Scientific / Metrology Instruments

Ultra-High Mass-Resolution MALDI-TOFMS System

Solutions for Innovation

JMS-S3000

SpiralTOF™-plus 2.0

The JMS-S3000 is a MALDI-TOFMS that incorporates JEOL's unique SpiralTOF ion optics system. Featuring unprecedented levels of mass resolving power and sensitivity, the system has been acknowledged for its distinctive capabilities in many scientific studies.

JEOL Ltd.

Towards the pinnacle of MALDI-TOFMS

In pursuit of optimal performance,

Introducing JMS-S3000 SpiralTOF™-plus 2.0

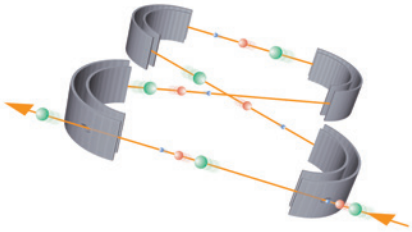
The JMS-S3000 is a MALDI-TOFMS* that incorporates the innovative SpiralTOF ion optics.
The JMS-S3000 has evolved into SpiralTOF™-plus 2.0 with much wider dynamic range.
The JMS-S3000 defines a new standard in MALDI-TOFMS performance and provides state-of-the-art analytical solutions for a wide range of research areas such as functional synthetic polymers, materials science, and biomolecules.

JMS-S3000 SpiralTOF™-plus 2.0

2003

Development of multi-turn time-of-flight mass spectrometer

- Development of "perfect focusing" and "multi-turn" technologies
- Realization of multi-turn time-of-flight mass spectrometer



2010

Initial introduction of SpiralTOF™

- Development of SpiralTOF ion optics
- Mass resolving power: 60,000
- Mass accuracy: 1 ppm (internal calibration)

2014

Improved version of SpiralTOF™ introduced

- Mass resolving power: 75,000
- Ultra-high mass-resolution MS imaging

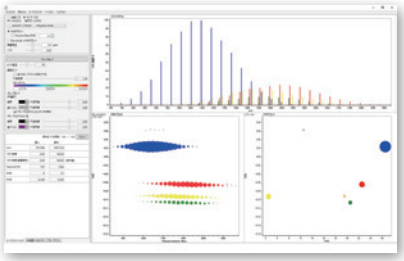
2015

Polymer analysis program

msRepeatFinder introduced

MS imaging data processing program

msMicroImager™ introduced



2019

SpiralTOF™-plus introduced

- Major enhancement in MS imaging capability

JEOL conducted collaborative research with the Graduate School of Science, Osaka University, to develop an ultra-high mass-resolution TOFMS that exceeds the reflectron used in the AccuTOF™ series by extending the flight distance. As the result, we proposed a multi-turn ion optics with a variable flight distance*1. However, in multi-turn TOFMS, there is a problem that faster (lighter) ions overtake slower (heavier) ions when the number of flight cycle is increased. The spiral trajectory ion optics system was proposed as a solution to this problem*2. JEOL has developed a SpiralTOF ion optics system based on the MULTUM II multi-turn ion optics developed by the Graduate School of Science, Osaka University, and In 2010, launched JMS-S3000 SpiralTOF™ by combining the SpiralTOF ion optics with a matrix-assisted laser desorption/ionization (MALDI) ion source. SpiralTOF™ succeeded in ensuring a long ion flight distance of 17 m in a limited space, achieving the highest mass resolution among all commercially available MALDI-TOFMS at the time.
The legacy of the SpiralTOF™ series continues to the SpiralTOF™-plus 2.0 (and beyond).

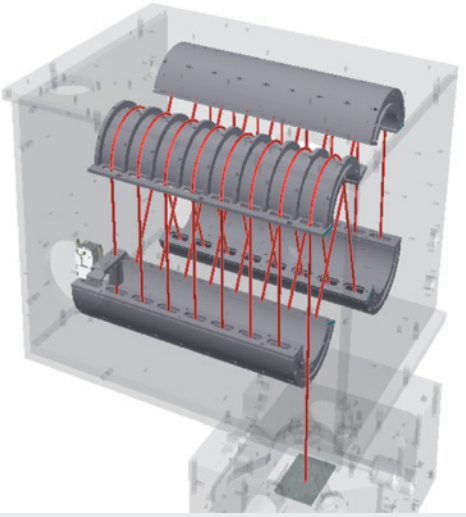
*1 Ion Optics for Multi-turn Time-of-flight Mass Spectrometers with Variable Mass Resolution: T. Matsuo, M. Toyoda, T. Sakurai and M. Ishihara, J. Mass Spectrom., 32 (1997), 1179-1185.

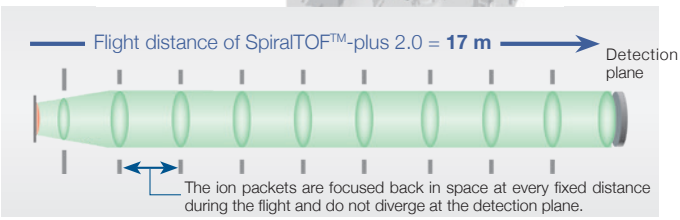
*2 Spiral Orbit Time of Flight Mass Spectrometer, Hisashi Matsuda, Journal of the Mass Spectrometry Society of Japan, 48, 303-305, 2000

MALDI-TOFMS for the next generation

Setting the new standard in MALDI-TOFMS performance

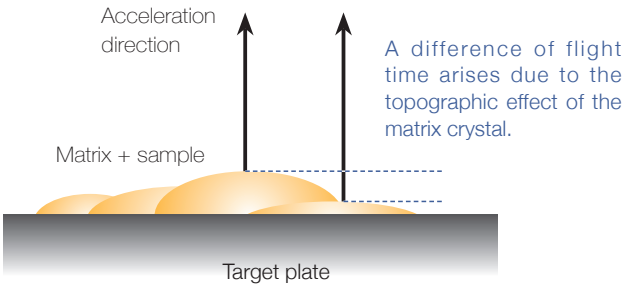
To improve the mass resolving power and mass accuracy of a time-of-flight mass spectrometer, the flight distance must be extended while keeping a group of ions having the same *m/z* (an ion packet) from diverging in space. The innovative SpiralTOF ion optics was developed by JEOL based on the "Perfect focusing[*1]" and "Multi-turn[*2]" principles. The ion packets are focused back in space at every fixed distance (i.e., each figure-eight trajectory) during the flight. Thus, even after the extended flight distance, the ion packets do not diverge at the detection plane, achieving high mass resolving power, high mass accuracy, and high ion transmission.



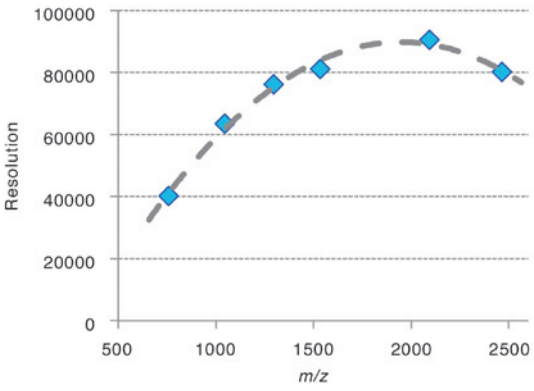


Reduced topographic effect of matrix crystal

The topographic effect of the matrix crystal leads to a difference in flight start position for the ions, resulting in a difference in flight time. In the conventional ion optics system, this time difference degrades the mass resolving power and also the mass accuracy obtained with external mass calibration. With its extended flight distance, the JMS-S3000 reduces this effect to the minimum and achieves highly reproducible mass resolving power and high mass accuracy with an external mass calibration.
High mass-resolution and mass accuracy can be maintained for imaging analysis of a biological specimen in which a large number of mass spectra are acquired across a large area and the specimen surface is likely to be uneven.

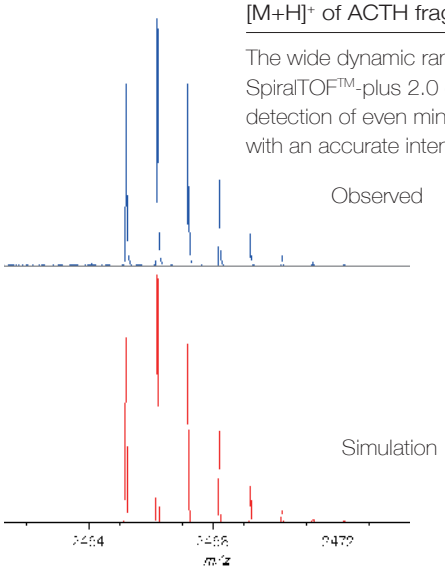


Mass resolutions observed with a mixture of peptide standards.



$[M+H]^+$ of ACTH fragment 18-39

The wide dynamic range of the SpiralTOF™-plus 2.0 enabled the detection of even minor isotope peaks with an accurate intensity ratio.

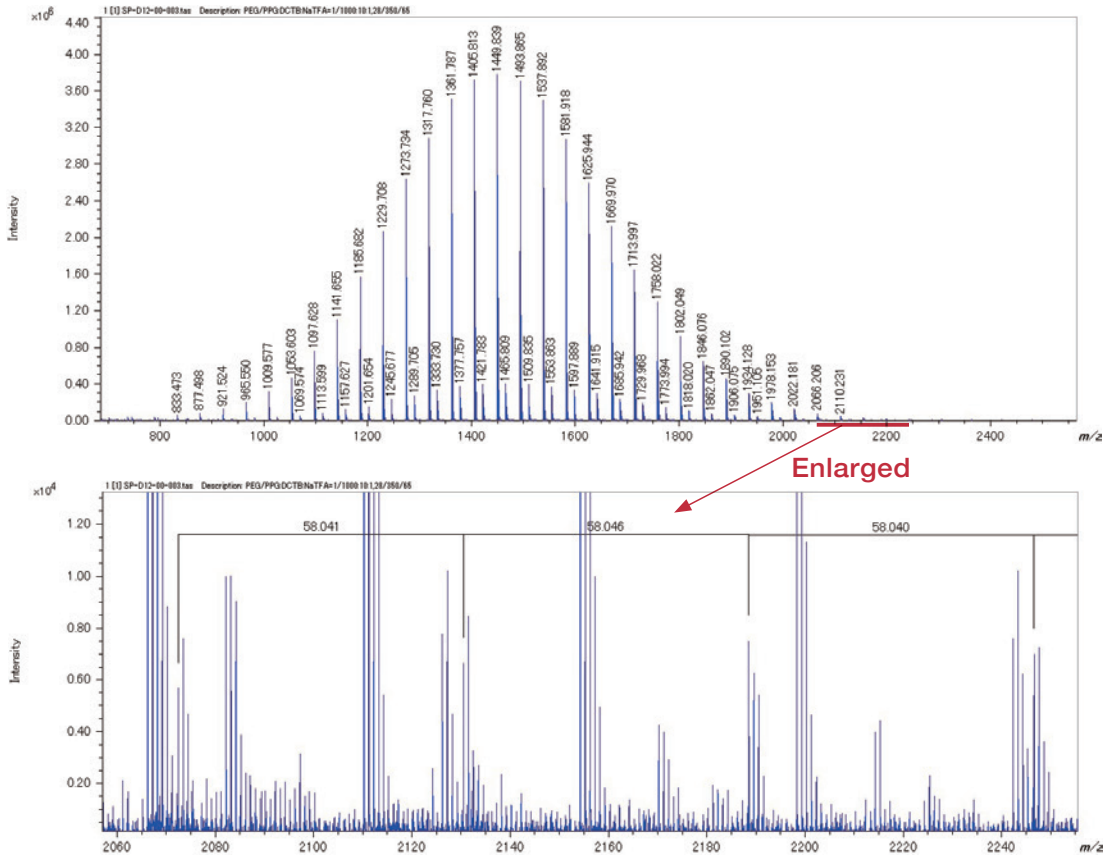


* 1 Perfect Spatial and Isochronous Focusing Ion Optics for Multi-turn Time of Flight Mass Spectrometer: M. Ishihara, M. Toyoda and T. Matsuo, Int. J. Mass Spectrom., 197, 179-189, 2000
* 2 Multi-turn Time-of-Flight Mass Spectrometers with Electrostatic Sectors: M. Toyoda, D. Okumura, M. Ishihara and I. Katakuse, J. Mass Spectrom., 38, 1125-1142, 2003
* 3 Japanese patents 4980583, 5238054, 5226824 US patents 7504620, 7910879, 8237112 (as of August 2021)

The SpiralTOF™-plus 2.0 has realized a wide dynamic range by greatly improving the detection system. This makes it possible to simultaneously detect peaks with ion intensity differences of about 4 orders of magnitude. Also, the analysis of trace components has become easy in mass spectrometry imaging measurements, in addition to the conventional bulk sample measurements. Below is the measurement example of a mixture of polyethylene oxide and polypropylene oxide in the ratio of 1,000:1. In the case of polymer analysis, when combined with the Kendrick Mass Defect (KMD) analysis, it is possible to analyze trace components that are otherwise difficult to detect.

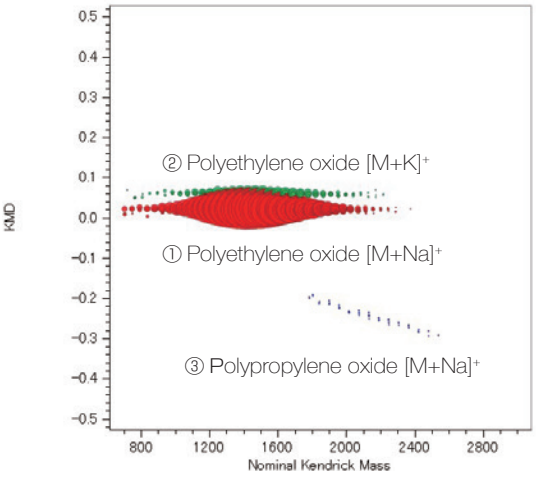
The mass spectrum of a mixture of polyethylene oxide and polypropylene oxide in the ratio of 1000:1.

The SpiralTOF™-plus 2.0 can realize a wide dynamic range and calculate the molecular weight distribution of trace components.



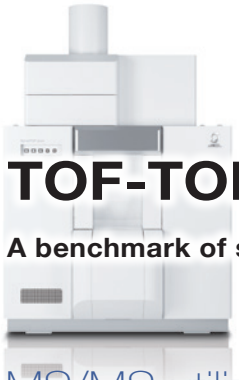
The intensity axis is enlarged 270 times.

KMD Plot (Base unit: EO)



Calculated values of molecular weight distribution

	Total ion intensity (%)	Number average molecular weight	Weight average molecular weight	Polydispersity
①	89.83	1460.80	1492.87	1.0220
②	10.00	1480.46	1515.30	1.0235
③	0.17	2112.30	2132.53	1.0096



TOF-TOF Option

A benchmark of structural elucidation by MS/MS

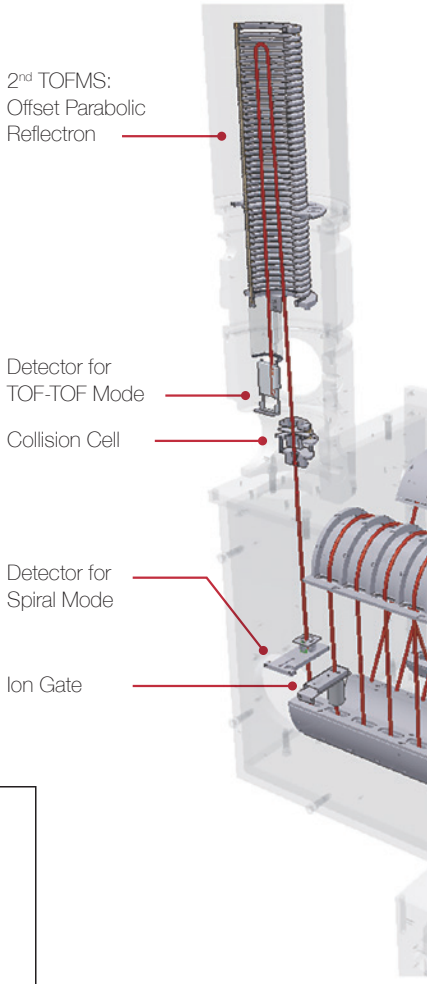
MS/MS utilizing the high selectivity of the SpiralTOF ion optics

Features

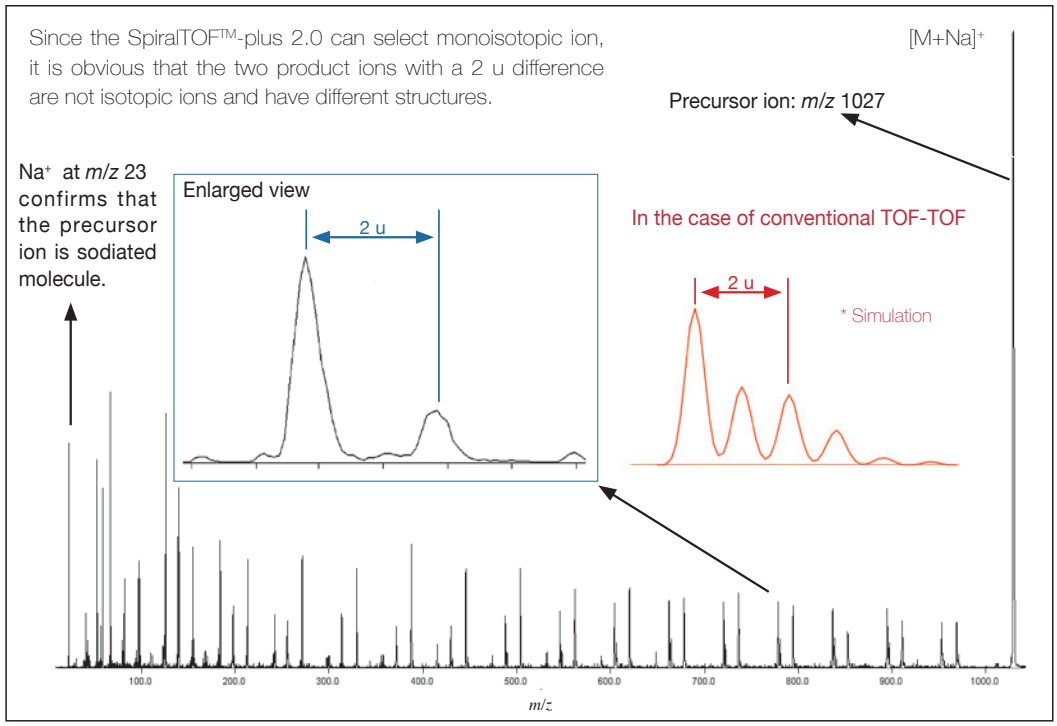
- By adopting the SpiralTOF ion optics as the first MS, the high precursor ion selectivity can be realized. The monoisotopic peak of precursor ions can be properly selected.
- High-energy collision-induced dissociation(HE-CID) allows for the acquisition of product ion mass spectrum rich with structural information.
- Offset parabolic reflectron, JEOL's patented technology, enables acquisition of all product ion information from *m/z* 5 to the precursor ion, and facilitates to obtain structural information of high reliability.

Usage

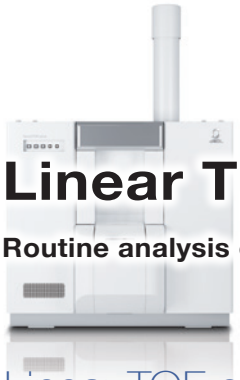
- In structural analysis of organic compounds, the accuracy of composition determination using accurate mass in Spiral mode can be improved by determining the adduct ion, in addition to the structural information obtained by HE-CID.
- In elucidation of amino acid sequences of a peptide, distinguishing structural isomers such as leucine and isoleucine is possible, as a feature of HE-CID. It is also possible to confirm the presence/absence of amino acids in a peptide by the presence/absence of immonium ions. (refer to p.21).
- For the analysis of additives, surfactants, and lipids, the structural analysis of alkyl chains is important. With HE-CID, it is possible to estimate the alkyl chain length and the positions of double bonds (refer to p.22, 23, 24).
- For structural analysis of polymers, it is possible to confirm the ion type (adduct ion) and the mass of the end groups from the product ion mass spectrum. It is possible to improve the accuracy in structure elucidation in combination with the elemental composition estimation result with the Spiral mode (refer to p.10).



Product ion mass spectrum of poly(oxypropylene)



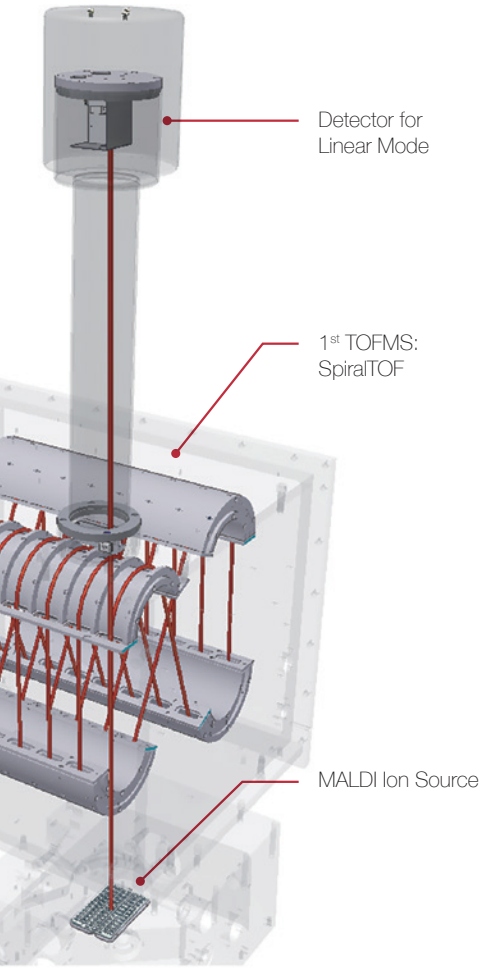
* Japanese patents 4688504, 5220574 US patents, 8330100 (as of August 2021)



Linear TOF Option

Routine analysis of high molecular weight compounds

Linear TOF option looking over a wide mass range



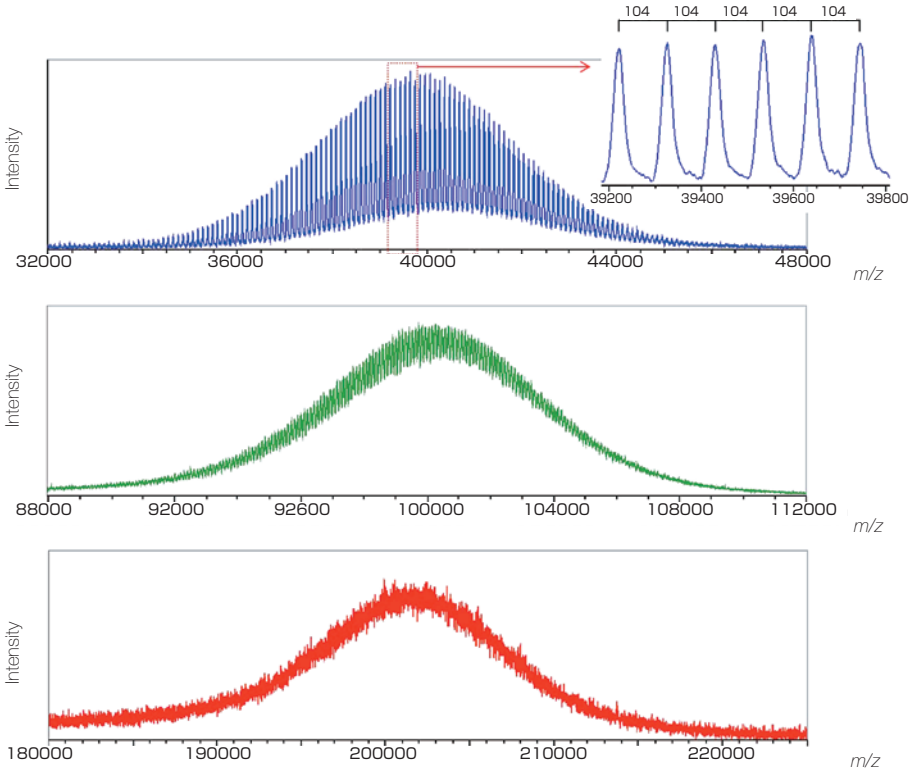
Features

- In the Linear TOF option, the ions travel from the ion source to the detector unaffected.
- When ions undergo post source decay (PSD) in flight, the produced fragment ions and neutrals continue to fly at the same velocity as before fragmentation. Hence, in a Linear mode mass spectrum, they are detected as the same signal as that of the ions that have not fragmented. Therefore high molecular weight compounds that tend to undergo PSD can be measured with high sensitivity in the Linear mode.
- The combination of Spiral and Linear modes further expands the range of analytes that can be measured.

Usage

- Useful for screening of molecular weight distribution of polymers.
- It is possible to calculate the molecular weight distribution & polydispersity of polymer samples with various masses ranging from several thousands to several tens of thousands.
- It is possible to measure high-mass samples of molecular weight over 10,000 Da such as intact proteins, with high sensitivity (refer to p.19)
- It enables high-sensitivity measurement of samples that can easily undergo PSD, such as proteins and polysaccharides.

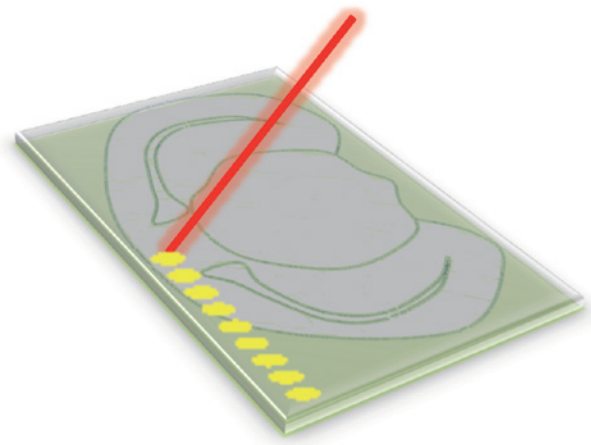
Mass spectra of poly(styrene) 40K, 100K, and 200K



Mass Spectrometry Imaging Analysis

Why high mass-resolving power is required for MS imaging?

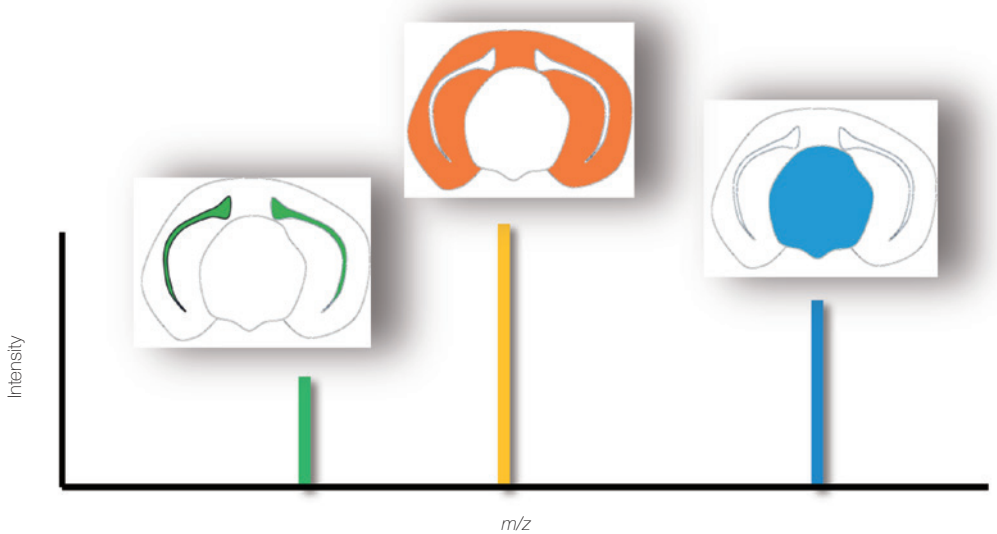
MALDI MS imaging was initially developed to focus on high molecular weight compounds such as proteins and peptides. However, with the expanding applications of MALDI MS imaging, the interests have shifted to include smaller molecules such as lipids, pharmaceuticals, and pharmaceutical metabolites. Conventional MALDI - reflectron TOFMS has difficulty discerning small molecule signals from those of matrix. In the case of MALDI MS imaging, signals from unwanted molecules on the specimen surface will often interfere with signals from the target analytes. High selectivity by means of high mass-resolving power is essential for obtaining reliable target analyte spatial distributions.
The SpiralTOF™-plus 2.0 with its high mass-resolving power is indispensable for MALDI MS imaging.



A tissue section is placed on an ITO-coated glass slide, and matrix solution is sprayed onto the surface.

The specimen is moved beneath the focused laser beam to create a time dependent series of mass spectra where each time corresponds to a specific spatial location. Analysis of the data allows the researcher to visualize the spatial distribution of specific compounds on the sample surface.

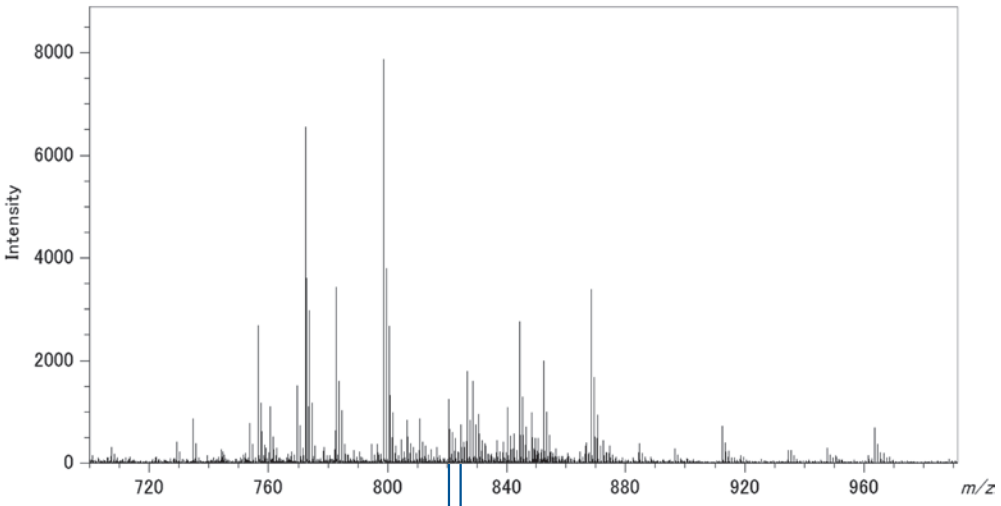
Mass spectrometry imaging data can be analyzed with the JEOL msMicroImager™ software or converted to a common data format imzML which allows data analysis by SCiLS Lab MVS (optional) or other third-party software such as BioMap.



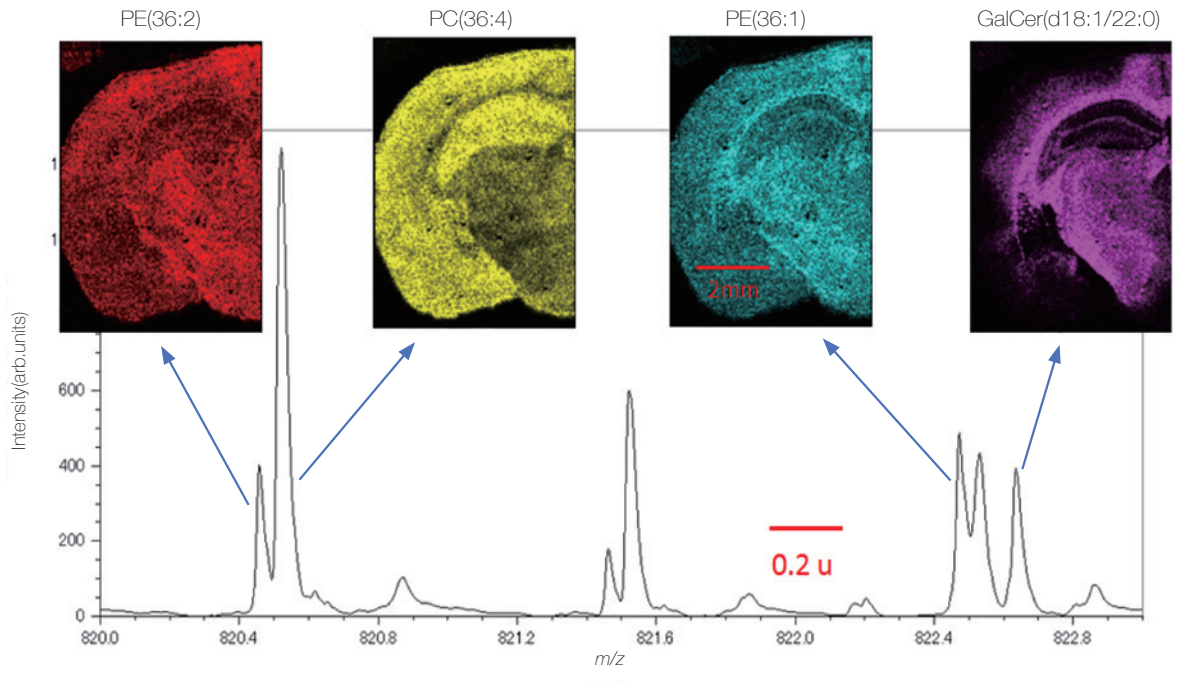
Mass Spectrometry Imaging Analysis of Lipids in Mouse Brain Tissue Section

Mouse brain sections contain a variety of lipid classes. A mass spectrum obtained from the tissue section is highly complex, especially in the region of *m/z* 700 - 1,000. Many of the peaks in the mass spectrum are less than 10% of the base peak, representing minor components. MALDI MS imaging of lipids requires a mass-resolving power high enough to separate the minor peaks from interferences. The bottom mass spectrum below shows the expansion of *m/z* 820 - 823. Many peaks were separated from each other by less than 0.1 u. The high mass-resolving power of the SpiralTOF™-plus 2.0 clearly separated these isobaric peaks, thus allowing the elucidation of 4 lipid elemental compositions. Moreover, each lipid clearly showed a different spatial distribution. Elucidation of elemental compositions and accurate determination of spacial distributions for each lipid would be difficult with a conventional reflectron TOFMS with moderate mass-resolving power.

Averaged mass spectrum of a mouse brain tissue section



Separation of isobaric ions and their MS images.



PE: Phosphatidyl ethanolamine, PC: Phosphatidyl Choline, GalCer: Galactosylceramide

The data were acquired in a joint research project with the Mass Spectrometry Group, Project Research Center for Fundamental Sciences, Graduate School of Science, Osaka University.
The tissue section specimen was provided by Awazu laboratory, Division of Sustainable Energy and Environmental Engineering, Graduate School of Engineering, Osaka University.

Polymer Analysis

Why is the SpiralTOF™-plus 2.0 good at analyzing synthetic polymers?

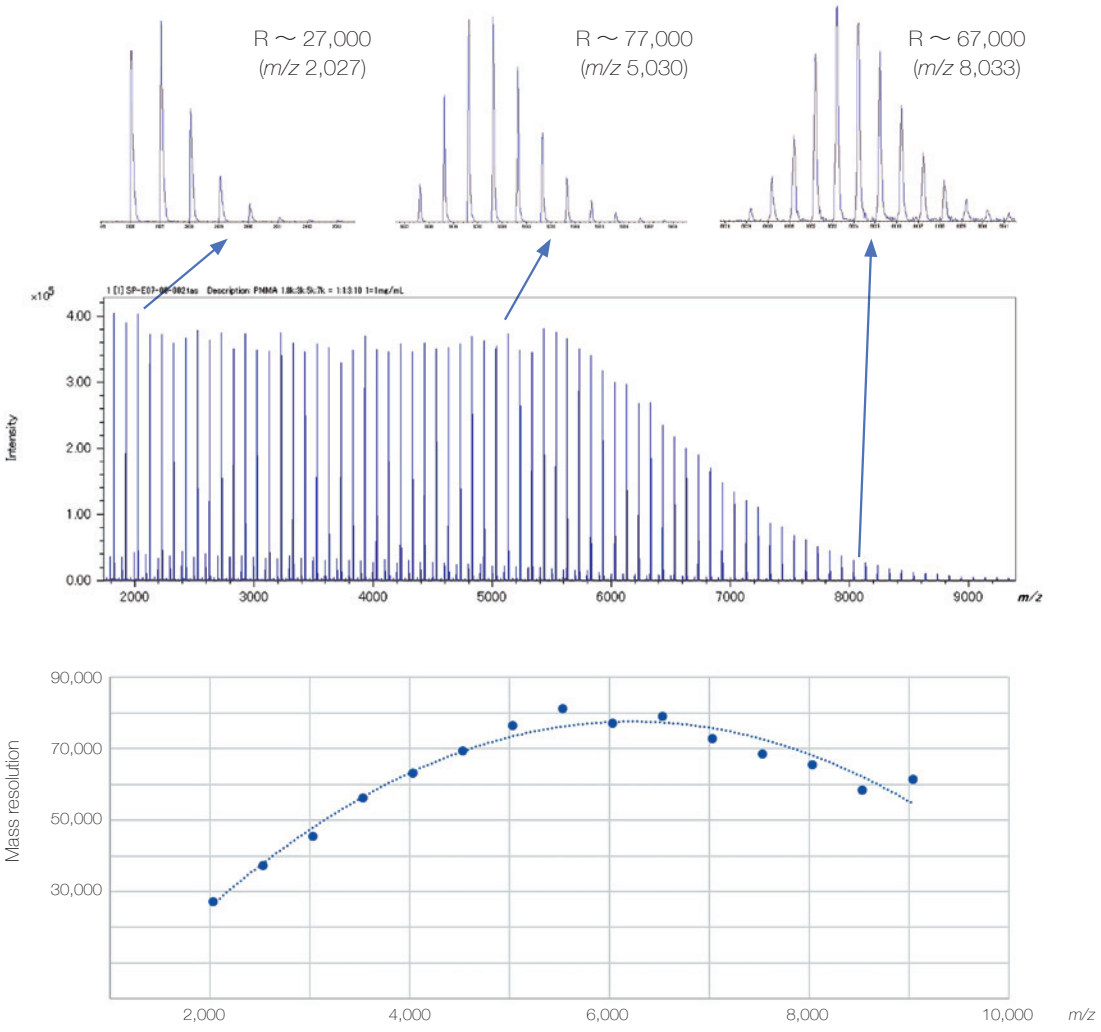
Synthetic polymers are polydisperse which means that they have a molar mass distribution. As a result, homopolymers with a variety of end groups and copolymers are highly complex mixtures. It is important to maintain ultra-high mass resolution over a wide mass range for the analysis of synthetic polymers. It is also important to resolve trace components from major components and other unwanted interferences. The SpiralTOF™-plus 2.0 ion optics, which consists of energy-filtering electric sectors, eliminates chemical noise derived from post source decay (PSD) and resolves trace components from other sample components. Synthetic polymer analysis requires high mass-resolving power over a wide mass range and wide dynamic range with low chemical noise. The SpiralTOF™-plus 2.0 satisfies both requirements. JEOL also provides optional software specifically designed to analyze complex mass spectra of synthetic polymers.

MALDI-TOFMS mainly produces single-charge ions, so polymer of high polydispersity is observed over a wide mass range.

The figure below shows the analysis example of polymethylmethacrylate (PMMA) at *m/z* 2,000 to 9,000. The SpiralTOF™-plus 2.0 can realize high mass resolving power and high mass accuracy over a wide mass range, due to the features of the SpiralTOF ion optics.

Mass spectrum of polymethylmethacrylate (PMMA) (*m/z* 2,000 – 9,000)

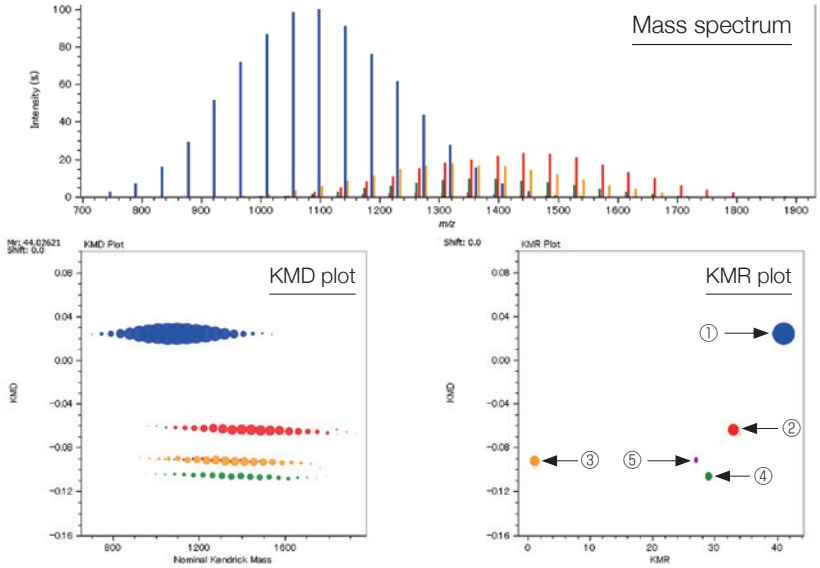
The SpiralTOF™-plus 2.0 achieves high mass resolving power over a wide mass range which is required for the analysis of polymers.



End-group analysis of polymers

By combining SpiralTOF™-plus 2.0 with msRepeatFinder (optional), mixtures of homopolymers with different end groups can be separated and grouped. For each group, it is possible to calculate the index values of molecular weight distribution (number average molecular weight, weight average molecular weight, and polydispersity).
It is also possible to elucidate the elemental compositions of polymer end groups from the accurate masses. However, it is not possible to determine the degree of polymerization (or the mass of an end group) or adduct ion information of a polymer species from the accurate mass alone. By utilizing the functions of TOF-TOF option, it is possible to determine the information.

Mass spectrum of a polyethylene oxide mixture with different end groups



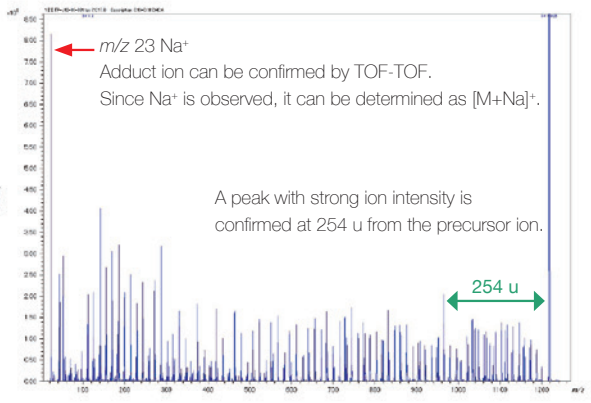
$[HO\text{-}(C_2H_4O)_n\text{–}R + Na]^+$
① R = H
② R = $C_{12}H_{25}$
③ R = $C_{16}H_{33}$
④ R = $C_{18}H_{37}$
⑤ R = $C_{18}H_{35}$

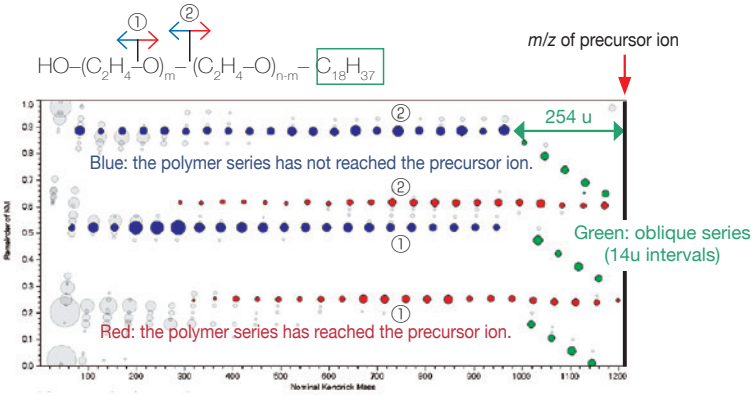
	Total ion intensity	Weighted-average of KMD	Weighted-average of NKM	Number average molecular weight (Mn)	Weight average molecular weight (Mw)	Polydispersity
①	826378	0.0245	1092.1	1092.8	1109.3	1.015
②	239802	-0.0635	1433.7	1434.5	1453.0	1.013
③	175311	-0.0920	1347.5	1348.3	1366.1	1.013
④	90119	-0.1060	1371.1	1371.9	1387.5	1.011
⑤	17689	-0.0912	1279.8	1280.5	1291.2	1.008

The elemental composition elucidation result of the end group for group ④ is shown. The 4 candidates have the same elemental composition, but different degree of polymerization. The information obtained from the TOF-TOF option are utilized to narrow down the candidates. Since a *m/z* 23 peak was observed in the product ion mass spectrum, it is known to be an Na adduct ion. The characteristic neutral loss indicates that the size of one end group is about 254 u and the other is relatively small. As a result, we could estimate that it was the polyethylene oxide which has an end group of $C_{18}H_{37}$ /OH.

No.	End group composition formula	Monomer	n	Adduct ion	Mass	DBE	Mass Error (modulus; mDa)	Mass error (mDa)	Mass Error (modulus; ppm)	Mass Error (ppm)
①	$C_{16}H_{34}$	C_2H_4O	22	Na	1217.83200	-0.5	2.2767	-2.2767	1.8695	-1.8695
②	$C_{18}H_{38}O$	C_2H_4O	23	Na	1217.83200	-0.5	2.2767	-2.2767	1.8695	-1.8695
③	$C_{20}H_{42}O_2$	C_2H_4O	20	Na	1217.83200	-0.5	2.2767	-2.2767	1.8695	-1.8695
④	$C_{22}H_{46}O_3$	C_2H_4O	19	Na	1217.83200	-0.5	2.2767	-2.2767	1.8695	-1.8695

Product-ion mass spectrum and RKM plot of group ④



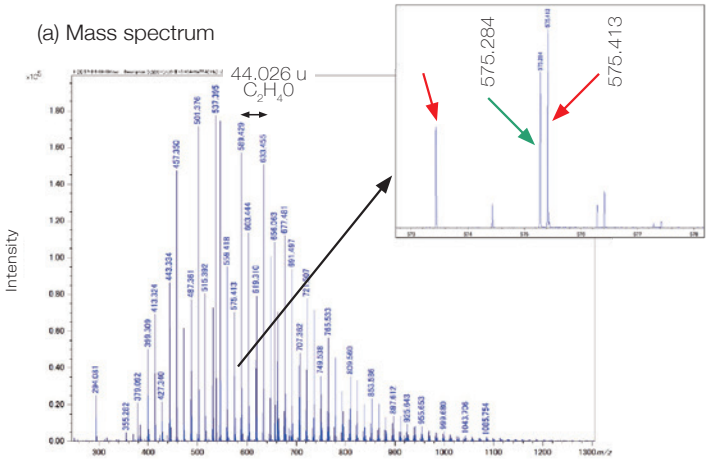


Analysis of an anionic surfactant

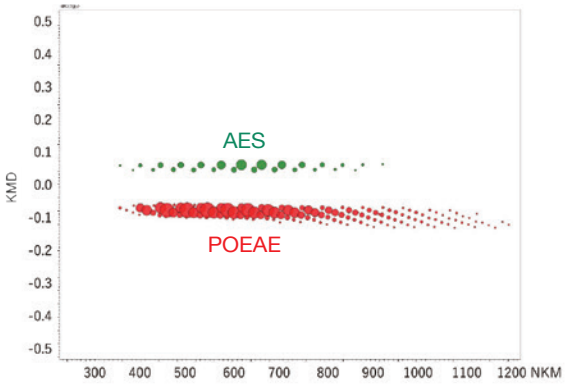
It is sometimes highly effective to analyze an anionic surfactant, which has a sulfate group or phosphate group as an end group, in the negative ion mode. Below are the analysis examples of detergent containing alkyl ether sulfate ester (AES) and polyoxyethylene alky ether (POEAE). In the positive ion mode, POEAE was mainly observed. However, by using KMD plots, AES can be also confirmed. On the other hand, only AES was observed in the negative ion mode. By obtaining product-ion mass spectrum in the negative-ion mode with the TOF-TOF option, it can be estimated that the end groups are alkyl chain($C_{14}H_{29}$) and sulfate group respectively.

Positive ion mode

(a) Mass spectrum

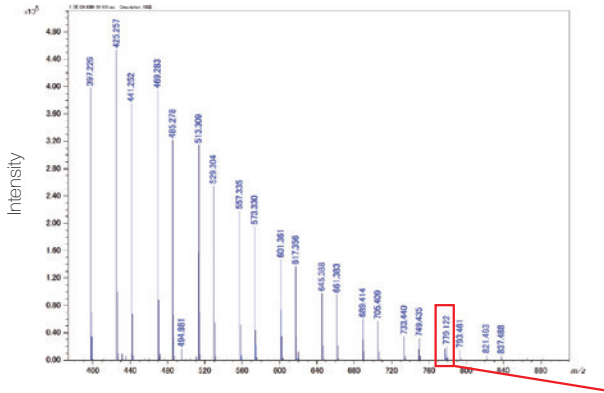


(b) KMD plot

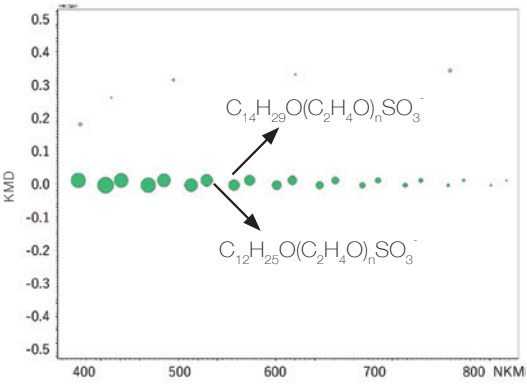


Negative ion mode

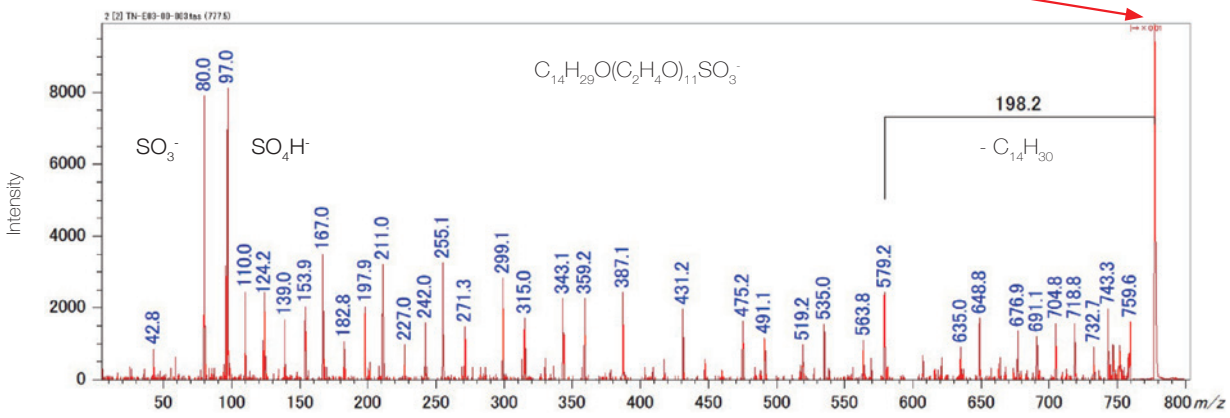
(a) Mass spectrum



(b) KMD plot



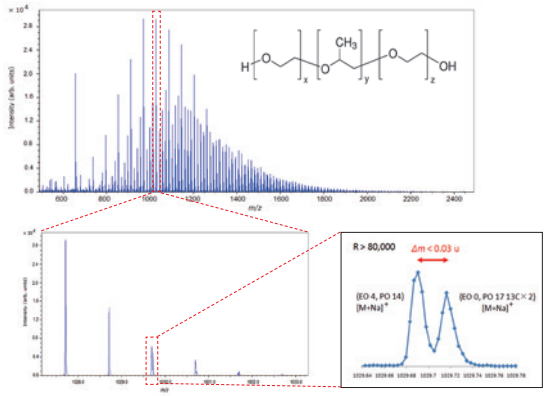
MS/MS

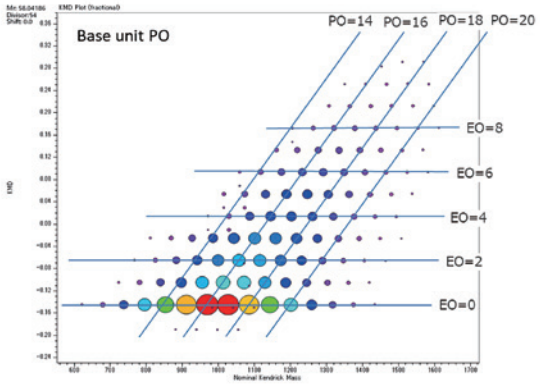


Analysis of copolymers

It is important to use high mass resolution to analyze copolymers, which consist of two or more species of monomer. The SpiralTOF™-plus 2.0 can separate many isobaric ion peaks (which have the same nominal mass but different accurate mass) on a mass spectrum. Since the mass spectra of copolymers are complicated, it is not practical to assign peaks one by one. The KMD analysis using msRepeatFinder(optional) makes it possible to visualize the distribution of polymer species. Below is the analysis example of EO-PO block copolymer. The enlarged mass spectrum shows that peaks that are less than 0.03 u apart are clearly separated by a high mass resolution. By visualizing the mass spectrum by using KMD plot(base unit: PO), a lattice is seen reflecting the PO distribution on horizontal axis and the EO distribution in a diagonal direction.

Mass spectrum and KMD plot of EO-PO block copolymer

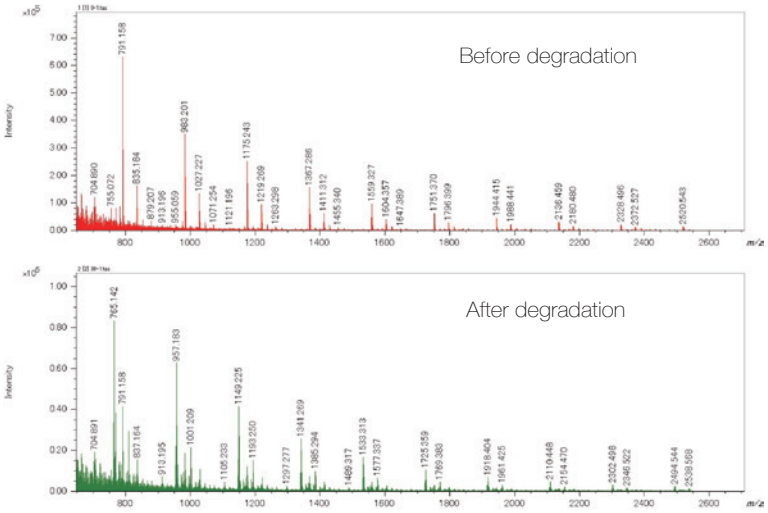




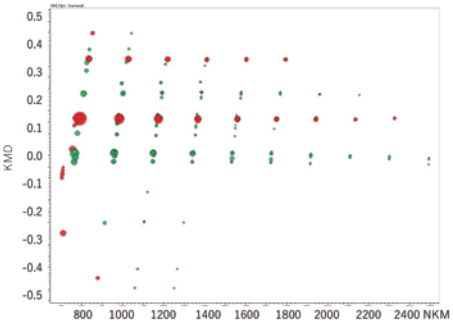
Differential analysis of 2 polymer samples

The differential analysis of the end groups and molecular weight distributions of polymer samples is very important for checking the degradation of a sample, difference between production lots, and difference in the synthesis processes. msRepeatFinder(optional) can perform the differential analysis of two samples. Below is the application example used for the degradation analysis of polyethylene terephthalate. The bottom left shows the mass spectrum before and after the degradation. Before the degradation, cyclic oligomers, and after the degradation, the series having the COOH/COOH end groups were observed as major components respectively. For performing a differential analysis, each sample was measured three times. The bottom right is the result of the differential analysis shown in KMD plots. The red shows the stronger peaks before the degradation, while the green shows the stronger peaks after the degradation. In addition, a volcano plot can be created to confirm the components that differ with statistical significance between 2 samples.

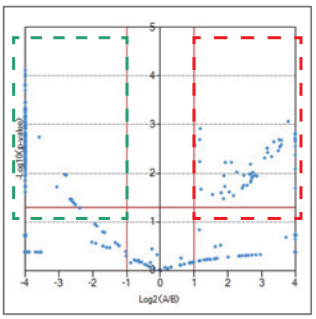
Mass spectra of PET samples before and after degradation



KMD plot of differential analysis result



Volcano plot of differential analysis result



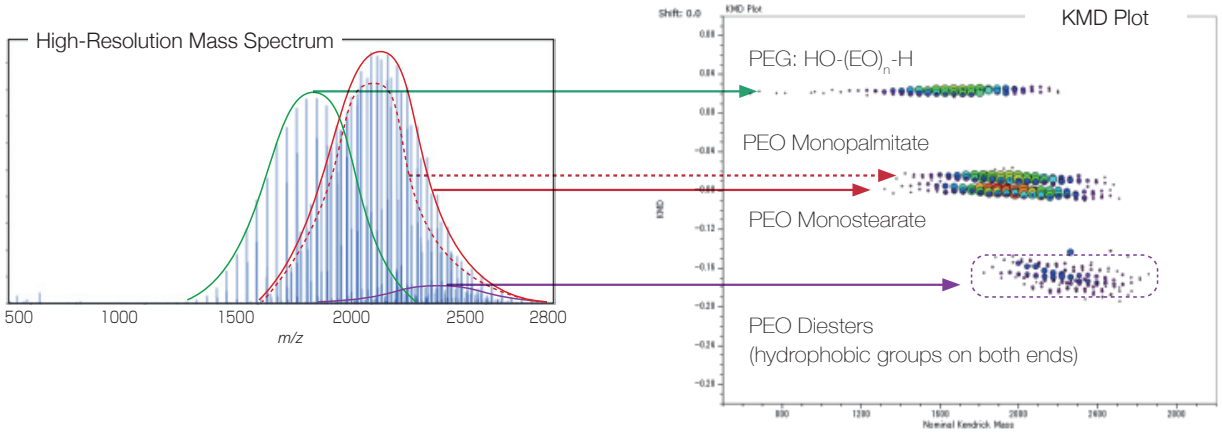
A Wide Range of Applications

Polymers

Compositional Analysis of an Industrial Surfactant*

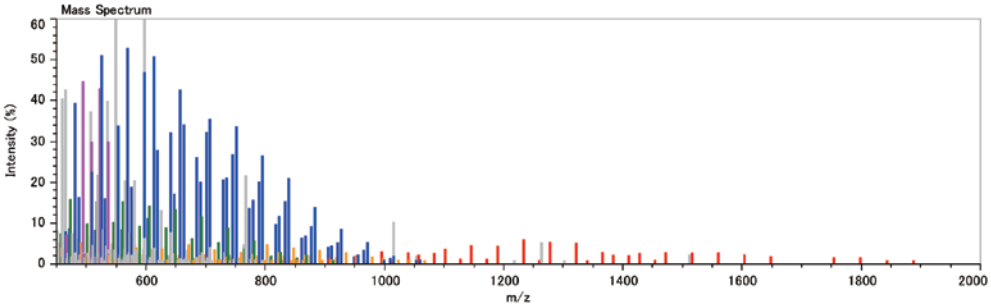
Molar mass and compositional distributions of an industrial surfactant were analyzed by using a KMD plot. The sample was marketed as "polyethlene oxide (PEO) monostearate." The KMD plot revealed that the sample contained not only monostearate but also monopalmitate, molecules with hydrophobic groups on both ends (distearate, dipalmitate, and monostearate-monopalmitate,) and free, unreacted polyethylene oxide.

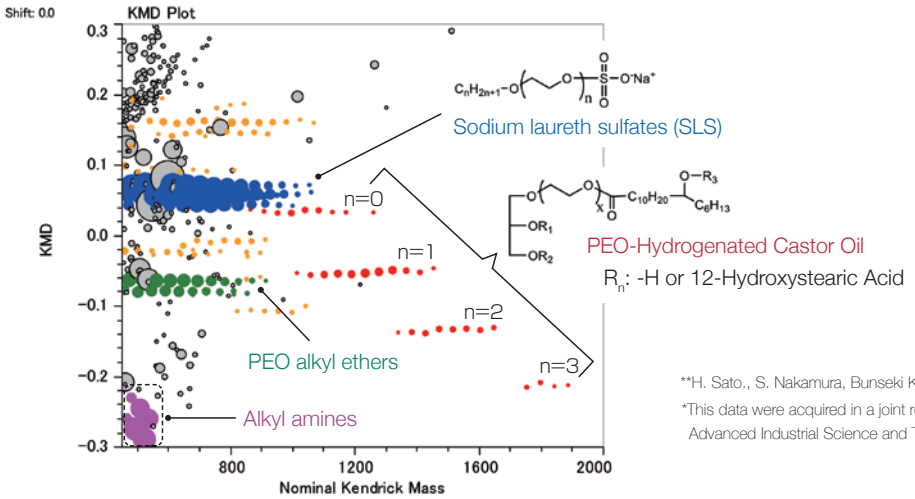
Sample: "polyethlene oxide monostearate"



Compositional Analysis of Surfactants in a Hair Shampoo*

Surfactants in a commercial hair shampoo were analyzed. A large fraction of the major component, sodium laureth sulfate (SLS), was washed out on the target plate** in order to detect minor components. The acquired mass spectrum was highly complex, but the KMD plot facilitated clear visualization of various components down to the trace ones. The compositional distribution of PEO hydrogenated castor oil, which is known to be difficult to analyze, was clearly visualized.



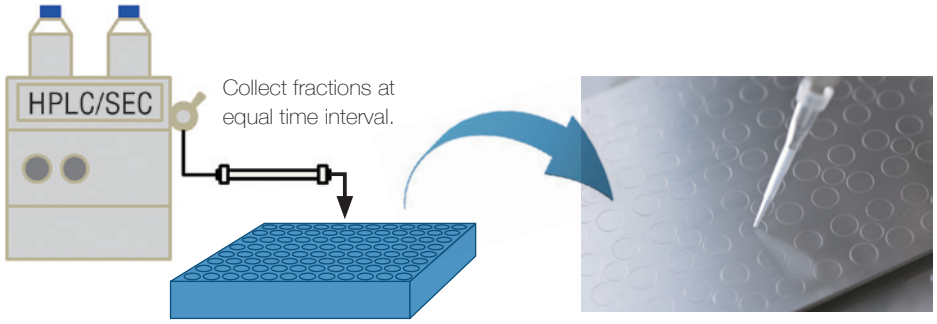


**H. Sato., S. Nakamura, Bunseki Kagaku,

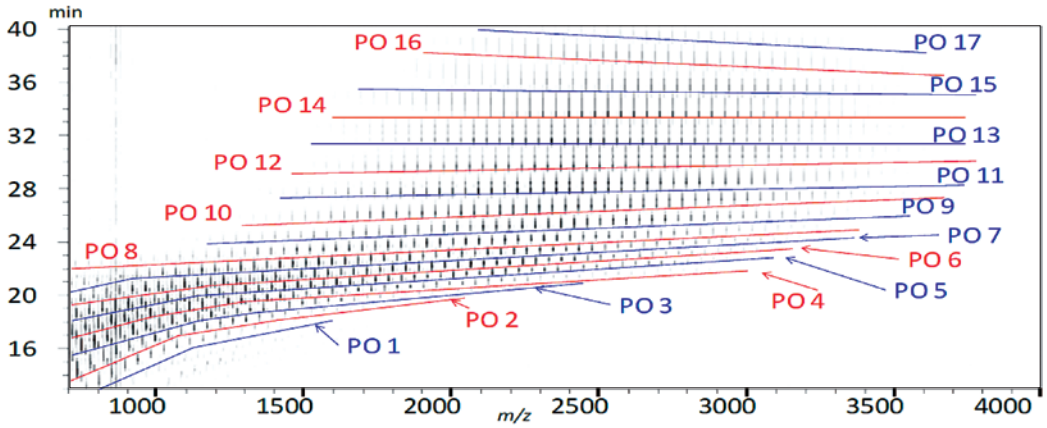
*This data were acquired in a joint research project with the National Institute of Advanced Industrial Science and Technology (AIST)

LC-MALDI Analysis of an EO-PO Random Co-polymer (MSTips No. 203)

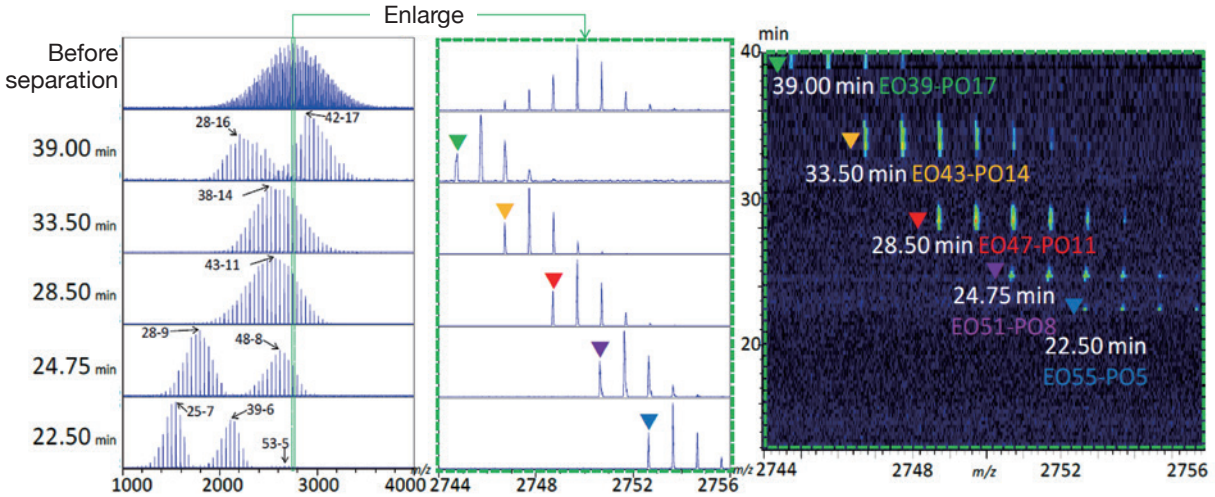
Since MALDI cannot be directly coupled with a chromatograph, detection of very minor components in a highly complex mixture can be difficult. Fractionating a complex sample with high-performance liquid chromatography (HPLC) or size exclusion chromatography (SEC) reduces ion suppression effects, thus facilitating the detection of many more components in the sample.
To do this, the eluent from the major peaks in a HPLC/SEC chromatogram can be fractionated, or eluent fractions can be collected at equal time intervals. Each fraction is then mixed with matrix and cationization agent solutions and deposited on the target plate. A mass spectrum of each fraction is then acquired in an automated fashion and visualized as 3 dimensional data.



Result of EO-PO random copolymer analysis by LC-MALDI (Survey View heat map)
Separation by HPLC and change of molecular weight distribution are visualized.



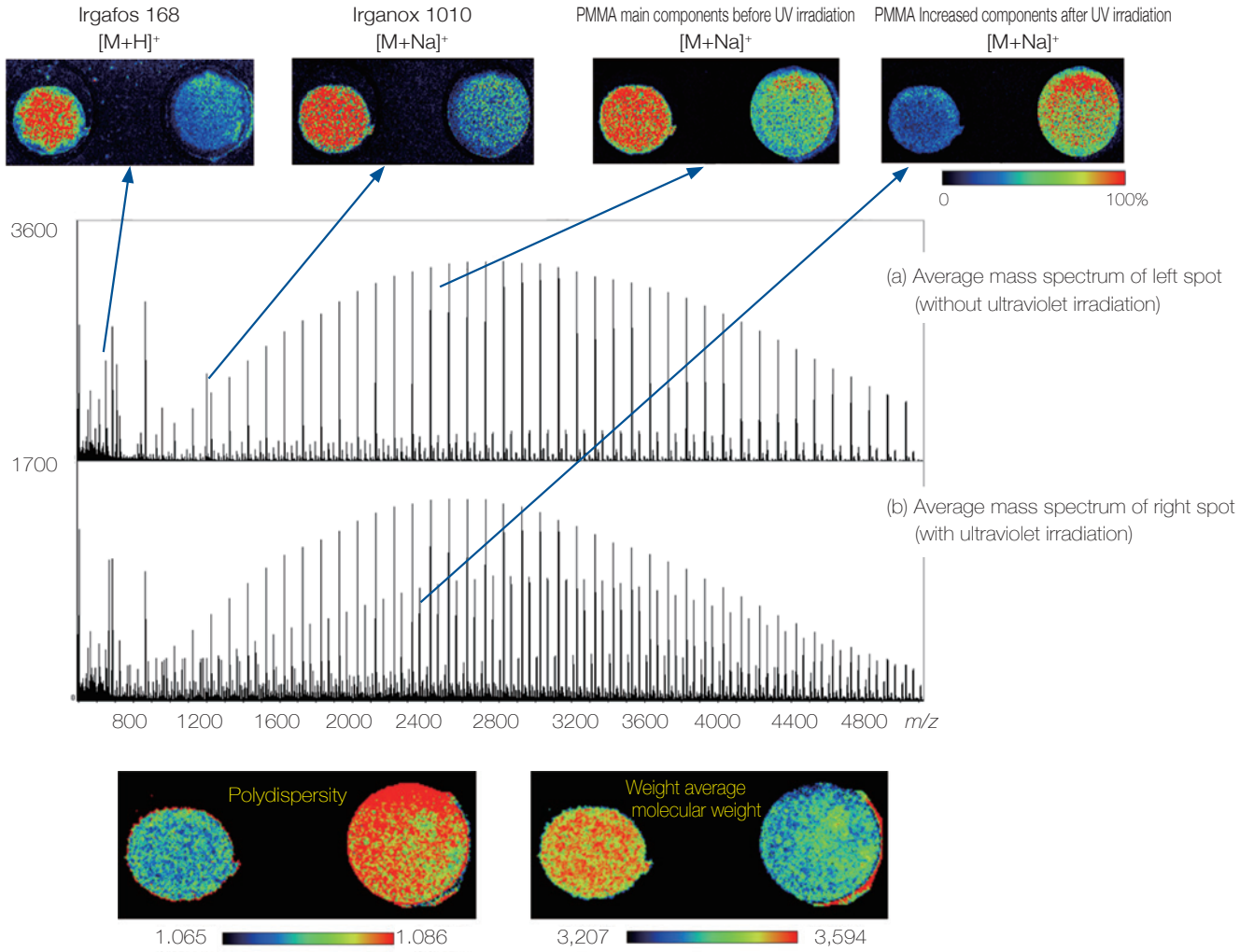
Change of mass spectra based on the retention time.
Many new peaks were observed as ion suppression was reduced by HPLC fractionation.



Mass spectrometry imaging of polymers

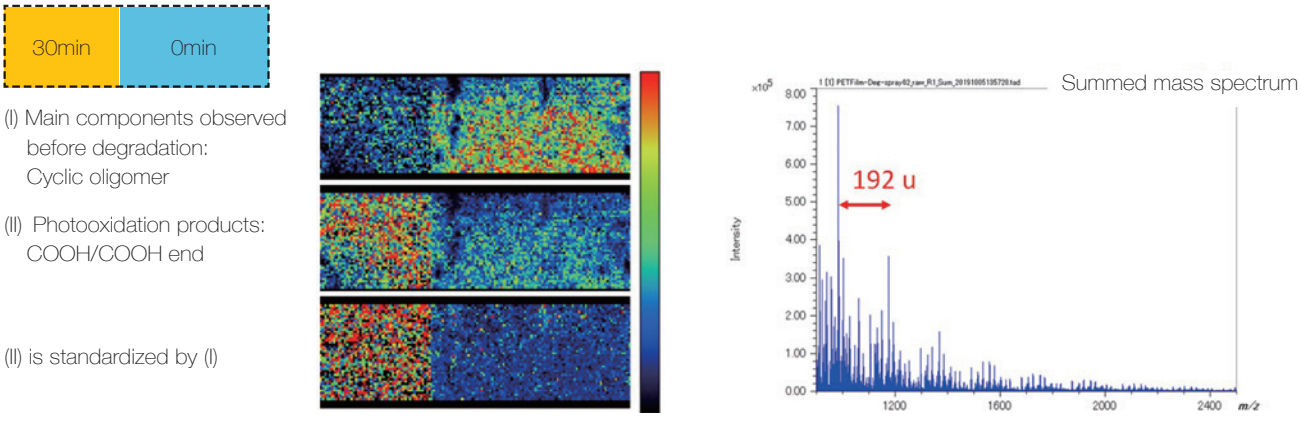
Mass spectrometry imaging can be applied to polymers. Two spots are prepared by adding two antioxidants - Irgafos 168 (BASF) and Irganox 1010 (BASF) - to polymethylmethacrylate (PMMA). The ultraviolet irradiation was performed to the right spot only and its degradation was visualized by using mass spectrometry imaging. For polymers, it is possible to visualize the quantitative change in both polymers and additives. It is also possible to capture the changes in the average molecular weight and polydispersity.

MS imaging of PMMA, Irgafos 168, and Irganox 1010



Surface analysis of polymeric materials

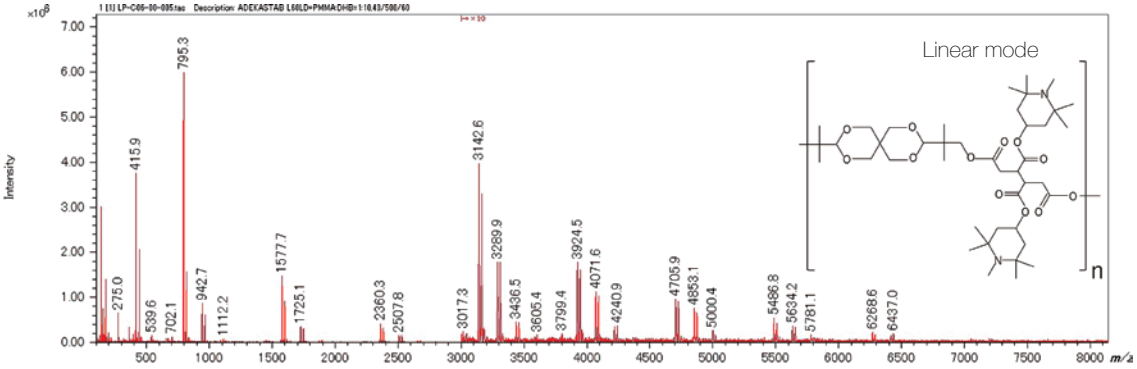
Use of mass spectrometry imaging makes it possible to analyze the localization of a compound on the film surface. Below illustrates the change of oligomer on the surface of polyethylene terephthalate film, by photooxidation degradation through ultraviolet irradiation.



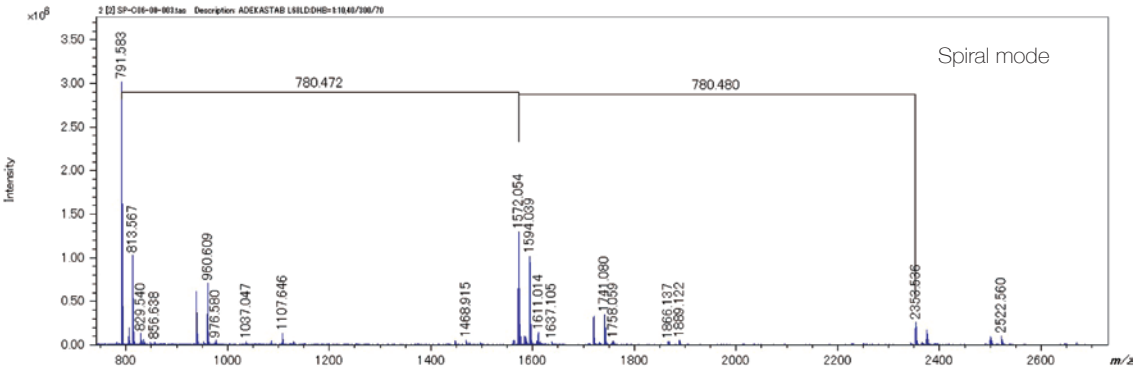
Measurement of high molecular weight additives

MALDI is capable of soft ionization of high molecular weight additives. The figure below shows a measurement example of ADK STAB LA68 (ADEKA), a high molecular weight hindered amine light stabilizer.
It is possible to check the molecular weight distribution in Linear mode and estimate the elemental composition in Spiral mode.

Mass spectrum in Linear mode (*m/z* 200 - 8,000)

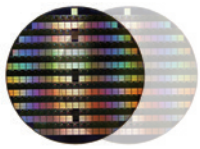


Mass spectrum in Spiral mode (*m/z* 800 - 2,700)



A Wide Range of Applications

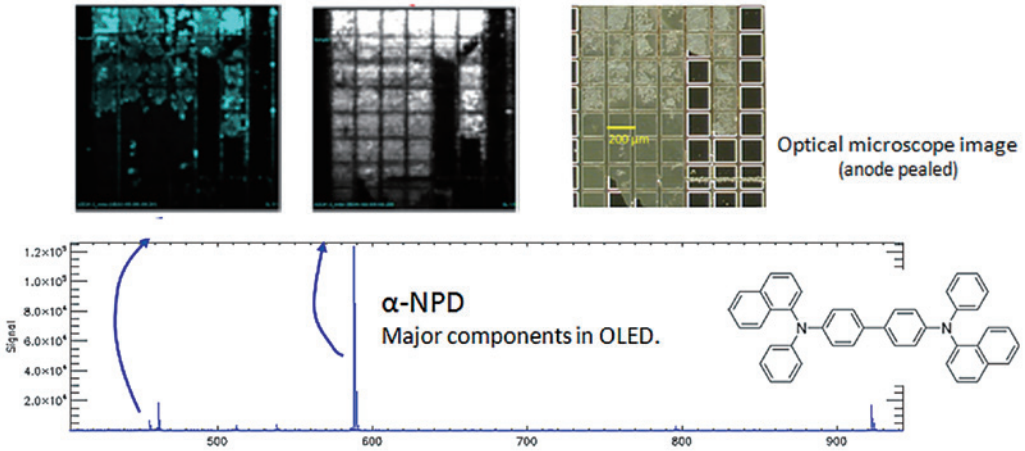
Organic Electronic Materials



It is important to understand the deterioration mechanism of organic electric materials in order to prolong the life time of the device. MS imaging allows the determination of spatial distributions for specific compounds. By comparing a MS image with an optical microscope image that shows deteriorated areas, compounds specific to the deteriorated areas can be differentiated.

Deterioration analysis of an organic light-emitting diode panel*

Top, from left to right: MS image of *m/z* 456 (a compound specific to the deteriorated area), *m/z* 588 (α-NPD; the major component), optical microscope image. Bottom: average mass spectrum of the whole observed area.



* This data was acquired in a collaborative research effort with AGC Inc.

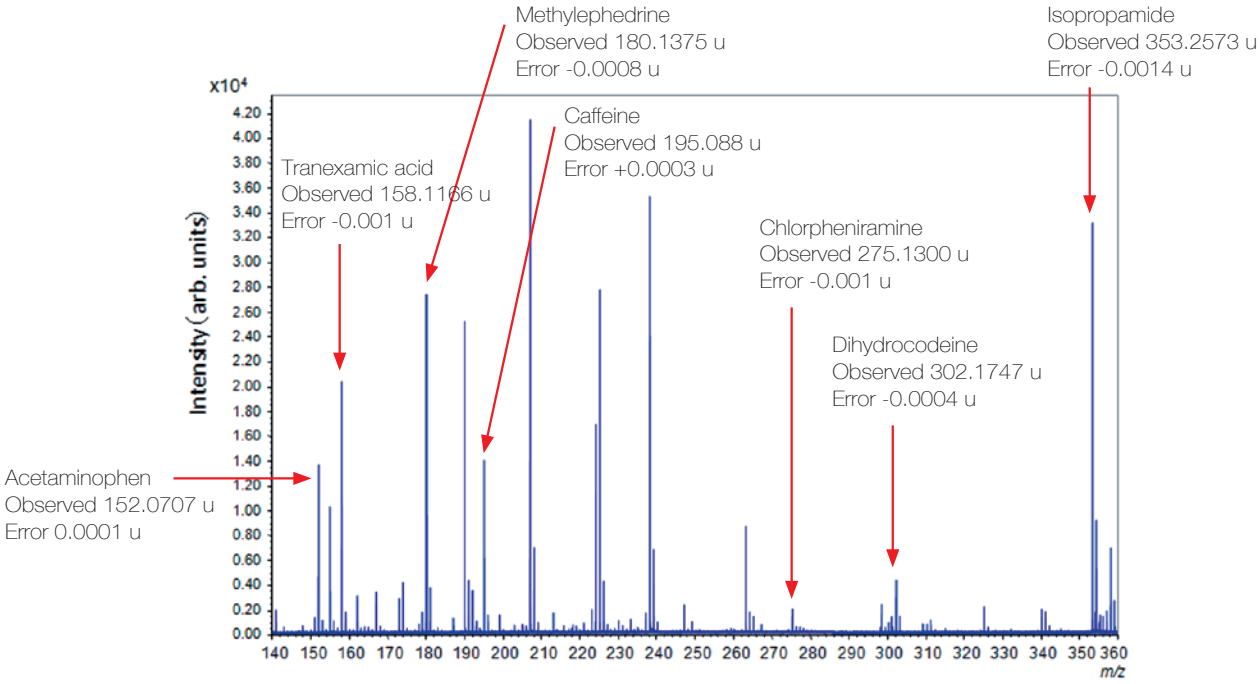
A Wide Range of Applications

Organic Chemistry

The SpiralTOF™-plus 2.0 facilitates accurate mass measurements of small and large molecules.
Previously, MALDI-TOFMS systems were not suitable for the analysis of small molecules as matrix-derived peaks and continuous chemical noise interfere with the signal from analyte molecules. The SpiralTOF ion optics have solved these problems.

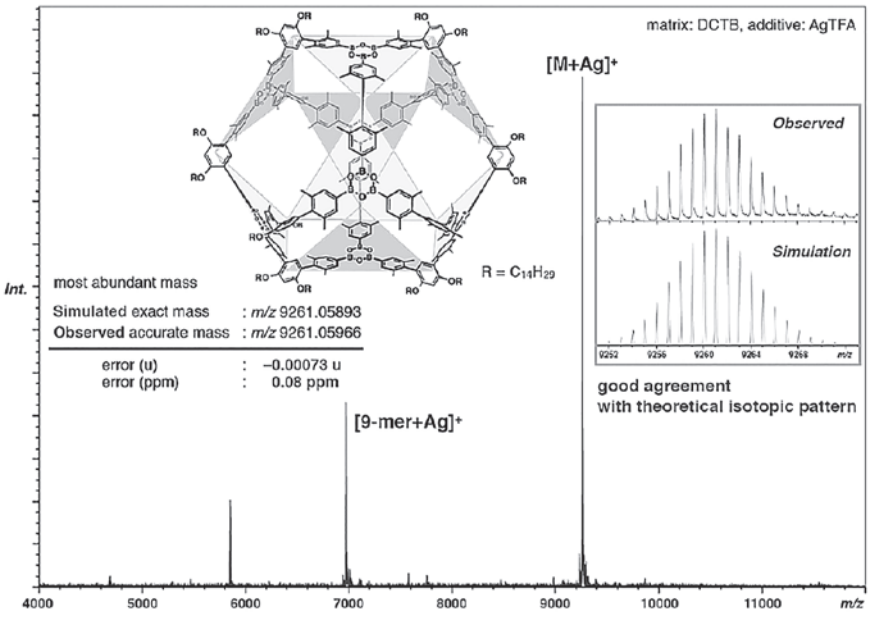
Analysis of a common cold medicine (MSTips No. 241)

The masses of the 7 active ingredients have been determined within 0.0014 u. Matrix-derived peaks have been used as internal mass references.



Analysis of boroxin cage 12-mer *

Isotopic peaks are completely separated in the high-mass region thanks to the ultra-high mass-resolving power. For high molecular weight compounds, the abundance of the monoisotopic ions are very small and difficult to observe. The elemental composition of the molecule can be confirmed by the observed *m/z* of the most-abundant ion and/or comparing the isotopic peak pattern with that of the simulation.



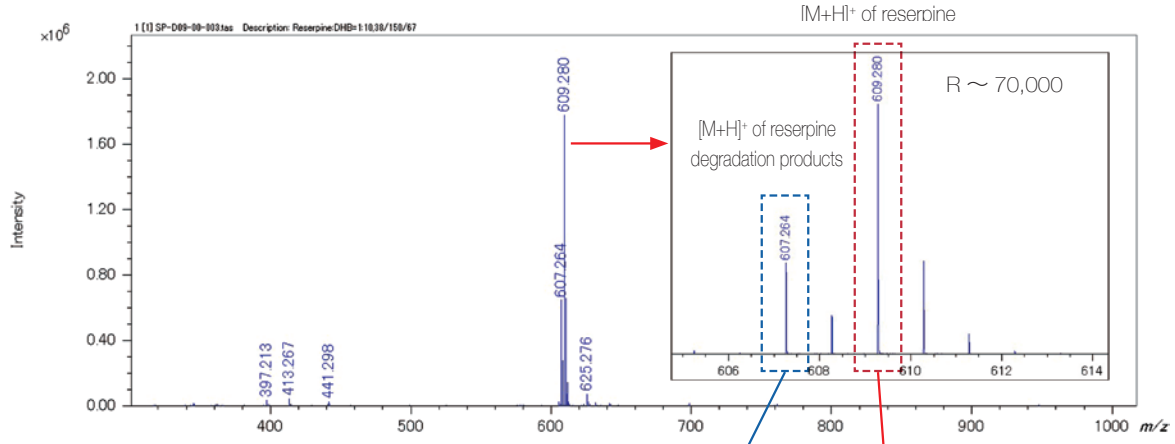
(Sample courtesy of Prof. Iwasawa, The Tokyo Institute of Technology)

* Self-Assembly of Nanometer-Sized Boroxine Cages from Diboronic Acids, Ono, K., et al., J. Am. Chem. Soc. 2015, 137 (22), 7015-7018, DOI: 10.1021/jacs.5b02716

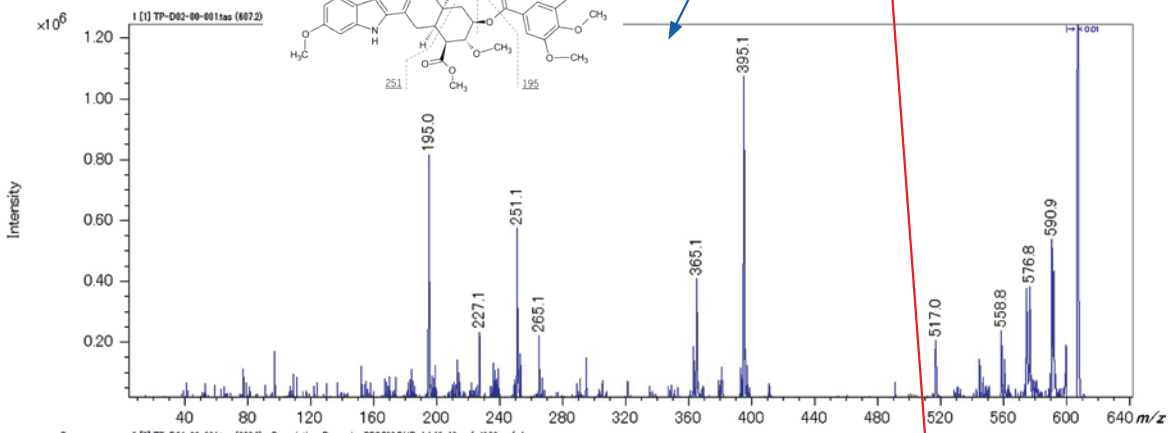
Structural analysis of small molecules

Below is the structural analysis example of reserpine after photodegradation. The $[M+H]^+$ of reserpine and its degradation products were observed with a 2 u difference. It is possible to obtain the product ion mass spectrum for each by the high precursor ion selectivity of SpiralTOF™-plus 2.0's TOF-TOF option. The product ion mass spectra are quite different between the two, and the structure can be elucidated from the characteristic product ions of each.

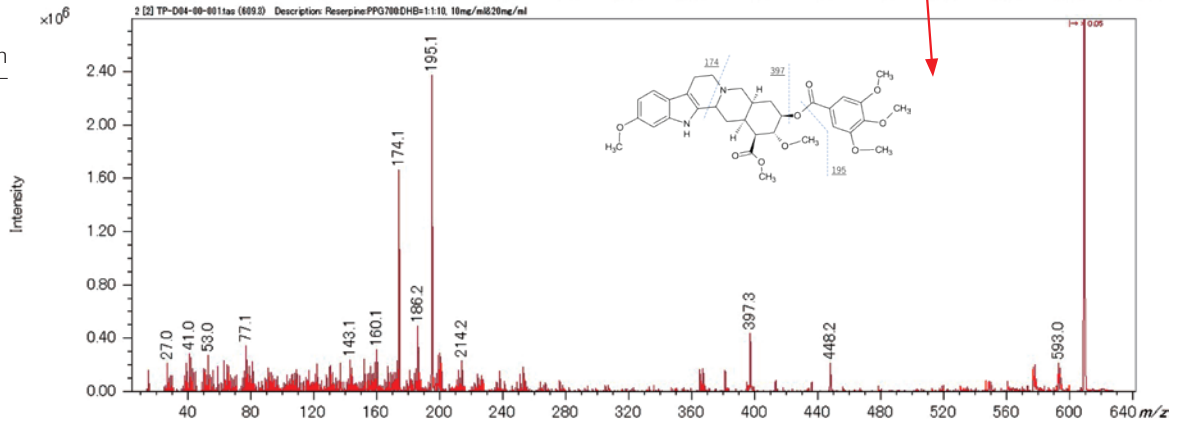
Mass spectrum of mixture of reserpine and its degradant



Product ion mass spectrum of a reserpine degradant



Product ion mass spectrum of reserpine

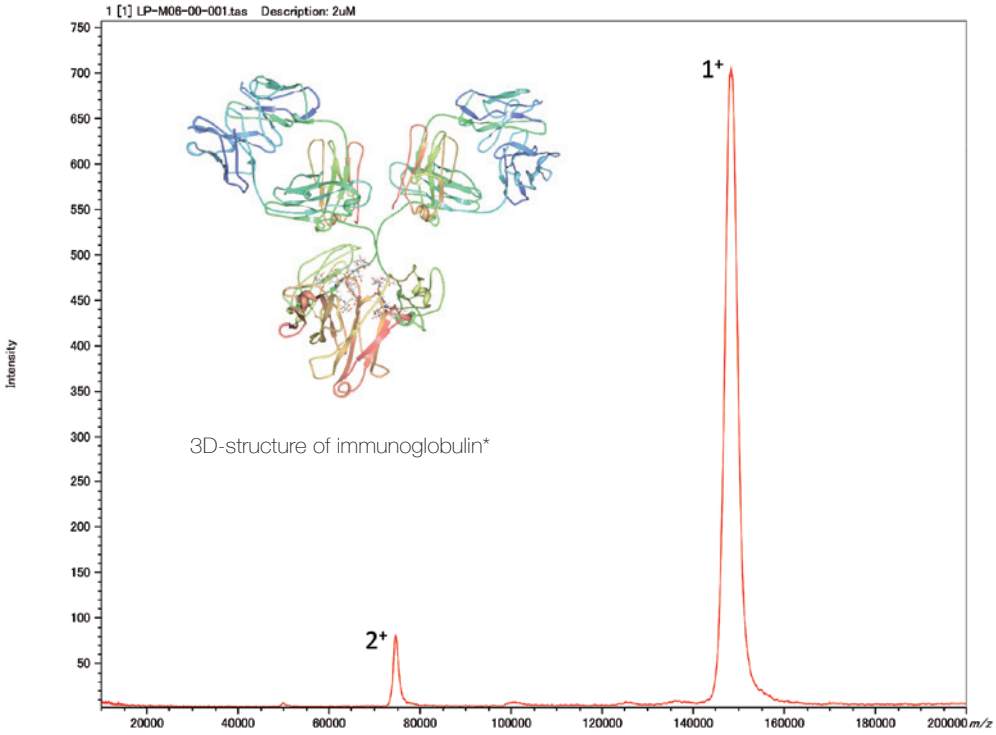


A Wide Range of Applications

Proteins

The molecular weight of an intact protein can be measured by using linear mode.

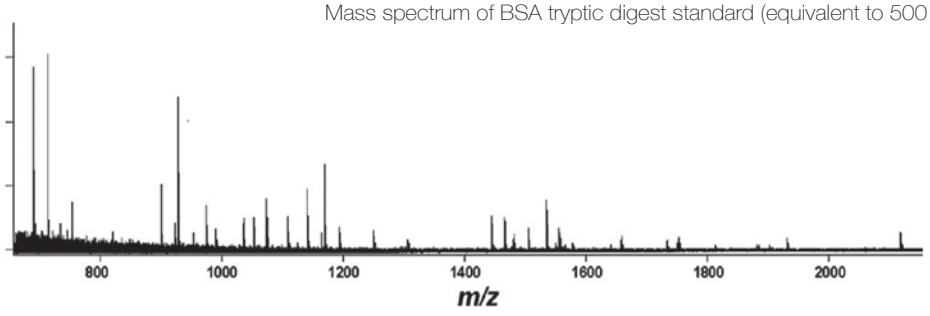
A mass spectrum of intact immunoglobulin G (IgG) measured with linear mode



For the detailed analysis of a protein, not only the intact protein but also enzymatic digest of the protein can be analyzed. Peptide mass fingerprinting allows identification of a protein.

Mass spectrum of the tryptic digest of bovine serum albumin (BSA) and the results of the peptide mass fingerprinting.

Mass spectrum of BSA tryptic digest standard (equivalent to 500 amol)



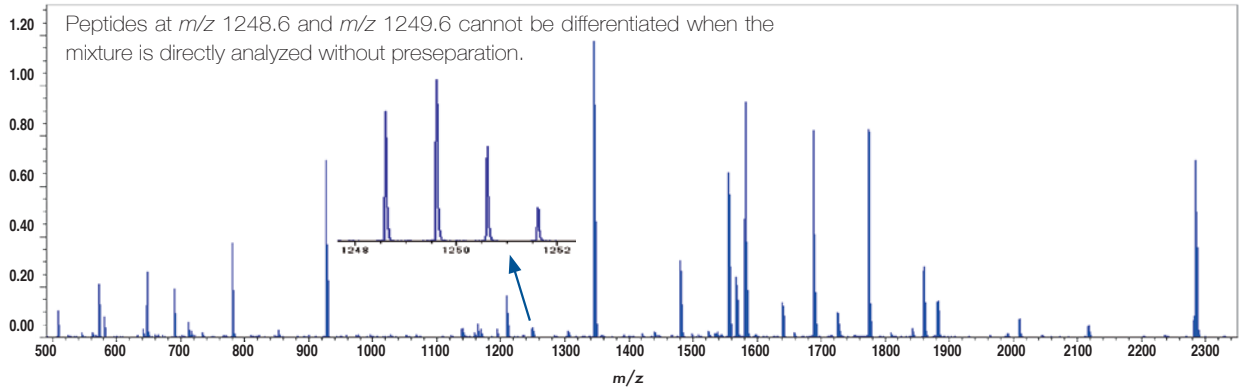
Amount (fmol)	Number of peptides matched/searched	Sequence coverage (%)	MASCOT score
50	52/81	75	570
10	41/79	64	390
5	36/77	54	351
1	28/57	43	255
0.5	31/52	46	306
0.1	12/34	18	92

* 3D-structure of RCSB PDB (www.rcsb.org) ID 1IGY (Harris, L.J., et al. (1998) J.Mol.Biol. 275: 861-872) created with Protein Workshop (Moreland, et al. (2005) BMC Bioinformatics 6:21).

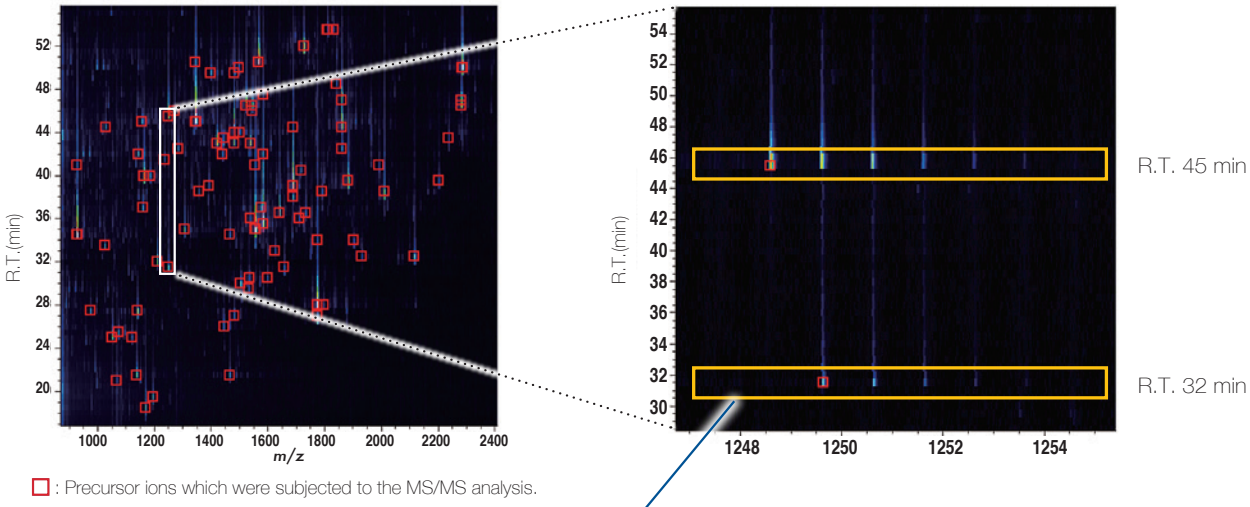
For more detailed amino acid sequence determination, MS/MS Ion Search is available. More accurate protein identification is possible with MS/MS Ion Search as proteins are identified based on the amino acid sequences of the enzymatic digests. With the LC-MALDI method, analysis of low abundance peptides or analysis of a mixture of peptides are possible. Ion suppression is significantly reduced as peptides are fractionated by LC.

LC-MALDI analysis of the enzymatic digest of a protein mixture and identification of the proteins by MASCOT MS/MS Ion Search

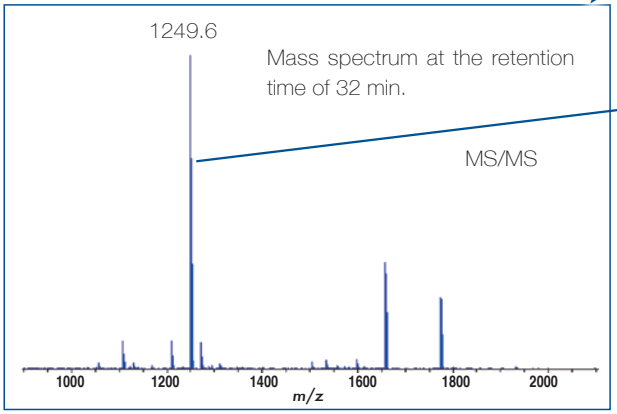
MALDI mass spectrum of the tryptic digests of bovine serum albumin and chicken egg ovalbumin.



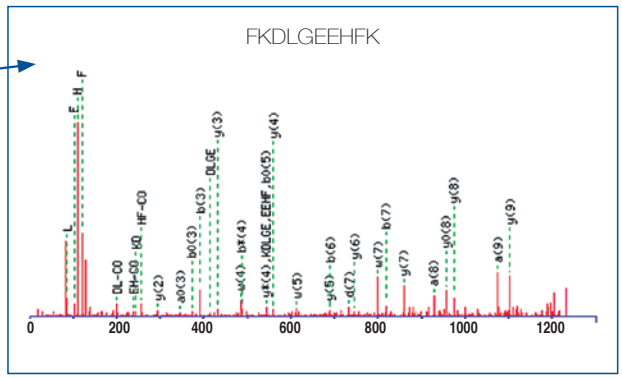
The result of the LC-MALDI analysis by fractionating the peptide mixture with HPLC (Survey View heat map.)
More peptides were observed by fractionating the mixture with HPLC as ion suppression was significantly reduced.
Peptides at *m/z* 1248.6 and *m/z* 1249.6, which could not be differentiated in the mass spectrum of the mixture, are clearly separated.



: Precursor ions which were subjected to the MS/MS analysis.



The product ion mass spectrum and MS/MS Ion Search result for the *m/z* 1249.6 precursor ion observed at the retention time of 32 min.



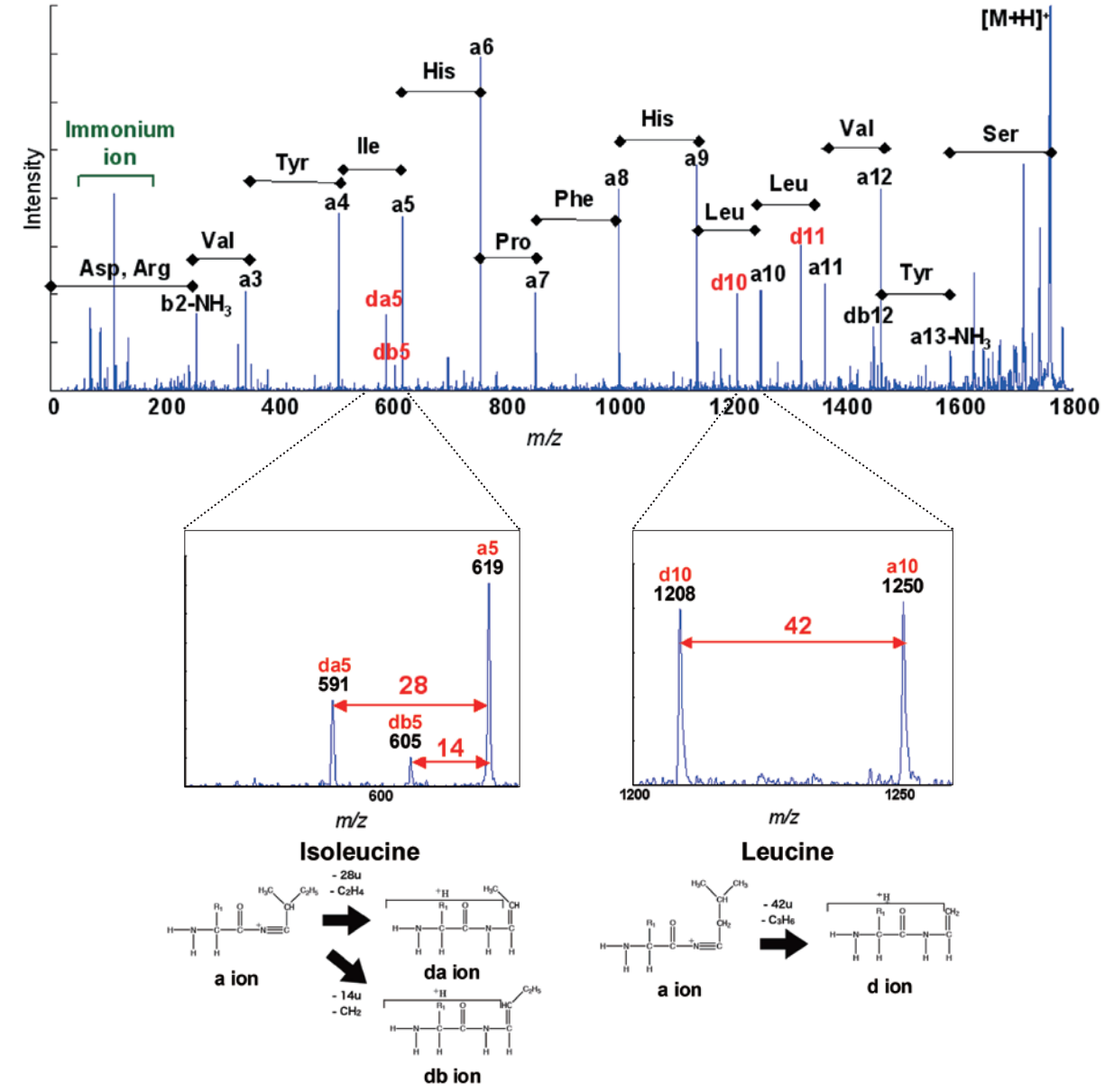
A Wide Range of Applications

Peptides

With the TOF-TOF option, de-novo sequencing of an unknown peptide that is not present in the database is possible. With HE-CID fragmentation, an amino acid sequence from the precursor ion down to immonium ions can be determined. Leucine and isoleucine are known to be differentiated with HE-CID*.

Amino acid sequence determination of renin substrate tetradecapeptide (MSTips No. 180)

Asp-Arg-Val-Tyr-Ile-His-Pro-Phe-His-Leu-Leu-Val-Tyr-Ser



Leucine and isoleucine can be differentiated by the d ions derived from side chain fragmentation.

* Kitanaka, A., et al., N-Terminal Derivatization with Structures Having High Proton Affinity for Discrimination between Leu and Ile Residues in Peptides by High-Energy Collision-Induced Dissociation, Mass Spectrometry, 5, A0051, doi: 10.5702/massspectrometry.A0051 (2016)

A Wide Range of Applications

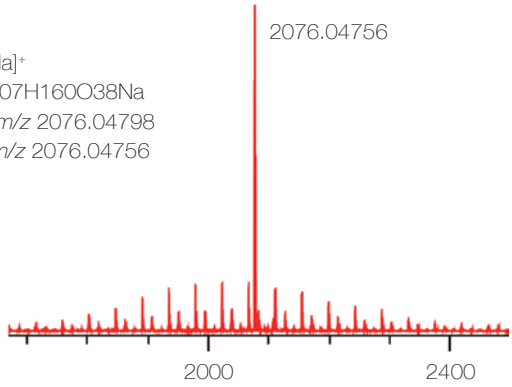
Natural Products

HE-CID can be utilized for the structural elucidation of natural products as a complementary technique for NMR, which provides a wealth of structural information. With the SpiralTOF™-plus 2.0, the accurate mass measurement facilitates elemental composition determination of unknowns. With the TOF-TOF option, the product ion mass spectrum for the mono-isotopically selected precursor ion can be measured. Mono-isotopic selection of the precursor ion facilitates unambiguous interpretation of the product ion mass spectrum since all of the product ions observed are also mono-isotopic.

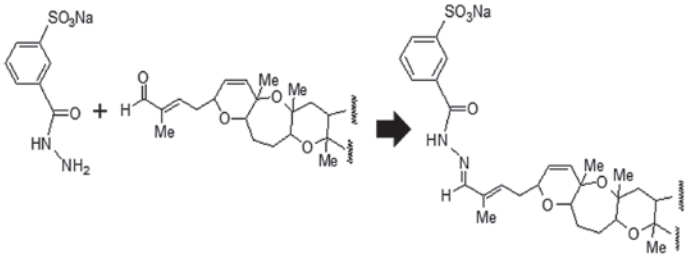
Structural elucidation of brevisulcenal-F*

1. Accurate mass measurement for elemental composition determination

KBT-F $[M+Na]^+$
Formula: C107H160O38Na
Calculated: *m/z* 2076.04798
Measured: *m/z* 2076.04756

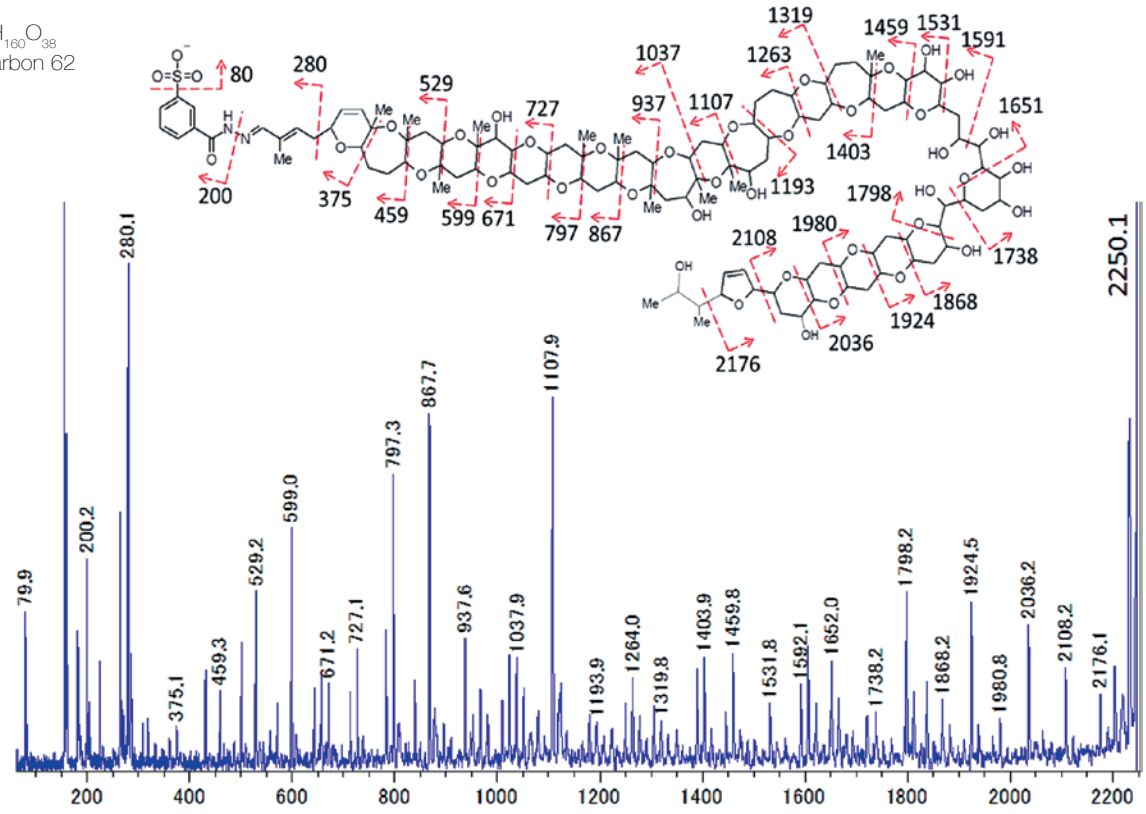


2. Derivatization to facilitate charge remote fragmentation



3. Acquisition and analysis of the product ion mass spectrum

Formula: $C_{107}H_{160}O_{38}$
Asymmetric carbon 62
Ether ring 24



* Hamamoto, Y. et al. Brevisulcenal-F: A polycyclic ether toxin associated with massive fish-kills in New Zealand. Journal of the American Chemical Society 134, 4963-4968, doi:10.1021/ja212116q (2012).

Lipids

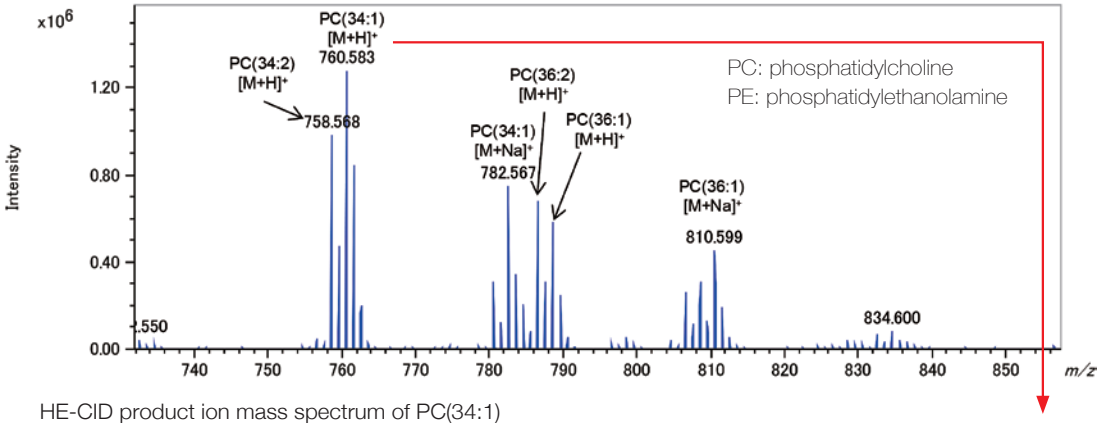
Why is the SpiralTOF™-plus 2.0 good at analyzing lipids?

Lipid molecules contain fatty acids and alkyl chains. Within a class of lipids, there is a wide variety of compounds due to the difference in alkyl chain length and number of double bonds. The molecular mass shifts 14 u with one methylene group and -2 u with one double bond. The SpiralTOF™-plus 2.0 with TOF-TOF option can completely isolate precursor ions that differ by 2 u - an essential feature required for the detailed structural analysis of a lipid mixture by tandem mass spectrometry. HE-CID can fragment C-C bonds in alkyl chains due to charge remote fragmentation, and double bond positions can be elucidated due to the fact that they are harder to cleave.

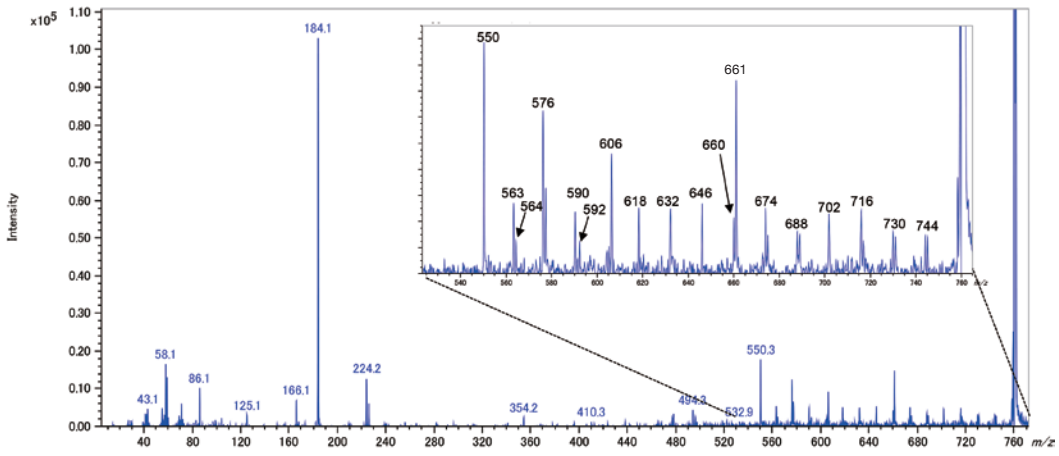
Analysis of phospholipids in hen egg yolk (MSTips No.185)

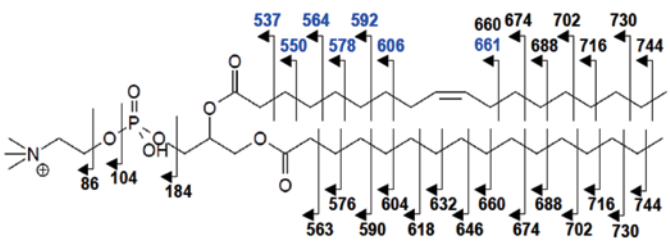
Lipids in hen egg yolk were extracted and analyzed in positive ion mode. A variety of phosphatidylcholines (PCs) were detected in the sample. In the example below, the product ion mass spectrum from the protonated molecule [M+H]+ was acquired for PC(34:1). Product ions derived from the fragmentations within the fatty acid chains were observed, which provided the information necessary for determining the fatty acid composition and double bond position.

MALDI mass spectrum of phospholipids from hen egg yolk



HE-CID product ion mass spectrum of PC(34:1)

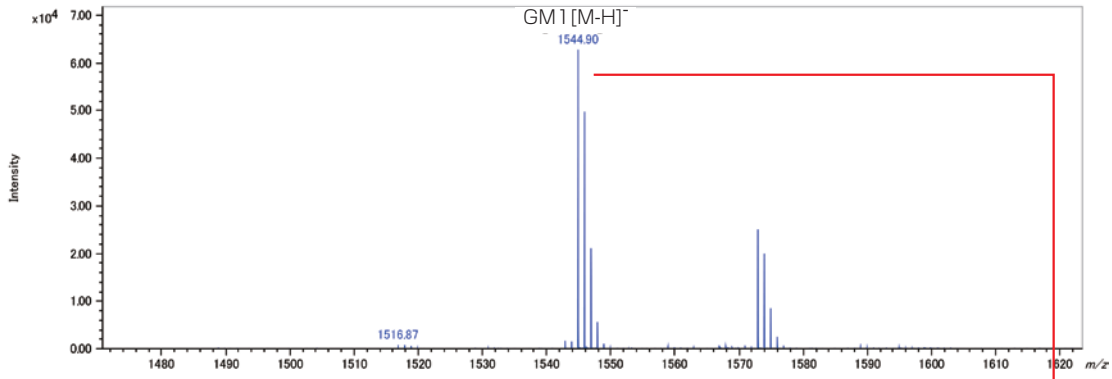




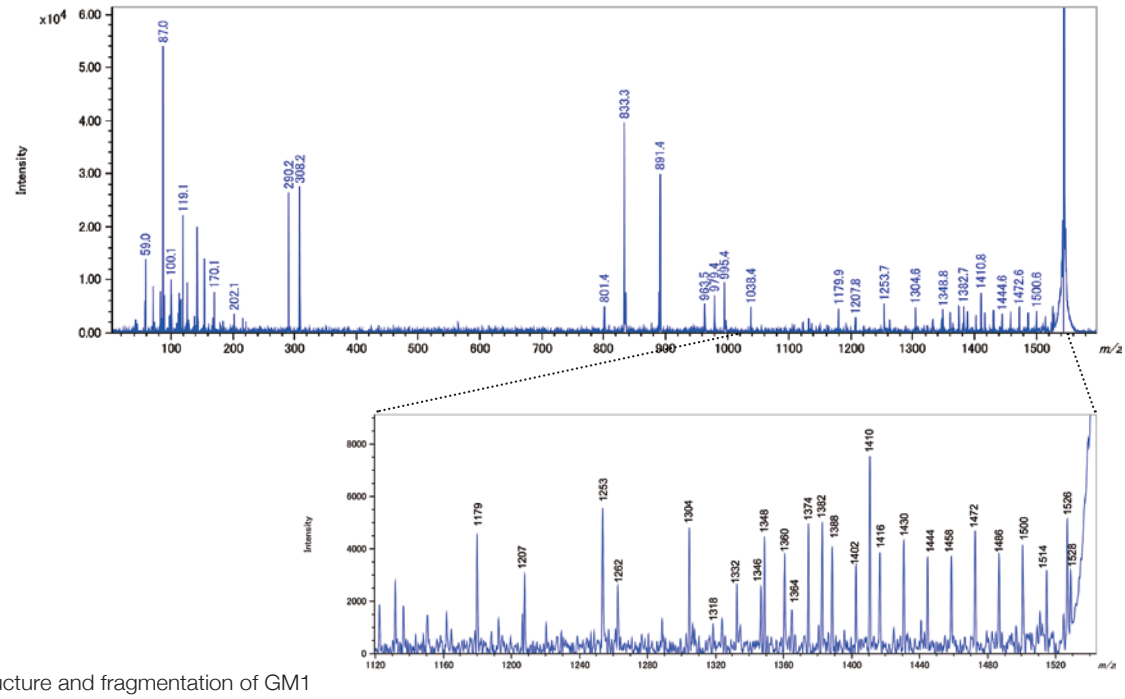
Analysis of ganglioside GM1 (ovine brain) (MSTips No.187)

Ganglioside GM1, a glycolipid abundant in brain and nerve cells, was analyzed in negative ion mode. Product ions derived from the cleavage within the fatty acid and ceramide were observed in the product ion mass spectrum of the deprotonated molecule $[M-H]^-$. The composition of the fatty acid and ceramide as well as the structure of the glycan were determined with this method.

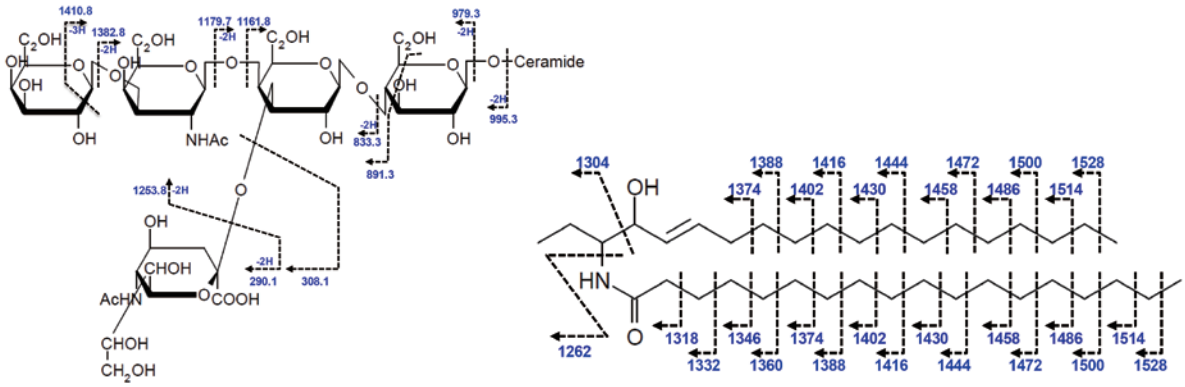
MALDI mass spectrum of GM1



HE-CID product ion mass spectrum of GM1. The region showing product ion peaks derived from charge remote fragmentation is shown at the bottom.



The structure and fragmentation of GM1



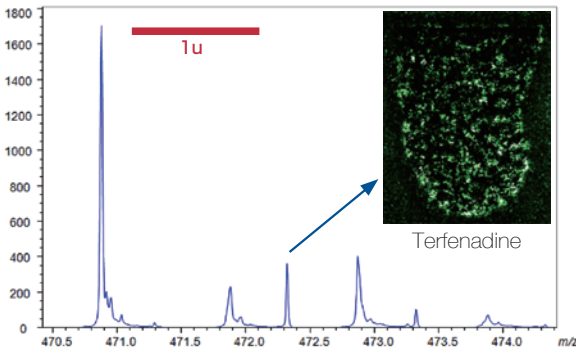
A Wide Range of Applications

Pharmaceuticals

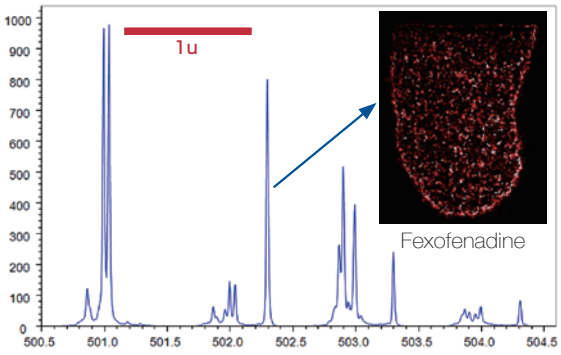
With the high mass-resolving power of the SpiralTOF™-plus 2.0, accurate spatial distributions for pharmaceuticals and their metabolites in a tissue section can be determined despite the presence of abundant interfering compounds in the tissue. HE-CID product ion mass spectra can be directly acquired from the tissue section, facilitating the structural identification of the target analytes.

Analysis of terfenadine and its metabolite, fexofenadine, in a mouse kidney section (MSTips No. 212)

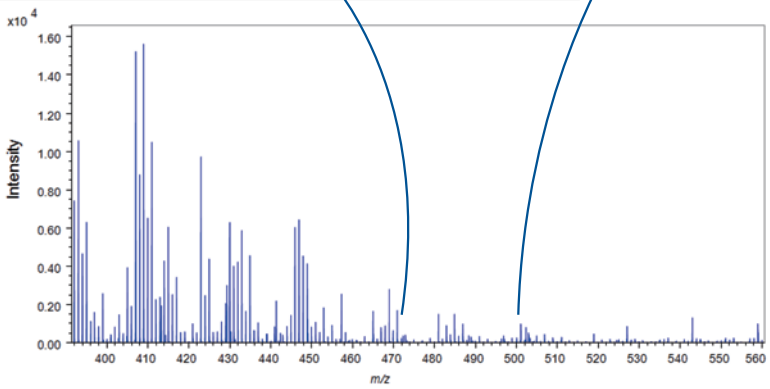
Mass spectral peak and MS image of terfenadine



Mass spectral peak and MS image of fexofenadine

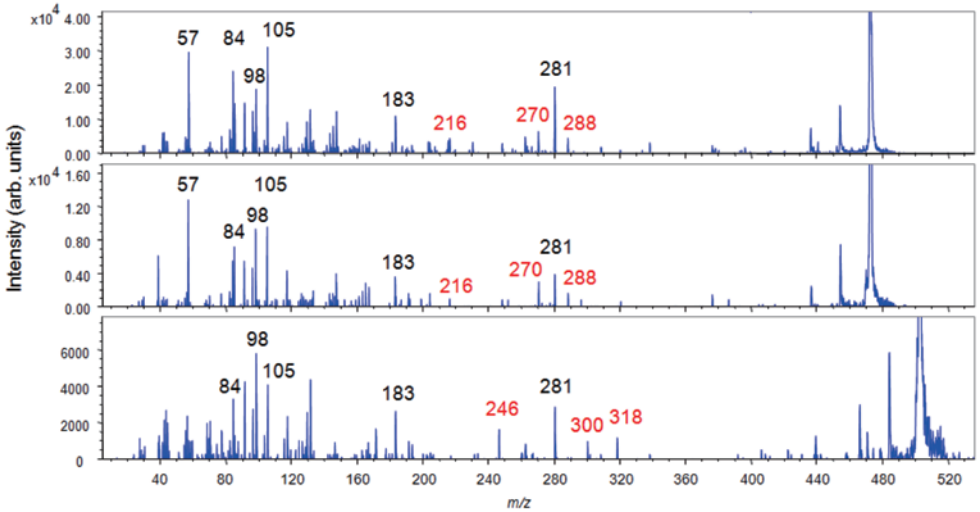


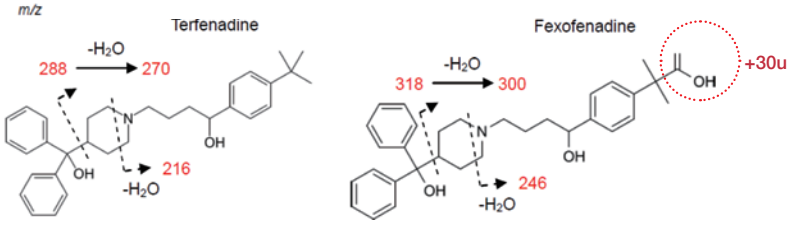
Averaged mass spectrum of a mouse kidney section that was administered terfenadine.



HE-CID product ion mass spectra of terfenadine and fexofenadine.

MS/MS analysis allows structural elucidations of compounds on a tissue section.





(Specimen courtesy of the pharmacokinetics research center, Daiichi Sankyo Co. Ltd.)

Options

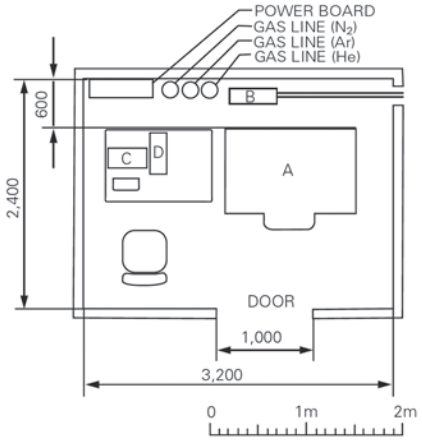
For MS imaging

	Model name	Description
Target plates	Adapter for glass sample plate	For ITO glass sample plates (Hudson Surface Technology; HST)
	ITO glass sample plate	Slide glass, 0.7 mm thick, 25 pc/pkg
	Multi-target plate	For thick specimens Indentations for 0.5 mm thick and 1.0 mm thick specimens.
Software	MS-56530MSI MS Imaging Support Program	1D (line) scan and 2D scan (imaging) data acquisition. Convert MS imaging raw data into imzML format.
	msMicroImager™ MS-56550MSIV MS Imaging Viewer Program	Read MS imaging raw data acquired by msTornado™ Control. Perform pixel binning. Extract and export MS images. Export mass spectra of the regions of interest. Browse MS images. Change color map of the images. Perform arithmetic operations between MS images. Overlay MS images. Generation of images based on average molecular weight and polydispersity.
	SCiLS Lab MVS (Bruker Daltonik GmbH)	Comparative analysis, co-localization analysis, spatial segmentation, component analysis, classification model calculation, organizational quantification

For polymer analysis

	Model name	Description
Target plates	96-spot hairline finish plate	Suitable for use with organic solvents.
	Adapter for µFocus plates (HST)	The adapter to hold and use µ Focus plates (HST).
	Various one-time use plates (HST)	One-time use plates by HST
Software	msRepeatFinder MS-56560REP Repeating Structure Analysis Program	Import peak list (centroided mass spectrum). Display a centroided mass spectrum. Create KMD plot, KMR plot, Fraction Base KMD plot, and RKM plot. Grouping (coloring, calculate relative ion intensity w.r.t. sum of all groups, calculate average molecular weights) Elucidate elemental composition of monomer and end group. 2 sample comparison function.

Installation requirements



Power supply*

Mass spectrometer (including RP)	Single phase AC200 V or 220-240 V, 50 Hz, 30 A AC200 V-210 V or 230-240 V, 60 Hz, 30 A
Data system	Single phase AC 100-240 V, 50-60 Hz, 15 A
Grounding	100 Ω or less

Gas supply

● Nitrogen gas	
Pressure	0.45±0.05 MPa
Purity	97% or better
● Helium gas for CID (for TOF-TOF option)	
Pressure	0.45±0.05 MPa
Purity	99.999% or better
● Argon gas for CID (for TOF-TOF option)	
Pressure	0.45±0.05 MPa
Purity	99.9 % or better

Installation room

Floor space	3200 mm×2400 mm
Static magnetic field	5×10^{-4}T or less
Variable magnetic field	1×10^{-6}T or less
Floor vibration	
Amplitude (p-p)	25 µm or less
Acceleration	0.1 m/s² or less
Room temperature	
Temperature range	20 to 27 °C
Temperature stability	±3 °C/h or better
Maximum heat generation	20,300 kJ/h (MS+data system)
Humidity	30 to 70% (no condensation)
Ventilation facility	required for the rotary pump

* For details of installation requirements, please inquire a local sales office for details.

* Power supply requirement depends on specific configuration sold in each territory. Please inquire a local sales office for details.

	Name of unit	Width (mm)	Depth (mm)	Height (mm)	Weight (kg)
A	MALDI-TOF basic unit	1300	1000	1190	765
	+TOF-TOF option			1920	874
	+Linear TOF option			1920	775
	+TOF-TOF+Linear TOF			1920	884
B	Rotary pump	158	491	261	26.3
C	LCD monitor	506	253	477	8.5
D	PC	168	456	450	15.1

To place the rotary pump (RP) behind the basic unit, the distance from the rear of the basic unit to the room wall must be 600 mm or more.
- An exhaust duct or port is needed for the rotary pump (RP).
- The table for PC and printer must be provided by the customer.

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