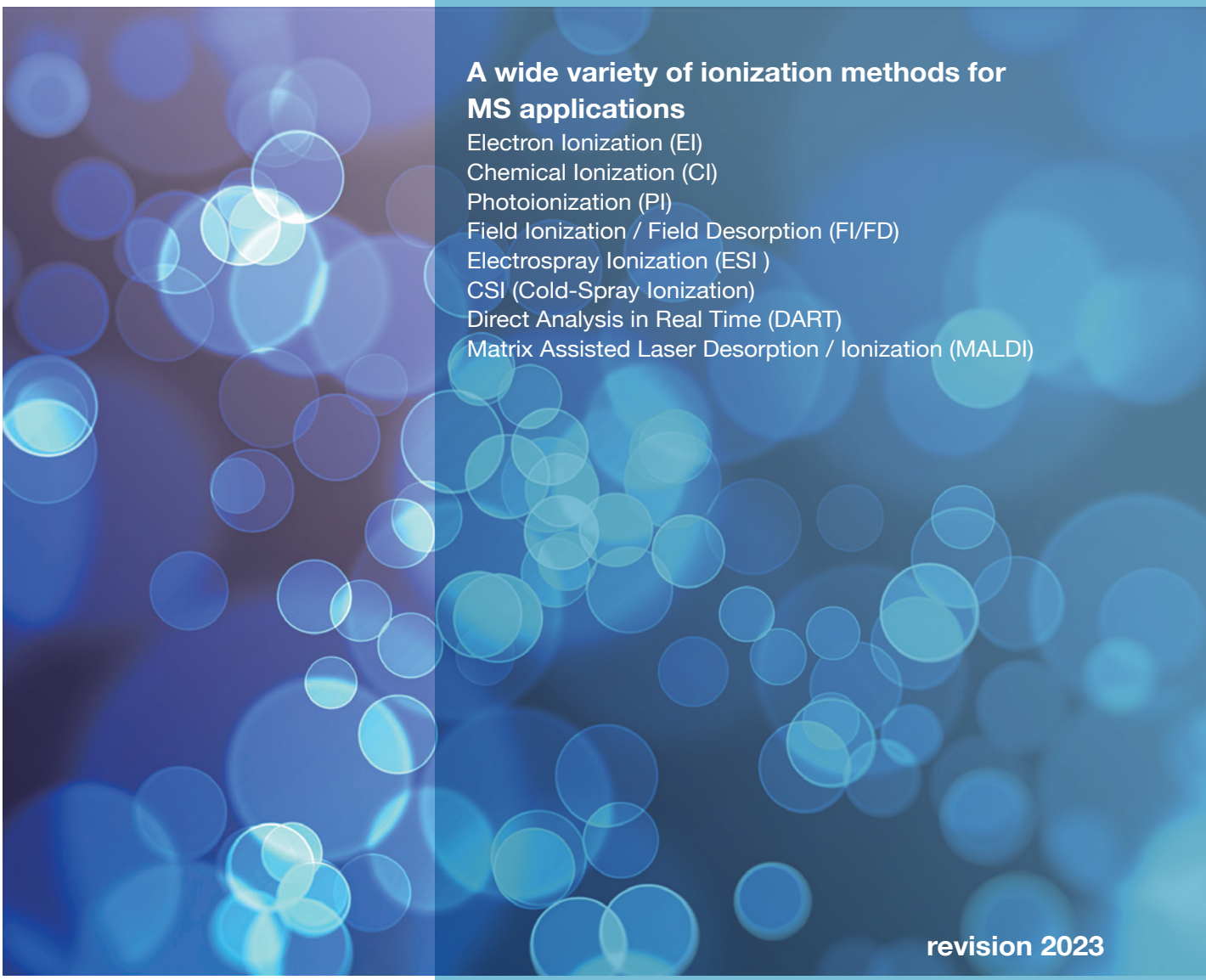
JEOL

Solutions for Innovation

Scientific / Metrology Instruments
Mass Spectrometry Guidebook

Ionization Methods for JEOL Mass Spectrometers

- A Guidebook -



A wide variety of ionization methods for MS applications

Electron Ionization (EI)
Chemical Ionization (CI)
Photoionization (PI)
Field Ionization / Field Desorption (FI/FD)
Electrospray Ionization (ESI)
CSI (Cold-Spray Ionization)
Direct Analysis in Real Time (DART)
Matrix Assisted Laser Desorption / Ionization (MALDI)

revision 2023

JEOL Ltd.

A wide variety of ionization methods for MS applications

JEOL mass spectrometers support a wide variety of ionization methods, including the ones compatible with chromatography, the ones for direct sample introduction, hard ionization, soft ionization, etc.

This guidebook introduces the principles and features of these various ionization methods, as well as their applications.

JEOL
Mass Spectrometers

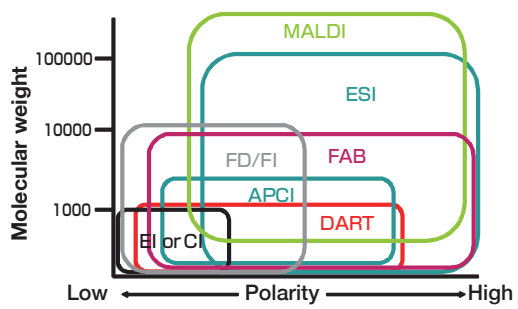
	EI	CI	PI	FI	DEI*	DCI*	FD	MALDI	DART	APCI	ESI	CSI
GC-QMS JMS-Q1600GC UltraQuad™ SQ-Zeta	●	●	●		●	●						
GC-TQMS JMS-TQ4000GC UltraQuad™ TQ	●	●	●		●	●						
GC-TOFMS JMS-T2000GC AccuTOF™ GC-Alpha	●	●	●	●	●	●	●					
GC-HRMS JMS-800D UltraFOCUS™	●											
MALDI-TOFMS JMS-S3000 SpiralTOF™-plus								●				
DART™, LC-TOFMS JMS-T100LP AccuTOF™ LC-Express									●	●	●	●

Ionization methods marked by deep blue can be combined with chromatography including GC and LC.
* DEI and DCI represent EI and CI using a platinum filament direct exposure probe.

Topic 1

Applicable ranges of ionization methods

There is no one ionization method to support all applications. You need to select an ionization method best suited for your applications. The table on the left shows the ionization methods you can use with JEOL mass spectrometers. As the table demonstrates, JEOL mass spectrometers support a variety of ionization methods. The figure below shows the molecular weight and sample polarity suitable for each ionization method.



Topic 2

Soft ionization methods for JEOL mass spectrometers

Soft ionization gives little internal energy to sample molecules, produces fewer fragment ions, and makes it easier to observe molecular ions from ionized sample molecules. Ionization may be accomplished in various ways: by the direct interaction of sample molecules and electrons, through the ion molecular reaction between ionized reagent gas and sample molecules, etc.

On the other hand, hard ionization imparts excess internal energy to sample molecules and produces a large amount of fragment ions. Fragment ions, containing partial structural information of sample molecules, are effective for structural analysis. Electron ionization (EI) is a typical hard ionization method.

JEOL mass spectrometers support a variety of ionization methods. Selecting an ionization method optimum for the samples and applications makes it possible to acquire the best results.

Topic 3

Ionization methods for analysis of complex mixtures

Complex mixture samples, if ionized as they are, will produce mass spectra showing peaks from various components at once, making the analysis extremely difficult. Chromatographic separation is effective for analyzing mixture samples.

Different types of chromatography are available: gas chromatography (GC) using the interaction between a vaporized sample and a column liquid phase; liquid chromatography (LC) using the interaction between a sample solution and a column solid phase. Ionization methods compatible with GC and LC are listed below.

GC: EI, CI, PI, FI
LC: ESI, APCI

Topic 4

Analysis of insoluble samples

Samples that are insoluble or dispersed in solvents are difficult to analyze in GC or LC. Direct sample introduction is effective for such samples.

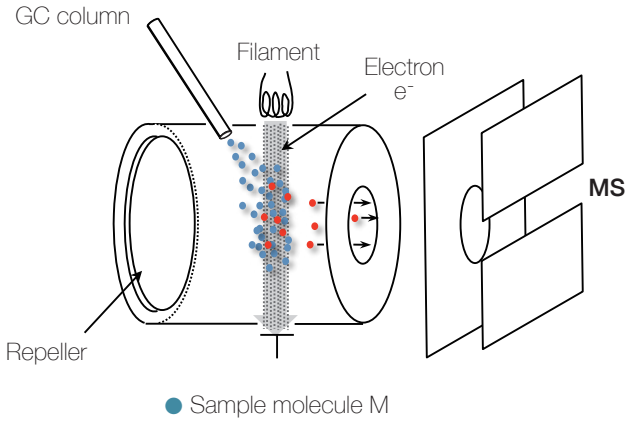
Direct sample introduction, designed to ionize an entire sample introduced into a mass spectrometer at once, is effective for analysis of pure compounds. For analysis of mixture samples, soft ionizations make it possible to identify components from molecular ions and cation adducts. Direct sample introduction methods supported by JEOL mass spectrometers are listed below.

DEI, DCI, FD, MALDI, DART

Electron Ionization (EI)

This is the ionization method most widely used for GC-MS. It is designed to produce ions by irradiating thermal electrons emitted from a filament to gaseous sample molecules. It is suitable to be combined with GC because sample molecules need to be in gas phase for ionization. EI, being the hardest ionization technique, produces many fragment ions. Because the relative intensity of each ion observed (spectral pattern) has high reproducibility, components are easily identified by comparing the acquired spectrum against the EI mass spectrum library database. The database contains more than 300,000 compounds, supporting various GC-MS applications.

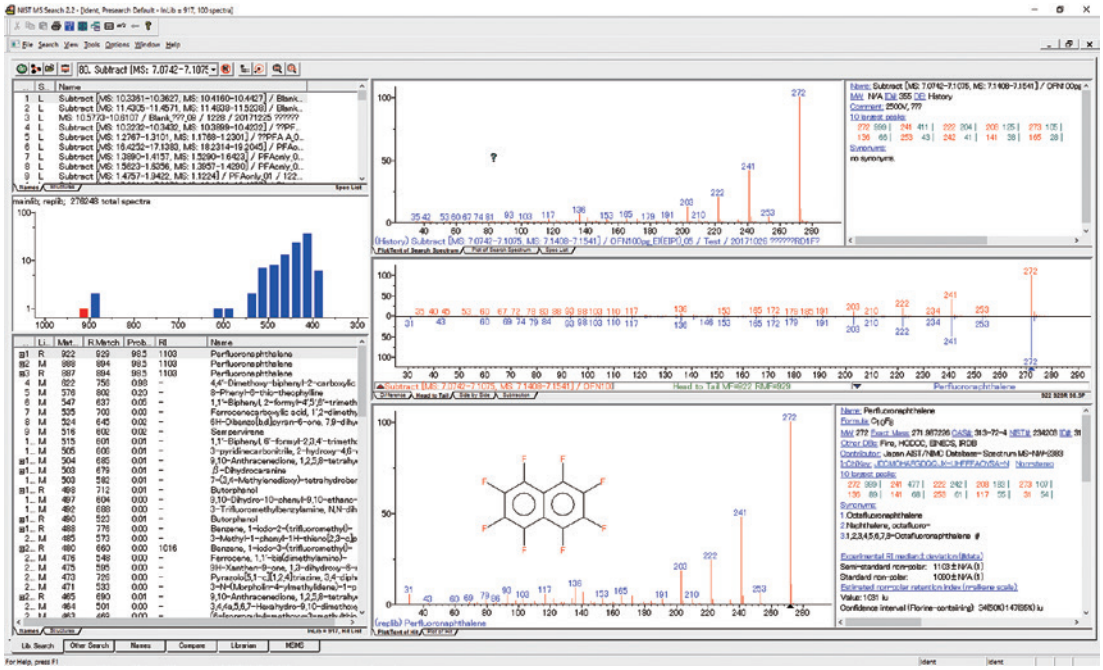
Electron ionization (EI)



$M + e^- \rightarrow M^{+\cdot} + 2e^-$

$M^{+\cdot} \rightarrow m^+ + n^\cdot$

EI application: NIST library search



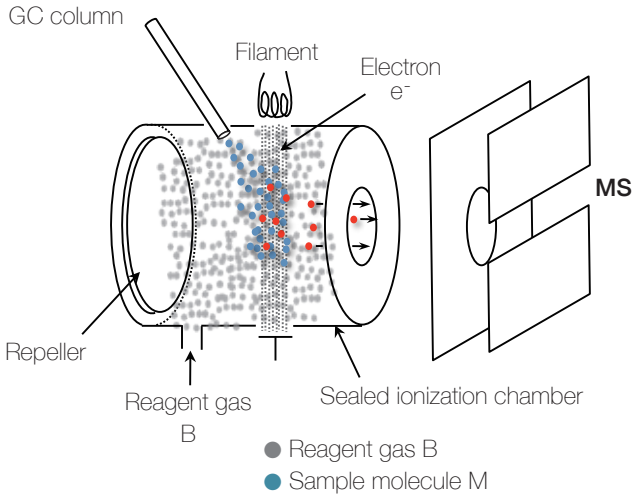
Result of NIST library search for octafluoronaphthalene

Source)
· The NIST Mass Spectral Search Program for the NIST/EPA/NIH Mass Spectral Library

Chemical Ionization (CI)

This is a typical soft ionization method used for GC-MS. A reagent gas is introduced into a highly airtight ionization chamber (approx. 10^{-2} Pa), and the reagent gas (B) is ionized by thermal electrons. Sample molecules (M) are then introduced to produce protonated molecules and other types of ions through the ion molecular reaction with the reagent gas ions. Compared to EI, CI is a soft ionization method, one of the techniques effective in determining the molecular weight of an unknown sample. For the reagent gas, methane, isobutane, and ammonia are primarily used. When methane and isobutane reagent gases are used, $[M+H]^+$ ions are observed; when an ammonia gas is used, $[M+NH_4]^+$ ions are observed.

Chemical ionization (CI)



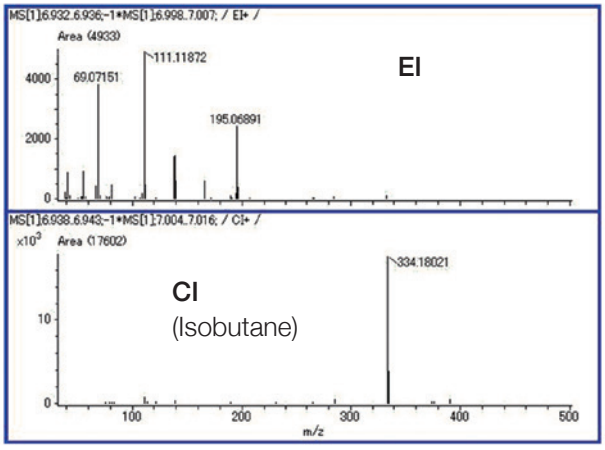
Proton adduct (most predominant reaction)
$M+[B+H]^+ \longrightarrow [M+H]^+ + B$

Reagent gas adduct
$M+[B+H]^+ \longrightarrow [M+B+H]^+$

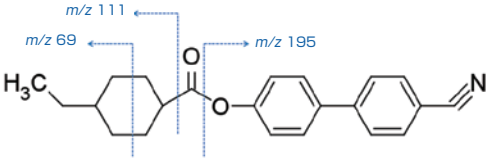
Hydride ion abstraction
$M+[B+H]^+ \longrightarrow [M-H]^+ + [B+2H]$

Charge exchange
$M+B^{+\cdot} \longrightarrow M^{+\cdot} + B$

CI application: Qualitative analysis of an unknown compound



Mode	Obs.*m/z*	Error (mDa)	Formula
EI+	69.0715	1.1	C_5H_9
	111.1187	1.3	C_8H_{15}
	195.0689	1.4	$C_{13}H_9NO$
	333.1743	1.4	$C_{22}H_{23}NO_2$
CI+	334.1802	-0.5	$C_{22}H_{24}NO_2$

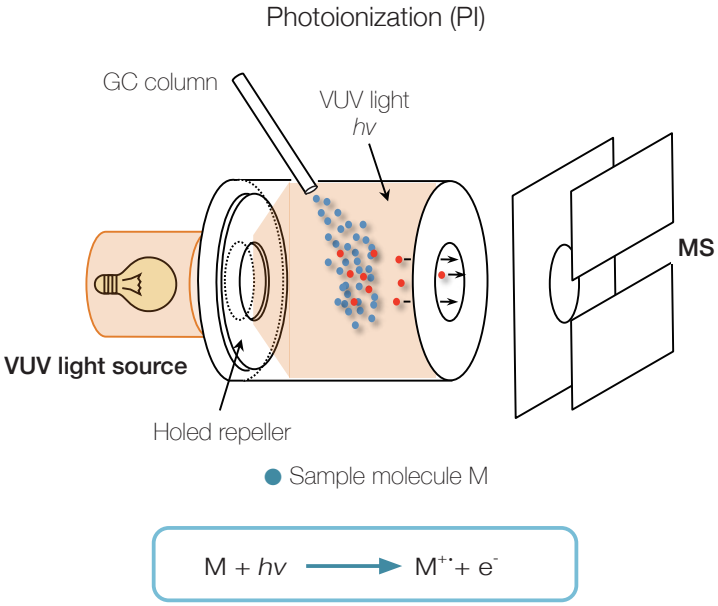


Unknown compound in liquid crystal mixture
Mass spectra of EI and CI

Exact mass results and
Estimated chemical formula

Photoionization (PI)

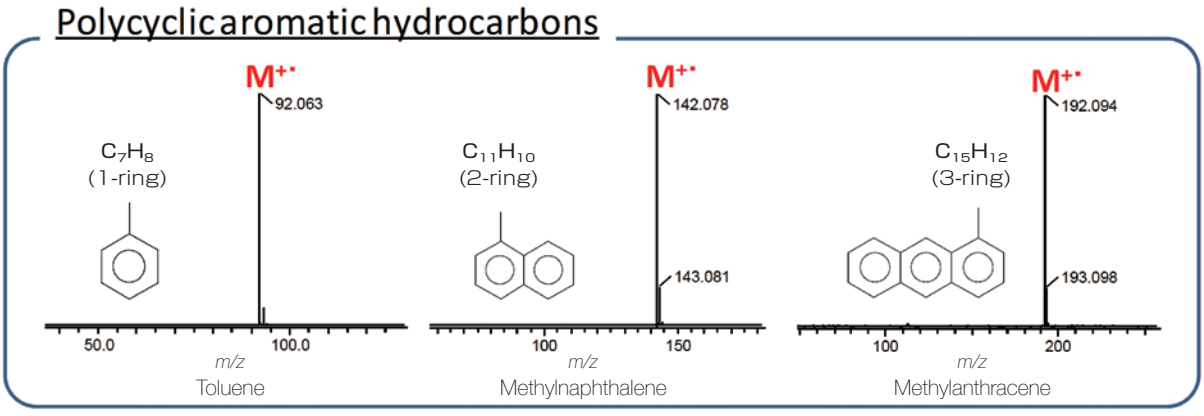
Photoionization is designed to irradiate vacuum ultraviolet (VUV) light inside an ionization chamber to provide photon energy at 8 to 10 eV to sample molecules.
It is a soft ionization method featuring low ionization energy, suppressing fragmentation, because the ionization energy for typical organic compounds is 8 to 11 eV. Compounds that absorb ultraviolet light, such as aromatic compounds, tend to have higher sensitivity compared to other compounds.
Photoionization is one of the soft ionization methods for GC-MS that require no reagent gas. It is easy to use and is effective in estimating the molecular formula of an unknown compound.



PI ion source flange for JMS-Q1500GC

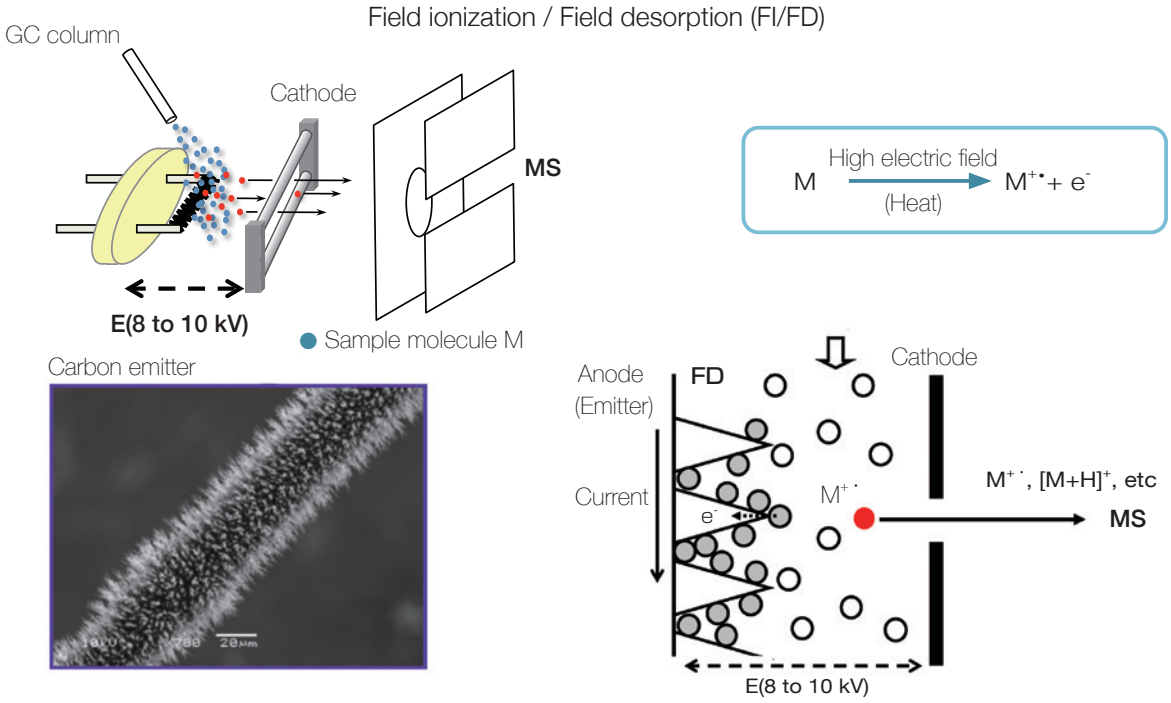
PI ion source flange for JMS-T2000GC

PI application: Analysis of aromatic compounds

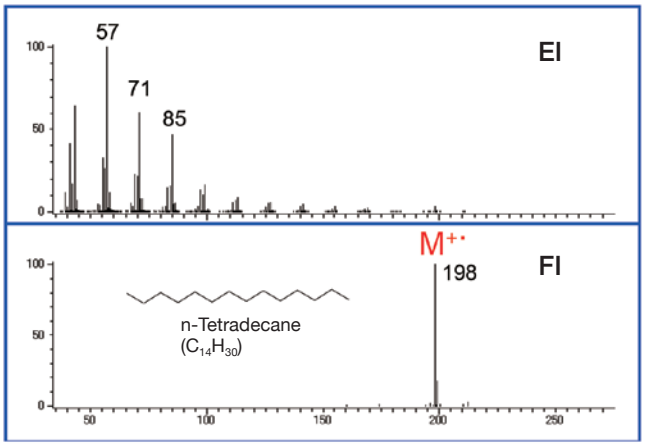


Field Ionization / Field Desorption (FI / FD)

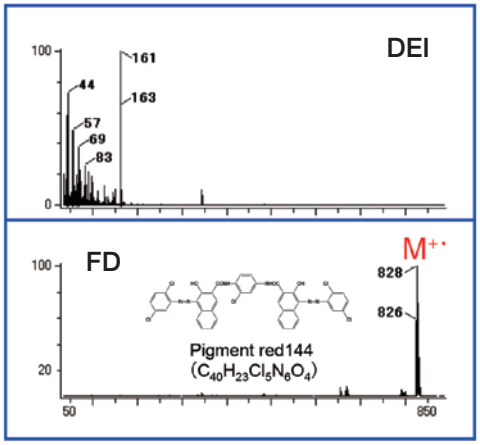
FD and FI are ionization methods based on the same principle. In this method, a voltage of about 8 to 10 kV is applied between the emitter and the counter electrode (cathode), and the electrons in the sample molecules move to the emitter due to the tunnel effect, thereby ionizing the sample molecules. It is called FI when gaseous sample molecules approach the emitter and are ionized, and it is called FD when the sample is applied to the emitter in advance and measured while being heated. FI is an ionization method for GC, and FD is an ionization method for direct sample introduction. The internal energy given when ionized by FD and FI is 1 eV or less, which is considerably smaller than that of EI and CI. Therefore, FD and FI are soft ionization methods with little fragmentation. Both methods are effective for detecting molecular ions, and FD is particularly effective for ionizing thermally unstable and non-volatile compounds.



FI/FD application: Molecular ions detected in a low-polarity compound and a refractory compound



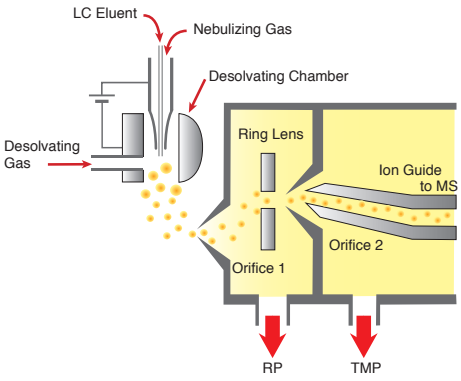
Mass spectrum of n-tetradecane
Top: EI; bottom: FI



Mass spectrum of pigment red 144
Top: DEI; bottom: FD

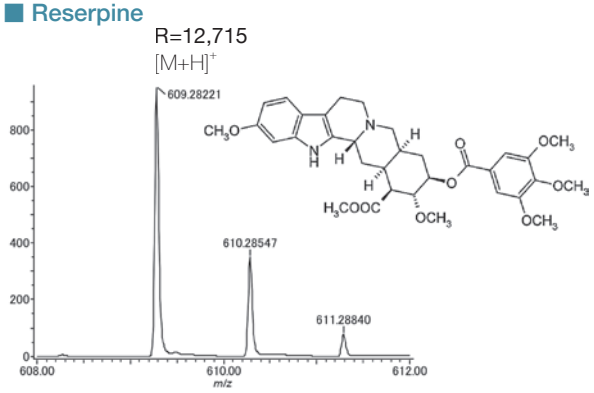
Electrospray Ionization (ESI)

This is the most widely used atmospheric pressure ionization method using electrospray phenomenon. A sample solution is injected into a capillary, and is ionized by applying high voltage between the capillary and the counter electrode (orifice electrode). Using the lowest ionization energy among all ionization methods, ESI is the only ionization method that acquires molecular weight information from biopolymer samples as well as coordinate bond compounds including organometallic complexes. When used for proteins, peptides, and nucleic acids etc., they are observed as multiply-charged ions.

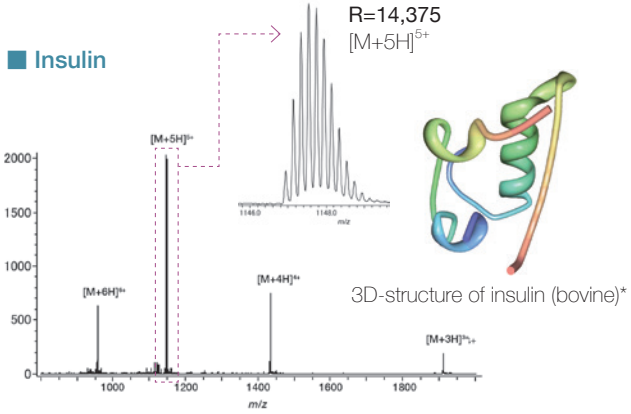


Schematics of the orthogonal electrospray ion source

■ Reserpine



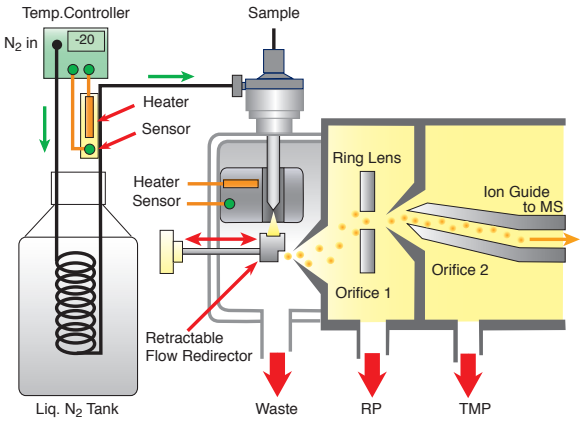
■ Insulin



3D-structure of insulin (bovine)*

Cold-Spray Ionization (CSI)

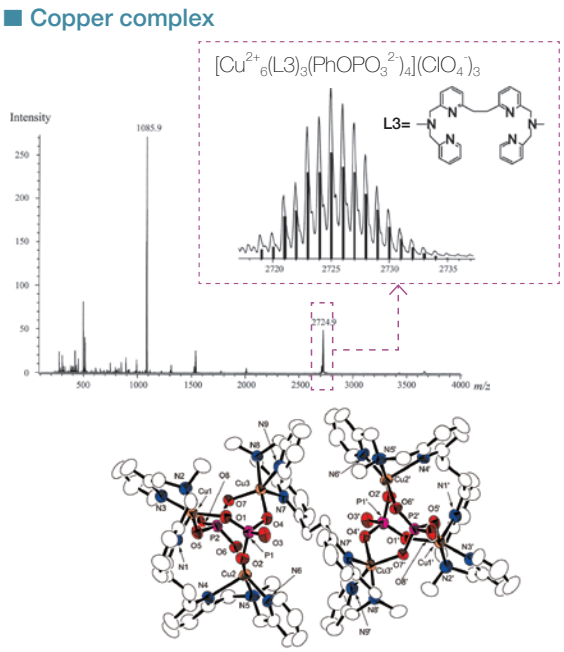
CSI is a low temperature ionization method using a cold nitrogen gas as the nebulizing gas for ESI ion source. It is effective in ionizing biological molecules, reaction intermediates, host-guest complexes, and various aggregates in solutions in addition to metal complexes that are difficult to be analyzed by ESI.



Schematics of the ColdSpray ion source

ColdSpray ionization was developed by Prof. Kentaro Yamaguchi, et al., of Kagawa School of Pharmaceutical Sciences, Tokushima Bunri University (previously Chiba University) and the result of a project funded by the Japan Science and Technology Agency (JST).
Reference: Cold-Spray ionization mass spectrometry: principle and applications K. Yamaguchi, J. Mass Spectrom, 38, 473-490 (2003)

■ Copper complex



ORTEP diagram of the complex $[Cu^{2+}_6(L3)_3(PhOPO_3^{2-})_4]$

(Data courtesy of Prof. Masahito Kodera, Doshisha University)

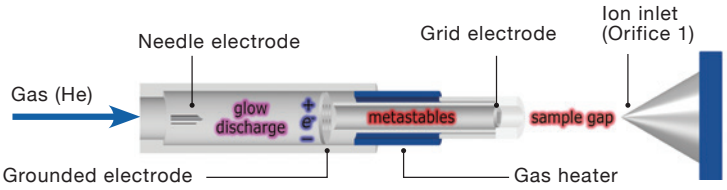
Direct Analysis in Real Time (DART)

A typical ambient ionization method, DART™ ionizes samples in atmosphere without preparation. The ionization process of DART™ is based on the interaction of excited atoms/molecules with an atmospheric gas and sample. A helium gas introduced to DART™ produces a plasma through the discharge from a needle electrode. The plasma contains ions, electrons, excited (metastable) atoms and molecules. Most of the charged particles in the plasma are removed by a ground electrode, emitting only the excited neutral gas molecules to atmosphere. The gas is heated as needed to promote vaporization of the sample and thermal desorption from the substance surface.

Positive ions

Excited helium atoms react to water in atmosphere, producing protonated water clusters. These react to an analyte (M), producing protonated molecules.

$He(2^3S) + H_2O \rightarrow H_2O^{+\cdot} + He(1^1S) + e^-$
$H_2O^{+\cdot} + H_2O \rightarrow H_3O^+ + OH^\cdot$
$H_3O^+ + nH_2O \rightarrow [(H_2O)_{n+1} + H]^+$
$[(H_2O)_{n+1} + H]^+ + M \rightarrow [M + H]^+ + (n+1)H_2O$



Negative ions

Excited helium atoms react to an exit grid electrode and neutral atmospheric gas (N), producing electrons through penning ionization. These electrons collide with gas (G) in atmosphere, rapidly losing speed, and react with oxygen in atmosphere, producing oxygen anions.

$He(2^3S) + N \rightarrow N^{+\cdot} + He(1^1S) + e^{-*}$
$e^{-*} + G \rightarrow G^{-*} + e^-$
$e^- + O_2 \rightarrow O_2^{-\cdot}$

These negative ions further react to sample molecules (M), producing negative ions of the analyte.

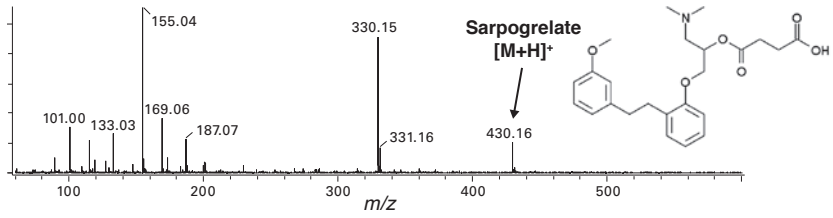
$O_2^{-\cdot} + M \rightarrow [M - H]^- + OOH^\cdot$
$O_2^{-\cdot} + M \rightarrow M^{-\cdot} + O_2$
$O_2^{-\cdot} + M \rightarrow [M + O_2]^{-\cdot}$

At the tip of a glass rod

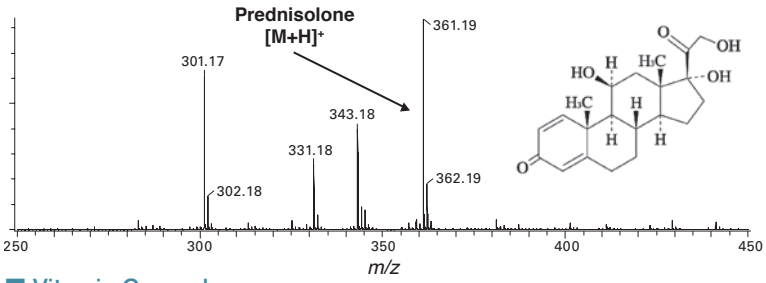
Held between tweezers

Powder wrapped in a ceramic sheet

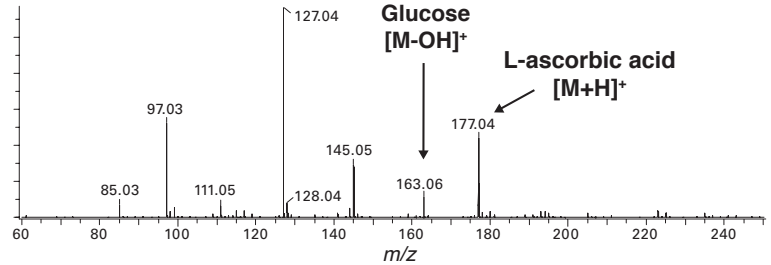
■ Antithrombotic drug



■ Steroid tablet

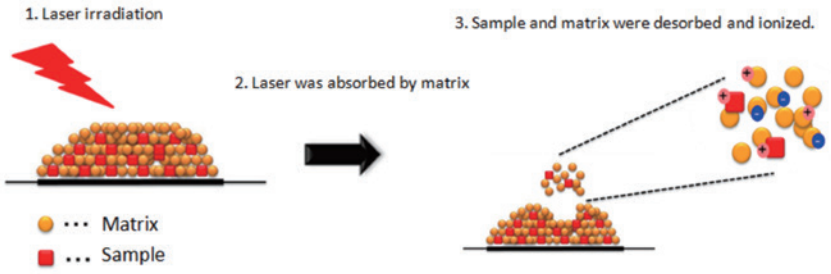


■ Vitamin C powder

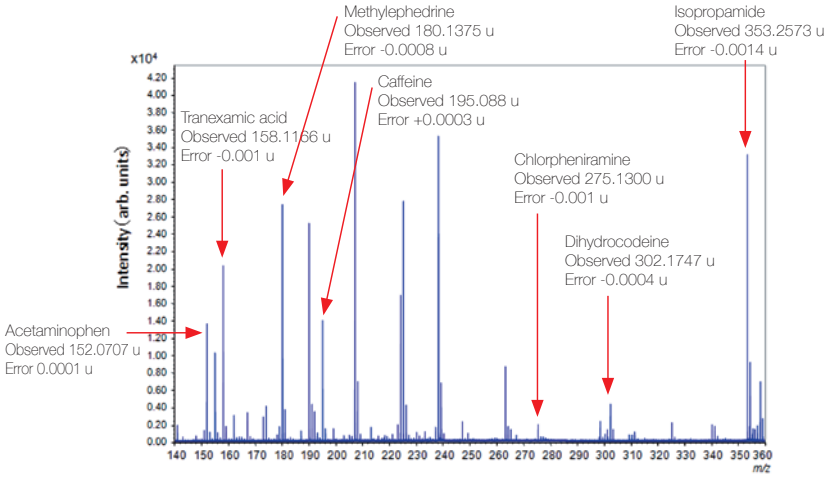


Matrix Assisted Laser Desorption/Ionization (MALDI)

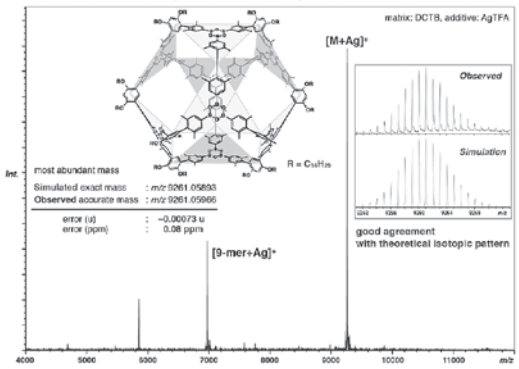
MALDI is a typical soft ionization method besides electrospray ionization (ESI). A solution of ionization promoter called matrix and sample solution are mixed and dropped onto a stainless plate. As it dries, the mixture forms a cocrystal, to which ultraviolet laser is irradiated, ionizing sample molecules. By selecting an appropriate matrix for the sample, MALDI can ionize low to high molecular weight samples-from a few hundreds Daltons to hundreds of thousands of Daltons. Because singly charged ions are primarily produced, the horizontal axis equals the mass of molecule, making it easy to interpret mass spectral data.



Cold medicine

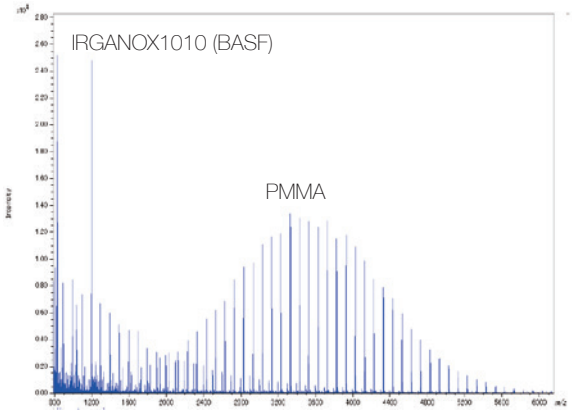


Boroxine cage



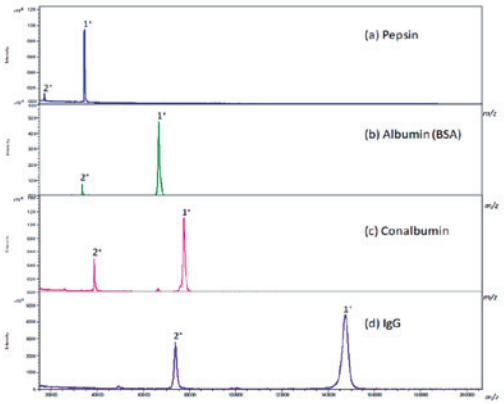
(Sample courtesy of Prof. Iwasawa, The Tokyo Institute of Technology)

Additives in polymer



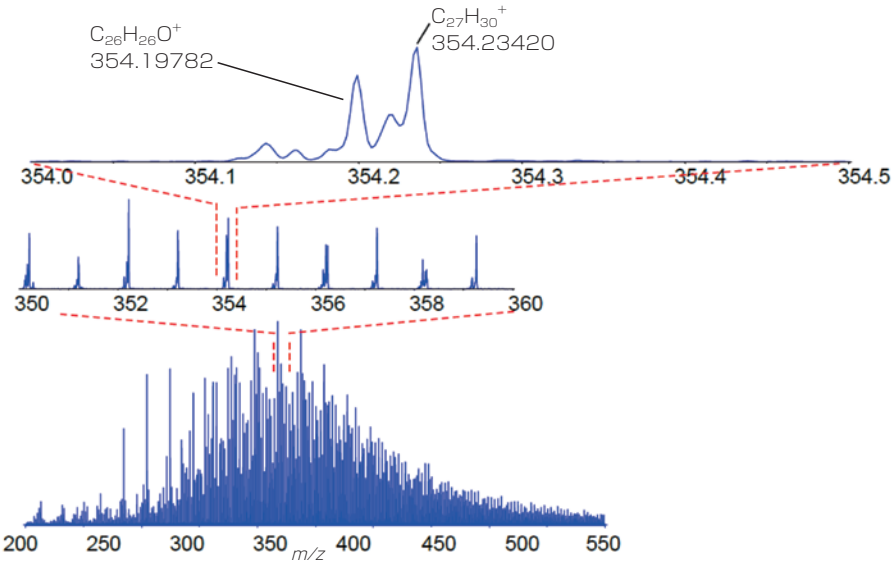
* Irganox is a registered trademark of BASF

Protein



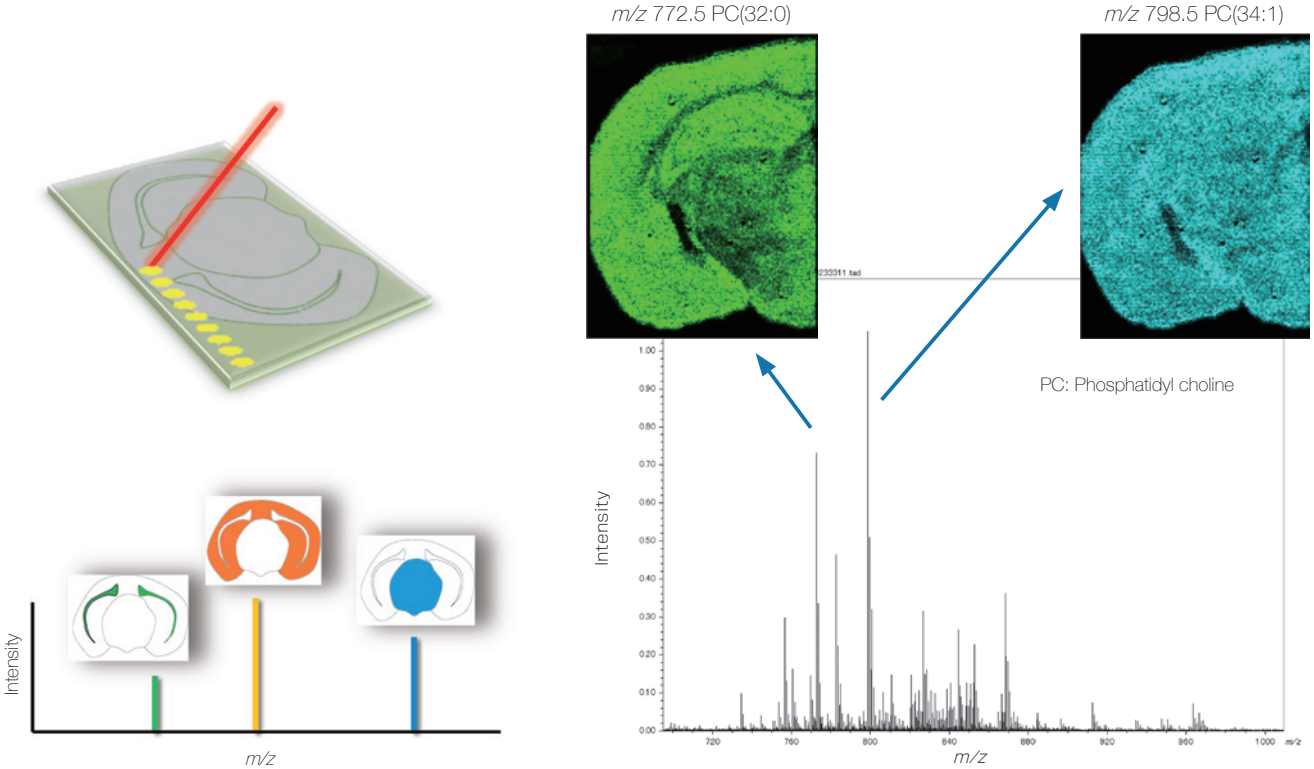
Some of the low molecular compounds can be ionized without a matrix. This type of ionization process is called laser desorption ionization (LDI). Typical compounds subjected to this ionization method include polycyclic aromatics, pigments/dyes, and organic semiconductor compounds, such as organic electroluminescence compounds.

■ Sample extracted with dichloromethane from Tokyo Bay sediments



MALDI also supports mass spectrometry imaging that maps organic substances on the sample surface. A sample section is placed onto a conductive plate (ITO slide glass), and coated with a matrix. The sample is subjected to laser irradiation at an interval of 10 to 100 µm to acquire mass spectral data.

■ Lipid distribution on a mouse brain section



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JEOL Ltd.

3-1-2 Musashino Akishima Tokyo 196-8558 Japan Sales Division Tel. +81-3-6262-3560 Fax. +81-3-6262-3577

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