This page is for a novel technology produced by a company **Shimadzu corporation** through a collaboration with researchers based on results of Biophysical studies

High spatial resolution imaging mass spectrometry with atmospheric-pressure ion source

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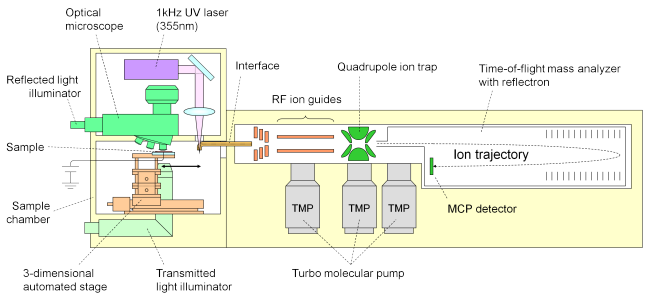
Advantage of an atmospheric pressure (AP) imaging mass spectrometry (IMS)

IMS is used to visualize the surface molecular distribution of objects. This analyzing method is extremely useful as a way of imaging for simultaneous and/or non-targeting analysis like omics-analysis because this method does not require any labels or specific probes. This character enables us to visualize the distribution of metabolites that are difficult to make labels including small organic molecules, lipids, and some proteins. The biological knowledge with IMS has increased. On the other hand, since traditional instruments of IMS are coupled with vacuum ion-source chamber for effective ionization, liquid or volatile metabolite cannot be measured by evaporating and histological information may be lost by shrinking of tissue sections. In addition, traditional instruments of IMS only have low magnification camera as machinery for the observation of tissue. The magnification is not enough to obtain histological information of cell level or organ functional unit. Therefore, we developed a mass microscope equipped with AP ion-source chamber and optical microscope[1]. AP ion-source chamber is efficient in IMS of volatile metabolites like taste/flavor molecule, and the high magnification lens are available for observation of cellular-level structure of the tissue sections. We applied the mass microscope for the IMS of fresh ginger rhizome, indicated several specimen including the metabolite of ginger taste, and demonstrated the organelle-level characterization (Fig. 2).



(Fig. 1) Scheme of the mass microscope

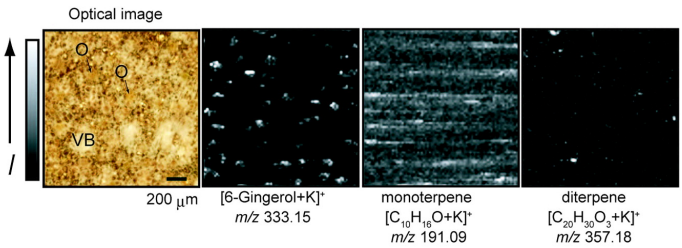
Matrix for high spatial resolution IMS

Matrix is very important and useful material for MALDI-IMS of biomolecules in tissue section. The characters of these co-crystals affect the spatial resolution and the signal intensity. The formation of bigger crystal alters the microscopic distribution of biomolecules by the molecular intermixture between adjacent sites in the co-crystallization process. The ununiformities of crystal lead to instability in mass spectra between measurements. To solve these problems, the matrix sublimation method was developed[2]. We developed automatic and stable sublimation instrument equipped with measurement of thickness of coated matrix based on that method. The crystal of sublimation coated matrix is nano-level size. Currently, we are analyzing single cell with this instrument.

Reference

1. Harada T et al., Visualization of volatile substances in different organelles with an atmospheric-pressure Mass Microscope. **Anal Chem.**, 81(21), 9153-7, 2009

2. Hankin JA et al., Sublimation as a method of matrix application for mass spectrometric imaging. **J Am Soc Mass Spectrom.**, 18(9): 1646-52, 2007



(Fig. 2) Spatial distribution of 6-gingeol ($[M+K]^+$, m/z 333.15) (Reprinted and modified from Ref.1)

A novel technology developed by studies of Biophysics

Imaging Mass Microscope "iMScope *TRIO*".

Shimadzu corporation

Imaging Mass Microscope "iMScope TRIO", visualizing the distribution of bio molecules in organ, is the new instrument for MALDI imaging MS (IMS) with high special resolution than ever.

We have developed a mass microscope equipped with an atmospheric pressure ion-source chamber for Matrix assisted laser desorption /ionization (AP- MALDI) and a quadrupole ion trap time-of-flight (QIT-TOF) analyzer. The optical microscope combined with the mass spectrometer permitted us to precisely determine the relevant tissue region prior to performing imaging mass spectrometry (IMS). An ultraviolet laser tightly focused with a triplet lens was used to achieve high spatial resolution (Max:5um). An atmospheric pressure ion-source chamber enables us to analyze fresh samples with minimal loss of intrinsic water or volatile compounds.

iMlayer is also our newly developed instrument. It is for sample preparation. This matrix vapor deposition system is well controlled Matrix thickness and makes finer and more reproducible matrix layer. The result of mass analysis with finer crystallized matrix shows sharper images than spraying of tissue sections.

We performed simulation of spatial resolution required to visualize the pigment layer of retina.The imaging mass analysis was used iMScope TRIO to pigment layer of rat's retina. Only 10um or less laser diameter can be distinguished the three layered of phosphatidylcolines(PC) near pigment layer of retina. And Matrix deposition system also contributed for high special resolution imaging. Used for observing the distribution of drugs in micro areas or localized accumulations of metabolites.

iMScope TRIO is useful tool to determine the drug, its metabolites and candidate biomarker molecules with high special resolution. Also iMScope data acquisition and statistical analysis of dedicated software are effective to discover biomarker.