An overview of Surface-Assisted Laser Desorption/Ionization mass spectrometry and its application to the biological research area

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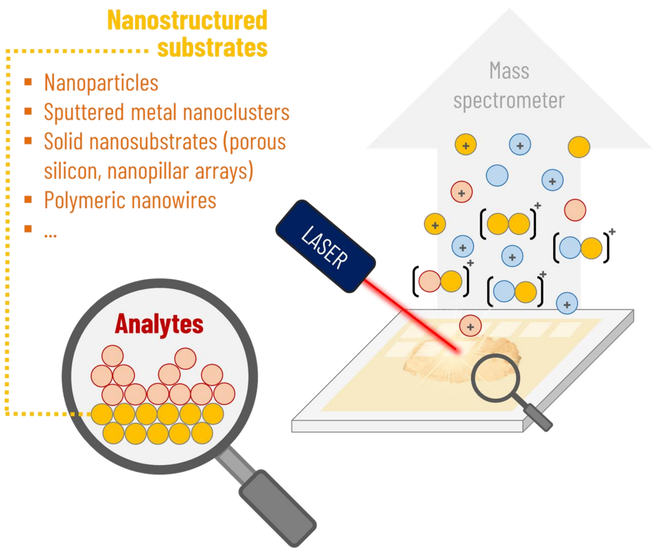
What is SALDI MS?

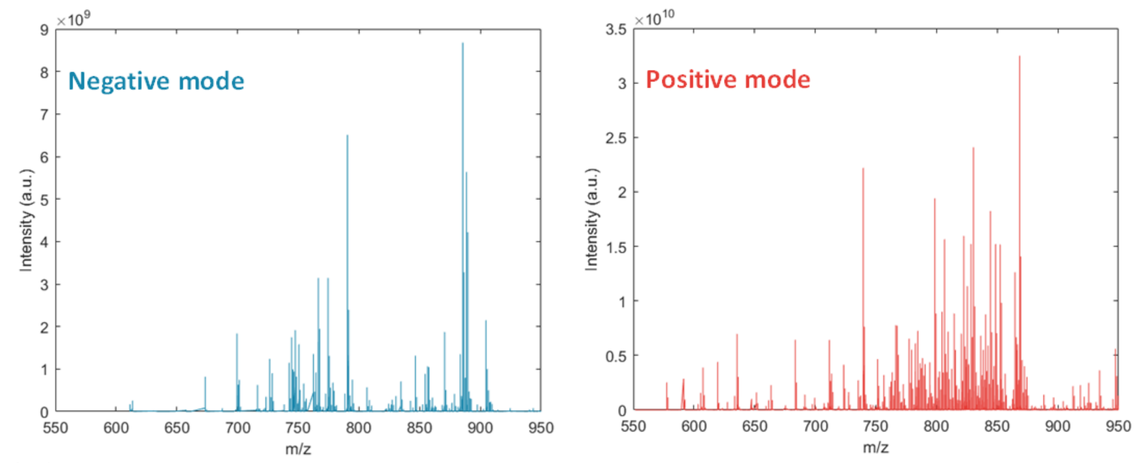
Surface-assisted laser desorption/ionization (SALDI) mass spectrometry (MS)

- SALDI = laser desorption technique, which employs **nanostructured substrates** instead of organic matrices (>< MALDI) to promote the analyte desorption and ionization.
- Nanosubstrates can be of **various morphology** and **chemical nature** (*e.g.* metal, metal oxide, silicon, graphite, polymer)
- The nanosubstrates play a key role in SALDI MS by **absorbing the laser energy**, promoting the analyte **desorption** (mainly through a **thermal** process) and providing a source of **ionization.**



Dual-polarity imaging of lipids

- **Highlighted SALDI capability**: **Dual-polarity** capability of gold nanoparticles (AuNPs).
- **Addressed scientific issue**: Some lipids are **preferentially detected** in the **positive** ionization mode, and others in the **negative** one. Thus, their MS analysis may be challenging.
- **Results**: We present a **SALDI MS imaging dual-polarity** approach to image the **lipids detected in both polarities** from the **same tissue section.** We show the **complementarity** of the dual-polarity data, regarding the **lipid coverage** and the **spatial distributions** of the detected lipids.

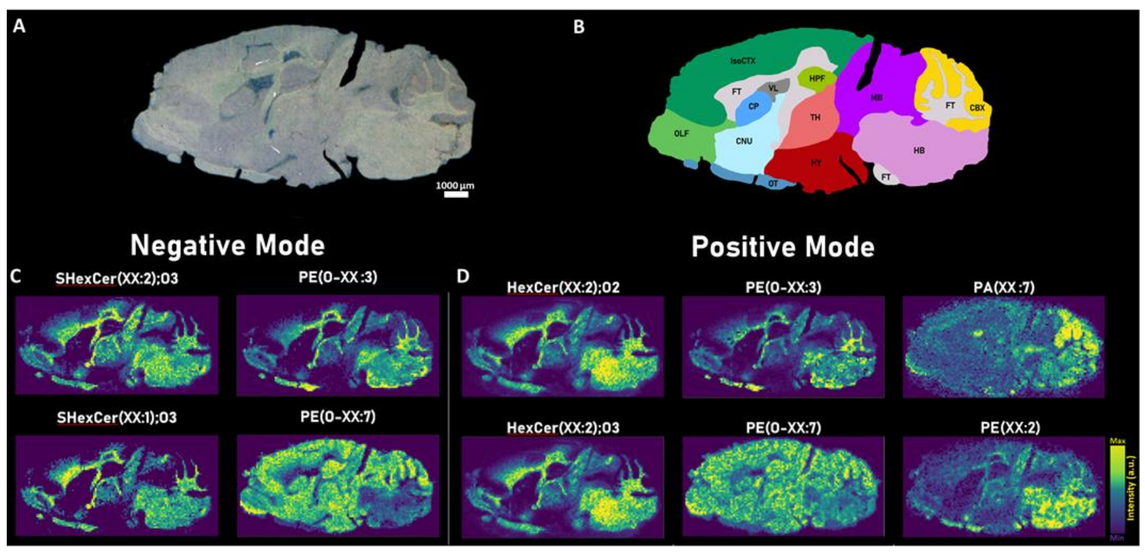


Filtered mean mass spectra acquired in the negative and positive ionization modes, resulting from the imaging of an entire mouse brain section by SALDI MSI, using AuNPs as nanosubstrates.

Lipids detected in the different ionization modes:

NEGATIVE: 27% | **BOTH**: 18% | **POSITIVE**: 55%

Proportion of the lipids detected in the negative, positive and both ionization modes. This illustrates the complementarity of the dual-polarity approach.



(A) Optical image of the AuNPs-covered mouse brain section. (B) Schematic annotation of the mouse brain anatomical regions, based on the Allen Mouse Brain Atlas (https://mouse.brain-map.org/). (C) Ion images of lipid families in the negative ionization mode. (D) Ion images of lipid families in the positive ionization mode.

Some advantages of SALDI MS

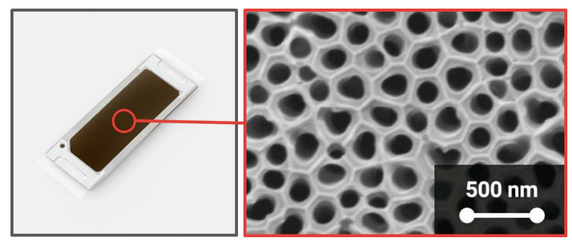
- **Limited chemical background** in the **low *m/z* range**:
  - ⇨ Particularly effective for the analysis of **small molecules** (< 900 Da)**.**
- The nanosubstrates **do not have to co-crystallize** with the analytes (as opposed to a MALDI matrix):
  - ⇨ Easier **sample preparation**;
  - ⇨ Access to **high lateral resolution** imaging (with appropriate sample preparation);
  - ⇨ Increased signal **reproducibility**.
- Most nanosubstrates can be used in **both ionization modes** (dual-polarity capabilities);
- The surface of the nanosubstrate can be **functionalized with ligands** to improve the sensitivity and selectivity of the analysis.

New blotting sample preparation

- **Highlighted SALDI capability**: **Blotting/imprinting** sample preparation using a solid nanostructured substrate.
- **Addressed scientific issue**: Agar-based microbial cultures require **laborious and time-consuming preparation** prior to **MALDI** MS analysis, For example, the MALDI sample preparation may require desiccation, potentially causing **sample deformation** and/or **degradation**. Other issues may be associated with the use and application of the matrix.
- **Results**: We present a **rapid and easy sample preparation** using a **DIUTHAME membrane** with a **blotting method** to image the metabolites in agar-based bacterial co-cultures.

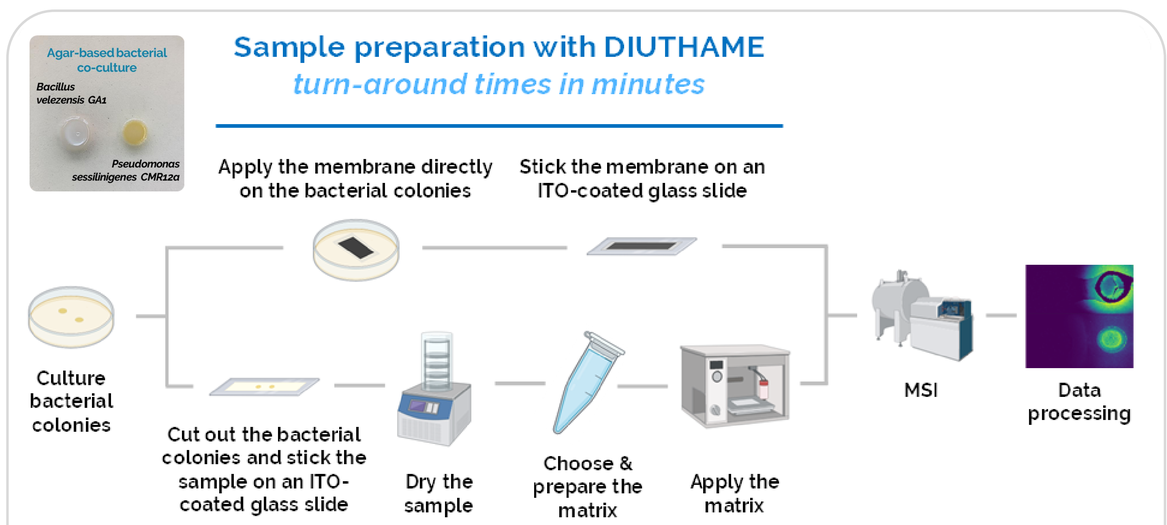
Desorption/Ionization Using Through-Hole Alumina Membrane, *Hamamatsu Photonics K.K.*

- **DIUTHAME:** Porous alumina (Al_2O_3) membrane coated with a 10-nm thick layer of platinum
- The DIUTHAME membrane is used (1) for the **transfer** of the metabolites from the sample to the membrane, and (2) as **assisting material** in SALDI MS imaging.

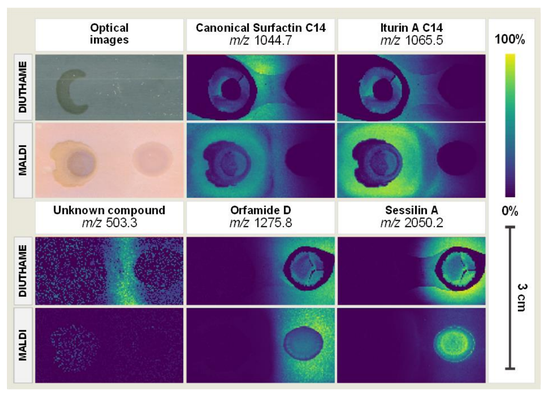


Courtesy of Hamamatsu Photonics K.K.

Methods



Results



Optical images of the bacterial co-culture and ion images of lipopeptides acquired by MALDI MSI and SALDI MSI with DIUTHAME, in the positive ion mode, delimiting 3 main regions of interest: (1) the Bacillus area (left), (2) the Pseudomonas area (right) and (3) an area at the interface between the two bacterial colonies.

PROS

- ☑ *Rapid & easy sample preparation*
- ☑ *Suitable for the analysis of small molecules with limited interference*
- ☑ *Effective in both ionization modes*
- ☑ *Potential preferential blotting ⇨ selectivity*

CONS

- ☒ *Imprinting failure ⇨ biased ion images*
- ☒ *Low signal intensity*
- ☒ *Membrane damage (tear)*
- ☒ *Potential preferential blotting ⇨ selectivity issues*

Conclusion & Perspectives

- **SALDI mass spectrometry** is particularly adapted for the analysis of **small molecules**.
- Due to the **unique capabilities** offered by the **nanosubstrates**, **novel** analytical **strategies** (for **sample preparation** and **data acquisition**) can be developed in SALDI MS (imaging).
- These **new analytical strategies** offer great prospects for studying **small molecules** in **complex biological samples,** such as lipids in mouse brain tissue sections or metabolites in agar-based bacterial cultures**.**

References

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