

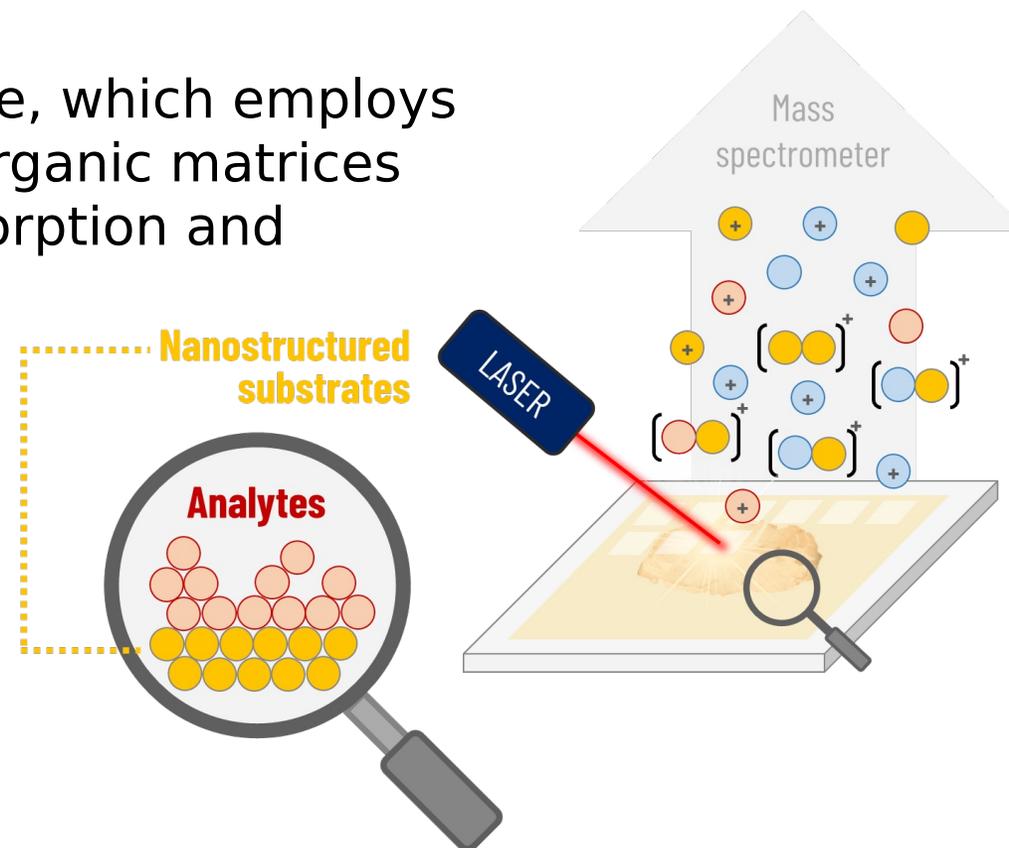
Introduction to SALDI MSI

Wendy H. Müller

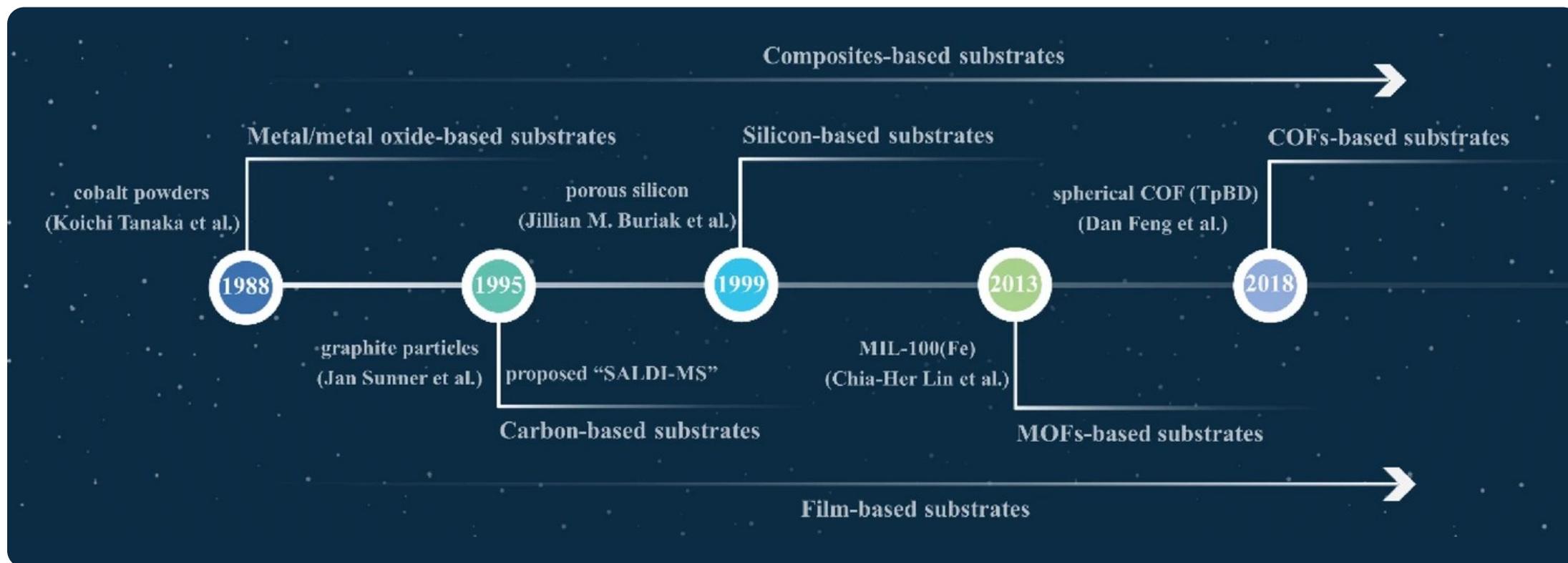
EU FT-ICR MS Network Short Courses (November 2022, Liège)

Introduction to SALDI MS

- **Surface-assisted laser desorption/ionization (SALDI)**
- **Laser desorption/ionization** technique, which employs **nanostructured surfaces** instead of organic matrices (>< MALDI) to promote the analyte desorption and ionization.
- Also known as:
 - DIOS (desorption/ionization on silicon),
 - DIUTHAME (desorption/ionization using through-hole alumina membrane),
 - NALDI (nano-assisted LDI),
 - NAPA-LDI (nanopost array LDI)
 - NIMS (nanostructure-initiator MS)
 - ...

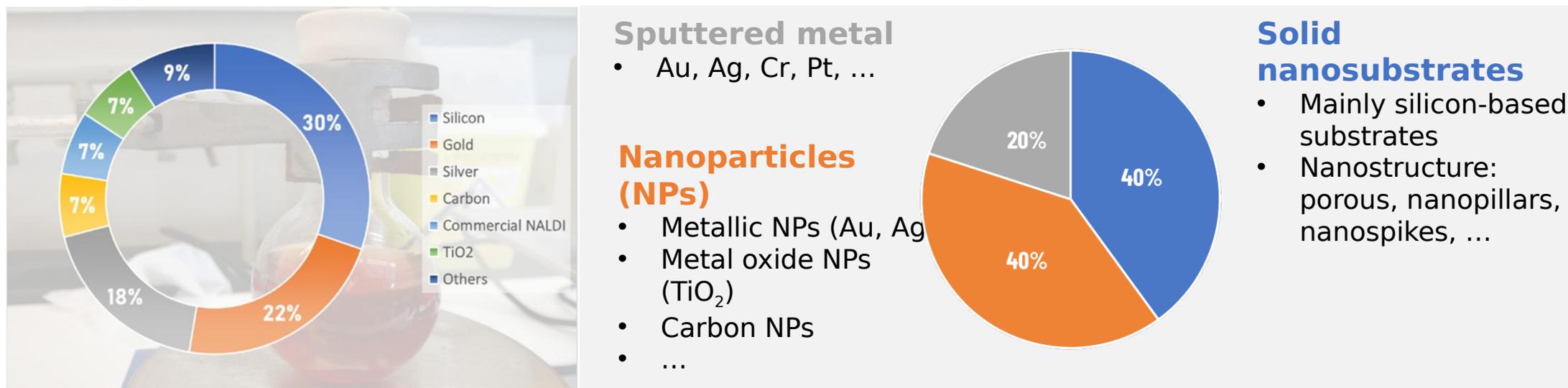


A brief history of SALDI MS



“SALDI” nanosubstrates

- Nanosubstrates can be of **various chemical nature** and **morphology**.



- The nanosubstrates play a key role in SALDI MS by **absorbing the laser energy**, promoting the analyte **desorption** and providing a source of **ionization**.

Fundamentals of SALDI

Desorption

- Mainly a laser-induced **thermal process**:
Rapid and highly localized (confined) heating of the nanosubstrate surface
- Other **non-thermal phenomena**:
Surface restructuring or destruction

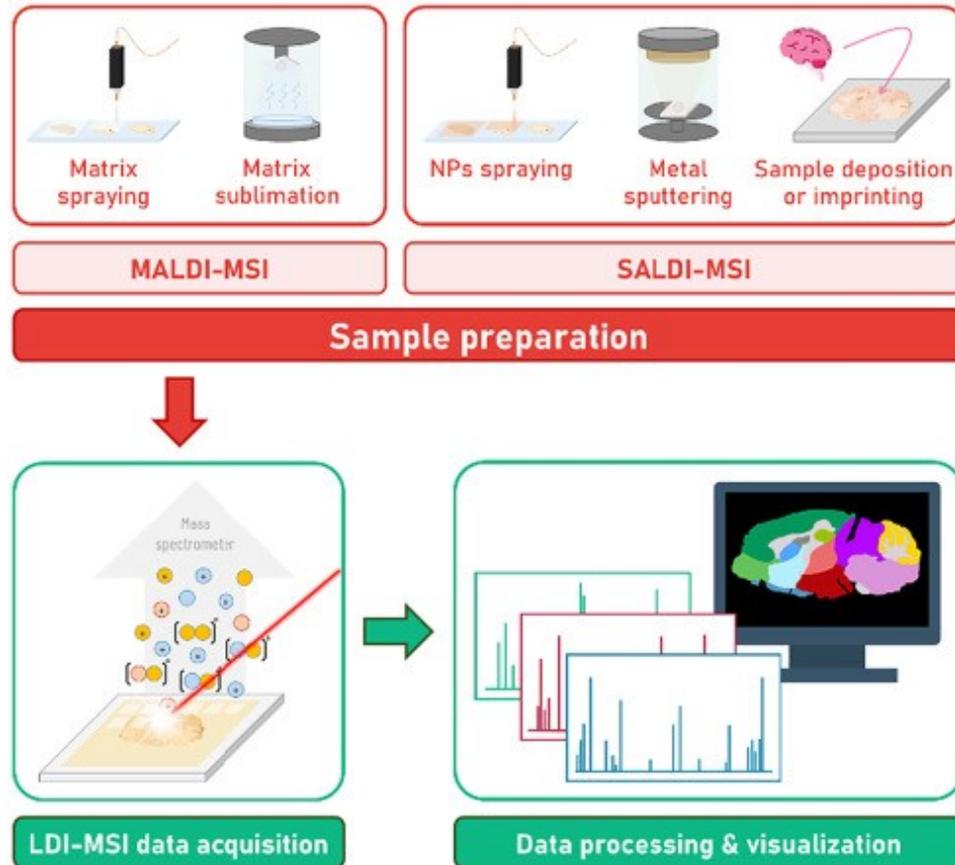
Ionization

- Mainly a **non-thermal process** promoted by various phenomena:
 - Charge transfers
 - Photo-ionization reactions
 - Surface melting/destruction
 - Presence of pre-existing ions in the sample
 - Emission of hot electrons by plasmonic materials
 - ...

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.

Analytical strategies for SALDI MSI

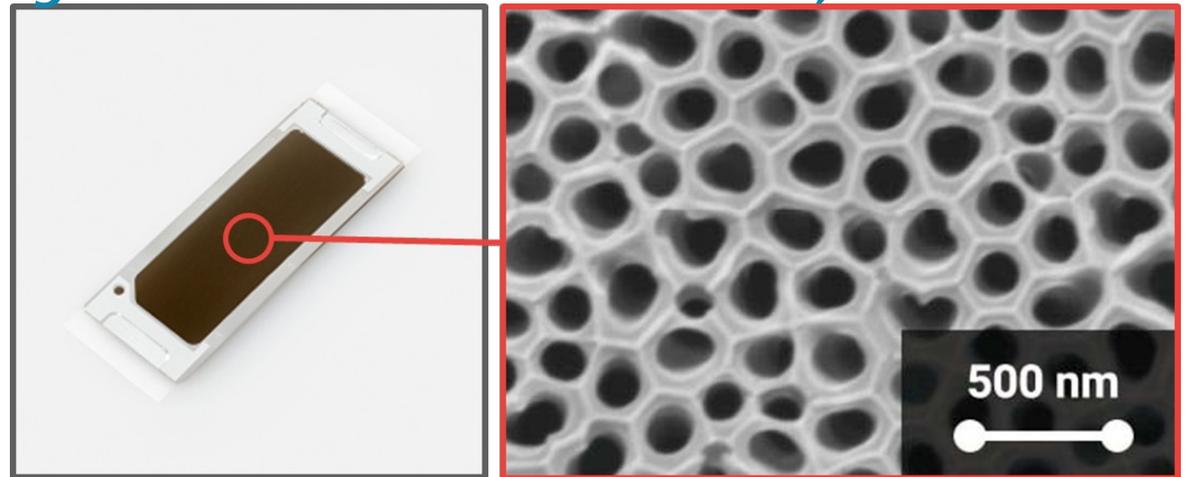


- The **main differences** in the MALDI vs. SALDI analytical procedures lie in the **application/use of the nanosubstrate**.
- The nanosubstrates offer **new analytical strategies**:
 - New **substrate application/use** for **sample preparation**: sputtering, deposition, imprinting/blotting
 - **Functionalization** of the sample surface
 - Acquisition of **dual-polarity** images
 - ...

Some applications of SALDI FT-ICR MSI in the MSLab

Imprinting sample preparation for agar-based samples

- **Addressed scientific issue:** Agar-based microbial cultures require **laborious and time-consuming preparation** prior to **MALDI** MS analysis,
- **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.

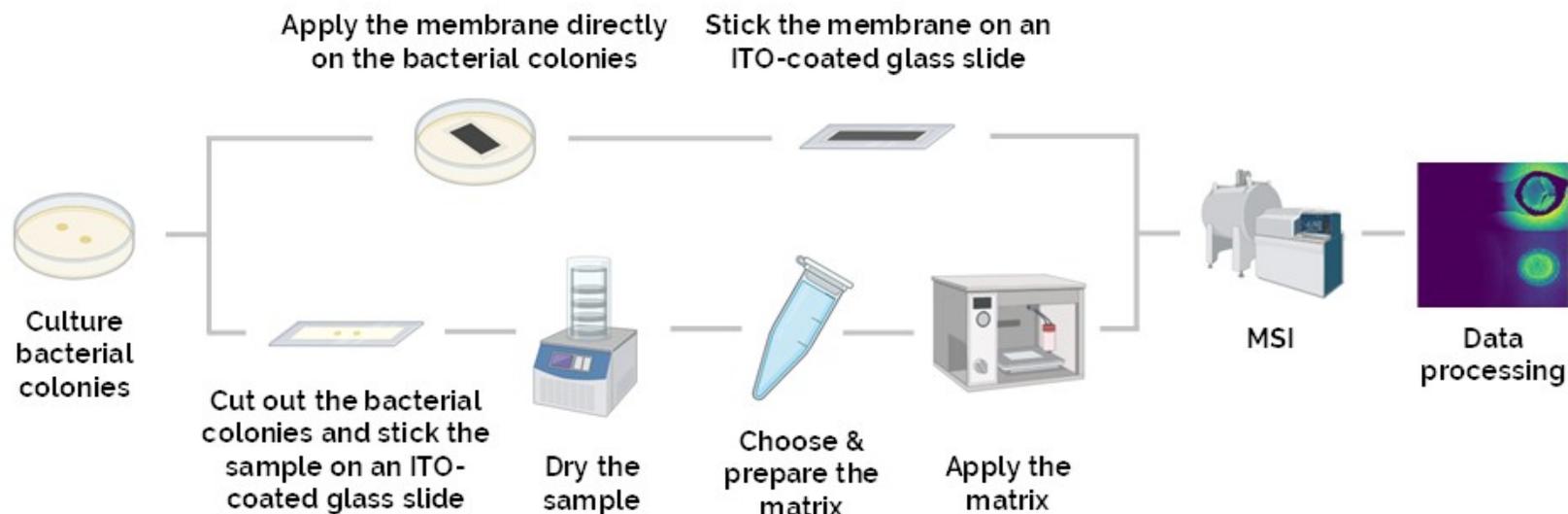
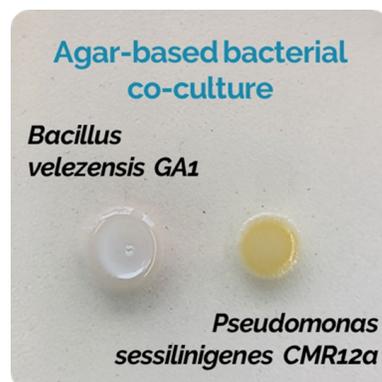


Some applications of SALDI FT-ICR MSI in the MSLab

Imprinting sample preparation for agar-based samples

Methods.

Sample preparation with DIUTHAME *turn-around times in minutes*

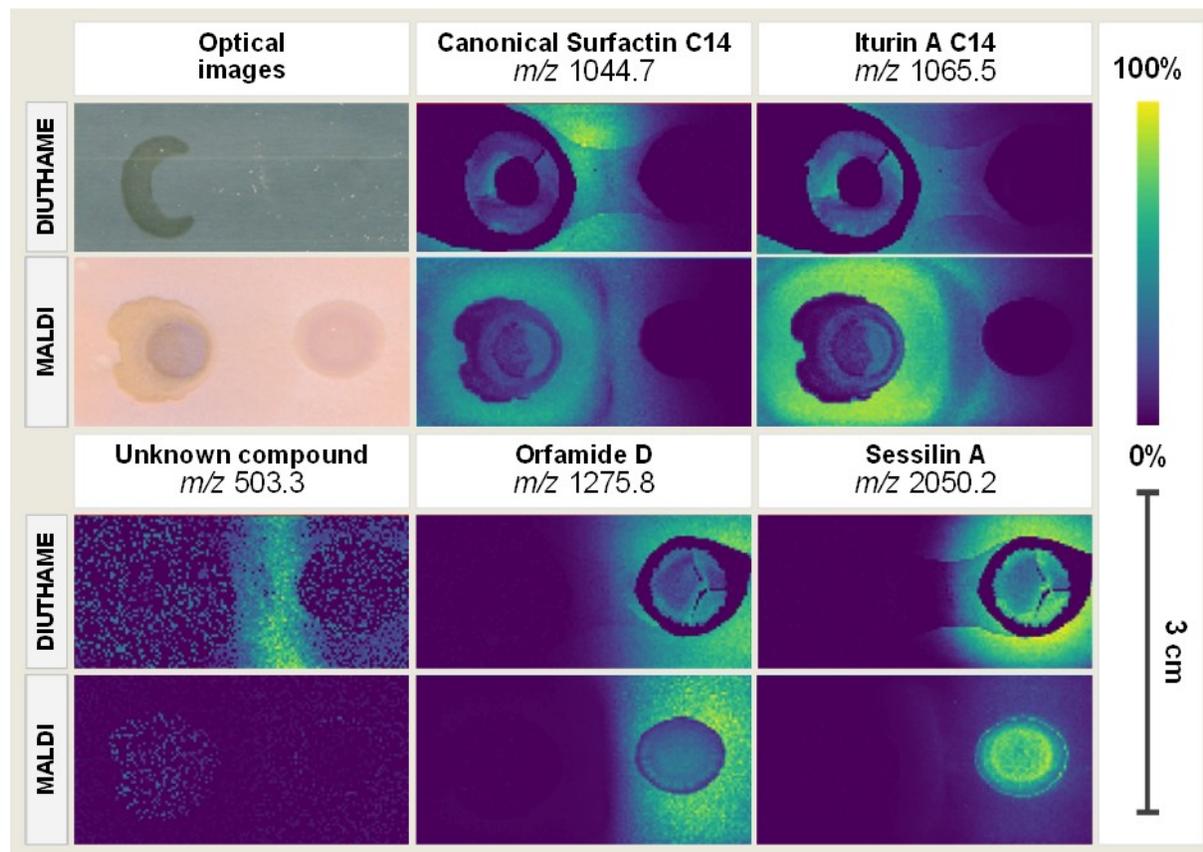


Sample preparation for MALDI *turn-around times in hours*

Some applications of SALDI FT-ICR MSI in the MSLab

Imprinting sample preparation for agar-based samples

Results



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

PROS

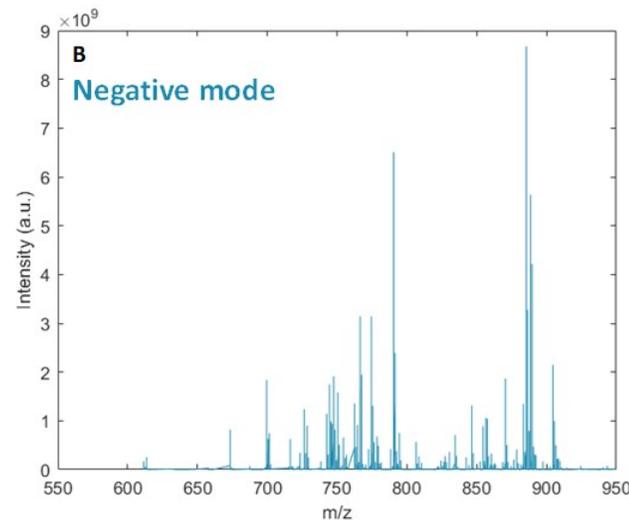
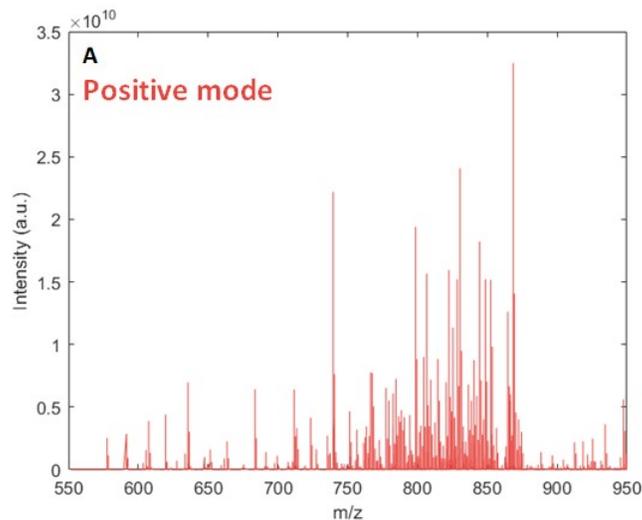
- ✗ *Imprinting failure* ☐ *biased ion images*
- ✗ *Low signal intensity*
- ✗ *Membrane damage (tear)*
- ✗ *Potential preferential blotting* ☐ *selectivity issues*

CONS

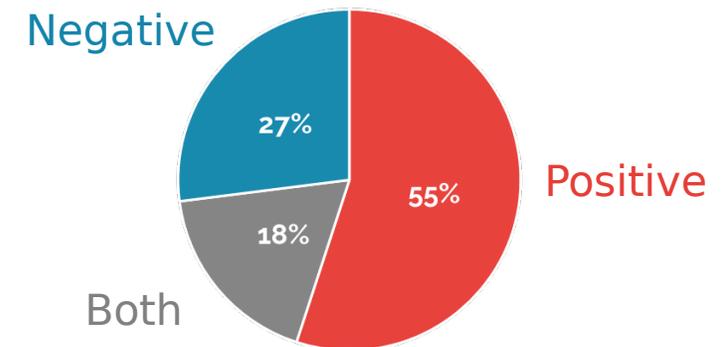
Some applications of SALDI FT-ICR MSI in the MSLab

Dual polarity imaging of lipids with 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.

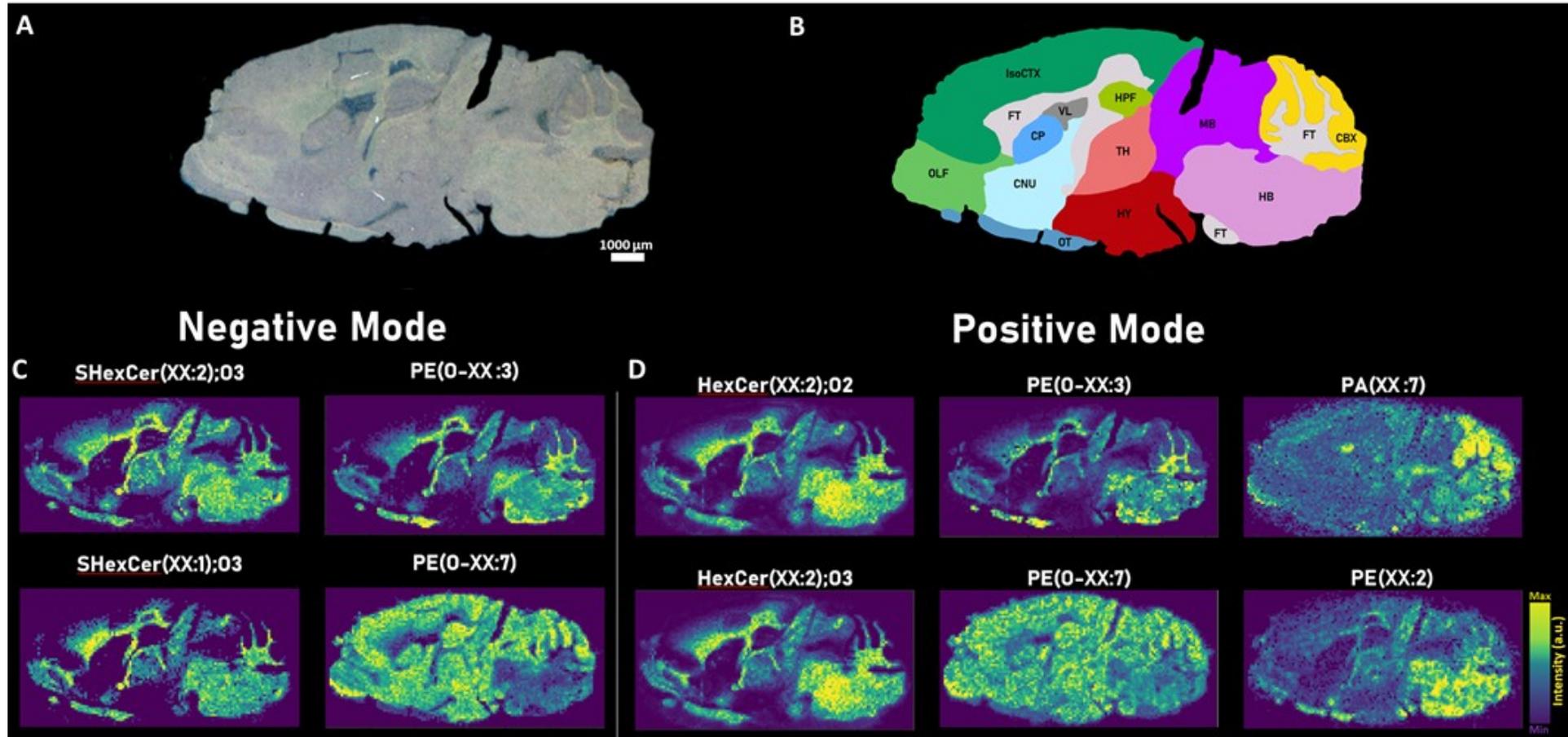


Lipids detected in the different ionization modes:



Some applications of SALDI FT-ICR MSI in the MSLab

Dual polarity imaging of lipids in mouse brain



Interested in SALDI MSI?

REVIEWS

- Müller, W.H., Verdin, A., De Pauw, E., Malherbe, C. & Eppe, G. (2022). Surface-Assisted Laser Desorption/Ionization Mass Spectrometry Imaging: A Review. *Mass Spectrometry Reviews*, 41 (3), 373-420
- Müller, W.H., (2022) Optimization of Surface-Assisted Laser Desorption/Ionization Mass Spectrometry – The quest for the Holy Grail from the study of thermometer ions. *Bulletin de la Société Royale des Sciences de Liège*, 91(1), 105-127
- Müller, W.H., De Pauw, E., Far, J., Malherbe, C. & Eppe, G. (2021). Imaging lipids in biological samples with surface-assisted laser desorption/ionization mass spectrometry: A concise review of the last decade. *Progress in Lipid Research*, 83, 101114

ARTICLES

- Müller, W.H., McCann, A., Argüelles Arias, A., Malherbe, C., Quinton, L., De Pauw, E. & Eppe, G. (2022) Imaging Metabolites in Agar-Based Bacterial Co-Cultures with Minimal Sample Preparation using a DIUTHAME Membrane in Surface-Assisted Laser Desorption/Ionization Mass Spectrometry. *ChemistrySelect*, e202200734
- Müller, W.H., Verdin, A., Kune, C., Far, J., De Pauw, E., Malherbe, C., Eppe, G. (2021). Dual-polarity SALDI FT-ICR MS imaging and Kendrick mass defect data filtering for lipid analysis. *Analytical and Bioanalytical Chemistry*, 413(10), 2821-2830.