Lipidomics is a subset of metabolomics which focuses on the characterization, identification and quantification of lipidic compounds in a living organism, relying mainly on mass spectrometry (MS). In recent years, advances in the field have led to the development of techniques enabling researchers to recover detailed lipidic compositions of samples, while also preserving spatial information. These techniques are categorized as Mass-Spectrometry Imaging (MSI). In a typical MSI assay, a sample is covered by a MALDI matrix (Matrix-Assisted Laser Desorption/Ionization). This matrix, when hit with a laser, rapidly heats up and transfers energy to the sample, ionizing and vaporizing it. The resulting ions are then funneled to an analyzer, usually a Time-Of-Flight (TOF) mass spectrometer, which produces a spectrum based on the mass/charge ratio of the ions.

The ions are identified by comparing the obtained spectrum to a library of reference spectra. Using this setup, experimentalists routinely attain a resolution of 40µm, while the most advanced equipment can be precise under 1µm (Chan *et al*, 2017), enabling single-cell lipidomics. With MSI, it is possible to detect heterogeneity in samples, but it suffers from lower sensitivity than other MS methods. To mitigate this drawback, researchers have developed assays combining MSI with more sensitive techniques, such as tandem MS. In these assays, two neighbouring pixels are analysed separately, one with MSI, the other with high resolution shotgun mass spectrometry. The data obtained this way offers lower resolution size (roughly 40µm), but provides a highly accurate and spatially constrained composition of the sample. Analysis time is longer, and it cannot be used with highly heterogeneous samples, but brings sensitivity to the single-molecule level.

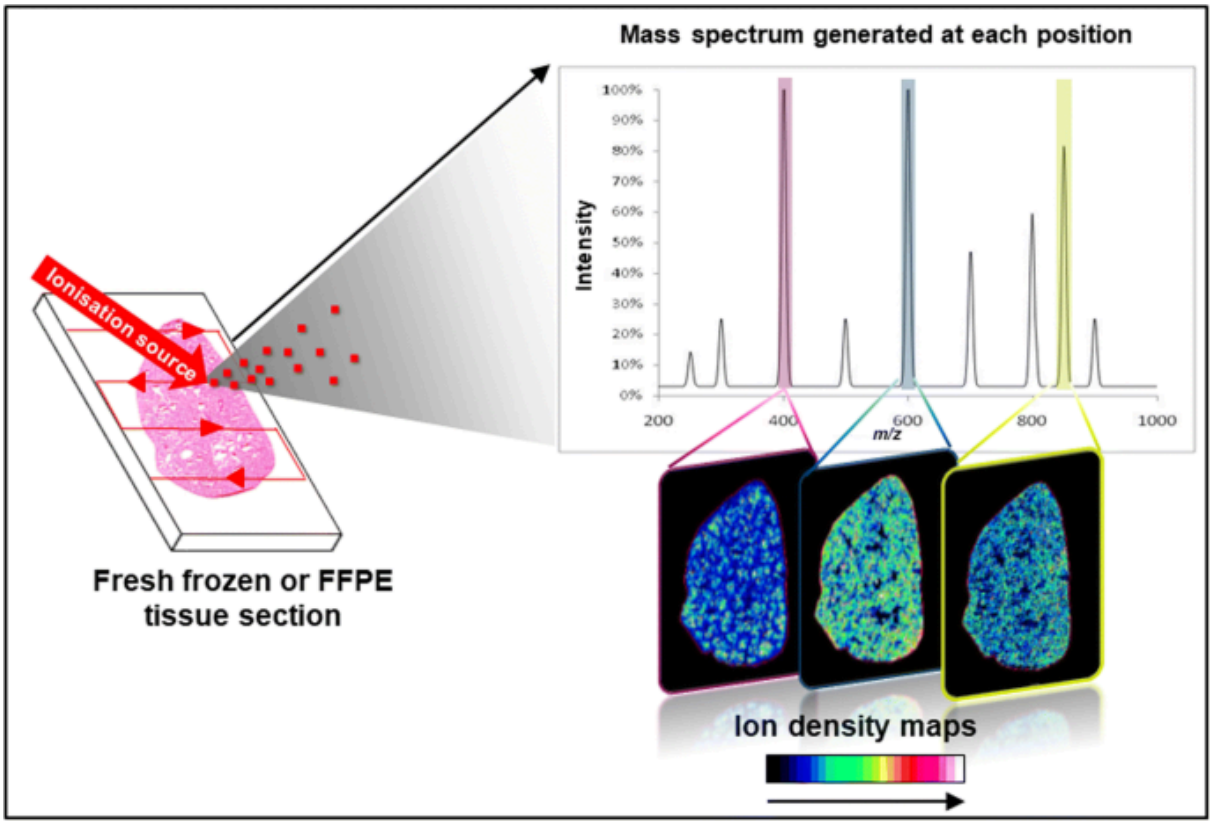


Figure 1: Principle behind Mass-Spectrometry Imaging. The sample is covered by a matrix, which ionizes its constituent when hit by a laser. The ions are then identified through mass spectrometry. As the laser hits one spot at a time, an image representing ion density can be constructed from the data.

Chan, Y. H. et al. (2024). Gel-assisted mass spectrometry imaging enables sub-micrometer spatial lipidomics. Nature Communications, 15(1), 5036.
Ellis, S. R. et al. (2018). Automated, parallel mass spectrometry imaging and structural identification of lipids. Nature Methods, 15(7), 515-518.
Porta Siegel, T. et al. (2018). Mass spectrometry imaging and integration with other imaging modalities for greater molecular understanding of biological tissues. Molecular Imaging and Biology, 20, 888-901.