

Matrix-assisted laser desorption/Ionization Time of Flight Mass Spectrometry (MALDI-TOFMS)

Matrix-assisted laser desorption/ionization (MALDI) time of flight (ToF) mass spectrometry is a powerful analytical tool used for the detection, identification, and structural characterization of macromolecules (peptides/proteins, DNA, sugars, and other metabolites & biomarkers, pharmaceutical drugs, clusters, and synthetic polymer mixtures) in the molecular mass range 500 Da to 500 KDa .

What is MALDI?

MALDI is a soft ionization technique used to generate intact large biological molecules in the gas phase without fragmentation. In MALDI fragile biological molecules (analyte) are mixed with UV/IR absorbing weak organic acids (matrix) in the molar ratios $\approx 1:1000$ in water/acetonitrile or ethanol solvents. The resultant analyte + matrix mixture is placed over a solid substrate (Stainless Steel/Gold) and allowed to dry in an airy ambience. The air-dried crystals (analyte+matrix) are then irradiated with a short/ultrashort (ns/ps/fs) pulsed UV/IR laser beam in a vacuum. The absorption of laser photons by matrix either by single or multiphoton absorption processes drives rapid heating and sublimation of sample which results in the formation of protonated/deprotonated intact analyte $[M\pm H]^\pm$ in the expanding matrix plume. The intact macromolecular ions thus generated by MALDI processes can be coupled to a time of flight (ToF) mass analyzer, which has an unlimited mass range.

What is TOF MS?

Charged ions of various sizes generated by lasers or other energetic ions are accelerated to high kinetic energy (keV) by the application of an electric field in the ion source region of the mass spectrometer. The high-velocity ions are then extracted and allowed to travel in the electric field-free drift space where they are mass separated according to their m/z value. The mass separated ions are then detected by an ion detector usually a microchannel plate (MCP) detector. The MCP generated signal is amplified by a preamplifier and acquired through a digital oscilloscope and transferred to a PC for signal processing and calibration.

Applications of MALDI Mass Spectrometry

MALDI mass spectrometry finds application in various fields viz., biology, biochemistry & biophysics, clinical microbiology, medicine, proteomics & genomic research, amino acid sequencing, peptide mass fingerprinting, generation of molecular clusters, biomarker (small molecule) detection for early identification of disease, identification of pathogenic bacteria, yeasts, fungi, etc. as well as in several other areas of science & technology where the mass characterization of the sample is critical for structural elucidation to determine their structure-function relationship. In recent times, MALDI-TOFMS have also been employed for SARS-CoV2 (COVID-19) diagnosis in human saliva due to its high-sensitivity and high-specificity species identification through proteomic profiling.