Matrix Assisted Laser Desorption Ionization (MALDI)

1. Either sample (A) is mixed with excess matrix (M) and dried on a MALDI plate or solutions of M and A are placed on the plate sequentially.
2. Laser flash ionizes matrix molecules.
3. Sample molecules are ionized by proton transfer from matrix: $\text{MH}^+ + \text{A} \rightarrow \text{M} + \text{AH}^+.$

Common MALDI matrices

MALDI Targets

2,5-dihydroxy benzoic acid crystallized on stainless steel target

2,5-dihydroxy benzoic acid crystallized on AnchorChip target

During solvent evaporation, sample shrinks onto the hydrophilic anchors (200-800 µm) in hydrophobic surroundings. Enhance sensitivity by a factor of 10-100.

Time of Flight (TOF)

\[
t = \frac{2zU}{L^2}m
\]

If $U = 20 \text{ KV}, L=1.8m, m = 1000 \text{ Da}, ze = 1$

\[
t = \frac{1.8m}{\sqrt{2 \times 20000V}} \times \frac{1000 \text{ Da} \times 1.660539 \times 10^{-24} \text{ kg Da}^{-1}}{1.602 \times 10^{-19} \text{ C}}
\]

\[
t = 2.9 \times 10^{-4}
\]

Instrument Schematics and tuning

Post Source Decay (PSD)

In Source Decay (ISD)

<table>
<thead>
<tr>
<th>Fragmentation location</th>
<th>Post source decay (PSD)</th>
<th>In source decay (ISD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>After source</td>
<td>yes</td>
<td>No</td>
</tr>
<tr>
<td>Precursor ion selection</td>
<td>&lt;4 KDa</td>
<td>1-100 KDa</td>
</tr>
</tbody>
</table>

Precursor Ion Selector (PCIS)

Electrostatic field perpendicular to the ion flight path deflects ions.

5-10 Da window

In FAST (Fragmentation Analysis and Structural TOF) method reflector voltage is reduced stepwise to guide fragments to the reflector detector.

Tandem MS

Linear or reflectron analyzer

Pulsed Ion Extraction (PIE) delay

Two Stage Ion Reflector

Ions with same m/z but higher kinetic energy penetrate deeper into reflector electrostatic field, delaying their arrival time at the reflector detector, which results in improved resolution.

Focus in time and space about 30% of difference in kinetic energy. Two stages minimize chemical noise.

Fragments and combined PSD spectra of Angiotensin II peptide