Bioimaging by Massive Cluster Impact (MCI)

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Abstract

We have adapted a massive cluster impact (MCI) glycerol electrospray source to a TRIFT 1 microscope-imaging time-of-flight mass spectrometer to explore bioimaging applications. The source generates highly-charged massive glycerol clusters: the distribution is very broad and the most probable clusters have masses of several million Da and ~ 100 - 150 charges. Acceleration through 13 kV gives impact kinetic energies ~1 - 2 MeV and target material is ejected following a shock-heating event. MCI generates intact biomolecular ions from neat (dried) samples of lipids, peptides and small proteins (up to lysozyme so far). The electrosprayed cluster beam cannot readily be focused (for microbeam imaging) or pulsed and so is operated continuously. Imaging is achieved using the stigmatic microscope imaging properties of the TRIFT 1; for time-of-flight operation the secondary ion beam is pulsed using blanker plates downstream from the sample. At the detector either a mass spectrum can be registered, or the beam can be chopped using a second set of blanker plates and a magnified mass-selected image can be registered. Image resolution of ~ 3 μm has been measured for grid-defined images of bradykinin and insulin molecular ions. In practice, for any imaging approach useable image resolution is limited by useful ion yields (intact molecular ions detected per molecule sputtered) that determine the number of ion counts achievable in a given pixel size from a given analyte concentration. Useful ion yields ~ 1 – 3 x 10^{-5} have been measured for MCI under imaging conditions for bradykinin and phosphatidylcholine. These values appear to be ~ 100 times greater than values estimated for Ar_{1000} clusters and would allow detection of ~ milllimolar concentrations of bradykinin in a 3 x 3 x 3 μm^3 voxel or ~ 10% lipid components in a 3 x 3 μm^2 pixel of a bilayer at 10 counts/pixel or voxel (signal/noise ~ 3). We are exploring lipid differences in cancer cell lines with the ultimate objective of adding biochemical image information at a sub-cellular level to cancer biopsy slides.