

Seminar

Exploring biomolecular complexes through the lens of native mass spectrometry

Debasmita Ghosh

Weizmann Institute of Science, Israel

Covalent and non-covalent interactions of biomolecules play a crucial role in defining their structure–function relationships. "Native" electrospray ionisation mass spectrometry (ESI-MS) aims to transfer these bonds from solution to the gas phase under gentle conditions, preserving their integrity. My research centres on understanding the complexes of nucleic acids, proteins and finally protein-protein complexes by native ion mobility-mass spectrometry (IM-MS).

Nucleic acid structures (G-quadruplex and single strands) were studied by native charging and supercharging. To assess ion structure preservation and conformational changes under supercharging, we utilised IM-MS. It separates ions based on electrophoretic mobility in helium, revealing their gas-phase compactness and conformational changes induced by supercharging conditions. Our results from IM-MS experiments matched with calculated structures and solution-phase UV-melting experiments. Some conditions led to native supercharging, shedding light on the ESI mechanism for oligonucleotides (in negative ion mode). Metal-bound proteins serve as precursors to fluorescent protein-protected noble metal clusters. Structural understanding of these clusters has been a challenge, despite their promising biomedical applications. I probed conformational changes of proteins due to noble metal ion binding by MS. My work combined IM-MS with Hydrogen/Deuterium exchange (HDX) MS and MALDI-MS to characterise these. The insights derived from spectroscopic measurements and simulations strongly support the MS findings. Furthermore, hierarchical self-assembled structures incorporating luminescent clusters was designed, which exhibits unique biophysical properties. In my current role, I look at direct exploration of protein-protein interactions within cell lysates through native MS approaches (direct-MS), with a particular focus on human cells. This approach has broad applications, including analytical understanding of protein-protein interactions, drug binding, and characterising therapeutic proteins.

Thursday, Nov 23rd 2023

4:00 PM (Tea / Coffee 3.45 PM)

Auditorium, TIFR-H