

Advances in Ultrahigh Resolution Mass Spectrometry Enable Exploration of Complex Biological Systems

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Abstract

Fourier transform ion cyclotron resonance (FTICR) mass spectrometry (MS) offers the highest mass resolving power and mass accuracy of any mass analyzer. Since all key measures of performance improve with increased magnetic field strength, a recently deployed 21T FTICR spectrometer offers unique capability to address the key knowledge gaps in functional understanding of complex microbiomes. For instance, global analyses of soil organic matter combined with omics workflows, provide information on identity and quantity of intact biomolecules (metabolites, proteins) derived from plants and microbes needed to uncover soil-microbe-plant-atmosphere relationships and interdependencies. Spatial heterogeneity and relationships can be tackled using ambient MS imaging techniques, which minimize perturbation to the tissue by limiting sample preparation and performing the analysis *in situ*. For instance, direct ionization by laser ablation electrospray ionization (LAESI) coupled with the 21T FTICR provided simultaneous spatial distributions for hundreds of biomolecules (metabolites, lipids, peptides, xenobiotics) in biological tissues, many of which could be annotated through resolved isotopic fine structure readout directly from a biological tissue. Similarly, ultrahigh resolving power is needed for characterization of intact proteoforms using top-down MS, an approach essential for physiologically relevant studies of microbes and higher eukaryotes. Advances currently in progress on the 21T FTICR platform have a potential to push the current limits of top-down MS and facilitate high-throughput comprehensive characterization of the functional proteomes. Specifically, we have demonstrated unprecedented acquisition rates and resolution for large intact proteins by coupling of the 21T FTICR, 4X frequency multiplication, ion trapping field harmonization, and spectral data processing methods.