

ANALYTICAL SEMINAR

Advancing by Simplifying: Novel Data Acquisition Strategies for Improved Top-Down and Middle-Down Mass Spectrometry

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Abstract:

The analysis of intact protein forms, or proteoforms, holds an important theoretical advantage over peptide-based approaches to proteomics. As posited by the “proteoform hypothesis”, the proteome-to-phenotype connection is better explained through the characterization of the actual molecules present in a cell or tissue, rather than by a catalogue of generically defined “protein groups”. However, the top-down approach to proteomics (i.e., the direct analysis of proteoforms) is particularly challenging as both intact and fragmentation mass spectra of proteoforms suffer from problems such as signal dilution and ion signal overlap.

One general strategy to mitigate these issues lies in spectral simplification. We will illustrate examples of the application of various strategies to reduce spectral complexity and achieve improved detection of intact proteoforms from complex mixtures and more confident assignment of protein modification sites. By leveraging the versatility of the architecture of tribrid Orbitrap instruments, these data acquisition methods combine techniques like differential ion mobility (high-field asymmetric waveform ion mobility spectrometry, FAIMS), gas-phase fractionation and ion-ion reactions (proton transfer reactions) to facilitate both targeted and untargeted proteoform characterization.



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