**NATIVE MASS SPECTROMETRY AS A STRUCTURAL BIOLOGY TOOL**

Vicki Wysocki

Department of Chemistry and Biochemistry, The Ohio State University, Columbus, OH 43210

Characterization of the overall topology and inter-subunit contacts of protein complexes, and their assembly/ disassembly and unfolding pathways, is critical because protein complexes regulate key biological processes, including processes important in understanding and controlling disease. Tools to address structural biology problems continue to improve. Native mass spectrometry (nMS) and associated technologies such as ion mobility and variable temperature electrospray ionization are becoming increasingly important components of the structural biology toolbox. When the native mass spectrometry approach is used early or mid-course in a structural characterization project, it provides answers quickly using small sample amounts and samples that are not fully purified. Integration of sample preparation/ purification with effective dissociation methods (e.g., surface-induced dissociation, SID), ion mobility, and computational approaches provide an MS workflow that is enabling in biochemical, synthetic biology, and systems biology approaches. Native MS can determine whether a complex of interest exists in a single or multiple oligomeric states, and surface induced dissociation can provide characterization of topology/intersubunit connectivity and other structural features. Examples will illustrate the coupling of SID to electron capture charge reduction and charge detection mass spectrometry for the characterization of protein and nucleoprotein complexes, including glycoproteins, adeno-associated virus capsids, and tau aggregates.

**References**

[1] Snyder, Harvey, Wysocki, V. H., Chemical Reviews, 2022, 122, 8, 7442–7487.

[2] Karch, Snyder, Harvey, Wysocki Annu. Rev. Biophys. 2022. 51, 157–79.