Ion/Ion, Ion/Neutral, and Ion/Electron Interactions for Rapid and Accurate Structural Biology

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Abstract: The combination of spray ion sources and high mass range mass spectrometers has led to the emergence in the past 15 years of native mass spectrometry. In native mass spectrometry, intact proteins and protein complexes from 5-5,000 kDa are measured under conditions that preserve the majority of tertiary and quaternary structure upon gentle lifting into the gas phase. Mass spectrometry provides speed, selectivity, and sensitivity for rapid (< s) analysis of these bio-ions, with gas-phase fragmentation reactions giving insight to the overall stability of protein domains and subdomains and information on molecular assembly. The nature of these gas-phase ions has not yet been completely characterized. If gas-phase ions are sufficiently close in structure to solution ions, the strengths of mass spectrometry make it an invaluable tool for structural biology, especially in combination with cryo-EM, due to the ability to examine selected structures in a heterogeneous ensemble of proteins by injecting only 10^{-11} to 10^{-12} moles of protein. Ion mobility measurements give information about the overall shapes and sizes of these structures and mass spectrometry reveals intact molecular weight. However, there are many possible structures that can be fit to a single ion mobility/mass spectrometry measurement. In the Webb laboratory, we use a combination of gas-phase irreversible and reversible covalent and strong electrostatic labeling strategies to reveal subtleties of gas-phase protein structure that previously have not been measurable for native-like protein ions. These measurements are used in combination with atomistic molecular mechanics to solve detailed gas-phase structures. In this talk, I will present an overview of our capabilities and recent advances from the group.