

## QCB Evenings

Wednesday, November 2 • 4:00pm • Chemistry C122

### **Toward Carbohydrate Sequencing: Mass Spectrometry and Ion Mobility-Mass Spectrometry-Based Approaches**

GABE NAGY, POHL LAB

Carbohydrate sequencing remains an unsolved task, largely because of the structural homogeneity of its monosaccharide constituents, especially as compared to other biomolecules such as peptides and nucleic acids. This structural homogeneity has greatly hindered its analyses with common analytical methods. Mass spectrometry, which measures the mass to charge ratio of an analyte, and ion mobility-mass spectrometry, which measures the shape to charge ratio of an analyte, have largely been considered as achiral techniques, that is, ones that are unable to discriminate amongst D/L enantiomers. Even more challenging is that up to 24 monosaccharide isomers, 12 D/L enantiomeric pairs, that differ only in their axial/equatorial orientation of their hydroxyl groups, in the case of the six-carbon hexose sugars, may exist in an entire analyte isomer set. This raised the question if such small structural differences in a monosaccharide isomer set would be sufficient enough to allow for complete individual discrimination. Herein is presented that through a variant of the fixed ligand kinetic method, where the dissociation rates of chiral non-covalent gas-phase complexes are measured, the complete individual discrimination of the 12 pentose isomers and 24 hexose isomers was possible through conventional mass spectrometry. Additionally, this information on suitable chiral gas-phase complexes to allow for the discrimination of monosaccharides with conventional mass spectrometry was applied to ion mobility-mass spectrometry, where the 16 aldohexose isomers were also individually discriminated based on their shapes as represented by collision-cross section values.

### **Ion Mobility-Mass Spectrometry Captures Multiple Conformational States on a Folding Landscape**

TARICK EL-BABA, Clemmer LAB

In solution, it is believed that unfolded proteins reach their native conformation through distinct folding intermediates. The alternative requires the unfolded conformations to undergo an unguided, diffusive search for the native structure, which would take an unrealistic amount of time. Theoretical models have shown that proteins likely fold by a guided conformational search through their multidimensional energy landscapes. However, the key to reconciling these two thoughts is capturing such intermediates experimentally, which remains challenging for most condensed-phase techniques. In contrast, biomolecules absent of solvent often form multiple structures, many of which have been shown to correlate well to their solution-phase counterparts. This makes studying the properties of isolated ions in the vapor phase ideal, as subpopulations are isolatable and easily characterized. In this talk, we probe the unfolding of the small protein ubiquitin by thermal denaturation in solution followed by structural interrogation of the solvent-free ions by ion mobility-mass spectrometry. We find evidence for at least eleven equilibrium folding states, three of which appear to be folding intermediates. Overall, these studies show that the solution-phase behavior of biomolecules can be preserved in the gas-phase. Our approach shows great promise in revealing the behavior of the multiple folding states that coexist in solution, which continue to elude detection by existing experimental techniques.

**All QCB Trainer Lab Personnel are invited to attend.  
Refreshments will be provided.**