Probing Biomolecular Structure via Anionic Gas Phase Microsolvation Studied by Cryogenic Infrared Action Spectroscopy

PhD Seminar

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Electrospray ionization (ESI) enables gentle transfer of biomolecules from solution to vacuum, allowing for the study of biomolecular structure under highly controlled conditions. However, inherent in the ESI process is the loss of solvent interactions, which stabilize the low-energy condensed-phase conformation. Specifically, the loss of ionic hydrogen bonds between solvent molecules and charged moieties can drive rearrangement via side chain collapse, as desolvated charged sites fold in to form intramolecular contacts that replace lost intermolecular interactions. To modulate this rearrangement process and examine the balance of inter- and intra-molecular stabilization, gas-phase microsolvation reagents can be used. Microsolvation reagents form non-covalent complexes with charge sites via hydrogen bonding, “capping” the charged site(s) to disfavor structural rearrangement in ESI mass spectrometry (ESI-MS) experiments. Diserinol isophthalamide (DIP), a novel reagent for the complexation of anionic carboxylate and phosphate moieties, was compared to commercially available reagents 1,1’-(1,2-phenylene)bis(phenylurea) (PBP) and triclocarban (TCC). Appreciable DIP complexation was demonstrated to the carboxylate moiety at the c- terminus of small model peptides as well as to phosphate groups in phosphorylated peptides, cyclic phosphates, and RNA dinucleotides in ESI-MS studies. To probe the effect of complexation on biomolecular structure in vacuum, cryogenic infrared action spectra were collected in the fingerprint region for a model deprotonated peptide, leucine enkephalin (YGGFL), with and without DIP. Significant differences in the spectra were observed upon adduction to DIP, most notably a large red-shift in the asymmetric stretch of the c-terminus carboxylate and a blue-shift of amide I bands. Preliminary electronic structure calculations predict that these shifts result from strong intramolecular hydrogen bonding between DIP and the c-terminus and a corresponding loss of hydrogen bonding with backbone amides.