

Ion Mobility-Mass Spectrometry: Challenges and Design Considerations for Future Instrumentation

David H. Russell*, Brandon T. Ruotolo, Kent J. Gillig, Holly A. Sawyer, Earle G. Stone and John McLean

Laboratory for Biological Mass Spectrometry, Texas A&M University, Department of Chemistry, College Station, Texas, United States of America

Modern biological mass spectrometry techniques provide significant advantages for rapid analysis of peptides and proteins. For example, high mass measurement accuracy can be used to determine the amino acid composition of peptides, and tandem mass spectrometry (MS/MS or MSⁿ) can be used to sequence unknown peptide and protein ions. In each of these experiments, mass spectrometry measures the mass-to-charge ratio of the analyte ions. To enhance structural information provided by mass spectrometry, a complimentary analyte separation technique, such as ion mobility (IM), can be combined with mass analysis. This report describes our recent advances in the coupling of ion mobility with mass spectrometry and directions for future instrumentation.

We have developed MALDI-IM-o-TOFMS and MALDI-IM-SID-o-TOFMS instruments for rapid analysis of peptides and proteins. The instrument designs are aimed primarily at the analytical challenges presented by proteomics and protein folding; however, the same instruments can be used to analyze a wide variety of ions, *i.e.*, industrial polymers, ionic clusters, as well as other types of biological molecules. Proteomic applications require high sensitivity, good resolution, and conformational selectivity that are lacking for current state-of-the-art instrumentation. To compliment the IM-MS protein/peptide folding studies, molecular modeling (simulated annealing) and gas-phase/solution phase H/D exchange studies are also used.

We have developed a periodic-focusing ion mobility drift cell that significantly increases sensitivity for peptide and protein analysis (sub-femtomole to femtomoles). This new drift cell design increases ion transmission efficiency by a combination of linear and non-linear electric fields within the drift cell without a concomitant loss of resolution. This instrument is readily applied to the analysis of protein digest mixtures. IM-MS peptide maps of protein digest fragments can also be screened according to their gas phase secondary structure (*i.e.*, helical peptides can be identified from a field of globular peptides). In addition, high throughput sequencing instrumentation for complex mixtures has been designed around a MALDI-IM-SID-o-TOFMS platform. In this design, proteolytically digested proteins are separated on the basis of ion mobility and then sequenced by surface induced dissociation prior to mass analysis.

This lecture will focus on the novel instrument development to address needs/challenges in the fields of proteomics and protein biophysics.
