"Targeting the untargeted: Structural mass spectrometry for the analysis of complex samples in systems, synthetic, and chemical biology"

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Abstract – One of the predominant challenges in systems-wide analyses is the broad-scale characterization of the molecular inventory in cells, tissues, and biological fluids. Advances in computational systems biology rely heavily on the experimental capacity to make omics measurements, i.e. integrated metabolomics, proteomics, lipidomics, glycomics, etc., accompanied with fast minimal sample preparation, fast measurements, high concentration dynamic range, low limits of detection, and high selectivity. This confluence of figures-of-merit place demanding challenges on analytical platforms for such analyses. Ion mobility-mass spectrometry (IM-MS) provides rapid (ms) gas-phase electrophoretic separations on the basis of molecular structure and is well suited for integration with rapid (us) mass spectrometry detection techniques. Furthermore, the timescales of this multi-dimensional separation are well suited for combination with fast condensed-phase separations such as GC, SFC, and UPLC (min) for enhanced separation selectivity as the sample complexity becomes ever more challenging. This report will describe recent advances in IM-MS omics measurement strategies in the analyses of complex biological samples of interest in systems, synthetic, and chemical biology. New advances in bioinformatics and biostatistics will also be described to approach biological queries from an unbiased and untargeted perspective and to quickly mine the data gathered to provide targeted and actionable information.

Bio – John A. McLean is Stevenson Professor of Chemistry at Vanderbilt University. Prof. McLean completed his Ph.D at George Washington University in 2001, where he made significant contributions in plasma spectrochemistry in the development of new technologies for the analysis of complex and limited radionuclide and biological samples. Subsequently, he performed postdoctoral research at Forschungszentrum Jülich in Germany and then as a postdoctoral at Texas A&M University with Prof. David H. Russell in biological mass spectrometry. Working with David Russell from 2001-2006, he constructed ion mobility-mass spectrometers capable of broad-scale analyses of complex biological samples on the basis of both molecular structure and mass. In 2006, Prof. McLean was recruited to Vanderbilt University as Assistant Professor of Chemistry through both the Department of Chemistry and the Vanderbilt Institute of Chemical Biology.

At Vanderbilt, McLean and colleagues focus on the conceptualization, design, and construction of structural mass spectrometers, specifically targeting complex samples in systems, synthetic, and chemical biology as well as nanotechnology. His group applies these strategies to forefront translational research areas in drug discovery, personalized medicine, and 'human-on-chip' synthetic biology platforms. Prof. McLean has received a number of awards, including the Agilent Thought Leader Award, Waters Center of Innovation, Excellence in Teaching Award from the student members of the American Chemical Society, a Defense Threat Reduction Agency Research Award, an American Society for Mass Spectrometry Research Award, a Spectroscopy Society of Pittsburgh Award, an R&D 100 Award, and the Bunsen–Kirchhoff Prize from the GDCh (German Chemical Society), among others.

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