

Bridging Native-MS in Academia and Industry: Nucleic Acids and Their Delivery

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Since the initial experiments performed in academia demonstrating the retention of noncovalent protein-ligand and protein-protein complexes in the gas-phase over twenty-five years ago, this unique application area of MS has grown into a fully established research field with applications for project support and progression within pharma.

Although native MS has most commonly been employed to study protein complexes, a small community has driven significant advances in native MS of nucleic acids. Simultaneously, the use of nucleic acids in a variety of forms has significantly grown in the biopharmaceutical industry, not least in the unprecedented advances in mRNA vaccines. Beyond the nucleic acids themselves, the delivery vehicle can be critical to success of nucleic acid therapeutics. A wide range of potential delivery options are available, ranging from antibody conjugates, lipid nanoparticles, or viral capsids. Native mass spectrometry is uniquely suited to characterize these complex biomolecules and support research and development for novel nucleic acid therapeutics.

Within this workshop, we will discuss the diversity of nucleic acid-based systems now being studied by native-MS in both academia and pharma as well as new technologies for studying these complex systems. Our focus is to bridge new technology and applications development in both academic and pharma research environments allowing for routine project support and progression for modalities that require native MS analytics.

Speakers:

Ghazaleh Yassaghi (University of Connecticut)

Lohra Miller (Indiana University)

Erin Panczyk (Mobilion)

Corinne Lutomski (University of Oxford)

Jared Kafader (Northwestern University)

Summary of Discussion:

The workshop began with a short introduction from Michael Marty to discuss the workshop goals and relationship with past native MS workshops. Then, each speaker presented a short introduction. Ghazaleh Yassaghi presented on native MS of nucleic acid complexes, and Lohra Miller presented on charge detection-mass spectrometry of large viral capsids. Erin Panczyk presented on SLIM ion mobility separations of nucleic acids. Corinne Lutomski spoke about native MS and CD-MS of protein complexes, and Jared Kafader spoke about Orbitrap-based CD-MS. Following the presentations, there was a vibrant discussion that included sample preparation methods, salt concentration, and differences in ionization modes. Significant contributions from the audience were helpful in framing the discussion. The overall outcomes of the discussion are that there is a lot of potential for native MS in nucleic acid research and, although there are differences with more conventional protein analysis, the methods are strong and worthy of broader research in academic and industrial settings.