Bridging Native-MS in Academia and Industry: From Direct nESI Infusion to Platform Sample Introduction and Routine Project Support

Date of Workshop: June 2, 2020

Organizers: Michael T. Marty and Iain D. G. Campuzano

Presenters and Titles of Presentations:

1. Joe Loo: History of native MS sample introduction
2. Vicki Wysocki: Online desalting for native MS
3. Evan Williams: Submicron nESI needles
4. Ashley Bell: CE-MS and CEIF-MS
5. Elizabeth Hecht: High throughput microflow online SEC desalting
6. Iain Campuzano: Native-MS on the FT-ICR and native MS-SEC on a ToF

Description of Workshop:

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.

The protein complexes investigated by native-MS have ranged from the initial demonstrations on simple protein complexes, through complex macromolecular machines, to the present-day analysis on polydisperse nanodiscs, membrane proteins, and mega-Dalton virus capsids.

What has remained relatively constant is sample introduction with single-shot, low-volume nanoESI capillaries. However, sample introduction for native-MS is beginning to evolve rapidly using more "platform" based technologies. There are now multiple examples within pharma, where native-MS is critical for project support and progression, but still remains niche, due to lack of robust, higher throughput introduction methods.

Within this workshop, we will discuss the diversity of samples now being analyzed by native-MS in both academia and pharma; new and evolving sample introduction methods ranging from single-shot nESI, to high-throughput automated native-MS acquisitions. 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.

Subject matter would include:

1. Sample diversity now being analyzed by native-MS; academia and industry
2. Improvements in single-shot nESI sample introduction (NanoMate and submicron emitters) and perceived challenges.

3. Platforming native-MS methods (SEC-MS and CEX-MS, cIEF-MS and high throughput native-MS sample introduction)
4. ToF, Orbitrap, and FT-ICR as native-MS instrument platforms.

Summary of Discussion:

The discussion centered on different ways to perform sample introduction for native MS and in particular on the electrospray conditions. There was a discussion of different separation strategies and technical details on the conditions. True to the title, there was a significant discussion of native MS in industry and how native MS is essential for answering specific problems. Additional discussion points focused on standard proteins versus therapeutic proteins analyzed by native MS. Also discussed was the apparent peak shape differences between oa-ToF and Orbitrap and levels of adducting as a function of activation.

The consensus among the presenters was that native MS has a major role to play in both academic and industrial research, and exciting ongoing research and future developments, such as instrument source design, promise to address some of the significant challenges in sample introduction.