Native MS Workshop June 2022, Minneapolis, MN

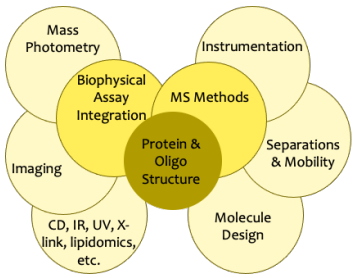
From Academia to Industry: How Native MS works with complementary technologies to elucidate protein structure.

Native MS is recognized as a cutting edge technique in the molecular characterization of protein targets and drugs. It can provide information regarding complex stoichiometry, structural integrity, noncovalent ligands, drug binders, and post-translational modifications. As research targets in academics and industry become more challenging, there is an increasing need to integrate native MS with other orthogonal technologies to solve structures at hand.

The last two years have witnessed a growth in complementary technologies or methodologies to native MS to assist in structural characterization. Exciting developments have been made in soft landing (interface of microscopy and native MS), binding interface elucidation (interface of cross-linking and native MS), and stoichiometry (interface of mass photometry, ion mobility, and native MS). This workshop will highlight the integration of traditional native mass spectrometry structural biology with these emerging complementary technologies. For newcomers to the field, the workshop will also seek to address which routine instrumentation may be desirable for inclusion in a new native MS lab looking toward structural characterization.

The native MS workshop has long supported collaboration between academia and industry. The panel of experts will sit on both sides, presenting work that is cutting-edge both in technique and application area. The workshop will deliver short lightning talks followed by a facilitated discussion.

Speakers
Anita Liu, Lead R&D Specialist, Anal. Chemistry, Regeneron
David Roberts, Graduate Student, Ying Ge Lab, UW
Weston Struwe, UKRI Future Leaders Fellow, U Oxford
Valérie Gabelica, Research Director, IECB, U Bordeaux, France
Zhuo Chen, Investigator, GSK
Michael Westphall, Distinguished Scientist, Coon Lab, UW



Organizers: Elizabeth Hecht, Ashley Bell, Justin Benesch

Summary of discussion:
The concept of structural mass spectrometry was approached by speakers through a range of different methodologies and for the purpose of answering diverse questions. Liu, Roberts, and Chen predominantly focused on utilizing TIMS or LC technologies to solve questions related to glycosylation heterogeneity. Speaking to concepts around the native state and the effects of electrospray on conformation, Gabelica presented a lightning talk around a bead ejection model for non-globular biopolymers, and spoke about the difficulties in using ion mobility to extract information on non-globular structures. Native MS coupled to photometry to solve glycoprotein and viral structures was discussed by Struwe, and emerging instrumentation to enable soft landing for Cryo-EM structures was presented by Westphall. The discussion centered around three main areas. In the first, terminology around “native” was discussed. This revealed a discrepancy between native biopharma applications, where it is often used for covalent molecule analysis for the sake of charge reduction, versus native academic applications, which tend to define the native state more at the tertiary and quaternary preservation level. The second level of discussion centered around what happens to native ions in the gas phase, where people made connections between Gabelica’s and Westphall’s talk to suggest that native states are in fact preserved when the kinetics are fast enough. Lastly, terminology and the need for high resolution mass spectrometry was discussed. The group as a whole remains optimistic about the intersection of new technologies to help answer questions around native states.

The online attendance was unknown and the workshop was well attended (room nearly full). There was engaging conversation. 1/3 organizers was unable to attend due to COVID, but the event was still able to proceed.