

## **Fundamentals Interest Group Workshop**

ASMS 2022, Minneapolis

### **Title: Isotopes - the Curse and Blessing of Mass Spectrometry**

Organizers: Alexandre Shvartsburg (Wichita State) and Alexander Makarov (Thermo Scientific)

Date: Tuesday, June 7, 2022

Attendance: 50 - 100

Our workshop has focused on the MS approaches utilizing isotope ratio measurements to push the science frontiers. We sought to illustrate how this fundamental, ubiquitous, and seemingly mundane concept still sparkles with abundant scientific, industrial, and clinical opportunities.

The presider A. Makarov opened by highlighting the definition and origin of isotopes and established MS applications based on the isotopic measurements. This set the stage for the short talks advancing new and often unexpected lines of research.

Richard Shanks (U. of Glasgow) presented a new concept expanding the  $^{14}\text{C}$  dating beyond the accelerator mass spectrometry (AMS). The group achieves efficient ionization employing a bright plasma source and suppresses interferences employing carbon-specific polarity reversal upon the collisions with isobutane gas molecules. The resulting instrument is competitive with AMS at ion energies under 30 kV, potentially enabling a much more compact and affordable platform.

Tim Csernica (Cal Tech) ventured into the growing field of site-specific measurement of isotope ratios for ever larger species using high-resolution MS. With sufficiently long acquisitions, those ratios for specific atoms within a molecule could be determined with high precision even for unlabeled samples. Applications include the prebiotic synthesis on carbonaceous meteorites and tracing the fluxes of serine synthesis in plants.

The talk “Just Add Water!” by John Kellie (GSK) was devoted to investigation of protein turnover *in vivo* using deuterated water. High-resolution MS separates the D-containing isotopologues of peptide fragments from the  $^{13}\text{C}$  and  $^{15}\text{N}$  isotopologues, significantly improving sensitivity.

Alexey Chernobrovkin (Karolinska Inst., Zubarev group) presented the isotopic measurements of protein digests at the amino acid level using the immonium ions common to peptides. The unexpected inexplicably high D content in proline/hydroxyproline in some animals (especially gray seals) was discovered, materially increasing the average hydrogen mass in these species. This effect was confirmed by the traditional isotope ratio MS.

Ryan Bomgarden (Thermo Scientific) conveyed the advantages, history, and perspectives of tandem mass tags for sample multiplexing in proteomics. He covered various strategies and challenges for a dramatic increase of multiplexing.

Alexandre Shvartsburg (Wichita State U.) concluded the workshop by discussing how the differential ion mobility spectrometry (FAIMS) can be combined with ultrahigh-resolution (Orbitrap) MS to delineate isomers not just by molecular geometry, but utilizing the isotopic fine structure. This new technique based on the structurally specific shifts between mass-selected isotopologues in IMS dimension brings closer the vision of “gas-phase NMR”.

The workshop concluded on time, with most questions coming from the speakers.