

MEASURING MASS OF MOLECULES: FROM ATOMS TO MOLECULAR MACHINES

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Starting from a brief introduction to mass spectrometry, this talk focuses on high-resolution accurate mass (HR/AM) analysis of atoms and molecules, especially Orbitrap mass spectrometry as the leading technique in this field. Basic principles of this technology are presented against a backdrop of its brief but colorful historic development.

Since its introduction the utility of the Orbitrap analyzer has been continuously extended by coupling with additional capabilities such as quantitative analysis, new fragmentation methods, different vacuum and ambient ion sources, imaging and ion mobility. These capabilities are exemplified for four major families of Orbitrap-based instruments, with numerous new modes of operation enabled by parallelization of detection and ion processing, and intricate coordination with different ion-optical devices. New modes of data-independent, targeted and top-down acquisitions are overviewed, including acquisitions at 40 spectra/second or at 1 million resolution setting.

The roadmap of future instrument innovations is overviewed. Major directions of progress include trap and instrument designs, analytical modalities, acquisition methods as well as signal processing. Special attention is devoted to analysis of proteins and protein complexes that poses unique challenges to mass spectrometry and drives the deep re-thinking of principles earlier validated on small molecules and peptides.

In conclusion, future trends and perspectives of Orbitrap mass spectrometry are discussed, including its inroads into emerging areas of mass spectrometric analysis. It is shown that Orbitrap-based mass spectrometers possess compelling potential as an (ultra-) high resolution platform not only for high-end proteomic applications but also for screening, trace and targeted analysis by LC/ and GC/MS.