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This talk presents first-hand a short but eventful history of Orbitrap mass spectrometry, from laying down the first principles to its current status as the leading mass spectrometric technique for high-resolution, high mass accuracy quantitative analysis.

Originating from an ideal (and therefore never realized) Kingdon trap, this analyzer can provide high performance analytical characteristics only when it is highly integrated with the ion injection process. The advent of pulsed injection from an external ion storage device allowed the Orbitrap analyzer to enter mainstream mass spectrometry, initially as a part of a hybrid instrument. Since its introduction the utility of the Orbitrap has been extended by coupling with additional capabilities such as higher-energy dissociation (HCD), ETD, FAIMS, UVPD, ion mobility and different ionization techniques such as MALDI, in-vacuum EI/CI, APPI, etc.

The widespread adoption and use of Orbitrap mass spectrometry has been driven by its characteristic ability to acquire high-resolution, high mass accuracy data for qualitative and quantitative analysis. Increasing speed of chromatographic separations imposes ever increasing requirements on throughput of mass spectrometric analysis and demand higher spectral acquisition rates, improved spectral quality and better control of different ion optical devices within mass spectrometers.

Recent improvements in these directions are exemplified for Q Exactive and Orbitrap Fusion families of instruments, with numerous new modes of operation enabled by parallelization of detection and ion processing and concerted operation of different ion-optical devices. A special emphasis is made on technical solutions that allow quantitative analysis in these instruments, despite Orbitrap analyzer being of an ion trapping type.

It is shown that quantitative analysis in Orbitrap mass spectrometry is now highly feasible due to a unique combination of high space charge capacity of the C-trap, improved control over the number of stored ions, intelligent filling and high sensitivity with built-in high mass accuracy, resolving power and dynamic range of analyzer. New modes of data-independent, targeted and top-down acquisition are overviewed.

In conclusion, future trends and perspectives of Orbitrap mass spectrometry are discussed, including its inroads into emerging areas of mass spectrometric analysis, such as analysis of intact proteins and protein complexes under native conditions, e.g. antibody-drug conjugates and antibody-antigen complexes. 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 and clinical analysis by LC/ and GC/MS.