Internal Calibration in Mass Spectrometry without Internal Calibrants

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High magnetic field Fourier transform ion cyclotron resonance mass spectrometry enables the molecular characterization of our planets' most complex mixtures. However, this capability comes at a cost. With the analysis of a single sample yielding 1K-1M+ individual mass spectral peaks, calibration and assignment of molecular formulas to all peaks in each spectrum becomes a daunting task. Thus, we developed an automated calibration method and an architecture for molecular formula assignment that utilizes only the information available in the periodic table.

Starting with the externally calibrated mass spectrum (**Fig. 1, top, left**), detected peaks (mass-to-charge (*m/z*) ratios and peak heights) are sorted from highest to lowest *m/z*. All *m/z* values are subtracted from the highest *m/z* and stored as a list of *m/z* differences ($\Delta(m/z)_{ij}$). The highest *m/z* is deleted, and the process continues until no peaks remain in the spectrum (mass difference analysis; middle, left). All $\Delta(m/z)_{ij}$ are then plotted as a histogram (number of times a $\Delta m/z$ occurs on the y-axis and $\Delta m/z$ on the x-axis). Since no two elements have the same exact mass, the mean $\Delta m/z$ of each histogram yields a unique elemental identification (bottom) but exposes an error in the mass spectral data due to suboptimal calibration. Since the calibration equation is known, we simply iterate the calibration coefficients until we move the mass difference histograms to their correct $\Delta m/z$ values (middle, right). Once optimized, the new calibration is applied, which substantially increases mass accuracy (top, right), without knowing the identity of any peaks in the spectrum.

Mass difference calibration enables rapid, automated, accurate recalibration of complex mass spectra and removes the largest source of variance (the scientist) in the process. It also drastically reduces data analysis times and staff involvement.

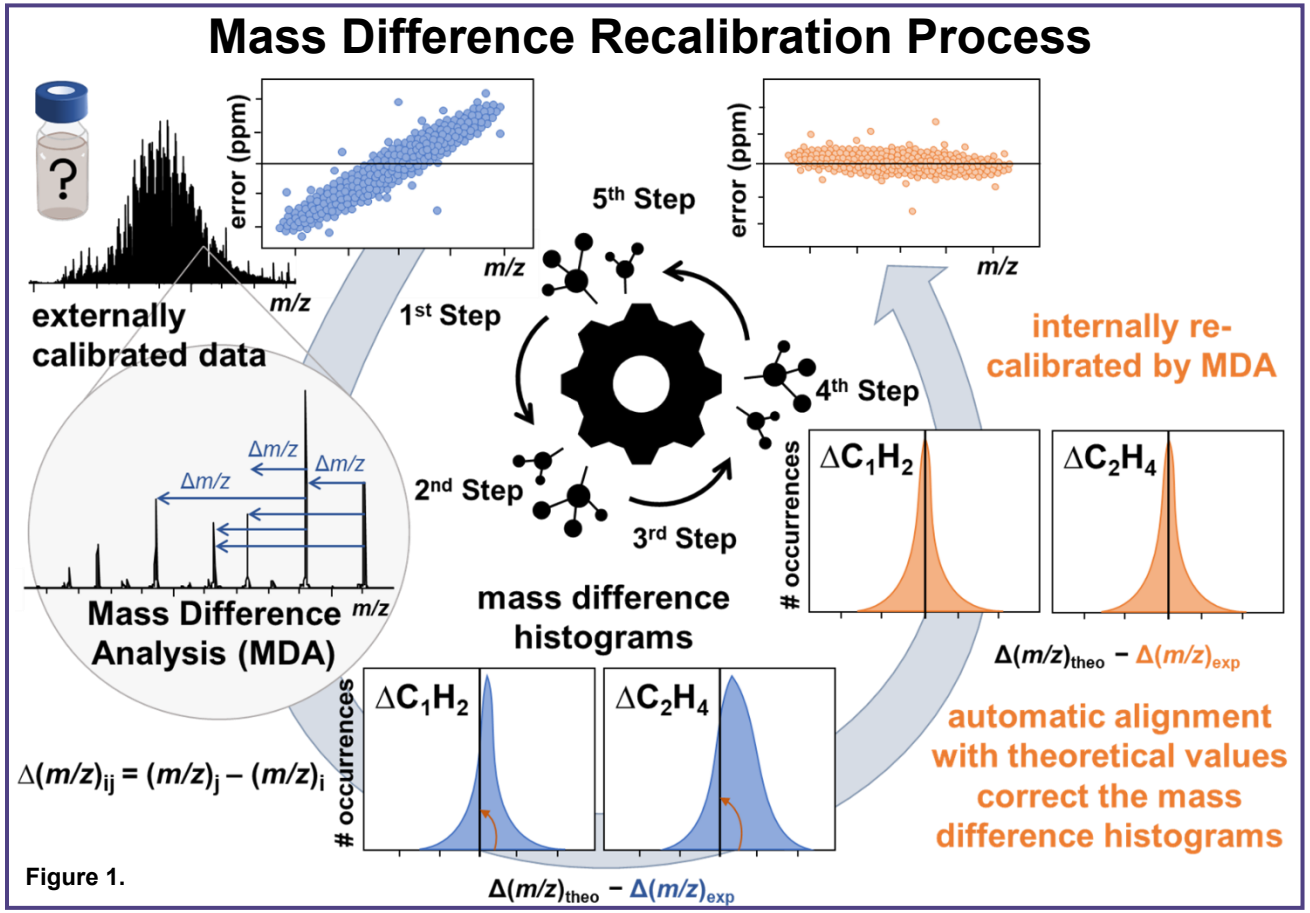

Figure 1.

Facilities and instrumentation used: Ion Cyclotron Resonance Facility, 21T FT-ICR Mass Spectrometer

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