Determining the isotopic structures of molecules by Orbitrap mass spectrometry

JOHN EILER[1], ELLE CHIMIAK[1], BROOKE DALLAS[1], JENS GRIEP-RAMING[2], DIETER JUCHELKA[2], NAMI KITCHEN[1], ALEXANDER MAKAROV[2], JOHANNES SCHWIETERS[2]

[1]Div. Geol. Planet. Sci., Caltech, Pasadena, CA 91125, USA
[2]Thermo Fisher Scientific, Bremen, Germany

Position-specific and multiply-substituted, or ‘clumped’, isotope compositions of molecules potentially constrain many features of their origin and evolution. We present the instruments, methods and initial applications of a technique for measuring molecular isotopic structures using an Orbitrap mass spectrometer, the Thermo Scientific Q Exactive GC.

The Orbitrap mass spectrometer achieves mass resolutions on the order of 500,000-1M in the mass range ~50-100 amu where most of the measurements we report were performed. This is sufficient to resolve all commonly encountered isobaric interferences, including those that are beyond the capabilities of even the most advanced magnetic sector instruments (e.g., distinguishing ^{13}C from ^{17}O bearing species at moderate mass). Through study of diverse organic and inorganic reference materials, we have established that standard errors in isotope ratios closely follow shot-noise limits, and are accurate within formal errors when standard/sample comparisons are made under controlled conditions. Thus, the accuracy and precision of Orbitrap based measurements of isotope ratios largely depend on experimental design rather than fundamental limits of the technology. External errors for measurements lasting ~minutes are as good as ±0.2 per mil (1SE) for relatively abundant isotopologues, and ±0.5-1 per mil for less abundant species. Perhaps most importantly, the Q Exactive GC combines the Orbitrap mass analyzer with a quadrupole mass filter and CID-type collision cell. This combination allows one to define analytical methods that quickly measure for proportions of large numbers of isotopologues of molecular and fragment ion peaks; this permits one to constrain diverse position-specific and clumped isotope species as part of a single, relatively time-efficient analysis. Finally, we have established that these capabilities can be applied to time-resolved peaks eluted from a GC, permitting study of complex mixtures. Sensitivity is sufficient to permit isotope ratio analysis of sub-nano-molar samples.

We will present the first applications of this system to the isotope structures of natural and synthetic amino acids. This work aims to use position-specific carbon isotope variations to constrain the origin and evolution of organic compounds in meteorites and terrestrial extreme environments. We intend to add to these constraints measurements of position-specific ^{17}O anomalies in meteoritic organic compounds.