Quick stable isotope analysis of multiple components in a complex mixture by Fourier transform mass spectrometry

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Recent developments in Fourier transform mass spectrometry facilitate high-resolution, high-precision measurements of molecular isotopic structure (i.e., site-specific and multiple substitution), using a Thermo Scientific™ Orbitrap™ mass analyzer coupled to Thermo Scientific Q Exactive GC™ and Q Exactive HF™ instruments. Precision of measurements on these instruments is constrained by the duration of eluted chromatographic peaks, shot-noise limits, and space charge effects within the Orbitrap, but can achieve ±0.015‰ for long integration times[1]. In this study, we observed natural abundance isotope ratios of molecular and fragment ions for a mixture of ~10 amino acids via direct injection of peaks eluted from the gas chromatograph[1], where each molecule in the complex mixture was analyzed for ~30 seconds. Altogether, direct analysis provides information on isotopic molecular structure for fragment ions of all eluted moleules in ~40 minutes (assuming appropriate standards in a standard mixture). Relative standard errors (RSE) for these measurements were as good as 33‰ for $\delta^{13}C$ values of major fragment ions for one injection; averaging across multiple injections (n=3) achieved RSE as good as 5.1‰. The direct injection method was designed to search for large site speicfic anomalies (~100‰) in extraterrestrial compounds, but, at best performance, isotope effects on the order of ~20‰ could be confidently recognized. To demonstrate the applicability of this method, we performed this direct analysis techinque on a mixture of amino acids extracted from the Murchison meteorite and identified site-specific ^{13}C enrichments ranging up to 120‰. These measurements provide information on precursor molecules in the solar system and extraterrestrial abiotic organic synthesis, and have implications for Early Earth origins of life chemistry.

1. Eiler, J. (Caltech) *et al.* Analysis of molecular isotopic structures at high precision and accuracy. *Int. J. Mass Spectrom.* **422**, 126–142 (2017).