Challenges Posed by Ultrahigh Resolution Complex Mixture Data

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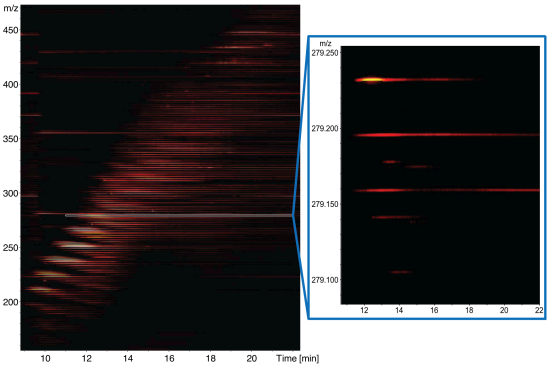
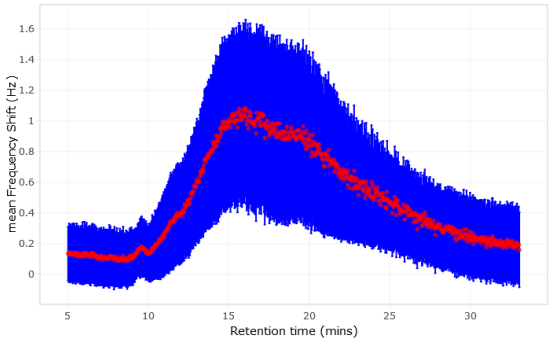
Background: Fourier transform ion cyclotron resonance (FTICR) mass spectrometry (MS) represents the state-of-the-art for ultrahigh resolution analysis of complex mixtures. As one example application, crude oil has been described as "nature's most complex mixture," containing tens or hundreds of thousands of different molecular formulae.[1,2] FTICR MS provides mass-to-charge ratio (*m/z*) information which can, in turn, be used to determine the masses of individual components and their molecular formulae. Following formula assignments and the use of visualization methods[3] sample data can be compared to highlight geographical relevance or the effects of industrial and environmental processes. For the next steps for the field, it is important to gain greater insight into the structures of the components, particularly with respect to physical properties and toxicity. To obtain structural information, it is possible to couple a mass spectrometer with chromatographic methods, including liquid chromatography (LC) and gas chromatography (GC).[4]



Challenges and objectives: During FTICR MS analysis, ions orbit within a small cylinder known as the ICR cell and the frequencies of the ions are inversely proportional to their *m/z* values. When very complex samples are analyzed, the large numbers of ions repel each other due to their charges and this causes frequency shifts. These frequency shifts affect resolution, mass accuracy, and peak shape, degrading instrument performance. When coupling chromatography, there is an added dimension of time: the number of ions within the ICR cell changes with scan number and therefore time. This means that the frequency shifts change as a function of time and makes calibration difficult, which is extremely important for analysis of complex samples; the objective is the development of a new calibration method for such data.



MSc and PhD Project: The MSc project will focus upon improved processing of complex, multidimensional data sets (e.g. GC-FTICR MS data). In-house software has been developed using R for processing and viewing such data. The project will focus upon the development of an improved calibration method to compensate for frequency changes as a function of time, taking into account the ions' masses, the individual and total number of charges, and signal magnitudes. Successful development of an improved calibration method would lead to implementation in the in-house software and, due to the widespread challenges, may also attract commercial interest by instrument manufacturers. Longer term (PhD) project work would include development of processing algorithms for multidimensional, complex data and new methods for comparing multiple complex data sets, which are essential next steps for the field.

References: [1] *Proc. Natl. Acad. Sci. U.S.A.* **2008**, *105*, 18090-18095 [2] *Biofuels* **2010**, *1*, 651-655. [3] *Mass Spectrom. Rev.* **2014**, *34*, 248-263 [4] *Anal. Chem.* **2014**, *86*, 8281-8288