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Short Bio

I am currently a Reader – Associate Professor at the University of Warwick, located in the UK. I began working with Fourier transform ion cyclotron resonance mass spectrometry and complex mixtures, including petroleum, in 2000. Working with 12 T and 15 T Fourier transform ion cyclotron resonance (FTICR) instruments, my research group focuses upon the use of ultrahigh resolution mass spectrometry to characterize complex mixtures, with particular interests in petroleum, transportation (including fuels and engine oils), energy from biomass (biofuels and bio-oils), environmental samples, archaeological samples, and development of advanced data processing and visualization methods. Since 2015, I have been a trustee and elected member of the executive committee of the British Mass Spectrometry Society (BMSS), previously holding the role of Education Officer and now serving as the General Secretary. I am also a member of the Royal Society of Chemistry's "Instrumental Analysis Expert Working Group," coordinated by the Analytical Methods committee.

Method Name in non-abbreviated full form

Fourier transform ion cyclotron resonance mass spectrometry (FTICR MS)

Method description in brief

In brief, a typical workflow for a complex sample would involve:

- Sample extraction and preparation in organic solvents
- Choice of appropriate ionization method (most commonly ESI or APPI, listed below)
- Use of a 12 T or 15 T FTICR mass spectrometer, listed below
- Multi-stage data processing and data analysis using software listed below

Details of Ion Cyclotron Resonance Laboratory at the University of Warwick

Our laboratory currently uses three mass spectrometers:

- 12 T solariX (FTICR MS)
- 15 T solariX 2xR (FTICR MS)
- timsTOF Pro (trapped ion mobility spectrometry, TIMS)

Note: both FTICR instruments have been modified.

Optional separation methods:

- nanoElute (liquid chromatography, LC) by Bruker Daltonics
- 7890A (gas chromatography, GC) by Agilent
- nanoACQUITY (liquid chromatography, LC) by Waters

Ionization methods include:

- Electrospray ionization (ESI)
- Nanospray
- Atmospheric pressure photoionization (APPI)
- Atmospheric pressure chemical ionization (APCI)
- Matrix-assisted laser desorption/ionization (MALDI)
- Laser desorption/ionization (LDI)
- Low temperature plasma (homemade)

Dissociation methods include:

- Collision-induced dissociation (CID)
- Infrared multiphoton dissociation (IRMPD)
- Ultraviolet photodissociation (UVPD)
- Electron capture dissociation (ECD)
- Electron-induced dissociation (EID)
- Electron transfer dissociation (ETD)

Data processing and analysis:

- DataAnalysis (Bruker Daltonics)
- Composer (Sierra Analytics, Inc.)
- KairosMS (Barrow Group, University of Warwick)

Applicability of method

- FTICR instruments can be tuned for different m/z ranges
- For petroleum-related samples, typical carbon number ranges can be 10-80, but can go higher or lower as needed (e.g. we have observed compounds with a carbon number >100)

- For petroleum-related samples, heteroatom classes typically include varying amounts of nitrogen, oxygen, and sulfur
- Variety of structural motifs and functional groups can be represented, as long as can be ionized (i.e. limitation of ionization method, not the FTICR mass analyzer)
- Most commonly used in semi-quantitative manner
- True quantitation (when using any variety of mass spectrometer, not only FTICR) would require coupling with chromatography, separation of isomers, use of authentic standards, and construction of calibration curves for signal response as a function of concentration; for targeted analysis of a limited number of components, this is possible but, for full and untargeted analysis of the most complex samples, this could require hundreds of thousands (or more) of standards, which is not viable
- Maximum ion population of ICR cell (a function of cell design and magnetic field strength) can limit detection; combined with minimum number of ions required to register a peak, these factors determine maximum number of peaks and dynamic range (very approximately order of 10^3)
- Resolving power is variable and depends on instrument design, magnetic field strength, and experimental parameters used
- Required resolving power to resolve a particular mass difference scales linearly with increasing m/z; two of the well-known "mass splits" associated with petroleum which need to be resolved are 3.4 mDa and 1.1 mDa, when sulfur-containing compound classes are present
- FTICR instruments typically operated with resolving power of an order of ~10^5-10^6 at m/z 400

Sample preparation required

- Samples can be used in solid form with LDI but, much more commonly, samples must be dissolved in organic solvents before use with most ionization methods (e.g. ESI, APPI, APCI, and more).

- Some samples will require prior separation, such as using Soxhlet extraction (note: involves heating) or open column chromatography. This can be performed to obtain a liquid sample from a solid material or for fractionation of petroleum on the basis of solubility, for example.

- Samples are finally diluted by orders of magnitude in organic solvents. Complex mixtures may be prepared as approximately 0.05 mg/mL, for example, depending upon the sample nature.

Method strengths

Fourier transform ion cyclotron resonance mass spectrometry:

- Unrivalled ultrahigh resolution and mass accuracy
- Ability to resolve peaks in complex mixtures; observe more components
- Accurate measurement of m/z; high confidence when assigning molecular formulae
- Can assign tens of thousands of molecular formulae in a single data set
- Has led to most detailed characterization of highly complex samples, such as petroleum, to date
- Due to not requiring chromatography, not directly limited by solubility or boiling point
- Can characterize samples that could not readily be analyzed by other methods, has also demonstrated risk of incorrect assignments using other methods
- Versatility:
    - Ability to change between ionization sources (note: important to differentiate between mass analyzer and an ionization method when discussing advantages and limitations)
    - Ability to combine with chromatography
    - Multiple dissociation methods available
    - Users can custom-design experiments
    - Flexibility of tuning, experimental parameters

Estimated time for analysis

Time required is variable and highly dependent upon nature of sample, experiment type, performance required, and amount of data analysis.

- Sample preparation: minutes if simply diluting for analysis, hours or days if performing prior extraction/fractionation
- Experiments: time must be allowed for tuning and initial checks, but data can be collected for simple experiments in approximately 10-30 minutes; users typically spend a full day on an instrument
- Data processing, analysis, and visualization: this is the majority of the time required and again depends upon needs, potentially ~80% of the total time

Method weaknesses

- User expertise required
- Instruments are expensive to purchase and run
- Use of cryogens; cost and availability
- Time and user interaction required; slower than other instruments and will not achieve optimum performance if using an autosampler
- Unless performing dissociation experiments for individual peaks, standard experiments for overall sample yield molecular formulae but not structures
- Instruments cannot be operated in the field, samples must be sent to laboratory

Result interpretation / visualisation / presentation

- Raw data (time domain) acquired using FTICR mass spectrometer
- Fourier transform and instrument calibration used to convert to frequency domain and, ultimately, mass spectrum
- Optional: absorption mode ("phasing") to increase resolving power and signal-to-noise
- Calibration of data set using reference list
- Assignment of molecular formulae, either individually/manually or based upon patterns
- Use of assignments list and in-house software for visualization; examination of data using different plot styles to check for features warranting further investigation

Relevant Papers

(1) **Review of petroleomics**
Lozano, D. C. P.; Thomas, M. J.; Jones, H. E.; Barrow, M. P. *Annual Review of Analytical Chemistry* **2020**, *13*, 405-430.

(2) **Differentiating industrial/environmental sample origins**
Headley, J. V.; Barrow, M. P.; Peru, K. M.; Fahlman, B.; Frank, R. A.; Bickerton, G.; McMaster, M. E.; Parrott, J.; Hewitt, L. M. *Rapid Commun Mass Spectrom* **2011**, *25*, 1899-1909.

(3) **Coupling GC with FTICR MS**
Barrow, M. P.; Peru, K. M.; Headley, J. V. *Anal Chem* **2014**, *86*, 8281-8288.

(4) **Simulated effects of exposure of crude oil to light**
Griffiths, M. T.; Da Campo, R.; O'Connor, P. B.; Barrow, M. P. *Anal Chem* **2014**, *86*, 527-534.

(5) **Analysis of sediment cores**
Thomas, M. J.; Collinge, E.; Witt, M.; Palacio Lozano, D. C.; Vane, C. H.; Moss-Hayes, V.; Barrow, M. P. *Sci Total Environ* **2019**, *662*, 852-862.

(6) **Interlaboratory study to compare sample analyses**
Hawkes, J. A.; D'Andrilli, J.; Agar, J. N.; Barrow, M. P.; Berg, S. M.; Catalán, N.; Chen, H.; Chu, R. K.; Cole, R. B.; Dittmar, T.; Gavard, R.; Gleixner, G.; Hatcher, P. G.; He, C.; Hess, N. J.; Hutchins, R. H. S.; Ijaz, A.; Jones, H. E.; Kew, W.; Khaksari, M.; Palacio Lozano, D. C.; Lv, J.; Mazzoleni, L. R.; Noriega-Ortega, B. E.; Osterholz, H.; Radoman, N.; Remucal, C. K.; Schmitt, N. D.; Schum, S. K.; Shi, Q.; Simon, C.; Singer, G.; Sleighter, R. L.; Stubbins, A.; Thomas, M. J.; Tolic, N.; Zhang, S.; Zito, P.; Podgorski, D. C. *Limnology and Oceanography: Methods* **2020**, *18*, 235-258.

(7) **KairosMS (software)**
Gavard, R.; Jones, H. E.; Palacio Lozano, D. C.; Thomas, M. J.; Rossell, D.; Spencer, S. E. F.; Barrow, M. P. *Anal Chem* **2020**, *92*, 3775-3786.

(8) **Assignment of 244,779 molecular formulae within a fraction of a petroleum sample**
Palacio Lozano, D. C.; Gavard, R.; Arenas-Diaz, J. P.; Thomas, M. J.; Stranz, D. D.; Mejía-Ospino, E.; Guzman, A.; Spencer, S. E. F.; Rossell, D.; Barrow, M. P. *Chem Sci* **2019**, *10*, 6966-6978.