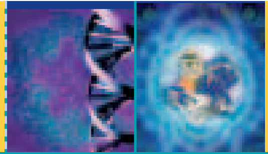
High-field FT-ICR MS



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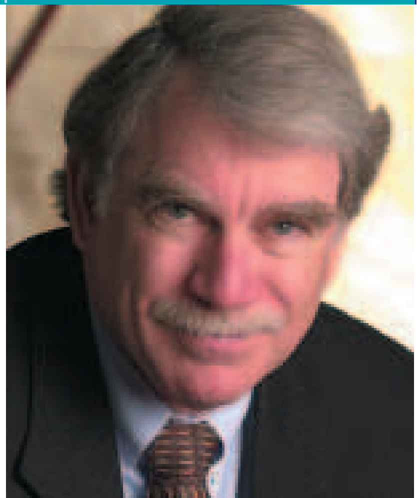
Mass spectrometry (MS) has become one of the most ubiquitous analytical techniques in use today. It represents a powerful tool in the study of all substances because it provides more information about the composition and structure of a substance from a smaller amount of sample than any other analytical technique.



Professor Alan Marshall of the National High Magnetic Field Laboratory explains the significance of superconducting magnet technology to FT-ICR MS

Of all the MS techniques currently available, Fourier Transform Ion Cyclotron Resonance mass spectrometry (FT-ICR MS) is arguably the most powerful. It offers 10-100 times higher mass resolution, mass resolving power, and mass accuracy than any other mass analysis technique. Alternatively, viewed only as a separation device, ultrahigh-resolution FT-ICR MS offers more than 100 times higher peak capacity than the most effective wet chemical separation methods (e.g., high performance liquid chromatography, capillary electrophoresis, polyacrylamide gel electrophoresis). This makes it possible to analyse complex mixtures with no prior chromatography.

Superconducting magnets: an integral part of FT-ICR

In FT-ICR MS, ion mass-to-charge ratio is obtained by measurement of the ion cyclotron frequency in a static homogeneous magnetic field, B. As with NMR, the quality of results produced is directly influenced by both the field strength and quality of the superconducting magnet at the heart of the instrument. ICR frequency is proportional to B. Thus, as in FT-NMR, FT-ICR resolving power increases linearly with increasing B field. Unlike NMR, however, six other essential FT-ICR parameters also increase linearly (highest non-coalesced mass, scan speed) or quadratically (ion kinetic energy, maximum number of trapped ions, upper mass limit, ion trapping period) with increasing B. These fundamental advantages result in improvements in other FT-ICR performance parameters: e.g., signal-to-noise ratio, dynamic range, mass resolution, mass accuracy, and mass selectivity for MS/MS.

Moreover, the various advantages may be exploited in combination, so as to produce even higher enhancement in a particular parameter.

Record-breaking MS

The 'flagship' of the NSF National High-Field FT-ICR MS Facility at Florida State University in Tallahassee is based on an Oxford Instruments 9.4 T superconducting magnet. This instrument is usually configured for electrospray ionisation and features a microelectrospray front end (for high sensitivity and easy operation in both positive and negative ion analysis) and ion accumulation and mass selection outside the magnet (for fast scan rate and high dynamic range). It also offers three fragmentation techniques for extensive structure elucidation.

The exceptional spatial homogeneity and temporal stability of the magnet mean that the system continues to be the highest performance electrospray FT-ICR mass spectrometer in the world. As a result, the 9.4 T spectrometer holds virtually all of the current world records for mass resolving power, mass, resolution, and mass accuracy.

The laboratory also uses a 7 T system, which is equipped with a microelectrospray source and has been dedicated to high sensitivity biological analysis. This spectrometer has demonstrated nano-LC sensitivity, with a repeatable detection limit of 300 attomoles loaded onto a column (in biological matrix). Absolute limits of 100 attomoles have been detected and repeated[1].

From forensics to petrochemicals to proteomics

Ultrahigh mass resolving power ($m/\triangle m_{50\%}$ > 300,000 over a wide mass range) offers two major advantages. First, it becomes possible to separate complex mixtures without prior chromatographic or gel separation. Second, accurate (to 1 ppm or better) mass measurement allows for direct determination of elemental composition ($C_cH_hN_nO_oS_s$ …) for molecules up to 1 kDa, and identification of up to hundreds of peptides in an enzymatic digest without prior chromatographic separation (Figure 1).

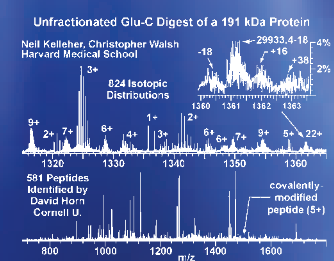


Figure 1: Identification of peptides

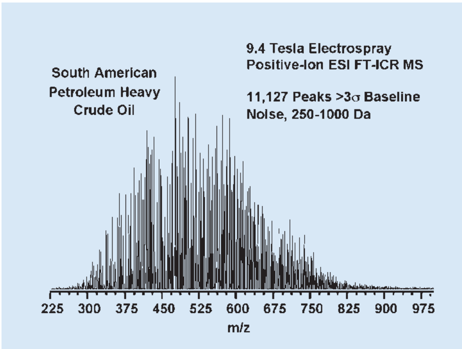


Figure 2: Determination of elemental composition for molecules up to 1 kDa

The ability to directly determine elemental composition from complex mixtures has applications in the field of forensics. Simple and rapid identification of ignitable liquids, for example, can prove essential in the criminal investigation of suspected arson fires. Here, FT-ICR MS has been used to yield molecular formulae from as little of 500 nL of accelerants such as petrol. Extraction and FT-ICR mass analysis of fire debris, from a controlled burn of a couch with lighter fluid and turpentine, also gave unique 'fingerprints' for each accelerant. These were obtainable even in the presence of compounds from both the couch and the combustion process[2].

The use of FT-ICR MS for complex mixture analysis has also been demonstrated in experiments with petrochemicals. Electrospray ionisation FT-ICR MS of South American crude oil gave a spectrum of more than 11,100 resolved peaks, of which more than 75% could be assigned to a unique elemental composition[3] (see Figure 2). The field strength of the magnet (9.4 T) was essential in order to obtain the resolution necessary for these experiments. Below 9.4 T it would be impossible to resolve between $-^{32}SH_4$ and $-^{12}C_3$ over the full mass range, as there is only 3.4 milli Da difference between these two moieties.

Another important application of complex mixture analysis is in the growing field of proteomics. Here, proteins are often identified based on the mass of one or more of their enzymatically-cleaved fragments. This has been carried out using FT-ICR MS, again removing the need for liquid chromatographic separation before analysis and thereby reducing time to results. Researchers identified a database protein from as few as one to three of its trypsin-cleaved fragments at a mass accuracy of approximately 10 ppm[4]. This application may be of particular value to the pharmaceutical industry, where time to results can be instrumental in reducing research and development costs for potential new drugs.

Conclusions

Finally, it should be noted that the main advantage of high field FT-ICR MS is the increased ease of obtaining results. With increasing magnet field strength, experiments that might have previously been considered remarkably difficult are now likely to become routine. The continuing developments in superconducting magnet technology should ensure that mass spectrometry remains one of the most ubiquitous and powerful analytical techniques for many years to come.

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