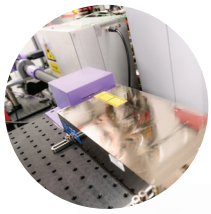
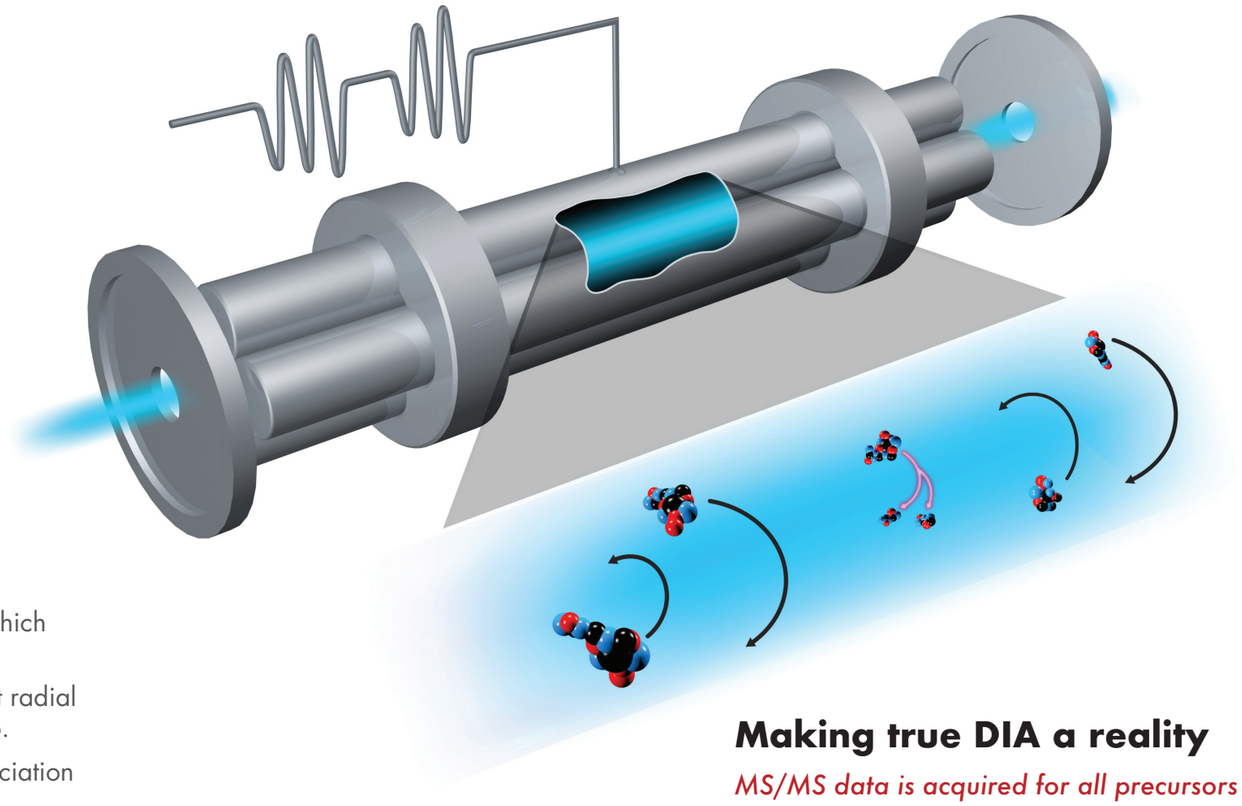
Total Correlation Mass Spectrometry

True DIA beyond the limits of current MS techniques

Total Correlation Mass Spectrometry (TOC-MS™) is a new approach to MS that enables true data independent analysis (DIA) by providing MS/MS data for every analyte in a complex sample. This novel technique eliminates the need to separate analytes prior to fragmentation, removing the dependency on chromatography and quadrupole isolation and increasing the speed of analysis.

TOC-MS enables simultaneous fragmentation of every analyte in the sample, followed by unambiguous automatic correlation of each precursor with its fragment ions using a Fourier transform approach. A single sample can be analysed in minutes, allowing rapid analysis of the most complex data sets.





How does TOC-MS work?

1. The sample is directly infused.
2. Precursor ions are held in a linear ion trap (LIT), to which an RF excitation pulse is applied.
3. The excitation pulse moves precursor ions to different radial positions within the LIT, depending on their m/z ratio.
4. Fragmentation is caused by an ultraviolet photodissociation (UVPD) laser beam in the centre of the LIT.
5. Ions are released from the LIT and move into the time-of-flight (TOF) mass analyser for mass detection.
6. Steps 2-5 are repeated rapidly using a sequence of excitation pulses – Stored Waveform Ion radius Modulation (SWIM) pulses.
7. A Fourier transform is applied to the data to match the precursors with their fragments; each fragment ion has a modulation pattern identical to its precursor ion.
8. The TOC-MS software provides a data plot showing the MS/MS spectrum for each precursor.

The UVPD laser has a Gaussian power distribution that decreases towards the edge of the beam. Consequently, precursor ions close to the centre of the beam fragment to a greater degree than those positioned closer to the edge. Modulating the amplitude of the RF excitation alters the position of a precursor in the LIT and, therefore, the laser beam, which results in changing ratios of precursor and fragment ions. The change in the abundance of each precursor is mirrored precisely by the corresponding inverse change in the abundance of its fragments, and direct correlation between the two can be identified using a Fourier transform.

TOC-MS can, therefore, unambiguously identify which fragments are associated with each precursor, even when large numbers of analytes are fragmented simultaneously.

Making true DIA a reality

MS/MS data is acquired for all precursors

- Enables true DIA for complex samples.
- MS/MS data for all precursor ions due to the technique's unambiguous and automatic correlation of precursors and fragments.
- Researchers are no longer limited to data from just the most abundant analytes – data can be acquired from every precursor present in the sample.
- TOC-MS does not require quadrupole filtering, so increased sensitivity can detect lower abundance analytes.
- Offers rapid analysis at mDa specificity.
- Complex samples with co-eluting peaks can be run at the speed of a quadrupole time-of-flight (QTOF) instrument – data acquisition takes minutes.
- Reduces data processing times from days/weeks to a few hours.
- Highly reproducible, due to the correlation of precursors and fragments.
- Reduces the need for separation and isolation techniques.
- No sample knowledge needed prior to data acquisition.
- Supplied as an upgrade to a range of QTOF instruments from different suppliers.
- Allows users to repurpose existing instruments.
- Rapid access to innovative new technology.

Potential applications

Lipidomics

The use of UVPD fragmentation combined with the automatic total correlation of precursors with their fragments means that the technique can be used to identify specific lipids. TOC-MS enables the precise identification of the head group and fatty acid chains, and the location of the double bonds. Multiple lipids can be detected and analysed simultaneously, as fragments can be correlated to the precursors.

Wastewater-based epidemiology

The complexity of wastewater has limited the use of data independent analytical techniques. TOC-MS has the ability to thoroughly profile wastewater by simultaneously providing structural and accurate mass data, as well as identifying where fragments are shared between multiple precursors. This allows users to rapidly detect related species – such as metabolites or illicit analogues of prescription medicines – and identify their structural differences. UVPD further enhances this ability by allowing for structural informative fragmentation of aromatic and cyclic rings, which is not possible by conventional MS/MS techniques.

Proteomics/multi-omics

TOC-MS's capacity to provide MS/MS data for all precursors in a complex sample means that it can provide game-changing improvements in data quantity and quality, which is valuable to researchers across all omics disciplines. The technique also provides high levels of sample reproducibility, as well as elevated sensitivity for analytes with lower abundancy.

Complex samples

Many industries have complex samples that rely on separation techniques to enable analysis of multiple analytes. TOC-MS increases the number of analytes detected, simultaneously improving the quality of the data by providing MS/MS spectra for every precursor. A key benefit of TOC-MS is that the total MS/MS data set will enable retrospective sample analysis when new analytes of interest are identified in a project.

Total correlation means *everything* to us

Get in touch now to discover the next generation of mass spectrometry and see how it can help propel your research forward.

Verdel Instruments Ltd.
Suite G1/2,
Building Three,
Watchmoor Park,
Riverside Way,
Camberley GU15 3YL
UK

Visit our website for more information.