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TIMSMRMS – THE NEXT GENERATION OF ULTRA-HIGH RESOLUTION MS INSTRUMENTATION

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Trapped ion mobility spectrometry (TIMS) has advanced greatly in recent years, yet FT-ICR MS has only had limited exposure to the IMS separation technique. A new FT-ICR MS based instrument has been designed, constructed, and characterised which overhauls the entire SolariX MRMS platform to benefit from various ion optic advancements, including a contemporary dual-accumulation and analysis TIMS cartridge as used on commercial TIMS Tof systems, creating the timsMRMS platform. The energy landscape of the system was retuned for ultra-low energy and low activation transmission of delicate analytes. Extensive ion current measurements were used to optimise each transfer and isolation region, with energy measurements informing optimum transfer and detection characteristics.

The timsMRMS system was modified to operate under gated TIMS (gTIMS) conditions using fast switching quadrupole as a gating element. gTIMS allowed time-binned analysis of TIMS-separated ions in order to accommodate the FT-ICR MS's variable, and longer detection times required for ultra-high resolution MS analysis. This decoupling of the IMS separation (millisecond timescale) and MS (second timescale) allowed for ultra-high resolution analysis and the ability to accumulate large ion populations for subsequent analysis, enhancing dynamic range for complex mixture samples such as alternative future fuels. Gated TIMS was optimised for a wide mobility range (e.g. 1/K0 0.01-2.3Vs/cm2) and was operated in both sweeping mode to study mobility of species, or filtering mode to pass individual species/isomers on for MSn and/or high resolution detection of gas phase fractionated ions.

Ultra-high resolution MS performance of FT-ICR and UHV was maintained; mass resolving power of several million in broadband mode, and over 14 million in narrowband mode was readily achieved. Front-end CID and in-cell ExD (ECD, EID, EDD) are compatible with up front gTIMS separation. Calibration against known compounds showed gTIMS elution voltage to mobility relationship was preserved to an R2 of 0.9999. The inherent mass accuracy of FT-ICR was achieved without compromise; 95ppb standard deviation for Tunemix ions 622-2722m/z on a 7T magnet system. Ion capacity improvements in the various ion traps within timsMRMS extends ion dynamic range to >12M ions analysed per scan event, adding to FT-ICR MS's high intensity dynamic range improve single intra-scan dynamic range to >5.4 orders of magnitude S/N.

To demonstrate the capabilities of the prototype system; a range of complex mixtures were analysed, such as Swannee river fulvic acids (SRFA) and alternative (green) future fuels. Combining ultra-high MS resolution and gTIMS allowed m/z specific IMS analysis to the milli-Dalton level, required for studying the isomeric complexity of such complex mixtures.[1]

Initial MALDI imaging analysis shows ≤10um microprobe spatial resolution with high spatial fidelity and 500,000-1,000,000 MS resolving power (at 400m/z) readily at 7T. Native protein conformer-selective ExD MSMS shows that conformer-dependent differences are retained from the separation event (TIMS) to the ExD probe event (ICR cell).

References:
[1] Wootton CA, Maillard J, Theisen A, Brabeck GF, Schat CL, Rüger CP, Afonso C, Giusti P. A Gated TIMS FTICR MS Instrument to Decipher Isomeric Content of Complex Organic Mixtures. Anal Chem. 2024 Jul 16;96(28):11343-11352. DOI: 10.1021/acs.analchem.4c01370

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FT-ICR MS, MRMS, TIMS, complex mixture analysis, protein, ExD, ECD.