The Triple-Quadrupole and the Beginnings of Analytical MS/MS

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TANDEM MASS SPECTROMETRY

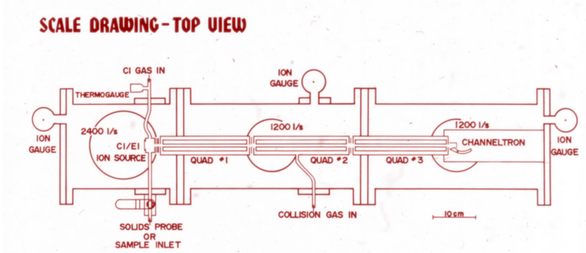
Up until the late '70s, the development of tandem MS was dominated by magnetic sector mass analyzers. The quadrupole mass filter (QMF) had an established reputation for residual gas analysis but in the late '60s Finnigan and others began marketing it as an analytical mass spectrometer. Success in competing with magnetic sector instruments wasn't realized until 1975 when Eichelberger[1] *et al* established a standardized method for tuning the QMF to obtain reproducible mass spectra among different QMF instruments. Such spectra also compared favorably with those from magnetic sector instruments.

THE TRIPLE QUAD

Despite a continued disdain for QMF analyzers among the larger mass spectrometry community, the idea that such an analyzer could be the basis for a tandem instrument was being explored by various researchers.

DRAWING OF THE FIRST YOST-ENKE QqQ INSTRUMENT

Note the presence of baffles separating q from the rest of the instrument to obtain higher collision gas pressures.



Photodissociation studies in the mid-70s led researchers at La Trobe and Utah Universities to create triple quadrupole instruments in which 'q' provided a cell for the photo-irradiation of ions selected by 'Q1'; the products of which were analyzed in 'Q3'. The concept of an analytical triple quadrupole (QqQ) mass spectrometer was developed further in 1975 when Enke and Yost proposed the concept to the National Science Foundation (NSF) and the Office of Naval Research (ONR). Funding from ONR arrived the next year and subsequently Yost left for Morrison's lab to perform the first QqQ experiments in the fall of 1977. Both laboratories at LaTrobe and Michigan State published papers utilizing the QqQ, LaTrobe for photodissociation and Michigan State for low energy collision induced dissociation. In 1978, both teams collaborated on publishing a joint paper describing their QqQ research.

James Douglas Morrison

Morrison about the time of his retirement from Latrobe University

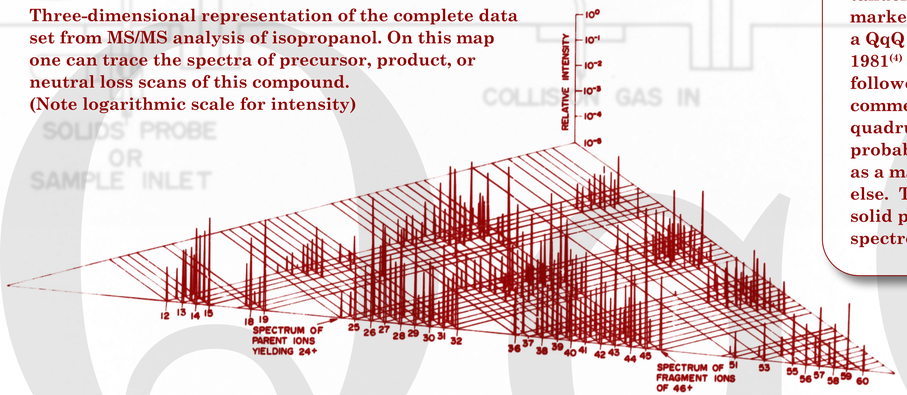
James Douglas Morrison was born in Glasgow Scotland in 1924. His undergraduate education at Glasgow University was accelerated so that he could enter the military after graduation. Fortunately World War II ended when he graduated in 1945 so he was able to continue his education under J. M. Robertson pursuing a doctorate in X-ray crystallography. In 1949, Morrison was encouraged by his graduate school colleagues to move to Australia and join the staff of the Australian Council for Scientific and Industrial Research (CSIR, later to become CSIRO).

Despite his training in X-ray crystallography, he was charged with putting to use a recently arrived CEC 21-102 mass spectrometer. He decided that the mass spectrometer provided 'a wonderful way to measure bond energies'. In due time, he abandoned the CEC instrument to build his own mass spectrometers after being awarded a Harkness Fellowship and spending a year at the University of Chicago working with Mark Inghram, one of Al Nier's early students. While there, he and Inghram built a photo-ionization source. His research in this area later led to the development of a triple quadrupole instrument. Morrison was a frequent visitor to the States, with stays at Princeton, the University of Chicago, and the University of Utah; as well as regular attendance at this conference from 1964 onwards.

LOW ENERGY CID (LE-CID)

Naturally, given the operating conditions of the QMF, the collision energy in q was orders of magnitude lower than that experienced in tandem instruments based on magnetic sector analyzers. While most believed, based on sector experience, that low energy collisions would be less efficient in producing fragments for further study, the opposite in fact was the case. Work presented at this conference in 1978 demonstrated that the use of the 'rf only' q as a collision cell led to high collision efficiencies; up to 65% at energies in the 5 to 20 eV range.[2]

Three-dimensional representation of the complete data set from MS/MS analysis of isopropanol. On this map one can trace the spectra of precursor, product, or neutral loss scans of this compound. (Note logarithmic scale for intensity)



COMMERCIAL DEVELOPMENTS

In 1980, Hunt, Shabanowitz and Giordani used Finnigan quadrupole parts to create the triple stage quadrupole (TSQ) tandem mass spectrometer[3], later marketed by Finnigan. Sciex produced a QqQ instrument, the TAGA 6000, in 1981[4] and Extranuclear and Nermag followed suit in later years. The commercialization of the triple quadrupole tandem mass spectrometer probably did more to 'legitimize' the QMF as a mass spectrometer than anything else. Today, the triple quad has earned a solid place as a powerful tandem mass spectrometry tool.

References

1. Eichelberger, J. W.; Harris, L. E.; Budde, W. L., *Reference Compound to Calibrate Ion Abundance Measurements in Gas Chromatography-Mass Spectrometry Systems.* Anal. Chem. 1975, 47 (7), 995-1000.
2. Yost, R. A., Enke, C. G., *Selected Ion Fragmentation with a Tandem Quadrupole Mass Spectrometer.* Bound volume of ASMS Proceedings, 1978.
3. Hunt, D. F.; Shabanowitz, J.; Giordani, A. B., *Collision Activated Decompositions in Mixture Analysis with a Triple Quadrupole Mass Spectrometer.* Anal. Chem. 1980, 52, 386-90.
4. *1981: TAGA 6000*
   Introduced in 1981, the TAGA 6000 was the first commercial triple quadrupole MS/MS instrument that spawned today's multi-million dollar mass spectrometry industry.
   (from http://www.sciex.com/timeline)

1971
- Morrison spends year at University of Utah as visiting Professor
- November: Morrison suggests QqQ to Futrell for collisional activation

1972
- Lampe constructs QQ for studying ion-molecule reactions

1973
- Denton constructs QQ (notch filter/mass analyzer)

1974
- Futrell and Vestal complete the QqQ at Utah and use it for photodissociation studies
- Enke conceives of an intelligent computer-controlled general analytical instrument

1976
- Cooks uses MIKES to perform mixture analysis

1977
- November: Morrison and McGilvery submit QqQ PD paper

1978
- May: Enke and Yost present first analytical QqQ paper at ASMS meeting in St. Louis
- Vestal & Mauclaire use QqQ for photodissociation exp.
- Cooks and Hunt both make tandem quadrupole instruments

1979
- Cooks' group investigates low energy CID with angle resolved MS
- LE-CID described in rf-only collision cell and metrics defined to characterize CID efficiency