Thermo Fisher Scientific: A Legacy of Over 70 Years of Innovation in Mass Spectrometry

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The mass spectrometry business of Thermo Fisher Scientific Inc. (TFS) has multiple pedigrees as the overall enterprise has been assembled by multiple acquisitions over the past 28 years. Portions of its ICP MS technology and its FT spectral processing technology have, respectively, VG/Micromass (Manchester, UK) and Nicolet Instruments (Madison Wisconsin, USA) heritage. The company's Orbitrap analyzer technology originated with HD Instruments of Manchester, UK. Its Field Asymmetric Ion Mobility (FAIMS) technology originates from Ionalytics (Ottowa, Canada). However the majority of TFS's MS enterprise traces its origins to Atlas MAT (Bremen, Germany) and Finnigan Instruments (Palo Alto, CA USA) .

With the acquisition of MAT by Finnigan Instruments in 1981, the combined enterprise became known as Finnigan MAT. Later, after acquisition by a subsidiary of Thermo Electron Inc. in 1990, the combined enterprise's name became successively Thermo Quest Inc. (1995), Thermo Finnigan Inc.(2000), Thermo Electron Inc (2002) and since 2006, Thermo Fisher Scientific Inc. The parallel timelines below attempt to illustrate the, at first, separate and, after 1981, joint history of the MAT and Finnigan legacy enterprises from their founding through to the commercial introductions of radial ejection quadrupole linear ion trap and Orbitrap analyzer technology . Naturally when trying to represent such a long rich history in such a limited space, there are inevitable omissions of noteworthy events. The author has tried to emphasize events and technological developments that were most influential to these enterprises and the practice of mass spectrometry in general. He has relied on the following documents and his own memory.

ten Noever de Brauw, Michael C. "A Short Story About the Life of Curt Brunnée."
Rapid com. in mass spec. 11.6 (1997): 708-713.
Brunnée, Curt. "50 Years of MAT in Bremen." *Rapid com.in mass spec.*11.6 (1997): 694-707.
Finnigan, Robert E. "Quadrupole mass spectrometers." *Anal. Chem.* 66.19 (1994): 969A-975A.

Ludolf Jenkel
He was the founder, technical visionary and driving force of the MAT enterprise during its early decades. His powers of persuasion must have been formidable. He served as the general manager of the organization from 1962 -1974.

Curt Brunnée
Joining MAT as a R&D scientist 1956, he served in multiple technical leadership roles including that of director of research for all of Finnigan MAT . His legacy as a scholar, scientist and developer of many MS instruments is reflected in the Curt Brunnée award which given to a promising young scientist who has made essential contributions to the field at each International Mass Spectrometry Conference.

Karleugen Habfast
He joined MAT as a R&D scientist in the early 1960's. Author of numerous patents and journal articles related to isotope ratio MS (IRMS) instrumentation, from the 1970s on into the 1990's he was the creative force that drove MAT's IRMS technology to preeminence.

Alexander Makarov
His invention of the FT Orbitrap analyzer and his technical leadership of the commercialization and continuing development of the technology has had a profound impact on the practice of mass spectrometry. In 2008, for this work he received the ASMS award for distinguished contribution.

1947 — Ludolf Jenkel, a young physicist, convinces his employer, Atlas-Werke AG (Bremen, FRG), to allow him half time leave to build a MS.

1948 - 1949 — The construction of the MS-1 prototype 60° Magnet Sector MS is completed in a rented room in the basement of a Bremen hospital. After some refinements, the instrument is sold to Bayer, AG. Thereafter L. Jenkel convinces Atlas to form a small division, **Mes und Analysen-Technik (MAT)**

1950 — **CH3** This was Atlas MAT's first product, It was single focusing Sector MS. It was not very competitive with the offerings of CEC and Metro Vick so for years Atlas MAT operated on the brink of dissolution.

1958 — **CH4** This was Atlas MAT's second product. It was also a single focusing sector MS, it was MAT's first truly competitive and successful product. After its introduction, the MAT enterprise became sustainable though not reliably profitable.

1962 — **CH4 GC/MS** It was the company's first offering to address the emergent GC/MS technique. Sales were slow until L. Jenkel, ignoring conference rules, set up an instrument and did demonstrations in a bar adjacent to the 1963 ASTM Conference (Proto-ASMS) .

1962 — **M86** This was MAT's first single focusing sector MS specifically marketed for Gas Isotopic Ratio Analysis

1963 — **AMP 3** Residual Gas Analyzer (RGA) It was the first commercial quadrupole mass filter (QMF) based MS instrument of any type. MAT did not begin to develop an analytical QMF MS till a decade later.

1966 — **SM1** (Organic MS) **SM1-F** (Inorganic/Spark Source MS). These were MAT's first high resolution MS instruments. They utilized a Mattauch-Herzog double focusing (EB) optics system.

1967 — **CH5** This replacement for the CH4 had a horizontal ion flight path, all solid state electronics and could attain resolutions of 10,000. Evolved versions of the CH5 were the mainstay of the MAT's Organic MS products through 1985.

1972 — **CH5 DF** It was the first double focusing sector MS of reverse (BE) geometry. This geometry enabled early MS/MS (MIKES type) spectra.

1977 — **MAT 44** GC/MS It was the first fully computer controlled quadrupole MS instrument. It featured fully hyperbolic profile QMF electrodes.

1978 — **MAT 250** (Gases) **MAT 260** (Solids) These fully computer controlled instruments shared a common analyzer platform that was specifically optimized for IRMS. They were the basis of a series dominantly successful IRMS instruments .

1981 — **MAT was acquired by Finnigan Instruments. The joint enterprise become known to customers as Finnigan MAT.** MAT had previously been acquired from Atlas by the Krupp Group AG in 1966 and then a by Varian Associates Inc .in 1967.

1985 — **HSQ 30** It was the first BEqQ geometry hybrid MS instrument. The prototype was built at Purdue U. as a joint project with the J. Amy led Purdue U. instrument facility, R.G. Cooks's laboratory and both Finnigan MAT's Bremen and San Jose sites.

1986 — **MAT 90** It was first fully computer controlled double focusing (BE) MS.

1992 — **MAT 900 S** It was a double focusing (BE) MS with novel scanning electronic imaging ion detection system.

1993 — **ELEMENT** It was the first high resolution double focusing sector ICP- MS. It enabled trace analysis to 1 part in 10^{16}

1996 — **MAT 262** A solids IRMS sector MS with a novel retarding quadrupole optics, it provided abundance sensitivity exceeding 10^{5}.

2000 — HD Technologies LTD of Manchester UK was acquired by what is now TFS. Thereafter A. Makarov and the development of his nascent Orbitrap technology relocated to the Bremen site .

2003 — **LTQ FT** It was the first commercial hybrid RF QLT – FTICR MS. Ion trap AGC enabled the ICR analyzer to produce high resolution accurate m/z spectra during LC/MS analyses. It featured parallel operation of FTICR (MS) and the QLT Analyzer (MS^2). It was developed was in collaboration with D. Hunt's group at U. Virgina.

2005 — **LTQ Orbitrap (Classic)** This hybrid QLT-Orbitrap was the first commercial MS with an Orbitrap analyzer. The development of novel scheme for ion injection into the Orbitrap involving pulsed ion ejection from a curved RF trap (C -Trap) and the development of a high precision Orbitrap structure enabled commercialization.

1958-1962 — Quadrupole (QMF) RGAs were constructed and used in K. Shoulder's Advanced Microelectronic Research Laboratory at Stanford Research Institute (SRI), Menlo Park CA

1963-1966 — R. Finnigan, and M. Uthe, leave SRI to join Electronic Associates Inc. (EAI), where they began an enterprise building and selling Quadrupole RGAs developed from the SRI designs.

1967 — **Finnigan Instruments Co.** was founded by R. Finnigan, M. Story, R. Hein (all from EAI) and W.Fies (from SRI) to commercialize quadrupole GC/MS technology. Principal investors were Roger Sant (Syntex) and T.Z. Chu (Varian Aerograph). T.Z. Chu later joined the company and served as president and CEO till it was acquired in 1990.

1968 — **Finnigan 1015** Quadrupole MS. With an upper m/z limit of 750 Th, it was the first commercial analytical quadrupole MS. A GC/MS version of the instrument appeared shortly thereafter.

1969 — System Industries Inc. was founded in space shared with Finnigan Instruments. Its initial product was a PDP 8 based MS Data system (DS) – **System 150** - based on the DS developed in J. Lederberg's laboratory at the Stanford U. Medical School for the first ever delivered Finnigan 1015 MS.

1970 — A **Chemical Ionization (CI)** option for the Finnigan 1015 was developed by M. Story with M. Vestal under contract with H. Fales and B. Milne of the U.S. National Institutes of Health.

1971 — US EPA Purchases 20 Finnigan 1015 GC/MS DS Instruments. It was the financial salvation of the enterprise. Over the next decade EPA and industry scientists establish quadrupole GC/MS DS as the technology of choice for priority pollutant analyses.

1976 — **Finnigan 4000** This was the first of a family of high performance QMF based GC/MS instruments that were not a direct evolution of the original Finnigan 1050.

1976 — **Moving Belt LC/MS Interface** It was the first LC/MS Interface and it enabled EI, CI and NCI of compounds eluting from an LC. W.H. McFadden led its Development.

1977 — **PPNICI** Pulsed Positive Ion - Negative Ion CI. The ability to analyze positive and negative ions in alternating scans was enabled by G. Stafford's invention of the negative ion conversion dynode detector.

1980-1981 — **TSQ** GC/MS. A small enterprise inside the Finnigan research group led by M. Story and C. Boitnott began building and marketing QqQ MS instruments based on the Finnigan 4000. R.Yost, D. Hunt and R.G. Cooks were early recipients of these instruments.

1982-1983 — The fully hyperbolic profiled QMF design developed by MAT was incorporated into the **Finnigan 4600** and its QqQ counterpart, the **TSQ 46**. To this day, all of the TFS's high performance QMF instruments have utilized hyperbolic profiled QMF s.

1983-1984 — **ITD 700** 3D Ion Trap GC/MS Detector It was the first commercial Paul type quadrupole ion trap MS. It employed G. Stafford's mass selective instability (MSI) scanning method and used Helium damping gas.

1986 — **TSQ 70** GC/MS Triple Quad This fully computer controlled QqQ instrument was designed to fully enable data dependent MS/MS methods. It utilized a curved collision cell to suppress excited neutral noise from FAB & LSIMS ionization.

1986 — **ITD 800** 3D Ion Trap GC/MS Detector The first ion trap MS to utilize the AGC concept for regulating trapped ion populations. Initially realized by D. Taylor and S. Bradshaw, AGC is an enabling technology for RF ion trap MS.

1985-1994 — Led by G. Stafford, Finnigan MAT R&E staff (often in collaboration with R. G. Cooks's group at Purdue U.) pioneered much of RF ion trap MS technology: ion trap CI , MS^n , MSI with resonant ejection, high m/z range scanning, high resolution scanning, isolation waveforms, external ion injection and the radial ejection MSI scanning linear ion trap concept.

1992 — A Heated Metal Capillary- Tube Lens-Skimmer API was Interface developed by M. Hail and I. Mylchreest based on B.Chait and his group's (Rockefeller U.) invention. This basic design is still used in many TFS LC/MS instruments.

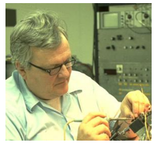
1995 — **GCQ and LCQ** These were fully automated GC/MS^n and LC/MS^n 3D ion trap instruments. The LCQ was an enabling tool for "Shotgun" proteomics methods.

2003 — **LTQ** This was the first commercial radial ejection MSI QLT MS. With a 30× higher ion capacity, and a 30× fold higher ion injection efficiency relative to its predecessor 3D QIT instruments, it could generate 5 quality data dependent MS/MS spectra/sec and MS^n (n>2) spetra without averaging.

2004 — Electron Transfer Dissociation (ETD) D.F. Hunt's Group at U. VA published and presented the first ETD results. The work was a collaborative effort between the Hunt Lab and TFS. An ETD product was introduced in 2006.

Robert Finnigan
His persistence in pursuing his vision of computerized QMF GC/MS instrumentation led to the founding of the company. Through the 1970s he worked closely with both US EPA and industry laboratories developing the studies and compiling the data to establish that quadrupole GC/MS DS systems were, both in terms of quality of data and cost effectiveness, the most effective instrumentation for priority pollutant analyses.

Michael Story
A Finnigan co-founder, his early contributions included refining the ultra high precision design and fabrication processes for QMF structures, ion source and vacuum system design, and the suppression of Helium related neutral noise. Later as VP of Research, he fostered the development of the first LC/MS interface, the mass selective instability ion trap MS, the organization's first commercial QqQ instrument and, after the acquisition of MAT, the integration of the MAT and Finnigan R&D efforts.



William Fies
A Finnigan co-founder, he developed the concepts for generation and precision control of the QMF analyzer voltages that are necessary to provide stability in m/z assignment, m/z resolution and ion transmission which enabled quantitative operation of analytical QMF MS instruments.

George Stafford
His invention of the negative ion conversion dynode detector was a practical enabler for negative ion MS. His invention of RF ion trap mass selective instability scan, for which he received the ASMS award for distinguished contribution in 2001, led to the commercialization of the RF ion trap. He served nearly 30 years as the technical leader of the company's ion trap MS R&D effort.