The History of Quadrupole Mass Spectrometry at VG - Micromass - Waters

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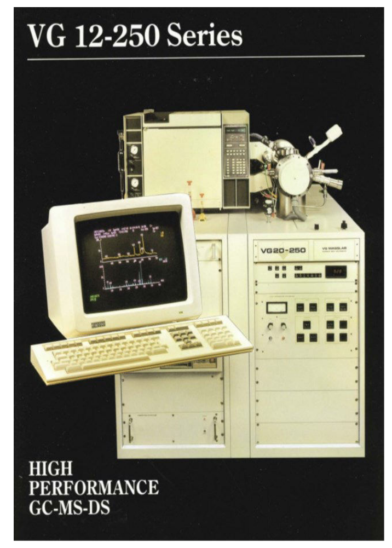
COMPANY BACKGROUND

VG Instruments was formed in 1962 (Vacuum Generators Limited) to provide ultra-high vacuum components and systems. In 1970, VG Micromass was formed to specialise in mass spectrometry and in 1974 was fragmented into four: VG Isotopes, VG Organic, VG Quadrupoles and VG Inorganic. VG Organic moved to Altrincham, South Manchester, UK, along with VG Data Systems. The rationale behind the repeated formation of small companies was Bernard Eastwell's 'Christmas card principle' : most people send Christmas cards to between 50 and 100 people, and this represents a natural maximum number of people with whom to associate in a company. In 1980, VG Analytical was formed, followed by VG Masslab (1984), VG Tritech (1985) and VG Biotech (1988).


VG Altrincham Facility *c.*2000

SINGLE QUADRUPOLES

The first quadrupole mass filters from the VG stable were introduced in 1971 by VG Quadrupoles, with the Q7 (m/z range 120) and the Q8 (m/z range 300), and were made available in either kit form or as complete analytical systems. Both the Q7 and Q8 used 6mm quadrupole rods for residual gas analysis (RGA) applications. These instruments were followed by the Q40 and Q50 devices that used 12mm and 18mm quadrupole rods, respectively (1).



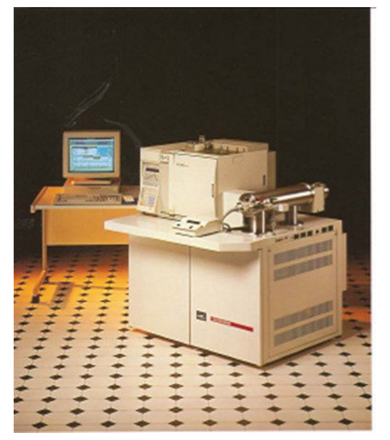
VG 12-250

The first computer-controlled quadrupole instrument was the VG12-250 introduced in the early 1980s by VG Masslab. The 12-250 was promoted as a 'compact, computer-controlled integrated mass spectrometer-data system package giving unprecedented high performance for LC-MS and GC-MS', and was available with EI/CI, Thermospray, moving belt LC-MS and Fast Atom Bombardment ion sources. The data system was a PDP11-73 with a massive 70MB system storage and a 90MB streaming tape.

In 1985, VG MassLab introduced the benchtop GC/MS TRIO-1 instrument with a *m/z* range of 1000, and incorporated the same quadrupole assembly as was used across all the quadrupole range. It had


TRIO 1

The second generation of the TRIO-1 in 1988, the TRIO 1000, saw the introduction of the PC-based data system and LabBase instrument control and data processing. The TRIO-2 was a research-targeted multi-inlet (GC/LC-MS) single quadrupole instrument with an increased mass range vs the TRIO-1.


TRIO 2

In 1993 VG Biotech introduced the multi-inlet Platform single quadrupole, a compact benchtop instrument intended as a detector for the chromatographer's bench. This was the first time that external design consultants were used by VG in the development of an instrument. Electrospray capabilities were updated to accommodate LC flow rates of up to 1.0mL/min that served to interface with 4.6mm HPLC columns. This was the first instrument to be launched with the Windows-based MassLynx data system. Other capabilities that were introduced with the Platform series included Open Access analysis for synthetic chemists, and the MaxEnt deconvolution software for use in the analysis of proteins. There were also a number of these instruments that were modified to deliver accurate mass measurement (<5ppm to m/z 500) in a routine environment using 18-bit Digital to Analog converters(2).


VG Platform

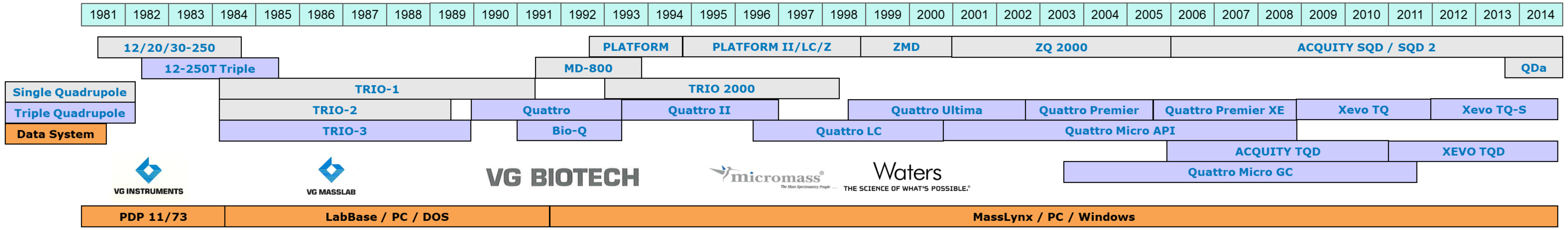

ZMD 2000

In 2000, a pair of instruments based on the same architecture was released - the Waters ZQ single quadrupole and the Quattro micro triple quadrupole. Both of these instruments were designed to be part of an LC-MS system.


ZQ 2000

The integration with liquid chromatography was taken a step further in 2005 with the delivery of the single and tandem quadrupole instruments designed to work with the ACQUITY UPLC system, cunningly entitled the SQD and TQD, facilitating method


ACQUITY SQD



1981 | 1982 | 1983 | 1984 | 1985 | 1986 | 1987 | 1988 | 1989 | 1990 | 1991 | 1992 | 1993 | 1994 | 1995 | 1996 | 1997 | 1998 | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014

Single Quadrupole
Triple Quadrupole
Data System

12/20/30-250
12-250T Triple
TRIO-1
TRIO-2
TRIO-3
MD-800
PLATFORM
PLATFORM II/LC/Z
TRIO 2000
Quattro
Bio-Q
Quattro II
Quattro LC
ZMD
ZQ 2000
Quattro Ultima
Quattro Premier
Quattro Premier XE
Quattro Micro API
Quattro Micro GC
ACQUITY SQD / SQD 2
ACQUITY TQD
Xevo TQ
Xevo TQ-S
XEVO TQD
QDa

VG INSTRUMENTS
VG MASSLAB
VG BIOTECH
micromass
Waters

PDP 11/73
LabBase / PC / DOS
MassLynx / PC / Windows

The current state-of-the-art single quadrupole, the QDa, was launched in late 2013, and specifically designed as a detector for use with liquid chromatography. The QDa was the first mass detector fully configured within an LC stack, with the intention of bringing the benefits of mass spectrometry to the chromatographer, and incorporated built-in calibration and operation with broad tuning parameters.


QDa

TANDEM QUADRUPOLES

The first triple quadrupole instrument from VG Masslab in 1984 was the TRIO 3 with dual optical detectors and controlled with a PDP11/73 data system. The dual detectors permitted switching between MS and MS/MS modes in 50ms, and allowed mixed mode scanning experiments as well as data-dependent analyses.


TRIO 3

The first, dedicated atmospheric pressure ionisation triple quadrupole was introduced in 1991 as the VG Bio-Q, with electrospray ionisation. The Bio-Q was marketed primarily for infusion analysis of proteins, in combination with MaxEnt deconvolution. This instrument was also the last quadrupole system that used diffusion vacuum pumps.


Bio Q

In 1994, the Quattro I was followed by the Quattro II which was a multi-inlet tandem quadrupole instrument, and was the last EI/CI/ Atmospheric Pressure Ionisation switchable tandem quadrupole, with all future tandem quadrupoles benefitting from being dedicated for vacuum or atmospheric based ionisation inlets.


Quattro II

The first benchtop triple quadrupole was the Quattro LC, introduced in 1996, which had mass range options of *m/z* 1,600 and *m/z* 4,000 depending on the target applications. This was the first Micromass instrument to use RF-transfer lenses between the ion source and the analyser. The Quattro LC also saw a move away from the embedded transputer control system to embedded PC control, as well as the introduction of the dual-orthogonal Z-spray API ion source, internally referred to as the 'goldfish bowl'.


Quattro LC

The introduction of the multiplex (MUX) interface in 1999 allowed for the introduction of 4 or 8 parallel LC streams simultaneously into the ESI source.

The drive for the highest possible levels of instrument sensitivity led to the exploration of multiple stages of differential pumping in the transport region between the ion source and the mass analyser. The Quattro Ultima was introduced in 2000, with two stages of differential pumping, and a revised detector with greater gain. This was superseded by the Quattro Ultima Platinum in 2002, which included for the first time, RF ion tunnels in place of the hexapole RF ion guides.


Quattro Ultima Pt

When it was introduced in 2001, the Quattro micro was the smallest tandem quadrupole instrument commercially available. This instrument was a start in addressing the increasing cost of laboratory bench space and the need to increase lab productivity. The Quattro micro was the first MS/MS instrument available for *in vitro* diagnostic (IVD) applications, with an initial focus on neonatal metabolic screening.


Quattro micro

In 2003, the Quattro micro GC was introduced, with direct probe EI/CI capabilities alongside a GC interface.


Quattro micro GC

With the adoption of faster chromatography and the need to quantify higher numbers of compounds to increase laboratory throughput, the speed of multiple reaction monitoring (MRM) analysis became limited by the residence time of the ions in the collision cells. This was addressed in the Quattro Premier with the introduction of a travelling wave (T-Wave) RF device as the collision cell between the two mass-analysing quadrupoles.


Quattro Premier

The ACQUITY SQD/TQD systems were the first quadrupole instruments designed to cope with UPLC separations in 2005. The next iteration, the Xevo TQD in 2010, included the addition of the universal ion source architecture, stacked-ring ion guides in the source transfer optics, and new


Xevo TQD

The Xevo TQ was introduced in 2008 as a high-performance instrument and brought the time-saving and consistency of automated acquisition and processing method creation to market, along with the capability to perform GC/MS on an atmospheric pressure ionisation mass spectrometer with the APGC interface. The Xevo TQ also saw enhancements in usability with the introduction of the Universal Ion Source that would allow for a full range of ionisation techniques to be used from ESI/APcI/EScI to APGC, APPI, ASAP, nano-ESI and Trizaic. The Xevo TQ also contained the T-Wave collision cell, and some new modes of operation were introduced with the ability to trap and release ions in synchronisation with the scanning of the second quadrupole mass filter.


Xevo TQ

In 2010, a breakthrough in ion optical design was made with the introduction of the StepWave ion guide, specifically designed to capture as much of the ion beam as possible from the atmospheric pressure region after entry into the high vacuum system of the mass spectrometer. The dual ion tunnel design of the Stepwave ion guide enabled the efficient extraction of ions from the primary plume entering the vacuum region, and the rejection of unwanted particles/neutrals.


Xevo TQ-S

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(1) R H Bateman in K R Jennings (Ed.) A History of European Mass Spectrometry, IM Publications, (2012).
(2) A N Tyler, E Clayton and B N Green, Anal.Chem. 68 (1996) 3561,