AGILENT IN MASS SPECTROMETRY

OVERVIEW

Mass spectrometry is a powerful technology for chemical analysis. It can be used to identify unknown compounds, quantify known compounds, and obtain information about chemical structure. The ability of mass spectrometry to do all of this for minute amounts of chemicals—often less than a billionth of a gram—make it a highly useful technique in both established and emerging branches of science.

Mass spectrometers work by determining the weights and numbers of molecules in a sample. Frequently they also fragment the molecules and determine the weights of the molecular fragments. The resulting information about the weights and abundances of the molecules and molecular fragments is collected and displayed in what are called mass spectra. Like a fingerprints, mass spectra can be used to positively identify chemicals.

Gas chromatography and liquid chromatography are techniques for separating complex mixtures of chemicals. A gas chromatograph (GC) or liquid chromatograph (LC) is very often combined with a mass spectrometer (MS) into a GC/MS or LC/MS system. Using chromatography before mass spectrometry makes it easier for the mass spectrometer to identify all of the individual chemicals in complex samples.

Agilent Technologies has long been a leading supplier of gas chromatographs, liquid chromatographs, and mass spectrometers. Its products have earned a reputation for excellent performance, reliability, and ease of use. Agilent's MS portfolio includes instruments built around five main configurations – single quadrupole, triple quadrupole, ion trap, time-of-flight (TOF) and quadrupole time-of-flight.

According to customer benchmarking studies, a shortcoming of MS systems to date has been their tendency to break down and require frequent servicing. Thus, when Agilent's engineers set out to create the new 6000 Series family of LC/MS systems—which includes single quad, triple quad, ion trap, TOF, and Q-TOF instruments—they focused not only on matching or exceeding the performance of competitive instruments, but also on creating a new standard for reliability.
APPLICATIONS

Mass spectrometry has long been a mainstay in applications that involve the analysis of small, thermally stable organic compounds, inorganic compounds, and metals. More recently, the development of new technology has dramatically increase the ability of mass spectrometers to analyze large, relatively fragile biological molecules such as proteins, opening vast new applications for MS. Important applications and markets for MS include:

**Pharmaceutical:** Mass spectrometry plays an important role in the entire life cycle of a drug, from discovery to development to manufacturing. In drug discovery, LC/MS systems are the method of choice for identifying and characterizing of drug candidates produced by combinatorial chemistry or extracted from natural products. They are also a primary tool used to check drug compound quality during manufacturing.

**Proteomics:** Proteomics is the large-scale analysis of proteins for disease research and drug discovery. MS analysis is a fundamental tool for proteomic research. In addition to LC/MS instruments for identifying and quantifying proteins in biological samples, Agilent has developed wide range of complementary technologies to help researchers prepare, separate, analyze, identify, and interpret challenging protein samples.

**Metabolomics:** This emerging area of research involves the study of large sets of metabolites found in tissue at a given time, looking for correlation with health or various diseases. Agilent is particularly well-suited to provide metabolomics scientists the tools they need, including: sample preparation supplies, GC/MS and LC/MS instruments, software for identifying and comparing compounds, and metabolite database and library to facilitate this research.

**Environmental:** The ability to identify and quantify pollutants is essential to maintaining a health environment. A mainstay of environmental testing, GC/MS is used to detect volatile organic compounds such as pesticides. Agilent is the worldwide leader in GC/MS. Inductively coupled plasma mass spectrometry (ICP-MS) helps identify and quantify inorganic compounds and heavy metals. LC/MS is a popular complement to GC/MS; it can analyze more fragile chemicals that may not stand up well to GC/MS analysis.

**Food safety:** GC/MS, LC/MS and ICP-MS are widely employed for food safety testing, which includes the analysis of additives, residues, contaminants, and toxins in agricultural products and foods. The need for food testing is growing rapidly, driven by the liberalization of global trade, a more stringent regulatory environment, and increased public awareness of food safety issues.

**Forensics:** Agilent is the worldwide leading provider of GC/MS systems for drug screening and toxicology. As with the environmental industry, Agilent LC/MS systems are beginning to be employed for forensic analyses as a complement to GC/MS. ICP-MS coupled to laser ablation (LA-ICP-MS) is also useful for measuring solid samples as well as for elemental fingerprinting of materials in forensic investigations.

**Homeland Security:** Agilent MS systems help government, military, law enforcement, and health agencies to quickly detect and identify chemical compounds that pose an environmental or health threat. GC/MS can analyze toxic gases and volatile organic compounds, while LC/MS is appropriate for low-volatility organic compounds. ICP-MS is suited to the analysis of toxic metals and metal-containing compounds.

**Hydrocarbon Processing/Energy Research:** HPI comprises the petroleum, petrochemical, fine and specialty chemical, natural gas, industrial gas, and fuel cell industries. Agilent mass spectrometers, particularly GC/MS systems, are routinely used to analyze product quality and process performance in QA/QC and process control. They’re also widely used to analyze feedstocks, intermediate products and finished biofuels.
**Semiconductor:** Agilent provides innovative and reliable ICP-MS instrumentation for accurate analysis of the ultra-high purity materials used in semiconductor fabrication. Major ICP-MS applications include the characterization of bulk and process chemicals used in semiconductor manufacture, the analysis of organic and metal contaminants on silicon wafer surfaces, and the analysis of volatile organic solvents used during the manufacture of final components such as disk drives and circuit boards.

**MAJOR PRODUCTS**

**5975C inert GC/MSD**—This market-leading GC/MS features novel Trace Ion Detection for unmatched signal-to-noise ratio, user interface that allows the electronic sharing of application methods. The redesigned hyperbolic mass analyzer features a higher mass range capability, providing quality data for higher mass range applications.

**7000A Triple Quadrupole GC/MS**—combines the reliability of the best-selling 5975C with the superior sensitivity and selectivity of a triple quadrupole instrument. This performance and reliability is anchored by Agilent’s proprietary, well-proven heated monolithic gold plated hyperbolic quartz quadrupole analyzer that is known for its superior stability.

**240 Ion Trap GC/MS**—This system combines the flexibility (multiple ionization and scan modes) of an ion trap MS with the rugged performance and advanced Capillary Flow Technology of the Agilent 7890A gas chromatograph. Applications include environmental analysis, materials testing, food quality measurement and a wide range of research and routine analyses performed in government and academic labs.
7200 Quadrupole Time-of-Flight GC/MS — It delivers a new level of chromatographic and spectral resolution to a wide range of biological and chemical analyses to help researchers coax more qualitative and quantitative information out of increasingly complex samples. Applications include environmental analysis, sports-doping detection, energy research, natural products research, and energy research.

6100 Series Quadrupole LC/MS systems — the 6100 Series dramatically reduces the size of Agilent's workhorse single quadrupole LC/MS. Offered in a range of price and performance combinations, these easy to use single quad systems have the ruggedness and reliability required for high-throughput applications. They are used in everything from environmental testing to pharmaceutical QA/QC. Recent advances provide industry leading scan speed and ultra-fast POS/NEG switching with excellent spectral quality.

6400 Series Triple Quadrupole LC/MS — The power of triple quadrupole (QQQ) instruments is their ability to quantify trace compounds in complex mixtures. The Agilent 6410 provides femtogram sensitivity with an unprecedented cost of ownership. The Agilent 6490 with iFunnel technology delivers breakthrough 10x more sensitivity than comparable instruments, boasting a zeptomole level detection limit.

6220 Accurate Mass Time-of-Flight LC/MS — The 6220 Accurate Mass TOF is ideal for high-throughput expression studies for metabolomics, product degradation studies, protein characterization, and metabolomics programs. Recent enhancements deliver exceptional accurate mass of better than 2-ppm mass accuracy combined with 20,000 mass resolution and 32 gbit/second high speed data acquisition.

6550 iFunnel Quadrupole Time-of-Flight LC/MS — Agilent's new bench-top 6550 dramatically redefines Q-TOF performance compared with other Q-TOF and orbital trap systems. It delivers unmatched sensitivity down to femtogram levels, exceptional data quality, and superior mass accuracy, mass resolution, dynamic range and speed.
6300 Series Ion Traps LC/MS systems – This upgraded family of ion trap LC/MS systems features four different instruments covering a range of budget and performance requirements. New libraries for drugs of abuse and pesticides are available to provide confident identification of critical compounds. Alternatively, the MS/MS spectra can be exported to a program that determines compound structures from fragmentation spectra. The full featured 6340 ion trap incorporates a patented device for electron transfer dissociation (ETD). Peptide fragmentation with ETD has proven very useful for precisely locating post-translation modifications. With attomole sensitivity the 6340 is the ideal LC/MS system for proteomics.

LC/MS Ion Sources – The ionization source is a critical component in mass spectrometers. Agilent has long been a leading innovator in ion source technology and offers the industry’s widest selection of interchangeable LC/MS ion sources. Of particular note are two recent inventions. Agilent HPLC-Chip/MS technology puts LC columns, fittings, and ion source components onto a polyimide chip the size of a microscope slide. This eliminates 50% of valving, tubing, and connections between a nanoflow LC and MS, dramatically increasing sensitivity, reliability, and ease of use. An automated interface between the LC and MS handles all connections and chip positioning.

The other major invention is the multimode source. Unlike any other LC/MS source, the multimode source can effectively operate in two of the most important ionization modes, electrospray (ESI) and atmospheric pressure chemical ionization (APCI), simultaneously. Since many compounds ionize well only by one technique or the other, the multimode source can double productivity when analyzing unknowns. It eliminates the need to run samples twice to ensure that all compounds are detected.

7500 ICP-MS – The Agilent 7500 ICP-MS comes in three models to precisely meet application requirements. The 7500a is a full-featured, high-performance ICP-MS system designed for flexibility and routine operation. For semiconductor applications, the 7500cs features a new high-sensitivity version of the ORS to resolve even the toughest analytical challenges faced by the semiconductor and research lab. The new Agilent 7500ce ICP-MS is specifically designed for trace-metals analysis in environmental applications, providing the highest sensitivity, interference reduction and stability for complex, high-matrix samples.
HISTORY

Prior to 1999, Agilent Technologies was part of Hewlett-Packard (HP). In 1999, HP announced a strategic realignment to create an independent measurement company composed of its test and measurement, chemical analysis, and medical businesses. This measurement company was named Agilent Technologies. Agilent became a fully independent company in June 2000.

1965 HP enters the analytical instrumentation field with the acquisition of GC manufacturer F&M Scientific Corporation of Avondale, Pennsylvania. The acquisition allows HP to further expand its measuring and testing expertise into the area of chemical analysis.

1976 HP introduces world’s first integrated, digital benchtop GC/MS system, the 5992. The 5992 also features the world’s first true hyperbolic chromium – molybdenum alloy (Cr/Mo) quadrupole mass filter.

1985 HP offers a thermospray interface – an early breakthrough in interfacing LC and MS instruments.

1988 HP introduces the 5971 MSD, the world’s first mass spectrometer to employ a true hyperbolic glass quadrupole.

1992 ShieldTorch interface developed for ICP-MS, which virtually eliminates Ar interferences, enabling ppt analysis of K, Ca, Fe by ICP-MS.

1994 HP introduces world’s first benchtop ICP-MS system, the 4500.

1997 HP introduces its first benchtop quadrupole LC/MS, the 1100 Series LC/MSD.

Mar 2000 Agilent introduces its first benchtop ion trap LC/MS, the 1100 Series LC/MSD Trap.

May 2001 Agilent introduces an atmospheric pressure photoionization (APPI) source for its quadrupole and ion trap LC/MS systems.

Jun 2002 Agilent introduces an atmospheric pressure matrix-assisted laser desorption/ionization (AP-MALDI) source.

Jun 2003 Agilent introduces its first benchtop time-of-flight LC/MS system.

May 2004 Agilent introduces breakthrough HPLC-Chip/MS technology.

Feb 2005 Agilent introduces first simultaneous multimode ion source for MS.

Jun 2005 Agilent introduces industry’s first GC/MS allowing electronic methods sharing.

Jan 2006 Agilent announces 1200 Series LC and 6000 Series LC/MS in the largest multi-product launch in company’s history.


Mar 2006 Agilent introduces most sensitive triple quadrupole mass spectrometer in its price class.

June, 2011
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<tr>
<th>Date</th>
<th>Event Description</th>
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<tbody>
<tr>
<td>May 2006</td>
<td>Agilent Technologies introduces innovative technology to separate proteins and peptides</td>
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<tr>
<td>May 2006</td>
<td>Agilent Technologies introduces mass spectrometry software that enables biomarker discovery</td>
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<tr>
<td>Feb 2007</td>
<td>Agilent Technologies Announces Shipment of 1,000th Rapid Resolution Liquid Chromatography System</td>
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<td>Feb 2007</td>
<td>Agilent Technologies Launches Metabolomics Initiative with New Web Site and Customized METLIN Database</td>
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<td>Feb 2007</td>
<td>Agilent Technologies Enhances MassHunter Software, Expands it to TOF Mass Spectrometer to Benefit Customers in All LC/MS Markets</td>
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<td>Jun 2007</td>
<td>Agilent Technologies' New GeneSpring MS Allows Users to Apply Tools, Visualizations to QQQ Data</td>
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<td>June 2007</td>
<td>Agilent Technologies Expands HPLC-Chip Line with High-Capacity Enrichment, Intact Protein Chips for Proteomics</td>
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<td>Nov. 2007</td>
<td>Agilent Technologies' New Accurate-Mass TOF and Q-TOF LC/MS Provide Unmatched Performance</td>
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<td>Feb 2008</td>
<td>Agilent introduces LC/MS software for browsing large sets of drug discovery data</td>
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<td>Mar 2008</td>
<td>Agilent Technologies makes powerful GC/MS capabilities accessible to a wider range of labs.</td>
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<td>Mar 2008</td>
<td>Agilent introduces LC autosampler with industry's lowest carryover</td>
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<td>Mar 2008</td>
<td>Agilent sells 500th triple quadrupole LC/MS</td>
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<td>Apr 2008</td>
<td>Agilent provides core instrumentation for University of Colorado Water Quality Lab</td>
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<td>Jun 2008</td>
<td>Agilent introduces 7000A triple quadrupole GC/MS</td>
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<td>Jun 2008</td>
<td>New Agilent triple quadrupole LC/MS breaks the femtogram detection barrier</td>
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<td>Jun 2008</td>
<td>Agilent introduces 6530 Accurate Mass Q-TOF featuring true High Definition TOF technology for superior mass accuracy, mass resolution, dynamic range, sensitivity and speed</td>
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<td>Jun 2008</td>
<td>Agilent introduces the first commercial GC/MS metabolite library</td>
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<td>Dec 2008</td>
<td>Agilent ships 10,000th 5975 Series GC/MS</td>
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<tr>
<td>Jun 2009</td>
<td>Agilent introduces next generation ICP-MS, offering unmatched data integrity, ease of use and smallest footprint</td>
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<tr>
<td>Jun 2009</td>
<td>Agilent QuEChERS method kits simplify food sample preparation for pesticide analysis</td>
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<tr>
<td>Oct 2009</td>
<td>Agilent and Institute for Systems Biology build MRM human protein atlas</td>
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Mar 2010  Agilent introduces transportable GC/MS for high performance out-of-laboratory analysis.

Mar 2010  Duquesne University and Agilent establish mass spectrometry center of excellence to study diseases, environmental issues

May 2010  Agilent completes acquisition of Varian, marking historic milestone for two Silicon Valley pioneers

May 2010  Agilent introduces triple quadrupole LC/MS with iFunnel Technology, delivering breakthrough 10x sensitivity

Nov 2010  Agilent expands LC/MS portfolio with ion trap instrument

Mar 2011  Agilent introduces ion trap GC/MS