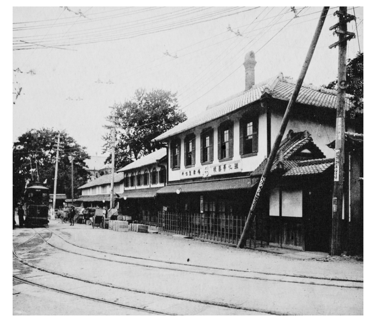
A History of Shimadzu and Mass Spectrometry Innovation

SHIMADZU
Excellence in Science

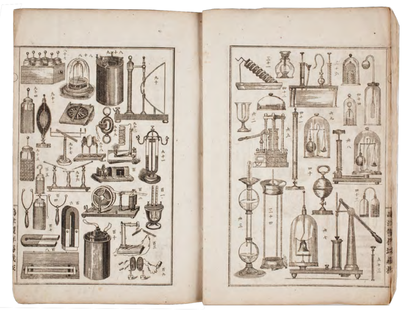
1875 Shimadzu Founded

The history of Shimadzu as a company begins with its founding in Kyoto, Japan in 1875 by Genzo Shimadzu Sr.



Genzo Shimadzu Sr.


Genzo absorbed knowledge enthusiastically by attending lectures at the Physics and Chemistry Research Institute and participating in experiments. Afterwards, he set to work repairing and maintaining foreign instruments. Genzo carefully studied each product from overseas as he repaired it with his nimble fingers. As it so happens, this was also a period of educational promotion by Japan's educational system. Until then, education had consisted primarily of reading, writing, and the abacus. But now, proponents began advocating the importance of the natural sciences. However, in those days, there was almost no educational equipment available in Japan for science education. It was at this point that Genzo decided to manufacture physics and chemistry instruments himself, with the goal of making Japan a leader in science. This decision marks the start of the Shimadzu Corporation. Around this time, Genzo began to create a Science Equipment Catalog List featuring 110 products in 5 categories.

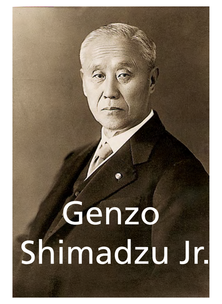
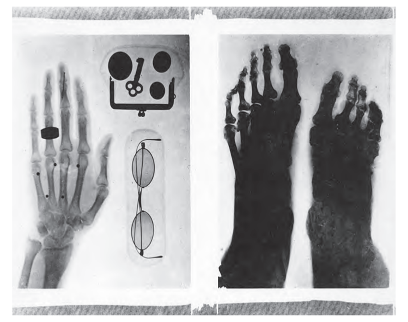

Science Equipment Catalog List

1877 Japan's First Manned Balloon Launch

Genzo Senior created a manned balloon based on a single illustration. By using his understanding of chemistry, he filled multiple sake barrels with metal and hydrochloric acid. They collected the hydrogen off-gas in tubes sending it to the balloon. As a result, he successfully launched Japan's first manned balloon. The event was promoted in response to the Kyoto Prefectural government's enthusiastic desire to stimulate public interest in scientific education.

1894 Expanding with the Times

The company was expanded by Genzo Jr. between 1894-1916 to grapple with emerging technologies such as batteries and X-ray equipment, which contributed to Japan's manufacturing industry as well as to advances in the medical field.

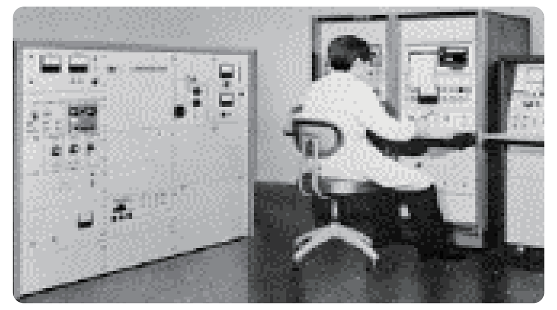

GS Storage Battery

Genzo Shimadzu Jr.


1957 First Shimadzu Gas Chromatograph was developed

Just five years after invention of the fundamental technique in 1952, Shimadzu developed its first commercial gas chromatograph, the GC-1A. The GC-1A was displayed in the spring of 1957 at the 10th annual meeting of the Japan Society for Analytical Chemistry. The GC-1A contained an integrated xy-recorder to plot the generated data. It came equipped with a TCD and its heating technology allowed for faster analysis of samples. In the first year, the unit was sold to a few customers mostly in the petrochemical and chemical industry. In 1958, Shimadzu developed the GC-2A which was the first GC to adopt a dual-column flow line with TCD allowing both sides of the detector to be used for sample analysis.

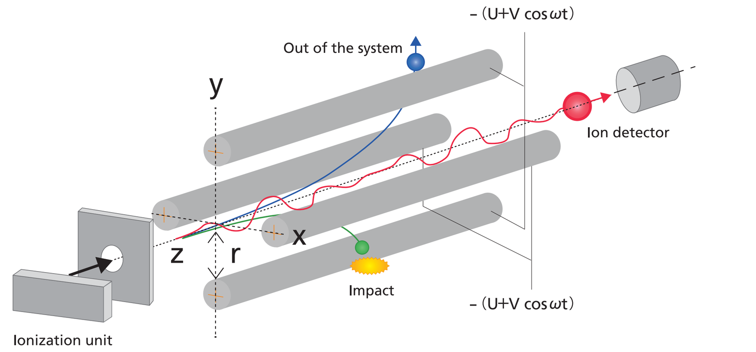
1970 First Mass Produced GC-MS to Japan

In cooperation with the Swedish firm LKB, Shimadzu introduced the world's first mass-produced GC-MS (magnetic sector MS) to Japan.[1] This formed a blueprint for future Shimadzu GC-MS devices. The LKB-9000 was revolutionary in that it could selectively remove the helium (mobile phase) from the mixture of gasses using a jet molecular separator, allowing the mass of each of the separated components of the sample to be measured.



1978 Era of Mass Spectrometry Innovation

Shimadzu engineers and scientists including Sumio Shibata, Norihito Inatsugu, Kiyoshi Shimizu, Tsunezo Takeda, and Kozo Miseki began developing the technology that would lead to our first GC-MS and LC-MS products. They worked on hyperbolic rod configurations and a soon-to-be patented deflector.[4]



1982 First Japanese Quadrupole GC-MS

Shimadzu released Japan's first general-purpose quadrupole GC-MS. The combination of high functionality and ease-of-use helped to popularize GC-MS technology in Japan. With the creation of the GCMS-QP1000, hyperbolic quadrupole technology was used. A cylindrical deflector was designed to achieve the optimum ion transmission independent of m/z. The addition of the cylindrical deflector allowed for more ions to be sent to the detector. The addition of more ions allowed for more of the higher mass ions to make it to the detector. This change made our system able to achieve a larger mass range.


GCMS-QP1000

1984 Modular Liquid Chromatograph

Shimadzu releases the LC-6A Series, one of the world's first modular LC systems, allowing for flexible arrangement of components. The pump utilized a single reciprocating plunger of 100 µL displacement. Considered unsuitable by today's pulsation standards, it nevertheless had a contoured cam and a compressibility correction circuit to allow rapid refill and compensation for solvent compressibility induced flow loss. A centralized system controller and a bench-top integrator with 176 Kbytes of memory presaged the days of PC hardware control and data processing.

1988 First Commercial MALDI-TOF MS Instrument

Shimadzu released the world's first commercial MALDI-TOF MS device, and subsequently produced various example analyses of high molecular weight compounds. This dramatically expanded the possible uses of mass spectrometry. Relevant papers were presented at the Japan-China Joint Symposium on Mass Spectrometry (Sept. 1987) and published in Rapid Communications in Mass Spectrometry, USA (1988).


From left, Koichi Tanaka (Shimadzu Corp.), Dr. Cotter (Johns Hopkins Univ.), Dr. Hotta (Kobe Women's Univ.), Dr. A. Burlingame (Univ. of California), Katsuaki Shiratsuchi (Shimadzu Corp.)

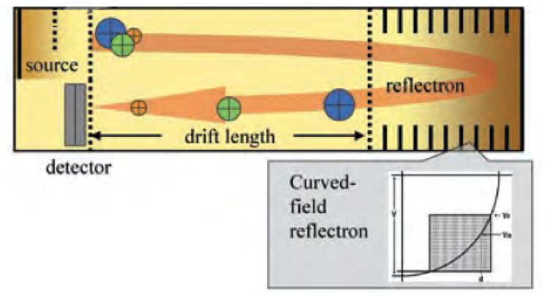
LAMS-50k in the background

1991 Shimadzu's Low-Pulsation Dual Reciprocating Pump

Ongoing LC development, driven by the demands of highly sensitive mass spectrometry detection, resulted in breakthroughs in hardware design, such as a low-displacement, low-pulsation, dual reciprocating pump. The LC-10AD pump utilized a 10 µL plunger displacement and an advanced 4-phase stepping motor (6400 pulses per rotation) with pressure feedback for steady solvent delivery. Combined with autosamplers that resist adsorption, provide multiple rinse options, and deliver sub-10 second injections, these HPLC front-ends were well suited for high-speed, high-sensitivity LC-MS/MS applications.

1993 Bob Cotter - Curved-Field Reflectron

Long-time collaborator Bob Cotter invented the curved-field reflectron with Tim Cornish at Johns Hopkins University. This technology was later commercialized in our AXIMA MALDI product lineup.[2] The curved-field reflectron improved upon existing reflectrons by focusing all ions to within a small region at the exit of the reflectron. Previous designs, such as linear field reflectrons, had to scan or step the potential gradient of the reflectron in order to focus ions across a mass range. The curved-field reflectron enabled the generation of seamless mass spectra (as opposed to the stitched mass spectra which were prevalent), enabling faster acquisition speed.



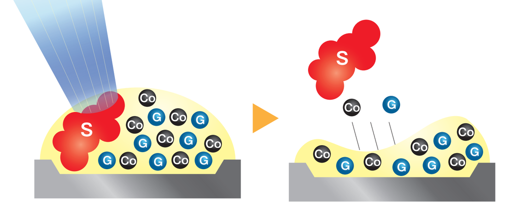
2002 First MALDI-QIT-TOF Instrument

The Axima MALDI QIT-TOF was the world's first commercially available instrument that combined a MALDI ion source with a quadrupole ion trap and a TOF analyzer. This design, first reported by He, Liu and Lubman[3], improved on traditional MALDI-TOF instruments by increasing detected ions' S/N (removal of high-intensity matrix peaks) and enabling multiple-stage MS/MS for extensive structural analysis of various biological compounds.

2002 Koichi Tanaka Shares Nobel Prize

Koichi Tanaka received the Nobel Prize in Chemistry for the development of soft desorption ionization methods for MS analysis of biological macromolecules. The Koichi Tanaka Mass Spectrometry Research Laboratory was established in 2003. Koichi Tanaka shared the award with John Fenn, honored largely for his contributions to the development of electrospray ionization, and Kurt Wüthrich, in recognition of his work in developing NMR techniques.

Tanaka began researching the development of the laser desorption ionization method in the early 1980s. While this method could easily handle comparatively small molecules, when the laser was used on biological macromolecules, it would decompose them into fragments. For this reason, the laser method was thought to be impossible for analyzing macromolecules. In experiments conducted by Tanaka and his colleagues, however, their laser-induced analysis had achieved high molecular weight results and it had been the use of a matrix to soften the power of the laser that made the analysis possible. The unique idea of adding cobalt ultra-fine metal powder to the matrix (patent: JP01731501) came from Yoshikazu Yoshida.


Progress stalled until an accidental mixing mistake occurred. Tanaka, responsible for the ionization work, including sample preparation, mistakenly mixed glycerin instead of acetone with cobalt. Instead of considering this a waste, Tanaka, told himself: "Mottai-Nai!" what a waste! (A term used by environmentalists to encourage people to recycle) and set it on a sample plate for future use, a stroke of fortune and, perhaps, intuition, that paved the way to future success.

Experiments continued and as the parameters fell into place, including using the accidental matrix, the measurable molecular weight reached 35,000. In August 1985, Tamio Yoshida and Tanaka jointly patented a sample preparation method, which came to be known as soft laser desorption, and sample holder for use with a laser ionization mass spectrometer (patent JP01769145).

At the 2nd Japan-China Joint Symposium on Mass Spectrometry, Tanaka presented Dr. Robert Cotter with the team's research results showing that detection had reached a mass number of 72,000. This was followed by his paper in Rapid Communications in Mass Spectrometry, seminal moments in Tanaka's history that led to him being awarded the Nobel Prize. Koichi Tanaka presently leads the Mass Spectrometry Research Laboratory at Shimadzu Corporation and is still making an impact in the world of Mass Spectrometry and analysis of biomolecules by unveiling an Amyloid Beta MALDI-based blood test and designing the world's first commercially available Digital Ion Trap (MALDImin-1).

References

[1] http://www.speciation.net/Database/Instruments/Shimadzu-Corporation/LAMS50K-MALDITOF-MS-;i2720

[2] Cornish, T.J.; Cotter, R.J. Non-Linear Field Reflectron, US Patent 5,464,985, November 7, 1995.

[3] He, L.; Liu, Y.-H; Zhu, Y.; Lubman, D.M. Detection of Oligonucleotides by External Injection into an Ion Trap Storage/Reflectron Time-of-Flight Device. Rapid Commun. Mass Spectrom. 1997, 11, 1440-1448.

[4] Takeda T.; Miseki, K. Quadrupole Mass Spectrometer. U.S. Patent 4,481,415 , November 6, 1984.

1875	Shimadzu Founded
1877	Manned Balloon Launch
1957	GC-1A
1970	Started Manufacturing GCMS Instruments in JAPAN
1981	GCMS-9020DF
1982	GCMS-QP1000
1983	Started Manufacturing Analytical Instruments in the US
1984	LC-6A
1987	GCMS-9100K
1988	LAMS-50K LCMS-QP1000
1991	LC-10A
1992	KOMPACT MALDI III/II
2002	Nobel Prize AXIMA-QIT
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