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SHIMADZU
Excellence in Science

MOMENTUM

Vol. 04
2016

Inspiration from natural sources

Feature 2 : Development of medical care infrastructure

Health-3 Project by Ministry of Health of the Republic of Uzbekistan

Shimadzu Technology Focus

The art of generating vacuums

COVER

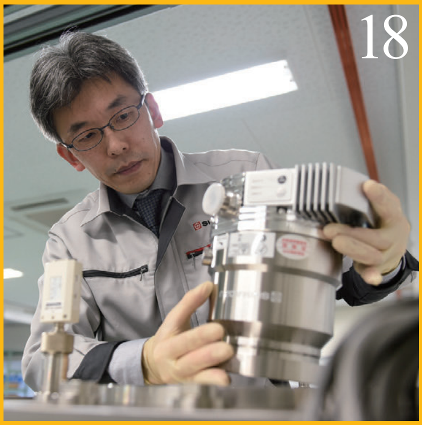
CHICAGO

UNITED STATES OF AMERICA

Chicago is an international city in the state of Illinois with the third largest population in the United States. Known as the birthplace of the skyscraper, there is so much to see in Chicago, whether strolling at ground level looking up or the magnificent vistas from the top of Willis tower. Chicago has many parks including Grant Park that encompasses the Art Institute, Field Museum of Natural History, Adler Planetarium, and the Shedd Aquarium, which also hosts live jazz music events at its lakeshore venue that offers spectacular views of the Chicago skyline. As for cuisine, Chicago is famous for roast beef and steak, deep-dish Chicago pizza, and hot dogs, to name just a few of the iconic culinary delights associated with the 'Windy City'.

Vol.04 2016

MOMENTUM



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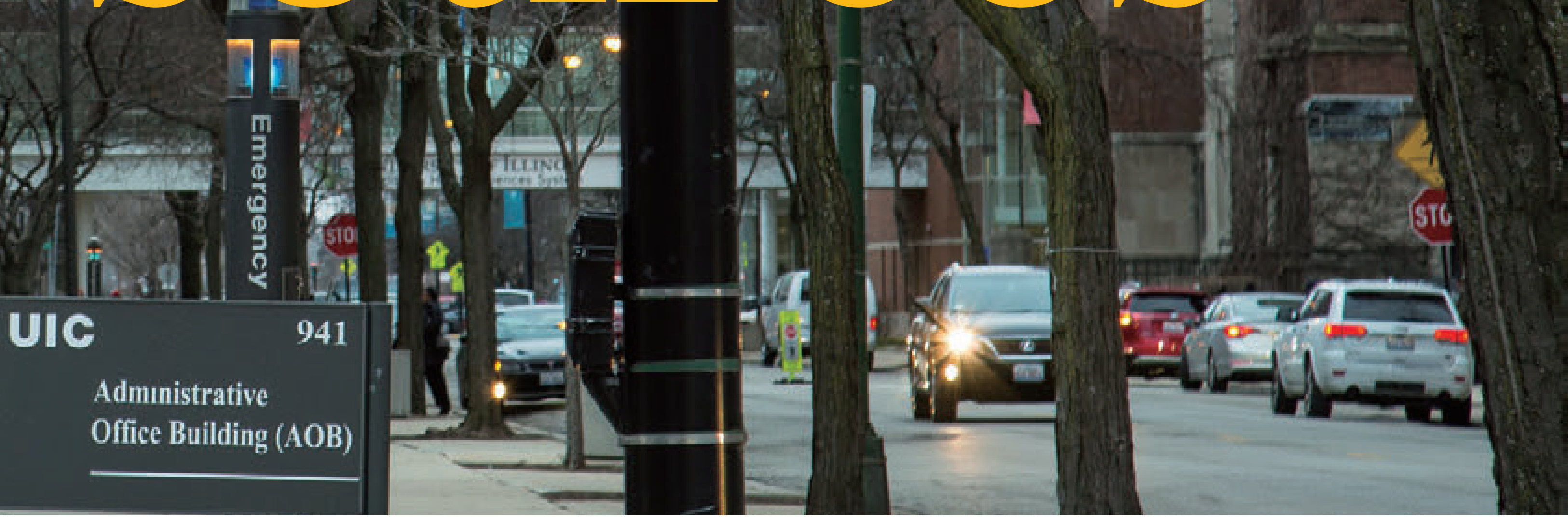
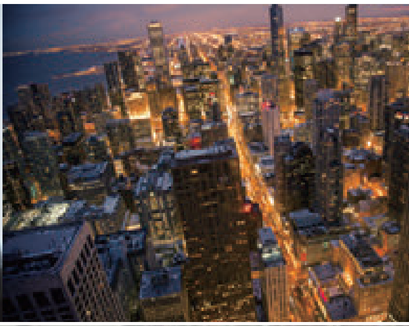
Inspiration from natural

Spotlight on the work of Richard van Breemen

A remarkably diverse and productive set of applications for the Shimadzu Corporation's mass spectrometry equipment have been pioneered by eminent researcher Richard van Breemen

sources





Richard van Breemen

Professor, Medicinal Chemistry and Pharmacognosy

Collaborations between the Shimadzu Corporation and renowned researchers across the globe have rarely been more productive than in recent years. Since the company was founded, Shimadzu's highly specialized equipment has enabled scientists to make breakthroughs in many different disciplines, from chemistry to medical science. The relationships between Shimadzu and their collaborative partners in research laboratories and academic institutions all over the world work both ways – researchers trained to use Shimadzu's instrumentation then find new and innovative ways of utilizing it, thus inspiring Shimadzu's engineers to build the next-generation of equipment.

The eminent researcher Richard van Breemen of the University of Illinois, Chicago, has had a long-standing and mutually beneficial relationship with the Shimadzu Corporation for the past 35 years. His connections with the company began during his degree at the John Hopkins University in Baltimore, where he was trained to use mass spectrometry (MS) equipment made by Kratos (which later become part of Shimadzu). In the first half of the 1980s, during his early career as a researcher in analytical chemistry for medical science, van Breemen was lucky enough to be taken under the wing of Robert Cotter, the American chemist whose research led to considerable advances in time-of-flight mass spectrometry and contributed to the development of 'matrix-assisted laser desorption ionization' (MALDI). Subsequent breakthroughs involving MALDI led to Shimadzu's Koichi Tanaka receiving the Nobel Prize for Chemistry in 2002.

"Cotter had a mantra that I've subscribed to ever since," recalls van Breemen. "He would say 'Never conclude that something can't be done!' To my mind, this sums up the attitude of all the scientists and technicians working on early versions of mass spectrometers in the 1980s. Their efforts to make technology such as liquid chromatography mass spectrometers (LCMS) actually work were truly heroic. Without companies like Shimadzu who were willing to push the boat out and work endlessly to develop the technology and make it more and more reliable, little of the work in analytical chemistry conducted in the last 30 years would have been possible."

What is mass spectrometry?

Mass spectrometry is a technique used by analytical chemists to determine the 'signature' of substance – in other words, its exact chemical make-up including details of the mass and elemental composition. It works by ionizing the substance, creating gas-phase charged molecules from which the mass-to-charge ratio of each can be determined. MS techniques can be used to disentangle the complexities of a substance, be it a naturally-sourced compound from a plant or a prescription drug made in a laboratory. By allowing scientists to ascertain the exact amounts of each constituent molecule that are found in a substance, MS can give great insights into how a particular compound functions and behaves.

There are many different types of MS, and Shimadzu has been a leading light in terms of developing and fabricating equipment to make MS work reliably and effectively in recent decades. van Breemen and his team work regularly, although not exclusively, with several types of MS including time-of-flight (or TOF-MS) mentioned above, as well as ion trap and triple quadrupole MS. Different information about molecules can be uncovered using different MS techniques. The complexity of the natural product mixtures being studied means that these MS-techniques are usually coupled in tandem with liquid chromatography (LCMS).

The concept of liquid chromatography has been around for many decades. This technique is based on the fact that a mixture of compounds will split into its component parts when dissolved in a liquid and passed through stationary phase. The classic illustration of this is to imagine a piece of paper with ink on it – when the paper is dipped into water, the ink will run. If you examine it carefully, you will see the ink has split into different pigments on the paper. This splitting is due to different constituents of the ink moving at different speeds through the stationary phase (the paper). A chromatographic separation allows scientists to simplify a chemical mixture which can then be measured for more detailed molecular information in a mass spectrometer.

The basic premise of MS is that charged molecules or ions can be separated from each other in the gas-phase based on their mass-to-charge ratio. For example, TOF-MS measures the time taken for each ion to travel a set distance to a detector inside the machine. Light ions travel faster, heavier ones take longer. Molecular ions (charged intact molecules) can fragment inside the mass spectrometer, and the various product ions can be recorded in a mass spectrum. Such tandem mass spectra provide structural information about the chemical makeup of each molecular ion. This gives more a more detailed description of the individual components which can be separated out using LCMS.

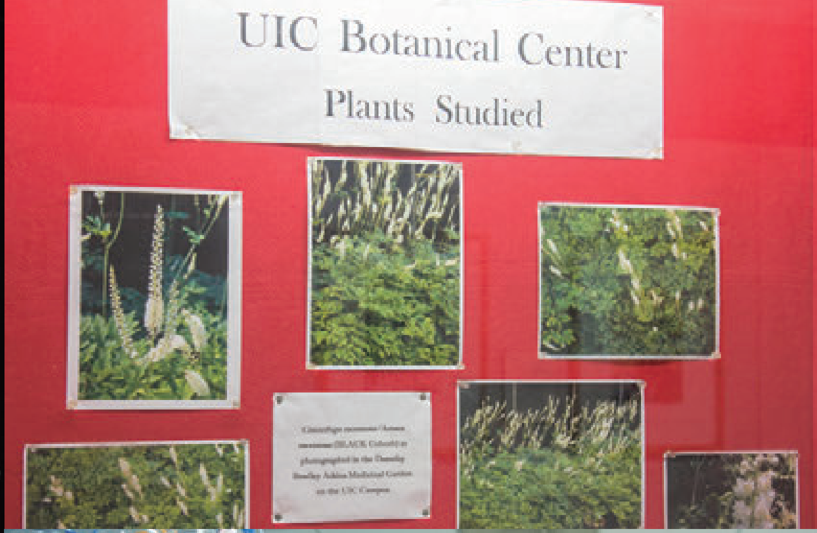
“We often use ion-trap TOF-MS, or IT-TOF, which can help us to figure out which components bind to a particular enzyme or receptor by measuring their relative masses,” says van Breemen. “In this technique, combined electric fields are used to trap the charged particles so we can then detect, measure and identify individual components, as well as analyze their behavior and interactions with other molecules.”

Richard van Breemen: A career built on MS

Throughout his early career, after graduating from John Hopkins School of Medicine in 1985, van Breemen trained in the use of MS, LCMS and their applications in medicine. He began by investigating the characteristics of natural products such as chlorophylls and carotenoids from plants. He is now considered to be a world-expert in MS techniques applied to natural products, and has pioneered a number of methodologies in the field.

“Everything I do uses MS,” he says. “I investigate drug metabolism and toxicology for existing medications and botanical supplements, alongside focusing on drug discovery from natural sources. I devote a considerable amount of time to the search for new anti-cancer drugs based on natural products from plants. In essence, I study mechanisms of action; investigating interactions between natural products and receptors and enzymes, working out what these compounds do and how they do it. Utilizing MS-based screening is the best way to do this.”

His initial mass spectrometry work on plant compounds led to



him being asked to join the Department of Medicinal Chemistry and Pharmacognosy at the University of Illinois at Chicago in the early 1990s, where he still works to this day. At that time, the natural products research team in Chicago was already actively searching for new cancer chemoprevention agents in nature, and would soon embark on the study of the safety and efficacy of botanical dietary supplements, as van Breemen explains:

“Our efforts were, and indeed still are, focused on examining in detail the compounds and molecules found in natural sources, in the hope of finding products that could be used in new medicines. We were also acutely aware of the rise in the use of dietary supplements – non-prescription, botanically-based products that claimed to relieve symptoms of many illnesses and conditions – and our unique chance to study these in more depth.”

These dietary supplements are marketed and regulated in different ways across the world, and every country has a different set of regulations to control them. The aim of the UIC Botanical Center, which is directed by van Breemen, is to provide overarching, detailed research into how these botanical supplements work and interact with the body, and indeed with prescription medications.

“Botanical supplements are often based on extracts from plants that were used in ancient cultures,” explains van Breemen. “By utilising the latest technologies and novel methods of determining the constituent parts of these supplements, we hope to reveal many new aspects of the products available on the market – investigating an old field with new twists.”

Botanical supplements case study: The menopause

One of the van Breemen group’s key areas of research is to examine the effects of using botanical dietary supplements to treat the symptoms of the menopause in women. Given the negative press surrounding the use of hormone replacement therapies, more women have been turning to alternative medicines such as licorice and black cohosh to relieve symptoms of cramps and hot flushes, for example.

“Although these supplements have been around for ages, there is a lot we still don’t know about them,” explains van Breemen. “We were intrigued to find out how botanical supplements actually work once inside the body, and current technology is finally allowing us to understand how they work – or indeed, if they work.”

In 2011, van Breemen led an investigation into the plant black cohosh, the roots of which have been used in traditional Native American medicines for centuries. His team were keen to add to understanding of the pharmacological profile of the plant, with a particular focus on the nitrogen-containing compounds, which had never been studied before.

They used a Shimadzu IT-TOF-MS to examine plant extracts, allowing them to determine exactly how many atoms of each element there were in the samples. They revealed a diverse set of 73 nitrogen-based metabolites (small molecules created as a direct result of metabolic processes) previously unknown to exist in black cohosh. Indeed, some of the molecules were completely new to science. Their findings may be significant in understanding the biology of the plant, its bioactivity and its efficacy as a dietary supplement.

Metabolites are of particular interest to scientists studying drug mechanisms of action, because many of these small molecules created during metabolism in the body become reactive – they trigger reactions which can prove significant in terms of a drug's or supplement's efficacy, or indeed can interfere with other drugs present in the body. Drug-botanical interactions are a serious consideration for researchers involved in drug discovery, as two or more substances taken together can negate each other, or in worst-case scenarios actually prove toxic.

Earlier this year, in March 2015, van Breemen published a paper describing a new methodology for detecting such reactive metabolites in dietary supplements using ultra-high-pressure LCMS (UHPLC). He became aware that existing technologies, which trapped reactive metabolites using glutathione (or GSH) and then scanned them using high-pressure LCMS, actually missed out some of the GSH conjugates in the final read-out.

To ensure all reactive metabolites could be identified in a single analysis, van Breemen and his team developed a new technique using UHPLC instead, and tested it on a licorice-based supplement called Glycyrrhiza glabra. Their screening test simultaneously measures both positive and negative ions in a single assay, allowing more of the metabolites to be identified than in previous tests. Their results indicated for the first time that licorice forms metabolites which are capable of reacting with biological nucleophiles when consumed as a supplement. Their UHPLC technique has the potential to transform this particular field of study, as van Breemen explains:

"UHPLC separations are fast and Shimadzu's triple quadrupole mass spectrometers are the fastest on the market today. The name UHPLC, as it might suggest, refers to the pressure used to pump solvent through the chromatographic column – it literally pushes the machine as hard as it can go! From this we gain fantastic productivity; in the search for reactive metabolites using UHPLC with fast scanning triple quadrupole mass spectrometry we were able to speed up the process ten-fold. The technology can also provide crucial support for clinical trials requiring rapid, accurate results."

Enhancing clinical medicine: A clear future for rapid analysis

This ability to generate results in minutes from mass spectrometry could prove vital for medical diagnoses, and van Breemen's group have recently been involved in a number of clinical-based support projects using Shimadzu's equipment. It is in this field that the brilliance of Shimadzu's partnerships with researchers comes to fruition. To give an example, van Breemen was asked by a pathologist at a local hospital if it were possible to predict how long an infected liver might function before it fails, purely by examining the constituent parts of a tiny piece of liver taken during a biopsy.

"If Shimadzu had not just released their latest mass spectrometer, the LCMS-8050, this particular project simply couldn't have been possible," describes van Breemen. "The biopsy samples were so small that no previous machine could have analyzed them accurately. I have no doubt that these are the kind of challenges Shimadzu's engineers will continue to rise to in coming decades. I look forward to seeing what they will come up with next!"

As mentioned, the relationship works both ways, and van Breemen is an expert at fine-tuning methods used with Shimadzu's equipment. In a paper published in November 2015, van Breemen describes a new assay capable of assessing drug-drug and drug-botanical interactions, which could have immense value for both clinical medicine and new drug development. Again using fast UHPLC equipment with a triple quadrupole mass spectrometer, the new assay measures ten different drugs at once in a cocktail, rather than individual species one at a time. The technique examines how each drug is transformed by liver enzymes in vitro, simultaneously measuring the resulting products and the rate at which the enzymes metabolize each drug.

"The second step once we have this information is to see what happens to the individual drugs' 'mechanisms of action' once we add a botanical supplement into the mix," explains van Breemen. "If there is an interaction between the supplement and a particular drug, or drugs, in the lab test, then it is highly likely there would be implications for that combination inside the body as well."

Trials of the new technique proved highly successful, with promising results in test runs using drugs with known liver enzyme inhibition activity. The team also conducted tests using the licorice-based Glycyrrhiza glabra, showing that their method was capable of illustrating the effect of a supplement on prescription drugs.

Cancer prevention case study: The search for promising targets and therapies

van Breemen and his colleagues are heavily involved in conducting analyses in the search for cancer prevention targets and therapies. They research potential proteins inside the body that could provide targets for anti-cancer drugs, as well as investigating products from natural sources that could provide the basis for developing such drugs in future. This versatility stems in part from the team's expertise in MS techniques, which can be used for both sides of the investigative process. In 2012, for example, van Breemen was involved in the development of a new method of screening for agents that could modify a human protein called Keap1. This protein is heavily involved in regulating antioxidant responses in the body, an important process that protects cells against carcinogens. This means Keap1 could prove to be a viable target for cancer prevention therapies.

A previous trial by the same team using MALDI-TOF MS provided some detail on potential agents for Keap1 modification, but van Breemen was not satisfied that all the interactions were detected using this method. He developed a second, more sensitive assay based on a simpler, one-step LC-MS/MS process. The assay proved to be 20 times more sensitive than the MALDI-based analysis, and was able to identify new potential chemoprevention agents that interacted with Keap1.

For a number of years, a molecule called lycopene found in tomatoes and other red fruit and vegetables has been under investigation as a possible drug candidate for cancer prevention therapy. Lycopene is known to be very safe for human consumption, and exhibits anti-inflammatory, anti-oxidant and anti-cancer properties. It is not yet clear whether the molecule is potent enough in its natural state to actively prevent cancer, however.

The study of lycopene is one of van Breemen's current projects, in which he is focusing on its potential as a therapy for prostate cancer. The slow growth of prostate cancer over years lends itself to intervention via cancer prevention therapy. To determine the potential of lycopene as a prevention tool, van Breemen and his colleagues must first unravel the mechanisms which occur inside the body when lycopene is consumed.

A significant step forward is described in van Breemen's 2013 paper in Cancer Prevention Research, wherein his team successfully identified how lycopene affects specific individual protein expression in human prostate cells in culture. Using HPLC-MS/MS equipment, they found that proteins linked with anti-cancer / anti-oxidant responses were upregulated following lycopene treatment. More specifically, proteins associated with apoptosis (programmed cell death) were upregulated, and they found increased levels of a class of protective enzymes which may help prevent cancer initiation. They also observed an anti-inflammatory effect in the prostate cells. Proteins involved in protecting cancer cell growth and cancer-inducing pathways were downregulated.

Crucially, finding these multiple protective effects on multiple molecular pathways would not have been possible without Shimadzu's latest HPLC-tandem mass spectrometry technology. Repeating these results in vivo (inside the body) has yet to be achieved, but van Breemen remains positive about the power of natural products to treat, and potentially prevent, cancer.

"More than half the drugs in use today stem from natural sources," he says. "Two thirds of cancer prevention drugs on the market are also from natural sources – there have to be more potential drugs out there that we haven't found yet. I'm determined to continue searching for compounds that could help us in the fight against all forms of cancer in future."

Shimadzu and van Breemen: A productive future

Given the scope for potential new discoveries that Shimadzu's equipment provides, it is vital that the corporation continues to work with experts in MS, such as Richard van Breemen, long into the future. Collaborations such as this yield significant and far-reaching results, aiding Shimadzu in its aim to contribute to society through the application of science and technology.

The Center for Botanical Dietary Supplements Research at the University of Illinois has recently been awarded funding for a further five years, and van Breemen is convinced that Shimadzu's wide variety of LCMS and IT-TOF equipment will continue to help them achieve the Center's goals.

"Our efficiency, accuracy and productivity are ultimately tied to the equipment we use," says van Breemen. "Shimadzu's unending support and their willingness to persevere in building high-performance MS instrumentation enables us to conduct accurate, relevant and unique scientific analyses of compounds which would otherwise remain a mystery. New drugs and anti-cancer therapies are out there, it is simply a case of finding them using the technology available to us."

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Republic of Kazakhstan
The Caspian Sea
Republic of Uzbekistan
Turkmenistan

Health-3 Project by Ministry of Health of the Republic of Uzbekistan

Shimadzu Corporation is providing technical support and diagnostic X-ray systems to Uzbekistan for the development of its medical care infrastructure.

Uzbekistan is located in Central Asia, and is completely landlocked—people are required to cross two national borders before they reach the sea. It prospered, historically, by being a midpoint on the Silk Road. Thirty million people live in a country that has 1.2 times the land mass of Japan. None of its rivers connect directly to the sea, and intensive farming is confined to an irrigated agricultural area that makes up less than 10 % of the entire country. The remaining land comprises the Kyzylkum desert and ranges of steep mountains.

The center of Uzbekistan has traditionally been home to oasis cities, which served as stopping-off points between East and West for traders on the Silk Road. Historically, Sogdian people from Iran inhabited the area, but in the 8th century it was conquered by the Arabs, who imposed the Islamic faith. In the 10th century, the Turks appeared, and the Turkic language began to spread throughout the area. In the 13th century, it became part of the Mongolian empire. Under Mongolian rule, many cities were subjected to massive damage, but they recovered quickly and by the 14th century the Timurid Empire had spread across a broad area from Central to Western Asia, becoming a powerful dynasty. After the Timurid Empire fell into ruin, the Uzbeks invaded from the north, and the state was established by the Uzbek people.

In the 19th century, it was absorbed into the Russian Empire, but with the dissolution of the former Soviet Union in 1991 it became the independent Republic of Uzbekistan. The country has rich natural resources of gold, cotton, natural gas and uranium, among other things, and has successfully worked to modernize its own industry, to the point where in the past few years it has achieved a minimum of 8 % economic growth. Since independence, however, health and medical care have been among its least developed areas, partly due to the economic difficulties the country faced immediately after independence, and there is a constant lack of resources throughout the medical sector, including a shortage of doctors, medical equipment, medicines and medical information. The standard of medical services generally provided is significantly low in comparison with developed countries, and in the Health Risk Map 2014 issued by SOS International, Uzbekistan is categorized as a country with high levels of medical risk. It also has very limited emergency provision, with ambulances said to take over an hour to arrive after an emergency call is placed, even in the city of Tashkent.


BOLA YILI
PARKENT TUMAN KO'P TARMOQLI
MARKAZIY POLIKLINIKASI

In 2011, the Uzbekistan government established a Health System Improvement Project with financial backing from the World Bank, and took the decision to completely renew the diagnostic X-ray imaging systems in 12 regional hospitals. These nationwide facilities are being updated in stages, in a rollout that will take until 2018. Shimadzu Corporation has local staff positioned in Germany, Russia, and in the past in the capital of Uzbekistan, Tashkent, and has for many years been involved in providing medical equipment to Uzbekistan since the days of the Soviet Union and during the period of confusion that followed independence. Shimadzu has also provided technical support and contributed to raising the overall level of medical care in the country.

This renovation of facilities requires reliable, high-quality equipment that will continue to operate over the mid-to-long term. As a result of the durability of equipment Shimadzu has provided in the past, its history of providing support if anything breaks down, and the trust Shimadzu has built up with its local partner, Shimadzu was entrusted to deliver 58 imaging systems and fluoroscopy systems each during the first phase of the project in 2012, and a further 40 imaging systems and 60 fluoroscopy systems during the second phase of the project in 2015. The Ministry of Health and the hospitals to which this equipment has been delivered have shown great excitement and anticipation about the increase in standards that these latest diagnostic X-ray systems will bring to medical facilities nationwide. Shimadzu intends to provide full support, based on an understanding of the perspectives of both medical professionals and patients in Uzbekistan, in order to further contribute to improvements in medical services.







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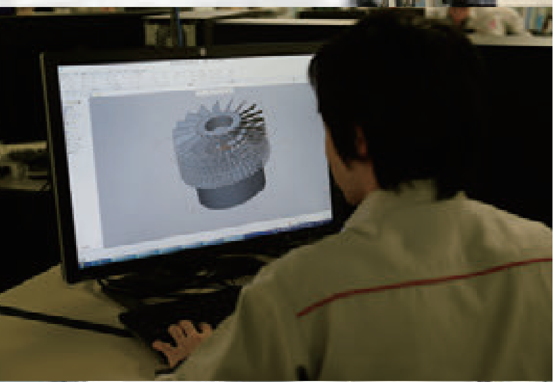
The art of generating vacuums

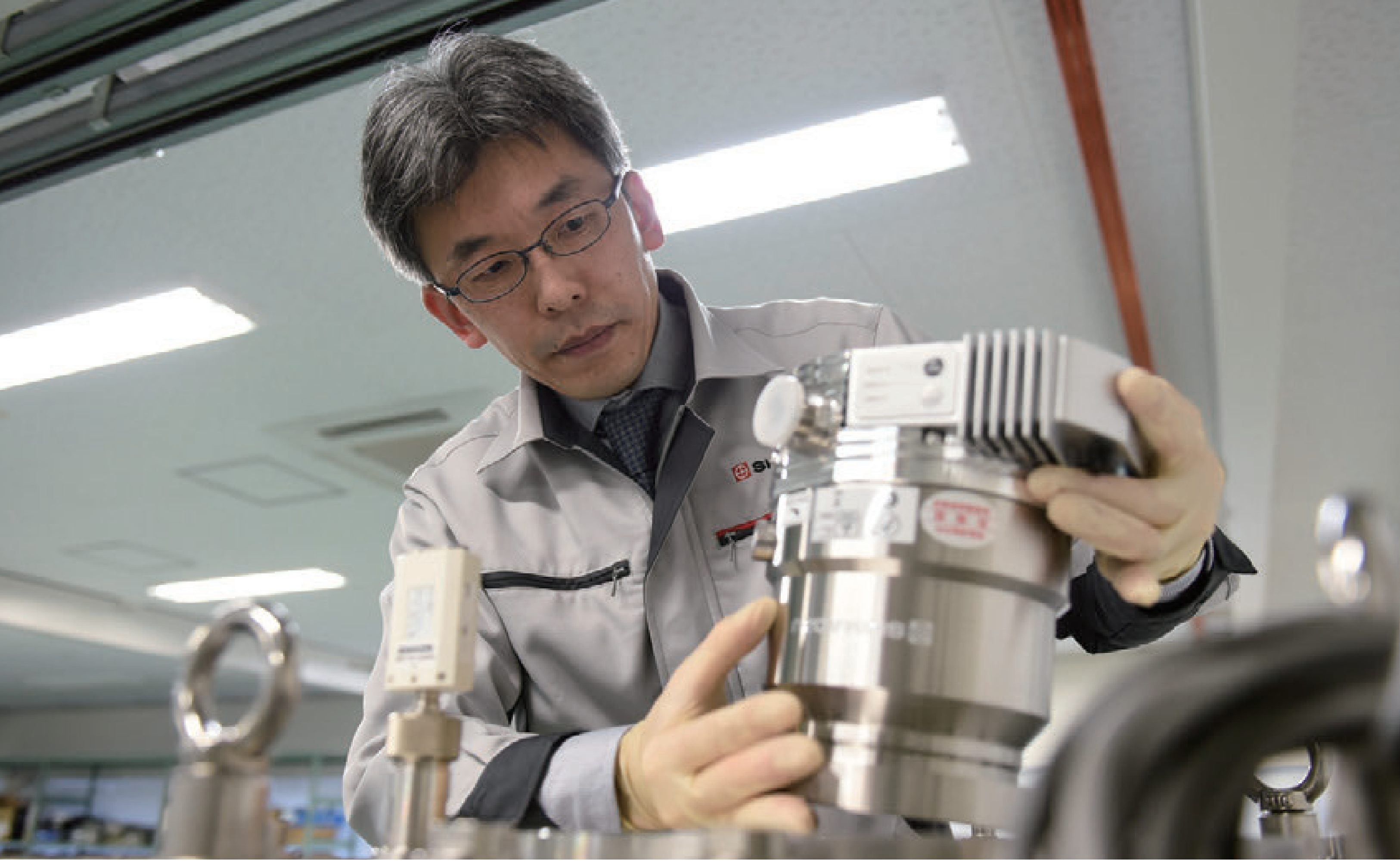


Insights into the innovative engineering at the heart of Shimadzu's turbo molecular pumps

The Shimadzu Corporation is one of the world's leading manufacturers of turbo molecular pumps (TMPs) for applications that include manufacturing semiconductor devices, solar cells, and flat panel displays. TMPs are used to create and maintain a high vacuum environment. The TMPs produced by Shimadzu exhibit world-class gas throughput and pumping speed to meet the increasingly stringent demands of semiconductor manufacture, for example in enabling manufacturers to deposit and etch thin films of semiconductors on large areas of silicon wafer.

TMPs generate a vacuum environment via the high speed rotation of turbines that enables vacuum pumping at the molecular flow level. The manufacture of semiconductors and flat panel displays requires clean, oil-free vacuum generation to maintain optimal device operation. The technical performance, reliability and global network of technical support offered by the Shimadzu Corporation have made Shimadzu TMPs integral components for these kind of applications. Shimadzu makes a wide variety of TMPs. all of which have different uses.

The high gas throughput TMP-2404/3304/4304 series has pumping speeds in the range 2100L/s to 4400L/s in addition to the temperature control function and special corrosion resistance coatings potentially have a wide range of potential applications.
Each TMP in the compact, energy saving TMP-X1605/V2304 series has an integrated power supply unit with a power consumption that is 15% less than models with separate power units.
The TMP-X3405/X4304 series also use the integrated power supply but in addition they have temperature control functions and corrosion resistance coatings for harsh processes used in manufacturing semicon-



ductors and flat panel displays (FPD).
Furthermore, the wide range TMP-203〜1003 series have excellent compression ratio and ultimate pressure level for realizing high vacuums.
Finally, the TMP-5305 series have maximum-class gas throughout and pumping speed of 5300 L/s and are expected to find applications for next generation 450nmm semiconductor wafer processing.
“We currently have a 30% worldwide market share of magnetic levitation TMPs,” says Tomoo Ota, General Manager, Turbo Molecular Pump Business Unit R&D Group, Semiconductor Equipment Division, Shimadzu Corporation. “The worldwide popularity of our TMPs reflects our history of innovative design and global technical support to meet the continuously changing needs of industry.”
Indeed, prototypes of Shimadzu TMPs are designed using the power of Japan’s fastest supercomputers, located in Kobe, Japan. “Shimadzu engineers use cutting edge modelling technology to simulate the performance of our TMPs,” says Tomoo Ota. “All our commercial TMP systems are manufactured in-house by Shimadzu. This guarantees the quality and performance of our products.”

New TMP with renewal bearing structure for next generation applications

In 2014, the Shimadzu Corporation launched the innovative TMP-B300 “hybrid-bearing” turbo molecular pump series for applications including the generation of ultra-high vacuums for analytical scientific research, as is required for mass spectrometers and scanning electron microscopes. The TMP-B300 series was developed for the US $150 million market of small-size TMPs for analytical scientific applications and general purpose equipment.

In vacuum-based industry and analytical scientific applications where ultra-high vacuums are required, TMP performance must satisfy stringent requirements. The TMP-B300 is a low power, compact 195 mm-high pump with an integral controller designed to be mounted vertically, upside down or horizontally in space-constrained environments. It allows a high foreline pressure of 1000 Pa to enable a small size backing pump such as a diaphragm pump. The device has an integrated control panel for ease of use, works at a low power consumption of only 180W at a pumping speed of around 280L/s.

Further information

Shimadzu turbo molecular pumps

http://shimadzu.com/industry/products/tmp/index.html

Strengthen Response to the Needs of the Chinese Market and Promote Joint Research and Development.

Shimadzu China Mass Spectrometry Center

abbreviated as the China MS Center ; Name in Chinese：島津中国質譜中心

Shimadzu Establishes Shimadzu China Mass Spectrometry Center to Strengthen Response to the Needs of the Chinese Market and Promote Joint Research and Development

In order to expand its share of the mass spectrometer market and to promote cutting-edge joint research and development in China, Shimadzu has established the Shimadzu China Mass Spectrometry Center (hereinafter the China MS Center) at the Beijing Branch of Shimadzu (China) Co., Ltd., a Shimadzu Group company in China. The opening ceremony for the Center was held on-site on October 26, 2015.

The Center is a facility established for the purpose of research and development with researchers in China who are performing advanced MS related research jointly with Shimadzu's mass spectrometry (MS) technology. The laboratories are equipped with high-end Shimadzu systems including liquid chromatograph mass spectrometers and gas chromatograph mass spectrometers. The Center will participate in the formulation of official analytical methods through new application development, and develop and improve high-end mass spectrometry systems. By providing solutions better matched to the Chinese market, Shimadzu aims to expand the market share of its core products, centered on mass spectrometers, and to further improve the Shimadzu brand image.

As of fiscal 2015, the China MS Center has 10 staff, and the number of staff will be expanded as the need arises. The Center addresses food safety as well as the clinical, pharmaceutical, and environmental fields, and by the end of 2016 plans to invest a

■Location : 6th floor of the building where the Beijing Branch, Shimadzu (China) Co., Ltd. is located 6F, China Life Tower, No. 16 Chao yang men wai Street, Chaoyang District, Beijing 100020 P.R. China
■Floor Space : 1,009m^2
■Main Systems : Triple quadrupole liquid chromatograph mass spectrometers. Triple quadrupole gas chromatograph mass spectrometers. Supercritical fluid extraction/supercritical fluid chromatograph systems. Imaging mass microscopes, and other systems

total of more than 460 million yen in research and development. The market in China is expected to expand with a background of increasing research investment in cutting-edge fields, as well as demands for speedy solutions to food safety and environmental issues, the mass spectrometer. In 2016 Shimadzu expects the scale of the mass spectrometer market in China to increase by approximately 1.3 times the value in 2013, so the goal is to succeed in the market through the activities of the China MS Center and improve our business performance. In addition, results obtained at the China MS Center will be fed back to Shimadzu in Japan and deployed to other regions, thereby leveraging the results in product and application development at various sites around the world.

At the opening ceremony held on October 26, Shimadzu President & CEO Teruhisa Ueda delivered the following message. “Recently, the development of mass spectrometry technology has been remarkable, and the scope of applications is expanding rapidly. At the Shimadzu China Mass Spectrometry Center, we will promote the joint development of analysis methods and applications better matched to the needs of the market, aiming to provide the solutions required by our customers in China. At the same time, I would like to see the Center develop as the foundation on which to build a close cooperative relationship with many customers involved in mass spectrometry. Research activities in mass spectrometry in China has impacts internationally, contributing significantly to this development. Under such circumstances, Shimadzu will work to contribute further to mass spectrometry technology in China and globally, through the activities at this Center.”

As the driver for its “global innovation center concept”, Shimadzu established the SSI Innovation Center at Shimadzu Scientific Instruments, Inc., a Shimadzu Group company in the USA, in July 2015. The China MS Center is another aspect of this concept. Shimadzu will investigate the subsequent establishment of such facilities at other sites around the world, aiming for business expansion.

Shimadzu Corporation Establishes Sales Subsidiary in Malaysia

Shimadzu Corporation has established a 100 %-owned sales subsidiary in Malaysia that is now in operation. The subsidiary strengthens the company's business structure within the ASEAN/India region, which is showing impressive economic growth and is expected to continue to do so in the future.

Shimadzu has recently been focusing on the growing market in the ASEAN/India region. The company is pressing ahead with the timely supply of products that meet local needs and the development of a wide variety of sales capabilities, as well as establishing a solid business foundation to ensure that Shimadzu can capitalize on growth opportunities in the region.

In addition to beginning direct sales of general purpose analytical instruments such as high-performance liquid chromatograph mass spectrometers for use in markets such as food, pharmaceutical, and petroleum chemistry, Shimadzu will use the existing specialist knowledge of its local distributors in large-scale models, testing machines and non-destructive inspection instruments in order to ensure that it delivers an even greater level of convenience and a stronger brand image to its customers.

In terms of medical systems, Shimadzu's X-ray systems are highly rated within Malaysia for their excellent quality and the support services that the company provides, and the company has a 25 % market share, which increases to above 50 % when general purpose X-ray systems for use in hospitals is included. Shimadzu aims to gain a greater foothold in the high-end device market for vascular imaging systems, with increasing efforts to open up the clinical medicine market.

The more than 50 employees of the new company will work to improve the brand image of Shimadzu within the Malaysian market, and to contribute to infrastructure, the environment, industry and medical care within Malaysia.

5th Shimadzu Global Pharma Summit 2015 Sees 200 Global Pharma Leaders Find Ways To 'Face Regulatory Challenges With Confidence' In Singapore

Organized by Shimadzu (Asia Pacific) Pte Ltd, the 5th Shimadzu Global Pharma Summit 2015 was held from 25-27 November 2015 at the Marina Bay Sands in Singapore. Shimadzu Global Pharma Summit is a platform for members of the global pharma industry to network, share, and discuss strategies for the future.

The theme was "Face Regulatory Challenges With Confidence". This year, one of the most pressing issues being faced by the pharma industry is meeting the demands of regulatory organizations.

The summit started with a futuristic laser-enabled Exordium. Next, Imura Kiminobu, MD, Shimadzu (Asia Pacific), Singapore and Akira Nakamoto, Chairman, Shimadzu Corporation, Japan, addressed the audience. Mr Nakamoto said that, "Shimadzu, together with our clients, has been deeply involved in adhering to compliance and we could all use this platform to share our thoughts and help to contribute towards compliance of each and every one of you."

PITTCON® CONFERENCE & EXPO 2016 March 6 – 10, 2016, Atlanta, Georgia USA

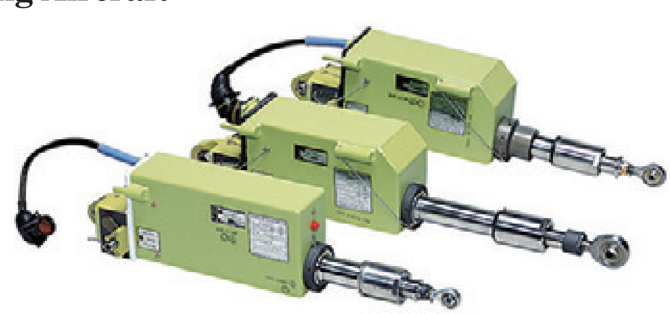
Pittcon is a major event for the global laboratory marketplace, showcasing technologies and instruments for a broad range of applications. At Pittcon 2016, Shimadzu featured our extensive portfolio of innovative, proven products designed to address customers' specific laboratory workflows in a variety of markets. One highlight was the release of the new ICPMS-2030 Inductively Coupled Plasma Mass Spectrometer, offering sensitive, trace element analysis for environmental testing, food studies, and pharmaceutical work. An exciting new feature at Pittcon 2016 was the addition of a live demo area. Shimadzu provided live demos of unique techniques in spectroscopy and elemental analysis direct to attendees. Moreover, we had a full technical program, including networking sessions, posters and oral presentations covering a variety of topics, from food safety analysis via SFE/SFC/MS and mass spectrometry applications for environmental and petrochemical markets to RoHS Directive related application. For more details on posters that Shimadzu presented at Pittcon 2016, visit our website at
http://www.shimadzu.com/an/news-events/2016/pittcon.html

Expanding Global Strategic Products and Commercial Aircraft Equipment Business Shimadzu Supplying New Equipment for Boeing Aircraft

Shimadzu Corporation announced it is delivering new orders for three components to be fitted on aircraft made by Boeing, the world's largest aircraft manufacturer.

The equipment includes:
"APU Air Inlet Door Actuator" for Boeing 737 MAX
"APU Air Inlet Door Actuator" for Boeing 777
"Ground Spoiler Control Module" for Boeing 737 MAX

Shimadzu has positioned these commercial aircraft sector products as global strategic products. The Boeing 737 MAX is scheduled to make its maiden flight in 2016, and according to Boeing's press release, as of September 15, 2015, orders for 2,869 airplanes from 58 airlines around the world have been received.



Reference Image: APU Air Inlet Door Actuator products of the same type that will start to be delivered this time

Created an Induction Electrostatic Generator when he was only 15 –Passion of Genzo Sr. inherited by Genzo Jr.–

When Genzo Shimadzu Sr. passed away suddenly in 1894, he was succeeded by his 25 year old eldest son Umejiro, who took the name Genzo Shimadzu Jr. and became the business owner.

When he was only 15 years old (1884), Genzo Jr. created an “induction electrostatic generator” to generate electricity. In Japan, electricity was part of the curriculum of physics and chemistry in 1868 and students were taught about electric generators.

Owever, “generator using friction” was introduced in the teaching material, which Genzo Sr. produced. Umejiro learned about the induction electrostatic generator invented by Wimshurst in England in 1883 from available literature and created his own induction electrostatic generator looking at the illustration of Wimshurst’s generator in 1884. Umejiro’s induction electrostatic generator was more powerful then generators that used friction.

Genzo Senior’s passion for physics and chemistry and talent were inherited by Umejiro who showed a strong interest in physics and chemistry even when he was a small child. Umejiro frequented the Physics and Chemistry Research Institute and gained scientific knowledge by handling unusual experimental devices for physics and chemistry and peeking in on experiments being conducted. It is said that Umejiro created most of his new scientific instruments, including the induction electrostatic generator, by creating prototypes after studying illustrations found in scientific publications, including those of French physicist Ganot as the most reliable information source and then repeatedly carrying out experiments.

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