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MOMENTUM

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Research that could save thousands of women's lives

Feature 2 : Planetary Science
Butterfly hovering in space and the search for life beyond our solar system

Feature 3 : Food Science and Metabolomics
Focus on metabolomics for food science

Message from Teruhisa Ueda, 12th President & CEO of Shimadzu Corporation
Listen Carefully and Perfect Our Technology

Contents

Vol.03 2015

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Message from Teruhisa Ueda, 12th President & CEO of Shimadzu Corporation

Listen Carefully and Perfect Our Technology

This year marks the 140th anniversary since Shimadzu Corporation was founded. After overcoming countless difficulties, we are now in the process of firmly establishing Shimadzu as a company that operates globally. More than anything, this progress was achieved due to the generous support from all of you. Thank you. We are sincerely grateful.

It is in this celebratory year that I have been appointed to succeed Akira Nakamoto as president and CEO. I hope I can rely on your ongoing support.
When I was first appointed, I asked all Shimadzu Group employees to listen carefully to the customer. Visit the sites where customers are researching and developing new products, where they are providing healthcare, or where they are manufacturing products, more often than you have until now, to find out what they think about our products and what they truly want. Furthermore, sales and R&D personnel are working as one to determine their response and earn their trust.
As one measure for listening to customers, we are working on establishing innovation centers in various countries around the world. These centers will be staffed by R&D personnel that can respond quickly to customer requests. As society becomes increasingly sophisticated and changes at an increasingly fast pace, our aim is to satisfy customer needs as reliably as possible. Meanwhile, we will allocate a larger share of resources on R&D for new business operations and strengthen our ties with academic and research institutions involved in advanced research. In addition to providing our technology, such collaborations will help us absorb new knowledge and accelerate the process of increasing our technical capabilities.

“Contributing to Society through Science and Technology”
This corporate philosophy that has served as the basis for all our business operations is still just as vital as it was 140 years ago. It represents proactively working to make society a more convenient, safe, and secure place by supporting the business activities and measures of our customers and by sometimes taking the lead in industries ourselves. Through such efforts, we can make an even bigger contribution to society.
Expect great things from Shimadzu in the future as well.

12th President & CEO of Shimadzu Corporation

Teruhisa Ueda

After performing the elite official Kurosaki role in the mega Japanese hit TV drama "Hanzawa Naoki", Ainosuke Kataoka - 6th generation of the famous Kabuki theatre family - leapt to fame as a popular onscreen actor. We were curious to learn more about this unique persona, and the unusual jump he has made in combining a career in both traditional Kabuki theatre and the world of stage and screen. How did he become so active in such a wide range of shows, working in films,dramas, as an anime voice actor, and as the host of a variety of shows, as well as Kabuki? In an extensive interview, we asked Ainosuke Kataoka about his career, the balance of "tradition and innovation" in classical performing arts and his passion and affection towards Kamigata Kabuki.

Kabuki's Ainosuke Kataoka : A rising star of stage and screen

Inherit the

Kamigata Kabuki: A time of crisis?

When Kataoka was invited to appear as a guest on the talk show "Waratte Iitomo!" in March 2014, he deliberately asked the audience how many of them had been to Kabuki theatre in the last year, during the '100 people survey' segment of the show. Only one person out of 100 said they had. This is increasingly the case with Kabuki, a traditional theatrical performing art from Japan. Kabuki theatre combines dance and drama, with the actors dressed in elaborate costumes and make-up. Men play all the parts, including female roles, and the art of Kabuki runs deep with tradition. The plays are long, often lasting most of a day, and in recent years the number of people coming to the live shows has decreased considerably.

"I asked this question on purpose during the live program, but I myself felt tense inside," explains Kataoka. "My intention was to pass on the message that people who care about Kabuki, those who wish to preserve the traditions as I so passionately do, should be extremely concerned by this crisis." .

In an attempt to remove the image that "Kabuki is difficult to understand", Kataoka made a decision to participate in at least one film or drama, alongside appearing in Kabuki, every year. "Although I wanted to know how I would be accepted as an actor in productions such as film and drama, I also needed to highlight to people the existence of such an actor and help them learn more about Kabuki."

When Kataoka was a young child, he wanted to live just like a Kabuki actor would have done in the past. "However, when I looked around when I was 20 years old, there were only 3 or 4 top actors acting Okina role in Kamigata Kabuki," says Kataoka. "I was stunned. Although Kabuki was originated from Kyoto, only a few actors could still speak the Kansai dialect. Would Kamigata Kabuki be extinct if such situation continues? I recognized early on the sense of crisis in the world of Kabuki with a great degree of restlessness."

A fascination with Kabuki from a young age

Kataoka was born into an ordinary family without any connection to Kabuki. His home as a child was a backstreet workshop, with dumpers coming in and out every day around his home. "My birth father told me I needed to learn a trade outside the neighborhood because it was dangerous for me at home," describes Kataoka. "When

smell

KABUKI ACTOR AINOSUKE KATAOKA

he applied to the child role recruitment of production company Shochiku Geino on my behalf, I got in. While undergoing voice training and performance exercises once a week, I started to accept jobs little by little, beginning with a role in NHK's series TV novel, "Don't Need That Until I Win".

Kataoka first became aware of Kabuki during grade 2 in elementary school. When he first accepted a Kabuki job, it was a total culture shock. "It looked like a theme park through the eyes of a child," he recalls. "I had never seen anyone paint his face before, and big brothers and uncles suddenly became beautiful women. Gorgeous flowers, costumes and the equipment for midair stunts were also interesting. I fell in love with Kabuki that first day."

A lucky break

Kataoka participated in Kabuki performances from time to time after that, but he often struggled in class and was ready to give up performance. Then he met his now adoptive father, Hidetarou Kataoka, and everything changed. When the elder Kataoka watched the young actor on stage, working honestly as a sword-bearer in "Kanjincho", he thought noted how the child seemed to love performing, and offered to accept Ainosuke Kataoka as an apprentice. However, Kabuki theatre remained very much a kinship-oriented world, and Kataoka was concerned that he would never become a Kabuki actor as he was from an ordinary family with no connections. His birth parents were concerned, but the young Kataoka remained determined. He finally became a pupil of 13th generation Nizaemon Kataoka, the father of Hidetaro Kataoka as a Heyago, and was given the name of Chiyomaru.

"Before graduating from high school, I became the adopted son of Hidetaro Kataoka just as I received the adult name of Ainosuke," explained Kataoka. "My real father said then 'if you can stand at the

starting-line and become a Kabuki actor as an adopted son, we will let you go'. My parents sent me away, saying 'A career is important for men. Just go for it if you want to live in the world of Kabuki for the rest of your life. We cannot do anything for you as parents from now on.' I didn't really understand the meaning of being an adopted son at that time, but now I know it was a very difficult choice for them to make."

Kataoka recalls having to work incredibly hard when he first began to accept roles, and he found the task of playing many different 'background' characters incredibly challenging. He had to play his roles with great care, trying not to get in the way of leading roles whilst making sure not to let his own role 'die'. The sense of existence, of 'performing you', as Kabuki actors call it, proved very difficult for Kataoka to grasp. It was not easily learnt overnight, and he remembers studying the seniors' performances intensely in order to learn the 'steal arts' of truly becoming a character.

"Shape" and "mind" help to express each other

The beauty of style is important for Kabuki, but it is not only composed of the shape of the body; and every shape has its own meaning, expressing the mind of the dramatic personae. Unlike other productions like film and drama, there are no stage producers or directors in Kabuki. In the world of film, actors learn much about the expression of characters from producers and directors, and have the added value of observing their performances as a whole in the final film. This is invaluable, but because Kabuki is very traditional, the actors have to learn to 'inherit' the shape and expression of their clan's style, as Kataoka explains:

"For example, I learned the Yasuke role of selling sushi in "Yoshitsune Senbonzakura" from my father Hidetarou, and he also learned this from his father, 13th generation Nizaemon. So when you watch the Yasuke role I played, you are actually watching the Yasuke produced by Hidetarou, 13th generation Nizaemon, and ancestors many generations before, channeled through me. Their 'shapes' are left to travel through the centuries."

These shapes express the "heart" of Japan's traditional "Wa". Since there is "heart" in them based on so many generations, these works can be watched repeatedly for many years and remain charming. But how much this can be expressed and understood in the present age really depends on each individual actor.

Why is Kabuki needed in the present?

Over the years, many Kabuki scripts have fallen by the wayside, but recently many have also been dug up and efforts have been made to re-produce them for the modern age. Two years ago, for

example, “Shin Hakkenden” based on the classical Kabuki script was performed for the first time in 11 years, and the new Kabuki “GOEMON Ishikawa Goemon” that has also been adapted by flamenco was performed last year. Tsubasa Imai from Tacky & Tsubasa performed for the first time in Kabuki at Johnny’s Office.

Kataoka feels strongly that it is necessary to produce new products that could live on for many years, instead of just performing the older, traditional ones. As he points out, even the newest shows would be considered classics if performed regularly for the next one hundred years.

It is said that the etymology of Kabuki stems from ‘inclination of the heart’, and ought to include unconventional novelty and the spirit beyond common sense. After all, in order to inherit something without it being merely a shell, new challenges from time to time are required. “Following the death of Mr. Kanzaburo (Nakamura), I am keenly aware that we can enjoy Kabuki today only because the seniors have cut a path for us,” says Kataoka. “While inheriting the long history and tradition, we can also decide what we should leave for the future generations in several hundred years time. I would like the audience to feel the tracks of history while watching Kabuki.”

The fun of performance cannot be created by one person. No matter how hard the lead role performer works, it still would not result in a good performance if there are rickety surroundings. On the other hand, if those creating the background can perform properly, the lead role will create wonders. “In the world of Kabuki, people in their 40s are still rookies,” says Kataoka. “I will continue to train myself as an actor and raise the next generation at the same time, thus continuing and hopefully rejuvenating the amazing tradition that is Kabuki.”

6th generation Ainosuke Kataoka

Born in Osaka, Japan in 1972. Kabuki actor. He belonged to Shochiku Geino from 5 years old and began to perform on the Kabuki stage from 7 years old. With Hidetarou Kataoka’s eye on him, he became a Heyago of 13th generation Nizaemon Kataoka at 9 years old. He got the name of Chiyomaru Kataoka and performed in Kabuki for the first time as a sword-bearer in “Kanjincho”. He became the adopted son of Hidetarou Kataoka in 1992 and succeeded the name of Ainosuke Kataoka as the 6th generation. While attracting people’s attention mainly as an actor of Kamigata Kabuki, he was also popular after playing the elite officer Shunichi Kurosaki in TV drama “Hanzaki Naoki” in 2013. He is also active across a wide range of productions including participating the theatre “Sake and Tears and Jekyll and Hyde” produced and acted by Kouki Mitani, playing Kazuo Umezu role in film “Mother”, and playing the Ubaune role as a voice actor in “Film: Yokai Watch – the Secret of Birth, Mew”, to name but a few.

Research that could save thousands of women's lives

Spotlight on Michelle McIntosh

A new method of delivering the life-saving hormone-based drug oxytocin to new mothers has been developed by researchers in Australia with the help of Shimadzu's high-spec instrumentation

The Shimadzu Corporation prides itself on providing the ways and means for scientists across the world to make significant breakthroughs in all disciplines. Researchers in the medical sciences, for example, frequently use the equipment, instruments and analytical methods pioneered by Shimadzu to develop new drugs, life-changing treatments and aid in the understanding of complex diseases.

Michelle McIntosh from the Monash Institute of Pharmaceutical Sciences in Melbourne, Australia, is a world-leading researcher in the field of pharmacokinetics and drug delivery. McIntosh and her team have been in the media spotlight recently for one particular project, which has received large amounts of funding and attention from philanthropic and healthcare associations across the globe, and could help save 1.4 million lives in the next decade.

The project in question aims to create a new, inexpensive and easy-to-use method for delivering the hormone-based drug oxytocin to mothers immediately after childbirth. The drug can prevent the potentially fatal condition of postpartum haemorrhage: the excessive loss of blood after birth. The project is specifically targeted at helping mothers in developing nations, where the healthcare infrastructure is not able to support the injected form of oxytocin that is widely given in developed countries.

McIntosh and her team are working to create an aerosol inhalation system to deliver oxytocin – a simple product which can be used without highly trained medical personnel, or could even be self-administered if necessary. The new inhaled version of the drug also has a longer shelf-life than the current aqueous oxytocin solution used for injections and does not require refrigeration for storage.

"In 2011, at the Saving Lives at Birth Development XChange, this project was identified as one most likely to be transformational in maternal and neo-natal healthcare," explains McIntosh. "The Peer Choice award was presented by Hilary Clinton. We also went on to win the same award again in 2013." In 2013, the Monash project won The Australian Innovation Challenge, both in the Health category and as the overall winner. "The project has had a lot of significant supporters, encouraging us and providing us with the resources that we need to take it forward into a clinical development stage," [5] states McIntosh.

Current funders of the project include the United States government, through their International Aid Agency, and also the McCall MacBain Foundation, Grand Challenges Canada and the Planet Wheeler Foundation. "Recently we signed a co-development agreement with GlaxoSmithKline, the leading respiratory drug delivery company. This partnership will take us through human clinical trials, and will ultimately lead us to the production and dissemination of the final commercial product."

The Monash Institute of Pharmaceutical Sciences

MIPS

During the course of the product development, equipment and instrumentation made by the Shimadzu Corporation has proved critical to McIntosh and her fellow researchers. In fact, McIntosh has had a lengthy, and very fruitful, relationship with Shimadzu. McIntosh studied for her undergraduate pharmacy degree at Monash, followed by her PhD. She then moved to the University of Kansas in the USA, where she did her post-doctoral training in drug delivery research, and first became familiar with Shimadzu analytical equipment.

"In the early 2000s, I was awarded a grant from Shimadzu in the US to assist in the purchase of the department's first Liquid Chromatography (LC) Mass Spectrometer (MS), which was a 2010 single quadruple system," describes McIntosh. "I received training at the Shimadzu Maryland laboratories, and when I returned to Monash in late 2006 the first instrument I purchased was a Shimadzu LCMS 2010."McIntosh has continued her partnership with Shimadzu, and their collaboration is going from strength to strength. Recently they secured funding to establish a new, state-of-the-art laboratory at Monash, which will support future drug development projects for global health, as well as further supporting the oxytocin project. This laboratory is in addition to the Shimadzu Chromatography Laboratory, a unique, specialized teaching facility already in place at the university.

Fatal blood loss after delivery

Postpartum haemorrhage (PPH) is the excessive loss of blood (over 500ml) following childbirth, and in some cases it can be fatal within two hours if the appropriate medical care is unavailable. PPH is most commonly caused by a loss of muscle contraction in the uterus, a condition known as 'uterine atony', which would ordinarily stem the flow of blood. Other possible causes include lacerations to the birth canal, uterus or vagina, a retained placenta or blood clots. The condition is treatable via injections of oxytocin, a hormone naturally produced in the body which is strongly expressed during labour and childbirth. Oxytocin is classed by the World Health Organisation as an 'essential medicine'. It works by increasing uterine tone, helping blood flow return to normal.

The incidence of PPH is under control in developed countries, because women are automatically given a dose of oxytocin via injection within one or two minutes of giving birth. As McIntosh said in a recent interview for The Australian Innovation Challenge, however, "every three or four minutes, somewhere in the world, there is a mother who will bleed to death immediately after childbirth, and the greatest tragedy is that it is preventable." [6] In developing countries, particularly in rural areas with low resources, PPH is still a major cause of death; over 150,000 women

Dr. Michelle McIntosh

Senior Lecturer, Faculty of Pharmacy and Pharmaceutical Sciences

die each year as a direct result of the condition. In a paper on the PPH project published in PLOS One in 2013, the Monash team stated; "while current estimates attribute 35% of all maternal deaths [worldwide] to PPH, this statistic may be as high as 50% in some resource-poor settings." [3]

One of the main reasons for this is that the aqueous form of oxytocin used for injections requires safe storage and administration: the solution must be kept refrigerated and requires skilled professionals to administer the injection correctly. There is also the risk, as with any method involving needles and syringes, of needle-stick injuries, contamination and the transmission of blood-borne diseases. The infrastructure available in developing countries, particularly in rural areas, simply cannot meet these demands.

A simple solution via inhalation

"Ultimately, what I think everyone on the oxytocin project team would like to see is that it is just as safe for a woman to give birth in India, or in sub-Saharan Africa, as it is in Australia," says McIntosh. "So we'd really like to improve access to medicine so that women all around the world can be treated with life-saving drugs." [5]

In order to tackle the problems with oxytocin in an injected form, McIntosh and her team have been working on a new method of administering the drug via inhalation. The oxytocin itself is used in dry powder form, instead of aqueous solution, and the team's new collaboration with GlaxoSmithKline will allow them access to the company's low-cost inhaler devices, which are easy to use and disposable after a single use. The dry powder will have a much longer shelf-life compared to the injectable product which degrades quickly if not stored in refrigerated conditions, and considerable thought has gone into its design and components to ensure it is resistant to the high temperatures and fluctuating humidity likely to be encountered in many countries.

Inhalation of drugs into the lungs for absorption into the blood stream is not a new concept, but it is technically very difficult to achieve. At present, there are no products on the market for systemic delivery of a drug via the lungs. Initial investigations into various lung-targeted delivery methods began around fifteen years ago, and since then there has been increasing interest in the techniques. It appears that vaccine inhalation into the lungs may actually trigger a better immune response than injections. As such, lung-targeted delivery methods are of great interest to scientists developing immunisation programs. "At Monash, in addition to the PPH project, we currently have a number of research projects underway investigating vaccine formulations for lung delivery," states McIntosh. "The aim is to achieve both mucosal and systemic immune responses in the body via these new methods."

As McIntosh and co-workers stated in a review paper published in Cell Press in 2011, drug delivery straight to the lungs makes use of the "unique physiology of the respiratory system." [1] The large surface area of the lung, combined with its extensive vascular system and thin layers of tissue "might facilitate efficient systemic delivery of [drugs], thereby reducing the dose required." [1] In the 2013 PLOS One paper on their PPH project, McIntosh adds; "Given that [the lung] is the only organ through which the entire cardiac output passes, potential exposure of the blood to a bioabsorbable drug is therefore high." [3]

Developing the dry powder form of oxytocin

In order for McIntosh's concept to work, the team needed a way of creating an ultra-fine powder form of oxytocin. The Shimadzu analytical equipment at the Monash Institute has proved invaluable in the progression of McIntosh's project, providing the team with highly specialized, precision instrumentation with which to thoroughly examine oxytocin. Their work on the hormone has extended beyond the current project, leading to investigations into the molecular mechanisms inherent in oxytocin which determine its stability. These insights will prove useful in future applications.

In order to successfully delivery oxytocin to the lungs, the researchers needed to engineer particles to a specific mass and diameter (less than 5 micrometers) that would be readily delivered to the deep (alveolar) regions of the lungs. Once dissolved, the oxytocin could be absorbed via the lung epithelium into the blood stream.

The team decided on a spray-drying method to produce dry powder from aqueous oxytocin. As mentioned in the 2013 paper; "Co-formulation of peptides with sugars and amino acids is known to enhance the aerosolisation and fine particle fraction of powders." [3] To this end, McIntosh and co-workers incorporated the sugar mannitol, and two amino acids, glycine and leucine, as carriers into the spray-drying process. These particular carriers were carefully chosen because they do not interfere with oxytocin or affect its activity.

The team successfully created a powder with average particle diameter of around 2 micrometers. The particles are spherical and smooth in shape, enabling them to pass easily through the respiratory system.

Experiments on female sheep, discussed in the same paper, verified that inhaling the drug caused no irritation or airway distress. The drug reached the uterus via systemic circulation as anticipated, and facilitated the contraction of the uterine tissues in the same way as the injected form would. In fact, McIntosh and her team found that the dry-powder inhalation method elicited a faster response from the uterine tissues than the injected form.

Maintaining concentration and extending shelf-life

Given than many developing countries are in the warmer parts of the world, it was crucial that the drug retained both its potency and its stability, without the need for refrigeration, at temperatures of up to 50C. McIntosh needed to create a product that would remain safe in storage under high temperatures.

A key part of the development process involved the use of Shimadzu's high performance liquid chromatography (HPLC) equipment coupled with a mass spectrometer (MS). The high sensitivity and efficiency of the instrumentation allowed McIntosh and her team to create an extremely sensitive bioanalytical assay to

monitor the absorption and distribution of oxytocin after lung delivery.

Chromatographic techniques allow the careful separation of all components in a mixed substance. The individual constituents can then be identified, and the relative amounts of each can be verified using mass spectrometry. The team wanted to make sure that the dry powder held the correct concentration of oxytocin after the spray-drying process, and also that it retained the correct concentration once it had been kept in storage. The sample preparation process is far easier thanks to the sensitivity and selectivity of the Shimadzu equipment.

McIntosh and her team carefully monitored the percentage content of oxytocin and its carriers (mannitol, glycine and leucine) in different powder samples following the spray-drying process. They also monitored the powders over time, after storage at different temperatures. Following analysis conducted with Shimadzu's analytical equipment, the researchers were able to prove the enhanced stability of the dry powder form of oxytocin at temperatures up to 50C.

Furthering understanding of oxytocin

As a direct result of the PPH project, McIntosh and her team have contributed significant data and information about the oxytocin molecule itself. In a parallel piece of research, the Monash researchers investigated the mechanisms at the heart of oxytocin degradation. The deterioration of the hormone occurs naturally over time when kept in liquid form and, although refrigeration can slow the process, the degradation of aqueous oxytocin solution is of concern to healthcare professionals all over the world.

The researchers found that the oxytocin molecules undergo a variety of alterations when subjected to different environmental conditions. When oxytocin was stored at temperatures above 4C, the team identified a number of products resulting from so-called 'deamidation' – a chemical reaction which results in damage to the side chains of amino acids. Deamidation occurs far quicker as the temperature rises. They also uncovered linkages between the oxytocin molecules (polymerisation) which the researchers believe reduce the oxytocin's potency and activity.

Central to these investigations has been the Shimadzu 8030 and 8050 mass spectrometers coupled to an ultra-HPLC. The sensitivity of the equipment allowed the researchers to analyze oxytocin degradation under both standard and accelerated storage conditions. These problems appear to occur when oxytocin is stored in liquid form. The new dry-powder formulation could prove significant in overcoming these issues.

There has also been some concern over the stability and effectiveness of the aqueous oxytocin if it is inadvertently frozen en route to healthcare centers. This can happen on occasion during transportation and storage in remote areas of the globe. In a letter submitted to The New England Journal of Medicine in May 2013 [2], McIntosh and co-workers sought to reassure healthcare professionals that oxytocin retains its stability and effectiveness, even after several freeze-thaw cycles in temperatures as low as -20C.

In their study, the team used Shimadzu's HPLC instrumentation coupled with triple-quadruple MS equipment to verify the percentage and stability of oxytocin in the samples. They stored samples at -5C and -20C for seven days, and subjected another batch to repeated freeze-thaw cycles for five days. The researchers found no significant difference in oxytocin levels, or its activity, in the temporarily frozen samples when compared with a control batch kept at 4C for seven days.

A bright future for the PPH project

The PPH project is now entering a very exciting stage, because of the recently acquired funding and partnerships with a network of international sponsors to take the oxytocin inhalation product to clinical trials.

"The deal secured in September 2014 with GlaxoSmithKline means we can begin the first stage of testing in humans, to confirm that what we've seen in our pre-clinical development is replicated," explains McIntosh. "We're quite confident that it will be because oxytocin is a very old drug which has been used for a long time, and there is a substantial evidence base that it's safe. We have to get this first set of data from humans to present to the authorities who approve drug products." [6]

The researchers have already started using the new ultra-sensitive LCMS-8050 equipment made by Shimadzu which has recently been delivered to the Monash labs. The hope is that this instrumentation will come in handy during the clinical trials, allowing the team to study and monitor the delivery of oxytocin in humans. The LCMS-8050 is of particular interest, because it does not need the time-consuming pre-concentration of samples that less sensitive equipment required. The new equipment will also help them reduce their costs associated with sample preparation and allow them to increase sample throughput.

In a recent interview with the Shimadzu Journal, McIntosh explained that examining the mechanisms in oxytocin at the concentration ranges specific to their project is immensely challenging. She is certain that the new Shimadzu technology will allow fast scanning and fast switching for a definitive and accurate set of data.

Another significant issue, which McIntosh is very keen to publicise, is that education will play an important part in the dissemination of the product throughout the world, once it becomes commercially available. In an interview on Australian radio in 2013, McIntosh said; "There's a big role in education, in women being aware that this drug option is there and available to them, and also informing them that when they do get it, it's stable." [6]

Continuing support long into the future

As mentioned earlier, Shimadzu have recently partnered with Monash Institute of Pharmaceutical Sciences, the Helen Macpherson Smith Trust and PerkinElmer (a fellow analytical equipment developer) to establish the HMS Trust Laboratory. This world-class translational pharmaceutical science laboratory within Victoria will directly support capacity building, skills growth and educational advancement in the field of pharmaceutical science. The laboratory, due to open in the first half of 2015,

will house unique instrumentation accessible to all researchers within Melbourne and Australia, and will provide a transformative capability to advance and accelerate the translation of basic research into new medicines.

McIntosh and her team hope to share their knowledge and experience in the development of pharmaceutical products with other groups developing new medicines. The laboratory will house four Shimadzu LCMS systems, three HPLCs, an X-ray diffractomer and the first MALDI 7090 instrument in Australia. The MALDI 7090 will be used for macromolecular characterisation as well as mass spectrometry imaging. This will provide an unprecedented level of insight into the biodistribution of drugs and their metabolites.

The Shimadzu Corporation are looking forward to continuing their strong support of Monash Institute of Pharmaceutical Sciences, and indeed of Michelle McIntosh and the PPH project - an endeavour that encompasses the core beliefs of the company.

"We have a responsibility to share our knowledge and our capabilities to help people all around the world," says McIntosh. "The privilege of working on a project like this is what really motivates me; it makes it easy to come to work. I really believe that the future of this project is truly exciting." [6]

Creating a world where there is 'Excellence in Science' is Shimadzu's goal, and the corporation very much believe that Michelle McIntosh and her team are representative of this philosophy. As McIntosh herself says, she feels they are ready to make "a tangible difference" to healthcare around the world. [5]

A strengthening relationship between Shimadzu and Monash: The Shimadzu Chromatography Laboratory

The Shimadzu Corporation teamed up with the Monash Institute of Pharmaceutical Sciences in 2011 with a five-year partnership to create a new state-of-art analytical laboratory on site at the university. The lab comprises Shimadzu chromatographic equipment and analytical techniques for separating, identifying and analyzing complex substances, such as blood plasma. It is very similar in terms of technology and set-up to the types of labs found in industrial settings.

The lab is specifically designed for undergraduate teaching – aiming to foster the next generation of scientists in a unique training facility. The students are given the chance to try hands-on, problem-solving tasks which really challenge their practical skills. This gives them a head-start in the skills and mental agility required when facing tough technical challenges in their later careers.

Students of the Bachelor of Pharmaceutical Sciences degree graduate from Monash with a comprehensive skill set in maintaining and operating HPLC and other chromatographic instruments, as well as the ability to analyze and validate data from these techniques. These skills are highly sought-after in both industrial and academic settings, and both the university and Shimadzu hope that experiences gained in the lab will give Monash students the edge in applying for their first jobs.

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Butterfly hovering in space and the search for life beyond our solar system

A scientist's dream of finding life on other planets

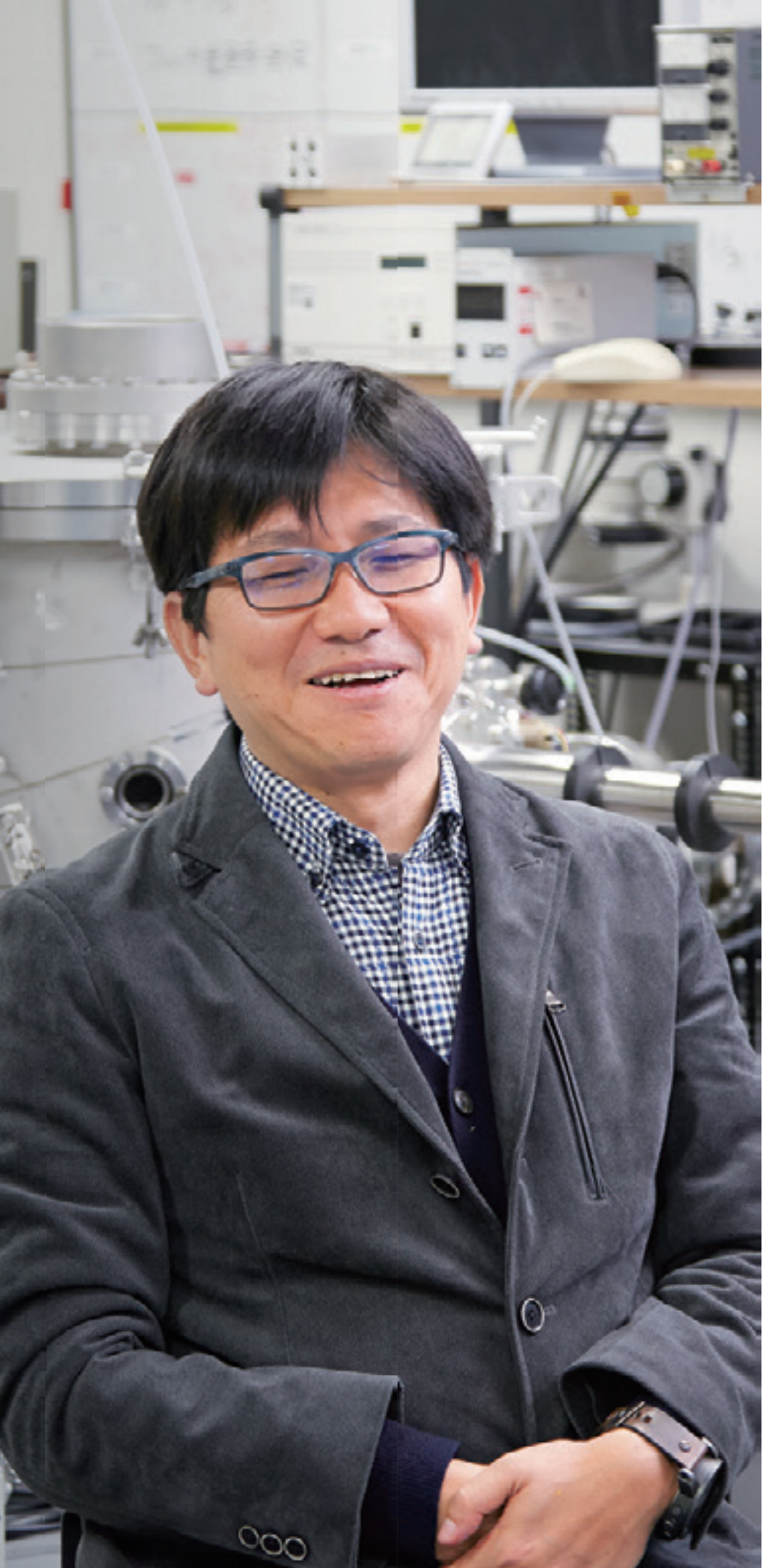
The universe is full of mysteries. How was our solar system formed? Why was a life-bearing environment created only on Earth? These questions still remain to be solved by future research. With passion and advanced technologies, scientists are now endeavoring to unveil the true nature of our universe.

Professor Ichiro Yoshikawa

Space and Planetary Science Group, Department of Earth and Planetary Science, Graduate School of Science, The University of Tokyo

Profiles

Graduated from the University of Tokyo School of Science. He worked as an assistant at the Institute of Space and Astronautical Science (ISAS), while on a doctorate program at the University of Tokyo in 1998. Currently, he specializes in measuring extreme ultraviolet light and is working on analysis of the atmospheres of the Earth and other planets within the solar system, as well as terrestrial atmospheres outside the solar system. In 2005, he returned to the University of Tokyo to participate in projects such as the Kaguya lunar orbiter. In 2013, he joined a project to launch the Hisaki Spectroscopic Planet Observatory to study the mechanisms behind atmospheric escape on Venus and Mars and to analyze the electron heating mechanisms in the Jupiter's magnetosphere.



"My ambition is to search for life beyond our solar system," says Ichiro Yoshikawa, Professor, Space and Planetary Science Group, Department of Earth and Planetary Science, Graduate School of Science, The University of Tokyo. "This is what I want to do during my lifetime. To this end, it is not too early to embark on such a mission and send a space probe outside our own solar system. Fortunately, however, we now have "HISAKI" which will show us the direction of stars potentially having a 'wet environment' suited to biological activities. By focusing on these stars, we might be able to find and communicate with extraterrestrial life."

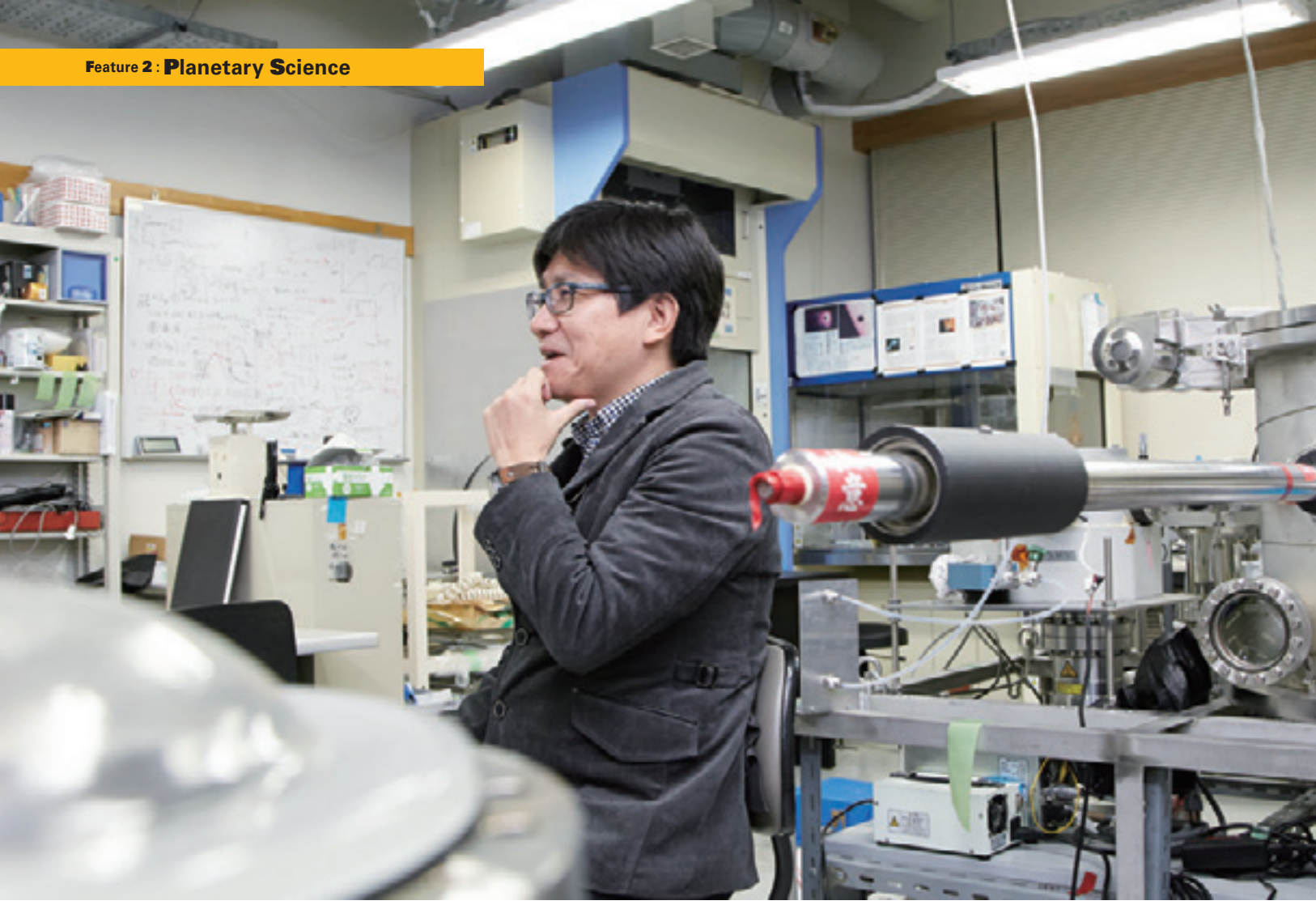
Boundary between Earth and outer space

In September 2013, the Spectroscopic Planet Observatory for Recognition of Interaction of Atmosphere "HISAKI" (SPRINT-A), a space telescope equipped with an extreme ultraviolet (EUV) spectroscope, was launched by the Epsilon Launch Vehicle. EUV is extremely short wavelength ultraviolet light. Under EUV light, the Earth looks quite different from the blue round sphere that we usually see; it appears like a butterfly spreading its wings which are 5 to 6 times as long as the Earth's radius with their roots extending from the North and South poles.

What becomes visible is plasma (ionized gas) that surrounds the Earth.

Yoshikawa explains that, "This is the boundary between Earth and outer space. The inside the wings is what we call the 'plasmasphere' where matter from the Earth exists in an ionized state, while the outside is the outer space where solar winds blow harshly."

Yoshikawa is a leading scientist in the area of planetary atmospheres and he led the development of the EUV telescope onboard HISAKI. The main objective of HISAKI, the world's first space telescope for remote observation of planets, is to explore the atmospheres of planets including Venus, Mars, and Jupiter from



orbital positions around the Earth.

Detailed analysis of the spectrum of EUV light from planets reveals differences in wavelength (color) depending on the composition of the atmosphere. Hence, on the basis of such differences, atmospheric constituents of planets can be investigated. Shimadzu Corporation developed and manufactured the diffraction grating, a key device used in the spectrometer loaded onto HISAKI.

Geomagnetic field to deflect solar wind

It is not widely known but the Earth's atmosphere constantly escapes into space. However, around 0.1% of land surface atmosphere is contained in the plasmasphere.

How does this happen?

When oxygen and nitrogen molecules that float up in the air defying the pull of gravity reach a certain altitude, their electrons are stripped off due to interaction with ultraviolet light and X-rays contained in sunlight, thereby turning oxygen and nitrogen into positive ions (O_2^+, N_2^+, NO^+, O^+, N^+) , that is into a plasma. Trapped by the Earth's magnetic field lines, these ions start to move around in a growing spiral orbit and form a thin layer, analogous to a huge soap bubble floating in space and preventing atmospheric dissipation.

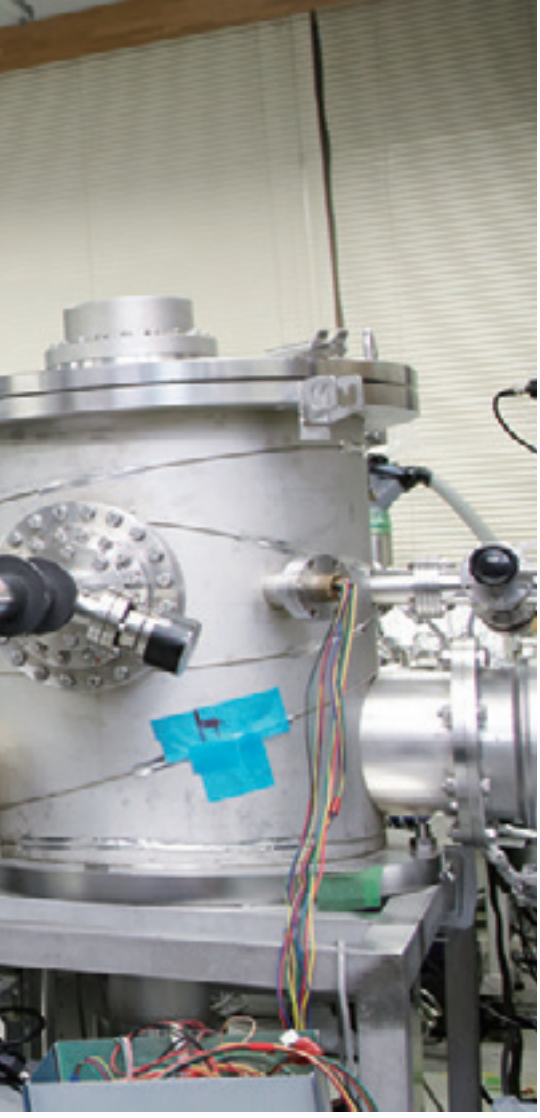
Solar activity varies with time and increases and decreases over a monthly cycle. When solar activity is high, turbulent solar wind blow, and strip away the Earth's plasma atmosphere. Although several tonnes of plasma atmosphere leaks away every day, the Earth constantly generates new atmosphere from its constituents. Hence it is commonly believed that terrestrial atmosphere will not be depleted for billions of years in the future.

"If the Earth's magnetic field were weaker than it is now, solar winds would reach the Earth's surface with much more atmosphere escaping, making Earth unable to accommodate life. Indeed, due to the weakness of the magnetic fields of Venus and Mars, it has been found that far more volume of atmosphere is escaping from these planets," says Yoshikawa.

Mystery of Venusian thick clouds

Here we come across another question. Venus has a thick atmosphere and atmospheric pressure at the surface is approximately 90 bar. Since the atmosphere is mostly carbon dioxide, 96% by volume, the surface temperature reaches 400-500 degrees Celsius due to greenhouse effects. So the question arise as to why Venus has a denser atmosphere than Earth even though far more of the atmosphere escapes than the Earth?

"This is a paradox," says Yoshikawa. "Venus is close to the Earth in terms of



mass. Since Venus is closer in distance to the Sun, it is exposed to harsher solar winds with more atmosphere escaping than Earth. However, Venus still has a thick atmosphere. As yet, we do not have an answer to this question."

One of the missions of HISAKI is to observe the atmosphere of Venus. So far, analysis of atmosphere samples captured by a number of probes flying by Venus has revealed its composition and the presence of oxygen molecules, which are transformed into a plasma in the escaping atmosphere.

It is well known that the atmosphere of Venus is mostly carbon dioxide with a large volume of oxygen ions escaping. The estimated escaping volume, however, varies over four to five orders of magnitude. "This is weird enough, but there is another confusing fact," says Yoshikawa. "The escape of carbon ions has not been observed. Hence there are several theories about the origin of the Venusian atmosphere. If carbon ion escape is observed, we can take another step to unravel this mystery."

Is the universe full of life?

There are many other interesting phenomena in planetary atmospheres. Lo, a moon of Jupiter, is known for its tremendous volcanic activity. The plumes generated by active volcanism are released into space. The plumes are turned into plasma under the intense heat of volcanic activity, which is trapped by the magnetic field lines of Jupiter, thereby forming clouds that wrap around the planet. The ions of sulfur and sodium contained in the plumes emit light in the clouds. Such phenomenon has also been observed on the surface of Jupiter where the magnetic field lines reach, and notably, these ions emit light almost simultaneously with those in the clouds.

"This phenomenon is similar to the Aurora observed on Earth and is considered to be caused by highly energized ions reaching the Jovian atmosphere by chance," explains Yoshikawa.

The problem is the velocity of these excited ions. Emission of light in the orbit of Lo and the surface of Jupiter occurs almost simultaneously and sequentially. If transported by convection of the magnetic field lines, the ions cannot move fast enough to cause simultaneous emission. Since the magnetic field lines act like violent storm for electrically charged molecules, it is usually not presumable that the molecules go across the magnetic field lines to take a shortcut. However, there is no other explanation for this phenomenon.

"What is the force that drives this phenomenon? Are there any mechanisms that we have never considered? I am looking forward to tackling these questions in my future research."

Meanwhile, Yoshikawa turns his eyes toward outside our solar system. "Thanks to the excellent resolution of HISAKI, we will be able to analyze atmospheric constituents of planets of other solar systems. Abundance of carbon and oxygen ions will, if found, would be proof of wet environment. It is conceivable that life exists out there."

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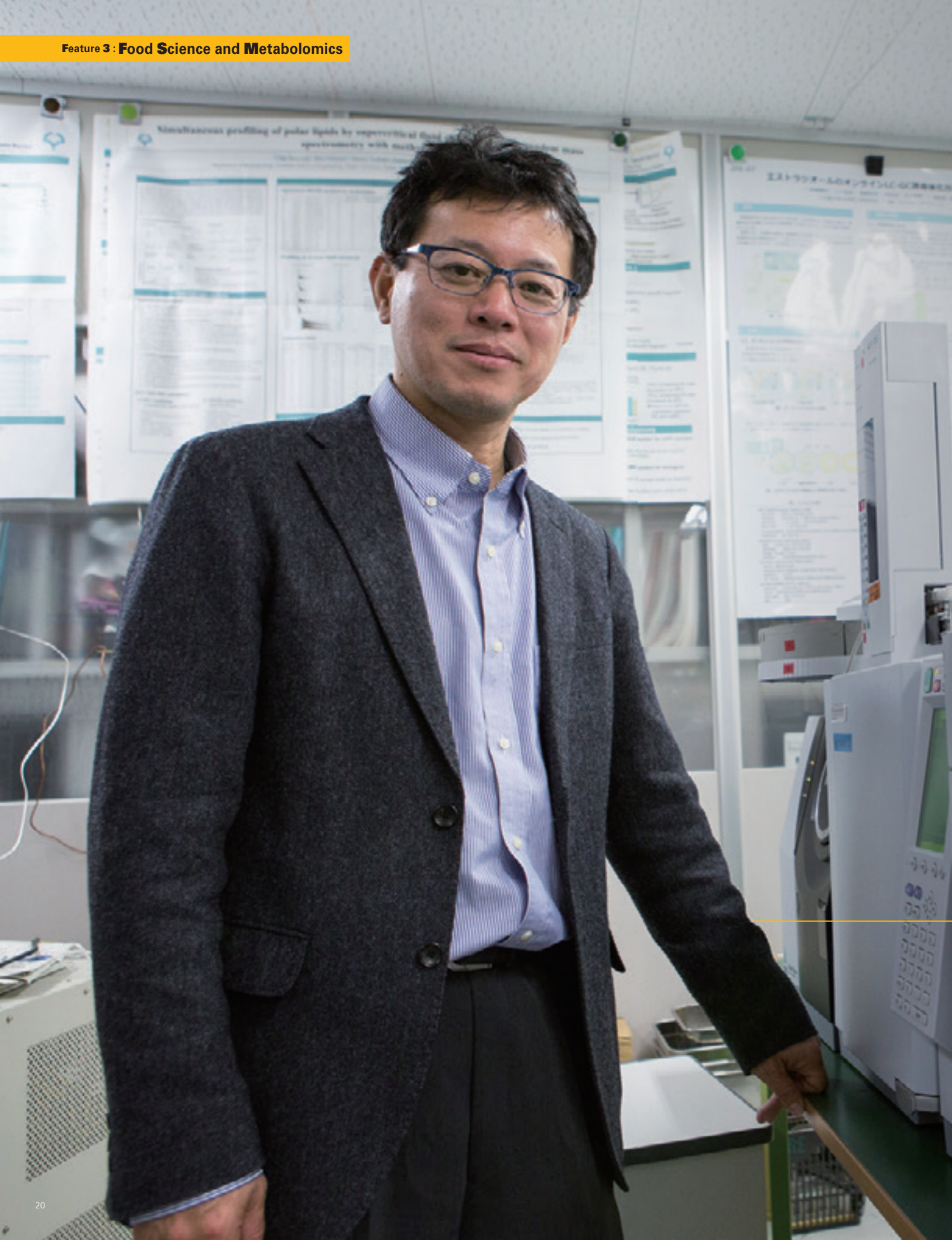
Further information
Ichiro Yoshikawa

Department of Earth and Planetary Science, University of Tokyo
https://secure.eps.s.u-tokyo.ac.jp/en/member/index.php?_urid=1684&_lang=en



Focus on metabolomics for food science

“My research reflects my love of food!”

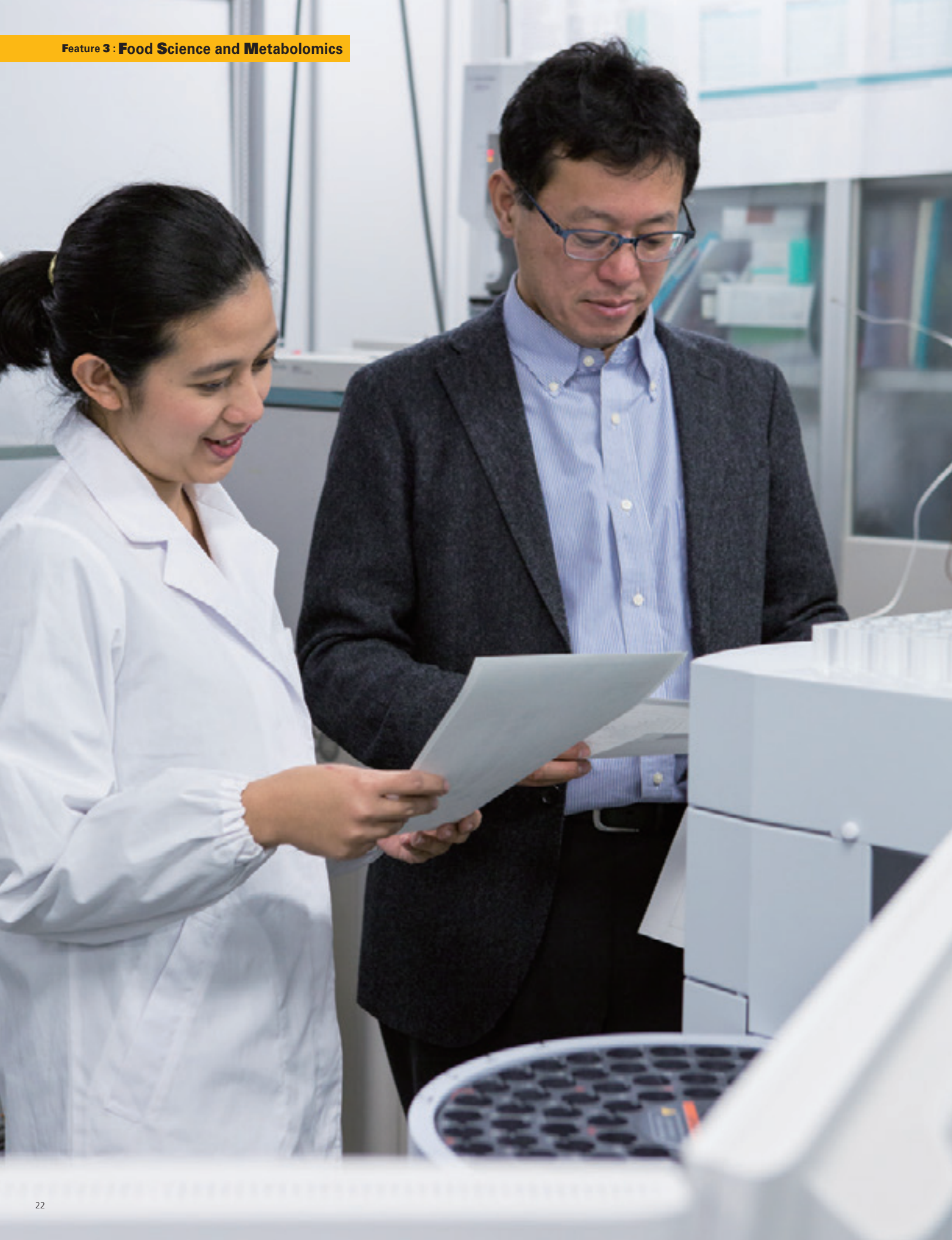
Research in the field of metabolomics involves analysis of chemical markers or ‘fingerprints’ that are produced by well-defined processes that occur in in biological cells. For example, analysis of urine, saliva or sweat gives doctors critical information about a person’s health, including the early warning signs of the possibility of diseases such as diabetes for patients with high glucose levels. The Fukusaki Lab. has been involved in food metabolomics research since 2007 and has produced highly cited publications on analysis of the quality of food, such as green tea and watermelon.

Professor Eiichiro Fukusaki

Department of Biotechnology, Graduate School of Engineering, Osaka University.

Profiles

Professor Eiichiro Fukusaki is head of the Metabolomics Lab at the Department of Biotechnology, Graduate School of Engineering, Osaka University. In 1985, Fukusaki joined Nitto Denko Corporation after graduating with a master’s degree from Osaka University. In 1995 he left his position as Deputy Chief Researcher, Center of Core Technology at Nitto Denko Corporation and returned to Osaka University where he was given a full professorship in 2007. Professor Fukusaki has published more than 200 technical articles, book chapters and reviews and holds 17 Japanese and eight international patients. He works actively with collaborators from 30 other academic institutes, as well as industrial partners in areas including pharmaceuticals, medicine, and the food industry. He received the “Saito Award” from the Society of Biotechnology of Japan in 2004.



"In 1985 I graduating with a master's degree from Osaka University and joined a company where I focused on organic chemistry, in particular mass spectroscopy and nuclear magnetic resonance," says Professor Eiichiro Fukusaki, Department of Biotechnology, Graduate School of Engineering, Osaka University. "In 1995 I returned to Osaka University as an associate professor to a department that specialized in fermentation. This is when I made the decision to start research in 'metabolomics' and established this laboratory." Fukusaki has published more than 200 scientific articles including book chapters and reviews, and holds 17 Japanese patents and eight patents valid in other countries. He collaborates with over 30 academic institutions and major companies in areas including food, medicine, and pharmaceuticals. In 2004 Professor Fukusaki was awarded the 'Saito Award' by the Society of Biotechnology, Japan.

Collaboration with Shimadzu Corporation

"My group has extensive expertise in analyzing the metabolomic fingerprints of a wide range of living things including medicine and food," explains Fukusaki. "Our research on metabolomic profiling of Japanese sake, green tea, soy sauce, and cheese reflects my love of food!"

Professor Fukusaki and his group conduct their research in close collaboration with industrial partners. For example, recent research on soy sauce, cheese, and Japanese sake was carried out with internationally renowned companies specializing in the manufacture of these food products. "We also work closely with Shimadzu Corporation on the development of analytical instrumentation and protocols for our research," says Fukusaki. "We have a long-standing and strong relationship with Shimadzu Corporation that has been pivotal in our ability to demonstrate the power of metabolomics in the food industry as well as medicine and pharmaceuticals. We rely on many analytical instruments developed and manufactured by Shimadzu Corporation, such as the GCMS-QP 2010 Ultra gas chromatography mass spectroscopy system. The instrumentation is crucial for our research on authentication purposes, prediction of food sensory attributes, and the identification of metabolites responsible for flavor, aroma, and other characteristics of food."

Fukusaki and his group believe that major advantageous features of gas chromatography mass spectroscopy (GC–MS) include the ability to quantitatively measure many metabolites in a single-step with high sensitivity and reproducibility. It is also easy to access vast data bases and compound libraries—such as the National Institute of Standards and Technology mass spectral library—to identify compounds without the necessity for time consuming experiments with standardization compounds. Fukusaki notes that compared with other analytical methods, GC-MS enables relatively easy identification of compounds of the reproducibility in obtaining unique mass spectra of different compounds.

The quest to quantify genuine Kopi Luwak—the world's most expensive coffee

"Kopi Luwak are Indonesian words for coffee and the Asian palm civet," explains Sastia Prama Putri, special appointed Assistant Professor at the Fukusaki Laboratory. "I suggested using metabolomic profiling to investigate the authenticity of Kopi Luwak when I joined the lab in early 2011 because detecting counterfeit and impure Kopi Luwak is a big problem in my country, Indonesia."

The history of Kopi Luwak can be traced back to the mid-1800s when Indonesian farmers noticed that the cat-like palm civets ate certain coffee fruits and left undigested beans in their excrement. The farmers collected and processed these beans to produce their own coffee. Rumor of the Kopi Luwak spread to the west, leading to the dawn of the world's most expensive coffee made with the assistance of the civets.

One cup of Kopi Luwak can cost as much as $100. The process of making Kopi Luwak starts with high quality coffee beans. Next the beans are fed to palm civets for them to undergo the partial fermentation inside the creature's digestive tract, where the exterior fleshy parts of the beans are digested. The remaining intact beans are excreted after a day or so. The process of producing coffee with these beans continues with cleaning the beans, then further fermentation, after which the beans are dried and roasted before finally being ground and brewed. The passage of the beans through the digestive system of palm civets and subsequent processing gives the highly desired flavor of this expensive brew sold for around $300 to $700 per kilogram.

Needless to say, Kopi Luwak is a lucrative business but it is prone to counterfeiters and fakes. So, how can you tell the difference between genuine Kopi Luwak and fakes? "We decided to devise a proof of concept procedure based on metabolomics to detect genuine Kopi Luwak," says Putri. "I contacted the Indonesian Coffee and Cocoa Research Institute (ICCRI) to

Sastia Prama Putri

special appointed Assistant Professor at the Fukusaki Laboratory, Graduate School of Engineering, Osaka University, Japan

Dr Putri received her doctorate "on the discovery of novel bioactive compounds from natural products" from the International Center for Biotechnology, Osaka University. Since joining the metabolomics laboratory in 2011, Dr Putri has actively promoted metabolomics to scientific communities in Indonesia, her home country.

ask for their cooperation. They supplied us with a wide range of high quality samples. This international collaboration enabled us to conclude our initial experiments in around one year."

The team developed a metabolomic based process to assess the authenticity of Kopi Luwak which consists of mixing coffee samples with water, alcohol and chloroform to extract signature-chemicals that are responsible for the flavor of coffee. These were then analyzed with Shimadzu Corporation gas chromatography mass spectroscopy instruments. The researchers conducted experiments with 21 different samples: genuine Kopi Luwak; regular coffee; a mixture of 50% Kopi Luwak and 50% regular coffee; and a concoction made from coffee beans that had undergone chemical treatment to mimic the environment the beans would be exposed to in a mammal's digestive tract.

"Our findings were clear," explains Putri. "Genuine Kopi Luwak had significantly higher concentrations of citric acid and malic acid [1]. We also found a higher ratio of inositol to pyroglutamic acid in the real Kopi Luwak. Although there have been reports on using a so-called 'electronic nose' to discriminate between Kopi Luwak and regular coffee, our paper is the first to describe the metabolites that actually make the differences."

These results were obtained using 21 different samples of coffee. The Fukusaki Lab plans to extend this series of experiments to include more 'markers' to elucidate further unknown metabolic reactions that occur during the passage of the coffee beans through the digestive tract. This will help in quality checks and give clues about the origin of the flavor of Kopi Luwak.

An important outcome of this research was that Fukusaki and his colleagues not only defined the key signature chemicals in authentic Kopi Luwak but also established the 'gas chromatography flame ionization' (GC-FID) method for testing. The GC-FID is less expensive than GC–MS, thereby making it more accessible to workers in the coffee industry in Indonesia.

Putri wants to build her experience of setting up this international collaboration to initiate new projects. "Metabolomics to improve post-harvest technology for food products, and 'nutri-metabolomics' - connecting food intake to improving human health - are two areas I want explore in the future." Specifically, Putri and colleagues are devising tests for checking the authenticity of the ingredients used to make 'birds nest soup', as well as the peel of fruit from mangosteen trees (that grow in Indonesia), used in traditional medicine in Southeast Asia.

Research highlights, reviews and books

1. SP Putri, T. Bamba & E. Fukusaki, Application of metabolomics for discrimination and sensory predictive modeling of food products. Chapter 5 of Metabolomics - food and nutrition (e-book). Future Science, London, UK. December 2013, Pages 54-64
   doi: 10.4155/ebo.13.503.

   Putri etal describe the potential of metabolomics as a "as a valuable postgenomic research tool" in food science for monitoring the quality of food from pre-harvest to post-harvest storage and logistics. The authors describe the pertinent characteristics of "predictive metabolomics for the prediction of sensory characteristics of food as well as comparative metabolomics for the discrimination of food products". The chapter covers the use of metabolomics for quality control and process management in food science as well as shedding light on the potential of metabolomics for elucidating the mysteries of the relationship between nutrition and health.

2. K. Jumtee, T. Bamba, and E. Fukusaki, Fast GC-FID based metabolic fingerprinting of Japanese green tea leaf for its quality ranking prediction, Journal of Separation Science 32, pp.2296-2304, (2009).
   Metabolic fingerprinting of plants requires fast, high throughput analytical instrumentation. Currently GC-MS is widely used because it is robust, sensitive and reproducible but it has the drawback that compounds that form ions during electron impact ionization cannot be detected. Here, the authors describe the potential of gas chromatography flame ionization detection (GC-FID) as a rapid and inexpensive method for fingerprinting metabolites extracted from Japanese green tea leaves to assess the quality of the tea.

3. Mass Spectrometry-Based Metabolomics: A Practical Guide, Edited by Sastia Prama Putri, Eiichiro Fukusaki, November 25, 2014, CRC Press.

In an easy-to-follow style, this book describes the pertinent features of research in metabolomics including and analytical protocols for widely used samples, and reference library of metabolite profiles.

Selected publications in food science

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A flourishing partnership with world-leading chromatography expert Luigi Mondello

The Shimadzu Corporation has long enjoyed a fruitful collaboration with Italian scientist Luigi Mondello, a leading light in the field of analytical chemistry

The ability to accurately identify all the components in a mixture is crucial in many fields of analytical chemistry, such as food science and the petrochemical industry. The most well-known method for separating individual components of mixed substances is chromatography – a group of laboratory techniques in which a mixture carried by a fluid (the 'mobile' phase) moves across another material (the 'stationary' phase). The individual constituents of the mixture are forced to separate because they travel at different speeds through the stationary phase. There are many different types of chromatography, each useful for a different purpose, and the Shimadzu Corporation has long been at the forefront of chromatographic technology.

A long-standing partnership

Shimadzu's advances in chromatographic techniques and the design of new equipment have been helped considerably by a partnership forged twenty years ago with a high-flying academic researcher from Italy, Luigi Mondello. A world expert in the field of chromatography, Mondello has enjoyed considerable success over the years and has been awarded several medals and scientific accolades for his advances in chromatographic techniques and their application in analytical sciences. His main focus of research is in food science, investigating the natural constituents and the contaminants in the food we eat.

"I have used equipment made by Shimadzu since I was a graduate student; we began collaborating at that point and our scientific partnership has continued to this day," explains Mondello. "The collaboration with Shimadzu has been extremely productive for both sides. Shimadzu have helped us to meet our analytical goals, and we have supported and aided them in customizing new equipment to meet the requirements of current global research."

Mondello's laboratory at the university is over 1000 square meters in size and 90% of all their equipment is from Shimadzu. In fact, Mondello has at least one of every piece of equipment and technology designed by Shimadzu in his laboratory. He helps the company decide which systems to commercialize by running prototypes and trialling new concepts. The partnership is truly beneficial to both parties, as well as to the next generation of scientists, as Mondello describes: "The collaboration with Shimadzu offers an unprecedented opportunity for our students, who are exposed to state-of-the-art instrumentation while they are training in our laboratory."

What is chromatography?

Basic chromatography, first discovered in 1900, involves the simple separation of components in a mixture, making use of the fact that when a mixture is dissolved in a liquid or gas, the different constituents flow at different rates, causing them to separate. Take printing ink on paper, for example. If printed paper is held upright in a container of water, the water will gradually move up the paper, taking the ink with it. Different components of the ink move at different rates, and a clear separation pattern appears. This pattern can then be analyzed in order to identify the constituents of the ink.

Chromatography has come a long way since the turn of the last century. There are now many different forms of the technique, utilizing the properties of different liquids and gases as the mobile phase where the substance to be analyzed (or the 'analyte') is dissolved. Equally, the methods and materials used for the stationary phase (the paper, in the example above) have also changed considerably.

It is now possible to use different materials for the columns used in the stationary phase. So-called 'normal-phase' (NP) separation uses resins made from silica or aluminium oxides, which are hydrophilic, meaning that any water-attracting molecules in the analyte are absorbed and hydrophobic molecules pass through.

However, hydrophilic molecules can be forced through normal-phase without being absorbed if the polarity of the liquid in the mobile phase is increased. The more recently developed 'reverse-phase' (RP) separation uses columns made from hydrophobic material, meaning that the opposite absorption occurs – hydrophobic molecules are attracted to the RP column, unless the polarity of the liquid phase is decreased.

Chromatography, now often used in combination with mass spectrometry, is used in multiple settings for many purposes, from analyzing food samples for contaminants to examining the substances present in plant extracts and even oil samples.

Luigi Mondello's career: a tour through recent developments in chromatography

Through his partnership with Shimadzu and his drive to continuously improve chromatographic techniques, Mondello's career spans much of the recent history of new techniques in analytical chemistry. After graduating with a degree in Chemistry in 1991, Mondello moved to Leeds in the UK to complete his postgraduate studies. There he began working on multidimensional chromatography. Instead of passing a small amount of analyte through one chromatographic cycle, in multidimensional chromatography the analyte is passed through two separation stages. The second stage is different from the first in terms of the materials used or the temperature at which it runs, meaning that any constituents that were weakly separated in the first run may appear more strongly in the separation bands from the second run. This allows for a higher resolution, more robust and accurate set of results.

In 2004, Mondello and his team published results from a novel multidimensional high performance liquid chromatography (HPLC) technique. The team created a two-stage separation using a microbore silica column which operated in NP mode in the first separation, and a monolithic column operating in RP mode in the second run. This was the first 'interfacing' of NP and RP systems.

"We tested the technique on the components of lemon essential oil," describes Mondello. "The new, fully-automated and low-cost method achieved complete separation of all the components in the sample."

This was one of the first examples of a so-called 'coupled' chromatographic technique: combining two forms of liquid chromatography together in NP and RP phases. One of the main advantages of multidimensional comprehensive HPLC is that entire samples are subjected to the two separations, each at high resolution, which dramatically enhances the capacity of the technique to analyze highly complex mixtures. However, HPLC cannot be used for every sample type, so further research was required into other coupled techniques.

Over the past decade, Mondello has gone on to develop many variants of liquid-liquid (LCxLC), gas-gas (GCxGC) and liquid-gas (LC-GC) chromatography, all with Shimadzu's high-spec equipment as the basis of his research.

Into the fast lane: Developments in fast gas chromatography

The capabilities of gas chromatography have expanded considerably in recent years. The combination of 2D gas chromatographic

techniques with mass spectroscopy (MS) in the last decade, for example, has allowed scientists to examine samples with high levels of sensitivity and specificity. GC is very useful as it can be used to examine volatile substances – such as substances in the petrochemical industry, which LC cannot. GC-MS systems are used in all kinds of forensic analysis – for identifying explosives or food contamination, and even as scanners for identifying drugs in luggage at airports.

Mondello is leading the way in the development of 'fast gas chromatography' methods, which give results in real-time and allow rapid, accurate analysis. "These techniques are very useful if immediate answers are required, or if you have a vast number of samples to work through," explains Mondello. "Concerning the analysis of food contaminants, for example, the complexity of the matrix and the presence of unidentified compounds at very low levels mean that we need devices that work to a very high level of specificity and at high speed."

Mondello recently published results of an investigation into food contamination from paperboard packaging using GCxGC-MS. Mineral oil products, such as aromatic hydrocarbons, leech into food from the ink used on packaging. Mondello analyzed pasta, rice and icing sugar from supermarkets, with pasta found to be most contaminated with aromatic compounds. "The results from experiments such as these must be absolutely accurate so that marketing and food standard agencies know exactly what compounds are present in foodstuffs," explains Mondello.

Shimadzu and Mondello continuously work to upgrade current multidimensional systems to meet these demands, and have recently moved into designing innovative dedicated software and producing GC-MS spectra libraries for reliable compound identification.

The rise of a new company: Chromaleont

Mondello set up a start-up company running from the University of Messina in 2007. The company, called Chromaleont, has shared projects with Shimadzu, producing, updating and promoting the software and spectra libraries for chromatographic techniques, as well as providing a base for analytical scientists to test new instruments and ideas.

"Chromaleont is a society that offers solutions for the development of analytical instrumentation and dedicated software for chemical analysis, as well as consultancy in the field of separation science," explains Mondello. "Its mission is to push the limits of separation science forward, while proposing the simplest solutions. The goal is the creation of a team of research specialists converging from different areas to realize innovative and ambitious projects in our field."

Chromaleont is currently involved in trialling prototype instruments and associated advanced analytical techniques for Shimadzu, including a four-dimensional GC system, combining a first stage pre-purification liquid chromatography step followed by GC-GC-GC. "This allows the pre-separation of a sample into chemical classes, and the removal of non-volatile matrix components which are likely to contaminate the GC system," describes Mondello. "It is also possible to inject higher sample amounts, collect low-level constituents in a relatively short time, and all in a fully automated fashion."

Current research and prototyping at Mondello's laboratory

Mondello and his team of researchers are currently involved in the development of other prototypes for Shimadzu at their laboratory, which, in Mondello's words, "represent a paradigm shift in chromatography separation." Two such pieces of equipment, which are now being marketed by Shimadzu, are the multidimensional comprehensive LC model named Nexera-e, and a GC counterpart named 5D Ultra-e.

Nexera-e combines two independent separation modes with a new switching valve design, enabling separation of even the most complex mixtures and providing a new level of knowledge and understanding of sample analytes. This is especially beneficial to the analysis of pharmaceutical impurities, food extracts, natural products and synthetic polymers.

"The 5D Ultra-e is a five-dimensional chromatography system (LC-GCxGC-MS/MS), and is currently installed at the Hong Kong government laboratories," says Mondello. "We have successfully used it to tackle the challenging task of coal tar analysis, using HPLC to pre-separate the sample into three fractions (non-aromatic, aromatic, and oxygenated compounds)."

The future of chromatography: Down to the nano-scale

As well as the continued advances and proliferation of multi-dimensional and fast chromatography, Shimadzu and Mondello are looking ahead at the possible miniaturization of chromatographic techniques. This is a major emerging trend in the field of separation science, with clear benefits in reducing solvent and sample consumption and costs, while at the same time reducing environmental impacts.

"In this context, we are focusing on the development of a nano liquid chromatography (NanoLC) system coupled online to an electron impact mass spectrometer (EI-MS), again in collaboration with Shimadzu," says Mondello. "Such a configuration allows for direct introduction of a tiny amount of LC effluent into the mass spectrometer. The analytes can then be vaporized, ionized and detected without any interference. It may also lead to the construction of an EI mass spectral database of non-volatile and thermally unstable compounds. This would represent a significant breakthrough for the identification of complex samples in future."

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Chromaleont Company profile brochure 2015

Shimadzu Latin America S.A.

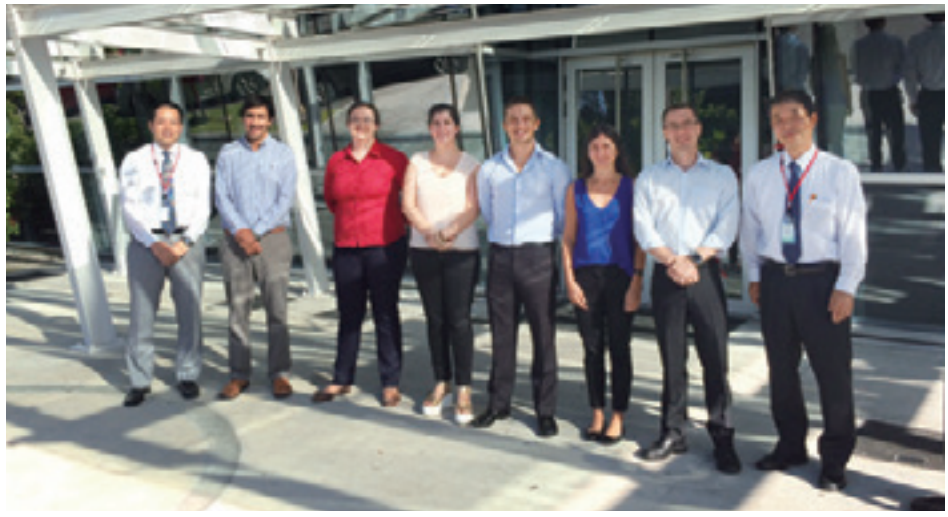
Launch of Shimadzu Latin America (SLA) in Uruguay

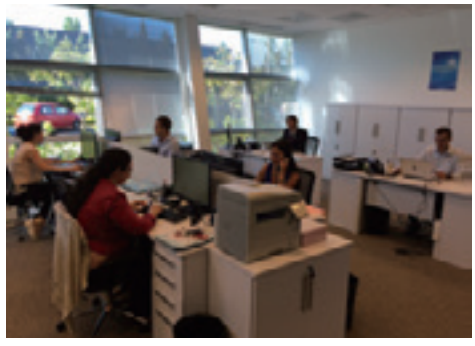
SLA is strategically located in Uruguay to support customers in Central and South America

Shimadzu Corporation established a wholly owned subsidiary Shimadzu Latin America S.A. (SLA) in Uruguay in order to strengthen the company's sales and distribution of analytical and measuring instruments and medical systems and also provide better support for customers and distributors in Central and South America.

Shimadzu Corporation established Shimadzu do Brasil Comercio Ltda. (SBL) in Sao Paulo, Brazil in 1997 to provide sales services and advise distributors in Brazil and other countries in Central and South America. However, as businesses in the area expanded, SBL could not cover all of Central and South America.

Uruguay is located between Brazil and Argentina. The capital Montevideo has good access to major cities in South America. It is 30 minutes to the Argentine capital Buenos Aires by air and two hours to Sao Paulo in Brazil where SBL is located by air. Moreover, Uruguay has some advantageous features. It has a free-trade zone where foreign-capital organizations can establish a company easily, and the degree of financial freedom is high as compared to surrounding countries. Since Uruguay's national language is Spanish, SLA located in Uruguay is expected to help to improve the company's marketing ability and provide better support for customers and distributors in other Spanish-speaking countries in Central and South America as compared to SBL in Brazil whose national language is Portuguese.





Completion of New Shimadzu Subsidiary Manufacturing Plant in Long Beach, California

Shimadzu Precision Instruments, Inc. has completed a new manufacturing plant for commercial aircraft equipment at Douglas Park in Long Beach, California. With the doubled total floor space and newly added faculties for parts machining and surface treatment, it will strengthen its capabilities as a manufacturing plant. This plant will increase product development speed and the ability to provide high-quality, competitively priced products and services tailored to customer needs.

Location: 3645 North Lakewood Blvd., Long Beach, CA 90808
Total Floor Space: 5,462 m^2 (of this, plant floor space is 4,135 m^2)
Start of Operations: June 2015
Primary Products Manufactured: Engine accessory gearboxes, flight control systems, landing gear, cargo door actuators, etc.

Shimadzu Corporation Establishes Sales Company in Malaysia—New Analytical and Measuring Instruments Plant Also Scheduled to Start Operations in 2016—

In order to strengthen their business operations in the ASEAN and Indian regions, Shimadzu Corporation has established Shimadzu Malaysia Sdn. Bhd., a sales company in Malaysia.This subsidiary has now started operations. In 2016, Shimadzu Corporation also plans to establish a new manufacturing base for analytical and measuring instruments in Malaysia, to strengthen their capabilities in terms of both manufacturing and sales. Thus, Shimadzu intends to establish a timely product supply system and extensive sales capabilities that can focus on the needs of the ASEAN and Indian regions.

Shimadzu Malaysia Sdn. Bhd.
Location: Nouvelle Industrial Park 2, Petaling Jaya, Selangor, Malaysia
Total Floor Space: About 945 m^2, of which 160 m^2 is an application laboratory
Business Description: Sales and service of analytical and measuring instruments and medical systems in Malaysia

25th Anniversary of the Establishment of Shimadzu (Asia Pacific) Pte. Ltd. (SAP)

This year marked the 25th anniversary of the establishment of Shimadzu (Asia Pacific) Pte. Ltd. (SAP), a base in Singapore for Shimadzu's Asian operations.
In 1990, SAP was changed from a Shimadzu's local office to a subsidiary company. It began operations with 15 staff members. SAP afterwards established its own subsidiaries in the Philippines, India, and last year in Malaysia, and current sales have grown to about 14 times the initial level.
As the customer service base, SAP will continue to expand operations in the Asian region, where high growth is expected.

Published the Latest Science and Technology Magazine

Genzo Sr. created the Physics and Chemistry Industrial Arts Journal in July 1886 (19th year of the Meiji period). This monthly magazine featured the latest theories and information about physics and chemistry, and was produced in association with learned people who had studied abroad in Western countries. It explored academic theories focusing on up-to-date knowledge and introduced practical science and technology by quoting from other science magazines published in the West.

By looking at an advertisement in the first issue of the Physics and Chemistry Industrial Arts Journal, we can see that the business at the time was described as “the manufacture and sale of instruments for physics and chemistry and various machines. “ In the fifth issue, we can see that the business had expanded with “the tuning of medical equipment” added to the description. In the eighth issue, in addition to the above description, the distributors they had established were introduced—two in Kyoto, three in Osaka, and one in Okayama and Kanazawa respectively—which reveals they had expanded their sales channels as well.

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