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New Analytical Chemistry

from Keio's Faculty of Science and Technology

Medical and environmental sensing chips that can be made with an inkjet printer alone.

Citterio, Daniel

Associate Professor
Department of Applied Chemistry

Introducing Researchers

Featured in this issue is Associate Professor Citterio, Daniel, who focuses on the development and practical implementation of a handy sensing chip fabricated by the inkjet printing technology.

Creating Paper-based Sensors Using Inkjet Printer

Development of handy sensing chips for medical and environmental uses

The condition of one's health can be judged by simply putting a drop of saliva or urine on a piece of paper and observing a color variation. Or the degree of river pollution can be determined from a small quantity of river water . . . The development of such handy sensing chips is now in progress. All that is required to create the sensing chip is paper and an inkjet printer. We listened to Dr. Citterio who addresses the development of innovative, highly useful sensors by combining existing technologies with new "chemical sensing inks" specifically designed for this purpose.

Fantastic paper-based sensors . . . No special equipment, not even a power supply, is required to use them!

"What I'm focusing on are chemical sensors and biosensors that can be carried and handled by anyone and anywhere, making measurement quite easy," remarks Associate Professor Citterio.

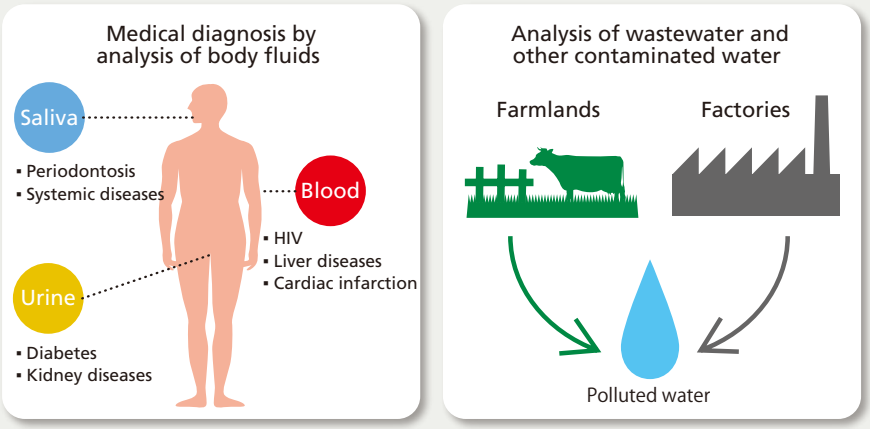
Among familiar examples of chemical sensors are litmus paper for pH measurement and gas leak detectors. Furthermore, biosensors make use of biomolecules such as enzymes and antibodies to selectively recognize target substances. One well-known example are pregnancy test kits. What Dr. Citterio aims to develop are handy sensing systems that will allow instantaneous visual recognition, like that of a color variation on litmus paper.

"In particular, I'd like to create handy sensing systems for medical and environmental applications. When it comes to health management and medical diagnosis, the sensing system will allow you, while at home, to check urine, saliva or blood for protein, blood sugar and hemoglobin conditions, for example. Regarding environmental applications, the system will make it possible to easily check drinking or lake water for pH value or for the existence of contaminants such as lead, cadmium and other heavy metals as well as nitrite, arsenic, herbicides and pesticides. Effective combination of already established sensing technologies and their adaptation towards new inkjet printable materials is my approach to the development of easy-to-use and highly practical systems."

With this approach in mind, Dr. Citterio decided to employ "paper" as the sensor substrate – filter paper made of cellulose fibers. He thought paper would be ideal as it is available anywhere easily and for a low price, lightweight and handy to carry, mailable, easily storable, and can be burned or discarded after use. Presently available systems for medical and environmental analysis are of a large scale, their use requiring an air-conditioned laboratory and cooling equipment like a refrigerator. But a paper-based system would eliminate the need for such equipment or even a power source. This means great advantages when used at home and at fieldwork sites and in developing countries where medical facilities are poor or insufficient. What's more, it can be used easily even under emergencies.

"In the world of chemistry, paper has been used since ancient times. Chemicals can be fixed to it and it's capable of wicking a solution by means of the capillary action phenomenon. One fine example is the established technology known as paper chromatography used to separate chemical substances by virtue of these filter paper characteristics.

The amount of reagent consumption would be minimized if various kinds of tests can be conducted by dropping only one drop of sample on to a small piece of paper. Given some reagents for example based on antigen-antibody reactions are costly, it is very important to reduce reagent consumption by reducing the chip size itself.

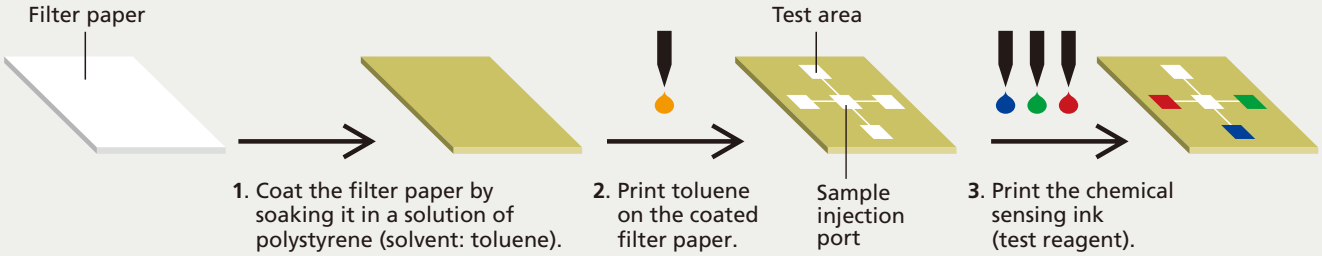


Handy medical/environmental sensing chip
The use of this chip allows anyone to conduct medical tests with only a small amount of body fluid (saliva, blood, or urine) and to check wastewater or river/lake water quality – at low costs, promptly and easily.

Making chips with one single inkjet printer

In reality, several research groups recently began pursuing the method of using paper as sensor material. However, the originality of Dr. Citterio's team lies in the use of an inkjet printer based on the piezo method (a method of jetting out ink by means of a piezoelectric element when voltage is applied to the print head).

"Since more than ten years ago, research efforts have been increasingly made on Micro-TAS (Micro-Total Analysis Systems) – devices for the analysis of chemicals by combining microscopic



How to make a medical/environmental sensing chip

The sensing chip is made using the following processes ; (1) Soak the filter paper in a solution of polymer (polystyrene) for coating, making it hydrophobic ; (2) Use an inkjet printer to discharge an organic solvent (toluene) and make a channel. Polymer on the part to which toluene was applied is dissolved, thereby creating a hydrophilic channel ; (3) Then use the inkjet printer to print the sensing ink (test reagent) on the test area at the end of the channel.

flow-channels, reaction chambers and mixing chambers on a minute chip. Glass and plastic chips have been used until recently. In 2007 Professor Whitesides of Harvard University proposed paper chips as a cheaper and easier solution.

In association with paper, Dr. Citterio's team set their eyes on an inkjet printer capable of jetting any desired controlled amount of ink. Today, inkjet printing has grown into a highly generalized technology, finding wide applications not only for paper printing, but also for large-size color display films through to the production of microscopic items such as semiconductor substrates. This advantage makes the inkjet printer very attractive, Dr. Citterio says.

"To make a chip, you basically put the required reagents in the ink cartridge and print onto paper. Then, simply use a pipette to apply a sample like blood or urine. Soon a reaction occurs. Besides, we are not only able to print chemical reagents, but we also create microfluidic channels on the chip using the inkjet printer. It will be highly cost-saving if we can perform the entire chip-making process with a single printer, you know."

The keys: the sensing ink and chip's microfluidic channel design

The greatest challenge involved in the chip-making process is the development of multiple functional chemical and biochemical sensing inks. For this purpose, the creation of chemically functional materials in nanoparticulate form is essential.

"With ordinary printer nozzles, there are limitations to the liquid viscosity and particle size that can be discharged. Also, you must ensure that the normally water soluble reagents are not washed away by the flowing sample, but stay firmly on the test area so that color change occurs uniformly, in a repeatable manner. So it becomes important to exert ingenuity such as the use of small polymeric particles in the ink to prompt the reagent adsorption onto the paper.

Although we still have a number of chemical and physical problems to be solved, it would be fantastic if in the future we could develop a sensing system with which we can perform everything with an ordinary printer we're using at home."

Another challenge Dr. Citterio is intent on is the design of the microfluidic channels to be patterned on the paper substrate – only 500μm in width.

"We are making the flow-channels and sensing areas by printing a pattern on a piece of filter paper that has been dried after being soaked in a solution of a highly hydrophobic polymer known as polystyrene. Here we use toluene as the ink, an organic solvent that dissolves polystyrene. In other words, only the flow-channel and sensing area parts become hydrophilic. Chemical and biochemical sensing inks are printed onto those sensing areas to make the final chip.

If we succeed in making a good pattern, it will be possible to have one single piece of paper accommodate multiple test items."

Currently Dr. Citterio is also studying a method of drawing a pattern using a material that is more environment-friendly than toluene, accelerating the research work aiming for completion and launch within a few years' time.

(Reporter & text writer: Madoka Tainaka)

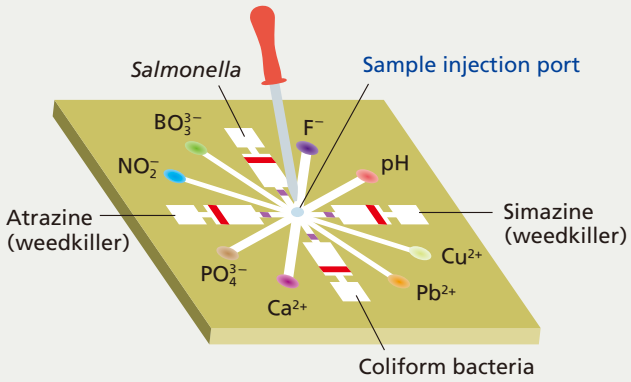


Fig. A: Water-quality testing chip

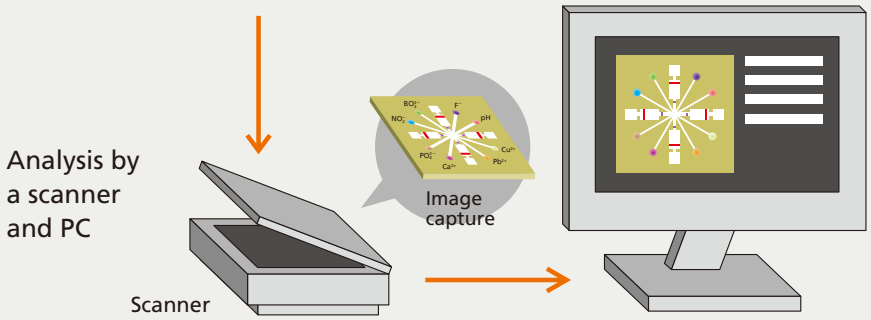


Fig. B: PC and color analysis software package

A handy system anyone can use anywhere

When making a sensing chip, you print the sensing inks (test reagents) for your targeted test items such as *Salmonella* and ingredients of weedkillers (Simazine and Atrazine) on the chip. Then, by simply placing one drop of the sample into the sample injection port, reactions will occur in the respective areas, making it possible to measure multiple test items simultaneously (Fig. A). This sensing chip is not only suitable for visual judgment, but it is also capable of quantitative analysis if used together with a scanner. Systemizing it by combining with a PC, you can create an easily portable, epoch-making sensing system (Fig. B).

Japan is complete with an excellent research-encouraging environment

Mr. Citterio is devoted to the development of handy paper-based sensors that anyone, not only specialists, can handle with ease. Eight years have passed since Mr. Citterio, born in Zurich, Switzerland, came to Japan to engage in research work. He praises Japan as an attractively fertile soil for research pursuits thanks to strong bonds among researchers as well as an excellent research environment relatively favored with both ample budgets and advanced facilities.

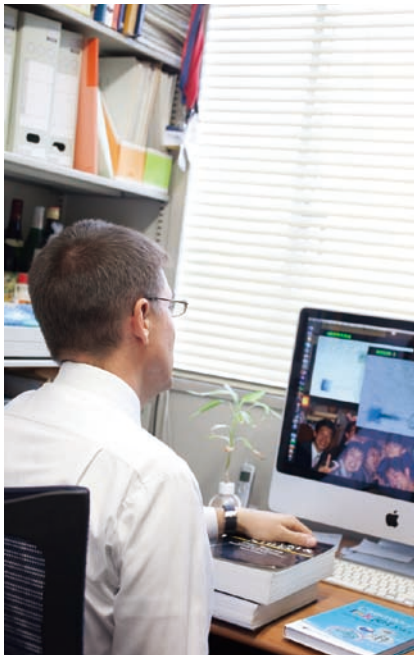
When did you come to Japan?

My first visit to Japan was in 1996 when I was a doctor course student at the Swiss Federal Institute of Technology in Zurich (ETHZ). At that time I had an opportunity to participate in a joint project and belonged to the Chemical and Biosensor Laboratory at the University of Tokyo's Graduate School of Science, staying for three months.

With universities in Europe, students in natural sciences usually find employment after completing a doctor's course and then pursuing postdoctoral studies overseas for at least one year. Many of my fellow students liked to study in the United States, but I didn't want to go there. This was because, rather than for the sake of research only, I also wanted to broaden my horizons in life. In other words, I wanted to take up new challenges in a land where culture and language are totally different. So I made up my mind to study as a postdoctoral fellow in Japan, the destination I had visited as a doctor course student.

To tell the truth, during my first visit to Japan I had an opportunity to visit Keio University for only one day. On that occasion I paid a visit to Professor Suzuki's lab, to which I belong now. I learned that Professor Suzuki's lab is engaged in research close to that of mine. Finding that students there were all open-minded and easy to communicate with, I had a good impression of Keio.

It was in March 1998 that I revisited Japan as a postdoctoral fellow of Keio University. My initial plan was to stay for one year. But as I got accustomed to my research life in Japan, I began to think it would be a waste of precious opportunity if I left Japan as initially planned. Our lab's atmosphere was so comfortable that I postponed my return again and again. As a result, I had stayed in Japan for four and a half years in total.



Did you acquire your Japanese language ability in those days?

Yes. In my early years I could hardly speak Japanese, which put me in trouble even for shopping and other daily matters. But my Japanese gradually improved thanks to once-a-week Japanese lessons from a private teacher and daily communication with students on the campus.

Later, in 2002, I returned to Switzerland and began to work as an assistant professor at a university. Meanwhile, I became interested in patents by that time because our Keio lab had obtained several patents. So I acquired a patent attorney qualification by entering a university again to study.

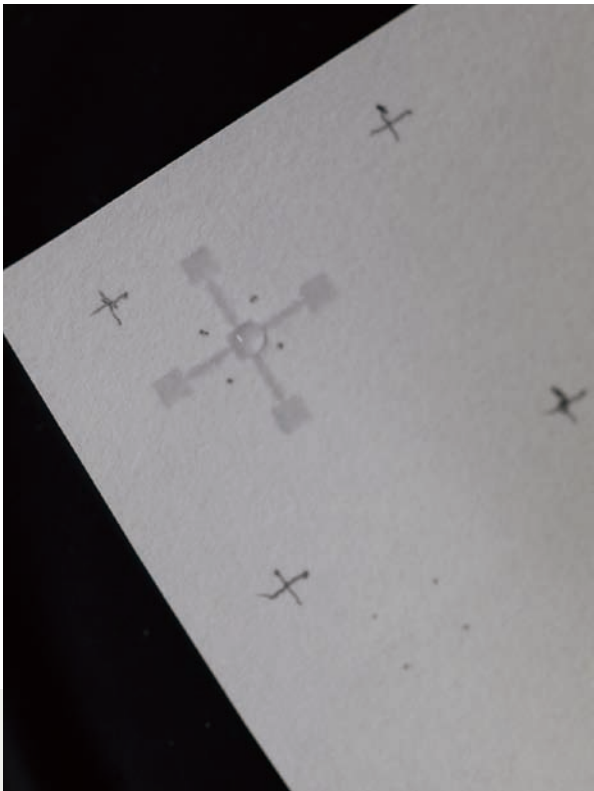
Armed with these careers, I once found employment with a Swiss chemical maker, but left this company a year later and returned to Japan.

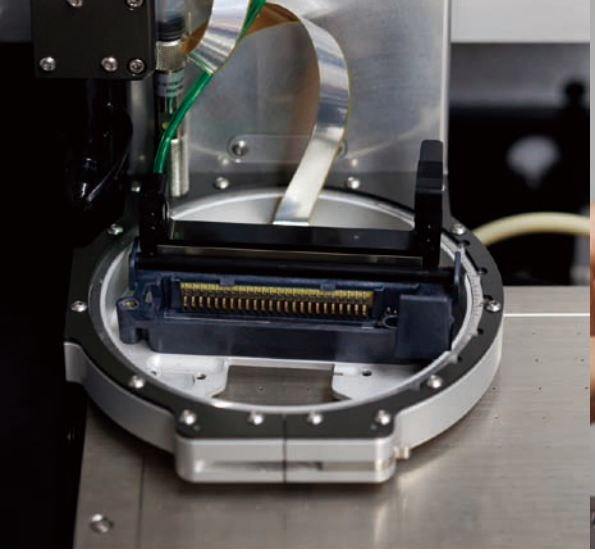
Why?

I had long enjoyed a life steeped in unrestricted research activities, conducting experiments at university labs and writing theses. But the moment I joined the company, such lifestyle was lost, which caused me to entertain anxiety about my future. I thought I was a researcher type after all.

In the meantime, Professor Suzuki was kind enough to invite me to participate in a new project. I thus came back to Keio University's Faculty of Science and Technology in 2006 as a non-tenured associate professor. From the academic year 2009, I became a full-time associate professor.

From 2007 on I focused on research into paper-based chips using the inkjet printer. I think Keio is complete with a





superb environment for researchers.

You mean it's a favorable environment for researchers?

When we propose a research project and it is accepted, the university offers an adequate support environment and we can proceed with the project almost unrestrictedly. This is a great merit.

Things seem to be changing a bit these days. Even so, I think Japan still offers an environment in which research budgets are available relatively easily. I also notice strong bonds existing among researchers like Professor Suzuki. They all value mutual human connections, which is good. For example, even when you want to know about something that is outside of your own specialty field, you can consult a specialist of that particular field through a network – a great environment.

By the way, is your name Italian?

Yes. This is because my ancestors immigrated from the northern part of Italy to Switzerland. My father was born in Switzerland while my mother had two nationalities: German and Swiss. My mother tongue is German.

Incidentally, as a small boy I was not particularly interested in becoming a scientist. Rather, I wanted to become a pilot but gave up the dream because of weak eyesight. Somehow I was good at foreign languages (English, French, Italian and Latin) at school, which made my teacher recommend me to major in foreign languages in the future. Though I undoubtedly liked foreign language study, I didn't think I would choose foreign language study itself as my profession.

What I am today as a researcher may partially be the influence of a high school chemistry teacher who lived in a neighboring condominium. I still remember him telling me many things about chemistry while giving me a ride to school. At one time I was absorbed in a chemical experiment kit for junior high school students. Due to failure of an experiment one day, I discolored the wallpaper of my room into brown. (laughter)

You like to use your own hands to create something, don't you?

Yes, I do. In fact, I'm also good at cooking. In a way cooking is similar to chemical experiments, you know. In Japan I've been living in the Hiyoshi area. Living a single-life, when I have time I often invite friends or some of my students and treat them to dishes of my own cooking.

Since I like to move not only my hands but also the whole body, I often enjoy outdoors on days off – activities like cycling, skiing and hiking. I was surprised to find few young Japanese people taking up hiking as outdoor recreation. Given superb scenic attractions in Japan, I'd like more and more students to enjoy what nature has to offer. I recover vitality needed for research work through such outdoor leisure activities.

◎ **Just a word from . . .** ◎

● A student: Daniel-san is frank and easy to communicate with. All of us follow him like one of our seniors. Not only does he allow whatever we like to challenge, but also he is always willing to give advice. He is a truly reliable teacher.

(Reporter & text writer: Madoka Tainaka)

For the full text of this interview, please refer to:

http://www.st.keio.ac.jp/kyurizukai

Citterio, Daniel

By creating and combining functional materials (dyes, polymers, etc.), his research work focuses on the development of (bio) chemical sensors for application in industrial, medical, and environmental analysis. Born in Zurich, Switzerland, he graduated from the Department of Chemistry of the Swiss Federal Institute of Technology (ETHZ) in 1992 and obtained his Doctor degree from the same school in 1998. After postdoctoral research at Keio University, he became a research associate at ETHZ. Through postgraduate studies, he obtained a Masters degree in Intellectual Property and joined a Swiss chemical manufacturer as a patent attorney. In 2006, he returned to Keio University, were he became a tenured Associate Professor at the Department of Applied Chemistry in 2009.

"I love conducting experiments and writing theses in my lab … I found myself suited to be a researcher."

Q&A with Associate Professor Citterio

Q : Why did you choose Japan and what merits did you find in working here?
A : I chose Japan because I wanted to lead a challenging life as a researcher in an environment with a different cultural background. Once settled in Japan, I found this country very favorable for my research activities. First of all, I found it relatively easy to obtain research funds. Another merit was easy access to a network of human connections, which is vitally important for developing research work in this country. In this respect I owe much to my teacher, Professor Suzuki, who is a leading figure in his field and keeps many valuable connections in and outside of Keio.

"Japan as seen from foreign countries; Foreign countries as seen from Japan"

Q : When it comes to studying overseas, Japanese students appear rather reluctant whereas students from other Asian countries are very positive. What do you think?
A : According to my observation, Japanese students are also motivated to do so. Given the prolonged recession, they tend to become hesitant for fears that the chance of finding employment may be delayed by at least one year. Some students opt to study abroad only after having secured their employment though . . . I'm always trying to take students with me to participate in international conferences. This often turns out successful because such occasions stimulate students' intellectual appetite and motivate them to study overseas.

I think that Keio University is providing its students with sufficient opportunities in this respect. Keio maintains double-degree programs* with some overseas universities and an internship collaboration agreement with the Swiss Federal Institute of Technology Zurich (ETHZ), my alma mater. Opportunities are not few. The foremost reason for this problem is that students are concerned about employment. This is my impression.

Q : In what ways do you think human connections are important in Japan?
A : In Japan human relationships among researchers are strong and exchange of information among them is relatively open. Though I have no experience of working in the United States, my impression is that individual researchers there are more inclined to protect their own worlds than those in Japan.

(*Double-degree program: This program allows a student to obtain double degrees simultaneously from Keio and an overseas counterpart in agreement if the student has completed a specified curriculum mutually agreed upon by the two universities. Currently Keio University (Faculty and Graduate School of Science and Technology) maintains such programs with Intergroupe des Ecole Centrale (France) and Lund University (Sweden).)

"Encouragement of Cosmopolitanism"

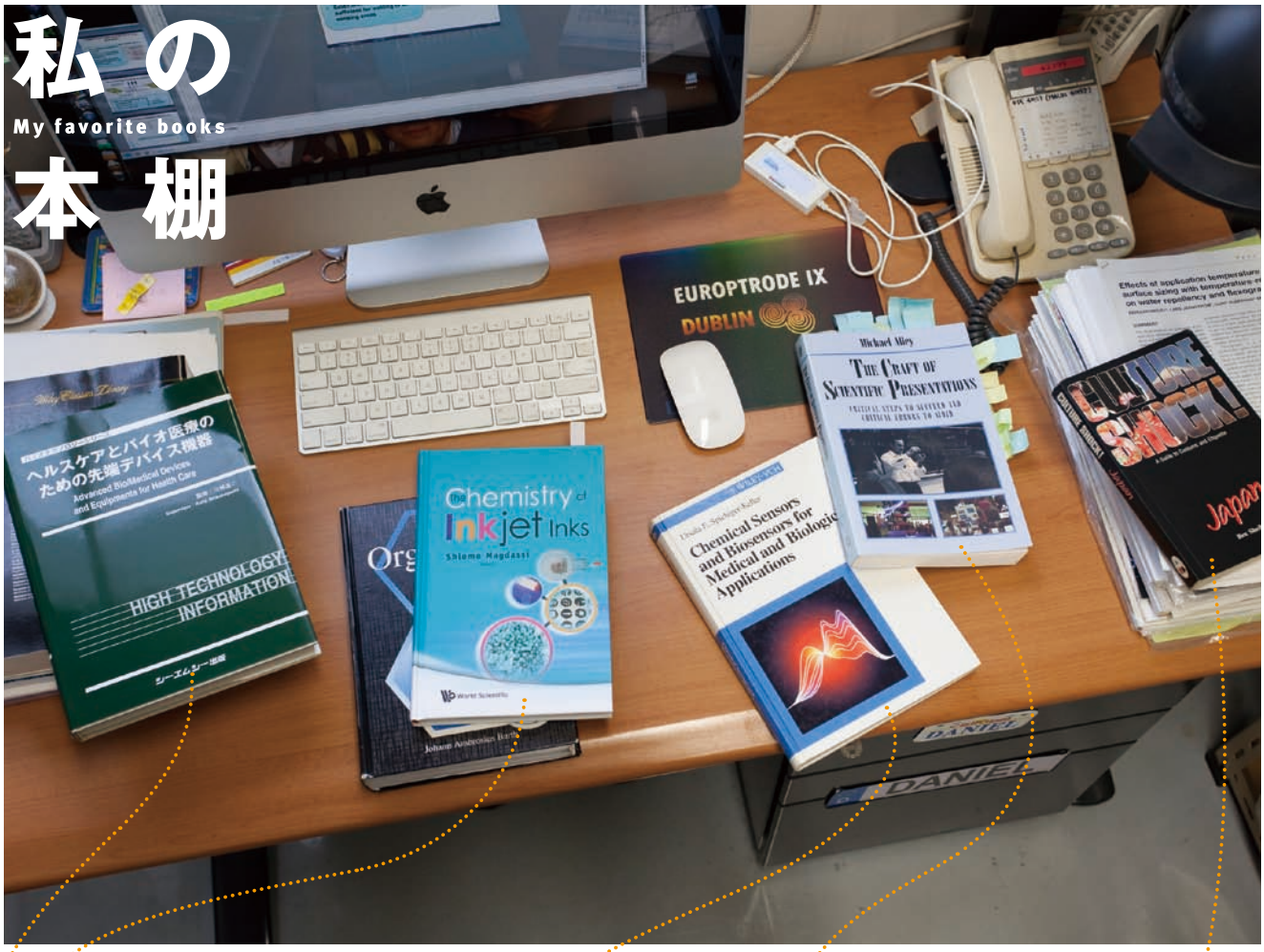
Q : What points do you think are important for Keio students to develop activities on international scenes?
A : First and foremost is the ability to communicate in English. Suppose you can communicate fully in English when participating in an international conference, even if you are a master's course student you'll be able to make a presentation on one-of-a-kind research achievements of your own, which gives you great confidence as a researcher. If you lack the ability to communicate in English, especially that concerning your own specialty field, the hurdles will remain high. So I'm always telling my students to lower the hurdles of language to begin with.

Q : Mr. Citterio, you are proficient in Japanese in addition to German (your mother tongue) and English. Do you have an aptitude you can recommend to Keio students?
A : To learn Japanese, I began by listening to rinko* sessions held in Japanese in our lab and at seminars. To master technical terminology, listening is particularly important since good dictionaries are rarely available. As for English, I'd suggest students listen to lectures by overseas researchers. By merely listening to lectures in English, you can substantially increase your knowledge of English technical terms. I'd like them to avail themselves to such opportunities as much as possible. This is the way I learned Japanese. So I can now read theses written by students in Japanese, although I still find it difficult to read more common Japanese sentences as found in magazines and the like.

(*Rinko: Rinko is an occasion where students report on the progress of their respective research activities and discuss their contents and directions. In some cases, rinko is held to read imported books and original theses with students taking turns, or to solve fundamental problems.)

私の本棚

My favorite books



The Chemistry of Inkjet Inks -In English

This book is relatively new in my personal library. As an Analytical Chemist specialized in the development of chemical sensors, I felt that I did not have sufficient background knowledge about inkjet printing inks. However, in my recent research, I need to transform the reagent mixtures required to create a chemical sensor into an inkjet printable liquid. The book summarizes most of the important facts and properties that are important for inkjet printable fluids. I think that the information presented in this book would otherwise only be accessible by extensive search of the patent literature.

Advanced Bio/Medical Devices and Equipments for Health Care -In Japanese ヘルスケアとバイオ医療のための先端デバイス機器

In this book, my name appears as a coauthor (of one chapter), since one of my graduate students summarized his research work on inkjet printed healthcare chips. Each chapter introduces a different device/technology, which is still not standard in health care, but which might become so in the future. Hopefully, our own inkjet technology will be among those. The book provides an overview over the latest research progress at Japanese universities, research centers and companies.

Chemical Sensors and Biosensors for Medical and Biological Applications -In English

This is a very relevant scientific textbook in my research field. At the same time, I have a specially close "personal relationship" to it. The author of this book is my former Ph.D. supervisor at the Swiss Federal Institute of Technology (ETH), and it was actually written while I was a doctoral student. Therefore, most of my former laboratory colleagues and I have at some time been involved in the "creation" of this book, both by providing scientific data and by supporting the editing and formatting of the text. The present copy of the book is actually a gift including a personal handwritten note from the author, which I received on the occasion of completing my doctoral thesis. I still refer to this book in my daily scientific work.

The Craft of Scientific Presentations -In English

This is a book that I can recommend for all scientists, no matter whether being a student or a professor. Before I first read this book, I could not imagine that a systematic introduction into the "art" of scientific presentations would be so helpful. The book provides not only good advice for presenters, but it is also fun to read. It makes you think more about your own style of presentation, about what could go wrong during a scientific talk, and about the way that you design your presentation slides. I am using this book as the basis of my graduate student course "Presenting and Discussing Scientific and Technical Subjects in English".

Culture Shock Japan -In English

I bought this book shortly before coming to Japan for the first time in my life in 1996 as a visiting student at Tokyo University. The book is intended to act as a guide to customs and etiquette for "gaijin" who are not familiar with Japanese tradition and behavior. I must say that the book was indeed helpful, especially during my first few months in Japan. I remember for example referring to it before attending a Japanese wedding ceremony for the first time. On the other hand, daily life in Japan taught me that not everything is as "strange" as described in the book. At the end of the book, there is a quiz where you can test your knowledge about Japanese customs. How about testing yourself to find out "how Japanese" you really are?

Spin-offs Coming into Bloom

Associate Professor Citterio's research project is an outcome of a flexible concept: "Wouldn't it be possible to create sensors for medical and environmental applications using the micro-nozzle technology originally developed for printing?" There are similar cases like this where a certain technology, originally developed for another purpose, can bloom into a new, unexpected flower by adding some novel ingenuity to it. These are known as technological "spin-off", representative examples being space development technologies.

The laser, now popular in lighting and other fields, was developed for the Apollo Program to accurately measure the distance between the Earth and the Moon. Today its applications range widely from CD and DVD equipment, processing equipment and medical equipment through laser fusion.

Laser equipment for space use must clear various requirements, such as being lightweight, robust, compact and high performance capable. For example, what is known as the truss was contrived by combining triangular frames in order to make a robust cylindrical structure with a limited material. An application of this technology in beverage can design is the shiny "diamond-cut can" for the popular "Can Chu Hi" alcoholic drink, which won a packaging design prize in Japan. In another example, the idea of small CCD camera, developed to monitor plant experiments in the Space Station, is applied to a pill-type gastroscope (9mm in diameter and 23mm in length).

Furthermore, the "organic waste treatment technology" vitally needed for humans to stay in outer space over a long period is applied to waste treatment technologies on Earth – typically, the recycling of organic waste from alcoholic beverage production processes and excretions from livestock farming into water or energy resource, thus contributing to environmental betterment.

What flowers will advances of Mr. Citterio's research bring next? Expectations are high.

Science and Technology **Information**

The 11th KEIO TECHNO-MALL 2010 held under the theme "Transcendental Powers"

http://www.kll.keio.ac.jp/ktm/
December 10 (Fri.), 2010 (10:00 ~ 17:00)
Tokyo International Forum (Halls B7 & B5)
Admission free, no prior registration required

KEIO TECHNO-MALL is an annual science and technology exhibition held by the Keio Leading-edge Laboratory of Science and Technology (KLL). It introduces a diversity of research achievements and new technologies developed by Keio University with approximately 70 booths for demonstrations and exhibits. This year's concurrent main event will feature a talking session by guests under the theme "Process from Research to Commercialization: Roles played by academia, industry and the government, and the future."

Strategic Management Chair for Creating Innovations (a Sony-donated chair) Open Symposium 2010 "Toward a New Phase of Development of Humankind and Society: The Future of Science, Technology and Humankind"

http://www.koukai-sympo.net/
January 14 (Fri.), 2010 18:00~
Kyosei-kan Fujiwara Hiroshi Memorial Hall on the Keio University Hiyoshi Campus
Admission free; Prior applications required

This event is the last of a 3-round-series open symposium by an endowed chair established at the Keio Graduate School of Science and Technology. Mr. Mario Tokoro, President of Sony Computer Science Laboratories, Inc. will preside over the symposium, inviting Professor Junichi Rekimoto (Graduate School of Interfaculty Initiative in Information Studies, The University of Tokyo) and other scientists for discussion. Please apply for participation at the above URL. A movie showing last year's symposium is available:
Open Symposium 2009 http://21722lab.jp/#/basic/detail?id=361

A scene from Open Symposium 2009

Editor's postscript

As I knocked on Associate Professor Citterio's lab for an interview, students rushed around Mr. Citterio in a moment at his welcome and began talking cheerfully. As you can see in "Just a word from . . ." at the end of the interview (page 5), Mr. Citterio is called by his first name "Daniel-san" by his students and apparently maintains frank and friendly communication with them. When we were about to take photos for the "My favorite books" corner, Professor Koji Suzuki of the same lab popped in and said "How about this book?" I could feel a truly harmonious and cooperative atmosphere prevailing in this lab.

The next issue will feature an up-and-coming assistant professor from the Department of Systems Design Engineering. Please look forward to the next issue. (Saori Taira)

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