Tune

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Tohoku University Research News of Engineering

Mitsuo UMETSU

Hitoshi SHIKU

Research Highlight

Takayuki NARUSHIMA   Ko-ichiro MIYAMOTO

TOHOKU UNIVERSITY

General Introduction

Known worldwide as a leading university in Japan with particular strengths in engineering and science (especially chemistry) not to mention in biomed, Tohoku University is home not only to its superb engineering institutions but also its affiliate research institutes. The entities range from those studying advanced materials and fluid mechanics – the latter involving the micro/nano varieties as well – to units focused on metallurgy and robotics, again covering the micron and nanometer size regions.

Internationally, there are moves to design matter at all size levels also. The trend is exemplified by use of CRISPR-Cas, a technique born in Japan, for genomes while design efforts related to atomic structures are ongoing around the globe. Tohoku University Engineering Faculty members, in addition to those we highlighted in this issue, are actively scrutinizing the minute frontiers of research too. Said pursuits promise to bring forth paradigm shifts in terms of life science and nanotech.

The last big leap related to such research areas took place with the discovery in 1982 of the genzyme. The decades that followed saw marked advances in the field of molecular biology, according to an observation made by engineer-writer Kouichi Ishii. In his “biobusiness handbook” which was published by Oriental Economist soon after Dolly the sheep's cloning, it was portended that engineering at genetic levels and beyond would become prevalent.

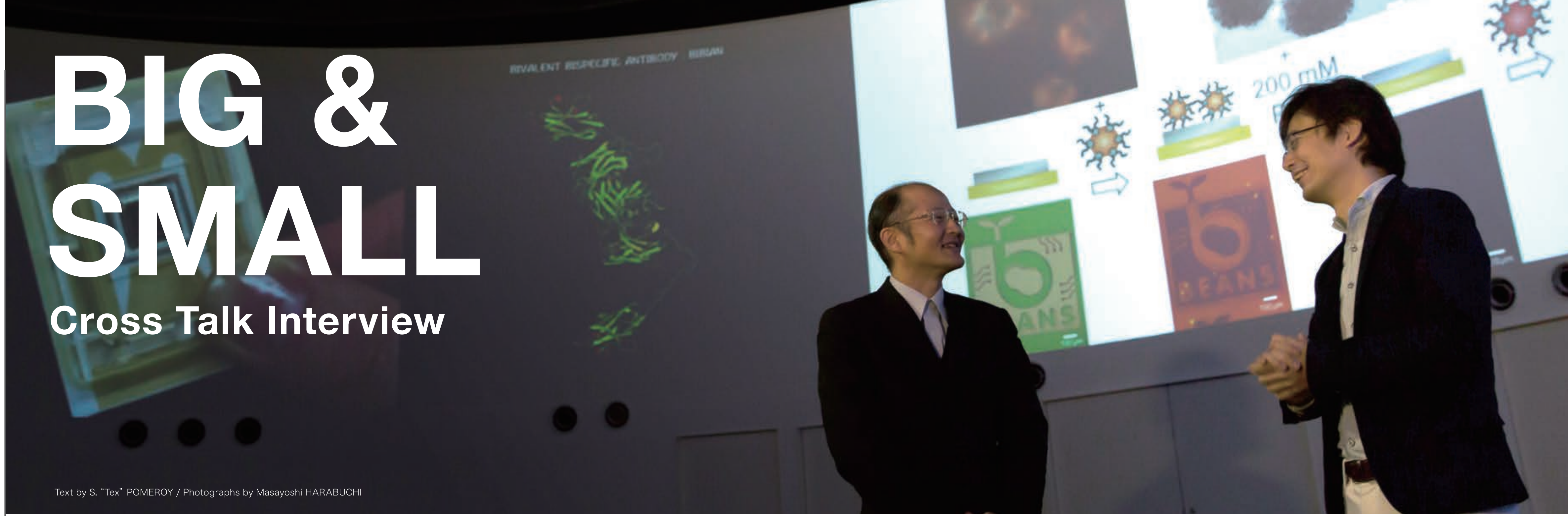
Today, fundamental technologies to fabricate integrated biodevices including biologically-benign microfabrication and characterization for biomaterials in nanometer domains, along with movement technology for solutions and biomaterials, have come to the fore. Currently, on-chip genetic engineering systems to realize simple genetic manipulation on a single chip is undergoing development. This chip will enable rapid and comprehensive analysis of gene and protein functions.

It may even be that “Tangible Bits” efforts being spearheaded by the Japanese MIT Media Lab Associate Director will lead to supersmall manipulations via hands-on simulation becoming realized. Indeed in the very near future my late collaborator Kouichi's predictions could come to pass, judged from the current state of affairs. Hopefully, this journalist would be fortunate enough to witness more progress, including those emanating from Aobayama campus, related thereto in the dozens of years to come.

S. “Tex” POMEROY
Journalist

BIG & SMALL

Cross Talk Interview



Text by S. “Tex” POMEROY / Photographs by Masayoshi HARABUCHI

Planning For Bigger Things By Pursuing Nano-level Structures

Life Science-related Efforts in Engineering

Recent decades have seen major advances related to life science, especially for the building block of life: cells (encompassing induced pluripotent stem aka iPS ones and otherwise), proteins, amino acids... . The respected magazine “Science” for example cited as one of the Top Ten science stories of 2016 the synthesis of a “minimal” bacterial genome, that is, the assembling a set of genes in full for an organism using the minimum amount required.
Yet what is an organism, a living thing? This is also a question being delved into by researchers around the world. But indeed there still remains many mysteries to be solved, such as that of the virus, which defies the definition of a living organism, not to mention things like the mechanism of certain proteins in triggering ailments like bovine spongiform encephalopathy (BSE). Meanwhile there has been links made from the organic to inorganic materials thanks to furtherance of research activities at the nanometer level. Actually, considering that the design of micromachines was awarded the Nobel Prize in 2016, possibilities have been opened up ahead of “cyborg-like cells” being realized in the not-too-distant future.
In line with such moves, we would like to place the spotlight on two researchers in the engineering field pursuing activities related to this leading-edge sector, Prof. Mitsuo Umetsu with the Department of Biomedical Engineering, Graduate School of Engineering at Tohoku University and Prof. Hitoshi Shiku, working now at the Graduate School of Engineering, Tohoku University.

Organically Speaking: Life Science and Engineering

Living beings are made up of materials, conventionally organic chemicals. For example, in explaining to nonbiologists and those unfamiliar with genetics in a very roughshod manner – “clemency” requested herewith – the basic building blocks of a living body are based on deoxyribonucleic acids (DNA), a set of biopolymer strands in a double-helix form made up of certain types of amino acids and a sugar known as deoxyribose, the namesake item.
Such DNA is found “packaged” in a unit called the chromosome; as with the abovementioned “genome” these “ome” words can be thought as “package” (and the study of those touting “-ome” at the end are referred to by “-omics” as in “genomics” or “proteomics”). Proteins and cells are derived from amino acids as transcribed by ribonucleic acids carrying genetic codes as based upon the DNA.
When put together as a system, unicellular and higher living units become realized. Thus, life science is of interest as human beings are also living units, and upon attempting to gain a good “Quality Of Life” for themselves, people are seeking for ways to manipulate materials to improve their lot. These days, the ability to discern and alter materials at the nanometer level has led to protein engineering, among other types of nano-level engineering.

Think Big, Design Small

– Prof. Hitoshi Shiku, Systems Specialist, and Prof. Mitsuo Umetsu, Design Expert

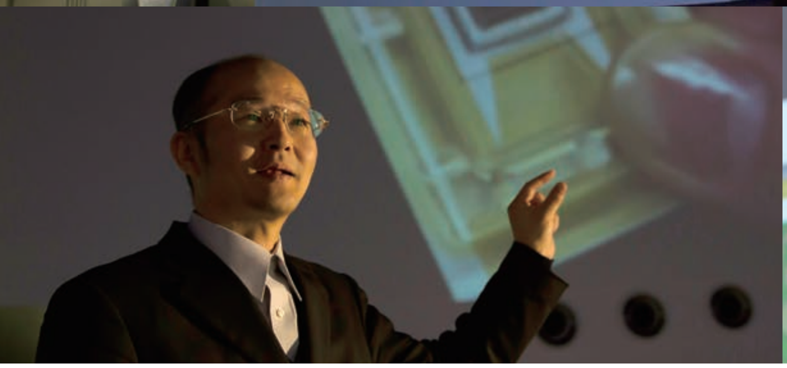
Dr. Shiku: I am by training an electrochemist who looks – both figuratively and literally – at things from the systems perspective. I believe I can observe and handle systems at the microscopic frontline, while retaining the overall view from a systematic standpoint. I suppose I took in a global vista, garnering a wider view by having spent time overseas at Department of Chemistry, the University of Kansas for post-doc work.

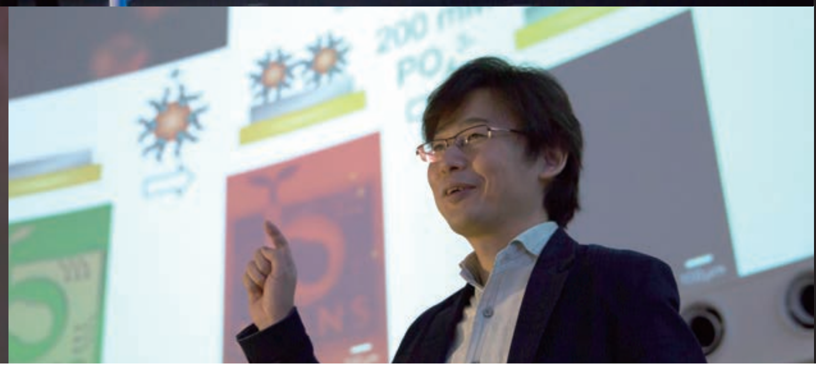
Dr. Umetsu: In contrast then I'm an expert as to design at the nanometer order, handling amino acids, proteins and peptides, having been involved in the pharma field, covering from drug design to delivery. Being part of the biomedical engineering thrust at Tohoku University, I've handled in-vitro (“wet”) activities in addition to “dry” data-driven efforts.

The Name Of The Game - Hybridization and Variety

Dr. Shiku: Although our operational bases are in close proximity to one another, it may be said that it could be better to have a third party assist in linking up the two research efforts in a more “organic” manner. This is because we both need to concentrate thoroughly on research fronts due to the competitive nature for our fields of choice.
Dr. Umetsu: Regarding hybridization, with the design at a grander scale to be implemented with proper fusion at the component level (organic bases needing integration into inorganic parts, such as cell surfaces being melded into metallic electrodes), a “bridger”... analogous to a bee assisting with cross-pollinations.. may be quite useful. And I like bees – especially their hives made up of hexagonal “cells”... quite symbolic.
Dr. Shiku: Yes, we could expect even more “variety” when it comes to Research & Development, should manufacturers or other business entities come to contribute to the work schemes, as it is quite variety ladened though. It would be intriguing to guess the outcome as to exactly how issues like relationships with industry and government sectors will be dealt with under such a set-up.
Dr. Umetsu: Indeed, such a third party might help us to work even more closely. Biodiversity is important in the environmental sciences and variety, to engineering.

M.UMETSU × H.SHIKU





The Big Picture

Dr. Shiku: Now, for interesting activities you were involved in that I'm aware of, there was the Bio Electromechanical Autonomous Nano Systems (BEANS) project run by the Micromachine Center and backed by Ministry of Economy, Trade and Industry-affiliated New Energy & Industrial Technology Development Organization (NEDO). Concluded several years ago, I believe BEANS produced many results related to Micro-Electro-Mechanical Systems (MEMS) and microfluidics, as represented by small "cells on chips" among other manifestations that are linked to my research too. The leader of this effort I remember was known for growing a human ear on the back of a mouse, a sensational way to catch the eye!

Dr. Umetsu: Indeed. By the way, I heard that NEDO began expanding into life science-related activities due to biomass and associated research. It should be noted that after all, even at the cellular level there is energy being produced by the mitochondria.

Dr. Shiku: Quite right. Without fuel, or in living organisms' case, foodstuff, the "system" obviously cannot be sustained so I think you may be correct. As to why they named the project BEANS, I can but only guess but possibly had something to do with Jack and the beanstalk. Maybe was trying to take in the "big picture" from above, the bird's-eye-viewpoint. Speaking of naming, can you tell us about BIBIAN?

'BIBIAN'

Dr. Umetsu: As to my past work, I have been involved in producing antibodies as part of a "smart unit" to defeat cancer and combat diseases, aiming for better selectivity of such treatment agents. In this vein, I prepared a bispecific and bivalent antibody which I called 'BIBIAN'... named in a nod to a versatile TV personality from Taiwan. She was popular in Japan some years back.

Dr. Shiku: I see, BIBIAN is an acronym for "Bispecific and Bivalent Antibody"! Ingenious!

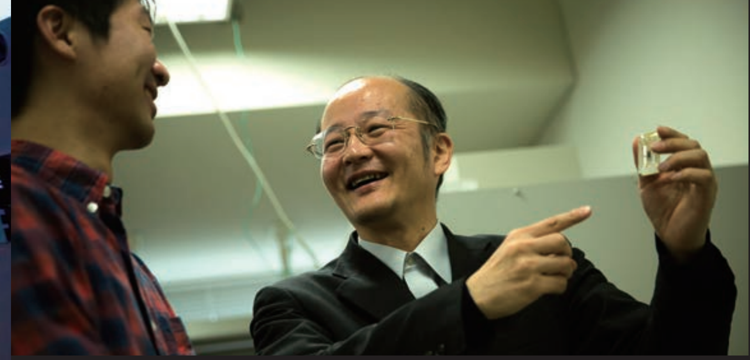
Dr. Umetsu: Thank you! I even considered using "Smart Unit" after it but I thought that would have been a tad too much.

Dr. Shiku: You are also involved in drug design. Can you elaborate further on this for our readers' benefit?

Dr. Umetsu: Considering the rapidly-greying society, in particular in Japan, I was looking to improve the situation faced by those suffering from kidney disorders, and I searched for means to "revitalize" remaining normal renal cells. Just as with prospects of human kidneys being grown in pigs thanks to genetic engineering, there is the outlook for design allowing stem cells to be grown into full-sized kidneys.

Dr. Umetsu's Biotech Definition

Biotechnology (in the context here) refers to any technological applications of biological systems, such as enzymes, microorganisms, plant cells and animal cells, to make or modify products or processes for specific purposes. This includes recombinant gene based and/or tissue culture based processes that have only been developed during the past three decades. Issues related to biotechnology are genetic engineering, biological membrane transport and chemical biology process. Synthesis of biochemical components, genetic engineering, biomedical engineering, membrane transport system and glycotechnology are also related generally.



Platform: Dr. Shiku's Research

Development of Microbiosensing Devices

Microfabrication technologies and localized chemical reactions at solid surfaces were used to fabricate integrated biodevices and develop characterization methods. Collaboration with industries is now going on to apply these biodevices to environmental monitoring, health monitoring, diagnosis, drug screening and order-made medical treatment.

Characterization and Utilization of Cellular Functions

Developed was a novel characterization system for single cells by capturing electrical, electrochemical and photonic signals in micro/nanometer spaces. This system will have an impact not only on the cellular engineering but other related areas. Also developed was a novel characterization system for early embryos and micro tissues. This system will be a fundamental tool to explore cellular engineering in the next generation to realize practical infertility treatment and tissue engineering.

Development of Intelligent Biosystems

Developed were fundamental technologies to fabricate integrated biodevices, including biologically-benign microfabrication technology, movement technology for solutions and biomaterials, characterization technologies for biomaterials in nanometer domains. Also developed was an on-chip genetic engineering system to realize simple genetic manipulation on a single chip. This chip will enable a rapid and comprehensive analysis of gene and protein functions.

Synergy and Beyond

Synergy Aimed For

Dr. Shiku: Ah, yes, I have been working to produce scaffolding for stem cell use in growing organs. Actually, we two have recently been talking of collaboration even though there is yet a "bridger" to be found. I think our combination – "chemistry" as it were – bodes well for synergy to be realized.

Dr. Umetsu: I am currently looking to apply Artificial Intelligence (AI) to design efforts, and possibly making molecular recognition of drug candidate easier. In the medical arena there are robots and Internet-of-Things or so-called IoTs being adopted these days.

Dr. Shiku: I believe AI can likely be adopted for the design of systems as well, we have a huge amount of data to deal with too. Speaking of IoT, we obtain a great deal of information from the sensors and other equipment being used to carry out measurements and evaluate materials.

Dr. Umetsu: We should combine forces to deal with such issues then! I think we can not only produce synergy but then go beyond, maybe not for using the microgravity environment in space to make protein crystals but perhaps work jointly as regards intellectual property. * Time now for teamwork to begin?

Porro Unum Est Necessarium

Dr. Shiku: Teamwork is important and now that I have known you for many years I am certain we understand each other well. I observed in the U.S. during my post-doc days that teamwork is a great motivator.

Dr. Umetsu: Yes! As you probably know, I like Roman history and have several Latin words that I am fond of. But, I think the Latin phrase that goes "Porro Unum Est Necessarium" which roughly means "Moreover, one thing is needed" befits the role teamwork can play. In the future we may gain other teammates but let's look to work together in this interesting scientific field.

Dr. Shiku: True, we could possibly gain more when other bio-related units of Tohoku University join us at the Aobayama campus in the near future. 2017 hopefully will be a great year to start new endeavors.

*[Though the Japanese system still does not allow patenting of medical acts unlike other advanced countries, it recently paved the way for supplementary foodstuff patenting. Accordingly there is some notable movement in this front entailing university-backed startups, such as those at Tohoku University in the form of an "antidote" to hangovers that follow drinking sessions.]

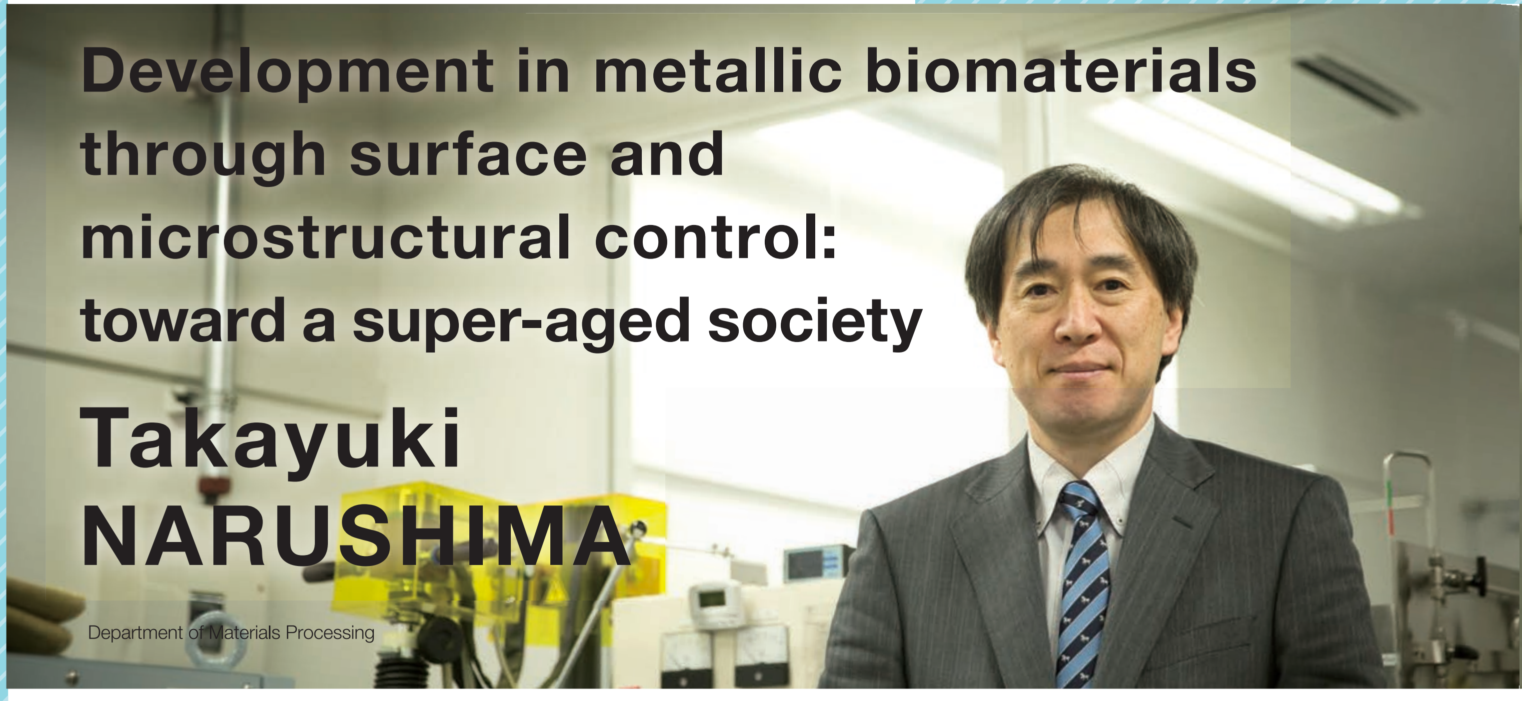
Dr. Mitsuo UMETSU

He received his Doctor's degree from Tohoku University in 2000. After he studied at Leiden University in the Netherlands as a JSPS Postdoctoral Fellow for Research Abroad, he was a research associate in the Graduate School of Engineering and in the Institute of Multidisciplinary Research for Advanced Materials, Tohoku University, in 2001-2006. In 2006, he was an associate professor in the Graduate School of Engineering , Tohoku University, and he is a professor in the same university from 2014.

Dr. Hitoshi SHIKU

He received his Doctor's degree from Tohoku University in 1997. He was a research fellow for young scientist of Japan Society for the Promotion of Science (JSPS) in 1996-1998, and a postdoctoral fellow of the University of Kansas in 1998-1999. After that, he joined Regional Joint Research Project of Yamagata prefecture, Japan Science and Technology Corporation (JST) as a senior researcher of Yamagata Public Corporation for the Development of Industry in 1999-2003. In 2003, he was an assistant professor in the Graduate School of Environmental Studies, Tohoku University. From 2016, he is a professor in the Graduate School of Engineering, Tohoku University.

Photographs by Masayoshi HARABUCHI



Development in metallic biomaterials through surface and microstructural control: toward a super-aged society

Takayuki NARUSHIMA

Department of Materials Processing

The proportion of elderly people in the population is rapidly growing worldwide. It is predicted that the numbers of patients suffering from falls due to aging and deterioration of bodily functions will increase in this super-aged world; at the forefront of this is Japanese society, which is graying at an unprecedented rate. In order to improve the quality of life (QOL) for these patients, devices for reconstructing bodily functions will become essential. Metals are candidates for materials of these devices used with the human body, in the form of implants, because of their strength, ductility and durability; actually, 80% of all implants today are made from metals. Our group focuses on the use of metallic biomaterials on the basis of physico-chemical approach.[1]

We are working on the research to make stent* (Fig.1) more reliable and more durable by controlling microstructure of NiTi and Co-Cr alloys, mainly used as materials for self- as well as balloon-expandable stents, respectively. Both the fatigue strength of NiTi and the ductility of Co-Cr alloys have been improved through precipitation and phase-transformation control [2].

Another study in our group is surface modification of metallic biomaterials, especially Ti and Ti alloys, giving these both the antibacterial activity and bone compatibility. It is well known that Ti possesses the unique property of osseointegration, which refers to direct connection from Ti to bone at the optical microscopic level. However, the fixation is influenced by the state of bones and interface. Therefore, surface modification is required for improving bone compatibility of Ti implants.For this reason, we prepared bioceramic coatings of bioresorbable ACP(amorphous calcium phosphate) (Figs.2 and 3) and photocatalytically-active TiO_2 on Ti [3].

*A mesh tube medical device to spread the human body of the tubular part such as blood vessel from inside the lumen. The vascular stent market is more than ten billion US dollars and steadily increases year over year.

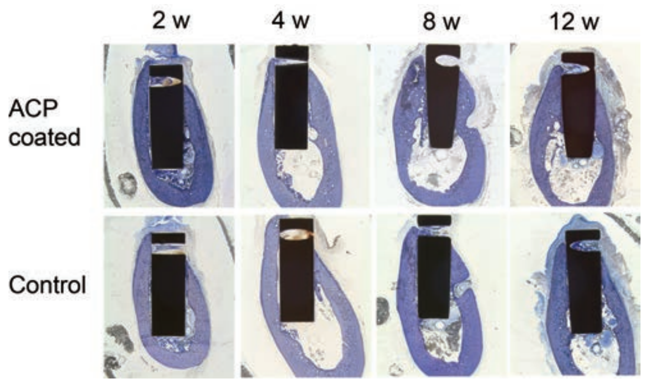


Fig.2 Interface between Ti implant and bone

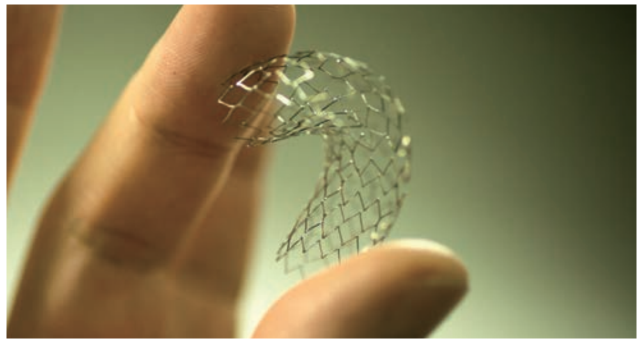


Fig.1 Vascular stent made of Cu-Cr alloy

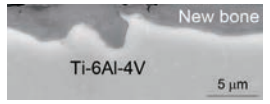


Fig.3 New bone formation on ACP-coated Ti

Profile:
Takayuki Narushima received his B.S., M.S. and Ph.D. degrees in Engineering from Tohoku University, Japan, in 1985, 1987 and 1994, respectively. He joined the Department of Metallurgy at Tohoku University as a Research Associate from 1987 to 1994 and as an Associate Professor from 1994 to 2004. He was a Professor in the Tohoku University Biomedical Engineering Research Organization (TUBERO) and has been a Professor at the Department of Materials Processing at Tohoku University since 2007. From 1998 to 1999, he was a Research Fellow at the University of California, Berkeley. His current research interests include microstructural control in metallic biomaterials such as Co-Cr and NiTi alloys in addition to biofunctionalization of Ti and Ti alloys through surface modification using bioceramics.

[1] T. Narushima: New generation metallic biomaterials, Metals for biomedical devices, Ed. M. Niinomi, Woodhead Publishing Limited, (2010), 355–378.
[2] Microstructure and mechanical properties of heat treated Co-20Cr-15W-10Ni alloy for biomedical application, K. Ueki, K. Ueda and T. Narushima Metall. Mater. Trans. A, 47 (2016) 2773–2782.
[3] T. Ueda, N. Kondo, S. Sado, O. Gokcekaya, K. Ueda, K. Ogasawara and T. Narushima: Ceramic coating of Ti and its alloys using dry processes for biomedical applications, Interface Oral Health Science 2016, Innovative Research on Biosis-Abiosis Intelligent Interface, Ed. K. Sasaki, O. Suzuki and N. Takahashi, Springer, (2017), 23–34

Toward a palm-top chemical imaging system for biomedical applications

Ko-ichiro MIYAMOTO

Department of Electronic Engineering

Recent years have seen a rise in the number of Japanese allergy patients, especially younger people. It is generally known that allergy symptoms to certain chemicals or foodstuff could be extreme, even life-threatening in some cases. Thus there are increasing calls for efficient methods to test the safety of specific chemicals and other substances. In addition, there are demands concerning the screening for efficacy of chemical compounds under consideration as drug candidates. The so-called "cell-based assays" - testing with cultured human cells - is commonly used in such cases. In 2016 my colleagues and I launched a project to develop a novel sensing system for a particular type of cell-based assays (Fig.1). This project is founded upon the results of our research endeavors over the past decade.

The project's first key technology is the "miniaturized" chemical imaging sensor [1]. Said sensor utilizes the measurement principal behind light-addressable potentiometry, enabling visualization of ion, pH and impedance distributions. We proposed use of a light spot on a small display panel as light source to replace scanning optics in use with conventional systems. Both the size and costs can be reduced by a factor of nearly 100 (Fig.2 (Left)).

The second key technology is impedance mapping of a cultured cell layer [2]. A cell layer's defect and the recovery process thereof can be monitored by means of impedance distribution as visualized through application of the chemical imaging sensor (Fig. 2 (right)). Quantitative and label-free monitoring of the cell layer's barrier function would produce useful information for cell-based assays. By combining the two aforementioned key technologies, our new project aims to realize innovative cell-migration assays using a palm-top chemical imaging system. We foresee this providing a powerful tool for testing and screening of chemicals, drugs and so forth. My dream for the future is that the palm-top chemical imaging sensor will be adopted widely for clinical examinations and pathological diagnosis, among other activities.

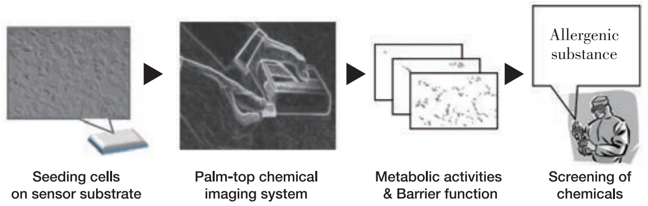


Fig.1. Palm-top chemical imaging system

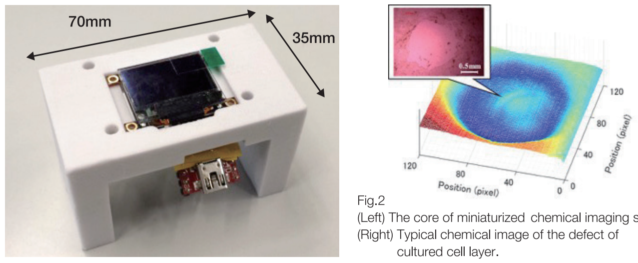
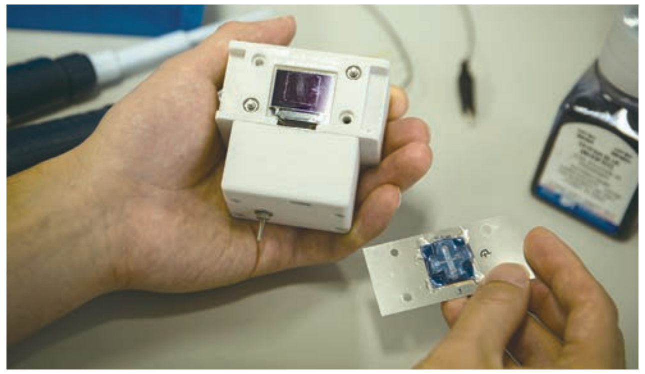


Fig.2
(Left) The core of miniaturized chemical imaging system
(Right) Typical chemical image of the defect of cultured cell layer.



Profile:
Ko-ichiro Miyamoto received BE, ME and PhD degrees from Tohoku University in 2002, 2004 and 2006, respectively. His PhD degree is for his study on the bio-molecular sensing using infrared absorption spectroscopy. Since 2006, he was an assistant professor at the Department of Electronic Engineering, Tohoku University. Since 2013, he is an associate professor. His research subject is on the application of silicon-based chemical sensors for bio-sensing.

[1] "Miniaturized Chemical Imaging Sensor System Using an OLED Display Panel" K. Miyamoto, K. Kaneko, A. Matsuo, T. Wagner, S. Kanoh, M. J. Schöning and T. Yoshinobu, Sensors and Actuators B, 170 (2012) pp.82-87.
[2] "Visualization of the Recovery Process of Defects in a Cultured Cell Layer by Chemical Imaging Sensor" K. Miyamoto, B. Yu, H. Isoda, T. Wagner, M. J. Schöning and T. Yoshinobu, Sensors and Actuators B, 236 (2016) pp.965-969.

News

Tohoku University Engineering Summer program 2016

From July 27 to August 7, the Graduate School of Engineering, Tohoku University offered for the seventh consecutive year a two-week graduate level summer program. This year the program focused on "Robotics" and "Electrical and Electronic engineering", a program designed to inspire graduate level students or young professionals in the field of Engineering. The summer program has been a success with more than 60 participants coming from 18 different countries. In addition to a series of English lectures and hands-on on respective specialities the summer program included various activities that exposed the participants to Japanese culture to enrich their academic experience. The overall program aimed at providing students with rich academic and cultural experiences for their academic and global insight.

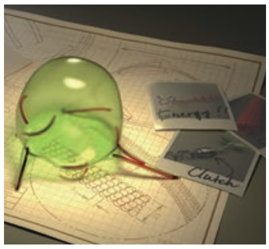
14th Prime Minister's Award received by Professor Endoh

Tohoku University's Tetsuo Endoh, Tokyo Electron Limited's Gishi Chung and Keysight Technologies Inc.'s Masaki Yamamoto have been awarded the 14th Japan's Prime Minister's Award for Contribution to Industry-Academia-Government Collaboration. The award recognizes outstanding achievements or pioneering efforts in industry-academia-government collaboration, especially by leaders in businesses, academia and public research institutions. The collaboration brought expertise from scientists at Tohoku University and partnered them with major global companies Tokyo Electron and Keysight Technologies to research and develop innovative integrated electronics systems. Together, the group has developed high tech equipment for manufacturing and evaluating STT-MRAM (Spin Transfer Torque - Magnetoresistive Random Access Memory).

Tohoku University Again in Top Tier at BIOMOD

Tohoku University's 'Team Sendai' came in second place at the 2016 International Biomolecular Design Competition, held in Cambridge, Massachusetts. Widely known by the nickname of BIOMOD, this competition brings up to 30 teams made up of undergraduate students from around the world to showcase their prowess in designing molecule-sized objects. Since the event was launched by the Wyss Institute at Harvard University in 2011, the Tohoku University representatives have consistently been one of the top awardees. During the English-only competition which helps prepare students for making pitches and scholarly presentations on the global stage a wide range of engineering knowledge covering from chemical, electrical/electronic to mechanical, not to mention disciplines like biology, chemistry and physics, are put to use in both design and characterization of molecules. Thus, an interdisciplinary education is needed to gain recognition in this international competition, though some assistance in handling design software is available from the host institution.

Molecular robot developed by integrating molecular machines



Led by Graduate School of Engineering Associate Professor Shin-ichiro Nomura, a joint Tohoku University/Japan Advanced Institute of Science & Technology research group has realized a molecular robot consisting of biomolecules like DNA and protein. By integrating molecular machines into an artificial cell membrane, a molecular robot sized about a millionth of a meter small was produced. It is not only the size of a cell but can alter its shape in response to specified DNA signals. This is the first time for a molecular robot system can recognize such signals to start and stop its shape-changing function. This opens up the way for molecular robots to act similarly to living organisms when it comes to important functions. In the not-too-distant future, it may perhaps be plausible that such sophisticated biomolecules as DNA and protein can be used in a molecular robot form to supplement vital functions in those patients whose crucial cell functions have deteriorated. (Photo, courtesy of Sho Aradashi)

Upcoming Events in Sendai

56th Annual Conference of JSMBE
May 3-5, 2017,
Tohoku University, Sendai, Miyagi
http://www2.idac.tohoku.ac.jp/jsmbe56/

Biomagnetic Sendai 2017
May 22-24, 2017,
Sendai International Center.
http://www.c-linkage.co.jp/isacm2017/index.html

International Disaster and Risk Conference 2017
November 25-27, 2017,
Sendai International Center.
http://idrc.info/2017/

International Conference on Solid State Devices and Materials
September 19-22, 2017,
Sendai International Center.
http://www.ssdm.jp

TOHOKU UNIVERSITY

Tohoku University Research News of Engineering

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