Mitsuo UMETSU

Research Highlight
Takayuki NARUSHIMA

Hitoshi SHIKU

Ko-ichiro MIYAMOTO
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 genezyme, the decades that followed saw marked advances in the field of molecular biology, according to an observation made by engineer-writer Kouichi Ishikawa. 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 bio-devices 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 Material Associates Director will lead to supramolecular manipulations via hands-on simulation becoming real. Indeed in the very near future my late collaborator Kouchi'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 Aoba-yama campus, related therein in the dozens of years to come.

S. "Tex" POMEROY
Journalist

The Name Of The Game - Hybridization and Variety

Dr. Shikui: Although our operational bases are in close proximity to one another, it may be noted that it is 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 biologic parts, such as cell surfaces being melded into metallic electrodes), a "bridge"... analogous to a bee assisting with cross-pollinations... may be quite useful. And I like bees - especially their lives made up of hexagonal "cells"... quite symbolic.

Dr. Shikui: 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 laden 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 setup.

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.

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 rough-hand manner - "clenancy" 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 nomenclature term.

Such DNA is found "packaged" in a unit called the chromosome; as I believe the above mentioned "genoma" these "ome" words can be thought as "package" (and the study of those touting "ome" at the end are referred to as "-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 larger 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, those 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 Shikui, Systems Specialist, and Prof. Mitsuhiro Umeda, Design Expert

Dr. Shikui: 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 frontiers, 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.

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 (encapsulating induced pluripotent stem cells (IPs) 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 organ for using the minimum amount required, 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 defines 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 furthureance of research activities at the nanometer level. Actually, considering that the design of microchips 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. Mitsuhiro Umetsu with the Department of Biomedical Engineering, Graduate School of Engineering at Tohoku University and Prof. Hitoshi Shikui, working now at the Graduate School of Engineering, Tohoku University.
The Big Picture
Dr. Shiku: Now, for interesting activities you were involved in that I’m aware of, there was the Bio Electro-mechanical Autonomous Nano Systems (BIAN) 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 BIANs 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 “next generation” which obviously cannot be sustained so I think you may be correct. As to why they named the project BIANs, I can but only guess but possibly something to do with Jack and the beanstalk. Maybe was trying to take the “big picture” from above, the birds-eye’s viewpoint. Speaking of naming, can you tell us about BIBIAN?
Dr. Umetsu: BIBIAN,
BIAN: 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 “Biocompatible and Bivalve 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 topic for our readers’ benefit?
Dr. Umetsu: Considering the rapidly-growing 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 designing allowing stem cells to be grown into customized kidneys.

Synergy and Beyond
Synergy Aimed For
Dr. Shiku: Ah, yes, I have been working to produce scaffolding for stem cells: we are growing organs. Actually, we two have recently been talking of collaboration even though there is yet a “bridge” 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 IoT 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.
Synergy Aimed For
Dr. Shiku: Our goal is not only to produce synergy but then to go beyond, maybe not for using the microgravity environment in space to make protein crystals but perhaps work jointly as regards intellectual property.
Dr. Umetsu: I think that teamwork is a great motivator. We have known you for many years. I am certain we understand each other well. We observed in the U.S. during our post-doc days that teamwork is a great motivator.

Development of Intelligent Biosystems
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. We have known you for many years. I am certain we understand each other well.

Platform: Dr. Shiku’s Research
Dr. Shiku: Yes! As you probably know, I like Russian history and have several Latin words that I am fond of. But, I think the Latin phrase that goes “Porro Unum Est Necessarium” means “Moreover, one thing is needed” before the role teamwork can play. In the future we may gain other teammates but let’s work to look together in this interesting scientific field.
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. Mitsuaki UMETSU
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 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, biomechanical engineering, membrane transport system and glycochemistry are also related generally.

Dr. Mitsuo UMETSU
He received his Doctor of Science 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, from 2001-2005. In 2005, he was appointed professor of the Graduate School of Engineering - Tohoku University, and has been a professor in the same university from 2012.

Dr. Hidachi SHIKU
He received his Doctor of Science degree from Tohoku University in 1991. He was a research fellow for young scientists at Project of the Promotion of Science (COE) from 1985-1989, and a coordinator under Project of the Promotion of Sciences, Project of the Promotion of Science (COE) from 1999-2000. He won the National Science and Technology Prize of Japan in 1993, and the National Science and Technology Prize of Japan in 1999.
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 the Japanese society, which is graying at an unprecedented rate. In order to improve the quality of life (QOL) for these patients, devices for constructing biomaterials whose surface and microstructure 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, 40% 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 anti-bacterial 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 bioactive coatings of bioreabsorbable ACP (amorphous calcium phosphate) (Figs. 2 and 3) and photocatalytically-active TiO2 on Ti.[3]

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 foodstuffs 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 on enhancing the improving efficiency 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.4). This project is founded upon the results of our research endeavors over the past decade. The projects first key technology is the “miniatized” chemical imaging sensor.[4] Said sensor utilizes the measurement principal behind light-addressable potentiometry, enabling visualization of ion, pH and impedance distributions. We proposed the 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[5]. 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.

[1] Takayuki Narushima received his B.S., M.S., and Ph.D. degrees in Engineering from Tokyo University, Japan, in 1983, 1985, and 1988, respectively. He joined the Department of Materials Science and Engineering at The Ohio State University (OSU) in 1988, and has been a Professor at the Department of Materials Science and Engineering at Tokyo University since 2007. From 1986 to 1987, he was a Research Associate at the University of California, Berkeley. His current research interests include microstructural control in metallic biomaterials such as Co-Cr alloy and NiTi alloys as well as the biocompatibility and mechanical properties of these materials.


[4] Koichiyo Miyamoto received B.E., M.E., and Ph.D. degrees from Tohoku University in 2003, 2005, and 2009, respectively. His Ph.D. degree is for his study on the biocompatibility of nanomaterials obtained through electrospinning. Since 2009, he has been an associate professor at the Department of Mechanical Engineering, Tohoku University, Japan. Dr. Miyamoto is an author of over 30 papers on the application of bio-inspired nanoparticles for biomedical engineering.

[5] Koichiro Miyamoto received B.E., M.E., and Ph.D. degrees from Tohoku University in 2003, 2005, and 2009, respectively. His Ph.D. degree is for his study on the biocompatibility of nanomaterials obtained through electrospinning. Since 2009, he has been an assistant professor at the Department of Mechanical Engineering, Tohoku University, Japan. He is an associate professor. His research subject is the application of bio-inspired biomaterials for biomedical engineering.
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 specialties 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 BIOMOC, 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 also shape in response to specified DNA signals. This is the first time for a molecular robot system can recognize such signals and start 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/jsmbe66/

Biomagnetic Sendai 2017
May 22-24, 2017,
Sendai International Center,

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

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