NIMS NOW International

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Special Feature
Nanobiomaterials

Cell culture laboratory (clean room)

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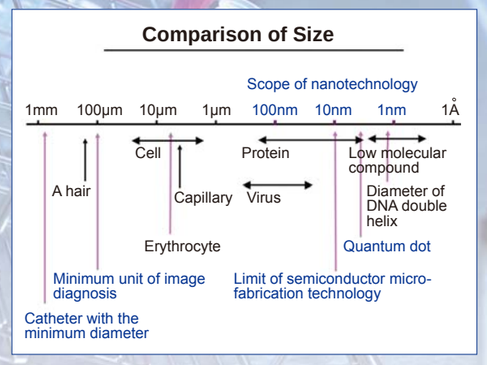


Introduction

Nanobiomaterials — What are they?

"What are nanobiomaterials?" Even nanobiomaterials researchers themselves may have had to stop and think when they try to define this field. This field of research is particularly diverse and wide-ranging, as readers will see in the individual articles covered in this special feature. The researchers come from various different science and engineering backgrounds, including polymer chemistry, electrical engineering/electronics, mechanics, solid-state physics, materials science, and biosciences and so on.

The living organisms have various nanoscale structural and functional units, ranging between 100nm and 1nm where nanotechnology research is focused. These units are then organized into higher-order structures. Nanobiomaterials research is motivated and inspired by what we can learn from the living organisms and how we can mimic their functions. The unique phenomenon in the nanodomain, which we focus on in our research and utilize in our methodologies, can be thought of as the natural course of events.

Nanobiomaterials may revolutionize healthcare

Lets look at the objectives of nanobiomaterials research in more detail. One of the major drives is to develop advanced medical applications.

Nanobiomaterials research with therapeutic applications includes regenerative medicine aimed at regenerating tissues and organs, drug delivery systems that allow the delivery of drugs at the right time and to the right targets, or materials research for artificial livers and kidneys. In this special feature, we look at artificial bone, artificial corneas, and the importance of scaffolds in regenerating tissues and organs.

Research into diagnostic or analytical techniques also makes an enormous contribution to the practice of medicine. R&D is underway into numerous techniques, including biochips, biosensing, bio-imaging, and nanocapsules. Here, we look at the latest biotransistors and biochips that play a role in telemedicine and in-home care.

Much of this research is pursued in collaboration with medical doctors. Nanobiomaterials research has the potential to revolutionize healthcare, but needs to be underpinned by strong social infrastructure if the developments are to be fully applied.

Computing using biological principles

Another objective for nanobiomaterials research is the development of engineering outcomes. Such research draws on distinct functions within the living organisms—the systems for self-organization, processing feedback, learning, and simultaneous processing of multiple signals—and tries to reproduce this functionality using engineering approaches. A good example is drawing on human brain functionality to create a new computing concept. Here, we discuss the work of researchers engaged in the development of nano-measuring technologies for application to new computing concepts.

Interesting results are also being generated by the research that takes substances found in the living organisms and uses them as materials eliminating their biological role. Examples include molecular motors, nano-machines, or DNA nanostructure techniques. This special feature discusses the use of DNA as a material, an unusual approach that may come as a surprise to readers.

At NIMS, our Biomaterials Center is developing an impressive portfolio of nanobio research with a materials slant. We hope NIMS WEEK in July (http://www.nims.go.jp/nimsweek/09) will give visitors a greater understanding of how we are combining disciplines to further this field of research.

Artificial bone that more closely resembles living bone

Ceramic Biomaterial Group, Biomaterials Center
Masanori Kikuchi, PhD

Many people have images that bones are perpetual mineral substance. Some people even think that artificial materials with a certain mechanical strength are sufficient for replacement of bone lost through illness or injury.

In reality, bone is a living organ that metabolizes actively. Every bone in our body undergoes a constant cycle of resorption and formation, and all our bones are completely replaced every few years. That is, repeating cycle of destruction and construction driven by the coupling of osteoclasts that resorb bone and osteoblasts that form bone.

Our group has been working on the development of artificial bone for regenerating living bone based upon materials science, in collaboration with clinicians including orthopedic surgeons.

Human bone comprises 65% hydroxyapatite, 25% collagen, and other substances, mainly water. In bones, the collagen fibers and crystal axes of apatite align each other, but the mechanism controlling this oriented structure is not yet fully understood. Today, many scientists think that bone may be formed through the spontaneous orientation of the collagen molecules and apatite crystals via the interaction of interfacial structures with surrounding environment. Collagen molecules are approximately 300 nm in length, while apatite crystals in the bone are 30–40 nm. Thus, bone is a nanocomposite with ingenious nanostructure as a part of living body which is usually described as a conglomerate of nanomaterials. Our goal is to reproduce the architecture and the function of the bone using an engineering approach.

Artificial bone is used in the field of orthopedic surgery to treat bone fractures and defects after bone tumorectomies; it is also used in the field of oromaxillofacial surgery to treat jawbone defects caused by periodontal disease. Autogenous bone grafts, which require harvesting bone from the patient's own ilium (hipbone) or fibula (lower leg bone) to graft into the bone defect, account for 80% of therapeutic procedures today. Although the use of autogenous bone has several advantages that the graft can transplant patients' own cells at the same time without risk of rejection or infection, the procedure does involve injuring a healthy part, which is not desirable. Further, the amount of autogenous bone harvested would not be always sufficient.


The porous artificial bone that deforms like a sponge, developed by our team.

The artificial bone being developed by our team for practical application comprises a porous material composed of a 4:1 composite of hydroxyapatite and collagen with a nanostructure similar to that in living bone. By adjusting the temperature and pH of reaction solution, we can promote the simultaneous formation and coprecipitation of apatite nanocrystals and collagen fibers to create a fibrous composite with a nanostructure similar to bone. By controlled freeze-drying of this composite, we have created a porous artificial bone that deforms like a sponge. We implanted this material into dog tibia and confirmed osteoblasts and osteoclasts activity worked within the material to replace it with newly-regenerated bone. After 3 months from the surgery, the dog was able to run again.

Further, we are developing advanced materials with better cell responsiveness that have nanostructures of higher order. This will open new prospects for our materials lab.

Porous materials essential for tissue engineering

Polymeric Biomaterial Group, Biomaterials Center
Guoping Chen, PhD

Regenerative medicine involves the use of cells to regenerate organs or tissues for transplantation in order to cure some diseases or defects in the body. Research into tissue regeneration using cells and other materials took off in the late 1980s. This discipline is known as tissue engineering. Today, tissue engineering has been used to develop tissues such as skin, cartilage, cornea, and bone, which have relatively simple structures and functions and for which cell culture is relatively easy. The regeneration of organs with more complex functions, such as kidney, liver, and pancreas, is still at the research stage.

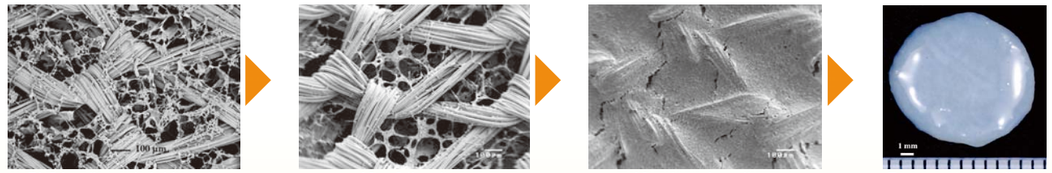
Tissues can be created by inoculating three-dimensional porous materials with cells and culturing in the presence of nutrients to stimulate cell proliferation. The porous materials used are called scaffold. Our group is developing functional scaffold for efficient tissue regeneration.

What properties must scaffold have? The cells must easily adhere onto and develop in the scaffold, which must be absorbed by the body once it has played its role. Efficient tissue generation requires that the cells penetrate deep within the scaffold. To achieve this, the surface of the scaffold must have numerous pores that penetrate through to the interior. Materials used for scaffold include synthetic polymers such as poly (lactic acid) (PLA), poly (glycolic acid) (PGA), or poly (lactic-co-glycolic acid) (PLGA); natural polymers such as collagen or hyaluronic acid; and composites of these materials.

We need to develop sophisticated techniques to make porous scaffold from these materials with the appropriate pore structures. Here we describe a template method and a hybridization method developed by our group.

We first developed a method to produce an ice particle mold and used this to create a material with funnel-shaped pores on the surface. Ice particles are 100–1000μm in diameter made by spraying water onto a surface with specific hydrophilic and hydrophobic properties and then frozen. We use this as a template by applying an aqueous collagen solution onto the surface and then freeze-drying to remove the ice particles. This process produces a collagen sponge with large pores on the surface where the ice particles were and small pores penetrating into the interior. The collagen sponge has been proved useful in the regeneration of skin tissue.

We have also combined collagen and a biodegradable synthetic polymer to produce a strong, highly biocompatible hybrid porous material (PLGA-collagen hybrid mesh). We



PLGA-collagen hybrid mesh — After 24h culture — After 4 weeks culture — Regenerated cartilage

have used this as a scaffold to generate cartilage tissue. The scaffold gradually breaks down and is absorbed and replaced by an extracellular matrix from the cultured cells. We have successfully used this to regenerate human articular cartilage. Many elderly persons suffer from osteoarthritis, so the regeneration of cartilage has particular promise in today's aging society.

The development of high-performance scaffolds is one of the most important steps in the practical application of regenerative medicine.

Nanofibers-made artificial cornea

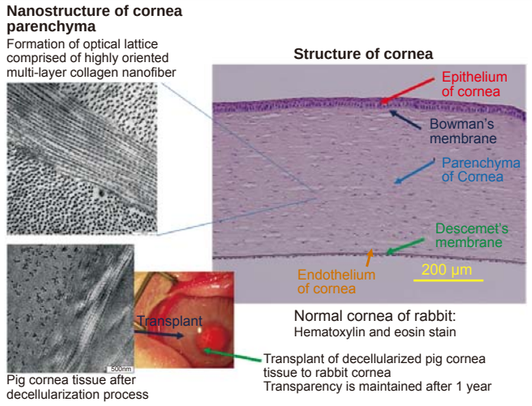
Biofunctional Materials Group, Biomaterials Center
Hisatoshi Kobayashi, PhD

I would like to talk about the basic thinking behind why nanomaterials are chosen for use in the body. The body comprises cells and extracellular matrices that are highly organized. Cells are the unit of life; they comprise a cell membrane surrounding a micron-scale closed space that contains a mix of functional elements such as nanoscale vesicles, cytoskeleton proteins, and genes. The surface of the cell membrane also has various nanoscale functional groups, including various receptors and channels. As such, cells can be thought of as comprising nanofiber and nanoparticle components. The extracellular matrix is also fibers with nanoscale diameters, comprising an aggregate of sugar moieties and proteins so-called glycoprotein.

In order to create sophisticated functional materials for use within the body, I adopt the same strategy as that chosen by living entities, namely using nanofibers and nanoparticles as a base to create higher-order structures and functions. Taking the same approach as seen in nature may seem like a shortcut, and it is inevitable in my view. Nanobiomaterials research was born out of scientists learning from the living body, as the available technologies for creating materials gradually scaled down to the nano level. Our immediate goal is to create higher-order functions by controlling nanostructures, for both bottom-up and top-down approaches to making biomaterials.

Regardless of the method used, we need platform technologies to handle polymers. Our research tries to reproduce higher-order functions using polymer nanofibers. The bottom-up method involves blowing out a polymer material from the tip of a stainless steel needle in a high-voltage DC field and electrospinning to draw out the fibers in a collector. This method produces 10μm–100nm nanofibers and we can control the higher-order structure of the fibers to be, for example, monofilament nanofibers, aligned nanofibers where the fibers are oriented in the same direction, sponges, or nonwoven mats.

My career has been dedicated to making artificial corneas out of nanofibers. The cornea is a transparent tissue



some 800μm thick present as the outermost layer of the eyeball; it mainly comprises collagen fibers and cells. Corneal transparency is due to high-level nanofiber ordering such that the cornea has a lattice-like structure with multiple layers of nanofibers oriented alternately at 90-degree angles to each other. Corneal transplantation is important as damage to the cornea can cause opacity and vision loss. However, there is a chronic shortage of donors and long-term graft survival only occurs in 70–80% of cases. The concept of producing artificial corneas has been around for a long time.

We have tested polyvinyl alcohol (PVA) nanofibers as an artificial material for corneas. In the future, we may be able to make corneas by controlling fiber orientation in a magnetic field. We are also involved in an industry-academia partnership to test a top-down method that involves extracting only the collagen fibers from porcine cornea by eliminating the cells under ultra-high pressure, transplanting into rabbits, and growing cells to produce a cornea. Our results show that the cornea has remained transparent and healthy one year after transplantation.

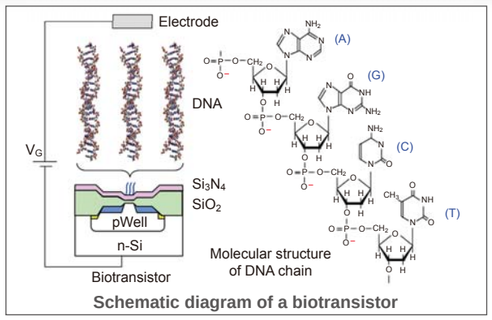
Biotransistor as a new testing method for advanced biomedical applications

Managing Director, Biomaterials Center
Yuji Miyahara, PhD

The micro total chemical analysis system (μTAS) has been widely adopted as a lab-on-a-chip system in experimental laboratories and in microchips used for clinical research. The system involves semiconductor microfabrication technologies but does not utilize semiconductors as electronic materials. "Biotransistors", however, do use this property of semiconductors.

Field effect transistor (FET) gates (electrodes) used in integrated circuits are sensitive to external electric charge. DNA is negatively charged because it contains phosphate groups. Attaching a single strand of DNA to a gate surface and then hybridizing this with a complementary strand would increase the negative charge. We therefore conceived of using a transistor to detect changes in charge, as a result of hybridizatrion.

This method can be used to detect single nucleotide differences in DNA (single nucleotide polymorphisms or SNPs). We first prepare two types of short DNA fragments, one with an adenine (A) terminus and the other with a guanine



Schematic diagram of a biotransistor

(G) terminus for example, and attach to separate transistor gates. If we then introduce the same target DNA into each gate, the DNA hybridizes to form a double strand; the addition of polymerase synthesizes a polynucleotide through an extension reaction as long as the strand terminus is complementary.

This increases the negative charge at the gate. This can therefore be used to distinguish between different nucleotides at the termini. SNP detection technologies are seen as extremely important in understanding disease and an individual's make-up that may determine susceptibility to disease.

We have also conceived a method using a transistor to detect single nucleotide extension reactions. A DNA probe made up of 11 nucleotides and target DNA made up of 21 nucleotides are both fixed onto transistors. Repeated reaction cycles with C, A, G, and T causes the take-up of nucleotides complementary to the target DNA, strand elongation, and the formation of a double strand. This increases the negative charge, so we can detect an electric signal change. This method can be used to analyze unknown base sequences.

Research is underway in the US to develop methods that allow an individual's entire genome to be sequenced easily and cheaply. For this to become a reality, we need to develop next-generation sequencing methods to replace the current DNA sequencers. Our technology is a possible candidate, in my view, as it could be used in the massively parallel analysis of short DNA sequences and combined with bioinformatics technologies.

We are also looking to develop other applications, including the analysis of cells, sugars, and lipids. Our method may also prove useful in the screening of candidate drug compounds. Biotransistors that can directly detect molecular charge could meet wide-ranging demand for non-invasive testing methods that can even be used at small-scale institutions.

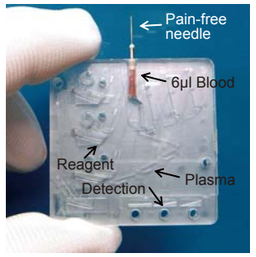
Biochips for in-home diagnostics

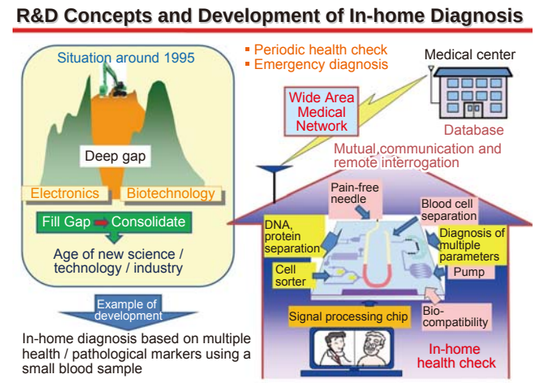
NIMS Honorary Fellow
Yasuhiro Horiike, PhD

Around 1995, I have got the idea and began researching of a healthcare chip that would allow multiple tests to be performed simultaneously on blood samples taken at home. Since then, I have been engaged in R&D into methods to test and measure various parameters, such as lipids, blood electrolytes, blood glucose or viral infections to a high degree of sensitivity, using only minute blood samples of around 6μL and tested on a small chip produced using semiconductor microfabrication technologies.

The diagnostic chip capable of testing three parameters simultaneously (triglyceride, total cholesterol, HDL cholesterol) developed by my team comprises a 4x4 cm square chip made up of three polycarbonate layers. The chip features a superfine, pain-free needle with a smooth interior; when the device is used to pierce a blood vessel, the patient's blood pressure drives blood into the chip. The chip is spun to create a centrifugal effect to separate out the plasma, which then flows through various microstructures via in-built channels and is mixed with accurately measured amounts of reagent before arriving at the test cell. This chip can be inserted into a measuring instrument and the data sent to hospital for diagnostic assessment by a physician. We hope that it will prove useful in managing lifestyle diseases.

Our diagnostic chip for infectious disease can be used in the diagnosis of viral infections, such as AIDS, hepatitis B, or hepatitis C. This chip has two layers; the upper layer has a micropillar structure produced using atomic layer deposition to create multiple silicon pillars coated with an aluminum oxide film. When DNA is introduced into this layer, the negatively charged DNA adheres to the positively charged aluminum oxide in acidic solution. After washing, the DNA is removed in alkaline solution and introduced into a nanogap array in the lower layer. We discovered that the DNA caught in the nanogap at the time of introduction is in the





form of single strands and will extend out. The addition of target viral DNA that has been fluorescently labeled results in hybridization with the test DNA, allowing diagnosis of the infection.

When designing a chip, we produce a mold of silicon or other material for each of the test reactions, create prototypes through press molding on resin, and then combine the prototypes to determine the final structure. Diagnostic chips are widely considered advantageous because they only require minute amounts of blood, but this is actually a major disadvantage when trying to detect viruses present in low concentrations in the blood. In order to overcome this, we need to establish a signal amplification technology to concentrate the test materials and further increase sensitivity.

Research into various types of diagnostic chips took off in the late 1990s. In the near future, I expect social infrastructure to mature such that diagnostic chips can be applied and more widely used. Diagnostic chips should be able to contribute in a number of ways, for example in reducing healthcare costs in our aging societies, enabling diagnostic tests to be performed on ships or airplanes and in sparsely populated areas such as remote islands lacking healthcare infrastructure, or supporting rapid diagnosis in infants.

Technologies to measure living cells

MANA Nano-Systems Field, Nano Functionality Integration Group
Tomonobu Nakayama, PhD

My interest in the biosciences was sparked by the idea that in the future computers could be developed using completely new principles, liberating them from the operating principles in use today. This concept has also arisen in discussions with Prof. Masakazu Aono, the Director-General of the International Center for Materials Nanoarchitectonics (MANA).

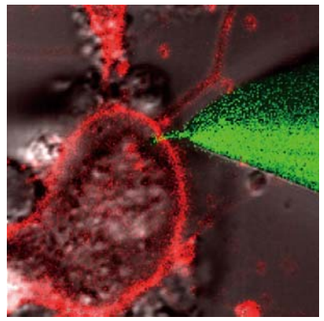
I attribute the flexibility, fuzziness, and accuracy of the brain to operating principles such as parallel processing or learning effects achieved through a network of cells. You may be surprised to learn that a single human brain has 10^{15} synapses, which is on a par with the total number of transistors in all the computers around that world connected to the Internet.

Moreover, a single human brain operates using only 10W of power. Can we create such an information processing system using the materials technologies under our control? I think that synapses may be the key to such developments. It may be difficult to mimic the synaptic function alone, however, as the entire nerve cell probably plays a role.

My research background is in solid-state physics and I have worked on developing scanning-probe microscopy methods for inorganic and organic nanostructure research. To explore nanomaterials research, I developed a multiple-scanning-probe microscope that enabled nanoscale physical measurements not previously possible. I am now hoping to link this work with bionanotechnologic research.

Biology textbooks show schematic models of cell signaling mechanisms, but no one has ever directly observed such reactions occurring in living cells. We need to use nanotechnologies to better understand the mechanisms behind cell signaling at a molecular level. Ion channels are nanoscale terminals that act as the site of information input and output for cells. We have developed nanoprobes capable of detecting individual molecules to allow us to access these channels. We have developed probes that detect pH and probes that detect the characteristic vibration modes that occur when the probe nears an individual molecule. We can now understand slight environmental changes in minute spaces. We want to apply these technologies to learn about living cells and how they function as networks. Cells have systems for the parallel processing of many types of signals and multiple molecules. Our expertise in multi-probe technologies should enable the simultaneous measurement of large volumes of data.

Our goal is to utilize the nanotechnologies developed thus far to further our understanding of cells, learn how the brain operates, and pave the way for neural computers.



Measuring nerve cells using a nanoprobe: Fluorescence microscopy using color-coding to show the nerve cell membrane (red) and the nanoprobe (green).

Making functional materials from DNA

Nano-Architecture Group, Organic Nanomaterials Center
Hidenobu Nakao, PhD

DNA is a biomolecule that provides the genetic blueprint for an organism. However, DNA has a completely different appeal and wide-ranging potential if we think of it as a chemical or a raw material. I am looking into how we can turn this abundant and vital natural macromolecule into a useful material.

The DNA double helix is around 2nm in diameter and can be several μm or more in length. It has a highly regular configuration and is extremely functional. The presence of phosphate groups on the DNA chain makes the molecule anionic, enabling electrostatic interactions with various substances.

Carbon nanotubes — an artificially made nanomaterial — have a similar diameter and size as DNA. They have greater mechanical strength than DNA, but are not readily soluble in solvents and surface modifications are difficult to achieve.

DNA usually exists as a clew in aqueous solution, so it needs to be straightened out before it can be used as a nanomaterial. Having achieved that, DNA could be used as a functional material if combined with metallic nanoparticles or organic polymers. We may be able to manipulate DNA using atomic force microscopy (AFM).

Thus far, many researchers have tried electrospinning and other methods for one-dimensional DNA stretching. Here I describe an exceptionally easy-to-use and cheap method which I developed recently.

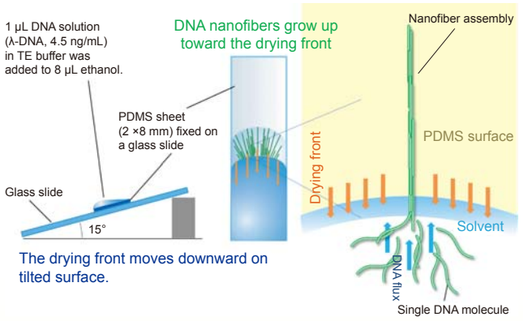
The method utilizes the fact that DNA is not readily soluble in ethanol. I mix ethanol with an aqueous DNA solution, drop this onto a hydrophobic silicon rubber sheet, and rest this sheet at a very slight incline. The resulting interface migration causes nanofibers of DNA aggregates to extend and separate away from the sheet surface starting at the upper edge of rapidly evaporating solvent droplets. The fibers produced in this way are several dozen nm in diameter and 1mm in length.

The pattern of DNA nanofibers produced on the flexible sheet surface can be transferred as is onto a glass sheet. Complex two-dimensional patterns can be formed by repeating this transfer process.

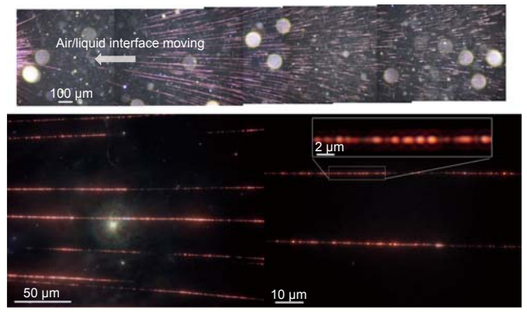
Various applications spring to mind. For example, a disposable sensor could be produced by attaching substances that react to blood sugar or various allergens to the DNA nanofibers and transferring the sheet of DNA nanofibers produced onto an electrode pattern.

It is also possible to produce a functional material that utilizes the space within the DNA double helix. Cationic organic dyes with at least three aromatic rings can be easily inserted, and fit well, into the inner space in the DNA helix. A row of dye molecules oriented the same way may be useful for laser oscillation.

There is a long way to go before the results of this research can replace the devices in use today. Our goal is to establish platform technologies that will allow us to combine our research with various other techniques in order to expand the possible applications.

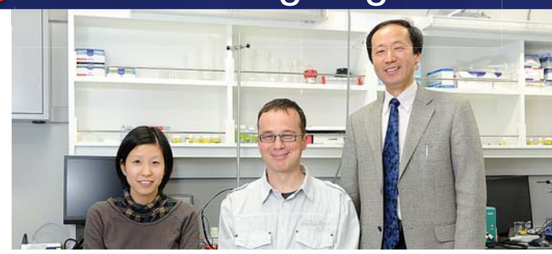


Producing DNA nanofibers using a solvent evaporation method



DNA nanofibers attached with gold nanoparticles

Creation of Functionalized Biodevice by Nanostructural Control of Solid/Liquid Interface



Biomaterial System Group, Biomaterials Center

Managing Director
Chiho Kataoka Martin Pumera Yuji Miyahara

In recent years, great progress has been achieved in nanotechnology and life science, and it has become possible to associate biological phenomena with nanometer-scale science. The research in nano-biology is expected to contribute to a wide range of fields including medical care and drug discovery. We are currently working on biodevices which convert protein-DNA binding, cell properties, and other phenomena to electrochemical signals by chemically and physically controlling the nanostructure of the solid/liquid interface. Although many biosensors are based on a variety of detection principles, an advantage of the electrochemical biosensor is the simple detection procedure, in which labeling of biological materials such as fluorescence labeling is not necessary. Our current research themes are (1) development of a DNA sequencing method using field-effect transistors, (2) elucidation of the working principle of field-effect based biosensors which are used to detect cellular properties and functions, and (3) development of highly sensitive biodevices using carbon nanotubes. This article describes research (2) on cell membrane devices.

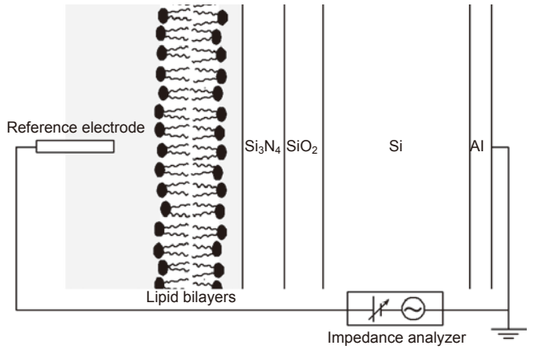


Fig.1 Detection of a lipid layer using a field effect device. The distribution of electrons and holes in the semiconductor (Si) is read as electrical signals.

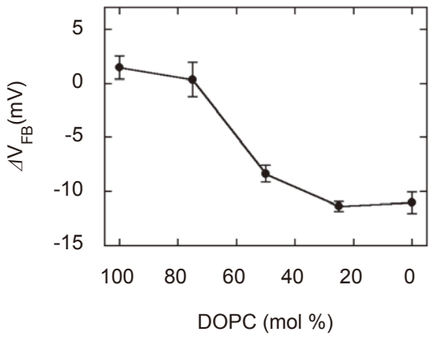
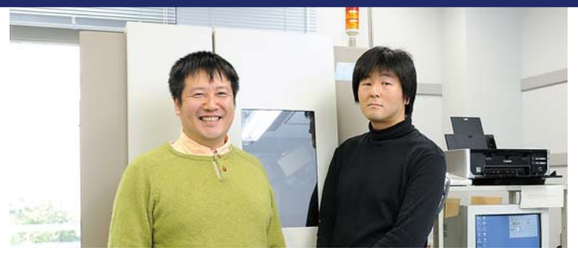


Fig.2 Relationship between the DOPC ratio in a DOPC/DOTAP film and device response ΔV_{FB}. DOPC: 1, 2-dioleoyl-*sn*-glycero-3-phosphocholine, DOTAP: 1, 2-dioleoyl-3-trimethylammonium-propane (chloride salt).

Field-effect devices are generally fabricated from an insulating film/semiconductor substrate, and the recognition element is fixed to the insulator surface. Changes in the electrical charge at the insulator surface are then detected as changes in the conductivity or capacitance of the semiconductor. We formed lipid bilayers which are good model systsms of biological membranes on the device surface (**Fig. 1**) and investigated the capacitance change. In a lipid bilayer, lipid molecules are self-assembled in a way that the hydrophobic group is oriented inside and the hydrophilic group is oriented to the outside aqueous phase. Because the structures (thickness: several nm), electrical charge, chemical compositions, and other properties of lipid bilayers can precisely be controlled, it is possible to elucidate the detection principle of field-effect devices which are used to obtain the information on cell membranes. For example, as shown in **Fig. 2**, our studies revealed that device response changes depending on the content of charged lipids. We believe that these results are essential in understanding hybrid systems consisting of cells and devices. In the future, we will continue to investigate the hybridization of cell membranes and biodevices, and will work to understand the operating principles of cell membranes devices and develop biodevices with new functions.

Novel Porous Apatite Artificial Bone

Ceramic Biomaterial Group, Biomaterials Center



Group Leader
Masanori Kikuchi　　Yasushi Suetsugu

Human bones are formed by alignment of nano-crystals of apatite, which is a type of calcium phosphate, along collagen fibers, which are a type of protein. When an artificially-synthesized porous apatite ceramic material is implanted in bone in a living body, newly-formed bone penetrates into the pores while bonding directly with the artificial material. Because apatite is originally a component of bone, harmful effects on the body are not a concern. This means that apatite is an extremely good material for artificial bones in grafting procedures to regenerate bone defects.

When porous ceramics are manufactured by the conventional technique, a material with a structure containing randomly-dispersed pores having a particle-like shape is obtained. To enable easier penetration of the newly-formed bone material, we developed a technique for producing a porous apatite material containing tube-shaped pores aligned in a single direction using the crystal growth of ice. Concretely, first, fine particles of apatite are synthesized and dispersed in water, and an organic polymer is then added to solidify this solution into a jelly. When this is cooled from one direction, numerous thin ice columns form aligned in that direction. As illustrated in **Fig. 1**, a porous material can be produced by extracting the ice columns using freeze-drying process, and then sintering the material at high temperature. In the material obtained in this manner, the tubular pores are aligned in one direction and pass virtually through the entire material.

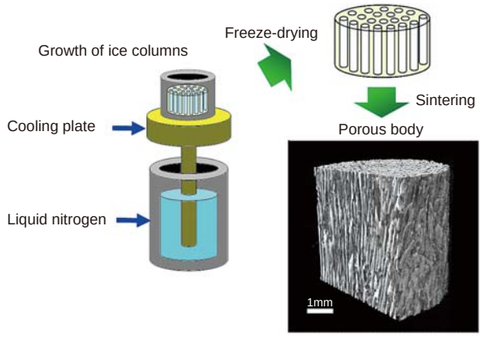


Fig.1 Method of producing porous apatite with pores aligned in one direction.

A porous body of this material was implanted in the thighbone of a rabbit, and was removed and subjected to mechanical tests at set intervals. It was found that strength against compressive loading in the pore direction increased with time after implantation, reaching 47MPa after 12 weeks. As shown in **Fig. 2**, this was clearly higher than that of a porous body with a random structure which was used for comparison. This is equivalent to approximately 1/2 of the strength of the hard part on the outside part of the bone. This remarkable increase in strength is considered to be due to the fact that the collagen fibers and apatite crystals of the new bone which formed inside the pores were aligned parallel to the tubular pores, and as a result, could effectively support compressive loading in that direction. High expectations are placed on the application of this material as an artificial bone which promotes the regeneration of bone having a micro-structure closer to the natural state.

This material was jointly developed with Kuraray Co., Ltd., and in vivo functional evaluations were performed with the cooperation of the Department of Orthopedic Surgery of the University of Tsukuba. We wish to express our heartfelt thanks to all those concerned, and particularly to Prof. Naoyuki Ochiai, Dr. Masataka Sakane, and Dr. Masashi Iwasashi (now at Showa General Hospital) of the University of Tsukuba, and to Mr. Tatsuhiko Higaki and Mr. Yuji Hotta of Kuraray Co., Ltd.

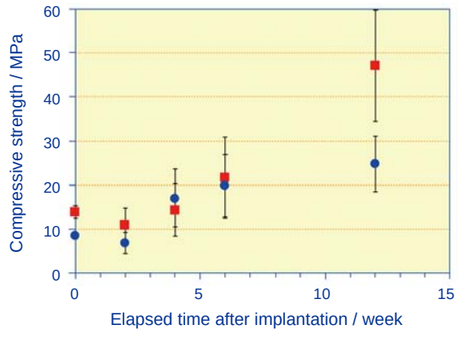


Fig.2 Change in compressive strength of porous apatite material implanted in the medullary cavity of a rabbit thighbone
■: Porous material having pores aligned in one direction (loading direction is parallel to pore direction)
●: Porous material with random structure

Production of Urban Ores Using Ball Mill for Saving Time and Effort

Center for Material's Scientific New-Deal
Basic Research Group, Exploratory Materials Research Laboratory for Reliability and Safety†

Managing Director
Kohmei Halada　　Nozomu Katagiri　　Kiyoshi Ijima†

With the increased risk associated with the consumption of natural resources, as exemplified by the recent rapid rise and fall in the prices of rare metals, there is a growing recognition that we should make active use of Japan's "urban mines."* In a previous report (November 2008), we estimated the amount of the urban ores accumulated in Japan as equivalent to approximately 16% of the world's current reserves of gold, or roughly 6,800 tons, and 22% (60,000 tons) of the world's reserves of silver. That study also revealed that Japan has large accumulations of other metals, such as indium, tantalum, etc.

Those values show the maximum potential for recycling, but never mean that the same amounts can be recycled immediately. This is because neither a high efficiency, low cost recycling process nor collection routes for used devices has been established. Furthermore, the recycling cost (mainly labor cost) may be higher than the value of the materials recovered because the amount of rare metals contained in each used device is so small. Therefore, we proposed a method which solves those issues by taking advantage of the properties of the substances which are to be recovered.

If roughly crushed cell phones are treated with a ball mill, which offers appropriate conditions for this process, plastics, aluminum, board materials, and other structural parts in which strength is required will not be crushed and will remain as relatively large sheet-shaped fragments. (**Fig. 1**, center) On the other hand, because the LSI chips, parts, etc. which contain the rare metals are brittle, these parts can be selectively separated and powdered, and can be concentrated as "urban ores." (**Fig. 1**, bottom right) For example, this process makes it possible to concentrate the gold content of the boards in cell phones by several times. This urban ore is equivalent to the fine ore in natural ores, and can be further concentrated by treatment processes such as wind separation, magnetic separation, and ore floatation. Depending on the case, it may also be possible to recycle the urban ore directly to the refining process. The ball mill is a simple device, in which roughly crushed cell phones are merely introduced into a drum-shaped container containing a large number of hard balls and then rotated. (**Fig. 2**) It only requires electric power to rotate the mill. Absolutely no heat or water is required. For this reason, this equipment can easily be installed in the outskirts of urban areas where large numbers of used devices are able to collect as a small scale treatment process, and thus can build a system for the recycling chain from the cities where products are consumed to the refineries.

* http://www.nims.go.jp/ecomaterial/hal/MR/UM/index.html

Fig.1 Outline of treatment process
Used cell phones (left) which have been roughly crushed to a size suitable for charging into the ball mill are treated by the ball mill (center). Plastics, aluminum, board materials, etc. remain in fragment form (upper right). LSI chips, parts, etc. packaged on the boards are selectively separated and crushed, and are concentrated as powder "urban ore."

a) Planetary ball mill　b) Charged board fragments and balls
c) Shape and size of balls (crushers)

Fig.2 a) Ball mill actually used (planetary ball mill)
b) Roughly crushed used cell phones are placed into a container containing balls made of a hard material.
The container is set in a planetary ball mill device (a), and the container itself rotates (self-revolution) while revolving around the central axis of the device.

SPECIAL Interview

No Run-Of-The-Mill Research for Leading Light of Nanomaterials Research

Z.L. Wang And The Nanotech Factor: Much Zeal For Nanotech At Georgia Tech

Dr. Zhong-Lin (Z.L.) Wang, Distinguished Professor at the Georgia Institute of Technology (Georgia Tech) School of Materials Science and Engineering as well as Director of the Georgia Tech Center for Nanostructure Characterization in the U.S., was in Japan for the Second MANA International Symposium organized by the International Center for Materials Nanoarchitectonics (MANA), held from February 25, in Tsukuba. Many of his papers have been placed in the high-impact category, putting Dr. Wang on the Top Ten list of academics having a great impact on the materials research field. Also a MANA Satellite Principal Investigator for NIMS, he said that NIMS impressed him with its facilities, not to mention the global network, that the institution has at its disposal, in addition to the sparkling initiatives such as providing a melting-pot setting for those from various disciplines having differing cultures of research.

What is your research forte?

At the Georgia Tech School of Materials Science and Engineering, I am carrying out a gamut of nanotech research activities, from biotech and electronics areas as exemplified by the Biotemplated Nanofabrication and Bio-inspired Nanotechnology as well as Quasi-aligned Ga_2O_3 nanowires papers grown on brass wire meshes (and their electrical / field-emission properties) to energy and medical applications, like for photovoltaic systems in the form of improved solar cells or systems for in-vivo detection of cancer cells. Currently the Georgia Tech nanotech research effort that I lead is in particular targeting work as related to nanogenerators and nanopiezoelectronics. Regarding piezoelectricity, I would like to note that I am working to fabricate novel devices such as functional oxide nanobelts as seen from the perspectives of materials, properties and nanodevices. Recently, the Technology Review published by MIT covered the piezoelectric-effect experiments our research group conducted based upon a mouse-driven system, wherein the biomechanical energy is converged into electricity. [Further details can be found at

http://www.nanoscience.gatech.edu/zlwang/index.html]

You have visited Japan in the past but how did you find things this time?

At the symposium that I attended this time, presentations were given by invited speakers from around the world and by members of MANA and the International Center for Young Scientists (ICYS), covering the four fields of Nano-Materials, Nano-Systems, Nano-Green and Nano-Bio. The symposium's main aim was to bring together experts in these fields, in addition to promoting research achievements of the MANA project. I chaired, together with Dr. Katsuhiko Ariga of NIMS, the first of two sessions on Nano-Materials, held on the opening day of the symposium. The invited speaker for this session was Prof. Gerhard Wenz of the University of Saarland, thus the main figures in just this single session represented the leading scientific communities to be found in Asia, the Americas and Europe. It appears that the global network as I mentioned was indeed highlighted here.

What is your view concerning nanomaterials research today?

Concerning the arena I have chosen to enter, I would like to state that I see nanomaterials research, in which I am generally involved, to be a wide-ranging field. However, I wish to underscore the need to maintain focus in order to become a world champion in certain spheres, resisting the temptation to over-diversity and succumbing to run-of-the-mill roles. Actually, not only do I wish my philosophy to provide a guide for other researchers, but the results of my work offer good changes to everyone's daily life overall, by paving way for innovations that can save energy and improve health among other things.

What is your role at the university?

As a professor at technical university, I hope to stress the need for teamwork and the requirement to have people grow in order to make innovations such as those I just described possible. I believe the best way to do so is to make sure ones students as well as ones colleagues find joy as I find joy in my research upon working. This is in line with one of my favorite quotes, If you want to do something well, you must love it; specifically for my students, I tell them that "My office doors are always open and available to offer assistance, not only as your teacher but as your friend." It is my stance regarding my students, that your success is my success and we can all gain from conducting research together.

How do you cope with your busy schedule?

I have several other favorite quotes, namely "If you have ten minutes, do a ten-minute thing" and "Do not touch the same piece of paper twice" (although a very difficult piece of advice to put into practice), these are sayings that enable me to cope with my schedule. In addition, there is an all-time favorite –"persistent, consistent"– certainly a masterpiece of advice for anyone interested in gaining material results in life.

NIMS NEWS

NIMS is Japan's Leader in the Citation Index for Papers in Materials Science

(May 1, 2009) NIMS reached the 10,000 level in the new Citation Index (CI) for papers in the Materials Science field during the period from January 2005 to February 2009. The Citation Index is one of the Essential Science Indicators (ESI) published by Thomson Scientific. NIMS moved ahead of Tohoku University and now ranks No. 3 in the world.

In 2008, the number of papers (SCI papers) published by NIMS researchers in the scientific journals surveyed in the ESI increased slight, from 1125 during the previous year to 1163. However, the average Impact Factor (IF), which is an index of the impact of the journals carrying papers, climbed from 2.35 to 2.45, reflecting the NIMS policy of changing the institute's focus from quantity to quality.

Citation Index (CI) in Materials Science Field
(January 2005 – February 2009)

Rank	Institution	Country	No. of Citations
1	Chinese Academy of Science (CAS)	China	32,241
2	Max Planck Institute	Germany	14,607
3	National Institute for Materials Science (NIMS)	Japan	10,003
4	Tohoku University	Japan	9,845
5	National University of Singapore	Singapore	9,460
6	National Tsing Hua University	China	8,840
7	Massachusetts Institute of Technology	USA	8,271
8	National Institute of Advanced Industrial Science and Technology (AIST)	Japan	7,465
9	Centre national de la recherche scientifique (CNRS; National Centre for Scientific Research)	France	7,049
10	Consejo Superior de Investigaciones Científicas (CSIC; Spanish National Research Council)	Spain	6,884

MANA Receives a High Evaluation in the WPI Program

The International Center for Materials Nanoarchitectonics (MANA), which NIMS operates as a World Premier International Research Center (WPI), together with the IPMU* at the University of Tokyo, received a high evaluation from the Program Committee for its activities during fiscal year 2008. MANA received high marks for operation appropriate to the WPI concept, particularly in that more than 50% of its researchers were foreign nationals (see accompanying table), and full administrative support is provided using the English language. Based on these results, ¥125 million was added to the Center's operating subsidy for fiscal year 2009, bringing the total to ¥1,475 million.

The aim of this program is to create research centers with "global visibility," which can boast the world's top level of research, by bringing together frontline researchers from around the world in an outstanding research environment. The program was launched in 2007 by Japan's Ministry of Education, Culture, Sports, Science and Technology (MEXT), which will provide support for a 10 year period. In 2007, NIMS was selected as one of 5 host institutions in Japan, along with the University of Tokyo, Kyoto University, Tohoku University, and Osaka University.

*IPMU: Institute for the Physics and Mathematics of the Universe

Composition of MANA members
(as of April 2009)

Position	No.	Non-Japanese
Senior Researcher	29	9
General Researcher	57	12
Postdoctoral Fellow	73	59
Student	27	17
Total Researchers	**186**	**97**

(Ratio of foreign researchers: 52%)

Staff	32	4
Total	**218**	**101**

NIMS Signs Agreement on International Joint Graduate School with the University of Pardubice (Czech Republic)

(April 20, 2009) NIMS and the University of Pardubice in the Czech Republic signed an agreement on an international joint graduate school. In the past, the two organizations have conducted joint research on sensor materials and other subjects, and NIMS has received students under an internship program. Under this agreement, NIMS will receive graduate students in doctoral courses. The University of Pardubice plans to send the first two students to NIMS this fall.

At the signing ceremony: Prof. Jiří Málek, Rector of the University of Pardubice, and Dr. Tetsuji Noda, Vice-President of NIMS.

NEW NIMS Partnerships

GE and NIMS Sign MOU to Strengthen Technological Ties

(May 27, 2009) GE and NIMS signed a Memorandum of Understanding to explore new technological collaboration opportunities. Under the agreement, GE's Global Research Center and NIMS will focus on the development of mutually beneficial partnerships through spontaneous dialogue, researcher exchanges and joint seminars over the next five years. GE and the NIMS will look to identify future projects in the field of materials science and engineering that help promote a cleaner, more sustainable energy portfolio and environment.

Mr. Mark Little (left), Director of GE Global Research and Prof. Teruo Kishi, President of NIMS.

KMAC (Korea): Promoting Research Cooperation and Exchanges of Human Resources

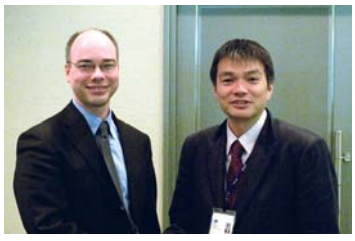
(April 19, 2009) NIMS and the Korea Materials and Components Industry Agency (KMAC), which is part of that country's Ministry of Knowledge Economy (MKE), signed an MOU aimed at promoting a program related to research cooperation and exchanges of human resources. The purposes of this program are to conduct joint research in which NIMS will receive researchers from Korea, with the costs to be borne by the Korean side, and to vitalize human exchanges. More concrete details will be worked out in the near future, and the program is expected to be launched within the present fiscal year.

At the signing ceremony: President Joon-suk Jung of KMAC (left), and Dr. Yukichi Umakoshi, Vice-President of NIMS.

Victoria University (NZ): Research and Development of Functional Optical Nanomaterials

(April 24, 2009) The NIMS Quantum Beam Center and Victoria University of Wellington, New Zealand, signed an MOU on "Research and Development on Functional Optical Nanomaterials." This is the first MOU that NIMS has concluded with a research institute in New Zealand.

In research on optical nanomaterials, Victoria University is a leader in fabricating metallic nanoparticle materials with a variety of shapes using chemical growth methods, while NIMS is a leader in the experimental evaluation of nonlinear optical properties. The two organizations will conduct collaborative interdisciplinary research and development of functional optical nanomaterials taking advantage of their respective strengths.



Dr. Richard Tilley, Senior Lecturer of Victoria University (left), and Dr. Yoshihiko Takeda, Senior Researcher of NIMS Quantum Beam Center.

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