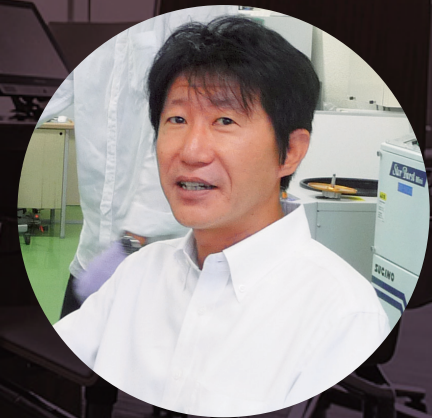


# Free Architectural Design and Synthesis of Nanocomposites

In recent years, nano-sized materials have been attracting tremendous attention in many research fields such as structural materials, cosmetics and medicine. The reason for this is that the unique physical properties of nanomaterials, such as quantum, surface and interface effects, facilitate the development of many new applications for these materials.

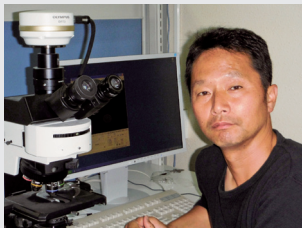


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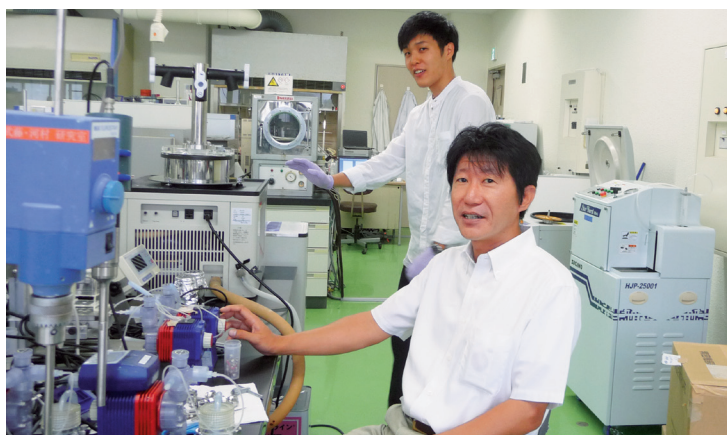
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# Free Architectural Design and Synthesis of Nanocomposites

Hiroyuki Muto



Hiroyuki Muto and one of his student

In recent years, nano-sized materials have been attracting tremendous attention in many research fields such as structural materials, cosmetics and medicine. The reason for this is that the unique physical properties of nanomaterials, such as quantum, surface and interface effects, facilitate the development of many new applications for these materials. Until now however, nanomaterials' complexity hindered their effective utilization; resulting in little progress in their practical applications. Nevertheless, Dr. Hiroyuki Muto, professor of Institute of Liberal Arts & Science and Department of Electrical and Electronic Information Engineering (acting), had developed a simple but novel method that enables the synthesis of uniform nano-sized composite materials utilizing electrostatic interactions. Currently, Dr. Muto is advancing his research towards the mass production of nanomaterials.

Interview and report by Madoka Tainaka

## The key is “electrostatic interaction”

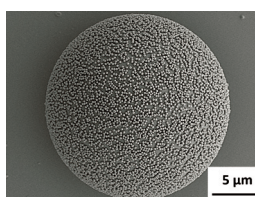
“I think many of you know very well what a carbon nanotube is. However, if I ask you about the practical applications of a carbon nanotube, I doubt many of you would be able to answer my question, which would be fair enough, as few practical applications currently exist.

A carbon nanotube is a thread-like material that can conduct electricity and upon mixing with translucent materials, it can be utilized in many applications such as touch panels and solar panels. However, during preparation, carbon nanotubes tend to shrink into a ball of thread or harden upon mixing. Moreover, as it is difficult to obtain a uniform mixture of carbon nanotubes, a large amount is usually required during the mixing process. As carbon nanotubes are very expensive, it is not therefore easy to practically fulfill their immense theoretical potential.,” explains Dr. Muto.

In the conventional fabrication of composite materials, the required raw materials are mechanically stirred in a container with sticks or hard balls, which is also known as ‘mixing’. In reality, it is actually very difficult to obtain a very well balanced and distributed mixture. Despite the adoption of various measures to improvise the mixing process such as chemi-

cal additives and controlling the level of force and time during mixing, crucial issues such as structural decomposition resulting from the impact of mixing remained unresolved. Therefore, it is almost impossible to synthesize minute/fine composites by just mixing the materials.

“When materials with different specific gravities are mixed, they tend to separate and resist uniform mixing. It is also a challenge to mix the proper amount of conductive materials (as mentioned previously for carbon nanotubes) and at the same time align them in a continuous arrangement. Therefore,



Adhered nano-sized materials around a micro particle

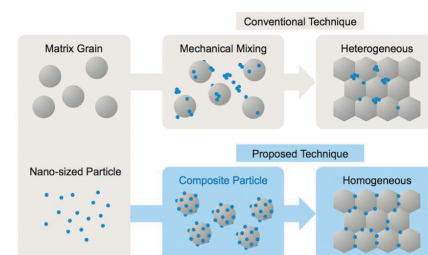
we came up with the idea of synthesizing a composite material by adhering nano-sized materials around a micro particle that is used as the parent material (matrix).”

The principle of adhering the nano-sized materials onto the matrix particle is based on “electrostatic interaction.” Electrostatic interaction is the force that acts between positive and negative charges. Dr. Muto has succeeded in

using this well-known physical phenomenon to construct composite materials in a simple manner.

## Synthesizing a wide variety of composite materials by freely controlling the surface electric charges of a particle

This method for synthesizing a composite material is very simple and easy to understand.



Concept of development for novel nano-composite via composite particle

“First, the electric charges on the surface of the matrix particle and the nanomaterial (which is the additive) are controlled to be either positive or negative, in order to generate opposite polarities. Then, both materials are added into a solution such as water and stirred in such a way that the nanomaterial is successfully absorbed onto the surface of the matrix particle. The

preparation procedure involves the addition of the materials into a polyelectrolyte solution (a material that produces polymer ions upon dissolution in water, such as the positively charged poly diallyldimethylammonium chloride or the negatively charged sodium polystyrenesulfonate) so that the surface of each material has either a positive or negative charge. This method enables quick room-temperature synthesis of composites, without being affected by the specific gravity difference of the constituent materials. Moreover, the amount of nanomaterials absorption can be freely regulated", Dr. Muto explains.

Firstly, all materials have their own specific electric charge. For example, if silica (silicon oxide) is added into neutral water, it would become negatively charged. However, this does not always occur, and in some circumstances, the electric charge may be too weak and cannot be used as it is. However, Dr. Muto explains that if a polyelectrolyte is used, it is possible to charge the material uniformly with a strong electric charge. In addition, the alteration of electric charge between positive and negative is possible regardless of the original surface electric charge of the particle. By adopting this method, it is feasible to synthesize composites with various functionalities depending on the combinations of matrix particles and nanomaterials that are absorbed.

"Actually, this method is based on electrostatic interaction, which is already used in the synthesis of functional "nano" thin films (two-dimensional structures). So although the method is not new, we succeeded in using it for the first time to synthesize integrated three-dimensional architectural nanocomposites that consisted of particles of various sizes. When the composite is dried, it is applicable as a powder. By increasing the concentration, it can be utilized as a paste. In powder metallurgy, the composites can also be pressed, formed, and hardened thermally into a block. One of the

highlights of this method is the ability to synthesize and design the dimension or form of the nanomaterials in order to utilize their properties in accordance to the specific requirements", Dr. Muto proudly explains.

The composite particles synthesized in this way are bound strongly, which makes the material stable and more energy efficient compared to those synthesized by mechanical mixing. This method was not originally suitable for materials that did not possess wettability, water solubility or buoyancy because this process involves dissolution into a solvent. However, through the application of many creative ideas, it has become applicable for almost all materials at this point.

As an example, Dr. Muto worked on the development of a conductive material using carbon nanotubes. In this project, Dr. Muto succeeded in synthesizing a material that has high transparency, while greatly reducing the amount of carbon nanotubes used.

### Working on the development of a manufacturing process towards mass production

Owing to the superiority of this research, it was adopted as one of the Industrial Technology Research Grant Programs of the New Energy and Industrial Technology Development Organization (NEDO) from 2009 to 2012. From 2015, the research has advanced further into the Innovative Design and Production Technology project in the Cross-ministerial Strategic Innovation Promotion Program (SIP) of the Cabinet Office. Currently, Dr. Muto is working on the process development that enables mass production of composite nanomaterials (composite particles). Moreover, industries in various fields are expressing their interest in this technology.

In relation to his goal, Dr. Muto said, "Material study does not immediately come across as a glamorous field of study, but in fact it has

great influence on society. For example, just by changing the composition of a material, its strength can be doubled or reduced to half. It is therefore challenging. The production rate varies for different materials, but in the near future, I hope to be able to produce about 10 kg of composite particles per hour." It is very exciting to see what kind of novel materials will be synthesized with this method developed by Dr. Muto.

This study was supported by Cross-Ministerial Strategic Innovation Promotion Program (SIP) of Council for Science, Technology and Innovation (CSTI), Japan.

#### Reporter's Note

Toyohashi University of Technology has many members who graduated from a technical college, as the university promotes collaborations with other technical colleges. Dr. Muto himself has also graduated from the National Institute of Technology, Fukushima College.

"People from technical colleges are accustomed to experiments, and many of them enjoy the process. Therefore, they share the tendency of trying out their ideas hands-on. This research started in the same way too, where I tried my idea in an experiment and surprisingly, the result was better than expected." Dr. Muto laughed.

Dr. Muto was originally working on research regarding the fracture mechanics of materials. He chanced upon his current research when he first started to synthesize his own ceramics for evaluation purposes. It's safe to say that Dr. Muto's significant research results are the fruit of his dedicated attitude toward experiments.

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#### Dr. Muto and his research colleagues were awarded the "Editor-in-Chief's Featured Article" by the Journal of Supercritical Fluids (Elsevier)

This is an award given to the top three papers chosen from all published articles in 2014 by the editorial committee of the Journal of Supercritical Fluids.

#### Awarded to

Kiyoshi Matuyama, Yu-ki Maeda, Takaaki Matsuda, Tetsuya Okuyama (National Institute of Technology, Kurume College), Hiroyuki Muto (Toyohashi University of Technology)

University of Technology)

#### Title of awarded article

Formation of poly (methyl methacrylate)-ZnO nanoparticle quantum dot composites by dispersion polymerization in supercritical CO<sub>2</sub>.

By TUT Research editor



## ナノ複合材料を微細に、自在にデザインする

近年、構造材料から化粧品、新薬にいたるまで、ありとあらゆる分野において、ナノサイズの物質が注目されている。その理由は、「量子効果」や「表面・界面効果」といった、ナノ物質特有の物性により、材料に新しい機能を付加できる点にある。しかし、実際にはナノ物質を使いこなすことは難しく、実用化はさほど進んでいない。そうした中、武藤浩行教授は、「静電相互作用」を利用して、ナノサイズの複合材料を均質に、しかも自在にデザインする手法を開発。量産化へ向けて、研究を加速させている。

### ■ カギは「静電相互作用」にあり

「皆さん、カーボンナノチューブはよくご存知だと思いますが、実際に何に使っているかという、すぐに思いつかないのではないのでしょうか。それもそのはずで、じつは、まだほとんど実用化には至っていないのです。」

カーボンナノチューブは糸状の電気を通す物質で、透明な物質に混ぜれば、タッチパネルや太陽光パネルなど、さまざまな用途に使うことができます。しかし、いざつくるとなると、物質と混ぜる際に糸状にかたまってしまうり、均質に適量を材料に入れることが難しくなったりして、現状は大量に混ぜなければなりません。とても高価な物質ですから、なかなか実用化に結びつかないのです」と武藤教授は説明する。

従来、複合材料をつくる際に、多くの場合、容器の中で棒や硬い球などを用いて機械的に攪拌する、つまり「混ぜる」という手法がとられてきた。しかし物質を均質に混ぜるのは容易ではない。物質同士が混ざりやすいように薬品を使ったり、攪拌する強さや時間を変えたりするなど、さまざまな工夫が凝らされてきたが、混ぜる際の衝撃で物質の構造が壊れてしまうなど、いくつもの課題があった。そもそも、ただ混ぜるだけでは、複合材料を微細にデザインすることは難しい。

「当然、比重が違うものを混ぜると分離してうまく混ざりませんし、さきほどのカーボンナノチューブのように、導電性の材料を適量入れて、連結するように配置することも困難です。そこで我々が思いついたのが、母材(マトリックス)となるミクロの粒子のまわりにナノ物質をべたべたと貼付けて複合材料をつくるという方法です」

このとき、マトリックス粒子にナノ物質を吸着させる役割を担うのが「静電相互作用」である。静電作用とは、正(プラス)と負(マイナス)の電荷の間に働く引力のこと。この一般的にもよく知られた物理現象を利用して、武藤教授は複合材料を簡便につくることに成功したのである。

### ■ 粒子の表面電荷を自在にコントロールし、多種多様な複合材料をつくる

そのつくり方は、じつに単純明快だ。

「マトリックス粒子の表面の電荷と添加物となるナノ

物質の表面電荷を、それぞれプラスとマイナス、すなわち相反するように制御しておいて、その二つの物質を水などの溶液の中に入れて、ぐるぐるかき混ぜて吸着させるだけです。そのための前処理として、それぞれの物質の表面がプラスかマイナスの電荷を帯びるように、高分子電解質(水中で解離して高分子イオンとなる物質)の溶液(例えば正電荷を持つポリジアリルジメチルアンモニウムクロリドや負の電荷を持つポリスチレンスルホン酸ナトリウムなど)の中に入れて反応させ、表面の電荷を変化させておきます。この方法であれば、常温で、素早く、物質の比重差にも左右されることなく、複合材料を創製できる。しかも吸着させるナノ物質の数なども自在にコントロールできるのです」と武藤教授は語る。

そもそも、どのような物質も、それぞれ固有の電荷を持っている。例えば、シリカ(酸化ケイ素)であれば、中性の水の中に入れてはマイナスとなる。しかし、それらは必ずしも均一ではなく、電荷の弱い場合もあり、そのままでは使いづらい。しかし、高分子電解質を使えば、物質に均一に強い電荷を帯びさせることができるのだという。しかも、粒子が元来持つ表面電荷の正負にかかわらず、電荷を自在に変えることもできる。これにより、マトリックス粒子と吸着させるナノ物質の組み合わせ次第で、さまざまな機能を持たせた機能性微粒子の創製が可能になった。

「じつは静電相互作用というのは、機能性「ナノ」薄膜(二次元構造)をつくる際に使われていた手法です。それを我々は粒子などの三次元構造に応用し、集積化に用いることで、さまざまなナノ集合複合体をつくることに成功しました。乾かせばパウダー状にもなるし、濃度を上げてペースト状にすることも、粉末冶金といって、プレスして成形して焼き固めて塊にすることもできる。まさに自在に材料をデザインできる点が大きな特長です」と、武藤教授は自負する。

こうしてできた複合粒子は、非常に強い力で結びついているため、安定した材料となる。しかも、機械で混ぜる方式に比べると、エネルギー効率もいい。もともと、溶液を使うことから濡れ性のない物質や水に浮く物質、水に溶ける物質の創製には不向きだが、さまざまな工夫により、現在ではほぼすべての材料を扱うことができるようになりつつあるという。

その一例として、武藤教授はカーボンナノチューブを用いた導電性材料の開発に取り組んだ。これにより、カーボンナノチューブの添加量を通常よりも大幅に減らし、かつ、きわめて透明度の高い物質をつくることに成功したのである。

### ■ 量産化に向け、製造プロセスの開発に取り組む

その研究の優位性から、2009～2012年には、NEDO(独立行政法人新エネルギー・産業技術総合開発機構)の産業技術研究助成事業として採択されたほか、2015年からは内閣府のSIP(戦略的イノベーション創造プログラム)の革新的設計生産技術のプロジェクトの中で研究を深化させている。現在は、複合ナノ材料(複合粒子)を連続的に大量に生産するためのプロセス開発に取り組む。一方で、さまざまな分野の企業からの引き合いも来ているという。

「材料研究というのは、一見、地味な分野ではありますが、材料の特性を変えることで、強度を倍にして半分の薄さにできることといったように、社会に大きなインパクトを与えることができるのです。それだけにやりがいもあります。物質により違いはありますが、数年後には、時間あたり10kg程度の複合粒子をつくれるようにしたいですね」と、武藤教授は抱負を語る。今後、この武藤教授が開発した手法により、どのような夢の材料が開発されるのか、大いに楽しみだ。

取材・文=田井中麻都佳

### 取材後記

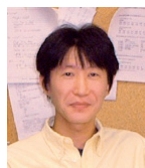
豊橋技術科学大学は、高専との連携を進めていることから高専出身者が多い。武藤教授ご自身も、福島高専のご出身だという。

「高専出身者は、実験に慣れていて、楽しんで取り組む人が多い。だから、何でも実際に手を動かして試してみようとするんですね。現在の研究も、実験してみたらいいのほかつまらないうのが、最初のスタートだったんですよ」と、武藤教授は笑う。

もともと材料の破壊力学の研究を手掛けていたという武藤教授。評価するセラミックスを自らつくり始めたことが、現在の研究へとつながった。まさに、実験を厭わない姿勢が、大きな研究成果を引き寄せたと言えるだろう。

### Researcher Profile

Dr. Hiroyuki Muto studied at Toyohashi Tech, and received his PhD. in 1997, Japan. Since 1997, Dr. Muto has been involved in researching the deformation and flow mechanism of brittle ceramic materials at elevated temperatures at Toyohashi Tech. He was involved in the development of nanocomposite ceramic materials. He was also a visiting research associate of Professor David Wilkinson's group in the Department of Materials Science and Engineering at McMaster University from 2005 to 2006. Currently, Dr. Muto is a professor in the Institute of Liberal Arts and Sciences at Toyohashi University of Technology, Japan. He has more than 15 years of research experience in materials science, and has published extensively in peer-reviewed journals.



### Reporter Profile

Madoka Tainaka is a freelance editor, writer and interpreter. She graduated from the Department of Law, at Chuo University, Japan. She served as a chief editor of "Nature Interface" magazine, and on the committee for the Promotion of Information and Science Technology at MEXT (Ministry of Education, Culture, Sports, Science and Technology).



# Job-sharing with nursing robot

Conciliatory approach to human-robot symbiosis through development of “Terapio” medical round support robot  
By Ryosuke Tasaki

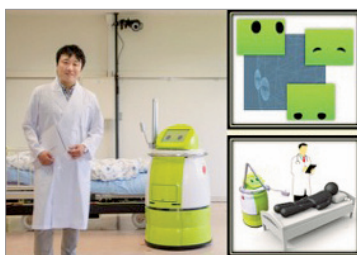
Ryosuke Tasaki and Kazuhiko Terashima have organized a cooperative project team to develop a new robot designed to help Japan cope with medical care in the eventuality of the predicted massive earthquake striking the country. This team consists of engineering researchers, medical doctors, and software/hardware companies in Fukushima and Toyohashi. They set about determining the factors that are most important to hospital patients in modern society, after which they set about developing the world's first medical round robot capable of job-sharing, making more time for face-to-face nursing care.



Given the aging of the population and the low birthrate both in Japan and elsewhere, healthcare professionals are in short supply and unevenly distributed, giving rise to a need for a method of performing simple tasks that does not rely on humans. Although increasing numbers of medical institutions have introduced electronic medical records, a variety of issues remain unresolved, such as the inconvenience of data recording and the high costs associated with data input.

The use of robots to support medical care data management and the delivery of resources at the medical front—thus allowing humans to concentrate on those tasks requiring knowledge, skill, and experience—is expected to contribute to the enhancement of the quality of healthcare services.

Ryosuke Tasaki, Kazuhiko Terashima and their colleagues have developed “Terapio” a next-generation robot that replaces the conventional medical cart used by healthcare staff during their rounds in a hospital. Terapio assists staff in delivering resources and recording information on their rounds, and is also capable of friendly communication.



“Terapio” medical round support robot

Terapio is an autonomous mobile robot that can track a person. It uses a differential-drive steering system to provide both quiet operation and smooth omnidirectional mobility. It recognizes its environment and autonomously tracks a specified human while avoiding obstacles. Using its ring-shaped power-assist handle, an operator can control the robot accurately by applying a slight force.



Human-tracking field test in a hospital

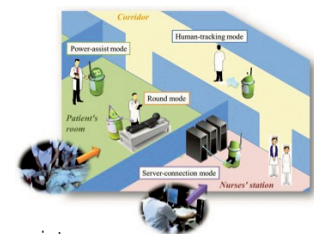
Terapio can also record patients' personal and vital signs data as well as displaying data, such as the patient's health records. In terms of its exterior design and color scheme, Terapio is suitable for use in medical institutions. The touch panel on the top of Terapio is used for operating the robot and inputting/displaying data from the rounds. It is designed such that the operator and patient can recognize the robot's status and actions by expressions shown on the display that change according to the robot's operation mode, which are “power assist,” “tracking,” and “rounds.”

The LCD display on the top of Terapio serves as the robot's “face.” It changes its expression by changing the shape of its “eyes.” These eyes give Terapio a human-like, friendly, and communicative persona which are a step up from the plain

functionality of a hospital cart.

“As we were developing Terapio, we could clearly imagine the human-robot symbiosis. By constantly promoting the pursuit of system integration technology, life with robots can become a reality in the near future,” said assistant professor Ryosuke Tasaki. “An ongoing daily effort to incorporate high-tech robotics into our activities will be the best way to realize life in our future society.”

When medical and nursing care workers are released from menial and back-breaking work by sharing their duties with a robot, they will be able to concentrate more on interacting with their patients and providing knowledgeable, kind, and compassionate care. Terapio can also elicit warmth from the humans with which it interacts. The More Information Back Next researchers expect that similar research will become widespread in the future as more people adopt a conciliatory approach to human-robot symbiosis.



Round assistance

## Reference

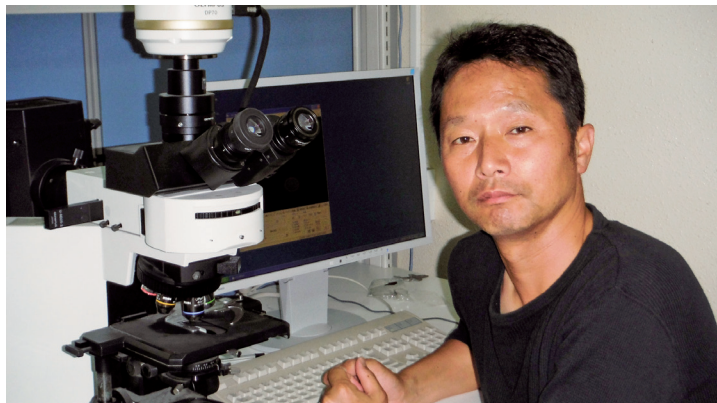
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# Autophagy defect causes loss of muscle in aging

Unbalanced p62/SQSTM1 and LC3 expression in sarcopenic muscle of mice

By Kunihiro Sakuma

Kunihiro Sakuma and his colleagues in cooperation with researchers at Kyoto Prefectural University and the Health Science University of Hokkaido, have detected marked upregulation of p62/SQSTM1, but not LC3, protein levels in the cytosol of sarcopenic muscle fibers in mice. This unbalanced expression appears to induce an autophagic defect in skeletal muscle and consequent loss of muscle mass. This finding contributes to our understanding of the molecular mechanism of sarcopenia, or muscle aging.



Sarcopenia is the aging-related loss of skeletal muscle mass and strength. Preventing sarcopenia is important for maintaining a high quality of life (QOL) in the aged population. However, the molecular mechanism of sarcopenia has not yet been unraveled and is still a matter of debate. Determining whether the levels of autophagy-related mediators (e.g., p62/SQSTM1, LC3, etc.) in muscle change with ageing is important to understanding sarcopenia. Such information could enhance the therapeutic strategies for attenuating mammalian sarcopenia.

In previous studies, autophagic defects were detected in the sarcopenic muscle of mice, rats, and humans. However, all

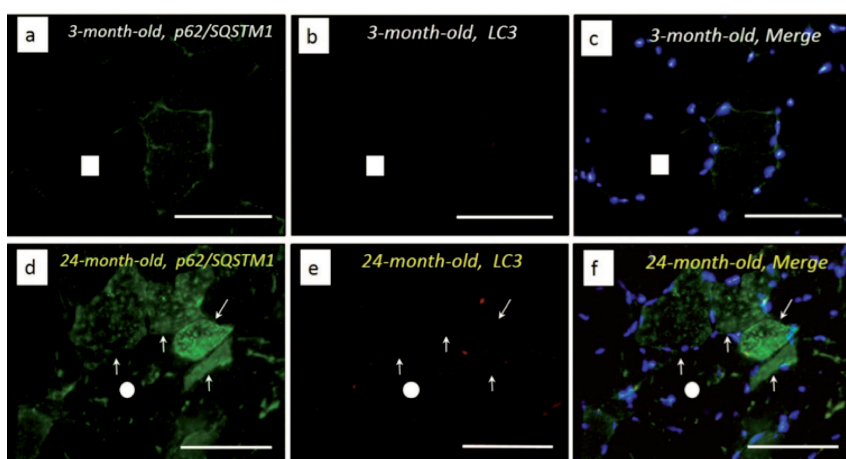
these studies involved only western blotting analyses of crude not cell-fractionated muscle homogenates. Thus, these data were insufficient to describe the adaptive changes in autophagy-linked molecules within sarcopenic muscle.

Associate Professor Kunihiro Sakuma and his colleagues at Toyohashi Tech found a marked accumulation of p62/SQSTM1 in the sarcopenic quadriceps muscle of mice using two different methods (western blotting of cell-fractionated homogenates and immunofluorescence). In contrast, the expression level of LC3, a partner of p62/SQSTM1 in autophagy progression, was not modulated.

The detected autophagic defect improves our understanding of the mechanism underlying sarcopenia. The researchers would like to further study this mechanism with an aim to attenuate sarcopenia by ameliorating this autophagic defect using nutrient- and pharmaceutical-based treatments.

## Reference

Sakuma, K., Kinoshita, M., Ito, Y., Aizawa, M., Aoi, W., and Yamaguchi, A. (2015). p62/SQSTM1 but not LC3 is accumulated in sarcopenic muscle of mice, *Journal of Cachexia, Sarcopenia, and Muscle*, DOI: 10.1002/jcsm.12045 (Published online before print)



Bar = 50  $\mu$ m

p62/SQSTM1 but not LC3 is markedly expressed in the cytosol of muscle fibers of sarcopenic mice.

## Molecular modeling of novel potent agents for treating Alzheimer's disease

Novel curcumin derivatives proposed for inhibiting the production of amyloid-beta peptides, which are the main causal agents of Alzheimer's disease.

By Noriyuki Kurita

Noriyuki Kurita and his colleagues in cooperation with the Ukraine National Academy of Sciences proposed novel agents for inhibiting the production of amyloid-beta ( $A\beta$ ) peptides, which are involved in the pathogenesis of Alzheimer's disease. Using state-of-the-art molecular simulations, interactions between amyloid precursor protein (APP) and curcumin derivatives were investigated, to elucidate the specific derivative that binds strongly to APP and inhibits the pathogenic  $A\beta$  production. The results contribute to developing new medicines that suppress  $A\beta$  peptide production.



Graduate students from left: Hiromi Ishimura and Ryushi Kadoya

Alzheimer's disease (AD), a severe form of dementia among aged individuals, is caused by accumulation of amyloid-beta ( $A\beta$ ) peptides in the brain. Numerous types of agents have been developed to suppress the production of  $A\beta$ , by inhibiting the secretase-mediated cleavage of amyloid precursor protein (APP) into  $A\beta$  peptides.

However, because the secretases also play important roles in the production of vital proteins for the human body, inhibitors of the secretases have increased risk for side effects.

Associate Professor Noriyuki Kurita and Toyohashi Tech graduate students in cooperation with a researcher at the National Academy of Sciences in Ukraine, proposed new agents for protecting the cleavage site of APP from attack by  $\gamma$ -secretase, based on results evaluated by their state-of-the-art molecular simulations.

They carried out a world-first investigation into the specific interactions between a short APP peptide and curcumin derivatives, using protein-ligand docking as well as ab initio molecular simulations. Curcumin is a constituent of turmeric, which is a yellow spice commonly used in Indian cuisine. The simulated results elucidated the specific curcumin derivative and showed that it bound more strongly to APP and inhibited the binding of secretase to APP more than the other derivatives did. Moreover, some novel curcumin derivatives were proposed as potent inhibitors of  $A\beta$  peptide production. These derivatives are novel agents for sup-

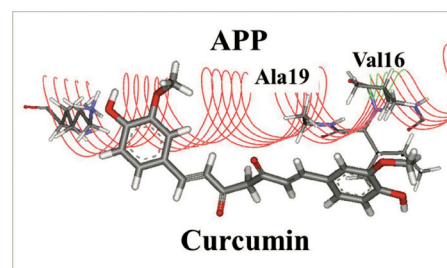
pressing AD and are proposed based on the novel concept of preventing APP cleavage. However, this does not imply that the consumption of Indian cuisine suppresses AD.

The First author, graduate student Hiromi Ishimura said, "We have also been studying the aggregation mechanism of  $A\beta$  peptides by using molecular dynamics simulations (Okamoto et al. *Journal of Molecular Graphics and Modeling*, 50, 113-124, 2014; Yano et al. *Chemical Physics Letters*, 595-596, 242-249, 2014). By combining the present ab initio molecular simulation and the molecular dynamics simulations, we will be able to elucidate the mechanism and propose potent inhibitors for suppressing the aggregation of  $A\beta$  peptides. These inhibitors are used as a therapeutic agent for ADs."

Associate Professor Noriyuki Kurita said, "Our present molecular simulations elucidated that curcumin can bind APP and inhibit the cleavage of APP by secretase. Curcumin is a natural product contained in the root of *Curcuma Rhizoma*. In the laboratory of our collaborator at the National Academy of Sciences in Ukraine, our proposed curcumin derivatives will be synthesized and their effects on experimental animals with ADs will be investigated."

Our developed state-of-the-art molecular simulations can be applied to the study of other vital proteins that play important roles in the pathogenesis of numerous diseases. In developing countries such as Ukraine, tuberculosis (TB), which is a severe infection caused by

*Mycobacterium tuberculosis* is prevalent. In fact, about 9 million people are infected with TB worldwide and 1.5 million died from this infection in 2013. Therefore, the urgent development of novel drugs for TB is necessary. We are currently performing molecular simulations to propose novel potent inhibitors of a protein that reduces the blood level of anti-tubercular as well as anti-human immunodeficiency virus (HIV) agents. This collaborative study with Ukrainian researchers will be applied to the "Science and Technology Research Partnership for Sustainable Development Project" organized by the Japan Science and Technology Agency (JST) and the Japan International Cooperation Agency (JICA) in 2015.



Specific interactions between amyloid precursor protein (APP) and curcumin indicating that curcumin protects the APP attack site (Ala19) of APP from the  $\gamma$ -secretase

### Reference

Ishimura, H., Kadoya, R., Suzuki, T., Murakawa, T., Shulga, S., and Kurita, N. (2015). Specific interactions between amyloid- $\beta$  peptide and curcumin derivatives: ab initio molecular simulations. *Chemical Physics Letters*, 633, 139-145, DOI: 10.1016/j.cpllett.2015.05.023

# Super small needle technology for brain

Dissolvable material expands opportunities of flexible microneedles for brain penetrations

By Takeshi Kawano

The interdisciplinary collaborative research team led by Associate Professor Takeshi Kawano has now developed a methodology for brain penetration of sub-5 $\mu$ m diameter flexible needles. This should further reduce invasiveness and provide safer tissue penetrations than conventional approaches.



Microscale needle-electrode array technology has been enhancing brain sciences and engineering such as electrophysiological studies, drug and chemical delivery systems, and optogenetic applications.

However, one enduring challenge is to reduce the tissue/neuron damage associated with needle penetration, particularly for chronic studies and future medical applications. A way to solve the issue is to use microscale diameter needles (e.g., < 5 $\mu$ m) along with a flexible property, but such fine needles struggle to penetrate the brain and other biological tissues due to the needle buckling or fracturing before penetration.

Now, Takeshi Kawano at Department of Electrical and Electronic Information Engineering and his colleagues have developed a methodology to temporarily enhance the stiffness of the long, high-aspect-ratio flexible microneedle (e.g., < 5 $\mu$ m in diameter and > 500  $\mu$ m in length), without affecting the needle diameter and flexibility within tissue. The approach is realized by embedding a needle base in a film scaffold, which dissolves upon contact with a biological tissue. Here silk fibroin is used as the dissolvable film because it has a high biocompatibility and is known as a biomaterial used in bio-

implantable devices.

“We investigated how to prepare the silk base scaffold for microneedles, made a quantitative analysis of the needle stiffness, and investigated the penetration capability using a mouse brain in vitro/in vivo. In addition, as an actual needle application, we demonstrated particle depth injection into the brain in vivo”, explained the first author Master student Satoshi Yagi and PhD candidate Shota Yamagiwa.

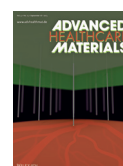
The leader of the research team, Associate Professor Takeshi Kawano said “Preparation of the dissolvable base scaffold is very simple, but this methodology promises powerful tissue penetrations of numerous high-aspect-ratio flexible microneedles, including recording/stimulation electrodes,

glass pipettes, and optogenetic fibers.” He also added, “This method has the potential to reduce invasiveness and provide safer tissue penetration than conventional approaches.”

#### Editor's Note

This study was featured in the Inside Front Cover page of the *Advanced Healthcare Materials*, Volume 4, Issue 13, September 16, 2015.

<http://onlinelibrary.wiley.com/doi/10.1002/adhm.v4.13/issueoc>

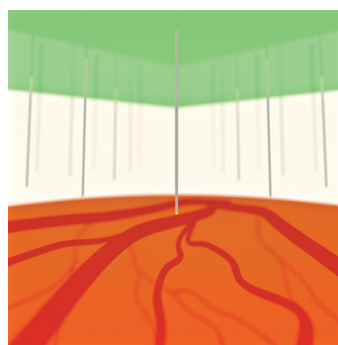


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#### Reference

Yagi S, Yamagiwa S, Kubota Y, Sawahata H, Numano R, Imashioya T, Oi H, Ishida M, and Kawano T. (2015).

Dissolvable base scaffolds allow tissue penetration of high-aspect-ratio flexible microneedles, *Advanced Healthcare Materials*, 4(13), 1949–1955, DOI: 10.1002/adhm.201500305



Flexible high-aspect-ratio microneedles penetrating brain tissue



## Pick Up

### Two world-leading collaborative research laboratories established

Toyohashi Tech established the “Mind & Brain Laboratory for Perceptual and Cognitive Processing” with Dr. Shinsuke Shimojo of California Institute of Technology (Caltech), and “AIST-TUT Advanced Sensor Collaborative Research Laboratory” with the National Institute of Advanced Industrial Science and Technology (AIST).

These laboratories were established in Toyohashi Tech on July 1st 2015, with the aim of promoting the advancement and diversification of Toyohashi Tech’s research by collaborating with world-leading global research institutions.



President Onishi, Dr. Shimojo, Dr. Nakauchi, Dr. Hara

#### Prof. Shimojo (Caltech)–TUT International Collaborative Research Laboratory

– Mind & Brain Laboratory for Perceptual and Cognitive Processing –

##### Research Content & Goal:

To pioneer neuroscience that leads to a deeper understanding of humanity and society. This will be achieved by elucidating the underlying workings of the brain through neurocognitive approaches such as non-invasive brain function measurement techniques. In this way a greater understanding will be acquired of how the brain serves as the foundation for human reason, mutual understanding, action, and perception so in essence we will rapidly increase our scientific understanding of human nature. Our laboratory will be working on this project in collaboration with Toyohashi Tech’s doctoral degree education leading program. This alliance increases our confidence that we can foster first class human resources who will be at the cutting edge of future neuroscience.

##### Organization:

California Institute of Technology (Caltech)	
Shinsuke Shimojo	Gertrude Baltimore Professor of Experimental Psychology, Division of Biology and Biological Engineering
Toyohashi University of Technology (Toyohashi Tech)	
Shigeki Nakauchi	Professor, Department of Computer Science and Engineering
Michiteru Kitazaki	Associate Professor, Department of Computer Science and Engineering
Hiroshi Higashi	Assistant Professor, Department of Computer Science and Engineering
Tetsuto Minami	Associate Professor, Electronics-Inspired Interdisciplinary Research Institute (EIIRIS)

#### AIST–TUT Advanced Sensor Collaborative Research Laboratory

##### Research Content & Goal:

Sensors detect various data all around us, from information about water quality and viruses to temperatures and humidity. In the context of greater interconnectivity of the physical and cyber worlds, their importance continues to grow. This laboratory aims to promote academic research and practical applications in sensor development and to avoid passing through a so-called “death valley” by working in collaboration with the National Institute of Advanced Industrial Science and Technology. The goals of this collaboration are to maximally reduce the time it takes from basic research on innovative sensors that meet various needs, including sensing data that was thought to be impossible at first glance, to implementation in society, to advance low-cost research and development, as well as to research technologies that are able to be manufactured (minimal manufacturing techniques). This laboratory aims to be active in research on theories of minimal manufacturing techniques for sensors, the development of sensors, research and development for cutting-edge sensing chips based on those techniques, and building a place for open innovation in the sensor sector.



Dr. Hara, Dr. Chubachi (AIST president), President Onishi, Dr. Sawada

##### Organization:

National Institute of Advanced Industrial Science and Technology (AIST)	
Shiro Hara	Group leader, Minimal System Group of Nanoelectronics Research Institute
Toyohashi University of Technology (Toyohashi Tech)	
Kazuaki Sawada	Professor, Department of Electrical and Electronic Information Engineering
Kazuhiro Takahashi	Lecturer, Department of Electrical and Electronic Information Engineering
Tatsuya Iwata	Assistant Professor, Department of Electrical and Electronic Information Engineering

## Open Campus achieves record number of participants

The 32nd Open Campus event was held on August 22nd 2015 and achieved a record high attendance of 2,940 people.

On top of our usual range of popular activities and events (scientific experiments for kids, laboratory tours, exhibitions of club activities, etc.), we added a live radio show broadcast by FM Toyohashi. This year's eco-bag, designed by Masami Takahashi (advisory designer of Toyohashi Tech), was also very cute and a big hit with participants.



### Open Campus 2015:

<http://www.tut.ac.jp/exam/opencampus/opencampus2015/> (Japanese version only)



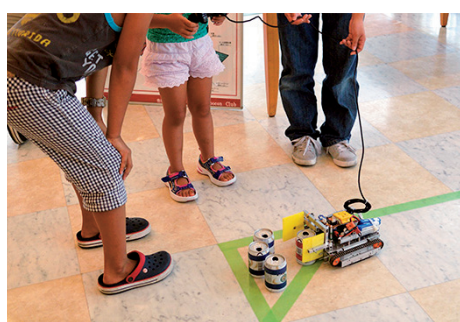
Eco-bag for 2015



Admission briefing



Hands on experiments for kids



Robot performance



Live broadcast on FM Toyohashi



Open laboratories

## International student program 2015

17 students, representing 5 partner universities from 4 countries in Asia, were invited to join a program at Toyohashi Tech which ran from August 31st to September 5th. This program has been held every year since 2003 with the aim of contributing to the development of innovative leaders among the next generation of Asian scientists and engineers. The visiting students could experience first hand our cutting edge laboratories as well as participate in group discussions with 18 students from Toyohashi Tech on subjects beyond the

fields of culture and language. Basic Japanese language classes, opportunities to sample traditional Japanese culture and visiting a local facility for sustainable energy and resources were also included to give the students a better understanding of culture and technology in Japan.

This program is supported by Japan-Asia Youth Exchange Program in Science (SAKURA Exchange Program in Science) 2015 of Japan Science and Technology Agency.



### Editorial Committee

The Toyohashi University of Technology (TUT) is one of Japan's most innovative and dynamic science and technology based academic institutes. TUT Research is published to update readers on research at the university.

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