Impact Objectives

- Develop a fabrication process of sophisticated nanostructures with spatio-temporal controllability
- Explore the use of actively tunable plasmonic structures

Pioneering research in nanostructures

***Associate Professor Hideyuki Mitomo** is creating innovative devices and he describes the important real-world applications they may have*

Could you outline the focus of your research?

My research focus is on the fabrication of highly designed metal nanostructures, including 3D and 4D structures, which are realised using spatio-temporal control. Living organisms have made great systems using only limited and familiar elements, such as carbon, nitrogen, hydrogen, oxygen and phosphorus. They are likely driven to do so as a survival strategy. So, biomacromolecules, such as proteins, DNAs and lipids, can have great functions due to the sophisticated nanostructures formed through self-organisation. They are soft matter and we are interested in their flexible structures and/or dynamic conformation changes, including assembly and disassembly, as a source of emergent functions.

What is the goal of this work?

As it is possible to handle various elements, it is expected that we can prepare highly functional devices, which never exist in living organisms and nature known as meta-materials, once we have developed a fabrication process of sophisticated nanostructures made of metals or other elements.

How did your background lead you to research of this type?

When I was a student, I learned about life sciences, especially proteins and lipids. I was particularly interested in self-assembly, and molecular recognition or functions were my interest. So, I conducted research on membrane proteins and lipid membranes. I later moved to the Research Institute for Electronic Science at Hokkaido University, where I was introduced to metal nanostructures and began using metal nanoparticles. Metal nanostructures are very interesting functional materials.

What do you anticipate the impact of your studies will be?

I am interested in the use of plasmonic structures. Plasmonics is a relatively new research field. But there is already a huge number of reports on the science and applications, such as photonic antennae and sensors, for example. Understanding in this area is greatly expanding and creating new possibilities. I believe our approach has significant potential at some parts.

You are interested in how active structure changes of metal nanostructures can produce different functions. Can you talk about what this involves?

For active structure changes, there are many examples in living organisms, one of which is enzymes. They form open structures and wait for targets. When they catch a target, they start working as a catalyst. Once they've finished their work, they return to being open structures. This open form is conducive to efficiently catching targets. Think of it as a ball being caught by a glove in baseball. We are looking at the active gap tuning of gold nanoparticle arrays and orientation control of the gold nanorod arrays. Using this system, we can develop tunable optical antennae or plasmonic devices and, in the future, even more impressive devices. In our system, instead of molecules, we are using more attractive components with plasmonic functionalities and so we anticipate that it has great potential.

Are there any results so far that you are particularly pleased with?

We've developed a SERS (surface enhanced Raman scattering) system, which is a very useful sensing approach, with actively tunable plasmonic structures. This is a typical and essential example of work I am proud of. This will be a useful device for biosensing, which is very important in medicine and social security. I believe we can make additional useful and functional devices in the near future.

What are your next research plans?

I plan to continue basic research, using anisotropic structured nanoparticles, prepare more sophisticated structures and look into precisely controlling their structures. I am also eager to forge future collaborations that will expand our systems and help us to develop invaluable devices with very real applications.

Learning from living things

*Scientists at the **Molecular Device Laboratory, Hokkaido University** are taking inspiration from living things in their creation of self-assembled nanoparticles, which could ultimately be used in a range of bioengineering applications*

There is a lot to be learned from nature, in countless ways. Just one of these ways is observing and replicating the complex structures found in nature, particularly on the nanoscale where all is small but mighty. Imagine if you could take inspiration from natural nanostructures to create impressive nanorobots with a number of exciting applications? At the Molecular Device Laboratory at Hokkaido University in Japan, an intrepid team of researchers is looking into fusing biomolecular science and nanotechnology to create powerful bio- or nano-devices with manifold applications.

The research work is funded by a Grant-in-Aid for Scientific Research (KAKENHI) from JSPS and some other funding sources. Associate Professor Hideyuki Mitomo heads up the group, working alongside Professor Kuniharu Ijiro, and some collaborators including a collection of ambitious students. Their work relates to the themes of material science, nanotechnology and life science. For Mitomo, an original interest in life sciences (molecular biology), especially proteins and lipids, transformed into an avid interest in metal nanostructures and nanoparticles. And now he is combining the two in pioneering research.

THE PERFECT FUSION

This research surrounds an exciting area, the emergent fusion of biological functions and nanotechnology. This means that the researchers are exploring the functional features of biomolecules and nanotechnology, with a focus on metal nanoparticles. They are interested in how the two can work together; combining their respective attributes with impressive results. To this end, Mitomo and the team are looking at developing nanodevices using soft matters such as biomolecules, as well as creating biodevices using metal nanoparticles. 'The former pertains to the application of biomolecules to nanotechnology,' highlights Mitomo. 'In essence, the researchers are working to create functional molecular devices by using biomolecules such as proteins, nucleic acids, lipids and sugars, or at least their features.' The latter involves the use of nanomaterials for biological applications. The team believes this work could produce devices that will be useful in a range of biological fields. A good example of this is drug delivery carriers being able to control properties such as the size and shape could be extremely useful here.

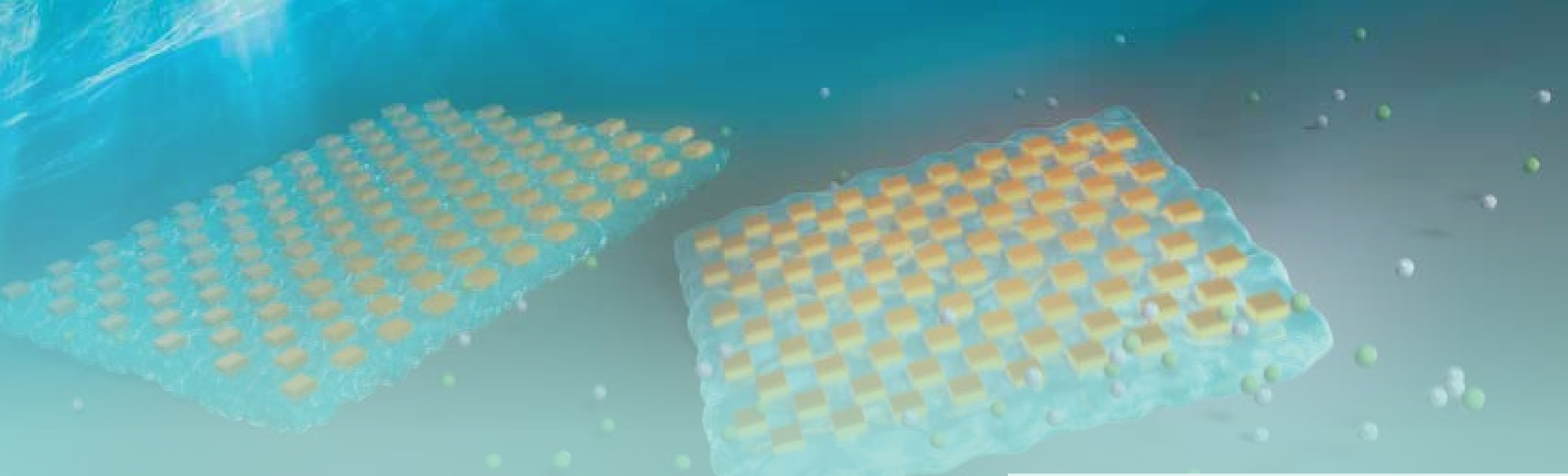
One particular area of interest for Mitomo and the team is the creation of 4D metal nanostructures. These nanostructures are built incorporating lessons from nature. They mimic the sophisticated systems of living organisms. 'Enzymes show dynamic structural changes in their activity, which is why they are sometimes referred to as 'Pac-Man'. Lipids form membranes and small capsules via self-assembly and dynamic structural changes as budding and fusion, providing active substance transportation functionality,' explains Mitomo. 'Actin protein forms actin filaments and work as a cytoskeleton via active assembly/disassembly tuning. So, we can learn from living things that sophisticated nanostructures can provide highly functional devices.'

An example of the enzymes that Mitomo is referring to is CRSPR enzymes. They are likened to Pac-Man as they have the ability, once activated, to chew up RNA. There are other functions they can do too, and it is these Mitomo is looking into. He provides an insight into what the creation of 4D metal nanostructures involves. 'It's like a functional nanomachine or nanorobot,' he says. 'If you can imagine how an enzyme works like Pac-Man, you can feasibly understand how a metal or robotic Pac-Man can work even better and be ascribed various functions.'

GOING FOR GOLD

One line of investigation for the team is 'Structure Control of Self-assembled Gold Nanoparticle Arrays'. First, it is important to note that metal nanoparticle arrays have become an exciting platform for manipulating light-matter interactions at the nanoscale which, in turn, creates a number of possible applications. In terms of research work, Mitomo's focus is on the polymer-assisted self-assembly of gold nanoparticles (AuNPs). 'AuNPs show localised surface plasmon resonance (LSPR), which means that a collective oscillation of electrons at the AuNP surface is induced by the irradiation of light with a specific wavelength,' he confirms. This can vary depending on the size and shape of the AuNP, as well as the distance between AuNPs. Polymers can be used to help tune the assembly of AuNPs.

The research theme of 'Structure Control of Self-assembled Gold Nanoparticle Arrays' encompasses two research studies: 'active control of the self-assembled AuNP film on the hydrogel' and the other is 'orientation control of the gold nanorod (AuNR) arrays on polymer-grafted substrates'. In the



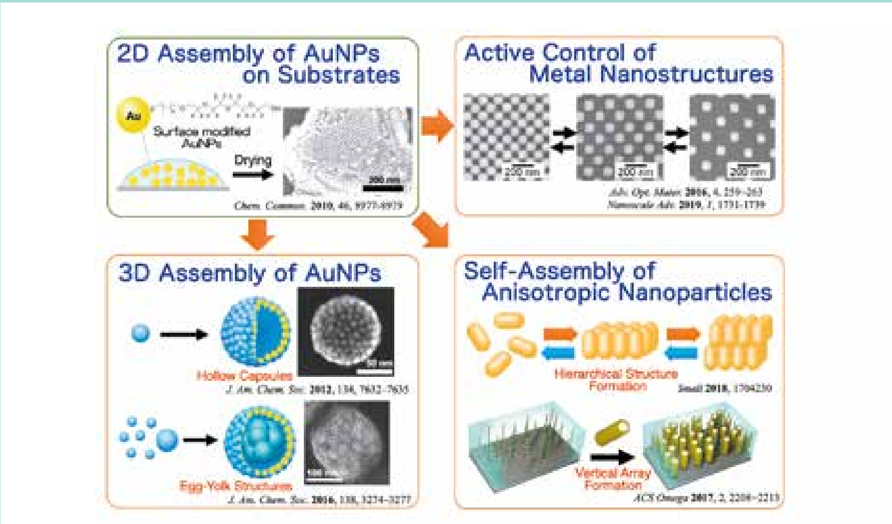
former, Mitomo and the team prepared self-assembled AuNP thin films on the solid substrate and transferred them onto the polymer hydrogel. They then tuned plasmonic properties depending on the volume change of the gel, as the gap distance of AuNPs in the film was changed. 'We found that by actively controlling the gap distance induced increased signals of surface-enhanced Raman scattering (SERS) through the improvement of the insertion efficiency of target molecules for the detection into the gaps as hot spots,' observes Mitomo. In the latter study, the researchers established a new simple method for the preparation of vertically aligned AuNR arrays with controlled density. Now they are working on active tuning of their orientation by stimuli.

Building from this, the researchers are looking at how they can selectively introduce target matter into hotspots, which can increase SERS intensity. 'Our strategy is using the lipid membrane. First, we entrap them onto the lipid membrane and then we work on the two dimensional,' Mitomo confirms. The team is also looking into other structures that are composed of anisotropic nanoparticles, but this is more challenging. 'They are more attractive due to their functionality but challenging,' he reveals.

LEARNING FROM ENZYMES

The researchers are interested in the potential of active plasmonic substrates, in particular. In previous work they found that active tuning of the gold nanogaps (they are in their open form for the insertion of target molecules and in their closed form for the detection) enabled them to function like enzymes. They also explored the use of thermo and/or photo-responsive nanoparticle vesicles, which they believe has potential to be used as a drug delivery system.

The research team has made impressive headway in its work to date, particularly given that it is a small team. This is one of the reasons why Mitomo values collaboration so highly. 'Resources are limited and we are chemists, which means we don't have in-depth knowledge on physics or other fields. Therefore, partnerships and collaborations are really important for us,' he explains. 'In particular, in order to apply our systems to real applications and to understand their photonic or plasmonic properties, a number of researchers with different backgrounds are required.' Indeed, Mitomo welcomes new research collaborations which could help expedite his important work and faster bring about real-world applications.



Recent advances on nanoparticle assemblies for sophisticated nanostructures

Project Insights

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BIO

Dr Hideyuki Mitomo received his PhD in 2007 from the Tokyo Institute of Technology. From 2007 to 2009 he worked at Lehigh University in USA as a postdoctoral researcher. After working as a postdoctoral fellow at the Research Institute for Electronic Science at Hokkaido University, he became an Assistant Professor at Hokkaido University in 2011 and he was promoted to an Associate Professor in 2017. He is currently an Associate Professor at the Research Institute for Electronic Science (RIES), and the Global Institution for Collaborative Research and Education (GI-CoRE) at the Hokkaido University.

GI-CoRE Hokkaido University Global Institution for Collaborative Research and Education

RIES Hokkaido University Research Institute for Electronic Science

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