HOKKAIDO UNIVERSITY

Hokkaido Universal Campus Initiative (HUCI) Report

Tackling Global Issues Vol.1

Soft Matter: Material of the Future

– The era of soft matter
– Hydrogels as promising materials
– Soft crystals and molecular machines
– Soft matter in medicine
– Soft matter: Past, present and future


Be ambitious.
Inazo Nitobe.

PREFACE

Hokkaido University has consistently pushed the boundaries of knowledge through innovative research for the past 142 years, and this approach will continue as we stride confidently toward the future.

Hokkaido University originated as Sapporo Agricultural College, which was established in 1876 as Japan's first modern higher educational institution to grant bachelor's degrees. Dr. William S. Clark, who was invited from Massachusetts Agricultural College, taught agricultural and other modern sciences in English as well as Bible-based moral education, setting a course for what has become one of Japan's leading universities. In 1877, the college accepted as a student Inazo Nitobe, who later became a professor of the college and principal of Dai-ichi High School before serving as an undersecretary general of the League of Nations from 1920 to 1926. Nitobe, who famously said "I wish to be a bridge across the Pacific," authored *Bushido: The Soul of Japan*, which is renowned internationally as a classic exploring the ethos of his nation. Nitobe's spiritual legacy is still very much alive and well in Hokkaido University's traditions.

Hokkaido University's established status as a top national university was enhanced even further when Dr. Akira Suzuki received the Nobel Prize in Chemistry in 2010, becoming the university's first faculty member to receive a Nobel Prize. Suzuki was born in Hokkaido and received a Ph.D. from Hokkaido University. In 1979, Suzuki announced "Suzuki-Miyaura cross-coupling reactions" as a pivotal palladium-catalyzed reaction in organic chemistry, paving the way for numerous industrial applications in everyday items such as pharmaceuticals and liquid crystal materials. We are immensely proud of the tremendous contribution Suzuki's research has made to academic and industrial fields alike.

In 2026, Hokkaido University will observe the 150th anniversary of its founding. To mark this upcoming milestone, the university formulated a concrete action strategy under the slogan of "Contributing Towards the Resolution of Global Issues." One effort to translate this strategy into action is the establishment of an international research and educational organization called the Global Institution for Collaborative Research and Education (GI-CoRE). GI-CoRE aims to conduct international joint research by inviting the world's best researchers to Hokkaido University. The university is committed to tackling global challenges through interdisciplinary approaches and with open-minded thinking by spearheading collaborations among different research fields. Soft matter, which will be spotlighted in this magazine, is one of the university's focuses and one of six areas promoted by GI-CoRE.

Hard matter served as the locomotive for past industrial revolutions. In more recent times, soft matter has rapidly attracted attention around the world as the group of new substances that hold the key to solving important global issues in the 21st century, such as building a sustainable society, developing sophisticated medical technology and dealing with problems associated with an aging population. Hokkaido University is at the forefront of soft matter research. In April 2018, the university established the Division of Soft Matter at the Graduate School of Life Science to further improve the educational and research regime specializing in soft matter science and to develop human resources who will lead the world in this field.

We hope readers of this magazine will gain insight into how Hokkaido University is striving to solve global issues by promoting joint research that transcends the boundaries of nations and academic fields. Spearheading soft matter research is a mighty challenge, but we are confident of meeting our goals in this field.

Masanori Kasahara, M.D., Ph.D.
Executive Director
Institute for International Collaboration

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The era of soft matter

It is no exaggeration to say the progress of mankind has been aligned with material revolutions. Some time periods are even named after materials: the Stone, Copper, Bronze and Iron ages. The era of hunters, dating back millions of years, was marked by the use of tools made from stone, followed by agricultural societies characterized by ceramics. In city-states, which rose around 1000 BC, metals began having an impact on people's lives. In modern times, the 19th century was the age of iron and steel that led to the first Industrial Revolution, and the 20th century saw the advent of more sophisticated materials like polymers that ushered in the spread of plastics.

Our understanding of condensed matter physics deepened in the 20th century, paving the way for the development of electric, electronic and other devices that are taken for granted today. Key materials for these objects were hard matter such as metals and semiconductors. In the 21st century, we have entered an era of soft matter. Look at things around you. Cathode-ray tube displays have been superseded by liquid crystal displays, and a considerable number of beverages are now packaged in plastic containers. Hard and heavy materials have increasingly been replaced by soft and light materials. Because the latter materials require less energy to transport and are considered essential for creating a sustainable society, efforts to advance the study of soft matter are expected to accelerate.

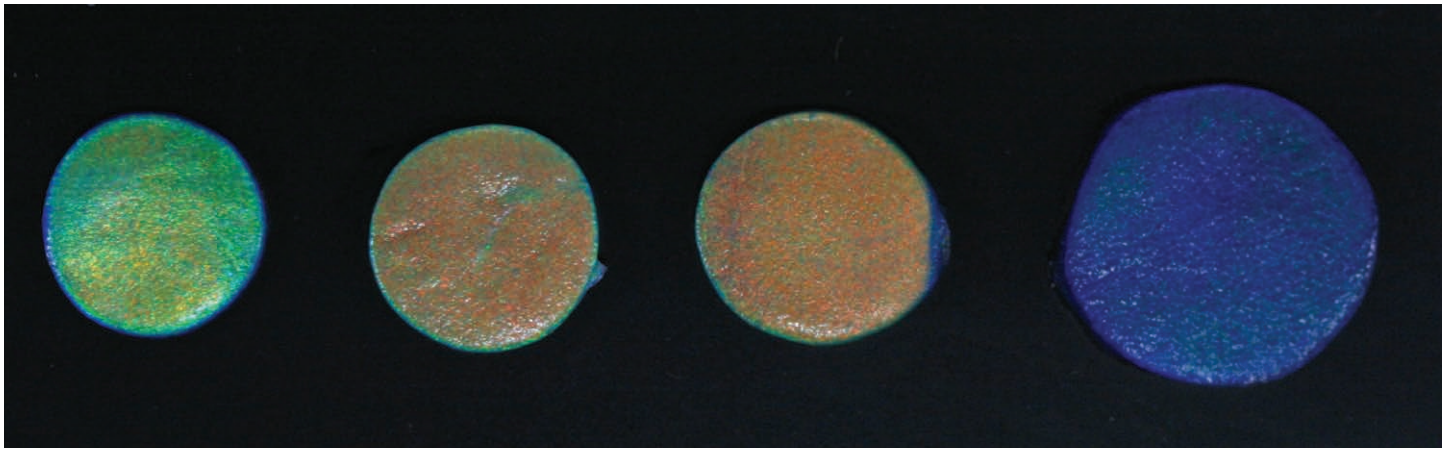
What is soft matter?

As the name suggests, "soft" substances are collectively called soft matter. But what does soft mean? In physics, the "hardness" and "softness" of substances are defined by their response to external forces. While hard matter shows certain resistance to external stress and conditional changes such as room temperature, light and pressure, soft matter materials easily flow and deform in response to such external stimuli. They may be elastic, viscous or both, with their phases changing when undergoing deformation. Take toothpaste as an example. It behaves like a solid when it sits on a toothbrush, but it flows like a fluid when squeezed from a tube. A precise definition is difficult for soft matter because it has a wide range of properties that are somewhere between solids and liquids. Such properties allow soft matter to take various forms.

Typical soft matter materials include colloids, polymers, surfactants, liquid crystals and gels. They are found in everyday objects ranging from paints, soaps and fabrics to food such as tofu, milk and yogurt. Even our bodies are made of soft matter, except for hard tissues such as bones and teeth. Today, soft matter is ubiquitous, but it is a relatively young academic field. Many aspects of soft matter remain a mystery.

Soft matter is characterized by its structural and dynamic complexity. In hard matter, the arrangement of atoms is highly ordered, enabling researchers to understand or predict the overall properties and behavior of a material from its average molecular arrangement and components. However, gaining such a clear, overall picture of soft matter from a partial analysis is not easy because its structures and dynamics are heterogeneous and hierarchical on every scale from microscopic to macroscopic. What soft matter materials have in common is that they consist of large molecules or an aggregate of molecules that moves collectively. They are held together by weak intermolecular interactions. These features give soft matter such characteristics as strong and nonlinear reactivity to external forces as well as a slow and non-equilibrium response to external stimuli.

Although soft matter shares certain common characteristics, it does not have fundamental encompassing theories like hard matter, which is marked by general relativity and quantum mechanics. The field of complex soft matter grew out of the traditional field of condensed matter



physics. Condensed matter physicists in the early 20th century generally looked into tiny details of properties of relatively simple substances in solid and liquid states. The field of soft matter rose to prominence after French scientist Pierre-Gilles de Gennes received the Nobel Prize in Physics in 1991 "for discovering that methods developed for studying order phenomena in simple systems can be generalized to more complex forms of matter, in particular to liquid crystals and polymers." Currently known as the "father of soft matter," de Gennes pioneered the field by seeking to understand soft matter in terms of physics.

Since then, the field has rapidly grown by incorporating aspects of different disciplines including physics, chemistry, engineering and biology. Because of soft matter's properties and behavior, hopes are also high that exploring life science from the standpoint of soft matter could unravel the fundamental principles of life.

Future to be shaped by soft matter

Soft matter has attracted global attention not only as a promising field but also for its high potential for practical applications. In recent years, hydrogels have become a high-profile element in soft matter research alongside liquid crystals and rubbers. Hydrogels, whose soft and hydrated forms exhibit some similarities to human tissues, have shown significant possibilities for various medical applications, from biomaterials for artificial joints to advanced materials that will help regenerate cartilage and discover cancer at an early stage. Indeed, hydrogels have already been used to make highly functional contact lenses and some medical devices that require direct contact with the human body.

Versatile soft matter could form key future technologies in many other industries, including electronics, automobiles and aviation, as well as areas of the environment and robot engineering. For example, soft matter could enable development of water purification technology, and a robot with artificial intelligence could improve nursing and other services for a welfare-oriented society. Using soft components in automobiles would enhance the safety of passengers because such materials can absorb the energy from collisions. More sustainable soft substances with higher energy efficiency would help cut energy consumption, while soft construction materials could increase buildings' resistance to natural disasters such as earthquakes. Daily items like clothes, food and cosmetics would also become more sophisticated and functional as our understanding of soft matter deepens.

Despite the myriad possibilities, the mechanical weakness of soft matter materials has limited their applications. A major challenge is to toughen the materials while retaining their softness. In recent years, significant progress has been made to solve this problem. But many hurdles remain, especially in cases in which the materials are applied to the human body. These materials must be nontoxic and nonhazardous, and their quality must be strictly controlled.

This publication features studies that offer leads or models for solving such issues while giving a glimpse into efforts by researchers dedicated to developing highly functional soft matter materials. Seemingly unrelated advanced areas of soft crystal and active matter are also covered in this publication.

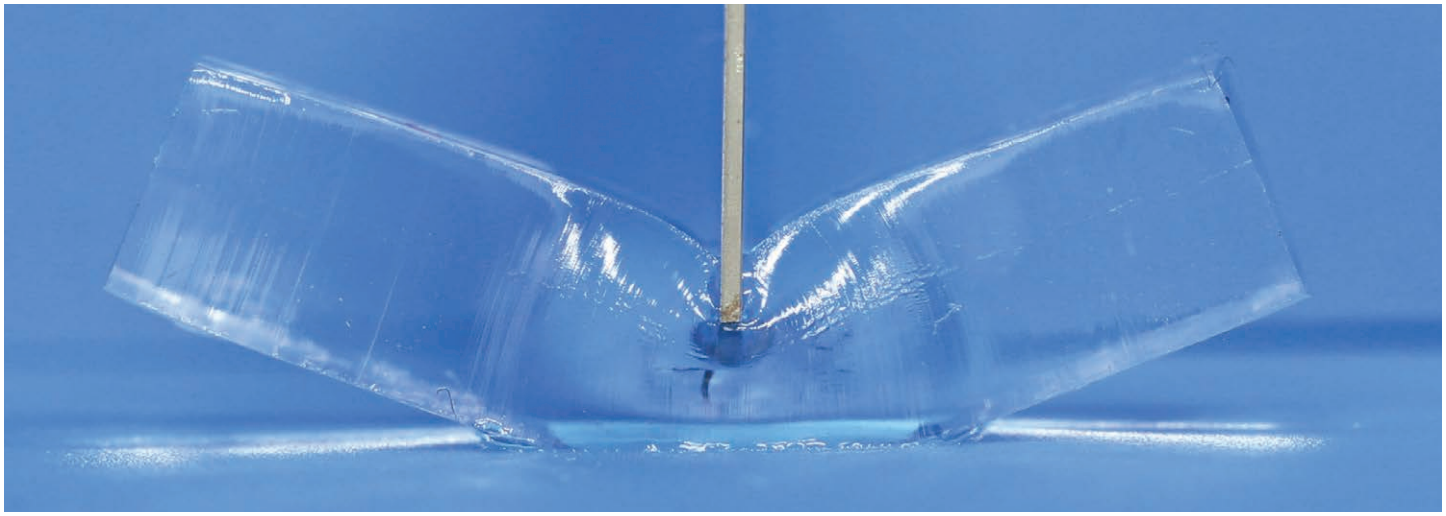
CHAPTER

1

Hydrogels as promising materials

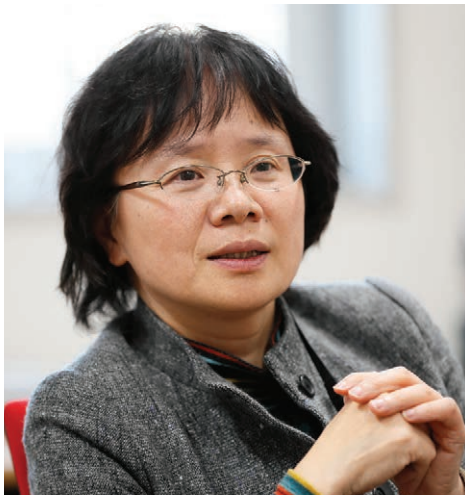
The invention of double network (DN) gels has rewritten the conventional concept that hydrogels are mechanically weak materials, opening up a whole new field in materials science. This chapter features four brilliant scientists who work on the extremely tough hydrogels, as well as hydrogels with unique and promising properties.

Extremely tough double network hydrogels open up numerous potential applications



Double network (DN) hydrogels challenge the conventional wisdom that hydrogels are weak materials.

When physicist Jian Ping Gong came to Japan about three decades ago, gel research was a minor scientific subject. Many researchers considered gels to be of little use as a material due to their structural complexity and mechanical weakness. Gong certainly thought so, too, but she took a bold step into a "messy" field.



Professor Jian Ping Gong

"Hydrogel was not a hot topic. Scientists thought it's no use and didn't even know how to characterize this kind of material. The structure is not in order, so you can't use X-rays or any other devices to examine it. Especially for physicists, it's a mess," Gong said.

But, over the years, things have changed. Hydrogels are now emerging as a high-performance material with numerous potential applications and Gong has become a leading figure in the field of soft matter.

DN gels based on opposite networks

Gong's team has opened up possibilities for hydrogels by developing double network (DN) gels. DN gels have attracted attention as an innovative material that has high water content, excellent mechanical strength and toughness. Despite containing about 90 percent water, the DN gels have compressive

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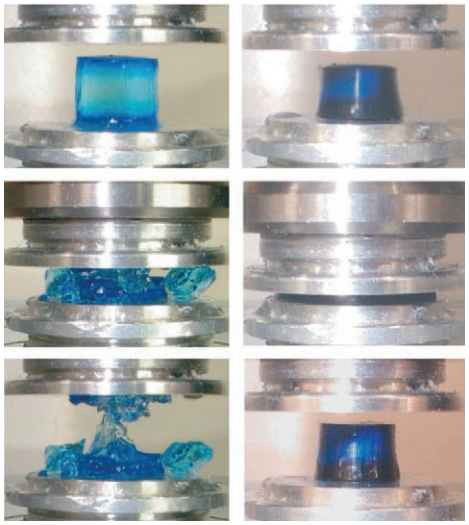


The DN gel sustains a high compression. Fracture stress for PAMPS single network gel and PAMPS/PAAm DN gel were 0.4 MPa and 17.2 MPa, respectively. (Gong J.P. et al., *Advanced Materials,* July 17, 2003)

fracture stress about 100 times stronger than conventional single network gels. The novel gels also do not fracture up to a compressive strain of 90 percent, making them tough enough to withstand being run over by a large truck. Their fracture energy is comparable to rubber and soft load-bearing tissues like cartilage.

DN gels are synthesized by combining two networks with opposite characteristics. The networks are separately cross-linked, tightly in the first one and loosely in the second one. The former network is composed of rigid and brittle polyelectrolytes such as poly (2-acrylamido-2-methylpropanesulfonic acid) or PAMPS, while the latter is made of flexible and stretchable neutral polymers such as polyacrylamide (PAAm).

Hydrogels are structurally heterogeneous, a property that was believed to cause their weakness. In a bid to toughen the gels, some scientists formed a hydrogel with a homogeneous structure. That gave the gel elastic stability and mechanical strength, but it remained brittle. Its fracture energy indicates a low resistance against crack propagation, making it easy to break once a crack is induced. Gong, meanwhile, considered that the weakness of hydrogels was due to the lack of an energy dissipation mechanism during deformation, and took a different strategy by inducing a new heterogeneous structure preferentially. Gong's approach worked.

This technique made it possible to create hydrogels with an unprecedented level of toughness. The DN concept, which was first reported in 2003, has opened a whole new area of polymer science. This groundbreaking discovery challenged the common belief that hydrogels are mechanically weak materials.

Discovery of 'sacrificial bond' principle

The first hint for creating such a tough gel was received accidentally by one of Gong's students, Takayuki Kurokawa, who is now a Hokkaido University professor, during an experiment to reduce sliding friction of gels. Although creating tough gels was possible after finding the opposite networks, the principle behind their toughness had remained a mystery. Gong said her team repeatedly made assumptions and devised experiments to test them, but to no avail.

> "This principle is universal. Using this concept, we can design tough materials, not only hydrogels but also other things."

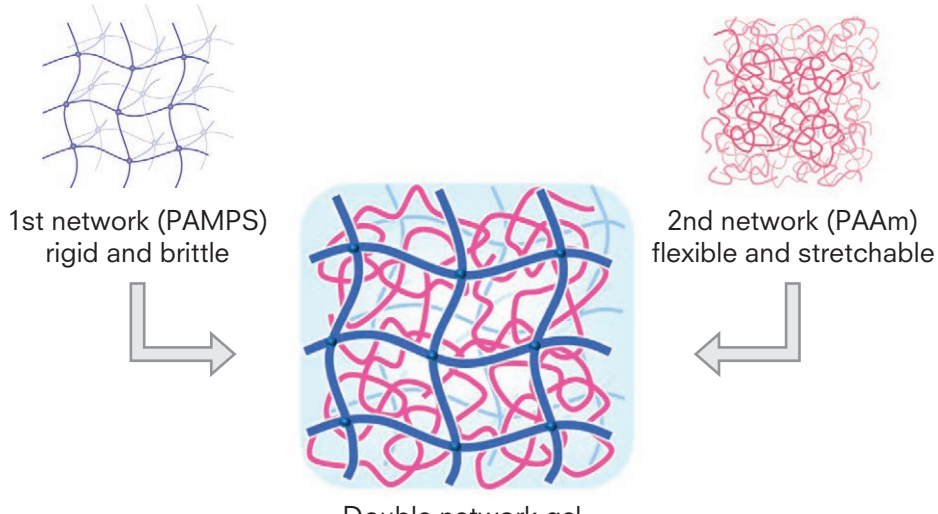
Eventually, the answer was found to be something that seemingly defied common sense. The toughness comes from the first network's brittleness.

Her team found that the rigid, brittle network serves as a "sacrificial bond" by effectively dissipating energy and preventing catastrophic crack propagation through its internal fracture, while the soft, stretchable network sustains stress. Because the toughness is reinforced by sacrificing the brittle bonds, they are called sacrificial bonds, a term originally used to describe the phenomenon of toughening bones. With a mechanically fragile structure used to toughen a material as a whole, this principle offers a sea change in thinking about a toughening mechanism.

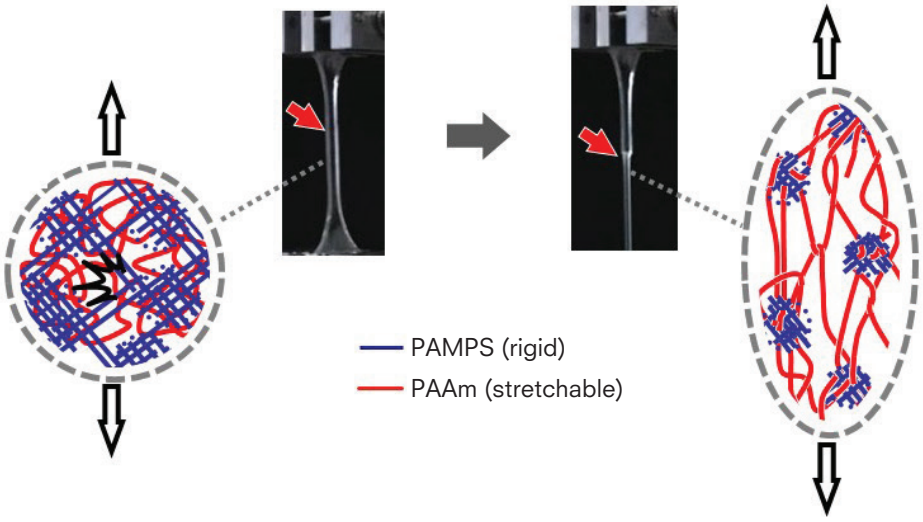
"It took about seven years to come up with this principle," Gong said. "This principle is universal. Using this concept, we can design tough materials, not only hydrogels but also other things." This principle now guides a new research field in tough soft materials and scientists around the world are following Gong's footsteps.

Encountering the giant

Gong prefers using a "rough sketch" when pursuing her research. Such



DN gels are synthesized by combining two networks with opposite characteristics: the first network is composed of rigid and brittle polyelectrolytes such as PAMPS, while the other is made of flexible and stretchable polymers such as polyacrylamide (PAAm).



The rigid and brittle PAMPS network serves as a "sacrificial bond" by effectively dissipating energy while the soft and stretchable PAAm network sustains stress.

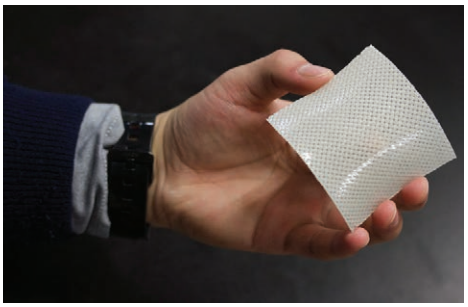
thinking came from Pierre-Gilles de Gennes, a Nobel laureate known as a pioneer in the soft matter field. Knowing him as a young scientist, she was fascinated with his "Impressionist" approach. Like Impressionist artists trying to capture a subject with simple brush strokes, de Gennes sought to obtain the essence of a physical matter based on a qualitative analysis instead of a numerical analysis. This style helped Gong make headway in her complex gel research.

"It's not necessary to understand every detail quantitatively if I have a rough idea," Gong said. "I'm a physicist, but I'm not very meticulous. So I think this research topic suits my personality."

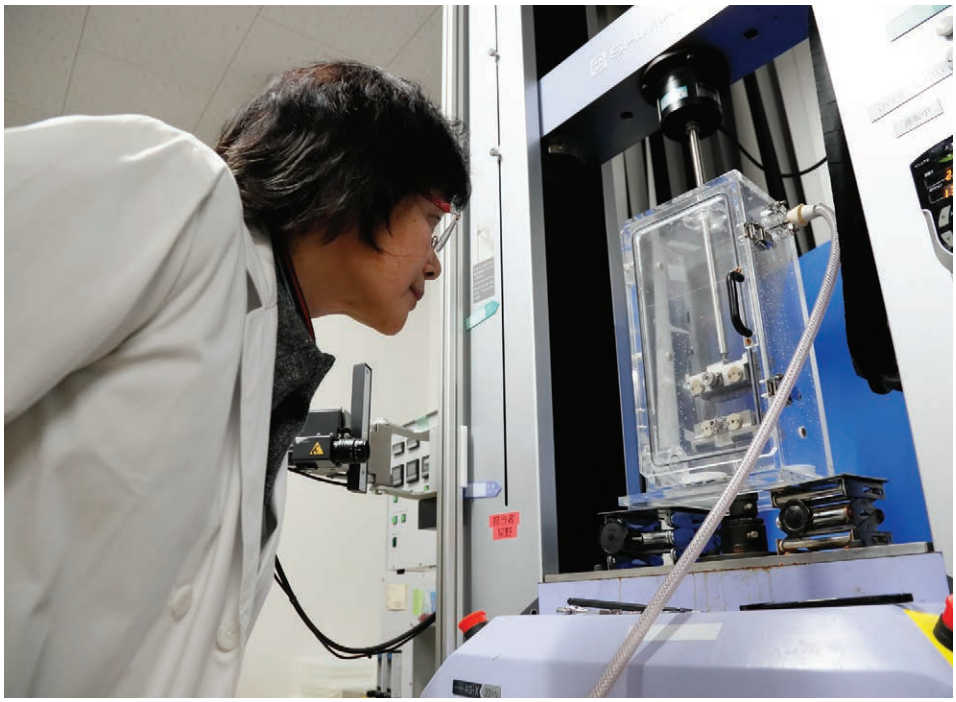
> "It's not necessary to understand every detail quantitatively if I have a rough idea."

Efforts to make gels even tougher

Her team's quest to toughen hydrogels has continued. It recently created hydrogels reinforced with glass fiber fabric, which makes the gels bendable but five times tougher than carbon steel. The team found the fiber-reinforced hydrogels are 25 times tougher than glass fiber fabric and 100 times tougher than conventional hydrogels based on fracture energy. The increased toughness stems from dynamic ionic bonds between the fiber and hydrogels and within the hydrogels, according to the team.

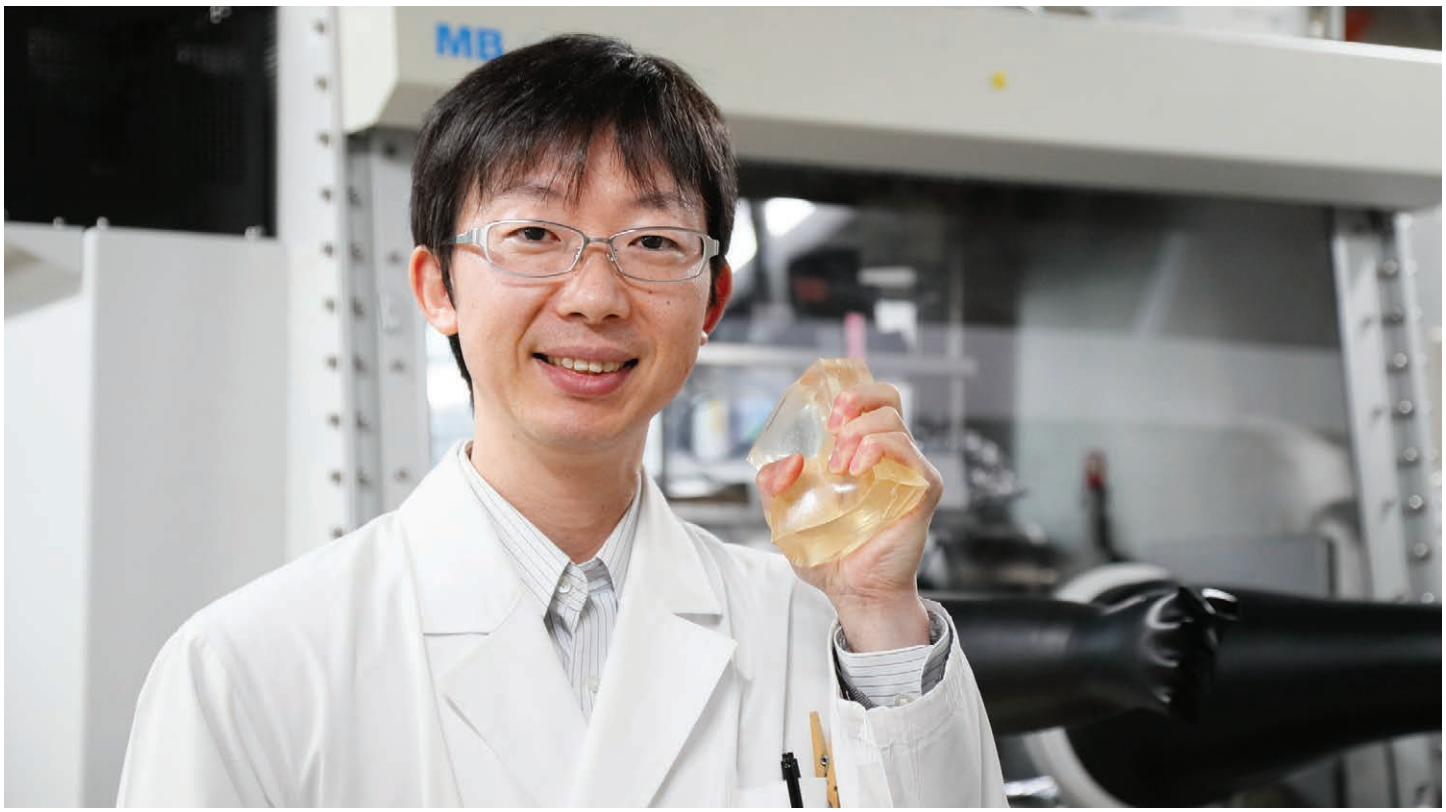


The fiber-reinforced hydrogel that is 25 times tougher than glass fiber fabric and 100 times tougher than conventional hydrogels.



Based on the sacrificial bond concept, Gong's team also has invented other types of gels including self-healing tough hydrogels. These efforts have raised hopes the gels could have practical real-world applications, notably in medical areas. Hydrogels share similar characteristics with biological tissues, including low surface friction, large thermal conductivity and high shock-absorbing ability. Demand is expected to be high for such biocompatible materials in nations with rapidly aging populations, such as Japan. Hydrogels have the potential to improve people's quality of life, a key issue in the 21st century. "Producing biological tools is our ultimate goal," Gong said.

Interdisciplinary lab culture leads to DN gel breakthrough



Professor Takayuki Kurokawa encountered the new-type hydrogel that was extremely tough when he was conducting an experiment to reduce surface friction of gels.

It started accidentally in 2000. Takayuki Kurokawa had a habit of squishing gels used for lab experiments. He liked the feeling of doing so with his fingers. One day, he found a gel so tough that he couldn't break it even by applying extra weight when he held it.

"It was very tough," Kurokawa recalled. "I was excited because I had never touched such a tough gel before." This chance discovery led to his laboratory's development of double network (DN) gels that have excellent mechanical properties.

At that time, Kurokawa, who is now a Hokkaido University professor, was a first-year master's student and conducting an experiment to reduce friction by forming polymer brushes on the gel's surface. Kurokawa presented the tough gel at a lab meeting only because a device to measure friction happened to be out of order and he had nothing but the gel to report. His finding was immediately recognized as a big one and prompted faculty members of the lab to make special arrangements to further investigate the gel.

"I never imagined this could be a breakthrough. I had no clue why the gel became so tough," Kurokawa said.

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Based on the way Kurokawa created the gel, skilled lab researchers sought to optimize the process and conditions for toughening gels by testing various polymer combinations and adjusting the amount of chemical reagents. After years of experiments and theoretical calculations, the team figured out the toughening mechanism. DN gels are made by combining two networks of polymers, one of which is rigid and brittle while the other is flexible and ductile. The team discovered that the rigid and brittle network dissipates energy when it breaks and gives DN gels their toughness through these "sacrificial bonds." Discovering the sacrificial bond principle was a major leap forward in gel research. However, the full picture of the material's complex properties remains unknown. Kurokawa said, "That's kept me interested."

Lab's culture allows 'detours'

Kurokawa pointed out that a "lack of experience" often can be an advantage in making new breakthroughs by challenging established science unknowingly. Researchers without preconceived ideas tend to find "seeds" that could yield something new and unexpected. He said the strength of the lab, currently led by Professor Jian Ping Gong, comes from its teamwork in which premature discoveries are followed up by faculty members and senior researchers who know ways to explain the phenomena with theories and advanced experimental skills.

Kurokawa also said the lab allows researchers to pursue their curiosity. This culture was cultivated largely by Yoshihito Osada, a former vice president of Hokkaido University who once led the university's gel research. Kurokawa remembers Osada often told his students not to aim for their research goals alone and encouraged them to make and enjoy "detours." As a result, researchers at the lab feel free to investigate new topics, including those unrelated to their original research.

The field of soft matter is characterized by its interdisciplinary nature that brings together people with various backgrounds, including physicists, chemists, engineers and biologists. This often enables a wide range of experiences, standpoints and approaches to generate synergistic effects. Kurokawa saw such robust interplay firsthand as Osada, a chemist, and Gong, a physicist, persuaded researchers from different areas of expertise to collaborate on gels.

"We've continued to embrace this collaborative culture. We always try to work as a unified team," Kurokawa said.

'Innovative' measuring technique for gels

Kurokawa's research now focuses on using a microelectrode technique to

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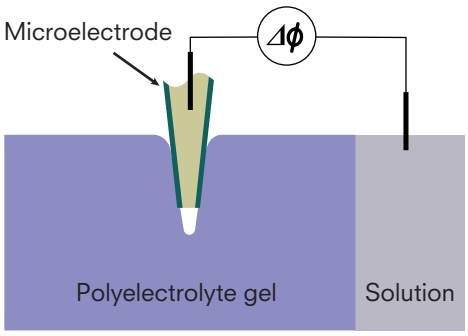
measure the spatial distribution of the electric potential of polyelectrolyte hydrogels. He described gels as "materials that cannot be seen quantitatively" because of their complex and heterogeneous structures, so establishing a measurement method for the quantitative study of gels has been long awaited.

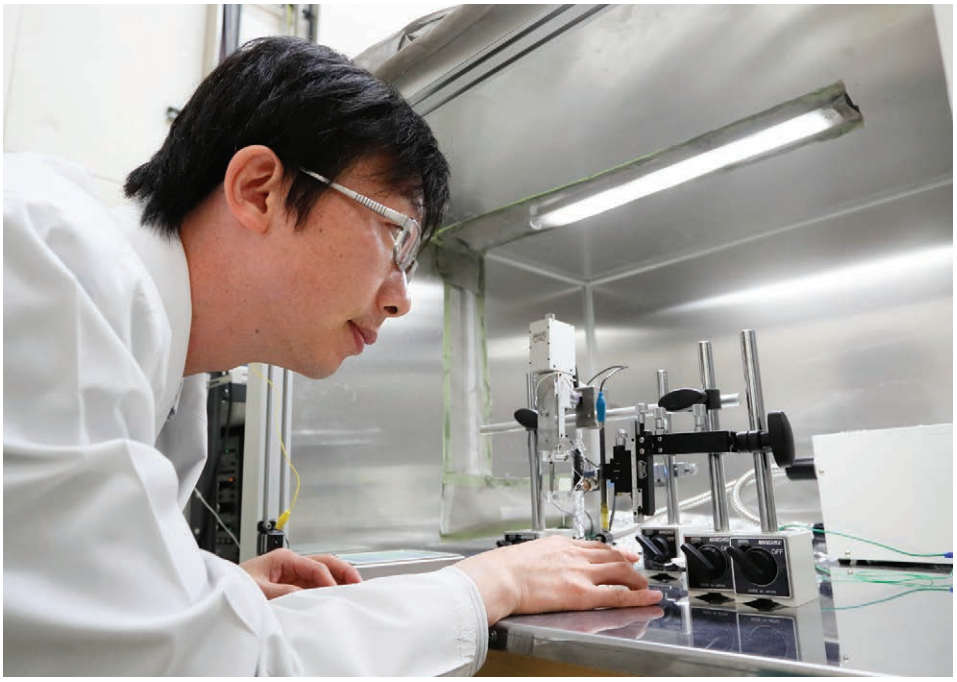
In 2016, Kurokawa reported a new method to gauge the ionic concentration in hydrogels. This method offers a powerful tool to characterize the internal structure of gels and further investigate the mechanisms of sacrificial bonds. "Measuring the behavior of polyelectrolytes quantitatively is challenging. But it's significant that we've introduced a new measurement method to the field of soft matter," Kurokawa said.

Given that hydrogels have a nanoscale network mesh, firmly connecting the microelectrode to the hydrogel was a major challenge. Kurokawa made accurate measurements possible by applying a microelectrode with an extremely thin tip wall and by using a micromanipulator to precisely control the microelectrode's position in the gel.

Local ionic concentrations change when stress is applied, so their technique would be instrumental in developing various sensors. Kurokawa envisions a sensor with the ability to detect pressure distribution and strength, similar to that of a human finger.



The microelectrode with a very thin tip wall is introduced into a gel using a micromanipulator for precise measurements.



This new device enables precise measurements of local ionic concentrations in hydrogels, which provides clues to its internal structure.

Identifying social needs is essential

Kurokawa's focus is primarily on the fundamental science of gels. Identifying social needs is vital to setting the course of his research, so meeting and listening to people in different areas is essential.

"Finding out the needs of people who want to use gel as a material makes me realize what we don't know about gels as well as what we should do with them," said Kurokawa, who frequently participates in events where he meets company representatives.

It is said to take 40 years for a material to be put into practical use after its invention. Efforts by private companies also will be crucial for turning gels into materials that are widely used.

"As basic scientists, our role is to present principles behind a material, but I'm willing to help companies speed up the process of adopting it for industrial use," Kurokawa said.

> "Finding out the needs of people who want to use gel as a material makes me realize what we don't know about gels."

SOFT MATTER USED HERE

Tire

Safe and diverse molecular design

by Bridgestone Corporation

BRIDGESTONE

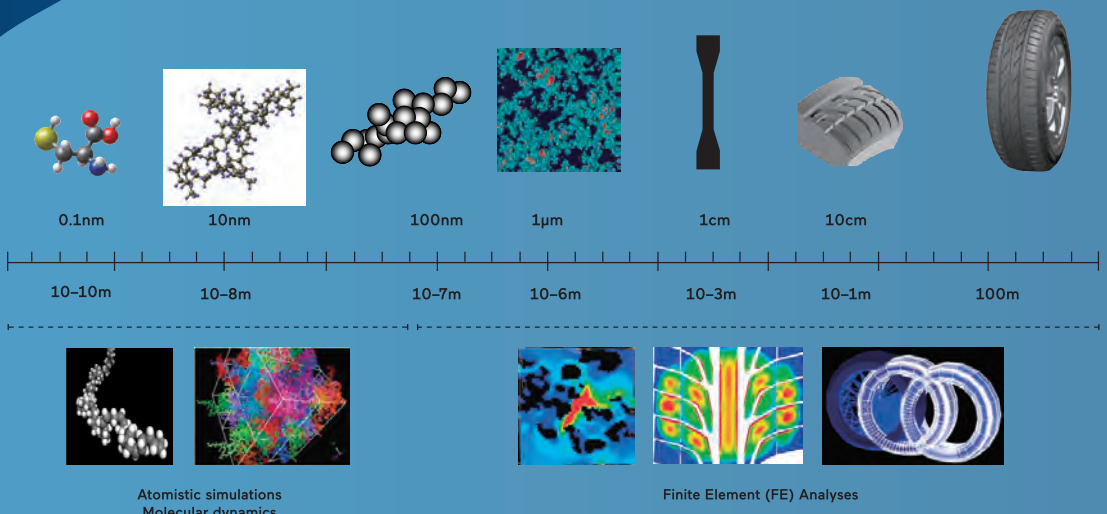
The history of rubber dates back to 1495 when Italian explorer Christopher Columbus discovered Haiti in the West Indies and brought back natural rubber to the West. Natural rubber became an industrial product of great value, and in 1839 American inventor Charles Goodyear and his associates vulcanized rubber, vastly improving his elasticity. In 1888, Scottish inventor and veterinary surgeon John Boyd Dunlop created pneumatic tires, a major development leading to the invention of automobile tires in the late 19th century. This has provided the foundation for other technological innovations by a large number of companies looking to enhance tire durability, reduce unwanted noise, and make other improvements. Due to advancements in soft matter research, fine tune adjustments to materials and molecular modifications to rubber are now possible. Technology has been evolving through greater nano-scale control of materials. In order to make tires safer, materials can be manipulated to satisfy various performance needs related to fuel efficiency, wet-grip, etc.

Above and right

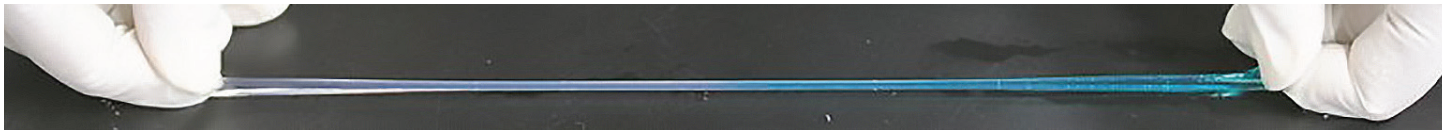
BLIZZAK VRX2, the latest studless tire utilizes this technology.

Below

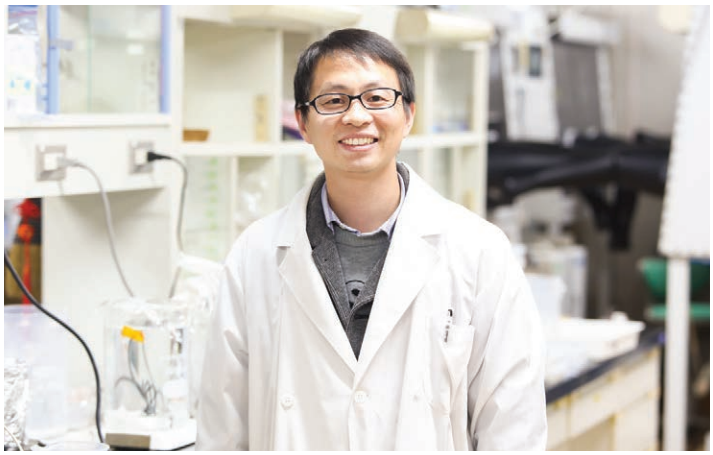
Multi-Scale Design



Tapping the world of polyampholytes to make a self-healing gel



The self-healing gel that was cut and then rejoined maintains its tensile strength. (Ihsan AB et al., *Macromolecules*, May 23, 2016)



Dr. Tao Lin Sun

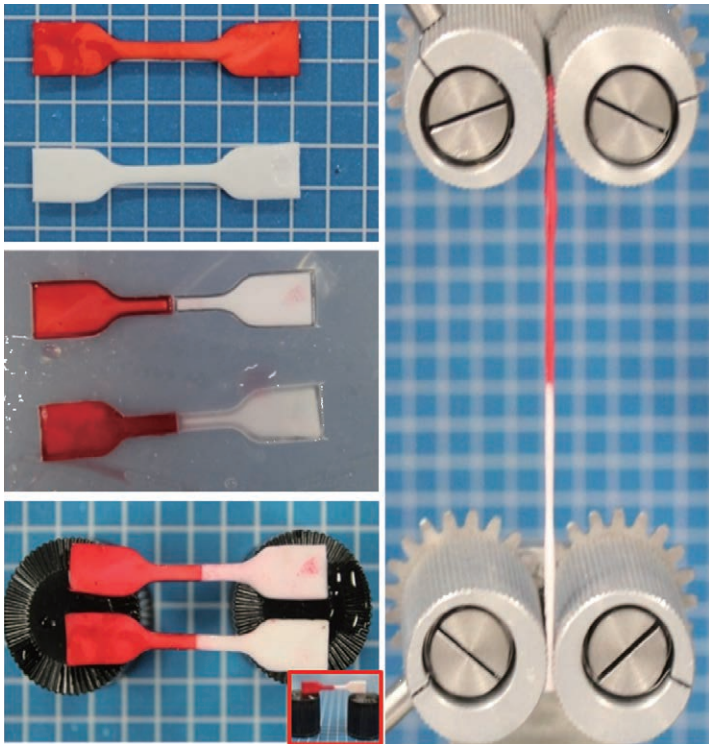
Tao Lin Sun came to Hokkaido University in 2009 to pursue a doctorate degree on soft matter after seeing scientific papers authored by Professor Jian Ping Gong, one of the world's top scholars in that field.

"While I was a graduate student at the University of Science and Technology of China, I focused on soft matter such as rubber-like materials," said Sun, who was an assistant professor at Hokkaido University until December 2017. "I was so excited about Professor Gong's work. It really inspired my research."

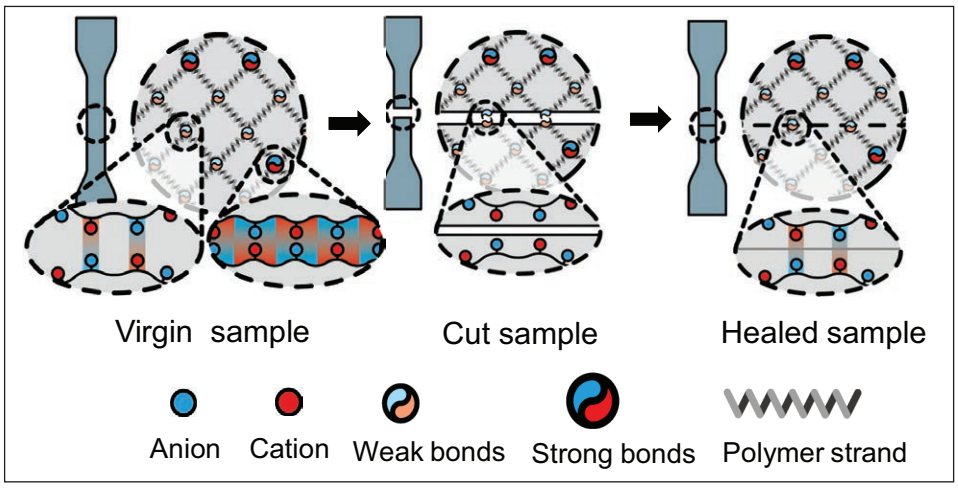
Under Gong's guidance, Sun initiated a study of self-healing gels, determinedly conducting experiments on roughly 15 different monomers – a chemical compound that can undergo polymerization. One year later, Sun's endeavors produced a success: He developed a self-healing gel that is very tough, exhibits excellent mechanical properties and endures autonomous healing and repairing after undergoing damage – all properties shared by living tissues.

When the gel is cut into two pieces, the cut surfaces can connect to each other like a healing wound. When the ruptured surfaces come in contact, a large number of damaged ionic bonds near the surfaces re-form across the interface, thus healing the gel.

> "It was amazing. Nobody, including me, thought polyampholytes could make this kind of gel."



This gel composed of polyion complex, not polyampholyte, also shows self-healing properties. The gels colored red and white were cut and then reconnected (left images). The self-healed gel retained its tensile strength (right image). (Luo F. et al., *Advanced Materials*, March 23, 2015)



The weak ionic bonds serve as dynamic and reversible sacrificial bonds giving the gel toughness and self-healing properties. (Ihsan AB et al., *Macromolecules*, May 23, 2016)

Macromolecule with both positive and negative charge is vital

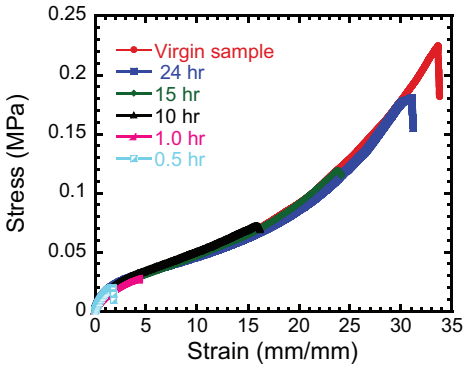
The key to Sun's gel is polyampholytes – macromolecules that have a mixed anion (negatively charged ions) and cation (positively charged ions) character. This class of gel is synthesized simply by copolymerizing a charge-balanced amount of oppositely charged monomers at high concentration so the polymer chains entangle to form gels.

"It was amazing," Sun recalled, pointing to the fact that most hydrogels do not have autonomous healing or repairing functions. "When I announced the finding at a group meeting, Professor Gong and the other professors were so excited. Nobody, including me, thought polyampholytes could make this kind of gel."

The polyampholyte chains' charge distribution is random, leading to the formation of multiple ionic bonds, of both intrachains and interchains. The strong ionic bonds of interchains, stabilized by entanglements, serve as permanent cross-linking, or a bond that links one polymer to another.

Meanwhile, the weak ionic bonds, of both interchains and intrachains, serve as dynamic and reversible sacrificial bonds to dissipate energy. The reversible sacrificial bonds give toughness to the material because the gel can make a self-recovery after a large deformation – thanks to the breaking and re-forming of weak ionic bonds.

Sun said the higher the proportion of weaker bonds to total bonds, the more efficient the self-healing function becomes, demonstrating that self-healing is due to the re-forming of dynamic weak bonds. Cross-linking formed by strong ionic bonds, meanwhile, reduces its efficiency. While high temperatures substantially accelerate self-healing kinetics, the healing efficiency is excellent when conducted at room temperature, but above a softening temperature. The gel's rigidity also affects the self-healing efficiency. If the gel is rigid, the cut surfaces cannot come in full contact. Soft gels, on the other hand, form a good contact between the surfaces, which improves its self-healing efficiency.



The stress–strain curves showing tensile strength after healing. The virgin sample and healed samples were measured at room temperature. Cut pieces were reconnected immediately after cutting and healed in water for different times at 25℃. (Ihsan AB et al., *Macromolecules*, May 23, 2016)

Looking ahead

Sun said one of his priorities is to make the polyampholyte gel much tougher. This would potentially help biomaterials become widely used in the future.

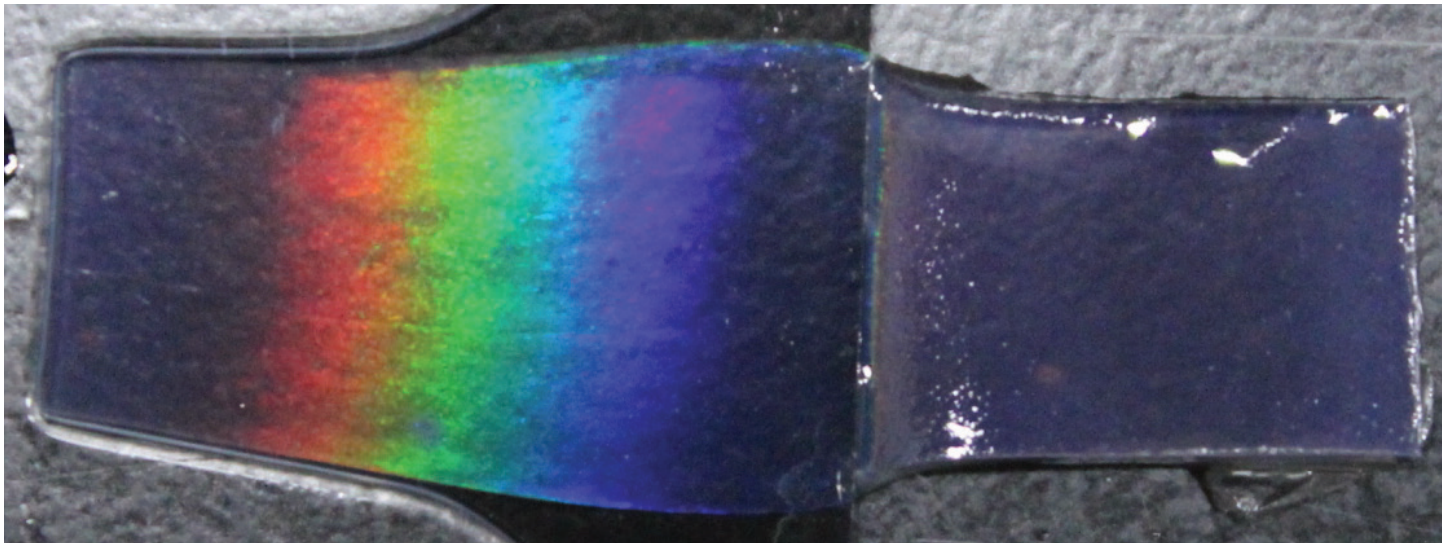
> "This kind of gel is very new, and you need knowledge in so many areas, such as chemistry, physics and life science."

"I focus on fundamental research so the mechanical behavior of hydrogels can be understood," Sun said. "I want to understand the internal structure that makes the gel very tough. If we accurately identify this mechanism, we can design much tougher gels for applications such as biomaterials and industrial use, including tires. That is my immediate goal." Sun's long-term goal is to make super-tough materials that can be used for artificial bones and teeth.

Sun is convinced that hydrogels will be a material for the next generation. "This kind of gel is very new, and you need knowledge in so many areas, such as chemistry, physics and life science," Sun said. "The challenge is how to connect the internal structural change with microscopic deformation. If we uncover this connection, we will know how to address problems associated with making hydrogels tougher. We want to construct a mathematical model to describe this connection."

*Dr. Tao Lin Sun has been conducting his research at South China University of Technology since January 2018.

Inventing multifunctional hydrogel that changes color under stress



The PDGI/PAAm^2 gel showing a complete visible spectrum by applying a compressive strain gradient. (Haque M.A. et al., *Chem. Mater.*, November 11, 2011)

Dr. Md. Anamul Haque, a Bangladeshi chemist, spent many hours at his Hokkaido University laboratory in 2010 trying to produce a hydrogel with a hierarchical structure, a daunting challenge that had to be overcome to make the gel exhibit magnificent colors when subjected to mechanical stimuli.

"The most difficult part was to make the bilayers of surfactant in a precursor solution aligned and layered in a gel," recalled Haque, who was a doctoral student at the university at that time. "I tried many kinds of gels, probably 20, and different methods for six months." He was eager to make such a gel, which shares many properties with biological soft tissues, because it could pave the way for making artificial blood vessels as well as sensors that can be used for studying artificial tendons.

The breakthrough came when Haque applied strong shear, a flow induced by force, to a precursor solution containing the surfactant dodecyl glyceryl itaconate (DGI), acrylamide, and a cross-linker prior to the polymerization. The shear flow allowed lamellar bilayers of self-assembled DGI to align in one direction, while stacking the bilayers periodically to give the gel a thin photonic crystal structure. His gel has as many as 4,000 layers.

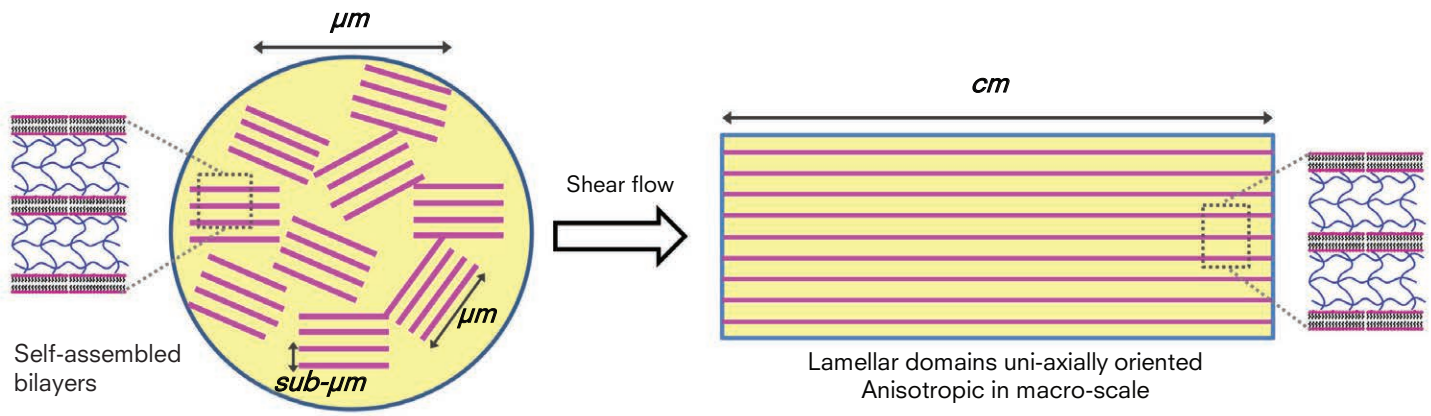
Haque stayed at the university as a doctoral student and

"The most difficult part was to make the bilayers of surfactant in a precursor solution aligned and layered in a gel."

a postdoctoral fellow through 2013 before returning to the University of Dhaka, where he worked as an assistant professor. Haque returned to Hokkaido University in 2015 for a two-year program under the JSPS Postdoctoral Fellowships for Research in Japan. He studied various functions of the gels he developed and an optimized method to synthesize the gel. The new suction method to apply the shear flow is effective for making a uniform DGI lamellar phase.

Creation of anisotropic gel

Haque became fascinated with hydrogels after learning of double network gels being developed by Professor Jian Ping Gong's team. "It was amazing because the gels I knew were very weak, like fruit jelly. But her gels were very tough and strong," Haque said.



Bilayers of DGI are stacked periodically with polymerized AAm in between the bilayers (far left). By applying strong shear flow prior to polymerization, bilayers of DGI align in one direction giving the gel a photonic crystal structure. (Haque M.A. et al., *Soft Matter*, June 15, 2012)

Dr. Md. Anamul Haque

Under Gong's instruction, Haque started conducting research on gels that have structural color and also change color when subjected to mechanical stimuli. The gels exhibit structural color by multilayer interference according to Bragg's law of diffraction.

The hydrogel Haque developed with the shear flow method has additional functions related to structural color and beyond. First, the gel's color can be reversibly tuned by compressive and tensile stimuli, changing the color from red to blue, depending on the intensity of force applied perpendicular to the bilayers. How the gel emits color is influenced by the alignment of bilayers, the number of layers, and the distance between layers.

Due to the uni-axial orientation of the bilayer, the gel possesses superb functions that have never been realized before, such as anisotropic modulus and one-dimensional swelling, which are properties of biological tissues.

> "One-dimensional swelling is also important for the ensuing materials that will be created."

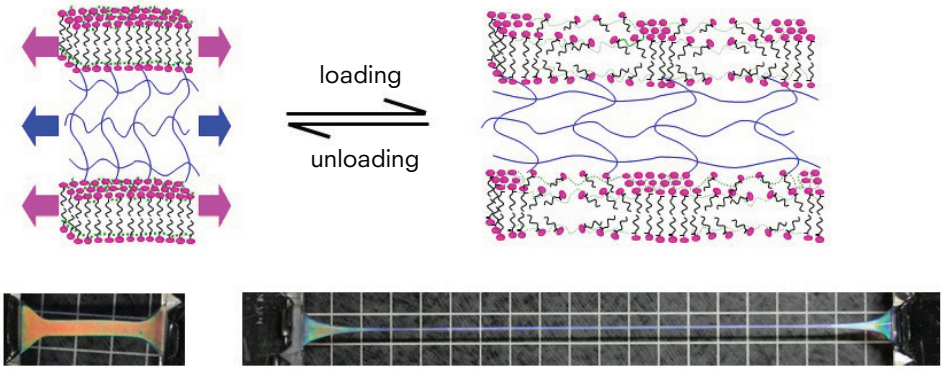
"Anisotropic means that if you change its direction, it can change its property," Haque explained as he showed the gel. "If you look at an angle of 90 degrees to the gel surface, it is orange or red. But if you reduce the angle to about 50 degrees, it becomes blue."

That the bilayer has one-dimensional swelling is also important for making the gel closer to biological tissues. "The bilayer can swell vertically, but not horizontally," he said. "One-dimensional swelling is also important for the ensuing materials that will be created. In the field of material engineering and mechanics, this type of system could be considered for modeling and designing functional materials for various purposes."

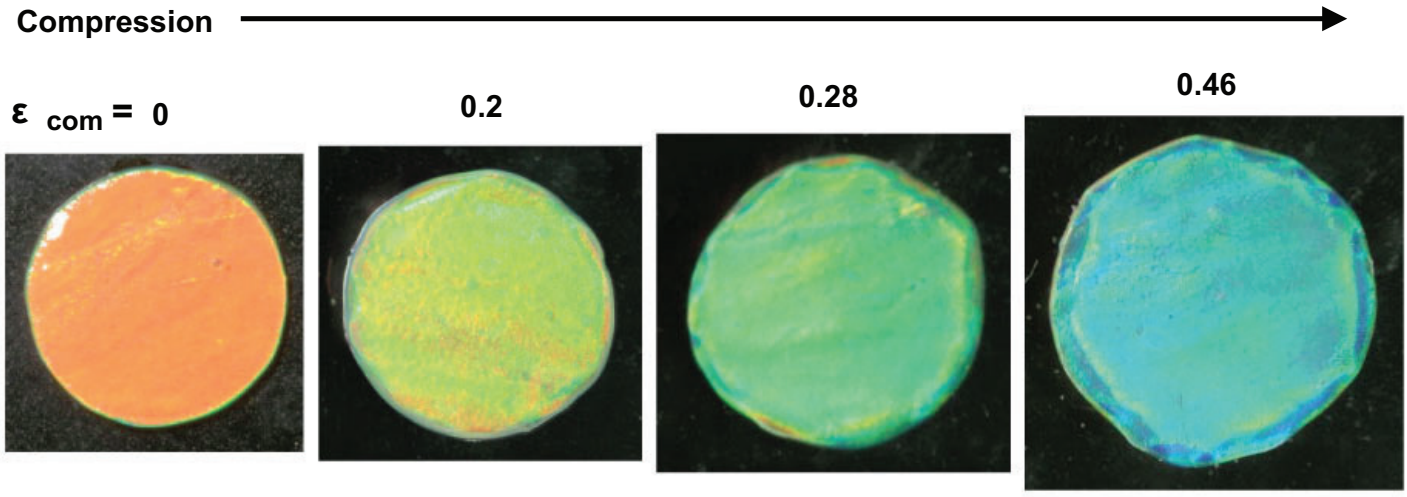
Reversible gel

Furthermore, the gel is reversible when subject to compression and tensile stimuli, a property most hydrogels lack. Haque's gel is comprised from rigid, hydrophobic polymeric-DGI (PDGI) and soft poly-acrylamide (PAAm), and has a typical double network (DN) structure.

The bilayers sustain compression and tensile stress and they yield at a large stress due to the dissociation of the hydrophobic packing of PDGI molecules. The molecules recover to



The gel is reversible when subject to tensile stimuli. The rigid PDGI bilayers serve as reversible sacrificial bonds to delocalize the stress and enhance crack resistance. (Haque M.A. et al., *Macromolecules*, October 31, 2011)



The gel's color can be reversibly tuned by compressive stimuli, changing the color from red to blue, depending on the intensity of force. (Haque M.A. et al., *Advanced Materials*, September 13, 2010)

the association state after removal of the stress. Thus, the rigid bilayers serve as reversible sacrificial bonds to delocalize the stress and enhance crack resistance.

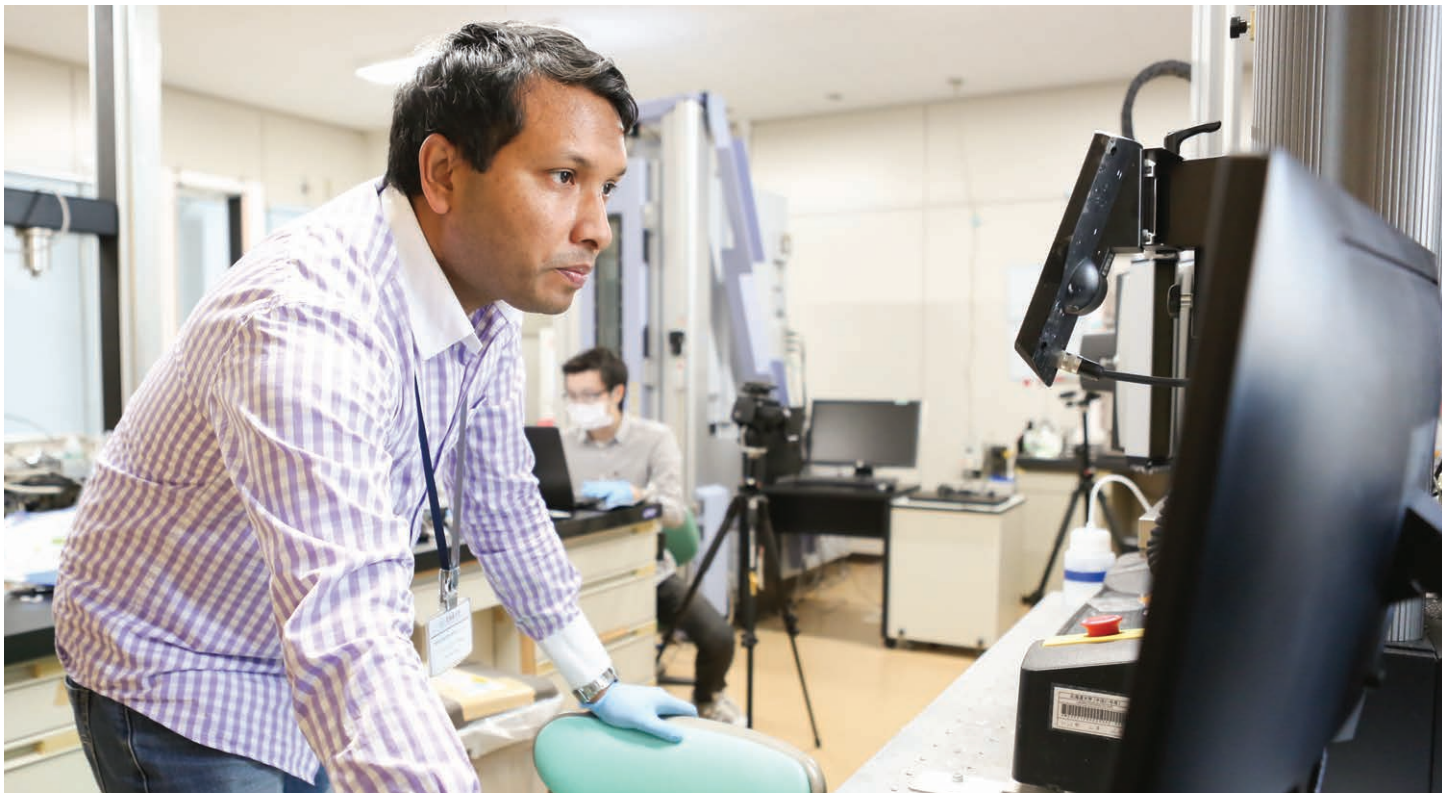
"Even if molecules are disassociated, they come back to where they were after the stress is released," Haque said. The recovery has two stages: Nearly 80 percent is recovered quickly after unloading, which is followed by a slow recovery stage that takes about 15 minutes. "The slow recovery could be an issue during practical use but I have improved the immediate recovery after unloading by adding a third polymer to the gel. Furthermore, a student of our team has shown the recovering process and color tuning response can be significantly shortened to a few milliseconds by hydrolyzing the PAAm network of gel."

Seeking bigger and stronger gels

Although the gel has a vital reversible function, it is not as strong as other gels developed by this lab. Haque believes the anisotropic gel must be stronger before it is ready for practical application. The chemist also wants to devise a method for producing much bigger gels from its current size – several centimeters wide and long and one millimeter thick.

Haque said possible applications of his gel include using it to make artificial blood vessels as well as using its ability to change color as a sensor to gauge the local force in tendons or muscles.

In December 2017, Haque returned to his position at the University of Dhaka, but he will conduct further research on hydrogels in collaboration with Gong.



Soft matter: Past, present and future

Michael Rubinstein, University of North Carolina at Chapel Hill[1]
Costantino Creton, L'École supérieure de physique et de chimie industrielles de la ville de Paris (ESPCI Paris)
Jian Ping Gong, Hokkaido University

The three globally prominent experts in soft matter science gathered in Hokkaido on August 2, 2017, to discuss soft matter as an interdisciplinary challenge, its impact on society, and their resolve to create academic societies for scientists working in the broad field of soft matter. Rubinstein and Creton visited Japan to teach at the International Soft Matter Summer School in Hokkaido 2017[2] and this special discussion was held on the sidelines of it.

Michael Rubinstein (left), Costantino Creton (middle), and Jian Ping Gong during their roundtable talk

First encounter with soft matter

Dr. Jian Ping Gong (Chair): First of all, I'm very happy to have this discussion with the unit leaders of Global Station for Soft Matter (GSS)[3] who have greatly helped the startup of GSS in 2016 and continue to work with us. I would like to start by discussing what attracts us to the new research area of soft matter. For me, soft matter is such a big field. It is even difficult to define soft matter because it covers almost everything. That's why I see huge potential in it.

Dr. Costantino Creton: I really like the interdisciplinary aspects. I got into this field by chance from the hard materials science field. When I came to ESPCI in France, I learned about more aspects of soft matter and I learned from the techniques and thinking of people in different fields to approach problems in a more multidisciplinary way. I especially like working on fundamental problems, materials and issues that are relevant in daily life and in industrial applications.

[1] Dr. Rubinstein became a professor at the Departments of Mechanical Engineering & Materials Science, Biomedical Engineering, Chemistry and Physics of Duke University in January 2018.

[2] The summer school, which was organized by Hokkaido University's Global Station for Soft Matter, was held from July 30 to August 5 and August 7 to August 11, 2017.

[3] Established on April 1 as one of Hokkaido University's key research hubs to facilitate the development of soft matter, which is expected to help solve problems associated with an aging population, environmental pollution and resource shortages, among other global issues.

> Soft matter is such a big field. It is even difficult to define soft matter because it covers almost everything. That why I see huge potential in it.
>
> – Jian Ping Gong

Dr. Michael Rubinstein: I started initially in experimental particle physics, but I later decided to study theoretical physics. I went to a graduate school and was assigned to a particle theory group. During my first year I discovered another area of theoretical physics, called condensed matter, which is related to something you can touch.

After I finished my PhD, I worked at Bell Labs, which was the best place for condensed matter, and the position I found was in polymers. I was scared to leave "proper" physics, as polymers were not considered a standard part of physics, but I found this is a great area to do research in. Working in industrial labs, such as Bell Labs, IBM or Kodak, encourages one to work with specialists in a variety of fields. The exciting thing is that you have an unlimited number of problems to solve, and each of them also has direct applications.

Gong: Soft matter has become prominent over the past two decades or so. The term "soft matter" was first used about 25 years ago, wasn't it?

Creton: French Nobel Prize laureate Pierre-Gilles de Gennes made the term popular. Maybe some other people had used this term before, to distinguish soft matter, which has weak interactions between molecules or atoms, from hard materials that have strong interactions.

Initially, soft matter referred to liquid crystal physics, polymer physics, complex fluids, and colloid physics with weak interactions. In American universities, solids are handled in materials science departments while fluids in general are handled by chemical engineers. De Gennes pointed out that they had more similarities than differences and the physics of these materials could be considered in a unified way. In France, people created a community centered around soft matter, which slowly expanded in Europe.

Rubinstein: This shows many common features and concepts can be exchanged and used in different academic fields. This helps to define a new area that's initially just a research field, but later becomes a new area of science.

Gong: So this field is quite interdisciplinary and covers a huge area.

Rubinstein: Each subfield is much older, but they were not directly connected. Polymers have a history of over 100 years and colloids have been used for thousands of years. But only 25 or 30 years ago, it became apparent that these fields have similar concepts.

Creton: That started with conferences where people came together under the same umbrella. Even our laboratory, which was called polymer something, has had "soft matter" in its name since about five years ago.

Rubinstein: Just like textiles use different components together, now we pull different elements into a complex field like biology. You have to use all those elements together and see how they interact and how they can make something interesting and useful. That's why this unifying approach is so attractive.

Soft matter in medicine and biology

Gong: As Michael mentioned, soft matter has a wide range of potential applications to our everyday life. Among them, biomedical applications of polymers like gels have drawn considerable interest.

Rubinstein: That's true. This will happen in two ways – one is developing gels that heal injuries, and the second is understanding how biophysical conditions of a disease develop from the perspective of soft matter.

Jian Ping Gong

Gong: Could you give some examples?

Rubinstein: When I was discussing this with people from medical school, I began to figure out what different lung diseases have in common. We looked at cystic fibrosis, chronic obstructive pulmonary disease and asthma. Mucus becomes too concentrated. Mucus is a biological gel that forms a protective layer in our lungs. It catches all pathogens and environmental toxicants we breathe in and clears it out of our lungs.

However, if the mucus gel becomes too concentrated, it sticks to the surface of the lungs and cannot flow. So, the question becomes how we can change the properties of this gel so it doesn't stick as much. This could be answered by using ideas and methods from material science of rubbers and gels, which are not known in medical fields. Mucus follows the

> The exciting thing is that you have an unlimited number of problems to solve, and each of them also has direct applications.
>
> – Michael Rubinstein

Michael Rubinstein

same laws as synthetic gels. Doctors were happy to learn about new field of soft matter because it enabled them to develop new treatments, and we were happy that we could help patients using concepts we were already familiar with.

Gong: When we developed tough hydrogels with low friction or some specific surface property, we asked medical doctors at our university about possibilities for collaboration and possible applications. Some of them became interested in working with us. There is no soft articular cartilage made from soft matter so far. Current treatment uses hard matter like metals. The patient's bone is cut and entire artificial joints are implanted. If we develop soft materials like hydrogels with properties similar to real cartilage, it will dramatically change this treatment.

Creton: A small proportion of medical doctors and biologists are interested in working with physicists, but this proportion is increasing. Success stories, like Hokkaido University, make it more interesting from the application point of view and also from the perspective of understanding life.

> "Life is not stable; if you are stable, you are dead. Cells are always moving in and out. This is where physicists can help."
>
> – Costantino Creton

For instance, real cells are very complicated. Physicists developed artificial cells (lipid membranes) that resembled real cells, while looking for models of deformed cells to understand how their elasticity played a role in the deformation. They investigated the combination of some physics aspects of the cell such as thermal fluctuations and added living features, such as molecular motors that produce energy and work in a steady state outside of thermodynamic equilibrium.

It is important to note that life is not stable; if you are stable, you are dead. Cells are always moving in and out. This is where physicists can help. They know about these fluxes and how things can be in a steady state, so they study these features of life in simpler systems where you have this behavior without the full complexity of the cell.

Gong: In biology, a very interesting problem is how the shape of, for example, a nose or ear develops and forms. We benefit from understanding new uses of soft matter concepts and mechanical concepts, and how mechanical constraints, tension and stress can explain how the shape develops. If we want to make artificial actuators, learning from how plant cells are distributed enables the development of gels with gradient structures so they can bend.

More potential uses ahead

Gong: Beside medicine and biology, what are other future applications of soft matter?

Creton: To save energy and cut carbon dioxide emissions, the automobile industry is currently developing lighter vehicles made with materials that have the same strength and properties as conventional vehicles. The vehicle's most important part is the body, which is now increasingly made from plastic composites. The biggest limitation at the moment is still cost.

Also, there is research into biomedical and flexible electronics. Sensors placed on the skin can provide electrical information and measurements. Sensors placed inside the body should be flexible, adhere to living tissues and be durable.

Gong: Solar panels are made of heavy glass plates. If we develop durable, highly efficient polymers, it will tremendously change the current situation. Using lighter panels will reduce the hefty transportation cost shouldered by solar panel producers.

Creton: Old tires are burned, but researchers are investigating whether chemistry offers a way for them to be recycled. Painters want safe paints with no toxic or smelly fumes. Unfortunately, the better paints use solvent that smells bad. Researchers are trying to develop completely water-based paints that don't stink.

Collaboration among scientists

Creton: If people from different fields want to conduct research together, it is easier if they are in the same place. After a while, people start thinking maybe we should teach this topic and ask the students to learn about fluids, solids, polymers, colloids and biophysics in the same program so they get a degree in this area. For example, chemistry and physics could become a joint program.

Gong: You both spend a lot of time thinking about how to organize this and make this interdisciplinary program work. Polymer physics and polymer chemistry are huge fields so such a curriculum is not common.

Rubinstein: It's like the fable about the elephant that walks into a village and several blind men try to figure out what it is. One touches the trunk and says the elephant is like a garden hose, another feels the body and says the elephant is like a wall, and another touches the tail and says the elephant is like a rope. Unless they start communicating, they will never have a full, accurate picture of an elephant.

Similarly, knowing just physics or just chemistry or just mechanics will not be enough to solve some complex

problems. We need a collaboration of scientists from several disciplines. Eventually we will train new scientists who can understand all these fields, but it will take at least 10 years to develop an undergraduate and graduate curriculum.

Creton: Our students in ESPCI Paris have to learn physics, chemistry and biology. It's not optional. Every student receives multidisciplinary training.

> "Unless they start communicating, they will never have a full, accurate picture of an elephant."
>
> – Michael Rubinstein

Gong: Why did soft matter science originate in France?

Creton: It was really de Gennes. He was a brilliant, respected physicist. He convinced bright young students, who would normally lean toward high-energy physics, plasma physics or astrophysics, that soft matter was physics. In 1970, most people thought soft matter was not physics. He still influences many people in this field.

Gong: Most professors in the physics department consider physics to be astrophysics, elemental particle physics or solid state physics. They think soft matter has a lower status than these core subjects.

Rubinstein: I think this is true in many U.S. universities, too. Soft matter in the United States developed slightly differently because it emerged from industry. In the 1970s, Exxon Research and Engineering Company assembled many brilliant scientists to work together on oil exploration, oil processing, colloids and polymers. When the lab reduced the number of scientists, some of them moved to universities. That's how soft matter, which at that time was called complex fluids, originated out of one center. The most prominent soft matter scientists in the U.S. are directly or indirectly related to Exxon labs.

Creton: In the United States, complex fluids and polymer physics are still kind of emerging.

Rubinstein: Right, but historically soft matter first emerged in Europe. Several researchers from different labs worked together, and that's how the international soft matter conference started in Europe. Many collaborations formed between countries and between different fields like chemistry and physics.

Creton: The European Union funded these projects and so several large multinational, multilab projects on topics related to soft matter became more permanent. The international soft matter conference started from one of these large network groups.

Rubinstein: In that sense, the United States lags Europe but soft matter scientists are trying to build similar organizations. There are efforts at different universities to start soft matter centers or departments. Hokkaido University is one of the first examples of building international collaboration in this field.

Gong: Japan has a small soft matter community, whose members are mostly physicists. We have a large polymer science community and developed colloid and biology science communities. These fields fall under the soft matter umbrella but still operate separately. Future development of the soft matter community depends on somehow joining these communities. Otherwise, we will be left behind.

Rubinstein: Two months ago, I was asked to chair the working group on soft matter of the International Union of Pure and Applied Physics. There are three subgroups – one each for North America, Europe/Africa and Asia/Australia. Our task this summer was to identify soft matter communities within each of the Asian countries. Some of them are in contact with each other, but some don't even communicate.

We are trying to establish an umbrella society that would allow soft matter scientists to easily communicate with each other. Right now, they are self-organized, small communities at a grassroots level, but the challenge is to integrate them within a country and between neighboring countries.

Gong: Government funding is vital. If governments craft policies for funding and encouraging soft matter interdisciplinary collaborations, it will substantially change the situation.

Creton: The European Union's Horizon 2020 research and innovation program covers applied and fundamental research and training of students. This program is available for everyone in Europe. In addition, each country has a national funding program.

Soft matter at Hokkaido University

Gong: Beside your primary responsibilities in your universities, you two are also members of the Global Station for Soft Matter at Hokkaido University. What are the strengths and weaknesses of soft matter research in Hokkaido University?

Creton: One strength is the integration of chemistry and materials science that created interesting new ideas and solutions. It's an effective way to cooperate, devise new ideas and inspire others. I think this work has influenced many people all over the world. That will continue because there is a system that identifies creative people, selects the right projects and produces good results.

Costantino Creton

As for weaknesses, I think more international collaboration is needed, and there needs to be more exchanges by sending students abroad.

Rubinstein: Hokkaido University is among the world's best for gel research. A weakness, not of the group but of the university, is that it covers only a narrow segment of soft matter. Soft matter is a broad field and there are different approaches and different angles. You need younger and senior people in complementary areas that are not necessarily overlapping with gels. That would enhance education of students in the groups because they will see other techniques and exchange ideas.

This weakness can be rectified by bringing in other groups in different departments, such as physics or chemistry, material engineering and medicine. This is what is happening at the International Soft Matter Summer School, which is taking place right now and bringing together scientists and students from different soft matter fields.

> "If everybody agrees, there are usually not many new ideas. When people start disagreeing, you think a little harder."
>
> – Costantino Creton

Future challenges

Gong: Let's conclude today's discussion by determining major challenges that remain in soft matter science.

Rubinstein: Life is based on soft matter. We know that this complex system works because we exist, but we do not yet fully understand how it works. Can we understand it well enough to design life, using similar or slightly different principles from synthetic materials without proteins and DNA? Can we make artificial cells without using lipids in cell membranes? I don't think it will be easy to do this in the next 25 years but I'm sure it's possible.

Creton: One fascinating thing is the dramatic progress made in the medical field to replace defective body parts with artificial parts. Understanding how the brain can command body parts and functions would be fantastic. There also are challenges in energy and the development of better batteries.

Rubinstein: To solve these problems, we need scientists who understand electronics, biology, polymer gels, colloids and other fields.

Creton: It's essential to have people with different viewpoints. If everybody agrees, there are usually not many new ideas. When people start disagreeing, you think a little harder. In our group, there's no real official boss, so you work with colleagues and they have different areas of expertise. We are independent but we decide to work together on some projects. This sparks some interesting new ideas on complicated multidisciplinary problems. It's an effective way to untangle difficult problems.

> "You are trying to develop something useful but in the process of that you discover some fundamental new laws of nature."
>
> – Michael Rubinstein

Rubinstein: Great discoveries can come from trying to solve very practical problems. You are trying to develop something useful but in the process of that you discover some fundamental new laws of nature.

Creton: I think you can apply fundamental science to solve practical problems, and sometimes from the practical problem you get an idea for some new fundamental science. They feed off each other.

Gong: Many fundamental problems appear initially in terms of practical questions, coming from industry and other sectors. I strongly felt this when I visited the ESPCI. Many people are doing fundamental work but they are from the industrial sector.

Creton: I'd also like to support young scientists working in similar areas to

mine and I would be delighted if this interdisciplinary, collaborative approach carries on after me. For young scientists, I would recommend to allow enough time to select an ambitious and challenging problem. Once this is done, spend time thinking carefully about it, form your opinion, and don't necessarily do the most fashionable activity.

Gong: I would like to think about how to maintain the superb hydrogel research conducted at this university and how to make a good platform for younger generations who will carry on this work. If these hydrogels can be put to practical use, as artificial cartilage or even new materials, I will be very happy.

I have many students from China who are talented but feel a lot of pressure. I suggest they select a topic they really like and don't worry about what people think of them. Of course, it's not easy, but this makes science so interesting and as a result they will produce good, original research.

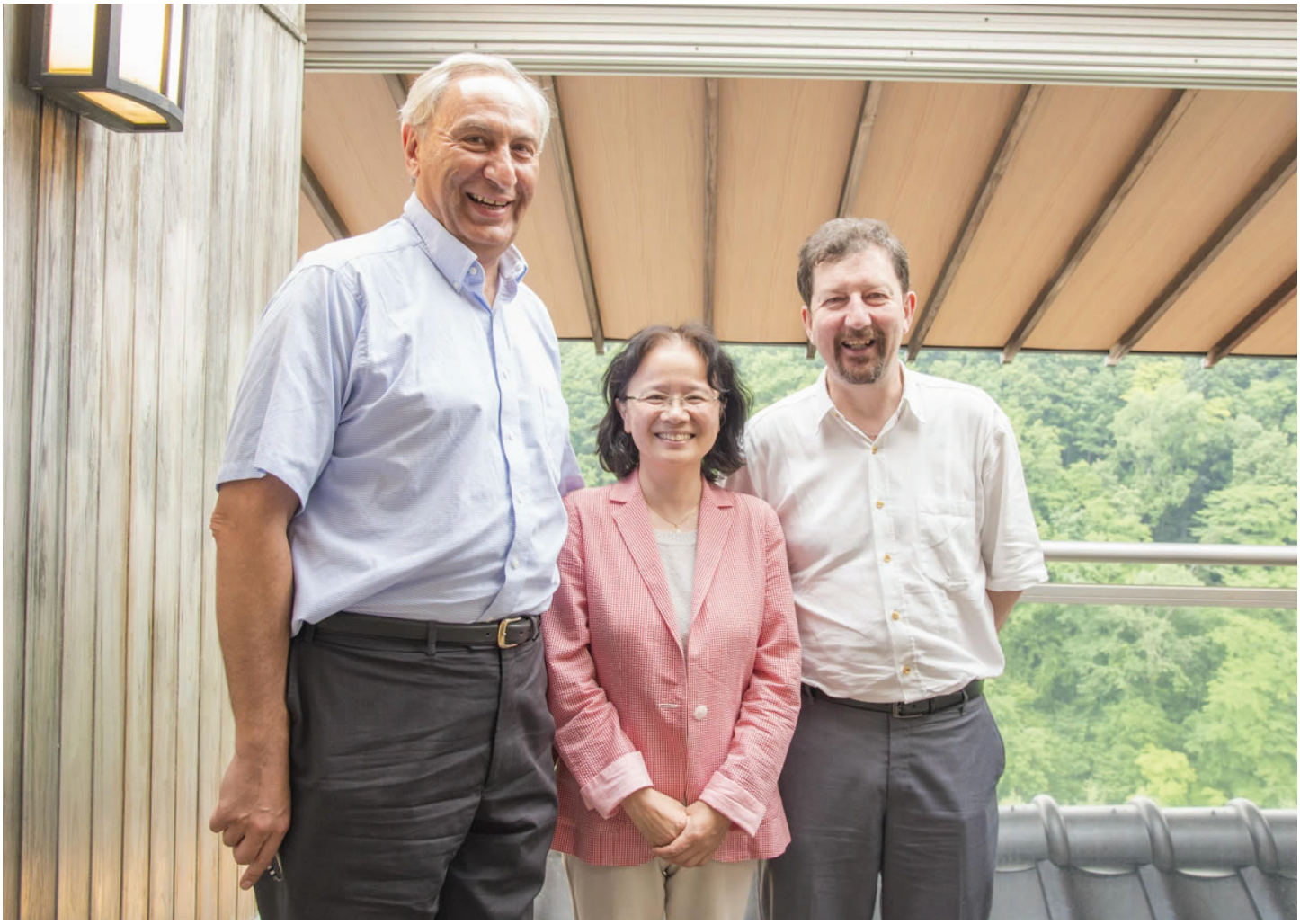
Rubinstein: In my case, a short-term goal that will be extended is to create this international soft matter society that will connect different groups of people in different disciplines and in different countries. I hope to launch an American soft matter society that will connect societies for physics, chemistry, chemical engineering, materials science and biophysics.

In terms of education, my goal is to find the best teachers in different disciplines, organizing them in Asia, Europe and the United States. The idea is to record full lectures and courses at different universities and make those courses available to students and professors all over the world so as to create a very broad soft matter curriculum.

This ambitious plan probably will need at least 15 years to complete. My advice to younger people is to find challenging problems, talk to and learn from as many experts as you can, and try to broaden your background as much as possible because learning different techniques is really crucial to answering complex questions.

> "Spend time thinking carefully about it, form your opinion, and don't necessarily do the most fashionable activity."
>
> – Costantino Creton

Gong: Thank you very much for your time and wonderful discussion. I hope our discussion will inspire other scientists, young students and everyone in many other fields. I also hope that we achieve our research goals in the future.



International Soft Matter Summer School 2017

The International Soft Matter Summer School 2017 was held in Hokkaido, Japan, from July 30th to August 11th to discuss the fundamentals of soft matter science, an emerging research field to develop innovative soft materials through interdisciplinary studies. The event, coordinated by Michael Rubinstein, Costantino Creton and Jian Ping Gong whose round table discussion is featured in this magazine (see p. 20), brought together 13 internationally renowned scientists and young researchers from all around the world.

It was hosted by the Global Station for Soft Matter (GSS) of Hokkaido University's Global Institution for Collaborative Research and Education (GI-CoRE) and the Graduate School of Life Science, and was held in conjunction with the Hokkaido Summer Institute (HSI) which attracted more than 50 graduate students to the program from Japan and abroad.

The first seven days of the program took place at the Otaki Seminar House located in the countryside outside of the university's Sapporo campus. A series of lectures on varying subjects, yet with a particular focus on polymer science, were given by world-leading scientists and lively discussions followed each lecture. Poster sessions were held to share the most up-to-date findings and exchange ideas. While lectures were not in session, some participants enjoyed Nordic walking in Otaki and a boat cruise at Lake Toya for a break. The intensive lectures continued on the Sapporo campus from the eighth day.

During the course, graduate students were divided into groups to work on assigned tasks. Assisted by young researchers, the students put their heads together to devise possible solutions for the tasks by utilizing the knowledge learnt during the course. They later gave presentations on their topics.

"The subjects taught in this summer school are so diverse and interdisciplinary. It's not easy for me to go beyond my area of expertise, but I believe having discussions with people from other disciplines is very important and will help my future research," said one of the participants Zhongtong Wang from Xian Jiaotong University in China.

The summer school, with its intensive and diverse program, was highly successful in putting into practice current interdisciplinary frameworks of soft matter.

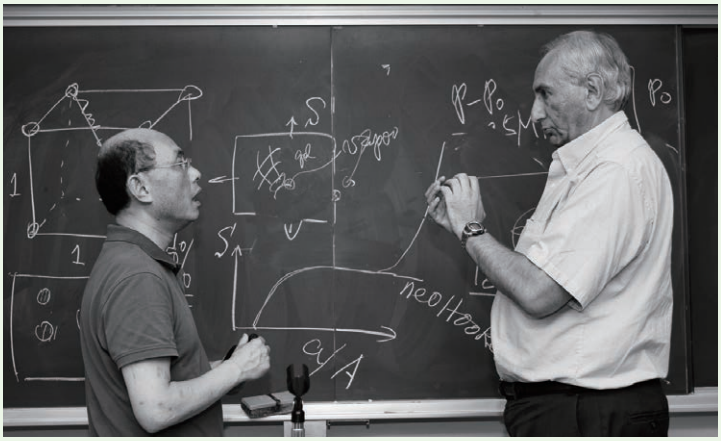


Photo taken by Tomas Sedlacik

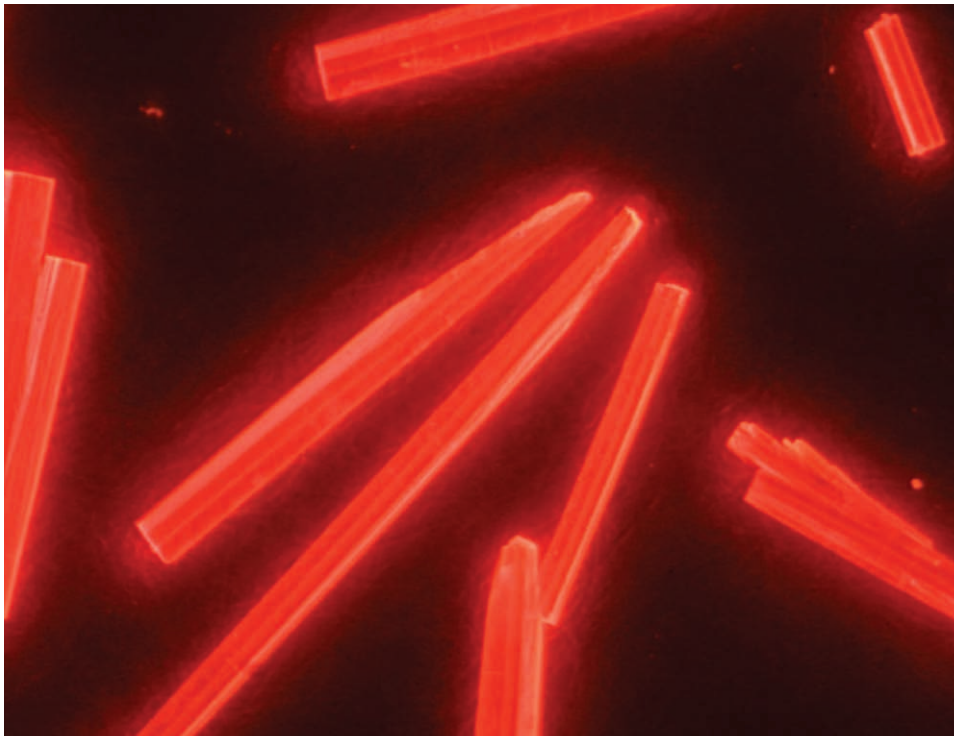
CHAPTER

2

Soft crystals and molecular machines

This chapter introduces the development of unique crystals that change color and other properties in response to external stimuli – research that could lead to the development of super sensitive sensors and smart responsive materials. Also featured is two scientists' quest to develop molecular machines that bring us closer to creating nano-robots that can be used in medicine and industry.

Crystals change color in response to vapor stimuli



Stimulus-responsive crystals emitting strong luminescence.

Generally, a crystal is the solidification of chemical compounds in which molecules are neatly aligned. It requires a considerable amount of energy to change the robust crystal structure of inorganic substances, but those among organic crystals – which likewise have orderly aligned molecules – undergo structural transformation with a small input of energy. Such molecular crystals, which exhibit clear visual changes in response to weak stimuli, are termed "soft crystals."

Masako Kato of Hokkaido University, who has long been fascinated with luminescent metal complexes, noticed something unusual when she was examining how platinum complexes become excited when irradiated with light.

"Platinum complexes diffused in a solution do not shine, but do emit light after they are crystalized with a regularly aligned structure, where platinum atoms are located with a short contact forming electronic interactions. That's why we were crystalizing platinum complexes," Kato said. However, in experiments they conducted in the early 2000s, they discovered a particular crystalized platinum complex didn't shine at all. "I was puzzled because the crystal, when I examined its structure, was supposed to emit light," Kato said.

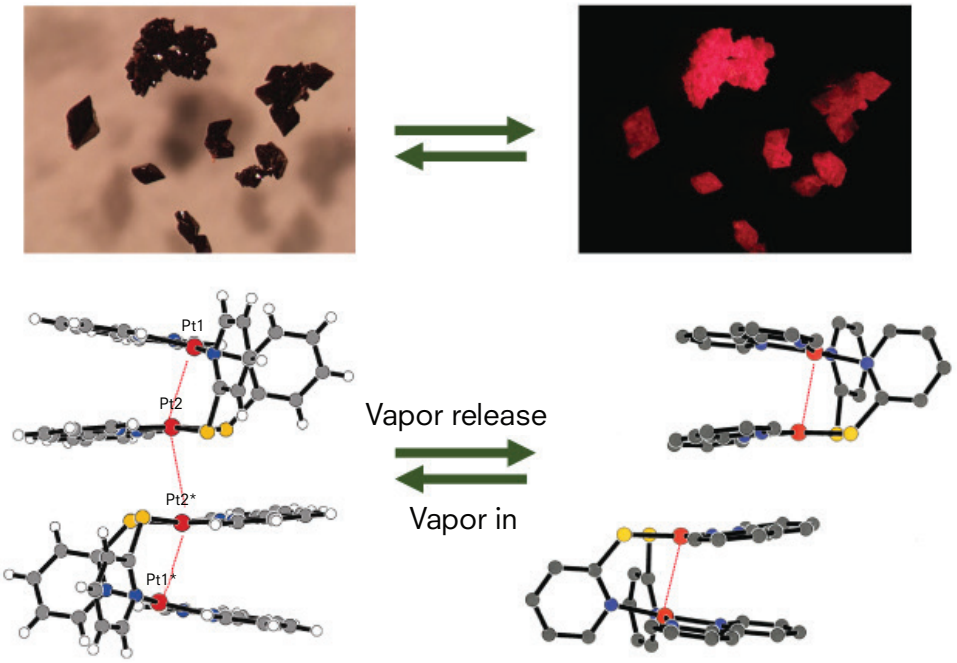
> "I was puzzled because the crystal, when I examined its structure, was supposed to emit light."

"I talked to my student who conducted the experiment about what went wrong, and left the crystals as they were. Surprisingly, after a few hours, we found the crystals started shining. We later found that acetonitrile had snuck into the crystals, and that was vital to understanding the phenomenon."

When crystalizing molecules in a solution, solution molecules can often get into the crystals, not as an impurity, but rather as constituents of the orderly aligned molecules in the crystal. For example, water molecules often enter the crystal structure. In the experiment conducted by Kato's team, acetonitrile – which was used as an organic solvent – penetrated the crystals and prevented them from shining. When the temperature rose with light irradiation, the acetonitrile vaporized and allowed the crystals to emit light.

The reverse was also true. The crystal

Professor Masako Kato



The luminescence of crystals of a platinum complex, syn-$[Pt_2(pyt)_2(bpy)_2](PF_6)_2$, changes between dark-red and light-red forms with or without acetonitrile vapor, respectively. (Kato M. et al., *Angewandte Chemie International Edition,* August 30, 2002, Kato M., *Bull. Chem. Soc. Jpn* review, 2007)

> "Since we didn't know – and still don't – the principles behind the crystal's structural change upon the uptake of vapor molecules, the only option was to study how crystals of newly synthesized metal complexes changed when exposed to various kinds of vapor."

switched back to the non-emissive state immediately upon exposure to acetonitrile vapor. Platinum complexes are known to change their color and luminescent properties based on their metal-metal interactions. The team investigated possible structural changes in the crystal that causes the luminescent switch and found acetonitrile alters the spatial arrangements of platinum ions.

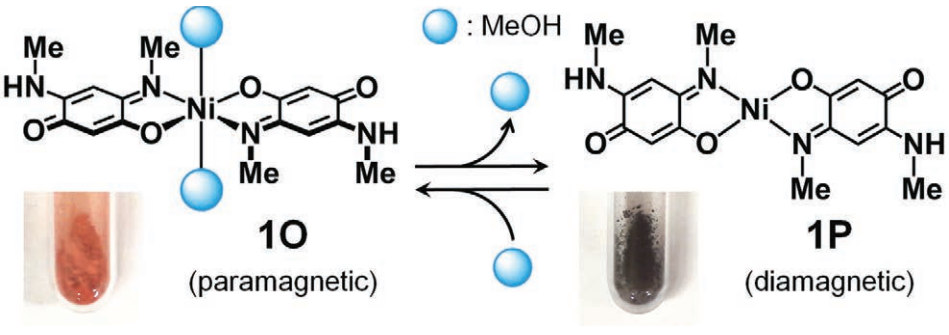
The discovery of a crystal that changes its property by the uptake of vapor molecules prompted Kato's team to begin researching vapochromism in earnest.

"Since we didn't know – and still don't – the principles behind the crystal's structural change upon the uptake of vapor molecules, the only option was to study how crystals of newly synthesized metal complexes changed when exposed to various kinds of vapor," Kato said. "We also made crystals with porous supramolecular structures to make it easier for vapor to penetrate into crystals."

During years of research, Kato's team succeeded in synthesizing metal complexes that exhibit various vapochromic responses. To cite one example, Kato developed a nickel (II) complex that changes color and magnetism by taking up alcohol. The complex changes from paramagnetism to diamagnetism when exposed to ethanol vapor, but changes from diamagnetism to paramagnetism when exposed to methanol, also a kind of alcohol but with a different toxicity to a living body.

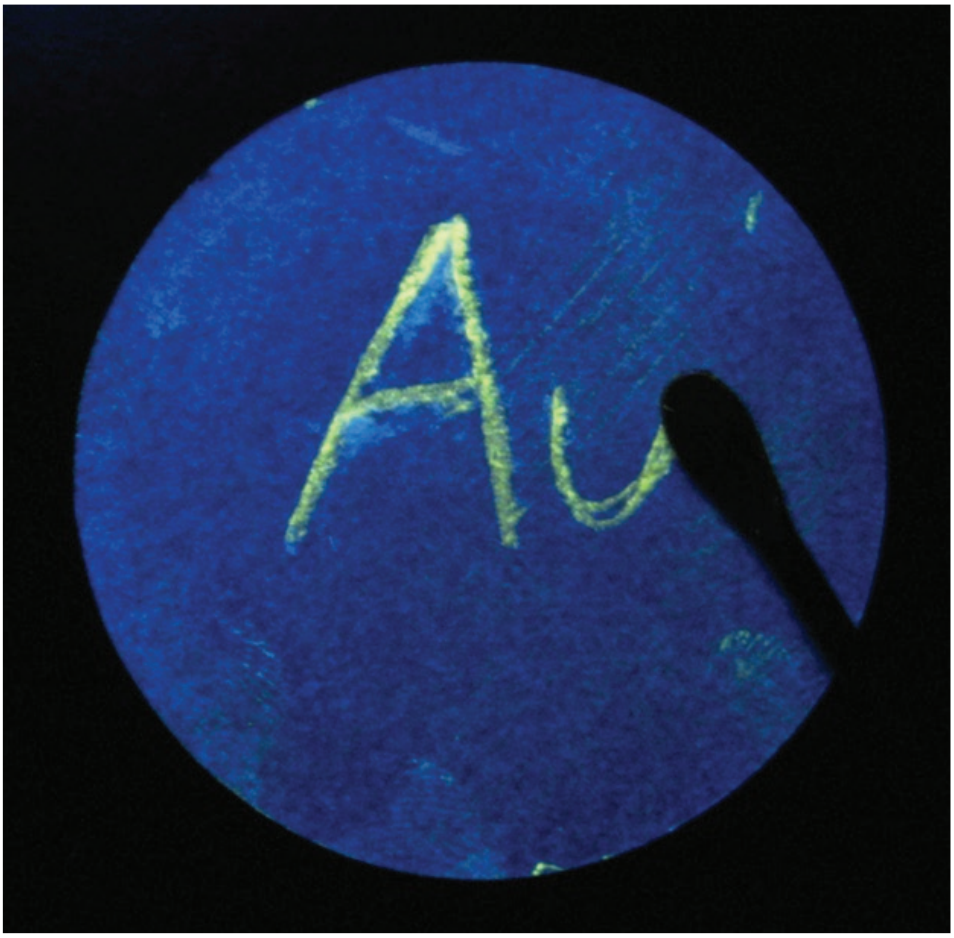
Such a system has high potential for applications in chemical sensors and smart responsive materials. Vapochromic materials capable of switching color and their spin state are particularly promising for developing rewritable optical and magnetic memory devices. Kato will continue focusing on fundamental chemistry research to unravel the mechanism that triggers vapochromism, which could open up avenues for designing a wide range of vapochromic materials.

Kato has launched a project to research soft crystals more comprehensively, together with Professor Hajime Ito of Hokkaido University, who is researching mechanochromism, in which the optical properties of crystals change upon mechanical stimuli. Kato, a synthetic chemist by training, plans to encourage the participation of researchers from different fields, such as computational chemistry and theoretical chemistry, in their efforts to understand the principles behind crystal structural change that happens with weak stimuli.



The nickel (II) complex that changes color and magnetism by taking up alcohol. (Kar P. et al., *Angewandte Chemie International Edition,* January 23, 2017)

Insatiable pursuit of new mechanochromic molecules



A mechanochromic compound on a filter paper changed its luminescent color from blue to yellow when scratched with a spatula.

The past decade saw rapid growth in the research of mechanochromic materials as interest soared in their mechanisms and potential applications. Mechanochromism is a phenomenon of color change that occurs when chemicals in solid state are subjected to mechanical stress such as grinding, rubbing, milling and crushing. The "smart material" could potentially pave the way for a wide range of applications such as bioimaging reagents, pressure-sensitive sensors and security inks that can detect tampering in packaging.

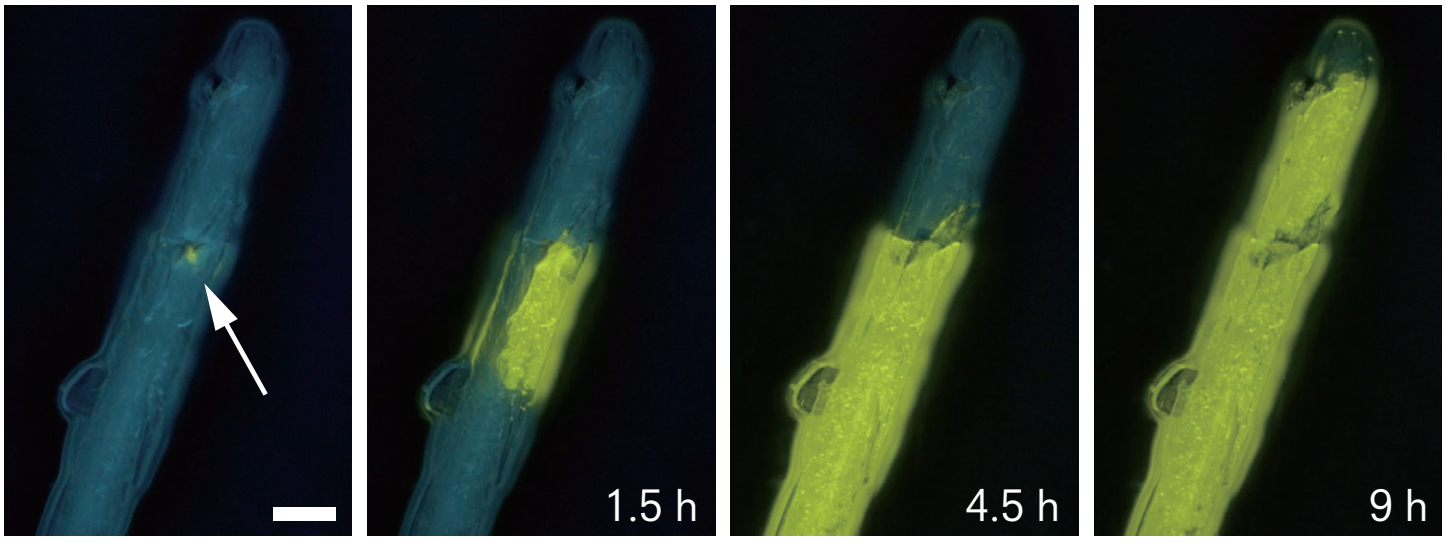
Hajime Ito of Hokkaido University's Organoelement Chemistry Lab is one of the world's leading scholars in the field of mechanochromism. Ito had been researching metal complexes as an academic interest, but it was only around 2007 when he started to research mechanochromism. One day, Ito asked one of his master's students to report on catalytic activity in a certain gold(I) complex.

"The complex did not show any catalytic activity at all, so we decided to investigate its crystal's luminescent property because it was widely known that gold(I) complexes emit light," Ito said."When we applied mechanical stimuli to the crystals under UV light, a luminescent color change was observed. I was amazed and thought this would be an interesting subject to pursue."

In those days, little was known about which molecular crystals show mechanochromism, or how molecules should be crystalized to exhibit this property. It was almost impossible to predict what structure organic compounds would take when they are crystalized, let alone to conduct molecular design based on the principles behind mechanochromism.

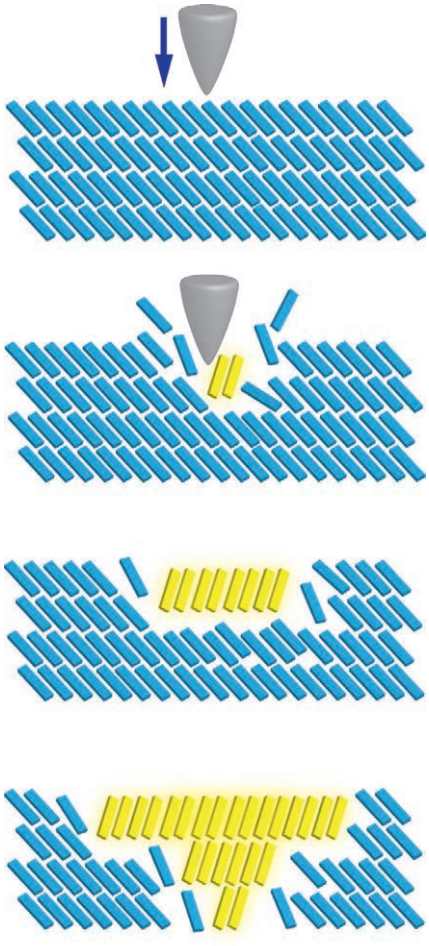
"When we applied mechanical stimuli to the crystals under UV light, a luminescent color change was observed. I was amazed and thought this would be an interesting subject to pursue."

Professor Hajime Ito



A small pit (white arrow) was introduced by pricking the fixed sample of phenyl(phenyl isocyanide) gold(I) complex with a needle. The phase transition gradually spread over the entire crystal after 9 hours and changed its color. (Ito H., et al., *Nature Communications,* 2013)

Crystals of numerous types of gold(I) complexes were made at Ito's laboratory and subjected to mechanical stimuli to find out how light wavelengths emitted by crystals will change. Ito's team was not trying to make elaborate gold(I) complexes,



The phase change first occurs at the initial contact area and subsequently progresses through the entire crystal, accompanied by a luminescence color change. (Ito H., et al., *Nature Communications,* 2013)

but those with a simple structure with some chemical modifications. The aim was to identify a law governing mechanochromism to find out which molecules possess this property.

Molecular domino transformation discovered

After extensive experiments, Ito's team discovered a phenomenon called "molecular domino transformation" in which a small stimulation can change the molecular level structure, setting off a phase change of the crystals. This phase change is amplified through a self-replication mechanism, causing a drastic change in the crystal properties.

"So far, around 500 mechanochromic molecules, including ours, have been reported," Ito said.

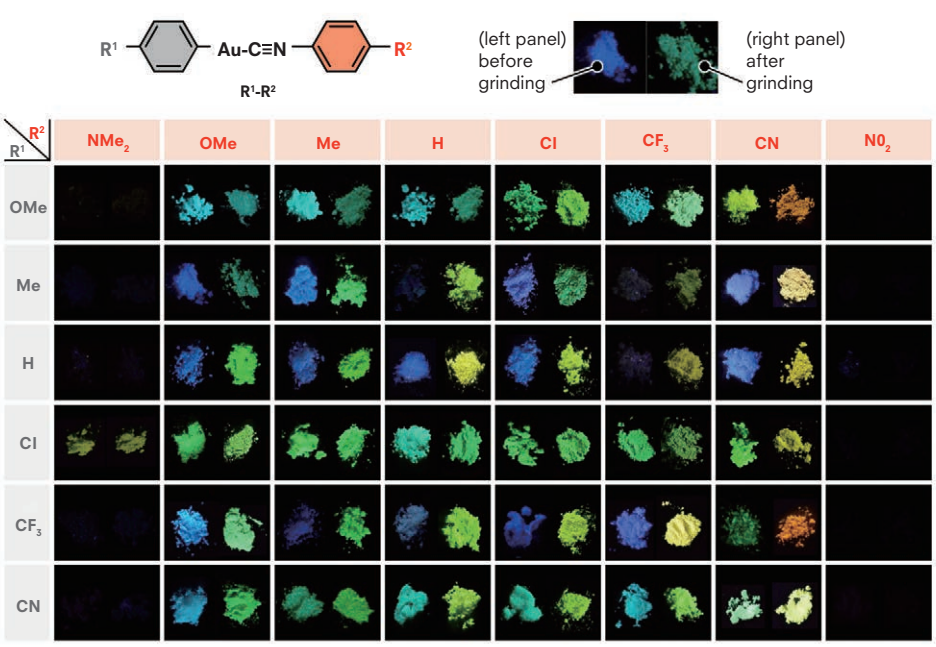
"Of them, 90 percent involve the transformation from crystals to amorphous solids, which is a non-crystal state. The phenyl(phenyl isocyanide)-gold(I) complex we developed, on the other hand, exhibits a crystal-to-crystal phase transition triggered by a small mechanical stimulus. We observed the domino transformation for the first time in 2013."

> "Theoretically speaking, it could lead to the development of a supersensitive sensor that can detect any change occurring even in a single molecular level."

The team found a rapid crystallization causes gold(I) complexes to be twisted, allowing them to transform to more stable, less twisted crystals upon a small stimulation. The phase change first occurs at the initial contact area and subsequently progresses through the entire crystal. The phase change was accompanied by a drastic luminescence color change caused by the switching of the intermolecular interactions.

This finding represented a significant step forward because Ito's team was able to shed light on one aspect of mechanochromism, which had long been shrouded in mystery. "Theoretically speaking, it could lead to the development of a supersensitive sensor that can detect any change occurring even in a single molecular level," said Ito. "Furthermore, the results can be used to help prevent medicines and organic semiconductors from degrading due to small external stimuli."

In 2016, Ito's team synthesized 48 organic compounds containing gold atoms or gold(I) isocyanide complexes – 28 of which were found to be mechanochromic, emitting changing colors such as blue, green, yellow



Forty-eight compounds containing gold atoms or gold(I) isocyanide complexes were developed by Ito's group, 28 of which were found to be mechanochromic. (Seki T. et al., *Journal of the American Chemical Society*, May 10, 2016)

and orange upon stimulation. Detailed analyses of the crystals revealed various molecular arrangements as the key to understanding their luminescent properties.

Since then, Ito's team has been able to strategically conduct molecular design – albeit roughly – based on these molecular analyses, resulting in the successful synthesis of a string of new mechanochromic molecules.

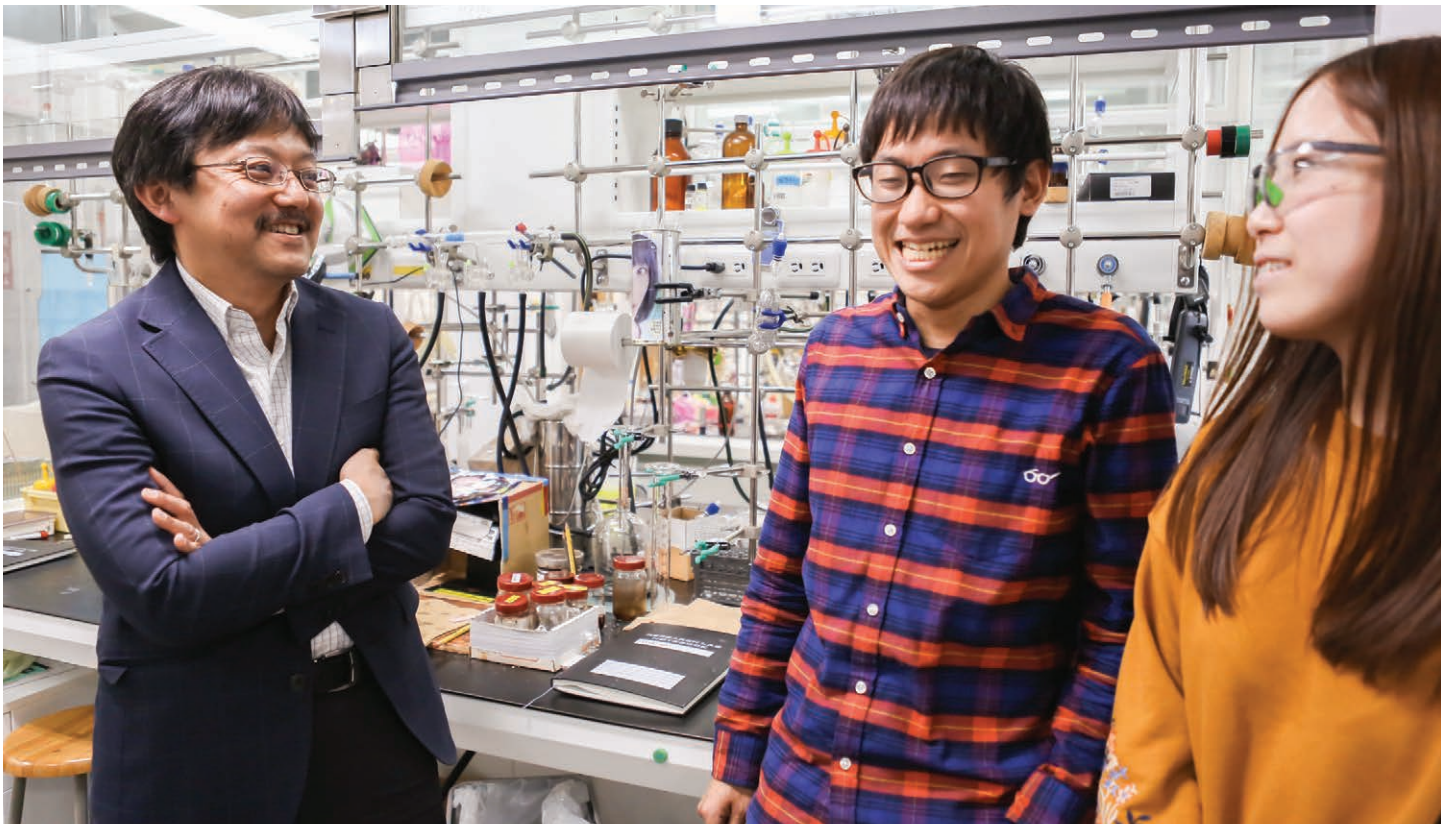
Emitting invisible light after being ground up

In 2017, the team found a gold compound called 9-anthryl gold(I) isocyanide complex, which produces a visible blue light but emits invisible infrared when ground to a fine powder. This was the first time a mechanochromic molecule was found to emit invisible light after being ground up.

"We examined how the light wavelength changes when gold atoms in gold(I) complexes bond with phenyl, naphthyl or anthryl groups, on the assumption that the wavelength will become longer after a crystal structural change," Ito said. "All complexes we examined emitted light with a longer wavelength, but the complex that bonded with an anthryl group produced a much longer wavelength than we expected – changing from blue light to infrared."

Further research on mechanochromic molecules is necessary before material made of them can be used for practical applications. In particular, Ito said gold(I) complexes must be made durable and stable at room temperature. The gold(I) complexes he developed so far disassemble easily and must be stored in a refrigerator.

Ito intends to focus on fundamental research into mechanochromic molecules to unlock more of their mysteries and spearhead global efforts to unravel the principles governing mechanochromism.



SOFT MATTER USED HERE

Separator

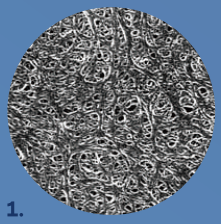
Unsung hero for storage batteries

by Asahi Kasei Corporation

AsahiKASEI

It is said that the history of the battery begins with the invention of the first electric battery made by Italian physicist Alessandro Volta in 1799. In 1859, the lead-acid battery was invented, and in the 1990s came the lithium-ion battery (LIB) that now meets the demand for smaller and lighter rechargeable batteries for portable electronic devices, electric vehicles, and renewable energy such as photovoltaic solar energy accumulation.

The LIB performs charges and discharges by lithium ion transfer. It is comprised of a cathode, an anode, an electrolyte and a separator, which isolates the two electrodes. The separator is a thin film with many small pores which allow lithium ions to pass through freely. If a short circuit occurs, the separator melts and the pores close. This shut down function (fuse function) prevents major accidents and is fundamental safety technology that can be utilized in soft matter.



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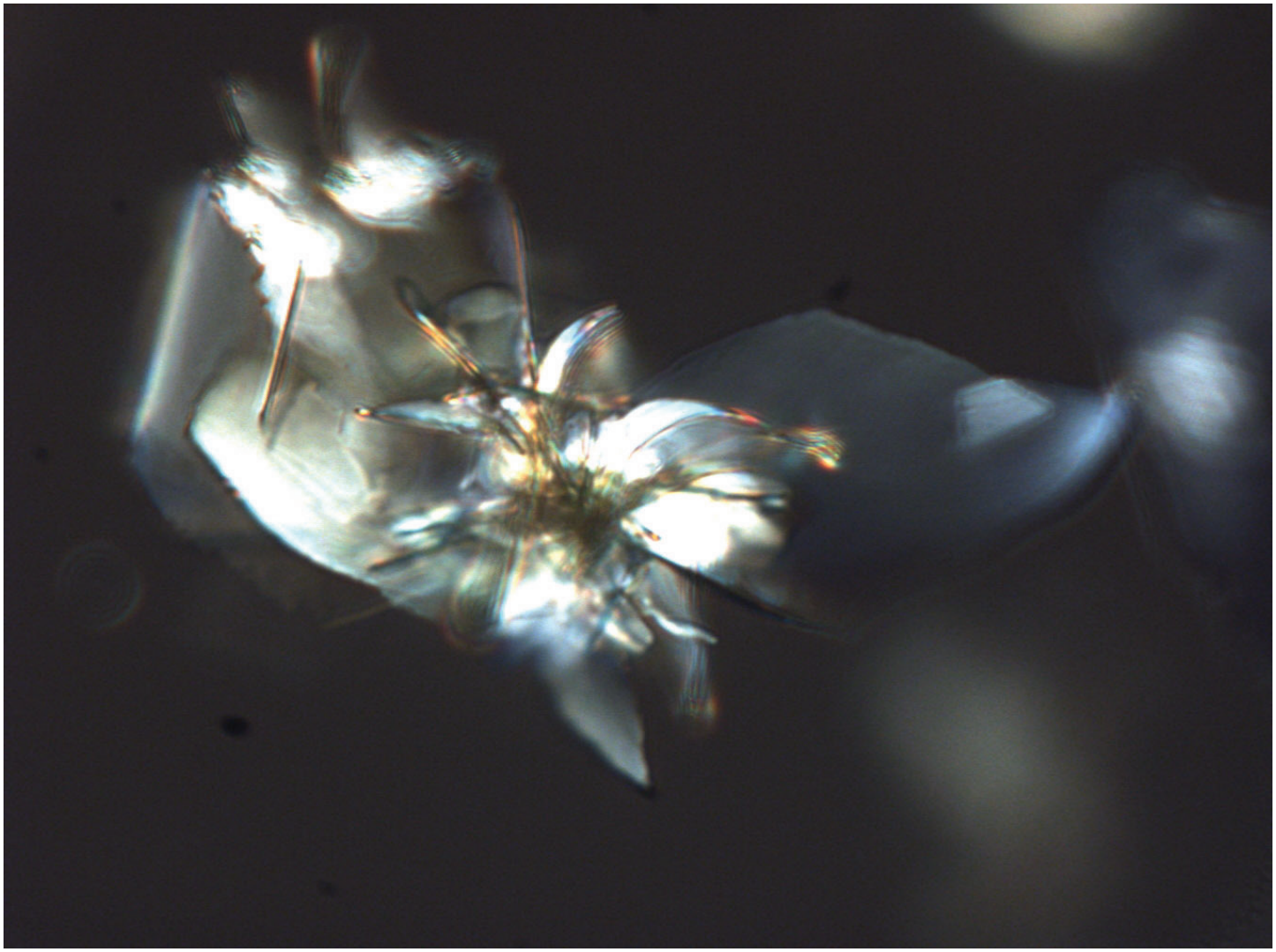
Upper right and below

1. Electron microscope view of the separator

2. Hipore™ LIB separator



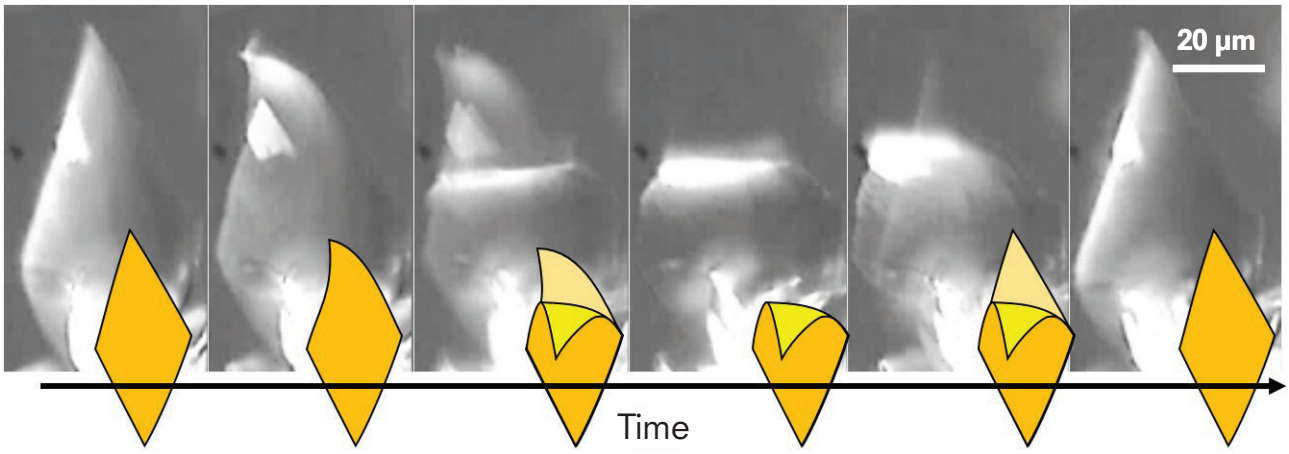
The crystal dancing under blue light.

The quest to make a synthetic molecular motor

Organic chemist Yoshiyuki Kageyama never imagined crystals would make a rhythmical motion until 2013, when one of his graduate students irradiated light on them on a whim.

The team was originally focusing on liquid crystals, not crystals, to make a molecular motor. "At that time, I firmly believed crystals would not move so easily," Kageyama said, recalling the day his student, Tomonori Ikegami, reported the incidental finding. "He wondered if he should even report the observation because it had little to do with his own project. I told him this was a huge discovery. Indeed, the crystals repeatedly fluttered when subjected to visible light."

> "At that time, I firmly believed crystals would not move so easily."



The crystal composed of azobenzene and oleic acid showed a repetitive fluttering motion under blue light.(Ikegami T. et al., *Angewandte Chemie International Edition*, May 19, 2016)

Kageyama started researching molecular machines two years earlier with the goal of producing a rhythmical motion in chemical compounds, something similar to heartbeats, cell division and molecular motors found in biological systems. For artificial molecular machines to act like biological molecular motors, they must move autonomously without external cues.

Despite the major discovery, the mechanism behind the fluttering motion remained a mystery. Kageyama and his research team spent another year trying to elucidate why crystals move when powered by visible light.

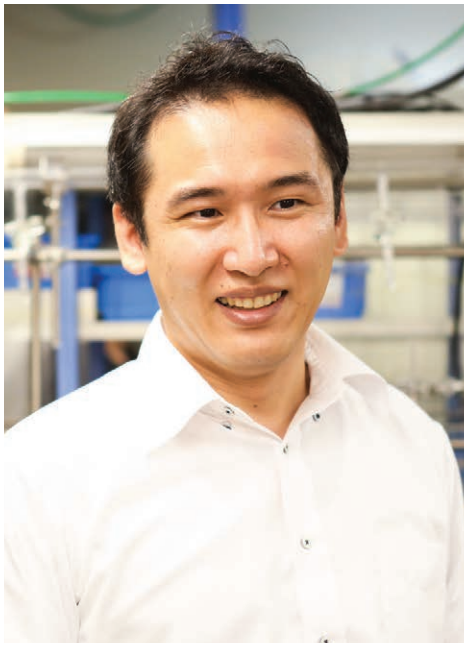
The team ultimately found that the crystal's phase transition is the key factor causing the fluttering motion. Their crystals were made of azobenzene, a chemical compound composed of two phenyl rings linked by a N=N double bond, which is commonly used for dye manufacturing, and oleic acid, generally found in cooking oil.

Azobenzene molecules take two structures, *cis* and *trans* isomers, repetitively converting from one form to the other under blue light. The team discovered the changes in the ratio of the isomers result in the phase transition of the crystal that causes changes in its shape. "As *cis-trans* transition repeats under the light, the crystal repeats the phase transition resulting in the oscillatory fluttering motion. The oscillation frequency increased when the light intensity was increased. Some crystals even exhibited swimming-like motions in water," Kageyama explained.

"We are pursuing chemical materials that can move autonomously. We call them 'active matter' as opposed to 'responsive matter,' which moves in response to changing stimuli from outside."

Receiving global attention

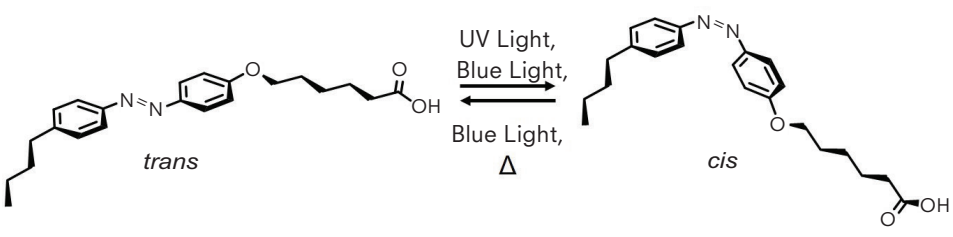
The research results were published in a German scientific journal, *Angewandte Chemie International Edition*, in July 2016. "It was the first time an artificial molecular motor had been reported," Kageyama said, "based on *cis* and *trans* transition of a simple molecule." The team's finding received global attention in the field and was covered by a number of news outlets. Kageyama introduced his finding to Bernard L. Feringa, who won the 2016 Nobel Prize in Chemistry with two other chemists for their design and production of molecular machines, when the Dutch chemist visited Hokkaido University in 2016.



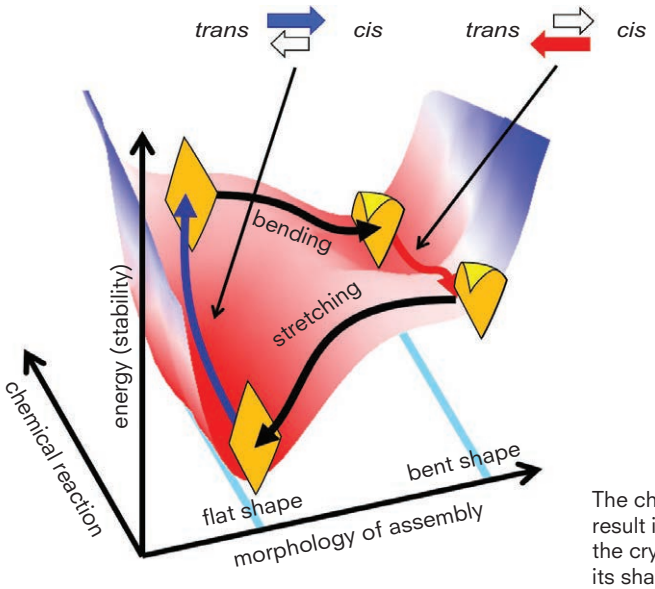
Assistant Professor Yoshiyuki Kageyama

"Dr. Feringa was surprised when he saw the phenomenon and asked why such a thing occurs," Kageyama recalled. "When I explained it in detail, he immediately understood. I hope I was able to give him some ideas."

"As far as my definition goes, an artificial light-driven molecular motor must continue to convert light energy into mechanical energy," Kageyama said. "This requirement has been met



Azobenzene molecules take two structures, *cis* and *trans* isomers, converting from one form to the other under blue light.



The changes in the *cis-trans* ratio result in the phase transition of the crystal, causing changes in its shape.

only by two motors so far – one made by us, and the other made by Dr. Feringa."

Daunting challenges remain

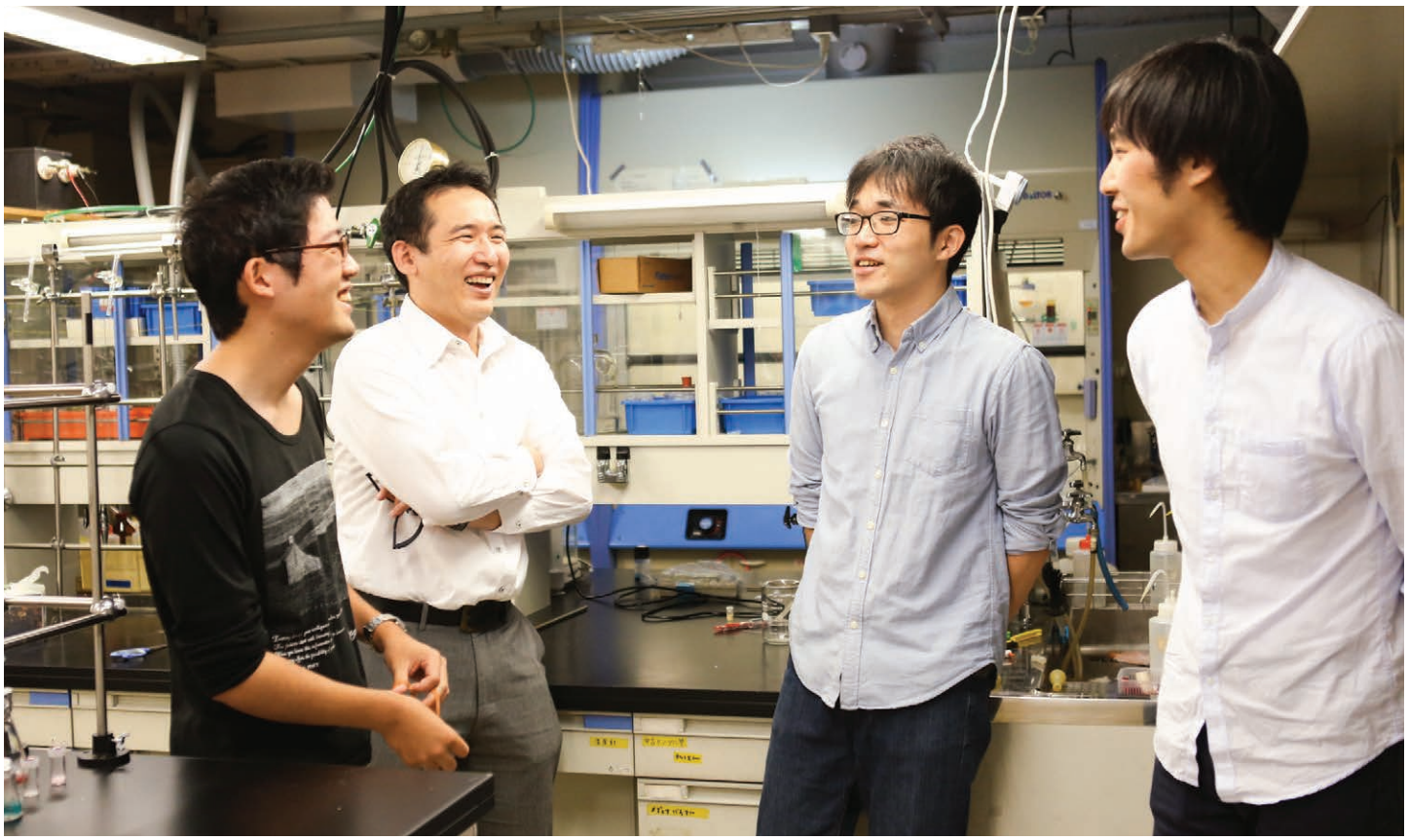
Many researchers around the world are intensively studying molecular motors, which could lead to the development of molecular robots capable of handling various tasks at a microscopic level – a potentially revolutionary breakthrough.

"In my view, molecular motors will not bring about a revolution equivalent to the Industrial Revolution because they function in a tiny world that the naked eye can't see," Kageyama said.

"But once the systems for molecular motors to work are more carefully designed, we could replace large machines with tiny ones. For example, I think molecular robots with the ability to move continuously and generate flows of liquid will be able to handle dialysis or seawater desalination very cheaply. Such robots might appear sooner than we think."

However, daunting challenges remain before molecular robots can be put into practical use. "Artificial motors are more easily designed for their functionality compared to biological motors, but new technologies are needed to assemble motors and other parts into a robot at the microscopic level," Kageyama said.

> "New technologies are needed to assemble motors and other parts into a robot at the microscopic level."



DNA computing brings molecular robot a step closer to reality

Associate Professor Akira Kakugo

In 2016, Akira Kakugo and his research team introduced a novel approach for sensing surface mechanical deformation of a soft material. One year later, Kakugo had not only the sensor but also a processor and an actuator – the three essential components for producing a molecular robot.

To measure the surface deformation of a soft material, the team utilized cellular proteins called microtubules and kinesins. Microtubules are filament-shaped proteins that serve as railways in the cellular transportation system, while kinesins are motor proteins that run on these railways. The team, however, took a reverse approach: kinesins are fixed on the surface of a soft material to allow microtubules to move around on them, like railways running on motors. This method allowed the team to successfully measure the surface deformation by detecting changes in the moving patterns of microtubules. "They move randomly but show different patterns as the surface deforms. The patterns reflect the direction and degree of deformation," Kakugo explained.

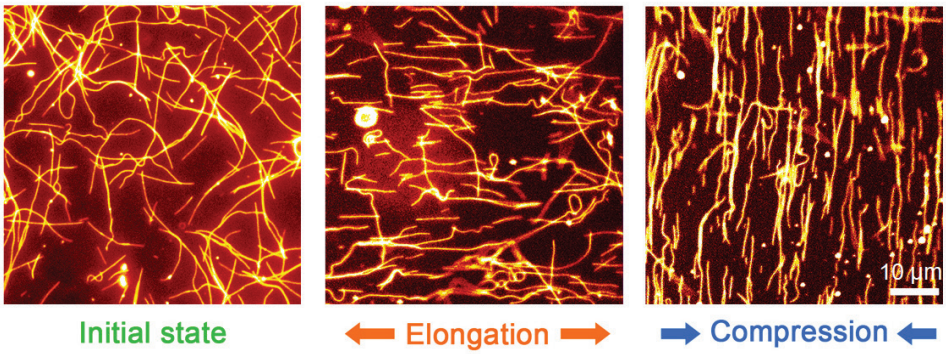
"A moving sensor was a novel concept when we published the paper in 2016," Kakugo said. "Since we got molecules that move autonomously and randomly in a test tube, the next question became how to control their random movement to produce collective motion."

Let DNA take control

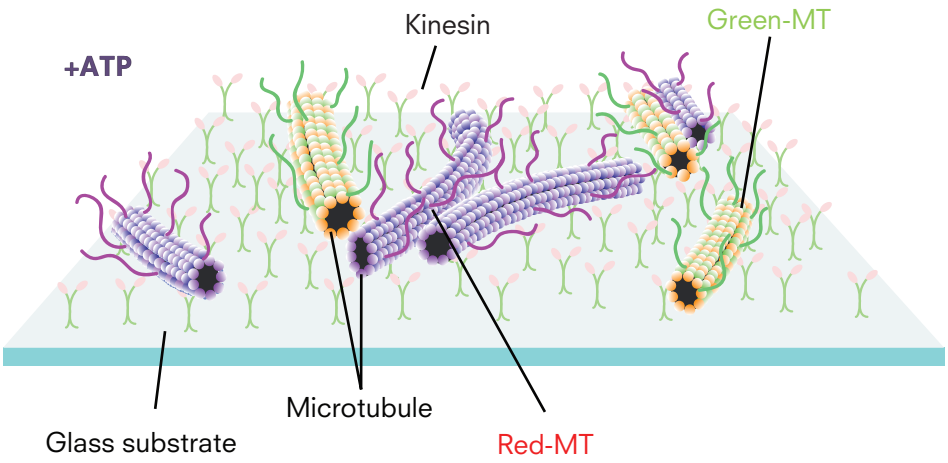
"Collective motion" is the key concept when they guide moving molecules. "When molecules act as a group, new properties that cannot be possessed by individual molecules appear, which we call 'emergence'," Kakugo explained. Such new properties are exemplified by division of labor, enhanced robustness and effectiveness, and flexibility that allows them to swiftly respond to a changing environment. Importantly, collective motion will enable molecules to work as an actuator, a device for moving something, when built in a molecular robot.

After testing several options, the team devised the idea of using a DNA computer to control the motion of microtubules. "Combining DNA with microtubules sparked a breakthrough in our research," Kakugo said. A molecular machine built on such a concept had been nonexistent when they reported the discovery in early 2018.

> "Since we got molecules that move autonomously and randomly in a test tube, the next question became how to control their random movement to produce collective motion."



The team successfully measured the surface deformation by observing changes in the patterns of moving microtubules. (Inoue D. et al., *Nature Communications,* Oct 3, 2016)



Microtubules (MT) interact with each other through DNA molecules while moving around on the kinesin motors. Microtubules were labelled with green and red fluorescence for observation. (Keya J. J. et al., *Nature Communications,* January 31, 2018)

But how can DNA, an essential element of life, control the physical movement of other molecules? In the team's experiments, DNA – homophilic molecules that bind to each other when they have complementary sequences – are attached simply to microtubules. Also added were DNA molecules, or input DNA, that intermediate interactions between DNA-attached microtubules.

When this system was introduced, DNA-attached microtubules stopped moving randomly but started swarming and self-organizing into different shapes that exhibited various patterns of movement. "We could make different patterns of collective motions by changing the programs in the DNA sequence, therefore changing the interactions between them," explained Kakugo. They also showed the swarming motion could be modulated by changing the rigidity of microtubules.

Focusing on collective motion of birds

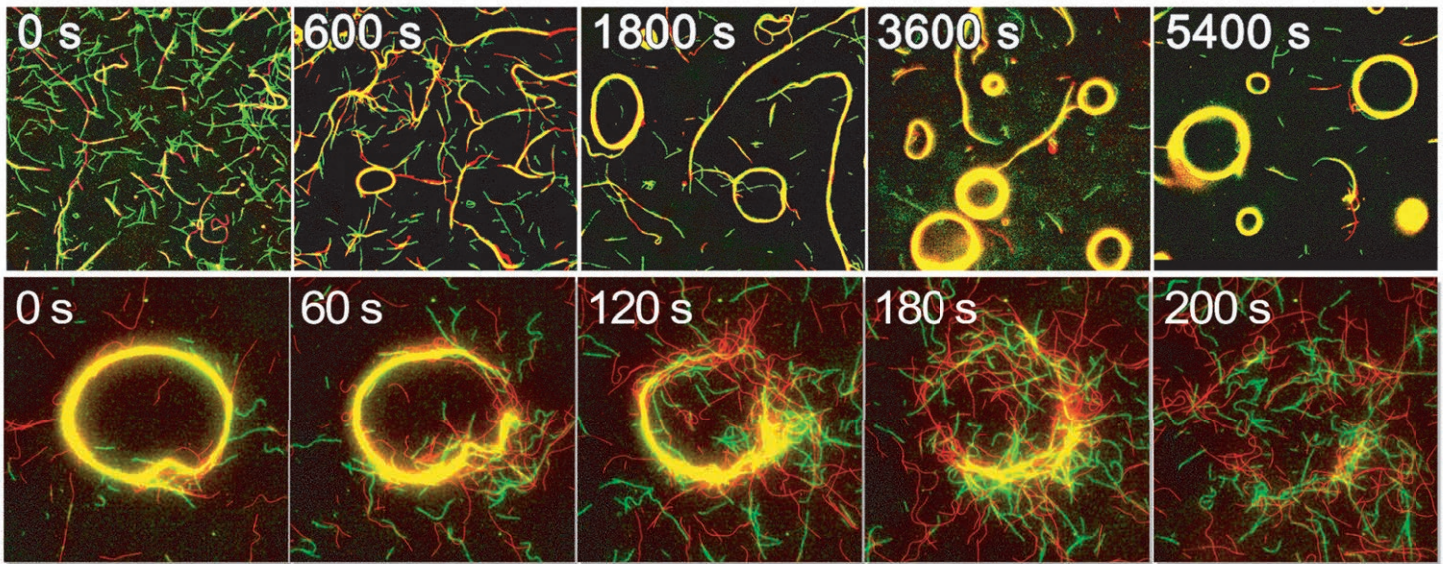
The breakthrough was made possible mainly because of his application of the Boids model, an artificial life simulation to replicate the aggregation motion of a flock of birds, herd of land animals or school of fish. Kakugo introduced the concept to DNA computing for the first time.

"DNA-attached molecules acknowledge their comrades through contact and the exchange of information," Kakugo said, showing a video to demonstrate how a flock of molecules make translational motions or rotational motions – clockwise or anticlockwise – like fish. To realize the flocking behavior, three factors in the Boids model – attraction, repulsion and alignment – had to be programed in the DNA sequence. His team also added azobenzene to the system, a chemical that binds to DNA and changes its structure in response to light. This enabled them to switch the DNA computer on and off by using light. (See a related movie at https://goo.gl/JVmXXV.)

Learning from a flea

Kakugo is now trying to build a system in which actuators are hierarchically ordered to enhance their scalability, complexity of movements and intelligent behavior. "The concept might be easier to understand if you imagine the Transformers

> "When molecules act as a group, new properties that cannot be possessed by individual molecules appear, which we call 'emergence'."



The flexible (low rigidity) microtubules formed swarms with circular motions (top). A swarm of microtubules was disassembled by adding input DNA with a certain sequence (bottom). (Keya J. J. et al., *Nature Communications,* January 31, 2018) See related movies at https://goo.gl/dfDLje.

(Photo: xpixel/shutterstock)

The team applied the Boids model to DNA computing, an artificial life simulation to replicate the aggregation motion of a flock of birds, herd of land animals or school of fish.

> DNA-attached molecules acknowledge their comrades through contact and the exchange of information.

or Microbots (in Big Hero 6) featured in U.S. movies," he said.

To attain this goal, he has to increase the number of sensors from the current one, a light sensor, to make it behave intelligently. A temperature sensor is a prime candidate for the next step.

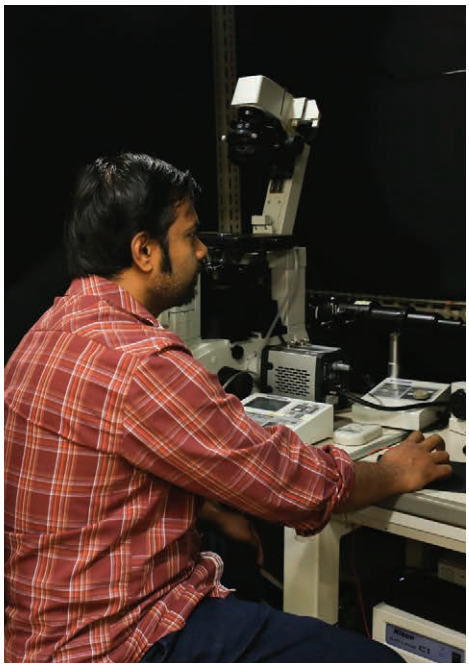
"A flea is a primitive creature, but it has three sensors, for light, temperature and butyric acid," Kakugo said. "It climbs up a tall tree when sensing light, jumps off the tree when sensing butyric acid in animal perspiration, and bites when sensing a certain temperature on the animal. That's how fleas can suck blood. With only three sensors, they appear to be behaving intelligently."

More challenges lie ahead

Although research into molecular motors has made considerable progress, Kakugo has identified several challenges that must be overcome before they are put into practical use.

First, researchers must boost the robustness of biological materials for use in medical fields and industries "Present actuators based on biomolecules are prone to degrade, so we might be able to start with a disposable motor for practical use to spearhead ensuing research," Kakugo said.

It is not easy, however, to engineer matter that moves actively in the current academic framework. The discipline of physical chemistry handles matter with equilibrium dynamics, but Kakugo handles active matter that moves autonomously with nonequilibrium dynamics, in which energy and substances come and go. "I think we must establish a new interdisciplinary framework for active matter if we want to see major advances in this field," he said. "To realize life-like behavior of molecular robots, incorporating algorithms of artificial intelligence would be particularly exciting."



COLUMN

From nonlinear physics to ethology in active soft matter

Professor
Toshiyuki Nakagaki

Director, Research Institute for Electronic Science, Hokkaido University
2008 and 2010 Ig Nobel Prize awardee

The aim of "physical ethology"—a term of our own creation that is not yet widely used—is to apply physical methods to ethology, or the study of animal behavior.

In my case, focus goes to the basic unit of life—the cell—primarily using unicellular organisms such as amoebas and ciliates as materials in our models. In their own way, these organisms exhibit context-dependent behavior within complex environments. They learn from periodic events and spatial configurations, solve mazes, and attempt to exhibit individuality.

While we have known for over a century that unicellular organisms possess an astounding variety of high-level capacities, insights into the inner workings of these capacities have been few and far between. Yet recent developments in cell physiology have put us closer to understanding their pivotal inner workings: The dynamics of intracellular actomyosin in amoebas and the dynamics of membrane potentials that control ciliary beats in ciliates for examples. Thus we are on the verge of seeing the possibilities of physical ethology come to fruition.

Cell bodies and the environments that envelop them are soft, wet, and highly variable. Conventionally, rheology has been used as the basis for formulating these dynamics. In addition, with an emphasis that the subjects are in non-equilibrium states, other methodologies such as dissipative structure theories and nonlinear physics that can handle spontaneous formation of orders and patterns are needed.

Nonlinear physics is used for interpreting complex or animate phenomena on everyday scales that can be applied across a wide variety of conventional fields, from the movements of unicellular organisms to the phenomena of human societies. Naturally, nonlinear physics can also be applied to the microscopic world or the vastness of cosmology. It extends beyond the boundaries of conventional physics, which is why it is often referred to as nonlinear science.

Mathematically speaking, independently of physical entities, all physical states exhibit common behaviors when moving within complex interactions. Professor Yoshiki Kuramoto[*1], one of the founders of nonlinear science, called this an "invariant (immutable) structure" when discussing his own theory of reduction.

Unexplored fields are still being opened up on scales that are more familiar to us, or rather, on scales that are completely divorced from quantum mechanics and particle physics. These fields are often underestimated or not considered to be essentially new areas of scientific inquiry, but that is not the case.

As an example of this kind of phenomenon, let me examine the oxidation-reduction reaction of malonic acid, which is also known as a Belousov-Zhabotinsky reaction, or BZ reaction. When a thin layer of reaction solution is poured into a petri dish about the size of the palm of a hand and let stand, the oxidation state of the reaction solution becomes spatially heterogeneous, and spiral patterns appear in the areas of heterogeneity. Shockingly, these spiral patterns start to rotate and move around in the petri dish. These rotating spiral waves arise out of the coupling of a nonlinear chemical reaction rate and a diffusion phenomenon.

Such rotating spiral waves are not only encountered in BZ reactions, but can be seen in totally different systems, such as a heart that beats faster even in rest. When a heart beats normally, a contraction wave disseminates throughout the entire organ, but if for some reason this wave turns into a rotating spiral wave, it can create a state of tachycardia

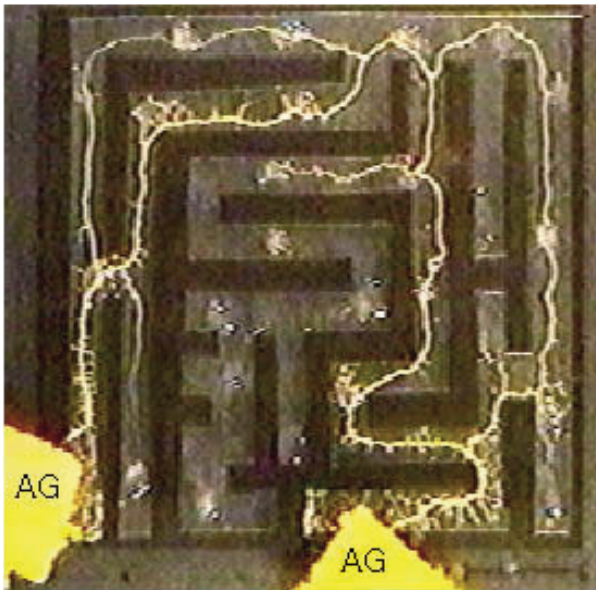
*1 Professor Yoshiki Kuramoto once held a special appointment at Hokkaido University and is currently a professor emeritus at Kyoto University.

and soon after a state of fibrillation, otherwise known as a heart attack. This rotating spiral wave occurs when the chemical reactions that promote muscle contraction coupled with diffusion of reactants and products throughout the cardiac tissue.

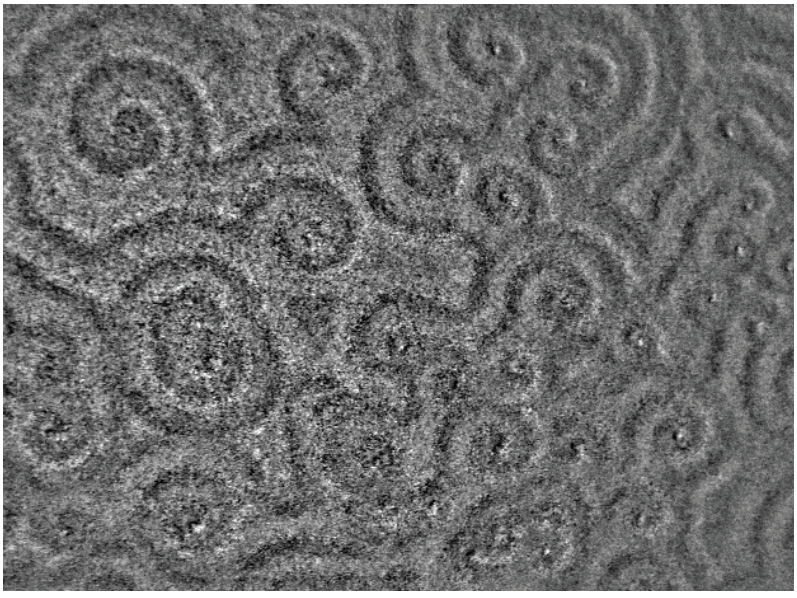
Another example is a type of soil-dwelling amoeba called a cellular slime mold. In states of starvation, several thousand amoebas congregate to form a fruiting body (structure that holds a large number of spores on top of a stalk) to complete the life cycle. Amoebas—unicellular organisms—are able to exhibit this kind of social behavior because of the rotating spiral wave motions that groups of amoebas create. The cells attract each other and communicate by releasing chemical compounds. The nonlinearity and diffusion of these release reactions combine to create waves of collective motion in which cells gather around rotating spirals.

Amoebas that live in the ground and chemical reactions that occur in petri dishes may play a big role in solving the fundamental dynamics involved in heart attacks, which are a major problem, both medically and for society. The strange depths of nonlinear science are what link these profound mysteries, demonstrating one of the possibilities of the soft matter sciences.

To come back briefly to physical ethology, the source of the ingenious social behavior of soil amoebas is the rotating spiral wave. These waves are a kind of information-processing mechanism comprising entire groups of amoebas, and can offer clues for explaining algorithms of natural intelligence. This is another area of possibility the soft matter sciences will be taking on.



Maze-solving by an amoeboid organism
(Nakagaki, T. et al., 2000, *Nature* 407, 470)



Spiral patterns appear when many cellular slime mold amoebas aggregate to become multicellular

SOFT MATTER USED HERE

lens

The parts of the human eye

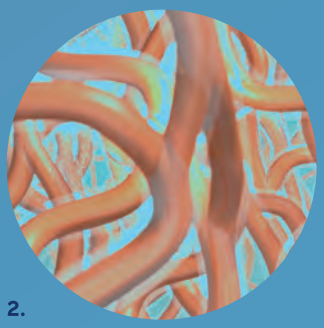
by Menicon Co., Ltd

Menicon

1.

CONTACT LENS (SILICONE HYDROGEL)

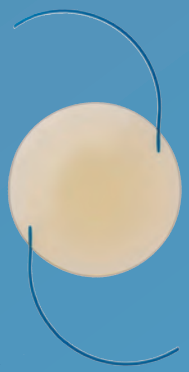
The idea of contact lenses was first thought of by Leonardo da Vinci during his experiments in the early 1500s. There have been many prominent scientists involved in the development of contact lenses, with the material evolving from acrylic resin to hydrogel, and now to silicone hydrogel. The amphiphilic gel material shown here has a co-continuous structure involving a mixture of water and water-soluble substances which are malleably interweaved — exemplifying the potential of soft matter.



2.

Above and right

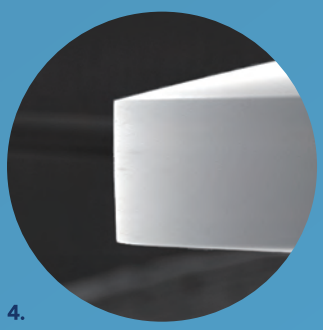
1. Contact Lens "PremiO"
2. Visualization of polymer structure



3.

INTRAOCULAR LENS (IOLs)

Lenses were clouded by cataracts which had been long been removed by surgery. In 1949, English ophthalmologist Sir Harold Ridley noticed that when splinters of Perspex (acrylic sheet) from aircraft cockpit canopies became lodged in the eyes of wounded pilots they did not trigger rejection, leading him to propose the use of IOLs. Since the development of materials using PMMA, insertion surgery has been applied in various countries. The material has continued to be developed and is now replaced by acrylic foldable intraocular lenses which have excellent flexibility, enabling improved cataract surgery.



4.

Above and left

3. Intraocular lens "AvanseePreset"
4. Electron microscopic view of IOLs (100x)

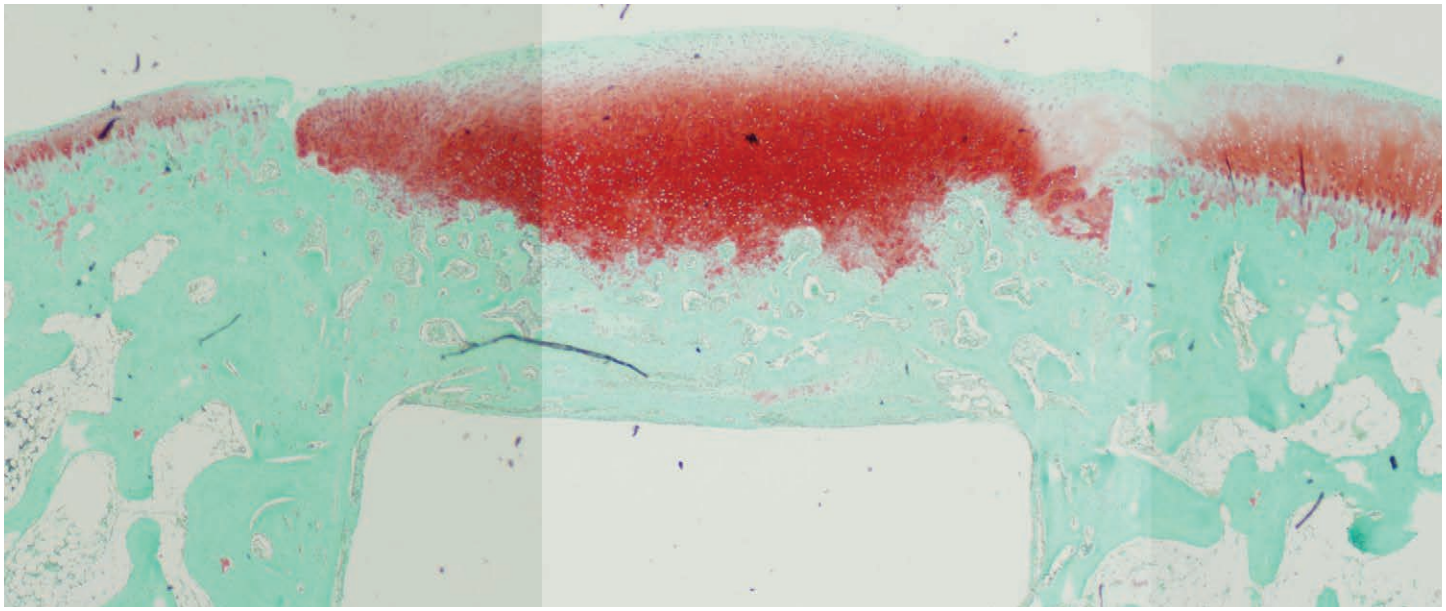
CHAPTER

3

Hydrogels in medicine

Hydrogels, which are soft yet tough, share properties similar to living tissues, making them an ideal substitute for cartilage. Moreover, recent studies have demonstrated that hydrogels can influence cell fates. They can induce the regeneration of cartilage tissue in vivo, which had been regarded impossible, and even reprogram cancer cells into stem cells. This chapter sheds light on the challenges to bring the fruits of hydrogel research into medicine.

Hydrogels as inducer of cartilage regeneration



Cartilage tissue induced by the DN gel (Yasuda K. et al, *Macromolecular Science,* April 8, 2009)

Kazunori Yasuda, an orthopedic surgeon of the Hokkaido University Hospital, had long been looking for a material suitable for cartilage substitute to treat orthoarthritis when he encountered the new hydrogel in 2003. It was Professor Yoshihito Osada and his Associate Professor Jang Ping Gong who visited Yasuda and asked whether the newly developed hydrogel could be used for medical purposes. At that time, Osada was conducting research on various gels, and Gong had succeeded in making double-network (DN) gels which were extremely tough and defied the notion of gels being weak.

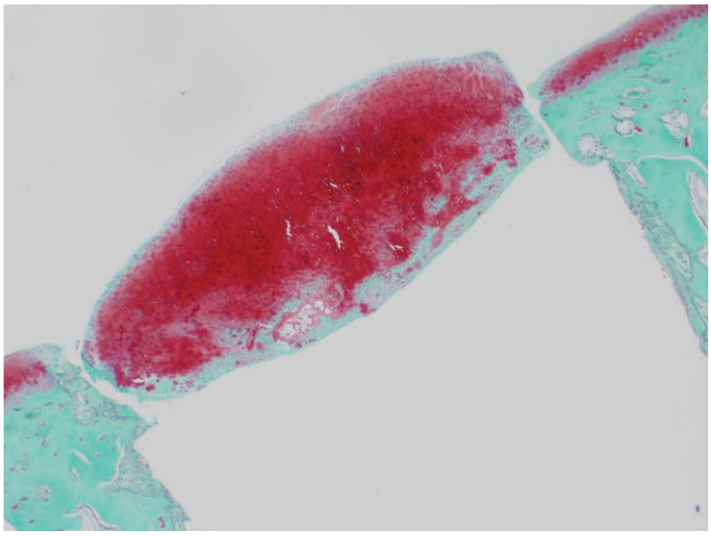
"When I touched the gel, I instinctively thought this material is cut out for a cartilage substitute. It had a low sliding friction and high elasticity," Yasuda said. This encounter set out his research on the DN gels as biomaterials.

During the years of attempts to optimize the DN gel, however,

> "When I touched the gel, I instinctively thought this material is cut out for a cartilage substitute. It had a low sliding friction and high elasticity."

Yasuda came across an even more astonishing discovery. "It was a total coincidence," Yasuda recalled. His research team was conducting in vivo experiments, implanting a DN gel plug as an artificial cartilage, consisting of poly-(2-acrylamido-2-methyl-propanesulfonic acid; PAMPS) and poly-(N,N'-dimethyl acrylamide; PDMAAm), into an osteochondral defect created in a rabbit knee. It was to evaluate whether the implanted artificial cartilage has detrimental effects on the normal cartilage on the opposite joint surface. "When I saw what my student said was a 'failed sample,' a thick mass of regenerated cartilage was growing out on the DN gel."

Professor Kazunori Yasuda



A thick mass of cartilage-like tissue growing out of the defect in a rabbit knee.

In the failed sample, the patella, or the kneecap, on the opposite side was dislocated, allowing the cartilage-like tissue to grow on the DN gel. "Since it had been believed hyaline cartilage could not spontaneously regenerate in vivo, I was really startled," Yasuda said.

Verify cartilage regeneration in vivo

Although Yasuda was first interested in the DN gel as a cartilage substitute, the unexpected discovery prompted the team to further investigate the gel's regenerative property. In their following experiments, a plug of PAMPS/PDMAAm DN gel was implanted at the bottom of a large osteochondoral defect in a rabbit knee joint, leaving a cavity above the gel vacant to allow tissue regeneration.

Two weeks after the implantation, a cartilage-like tissue appeared near the cavity wall. The regenerated tissue continued growing, and, at four weeks, reached a sufficient volume to fill the defect. On the other hand, the untreated defect was filled with fibrous and bone tissues even after four weeks.

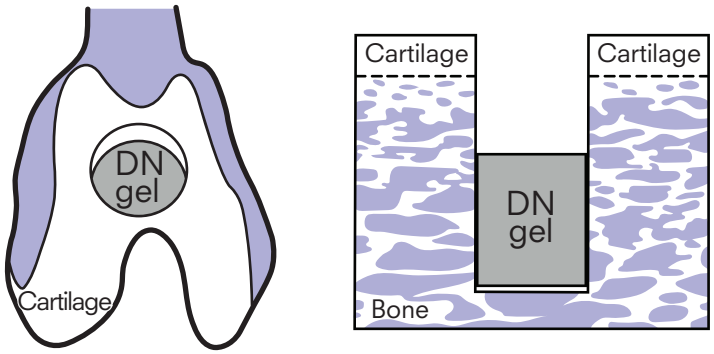
The team then examined gene expressions in the regenerated cells, which confirmed high expressions of proteoglycan, type-2 collagen, Aggrecan, and SOX9 mRNAs, indicating they were indeed cartilage cells. In 2009, the team published its finding in *Macromolecular Bioscience*. It was the first academic report that the DN gel could spontaneously regenerates hyaline cartilage. "Our discovery gave a significant modification to the commonly-established medical concept that cartilage cannot regenerate," recalls Yasuda.

In the following years, while finding the regenerated tissue has a similar gene expression profile to that of normal cartilage cells, the team also looked into the mechanism of regeneration. This research led to the recent discovery that the PAMPS gel, a component of the DN gel, activates TGF-β/BMP signaling pathway in mouse chondrogenic cells and this activation plays a pivotal role in the cartilage differentiation.

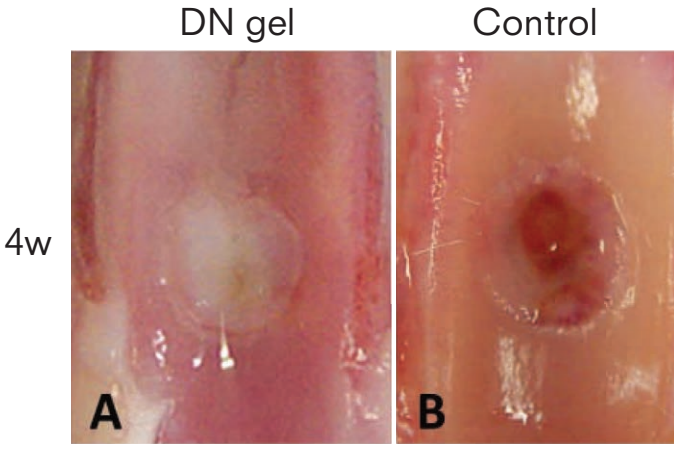
Most recently, to make a step towards a clinical research, Yasuda's team conducted experiments using a sheep model which proved the short-term efficacy of the cartilage regeneration strategy using the DN gel.

> "Our discovery gave a significant modification to the commonly-established medical concept that cartilage cannot regenerate."

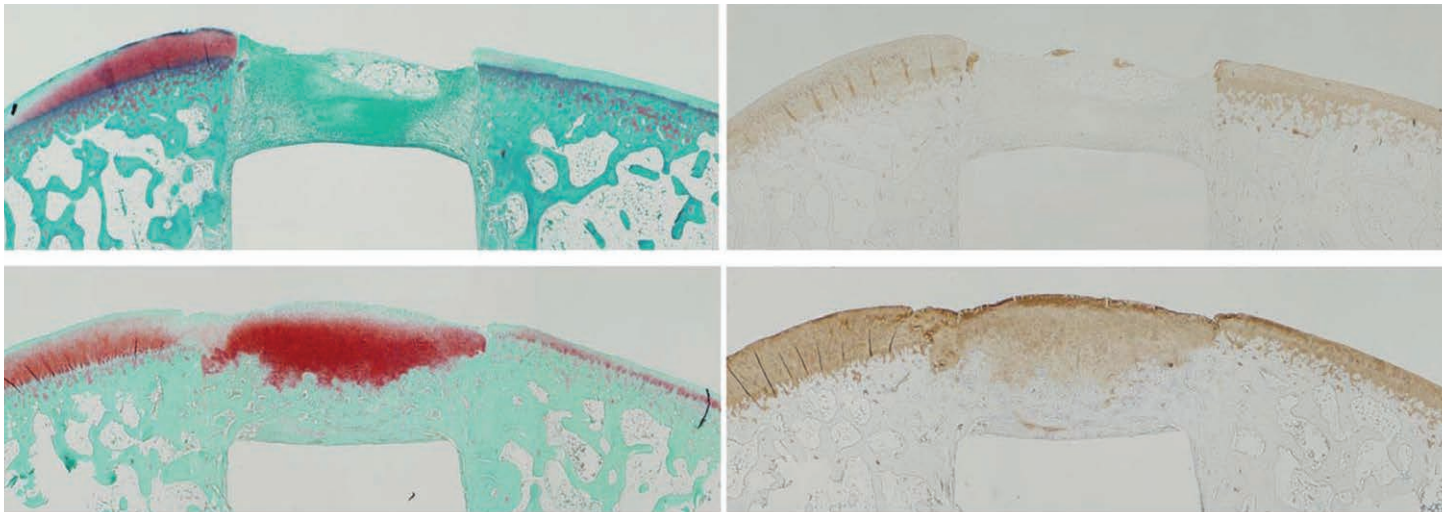
Going back to the beginning, Yasuda also continues to work on the DN gels as a cartilage substitute to establish a new treatment for orthoarthritis. Currently, his team conducts a pre-translational study with a company to develop an artificial cartilage. If such method is established, it will present a concept different from current treatments using tissue-engineered cartilage, cell-seeded scaffold-material, or acelluar polymer scaffolds with signaling molecules. With the dual properties of the DN gel, as substitute or inducer of regeneration, Yasuda is



A DN gel plug was implanted at the bottom of a osteochondoral defect in a rabbit knee joint, leaving a cavity to allow tissue regeneration.



A cartilage-like tissue filled the defect four weeks after the DN gel implantation. (Kitamura N. et al. *The American Journal of Sports Medicine,* April 1, 2011)



At four weeks (bottom panels), a cartilage-like tissue rich in proteoglycan (red) filled the defect and expressed the type-2-collagen (brown), which were not observed at 1 week (upper panels). (Yasuda K. et al., *Macromolecular Science,* April 8, 2009)

bringing novel strategies to articular cartilage treatments.

Promoting material genomics

Beside medical application, hydrogels has a major potentiality as a tool to unravel the mechanism of cellular phenomena and therefore contribute to basic research, according to Yasuda.

"Hydrogels are much simpler than a complex environment within the body, and yet able to elicit cellular responses. By using materials like hydrogels, we might be able to unlock the mystery of life much faster," Yasuda explained.

> "By using materials like hydrogels, we might be able to unlock the mystery of life much faster."

In fact, since 10 years ago Yasuda has been proposing what he calls "material genomics," which tries to exhaustively investigate changes in cells and gene expressions that occur at the contact with varying materials.

As an example for this, Yasuda cited a collaborating research led by Professor Shinya Tanaka to induce the creation of cancer stem cells with a DN gel and then to discover the mechanism involved in reprograming ordinary cancer cells to stem cells.

"I want students to know that materials can have unpredictable effects," Yasuda said. "I want them to broaden their perspectives as they conduct research, while working jointly with researchers from different fields. A new idea can lead to a completely unexpected result, engineering a breakthrough."

A breakthrough in the potential application of hydrogels as a cartilage substitute

Assistant Professor Takayuki Nonoyama uses a transmittance electron microscope.

Takayuki Nonoyama was asked to conduct research on a hydrogel that adheres to bones in 2013, right after he took up the position of specially appointed assistant professor at Hokkaido University's Laboratory of Soft and Wet Matter Science.

The person who gave him this research topic was Professor Kazunori Yasuda, an orthopedic surgeon at Hokkaido University Hospital, who has extensively researched the application of double network (DN) gel as artificial cartilage. As Japan's population grays, the number of people suffering knee pain due to cartilage abrasion or loss is rising, and one in five middle-aged and elderly people in Japan have osteoarthritis.

DN gels are tough yet soft and flexible, and their low sliding friction on solids makes them promising as materials for artificial cartilage. Yasuda's long-cherished goal is to develop a gel capable of bonding to bones so the gel can be fixed at the knee joint to function as cartilage, which does not regenerate spontaneously in vivo when damaged. One stumbling block was that DN gels usually have poor adhesion to solids because their main component is water – accounting for more than 90 percent of a gel's weight in some cases.

However, Nonoyama, a young scientist who as a graduate student

> It was quite surprising that osteogenesis penetrated into the HAp/DN gel region.

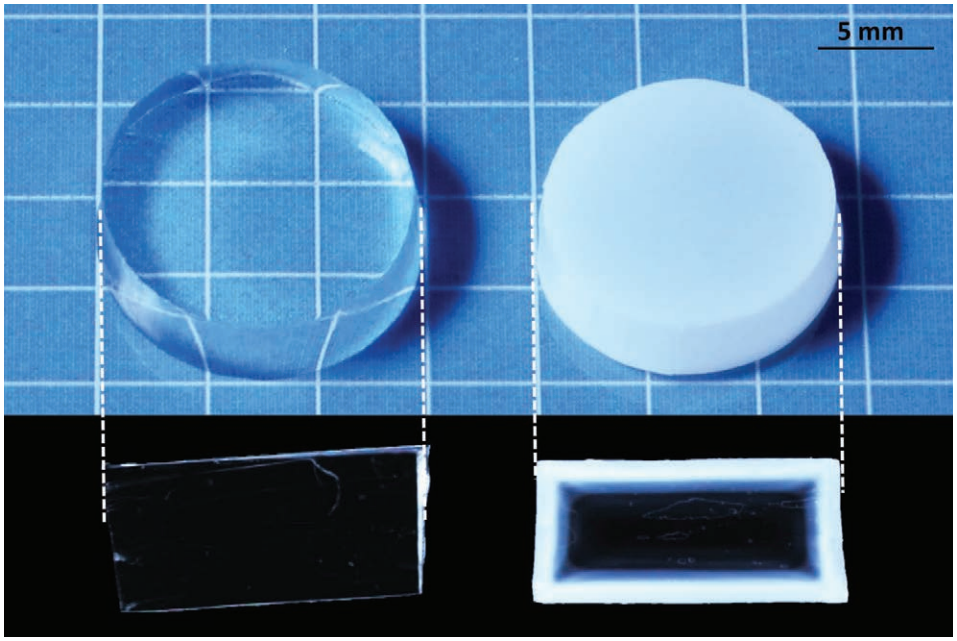
had researched inorganic compounds rich in biominerals, such as vertebrata bones and mollusk shells, immediately had an idea that could solve this problem. "I suggested coating the DN gel's surface with hydroxyapatite, which is the major inorganic component of bone," Nonoyama said.

Nonoyama might not have realized the magnitude of his proposal at that time, but the idea eventually led to a breakthrough that surprised many of his bosses and colleagues: the development of a hydrogel that strongly bonds to bones by inducing spontaneous bone formation in the gel's surface layer.

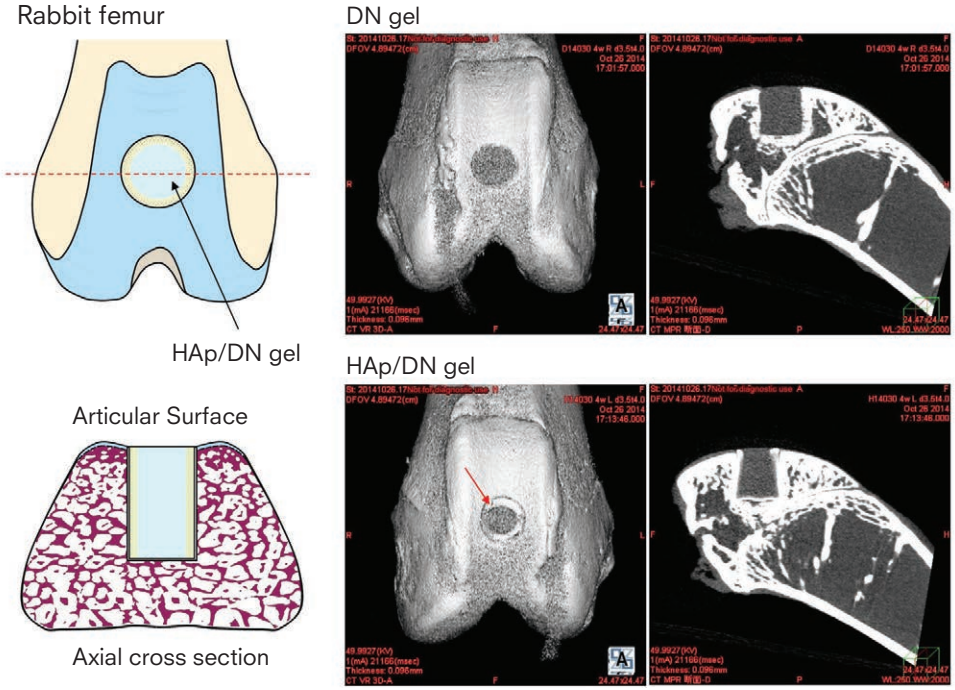
Putting an idea into practice

Nonoyama and other researchers selected a DN gel consisting of poly(2-acrylamido-2methyl propanesulfonic acid) as the brittle first network and poly(N,N-dimethylacrylamide) as the ductile second network.

But merely coating hydroxyapatite (HAp) on the DN gel would not be enough to strongly bond the gel with bones, so the gel likely would not stay fixed in the knee joint. Soft supporting tissues in the human body, such as cartilage and ligaments, are firmly attached to bones. To address this problem, Nonoyama alternately dipped the DN gel in solutions of calcium chloride and dipotassium hydrogen phosphate to obtain an HAp/DN gel. These ionized components of HAp could permeate the DN gel's surface while crystalline HAp could not.



Micro CT images showing a DN gel plug and a HAp/DN gel plug in a rabbit's femoral groove four weeks after implantation. Red arrow indicates integrated region of HAp/DN gel and bone tissue. (Nonoyama T, Wada S, et al., *Advanced Materials*, August 17, 2016)



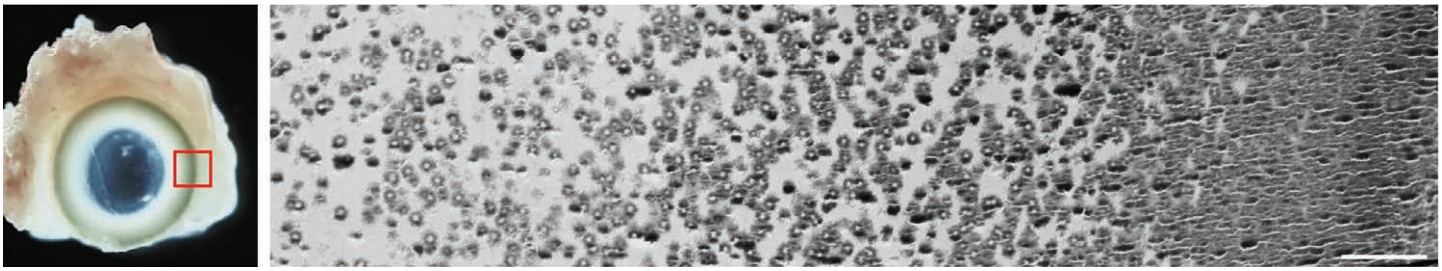
Micro CT images show implanted DN and HAp/DN gel has plugged into a rabbit's femoral groove four weeks after implantation. Red arrow indicates integrated region of HAp/DN gel and bone tissue. (Nonoyama T, Wada S, et al., *Advanced Materials*, August 17, 2016)

Spontaneous bone formation

The team conducted in vivo experiments to verify the HAp/DN gel's performance. The gel and uncoated gel were transplanted into defected bones in rabbits. Four weeks later, the team observed the HAp-coated gel had bonded very strongly to the bones, while the uncoated gel had not bonded at all. Observations by transmission electron microscopy into the gel's surface layer revealed the newly formed bone component in the defected area had penetrated into the surface layer, connecting the bone and the gel seamlessly.

"It was quite surprising that osteogenesis penetrated into the HAp/DN gel region," Nonoyama said.

This represented the first time a bone had been robustly fused with a tough hydrogel, a breakthrough toward the potential application of such hydro



Transmittance electron microscope image (right) showing gradient distribution between HAp/DN gel (left side) and bone tissue (right side) with no clear border. This indicates osteogenesis penetrated into the HAp/DN gel, fusing artificial gel and biological tissue together. (Scale bar=5μm) (Nonoyama T, Wada S, et al., *Advanced Materials*, August 17, 2016)

gels as substitutes of soft supporting tissues. The team is in a tie-up with a company to conduct joint research to put the gel into practical use as a cartilage substitute.

"Originally, we thought adhering bones to the gel surface would have been a great achievement," Yasuda said. "But we did more than that. HAp formed nanocrystals inside the gel, which then bonded with collagen and calcium to form bones. It is spontaneous bone formation. I was astonished by this finding."

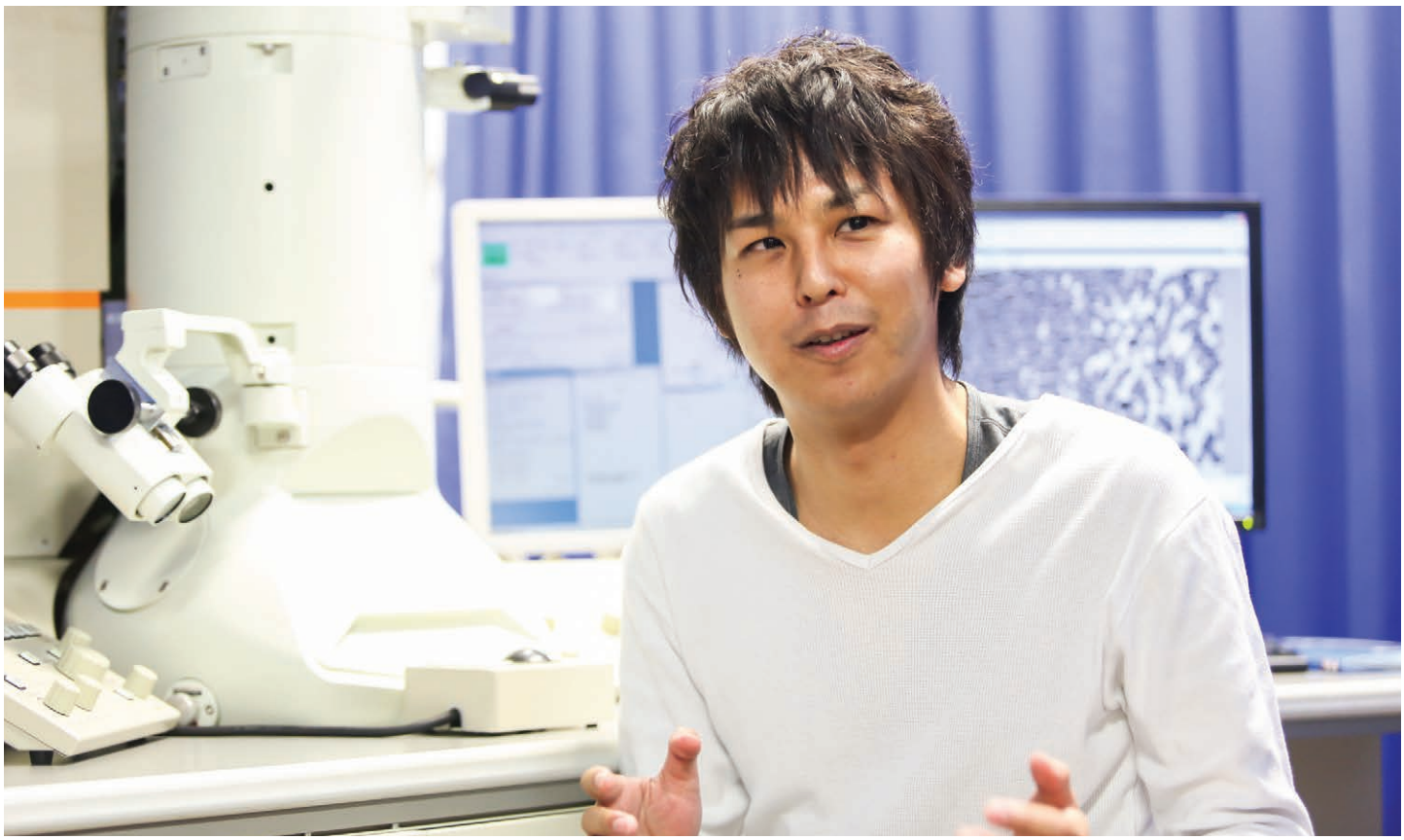
"We need to further improve the gel before actually using it in a patient. For instance, we must make sure the gel will not degrade for several decades after being implanted in the body," Nonoyama said, adding durability and safety remain major challenges to be overcome before the gels are put into practical use.

In the long run, Nonoyama hopes to utilize a DN gel as a scaffolding-like material to induce bone regeneration.

"Having experienced bone fractures twice myself, I know how burdensome it is to undergo surgery to fix a broken bone with a metal pin and go through another to retrieve it," Nonoyama said.

"A hydrogel scaffold must gradually biodegrade as bone regenerates so the patient won't need the second surgery. I am convinced we will be able to do this with DN gels in the future."

> "Having experienced bone fractures twice myself, I know how burdensome it is to undergo surgery to fix a broken bone with a metal pin and go through another to retrieve it."



My memories of Pierre-Gilles de Gennes

Professor
Ko Okumura

Department of Physics,
Ochanomizu University

From September 1999, I began to work with Pierre-Gilles de Gennes in Paris. My stay in Paris was limited only to a half year and my previous research fields were completely unrelated to soft matter physics.

At that time, de Gennes had two offices in Paris. One was in the Collège de France (CDF) and the other was in École supérieure de physique et de chimie industrielles de la ville de Paris (ESPCI or PC). In this article, I will call de Gennes PGG, since this was what many people around him in Paris affectionately called him. Basically, PGG was based in PC, of which he was the president or director, and visited CDF a few times a week. CDF is a very prestigious research institute in France and professors there give lectures that are open to the public; any citizen can attend the lectures free of charge, but the content is quite advanced and is appropriate for those who are conducting research on that particular topic. At CDF, PGG leaded a research unit comprising of a few experimental groups and a theoretical group.

Just after I arrived in Paris, PGG told me about nacre, which is a layered structure found on the surface of pearls or inside certain seashells. He had heard about this substance somewhere and was very excited about it because nacre shows a remarkable toughness due to its fine structure, and he explained to me a possible mechanism that provided this toughness. This is just a typical example of his behavior when he met a new problem. He was always filled with an exceptional curiosity, very open to many problems, and, once he set his mind on solving a problem, he soon came up with new ideas. Actually, I never saw him becoming dozy or falling half asleep while he was listening to someone talk. When the PGG group's weekly seminar started, he would swiftly walk to the lecture room with several sheets of paper, which always were documents he no longer needed. He would then fold one of the pieces of paper in half and then unfold it to make an ashtray. PGG would listen to the talk carefully and take notes on the remaining sheets of paper while smoking a cigar. The smoke would occasionally embarrass the speaker because PGG always had a seat beside the talker.

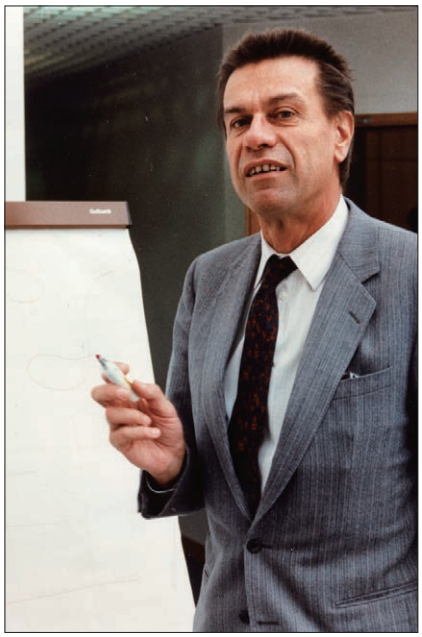
During our first discussion on nacre, I was struck by how he constructed his arguments, doing quick dimensional estimations and quoting numbers. Until then, I only knew the elegantly finished products of his research. However, after our discussion, I could not swallow what he had said; I started constructing an elastic theory for a layered structure in a certain limit in which the theory becomes simple and faxed my note on this to his office at PC. Soon after that, he visited me at the college and excitedly said to me, "This is useful!" and then quickly left. That was a happy moment for me because I had hoped to have a chance to impress him since my arrival in Paris. Surprisingly, during his regular lecture at CDF the following week, he talked about this theory on nacre in front of the public! I could not completely understand the class because it was given in French. However, I could easily imagine what he was talking about by looking at his drawings, equations and my name written on the blackboard. The topic of his course at CDF would change every year and, remarkably, the content usually consisted of what interested him and what he was thinking about at the moment of the lecture.

We frequently communicated by fax, although we were within walking distance. When PGG thought it necessary, however, he would suddenly turn up and we would have a brief discussion. When it was time to go, he almost always would say, "We will see," and then briskly

short, elegantly written and indicated he had completely understood my fax. His messages took me a long time to digest; his handwriting is elegant but not necessarily easy to read until one gets used to it. For some initial time, I was puzzled by the elegant faxes and wondered how he could always construct his arguments so stylishly. But later, I realized that he always tried to keep his own style even for me. One Sunday afternoon, when I happened to be working at CDF alone, which was rare for me, PGG suddenly appeared in front of me. "You should not work on Sundays!" he said, seemingly oblivious to the fact he was doing the same thing. He handed me a piece of paper and then briskly disappeared as usual. I was left holding a response to my fax, which he probably would have faxed to me the next day if I had not been there. On the piece of paper I could recognize many traces of words that had been erased and rewritten, which would have been covered when it had been sent by fax.

Ten years have passed since PGG died. David Quéré kindly sent me a book published in French that contains some of PGG's lectures, interviews and writing, both scientific and nonscientific. Reading this book brought me back some vivid memories of PGG. Especially, I will never forget the last time I saw him smile. It was about ten months before he died. I was saying goodbye in front of a rail station to which he had driven me from a mountain hut, where I spent a pleasant time with his family and found Françoise (Brochard-Wyart) to be an excellent mother and chef. On the way to the station, PGG had to stop the car several times on a country road because he was feeling unwell. I did not think it would be the last time I would see him.

A few months ago, at a conference in the United States, one young Japanese scientist approached me and said, "I might not be here today if I had not encountered the Japanese version of that book." The scientist was referring to PGG's last textbook, which I had translated into Japanese. A few minutes later, another young scientist approached me and said almost the same thing! However, this was not the first time: Such young researchers are not limited to talented Japanese physicists but include scientists active in engineering, which underlines the broad impact PGG had. In a sense, I believe that he is still alive and continues to influence enormously the next generation through his textbooks and articles.

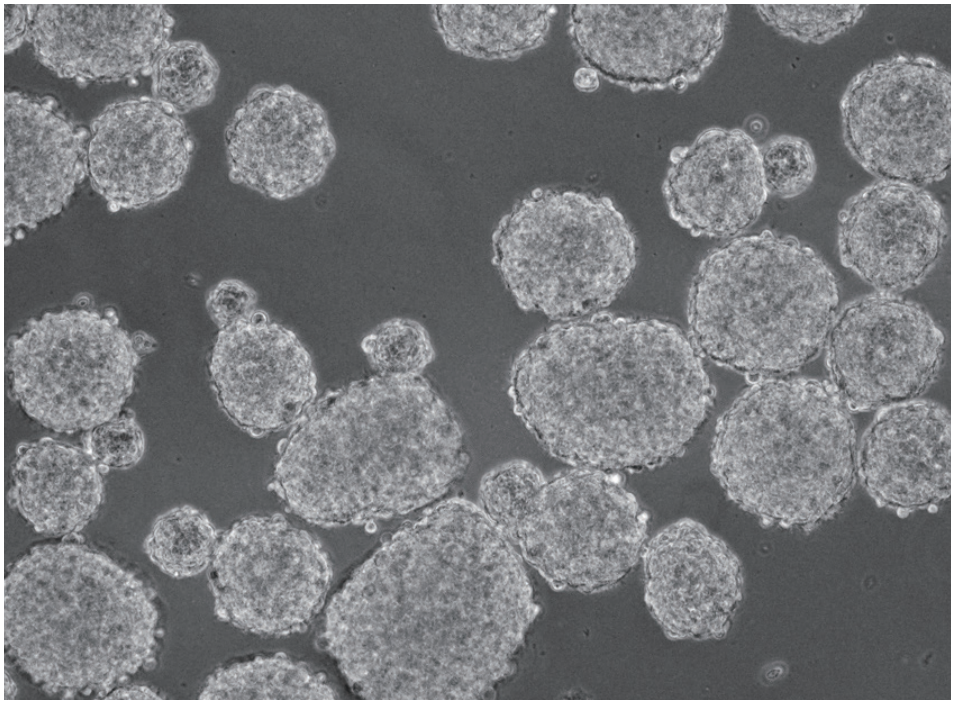


Pierre-Gilles de Gennes (PGG) lectures. Credit: AIP Emilio Segrè Visual Archives, Physics Today Collection

https://photos.aip.org/history-programs/niels-bohr-library/photos/de-gennes-pierre-b6

This article was written by Ko Okumura on October 9, 2017 on the basis of the following article published in Japanese: Ko Okumura (2007) "My Memories of PGG (P.-G. de Gennes)" *BUTSURI*, 62(8), pp. 634-635.

DN gels – a potential weapon to fight cancer



Spheres formed by patient-derived brain cancer cells on the double network (DN) gel.

Medical professor Shinya Tanaka was puzzled to see cancer cells spinning and quickly growing into spheres during a 2012 experiment on a double network (DN) hydrogel, a tough biomaterial developed by Hokkaido University's Laboratory of Soft & Wet Matter. He had placed brain cancer cells called glioblastoma on the DN gel, as a control for the experiment to explore how cartilage regenerates on the gel.

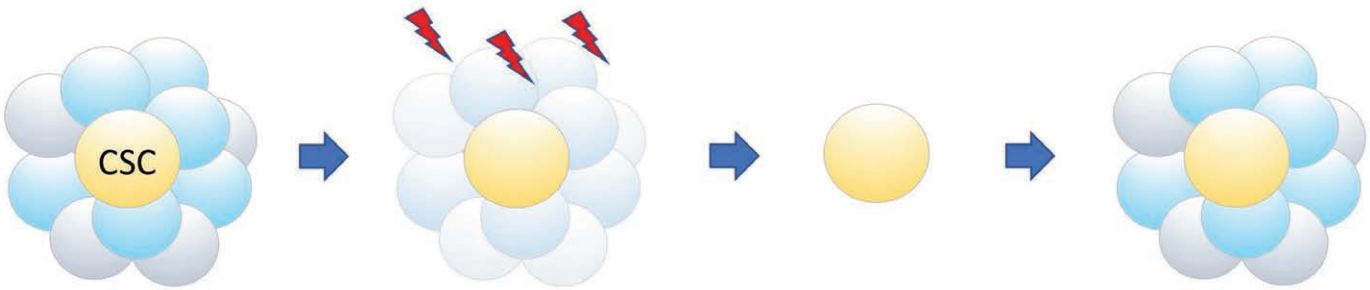
Tanaka used the cancer cells because he routinely examines such primary tumors as a pathologist. Glioblastoma is one of the hardest-to-cure cancer types with a poor postoperative prognosis. Its 5-year survival rate is approximately 8 percent.

"At first I thought the experiment was a failure. The spheres seemed to be made of dead cells," Tanaka said. He nonetheless decided to examine the gene expression patterns of the Yamanaka factors, or the four genes (Oct3/4, Sox2, Klf4 and c-Myc) identified by Nobel laureate Shinya Yamanaka as being essential to reprogram cells.

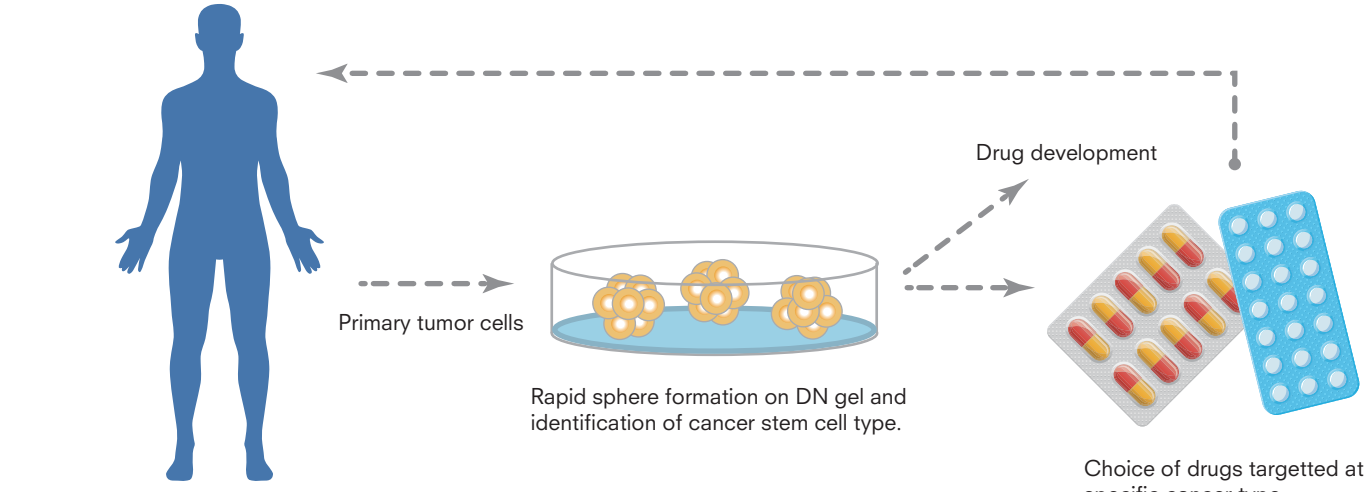
"I gave it a try because the spheres on the DN gel looked similar to those formed by Yamanaka's reprogramed cells, or induced pluripotent stem cells. Then, much to my surprise, I found there was a surge in the Yamanaka factors in our spheres."

This finding prompted Tanaka to embark on a quest he had never intended – to discover what happens inside the spinning spheres of cancer cells.

> "At first I thought the experiment was a failure. The spheres seemed to be made of dead cells."



Conventional cancer therapy kills differentiated cancer cells and their progenitor cells, but not cancer stem cells (CSCs), which can later trigger cancer recurrence.



Proposed tailored treatment for cancer patients and anti-cancer drug development utilizing cancer stem cells on DN gels.

Inducing the production of cancer stem cells

Subsequent research has indicated that the spheres grown on the DN gel contained a large number of cancer stem cells (CSCs), which are hardly found in primary tumors. Their preliminary experiments suggest that the CSCs are likely derived from differentiated cancer cells and their progenitors, both descendants of CSCs, implying the plasticity between those cell types. Tanaka and his team continue the investigation to characterize those cells.

A primary tumor is a heterogeneous mix of CSCs, progenitor cells and differentiated cancer cells. Only stem cells can trigger cancer recurrence or metastasis, but identifying them is extremely difficult because they only account for 0.0001 percent of tumor cells. CSCs are highly therapy resistant, which makes cancer treatment difficult. Even if only a small amount of CSCs remain after treatment, it raises the possibility of cancer recurrence or metastasis. This is because stem cells can reproduce themselves by cell division and at the same time produce more differentiated cells, or cancer cells in this case.

The use of DN gels, however, could facilitate the reprograming of progenitor and differentiated cancer cells into CSCs as well as multiplication of CSCs.

> “It looks like the cells are just growing into spheres, but something drastic is happening inside.”

“The proportion of CSCs in the overall tumor cells jumped to, say, 80 percent,” Tanaka said. “And it happened in just 24 hours. It looks like the cells are just growing into spheres, but something drastic is happening inside.”

“The DN gels could be stimulating the cells and inducing epigenetic regulation of gene expression,” Tanaka said. Epigenetic regulation is the modification of gene function without change in the DNA sequence.

Tanaka’s team has seen positive results showing DN gel-induced CSCs trigger cancer when they are implanted in mice. The team is also investigating whether the DN gels induce the production of CSCs of not only brain tumors but also colon, cervical, lung, oral, colorectal, bladder and other cancers, without adding any supplements or growth factors to the culture medium.

Professor Shinya Tanaka

DN gels key materials for curing cancers

DN gels have high potential in finding a suitable approach to treat cancer. "Further study should enable us to identify the type of recurrent cancer by determining the type of DN gel-induced stem cells," Tanaka said. "Since the cells grow very quickly on the gel, we could swiftly decide how to treat the patient by using molecular target drugs effective against the specific cancer type. Each cancer patient needs a different treatment approach, which I have been acutely aware of as a pathologist. The gel will enable a treatment tailored to each patient."

The gels also could help pharmaceutical companies develop cancer drugs to prevent a recurrence. CSCs produced from various cancers on the gels can be used to screen anticancer drugs selectively targeted at certain types of cancers. Using gel-induced CSCs is expected to slash the time required to develop new cancer drugs.

Tanaka is also hopeful that use of gels will lead to the production of healthy neurons that can be used to treat brain infarctions. "Some special gels are known to stimulate neural stem cells to differentiate into neurons and their supporter astrocytes. Gels could be novel tools to control cell differentiation in the future," he said.

Tanaka believes the gels will play an essential role in the global fight against cancer, together with single-cell analysis, which opened new avenues to characterize intra-tumor heterogeneity, identify cell types, among other steps, to guide diagnosis and treatment. "I think the gels can pave the way for making groundbreaking medical care a reality," Tanaka said.

> "I think the gels can pave the way for making groundbreaking medical care a reality."

SOFT MATTER USED HERE

acrylic sheet

The future of glass

by Mitsubishi Chemical Corporation

MITSUBISHI CHEMICAL

Above

Light Guide Panel (LGP) by Shinkolite™ LX

The origins of acrylic resin stems from German chemist Otto Röhm in 1927 when he invented the polymer Methyl Methacrylate (MMA). Its superior transparency compared to inorganic glass, its light weight, and durability lead to its widespread diffusion and use.

Acrylic resin is a highly functioning material used in technological innovations into the modern day because of its exceptional formability. Impact-resistant, scratch-resistant, durable, weather-resistant, fire-resistant, and self-extinguishing, the material has reached a point to where it can now be controlled using light by capitalizing on its unique optical properties. It acts as key example of a material playing a major role in the industrial application of macromolecules.

For example, modern day aquariums are now able to have tall water tanks in the shape of giant tunnels due to the durability and strength of acrylic sheets. Another example is the light guide panel, which is used for a variety of purposes, from edge lit illumination signage to displays. Nanoparticles dispersed in Methyl Methacrylate refract light allowing the whole surface of an acrylic sheet to be uniformly made bright, maximizing the efficiency light is utilized. These technological developments allow direct light (wavelengths) to be refracted, enabling optical characteristics to be easily controlled and for the whole surface of an acrylic resin plate to be uniformly made bright.

Left

Guests can pass through a walkway beneath the special transparent acrylic tank to view the penguins. Image by Sunshine Aquarium, Tokyo

Acrylic panels and tanks for aquariums using Shinkolite-technology.

(Image by Sunshine Aquarium)

Hokkaido University at a glance

Hokkaido University is one of the oldest, largest, and most prestigious universities in Japan. The university originates from the Sapporo Agricultural College, which was established in 1876 as Japan's first institution of higher education to grant bachelor's degrees. The university has 12 undergraduate and 21 graduate schools covering a wide range of disciplines in social and natural sciences, as well as humanities. Boasting one of the biggest campuses in Japan, the university houses cutting-edge research facilities, a university hospital, and one of the world's largest research forests.

HUCI

The "Hokkaido Universal Campus Initiative (HUCI)" is a reform program which aims to further internationalize the university as a whole to foster more world leaders who can contribute to the resolution of global issues. These leaders will be able to address contemporary issues, represent the frontier spirit as they forge new ways ahead, and contribute to the development of human welfare and society. The initiative began in 2014 and will be in effect until 2024, approaching the university's 150th anniversary in 2026.

12 undergraduate schools, **21** graduate schools

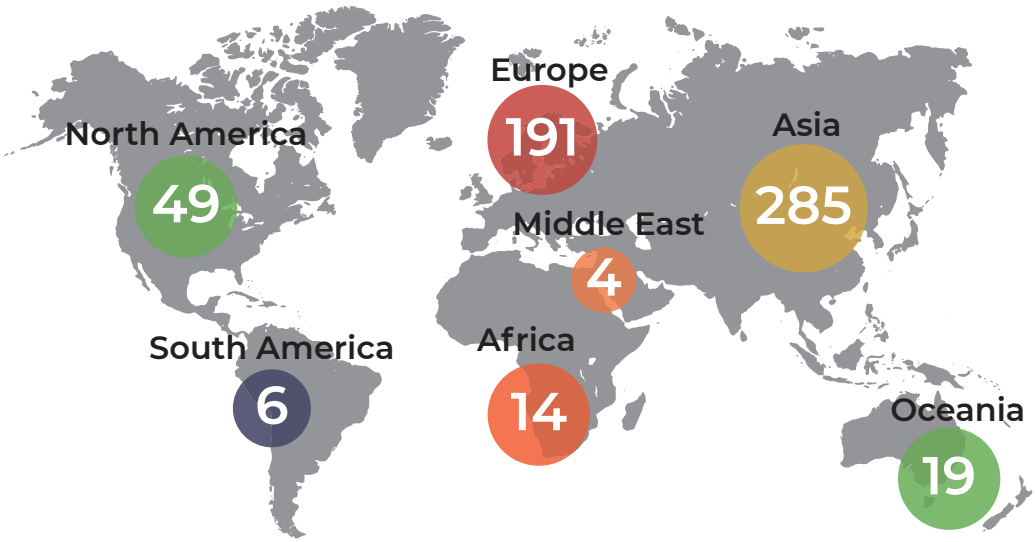
22 research institutes

4,000 staff members, **18,000** students

Thomson Reuters Rankings: **#95**

THE Japan University Rankings: **#8**

Data as of May 1, 2017

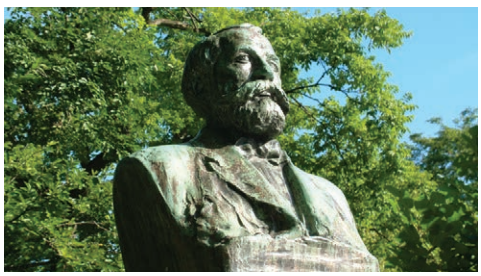


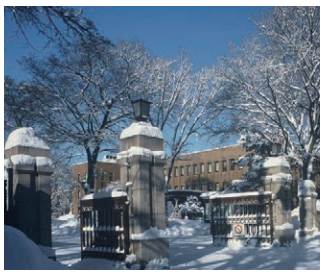
Hokkaido University
GI-CoRE
Global Institution for Collaborative Research and Education

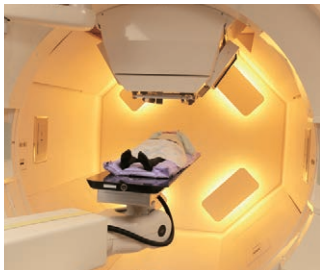
Global Institution for Collaborative Research and Education (GI-CoRE) is a faculty organization which brings together world-class researchers from around the world and within the University to promote international collaborative research and education. In 2016, the Global Station for Soft Matter (GSS) was established to further the progressive development of soft matter with the aim of solving social problems, such as aging, environmental pollution, and the lack of resources. GI-CoRE includes five other Global Stations covering Quantum Medical Science and Engineering (GSQ), Zoonosis Control (GSZ), Food, Land and Water Resources (GSF), Big Data and Cybersecurity (GSB) and Arctic Research (GSA).

New Division of Soft Matter, Graduate School of Life Sciences

Hokkaido University is one of the world's top-level research hubs for the study of soft matter and the success of GSS has led to the establishment of a new division focusing on soft matter within the Graduate School of Life Sciences in 2018. Its main objective is to educate and foster students with multi-disciplinary views beyond the conventional boundaries of science, technology, and engineering. The division will offer Master's and Doctorate courses in English, and will give students opportunities to utilize front-line research equipment for soft matter analysis.





On the cover

Photograph demonstrating the extraordinary strength of
a double-network hydrogel that resists slicing with a cutter.

J.P. Gong et al., *Adv. Mater.*, 15, 1155 (2003)
Double-Network Hydrogels with Extremely High Mechanical Strength.

HOKKAIDO UNIVERSITY

TOP GLOBAL UNIVERSITY JAPAN

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