Institute for Integrated Cell-Material Sciences

iCeMS

Our World, Your Future

Kyoto University

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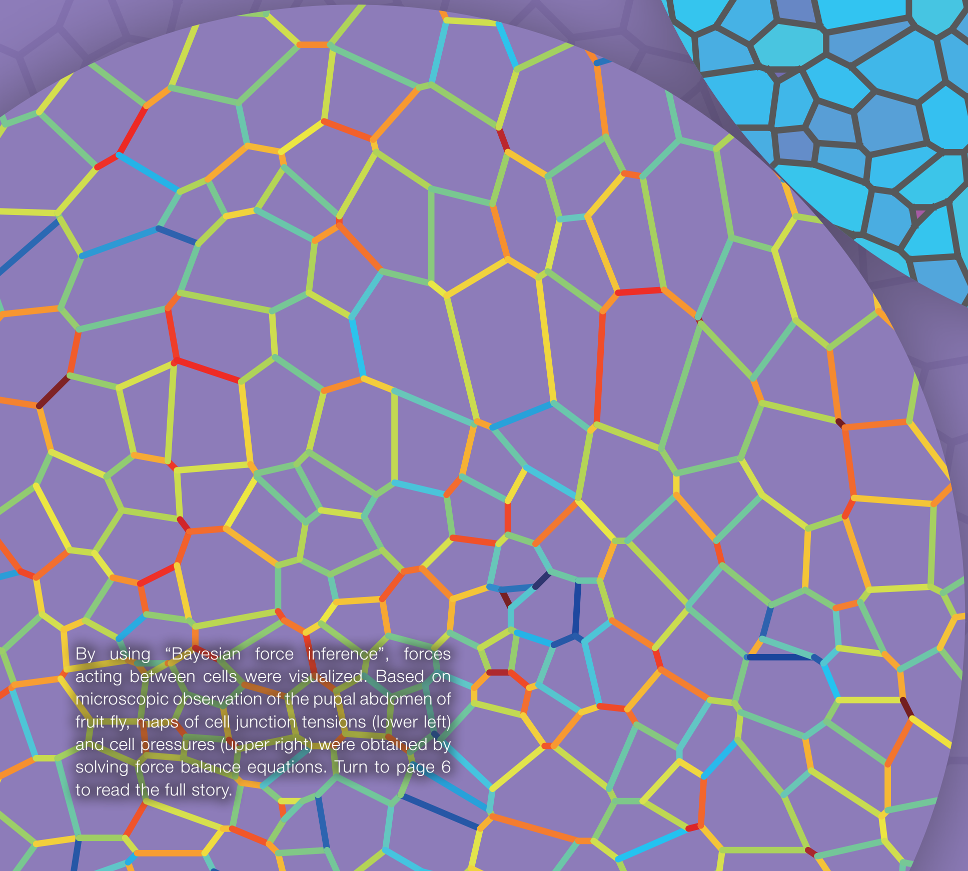


By using “Bayesian force inference”, forces acting between cells were visualized. Based on microscopic observation of the pupal abdomen of fruit fly, maps of cell junction tensions (lower left) and cell pressures (upper right) were obtained by solving force balance equations. Turn to page 6 to read the full story.

contents

Feature

Revival after a Century!

Mechanobiology has the potential to discover the secret of life

Bodies of living things, including mankind, consist of cells and tissues. How can a cell or tissue change its form or keep its structure? Life is still full of unknown secrets. There is a discipline that aims to elucidate the secret of life, known as "mechanobiology." This field of science, a challenge raised a century ago, has grown remarkably in this past decade, gradually elucidating the roles that physical forces play inside the body. In this issue, iCeMS researchers working in this challenging field introduce the fascinating points and prospects of mechanobiology.

Why mechanics?

Mechanobiology is a field of science that studies how forces produced within and between cells affect the functions of cells and tissues. The key word is force. Mechanics take place in every part of a living body. For example, a cell can move by kicking its substrate by virtue of action and reaction forces. Eggs or fertilized eggs are transported in the fallopian tube, while foreign substances are expelled from the airway by the motion of cilia. Thus, without a mechanics perspective, you cannot scientifically explain events taking place in your own body. Someday, when the mechanics of life are elucidated in detail, we may understand the workings of the human body and throw light on the differences between living and non-living things.

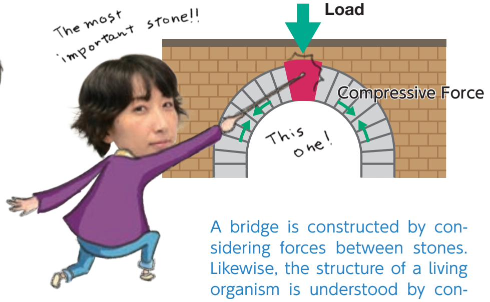
Kaoru Sugimura
Program-Specific Research Center
Associate Professor

Born in 1978 in Hyogo Prefecture. PhD, Graduate School of Science, Kyoto University. After working as a JSPS Research Fellow and RIKEN Postdoctoral Researcher, she served as an iCeMS Assistant Professor. In 2017, she took up her present post.

Naotaka Nakazawa
Program-Specific Assistant Professor

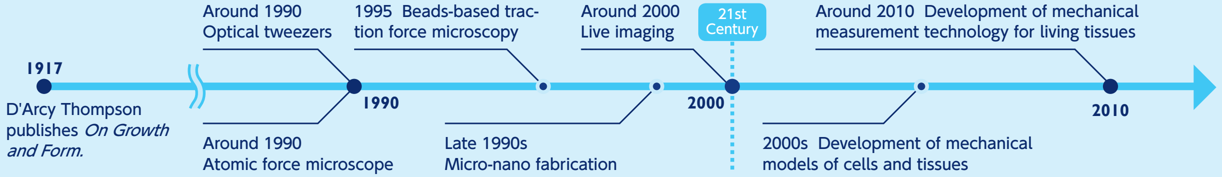
Born in 1984 in Gunma Prefecture. PhD, Graduate School of Industrial Science and Technology, Tokyo University of Science. He took up his present post in 2017 after serving as a Research Fellow at JSPS (DC1) and at the Mechanobiology Institute, National University of Singapore.

On firm ground, you can run fast; while on muddy ground, you will be running slowly. This is also true with cells. Cells can move by kicking their substrate.



A bridge is constructed by considering forces between stones. Likewise, the structure of a living organism is understood by considering the forces between cells.

Starting About a Century Ago : History of Mechanobiology

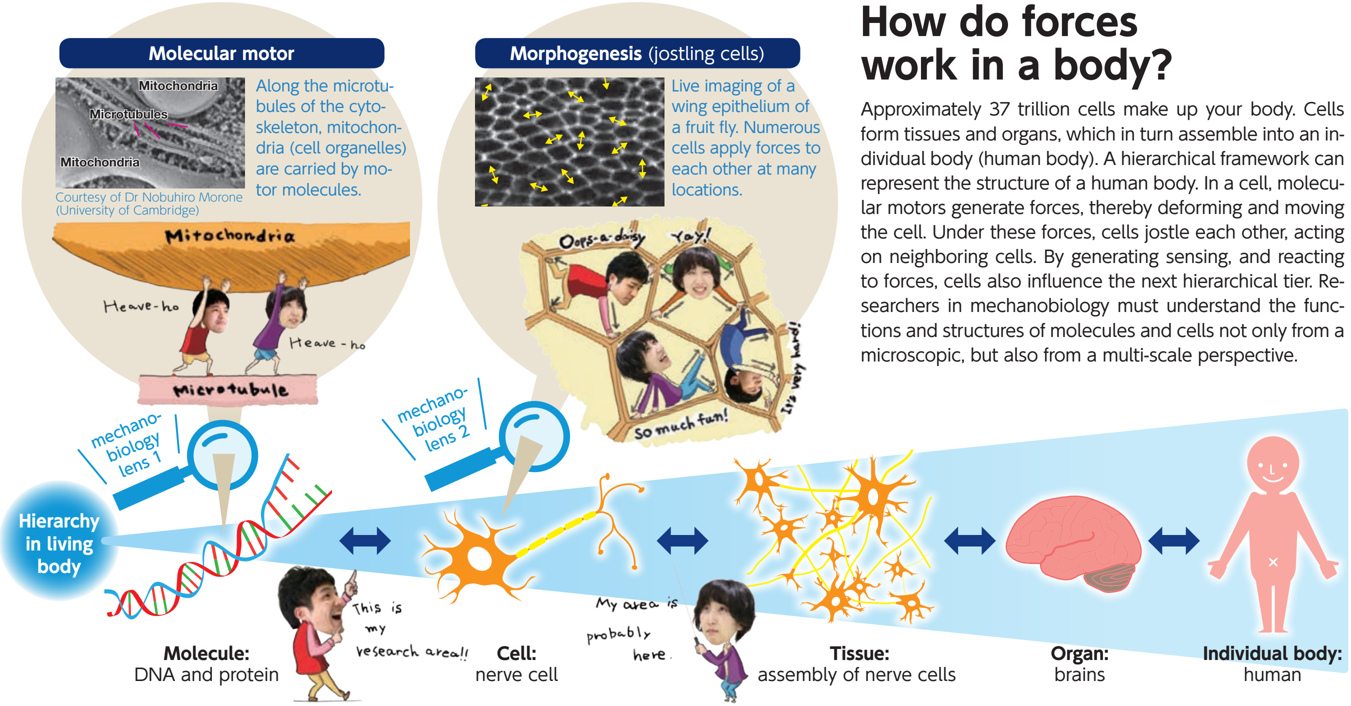


Although regarded as a new field of science, the origin of mechanobiology is not new, tracing back around a century ago. In 1917, the biologist D'Arcy Thompson published *On Growth and Form*. He proposed that physical or mathematical logic could explain the formation of the structures and patterns of animals and plants and that a living organism's form was related to mechanical forces. Nevertheless, techniques at the time were inadequate for thorough research, and Thompson's questions remained unaddressed for some time.

Around the turn of the century, many shifts in research perspective and technology occurred simultaneously in many fields of natural science including the development of mechanical measurement techniques, such as fluorescent imaging and micro-nano fabrication. These developments enabled researchers to quantitatively examine how mechanical forces organize the living system. Presently, knowledge and techniques from many fields are utilized to accelerate research activities. After a century, Thompson's questions have been revived, and researchers are addressing these challenges in a renewed effort.

Seeing through the lens of mechanobiology

Observations of life from a mechanical perspective and using advanced technologies that evolved in the 21st century have enabled researchers to understand cells and tissues in new ways. Let us briefly see the world through the lens of mechanobiology. It may lead to discoveries beyond generally accepted ideas.

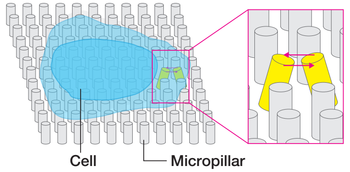


How do forces work in a body?

Approximately 37 trillion cells make up your body. Cells form tissues and organs, which in turn assemble into an individual body (human body). A hierarchical framework can represent the structure of a human body. In a cell, molecular motors generate forces, thereby deforming and moving the cell. Under these forces, cells jostle each other, acting on neighboring cells. By generating sensing, and reacting to forces, cells also influence the next hierarchical tier. Researchers in mechanobiology must understand the functions and structures of molecules and cells not only from a microscopic, but also from a multi-scale perspective.

The fate of a cell is determined by the mechanical environment

Cells not only sense forces, but they respond to the stiffness of the tissues around them. For example, mesenchymal stem cells differentiate into bone, muscle, or vascular endothelial cells and are highly regarded for their potential use in regenerative medicine. In 2006, it was found that substrate stiffness determines the type of cell into which these cells differentiate. For example, if the substrate is soft, the mesenchymal stem cell becomes a nerve cell; if hard, a bone cell; and if intermediate, a fat cell. The cell detects the substrate stiffness as a mechanical signal. Inside the cell, it is converted into a biochemical signal and transmitted to the nucleus. This process modulates gene expression to influence cell differentiation. In this way, the fate of a cell is determined by the mechanical characteristics of its environment.



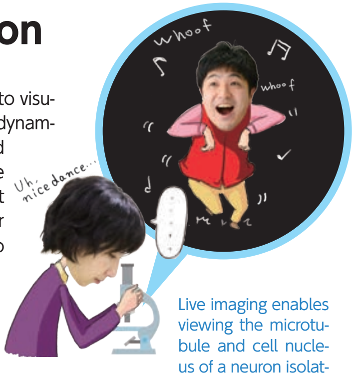
Culturing cells on a substrate that has micro-pillars makes it possible to visualize how the cells holds onto the substrate. The figure above schematically illustrates the behavior of the cells. The opposing red arrows, which indicate the directions of the motion of pillars, reveal that the cells are pinching the substrate.

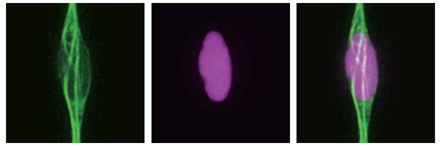
How do you pursue research? — Research methods and techniques

In the study of mechanobiology, it is necessary to look into the behaviors of cells and molecules in great detail. Various methods and techniques are used for this research, some of which are described below from the three perspectives of observation, measurement, and manipulation.

Observation (live imaging)

Live imaging enables researchers to visualize and externally observe the dynamics of living tissues and cells and the action of gene expression. The key is to attach a green fluorescent protein (GFP) or a similar marker to a living cell or protein. Doing so allows for observation of the behavior of cells or proteins in living tissue using a fluorescent microscope or other instruments.



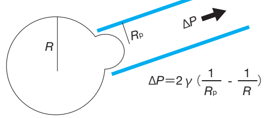


Live imaging enables viewing the microtubule and cell nucleus of a neuron isolated from the brain of a mouse. Left: microtubule (green); Middle: cell nucleus (magenta); Right: the superimposed image

Measurement

Direct contact with samples
(micropipette technique)

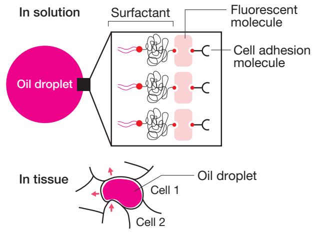
When the micropipette tip contacts a cell or tissue sample and a negative pressure is applied, the sample is sucked up. Based on the sample deformation, the sample's absolute value of surface tension is measured.



The surface tension is measured by controlling the vacuum level to make the sucked part of the sample a complete hemisphere.

Measuring method by using a force sensor
(oil droplet technique)

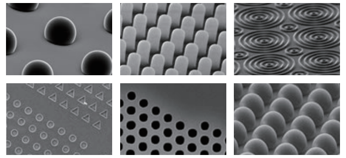
When an oil droplet is inserted between cells, the droplet is deformed due to the forces exerted by the neighboring cells. By previously measuring the surface tension of the oil droplet in a solution, the forces exerted by the neighboring cells can be calculated.



The oil droplet is coated with surfactant, fluorescent molecules, and cell adhesion molecules. Inserting the droplet between cells enables measurement of forces/stresses acting between cells.

Manipulation (microfabrication)

Polymer materials, such as polydimethylsiloxane and polyacrylamide, can bond cells when they are surface-coated with a protein that serves as a cellular scaffolding, In this process, it is possible to form scaffolding of various stiffness levels by varying the proportion of the cross-linking agent. Moreover, by combining the scaffolding with a microfabricated substrate, it becomes possible to change the cell adhesion pattern and form a channel for the passage of cells.



Images of various cell substrate surfaces taken with a scanning electron microscope. Using microfabricated molds and biomaterials, researchers can develop cell substrates with various structures and patterns.

Courtesy of Dr Gianluca Grenci (Mechanobiology Institute, National University of Singapore)

column Quantitative Data

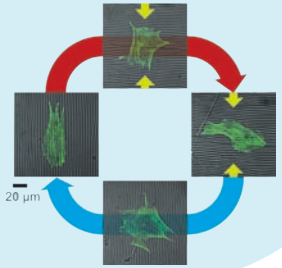
Information that can be measured, compiled, and analyzed with numbers are referred to as "quantitative data."
Full use of the above-described techniques enables obtaining quantitative data to analyze the complex workings of life. Scientific understanding of phenomena in mechanobiology, and in other fields as well, requires objective and detailed numbers that preclude subjective impressions and vague information. Researchers can construct theoretical models or discover unknown mechanisms of life by acquiring, comparing, and analyzing a vast amount of quantitative data on a daily basis.

iCeMS' Approach

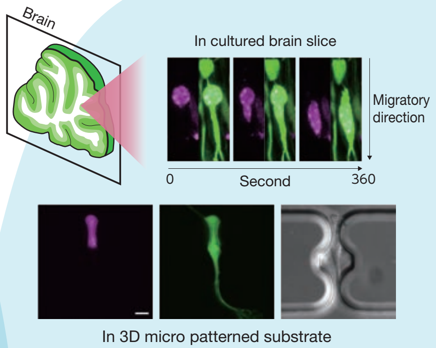
At iCeMS, some researchers work on mechanobiology. They all similarly aim to elucidate the workings of life from a mechanics perspective. However, their focuses vary in terms of scale. The following is an overview of the research.

Motomu Tanaka
Specially Appointed Professor (iCeMS-CiMPhy)

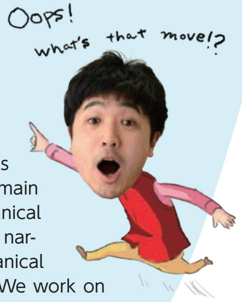
Tissues in our body, such as muscles, bones, and nerves, possess optimal levels of "stiffness/softness". Cells sensitively feel how stiff/soft their surrounding environments (called extracellular matrices) are, and they adapt their shape and function accordingly. Physicists are not only good at measuring the stiffness of cells and extracellular environments, but also creating an innovative way to calculate the order of cells and tissues. With aid of materials that can flexibly change their stiffness and orientation, we tightly collaborate with medical doctors and biologists, and elucidate how dynamic changes in the cellular environment affect the fate of cells, such as healthy cells becoming sick.



Observations of how cells react to a change in the topographic orientation. Cells that develop into muscles (myoblast cells) on a substrate with fine "wrinkles" adapt the shape and the order of cytoskeletons (green) in response to changes in the wrinkle direction.

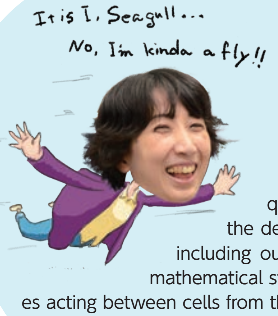


Top: Neuronal dynamics in cultured brain slice. (Magenta: cell nucleus; Green: cytoplasm). Neuronal migration is accompanied by the dynamic deformation of the cell nucleus.
Bottom: Neuronal migration in micro patterned substrate with a confined space (Magenta: cell nucleus; Green: cytoplasm). This pattern is modulated by microfabrication techniques. Scale bar = 5 µm



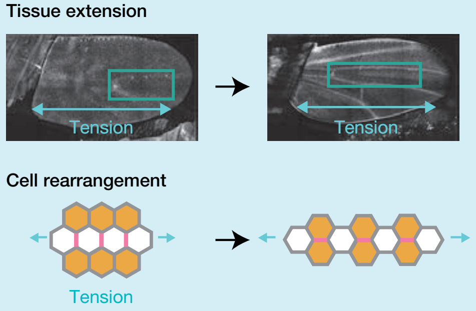
Naotaka Nakazawa

In the brain development, each newborn neuron migrates from its birthplace to its functional place through very confined spaces formed by complex neurite configurations and extracellular matrices. Many mysteries remain unsolved in this process, such as how mechanical force contribute to neuronal migration in very narrow spaces and how neurons respond to mechanical stress by confined space during its migration. We work on these questions focusing on the nuclear dynamics during the neuronal migration in nervous tissue.



Kaoru Sugimura

How do cells push and pull each other to trigger precise deformations of a tissue when shaping the body? The answer to this central question is essential for understanding the development of diverse forms in nature including our body. We have combined physics, mathematical statistics, and live imaging to infer forces acting between cells from the observed geometry of cells. By applying the method to fruit fly wing, we discovered that mechanical forces act as a messenger to transmit information between cells.



With wing epithelia of *Drosophila* (fruit flies), tensile stress along the proximal-distal direction of a tissue (the direction from inside to outside of the body) determines the direction of cell rearrangement. At the pink locations in the figure, cell junctions are remodeled and cells rearrange without being tore up under tensile stress.

The process by which cells proliferate and differentiate, growing from a fertilized egg into an organism body, is called "development". In the process, cells push and shove within the growing body, exerting force against one another. With the clarification of the chemical signaling pathways that control development, researchers turn to the question of how mechanical forces affect the shapes of organisms. Associate Professor Kaoru Sugimura's work is devoted to unraveling the mysteries of living organisms, a quest that centers on the "mechanical force in living things", as she gleans from a wide variety of fields, including imaging technology, soft matter physics, and mathematical statistics.

Expressing the mysteries of nature in astonishing new ways

Career summary on page 2

Kaoru Sugimura

Program-Specific Research Center Associate Professor

"This is live-cell imaging of a fruit fly wing," says Sugimura, as she turns the laptop on her desk to face us. The screen shows a fly wing taking form. Countless shining cells slowly migrate from the tip toward the body of the wing. The fantastic sight recalls the Milky Way twinkling in the night sky. "Fruit fly wings help us understand the fundamental logic of development. I've been using fruit flies for experiments and mathematical modeling since my student days. Collecting quantitative data is indispensable for my research, and flies are an outstanding tool for quantitative study of genetics and development. They are also easy to analyze. And so…." Her words speed up as her voice rises. The flies that gather around kitchen garbage might just annoy most people, but for Sugimura, they are special creatures that support her research. The way she talks about them gives us a sense that she sees them as more than experimental organisms - that she may actually feel affection for them, allowing some genuine feeling to filter through her scientific work. Where might this have come from?

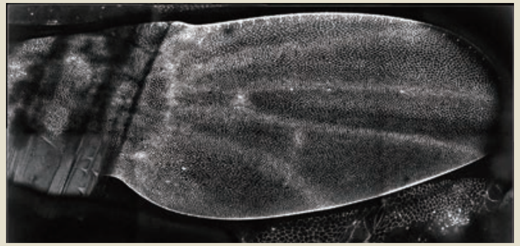


Image of a fruit fly wing, in which E-cadherin is labeled with GFP
A wing in the pupal stage. Observation of cell movement is enabled by fluorescently labeled E-cadherin, cell adhesion molecules. A pulling force acts from the body (left), and in response, cell groups flow from right to left.

Life direction changed by science experiments

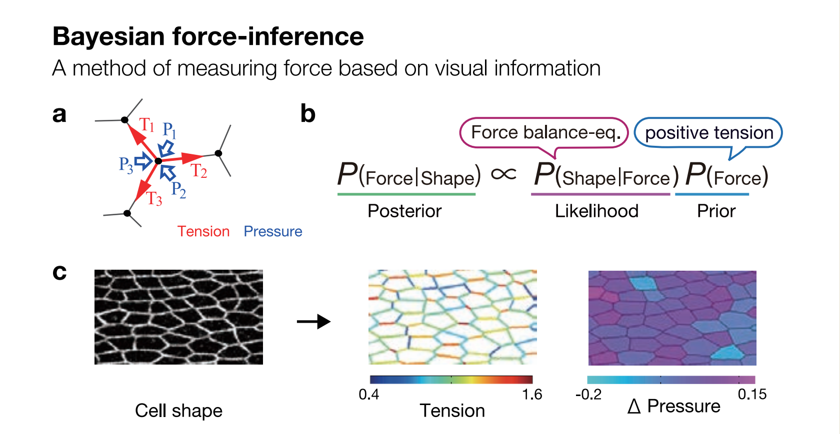
As a little girl, Sugimura was a bookworm. She would lose herself in endless books about anything that caught her fancy, from space and science to dinosaurs and stories. She had no interest in the toys and dolls that held the attention of girls around her, but she would beg her parents to buy her books. Spreading the wings of her imagination, she voyaged far through reading. "I wanted to grow up to be someone who expressed what the world is like. Sometimes I thought about being a writer or a film director, although, even as a child, I suspected my talents did not lie in those directions."

The turning point in her interest was a science class in middle school. Sugimura was totally absorbed even by simple experiments, such as observing a rolling ball or a swinging pendulum. "I was in a group of four girls doing experiments, and the other three weren't interested at all. But I got really excited. I thought to myself, this is something I could keep doing."

At first, it was physics and chemistry that held her interest. Compared to the physical sciences, where problems are precisely solved with mathematical formulas, biology seemed ambiguous and vague and therefore completely uninteresting. "Then during the summer break in my first year of high school, I happened to read a book about the beginnings of molecular biology, and the scales fell from my eyes. The workings of living organisms could be explained in logical terms! My inclination shifted 180 degrees. I suddenly knew I wanted to study biology from the perspective of physics, and it filled me with excitement."

An innovative method of quantitative research

About ten years later, as a researcher at RIKEN, she entered the emerging field of mechanobiology, a fusion of biology and physics. "In graduate school, I used live-cell imaging and molecular genetics to analyze the mechanisms of nerve cell dendrites. Just before finishing my PhD, I attempted a mathematical model of dendrite formation based on my own experimental observations. For this, I had to incorporate information from a variety of scientific fields. Later, through interactions with many scientists, including my current collaborator, I realized that mechanical force plays an important role in the process of development." At that time, very little progress had been made in



An inverse problem between cell shape and force is solved by using Bayesian statistics. It infers relative values of cellular forces from the observed geometry of cells.
a. Diagram of the force acting on the vertex of a cell. *T* denotes tension at the cell adhesion surface; *P* denotes cell pressure.
b. Formulation of the inverse problem derived using Bayesian statistics. The posterior distribution function, obtained by multiplying the likelihood function and prior distribution, gives the estimated value of forces.
c. Example of application of Bayesian force inference. Tension at cell junctions and cell pressures are shown (Image was take in fruit fly wing epithelium at 23 hours after pupation).

understanding this aspect of development, as the mechanics of biological tissue were still largely unknown. She plunged wholeheartedly into elucidating them.

Sugimura collaborated with Shuji Ishihara, an associate professor at the University of Tokyo, to measure physical forces in cells. They worked not by applying external force, but by visually quantifying the force received by individual cells. They established "Bayesian force inference" to estimate relative values of tension in surfaces contacted by other cells and pressures on the cells. "Simply put, the technique estimates the forces acting on cells by analyzing cell shapes in images. When force is applied to something, its shape changes. We set out to measure that force based on information from the shape, reversing the cause and effect relationship. With other methods, like using optical tweezers that apply external forces to cells, detailed information is obtained, though for relatively far fewer cells. With our method, although an estimate, the visual data measures some 20,000 cells at one time." Sugimura and her colleague devised this method by combining a mathematical statistics approach to physics and biology. This resulted in an innovative method of quantitative research and an original way to "express" the mechanisms of life.

Playing soccer on a futsal field with fellows from her graduate school days. Having played soccer since the first year of elementary school, she is relaxed. Even when busy, she manages to play once every two months, working up a sweat and renewing her energy for research. "My favorite position is central midfielder. I have a wide field of view, and I can think through each play. Just like scientific research, soccer is something I can't do without. Soccer is life!"

The mysteries of life are still quite profound

The results of her research at RIKEN were recognized, and in April 2011, Sugimura became a member of iCeMS. Ever since that first aspiration to be a scientist in middle school, she has had an inquisitive mind. "I want to uniquely express the mysteries of nature through my work. This idea has always sustained my work. Expression involves some individuality, and I'm just not interested in doing the same things as others. But I'm not like a chemist who starts from scratch and creates a new material. I want to take what's already in the natural world and express it in a way that anybody can understand."

The mysteries of living organisms are still quite profound. For example, the DNA contained in the nucleus of each human cell has a string-like shape, and when uncoiled, it is about two meters long. That is, packed inside a nucleus just ten micrometers in diameter is DNA about as long as a person is tall. Furthermore, rather than haphazardly crammed into the nucleus in the way we might stuff a closet, each type of cell, like muscle cells or nerve cells, has a characteristic arrangement. "Doesn't that make you wonder what it's all about? We can't elucidate even such basic mechanisms of life. If we bring together knowledge and ideas from, not only biology and physics, but various other fields as well, and if we investigate thoroughly, then hopefully we will understand what make living matter unique. I want to express the mechanisms of life from an original viewpoint that will astonish everyone."

Commemorative photo at the "Portraits of Thought" exhibition at the Kyoto University Museum. One of the drawings by Michael Whittle in this exhibition is based on a growth model for human neurons created by Sugimura.

The Other Half of iCeMS

ORSO: Overseas Researchers Support Office

Kazumi Arimoto

At iCeMS, English is the official language, and about 20 % of the researchers come from abroad. However, once these members take one step out of the building, they enter another land. People coming to Japan for the first time often encounter cultural differences and language barriers. Even given cutting-edge research facilities, they cannot concentrate on research without first having a stable living environment. One of iCeMS' major tasks is to maintain an environment where international researchers can feel relaxed and can concentrate. To this end, the ORSO is advancing efforts that are gradually spreading within Kyoto University. Kazumi Arimoto, who has worked for 7 years at iCeMS, talked to us about her job

ORSO supports in...

Obtaining a status of residence

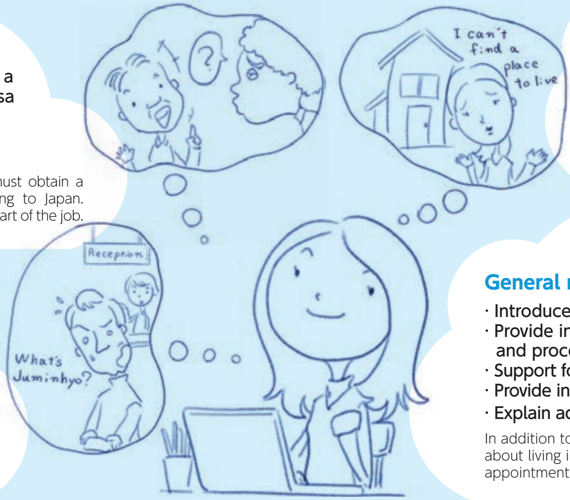
- Serve as a proxy applicant to receive a Certificate of Eligibility needed for visa acquisition
- Help with the renewal or changes of residency status

To work and live in Japan, overseas workers must obtain a status of residence in advance of their coming to Japan. Support for obtaining this is the most important part of the job.

Searching for housing

- Introduce university accommodation facilities
- Provide information about real estate agents who provide service in different languages

Provide residential information helpful for finding accommodation.



Employment procedure

- Confirm the necessary documents when overseas workers come to the university
- Support for opening a bank account
- Help with resident registration

General matters for living in Japan

- Introduce hospitals who provide service in English
- Provide information on childcare, schools, and procedures
- Support for obtaining mobile phones and credit cards
- Provide information about Japanese language classes
- Explain administrative procedures related to childbirth

In addition to the above, the ORSO responds to general requests about living in Japan and may accompany researchers to appointments, depending on the circumstances.

The range of support is infinite

Arimoto・For researchers coming to Japan, the first necessity is to obtain the status of residence. We coordinate with each department to examine and support the necessary preparations. In addition to such administrative procedures, it is also important that we respond to researchers' requests for consultation. Since the consultation can cover many aspects of life in Japan, the broad scope of this work cannot be easily summarized. In addition, we often receive unexpected consultation requests. For example, a researcher with an elementary school-aged child once asked, "I'd like you to tell me how to do the threadworm inspection." In his home country, there was no "threadworm inspection". At that time, I tried using an image of the procedure in English, and I remember struggling to pick the right words to explain. In this kind of situation, I first try to understand the matter well in Japanese myself and think about the best English words to explain with.

Responding with sincere feelings

Arimoto・Most people who come here to consult feel uneasy, so I take an affirmative approach, saying "Don't hesitate to ask for my help!" Sometimes we may get requests that we cannot solve directly, such as dealing with inadequate administrative procedures. Saying, "I do not know," will not solve such problems. We empathize with the request and try our best to affirm where the problem is and what should be done.

In any job, I think trust and sincerity are important for the relationships between people. If one party does not trust the other, then the message will not be communicated effectively. Whether a young researcher or a researcher already in an established position, my approach doesn't change. I try to respond to everyone in the same way.

iCeMS in brief

Research Highlights

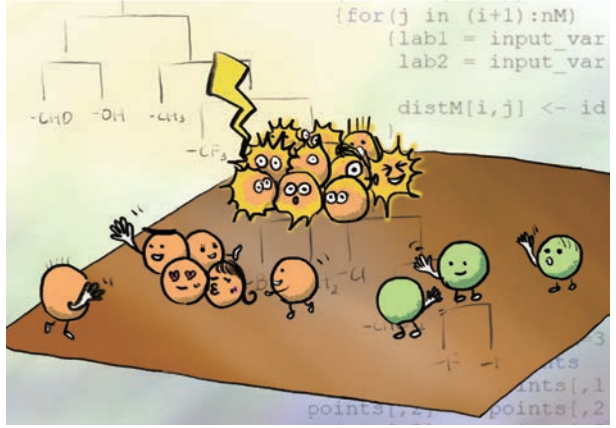
Creating guidelines for nanomaterial development using 'unsupervised machine learning'

Daniel Packwood and colleagues made use of mathematical science, theoretical chemistry, and materials science and succeeded in creating guidelines for machine learning, leading to protocols for assembling molecules on a desired substrate.

This 'machine learning' ascertains the relationship between chemical features of molecules and their assembly process, graphically summarizing the results. Analysis of these figures leads to these machine learning guidelines. Through this, it becomes possible to predict, for example, which molecule to employ for a linear supramolecular structure used as electrical wiring.

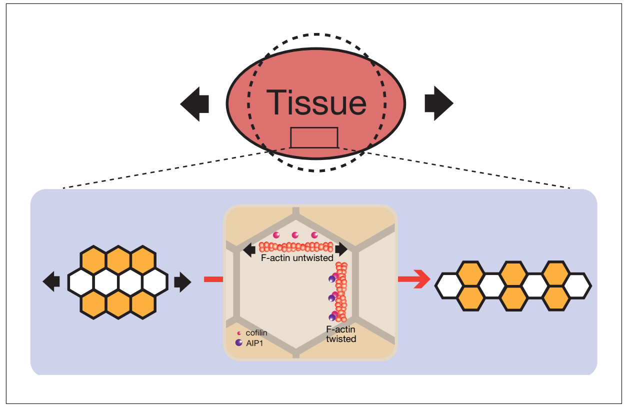
There are two types of machine learning, "supervised" and "unsupervised". The guidelines developed by this research can determine data group trends without knowing the correct and incorrect data solutions beforehand, a meaningful predictive application of "unsuper-vised machine learning".

This result contributes to the development of microdevice parts and will likely accelerate the development of nanoelectronics. In the future, it may also contribute to robot and soft display development, as well as the realization of ultra-low power consumption devices.



Molecules interact and align with each other in self-assembly.
Illustration by Izumi Mindy Takamiya

Daniel M Packwood, Taro Hitosugi (2018). Materials informatics for self-assembly of functionalized organic precursors on metal surfaces. *Nature Communications* 9, 2469



In response to tissue tension, cells change their position along the direction of tissue stress. AIP1 and cofilin maintain the structural stability of remodeling junctions to promote direc-tional cell rearrangement.

Keisuke Ikawa, Kaoru Sugimura (2018). AIP1 and cofilin ensure a resistance to tissue tension and promote directional cell rearrangement. *Nature Communications* 9, 3295

Mechano-sensing and resistance during development of the fruitfly wing

Kaoru Sugimura and Keisuke Ikawa have discovered new mechanisms of force sensing and force resistance during tissue development.

The global patterns of forces in a tissue (i.e., tissue stress such as tissue tension) control many aspects of development including cell proliferation, rearrangement, and polarity. However, the mechanism by which cells respond to and resist tissue stress during development remains unclear.

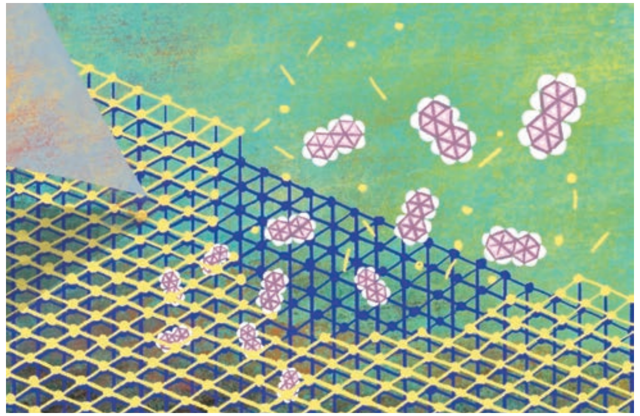
Sugimura's research group found that actin disassemblers, actin interacting protein 1 (AIP1) and cofilin, play a key role in sensing and resisting tissue tension to support directional cell rearrangement in the fruitfly wing. Tissue tension is converted into structural changes in the tiny actin filament, which are recognized by AIP1 and cofilin, leading to accumulation of AIP1 on the remodeling junction. AIP1 and cofilin promote actin turnover and strengthen the structural integrity of the remodeling junction. Future studies should explore whether the molecular mechanisms identified in the present study potentially function in other developmental contexts, such as cell proliferation and cell death.

Capturing the surprising flexibility of crystal surfaces

Susumu Kitagawa's group directly observes the crystal surface with an atomic force microscope. With this method, for the first time they observed the flexible and dynamic changes that occur on the surfaces of 'porous coordination polymer (PCP)' crystals.

When the porous crystal is exposed to certain molecules, its surface deforms from a square lattice structure to rhombic. Although the existence of porous crystals that flexibly change the structure when the concentration of molecules becomes equal to or greater than a certain value was known, how the surface behaved during this process remained a mystery.

This research found that the deformation of the surface of the porous crystal occurs at a lower concentration than for the deformation of the whole crystal. This means that the crystal surface has a more sensitive response than inside the crystal. The application of this phenomenon could lead to a wide range of nanotechnology, such as high-sensitivity sensors that detect trace amounts of substances and separation membranes that select substances at the nano level.



The team observed the fluctuations of the flexible PCP surface.
Illustration by Izumi Mindy Takamiya

Nobuhiko Hosono, Aya Terashima, Shinpei Kusaka, Ryotaro Matsuda, Susumu Kitagawa (2019). Highly responsive nature of porous coordination polymer surfaces imaged by in situ atomic force microscopy. *Nature Chemistry* 11(2), 109–116

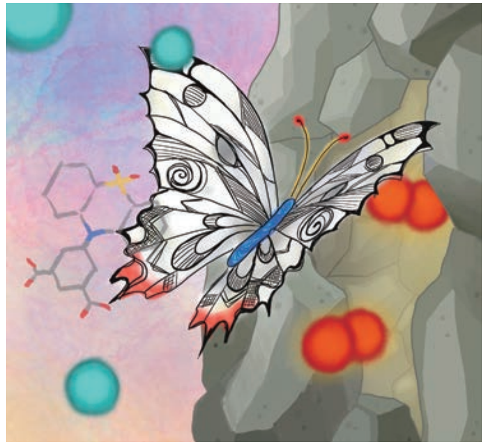
Materials that open in the heat of the moment

Susumu Kitagawa's group has developed a new porous material for sieving or storing different kinds of gas molecules.

They designed a porous coordination polymer that was formed of copper atoms linked by butterfly-shaped molecular "gates". This enables controling the pores' opening and closing according to temperature, allowing adjustment of the flow rate of gas molecules passing through the pores and the selection of gas types. This makes it possible to efficiently separate and store gases.

The research group succeeded in separating molecules with similar properties such as oxygen and argon, as well as ethylene and ethane by this method. Likewise, by controlling the release of the gas, the group also succeeded to slowly discharge the stored gas.

This research result can lead to further development of materials for gas separation and storage, with applications such as the separation of greenhouse gases and the storage of methane. It also has applications for a wide range of industries, such as material for the controlled release of ethylene gas, an important plant hormone for ripening fruits and vegetables.

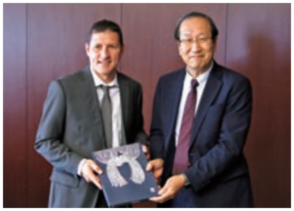


Butterfly-shaped ligands were the key to designing a material that can se-lectively absorb and store different gas molecules.
Illustration by Izumi Mindy Takamiya

Cheng Gu, Nobuhiko Hosono, Jia-Jia Zheng, Yohei Sato, Shinpei Kusaka, Shigeyoshi Sakaki, Susumu Kitagawa (2019). Design and control of gas diffusion process in a nanoporous soft crystal. *Science* 363(6425), 387–391

• What's new? •

iCeMS launches "Smolab" with CNRS, France



iCeMS established a joint laboratory "Small Molecule Lab (LIA-Smolab)" with the French National Center for Scientific Research (CNRS) and others. This collaboration aims to promote the development and application of "porous coordination polymer (PCP)" materials, which are filled with countless small holes that can take in gases. The October 9, 2018 signing ceremony was attended by Director Kitagawa and others. As PCP study further develops, the exchange between Kyoto University and French research institutions will also deepen.

iCeMS Caravan visits high school in Okinawa

iCeMS researchers held an "iCeMS caravan" on February 16, 2019 to deliver their original active-learning program to Kyuyo High School on Okinawa Island. High school students organized into groups to discuss the caravan lectures and gave presentations at the end of the program. The event was transmitted live to another room, where other participants, including families and teachers experienced the same process as the students in the main room. The program participants totaled more than 120.

Awards

- **Ryoichiro Kageyama receives the Naito Foundation Merit Award** (Nov 4, 2018)
- **Susumu Kitagawa Selected as the 2018 Highly Cited Researcher** (Nov 28)
- **Koichiro Tanaka receives the Nishina Memorial Prize** (Dec 6)
- **Aiko Fukazawa receives the Lectureship Award MBLA 2018** (Feb 1, 2019)
- **Hiroshi Kageyama receives the Inoue Prize for Science** (Feb 4)
- **French Maison de la Chimie awards Susumu Kitagawa the Grand Prix** (Feb 13)

Activities

- **iCeMS Science Festival 2018 held inviting High school students** (Nov 9, 2018)
- **KyotoU, UCLA hold joint symposium in California** (Nov 15–16)
- **iCeMS joins Instagram** (Dec 21)
- **iCeMS Participates in the WPI Science Symposium and Kagaku-Zammai in Aichi** (Dec 26–27)
- **iCeMS participates in the AAAS meeting in Washington DC** (Feb 14–17, 2019)

iCeMS Fund — Help us grow

At iCeMS, researchers from Japan and abroad devote themselves to research both day and night. Research results may sometime lead to applications, such as saving the lives of those suffering from incurable diseases or improving the global environment 100 years in the future. On the other hand, pure science we do may not be readily understood by people in the early stage. No one can predict the landscape we will be standing in after our challenges, however, we believe that our research will steadily advance science.

In order for iCeMS researchers to continue moving forward, it is necessary to establish a stable fiscal foundation. We appreciate your understanding of the activities and spirit of iCeMS, and we thank you for your continued support through the iCeMS Fund.

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Editorial note

We featured "Mechanobiology" in this issue. We spent time editing for the understanding of those not specialized in the field, but this was a super complicated theme (as we expected!) and we racked our brains so much. However, what is nice about iCeMS researchers is they always actively participate in the production of this newsletter series, and thanks to them, we have been able to deliver this completed issue to you.

In this issue "The Other Half of iCeMS" newly started. At iCeMS, not only researchers, but other staff members are also working to create the best research environment in the world. What do they do? What kind of people are they? We will deliver stories of the other very important half of our institute. Please let us know your thoughts.

Mari Toyama

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