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Osaka University

Research Profile

2019

A Collection of Twelve Impactful Articles
from Osaka University

Osaka University was founded in 1931 as one of the seven national universities of Japan and now has expanded to one of Japan's leading comprehensive universities. The University has embarked on an open research revolution with its vision of openness for 2021 from its position as Japan's most innovative university and one of the most innovative institutions in the world according to the Nature Index 2017 Innovation. The university's ability to innovate from the stage of fundamental research through the creation of useful technology with economic impact stems from its broad disciplinary spectrum.

Facts and Figures

Faculty and Staff *female staff
(as of May 1, 2019)

3,261
*587
Academic Staff

3,447
*2,263
Researchers, Administrative Staff, Medical Staff, etc.

Students
(as of May 1, 2019)

15,285
Undergraduate Students

8,031
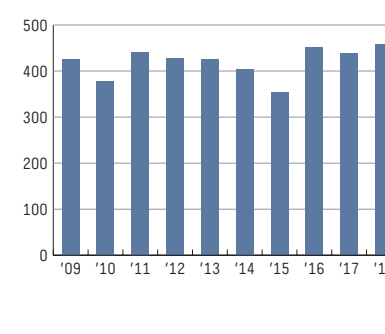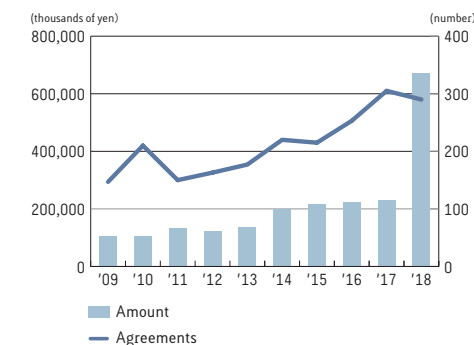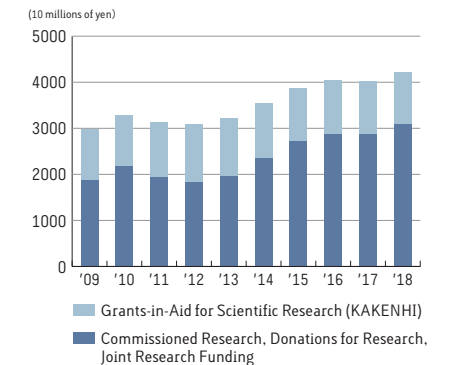Graduate Students

International Researchers
(Inbound) April 1, 2018 - March 31, 2019

Europe 265
Middle East 35
Asia 591
North America 100
Africa 33
Oceania 26
Others 19
Central and South America 21

Total 1,090

Budget FY 2019, in millions of yen

Revenues
157,952

Government Grants, etc. 4,062
Others
Funds for Facilities 8,878
Tuition and Fees 12,529
Industry-University Collaboration Research Revenues and Donations 30,585
9,076
Management Expenses Grant 50,962
41,860
Hospital Revenues

Expenses
157,952

Grant Program Management Expenses 4,062
Long-Term Debt Reimbursement 1,410
Facilities Expenses 8,878
Industry-University Collaboration Research Expenses, etc. 30,585
68,335
Education and Research Operating Expenses
44,682
Hospital Expenses

The Number of Invention Disclosures

'09 '10 '11 '12 '13 '14 '15 '16 '17 '18

License Agreements and Income
(including licensing, assignment and MTA)

(thousands of yen) (number)

'09 '10 '11 '12 '13 '14 '15 '16 '17 '18

■ Amount
— Agreements

External Funding

(10 millions of yen)

'09 '10 '11 '12 '13 '14 '15 '16 '17 '18

■ Grants-in-Aid for Scientific Research (KAKENHI)
■ Commissioned Research, Donations for Research, Joint Research Funding

Researchers have found that the structure of Parkinson's disease-associated protein aggregates can tell us, for the first time, about their movement through the brain. These new findings indicate that Parkinson's disease is a kind of amyloidosis, which has implications for its diagnosis and treatment.

Lewy bodies, primarily composed of α-synuclein proteins (α-syn), are the neuropathological hallmark of Parkinson's disease. However, we don't yet fully understand how or why they appear in the brain. Using state-of-the-art imaging techniques, researchers at Osaka University have found that Lewy bodies in Parkinson's disease brains contain α-syn protein aggregates (called amyloid fibrils) that can propagate through the brain. These findings, published in *PNAS*, support the new idea that Parkinson's disease is a kind of amyloidosis, which

is a group of rare diseases caused by abnormal protein accumulation.

"Our work follows on from *in vitro* findings that aggregates of α-synuclein that can propagate through the brain have a cross-β structure," says lead author of the study Dr Hideki Mochizuki. "Our study is the first to find that aggregates in Parkinson's disease brains *also* have this cross-β structure. This could mean that Parkinson's disease is a kind of amyloidosis that features the accumulation of amyloid fibrils of α-synuclein."
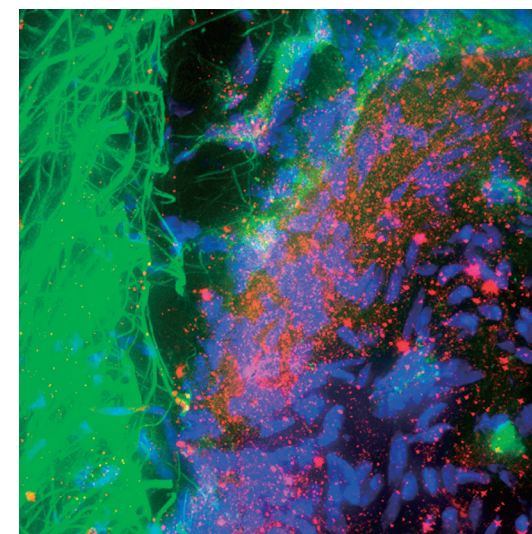
While immunostaining can tell us about the localization of a protein of interest, it doesn't tell us about its conformation. Electron microscopy can tell us about morphological features, but not about protein structure. Similarly, Fourier-transform infrared spectroscopy can tell us about the secondary structure of proteins, but not about their

fibrillary organization.

The researchers therefore teamed up with the large-scale synchrotron radiation facility, SPring-8, and used microbeam X-ray diffraction to visualize the ultrastructure of Lewy bodies in the post mortem brain slices of three patients with Parkinson's disease. Some of the α-syn aggregates did indeed have a cross-β structure, but there was quite a bit of variety in the state of amyloid proteins.

"One possibility is that this variability could indicate the different maturity stages of Lewy bodies," says Dr Katsuya Araki, first author of the paper. "This has obvious implications in the diagnosis of Parkinson's disease, and could also have therapeutic implications in the long run."

The researchers suggest that Parkinson's disease is a systemic (whole-body) amyloidosis rather than one that is localized to one part of the brain. This fits with the non-motor symptoms that patients experience before the onset of motor dysfunction and the multiple organ involvement of α-syn pathology. The findings from this work are highly applicable to the development of new diagnostic and therapeutic tools for the treatment of Parkinson's disease.

Hideki Mochizuki

Department of Neurology, Graduate School of Medicine

"The seeds of Parkinson's disease: Amyloid fibrils that move through the brain"

Using X-ray diffraction of post mortem brains, researchers find α-synuclein aggregates that can move through the brain before developing into Lewy bodies, the hallmark of Parkinson's disease

The red specks in this fluorescent micrograph of a section through a brain affected by Parkinson's disease are the protein α-synuclein, which is thought to cause the progressive degeneration of the neurons that leads to the symptoms of the disease.

[reference]

Araki K. et al. (2019) Parkinson's disease is a type of amyloidosis featuring accumulation of amyloid fibrils of α-synuclein. *Proceedings of the National Academy of Sciences* 116:36, 17963-17969. DOI: 10.1073/pnas.1906124116

https://resou.osaka-u.ac.jp/en/research/2019/20190820_1

The gut has a population of organisms that live within in it, called the gut microbiome, which are linked to human health and disease. Recent studies have shown that assessing the genetic changes in fecal samples can accurately reflect the status of the gut microbiome, and may be useful for the early diagnosis of diseases.
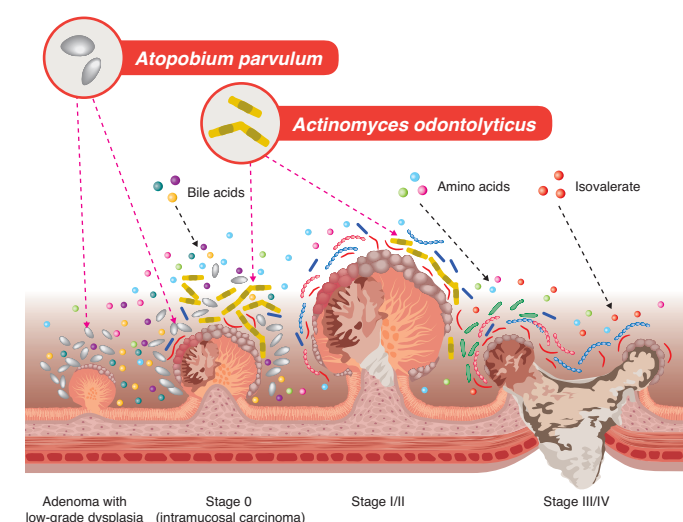
A group of researchers from Osaka University have reported increases in specific microbiome organisms that are linked to the neoplasms associated with colorectal cancer, such as intramucosal carcinomas and polypoid adenomas. Their results, published in *Nature Medicine*, reveal that these specific markers could help distinguish cases of colorectal cancer from healthy samples.

"We believe that colorectal cancer is fundament-

ally not only a genetic but also a microbial disease," says one of the study's corresponding authors, Shinichi Yachida. "Our results show that changes in the gut microbiome are present at the very early stages of colorectal cancer development, which could potentially provide vital diagnostic and causative clues for this disease."

Colorectal cancer, the third most prevalent cancer globally, is a relatively slow-moving disease—meaning it takes a long period of time before reaching its final, fatal stages. Therefore, early detection is crucial to ensuring effective treatment. The researchers used fecal samples from a little over 600 patients who underwent colonoscopy to assess the characteristics of their gut microbiota and how they relate to colorectal cancer.

"Our results revealed that colorectal cancer was linked to an increase in certain factors in the gut microbiome, as well as the presence of cancer-associated organisms," says the second corresponding author, Takuji Yamada. "Future studies will focus on the relationship between the gut microbiome and tumor characteristics in individual patients with colorectal cancer. This will help us understand the roles of the microbiome in the development of colorectal cancer."

Shinichi Yachida

Department of Cancer Genome Informatics, Graduate School of Medicine

"A gut feeling: Microbiome changes may mean early detection of colorectal cancer"

Researchers reveal specific changes in the gut microbiota at different stages of colorectal cancer that may lead to important detection methods or further understanding of colorectal cancer development

Atopobium parvulum

Actinomyces odontolyticus

Bile acids   Amino acids   Isovalerate

Adenoma with low-grade dysplasia   Stage 0 (intramucosal carcinoma)   Stage I/II   Stage III/IV

Microbial dynamics during multistep colorectal cancer progression: Graphic representation of major microbial and metabolomic alterations during multistep colorectal cancer progression

[reference]

Yachida S. et al. (2019) Metagenomic and metabolomic analyses reveal distinct stage-specific phenotypes of the gut microbiota in colorectal cancer. *Nature Medicine* 25, 968–976. DOI: 10.1038/s41591-019-0458-7

https://resou.osaka-u.ac.jp/en/research/2019/20190607_1

Collective cell migration, where groups of cells move together with a common purpose, is important for processes ranging from wound healing to tumor metastasis. Migrating cells respond to a combination of physical cues elicited by cell-to-cell contact and waves of chemical signals sent out by local cells to attract others to their location.

However, a team led by researchers from Osaka University have found that this combined approach may not be the case for cells at all stages of development.

In the study published in *Communications Biology*, the researchers used model organism *Dictyostelium iscoideum* to better understand the cues controlling collective cell migration during development. Referred to as social amoebae, unicellular *D. discoideum* cluster together in times of stress to form a multicellular aggregate called a slug.

Though their less-than-enticing name may inspire shudders in readers who have encountered their animal namesake, cells within the slugs seem to like getting up-close and personal: the researchers found that while free-living cells respond to waves of chemical stimuli, slug cells require physical interaction to induce migration.
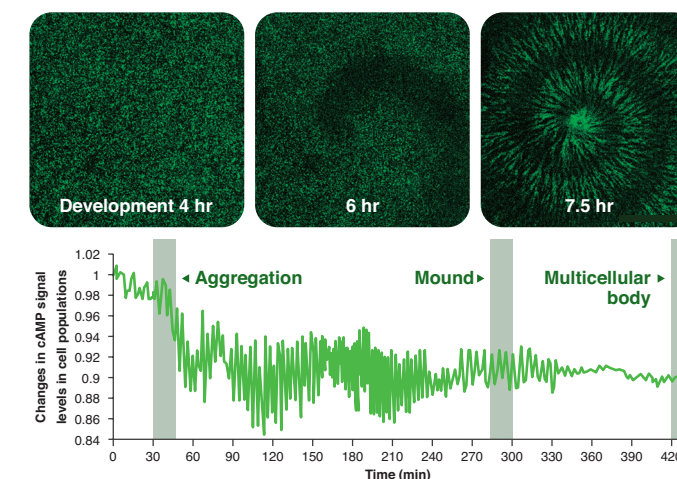
Hidenori Hashimura, lead author of the study, explained how they used changes in the intensity of chemical signals to deduce the importance of this type of signalling at different developmental stages. "Cyclic adenosine 3',5'-monophosphate (cAMP) is the only chemical guidance cue for cell aggregation. Using live cell imaging, we clearly observed waves of cAMP, which can be visualized using a green fluorescent probe, during the initial stages of cell aggregation," says corresponding author Yusuke V. Morimoto. However, it was revealed that the cAMP signals gradually disappeared during migration of the multicellular slugs.

"We found that the cAMP propagation waves thought to control mass cellular movement during all stages of *Dictyostelium* development actually disappeared once the cells aggregated into multicellular slugs," explains co-author Masahiro Ueda. "Although cell movement within the slugs was equal to that of cells in the early aggregation stage, the absence of cAMP signal waves suggested an alternative cue for collective cell migration."

The researchers proposed that "contact following", where physical contact between cells allows them to follow each other, is likely to be responsible for collective cell migration during the slug phase of *Dictyostelium* development.

This is the first time researchers have examined cAMP signal dynamics in the multicellular phase of *Dictyostelium* development and highlights the importance of examining cellular processes at all stages of development. More importantly, understanding collective cell migration cues is a vital step in developing methods to prevent metastatic cancer and promote wound healing.

Masahiro Ueda

Department of Biological Sciences, Graduate School of Science

"More physical than chemical: Researchers show what really gets cells going"

Researchers find that unlike their unicellular counterparts, aggregated social amoebae need physical contact rather than chemical signals to get them going


Top, fluorescence images of cAMP signals in aggregating cells. Bottom, changes in cAMP signal levels in cell populations during development.

[reference]

Hashimura H. et al. (2019) Collective cell migration of *Dictyostelium* without cAMP oscillations at multicellular stages. *Communications Biology* 2:34. DOI:10.1038/s42003-018-0273-6

https://resou.osaka-u.ac.jp/en/research/2019/20190206_e1
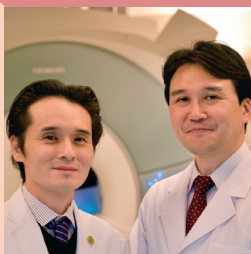
Researchers have developed a computer method that uses magnetic resonance imaging (MRI) and machine learning to rapidly forecast genetic mutations in glioma tumors, which occur in the brain or spine. The work may help glioma patients to receive more suitable treatment faster, giving better outcomes. The research was published in *Scientific Reports*.

Cancer treatment has undergone a revolution in recent years. Spurred by recognition that each cancer case is unique, the specific genetic mutations tumor cells carry are now sequenced to discover which chemotherapy drugs will work best. However, certain types of cancer, especially brain tumors, are less accessible for genetic testing. The tumor's genotype can't be found until a sample is taken during surgery, and this can significantly delay treatment.
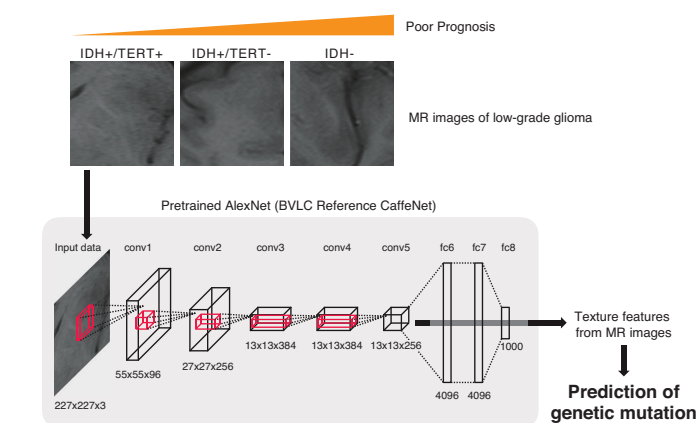
Glioma is a type of cancer that originates in the brain's supporting cells. Two types of mutations are especially important; these are changes in the gene for the enzyme isocitrate dehydrogenase (IDH) or the promoter region of telomerase (TERT). Identifying these mutations can help direct the proper course of treatment. The researchers produced a machine-learning algorithm that can predict which mutations are present using only the MR images of the tumors.

"Machine learning is increasingly used to diagnose medical images. But our work is one of the first to even attempt to classify something as hidden as the genotype based on image data alone," study first author Ryohei Fukuma explains. The algorithm was found to be significantly better at predicting the mutations compared with conventionally used radiomic features of the MR images, such as size, shape, and intensity.

To construct the algorithm, the researchers used a convolutional neural network to extract features from the MR images. Then, using a machine-learning method called support vector machines, they classified the patients into groups based on the presence or absence of mutations. "We hope to expand this approach to other types of cancer, so we can take advantage of the large cancer gene databases already collected" senior author Haruhiko Kishima says.

The end result could remove the need for surgical tissue sampling. Even more, it could lead to better clinical outcomes for patients as the process of delivering personalized medicine becomes easier and faster.

Manabu Kinoshita (left)

Graduate School of Medicine

Takufumi Yanagisawa (right)

Institute for Advanced Co-Creation Studies

"Peering into the genome of brain tumor"

Osaka University-led research introduces a machine-learning algorithm for predicting genetic mutations of malignant brain tumor types based only on MRI, offering promise for noninvasive diagnosis and faster treatment

MR images of gliomas were fed into a pre-trained deep neural network that can classify natural images. The activities of neurons in each layer of the network were used to characterize the textures of the MR images. These texture features were used to infer three key molecular subtypes of gliomas. The obtained algorithm was able to predict these molecular subtypes with an accuracy of 63.1%.

[reference]

Fukuma R. et al. (2019) Prediction of IDH and TERT promoter mutations in low-grade glioma from magnetic resonance images using a convolutional neural network. *Scientific Reports* 9:20311. DOI: 10.1038/s41598-019-56767-3

https://resou.osaka-u.ac.jp/en/research/2020/20200106_1

Masaya Yamaguchi

Department of Oral and Molecular Microbiology,
Graduate School of Dentistry

To successfully infect their hosts, bacteria need to evade the host immune system in order to reproduce and spread. Over the course of evolution, hosts — such as humans — develop increasingly sophisticated defenses against bacterial infection, while bacteria in turn develop new strategies to overcome these defenses in a biological arms race.

This competition has led to the development of antibiotic-resistant bacteria, for which few or no medical treatments are effective. Hence, there is an increasingly urgent need for novel drugs for use against such bacteria.

A research team has provided new hope in the battle against antibiotic-resistant bacteria by revealing a genetic factor that is important for the virulence of *Streptococcus pneumoniae*. This bacterium causes sepsis, pneumonia, and meningitis and is a major threat to public health globally. The team used molecular evolutionary analysis of gene sequences to identify a gene that has been largely prevented from mutating into other variant forms, suggesting that it is essential for the infection and/or reproduction of this bacterium.

In this work, reported in the journal *Communications Biology*, the team focused on genes encoding proteins called choline-binding proteins (CBPs), which are present on the bacterial cell surface and interact with the host's immune system.
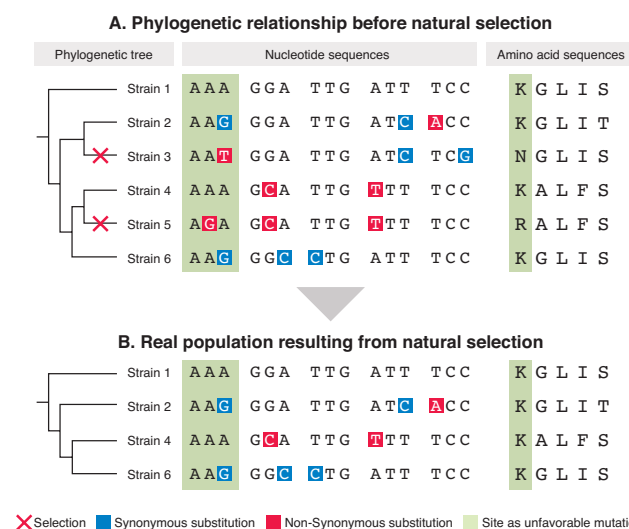
"We analyzed all the codons in genes encoding CBPs and compared their levels of diversity, reflecting how tolerant to mutation each gene is," Shigetada Kawabata says. "We found that, in the gene *cbpJ*, over 13% of codons were under negative selection, meaning that if mutations had occurred in these regions, they reduced bacterial survival and led to the mutant being eliminated from the population."

This finding led the team to investigate *cbpJ*'s effects. They found that when mice were intra-nasally infected with wild-type or *cbpJ*-deficient *S. pneumoniae*, those with the mutant bacteria were more likely to survive and had fewer bacteria in their lungs.

"We then cultured the *cbpJ*-deficient *S. pneumoniae* with neutrophils in medium and found that the mutant bacteria were generally less able to survive; however, when neutrophils were absent from the medium, they actually did better than the wild-type bacteria," lead author Masaya Yamaguchi says. "This suggests that *cbpJ* helps bacteria to evade detection and clearance by neutrophils."

The fact that the *cbpJ* gene is under strict negative selective pressure makes it a particularly attractive target for drugs, as this pressure would limit the likelihood of drug-resistant mutants emerging. This study also shows the value of molecular evolutionary analysis to identify new drug targets, including among pneumococcal virulence factors, especially when combined with traditional molecular microbiological approaches.

"Winning the arms race: Analysis reveals key gene for bacterial infection"

Researchers use molecular-level analyses of evolution to identify a key gene in bacterial infection, potentially providing a novel target for drugs that could minimize the incidence of bacterial resistance

Scheme for intraspecies molecular evolutionary analysis.
A. Random genetic drift induces synonymous and nonsynonymous mutations with equal probability. However, nonsynonymous mutations in essential regions are subjected to selective pressures. B. As a result of natural selection, synonymous substitutions are concentrated in important genes. Phylogenetic and molecular evolutionary analyses can detect significant accumulation of the substitutions.
(©2019 Yamaguchi M. et al., *Communications Biology*)

[reference]

Yamaguchi M. et al. (2019) Identification of evolutionarily conserved virulence factor by selective pressure analysis of *Streptococcus pneumoniae*. *Communications Biology* 2: 96. DOI: 10.1038/s42003-019-0340-7

https://resou.osaka-u.ac.jp/en/research/2019/20190311_1

Tsuyoshi Inoue

Advanced Pharmaco-science,
Graduate School of Pharmaceutical Science

For over 100 years, chemists have applied amounts of nitrogen fertilizer to soils to help feed the world; however, this leads to eutrophi-cation, an imbalance in the nitrogen cycle, one of the factors which causes destruction of the ozone layer. But now, researchers from Japan have experimentally verified the atomic-scale structure of an enzyme that may help to improve the environ-mental sustainability of this chemical reaction.

In a study published in *Proceedings of the National Academy of Sciences*, researchers from Osaka University used a technique called neutron diffraction crystallography to image the atom-by-atom architecture of an enzyme that belongs to a class known by the acronym CuNIR. If eutrophication progresses and excess nitrogen is present in the water and surrounding area, the large amount of plankton resulting from this excess will lead to water environmental problems, such as toxicity and odor, as well as various environmental problems, such as acid rain and ozone decomposition.
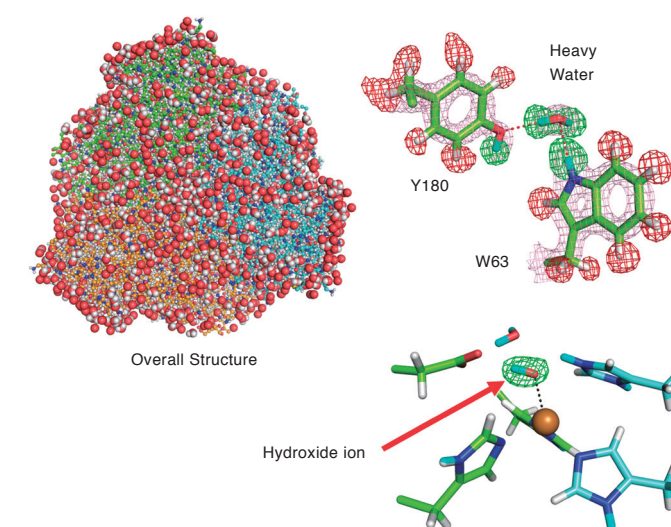
"Humanity needs to understand how nature performs this reaction so we can design an artificial reaction and perform it more efficiently," explains Tsuyoshi Inoue, a co-lead author of the study.

Previously, researchers haven't been able to see all of the atomic-scale detail of CuNIR enzymes, nor have they been able to avoid damaging these enzymes while imaging them. The Osaka University research team's imaging technique overcomes these limitations by using neutron diffraction. In doing so, the researchers experimentally verified theoretical calculations of the enzyme's structure.

These new experimental results clarified a long-standing, frustrating mismatch between lab work and calculations. "We confirmed details of copper binding and hydrogen bond dynamics that were predicted by theoretical calculations, but were obscured by experiments in the lab," explains Yohta Fukuda, senior author.

In addition to minimizing a global source of nitrogen pollution, the research team's findings may also be useful toward normalizing the nitrogen cycle. Inoue says: "Neutron diffraction crystallography may improve our understanding of enzymes that we can use to degrade nitrogen-containing pollutants throughout the environment."

"It's crystal–clear: Neutron beam uncovers reaction of the denitrification process in nature"

Researchers use neutron structure analysis to understand an enzyme that may help equilibrate nitrogen cycling in nature

Neutron crystal structure of CuNIR. Because neutron crystallography can visualize detailed protein structures including hydrogen, the smallest atom in this world, one can distinguish a hydroxide ion, a key intermediate of the chemical reaction, from a water molecule.

[reference]

Fukuda Y. et al. (2019) High-resolution neutron crystallography visualizes an OH-bound resting state of a copper containing nitrite reductase. *Proceedings of the National Academy of Sciences* 117:8, 4071-4077. DOI: 10.1073/pnas.1918125117

https://resou.osaka-u.ac.jp/en/research/2020/20200211_2

A team including researchers from Osaka University has produced a new molecular emitter for organic light-emitting diodes (OLEDs). Using rational chemical design with U-shaped synthetic building blocks, the scientists were able to arrange the electron donors and acceptors into a large ring called a "macrocycle." The wheel-shaped molecule could potentially be used not only in OLEDs but also in tiny, energy-efficient chemical sensors in the future.

Many modern televisions and smartphones use OLEDs to display pictures and videos. These devices can efficiently convert electricity into light because they are made from carbon-based molecules containing alternating single and double chemical bonds, an arrangement called π-conjugation. This configuration allows electrons to become highly mobile because they are effectively "delocalized" over large regions of the molecules, which tend to be long linear chains. When a molecule is electronically excited by external energy and then relaxes to the original state, the excess energy can be converted directly into light. By adding the right chemical functional groups to the molecule, a whole range of properties, such as emission colors and energy conversion efficiencies, can be fine-tuned.
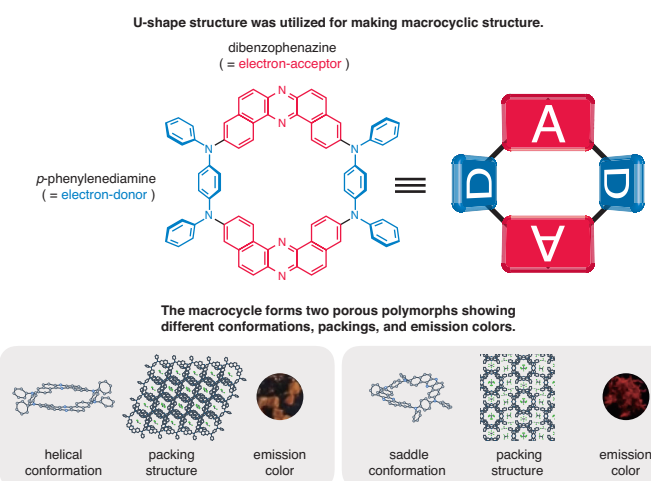
Now, a research team led by Professor Youhei Takeda has designed and synthesized an efficient macrocyclic OLED emitter in which donor and acceptor regions alternate in a permanently bonded ring structure. They found that OLED devices fabricated with the new macrocyclic emitter show much better efficiencies compared with linear molecular emitters (which act like open forms of the macrocycles), due to the fact that the macrocycles can more efficiently harvest ambient heat energy in a process called "thermally activated delayed fluorescence."

"Linear π-conjugated oligomers and polymers already play crucial roles in materials science, but we found ring-shaped macrocycles to be even better for many applications," says first author Saika Izumi. The team was able to create two different conformations, "saddle" and "helical", with different packing arrangements and emission colors. The nanoscale cavities inside the rings can be designed to interact with target molecules to create efficient and selective chemical sensors.

"Macrocycles can be arranged into highly-ordered 2D- and 3D-molecular assemblies that are much more difficult to achieve with linear analogs," explains senior author Youhei Takeda.

Possible future applications include the detection of chemical substances, such as water molecules or gases, based on the modulation of light emitted when the target substance is present inside the cavity.

Youhei Takeda

Department of Applied Chemistry, Graduate School of Engineering

"Light-up wheels: Unique organic light-emitting molecular emitters"

Researchers design and synthesize highly efficient carbon-based 3rd-generation OLED molecular emitters by linking the donor and acceptor modules into a ring, potentially paving the way for extremely sensitive nanoscale chemical detectors

U-shape structure was utilized for making macrocyclic structure.

dibenzophenazine (= electron-acceptor)

p-phenylenediamine (= electron-donor)

The macrocycle forms two porous polymorphs showing different conformations, packings, and emission colors.

helical conformation / packing structure / emission color

saddle conformation / packing structure / emission color

External quantum efficiency of the OLEDs fabricated with the macrocyclic TADF material achieved much higher value (11.6%) than those with conventional fluorescent materials.

Schematic explanation for the developed TADF-active macrocyclic material

[reference]

Izumi S. et al. (2020) Thermally activated delayed fluorescent donor–acceptor–donor–acceptor π-conjugated macrocycle for organic light-emitting diodes. *Journal of the American Chemical Society* 142:3, 1482-1491. DOI:10.1021/jacs.9b11578

https://resou.osaka-u.ac.jp/en/research/2020/20200108_2
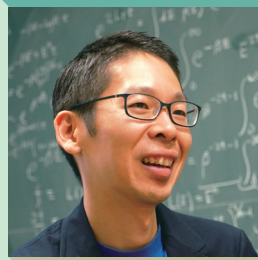
A research team from Osaka University, Nihon University and Chuo University has proposed a novel theoretical framework whose experiment could be performed in a laboratory to better understand the physics of black holes. This project can shed light on the fundamental laws that govern the cosmos on both unimaginably small and vastly large scales.

Recently, the world was transfixed when the first ever images of a black hole were released by the Event Horizon Telescope. Or, to be more precise, the pictures showed the bright circle, called an Einstein ring, made by the light that just barely escaped the grasp of the black hole's immense gravity. This ring of light was due to fact that, according the theory of general relativity, the fabric of spacetime itself becomes so contorted by the mass of the black hole that it acts like a huge lens.

Unfortunately, our understanding of black holes remains incomplete, because the theory of general relativity—which is used to describe the laws of nature at the scale of stars and galaxies—is not currently compatible with quantum mechanics, our best theory of how the Universe operates on very small scales. Since black holes, by definition, have a huge mass compressed into a tiny space, reconciling these wildly successful but thus far conflicting theories is necessary to understand them.
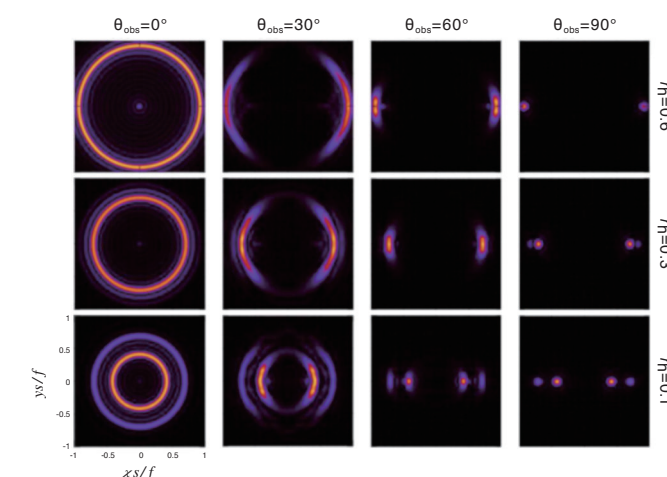
One possible approach for solving this conundrum is called string theory, which holds that all matter is made of very tiny vibrating strings. One version of this theory predicts a correspondence between the laws of physics we perceive in our familiar four dimensions (three dimensions of space plus time) and strings in a space with an extra dimension. This is sometimes called a "holographic duality," because it is reminiscent of a two-dimensional holographic plate that holds all the information of a 3D-object.

In the newly published research, the authors, Koji Hashimoto (Osaka University), Keiju Murata (Nihon University) and Shunichiro Kinoshita (Chuo University) apply this concept to show how the surface of a sphere, which has two dimensions, can be used in a tabletop experiment to model a black hole in three dimensions. In this setup, light emanating from a source at one point of the sphere is measured at another, which should show the black hole if the spherical material allows holography.

"The holographic image of a simulated black hole, if observed by this tabletop experiment, may serve as an entrance to the world of quantum gravity" says the author Hashimoto. The researchers also calculated the radius of the Einstein ring that would be observed if this theory is correct.

"Our hope is that this project shows the way forward towards a better understanding of how our Universe truly operates on a fundamental level," says the author Keiju Murata.

Koji Hashimoto

Department of Physics, Graduate School of Science

"Black hole holograms"

Researchers propose a new holographic method to simulate black holes with a tabletop experiment. This work may be crucial for solving one of the biggest mysteries in science - reconciling quantum mechanics and general relativity

$\theta_{obs}=0°$ $\quad \theta_{obs}=30°$ $\quad \theta_{obs}=60°$ $\quad \theta_{obs}=90°$

$\eta=0.6$ / $\eta=0.3$ / $\eta=0.1$

Theoretical prediction of the image of the black hole from the table-top experiment. The radius of the ring depends on the temperature. The image of the black hole is deformed as the observation point θ_{obs} is varied.

[reference]

Hashimoto K. et al. (2019) Einstein rings in holography. *Physical Review Letters* 123:031602. DOI: 10.1103/PhysRevLett.123.031602

https://resou.osaka-u.ac.jp/en/research/2019/20190730_1

Hirotaka
Koga

Department of Functionalized
Natural Materials,
The Institute of Scientific and
Industrial Research

The "Internet of Things" concept of interconnecting devices to streamline the experiences of the global population is reliant on sensors to acquire the real-world data. The extent of this reliance is illustrated by the dauntingly named "trillion sensors universe" initiative that was started to support the project. Optimizing the properties of sensor devices to achieve this abundance is therefore critical to establishing viable networks. Researchers at Osaka University have developed a paper-based disposable gas sensor that caters to widespread sensing. Their findings are published in *ACS Applied Materials and Interfaces*.

Issues such as the cost and sustainability of the raw materials used, the robustness and consistency of the devices, and their disposability and environmental impact are some of the criteria that must be addressed alongside the sensing performance when considering detection on such a large scale.

To fulfill these requirements, the researchers have developed a zinc oxide molecular sensor made from very fine nanowires that is supported by a biodegradable cellulose nanofiber backing and has graphite electrodes that can be drawn on with a pencil. The sensor was used to detect NO_2 gas—an important component of many industrial processes—and showed a performance comparable to that of available electrodes.
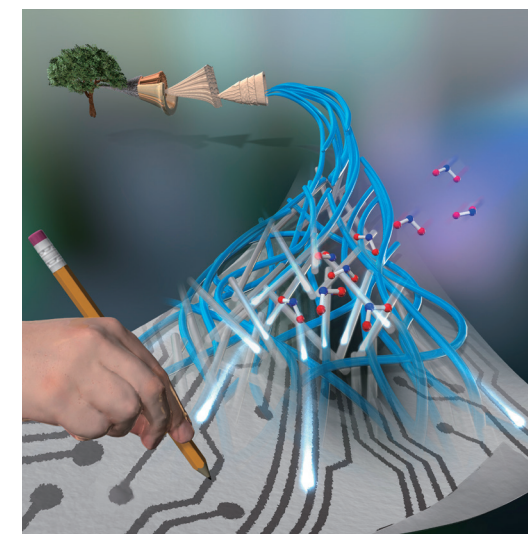
"Our design ticks many boxes for delivering economical and environmentally conscious molecular sensing on a large scale," study lead author Hirotaka Koga explains. "The zinc oxide nanowires offer a very large surface area for gas molecules to attach to, and the cellulose paper support is robust and can be cut very small—to just a few millimeters—with ordinary scissors. The sensors are prepared in a simple 2-step process, which makes them appropriate for widespread use."

When NO_2 molecules are present around the sensor they adsorb to the surface of the nanowires and the resistance increases as the gas molecules affect the electrons that carry current between the electrodes. The resistance increase is greater for more concentrated gas.

"We expect the many advantages of our device to make a significant contribution, particularly to molecular detection," Associate Professor Koga explains. "The accurate measurement of gas concentrations is important in many fields including healthcare, environmental protection, chemical production, and health and safety."

The researchers hope that the simple 2-step process can be extended for the detection of other gas molecules.

"New molecular sensor ticks the "trillion sensor universe" boxes"

Researchers report a robust lightweight low-cost molecular sensor based on paper for efficient gas detection

A paper-based molecular sensor device, which is constructed from a wood-derived cellulose nanofiber paper substrate, a zinc oxide nanowire sensor, and a pencil-drawn graphite electrode, demonstrates not only efficient molecular sensing but also cut-and-paste usability and easy disposability for future IoT society.

[reference]

Koga H. et al. (2019) Paper-based disposable molecular sensor constructed from oxide nanowires, cellulose nanofibers, and pencil-drawn electrodes. *ACS Applied Materials and Interfaces* 11:16, 15044-15050. DOI: 10.1021/acsami.9b01287

https://resou.osaka-u.ac.jp/en/research/2020/20200318_e1

Koh
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Over millions of years of evolution, insects have developed a wide array of impressive adaptations, some of which that they can wield in new and surprising ways. For example, trap-jaw ants have powerful, spring-loaded mouthparts that can snap shut at over 200 kph. This makes the mandibles among the fastest moving body parts in nature. Besides their fearsome chomping ability, trap-jaw ants have discovered that, by pushing with their hind legs while simultaneously "biting" the ground, an ant can send itself hurtling through the air to escape a predator or a deep pit. This innovative form of locomotion turns out to be very energy efficient, even when compared with sophisticated human-designed machines.
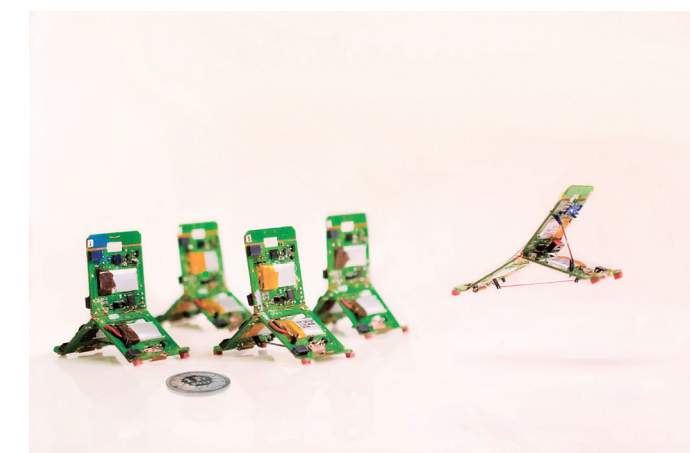
Now, Koh Hosoda at the Adaptive Robotics Laboratory, Osaka University together with his colleagues at Swiss Federal Institute of Technology Lausanne took inspiration from the trap-jaw ants to construct cooperative origami millirobots. Called "Tribots," these insect-sized, upside-down "Y"-shaped machines can crawl, leap, and even summersault over obstructions. The "muscles" of the Tribots are spring-like linear shape-memory alloy actuators. The hinge mechanism allows the robots to jump over previously impassible areas.

"The integrated design of the actuators and surface-mounted electronics enables us to miniaturize the robots," emphasize the authors. The team measured the mechanical power and energy "cost of transport," and found that Tribots surpassed the heavier jumping robots currently available.

Groups of Tribots can coordinate to accomplish tasks using division of labor. For example, one Tribot designated as the leader can command two others to move a box. This technology can be used to build scalable "colonies" of autonomous robots that might explore the surfaces of new planets.

"The ability to move over diverse terrain while accomplishing coordinated tasks sets these robots apart from currently available rovers," say the authors. "Here on Earth, Tribots might be deployed for search-and-rescue missions in the wake of natural disasters like floods or earthquakes."

"Designing minimal and scalable insect-inspired multi-locomotion millirobots"

An international research team constructed insect-size millirobots with the ability to fling themselves into the air like trap-jaw ants

Multi-locomotion millirobots inspired from trap-jaw ants ©Ahenishbek Zhakypov

[reference]

Zhakypov Z. et al. (2019) Designing minimal and scalable insect-inspired multi-locomotion millirobots. Nature 571, 381-386. DOI: 10.1038/s41586-019-1388-8

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Asako Miura

Social Psychology, Graduate School of Human Sciences

In an Internet-driven world, social media has become the go-to source of all kinds of information. This is especially relevant in crisis-like situations, when warnings and risk-related information are actively circulated on social media. But currently, there is no way of determining the accuracy of the information. This has occasionally resulted in the spread of misinformation, with some readers often bearing the brunt. In a study published in *Japanese Psychological Research*, scientists at Osaka University, including Prof Asako Miura, found a pattern through which information spreads on social media—which could help prevent the spread of fake news. Prof Miura says, "Dissemination of information through social media is often associated with false rumors. In order to prevent this, we wanted to unravel the underlying mechanisms by digging deeper into how these false rumors spread."

The scientists focused on Twitter, a popular site where users can disseminate or share information through the "retweet" feature. Conventional models of information diffusion fail to adequately explain the exact transmission route on social media, as they do not take into account individual user characteristics. Therefore, to study these characteristics, the scientists first selected 10 highly retweeted (more than 50 times) risk-related tweets. Based on Slovic's well-known definition of risk perception, a cognitive model used to assess how people perceive certain risks, they assessed whether users perceived these risks as "dreadful" (related to large-scale events with potentially dire consequences) or "unknown" (when the impact of the event is unknown). They then analyzed the personal networks of the users who tweeted/

retweeted particular tweets—specifically the number of followers, followees, and mutual connections.

They found that users with fewer connections tend to spread information arbitrarily, possibly owing to a lack of experience or awareness. But, users with a high number of mutual connections were more emotionally driven—they were more likely to spread dreadful information, possibly intending to share their reactions with the public. Prof Miura explains, "Our study showed the existence of an information diffusion mechanism on social media that cannot be explained by conventional theoretical models. We showed that risk perception has a significant impact on the 'retweetability' of tweets."

By identifying the user network characteristics on Twitter, this study potentially offers a solution to prevent fake news dissemination. These characteristics can be leveraged to maximize the spread of accurate information, ensuring that appropriate measures are taken. Prof Miura concludes, "Our research provides an opportunity for people to rethink how false information is spread and to deliver accurate information via social media."

"How dangerous news spreads: What makes Twitter users retweet risk–related information"

Scientists uncover how information related to potential dangers can spread on social media and how this can be prevented

©AlonzoDesign/Getty Images

[reference]

Komori M. et al. (2021) Spread of risk information through microblogs: Twitter users with more mutual connections relay news that is more dreadful. *Japanese Psychological Research* 63:1. DOI: 10.1111/jpr.12272

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Lianming Zhu

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Governments use special economic zones (SEZs) to incentivize firms to enter a region and form industrial clusters. This collective force, called an agglomeration economy, brings benefits such as greater productivity and wages, technological advances, and price impacts. SEZs have been around since the mid-20th century and are a popular strategy worldwide, but there have been few studies of their true success or failure, or looking at them over time.

In China, SEZs have been prominent in economic policy since 1979, which makes Chinese SEZs an ideal subject of study. A trio of Chinese researchers centered at Osaka University set out to intensively analyze the effects of these SEZs. Using data on over three million firms, they conducted a study focusing on a Chinese initiative to add hundreds of development zones between 2005 and 2008. They reported their findings in *American Economic Journal: Economic Policy*.

The researchers examined the local effects of SEZs on targeted areas, the SEZs' overall costs and benefits, and how zones' specific features affected outcomes. Key among the findings was that the SEZ initiative yielded around US$15.26 billion in net benefit over three years. The greatest positive effects were on capital investment, employment, output, productivity, and wages.

"We built a novel dataset that combined geocoded economic census data with comprehensive data on these SEZs," says study senior author Lianming Zhu. "We could see firms' ages, sectors, addresses, investment, employment, and output. We saw evidence of agglomeration economies and we also

found factors behind them."

Net entry of firms seemed to play a major role in the positive outcomes. Existing firms in the regions benefitted less. The researchers also found that firms in capital-intensive industries benefitted from SEZs more than firms in labor-intensive industries, likely owing to the zones' various subsidies for capital investment.

They additionally noted that China's SEZ policies underscore the importance of considering firms' particular circumstances. In China, SEZs offered a level playing field with better regulations and infrastructure, while maintaining advantages for large-sized companies. This heterodox approach may differ from Western approaches.

"Among economists, there's skepticism about SEZs," Zhu says. "Our study should help dispel that. This is the first strong evidence about SEZs' local economic effects and their benefits and costs. We also found factors that make them effective. Considering developing countries are seeking to attract domestic and foreign investment with SEZs, these are valuable findings that can be of global use."

"China's special economic zones found to reap billions of dollars in net benefits"

Study of a mid-2000s wave of new special economic zones in China finds net economic benefits of over US$15 billion thanks to capital investment, employment, business entries, and other factors

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[reference]

Lu Y. et al. (2019) Place-based policies, creation, and agglomeration economies: Evidence from China's economic zone program. *American Economic Journal: Economic Policy* 11:3, 325-360. DOI: 10.1257/pol.20160272

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