Laboratory Introduction 2020

NARA INSTITUTE of SCIENCE and TECHNOLOGY

Message from the President

Naokazu Yokoya, President

Nara Institute of Science and Technology (NAIST) is a national independent graduate school institution established in 1991, focusing on the advancement of information, biological and materials sciences. Since then, we have not only promoted research in these fields, but also realized human resource development through graduate education curriculum based upon world-class research. To this date, NAIST has sent out more than 8,000 master's and 1,600 doctoral graduates into society, and they now play key roles as active researchers and engineers throughout various fields around the world. This focus on contributing to education, research and development in the forefronts of science and technology is a distinguishing feature of NAIST.

Looking back at the 28 years of education and research performed at NAIST, we can see how our activities have been consistently recognized in the evaluations of the Ministry of Education, Culture, Sports, Science and Technology (MEXT). For example, NAIST was chosen by MEXT as one of 22 prestigious institutions to participate in the *Program for Promoting the Enhancement of Research Universities* (2013) to further strengthen the research prowess of institutions with considerable achievements. Furthermore, in 2014, NAIST was also selected as one of 37 institutions to participate in the *Top Global University Project,* which now supports NAIST in enhancing institutional internationalization to cultivate globally-minded professionals, and to lead Japanese higher education.

Today, globalization is being called for across all areas of society and NAIST has responded by strengthening globalization activities in education and research. To further develop education, NAIST maintains international offices in Indonesia and Thailand that serve as academic collaboration centers. Currently almost 25% of NAIST's student population consists of students from diverse countries and areas, and we plan to further support the growth of our global community. To advance research, NAIST is expanding its strategic collaborative network with institutions around the globe. Our faculty members are leading two satellite laboratories at partner universities in France and USA, as well as three joint research laboratories within NAIST in collaboration with American, Canadian, and French institutions.

NAIST's collaboration with industry and other non-academic institutions is also a significant priority for innovation. For example, NAIST is currently working with three corporations in Collaborative Research toward Future Innovation projects to create novel collaborative research.

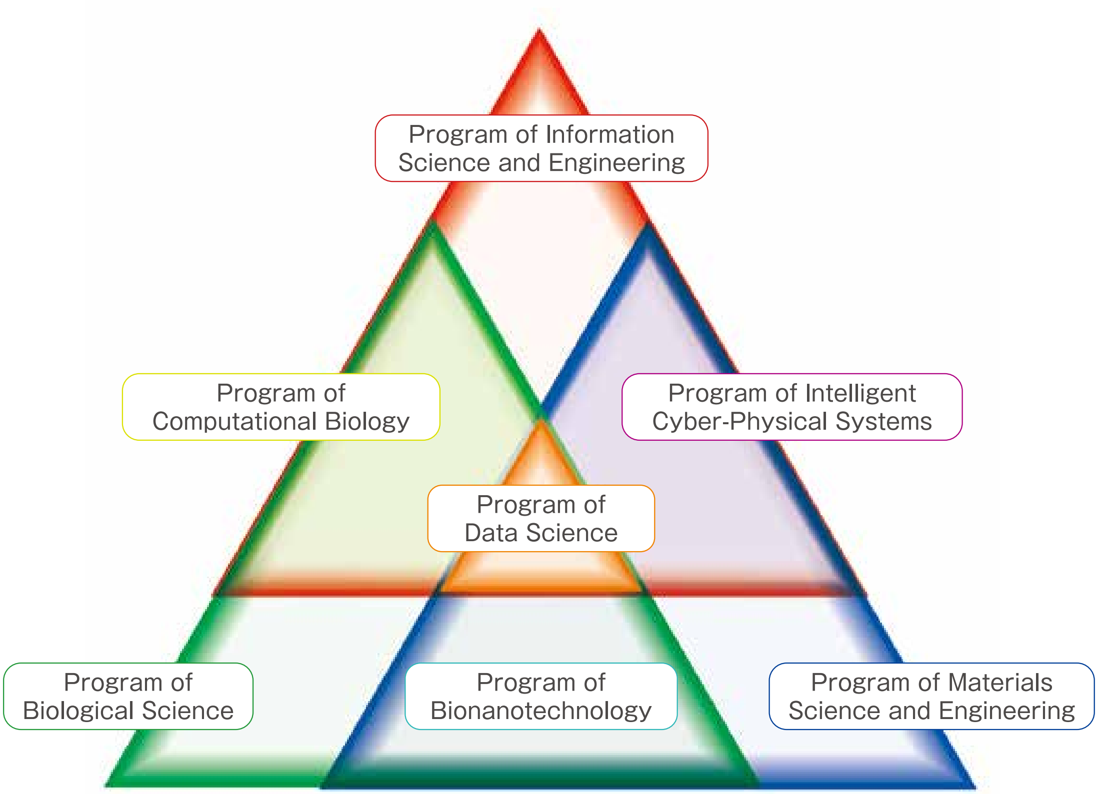
Science and technology are currently in a revolutionary era. Since its foundation, NAIST has continuously redefined the forefronts of science and technology. In order to respond flexibly to ever-evolving developments of science and technology, we have focused on fostering talented researchers and engineers who will lead tomorrow's discoveries and innovations. NAIST created the Graduate School of Science and Technology in April 2018 to further enhance interdisciplinary research and education. In our pursuit of a growing global presence, this transition is the largest challenge NAIST has undertaken.

As President of NAIST, I am proud to lead NAIST to continue to strive towards the challenges that lie ahead, and *-outgrow our limits-* to better the future through innovation and discovery in the years to come.

The Graduate School of Science and Technology

The forefronts of science and technology are developing and merging together at a striking pace. To continue to lead innovation, NAIST undertakes revolutionary research which moves ahead of current trends, especially approaching interdisciplinary research areas achieved through the removal of boundaries of traditional research fields. For this, in 2018 NAIST made the transition from its previous organization structured on its leading graduate education in the fields of information, biological and materials science to the Graduate School of Science and Technology offering seven new Education Programs.

The new integrated graduate school not only merged the existing three graduate schools into one, but also further expanded interdisciplinary and multidisciplinary research and education. The three core disciplines remain in the Programs of Information Science and Engineering, Biological Science, and Materials Science and Engineering. Amongst them are the Programs of Computational Biology, Bionanotechnology, and Intelligent Cyber-Physical Systems which include interdisciplinary areas of research, and the Program of Data Science which encompasses all three disciplines.



Program of	Program Outline
Information Science and Engineering	A focused information science program
Computational Biology	An interdisciplinary information and biological science program
Biological Science	A focused biological science program
Bionanotechnology	An interdisciplinary bioscience and materials science program
Materials Science and Engineering	A focused materials science program
Intelligent Cyber-Physical Systems	An interdisciplinary materials and information science program
Data Science	An interdisciplinary information, biological and materials science program

Program of Information Science and Engineering

A focused information science program which fosters students able to support today's dynamic advanced information society, implementing further achievements in information science in diverse fields and their wide-spread application. This program enriches students' broad interdisciplinary vision and cultivates cutting-edge specialized knowledge and skills covering computer hardware, software and information net work technology; computer/human interaction and media technology; and various systems to fully utilize robotics and computer technology.

Program of Computational Biology

An interdisciplinary information science and bioscience program which fosters students who are able to collect and analyze the huge amounts of data related to the phenomena of life, such as medical imaging data and the enormous amounts of bio-information concerning genes, proteins, and metabolism, while fostering persons who will undertake the development of these technologies.

Program of Biological Science

A focused biological science program which fosters students able to facilitate societal development and environmental protection through activities concerning areas such as the environment, energy, food supply, resources, life quality and health maintenance, within industry and public institutions foreign/domestic. This program enhances students' knowledge and cultivate expertise in areas from the basic principles of the phenomena of life to the biodiversity found at the molecular, cellular and individual level of plants, animals and microorganisms.

Program of Bionanotechnology

An interdisciplinary bioscience and materials science program which fosters students who pursue new trends in bioscience based on materials science understanding, and cultivates abilities necessary for the creation of novel functional materials to contribute to the future of society, including development of pharmaceuticals and medical engineering materials, development of new polymers which imitate biological functions, development of novel compounds to increase farming productivity, and exploration of new cellular engineering to support regenerative medicine through an understanding of the molecular foundation of biogenic activity.

Program of Materials Science and Engineering

A focused materials science program which fosters students with the foundational knowledge of materials science and advanced knowledge to fully utilize their expertise through a program spanning solid state physics, device engineering, molecular chemistry, polymeric materials and bionano-engineering, and undertake next generation science and technology to maintain affluent living and support societal development.

Program of Intelligent Cyber-Physical Systems

An interdisciplinary materials and information science program which fosters students able to holistically grasp areas including functional material design, devices with new functions and real-world sensing, analytical device design, system structuring to fully utilize analyzation results, and machine and robot control systems, who have specific, specialized knowledge and experience to support the social systems of this IoT era.

Program of Data Science

An interdisciplinary information, biological and materials science program which fosters human resources with a wide range of expertise in data-driven and AI-driven sciences related to information, biological, and materials science who will find hidden 'value' and 'truth' through data processing, visualization, and analysis of huge amounts of collected data to contribute to next generation of science and technology, and societal development.

Education Program	Denotation
Program of Information Science and Engineering	IS
Program of Computational Biology	CB
Program of Biological Science	BS
Program of Bionanotechnology	BN

Education Program	Denotation
Program of Materials Science and Engineering	MS
Program of Intelligent Cyber-Physical Systems	CP
Program of Data Science	DS

LABORATORY	IS	CB	BS	BN	MS	CP	DS
Computing Architecture	○					○	
Dependable System	○					○	
Ubiquitous Computing Systems	○	○				○	
Software Engineering	○					○	
Software Design and Analysis	○					○	
Cyber Resilience	○					○	○
Information Security Engineering	○					○	
Internet Architecture and Systems	○					○	○
Computational Linguistics	○						○
Augmented Human Communication	○						○
Network Systems	○	○				○	
Interactive Media Design	○					○	
Optical Media Interface	○	○				○	
Cybernetics and Reality Engineering	○					○	
Social Computing	○						○
Robotics	○	○				○	
Intelligent System Control	○	○				○	○
Large-Scale Systems Management	○					○	
Mathematical Informatics	○	○				○	○
Imaging-based Computational Biomedicine	○	○					○
Computational Systems Biology	○	○				○	○
Robot Learning	○					○	○
Communication							
Computational Neuroscience							
Humanware Engineering							
Symbiotic Systems							
Multilingual Knowledge Computing							
Next Generation Mobile Communications							
Optical and Vision Sensing							
Molecular Bioinformatics							
Digital Human							
Secure Software System							
Network Orchestration							
High Reliability Software System Verification							
Data-driven Knowledge Processing							

LABORATORY	IS	CB	BS	BN	MS	CP	DS
Plant Cell Function			○	○			
Plant Developmental Signaling		○	○				
Plant Metabolic Regulation			○	○			○
Plant Growth Regulation			○	○			
Plant Stem Cell Regulation and Floral Patterning			○	○			○
Plant Physiology		○	○				○
Plant Immunity		○	○				○
Plant Secondary Metabolism		○	○				○
Plant Symbiosis		○	○	○			
Molecular Signal Transduction			○	○			
Functional Genomics and Medicine			○				
Tumor Cell Biology			○	○			○
Molecular Immunobiology			○	○			
Molecular Medicine and Cell Biology			○	○			○
RNA Molecular Medicine		○	○				○
Stem Cell Technologies		○	○				
Developmental Biomedical Science		○	○	○			
Organ Developmental Engineering			○	○			
Systems Microbiology		○	○				○
Cell Signaling		○	○	○			
Applied Stress Microbiology			○	○			
Environmental Microbiology			○	○			
Structural Life Science			○	○			
Gene Regulation Research		○	○	○			○
Systems Neurobiology and Medicine		○	○	○			
Computational Biology		○	○				○
Molecular Microbiology and Genetics							
Quantum Materials Science					○	○	
Bio-process Engineering				○	○		○
Surface and Materials Physics					○		○
Nanostructure Magnetism					○		
Photonic Device Science				○	○	○	○
Information Device Science				○	○	○	○
Sensing Devices					○		
Organic Electronics					○	○	
Mesoscopic Materials Science					○	○	
Sensory Materials and Devices				○	○	○	
Synthetic Organic Chemistry				○	○		
Photonic Molecular Science				○	○		○
Photofunctional Organic Chemistry				○	○		
Functional Polymer Science				○	○		
Ecomaterial Science					○	○	
Advanced Functional Materials				○	○	○	
Supramolecular Science				○	○		
Complex Molecular Systems				○	○		○
Biomimetic and Technomimetic Molecular Science				○	○		
Nanomaterials and Polymer Chemistry				○	○		
Data Driven Chemistry							○
Materials Informatics					○		○

NAIST Website

https://www.naist.jp/en/

Contents

Division of Information Science

http://isw3.naist.jp/home-en.html

Division of Biological Science

https://bsw3.naist.jp/eng/

Division of Materials Science

http://mswebs.naist.jp/english/

Information Science Laboratories

List of Laboratories

Computing Architecture





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Research Areas

1. Power efficient near-data memory array accelerators for the Post-Moore Generation

Research and development of highly efficient computing systems, accelerators and LSIs for image processing and big data processing, such as graph processing and machine learning

- EMAXV,VR: A large-scale CGRA for image recognition
- IMAX: A small footprint near-memory accelerator for AI

2. Compact and efficient approximate computing VLSIs for the Post-Moore Generation

Research and development of reconfigurable approximate computing VLSI architectures with compact circuits, low energy, and function-flexibility for multi-operand computations, which can be efficiently employed in parallel computing tasks

- Various non-binary-based computing methodologies such as neuromorphic and stochastic computing for the Post-Moore generation
- Exploring analog-digital-hybrid CGRA platforms

3. Neuromorphic LSIs for the Post-Moore Generation

Research and development of super compact and low power neuromorphic integrated systems for artificial intelligence.

- Amorphous metal-oxide semiconductor thin-film synapses for 3D structures
- Neuromorphic architecture and leaning rules for astronomical scale integration
- Brain-type integrated systems with artificial humanity

4. Energy efficient system architecture for next generation machine learning

Research and development of next generation machine learning system architecture with edge computing

- Probabilistic reasoning algorithms with Bayesian networks

5. IoT + blockchain for secure smart systems

IoT and blockchain technologies are combined to develop smart systems such as smart healthcare systems, smart city management, etc. Secure health monitoring systems for hospitals are currently being researched.

Key Features

In our laboratory, we study state-of-the-art technologies for next-generation computing paradigms. Our goal is to realize environment-friendly, high-performance, and robust computer systems under energy constraints. From a wide viewpoint (from new theories to LSI implementations), we promote cutting-edge research and the highest degree of education within various research themes, particularly: high-performance, low-energy and dependable computation, and hardware/software co-design.

Fig. 1
Power Efficient Near-Data Memory Array Accelerators and FPGA Systems

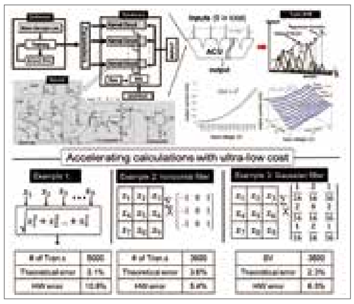

Fig. 2
Analog Accelerators

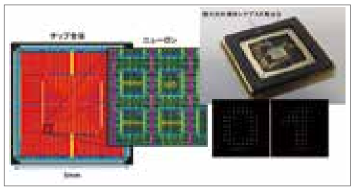

Fig. 3
Analog Neural Network LSIs

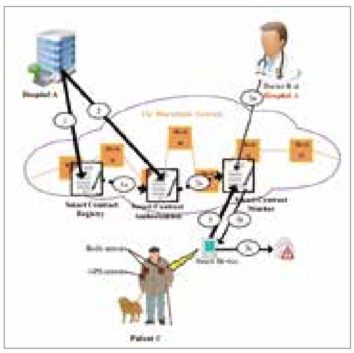

Fig. 4
Blockchains for IoT

Dependable System



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Research Areas

1. Distributed algorithms

We focus on designing algorithms to improve the dependability and performance of various distributed systems such as the Internet, ITS, IoT, blockchain (bitcoin), sensor networks, and nano-scale systems.

- Fault-tolerant distributed systems
- Wait-free distributed algorithms
- Self-stabilizing algorithms
- Mobile agent and robot algorithms
- Population protocols for nano-scale systems
- Dynamic distributed algorithms

2. Hardware design

We are conducting research on hardware dependability which ranges broadly across robust computing, VLSI design, CAD, testing, photovoltaic systems, security, and power converters using new wide-bandgap semiconductors.

- VLSI design for testability
- Test optimization through machine-learning-based analysis
- Dependability of neuromorphic computers
- Dependability of ReRAM based systems
- Hardware Security (Counterfeit and Trojan detection, PUF)
- Power device modeling
- Optimization of photovoltaic system power generation
- Decimal computing

Key Features

Today's information society is supported by various levels of advanced technology such as applications, systems, computers and VLSIs. The Dependable System Laboratory is pursuing research on safe and secure systems including distributed systems with hundreds of computers and VLSIs with billions of transistors. "Dependability" is a concept from the user's point of view, when systems can be used reliably and securely.

In order to achieve dependable systems, we need to consider various aspects of these systems from the user's point of view. For example, whether all the systems are completely tested before shipping, whether the systems can function correctly in the presence of faults, whether the systems can predict and avoid system failure caused by transistor aging, whether the system can handle malicious users, and whether the photovoltaic systems can efficiently generate power with partial shade or faulty cells. This laboratory performs research to improve dependability through various approaches.

The Dependable System Lab also fosters skills for logical thinking, presentation, design and analysis of algorithms, CAD tools, machine learning, software programming (C/C++, Java, Python, etc.) and hardware programming (Verilog/VHDL) through our research.

Fig. 1
Mobile robots

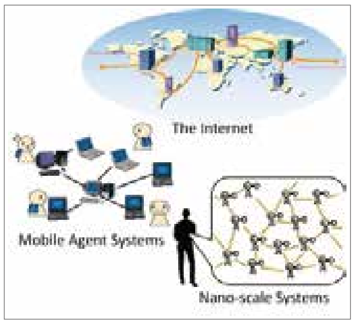

Fig. 2
Various types of distributed systems

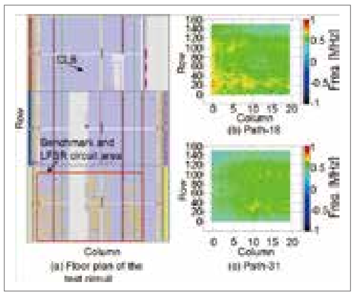

Fig. 3
Hardware security (Recycled FPGA detection)

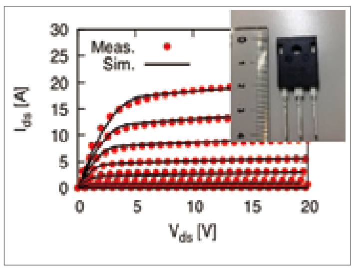

Fig. 4
Power device modeling

Ubiquitous Computing Systems





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Research Areas

Ubiquitous computing systems utilize many sensors and embedded/mobile devices in a harmonious manner and efficiently provide users with sophisticated services by recognizing real world contexts. Our lab conducts data collection, data analysis, and application development for solving the various challenging issues of real world. The main themes are as follows:

Smart homes

- Recognizing and predicting daily living activities in smart homes using sensor devices
- Elderly monitoring systems using BLE devices
- Smart appliance control

Smart life

- Sport sensing and coaching with accelerometers and EMG sensors
- Walking pace control through music tempo control
- Estimating physiological and mental states using various sensors
- Estimating QoL with wearable sensors

Smart city

- Participatory sensing systems
- Behavior change for smart community
- Dynamic video curation for smart tourism
- Edge/fog computing based IoT platform

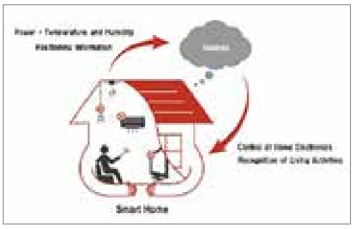

Fig. 1
Smart Home

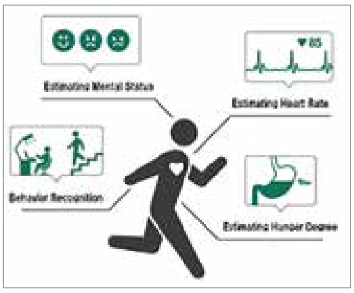

Fig. 2
Smart Life

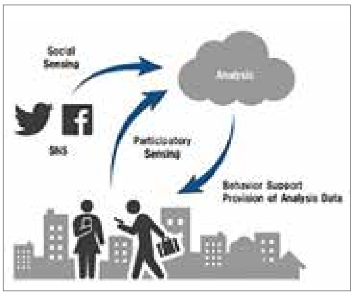

Fig. 3
Smart City

Key Features

We are conducting research using a smart home facility built within the university. This facility provides an actual home environment where various home appliances are deployed as in an ordinary household. In addition, this facility is equipped with special sensors including a high-accuracy indoor positioning system, wireless power meters, door sensors, and others. We are collecting data while subjects are actually living in this facility and develop various methods including activity recognition and automatic appliance control using the collected sensor data. We are also conducting research on smart life and smart cities through development of platforms for participatory sensing and IoT data processing as well as smart IoT devices including tiny all-in-one sensor boards and smart appliances.

Each student selects research topics according to his/her own interests through several brainstorming meetings with advisers. Advisers provide students with kind and careful direction to advance their research as well as suggestions to improve their programming, writing, and presentation skills. Students receive various opportunities to present their research results at domestic/international workshops and conferences.

Software Engineering

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Research Areas

1. Software data mining

- Software quality analysis and cost estimation
- Visualization and substantiation for software analytics
- Natural language processing in software development
- Data-driven software development

2. Free/libre and open source software engineering

- Expert recommendation models in open source development
- Communication analysis in open development
- Toward understanding open source ecosystems for user support
- Software repository mining and integration in open source system

3. Human factors in software development

- Measuring human brain activities to assess the program understanding processes
- Social analysis and game theoretical modeling
- Eye-tracking-based expertise analysis of online judging
- TaskPit: A software development task measurement system

4. Software protection

- Software obfuscation
- Software watermarking and birthmarking
- Software tamper-proofing
- Blockchain-based tracking systems

Key Features

The software engineering laboratory uses both theoretical and empirical approaches to address various problems related to software development, human computer interaction and software lifecycle management. We fully exploit the potential of students' curiosity and creative thinking and, together with conventional research theories and technologies, explore new topics in software engineering.

While actual software development often relies on project managers' intuition instead of sufficient evidence, our goal is to develop an empirically-guided software development environment where the software development process and product data are measured and decisions are based on the data. We also address current hot topics in software engineering such as open source software engineering, global software development and software protection.

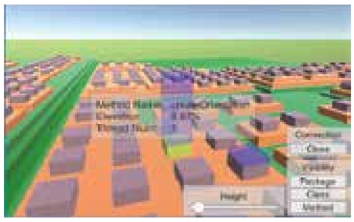

Fig. 1
Real-time Android application profiler

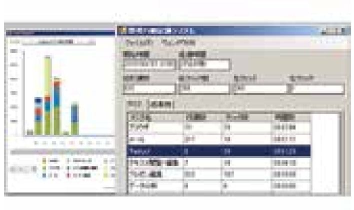

Fig. 2
TaskPit: A software development task measurement system

Fig. 3
A software engineering data analysis system

Software Design and Analysis






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Research Areas

1. Modeling and management / improvement of the software development process
- Process modeling / analysis / improvement
- Project information visualization & management support
- Social network analysis for open source projects
- Project re-player (virtual re-play of projects)
- Development process simulation

2. Repository mining
- History analysis of source code (code clones / design patterns)
- Finegrain process analysis of software maintenance
- Extracting topics from developers' mailing lists

3. Software design & verification
- Super-upper process design
- Searching / detecting design patterns
- System and software assurance
- Software risk analysis

4. Cloud infrastructure design
- Virtual computing environment deployment
- Software defined network (SDN) deployment
- Experiments on widely distributed systems
- High performance computing support
- Resource management

Key Features

In the Software Design & Analysis Laboratory, we conduct research on the methods and technologies which support the design / development of software and cloud computing systems. Our main focus is on the analysis and improvement of the software development process. Software technology is increasingly present in our daily lives, including various software embedded machinery and electronic devices for homes or mobile telephones and social infrastructures represented by cloud computing systems.

Fig. 1
Social network analysis tool for Open Source Software developments

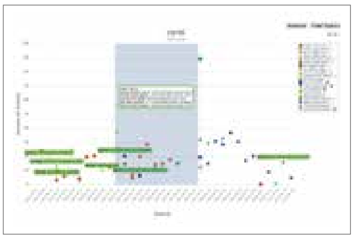

Fig. 2
Software development history visualization tool using topic extraction method

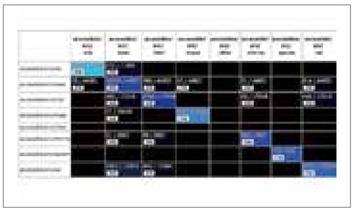

Fig. 3
Scatter plot for code clone analysis

Fig. 4
Demonstration environment for international OpenFlow network

Cyber Resilience


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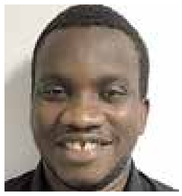
Assoc. Prof.
Daisuke Miyamoto


Assoc. Prof.
Hiroyuki Inoue


Assist. Prof.
Shigeru Kashihara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Research Areas

Our laboratory engages in education and research for cyber resilience. We focus on empirical research to improve resilience over physical and cyber spaces, and technology for its transfer into the real world. Our research areas include cybersecurity, networks, and society. In the cybersecurity area, standardization, malware, phishing, and forensics are important keywords. In the network area, QoE-driven management, softwarization (SDN, NFV, etc.), IoT, and wireless networks (LPWA, WLAN, etc.) are hot topics. In the society area, education, human behavior against security, security interfaces, gamification, and UAV (or drone) are active topics. These are only examples of what we do in order to improve resilience.

1. Towards making the Internet cyber-resilient

- Information infrastructure attack prevention and mitigation techniques
- Reliable communication over mobile networks
- Trusted identity management for modern applications and services
- Workload measurement and characterization
- Construction and management of resilient infrastructures
- Security risk assessment (cloud computing, IoT, etc.)
- IPv6 transition and verification methodologies
- Elastic mechanisms for efficient wireless/wired network management

2. Impacting society through cyber-resiliency

- Critical infrastructure security and resiliency
- Secure information distribution based on users' situation
- Gamification of cybersecurity
- Privacy protection
- Internet user experience quality improvement
- Learning the effects of cyber-resiliency on humanity

Key Features

The Internet has evolved to become essential to, arguably, all fields of industry and academia. At its inception, the Internet was used for basic electronic communications where users stored, processed, and transferred small amounts of data. Currently, the Internet encompasses more advanced technologies like social networks, cloud computing, big data, Internet of Things (IoT), augmented and virtual reality, etc.; in summary, it is becoming the world economy. Simultaneous to the universality of the Internet and its rapid growth, cyber threats are augmenting and globally proliferating at an exponential rate. Additionally, cyber threats are conquering domains like industrial control systems (ICS) that were, until recently, bereft of any types of internet-related security issues. In the Laboratory for Cyber Resilience, our goal is to build an Internet that, while intrinsically vulnerable, can contain any types of cyber-attacks and use the heuristics of the latter to build robust, dependable and more resilient architectures in order to make the cyber platform an environment that promotes efficiency, innovation, economic prosperity, academic development, safety, security and civil liberties.

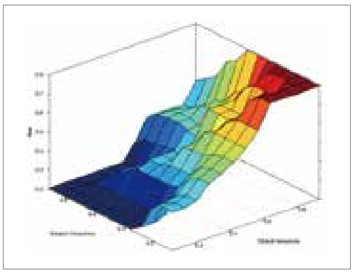

Fig. 1
Evaluation of a Risk-Adaptive Authorization Mechanism

Fig. 2
Malicious drone detection

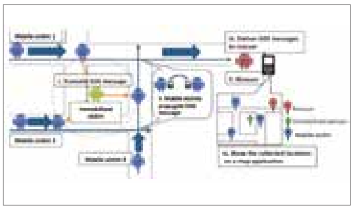

Fig. 3
Immobile victim's message propagation among visible victims' device and delivery to the rescuer

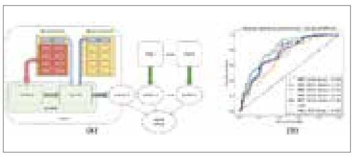

Fig. 4
AUROC value from a pair of normal dataset – VMM-based Anomaly Detection System

Information Security Engineering



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Research Areas

1. Electromagnetic (EM) information leakage

Research on the risk assessment of security degradation due to information leakage (Fig. 1) using electromagnetic (EM) signals generated from information terminals; we are also conducting researches on methodologies and techniques for countering this phenomenon (Fig. 2).

2. Intentional electromagnetic interference (IEMI)

Research on the risk assessment of security degradation associated with intentional electromagnetic disturbance in hardware and also on technologies for countering this phenomenon (Fig. 3).

3. Intentional modification of internal circuits (Hardware Trojan)

Research on risk assessment of security degradation due to malware implemented by intentionally changing the internal circuits of information equipment, and also on technologies for countering this occurrence.

4. Developing secret key-sharing frameworks and protocols based on information theory

Research on a cryptographic protocol, which is secure in terms of information theory. This stream of research is different from those on cryptosystems that base security on the difficulty of performing calculations, such as RSA public key and AES block cryptosystems.

5. Large-scale electromagnetic field simulation

Research on large-scale electromagnetic field simulation necessary for clarifying information security degradation mechanisms due to leakages or interfering electromagnetic waves, and for risk assessment at the early design stages of equipment (Figs. 4, 5).

6. Reliability of information communication systems

Research on approaches for designing information communication system equipment, which has little electromagnetic signal leakage from the viewpoints of environmental electromagnetic engineering (EMC) and electromechanical devices (EMD), and which is even tolerant against electromagnetic disturbances (Fig. 6).

Key Features

In the Information Security Engineering Laboratory, we conduct research on methods to ensure hardware safety, which is the bedrock of system information security. We also conduct research to ensure the security of the entire system, including the upper layers.

Fig. 1
Remote Visualization of Screen Images Using EM Emanation

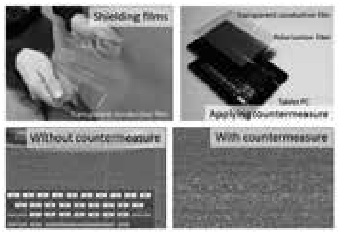

Fig. 2
Development of countermeasure to prevent EM display stealing from tablet PCs

Fig. 3
Visualization of the information leakage due to intentional electromagnetic interference (IEMI)

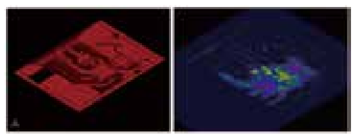

Fig. 4
Visualization of information leakage paths based on large-scale EM field simulation techniques

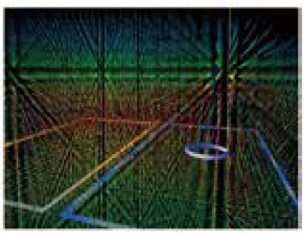

Fig. 5
Visualization of near fields disturbance during attack against a cryptographic module

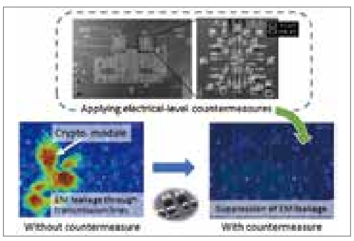

Fig. 6
Development of cost-effective countermeasures based on information leakage map

Internet Architecture and Systems




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Research Areas

1. Pervasive Computing / Ubiquitous Computing

In an environment which everything in real space is connected to the network (IoT, M2M environment) the information system analyzes and understands the sensor data and then controls remote devices and presents useful decision-making information.

- Public transportation big data analysis (ex. driving analysis)
- Indoor localization utilizing environment sensors and smartphone mounted sensors together
- Edge/Fog computing (Optimization of computing resource allocation for smart cities)

2. Disaster relief computing / networking

In large-scale disasters such as communication infrastructure being cut off, the use of satellite communication system becomes extremely important. We are conducting R & D on communication methods that make maximum use of limited resources of low bandwidth / high latency satellite lines. At the time of the initial disaster occurrence, on-site staff need to devote themselves to disaster response, and we are also discussing ways to provide the environment where terminals can be normally used as they are.

3. Operations technology for data centers and networks

We are working on operations technologies for data centers that is developing with higher performance and higher density with the spread of cloud computing. In particular, we are studying on the following technologies on data management for online storage for storing and sharing data in networks, resource management, and operations support for cloud service infrastructure and routing control for network traffic.

- Network storage system adaptation to data properties (object storage, distributed storage, access control)
- Technologies for virtual machine placement, data placement, traffic control and operations support considering energy saving and load balancing
- Next-generation traffic engineering for safe and effective data transport (IPv6 site multihoming, network auto configuration)
- Technologies for IPv4-IPv6 transition and IPv6 deployment

4. Cyber Security

Devices which are connected to the Internet are always threatened with malware and DoS attacks. With the spreading of IoT or M2M technologies, it is important to care about the vulnerabilities of various devices such as automobiles, robots, sensor nodes, etc. as well as servers and PCs.

- DoS attacks on industrial network and devices
- Car security
- Malware analysis

5. Transmission system using IP network of super realistic feeling space

Utilizing the method of transmitting super high definition 4K / 8K video and stereophonic sound using ultra high speed IP networks, we are studying video / sound / IP networks with the goal of forming a super-realistic space comparable to real space in remote places.

- Utilization of uncompressed video data for high quality / low latency
- IP network routing control methods for high reliability
- Adaptive use of compressing video data
- Approach to medical, museums, planetariums, etc.
- Application to the digital library system

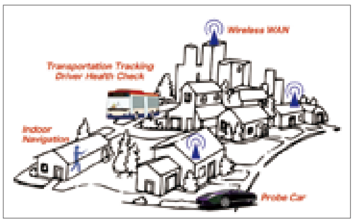


Fig. 1
Pervasive Computing / Ubiquitous Computing

Fig. 2
Disaster relief computing / networking

Fig. 3
Operations technology for data center and network

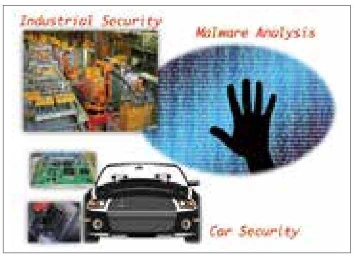


Fig. 4
Cyber Security

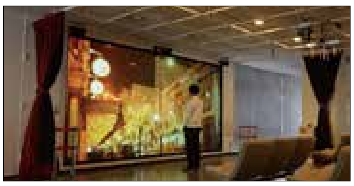
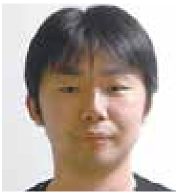


Fig. 5
Transmission system using the IP network of super realistic feeling space

Key Features

In our laboratory, students can study a variety of topics concerned with computer networks, from the network layer to the application layer. The strength of our laboratory is that students have opportunities to perform their research using actual computer network environments because all faculty members are engaged in the Information Initiative Center (ITC) of NAIST. Additionally, in some cases we develop devices to create appropriate research environments. Our laboratory welcomes students of all levels of expertise, providing seminars on basic theoretical and practical studies as well as advanced areas.

Computational Linguistics



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Research Areas

1. Making natural language processing resources publicly available

We believe that publicly available software and resources are important for the advancement of computational linguistics. Therefore, fundamental work in building essential resources such as dictionaries and annotated corpora is performed. Various widely used software tools are also maintained for core natural language analysis. Examples include:

- Software: Japanese Morphological Analyzer ("Chasen"), Dependency parser ("Cabocha"), Predicate Argument Structure Analyzer ("Syncha")
- Resources: NAIST Text Corpus, NAIST Japanese/English/Chinese dictionaries

2. Learning-based natural language processing and knowledge acquisition

Machine learning approaches are investigated to acquire linguistic rules automatically from large-scale text data. This approach enables us to build highly accurate and robust statistical natural language taggers and parsers. We also perform research in lexical and expert knowledge acquisition from scientific documents.

3. Applications

We explore novel applications that are enabled by computer processing of natural language. For example, our work in language learning assistance studies how computers can be used to help humans learn second languages. Our Scientific Document Analysis effort focuses on extraction of expert domain knowledge, automatic summarization and trend analysis of scientific fields by detailed analyses of scientific articles. Also, we have explored textual entailment, sentiment analysis, and information extraction.

Key Features

Natural languages are highly complex systems embodying various kinds of exceptions and subtle linguistic phenomena among beautiful grammatical structures. They are also systems for representing and describing our knowledge. To analyze and interpret languages computationally, one needs various theories and tools. Our lab organizes many research projects and reading groups focusing on areas from fundamentals to applications. Each group presents surveys of cutting-edge research topics and reads books and journals, while each project holds meetings on the research progress of its members. By participating in these reading groups and research projects, we encourage students to gain extensive knowledge on natural language processing that cannot be studied otherwise.

Fig. 1
Online demo of information extraction of restaurant reputations: Customer review positive/negative opinions extraction and summary

Fig. 2
A reading group session discussion

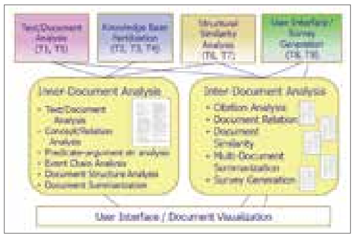

Fig. 3
Overview of scientific document analysis

Augmented Human Communication

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Go Beyond the Communication Barrier

The AHC Laboratory pursues research to solve problems related to human communication based on speech and language, paralanguage, and non-verbal information. By applying various artificial intelligence technologies including deep learning, our lab is pursuing tasks that were previously not able to be solved. Additionally, we seek knowledge related to human cognitive functions, as well as new information through brain measurement, and use it to perform research. Especially in research activities, we focus not only on theoretical aspects, but also on the applicability of technology, and aim at building prototype systems and validation. Below you can find our research areas.

NAIST launched the NAIST big data analytics project in April 2014, and subsequently the NAIST Data Science Center (NAIST DSC) in 2017. NAIST DSC focuses on material informatics, chemo-informatics, and social informatics by applying machine learning and artificial intelligence methodologies. The project also encourages close collaboration with industry. (For details, please see http://bigdata.naist.jp/ , http://www-dsc.naist.jp/dsc_en/)

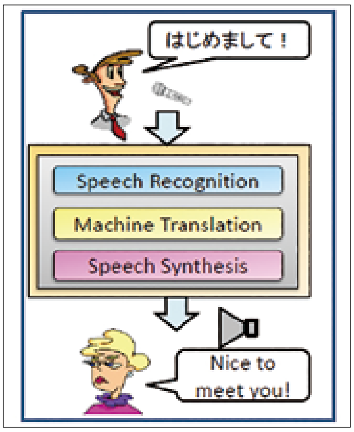

Fig. 1
Speech-to-speech translation

Research Areas

1. Real-time simultaneous speech-to-speech translation

Our current research project focuses on human-like simultaneous speech interpretation of complex utterances such as news and lectures, interpretation support technology for conferences attended by multiple speakers who speak multiple languages, and multimodal interpretation technology. (Fig. 1)

2. Natural Language Processing

Our research into natural language processing focuses on deep learning machine translation and natural language interfaces between humans and computers, thus allowing computers to understand natural language queries and commands so that they may answer questions and follow directions.

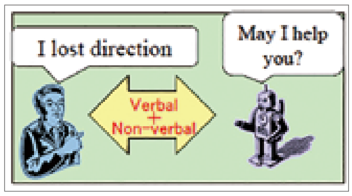

Fig. 2
A spoken dialogue system

3. Multi-lingual statistical speech processing

Speech recognition and synthesis are fundamental technologies for realizing natural human-computer interaction. We study statistical methodologies such as hidden Markov models, Gaussian mixture models, deep neural networks, and recurrent neural networks. We are extending these models for emotional, conversational spontaneous, and multilingual speech.

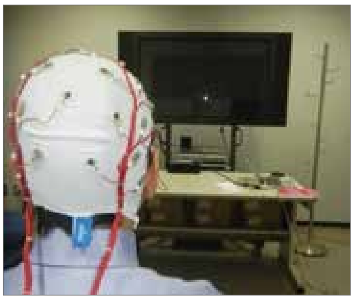

Fig. 3
An EEG measurement system

4. Goal-oriented and Chatbot-type Spoken Dialog System

We focus on new statistical dialogue models for natural dialogue using individuality modeling, verbal information, intonation, emotion, face and gesture information. (Fig. 2)

5. Brain Analysis for Verbal and Non-verbal Communication

Our research on cognitive communication analyzes brain activity to detect real-time communication difficulty using Electroencephalograms (EEG). We also perform research on support for communication disabilities such as autism and dementia. (Fig. 3)

6. Information Distillation

Research to summarize information that comes from a variety of complex data sources and to inform people of the summarized results in an understandable manner.

7. Knowledge Acquisition

Research on knowledge acquisition and understanding of objects in the real world to support the human-machine communication, in addition to available knowledge from a variety of information sources such as the Web.

Network Systems




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Research Areas

1. Digital TV on mobile receivers

In Japan, high definition television (HDTV) is provided using digital terrestrial television (DTTV) broadcasting. In addition to HDTV, a narrow band digital television service dedicated to handheld terminals, known as "One-Seg TV", is popular now. After the termination of analog TV services, multimedia broadcasting services have started using the vacated VHF analog TV band. However, it is difficult to improve reception reliability in mobile and handheld environments. This laboratory is working on developing low power-consumption and reliable handheld digital TV receivers using array antennas and radio signal processing techniques.

2. Mobile communication systems

With recent research and development activities, the bit rate of mobile communication systems, such as cellular systems and wireless local area networks (W-LAN), is increasing rapidly. However, its reliability is not satisfactory for error intolerant purposes, such as surveillance, networked robots, etc. In order to solve this problem, our laboratory studies key technologies including OFDM (Orthogonal Frequency Division Multiplex), MIMO (Multiple Input Multiple Output), diversity, and multihop mesh networks. We are working on implementing these technologies into specific systems such as W-LAN, WiMAX, and Zig-Bee.

3. Radio on fiber and distributed antenna systems

We are studying the Radio on Fiber (RoF) technique in order to construct a heterogeneous backhaul infrastructure for various types of broadband wireless signals such as LTE, WiMAX, mobile multimedia contents broadcasting, etc. In this regard, we also investigate sophisticated signal processing capabilities of distributed antenna system (DAS) in multi-user, MIMO scenarios for achieving further performance enhancement.

4. Wireless sensor networks

Although radio wave-based sensor systems, such as RADAR and GPS, are capable of measuring positions over a wide area, their function is limited. To enhance their applicability, we propose various kinds of sensing networks using radio waves, for example, rain rate estimation using millimeter-wave mesh links, intruder sensing in leaky coaxial cable infrastructure, and positioning sensors for medical applications using RFID tags.

5. Wireless power transfer

There has been an increasing demand for wireless power transfer (WPT) for mobile nodes. Although many WPT systems have been developed and are widely used, it is difficult to transfer power to moving nodes using WPT. In conventional WPT using electromagnetic coupling, the distance between the transmitter and receiver is limited to few tens of centimeters. The motion of the power reception nodes leads to a decrease in the power transfer efficiency due to impedance mismatching.

Network Systems Laboratory is now working on developing a wide-area WPT system using a parallel feeder line. This system is capable of accommodating mobile receiving nodes including vehicles.

Key Features

We do not only evaluate systems through theoretical analysis and computer simulation, but also implement them onto hardware using FPGA (Field Programmable Gate Array) and embedded systems. Students learn theories of signal processing and communication systems. In addition, they experience embedded system programming and digital circuit design.

Fig. 1
Highly reliable wireless communication system research and development

Fig. 2
Wireless sensor network container yard in Tarragona

Fig. 3
ESPAR antenna assisted receiver

Interactive Media Design

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Research Areas

Our vision is to introduce Augmented Reality (AR) into the everyday lives of the entire population. AR is a technology that enhances human vision with computer-generated graphics. In order to achieve our vision, it is imperative to merge three currently distinct research fields, computer graphics, computer vision, and human-computer interaction, into one.

1. Human-computer interaction
- User interfaces for 3D design (Fig. 1)
- Augmented Reality for rehabilitation support (Fig. 2)
- Sports training systems using Augmented Reality (Fig. 3)
- Human Robot Interaction (Fig. 4)

2. Computer vision
- Image-based 3D reconstruction
- Projection-based Augmented Reality (Fig. 5)
- Head-mounted display calibration

3. Computer graphics
- Generation of realistic Computer Graphics
- Development of new head-mounted displays (HMDs, Fig. 6)
- Computer Graphics applications for vision enhancement

Key Features

Our laboratory has a rich international flavor, with many international students and visiting international researchers gathering from every corner of the world. Therefore, we communicate in English in most meetings and events. We have various custom systems and special equipment and actively pursue creative research.

Dissertation supervision is carried out through frequent discussions in research subgroups, as well as in weekly lab meetings. In addition to supervising dissertations, we have weekly lunch talks about topics of interest and occasionally arrange research retreats.

Research Equipment

- Ubiquitous display system
- 270 inch display
- AR development environment
- A variety of latest Head-Mounted Display systems
- A steerable projector system
- A body scanning system

Fig. 6
Development of new head-mounted displays (HMDs)

Fig. 1
Tablet AR system for task support

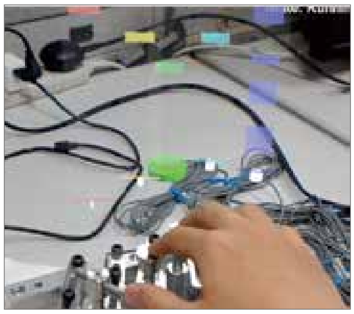

Fig. 2
Augmented reality for rehabilitation support

Fig. 3
Sports training systems using Augmented Reality

Fig. 4
TV chat robot

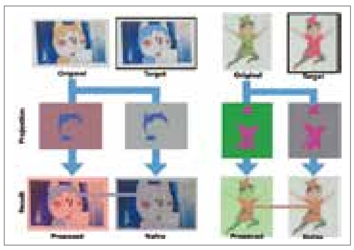

Fig. 5
Perceptual appearance

Optical Media Interface




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Research Areas

Our research interests stand on both computer vision and computer graphics techniques, which are inextricably linked together. Some of this research has interdisciplinary applications in areas such as autonomous robots, factory automation, medical services, and agriculture, and is performed in collaboration with other universities and companies.

1. Computer vision

We are interested in scene understanding via the analysis of light behavior such as reflections on surfaces and scattering beneath the surface. This is a key technology of 3D shape reconstruction and material estimation. (Fig. 1)

2. Computer graphics

We are developing new technology that supports the CG industry. Interpolating animation frames, automatic colorization, realistic material representation, and generation of novel 3D perceptions are examples of this. (Fig. 2)

3. Computational photography

Computational photography techniques generate images that are beyond ordinary camera limits by computing the distribution of light captured by modified cameras. We can control the camera parameters after the capture as well as visualize invisibles, for example, transparent surfaces, scenes through fog, hidden layers inside objects, etc. (Fig. 3)

4. Sensing system development

With the goal of correctly understanding scenes based on the physical phenomena of the real world, designing a measurement system that can acquire the high-dimensional light transport is an important project for of our laboratory. (Fig. 4)

Fig. 1
Estimating material and correct 3D shape

Fig. 2
Realistic computer graphics

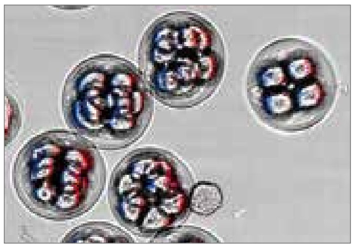


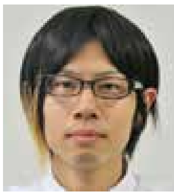
Fig. 3
Visualizing transparent shapes

Fig. 4
An optical measurement system

Cybernetics and Reality Engineering







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Research Areas

Humans have acquired new capabilities by inventing various tools long before computers came up and mastering them as if they were part of the body. In this laboratory, we conduct research to create "tools of the future" by making full use of virtual reality (VR), augmented reality (AR), mixed reality (MR), human and environmental sensing, sensory representation, wearable computing, context awareness, machine learning, biological information processing and other technologies (Fig. 1). We aim to live more conveniently, more comfortably, or more securely by offering "personalized reality" which empathizes each person. Through such information systems, we would like to contribute to the realization of an inclusive society where all people can maximize their abilities and help each other.

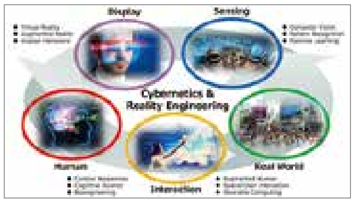

Fig. 1
Research fields

1. Sensing: Measuring people and the environment

We are studying various sensing technologies that assess human and environmental conditions using computer vision, pattern recognition, machine learning, etc.

- Estimation of user's physiological and psychological state from gaze and body behavior
- HMD calibration and gaze tracking using corneal reflection images

Fig. 2
Super wide field-of-view occlusion-capable optical see-through HMD

2. Display: Manipulating perception

We are studying technologies, such as virtual reality and augmented reality, to freely manipulate and modulate various sensations such as vision and auditory, their effects, and their display hardware.

- Super wide field of view occlusion-capable see-through HMD (Fig. 2)
- Gustatory manipulation by GAN-based food-to-food translation (Fig. 3)
- Tendon vibration to increase vision-induced kinesthetic illusions in VR
- A non-grounded and encountered-type haptic display using a drone

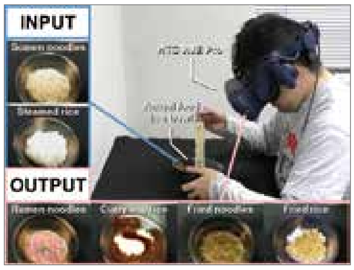

Fig. 3
Gustatory manipulation by using GAN-based real-time food-to-food translation

3. Interaction: Creating and using tools

We combine sensing and technologies to study new ways of interaction between human and human, and human and the environment.

- Controlling interpersonal distance by a depth sensor and a video see-through HMD (Fig. 4)
- Investigation on priming effects of visual information on wearable displays
- AR pet recognizing people and the environment and having own emotions

Fig. 4
Controlling interpersonal distance

Research Equipment

- A variety of head mounted displays (Fig. 5)

Fig. 5
A variety of head mounted displays

Research Grants, Collaborations, Social Services, etc. (2019)

- MEXT Grants-in-Aid (Kakenhi) (A x 2, B x 3, C x 2), SCOPE, JASSO, etc.
- Collaboration (TIS, CyberWalker, etc.)
- Steering / Organizing Committee members of IEEE VR, ISMAR, APMAR, etc.

Social Computing

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Research Areas

1. Social computing

The Social Computing Laboratory of NAIST was established in September 2015 to pursue cutting-edge research activities and is engaged in interdisciplinary research and education in a new scientific arena.

Our core technology is natural language processing, but we aggressively employ and collaborate with other fields in order to produce extensive applications, mainly in the medical and healthcare fields. Join us, and let's break new ground together.

2. NLP, web, medical & more

The mission of the Social Computing Laboratory is to explore a new interdisciplinary branch of informatics that is both practical and theoretical. Our research interests relate to healthcare and other real-life challenges, as well as to the application of natural language processing (NLP) and other information retrieval techniques.

Our approaches are:

Interdisciplinary and practical: We address practical problems in collaboration with experts from a wide range of fields, including informatics, medicine, biology, linguistics, psychology, and sociology.

Theoretical: In addition to practical informatics applications, scientific rigor is a major interest.

3. Research: Natural Language Processing + medical practice

Electronic medical records are now replacing traditional paper medical records, and accordingly, the importance of information processing techniques in medical fields has been increasing rapidly. ICT enables us to analyze voluminous medical records and obtain knowledge from the analysis, which would definitely bring more precise and timelier treatments in this field. Such assistance has much potential in saving more lives and further improving life quality. One of our goals is to promote and support the implementation of practical tools and systems into the medical industry.

4. Research: web mining

Social Network Services (SNS) potentially serve as valuable information resources for various applications. We have addressed and will be addressing web-based applications. For example, to date, most web-based disease surveillance systems assume that the web immediately reflects real disease conditions. However, such systems, in fact, suffer from time lags between people's web actions and real-time situations. We have taken this time gap into consideration and have been applying various technologies not only from our familiar NLP field, but also from other fields, such as simulation modeling and psychological modeling. Findings from this study will also directly contribute to healthcare.

Fig. 1
Web-based disease surveillance system "KAZE-MIRU"

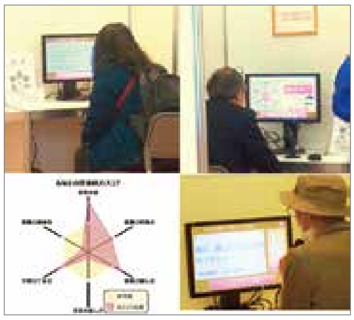

Fig. 2
We built a collection of elder's narratives.

Fig. 3
Our fields

Robotics




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Research Areas

A robot is an intelligent system that follows real-world dynamics while it interacts and communicates with human beings. Such a system requires sensing the real-world environment in real time (*real-time sensing*). In our laboratory, we develop real-time sensing technologies, such as robot vision and tactile sensing, and integrate them into intelligent systems.

1. Visual interface

Understanding the environment and generating robot motion play an important role in intelligent interaction among people, robots, and computers. We develop methods to recognize daily life environments so as to facilitate activities of people and robots.

- Modeling of human/environment in space-time (A-1)
- A service robot and interface (A-2)
- Human-robot interaction (A-3)
- Control, motion generation and machine learning (A-4)

2. Human modeling

We measure, analyze, and model human beings to understand human skills, as well as policy/strategy while carrying out various tasks. Our research topics include a human-sized robotic hand, evaluation of usability based on musculoskeletal models, power assistance, haptic devices, and the evaluation of surgical skills.

- Human support using human modeling technologies (B-1)
- A musculoskeletal model and its sports applications (B-2)
- Measurement and analysis of everyday activities (B-3)
- Rapid prototyping robotic hands (B-4)

3. Application

We construct various robot systems for applications in real-world environments. Research outputs on visual interfaces and human modeling are fundamental components to construct such systems.

- A humanoid robot: HRP-4 (C-1)
- An upper body humanoid robot: HIRO (C-2)
- An android robot: Actroid (C-3)
- Mobile robots: Pioneer 3DX (C-4)

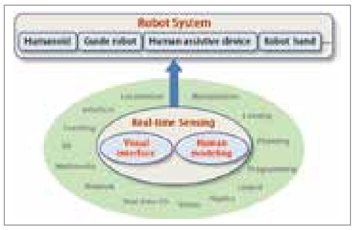

Fig. 1
Overview of our research

Fig. 2
Research area A: Visual interface

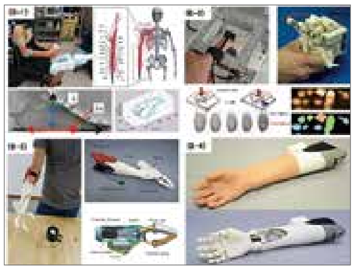

Fig. 3
Research area B: Human modeling

Fig. 4
Robots in our laboratory

Key Features

Robotics Laboratory members have various backgrounds which enable us to incorporate multiple technologies that intelligent robot systems require. By devoting our specialists to solve particular problems in robotics, we aim to transform our members' skills into improved intelligent robot technologies. Furthermore, many students have the opportunity to demonstrate our robots in different places, including stays in other research facilities. We always welcome new students to join our laboratory, and it's cooperative and friendly environment.

Collaborators & Research Activities

AIST, Georgia Tech., CMU, KIT, Tokyo Univ. of Science, Nara Medical Univ., National Inst. of Fitness and Sports in Kanoya, ATR, Osaka Urban Industry Promotion Center, Robotics Society of Japan, etc.

Intelligent System Control



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Research Areas

1. Control systems design

• Advanced robust/adaptive control

We study advanced theories in post-modern robust/adaptive control and their applications including current investigations into various schemes of feedforward learning control (feedback error learning). System identification and state estimation are also topics of interest. (Fig. 1)

• Networked dynamical systems

The goal of this research is to provide a better understanding of the dynamical processes taking place over complex networks, as well as developing effective strategies to control their behavior. Applications of this research direction can be found in a wide variety of contexts, from social networks to networked infrastructure and cyber-physical systems. (Figs. 2, 3)

• Positive systems

Positive systems are dynamical systems whose response signals to nonnegative input signals are constrained to be nonnegative and have applications in pharmacology, epidemiology, population biology, multi-agent systems, and communication networks. We are developing a novel framework toward the synthesis of positive systems based on geometric programming. Our application areas include product development processes, financial systems, data-center management, and systems biology.

2. Machine learning for robotics

• Biologically-inspired learning

We are studying new (reinforcement) learning structures inspired by animals and will convert mathematically convenient structures into ones suitable for real robotic problems. For example, we are developing new neural network dynamics, reinforcement learning schemes, reward reshaping to be optimized, and so on (Fig. 4).

• Physical human-robot interaction

We undertake development for next-generation robots that can physically interact with humans and aim to support various human motions: e.g., shared autonomy for autonomous driving car; adaptive robot control based on recognized human behaviors; multi-agent systems including humans (Fig. 5).

Key Features

We welcome motivated students from various fields including mechanical/electrical engineering, mathematical/physical science, as well as computer science. The faculty guides students individually, taking into account their backgrounds, and assists them in mastering mathematical system approaches by the end of their course. Thereby they acquire a wide range of technical skills from fundamental theories to applications. The students in our lab are highly motivated, diligent, cooperative and eager to learn from others. We anxiously await such students from all over the world.

Fig. 1
Networked control system

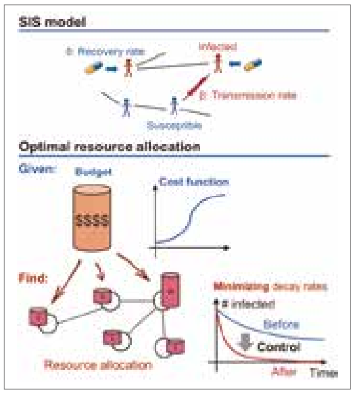

Fig. 2
Containment of epidemic spreading processes over complex networks

Fig. 3
Positive systems applications

Fig. 4
Robot control by reinforcement learning

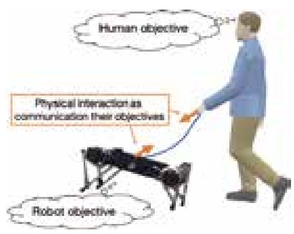

Fig.5
Multi-agent system for physical human-robot interaction

Large-Scale Systems Management




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Research Areas

1. System analytics and simulation

- Large-scale system modeling
- Markov analysis
- Queueing theory
- Simulation tools and techniques for large-scale systems
- Mechanism design
- Distributed virtual currency and smart contracts

2. Human-behavior-aware network systems

- Automation of hazard area estimation and evacuation guidance
- Crowd guidance for congestion alleviation
- Navigation for people with walking difficulty
- Delay tolerant networking

3. Ultra-scalable Blockchain technology

- Stochastic modeling and analysis of the fork mechanism of blockchains
- P2P networking technologies for high-speed block synchronization
- Block generation based on advanced data structure
- Innovative applications of highly-scalable blockchain technologies

4. Network design

- Next generation networks
- Cognitive radio
- Cloud computing
- Controllable P2P contents distribution systems
- Game-theoretic approach

5. IoT security

- Blockchain-based access control
- Physical layer security-based secure wireless communications

Key Features

The Large-Scale Systems Management Lab research aims to develop mathematical modeling and simulation techniques for design, control and architecture of large-scale systems such as computer/communication networks, with which the resulting systems achieve high performance, low vulnerability and highly efficiency energy. Our research focus is on network-science oriented design frameworks, fundamental technologies and highly qualified services, particularly for large-scale computer/communication network systems. The laboratory was established in June 2012, and we welcome students from abroad who have strong interest in theories and simulation skills for designing smart services over large-scale complex systems including Blockchains, data centers, cognitive radio networks, and energy-harvesting networks.

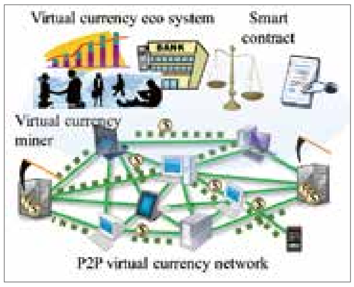

Fig. 1
Distributed virtual currency and smart contract network

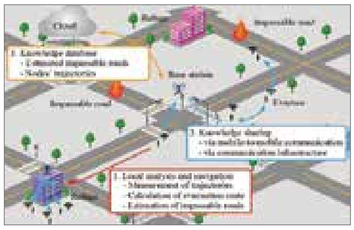

Fig. 2
Hazard-area estimation and evacuation guidance using trajectories of mobile terminals

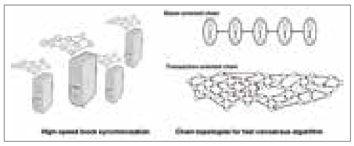

Fig. 3
Ultra-scalable blockchain technology

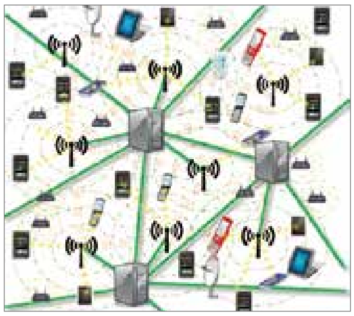

Fig. 4
Cognitive radio networks

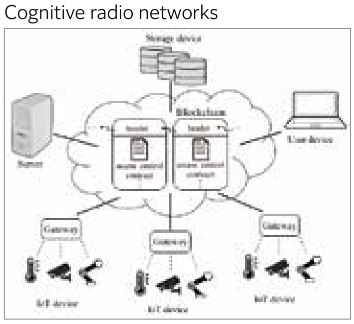

Fig. 5
Blockchain-based access control

Mathematical Informatics






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Research Areas

We study mathematical models for life sciences, from cell biology and neuroscience to medical science and social interaction. Our interdisciplinary research covers computation (machine learning), science (mathematical biology) and engineering (signal processing).

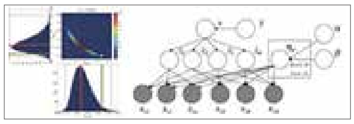

Fig. 1
Mathematical models in computation

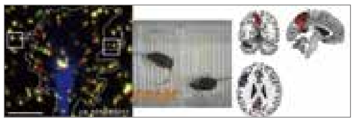

Fig. 2
Mathematical models in science

Fig. 3
Mathematical models in engineering

1. Machine learning

- Statistical learning theory
- Statistical signal processing based on Bayes theory
- Neural network theory
- Information geometry and information theory
- Factor analysis and sparse models
- Reinforcement learning theory and application

2. Mathematical biology

- Math models for cell biology
- Modeling and medical decision support for neuropsychiatric disorders
- Neural mechanisms of empathy
- Behavior analysis using smart sensors
- Cognitive interaction design and social interaction

3. Signal processing

- Advanced driver assistance systems
- Adaptive signal processing theory and application
- Non-invasive human-machine interfaces
- Anomaly diagnosis by big-data analysis
- Deep learning methods and application

Key Features

Mathematical informatics is interdisciplinary; faculty and students in our lab have a variety of backgrounds, such as mathematical engineering, electric and electronic engineering, mechano-informatics, statistical science, physics, psychology, social science and medical science. We welcome students from any background since "mathematical models are everywhere", as long as they are interested in mathematical models.

Imaging-based Computational Biomedicine




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Research Areas

We integrate biomedical imaging with information science approaches such as AI (Artificial Intelligence), especially deep learning, computational simulations, and augmented reality to create knowledge and foster innovation in the field of computational biomedicine. We currently have four main research areas (Fig. 1):

- AI-based human anatomy modeling (Fig. 2)

We create models of human anatomy for each individual subject from 3D biomedical images using AI technologies. We also create models of variability in anatomical shapes and image appearances throughout a population, which we call computational anatomy models. We further construct computational models of, for example, physical or physiological functions to seek comprehensive understanding of a subjects' body.

- Diagnosis and treatment planning (Fig. 3)

We develop systems to support critical decision-making in diagnosis and therapeutic planning. These systems integrate patient-specific biomedical simulations with human anatomy models and statistical (or AI-based) predictions based on clinical databases (known as "medical big data").

- Image-guided therapy (Fig. 4)

We are developing a surgical navigation system to provide surgeons with intraoperative guidance through real-time fusion of the surgical field and surgical plans on patient anatomy models. Our ultimate goal is to develop AI surgery systems to perform optimal surgery incorporating pre- and intra-operative patient conditions as well as postoperative predictions.

- Postoperative assessment (Fig. 5)

Medical treatment quality assurance requires proper assessment of the surgical outcomes, which are provided as training data of AI surgery systems. We develop methods to quantitatively evaluate the motion of patients who have had surgery on their musculoskeletal structures, such as in orthopedic and craniofacial operations, where detecting subtle changes in locomotion is crucial in predicting long-term outcome.

Key Features

Our laboratory features a highly integrated research environment for information science, biomedical imaging, clinical medicine, and other related technologies. We have a number of medical and technical collaborators, including companies, working together within Japan and throughout the world. We fully utilize our unique environment and our network of researchers to pursue our work in imaging-based computational biomedicine.

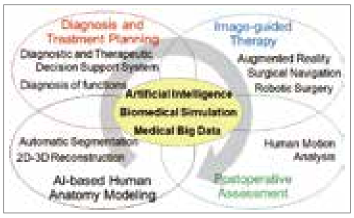

Fig. 1
Research areas in our lab

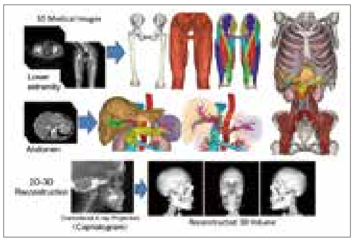

Fig. 2
AI-based human anatomy modeling

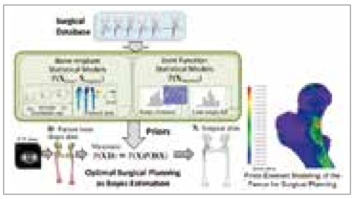

Fig. 3
Diagnosis and treatment planning

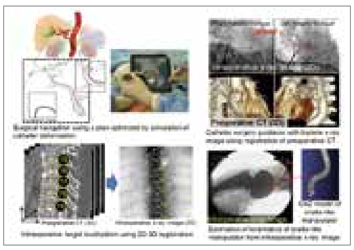

Fig. 4
Image-guided therapy

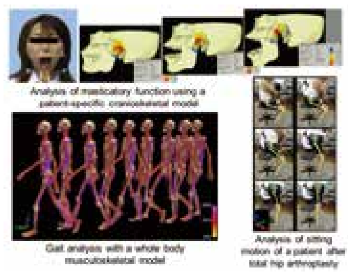

Fig. 5
Postoperative assessment

Computational Systems Biology

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Research Areas

1. Biomedical & health data science

In collaboration with medical hospitals and other academic institutions, we are developing various biomedical engineering technologies based on information technology and state-of-the-art deep learning techniques.

By incorporation of the strengths of the wearable/unconstrained sensing techniques and information technology such as deep learning techniques (CNN, GAN, etc.), we are developing health monitoring systems for daily use.

- A computer-aided diagnosis assistance system for medical images
- A wearable deep body thermometer monitoring system
- A cuffless blood pressure monitoring system
- A heart health monitoring system based on contactless electrocardiograph

2. Systems biology & bio data science

Huge biological data sets, such as more than 1,000 genome sequences, have caused a paradigm shift into a holistic approach to understanding living things as systems. In this field, we keep incorporating state-of-the-art data modeling/manipulating techniques such as deep learning techniques to better our understanding.

With the development of omics technologies, it has become imperative to systematically analyze all biological components (genes, mRNA, proteins and metabolites). To meet this challenge, we have developed a clustering algorithm (DPClus, BiClus) to extract highly connected clusters.

3. Metabolomes & drug discovery

Cells consist of a few thousand molecules. Of those, metabolites are mainly produced by enzymatic reactions. The objective of metabolome analysis is to comprehensively identify which particular metabolites affect cellular networks. As a metabolome analysis platform, we have developed a species-metabolite database, KNApSAcK, covering almost all reported metabolites. To date, 50,048 metabolites and 101,500 species-metabolite relationships have been accumulated. We could extract metabolic pathway information using Molecular Graph Convolution Neural Networks MGCNN.

Key Features

Regardless of research backgrounds, we enjoy an interdisciplinary field between information technology and bio-medical science to mine and integrate knowledge in biology, medical science and health-care. "Let's do research on what we want!" is the motto of our lab.

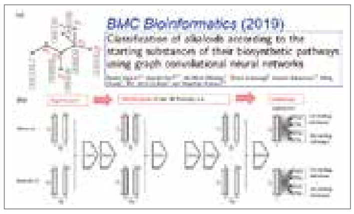

Fig. 1
Molecular Graph Convolution Neural Networks (GCNN) makes it possible to predict biological activity and metabolic processes for molecules.

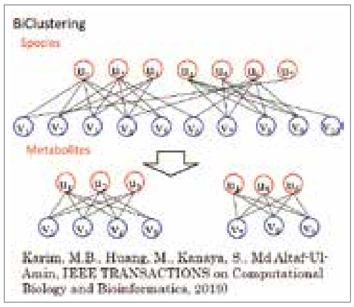

Fig. 2
The novel algorithm BiClustering (BiClus) has been developed in our lab, which makes it possible to create groups based on two different attributes.

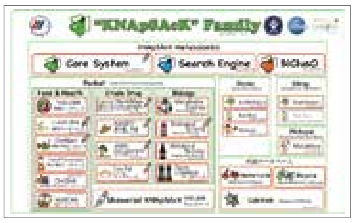

Fig. 3
Main page of "KNApSAcK Family DB"(http://kanaya.naist.jp/KNApSAcK_Family/). This DB has become a world standard database consisting of metabolite-species relationships and cited by very large number of scientific papers.

Robot Learning

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Research Areas

1. Machine learning algorithms for real-world robots

- (Deep) reinforcement learning
- (Deep) imitation learning
- Deep learning for dynamical systems
- Active perception
- Human-in-the-loop optimization

2. Real-world applications

- Smart manufacturing
- Human-assistive technology (exoskeleton robots, EMG interfaces, etc.)
- Chemical plant modeling and control
- Vehicle autopiloting

Research Equipment

- Nextage robot (Kawada)
- Baxter robot (Rethink)
- UR5 and UR3 (Universal robots)
- OP3 humanoid robot (Robotis)
- Various sensors (motion capture systems, EMG sensors, etc.)

Collaborators

University of Technology Sydney (Australia), Radboud Univ. (The Netherlands), Karlsruhe Institute of Technology (Germany), Edinburgh Univ. (UK), LAAS-CNRS (France), ATR, AIST, Shinshu Univ., Ritsumeikan Univ., Kansai Univ. (Japan), etc.

Research Statement

Robot learning (machine learning for robots) is an interdisciplinary field of various fields such as machine learning, artificial intelligence, robot engineering, control engineering, signal processing, optimization, and mechatronics. You may be able to find your approach by utilizing your field of expertise, skills, and experience (robot contests, programming contests, work, etc.). Please challenge yourself within robot learning research.

Fig. 1
Deep reinforcement learning for cloth manipulation

Fig. 2
Object search with Gaussian processes

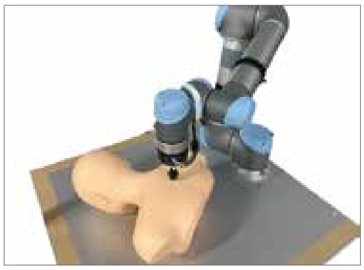

Fig. 3
Object shape estimation from tactile sensing

Communication (NTT Communication Science Laboratories)

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Assoc. Prof. Tomoharu Iwata

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Research Areas

1. Data mining from relational data including large and complex networks

We study basic technologies mainly based on statistical machine learning to understand huge, irregular and ever-growing relational data including complex networks, such as the Web and SNS, and then make effective use of them for knowledge navigation.

2. Understanding real world situations through sensor networks

We are interested in observing and interpreting the real world through a variety of sensing devices such as acceleration sensors, light sensors, GPS, cameras, and microphones.

Key Features

Our research activities include various phases, including proposing new theories and modeling, developing effective algorithms and data structures, and applying techniques to new interesting applications. We are interested in processing various data, such as Web and language data, speech sounds, images, and sensor data. Our everyday efforts are aimed at the world's first proposal and verification of new techniques, or the world's best performance of certain tasks. Students can use rich computer and human resources of NTT Communication Science Laboratories such as large clusters of high-performance servers. Each student receives a desk and personal computer and studies together with a group of researchers with which discussions occur naturally. More heated, in-depth discussions are also frequently conducted in discussion rooms.

Humanware Engineering (Technology Innovation Division, Panasonic Corporation)

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Assoc. Prof. Yoshikuni Sato

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Research Areas

1. Development of applied technologies for smart houses and for health support through biosensing
2. Nursing care support technology by combining sensing technology and artificial intelligence
3. Creating new solution areas for a better life and a better world

Key Features

"Humanware" is the core concept of this laboratory. It essentially extends the abilities of humans and supports better human life by the combination of sensor data and knowledge processing. It aims to achieve human-like intelligent information processing, five-sense communication, and soft-flexible robotics/mechatronics. The basis of information and communication technologies are artificial intelligence, machine learning, statistics, biosensing, etc. Our laboratory explores new research areas concerning smart houses and care support technology combined with human, social, and physical sciences.

Computational Neuroscience (ATR International)



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Research Areas

We aim to understand the human brain and to achieve new machine intelligence (artificial intelligence) based on brain information processing functions. We conduct research and educate students on computational neuroscience and cutting-edge machine intelligence with such methodologies as brain decoding, brain machine interfaces, neurofeedback, and robot learning at ATR, an internationally recognized computational neuroscience center.

Key Features

1. Machine intelligence for humanoid robot control
The framework for finding optimal behavioral policy can be formulated as a goal-directed decision-making problem. Using data-driven reinforcement learning algorithms, we construct machine intelligence for humanoid robot control to solve this decision-making problem.

2. Cognitive functions: understanding and manipulation
The brain is a huge information network. We tackle enigmas in relationships between the brain network and cognitive functions such as memory and thinking. We develop neurofeedback techniques for preventing impairments to cognitive functions due to brain diseases and aging.

3. Brain-Machine Interface (BMI) in daily life
By measuring brain activities in daily living environments, we develop techniques to estimate mental states such as stress and empathy. Based on them, we approach the neural bases of cognitive functions in natural situations to pursue social applications of neuroscientific knowledge, including human resource development.

4. Novel analysis methodology development to understand brain functions
We aim to provide new ways to understand brain functions by developing innovative analysis methodology using statistical and machine learning theory. In particular we emphasize the multimodal data integration approach to overcome limitations of single measurement data.

5. Neurofeedback
We integrate psychophysical, neuroimaging, and computational neuroscientific approaches and propose novel neurofeedback methods, developing effective methods for BMI, medical treatment, and communication applications.

6. Computational models of decision-making
Our goal is to understand how humans make decisions. Reinforcement learning models and economic theorems allow us to build neural computations for human decision-making. We apply them to solve social, economic, and medical problems.

7. Adaptive shared control for BMI exoskeleton robots
Since robots are expected to work closely with humans, the development of a shared control strategy is becoming an increasingly important research direction. We are constructing an adaptive shared control strategy for our brain-machine-interface (BMI) exoskeleton robot.

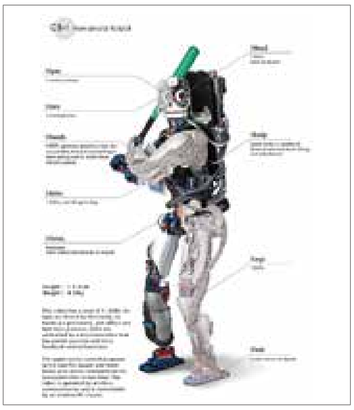

Fig. 1
Machine intelligence for humanoid robot control

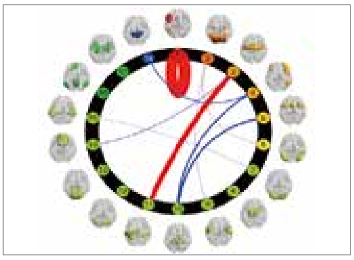

Fig. 2
Brain network supporting a cognitive function (working memory)

Fig. 3
Brain-Machine Interface (BMI) in daily life

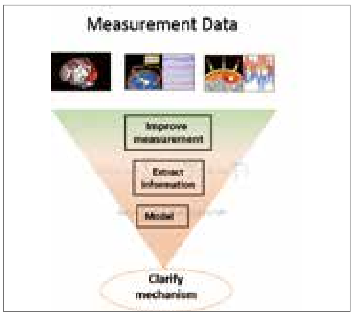

Fig. 4
Measurement data

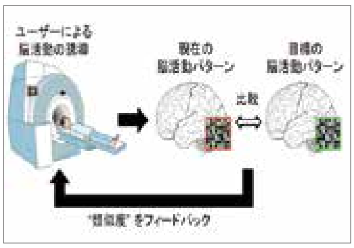

Fig. 5
Neurofeedback

Fig. 6
Computational model of decision-making

Fig. 7
Adaptive shared control for BMI exoskeleton robots

Symbiotic Systems *(NEC Corporation)*


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Research Areas

To enable machines (Artificial Intelligence, AI) to work in harmony with humans, we are involved in research and education of technology for precise real-time recognition and comprehension using sensors such as cameras, especially of real-world situations where there are many people and objects moving around and interacting.

In recent years, technological innovations based on deep learning techniques have dramatically increased the performance of AI, particularly with regard to image recognition. It is expected that this technology will be used in diverse applications including real-time analysis of security camera footage, and inspection/robotics in factories. However, AI currently requires not only large amounts of learning data to be prepared in advance, but also large amounts of adjustments to adapt to each installation site. As a result, there are still many issues to be overcome in order to apply AI to diverse real environments that change from one moment to the next.

To adapt to environmental changes, it is useful to capture changes in real-world conditions with faster real-time performance and in greater detail. In particular, if it is possible to perform not only spatial analysis of subjects that are targeted by most deep learning models, but also the detailed temporal analysis and comprehension, then it should be possible to grasp changes more reliably and adapt more easily to diverse environments. Specifically, at our laboratory we are mainly working on the following themes, but we also work on a wide variety of general recognition technologies primarily involving image recognition, such as improvements of deep learning itself.

1. High-speed-camera object recognition

Until recently, most image recognition studies have assumed a 30 fps frame rate (30 pictures captured per second). However, we aim to gain a deeper understanding of the real world by using a high-speed camera to obtain data with greater detail in the time axis (from 100 to 1000 fps) so that even fast-moving objects can be reliably tracked and evaluated without disturbing their motion, and so that tiny vibrations of objects can also be analyzed. This object recognition technology using high-speed cameras can achieve high speed inspection in, for example, the production of many models in small quantities where many different items are handled and each one has to be checked appropriately without interrupting the production process.

2. Individual object authentication

If it is possible to distinguish each individual item in a single camera image, then these items can be reliably tracked without having to perform constant sensing, and changes can be analyzed as they occur. With this as a broad theme, our aim is to individually identify and track any item in the real world by instantly capturing images with a camera and analyzing their detailed patterns instead of relying on special tags such as RFIDs. This will make it easy to find inefficiencies and optimize productivity, even in high-mix, low-volume production environments that are constantly changing, for example.

Key Features

1. Joint research and collaboration

We are continuing to strengthen our core technological ability while promoting joint research with various research institutions including the University of Tokyo and the RIKEN Center for Advanced Intelligence Project (AIP).

2. Open and global research environment

We invite many researchers and internship students from Europe, Oceania and Asia to the open laboratories at NEC. Students of our laboratory learn about various research fields and languages, while gaining a global point of view.

Multilingual Knowledge Computing (Fujitsu Laboratories Ltd.)

Prof.
Nobuhiro Yugami

Assoc. Prof.
Yuchang Cheng

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Research Areas

Explainable AI with Deep Tensor and Knowledge Graphs

Deep Learning is one of the most representative technologies in recent AI and shows high performance in pattern recognition and analysis. However, as it cannot explain the reasoning for its judgment, it is called "black box AI." Due to this limitation, it is difficult to apply AI to the fields requiring high reliability and persuasiveness such as healthcare, finance, and corporate management that especially need important decision-making.

Fujitsu Labs has developed the world's first machine learning technology called "Deep Tensor" that can directly analyze the relationships among numerous pieces of real-world data ranging from intercompany transactions to material structures. We also developed a technology for building a large-scale multilingual knowledge base, which is called a "knowledge graph" and consists of vast multilingual knowledge existing around the world such as academic papers in different languages, by using our unique knowledge computing technology. We combined these two technologies and developed novel technology that enables AI to explain the reasoning and basis (evidence) for its judgment by constructing a logical path from input to the AI inference result, which can be used by people securely. With this technology, we can realize explainable AI that overcomes the limitations of ordinary deep learning and it can be used by people with high confidence.

We are able to provide information on unknown causal relationships and academic papers supporting these to genomic medicine specialists, by using a knowledge graph consisting of the data stored in the open databases of life information science and the data in more than 10 million medical documents. We are trying to realize individual medicine optimized for each patient and find new treatments.

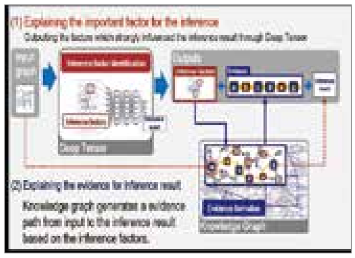

Fig. 1

Key Features

Our laboratory belongs to Fujitsu Laboratories Limited, located in Kanagawa Prefecture, Kawasaki City. We are researching and developing various multilingual knowledge computing technologies to develop AI. The AI that Fujitsu envisions is a "collaborative, human centric AI," and we are aiming for the realization of AI that supports greater business growth and efficiency for our customers.

Next Generation Mobile Communications (NTT DOCOMO, INC.)


Prof.
Yukihiko Okumura

Assoc. Prof.
Tetsuro Imai

■URL: http://isw3.naist.jp/Contents/Research/cl-05-en.html

Research Areas

Broadband multimedia mobile wireless communication systems

- Variable bit rate transmission techniques
  Power and bandwidth efficient resource allocation schemes for variable bit rate transmission, which is required for multimedia communication systems.
- Radio relaying schemes for MIMO wireless networks
  Radio repeaters expand coverage area without degradation in power and frequency utilization efficiency performance.

Key Features

Our laboratory is located in Yokosuka, Kanagawa. Students who plan to join our laboratory complete course work provided by the Network Systems Laboratory in the first year of the master's program. In the second year, students move to our laboratory in Yokosuka to start working with us.

Optical and Vision Sensing (Core Technology Center, OMRON Corporation)


Prof.
Masaki Suwa

Assoc. Prof.
Yoshihisa Ijiri

■URL: http://isw3.naist.jp/Contents/Research/cl-06-en.html ■Mail: suwa@ari.ncl.omron.co.jp, yoshihisa_ijiri@omron.co.jp

Research Areas

Vision sensing technology for factory automation, social systems and consumer products

1. Physics-based vision
3D sensing, vision-based 3D measurement/object detection, camera calibration

2. Computer vision
Object detection/recognition, character recognition, machine vision algorithms

Key Features

Students in our laboratory:

- Extract research topics that are closely linked to product commercialization. Research topics are directly derived from customers' problems in each application field.
- Frequently discuss ideas with company engineers
- Collaborate with overseas internship students

Molecular Bioinformatics (National Institute of Advanced Industrial Science and Technology)


Prof.
Yutaka Ueno

Prof.
Kazuhiko Fukui

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Research Areas

1. Omics-driven drug repositioning and repurposing
2. Bioinformatics tool integration for workflow analysis
3. Biological molecule structural analysis from electron microscopy images
4. A domain specific language for molecular model scripting animations

Key Features

- Graduate students' individual research projects and collaboration studies in bioinformatics areas are hosted at laboratories in the National Institute of Advanced Industrial Science and Technology (AIST).
- Experiencing a wide variety of research methods and techniques, and working with researchers from both biology and informatics fields.
- Various software systems for bioinformatics research projects developed in AIST in the last decade demonstrate the computational studies required for future problem solving.

Other Topics

- Software development for modern high performance computing
- Applications of haptic user interface devices for molecular modeling

Secure Software System (National Institute of Advanced Industrial Science and Technology)


Prof.
Yutaka Oiwa

Assoc. Prof.
Reynald Affeldt

■URL: http://isw3.naist.jp/Contents/Research/cl-10-en.html

Motivation

Safety and reliability of software and computer-based systems, based on both scientific theory and practical applications

Research Areas

1. Development process and tools for ensuring software reliability
- Quality management and improvements for software testing
- Analysis of software implementation/design
- Software development processes
- Software security assurance/certification

2. Fundamental theories/technologies for software safety
- Semantics and design of programming languages
- Software testing, model checking and formal analysis

3. Theoretical/practical aspects of computer security
- Software protection, intrusion detection
- Security protocols and cryptography

Digital Human (National Institute of Advanced Industrial Science and Technology)

Prof.
Mitsunori Tada

Assoc. Prof.
Akihiko Murai

■URL: http://isw3.naist.jp/Contents/Research/cl-08-en.html

Research Areas

Our laboratory is a part of Digital Human Research Group, Human Informatics Research Institute, National Institute of Advanced Industrial Science and Technology (AIST) under METI, located in Odaiba, Tokyo. Since our 2001 inception, we have promoted research projects with about 30 Japanese and international researchers and students from many fields to create computational models of human functions. We research the human appearance including its internal structure and functional neuro-musculoskeletal systems from the standpoints of modeling, computation, and measurement/visualization technologies. We work toward systems that adapt to individuals and their environments and support them suitably using digital human technology, a crucial function that has yet to be fully realized.

Prof. Tada works on modeling normalized/individual digital humans based on dimensional databases and statistics, and the development of motion measurement/analysis systems. Assoc. Prof. Murai works on modeling human neuro-musculoskeletal systems and the understanding of human motion generation/control mechanisms.

This course recruits students for the following research topics, which are part of ongoing research projects. Additionally, students may also propose related themes for their own research.

1. Digital human modeling

We lead research of modeling technology to reconstruct the human appearance and function on computers from anatomical knowledge and medical images of skeletons, muscle, and organs. This year, we will model detailed limbs, the trunk, and abdominal cavity based on the ongoing volumetric digital human model.

2. Understanding of human motion generation/control mechanisms

We measure human motion with optical motion capture systems and force plates, compute the joint angle and torque by kinematics and dynamics, and analyze the motion generation/control mechanisms based on robotics and statistics. This year, we will measure and analyze daily/athletic performance with the volumetric digital human model, applying statistical analysis and the feature extraction to analyze and modify these motion data.

Fig. 1
Digital human modeling based on anatomy and measurement

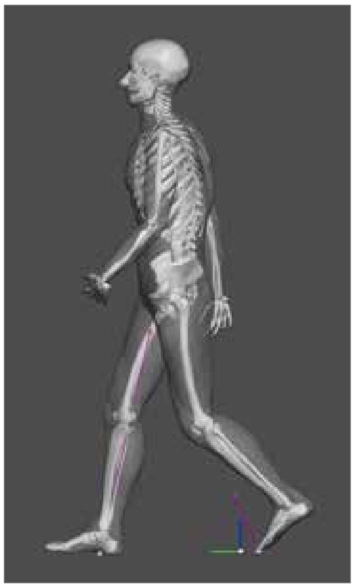

Fig. 2
Understanding human motion generation/control mechanisms using a digital human model

Fig. 3
Real-time motion measurement, analysis, and visualization

Network Orchestration (National Institute of Information and Communications Technology)


Prof.
Kazumasa Kobayashi

Assoc. Prof.
Eiji Kawai

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Research Areas

1. Virtualization technologies for network infrastructure
- Switch/router virtualization
- Software Defined Networking (SDN)
- Networking for cloud computing

2. Next- and new-generation network infrastructure technologies
- IPv6 and beyond-IPv6 technologies
- Infrastructure technology for service-oriented networks such as mobile networks, sensor networks, content-centric networks, etc.

3. Orchestration technologies for large-scale network infrastructure
- Management of wide-area and virtualized networks
- Advanced traffic engineering
- Multi-domain networks

Key Features

The Network Orchestration Laboratory is a collaborative laboratory with the National Institute of Information and Communications Technology (NICT). In particular, we are developing the JGN network testbed, a nation-wide experimental network infrastructure founded by NICT. JGN provides high-speed international connectivity to the United States, China, Singapore, and Thailand, and forms part of a global R&E network infrastructure. Those students who are interested in real-world ICT infrastructure technologies find great opportunities to conduct research not only utilizing the facilities of JGN, but also applying their products to JGN.

High Reliability Software System Verification

(JAXA's Engineering Digital Innovation Center (JEDI), Japan Aerospace Exploration Agency)


Prof.
Masafumi Katahira

Assoc. Prof.
Naoki Ishihama

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Research Areas

Recent embedded systems and infrastructure systems are recognized as the basis for accomplishing national and human safety. Assurance of high reliability in those systems is one of the most critical issues to increase the safety of the whole social system.

Based on the proven studies and practices concerning high reliability and safety in the field of space systems established by JEDI in JAXA, our "High Reliability Software System Verification Laboratory" is focused on research into software verification methodologies to achieve high reliability and safety in software that must function properly under extreme environmental conditions.

Assurance methods for verification completeness, such as End-to-End point of view for complex distributed software systems, are a recent key issue. In our lab, the main topics are reliability and safety verification methodology and reliability and safety assurance methodology.

The research outcomes are expected to be applied to practical uses for systems that require high reliability, not only in space systems but also in social core infrastructures.

1. Reliability and safety verification methodology

- Verification methods for robustness

We research and develop the assurance methods for verification completeness, and the key technologies for robustness verification including the non-functional specifications.

- Automated verification methods

We first research the analysis of system configurations, operational conditions and system error pattern models. Based on those concepts, algorithms and methodologies for the automated generation of verification cases and the automated success criteria of verification results are developed.

2. Reliability and safety assurance methodology

- Assurance methods for verification completeness

We research technology to evaluate verification completeness of whole End-to-End software systems based on verification information produced by various software systems.

- Assurance methods for defect propagation

We formulate systematic defect modes in the whole software system, then research and demonstrate the evaluation method of propagation effects into whole systems.

Key Features

In the first half of the master's program, students complete required coursework on NAIST's campus, and in the last half, determine the thesis themes and join the research of various technologies to produce high reliability and safety in systems, such as Independent Verification and Validation (IV&V), a model-based verification and system assurance, through project based studies and internships in JAXA. Most of the knowledge and skills experienced in our laboratory are highly concerned with science and industry, not only in the space domain but also in a broad range of industries, such as the automotive industry. Internships in JAXA Tsukuba Space Center are held during this period. For necessary topics, international collaborative studies with other international space agencies such as NASA are also performed.

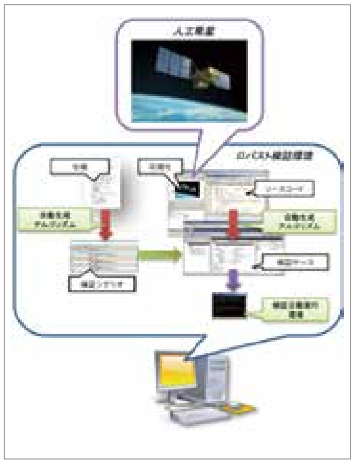

Fig. 1
The concept of robustness verification and automated environments

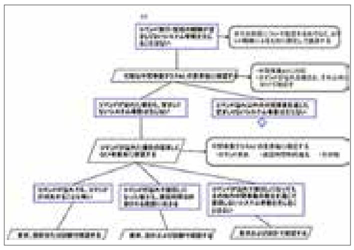

Fig. 2
An example of assurance methods for verification completeness using assurance cases

Fig. 3
JAXA Tsukuba Space Center

Data-driven Knowledge Processing

(National Institute of Information and Communications Technology(NICT))

Prof.
Kentaro Torisawa

Assoc. Prof.
Ryu Iida

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Research Areas

1. A study on intelligent dialog systems using big data

NICT Data-driven Intelligent System Research Center (DIRECT) strives to develop natural language processing systems that contribute to society. In particular, we are currently developing the dialog systems WEKDA and SOCDA. WEKDA is a spoken dialog system that can chat with users on a wide range of topics and give answers to spoken factoid/non-factoid questions using deep learning technologies and 4 billion web pages. SOCDA communicates with millions of disaster victims through a chat application (LINE) on smartphones and collects/provides disaster-related information from and to disaster victims. We are also trying to apply the technologies in WEKDA to spoken dialog systems that perform conversations with elderly people in order for them to have healthy and fulfilling everyday lives. In this research area, we pursue not only the further improvement of the above dialog systems but also the development of general technologies that enable intelligent conversations and debates using big data. Examples of research topics include “dialog strategies for educational purposes” and “automatic dialog strategy modification from user interaction”. The latter aims at developing dialog systems that can automatically change their dialog strategies according to users’ requests.

2. A study on question answering and hypothesis generation using big data

This research area focuses on 1) improving technologies of factoid/non-factoid question answering using knowledge obtained from a huge amount of web pages, 2) creating a new type of question answering task that has never been addressed in the field of natural language processing and 3) developing technologies for generating innovative hypotheses utilizing a huge amount of knowledge obtained from big data.

DIRECT has already developed the Japanese question answering system WISDOM X (https://wisdom-nict.jp/#top). This system gives answers to questions such as “why do sun flares occur?” and “what will happen if global warming persists?” using 4 billion web pages. Using it, we also succeeded in generating hypotheses that foresee facts reported in some scientific research paper. Here, “hypotheses” are not limited to scientific hypotheses: stories in novels can also be regarded as a certain type of hypotheses. Would it not be amazing if a dialog system could on its own start telling a story that was automatically constructed as hypotheses? Examples of research topics include “question answering methods that can provide multi-sentence answers to complex questions” and “story generation using question answering methods and big data”.

3. Study on fundamental natural language processing technologies that are applicable to big data

The above two research areas require syntactic analysis, semantic analysis, and context analysis of texts. These technologies have been studied for a long time in the field of natural language processing but, in most cases, satisfactory performance has never been achieved. In this research area, we develop such fundamental technologies that can be applied to big data. Examples of research topics include “general purpose zero anaphora resolution”.

Key Features

DIRECT currently employs dozens of human annotators who create high quality datasets for new tasks related to the above technologies. In addition, we have collected a huge amount of raw texts by crawling the web (More than 20 billion Japanese web pages and 1 billion English web pages.) and develop question answering, dialog systems and other technologies. We also have a variety of versions of the pre-trained state-of-the-art language models, such as BERT. Our facility is equipped with more than 500 CPU severs and more than 500 GPGPUs. Members of the Data-driven Knowledge Processing laboratory can utilize such resources and equipment for their research activities.

Cutting-edge Research Facilities

Stream pool
(Cybernetics and Reality Engineering Lab)

Wearable metabolic system
(Mathematical Informatics Lab)

Mobile robots
(Kilobot and Khepera IV)
(Dependable System Lab)

Baxter
(Intelligent System Control Lab)

Nextage
(Intelligent System Control Lab)

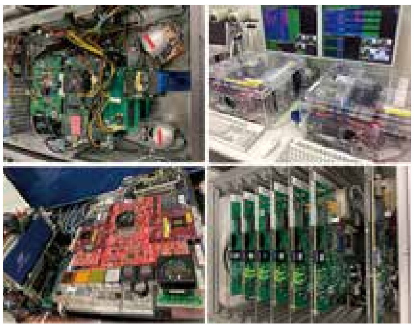
Universal Robot 5 (UR5)
(Intelligent System Control Lab)

Satellite communication vehicle
(Internet Architecture and Systems Lab)

Computation server
(Internet Architecture and Systems Lab)

Weight-bearing Open MRI System
(Imaging-based Computational Biomedicine Lab)

IoT acceleration by new devices
(Computing Architecture Lab)



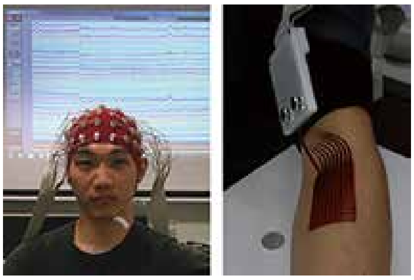
IoT/server acceleration by FPGAs
(Computing Architecture Lab)

GPU server system for deep learning
(Augmented Human Communication Lab)

Bigdata processing system
(Augmented Human Communication Lab)

Glasses-type eye tracking system
(Mathematical Informatics Lab)

Table-mounted eye tracking system
(Mathematical Informatics Lab)

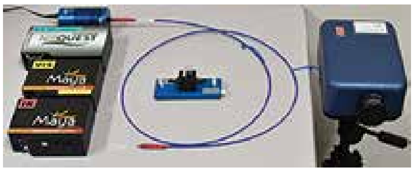


Multi-channel EEG/sEMG system
(Mathematical Informatics Lab)

Driving simulator system
(Mathematical Informatics Lab)

Optical motion capture system / EMG system /Force plates /Musculoskeletal simulator
(Mathematical Informatics Lab)

Multimodal Communication Robot
(Augmented Human Communication Lab)



Hyper-spectral camera and spectroscopes
(Optical Media Interface Lab)

IoT large-scale simulation environment FPGAs
(Computing Architecture Lab)

Smart home facility
(Ubiquitous Computing Systems Lab)

Electroencephalogram (EEG)
(Augmented Human Communication Lab)

Data analysis system
(Software Engineering Lab)

Virtual infrastructure system
(Software Design and Analysis Lab)

Ubiquitous display
(Interactive Media Design Lab)

Large-scale document processing system
(Computational Linguistics Lab)

Humanoid Robot HRP-4
(Robotics Lab)

Super-high definition image interactive system

Behavior media system
(Robotics Lab)

HIRO-NX
(Robotics Lab)

Tele-presence transmitter
(Network Systems Lab)

7-DOF manipulator controlled by pneumatic artificial muscles
(Mathematical Informatics Lab)

Biological Science Laboratories

Information Science

Biological Science

Materials Science

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Plant Cell Function



Prof. Takashi Hashimoto
Assist. Prof. Takehide Kato
Assist. Prof. Shinichiro Komaki

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Outline of Research and Education

We conduct extensive research, from basic to applied, concerning protein function, cell morphogenesis, signal transduction and regulation of gene expression in various plants, making effective use of molecular genetics and imaging technology on Arabidopsis thaliana, liverwort, and green algae.

Major Research Topics

1. Dynamic reorganization of microtubule cytoskeleton in response to environmental stimuli leading to stress adaptation

- Pattern formation of bio-polymer networks
- Regulators of microtubule dynamics
- Stress-induced reorganization of microtubule arrays
- Stress-signal transduction leading activation of tubulin kinase
- Novel growth arrest mechanisms by microtubule disassembly

2. Why and how plant pavement cells adopt a jigsaw puzzle-like shape

- Microtubule regulators generating complex cell shapes
- Bio-mechanics for local growth anisotropy
- Physical advantages for complex cell shapes

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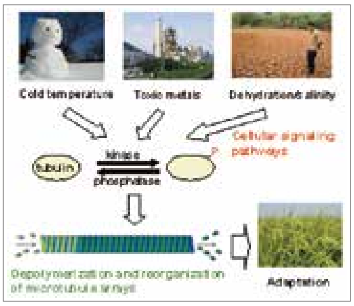

Fig. 1
Environmental stresses remodel the microtubule cytoskeleton by phosphorylation of tubulin subunits.

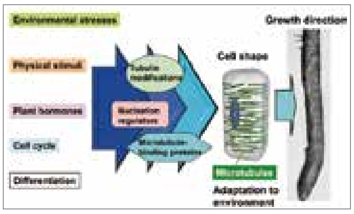

Fig. 2
The plant microtubule cytoskeleton remodels in response to developmental and environmental signals, and controls plant cell shape.

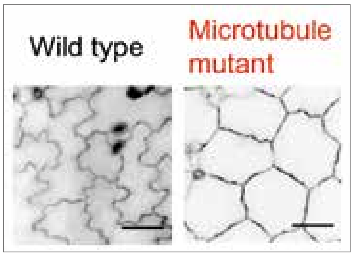

Fig. 3
Microtubules regulate plant cell shapes. Wild-type pavement cells of Arabidopsis cotyledons adopt a jigsaw puzzle-like shape, whereas the mutant cells of the microtubule regulator are polyhedoral.

Plant Developmental Signaling



Prof. Keiji Nakajima

Assist. Prof. Shunsuke Miyashima

Assist. Prof. Tatsuaki Goh

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Outline of Research and Education

Our scientific interests are centered around how plant cells acquire specialized functions and how they coordinately regulate plant growth and life cycles. Each student is engaged in a unique and important project that addresses central questions regarding plant growth and development. Our research is important not only to solve fundamental questions in basic biology, but also to gain the knowledge required to ensure food and energy security.

Major Research Topics

1. How root growth is regulated by endogenous and external cues

Roots have important functions, such as mechanical anchorage, nutrient and water uptake, and interaction with soil environments, and thereby support the life of whole plant bodies. In order to maximize such functions, root tissue organization, growth behavior, and metabolic activities must be precisely controlled by endogenous programs and environmental cues. While past studies have identified key regulatory factors of root development, how they coordinately regulate root growth is largely unknown. To achieve a breakthrough in this, we established a high-magnification live imaging technique to visualize gene expression and cellular/subcellular dynamics at the tip of growing roots for several days. Using this system, we are currently studying genetic and molecular mechanisms integrating endogenous and external cues to regulate root growth in changing environments (Fig. 1).

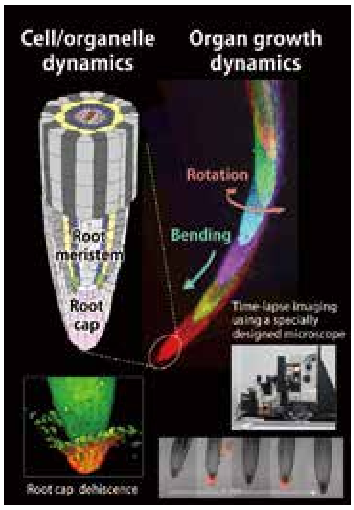

Fig. 1

2. How germ cell morphologies and functions are established in plants

Germ cells, such as eggs and sperm, are functionally specialized for sexual reproduction, and at the same time have specific genomic status enabling pluripotency. Germ cell differentiation in plants takes place deep inside reproductive organs in a relatively short time window, and hence is more difficult to study than somatic cells. We solved this problem through a complementary approach using the flowering plant Arabidopsis thaliana and the liverwort Marchantia polymorpha. We successfully identified evolutionarily conserved transcription factors that promote female sexual differentiation and egg cell formation in these distantly related land plants. Functional analyses of their target genes will reveal how germ cell-specific morphologies and functions are established in plants (Fig. 2).

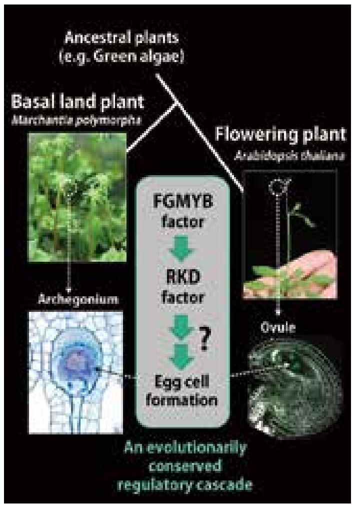

Fig. 2

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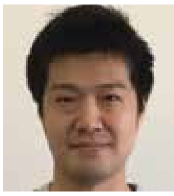
Plant Metabolic Regulation







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Outline of Research and Education

Our laboratory engages in research and education pertaining to the biotechnology needed to resolve the issues facing human beings in the 21st century, such as food, environment, and energy. Especially we are exploring the mechanisms of gene expression regulation for woody cell differentiation using omics technology to develop novel biotechnological tools for the establishment of a sustainable society.

Major Research Topics

1. Molecular mechanisms governing xylem cell differentiation

We identified a key regulator of the xylem vessel differentiation, Arabidopsis VND7 (VASCULAR-RELATED NAC-DOMAIN7), which is a plant-specific NAC domain transcription factor (Fig.1). To understand the molecular mechanism by which xylem vessel formation is regulated, we have been characterizing VND7 and its homologs through various approaches (Fig. 2).

2. Molecular and cell biological approaches to improve woody biomass

We are also conducting genomics, transcriptome, proteome and metabolome studies to reveal the molecular system of plant biomass biosynthesis, using not only model plants but also non-model practical plants.

3. Highly-efficient transgene expression systems in higher plants

Various gene introduction techniques have been developed in higher plants and attempts to produce useful genetically modified plants are actively conducted. However, in practical application, the low expression levels of the introduced genes is a major obstacle. Our laboratories are developing basic technologies to increase the expression levels of genes introduced into plants.

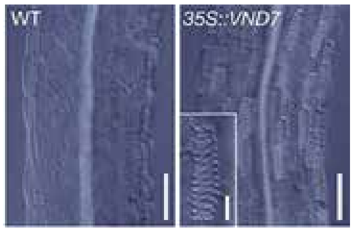

Fig. 1
VND7 acts as a key regulator of xylem vessel differentiation. Overexpression of VND7 induces transdifferentiation of epidermal cells into xylem vessel elements with spiral structures of secondary wall thickening (arrows) in hypocotyl. Bar=100 µm

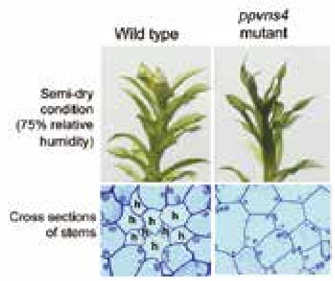

Fig. 2
Moss Physcomitrella patens ppvns mutants, a knock out mutant for one of VND-homologous genes, show the malformation of hydroids (h) in stems, thus leading to decreased water transport activity accompanied wilting phenotype under semi-dry conditions.

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Plant Growth Regulation

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Outline of Research and Education

Plants continuously produce organs throughout their life. This feature renders them distinct from animals, in which organ formation ceases soon after embryogenesis. We aim to understand the mechanisms of DNA polyploidization, stress response and stem cell maintenance that support sustained plant growth under changing environments. Our study will contribute to the development of technologies to increase plant biomass and food production.

Major Research Topics

1. Mechanisms for induction of DNA polyploidization

In many plant species, cells start DNA polyploidization after the cessation of cell division. DNA polyploidization causes enlargement of individual cells and organs; thus, it greatly contributes to plant biomass production. We are studying how cell cycle- and chromatin-level regulation is involved in the induction of DNA polyploidization, and developing technologies to enhance DNA polyploidization in crops and woody plants, aiming to increase food and biomass production.

2. Plant growth regulation in response to abiotic stress

Plant growth is usually inhibited under stressful conditions because plants need to use energy for coping with stress, rather than for organ growth. We have recently identified the signaling cascade that triggers cell cycle arrest in response to DNA damage and heat stress. We are studying how this cascade orchestrates expression of G2/M-specific genes and generating stress-tolerant plants by modifying the signaling components.

3. Maintenance of plant stem cells

Any plant has a long life span if the developmental program is optimized, and continues to grow throughout its life. This feature is derived from persistent proliferation of pluripotent stem cells scattered throughout the plant body. We are studying the molecular mechanisms of how stem cells are maintained and replenished in tissues to understand plant vitality.

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Fig. 1
Increasing plant biomass by enhancing DNA polyploidization.
Change in chromatin structure as well as in cell cycle progression is essential for induction of DNA polyploidization.

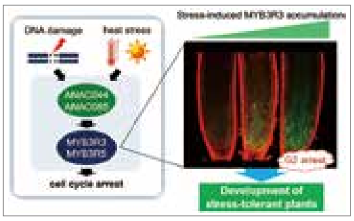

Fig. 2
A signaling module inducing cell cycle arrest in response to abiotic stresses.
Transcription factors MYB3R3/5 cause G2 arrest in response to DNA damage and heat stress. Suppression of the signaling cascade will enable us to generate stress-tolerant plants.

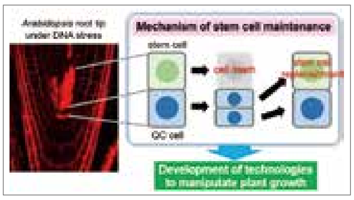

Fig. 3
Stem cell maintenance in the root tip.
Stem cell death, which occurs in response to DNA stress, is accompanied with the division of a neighboring QC cell, thereby replenishing stem cells.

Plant Stem Cell Regulation and Floral Patterning




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Outline of Research and Education

We are interested in a holistic view of gene regulation in plant reproduction, which leads to developmental robustness and coordination. We explore signaling and epigenetic control in stem cell maintenance, environmental response and fertilization. To reveal molecular mechanisms, we use *Arabidopsis* as a model plant for genetic, reverse-genetic, biochemical and genomics approaches, as well as Brassicas and rice, to study conservation and diversification. Our students work at the frontiers of plant molecular genetics, developing their research, presentation and writing skills.

Major Research Topics

1. Floral stem cell homeostasis

Flowers originate from self-renewing pluripotent stem cells in the floral meristems (Fig. 1). The maintenance and differentiation of stem cells are regulated by a well-coordinated interplay of cell-cell signaling and epigenetic regulation, leading to spatiotemporal-specific gene regulation. We study downstream cascades of the receptor kinase signaling pathway controlling stem cell homeostasis.

2. Stem cell termination and cell specification

In flower development, the stem cell activity is terminated in multistep pathways mediated by multiple transcription factors. We study transcriptional/epigenetic mechanisms and hormone signaling controlling stem cell termination and cell specification (Fig. 2).

3. Environmental response and acclimation

We study how plants memorize environmental temperature and light conditions and reveal the molecular mechanisms that confer the plasticity and robustness of the cascades under various environmental stimuli. These studies will serve as a basis of plant growth optimization for improved crop plant yields (Fig. 3).

4. Mechanisms of dominant/recessive relationships in plants

Pollen determinant genes functioning for self-incompatibility are governed by a complex dominance hierarchy. We study the mechanisms of these dominant/recessive relationships regulated by a small RNA-based epigenetic mechanism and its evolution in *Brassicaceae*.

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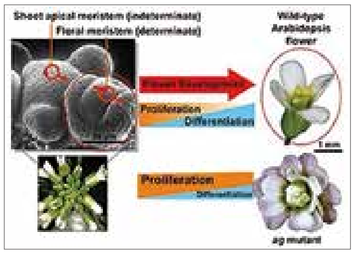

Fig. 1
Arabidopsis flower development
In flower development, the stem cell activities in the floral meristem are terminated (determinate), while the shoot apical meristem continues to grow.

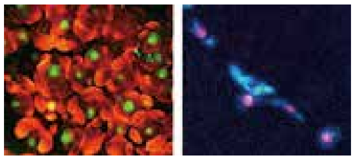

Fig. 2
Imaging of key transcription factors in floral meristems (left) and a differentiated myrosin cell (right)

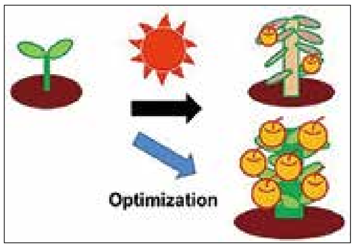

Fig. 3
Plant growth optimization
By revealing the mechanisms of floral stem cell regulation and environmental responses, we will develop a molecular basis for plant growth optimization for higher crop yield.

Plant Physiology

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Outline of Research and Education

Circadian clocks are molecular mechanisms used by plants and other organisms to predict and respond to environmental changes. Approximate 24 hour circadian rhythms affect many aspects of plant physiology, including cell elongation and photoperiodic flowering. To pinpoint how clocks function individual cells and tissues levels, we develop new methods for analysing gene expression with high spatiotemporal resolution. This is accompanied by the application of these to the control of photoperiodic flowering. Through this research, we seek a better understanding of plant physiology and development. We also attempt to identify gaps in our current understanding which can be addressed with greater precision.

Major Research Topics

1. Dissection of circadian clock functions at organ, tissue and cellular levels

Circadian clocks are used to predict the timing of transitions between day and night, and different seasons. In plants, the circadian clock modulates cell elongation, leaf movement, and flowering. We have shown that these responses can be explained by tissue-specific functions of circadian clocks. To explore the tissue and cell-type-specific functions of circadian clocks in further detail, we are investigating circadian rhythms with high spatiotemporal resolution and reveal signalling mechanisms with clear biological significance

2. Understanding and controlling photoperiodic flowering via the circadian clock

Photoperiodic control of flowering is a regulatory mechanism of key physiological importance mediated by the circadian clock. The molecular mechanisms by which the flowering hormone, florigen, regulates flowering have been extensively studied,but there are still questions to be answered regarding the integration of environmental signals into the circadian clock, and how seasonal information is extracted from circadian rhythms. We are assessing how light, temperature, nutrients and other external factors regulate photoperiodic flowering through circadian rhythms; while also applying this knowledge to control crop flowering time without genetic modification.

3. New technologies for high spatiotemporal analysis

To achieve high spatiotemporal analysis, we are developing new methods to precisely examine the function of the circadian clock. These include specific tissue/cell isolation, non-invasive measurement of tissue-specific gene expression, and an algorithm for a time-series single cell transcriptome. These new approaches provide novel ways to test our current understanding

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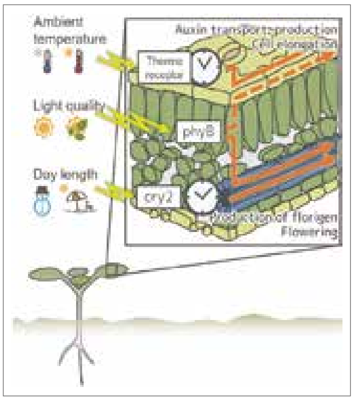


Fig. 1
Tissue-specific environmental responses through cell-type specific clocks. We found circadian clock functionality in specific tissues is required for specific physiological responses

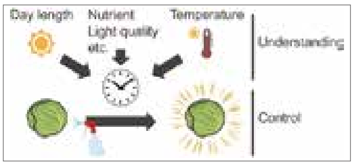


Fig. 2
Understanding clock-mediated flowering mechanisms allows for the manipulation of crop flowering times.

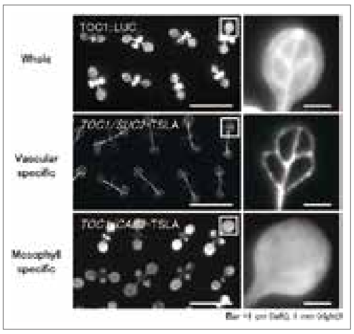
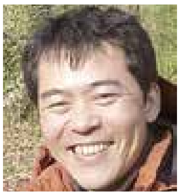


Fig. 3
Tissue-specific luciferase assay. Many clock genes including *TOC1* are expressed ubiquitously (top). Our technique enables us to measure tissue-specific dynamics of *TOC1* (middle and bottom), and this analysis shows tissue-specific circadian rhythms.

Plant Immunity



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Outline of Research and Education

In nature, plants cope with a wide range of microbes, which reside on the surface of or within plant tissues, under fluctuating environments. Plants accommodate and often exploit plant-inhabiting microbes in adapting to adverse conditions, despite an elaborate immune system to detect and repel microbes. We hypothesize that plants distinguish pathogens from non-pathogens in a context-dependent manner, by sensing "danger" signals generated upon pathogen attack in addition to microbial structures. We aim to decipher the molecular mechanisms by which plants integrate microbial and abiotic cues to fine-tune their associations with microbes and facilitate their adaptation to different habitats. Our major focuses involve immune receptor signaling and its modulation by abiotic stress sensing and signaling, defense-related transcriptional reprogramming, and infection strategies of pathogenic and endophytic microbes. Our studies are expected to reveal significant insight into the molecular basis for plant-microbe-environment associations, and thus offer new effective approaches to controlling plant health and growth in sustainable agriculture.

Major Research Topics

1. Danger sensing and signaling in plant-microbe interactions

2. Signal integration between biotic and abiotic stress responses

3. Endophytic and pathogenic microbes in plants

4. Plant-associated microbiomes

5. Transcriptional reprogramming and priming in plant immunity

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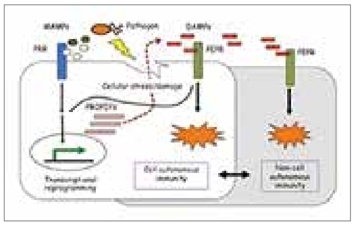

Fig. 1
The layered structure of microbe- and damage-signal receptor signaling provides an important basis for robust pathogen resistance and its fine-tuning.

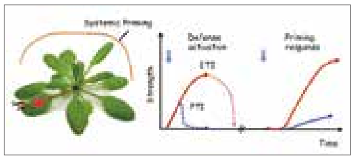

Fig. 2
Transcriptional reprogramming and priming in plant immunity. Following the initial defense activation (left arrow) upon recognition of pathogen-associated patterns (PTI) or effectors (ETI), defense-related genes become primed to allow faster and/or greater responses upon second stimulation (right arrow). Histone modifications provide a basis for this immune memory that is sustained in the generation and can be inherited by the next generation.

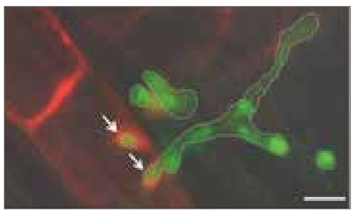

Fig. 3
Root colonization of endophyte Colletotrichum tofieldiae (Ct). Confocal microscope images of Ct constitutively expressing cytoplasmic GFP (green, labeled by dotted lines) and A. thaliana expressing VAMP722-mRFP (Red). Intracellular hyphae inside a root cortical cell are enveloped by PIP2A-mCherry-labeled host membranes (arrows). 8 day post inoculation. Bar = 10 µm.

Plant Secondary Metabolism


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Outline of Research and Education

Plant secondary metabolism (also called "specialized metabolism") produces compounds having several bioactivities such as resistance factors against various environmental stresses in plants, as well as health benefits for humans. Secondary metabolites are widely diversified in their chemical structures in nature (Fig. 1), since plants have adapted to environmental niches during long evolutionary periods using varied strategies such as gene duplication and convergent evolution of some key genes, which contributes to chemical diversity. Our laboratory focuses on model plants, crop species and medicinal plants for i) the analysis of the natural diversity of secondary metabolites, and ii) the functional genomics approach by translational analysis of omics studies (genomics, transcriptomics and mass spectrometry-based metabolomics). The specific goal is identifying key factors of natural chemical diversity and regulatory roles in plant secondary metabolism to enable the metabolic engineering of beneficial compounds.

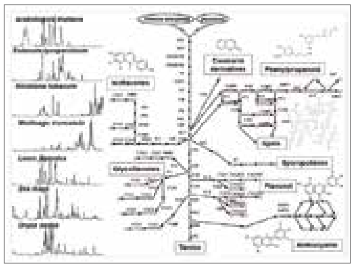

Fig. 1
Metabolic network of plant polyphenolic biosynthesis and their chemical diversity between plant species

Major Research Topics

1. Functional genomics approach by omics-based translational analysis

After completion of full-genome sequencing of huge array of plant species, the complete biosynthetic framework of each plant species still needs to be elucidated, since genome information is not sufficient to compute the size and framework of plant metabolism. We therefore perform metabolomic analysis to screen qualitative differences of metabolite levels between different species, tissues and natural mutants for refinement of recent models of biosynthetic framework (Fig. 2). After illustration of metabolic framework, genome and transcriptome data, as well as genome-wide resources such as quantitative trait locus (QTL) lines and wild accessions for genome-wide association studies (GWAS), are employed for translational analysis. We focus on the discovery of key genes involved in the creation of chemical diversity, and production of beneficial compounds.

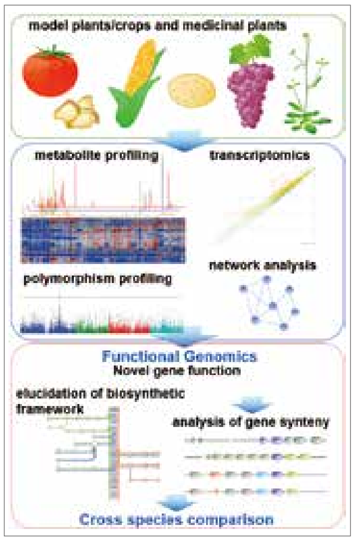

Fig. 2
Omics-based translational analysis using model plants and crops

2. Cross species comparison of the neo-functionalized genomic region

The range of genetics-based strategies for characterization of key genes described above provide several genes and genomic regions involved in neo-functionalization of plant secondary metabolism. "Neo-functionalization", which produces a totally new function after a gene duplication event, is a key factor of functional gene divergence. We therefore focus on the species-specific duplicated genes in these key genome synteny regions in order to discover new functional genes in plant secondary metabolism.

3. Regulation of metabolic networks during nutritional stresses

Nutrient deficiency in soil causes severe reduction in growth with low yields and crop quality. We investigate metabolic and gene expression changes of plants grown under nutrient deprivation stress. This study aims to: i) make an index of time-dependent metabolic changes, ii) evaluate the robustness of metabolic networks, and iii) find species-conserved metabolic makers for the effective breeding of plants having high nutrient-use efficiency or tolerance to nutritional stress.

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Plant Symbiosis


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Outline of Research and Education

Parasitic plants - major agricultural constrains in the world

Parasitic plants are able to parasitize other plants and rely on their hosts for water and nutrients. Several parasitic plants in the Orobanchaceae family, such as *Striga* (Fig. 1) and *Orobanche* spp., cause enormous damage to world agriculture because they parasitize important crops and vegetables. We are investigating molecular mechanisms underlying plant parasitism using the model parasitic plants *Phtheirospermum japonicum* and weedy parasite *Striga* spp. By combining molecular, genetic, cell biology and genomic approaches, we aim to understand the nature of parasitism and eventually develop novel control methods for weedy parasites.

Fig. 1
Sorghum field infested by *Striga* spp. (pink flowers) in Sudan

Major Research Topics

1. Identification of genes involved in haustorium formation

Parasitic plants form specialized invasive organs called "haustorium". The haustorium invades host roots, and eventually forms a vasculature connection between the host and the parasite to assimilate host nutrients (Fig. 2). To identify the genes involved in haustorium formation, forward and reverse genetic tools in *P. japonicum* were established. Screening of *P. japonicum* mutants which lack haustorium formation and identification of the causal genes by next-generation sequencing (Fig. 3) will isolate the essential genes in the haustorium formation. Furthermore, the genes upregulated during haustorium formation will be reverse-genetically analyzed.

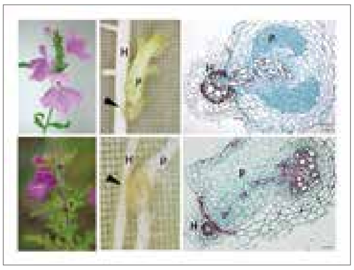

Fig. 2
Obligate parasite *Striga her-monthica* (upper panels) and faculta-tive parasite *Phtheirospermum japon-icum* (lower panels). Photos of flowers (left), host invading parasitic plant root (middle) and cross section of haustorium (right). H: host, P: parasite. Arrowheads indicate haustoria.

2. Plant-plant communication via small-molecular weight compounds

Parasitic plants recognize their hosts via small-molecular weight compounds secreted from the host plant (Fig. 4). For example, the obligate parasite *Striga* germinates in response to the plant hormone strigolactones. The haustorium formation is induced by derivatives of cell wall lignin; however, the nature of haustorium inducers has not been clearly understood. We are trying to identify novel haustorium inducing compounds.

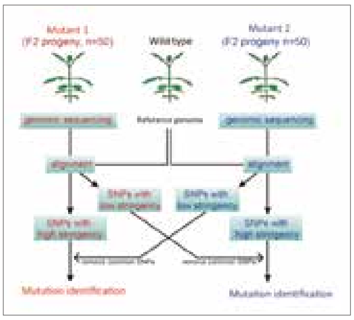

Fig. 3
Identification of the mutant causal genes using a next-generation sequencer

3. Comparative genomics of parasitic plants

Recent progress in next-generation sequencing technology enables us to acquire the complete genome sequence of any plant. We sequenced the whole genomes of *Striga* and *P. japonicum*. By examining these genome sequences, we found that parasitic plants have experienced evolutional events such as expansion of specific gene family and horizontal gene transfers from hosts. How did the plants obtain new genes, increase the copy numbers and eventually acquire a new trait? What is the genetic diversity among *Striga* species in Africa? We analyze genome evolution using bioinformatics tools.

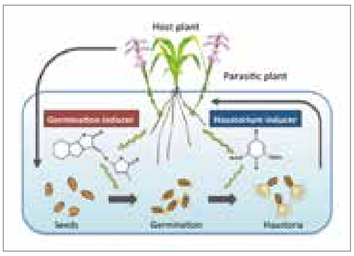

Fig. 4
Chemical communication between host and parasitic plants

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Molecular Signal Transduction



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Outline of Research and Education

Signal transduction is indispensable for organ development and homeostasis. Hormones and neurotransmitters induce a variety of cell responses mediated through membrane receptors and intracellular signaling pathways. Impairment of the signal transduction often causes disease. And with this, many drugs targeting these signal components are widely used today. Our laboratory is interested in cellular signaling systems with special emphasis on heterotrimeric G proteins. In our laboratory, faculty and graduate students are dedicated to cutting-edge scientific research and work towards a better understanding of how the human body functions and the alleviation of human disease.

Major Research Topics

1. Cellular functions and regulatory mechanisms of G protein signaling
2. Monoclonal antibodies against orphan adhesion GPCRs involved in tumorigenesis and neural function
3. Role of adhesion GPCRs in breast cancer
4. Formation and function of primary cilia

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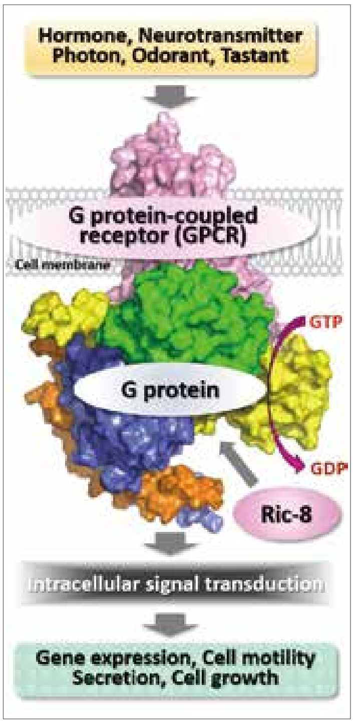

Fig. 1
Signal transduction mediated by G protein-coupled receptor

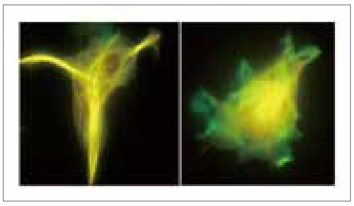

Fig. 2
G protein/PKA signal-regulated dynamics of a cytoskeleton in neuronal progenitor cells

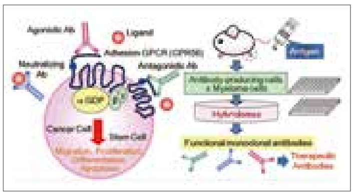

Fig. 3
Monoclonal antibody against orphan GPCR as a tool for signal analysis

Functional Genomics and Medicine


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Outline of Research and Education

In 1991 at Kyoto University, Ishida et al. discovered a novel gene in a project for the elucidation of the molecular mechanisms involved in the self-nonself discrimination by the immune system, and named it programmed death-1 (PD-1), hoping that it somehow plays a pivotal role when self-reactive (harmful) T lymphocytes (T cells) commit suicide by undergoing apoptosis. PD-1 is a type I transmembrane protein expressed on T cells that are activated by antigenic stimulation. Initially, the physiological function of PD-1 was elusive, but it was shown later that PD-1 downregulates excessive immune reactions. Recently, T. Honjo et al. (Kyoto Univ.) discovered that the cytotoxicity of T cells against some cancer cells can be induced by the antibody-mediated blockade of the above physiological function of PD-1. This anti-cancer strategy is now being widely performed in clinics of many countries, and the Nobel Prize 2018 in physiology and medicine was awarded to T. Honjo (and J.P. Allison). Unfortunately, however, the roles of PD-1 in self-nonself discrimination by the immune system still remain elusive. We conduct our research in the fields of immunology and molecular genetics to identify these roles.

Major Research Topics

1. Elucidation of the real physiological functions of PD-1

It is very strange that we can cure cancer by blocking the physiological functions of PD-1. What is then PD-1 doing in our body? Is PD-1 on our side (protecting us) or on the side of cancer cells (protecting them)? People believe that PD-1 is a negative regulator of the immune responses, but what kind of signals in the immune system is PD-1 suppressing? (Obviously, PD-1 is not an omnipotent negative regulator in the immune system) To answer these questions, we perform experiments in immunology and molecular biology by using a variety of genetically modified animals (including PD-1 knockouts).

2. Development of novel strategies in cancer immunotherapy

Cancer immunotherapy based on the blockade of the physiological functions of PD-1 is effective only upon a limited number of cancer patients. For instance, only about 20% of lung-cancer patients and only about 30% of melanoma patients show good responses to such a PD-1-blocking strategy. We try to improve this low efficacy of current cancer immunotherapy by creating a variety of “oncolytic” recombinant retroviruses.

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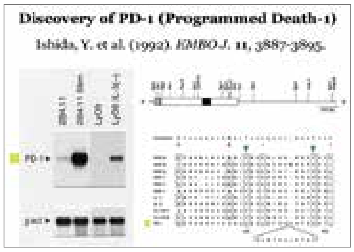

Fig. 1
Some people say that PD-1 was discovered only by chance.

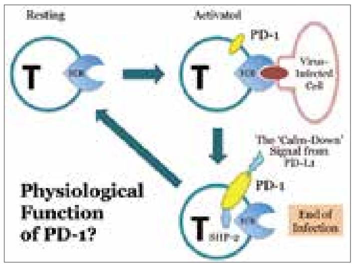

Fig. 2
PD-1 negatively regulates excessive immune reactions.

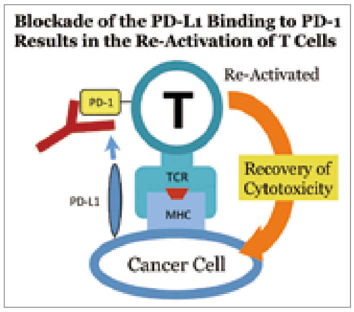

Fig. 3
Cancer immunotherapy using the anti-PD-1 blocking antibody.

Tumor Cell Biology


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Outline of Research and Education

We focus on the molecular mechanisms controlling proliferation, differentiation, and death of mammalian cells, and study the connection between cell cycle progression and oncogenesis, as well as differentiation, proliferation, and leukemogenesis in hematopoietic cells. These findings can be applied to regenerative medicine and cancer research. We use the following experimental systems:

- in vitro culture systems using mouse and human cell lines
- in vitro differentiation systems using ES cells and primary cultures
- mouse model systems using knockout and transgenic mice

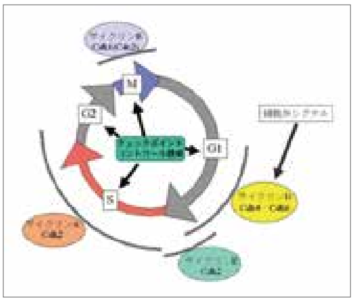

Fig. 1
Cell cycle and cyclin/Cdk complexes

Major Research Topics

1. Cell cycle control and oncogenesis

- Cell cycle control and oncogenesis: During the cell cycle, whether cells should proliferate or stop growing and prepare for differentiation is decided at the G1 phase. Therefore, we investigate the function of molecules that promote or inhibit the progression of the G1 phase such as cyclins, Cdks, Cdk inhibitors, and Rb tumor suppressor gene products (Fig. 1).
- Checkpoint control: The checkpoint mechanism is a means of monitoring and controlling the progression of the cell cycle. The central role in this checkpoint mechanism is played by the tumor suppressor gene product, p53. Recently, members of the p53 gene family, p63 and p73, have been identified. We are interested in the role of these molecules not only in oncogenesis, but also in the developmental program including morphogenesis (Fig. 1).
- Cancer and the cell cycle: Since cancer cells grow abnormally, they generally have abnormalities in the cell cycle control. We analyze the key molecules involved in cell proliferation, G1 regulation, and checkpoint control, and investigate the mechanisms involved in the abnormal growth of cells and cellular oncogenesis.

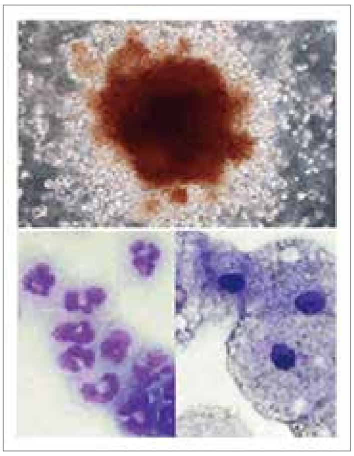

Fig. 2
A group of erythrocytes and leukocytes (upper), neutrophils (lower left) and macrophages (lower right), which were induced to differentiate from ES cells in vitro

2. Leukemogenesis

We investigate the molecular mechanisms underlying leukemogenesis, focusing on AML (acute myeloid leukaemia), MDS (myelodysplastic syndromes), and CML (chronic myeloid leukaemia).

3. Hematopoietic stem cells

We perform studies on hematopoietic stem cells present in the bone marrow, with the aim of developing in vitro amplification methods for hematopoietic stem cells. The results of these studies can be of benefit to regenerative medicine as well as leukemia research.

Fig. 3
A chimeric mouse generated by infusion of genetically modified ES cells

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Molecular Immunobiology



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Outline of Research and Education

Our body has an immune system to fight against microbial pathogens such as viruses, bacteria, and parasites. There are two arms of the immune system; innate and adaptive immunity. The innate immune system is the first line of host defense that detects invading microbial pathogens and plays a critical role in triggering inflammatory responses as well as shaping adaptive immune responses. In spite of its role in host defense, aberrant activation of innate immune responses is closely associated with exacerbation of inflammatory diseases, autoimmune diseases and cancer. Our aim is to uncover molecular mechanisms that control innate immune responses using tools of molecular and cell biology, bioinformatics and genetically modified mice, and seek a way to control immune diseases.

Major Research Topics

1. Analysis of innate immune signaling pathways

The innate immune system employs germline-encoded pattern-recognition receptors (PRRs) for the initial detection of microbes. PRRs distinguish self from non-self by recognizing microbe-specific molecular signatures known as pathogen-associated molecular patterns (PAMPs), and activate downstream signaling pathways that lead to the induction of innate immune responses by producing inflammatory cytokines, type I interferon (IFN) and other mediators. Mammals have several distinct classes of PRRs including Toll-like receptors (TLRs), RIG-I-like receptors (RLRs), Nod-like receptors (NLRs), AIM2-like receptors (ALRs), C-type lectin receptors (CLRs) and intracellular DNA sensors. Among these, TLRs were the first to be identified, and are the best characterized. The TLR family comprises 13 members, which recognize distinct or overlapping PAMPs such as lipid, lipoprotein, protein and nucleic acid (Fig. 1). We are focusing on the recognition mechanism of microbial components by PRRs and their signaling pathways, and understanding their roles in immune responses.

2. Analysis of RLRs

RLRs such as RIG-I and MDA5 are cytoplasmic RNA helicases that detect infection of RNA viruses. Upon detection of RNA virus, RLRs trigger intracellular signaling pathways by recruiting a mitochondria-localized adapter IPS-1, which further activates the transcription factors NF-kB and IRF3 that control expression of antiviral genes, including IFN and inflammatory cytokines (Fig. 2). We seek to understand molecular mechanisms underlying RLRs-mediated antiviral innate immune responses.

3. Analysis of sensing mechanisms of endogenous molecules by PRRs (Fig. 3)

Recent evidence has shown that innate immunity can react with endogenous molecules derived from necrotic cell death and this reaction is associated with inflammatory diseases. In addition, innate immunity also senses environmental factors such as asbestos and pollen, and causes cancer and allergic responses, respectively. We are seeking the recognition mechanisms of these molecules by innate immunity and its role in diseases.

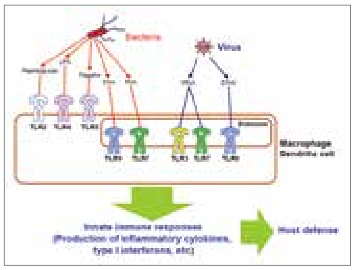

Fig. 1
Recognition of microbial components by Toll-like receptors (TLRs)

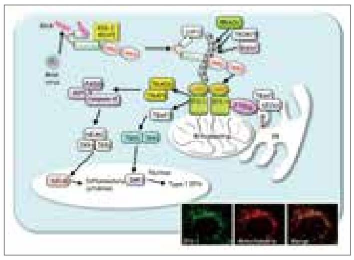

Fig. 2
Signaling pathways through RLRs, cytosolic sensors for RNA viruses

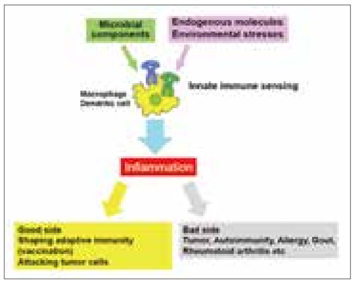

Fig. 3
Recognition of non-infection agents by innate immunity and its relevant in diseases

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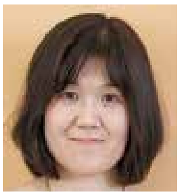
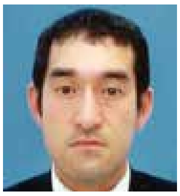
Molecular Medicine and Cell Biology

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Outline of Research and Education

The cellular membrane is the essential component of cells that distinguishes the inside and the outside of cells. While the membrane receives all of the stimulus affecting the cells, how it behaves is not well understood. Our lab focuses on the membrane-binding proteins connecting the membrane to the intracellular signaling for varieties of cellular functions including proliferation and morphological changes, using biochemical, cell biological, biophysical, and information techniques. The roles of lipid composition of the membrane, including the saturation or unsaturation of fatty acids, are examined using the membrane-binding proteins.

Major Research Topics

1. Elucidating cell-shape dependent intracellular signaling

The intracellular signaling cascade became understood by observing molecule-molecule interactions. However, the spatial organization of these signaling cascades had not been well studied. We found the BAR domain superfamily proteins that remodel membrane shape and then, presumably, dictate the intracellular signaling cascades. Thus, the important questions are how the BAR domain superfamily proteins are regulated, and how they assemble the downstream molecules.

2. Searching for new membrane binding proteins

Given the importance of membrane lipids as essential components of cells, we suppose there are many lipid-binding molecules that have not been clarified. We are searching for novel lipid-binding proteins using a variety of methods.

3. The importance of fatty acids in the membrane

Another point for understanding the cellular membrane is the importance of fatty-acid tails of lipids. Although the importance of saturated or unsaturated lipids in nutrients is well-known, the mechanism behind this importance is not understood at molecular levels in cell biology. We examine how fatty acids are important in intracellular signaling including that for cancer, using the proteins listed above.

4. Information science for cell biology

Image analysis using deep learning enables the recognition of the features stipulated by researchers. Such image analysis will reveal previously unrecognized features of protein localization for cellular morphology and will relate the cell morphology to cellular functions.

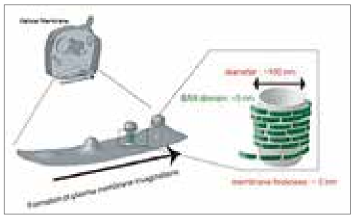

Fig. 1
Location of BAR domain functions in cells. The BAR domains function as polymers at submicron-scale invaginations, such as clathrin-coated pits and caveolae, as well as in protru-sions, including filopodia and lamel-lipodia. The typical scales for clathrin-coated pits and caveolae are 100-200 nm and 50-100 nm in diameter, respectively. The BAR domains have typically been approximated as arcs of 20-25 nm in length with a diameter of 3-6 nm. The membrane thickness is typically approximately 5 nm.

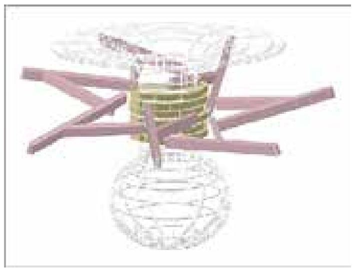

Fig. 2
Wire-frame model of the clathrin-coated pit. The BAR proteins are shown in yellow, and the actin cytoskeleton is shown in magenta. The membrane is in wire-frame. The actin filaments are thought to be finely organized on the nano-scale membrane invaginations of the clathrin-coated pits.

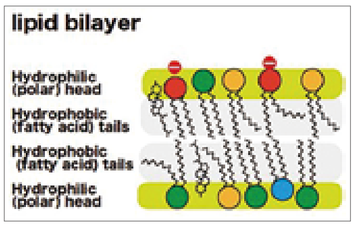

Fig. 3
Schematic diagram of the cellular membrane. Each lipid molecule con-sists of one hydrophilic head and two hydrophobic fatty-acid tails. There are varieties of combinations of the head, such as serine, ethanolamine, etc., and various saturated and unsaturated fatty acids, such as palmitic acid (saturated), oleic acid (monounsaturated), etc.

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RNA Molecular Medicine


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Outline of Research and Education

Advances in genomics technologies have transformed research and development strategies in biology and biomedicine, allowing us to access genetic information encoded in our DNA (Fig. 1). Our laboratory is interested in understanding how individual genes form large regulatory networks to control biological processes. In particular, we study how regulatory non-coding RNAs including microRNAs (miRNAs) contribute to gene regulation and how their misregulation leads to human health problems.

Research in our laboratory relies on a combination of traditional and modern techniques including biochemistry, genetics and computational biology. Students are expected to learn how to carefully interpret analysis results and develop strategies to answer biological questions by utilizing existing technologies or devising new techniques.

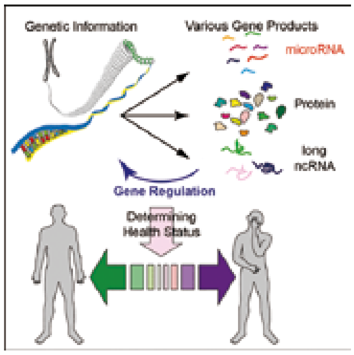

Fig. 1
Gene regulatory networks and their importance in normal development and physiology

Major Research Topics

1. How is expression of miRNAs controlled?

We have witnessed a paradigm shift in the research of gene regulation, and the importance of post-transcriptional regulation of protein-coding genes has now been broadly recognized. Expression of miRNAs should also be regulated at multiple levels (Fig. 2). Precise regulation of miRNA levels is important because misregulation of miRNAs often results in human disease. We study how miRNA levels are controlled under healthy and diseased conditions using genomic and biochemical techniques, and examine their biological significance at the cellular and organismal levels (Fig. 3).

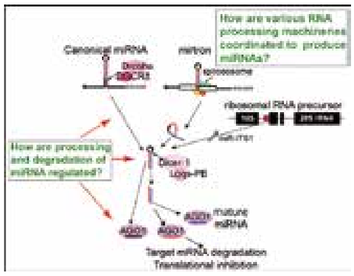

Fig. 2
microRNA processing pathway

2. Why are there many ways to produce miRNAs?

We discovered novel mechanisms of miRNA processing that use machineries known to produce other RNA families, such as mRNA introns and ribosomal RNAs (Fig. 2). This means that RNA processing machineries often have unexpected roles in gene regulation. We study the biological significance of non-canonical roles of various RNA processing pathways.

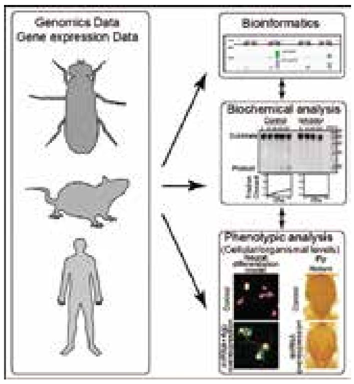

Fig. 3
Outline of research strategies

3. How have small RNA pathways changed in evolution?

Our previous studies revealed a variety of small RNA pathways including those that are only present in particular organisms functioning as natural defense systems (Fig. 2). To capture the full diversity of animal small RNA pathways, we are sequencing small RNAs from various animals by next generation sequencing. Discoveries of new small RNA pathways may pave the way for the development of novel technologies that complement the current CRISPR or RNA interference technologies.

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Stem Cell Technologies



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Outline of Research and Education

Pluripotent stem cells, such as embryonic stem (ES) cells and induced pluripotent stem (iPS) cells, have the abilities of unlimited self-renewal and multiple differentiations into all the tissue cells of the body. Therefore, these stem cells find potential application in regenerative medicine and drug discovery, and it is very important to strictly regulate this potent differentiation ability to induce multi-step differentiation of these stem cells toward functional tissue cells. During mammalian development, cells differentiate to form precise 3D structures of organs. Understanding of this process may contribute to the development of in vitro differentiation methods. Our goal is to understand the mechanisms of stomach and lung development to perform in vitro differentiation of pluripotent stem cells into these tissue cells. Moreover, we plan to develop in vitro disease models of these organs and technologies for regenerative medicine in the near future.

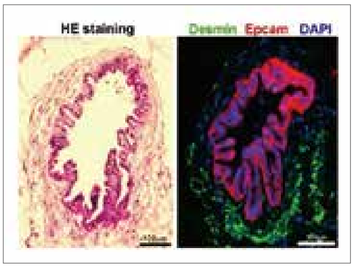

Fig. 1
Stomach tissue differentiated from mouse ES cells *in vitro* by 3D culture method. (Left) HE staining of the differentiated stomach organoid (day 56). (Right) Immunofluorescent staining of stomach organoid with Epcam antibody (red), Desmin anti-body (green), and DAPI (blue) for epidermis, mesenchyme, and nuclei, respectively. Stomach organoid with gastric glands and mesenchyme can be differentiated from ES cells *in vitro*.

Major Research Topics

1. Generation of gastric tissues and their disease models

Although the stomach is a major organ in our body, the mechanisms of its development are not well known. During early development, a primitive gastric tube developed from early endoderm is converted to stomach primordium, and further matures to fundus and antrum tissues covered with gastric glands. Recently, we developed an in vitro differentiation method of mouse ES cells to whole stomach tissue (Fig. 1). We think that this method could be a powerful tool to study the mechanisms of stomach development as well as serve as a unique model for various diseases such as gastric cancer (Fig. 2). We are currently investigating the mechanisms of gastrointestinal development, and studying these mechanisms using our in vitro model.

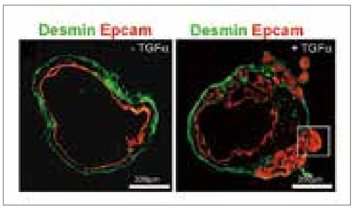

Fig. 2
A stomach disease model using *in vitro* differentiation method. (Left) Healthy control model. (Right) Ménétrier's disease model with massive gastric folds. This disease model can be generated by addition of TGF-α after day 28 of *in vitro* differentiation.

2. Differentiation of lung tissue and tissue regeneration

The lungs emerge as lung buds from the early gastric tube during development. These primordia proliferate, morphologically divide into multiple branches with the mesenchymal layer, and further differentiate into several kinds of epithelial cells to fulfill respiratory functions (Fig. 3). Recently, differentiation methods for these lung tissues have been investigated in the scientific community. We are also studying novel differentiation methods for these respiratory tissues.

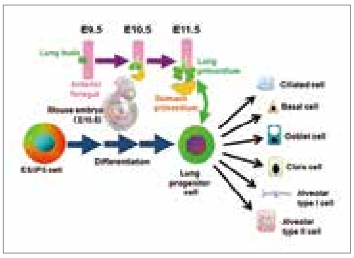

Fig. 3
During lung development, lung progenitor cells are generated in lung buds and can differentiate into various functional epithelial cells of the lung. These lung progenitor cells can be differentiated from pluripotent stem cells *in vitro*.

3. Stem cells in tumors

Patients with pancreatic cancer have a low survival rate because of a lack of early detectable symptoms and poor prognosis. Recent observations suggest the presence of a small number of stem cells in various cancers, which hamper effective cancer therapy. In our laboratory, we study the regulatory mechanisms of these cancer stem cells to decrease their functional potential.

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Developmental Biomedical Science

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Outline of Research and Education

The central nervous system, a critical organ for controlling individuals' body conditions, is comprised of a variety types of neurons, and its generation undergoes a number of regulatory steps mainly at the embryonic stages. We intend to elucidate the molecular mechanisms leading to this complexity by employing chick and mouse embryos, and mouse embryonic stem (ES) cells as experimental systems.

We are also interested in the homeostasis of functional neurons. By using model mice which develop particular inherited retinal diseases, we envisage proposing novel therapeutics for these related dystrophies.

Overall, our research program aims to be influential in cell and developmental biology and will furthermore be both scientifically and technically cross-disciplinary spanning basic biology and biomedical sciences.

Major Research Topics

1. Mechanisms leading to pattern formation and size control of the developing central nervous system

The neural tube is the embryonic tissue of the central nervous system where a number of functional neurons are produced and distributed in a quantitatively and positionally precise manner. This accuracy is mainly achieved by extracellular molecules including BMP, Wnt and Sonic Hedgehog (Shh). These molecules form gradients within the tissue and induce different types of neurons. In addition to the fate assignments, these signal molecules control proliferation of the cells. We are particularly interested in the relationship between cell fate determination and the proliferation of the cells.

2. Homeostasis of postnatal cells

How functional cells are maintained is also an important question. We possess genetically mutated mice that model retinal degeneration. While these mutant mice develop to normal retinal structure, the retina start to degenerate once their eyes open soon after birth. We are seeking the primary mechanisms leading to this retinal degeneration by using high-throughput sequence analysis and try to develop novel therapeutic methods.

In addition, our recent study has suggested that the retinal degeneration coincides with many more dystrophies in other organs. We are therefore aiming to propose further therapeutic methods through systemic analysis of these model mice.

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Fig. 1
A chick embryo incubated for 4 days

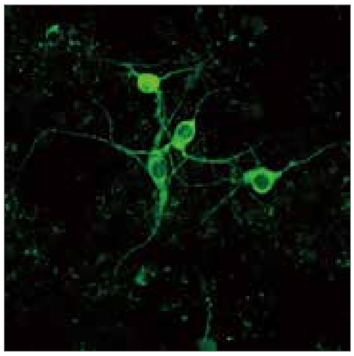

Fig. 2
Dopaminergic neurons cultured in vitro

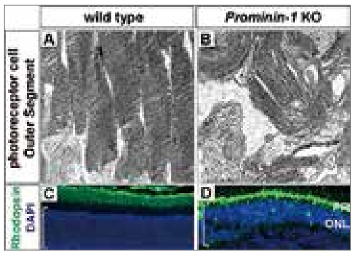

Fig. 3
Eye phenotype in Prominin-1 (Prom1) deficient mice. The outer segments are degenerated (A, B), and Rhodopsin proteins are misplaced in the photoreceptor cells of the Prom1-knockout eyes (C, D)

Organ Developmental Engineering

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Outline of Research and Education

In mammals, until the eight-cell embryo stage, fertilized eggs have totipotency, meaning that each cell can differentiate into all kinds of cell. In blastocyst-stage embryos just before implantation, the cells' fates are divided into the trophectoderm (TE), which will develop into placental tissue, and the inner cell mass (ICM), which has pluripotency in that its cells will develop into three germ layers, including germline cells. Embryonic stem cells (ESCs) were established from ICM, promoting the study of regenerative medicine and led to the discovery of induced pluripotent stem cells (iPSCs). We combine these early embryos, ESCs/iPSCs, and developmental technology with the aim of performing basic studies that will lead to regenerative medicine using animal models.

Major Research Topics

1. Model of organ formation using xenogeneic chimeras

Xenogeneic chimeras containing both mouse and rat cells were generated using blastocysts and ESCs (Figs. 1, 2). When we injected rat ES cells into blastocysts of nu/nu mice lacking a thymus, we could produce a rat thymus in chimeric animals. This indicates the formation of an organ from ES cells in xenogeneic conditions. Although this rat thymus could educate T-cells (Fig. 3), it was smaller than that of a mouse, and the functions of the educated T-cells were unclear. On the other hand, we could detect rat spermatozoa in mouse←rat ES chimeric testes. Rat pups were generated from rat spermatozoa in the xenogeneic chimeric testes by intracytoplasmic injections, and the normal germline potential of rat spermatozoa in the xenogeneic chimeric testes was demonstrated. Findings of the functions of organs, tissues, and cells developed in xenogeneic chimeras are valuable for future translational research.

2. Trials of novel animal models

Gene knockout animals can easily be generated using genome editing systems such as the CRISPR/Cas system. Using the combination of this system and ESCs/iPSCs, complicated gene modification can be performed. We aim to produce novel animal models using these technologies.

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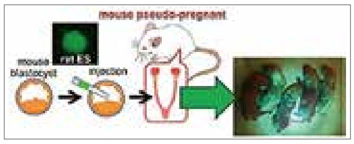

Fig. 1
Production of xenogeneic chimera
GPFP-expressing rat ES cells were in-jected into mouse blastocysts (mouse←rat ES chimera). We could obtain viable mouse←rat ES chimeras upon transplantation into the mouse uterus.

Fig. 2
Two kinds of mouse and rat xenogeneic chimeras
A rat-sized xenogeneic chimera which produced mouse ES cells injected into rat blastocysts (upper). A mouse-sized xenogeneic chimera which produced rat ES cells injected into mouse blastocysts (bottom).

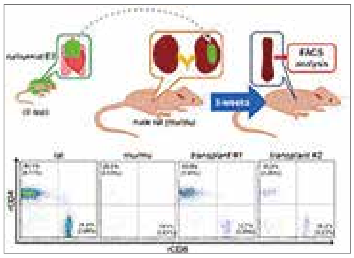

Fig. 3
The function of rat thymus in xenogeneic chimera
When rat thymus from a xenogeneic chimera was transplanted into renal subcutaneous tissues of nu/nu rat, rat T-cells were educated.

Systems Microbiology


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Outline of Research and Education

Escherichia coli is undoubtedly one of the most studied organisms in the world. Vast amounts of accumulated biological knowledge and methodologies make this organism one of the ideal platforms to analyze cells at the system level. Our lab is one of the leading groups performing post-genomic, system and synthetic approaches towards understanding the entire cell system of *E. coli*.

1. Genetic interactions

Normally cell systems can tolerate many kinds of perturbation, e.g. environmental stresses and genetic mutations. In *E. coli*, most single gene knockout strains do not exhibit substantial phenotypic changes. This characteristic is called "robustness" and is caused by the function of a network of compensatory backup systems. This is one of the main reasons why the computational design of a cell system has been unsuccessful so far. Genetic interaction analysis is one of the most powerful and reliable ways to identify and characterize cellular networks. To identify the complex cellular network structure in *E. coli*, we are performing high-throughput systematic genetic interaction studies using double-gene knockout strains as shown in Fig. 1.

2. Novel method for population dynamics by Bar-code strains

To monitor each strain's growth in a bar-coded single gene knockout strain library, named ASKA bar-coded collection. Each mutant has different 20nt DNA sequence as a molecular bar-code. Using a mixed culture of an entire set of knockout strains, we are now performing population analysis during the long-term stationary phase and sub-lethal concentration of antibiotics and determined each of strains behavior during stress conditions by deep-sequencing to elucidate the interaction between cells in the mixed culture as shown in Fig. 2. This new resource will accelerate population analysis in a variety of conditions.

3. Genome size design and cross-species transfer of DNA by conjugation

We have developed a very efficient method to construct double knockout strains using F plasmid based conjugal transfer system. The F (incF) plasmid has a narrow host-range but incP and incW plasmid families have much wider host-ranges. We are expanding our conjugation vector system from the F plasmid system to the incP and incW plasmids to enable the transfer of large DNA molecules from *E. coli* into other microbes. Our long-term goal is to design and construct bacterial genome-size DNA molecules and transfer large size genomes into the target micro-organisms to engineer cells as shown in Fig. 3.

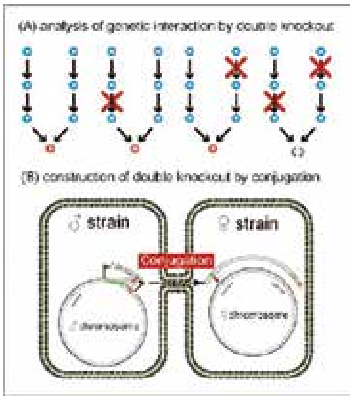

Fig. 1
(A) The concept of synthetic lethal/sickness analysis: Red circles represent essential metabolites for cells. If cells have redundant routes to produce essential metabolites, double deletion methods may identify such redundant steps of genes (enzymes). (B) The conjugation method to generate double knockout strains by combining single knockout strains

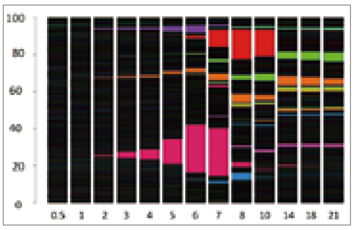

Fig. 2
The X axis shows time points of sampling and the Y axis represents population ration of all deletion strains

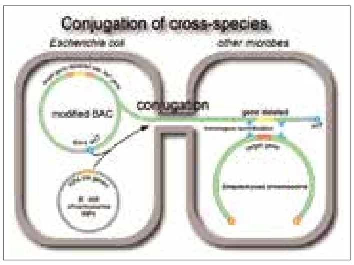

Fig. 3
Wide host-range incP family plasmid RP4 can deliver large DNA fragment by cross-species conjugation

Major Research Topics

1. Genetic interaction networks

2. Quantitative metabolic network analysis

3. Development of artificial chromosome and cross-species transfer systems of huge DNA

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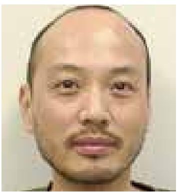
Cell Signaling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Outline of Research and Education

Our research aims to elucidate intracellular signaling networks that sense and transmit diverse extracellular stimuli, with particular focus on the signaling pathways involved in cancerous cell proliferation and metabolic syndromes such as diabetes. To identify and analyze novel components of the signaling pathways, the studies utilize the fission yeast *Schizosaccharomyces pombe*, which has been successfully used as a genetically amenable model system to investigate cellular regulatory mechanisms conserved from yeast to humans. Students in our laboratory are encouraged to design multifaceted approaches that logically combine research tools in molecular genetics, cell biology and biochemistry. Originally established in 1998 at University of California-Davis, our laboratory has been training researchers that serve the international scientific community.

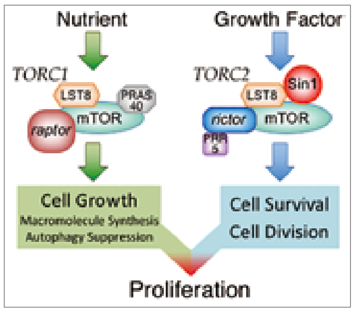

Fig. 1
The TORC1 and TORC2 signaling pathways integrate multiple stimuli to control cell proliferation.

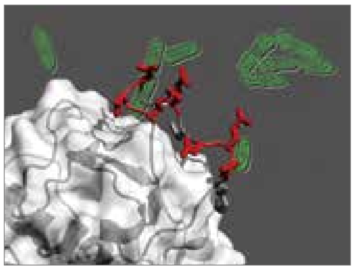

Fig. 2
The structure of the TORC2 subunit Sin1, whose function has been elucidated through genetic analysis in fission yeast (background).

Major Research Topics

1. TOR (Target Of Rapamycin) signaling pathways

TOR kinase forms two distinct protein complexes called TORC1 and TORC2, which mediate extracellular signals, such as nutrients and insulin/growth factors (Fig. 1). Deregulation of the TOR pathways is implicated in cancers, neurological disorders, diabetes and aging; therefore, comprehensive understanding of the TOR pathways is crucial for the development of informed strategies to treat these diseases.

2. Stress-responsive MAP kinase cascade

Stress-activated protein kinase (SAPK) is a member of the MAP kinase family that plays pivotal roles in cellular stress responses, including those of cancer cells exposed to cytotoxic therapies. Our goal is to discover cellular “stress sensors” that transmit signals to induce activation of SAPK.

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Applied Stress Microbiology




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Outline of Research and Education

Our research involves "Applied Molecular Microbiology". Our laboratory aims at basic studies in microbial science, particularly cellular response and adaptation to environmental stresses, and its practical applications in new biotechnology. To understand microbial cell functions, we analyze and improve various mechanisms of microorganisms from molecular, metabolic and cellular aspects. Our novel findings can be applied to the breeding of useful microbes (yeasts, bacteria), the production of valuable compounds (enzymes, amino acids) and the development of promising technologies (bioethanol, etc.).

Major Research Topics

1. Stress response and tolerance in yeast *Saccharomyces cerevisiae* (Figs. 1, 2, 3, 4)

We are interested in cellular response and adaptation to environmental stresses in the yeast Saccharomyces cerevisiae, which is an important microorganism as a model for higher eukaryotes. Yeast is also a useful microbe in the fermentation industry for the production of breads, alcoholic beverages and bioethanol. During fermentation, yeast cells are exposed to various stresses, including ethanol, high temperature, desiccation and osmotic pressure. Such stresses induce protein denaturation, reactive oxygen species generation, and lead to growth inhibition or cell death. In terms of application, stress tolerance is the key for yeast cells. We analyze the novel stress-tolerant mechanisms found in yeast listed below.

- Proline: physiological functions, metabolic regulation, transport mechanisms
- N-Acetyltransferase Mpr1: arginine biosynthesis, antioxidative mechanisms
- Nitric oxide (NO): synthetic mechanism, physiological roles
- Ubiquitin (Ub) system: protein quality control, Ub ligase Rsp5 regulation.

2. Development of industrial yeast based on novel stress-tolerant mechanisms

Through our basic research on novel stress-tolerant mechanisms, we construct industrial yeasts with higher fermentation ability under various stress conditions and contribute to yeast-based industries for the effective production of bread dough and alcoholic beverages, or breakthroughs in bioethanol production.

3. Endoplasmic reticulum (ER) stress and unfolded protein response (UPR)

We are pursuing the molecular mechanism by which ER stress triggers the UPR in yeast cells.

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Stress response and tolerance in yeast *Saccharomyces cerevisiae*

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Development of industrial yeast based on novel stress-tolerant mechanisms

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ER stress and UPR

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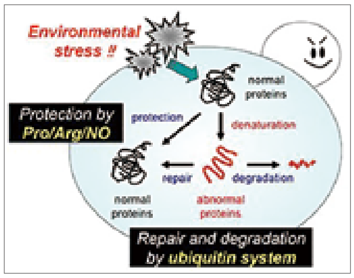

Fig. 1
Novel stress-tolerant mechanisms in *S. cerevisiae*

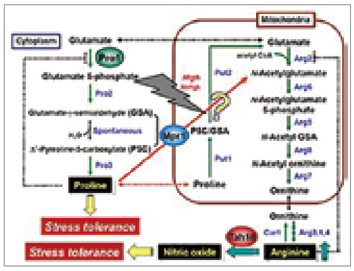

Fig. 2
Metabolic pathway of proline and arginine in *S. cerevisiae*

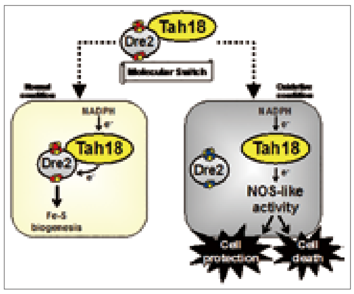

Fig. 3
Model of NO synthesis in *S. cerevisiae*

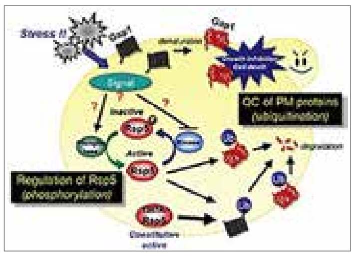

Fig. 4
Ubiquitin system under stress conditions in *S. cerevisiae*

Information Science
Biological Science
Materials Science

Environmental Microbiology

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Outline of Research and Education

Human beings have placed a heavy burden on the environment through modern mass production/consumption of petrochemical products which are not circulable. Microbes live in all environments and are deeply involved in the global homeostasis. Recently, we have discovered a microbe that degrades a plastic which was thought not to be biodegraded. Why do microbes possess such unique abilities? How did they attain them? To answer these questions, we study microbial molecules and assemblies. We believe that our studies will lead to solutions for the sustainable development of society.

Major Research Topics

1. Elucidation of a bacterial PET metabolism

Poly(ethylene terephthalate) (PET) is a material used for plastic bottles and polyester fibers. A bacterium that we discovered named *Ideonella sakaiensis* can degrade and metabolize PET. The fact that this bacterium nutritionally utilizes PET has been revealed through discoveries such as unique PET hydrolyzing enzymes. By unraveling bio-information such as genomes and transcriptomes and using genetic and biochemical methods, we aim to fully understand the molecular mechanisms involved in PET degradation.

2. Visualizing microbiology

Microbial research has been focused on analysis of cells that can be observed with an optical microscope, or molecules that can be followed by their presence such as enzymatic reactions. However, in recent years, it has been found that many microbes secrete much smaller structures than their cells. To open this new microbial world, we are trying to clarify the functions of these nanostructures using electron and super-resolution microscopes.

3. Plastic bioconversion

I. sakaiensis can eat PET. In other words, it has a metabolic system that can degrade and convert PET into energy and cellular components. We are attempting to breed the strains that produce high value compounds from waste PET products by modifying and/or enhancing their metabolism.

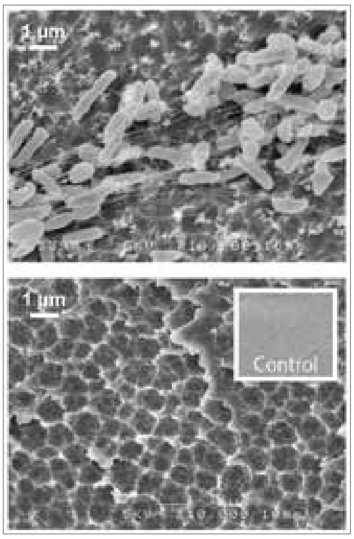

Fig. 1
A scanning electron microscopic image of *I. sakaiensis* cells grown on PET film (upper). The degraded PET film surface after washing out the adherent cells (lower).

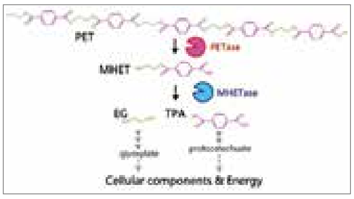

Fig. 2
Predicted PET metabolism by *I. sakaiensis*. Two unique enzymes, PET-ase and MHETase, are able to efficiently convert PET into its monomers.

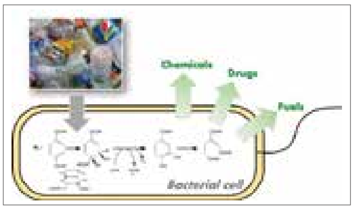

Fig. 3
Metabolic engineering to ferment waste plastic bottles into valued compounds.

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Structural Life Science



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Outline of Research and Education

In the cells, various proteins are involved in a variety of fundamental biological phenomena, especially motion. To understand life, it is crucial to know how these proteins function in the cell. Unfortunately, the molecular mechanisms of most of these proteins are still unclear. To unveil such mechanisms, our laboratory is working on various proteins. In particular, we are focusing on how proteins, small molecules, and ions are transported across membranes and how newly-synthesized proteins are folded into their functional states. This transportation and protein biogenesis are mediated by dedicated proteins including chaperones, proteases, transporters, channels, and translocases (Figs. 1, 2). Some of these membrane proteins can be drug targets. Also, there are proteins which drive the motility of the cell itself. Cilia and flagella are such organelles which are composed of over 600 kinds of proteins. To understand how these proteins work, it is crucial to know their detailed structures. Thus, our laboratory conducts fundamental research through structural biological analyses in combination with other newly developed methods.

The first step of our typical strategy is to elucidate the protein structure at the atomic and amino acid levels (Fig. 3). By obtaining detailed structural information of target proteins, much more insight into how these proteins function can be achieved. This is the greatest advantage of uncovering the details of protein structure. The next step is to reveal proposed molecular mechanisms based on protein's structural information by performing functional analyses. Recently, we are also attempting to visualize protein dynamics by single-molecule analyses. By utilizing several different methods for our research, our results provide new concepts that will change the contents of textbooks.

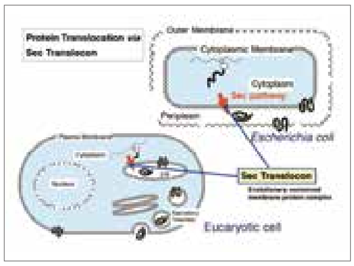

Fig. 1
Conserved protein translocation across the membrane via translocon.

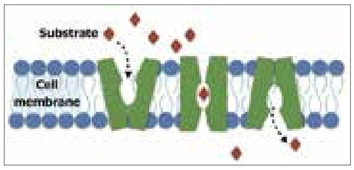

Fig. 2
Membrane transporter

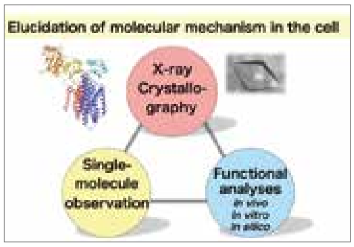

Fig. 3
Outline of our research

Major Research Topics

1. Transportation across cell membranes and protein biogenesis.

2. Molecular function and dynamics of proteins

3. X-ray crystallography and cryo-electron microscopy

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Gene Regulation Research

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Outline of Research and Education

Organisms are composed of various cells arranged in a well-coordinated manner. A fertilized egg repeats cell division and differentiates into the animal body in embryogenesis, in which various phenomena take place in a pre-determined order controlled by the inherent "biological clock" in each living body. We attempt to clarify the principles of animal morphogenesis through investigating the mechanisms of the "biological clock" that controls various life phenomena during embryonic development.

Major Research Topics

Research on somitogenesis in vertebrates as a model system for the biological clock

A mouse's body is composed of a metameric structure along the anteroposterior axis. For example, the spine is made up of the accumulation of multiple vertebrae, each of which is similar in shape. Such metamerism is based on the somite, which is a transient structure in mid-embryogenesis. Somites are symmetrically arranged on both sides of the neural tube as even-grained epithelial spheres that give rise to vertebrae, ribs, muscles and skin.

The primordium of the somite, located at the caudal tip of the mouse embryo, extends posteriorly. The anterior extremity of the somite primordium is pinched off to generate a pair of somites in a two-hour cycle, resulting in the formation of repeats of a similar size structure. On the basis of this finding, it has been considered that there is a biological clock, which determines the two-hour cycle, in the primordium of somites. The expression of several genes oscillates in the primordium of somites, corresponding to the cycle of somite segmentation, which serves as molecular evidence of the biological clock. We are exploring the mechanisms of the biological clock on the basis of such oscillatory gene expression.

Transcription factor Hes7 is specifically expressed in the primordium of somites (Fig. 1) and in a cyclic manner (Fig. 2). Through genetic and biochemical experiments, we have shown that Hes7 is involved as a principal factor in the mechanism for the biological clock that determines the two-hour cycle (Figs. 2, 3). We are conducting studies to understand the biological clock in a comprehensive manner.

Fig. 1
Transcription factor Hes7, serving as a molecular clock, is specifically expressed in the primordium of somites.

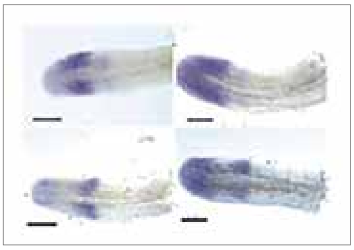

Fig. 2
The expression of Hes7 oscillates in the primordium of somites.

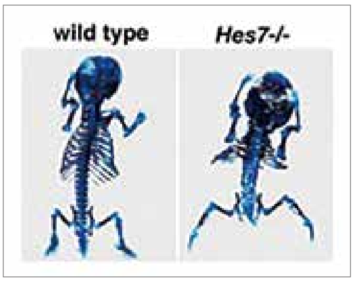

Fig. 3
In Hes7 knockout mice, somite segmentation does not occur cyclically and the metameric structures along the anteroposterior axis are lost.

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Systems Neurobiology and Medicine

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Outline of Research and Education

Neurons extend axons, and form elaborate networks in our brain; all the brain activities depend on neuronal networks. To establish proper neuronal networks, axons decide their migratory route in response to gradients of chemical signals in the brain. In addition to axons, various cells migrate within our body, thereby playing key roles in organ formation, immune responses, wound healing and regeneration. Disruption of axon guidance and cell migration is implicated in diseases, including birth abnormality, neuronal disabilities, immune disorders and cancer metastasis.

Our laboratory focuses on the proteins Shootin1a, Shootin1b and Singar, which we identified by proteome analyses, as well as their interacting proteins, Cortactin, L1-CAM and Rab33. We analyze the molecular mechanisms for axon formation, axon guidance, cell migration, and synaptic plasticity, using up-to-date methods including systems biology and mechanobiology. We also analyze actin waves, which is a new type of protein transport system for cell morphogenesis.

We expect that our studies will help us to understand the mechanisms underlying neuronal morphogenesis as well as the mechanisms underlying diseases including birth abnormality, neuronal disabilities, neuropsychiatric disorders and immune disorders, giving us a new window into therapeutic strategies for nerve injury, Alzheimer's disease, neuropsychiatric disorders and cancer metastasis.

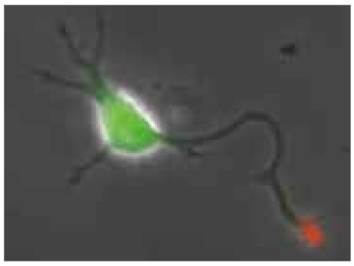

Fig. 1
Shootin1a (red) is a key molecule involved in axon formation and guidance [4, 5, 9, 10, 13, 15].

Fig. 2
Shootin1bb(magenta) is involved in neuronal migration [3, 7].

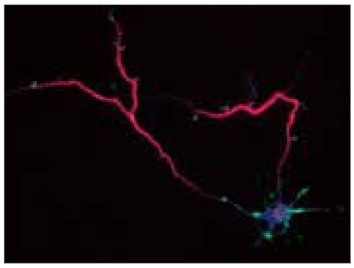

Fig. 3
Singar knockdown leads to formation of surplus axons [14].

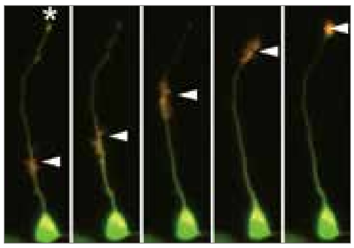

Fig. 4
Actin wave (arrow heads) migrating along an axon [6, 8]

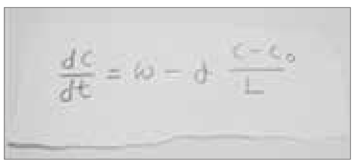

Fig. 5
An equation to describe shootin1a accumulation in axonal tip [12]

Major Research Topics

1. Neuronal network formation: axon guidance and cell migration

2. Synaptic plasticity: learning and memory

3. Actin wave: a novel mechanism for intracellular protein transport

4. Research in medicine: brain diseases and cancer metastasis

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(*Papers related to doctoral thesis)

Computational Biology


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Outline of Research and Education

Our laboratory aims to extract the principle between biological molecules and target biological function and phenotype by computationally analyzing experimental data. We quantitatively associate molecules with function and phenotype to elucidate the underlying mechanism as a set of interactions among various physical quantities. Biological molecules and biochemical interactions actually play an important role in the regulation of biological function and phenotype. Many of functions and phenotypes are expressed in quantities different from molecular concentration, and some of them actively interacting with molecules. In other words, biological system functions as the interactions of multimodal quantities beyond the biochemistry! We aim to understand biological functions and phenotypes as aspects of the multimodal system. To achieve this goal, we collaborate with experimental researchers and analyze experimental data using mathematics and computer programs.

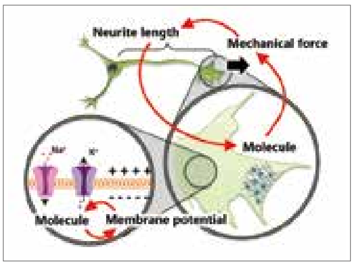

Fig. 1
Examples of system consisting of membrane potential and molecules, and system consisting of neurite length, mechanical force, and molecules. Signal transduction between various quantities are derived from experimental data. System can be reconstructed by integrating these signal transductions.

Major Research Topics

1. Systems biology on cell morphogenesis and migration (Fig.1)

- System between morphogenesis and molecules regulating cytoskeleton formation and mechanical force
- Cell taxis depending on substratum stiffness
- Neuronal axon guidance depending on membrane potential

2. Systems biology on tissue formation (Fig. 2)

- Cell communication and synchronization for development of vertebrates
- Angiogenesis based on cell morphogenesis and migration

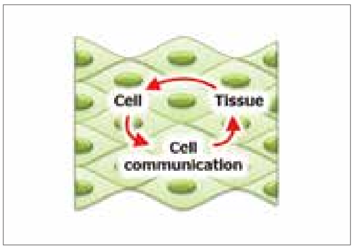

Fig. 2
Tissue formation can be regarded as the system consisting of cell, cell communication, and tissue itself. We aim to understand tissue formation as an aspect of such multimodal system.

3. Estimation of essential components by machine learning and control theory (Fig. 3)

- Molecular system identification using membrane potential time series and single-cell time series of nutrition response
- Computer-assisted diagnosis using human breath gas
- Estimation of essential kinases using inhibitor compounds
- Frequency response analysis of single-cell response data with system identification method
- Quantification of information transmission of signal transduction with Shannon theoretical approach

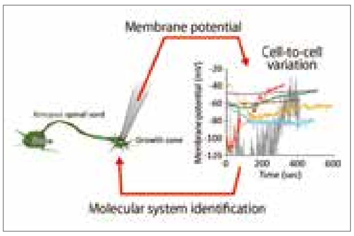

Fig. 3
Identification of molecular system from membrane potential time series. Measuring membrane potential is relatively easier than observing molecular interaction. Computation enables us to estimate intracellular molecular system from membrane potential.

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Molecular Microbiology and Genetics
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Outline of Research and Education

Global warming resulting from elevated CO_2 and global energy supply problems have been in the limelight in recent years. As these problems originate from rapid economic expansion and regional instability in parts of the world, broad knowledge of global economic systems as well as R&D is necessary to solve these problems. Fundamental research employing microbial functions to tackle the adverse effects of global climate change and mitigate energy supply problems is carried out in our laboratory.

Major Research Topics

1. Biorefinery

A biorefinery is the concept of production of chemicals and fuels from renewable biomass via biological processes. Biorefinery R&D is considered of national strategic importance in the U.S.A. (Fig. 1). A biorefinery can be divided into two processes: a saccharification process to hydrolyze biomass to sugars, and a bioconversion process to produce chemicals and fuels from the sugars. Based on a novel concept, we have pioneered a highly-efficient "growth-arrested bioprocess" as bioconversion technology to produce chemicals and fuels (Fig. 2). It is based on Corynebacteria that are widely used in industrial amino acid production. The key to high efficiency is the productivity of artificially growth-arrested microbial cells, cells with which we evaluate production of organic acids and biofuels. To efficiently produce these products, the cells are tailored for the production of a particular product using post genome technologies like transcriptomics, proteomics and metabolome analyses (Fig. 3).

2. Bioenergy and green chemicals production

Having established the fundamental technology to produce bioethanol from non-food biomass, we are now partnering with the automobile and petrochemical industries to explore commercial applications. We have also developed the platform technology to produce biobutanol, the expected next-generation biofuel, as well as a variety of green chemicals such as organic acids, alcohols and aromatic compounds from which diverse polymer raw materials used in various industries are produced.

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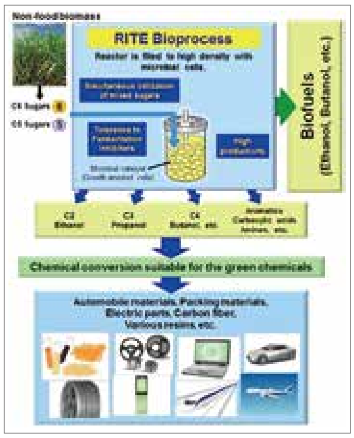


Fig. 1
The biorefinery concept

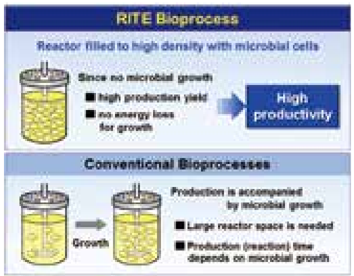


Fig. 2
Novel features of the RITE Bioprocess

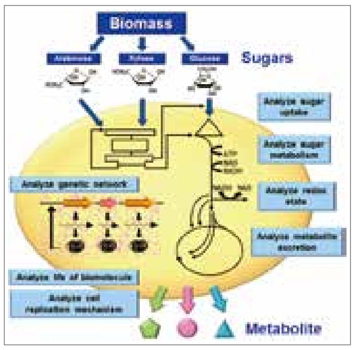


Fig. 3
Breeding of recombinant strains using system biology

Abundant Research Facilities

Each division is equipped with a variety of state-of-the-art equipment.
Shared equipment, among the most advanced available for biological science research in Japan, is provided at numerous locations within the division.

Transmission Electron Microscope

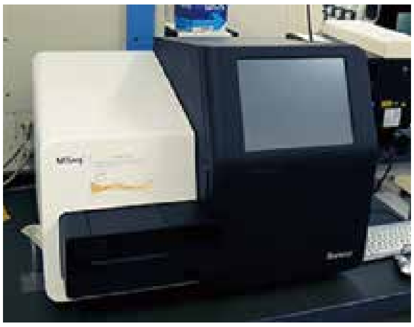
Scanning Electron Microscope

Confocal Laser Scanning Microscope

Light Sheet Fluorescence Microscope

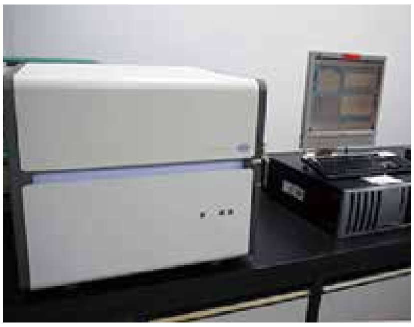
High Resolution Fluorescence Microscopy Imaging System

Flow Cytometer



Next Generation Sequencer

DNA Sequencer



Real-Time PCR System

Triple Quadrupole Mass Spectrometer

Protein Sequencer

Micro Focus X-Ray CT System

Cell Preservation Containers

Botanical Greenhouses

Animal Experimentation Facility

Radioisotope Facility

Materials Science Laboratories

Information Science

Biological Science

Materials Science

List of Laboratories

Physics Laboratories	Professor	Associate Professor	Assistant Professor	Page
Quantum Materials Science	Hisao Yanagi	Hiroyuki Katsuki	Atsushi Yamashita, Hitoshi Mizuno	79
Bio-process Engineering	Yoichiroh Hosokawa	Yalikun Yaxiaer	Ryohei Yasukuni, Sohei Yamada	80
Surface and Material Physics	Tomohiro Matsushita	Ken Hattori	Sakura Takeda	81
Nanostructure Magnetism		Nobuyoshi Hosoito	Takanobu Jujo	82

Device Laboratories	Professor	Associate Professor	Assistant Professor	Page
Photonic Device Science	Jun Ohta	Kiyotaka Sasagawa	Makito Haruta, Hironari Takehara	83
Information Device Science	Yukiharu Uraoka	Yasuaki Ishikawa	Mutsunori Uenuma, Mami Fujii, Juan Paolo Bermundo	84
Sensing Devices	Takayuki Yanagida	Noriaki Kawaguchi	Takumi Kato, Daisuke Nakauchi	85
Organic Electronics	Masakazu Nakamura	Hiroaki Benten	Hirotaka Kojima, Jung Min-Cherl	86
Mesoscopic Materials Science (with Panasonic Corporation)	Eiji Fujii, Hideaki Adachi	Tetsuya Asano		87
Sensory Materials and Devices (with Shimadzu Corporation)	Keishi Kitamura, Masaki Kanai	Shigeyoshi Horiike		88

Chemistry Laboratories	Professor	Associate Professor	Assistant Professor	Page
Synthetic Organic Chemistry		Tsumoru Morimoto	Hiroki Tanimoto	89
Photonic Molecular Science	Tsuyoshi Kawai	Takuya Nakashima	Yoshiyuki Nonoguchi, Mihoko Yamada	90
Photofunctional Organic Chemistry	Hiroko Yamada	Naoki Aratani	Hironobu Hayashi, Kyohei Matsuo	91
Functional Polymer Science (with Santen Pharmaceutical Co., Ltd.)	Takahiro Honda, Komei Okabe	Kazuhiro Kudo		92
Ecomaterial Science (with Research Institute of Innovative Technology for the Earth)	Katsunori Yogo, Kazuya Goto	Hidetaka Yamada		93
Advanced Functional Materials (with Osaka Research Institute of Industrial Science and Technology)	Yasuyuki Agari, Masanari Takahashi	Joji Kadota		94

Biomaterial Laboratories	Professor	Associate Professor	Assistant Professor	Page
Supramolecular Science	Shun Hirota	Takashi Matsuo	Satoshi Nagao, Masaru Yamanaka	95
Complex Molecular Systems	Hironari Kamikubo	Sachiko Toma	Yoichi Yamazaki, Yugo Hayashi	96
Biomimetic and Technomimetic Molecular Science	Gwénaël Rapenne	Kazuma Yasuhara	Toshio Nishino, Kenichiro Omoto	97
Nanomaterials and Polymer Chemistry	Hiroharu Ajiro	Tsuyoshi Ando	Nalinthip Chanthaset, Hiroaki Yoshida	98

Data Science Laboratories	Professor	Associate Professor	Assistant Professor	Page
Data-driven Chemistry	Kimito Funatsu	Tomoyuki Miyao	Swarit Jasial	99
Materials Informatics		Miho Hatanaka		100

Quantum Materials Science

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Education and Research Activities in the Laboratory

Electrons, when confined in a nanometer-sized space (1 nanometer = 10^{-9} m), remarkably begin to behave like waves. For example, an organic molecule can be considered as a quantum state in which electrons are confined in a nm space consisting of atoms connected together. Semiconductor nanoparticles show colors different from those of bulk solids due to this quantum size effect.

The Quantum Materials Science Laboratory studies molecules, crystals, nanoparticles, and ultrathin films of both organic and inorganic materials, utilizes various optics-based experimental approaches to clarify material properties from the viewpoint of quantum physics, and aims to create new functional materials that will be used in optical information-communication or environment-conscious devices in the future.

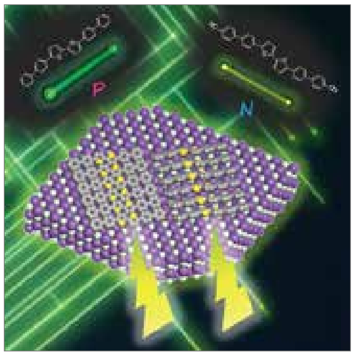

Fig. 1
A molecular crystal-based organic laser

Research Themes

1. Molecular electronics and photonics

By controlling molecular alignment and crystal growth, we develop efficient light-emitting materials such as nanowires, microrings and microdots specifically aiming to realize organic lasers.

2. Coherent control in various quantum systems

Using ultrafast lasers, we are attempting to observe and control quantum coherence in various quantum systems, such as polaritons in a microcavity, ro-vibrational states in solid para-H_2, and coherent phonons in organic crystals.

3. Photo-physical properties of nanostructured materials

We are working on optical functionality of nanostructured materials such as environment-conscious nanoparticles and impurity-doped nanoparticles.

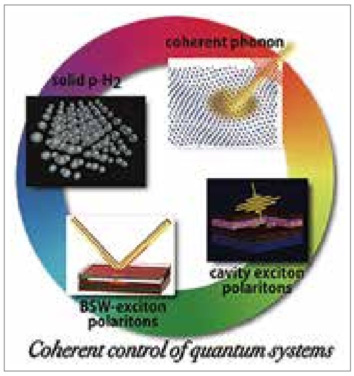

Fig. 2
Targets of coherent control

Fig. 3
Luminescence from impurity-doped semiconductor nanoparticles

Recent Research Papers and Achievements

1. H. Yanagi, F. Sasaki, and K. Yamashita, *Adv. Opt. Mater*. **7**, 1900136 (2019).
2. N. Kurahashi, V.-C. Nguyen, F. Sasaki, and H. Yanagi, *Appl. Phys. Lett*. **113**, 011107 (2018).
3. H. Katsuki, N. Takei, C. Sommer, and K. Ohmori, *Acc. Chem. Res*. **51**, 1174 (2018).
4. H. Katsuki, K. Ohmori, T. Horie, H. Yanagi, and K. Ohmori, *Phys. Rev. B* **92**, 094511 (2015).
5. A. Ishizumi, S. Fujita, and H. Yanagi, *Opt. Mater.* **33**, 1116 (2011).
6. H. Mizuno, K. Nagano, S. Tomita, H. Yanagi, and I. Hiromitsu, *Thin Solid Films* **654**, 69 (2018).

Bio-process Engineering




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Education and Research Activities in the Laboratory

The Bio-process Engineering Laboratory promotes developmental research of high-precision and fast manipulation methodologies for small biological materials, utilizing ultra-short pulse laser technology. When an intense femtosecond laser is focused in the vicinity of a micro-sized biological micro-object in a water medium, an explosion of water is induced at the laser focal point, and shock and stress waves from the explosion act as an impulsive force on the sample (Fig. 1).

We have developed several methodologies to manipulate single animal and plant cells utilizing this impulsive force. In addition, this laser manipulation technology has been combined with atomic force microscopes (AFM), microfluidic chip devices, and spectroscopy devices. The AFM is applied to quantify impulsive force and to analyze the sample oscillation induced by that force (Fig. 2). Microfluidic chip devices fabricated by MEMS technology realize sequential high-speed laser manipulation of biological micro-objects (Fig. 3). Spectroscopy devices are used to identify characteristics of objects manipulated by laser and/or microfluidic chip. Using these techniques, we successfully estimated the adhesion strength between mammalian cells (Ref. 5) and between sub-organelles in plant cells (Ref. 3). Furthermore, we apply such femtosecond laser-induced strong excitation phenomena to photoporation for living vertebrate embryos (Ref. 4) and alga (Ref. 1, Fig. 4). We successfully manipulated cells at 100,000/s (World Class) (Ref. 2). These activities and devices aim to open up entirely new areas of life and green innovation. The laboratory fosters human resources with a broad knowledge of engineering and science from areas ranging from physics and chemistry to biology and medicine. Laboratory members are ambitious to pursue a blazing trail in life science and engineering fields.

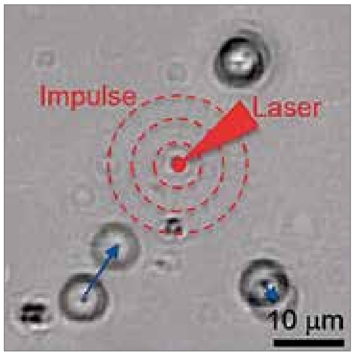

Fig. 1
Manipulation of microbeads by laser impulse

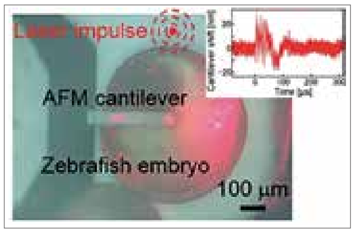

Fig. 2
Nanometer scale vibration of Zebrafish embryo induced by laser impulse and detected by AFM

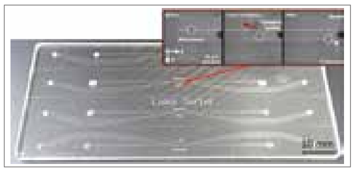

Fig. 3
High-speed laser manipulation in microfluidic chips.

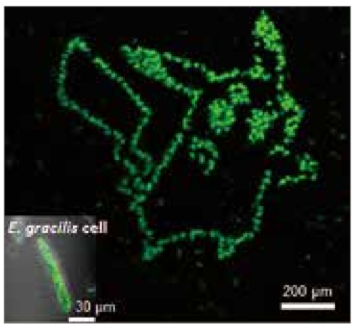

Fig. 4
Laser scanning photoporation of fluoresce probe molecules at single cell resolution

Research Themes

1. Kinetics of local explosions in water induced by ultrashort laser pulses, and its interaction with biological micro-objects
2. Development of new measurement methods to estimate internal stress in living tissues utilizing ultrashort lasers and atomic force microscopes
3. Development of new cell manipulation techniques in microfluidic chips
4. Exploration of the responsiveness of cells and living tissues to the environment stress and its application to cell manipulation

Recent Research Papers and Achievements

1. T. Maeno, T. Uzawa, I. Kono, K. Okano, T. Iino, K. Fukita, Y. Oshikawa, T. Ogawa, O. Iwata, T. Ito, K. Suzuki, K. Goda, Y. Hosokawa, “Targeted delivery of fluorogenic peptide aptamers into live microalgae by femtosecond laser photoporation at single-cell resolution,” Sci. Rep., 2018, 8, 8271.
2. T. Iino, K. Okano, S.W. Lee, T. Yamakawa, H. Hagihara, Z.Y. Hong, T. Maeno, Y. Kasai, S. Sakuma, T. Hayakawa, F. Arai, Y. Ozeki, K. Godab, and Y. Hosokawa, “High-speed microparticle isolation unlimited by Poisson statistics,” Lab Chip, 2019,19, 2669-2677.
3. K. Oikawa, S. Matsunaga, S. Mano, M. Kondo, K. Yamada, M. Hayashi, T. Kagawa, A. Kadota, W. Sakamoto, S. Higashi, M. Watanabe, T. Mitsui, A. Shigemasa, T. Iino, Y. Hosokawa, M. Nishimura, “Physical interaction between peroxisomes and chloroplasts elucidated by in situ laser analysis,” Nature Plants, 2015, 1, 15035.
4. Y. Hosokawa, H. Ochi, T. Iino, A. Hiraoka, M. Tanaka, “Photoporation of biomolecules into single cells in living vertebrate embryos induced by a femtosecond laser amplifier,” PLoS ONE, 2011, 6, e27677.
5. Y. Hosokawa, M. Hagiyama, T. Iino, Y. Murakami, A. Ito, “Noncontact estimation of intercellular breaking force using a femto-second laser impulse quantified by atomic force microscopy,” Proc. Nat’l Acad. Sci. USA, 2011, 108, 1777-1782.

Surface and Material Physics



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Education and Research Activities in the Laboratory

1. Research purpose and target

Functional materials are created by adding dopant atoms to the material or depositing atoms on the surface. The added atoms in bulk work as active sites and dramatically change the material's properties. Also slightly deposited atoms on surfaces can change structures and functionalities. Visualizing the three-dimensional atomic arrangement and understanding the function generation mechanism will bring about technological innovation. Our laboratory is the first in the world to develop atomic resolution holography (ARH) such as photoelectron holography (PEH) to visualize active sites, and in developing apparatus in SPring-8. Our laboratory studies surface structures, electronic states, optical properties, and chemical reactions using scanning tunneling microscopy (STM), Raman spectroscopy, reflection high-energy electron diffraction (RHEED), low-energy electron diffraction (LEED), angle-resolved photoelectron spectroscopy (ARPES), etc. For data science, we use a combination of scattering quantum mechanics and sparse-modeled machine learning, and density functional theory (DFT). Our aim is to clarify the physical properties of active sites and modified surfaces, while creating new functions from atomic and electron viewpoints. Our research targets include dopants in materials, atomically-controlled nano-films, nano-wires, nano-dots on surfaces, and artificially-strained sub-surfaces.

2. Educational policy

We provide education on experiments and physics combined with informatics. Also, we aim to develop important skills for researchers and professional engineers, which include an active attitude toward obtaining knowledge through acquisition of technical expertise (such as shop practices, machine control, and data analysis), cooperation with laboratory members, finding essential points based on logical thinking, presenting ideas, and managing activities. Students are expected to improve or create apparatuses before graduation. It is important for students to not only learn how to think systematically through seminars and lectures, but also to interact with external researchers in addition to the regular laboratory educational staff.

Research Themes

1. Atomic structural analysis of active sites in/on materials by PEH
2. Quantum theory of scattering combined with machine learning theory
3. Reciprocal space mapping (RSM) analysis of 3D-Si surfaces by RHEED
4. Growth of nano-films with surface modification by STM, LEED, RHEED
5. Quantization- and strain-modified electronic structure of crystals by ARPES
6. Raman spectroscopy and cathode luminescence of functional materials

Recent Research Papers and Achievements

1. T. Yokoya, T. Matsushita, *et al.*, Nano Lett. **19**, 5915(2019).
2. K. Hayashi, T. Matsushita, *et al.*, Science Advances **3**, e1700294 (2017).
3. N. Hirota, K. Hattori, *et al.*, Appl. Phys. Express **9**, 047002 (2016).
4. O. Romanyuk, K. Hattori, *et al.*, Phys. Rev. **B 90**, 155305 (2014).
5. S. N. Takeda, *et al.*, Phys. Rev. **B 93**, 125418 (2016).
6. T. Sakata, S. N. Takeda *et al.*, Semicon. Sci. and Technol. **31**, 085012 (2016).

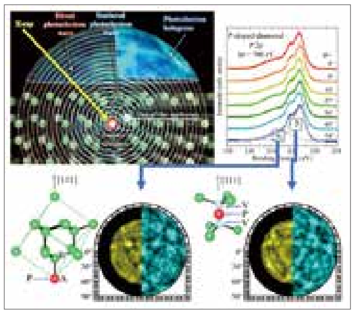

Fig. 1
Atomic structure of P dopants in diamond. [1] α: Substitutional site. β: PV split vacancy complex.

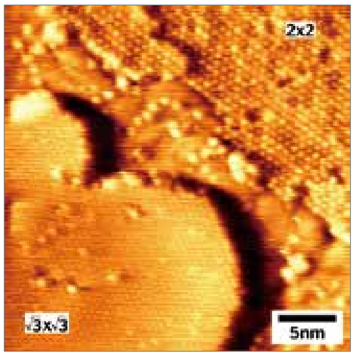

Fig. 2
Atomic-scale STM image of ultra-thin film and island of iron-silicides on a Si(111) surface.

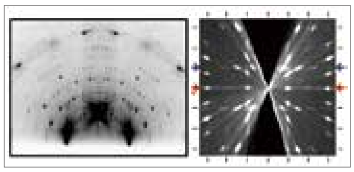

Fig. 3
RHEED pattern of Si(111)7x7 surface, and 3D-RSM of a 3D elongated island of α-$FeSi_2$(110) on Si(001).

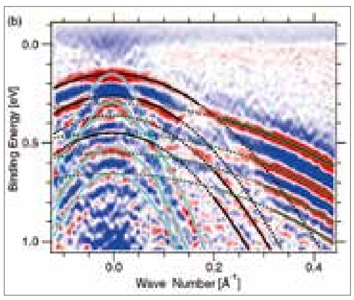

Fig. 4
Si valence subbands in p-type inversion layer.

Information Science
Biological Science
Materials Science

Nanostructure Magnetism


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Education and Research Activities in the Laboratory

In the Nanostructure Magnetism Laboratory, we use vacuum deposition and sputtering methods to produce metallic magnetic thin and multilayer films, and conduct basic research on magnetic phenomena specific to nanostructure thin films and the relationship between the structure of thin films and magnetism. The laboratory is characterized by research on “nanostructure magnetism” with synchrotron radiation X-rays. We are developing an X-ray magnetic scattering technique that enables element-specific magnetic structure analysis through the improvement of measuring methods, sensitivity enhancement and analysis precision.

Magnetic thin films and multilayer films with modulated structures at nanoscale can produce various magnetic structures and magnetization processes because of the effects of magnetic anisotropy in the individual magnetic layers, as well as the direct or indirect exchange coupling between the magnetic layers. Thus, we elucidate element-specific magnetic structures and vector magnetization processes by resonant X-ray magnetic scattering techniques, and reveal the generation mechanism of magnetic functionalities. In spin electronics, which is recently attracting attention, “magnetism in nonmagnetic layers” or “magnetism of conduction electrons” is related to the appearance of functionalities. The resonant X-ray magnetic scattering allows us to study the magnetism in nonmagnetic layers without being affected by the magnetism in ferromagnetic layers. We take advantage of these characteristics to advance our research on conduction electron magnetism.

In our laboratory, based on the specialized knowledge and experimental technology of solid state physics, especially of magnetism obtained from the above studies, we, for educational purposes, cultivate human resources with the ability to discover problems, explore solutions, discuss issues logically, give presentations on research results, and will demonstrate their ability in companies, universities, and research institutions after graduation.

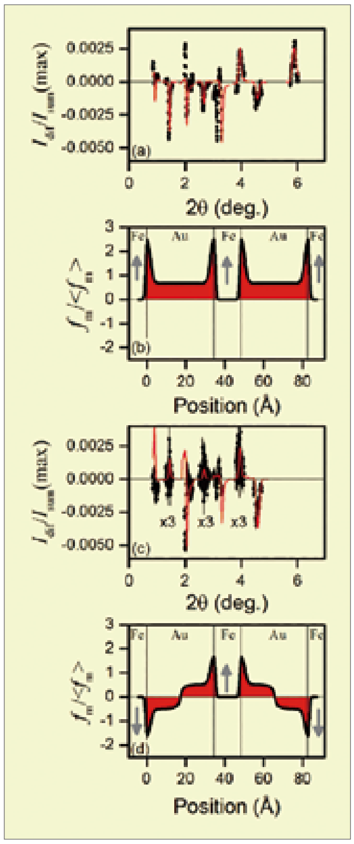

Fig. 1
Resonant X-ray magnetic scattering profiles in (a) parallel and (c) antiparallel states of Fe magnetizations measured near the Au L3 absorption edge, and induced magnetic structures of Au layers in (b) parallel and (d) anti-parallel states of Fe magnetizations.

Research Themes

1. Induced magnetic structures of nonmagnetic layers and their vector magnetization processes in the oscillatory interlayer exchange coupling systems such as Fe/Au and Co/Cu multilayers
2. Interface magnetism in the indirect exchange bias systems such as CoO/Cu/Fe and FeMn/Cu/Co trilayers
3. Induced magnetism of Pt layers in the Fe/Pt multilayers with perpendicular magnetic anisotropy

Recent Research Papers and Achievements

1. M. Lee, R. Takechi, and N. Hosoito, “Perpendicular Magnetic Anisotropy and Induced Magnetic Structures of Pt Layers in the Fe/Pt Multilayers Investigated by Resonant X-ray Magnetic Scattering”, *J. Phys. Soc. Jpn*. **86**, 024706-1-10 (2017).
2. S. Amasaki, M. Tokunaga, K. Sano, K. Fukui, K. Kodama, and N. Hosoito, “Induced Spin Polarization in the Au Layers of Fe/Au Multilayer in an Antiparallel Alignment State of Fe Magnetizations by Resonant X-ray Magnetic Scattering at the Au L3 Absorption Edge ”, *J. Phys. Soc. Jpn*. **84**, 064704-1-8 (2015).

Photonic Device Science




Prof. Jun Ohta

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Education and Research Activities in the Laboratory

1. Laboratory outline

The Photonic Device Science Laboratory researches and develops new optical functionality-based material science and device functions for fast, flexible processing of image information that promises to play a leading role in an advanced information society and a "super aging society." Specifically, we work on applying photonic LSI technology, which integrates semiconductor circuit technology and photonic technology, toward biological and medical field applications as shown in Fig. 1. Our typical research fields include bio-medical photonic LSIs and artificial vision devices.

2. Research activity and policy

With our research subjects crossing over various research fields, we actively pursue cooperative interdisciplinary studies. For example, we are conducting joint research on artificial vision with the Department of Ophthalmology of Osaka University Graduate School of Medicine and an ophthalmologic apparatus manufacturer and also performing joint research on bio-medical photonic LSIs with the Functional Neuroscience Laboratory of NAIST.

3. Education

The majority of students in the laboratory are requested to work on research subjects involving other fields. We provide introductory seminars, study meetings, and many opportunities to interact with researchers within and outside the university so that they can pursue their research smoothly and broaden their research perspectives.

Research Themes

1. Bio-medical photonic materials and devices
2. Micro-chemical photonic devices
3. Advanced image sensors and their application systems

Recent Research Papers and Achievements

1. T. Tokuda, T. Ishizu, W. Nattakarn, M. Haruta, T. Noda, K. Sasagawa, M. Sawan, and J. Ohta, "1 mm³-sized Optical Neural Stimulator based on CMOS Integrated Photovoltaic Power Receiver," AIP Advances **8**, 045018 (2018).
2. J. Ohta, Y. Ohta, H. Takehara, T. Noda, K. Sasagawa, T. Tokuda, M. Haruta, T. Kobayashi, Y. M. Akay, M. Akay, "Implantable Microimaging Device for Observing Brain Activities of Rodents," Proc. IEEE **105**, 158 (2017).
3. K. Sasagawa, T. Yamaguchi, M. Haruta, Y. Sunaga, H. Takehara, H. Takehara, T. Noda, T. Tokuda, and J. Ohta, "An Implantable CMOS Image Sensor with Self-Reset Pixels for Functional Brain Imaging," IEEE Trans. Electron Dev. **63**,215 (2016).

Fig. 1
Research fields of the Photonic Device Science Lab

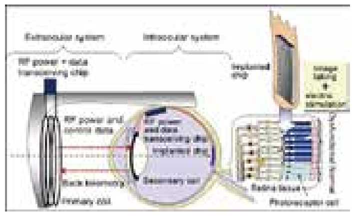

Fig. 2
Retinal prosthesis device

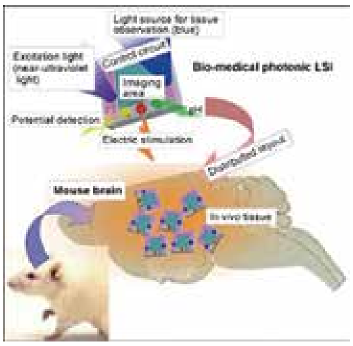

Fig. 3
Brain implantable microimager

Information Device Science





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Education and Research Activities in the Laboratory

Many daily necessities around us, such as TVs, computers, and mobile phones, are composed of silicon-based semiconductor devices. The Information Device Science Laboratory conducts research on information function devices that will support the next-generation information society. Key features of our research include the introduction of various new materials on silicon substrates, our own unique designs, and production of semiconductor devices that make the most effective use of their characteristics. Thus, we are working on producing semiconductor devices with innovative functions on the basis of skilled manufacturing

Research Themes

1. Transparent Oxide Thin Film Transistors
2. Printed/flexible displays for wearable devices
3. Printing technology for energy harvesting devices, solar cells
4. Power devices based on GaN, diamonds.

Recent Research Papers and Achievements

1. T. Takahashi, R. Miyanaga, M. N. Fujii, J. Tanaka, K. Takechi, H. Tanabe, J. P. Bermundo, Y. Ishikawa and Y. Uraoka, “Hot carrier effects in InGaZnO thin-film transistor”, Applied Physics Express 12, 094007 (2019).
2. J. Clairvaux, M. Uenuma, D. Senaha, Y. Ishikawa, Y. Uraoka, “Growth of InGaZnO nanowires vis a Mo/Au catalyst from amorphous thin film”, Appl. Phys. Lett. **111**, 033104 (2017).
3. J. P. Bermundo, Y. Ishikawa, M. N. Fujii, H. Ikenoue, and Y. Uraoka, “H and Au diffusion in high mobility a-InGaZnO thin-film transistors vis low temperature KrF excimer laser annealing”, Appl. Phys. Lett. **110**, 133503 (2017).
4. Kahori Kise, M. Fujii, S. Urakawa, H. Yamazaki, E. Kawashima, S. Tomai, K. Yano, D. Wang, M. Furuta, Y. Ishikawa, Y. Uraoka, “Self-heating induced instability of oxide thin film transistors under dynamic stress”, Appl. Phys. Lett. **108**, 02501 (2016).
5. Mutsunori Uenuma, Yasuaki Ishikawa and Yukiharu Uraoka, “Joule heating effect in nonpolar and bipolar resistive random access memory”, Appl. Phys. Lett. **107**, 073503 (2015).
6. Juan Paolo Bermundo, Yasuaki Ishikawa, Mami N. Fujii, Michel van der Zwan, Toshiaki Nonaka, Ryoichi Ishihara, Hiroshi Ikenoue, Yukiharu Uraoka, “Low Temperature Excimer Laser Annealing of a-InGaZnO Thin-Film Transistors Passivated by Organic Hybrid Passivation Layer”, Appl. Phys. Lett., (2015).

Fig. 1

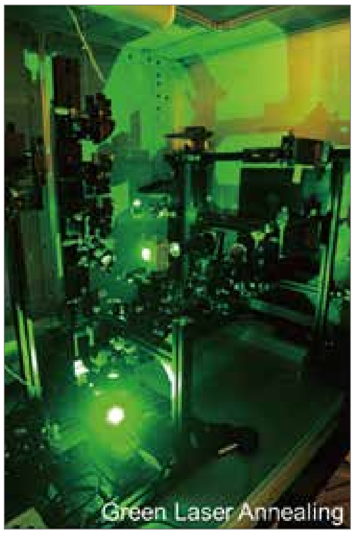

Fig. 2

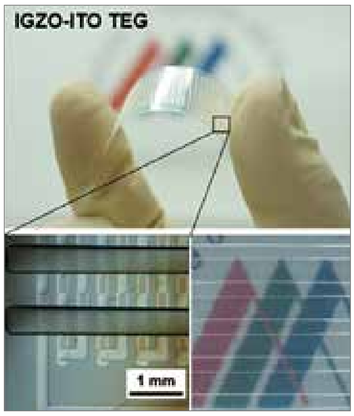

Fig. 3

Sensing Devices




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Education and Research Activities in the Laboratory

1. Measurements of ionizing radiations (for example, X-rays, γ-rays, charged particles and neutrons) using scintillators and dosimeters are our main focus of research.

2. Key areas of our studies are radiation physics, inorganic luminescent materials and photo-physics. It is preferable if the prospective student has a good understanding of physics described in the textbooks below.
- Solid state physics: Introduction to Solid State Physics (C. Kittel)
- Basic quantum mechanics: Principles of Quantum Mechanics (P. A. M. Dirac)

3. In our group, students are exposed to a wide range of experiments every day, and they learn and achieve experimental techniques to measure various ionizing radiations using inorganic phosphor materials. Typically, these phosphors (inorganic single crystals, ceramics and glasses) can be synthesized in the lab, and a variety of radiation-induced effects are characterized over a wide range of optical regions from VUV to NIR over a wide temperature range, 4-800K. Successful students may be involved in collaborative research with major university and industrial partners in Japan and overseas.

Fig. 1
Crystal, ceramic, and glass materials under UV excitation

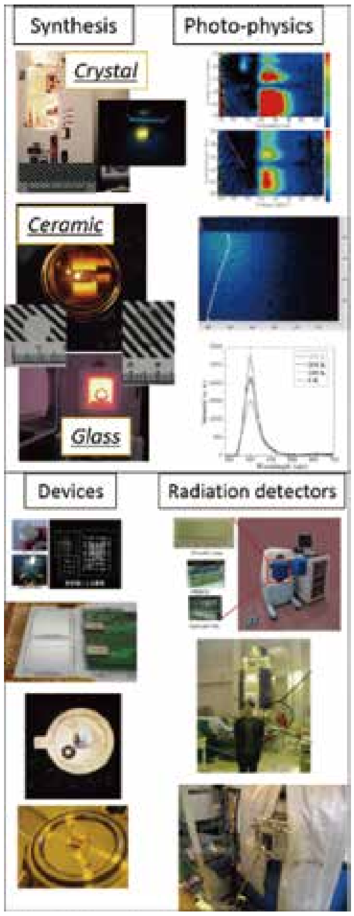

Fig. 2
Outline of studies in this group, from material synthesis to radiation detectors

Research Themes

1. Development of new scintillator materials and detectors for advanced radiation measurements
We synthesize inorganic crystal, ceramic and glass scintillators and characterize the fundamental scintillation properties. Successful materials will be further studied for state-of-the-art detectors.

2. Development of new dosimeter materials (OSL, TSL and RPL)
As for scintillator research, we synthesize inorganic crystals, ceramics and glasses for novel dosimeter materials. Our facilities offer comprehensive studies of different types of dosimetry. (OSL, TSL, and RPL)

3. Development of other phosphor materials
Besides radiation measurements, we also develop other types of phosphor materials, e.g., long persistent luminescence and stress luminescence.

4. Ionizing radiation detector applications
Promising samples are further advanced to develop detector instruments for medical, security and high energy physics applications.

Recent Research Papers and Achievements

1. Study of rare-earth-doped scintillators, T. Yanagida, Opt. Mat., 35 1987-1992 (2013).
2. Comparative study of ceramic and single crystal Ce:GAGG scintillator, T. Yanagida, K. Kamada, Y. Fujimoto, H. Yagi, T. Yanagitani, Opt. Mat., 35 2480-2485 (2013).
3. Development of X-ray induced afterglow characterization system, T. Yanagida, Y. Fujimoto, T. Ito, K. Uchiyama, K. Mori, Appl. Phys. Exp., 7 062401 (2014).

Organic Electronics




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Education and Research Activities in the Laboratory

Let's imagine electronic equipment that is easy to carry in a rolled state, a piece of fabric that generates electricity from the human body or a paper-like solar cell that generates electricity from light. Adding such unprecedented electronic functions onto various "surfaces", human life will become more comfortable and prosperous. We are pursuing the realization of such novel electronic devices through studies elucidating unique phenomena in organic solids and applying the findings to the device functions using knowledge of solid-state physics, electronics, surface science, polymer physics, and molecular science. Our laboratory utilizes unique approaches made possible by our original characterization tools and computer simulations.

We determine individual research projects ranging from basic science to development of operable devices, depending on the interests and aptitudes of the students. We foster independent thinking and a top-level mindset necessary for a researcher through collaborative research with institutes in Japan and overseas. Thus, we aim to cultivate researchers with a broad knowledge of science and a keen interest toward industrial applications.

Research Themes

1. Creation of "soft" thermoelectric materials

We are attempting to create novel thermoelectric materials and innovative flexible thermoelectric generators to convert exhaust heat from the living environment and the human body into electricity. We have found that the thermal conductivity of a carbon nanotube composite decreases to 1/1000 by forming molecular junctions between nanotubes with a specially designed protein. (Fig. 1) We are also trying to elucidate and control the *Giant Seebeck Effect* in organic semiconductors discovered in our laboratory (Fig. 2) with the aid of advanced measurement techniques, theoretical physics, and computational chemistry.

2. Elucidation of carrier transport mechanisms in organic semiconductors

We develop original characterization techniques, such as AFM Potentiometry, and perform studies to deepen understanding of the structure and the electronic functions of organic semiconductors.

3. Development of next-generation plastic solar cells

We develop next-generation solar cells based on semiconducting polymers. To elucidate the mechanisms that lead to photoelectric conversion, functional structures of the active layer have been visualized at the nanometer scale by conductive atomic force microscopy. (Fig. 3)

4. Flexible THz-sensing devices using organic-inorganic hybrid perovskite thin film

We study the origin of the strong absorption of terahertz wave by organic-inorganic hybrid perovskite thin film such as AMX_3 (A = MA or FA, M = Pb or Sn, and X = Cl, Br, I) and develop THz-sensing devices with them. (Fig. 4)

Recent Research Papers and Achievements

1. H. Kojima et al., "Universality of Giant Seebeck Effect in Organic Small Molecules", *Mater. Chem. Front*. **2**, 1276 (2018).
2. M. Ito, et al., "From materials to device design of a thermoelectric fabric for wearable energy harvesters", *J. Mater. Chem. A* **5**, 12068 (2017).
3. H. Benten et al., "Recent Research Progress of Polymer Donor/Polymer Acceptor Blend Solar Cells", *J. Mater. Chem. A* **4**, 5340 (2016).
4. Y. M. Lee, et al., "Surface Instability of Sn-based Hybrid Perovskite Thin Film, $CH_3NH_3SnI_3$: The Origin of Its Material Instability", *J. Phys. Chem. Lett*. **9**, 2293 (2018).
5. M.-C. Jung, et al., "Diffusion and influence on photovoltaic characteristics of p-type dopants in organic photovoltaics for energy harvesting from blue-light", *Organic Electronics* **52**, 17 (2018).

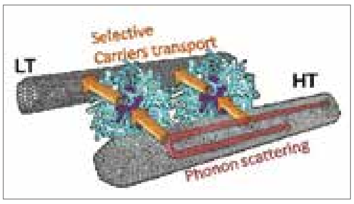

Fig. 1
A novel design of a thermoelectric nanocomposite using biomolecular junctions

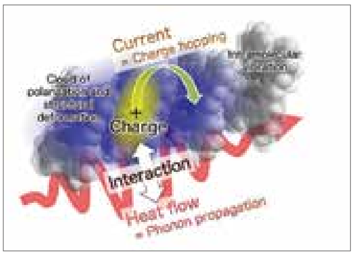

Fig. 2
Conceptual diagram of the *Giant Seebeck Effect*: a specific current-heat flow interaction in organic solids

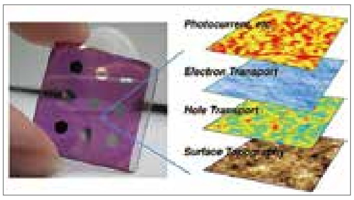

Fig. 3
Functional structures for photovoltaic conversion in plastic solar cells

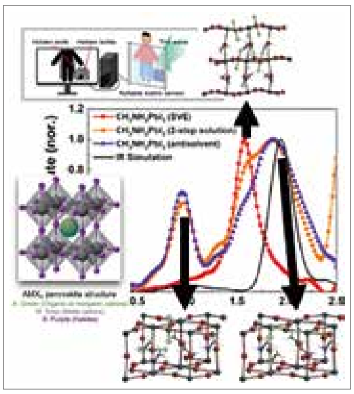

Fig. 4
AMX^3 perovskite structure and THz-absorption properties

Mesoscopic Materials Science *(with Panasonic Corporation)*



Prof. Eiji Fujii

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Education and Research Activities in the Laboratory

We aim to cultivate researchers who will carry out investigations on new physical phenomena and devices at the mesoscopic scale, and who will promote interdisciplinary research and open up new research areas. In the master's program, we first provide students with a basic education in order for them to grasp the reasons why our research is necessary for society, and why research in science and technology is essential for the development of humankind. Then, based on this education, students participate in our research activities in mesoscopic and nano fields, experiencing the joy of new discoveries and skilled manufacturing through experiments. Thus, we nurture researchers who can take on basic responsibilities in the development of new science and technology.

In the doctoral program, we not only provide guidance on specific research themes but also clarify the difference between science and engineering, thus providing students with adequate guidance so that they can, in a balanced manner, utilize both a scientific mindset that leads to paradigm shifts, and engineering knowledge that serves to realize scientific ideas.

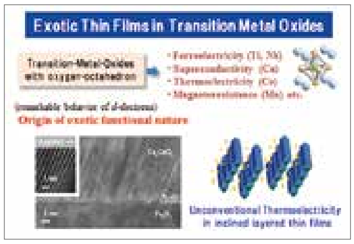

Fig. 1
A conceptual illustration of strongly correlated electronic materials and the layer-controlled thermoelectric thin film structure

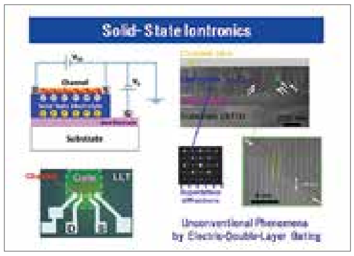

Fig. 2
A conceptual illustration of a solid-state iontronics device made of ion-conducting epitaxial thin film

Research Themes

We conduct research on exotic devices utilizing new physical phenomena in the mesoscopic region that take advantage of thin-film technology. Specifically, we are conducting research on novel energy conversion devices using strongly-correlated electronic materials and/or solid-state iontronics materials.

1. Strongly correlated electronic materials (Fig. 1)

Research of novel devices utilizing cross-correlated phenomena

2. Solid-state iontronics materials (Fig. 2)

Search for new phenomena using electric-double-layer derived in ion-conducting thin films

Recent Research Papers and Achievements

1. T. Asano, Y. Kaneko, A. Omote, H. Adachi, and E. Fujii, "Conductivity modulation of gold thin film at room temperature via all-solid-state electric-double-layer gating accelerated by nonlinear ionic transport", *ACS Appl. Mater. Interfaces* **9**, 5056-5061 (2017).
2. Y. Tanaka, S. Okamoto, K. Hashimoto, R. Takayama, T. Harigai, H. Adachi, and E. Fujii, "High electromechanical strain and enhanced temperature characteristics in lead-free $(Na,Bi)TiO_3$–$BaTiO_3$ thin films on Si substrates", *Sci. Rep.* **8**, 7847 (2018).
3. K. Umeda, M. Uenuma, D. Senaha, J. C. Felizco, Y. Uraoka, and H. Adachi, "Amorphous thin film for thermoelectric application", *J. Phys.: Conf. Ser.* **1052**, 012016 (2018).

Sensory Materials and Devices *(with Shimadzu Corporation)*

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Education and Research Activities in the Laboratory

We are advancing our research on sensor and device-related fundamental technologies such as microfabrication. We take advantage of these technologies to then conduct research on various devices such as electrophoresis chips, cell culture chips (Fig. 1), microreactors, electro-osmotic pumps, and vapor-liquid separation chips. Additionally, we are furthering research on biomaterial especially for tissue engineering (Fig. 2) and Gamma-ray image sensor systems (Fig. 3) to be applied in the medical diagnosis field, as well as working on the integration of these technologies to realize highly functional ultra micro chemical analysis systems (µTAS: Micro Total Analysis Systems).

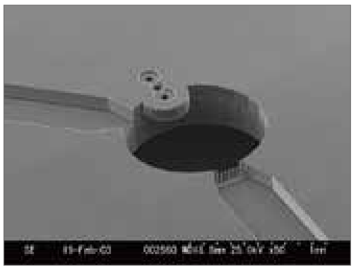

Fig. 1
Cell culture chips

Research Themes

Taking advantage of semiconductor manufacturing process technologies to apply micromachining to silicon and glass substrates of sub-micron dimensions, we develop functional devices with one-micron sized three dimensional structures that are used for chemical analysis and chemical manipulation (reaction or extraction).

We are also active in the medical diagnosis field, focusing on molecular imaging technology and X-ray imaging systems. We pursue the application of molecular imaging-related technologies such as positron emission tomography (PET) to medical diagnosis fields including cancer detection at its earliest stages. X-ray imaging systems are an important technology in the medical diagnosis field and we are investigating a phase contrast imaging system using an X-ray Interferometer.

Our laboratory research themes include:

1. Microchemical analysis systems
2. Microreactors and micropumps
3. Biomaterial for tissue engineering
4. Molecular imaging: Positron emission tomography
5. X-ray imaging systems

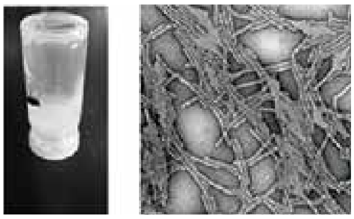

Fig. 2
A biocompatible polymer gel

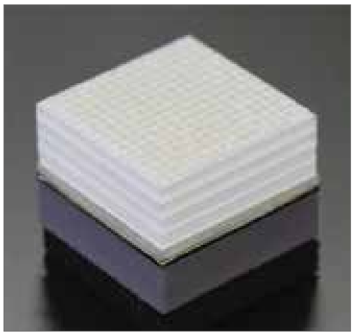

Fig. 3
A PET detector

Recent Research Papers and Achievements

1. Y. Ishii et al., "Timing performance simulation of TOF-PET detector using GATE v8.0", The 65th JSAP Spring Meeting, Tokyo, Japan (2018).
2. Y. Ishii et al., "Timing Resolution of GFAG Scintillators for TOF-PET", The 78th JSAP Autumn Meeting, Fukuoka, Japan (2017).
3. M. Nakazawa et al., "Development of a 64ch SiPM-based TOF-PET Detector with High Spatial and Timing Resolutions Using Multiplexing Architecture", IEEE Nuclear Science Symposium and Medical Imaging Conference (NSS/MIC), Atlanta, GA, USA (2017).
4. Y. Ishii et al., "Timing Resolution of GPS Scintillator with Several Ce Concentrations for TOF-PET", The 64th JSAP Spring Meeting, Kanagawa, Japan (2017).
5. Y Yamakawa et al., "Development of a dual-head mobile DOI-TOF PET system having multi-modality compatibility", Nuclear Science Symposium and Medical Imaging Conference (NSS/MIC), Seattle, WA, USA (2014).
6. KK. Miyake et al., "Performance Evaluation of a New Dedicated Breast PET Scanner Using NEMA NU4-2008 Standards", Journal of Nuclear Medicine 55(7), 1198-203 (2014).
7. Y. Kimura et al., "Novel system using microliter order sample volume for measuring arterial radioactivity concentrations in whole blood and plasma for mouse PET dynamic study", Physics in Medicine and Biology 58(22), 7889-903 (2013).

Synthetic Organic Chemistry

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Education and Research Activities in the Laboratory

Our philosophy in the Synthetic Organic Chemistry Laboratory is to cultivate, through the study on organic synthesis, abilities to (1) understand one another's research background, (2) make independent, logical research plans, and (3) consider and evaluate obtained results accurately to achieve rational conclusions (with a deep insight into the truth), in order to produce human resources possessing broad perspectives, flexibility and adaptability, and creativity, all of which are essential for researchers. Furthermore, in order to enhance students' presentation skills, we encourage them to present their research in various meetings and symposia.

Fig. 1

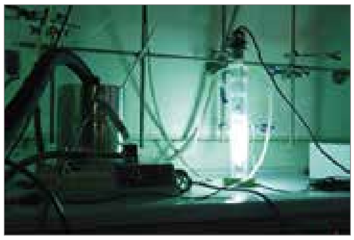

Fig. 2

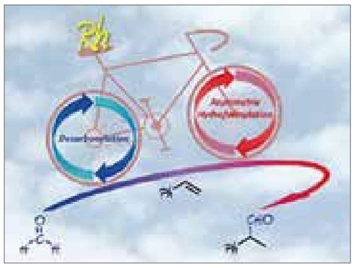

Fig. 3

Research Themes

Research in our laboratory focuses on photochemistry, natural product chemistry, and organometallic chemistry towards organic synthesis. We are interested in developing new photochemical and catalytic reactions to synthesize compounds of interest to the pharmaceutical industry, especially reactions that are stereoselective. We are also interested in the synthesis of natural products and functional organic materials utilizing developed methods. We are currently focused on our own research centered on the following themes:

1. Development of new methodologies for the synthesis of various functional polycyclic organic compounds, such as biologically active compounds and functional organic materials (Fig. 1).

2. Development of asymmetric photoreactions and devising a new microreactor system using a capillary reactor for organic synthesis (Fig. 2).

3. Development of new environmentally-friendly green organic synthesis processes using organometallic catalysts (Fig. 3).

Recent Research Papers and Achievements

1. J. Pan, T. Morimoto, H. Kobayashi, H. Tanimoto, K. Kakiuchi, *Heterocycles* **2019**, *98*, 519.
2. T. Yokoi, T. Ueda, H. Tanimoto, T. Morimoto, K. Kakiuchi, *Chem. Commun.* **2019**, *55*, 1891. (Selected as Cover Article)
3. H. Tanimoto, S. Ueda, T. Morimoto, K. Kakiuchi, *J. Org. Chem.* **2018**, *83*, 1614.
4. H. Tanimoto, J. Mori, S. Ito, Y. Nishiyama, T. Morimoto, K. Tanaka, Y. Chujo, K. Kakiuchi, *Chem. Eur. J.* **2017**, *23*, 10080. (Selected as Hot Paper and Cover Article)
5. S. Hikage, Y. Nishiyama, Y. Sasaki, H. Tanimoto, T. Morimoto, K. Kakiuchi, *ACS Omega* **2017**, *2*, 2300.
6. T. Furusawa, H. Tanimoto, Y. Nishiyama, T. Morimoto, K. Kakiuchi, *Chem. Lett.* **2017**, *46*, 926.
7. T. Furusawa, H. Tanimoto, Y. Nishiyama, T. Morimoto, K. Kakiuchi, *Adv. Synth. Catal.* **2017**, *359*, 240.
8. M. Nakano, Y. Nishiyama, H. Tanimoto, T. Morimoto, K. Kakiuchi, *Org. Process Res. Dev.* **2016**, *20*, 1626.

Photonic Molecular Science




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Assoc. Prof. Takuya Nakashima
Assist. Prof. Yoshiyuki Nonoguchi
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Education and Research Activities in the Laboratory

Research activity of this laboratory is focused on “Photonic Molecular Science”, a new research field covering molecules, polymers, coordination compounds and low-dimensional nanomaterials with advanced photo-functionality. We synthesize these new materials for future energy resource, sensors, displays and precision chemical fabrication processes. We welcome students who have been educated in chemistry and chemistry-related fields in Japanese and overseas universities. A small number of students may also join from solid state physics, material science and electronic engineering. Students are motivated to have advanced skills and knowledge on organic and inorganic chemical syntheses and material characterization, which are essential for future advanced researchers in chemistry, material chemistry and device science with photo-functionality. Our current research interest is dedicated to following topics.

Research Themes

1. Photoresponsive molecules composed of three-aromatic units showing photon-induced cyclization and color-change. Some of our compounds show a photochemical quantum yield of almost 100%, photo-induced generation of super-acid capable of triggering photopolymer patterning, ultra-efficient oxidative cycloreversion, and photoswitching of fluorescence.
2. Nanoparticles chemistry through surface molecular design for self-assembly, chiral chemistry, and composite materials.
3. Supramolecular functionalization of carbon nanotubes for thermoelectric energy conversion.
4. Coordination compounds based on structurally curved ligands and their supramolecular control of emission properties.

Recent Research Papers and Achievements

1. S. Yonezawa, R. Sethy, G. Fukuhara, T. Kawai, T. Nakashima, “Pressure-dependent guest binding and release on a supramolecular polymer”, *Chem. Commun.*, 55, 5793-5796 (2019)
2. M. Louis, R. Sethy, J. Kumar, S. Katao, R. Guillot, T. Nakashima, C. Allain, T. Kawai, R. Métivier, “Mechano-Responsive Circularly Polarized Luminescence of Organic Solid-State Chiral Emitters”, *Chem. Sci.*, 10, 843-847 (2019)
3. C. Martin, M. Minamide, J. Calupitan, R. Asato, J. Kuno, T. Nakashima, G. Rapenne, T. Kawai, “Terarylenes as Photoactivatable Hydride Donors”, *J. Org. Chem.*, 83, 13700-13706 (2018)
4. Y, Nonoguchi, K. Kojiyama, T. Kawai, “Electrochemical n-Type Doping of Carbon Nanotube Films by Using Supramolecular Electrolytes”, *J. Mater. Chem*. A, 6, 21896-21900 (2018)
5. Y. Hashimoto, T. Nakashima, M. Yamada, J. Yuasa, G. Rapenne, T. Kawai, “Hierarchical Emergence and Dynamic Control of Chirality in a Photoresponsive Dinuclear Complex”, *J. Phys. Chem. Lett.*, 9, 2151-2157 (2018)
6. J. Kuno, Y. Imamura, M. Katouda, M. Tashiro, T. Kawai, T. Nakashima, “Inversion of Optical Activity in the Synthesis of Mercury Sulfide Nanoparticles: Role of Ligand Coordination”, *Angew. Chem. Int. Ed.*, 57, 12022-12026 (2018)
7. T. Y. Bin, T. Kawai, J. Yuasa, “Ligand-to-Ligand Interactions Direct Formation of D2-Symmetrical Alternating Circular Helicate”, *J. Am. Chem. Soc.*, 140, 3683-3689 (2018)

Fig. 1
Schematic illustration for photoisomerization reactions of our unique photochromic molecule, which exhibits photoreaction with quantum yield of unity, a “photon-quantitative reaction”

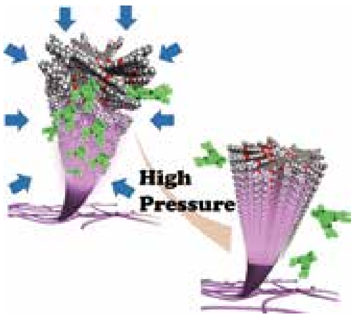

Fig. 2
Schematic illustration of pressure induced structural change and guest release in a supramolecular host-guest system.

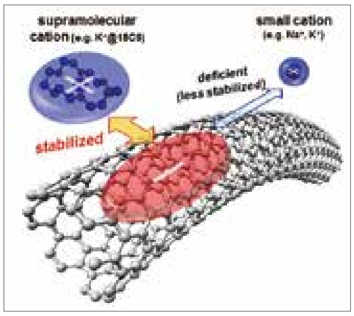

Fig. 3
A representative concept for supramolecular n-type doping of carbon nanotubes.

Photofunctional Organic Chemistry




Prof. Hiroko Yamada
Assoc. Prof. Naoki Aratani
Assist. Prof. Hironobu Hayashi
Assist. Prof. Kyohei Matsuo

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Education and Research Activities in the Laboratory

The Photofunctional Organic Chemistry Laboratory was established on January 1, 2011.

We focus on the development of functional organic materials including organic semiconductors for photovoltaic cells and organic thin-film transistors, highly fluorescent dyes, etc. on the basis of organic synthesis. In particular, acenes and porphyrinoids are our current target compounds. Students at our laboratory are encouraged to work independently and freely on their own original research themes.

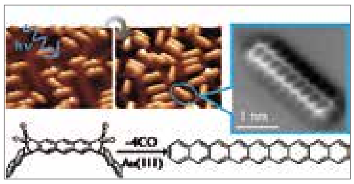

Fig. 1
A photoprecursor method for the longest acene “nonacene” synthesis

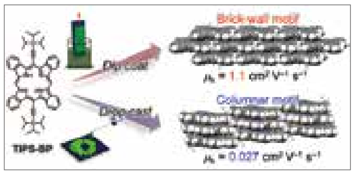

Fig. 2
An organic semiconducting thin-film for use in OFET devices

Research Themes

1. Development of high-performance molecular semiconductors for solution-processed organic electronic devices

We are trying to engineer well-performing organic semiconducting thin films for use in electronic devices such as organic field effect transistors. To this end, we employ a unique deposition technique called “precursor approach” (Fig. 1), and are preparing new compounds (Fig. 2)—typically derivatives of acenes and benzoporphyrin—that can be processed by this method (Fig. 3).

Fig. 3
Photo-irradiation process on making of organic thin-film devices

2. Development of graphene nanoribbons

We are investigating the surface-assisted graphene nanoribbon (GNR) synthesis that allows width, edge structure, and heteroatom incorporation to be modulated with atomic-level precision (Fig. 4). Our group is currently involved in, among others, collaborative projects of “Tailor-Made Synthesis of Graphene Nanoribbons for Innovative Devices” (JST CREST).

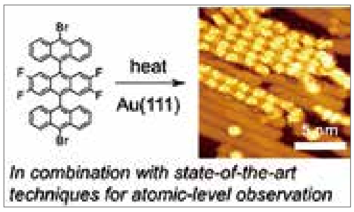

Fig. 4
On-surface synthesis of graphene nanoribbon (GNR)

3. Creation of unique carbon frameworks with remarkable optical/electronic properties

We have created various novel functional polycyclic aromatic hydrocarbons (PAHs). These compounds have near-infrared absorption properties, intensive light emission, or remarkable redox properties. For instance, a remarkably strained cyclopyrenylene trimer was synthesized and it underwent the first biaryl C-C σ-bond cleavage with $^1O_2$ (Fig. 5).

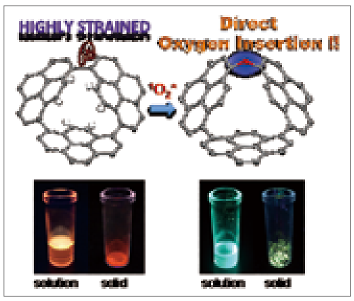

Fig. 5
A remarkably strained cyclopyrenylene trimer

Recent Research Papers and Achievements

1. H. Hayashi, H. Yamada, R. Fasel *et al*., On-surface light-induced generation of higher acenes and elucidation of their open-shell character, *Nat. Commun*., **2019**, *10*, 861.
2. K. Takahashi, M. Suzuki, Q. Miao, H. Yamada *et al*., Engineering Thin Films of a Tetrabenzoporphyrin toward Efficient Charge-Carrier Transport: Selective Formation of a Brickwork Motif, *ACS Appl. Mater. Interfaces*, **2017**, *9*, 8211.
3. H. Hayashi, J. Yamaguchi, H. Jippo, R. Hayashi, N. Aratani, M. Ohfuchi, S. Sato, and H. Yamada, Experimental and Theoretical Investigations of Surface-Assisted Graphene Nanoribbon Synthesis Featuring Carbon–Fluorine Bond Cleavage, *ACS Nano*, **2017**, *11*, 6204.
4. R. Kurosaki, H. Hayashi, M. Suzuki, J. Jiang, M. Hatanaka, N. Aratani, H. Yamada, A remarkably strained cyclopyrenylene trimer that undergoes metal-free direct oxygen insertion into the biaryl C–C σ-bond, *Chem. Sci*., **2019**, *10*, 6785. (Selected as an Inside Back Cover)

Functional Polymer Science (with Santen Pharmaceutical Co., Ltd.)



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Education and Research Activities in the Laboratory

1. Educational Purposes

We cultivate human resources with the ability to identify and solve research challenges, as well as those who can contribute to society through research activities in drug discovery based on synthetic organic chemistry. We provide research and education aiming to develop human resources who dream of performing skilled manufacturing and spare no effort in achieving their dreams. Thus, we place emphasis on the understanding of research backgrounds and positioning, experimental design and techniques, result analysis, discussion, and how to derive conclusions.

2. Guiding Principle

We provide guidance to students so that they can acquire the basic experimental capabilities to obtain correct and reliable data and, at the same time, give consideration to safety and health during actual chemical experiments.

Research Themes

New Drug Delivery System Project

The Functional Polymer Science Laboratory, a collaboration course between Santen Pharmaceutical Co., Ltd. and Nara Institute of Science and Technology, has been conducting research activity since April 2005. Our current main research focus is on new drug delivery systems (DDS) for the treatment of various eye diseases. Within ocular DDS development there are many challenging subjects for pharmaceutical and ophthalmologic sciences remaining, such as improvement of intraocular migration and intraocular sustainability of drugs. DDS for the eye are categorized into two main segments, anterior and posterior chambers (Figs. 1, 2). Now especially, sustained-release type DDS using inactive ingredients, such as an ascorbic acid ester derivative, are being studied to treat diseases of the posterior chamber of the eye (Fig. 3).

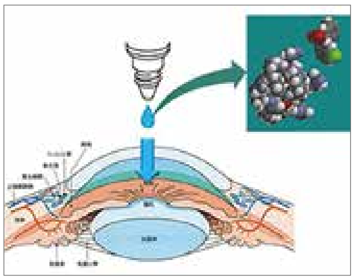

Fig. 1
DDS for eye disease (anterior chamber)

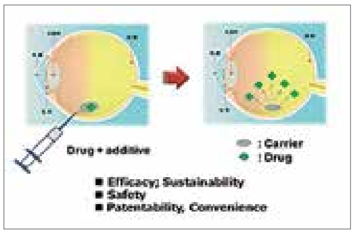

Fig. 2
DDS for eye disease (posterior chamber)

Fig. 3
Injectable gel for DDS using ascorbic acid ester derivative and its SEM image

Recent Research Papers and Achievements

1. T. Honda, et al. Bioorg. Med. Chem. Lett. 18, 2939 (2008).
2. T. Honda, et al. Bioorg. Med. Chem. 17, 699 (2009).
3. H. Tajima, et al. Bioorg. Med. Chem. Lett. 20, 7234 (2010).
4. H. Tajima, et al. Bioorg. Med. Chem. Lett. 21, 1232 (2011).
5. T. Honda, et al. Bioorg. Med. Chem. Lett. 21, 1782 (2011).
6. N. Kojima, et al.: Development of a novel in situ depot system using low molecular weight gelators. General Oral Presentation (27R-pm04), The 135th Annual Meeting of the Pharmaceutical Society of Japan in Kobe (March, 2015).
7. Y. Oyama, et al.: Possibility study of an ocular drug delivery system with using cell-penetrating peptides (CPPs). General Oral Presentation (27W-am07S), The 138th Annual Meeting of the Pharmaceutical Society of Japan in Kanazawa (March, 2018).

Ecomaterial Science (with Research Institute of Innovative Technology for the Earth)



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Education and Research Activities in the Laboratory

The Ecomaterial Science Laboratory, staffed by researchers of the Research Institute of Innovative Technology for the Earth (RITE), provides research and education on fundamental technologies to solve the global warming issues. We endeavor to develop advanced materials for CO_2 capture and H_2 energy production. Specifically, solid materials (e.g. zeolite, mesoporous silica, MOF) have been investigated in order to reduce the energy requirements and cost for CO_2 capture. Concerning CO_2-free, H_2-based energy systems generated by any renewable sources, it is necessary to develop efficient processes for the dehydrogenation of chemical hydrides such as methylcyclohexane or ammonia. We evaluate silica, zeolite and palladium membranes for the processing of chemical hydrides. We also develop innovative separation processes that can contribute to the prevention of global warming.

In our laboratory, we normally provide our students with OJT (on-the-job training) education through the projects conducted in RITE. The students can deepen their understanding of social contexts, causes and countermeasures concerning global environmental issues. They also learn fundamental knowledge of material science in relevant subjects such as physical chemistry, organic/inorganic chemistry, synthesis, and chemical engineering.

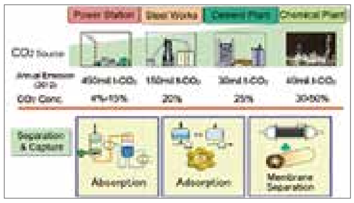

Fig. 1
CO_2 separation and capture technologies

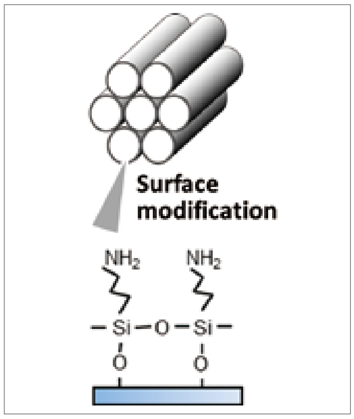

Fig. 2
Amine solid sorbent for CO_2 capture (amine-grafted mesoporous silica)

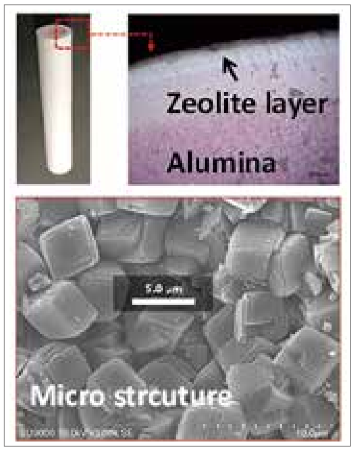

Fig. 3
Novel zeolite membrane for H_2 separation

Research Themes

Development of CO_2 capture technologies

Research on high-performance and energy-saving materials for gas separation in the fields of greenhouse gas mitigation, air quality control in space stations, etc.

- zeolite
- mesoporous materials
- polymeric materials
- metal organic framework (MOF)
- amine-based materials

Development of inorganic membranes for an H_2 energy society

Research on various separation membranes for use of inorganic materials.

- palladium (Pd) membranes
- zeolite membranes
- chemical vapor deposition (CVD) based silica membranes

Recent Research Papers and Achievements

1. Q. T. Vu, H. Yamada, K. Yogo, "Exploring the role of imidazoles in amine-impregnated mesoporous silica for CO_2 capture", Industrial & Engineering Chemistry Research, 57, pp. 2638-2644 (2018).
2. K. Kida, Y. Maeta, K. Yogo, "Preparation and gas permeation properties on pure silica CHA-type zeolite membranes", Journal of Membrane Science, 522, pp. 363–370 (2017).
3. M. Miyamoto, T. Nakatani, Y. Fujioka, K. Yogo "Verified synthesis of pure silica CHA-type zeolite in fluorite media", Microporous and Mesoporous Materials, 206, pp.67-74 (2015).

Advanced Functional Materials (with Osaka Research Institute of Industrial Science and Technology)



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Education and Research Activities in the Laboratory

Polymers, ceramics and metals are materials used widely in industry. Their applications are widespread from structural uses to a variety of functional uses. We devote our efforts to develop these materials and their nanocomposites to be applied in advanced industry. We focus on the nanostructure control of the materials to realize next generation electronic, optical, and energy devices. Another important challenge is the development of environmental-conscious material processing technology. Our laboratory is located in the Osaka Research Institute of Industrial Science and Technology, Morinomiya Center near the downtown area of Osaka city. Our laboratory conducts intimate collaborations with engineers from private companies; this leads to the rapid application of the developed materials into practical devices.

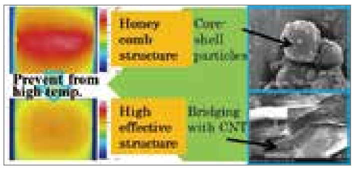

Fig. 1
Honeycomb structure of phenol resin particles with thermal conductive BN nanoparticles, or bridged structure of graphite plates with CNF has promoted thermal conductivity to increase immediately (two times).

Research Themes

1. Highly thermal conductive materials and transparent and highly thermal emissive coating materials

Super hybrid materials made up of honeycomb structures with nanoparticles show 10 W/(m K) of thermal conductivity with electric insulation, although those with co-continuous phases, made by SPS method have been developed to attain super highly thermal conductivity (> 120 W/(m K). Furthermore, those with both a high thermal emissivity (>0.9) and light transparency (haze<2%) have been developed, resulting in application to heat releasing materials in LED devices, communicators, robots and rockets.).

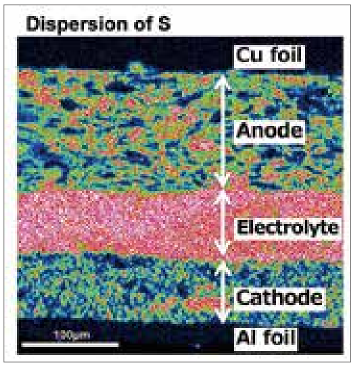

Fig. 2
A cross-section of an all solid state lithium ion battery. The layer by layer structure is composed of a cathode ($LiNi_{1/3}Co_{1/3}Mn_{1/3}O_2$with Li_3PS_4 and acetylene black), a solid state electrolyte (Li_3PS_4), and an anode (carbon with Li_3PS_4 and acetylene black).

2. Lithium ion batteries fully composed of ceramics

Our research is aims for the development of all solid state lithium ion batteries with high safety standards and high rechargeable capacity without liquid leakage. Our approaches to fabricate this lithium ion battery are economically and ecologically viable techniques expected to be used in industry. Core techniques employed are the slurry coating, aerosol deposition and the spray pyrolysis methods.

3. Biomass polymer materials with unique properties

A group of environmental and functional polymer materials, poly(lactic acid) materials, was developed to obtain properties of similar flexibility, high elongation and transparency to polyethylene, although they were perfectly biodegradable. Additionally, poly(lactic acid) can be synthesized to have high adhesion strength and unique rheological properties, because of high brunch chains and approximately 1 of Mw/Mn.

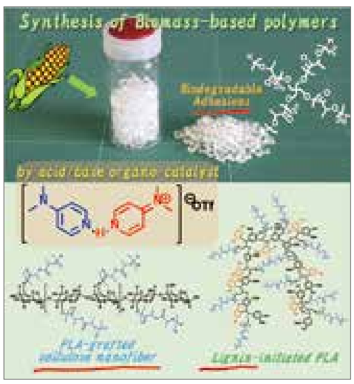

Fig. 3
Controlled synthesis of structure well-defined biomass-based polymers, as branched PLAs, PLA-grafted cellulose nanofiber and lignin-initiated PLA, by acid/base organo-catalyst for industrial use.

Recent Research Papers and Achievements

1. Y. Agari, K. Uotani, K. Mizuuchi, H. Hirano, J. Kadota, A. Okada, "Preparation and Properties of Al alloy/PPS Hybrid Materials with Co-continuous Phases by Spark Plasma Sintering Method", Asia Thermophysical Properties Conference 2016 (Yokohama).
2. M. Yamamoto, Y. Terauchi, A. Sakuda, M. Takahashi, "Binder-free sheet-type all-solid-state batteries with enhanced rate capabilities and high energy densities", Scientific Reports, vol. 8 1212 (2018).
3. J. Kadota, D. Pavlovic, H. Hirano, A. Okada, Y. Agari, B. Bibal, A. Deffieux, F. Peruch, "Controlled bulk polymerization of L-lactide and lactones by dual activation with organo-catalytic systems", Rsc Advances, vol. 4, 14725-14732 (2014).

Supramolecular Science




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Education and Research Activities in the Laboratory

We are performing new interdisciplinary researches in chemistry and biology. In living organisms, a variety of biomolecules such as proteins, DNA, and sugars form unique supramolecular assemblies to maintain biofunctions. Based on chemical knowledge of the functions and structures of these bio-supramolecules at the molecular level, our laboratory focuses on elucidation of the function mechanisms and design/applications of bio-supramolecules using various spectroscopic analysis methods, protein engineering techniques, and organic syntheses.

Research Themes

1. Elucidation and inhibition of protein denaturalization processes
Accumulation of proteins with unusual structures in tissues causes various diseases such as abnormal hemoglobin disease, Alzheimer's disease, and Parkinson's disease (conformational diseases). We investigate denaturalization of these proteins at the molecular level and develop strategies to inhibit the denaturalization.

2. Bio-supramolecule creation
We construct new protein supramolecules and polymers like puzzles, based on a new concept in which a building block protein is used as a structural unit (Fig. 1).

3. Functional protein creation by protein design
We design and make artificial proteins with multi-active sites exhibiting antibacterial activity and ligand binding properties (Fig. 2). These proteins are attracting attention in the biotechnology and pharmaceutical science fields.

4. Reaction mechanism elucidation of metalloenzymes
To understand the chemistry of life, we investigate enzymatic reactions using spectroscopic methods. For example, we elucidate the H_2 production and decomposition mechanisms of a metalloenzyme, hydrogenase.

5. Functional analysis of interaction fashions between biomolecules for medicinal chemistry
To understand and regulate bioreactions, we develop methods for bioreaction regulation based on interactions between biomolecules from the perspective of medicinal chemistry and chemical biology.

6. Functional protein creation through synthetic chemistry approaches
We aim at developing novel biocatalysts and artificial protein, or "molecular design-based functional biomolecules", and apply these biomolecules for organic syntheses and regulation of naturally occurring bioreactions. This strategy is based on complementary advantages of synthetic chemistry and biochemical approaches such as genetic engineering methods (Fig. 3).

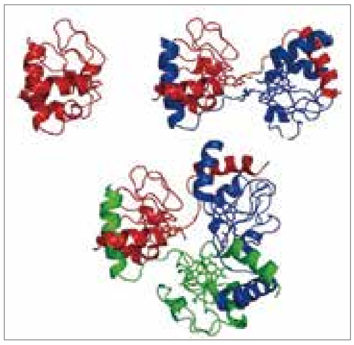

Fig. 1
Elucidated structures of cytochrome *c* supramolecules

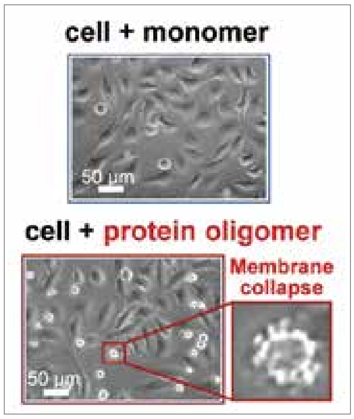

Fig. 2
Creation of antibacterial protein supramolecules

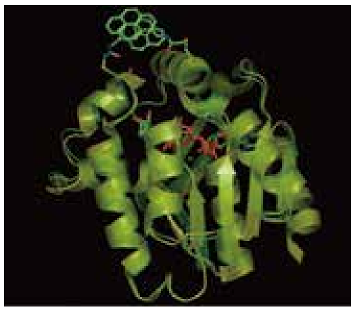

Fig. 3
X-ray crystallographic structure of an artificial fluorescent protein constructed by a combination of genetic and synthetic methods

Recent Research Papers and Achievements

1. H. Tai et al., *Angew. Chem. Int. Ed.*, 58, in press (2019).
2. T. Miyamoto et al., *ACS Synth. Biol.*, 8, 1112-1120 (2019).
3. A. Oda et al., *Chem. Asian J.*, 13, 964-967 (2018) (Front Cover).
4. T. Matsuo et al., *Chem. Eur. J.*, 24, 2767-2775 (2018).
5. Y. Shomura et al., *Science*, 357, 928-932 (2017).
6. K. Yuyama et al., *Angew. Chem. Int. Ed.*, 56, 6739-6743 (2017) (Hot Paper).
7. H. Kobayashi et al., *Angew. Chem. Int. Ed.*, 55, 14019-14022 (2016).
8. Y.-W. Lin et al., *Angew. Chem. Int. Ed.*, 54 511-515 (2015).
9. A. Fujii et al., *Bioconjugate Chem.*, 26 537-548 (2015).
10. T. Matsuo et al., *Bull.Chem. Soc. Jpn.*, 88, 1222-1229 (2015) (BCSJ Award).

Complex Molecular Systems

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Education and Research Activities in the Laboratory

The concerted actions of various molecules result in high-order functions that cannot be realized by individual molecules, as seen in various biological systems. The Complex Molecular Systems Laboratory, established on April 1, 2015, currently focuses on the complex molecular systems involving multicomponent biological molecules such as proteins. Weakly and/or strongly coupled proteins undergo regulatory dissociation and association in response to external stimuli, thereby exhibiting advanced biological functions. To determine the physicochemical properties of these molecular systems and to create new functional molecular systems, our laboratory employs various biophysical techniques, such as structural analysis using multiple probes (X-ray, neutron, and electron), spectroscopic measurements, protein engineering, and theoretical analysis.

Multidisciplinary knowledge is essential to clearly understand the characteristics of these complex molecular systems. We welcome students with various educational backgrounds such as physics, chemistry, material science, and biology. By enabling students to work on their own research theme independently, we encourage them to develop their own interests and to learn essential research skills, such as identifying problems to be solved, designing experiments that will yield solutions, and comprehensively interpreting experimental results.

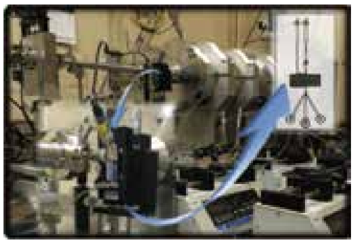


Fig. 1
Micro-fluidics based analyzer equipped for structure/interaction analysis of complex molecular systems

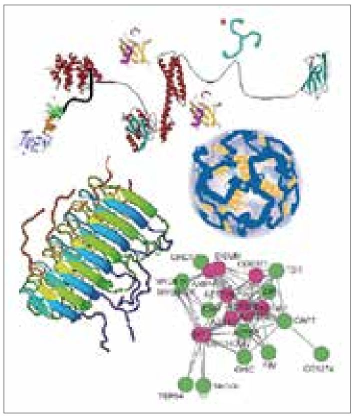


Fig. 2
Biological complex molecular systems

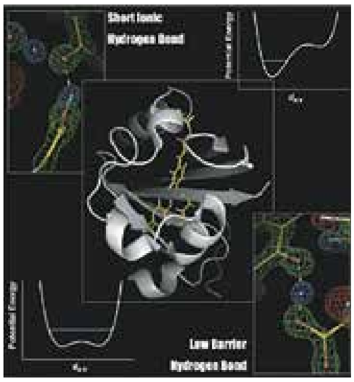


Fig. 3
Protonics in protein molecules

Research Themes

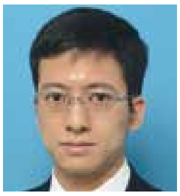
1. Development of analytical methods to investigate complex molecular systems (Fig. 1)
2. Investigation of the dynamical ordering of multi-component proteins (Fig. 2)
3. Creation of high-order self-assembled complex molecular systems (Fig. 2)
4. Detailed analysis of intramolecular actions in individual proteins responsible for the dynamical ordering of complex molecular systems in higher-class structural hierarchy (Fig. 3)
5. Development of rational molecular designs for novel synthetic proteins

Recent Research Papers and Achievements

1. K. Yonezawa, N. Shimizu, K. Kurihara, Y. Yamazaki, H. Kamikubo, M. Kataoka. "Neutron crystallography of photoactive yellow protein reveals unusual protonation state of Arg52 in the crystal." *Sci Rep* **7**(1):9361. (2017).
2. H. Kuramochi, S. Takeuchi, K. Yonezawa, H. Kamikubo, M. Kataoka, T. Tahara, "Probing the early stages of photoreception in photoactive yellow protein with ultrafast time-domain Raman spectroscopy", *Nature Chemistry*, 10.1038/nchem.2717 (2017).
3. Y. Yoshimura, N. A. Oktaviani, K. Yonezawa, H. Kamikubo, F. A. A. Mulder, "Unambiguous Determination of the Ionization State of a Photoactive Protein Active Site Arginine in Solution by NMR Spectroscopy", *Angewandte Chemie* **56**, 239-242 (2017).
4. F. Schotte, H. S. Cho, V. R. I. Kaila, H. Kamikubo, N. Dashdorj, E. R. Henry, T. J. Graber, R. Henning, M. Wulff, G. Hummer, M. Kataoka, P. A. Anfinrud, "Watching a signaling protein function in real time via 100-ps time-resolved Laue crystallography", *Proc. Natl. Acad. Sci. USA* **109** 19256-19261 (2012).
5. S. Yamaguchi, H. Kamikubo, K. Kurihara, R. Kuroki, N. Niimura, N. Shimizu Y. Yamazaki, M. Kataoka, "Low-barrier hydrogen bond in photoactive yellow protein", *Proc. Natl. Acad. Sci. USA* **106** 440-444 (2009).

Biomimetic and Technomimetic Molecular Science



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Education and Research Activities in the Laboratory

There are no physical limitations to the miniaturization of a machine down to the scale of a single molecule or conversely, to monumentalize a molecule until it becomes a machine. A molecular machine is a molecule designed to perform a function providing energy, data or/and orders to the molecule. Inspiration from mother nature and from modern technologies has given rise to the concept of biomimetic and technomimetic molecular machines respectively.

The Biomimetic and Technomimetic Molecular Science Laboratory studies molecules which can act as machines at the nanoscale. Thanks to an input signal as an energy source (light, electron or chemical) these molecular machines can produce a controllable motion and then to a useful output.

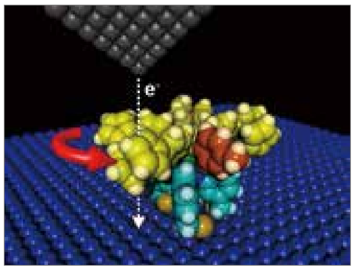

Fig. 1
A molecular motor rotating clockwise or counterclockwise by request.[5]

Research Themes

1. Technomimetic molecular machines

Technomimetic molecular machines are molecules designed to imitate macroscopic objects at the molecular level, and also to transpose the motions that these objects are able to undergo. Our originality is in the design of molecular machines and devices operating at the atomic scale for molecular mechanical applications: gears, vehicles, motors, etc. We are designing, synthesizing, organizing and synchronizing such molecular nanodevices to develop energy, communication and information transfer at the nanoscale under the action of light, heat or electrons.

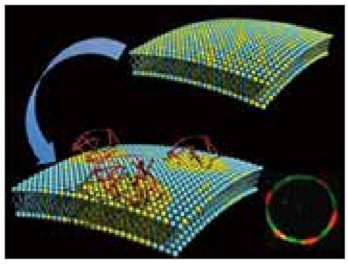

Fig. 2
Modulation of cell membrane structure by biomimetic molecular machines.

2. Biomimetic molecular machines

Membrane dynamics, such as morphological change of the cell membrane and molecular assembly in the membrane, are essential molecular mechanisms expressing and/or regulating various cellular functions. We design membrane-active agents which can trigger membrane dynamics and modulate biological functions learning from natural molecular machinery.

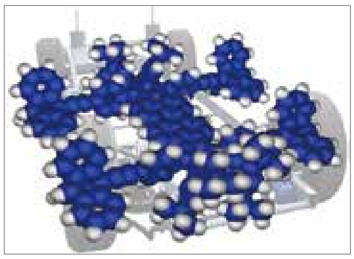

Fig. 3
Molecular nanovehicles which participated to the first Nanocar Race.[1]

3. Hybrid molecular machines

Hybrid molecular machines are based on biomimetic and technomimetic approaches to build new generation molecular machines and materials. Insertion of photo or electroactive molecular devices in membranes or in cells may induce some interesting biological activities.

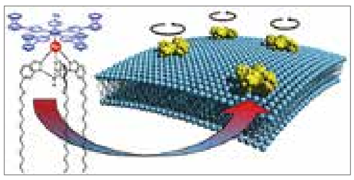

Fig. 4
A hybrid molecular motor designed to be inserted in artificial or cell membrane.

Recent Research Papers and Achievements

1. C. Kammerer, G. Erbland, Y. Gisbert, T. Nishino, K. Yasuhara, G. Rapenne, *Chem. Lett.* **48**, 299 (2019).
2. G. Rapenne, S.-W. Hla et al, *Nature Commun*. **10**, 3742 (2019).
3. Y. Zhang, H. Kersell, R. Stefak, J. Echeverria, V. Iancu, G. Perera, Y. Li, A. Deshpande, K.-F. Braun, C. Joachim, G. Rapenne, S.-W. Hla, *Nature Nanotech*. **11**, 706 (2016).
4. K. Yasuhara, J. Arakida, T. Ravula, S. K. Ramadugu, B. Sahoo, J. Kikuchi, A. Ramamoorthy, *J. Am. Chem. Soc*. **139**, 18657 (2017).
5. U.G.E. Perera, F. Ample, H. Kersell, Y. Zhang, J. Echeverria, M. Grisolia, G. Vives, G. Rapenne, C. Joachim, S.-W. Hla, *Nature Nanotech*. **8**, 46 (2013).

Nanomaterials and Polymer Chemistry

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Education and Research Activities in the Laboratory

Based on the concept of "molecular technology", this laboratory was established in 2015 to conduct research on functional materials in the field of polymer chemistry. Students who are interested in polymer synthesis and nanomaterials are welcome. The development of functional polymer materials requires knowledge of organic synthesis, analytical methods, and materials design, all of which are covered in the laboratory. Moreover, our functional materials will contribute to highly reliable medical devices as new therapeutic methods, new drugs, DDS, etc. We offer a thorough education to prepare students to become researchers through discussions, presentations, and participation in academic conferences and meetings.

Research Themes

In this laboratory, high-performance polymers and functional polymers are prepared by various approaches such as molecular design, polymer structure control, and effective polymer-polymer interaction.

1. General Synthetic Polymers
In order to give additional functions and higher physical properties, general synthetic polymers are modified. (Fig. 1)

2. Biodegradable Polymers
Multi-functional Biodegradable polymers are designed. (Fig. 2)

3. Amphiphilic Polymers
Functional materials are designed using amphiphilic polymers. (Fig. 3)

4. Nano Structure Control
In order to produce functional polymer materials, nanostructure control approaches are employed. For example, nano thin films for thermal storage materials and adhesives and nano particles for drug delivery systems.

5. Biocompatible coatings based on precisely designed polymers
Controlling of bio-interfacial water structure through precision polymer synthesis. (Fig. 4)

Fig. 1
Functional polyurethane through monomer design and oil gel using polystyrene

Fig. 2
Poly (trimethylene carbonate) derivatives for medical materials and antithrombotic surface materials

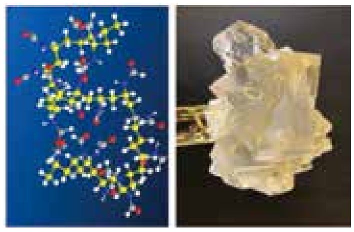


Fig. 3
Poly(N-vinylamide derivatives) for gas hydrate inhibitors

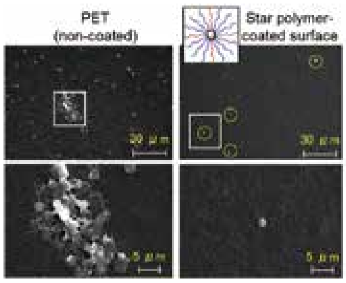


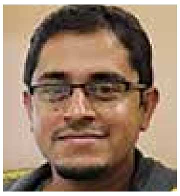
Fig. 4
Star polymer coating bearing biocompatible unit

Recent Research Papers and Achievements

1. N. Chanthaset, H. Ajiro*, *Materialia*, **2019**, *5*, 100178.
2. S. Seitz, H. Ajiro*, *Sol. Energy Mater. Sol. Cells*, **2019**, *190*, 57.
3. D. Aoki, H. Ajiro*, *Macromol. Rapid Commun.*, **2018**, *51*, 7845.
4. P. Charoensumran, H. Ajiro*, *Polym. J.*, **2018**, *50*, 1021.
5. K. Kan, H. Ajiro*, *Chem. Lett.*, **2018**, *47*, 591.
6. N. Chanthaset, Y. Takahashi, Y. Haramiishi, M. Akashi, H. Ajiro*, *J. Polym. Sci. Part A: Polym. Chem.*, **2017**, *55*, 3466.
7. R. Kawatani, Y. Nishiyama, H. Kamikubo, K. Kakiuchi, H. Ajiro*, *Nanoscale Res. Lett.*, **2017**, *12*, 461.
8. F. Nurlidar, M. Kobayashi, K. Terada, T. Ando, M. Tanihara, *J Biomat Sci, Polym Ed.*, **2017**, *28*, 1480.
9. Y. Kusumastuti, Y. Shibasaki, S. Hirohara, M. Kobayashi, K. Terada, T. Ando, M. Tanihara, *J Tissue Eng Regen Med.*, **2015**, *11*, 869.

Data-driven Chemistry





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Education and Research Activities in the Laboratory

Chemoinformatics is a research area where chemical problems are tackled using tools coming from informatics. The scale of problems varies from representations of a molecule to prediction of products at a chemical plant in the field of chemical engineering. These data can be efficiently and consistently handled with the use of computers, which is the main learning goal of this laboratory. An example topic may involve developing a methodology for affinity prediction using chemical structures. Constructing soft sensors, which are prediction models for unmeasured (or hard-to-measure) plant variables, is another topic required to handle increasing data in computers. Starting from the basics of machine learning, you will learn how to curate chemistry-related data and analyze them in order to obtain useful information.

Research Themes

1. Methodology development for affinity prediction

Virtual screening is a process which selects potential candidate compounds for a specific target from a compound pool. In ligand-based approaches, the principle that similar compounds show similar biological activity holds. This principle, however, is not necessarily true when focusing on ligand-protein binding mechanisms. Methodology development for extracting key information for this phenomenon in ligand-based approaches furthers improvement of virtual screening.

2. Constructing high predictive soft sensor models using limited data sources

Soft sensors are used to predict a property (i.e. yield or concentration of chemicals). Normally, constructing high-predictive soft sensors needs constant model updating and an adequate number of data. On the other hand, obtaining hard-to-measure data costs much (this is why soft sensors are needed in the first place). Reducing measuring frequency for the property but keeping high prediction ability is an important topic in this field.

Recent Research Papers and Achievements

1. S. Shibayama, H. Kaneko, K. Funatsu, Comput. Chem. Eng. 113, 86-97, 2018
2. T. Miyao, K. Funatsu, J. Bajorath, F1000Research, 2017, 6 :1285
3. T. Miyao, H. Kaneko, K. Funatsu, J. Chem. Inf. Model., 2016, 56, 286-299

Materials Informatics

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Education and Research Activities in the Laboratory

Theoretical and computational chemistry have contributed to a better understanding of the mechanisms and efficient molecular design for catalytic systems and functional materials. For the next challenge, we aim to devise a new research area by combining theoretical chemistry and informatics technology. Recently, along with the development of automated reaction path search methods, it has become possible to obtain big chunks of data regarding reaction pathways. Based on this data, we will extract the keys to determining reactivity and catalytic ability from a different viewpoint obtained by utilizing informatics technology, including machine learning and deep learning. Our material informatics strategy is applicable not only to chemical reaction systems but also to various functional materials. By using this strategy, we aim to construct a new methodology to accelerate the development of new functional materials.

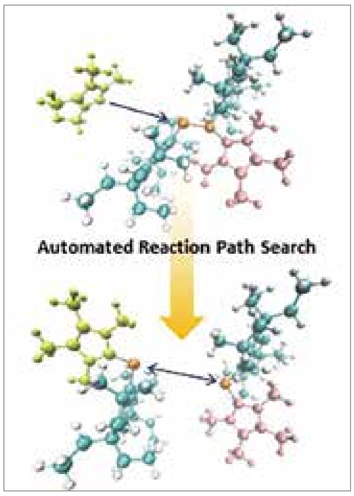


Fig. 1
Automated reaction path search by the "Global Reaction Route Mapping" strategy

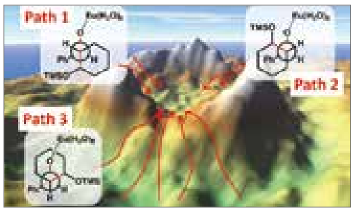


Fig. 2
Exhaustive sampling of the transition states of the stereo-determining step

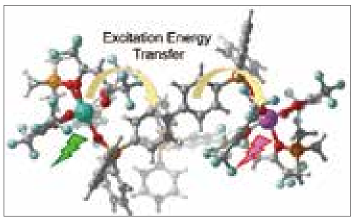


Fig. 3
Excitation energy transfer pathway of the thermometer using lanthanide luminescence

Research Themes

1. Automated reaction path search for catalytic reaction systems
   We explore the catalytic reaction pathways exhaustively by using a recently developed automated reaction path search method, called the Global Reaction Route Mapping (GRRM) strategy. This strategy gathers all the important intermediates and transition states automatically, which enables us to discuss the regio- and stereo-selectivity as well as reaction mechanism.
2. Mechanism studies and ligand design of lanthanide luminescent materials
   Lanthanide materials are widely used for display, optical fibers, in vivo probes and sensors. To understand the mechanisms and predict the luminescent properties of these materials, we study the potential energy surfaces of ground and excited states using our unique approximation method.
3. Finding the keys for efficient material design using informatics techniques
   The GRRM is very powerful tool to gather information about chemical reactions. However, it becomes difficult to analyze the calculation results because of the large amount of data in the intermediate and transition states. To analyze the data efficiently, we apply informatics techniques and aim to accelerate computational research.

Recent Research Papers and Achievements

1. A. Miyazaki, M. Hatanaka, "The Origins of the Stereoselectivity and Enantioswitch in the Rare Earth Catalyzed Michael Addition: A Computational Study", *ChemCatChem*, in press (2019).
2. M. Hatanaka, T. Wakabayashi, "Theoretical study of lanthanide-based in vivo luminescent probes for detecting hydrogen peroxide", *J. Comput. Chem.* 40, 500-506 (2019).
3. X.-F. Wei, T. Wakaki, T. Itoh, H.-L. Li, T. Yoshimura, A. Miyazaki, K. Oisaki, M. Hatanaka, Y. Shimizu, M. Kanai, "Catalytic Regio- and Enantioselective Proton Migration from Skipped Enynes to Allenes", *Chem*, 5, 585-599 (2019).
4. M. Hatanaka, A. Osawa, T. Wakabayashi, K. Morokuma, M. Hasegawa, "Computational study on the luminescence quantum yields of terbium complexes with 2,2'-bipyridine derivative ligands", *Phys. Chem. Chem. Phys.* 20, 3328-3333 (2018).

Research Instruments

Transmission Electron Microscope
(TEM)

Scanning Transmission Electron Microscope
(STEM)

Low Vacuum Scanning Electron Microscope
(LVSEM)

Nano-prober/EBAC

Scanning Probe Microscope
(SPM)

Focused Ion Beam
(FIB)

Double-focusing Mass Spectrometer

Electrospray Ionization(ESI) High Resolution Time-of-Flight Mass Spectrometer

MALDI-TOF Mass Spectrometer

High Resolution MALDI-TOF Mass Spectrometer

DART Mass Spectrometer

Wide-angle X-ray Diffractometer
(WAXD)

Single Crystal
X-ray Diffractometer and
Structure Analysis System

Small-angle
X-ray Scattering
Diffractometer
(SAXD)

600MHz
Nuclear Magnetic Resonance
(600MHz NMR)

500MHz
Nuclear Magnetic Resonance
(500MHz NMR)

400MHz Solid-state
Nuclear Magnetic Resonance
(400MHz Solid-state NMR)

Electron Spin Resonance
(ESR)

Electron Probe
MicroAnalyser
(EPMA)

Secondary
Ion Mass Spectrometer
(SIMS)

X-ray Photoelectron
Spectroscope
(ESCA)

Micro Raman
Spectrometer

Circular Dichroism
Spectropolarimeter
(CD)

Dynamic Light Scattering
Spectrometer
(DLS)

Spectroscopic Ellipsometer

Photoluminescence Lifetime Measurement System

Elemental Analysis
(EA)

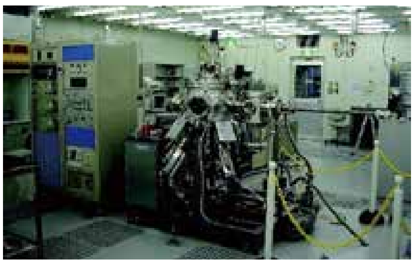
Inductively Coupled Plasma Mass Spectrometer
(ICP-MS)

Differential Scanning Calorimeter / Simultaneous Thermogravimetric Analyzer
(DSC / TG-DTA)

Photoelectron Yield Spectroscopy
(PYS)

Electron Beam Lithography Exposure

Projection Aligner



Oxide Complex Thin Film Coating Apparatus

High Purity Metal Sputter

Surface Profiler

NAIST®