Laboratory Introduction 2019

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 7,600 master's and 1,500 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 27 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 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.

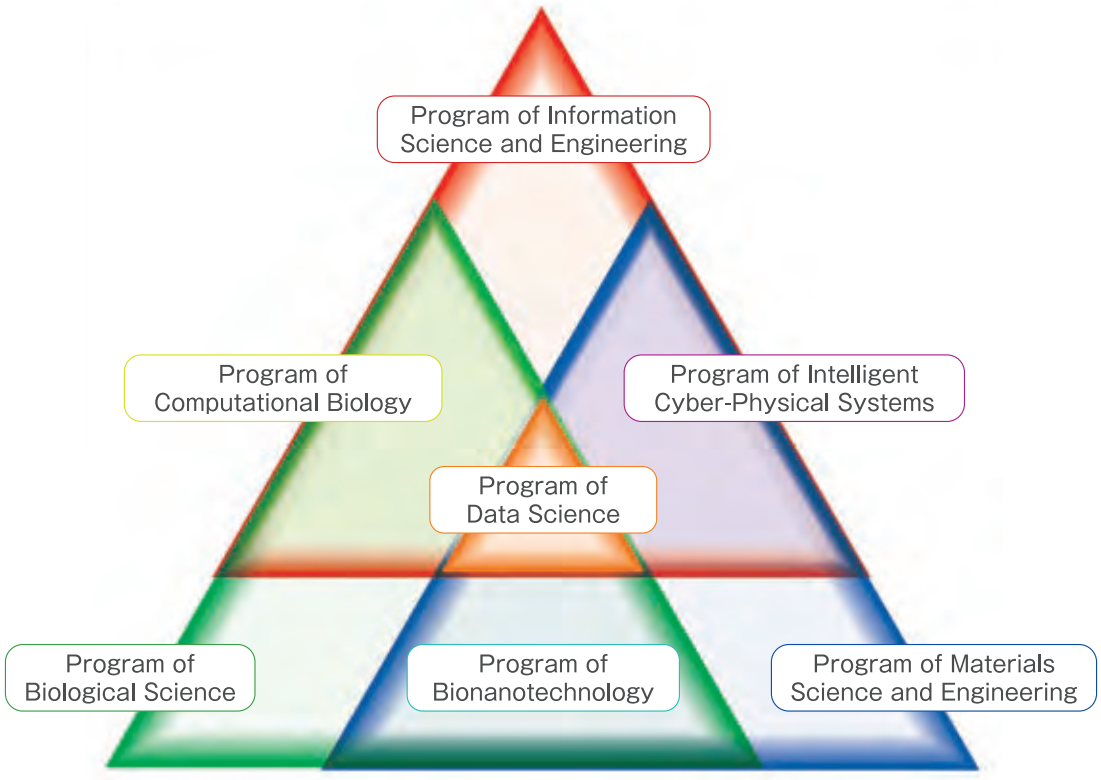
Science and technology are currently in a revolutionary era. Since its foundation, NAIST has continuously redefined the forefronts of science and technology. In order to respond flexibly to ever-evolving developments of science and technology, we have focused on producing talented researchers and engineers 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 *-out grow 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, NAIST made the transition from its previous organization structured on its leading graduate education in the fields of information, biological and materials science since 1991 to the Graduate School of Science and Technology offering seven new programs, as of April 1st, 2018.

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 cover interdisciplinary/multidisciplinary areas, 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 network 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	○	○				○	
Mobile Computing	○					○	
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	○	○				○	○
Robotics Vision	○	○				○	
Computational Neuroscience							
Network-Human Interaction							
Multilingual Knowledge Computing							
Next Generation Mobile Communications							
Optical and Vision Sensing							
Molecular Bioinformatics							
Digital Human							
Technology of Radiological Science							
Secure Software System							
Network Orchestration							
High Reliability Software System Verification							
Plant Cell Function			○	○			
Plant Developmental Signaling		○	○				
Plant Metabolic Regulation			○	○			○
Plant Growth Regulation			○	○			
Plant Stem Cell Regulation and Floral Patterning			○	○			○
Plant Physiology		○	○				○
Plant Immunity		○	○				○

LABORATORY	IS	CB	BS	BN	MS	CP	DS
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			○	○			
Microbial Molecular Genetics			○				
Systems Microbiology		○	○				○
Cell Signaling		○	○	○			
Applied Stress Microbiology			○	○			
Environmental Microbiology			○	○			
Structural Biology		○	○	○			
Structural Life Science			○	○			
Gene Regulation Research		○	○	○			○
Systems Neurobiology and Medicine		○	○	○			
Computational Biology		○	○				○
Molecular Microbiology and Genetics							
Medical Genomics		○	○				
Quantum Materials Science					○	○	
Surface and Materials Science					○		○
Photonic Device Science				○	○	○	○
Information Device Science				○	○	○	○
Synthetic Organic Chemistry				○	○		
Supramolecular Science				○	○		
Photonic Molecular Science				○	○		○
Photofunctional Organic Chemistry				○	○		
Sencing Devices					○		
Organic Electronics					○	○	
Bio-Process Engineering				○	○		○
Complex Molecular Systems				○	○		○
Biomimetic and Technomimetic Molecular Science				○	○		
Nanostructure Magnetism					○		
Precision Polymer Design and Engineering				○	○		
Data Driven Chemistry							○
Nanomaterials and Polymer Chemistry				○	○		
Materials Informatics					○		○
Mesoscopic Materials Science					○	○	
Intelligent Materials Science Laboratory							
Functional Polymer Science				○	○		
Ecomaterial Science					○	○	
Sensory Materials and Devices				○	○	○	
Advanced Functional Materials				○	○	○	
Humanophilic Innovation Project							

NAIST Website

http://www.naist.jp/en/

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Information Science

Division of Information Science

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

Biological Science

Division of Biological Science

http://bsw3.naist.jp/eng/

Materials Science

Division of Materials Science

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

Information Science

Laboratories

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Dependable System



Prof. Michiko Inoue
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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 spreads broadly across robust computing, VLSI design, CAD, testing, photovoltaic systems, security, and power converters using new wide-bandgap semiconductors.

- VLSI design for testability
- Reliable design and testing for memory
- Hardware Trojan detection
- Circuit and system mechanisms for high field reliability
- Test optimization through machine-learning-based analysis
- Circuit simulation of power converter
- Device modeling of SiC devices
- Optimization of photovoltaic system power generation
- Dependability of neuromorphic computers

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.

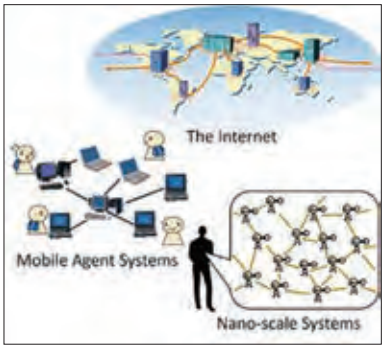

Fig. 1
Various types of distributed systems

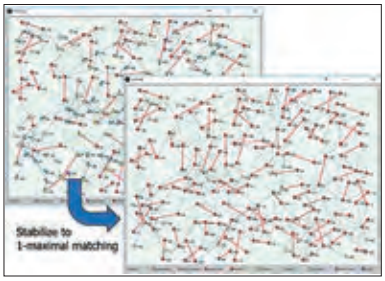

Fig. 2
Self-stabilizing algorithms

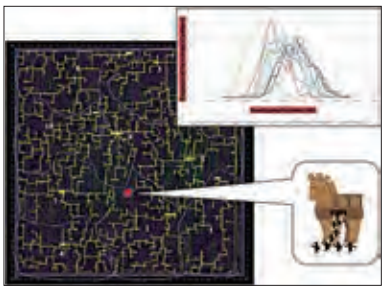

Fig. 3
Hardware Trojan detection

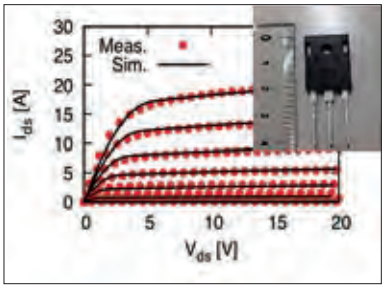

Fig. 4
Power device modeling

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:

- EMAX2: A memory-centric accelerator LSI for graph processing and stencil computation
- EMAX4: A high performance accelerator platform with heterogeneous commercial LSIs
- 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.

- Acceleration of deep learning applications such as CNN by using analog computational cores
- ACU: General purpose reconfigurable Approximate Computing Units for parallel computations
- 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

- Amorpous 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

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

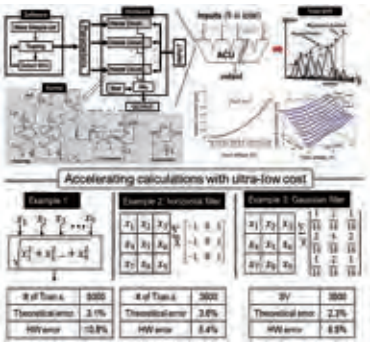

Fig. 2
Analog Accelerators

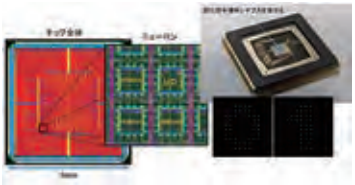

Fig. 3
Analog Neural Network LSIs

Research Areas (Cont'd)

4. Energy efficient system architecture for next generation machine learning

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

- Design methodology for next generation machine learning systems
- Spatiotemporal computation/data/communication optimization among edge and cloud computing
- Aggregation and compression for intermediate data in deep learning systems
- 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.

6. Wireless communication for IoT

Research and development of a low-cost low-power wireless communication transceiver for IoT applications. The transceiver follows IEEE 802.11ah standards. This research focuses on two layers: Physical (PHY) and Medium Access Control (MAC). The research basically has two stages: (1) software simulation on software (using Matlab C) to check the Bit Error Rate (BER) performance, throughput (data rate), etc. of systems; (2) hardware circuit design (using Verilog, Simulink, ModelSim, FPGA, etc.)

- VIT_DEC: A low complex K-best Viterbi decoder for error correction
- FEC_CONCAT: concatenating several FEC types such as LDPC, BCC, etc.
- Energy simulation of IoT sensor networks
- BER/PER simulation and hardware prototypes of the 802.11ah PHY layer
- 802.11ah MAC protocol

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.

Research Collaboration

Socio Next, Konica Minolta

Fig. 4
Blockchains for IoT

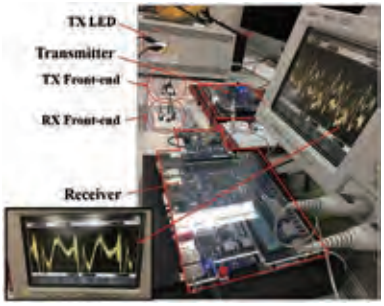

Fig. 5
Wireless Communication for IoT

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

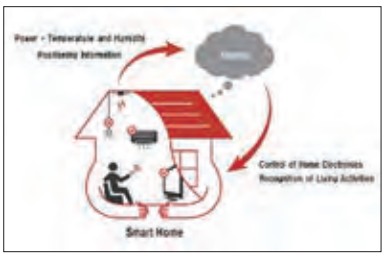

Fig. 1
Smart Home

Fig. 2
Smart Life

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.

Fig. 3
Smart City

Mobile Computing




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Research Areas

1. Distributed computing
- Video multicast streaming and grid computing via P2P overlay networks
- Fault-tolerant and autonomous adaptive algorithm design

2. Mobile computing
- Portable terminal low-power-consuming video streaming (Patent granted)
- Cooperative downloading and streaming by multiple portable terminals in ad hoc networks
- Low-power-consumption information gathering in wireless sensor networks, optimal sensor deployment in 3-dimensional environments, and underwater sensor networks
- Delay tolerant network applications
- Pedestrian and vehicle urban sensing
- Mobile data offloading

3. Ubiquitous computing
- UbiREAL, a simulator for virtual ubiquitous environments composed of sensors and consumer electronics (http://ubireal.org/)
- Consumer electronics intuitive remote controller with 3D graphic interface
- Power-saving support systems in smart homes
- Disaster emergency rescue support systems using ad hoc networks (http://etriage.jp/)

4. Intelligent Transportation Systems (ITS)
- Efficient information delivery via vehicle-to-vehicle and vehicle-to-road communication
- Navigation systems for tourists
- Traffic jam reduction via whole city traffic signal control and mass vehicle scheduling
- Pedestrian detection and alert system using directional antennas and vehicle-to-vehicle communication

Key Features

We work with a variety of research topics to realize distributed pervasive systems. Each master's course student starts his/her two year study by choosing an interesting research issue. Staff with different areas of expertise actively work with students to discover new perspectives towards each problem. We move forward through cooperation in pursuit of novel research results. Most master's course students attend domestic and international conferences to present their achievements. We encourage students to take such opportunities to let people know how important, difficult and interesting their work is.

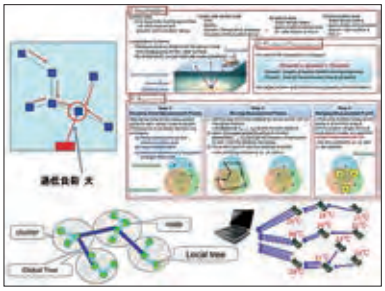

Fig. 1
Optimal sensor deployment in 3-dimensional underwater sensor networks

Fig. 2
Adjusting parameters for stereoscopic 3D video playback

Fig. 3
Cooperatively capturing and sharing video between vehicles

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 systems

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.

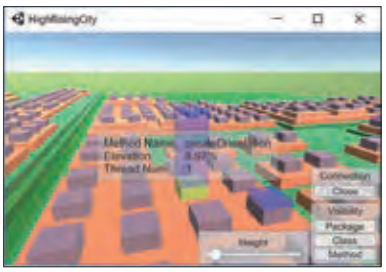

Fig. 1
Real-time Android application profiler

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 and 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

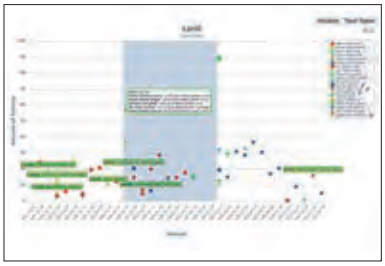
Fig. 2
Software development history visualization tool using topic extraction method

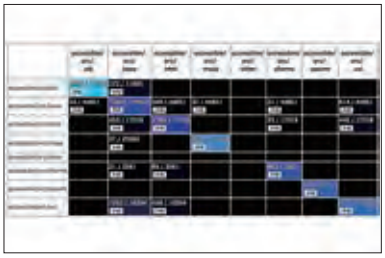
Fig. 3
Scatter plot for code clone analysis

Fig. 4
Demonstration environment for international OpenFlow network

Cyber Resilience


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Research Areas

We investigate all technical areas of resilience, from the three aspects of cybersystems, the Internet, and society. For cybersystems, security standards, malware analysis, phishing, and forensics are representative studies. Network security, DDoS, IPv6 transition, software network (SDN/NFV), and wireless networks (WLAN/LPWA) are major topics for the internet. Security standards, cybersecurity education, and UAV (or drone) are active topics for society. These are only examples of what we do in order to make everything resilient.

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.

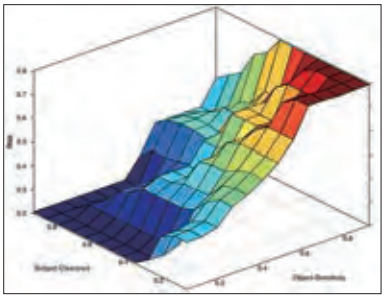

Fig. 1
Evaluation of a Risk-Adaptive Authorization Mechanism

Fig. 2
Malicious drone detection

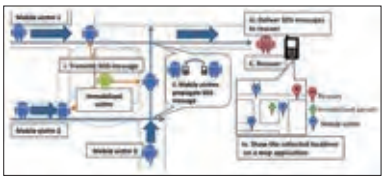

Fig. 3
Immobile victim's message propagation among visible victims' device and delivery to the rescuer

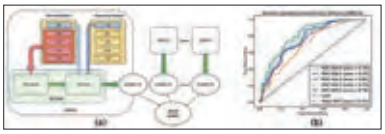

Fig. 4
4AUROC value from a pair of normal dataset – VMM-based Anomaly Detection System

Information Security Engineering

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Research Areas

1. Electromagnetic information leakage

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

2. Intentional electromagnetic interference (IEMI)

Research on the risk assessment of security degradation due to electromagnetic disturbance in hardware and also on technology for countering this phenomenon (Fig. 3).

3. Intentional modification of internal circuits

Research on risk assessment of security degradation due to malware implemented by intentionally changing the internal circuits of information equipment and also on technology 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 that 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 leakage or interfering electromagnetic waves, and for risk assessment at the design stages of equipment (Figs. 4 and 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 tolerant even to electromagnetic disturbance (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

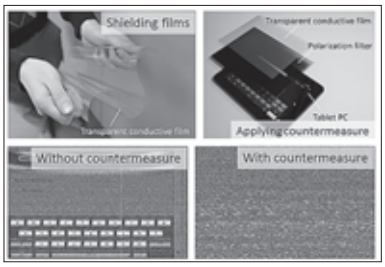

Fig. 2
Development of countermeasure to prevent EM display stealing from tablet PCs

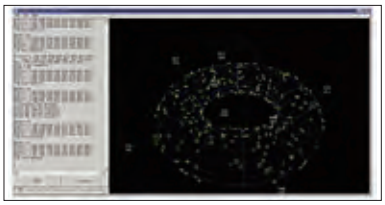

Fig. 3
Visualization of information leakage due to intentional electromagnetic interference

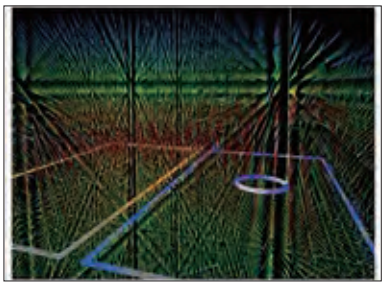

Fig. 5
Visualization of near fields disturbed during attack against a cryptographic module

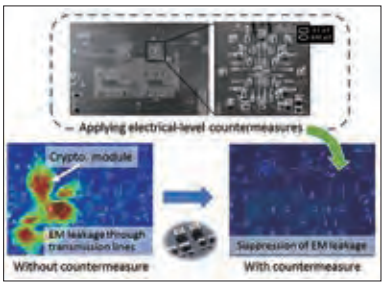

Fig. 6
Development of cost-effective countermeasures based on information leakage map

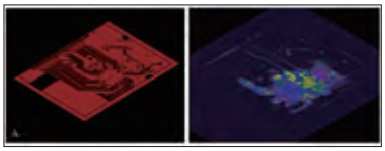

Fig. 4
Visualization of information leakage path based on large-scale EM field simulation

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) an 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 are developing higher performance and higher density with the spread of cloud computing. In particular, we study the following technologies of 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 by malware and DoS attacks. With the spreading of IoT or M2M technologies, it is important to consider 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 video data compression
- Approaches for medical use, museums, planetariums, etc.
- Application to the digital library system

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.

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

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

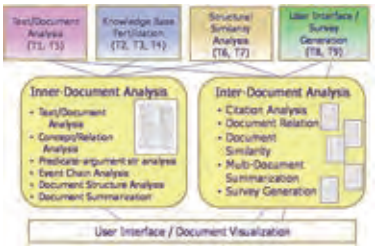

Fig. 3
Overview of scientific document analysis

Augmented Human Communication


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Assoc. Prof. Katsuhito Sudoh


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"Go Beyond the Communication Barrier" and "Next Generation Big Data Analytics"

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/)

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.

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.

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.

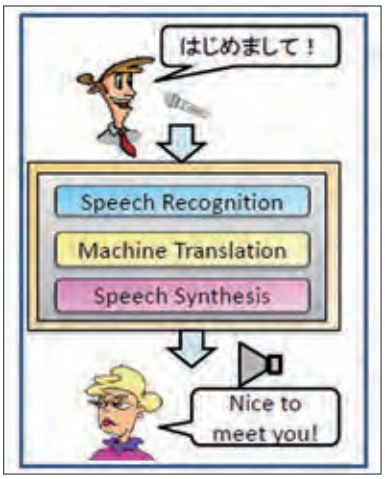

Fig. 1
Speech-to-speech translation

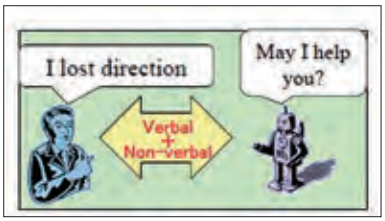

Fig. 2
A spoken dialogue system

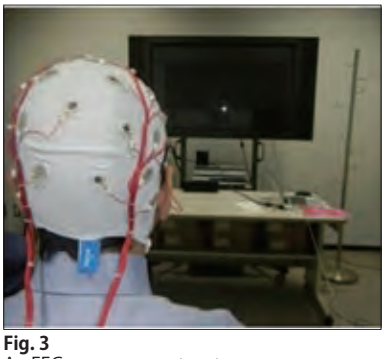

Fig. 3
An EEG measurement system

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 a 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. AR display technology
- High quality graphical rendering (Fig. 1)
- Projection-based displays (Fig. 2)
- Head-Mounted Display design
- Optical See-Through Head-Mounted Display calibration

2. AR user interface technology
- AR assistance systems based on sensing
- AR based communication between humans
- Interface technology for ubiquitous display environments
- Haptic for AR (Fig. 3)
- Sports training and healthcare
- Designing novel interaction methods for AR (Fig. 4)

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 sub-groups, 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 (Fig. 5)
- A steerable projector system
- A room-size visuo-haptic AR system
- A body scanning system (Fig. 6)

Fig. 1
High quality rendering technology for AR

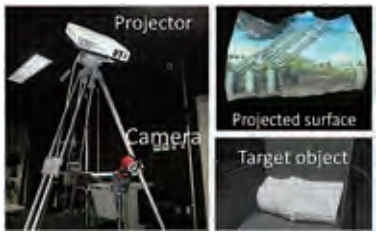

Fig. 2
Projection-based AR

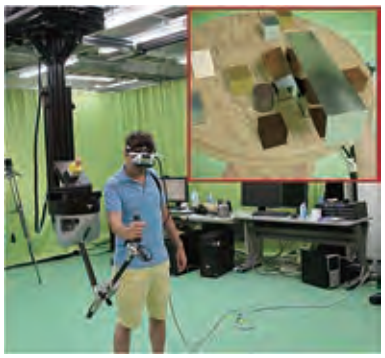

Fig. 3
Haptic feedback for AR

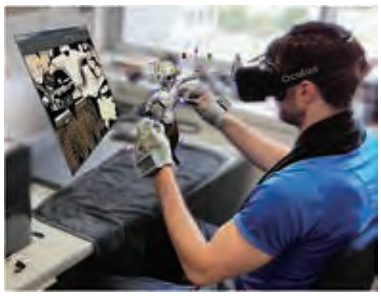

Fig. 4
Designing novel interaction methods for AR

Fig. 5
A variety of recent head-mounted display systems

Fig. 6
A photorealistic reconstruction of a human

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, and agriculture, and is performed in collaboration with other universities and companies.

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

2. Computer graphics
We are developing a new technology that supports the CG industry. Interpolating the animation frame, automatic colorization, realistic material representation, and generating a novel 3D perception are examples. (Fig. 2)

3. Computational photography
Computational photography techniques generates images that are beyond the ordinary camera limit 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, the transparent surface, scenes through fogs, hidden layers inside the objects, etc. (Fig. 3)

4. Sensing system development
Designing the measurement system that can acquire the high-dimensional light transport is an important development of our laboratory, because our goal is to correctly understand the scene based on the physical phenomena of the real world. (Fig. 4)

Key Features

The research topics in our laboratory include computer vision to understand scenes according to visual information obtained by a camera, and computer graphics to generate rich visual information for humans. We aim to realize new interfaces that enable humans and machines to interact through optical media based through cutting edge research.


Fig. 1
Estimating the material and correct 3D shape


Fig. 2
Realistic computer graphics

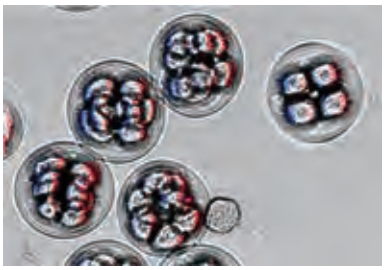
Fig. 3
Visualizing transparent shape

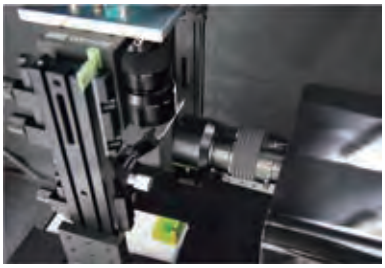
Fig. 4
Optical measurement system

Cybernetics and Reality Engineering


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Research Areas

Cybernetics is an academic field that unifies humans and systems. Reality engineering is used in the meaning of a superordinate concept bundling virtual reality (VR), augmented reality (AR), mixed reality (MR) and so on. In this laboratory, we are studying all of these, especially sensing, display and interaction technologies (Fig. 1).

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 human and environmental sensing, sensory representation, wearable computing, context awareness, machine learning, biological information processing and other technologies. In particular, by manipulating various sensations such as vision, 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.

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 drowsiness and degree of concentration from blinking and body movement
- Estimation of user's psychological state from gaze behavior
- HMD calibration and gaze tracking using corneal reflection images (Fig. 2)
- Pose estimation by wearable sensors (Fig. 3)

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 optical see-through HMD (Fig. 4)
- View expansion with a fisheye video see-through HMD
- Exaggeration of facial expressions using an eigenspace method (Fig. 5)
- Controlling interpersonal distance by a video see-through head mounted display with a depth camera (Fig. 6)
- A non-grounded and encountered-type haptic display using a drone

Fig. 1
Research fields

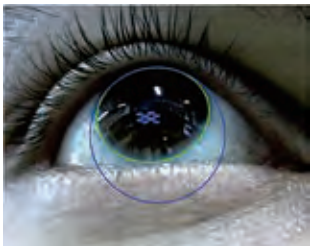

Fig. 2
HMD calibration and gaze tracking using corneal reflection images

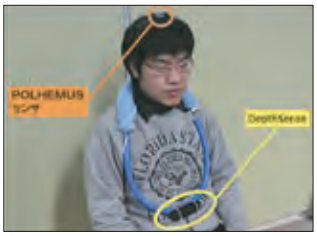

Fig. 3
Pose estimation by wearable sensors

Fig. 4
Super wide field of view optical see-through HMD

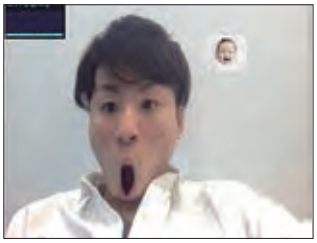

Fig. 5
Exaggeration of facial expressions using an eigenspace method

Research Areas (Cont'd)

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.

- AR pet recognizing people and the environment and having own emotions
- AR assembly support system that automatically recognizes assembly status
- AR furniture arrangement system that automatically transits to the optimal viewpoint (Fig. 7)
- AR pet with an emotion model (Fig. 8)
- Foot-based wearable interaction by a projector and a depth sensor (Fig. 9)

Research Equipment

- A variety of head mounted display (Fig. 10)

Research Grants, Collaborations, Social Services, etc. (2018)

- MEXT Grants-in-Aid (Kakenhi) (A x 2, B x 3, C x 2)
- Collaboration (TIS, CyberWalker)
- MIC Strategic Information and Communications R&D Promotion Programme (SCOPE)
- JSPS Program for Advancing Strategic International Networks to Accelerate the Circulation of Talented Researchers (CMU, JHU, TUM)
- JASSO Student Exchange Support Program (University of Oulu)
- Steering/Organizing Committee members of IEEE ISMAR, IEEE VR, APMAR, etc.

Fig. 6
Controlling interpersonal distance

Fig. 7
An AR furniture arrangement system that automatically shifts to the optimal viewpoint

Fig. 8
An AR pet with an emotion model

Fig. 9
Foot-based wearable interaction

Fig. 10
A variety of head mounted displays

Social Computing

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Research Areas

1. Medical application based on NLP

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. Besides, the uses of information and communication technology (ICT) in medical fields are said to be 10 years behind those in other fields. 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. Our goal is to promote and support the implementation of practical tools and systems into the medical industry, so that we can support physicians and medical staff in their decision-making and treatment. Additionally, we are gathering people interested in such issues to share our knowledge, so that we can facilitate communication between different specialties and have discussions between them to clarify issues to be solved, while defining necessary fundamental technologies.

2. Web mining for healthcare

Social Network Services (SNS) potentially serve as valuable information resources for various applications. We have addressed and will be addressing web-based disease surveillance systems. 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.

3. NLP as language ability test

We have investigated the relationship between cognitive ability and language ability, and are focusing on the creation of indicators to detect and screen language related diseases, such as Mild Cognitive Impairment (MCI), dementia, Autistic Spectrum Disorder (ASD), and many others. Recent medical studies on early detection methods (such as blood testing and detailed memory testing) have improved detection capabilities, but such methods are physically and/or mentally invasive. Instead, we are aiming for low or even non-invasive methods. Natural Language Processing (NLP)-based analytical methods have the potential of detecting cognitive ability deterioration quickly and easily.

Key Features

Our laboratory has been recently established to develop a new academic field, which can oversee the entire range from basic science to real-world applications. 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. Fig. 3 displays an example of our targets, involving medical fields, clinical fields, psychology, architecture, and much more.

Join us, and let's break new ground together.

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

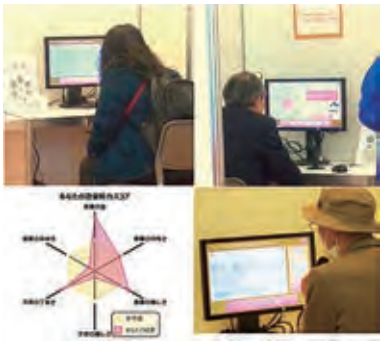

Fig. 2
We built a collection of elder's narratives.

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 realtime (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)

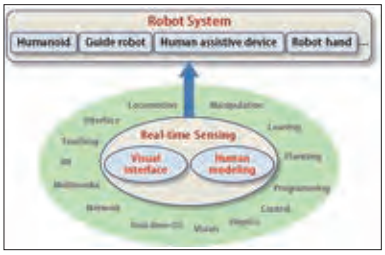

Fig. 1
Overview of our research


Fig. 2
Research area A: Visual interface

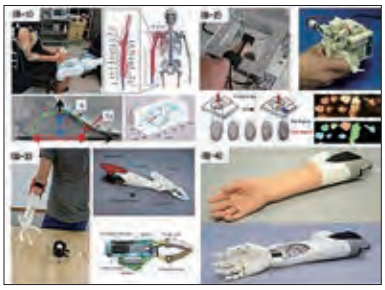
Fig. 3
Research area B: Human modeling


Fig. 4
Research area C: 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.

・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.

・Distributed control

We conduct theoretical and experimental studies on distributed LED lighting systems. We also study power demand-supply balance control for distributed generation network systems composed of multiple generators such as gas-engine and photovoltaic generators.

2. Machine learning for robotics

・Motor skill learning for humanoid robots

We are developing novel methods that enable robots to learn complex motor skills (e.g., biped walking, putting on T-shirts and clothing assistance) by optimal control and reinforcement learning.

・Truly autonomous robots

The ultimate goal of this research is to develop next generation autonomous robots that autonomously find multiple objectives, select what the robot wishes to achieve from among them, and acquire dynamic motions to achieve the selected objective.

・Constructing practical myoelectric interfaces for robot control

We construct myoelectric interfaces robust to postural changes, sweating, and muscular fatigue, using surface electromyograms (sEMG) *via* modern machine learning methods.

Key Features

We welcome motivated students from various fields including mechanical/electrical engineering and 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.

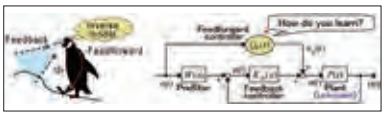
Fig.1
Feedback error learning control

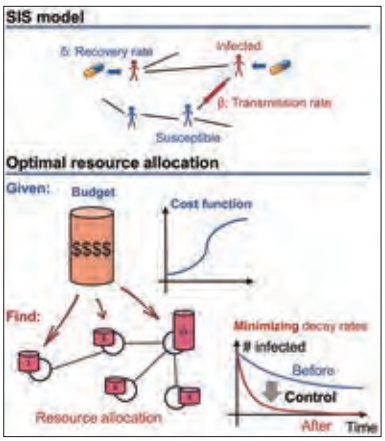

Fig. 2
Quantized control of a mechanical system

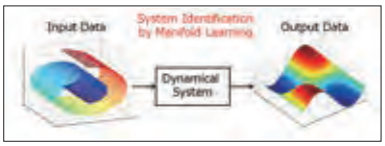

Fig. 3
System identification by manifold learning


Fig. 4
Motor skill learning by enforcement learning

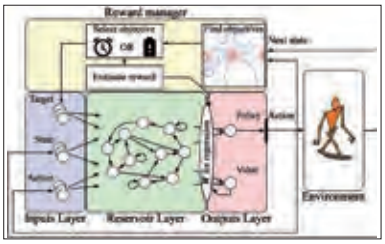
Fig. 5
Distributed lighting system and distributed generation network system

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

4. Algorithms for large-scale data processing
- Hadoop distributed processing systems/frameworks/clusters
- Task scheduling and file systems for cloud
- Online algorithms
- Large-scale graph and network algorithms
- Advanced data structure

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.

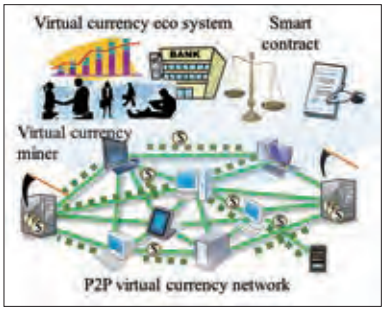

Fig. 1
Distributed virtual currency and smart contract network

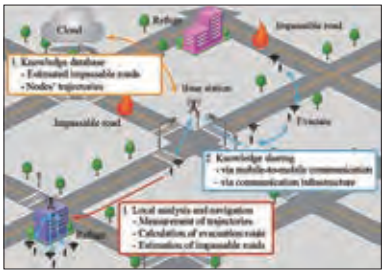

Fig. 2
Hazard-area estimation and evacuation guidance using trajectories of mobile terminals

Fig. 3
Cognitive radio

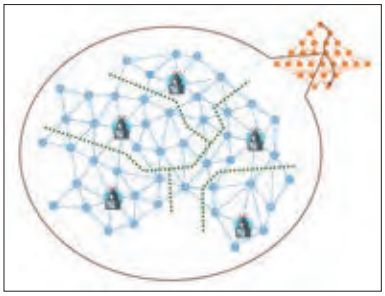

Fig. 4
Large-scale graph algorithms

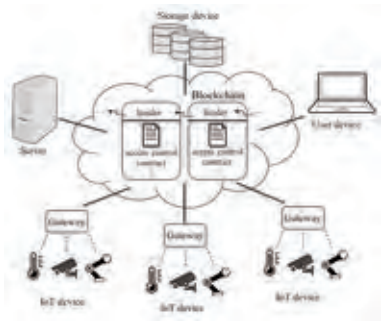

Fig. 5
Blockchain-based access control

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).

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

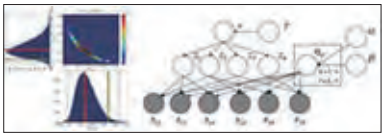

Fig. 1
Mathematical models in computation

Fig. 2
Mathematical models in science

Fig. 3
Mathematical models in engineering

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 machine learning including deep learning, computational simulation, and augmented reality to create knowledge and foster innovation in the field of computational biomedicine. We currently have four main research areas (Fig. 1):

・Virtualized human anatomy (Fig. 2)
We create models of human anatomy for each subject from 3D biomedical images. By integrating 3D image analysis and machine learning, we also create models of variability in anatomical shape and image appearance throughout a population. We call these computational anatomy models. We also 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 virtualized human anatomy and statistical predictions from 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 virtualized human anatomy. Our goal is to develop "intelligence" in surgery based on statistical learning and computational simulations. This will enable the prediction of changing conditions of patients during operations in order to perform optimal surgical procedures.

・Postoperative assessment (Fig. 5)
Medical treatment quality assurance requires proper assessment of the surgical outcomes. We develop ways to quantitatively evaluate the motion of patients who have had surgery on their skeletal structure, 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.

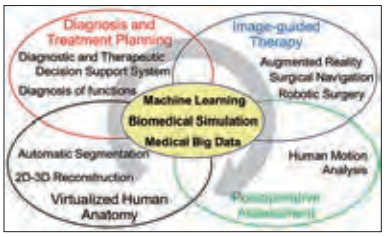

Fig. 1
Research areas in our lab

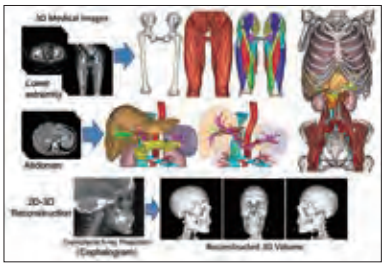

Fig. 2
Virtualized human anatomy

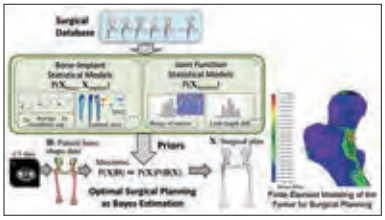

Fig. 3
Diagnosis and treatment planning

Fig. 4
Image-guided therapy

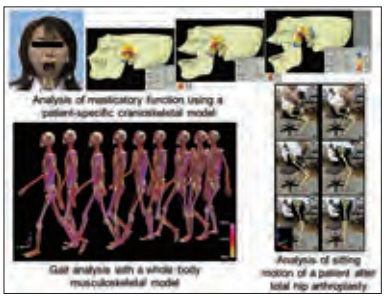

Fig. 5
Postoperative assessment

Computational Systems Biology


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Affiliate Prof.
Hidehiro Iida


Assoc. Prof.
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Assoc. Prof.
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Research Areas

1. Systems biology

Biology has been significantly advanced by reductive approaches. 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. We study these approaches by modeling several biological systems to elucidate cellular mechanisms. In this field, we keep incorporating state-of-the-art data modeling/manipulating techniques such as deep learning techniques to better our understanding.

2. Network analysis

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) to extract highly connected clusters.

3. Transcriptomes

A transcriptome is defined as a total set of transcripts in an organism. To elucidate transcriptome networks, we study transcriptome analyses using microarrays and new generation sequencers with the use of BL-SOM and novel methods.

4. Metabolomes

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.

5. Biomedical informatics

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.

- A computer-aided diagnosis assistance system for medical images
- A computer-aided educational system for radiologist training

6. Health informatics

By incorporation of the strengths of the wearable/unconstrained sensing techniques and state-of-the-art information technology such as deep learning techniques, we are developing health monitoring systems for daily use.

- A wearable deep body thermometer monitoring system
- A cuffless blood pressure monitoring system
- A heart health monitoring system based on contactless electrocardiograph

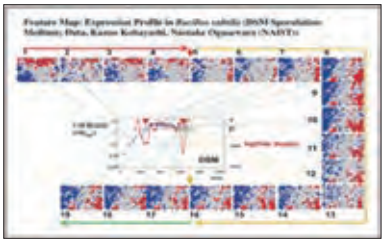

Fig. 1
Feature map: expression profile in *Bacillus subtilis*

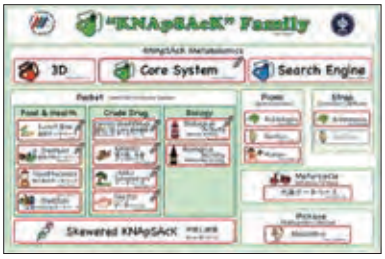

Fig. 2
Main page of "KNApSAcK Family"
(http://kanaya.naist.jp/KNApSAcK_Family/)

Research Areas (Cont'd)

7. Medical imaging

A cardiac MRI in clinical imaging for coronary arteries and decision support technology for motion compensation has been developed. Diffusion Tensor MRI (DT-MRI) and tractography techniques are being investigated for the analysis of human brain cognitive functions.

8. Volume visualization in biology

We have developed a high speed volume rendering method for visualizing high resolution microscopic 3D images such as two-photon microscopy techniques.

- Volume graphics
- Neuron tracing
- Microscope image analysis

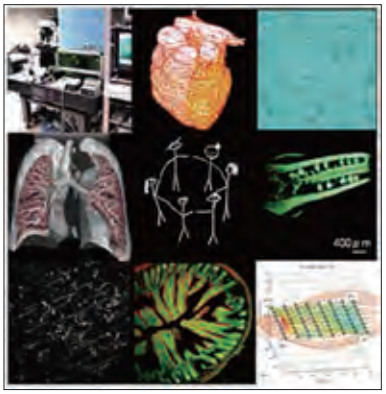

Fig. 3
Examples of biomedical imaging taken by various imaging schemes

Key Features

We work in an interdisciplinary field between information technology and bio-medical science. Our aim is to integrate knowledge in biology, medical science and healthcare. Students study a wide variety of technologies, such as signal and image processing, data-analysis and machine learning. We have been developing techniques to understand gene function and disease mechanisms.

Our laboratory members, who have come from a wide variety of backgrounds, aim to elucidate the robustness and diversity of biological systems through chemo- and bio-informatics. In our lab, students study a wide range of areas and attain broad perspectives. We always discuss important issues regarding research to enhance each other's knowledge.

Robotics Vision

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Assist. Prof.
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Research Areas

1. Assistive technology for disabled/older people

We focus on exploring computer vision possibilities for better enhancing robotics systems or wearable devices for better serving and helping disabled/older people, not just for safety purposes, but also for improving their quality of life and better engagement in society. We start with helping blind people "see" the attitudes and emotions of people who they are talking with using wearable cameras. Future research will cover other practical needs of different groups of people.

Fig. 1
Assistive technology for disabled/older people

2. First-person vision with wearable cameras and mobile computing

First-person vision lets computers/robots see what we see, in exactly the same viewpoints and potentially the same time spans, and therefore it may be a better way to understand human vision, interest, intension, and behavior. We use wearable cameras and light mobile computing devices (e.g. smartphones) to capture and process this data, and communicate with other resources. This research is expected to better solve many traditional computer vision problems including segmentation, detection, tracking and recognition, and also further many new applications.

Fig. 2
First-person vision with wearable cameras and mobile computing

3. Scalable visual recognition for dealing with large amounts of data

As the big data era comes, we are able to share and access large amounts of data, and connect countless amounts of sensors and devices. For computer vision, the critical research of visual recognition also goes from small-scale restricted data to large-scale real-world problems. We work on a representative task called large-scale across-camera person re-identification (with many cameras and people) to support large-scale real video surveillance systems. At the same time, we also look into more general problems such as image categorization and object recognition for investigating generic scalable visual recognition models. The research is also beneficial for our research on first-person vision.

Fig. 3
Scalable visual recognition for dealing with large amounts of data

Key Features

As one of the first two international collaborative laboratories established in NAIST, this laboratory is different from any other research or collaborative lab that you can find in the Division of Information Science. It is unique in:

- Being led by Prof. Takeo Kanade and closely collaborating with Carnegie Mellon University
- Gathering active and talented researchers with very diverse nationalities
- Targeting innovative research with global and long-lasting impact
- Effectively connecting NAIST researchers and international peers

Computational Neuroscience (ATR International)

Prof.
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Assoc. Prof.
Jun Morimoto

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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.

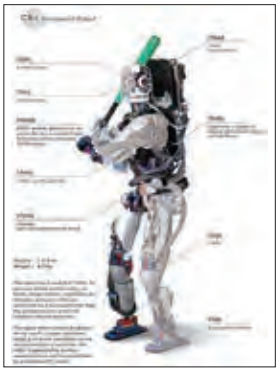

Fig. 1
Machine intelligence for humanoid robot control

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

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

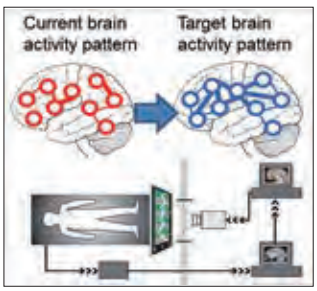

Fig. 5
Neurofeedback

Fig. 6
Computational model of decision-making

Fig. 7
Adaptive shared control for BMI exoskeleton robots

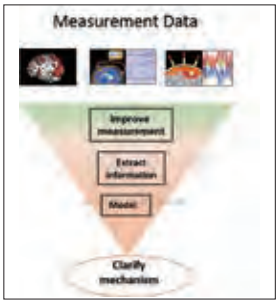

Fig. 4
Measurement data

Network-Human Interaction (Advanced Technology Research Laboratories, Panasonic Corporation)

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Takeo Azuma

Prof.
Yoshikuni Sato

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Research Areas

1. **Long-term care support with a combination of sensing technology and artificial intelligence**

2. **Improvement of recognition performance by multimodal input**

Key Features

With the recent aging of the population, bedridden prevention and reduction of nursing care burden are becoming social issues. Meanwhile, in the field of nursing care, the introduction of sensors to monitor the state of the elderly and electronic nursing care systems are being accepted. In this laboratory, we will conduct research aiming at realizing effective and efficient nursing care support based on prediction of elderly persons' states using sensing and artificial intelligence in cooperation with nursing care and medical facilities. Specifically, we will make efforts such as (1) quantitative evaluation of exercise and cognitive functions of the elderly from sensor information, and (2) preparation and improvement of care plans based on the grasping of the conditions of elderly people. Through these technologies, we aim to realize support to quantitatively grasp the state of elderly people who have traditionally relied on human senses, and to derive methods suitable for the maintenance and improvement of nursing care levels.

In relation to the recent remarkable progress in deep learning, multimodal input is expected to further enhance its performance. As an example of multimodal input, we are trying to improve recognition performance by inputting depth information in addition to two-dimensional images. Specifically, according to the framework of computational photography, depth information is acquired at the same time as two-dimensional image input by a light field camera, a multi-view camera, a multi-pinhole camera or the like, and these inputs are recognized and processed in order to improve recognition performance.

Multilingual Knowledge Computing

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Assoc. Prof.
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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.

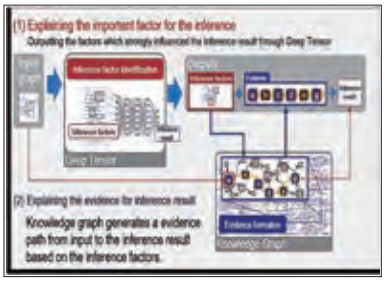

Fig. 1

Key Features

Our laboratory belongs to Fujitsu Laboratories Limited, located in Kawasaki City, Kanagawa Prefecture. 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.
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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)

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Yoshihisa Ijiri

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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 and camera calibration

2. **Computer vision**
Object detection/recognition, character recognition and 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. Interacting protein molecule simulation using atomic coordinates
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

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.

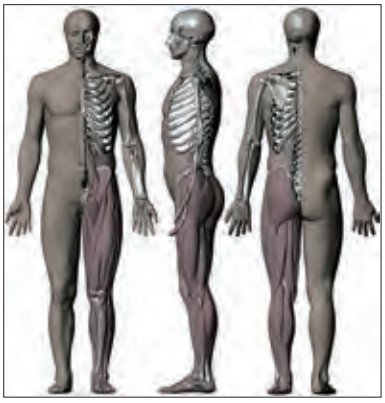

Fig. 1
Digital human modeling based on anatomy and measurement

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

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

Technology of Radiological Science (National Cerebral and Cardiovascular Center Research Institute)

Prof.
Takahiro Higuchi

Assoc. Prof.
Kazuhiro Koshino

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Research Areas

We develop image-based diagnostic tools to investigate the pathophysiology of diseases in the brain, heart and other organs (kidney, lungs, liver, pancreas, etc.), using nuclear medicine and molecular imaging techniques with PET (Positron Emission Tomography), SPECT (Single Photon Emission Computed Tomography) and MRI (Magnetic Resonance Imaging).

We aim to develop advanced high performance imaging techniques/devices and new tracers and image processing programs based on computer science, to quantitatively assess physiological functions in clinical application and pre-clinical animal studies.

1. Clinical diagnostic imaging
- Rapid and quantitative PET systems for cerebral ischemia
- Quantitative and standardized SPECT imaging
- MRI and data analysis for morphometry and neuroimaging

2. Molecular imaging for pre-clinical studies
- New therapy and drug evaluation
- Development of animal models of diseases

3. Key technology development for diagnostic imaging
- Image processing: Image reconstruction, motion correction, image registration
- Image analysis: Quantitative assessment of physiological functions (perfusion and metabolism, tissue viability, inflammation and receptor binding), modeling of input function for completely non-invasive imaging and morphometry on MRI images
- Tracer development for physiological functions

Key Features

Our laboratory is in a national center for advanced and specialized medical care and research, with scientific researchers working in a variety of fields such as computer science, physics, medicine, pharmaceutics and chemistry. We collaborate with clinical doctors, medical equipment companies, pharmaceutical companies, and domestic and international researchers.

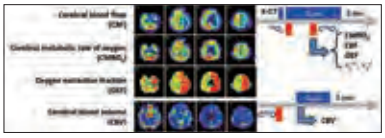

Fig. 1
Functional images obtained by our rapid and quantitative PET system.

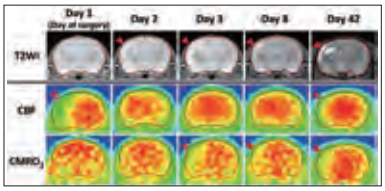

Fig. 2
Longitudinal observation of ischemic rat using a low invasive and hybrid PET and MRI imaging system.

Fig. 3
Imaging equipment dedicated to small animals in our laboratory.

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

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
- Networking for cloud computing
- Software Defined Networking（SDN）

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 technologiesfor large-scale network infrastructure
- Management of wide-area and virtualized networks
- Multi-domain networks
- Advanced traffic engineering

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

■URL:http://isw3.naist.jp/Contents/Research/cl-12-en.html ■Mail: { masa-katahira, ishihama }@is.naist.jp

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.

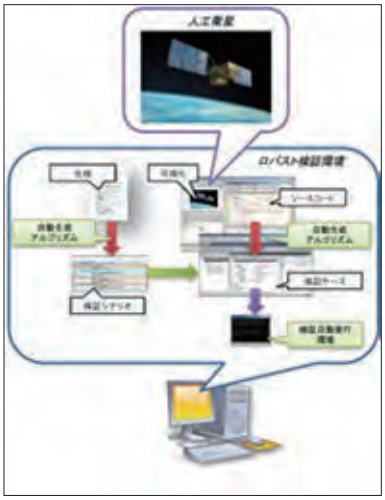


Fig. 1
The concept of robustness verification and automated environments

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

Fig. 3
JAXA Tsukuba Space Center

Cutting-edge Research Facilities

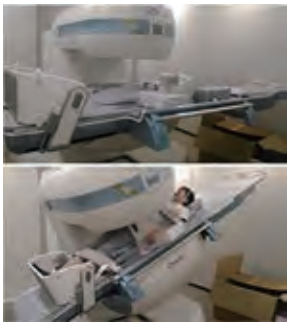
Baxter
(Intelligent System Control Lab)

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)

Experimental equipment for IoT acceleration
(Computing Architecture Lab)

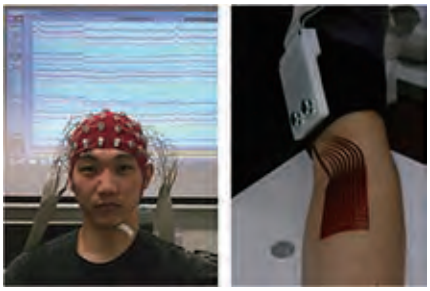
FPGA systems for large-scale applications
(Computing Architecture Lab)

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

Bigdata processing system
(Augmented Human Communication Lab)

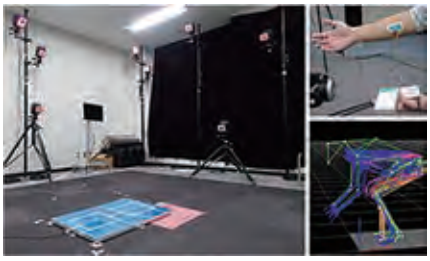
Glasses-type eye tracking system
(Mathematical Informatics Lab)

Table-mounted eyetracking system
(Mathematical Informatics Lab)



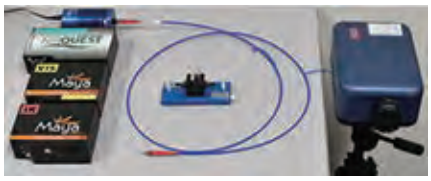
Multi-channel EEG/sEMG system
(Mathematical Informatics Lab)

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)

Large-scale simulation environment
(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

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Plant Cell Function




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Outline of Research and Education

We conduct extensive research, from basic to applied, concerning the cellular function, signal transduction and regulation of gene expression in higher-plants, making effective use of molecular genetics and imaging technology on Arabidopsis thaliana, tobacco, and tomatoes.

Major Research Topics

1. Dynamic reorganization of microtubule cytoskeletons in response to environmental stimuli and during plant growth

- Pattern formation of bio-polymer networks
- Regulators of microtubule dynamics
- Left-right asymmetry establishment in cell shape
- Stress-induced reorganization of microtubule arrays

2. Natural product biosynthesis and regulation

- Transcriptional regulation of defense metabolism
- Jasmonate signaling
- Identification of novel enzymes and transporters
- Plant metabolic engineering

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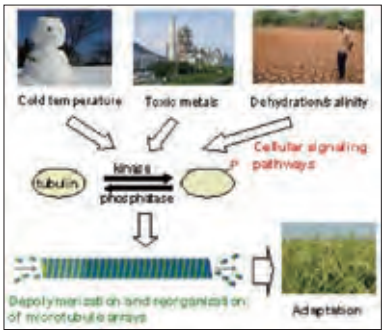

Fig. 1
Environmental stresses remodel the microtubule cytoskeleton by phosphorylation of tubulin subunits.

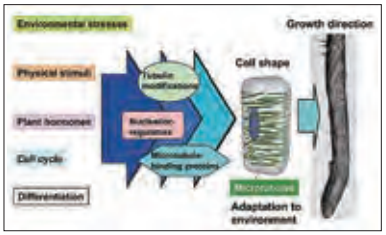

Fig. 2
The plant microtubule cytoskeleton remodels in response to developmental and environmental signals, and controls plant cell shape.

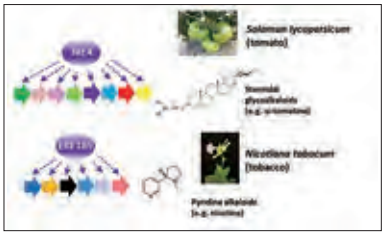

Fig. 3
Conserved transcription factors, JRE4 and ERF189, required for induced production of defense natural products in tobacco and tomatoes.

Plant Developmental Signaling


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Outline of Research and Education

Microscopic observation of plant sections allows one to realize the beautiful patterns of cells, each with a different shape and size (Fig.1). These cells are not only diverse in appearance, but are functionally specialized to play specific roles in each organ. These tissue patterns are produced from a single cell, the zygote. One of the most fundamental questions in plant developmental biology is how complex plant structures are derived from a single cell.

Our research group is trying to identify basic principles of plant development using model plant species. We aim to understand both intercellular and intracellular signal transduction pathways underlying the pattern formation and cell differentiation of roots and embryos, as well as cell reprogramming that triggers embryogenesis.

Major Research Topics

1. Cell-cell communication in tissue patterning

Due to the presence of rigid cell walls, plant cells are generally unable to alter their direction or position in the organ primordia. Therefore, timing and orientation of cell divisions, as well as cell fates, are determined by interpreting the positional cues of surrounding cells. Such developmental mechanisms rely on the presence of intimate cell-cell communication pathways. Our recent studies have revealed the presence of novel signaling pathways that allow regulatory molecules such as transcription factors and microRNAs to travel from cell to cell (Fig. 2). We are currently focusing on the generality of such cell-cell signaling pathway in root and embryo patterning.

2. Cell reprogramming and pattern formation during embryogenesis and germ cell formation

Embryogenesis of the Brassica family, including the model plant Arabidopsis, proceeds in a highly coordinated manner (Fig. 3). Similar to innovation of iPS cells, activation of an embryo- and germ cell-specific developmental program is initiated only after the reprogramming of somatic cells to the embryonic status. We have recently discovered a key reprogramming factor in Arabidopsis and bryophytes, and are currently investigating their mechanism of action. We are also constructing a translational approach that utilizes this reprogramming factor to propagate useful plant lines without waiting for the transition to the reproductive growth phase.

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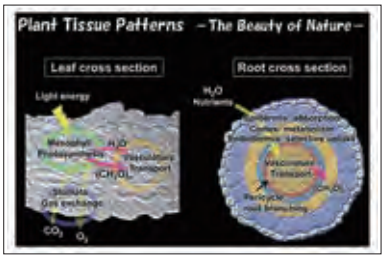

Fig. 1
(Left) In leaves, specialized cell types such as mesophyll, stomata, and vascular cells, are spatially arranged to maximize photosynthetic ability. (Right) Root tissues are organized into a concentric pattern that facilitates water and nutrient uptake, as well as their metabolism and translocation.

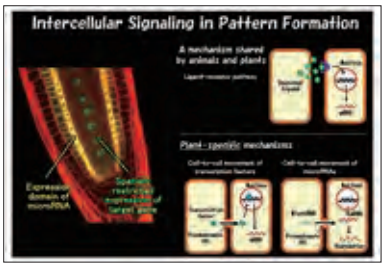

Fig. 2
Plant cells are connected with a cytoplasmic continuum termed plasmodesmata (PD). PD allows passage of regulatory molecules, such as transcription factors and small RNAs, thereby serving as a channel to transmit developmental signals.

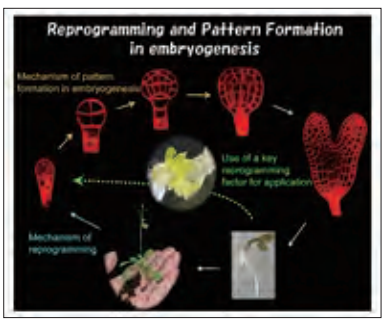

Fig. 3
Pattern formation in embryogenesis is triggered by cell reprogramming and proceeds in a highly coordinated manner. We study the mechanisms underlying embryonic pattern formation and reprogramming, as well as application of the reprogramming factors for efficient propagation of useful plants.

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 of higher plants

In order to transcribe foreign genes in plant cells more effectively, we are studying the factors that contribute to transgene-silencing, the relationship between chromatin/nucleosome structure around the promoter region and gene expression, identification and characterization of matrix the attachment regions, and improvement of transcriptional terminator regions.

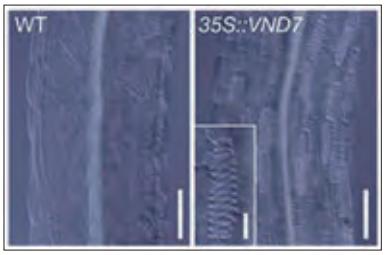

Fig. 1
VND7 acts as a key regulator of xylem vessel differentiation. Overexpression of VND7 induces transdifferentiation of epidermal cells into xylem vessel elements with spiral structures of secondary wall thickening (arrows) in hypocotyl. Bar=100 μ m.

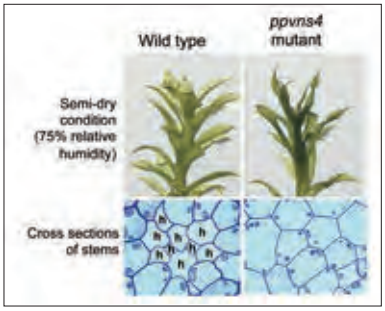

Fig. 2
Moss *Physcomitrella patens ppvns* mutants, a knock out mutant for one of VND-homologous genes, show the malformation of hydroids (h) in stems, thus leading to decreased water transport activity accompanied wilting phenotype under semi-dry conditions.

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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 are studying DNA polyploidization and stem cells that support sustained plant growth. We focus on the molecular mechanisms of DNA polyploidization that increases cell volume and organ size, and how plants preserve stem cells. We aim to understand the regulatory system underlying continuous plant growth, and to develop technologies to increase plant biomass and food production.

Major Research Topics

1. Mechanisms of induction of DNA polyploidization

In many plant species, cells start endoreplication after the cessation of cell division. This is an alternative type of the cell cycle, lacking mitosis and cytokinesis. As a result, DNA content in individual cells is elevated. The resultant DNA polyploidization causes enlargement of individual cells and organs (Fig. 1); thus, it greatly contributes to plant biomass production. However, the induction mechanisms of endoreplication have remained largely unknown. We recently found that regulation of chromatin structure plays essential roles in triggering endoreplication. Therefore, we are studying the epigenetic control of endoreplication, and developing technologies to induce DNA polyploidization, which may increase crop yield and woody biomass production (Fig. 2).

2. Maintenance of plant stem cells

The sequoia, the largest tree on the earth, has a life span of more than 3,000 years. It continues to grow throughout its lifespan, indicating that pluripotent stem cells function for a long time period under changing environmental conditions. How plants generate, proliferate, and maintain stem cells in tissues, however, remains elusive. We are studying the mechanisms of how the stem cell niche is regenerated through reprogramming, and how stem cells are replenished when they are lost owing to environmental stresses (Fig. 3). Our study will shed light on the pluripotency of stem cells and the process of tissue regeneration.

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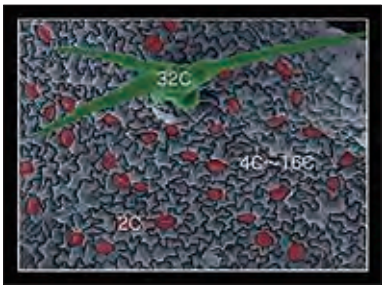

Fig. 1
Epidermal cells of an *Arabidopsis leaf.*
Each cell type has different DNA ploidy; stomatal cells (2C, red), trichomes (32C, green), and the other cell types (4C-16C). As the DNA content is elevated by endoreplication, the cells are enlarged.

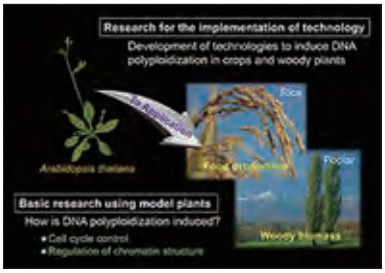

Fig. 2
Development of technologies to increase the yield of crops and woody biomass by induction of DNA polyploidization.

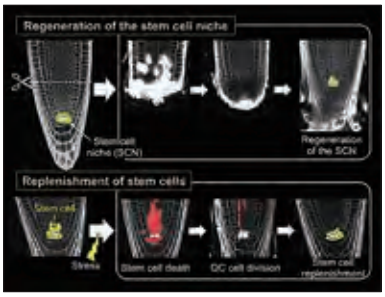

Fig. 3
Regeneration of stem cells in roots.
(Top) When the stem cell niche is removed by cutting the root tip, plants regenerate the stem cell niche through reprogramming. (Bottom) Environmental stress causes stem cell death, which is followed by division of quiescent center (QC) cells (white cells) to replenish 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*.

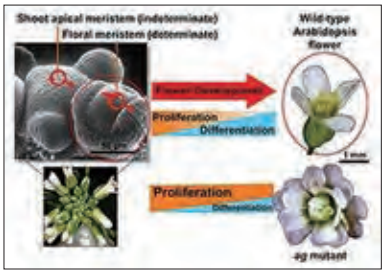

Fig. 1
Arabidopsis flower development
In flower development, the stem cell activities in the floral meristem are terminated (determinate), while the shoot apical meristem continues to grow.

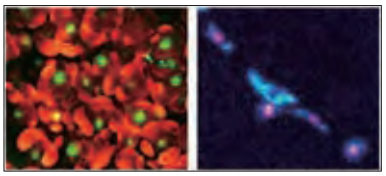

Fig. 2
Imaging of key transcription factors in floral meristems (left) and a differentiated myrosin cell (right).

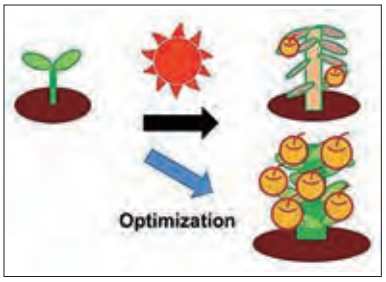

Fig. 3
Plant growth optimization
By revealing the mechanisms of floral stem cell regulation and environmental responses, we will develop a molecular basis for plant growth optimization for higher crop yield.

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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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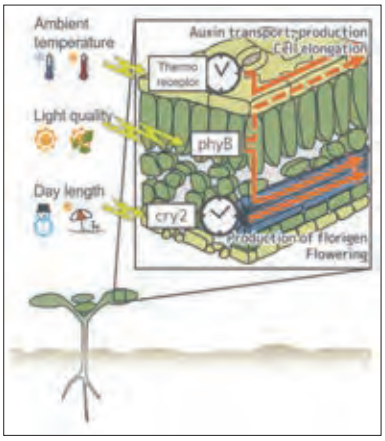

Fig. 1
Tissue-specific environmental responses through cell-type specific clocks. We found circadian clock functionality in specific tissues is required for specific physiological responses.

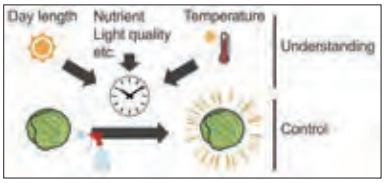

Fig. 2
Understanding clock-mediated flowering mechanisms allows for the manipulation of crop flowering times.

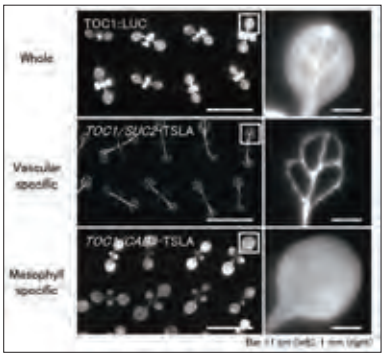

Fig. 3
Tissue-specific luciferase assay. Many clock genes including *TOC1* are expressed ubiquitously (top). Our tech- nique enables us to measure tissue-specific dynamics of *TOC1* (middle and bottom), and this analysis shows tissue-specific circadian rhythms.

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 disregard or tolerate the presence of these plant-inhabiting microbes at non-damaging levels, despite an elaborate innate 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 (DAMPs) generated upon pathogen challenge in addition to microbial signals (MAMPs). 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 functional interactions between MAMP and DAMP receptors, defense-related transcriptional reprogramming and infection strategies of pathogenic and endophytic microbes. Our studies are expected to reveal important insight into the principles with which plant-microbe associations and environmental factors influence each other, 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. **Modulation of plant immunity in fluctuating environments**
3. **Endophytic and pathogenic microbes in plants**
4. **Plant-associated microbiomes**
5. **Criptional reprogramming and priming in plant immunity**

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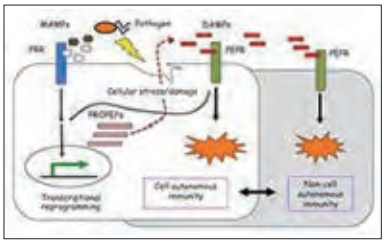

Fig. 1
Layered MAMP- and DAMP-receptor signaling provides an important basis for pathogen resistance.

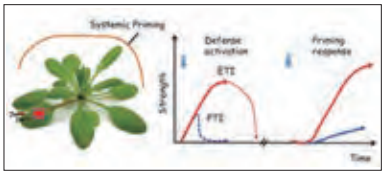

Fig. 2
Transcriptional reprogramming and priming in plant immunity. Following the initial defense activation (left arrow) upon recognition of pathogen-associated patterns (PTI) or effectors (ETI), defense-related genes become primed to allow faster and/or greater responses upon second stimulation (right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

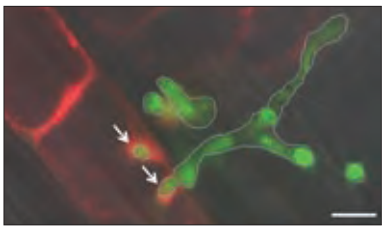

Fig. 3
Root colonization of endophyte Colletotrichum tofieldiae (Ct). Confocal microscope images of Ct constitutively expressing cytoplasmic GFP (green, labeled by dotted lines) and A. thaliana expressing VAMP722-mRFP (Red). Intracellular hyphae inside a root cortical cell are enveloped by PIP2A-mCherry-labeled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

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.

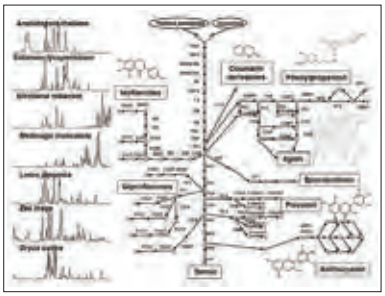

Fig. 1
Metabolic network of plant polyphenolic biosynthesis and their chemical diversity between plant species.

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.

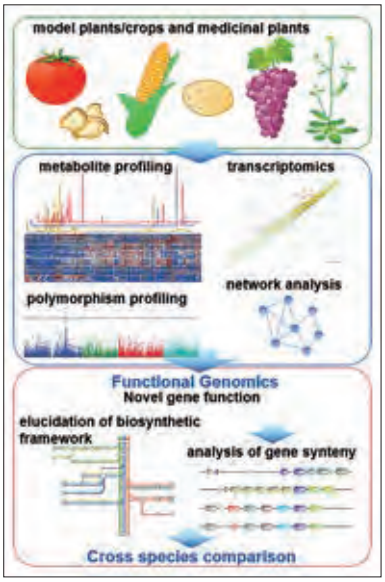

Fig. 2
Omics-based translational analysis using model plants and crops.

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.

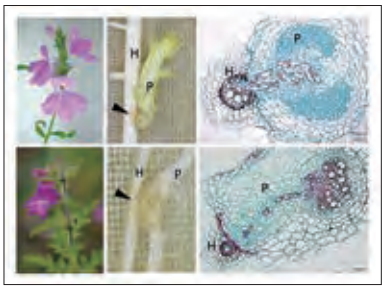

Fig. 2
Obligate parasite Striga hermonthica (upper panels) and facultative parasite *Phtheirospermum japonicum* (lower panels). Photos of flowers (left), host invading parasitic plant root (middle) and cross section of haustorium (right). H: host, P: parasite. Arrowheads indicate haustoria.

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 strigolactone, and its haustorium formation is induced by derivatives of cell wall lignin. However, some of our ***P. japonicum*** mutants do not respond to the known cell wall-derived chemicals, but are still able to form haustoria and parasitize hosts. We are trying to identify novel haustorium inducing compounds.

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.

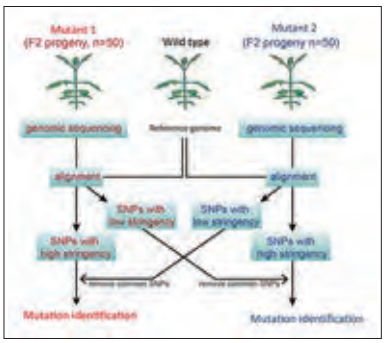

Fig. 3
Identification of the mutant causal genes using a next-generation sequencer.

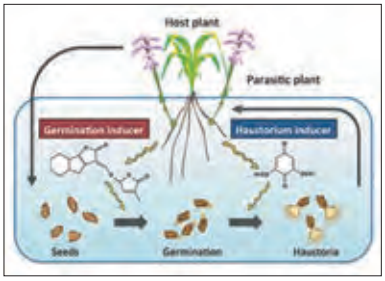

Fig. 4
Chemical communication between host and parasitic plants.

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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. **Molecular mechanisms of self-renewal, differentiation, and migration of neural stem cells**
3. **Monoclonal antibodies against orphan adhesion GPCRs involved in tumorigenesis and neural function**
4. **Regulation of primary cilia formation and function in mammalian cells**
5. **Molecular mechanisms of epithelial morphogenesis and cancer**

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

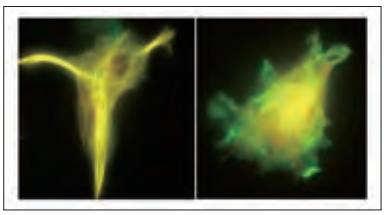

Fig. 2
G protein/PKA signal-regulated dynamics of a cytoskeleton in neuronal progenitor cells

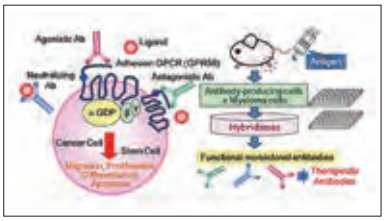

Fig. 3
Monoclonal antibody against orphan GPCR as a tool for signal analysis

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 of the immune system, and named it programmed death-1 (PD-1), hoping that it somehow played 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, researchers including T. Honjo (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. Unfortunately, however, the roles of PD-1 in self-nonself discrimination of the immune system still remain elusive. We conduct our research in the fields of immunology and molecular genetics to identify these roles.

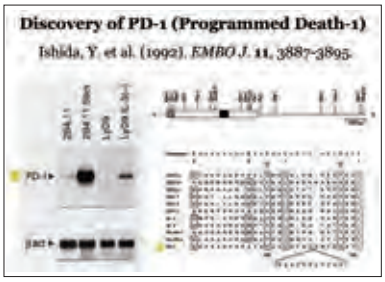

Fig. 1
Some people say that PD-1 was discovered only by chance.

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).

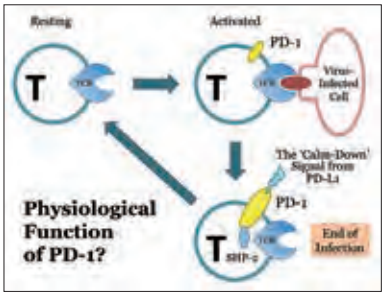

Fig. 2
PD-1 negatively regulates excessive immune reactions.

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.

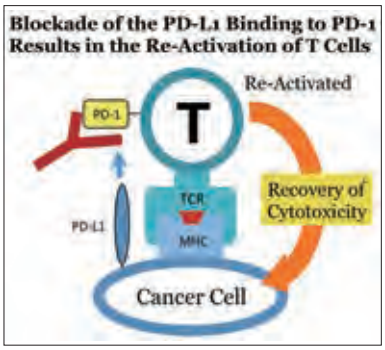

Fig. 3
Cancer immunotherapy using the anti-PD-1 blocking antibody.

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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

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.

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.

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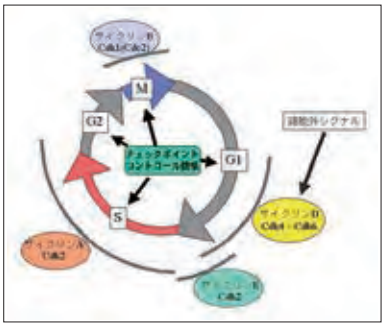

Fig. 1
Cell cycle and cyclin/Cdk complexes.

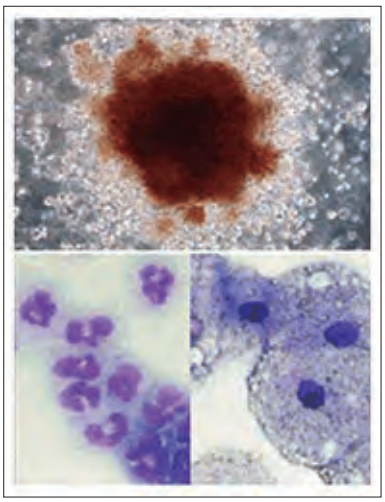

Fig. 2
A group of erythrocytes and leukocytes (upper), neutrophils (lower left) and macrophages (lower right), which were induced to differentiate from ES cells in vitro.

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

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.

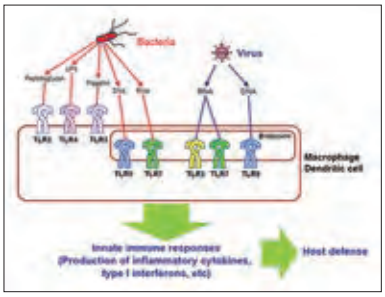

Fig. 1
Recognition of microbial components by Toll-like receptors (TLRs).

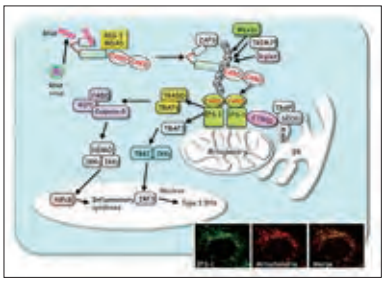

Fig. 2
Signaling pathways through RLRs, cytosolic sensors for RNA viruses.

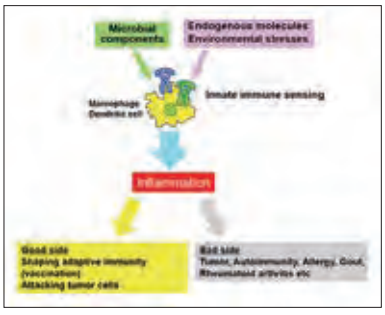

Fig. 3
Recognition of non-infection agents by innate immunity and its relevant in diseases.

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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. 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.

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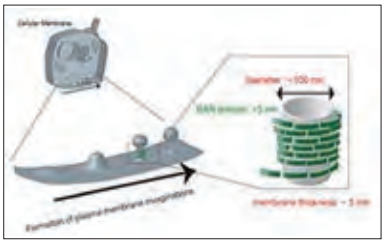

Fig. 1
Location of BAR domain functions in cells. The BAR domains function as polymers at submicron-scale invaginations, such as clathrin-coated pits and caveolae, as well as in protrusions, including filopodia and lamellipodia. The typical scales for clathrin-coated pits and caveolae are 100-200 nm 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.

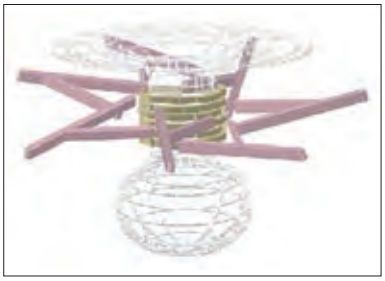

Fig. 2
Wire-frame model of the clathrin-coated pit. The BAR proteins are shown in yellow, and the actin cytoskeleton is shown in magenta. The membrane is in wire-frame. The actin filaments are thought to be finely organized on the nano-scale membrane invaginations of the clathrin coated pits.

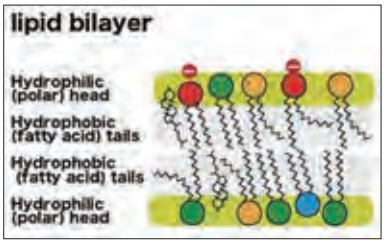

Fig. 3
Schematic diagram of the cellular membrane. Each lipid molecule consists of one hydrophilic head and two hydrophobic fatty-acid tails. There are varieties of combinations of the head, such as serine, ethanolamine, etc., and various saturated and unsaturated fatty acids, such as palmitic acid (saturated),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

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.

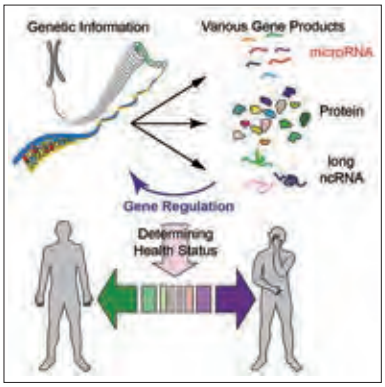

Fig. 1
Gene regulatory networks and their importance in normal development and physiology.

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).

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.

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.

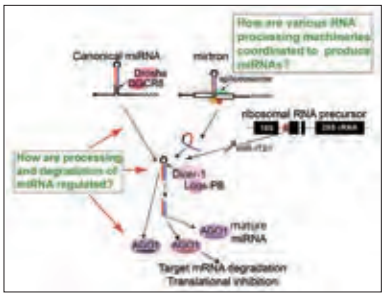

Fig. 2
microRNA processing pathway.

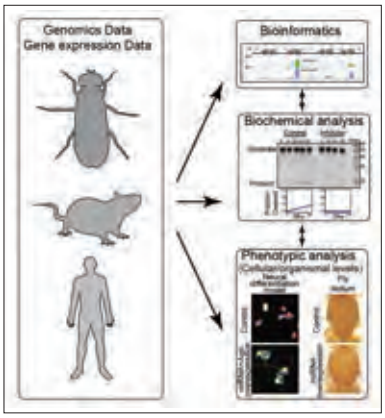

Fig. 3
Outline of research strategies.

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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.

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.

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.

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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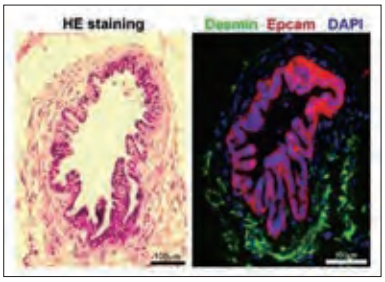

Fig. 1
Stomach tissue differentiated from mouse ES cells *in vitro* by 3D culture method. (Left) HE staining of the differentiated stomach organoid (day 56). (Right) Immunofluorescent staining of stomach organoid with Epcam antibody (red), Desmin antibody (green), and DAPI (blue) for epidermis, mesenchyme,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

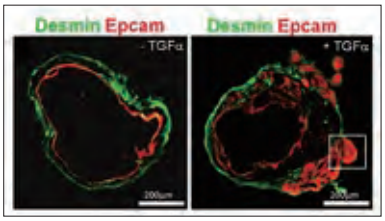

Fig. 2
A stomach disease model using *in vitro* differentiation method. (Left) Healthy control model. (Right) Ménétrier's disease model with massive gastric folds. This disease model can be generated by addition of TGF-α after day 28 of *in vitro* differentiation.

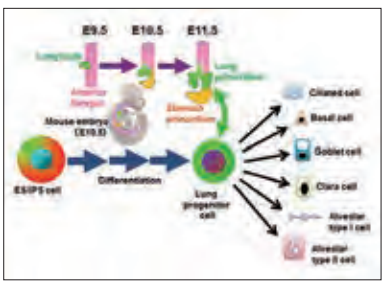

Fig. 3
During lung development, lung progenitor cells are generated in lung buds and can differentiate into various functional epithelial cells of the lung. These lung progenitor cells can be differentiated from pluripotent stem cells *in vitro.*

Developmental Biomedical Science

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Outline of Research and Education

One of the central questions of classical developmental biology is to understand how a limited number of genes produce a diversity of cell types. The developing central nervous system is composed of a number of different cell types, and we seek to elucidate the molecular mechanisms leading to this diversity by employing chick and mouse embryos as model organisms.

We are also interested in the homeostasis of functional neurons. We have been utilising model mice that have been shown to develop particular inherited retinal diseases, and propose novel therapeutics for these related dystrophies.

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

Major Research Topics

1. Transition of the intrinsic characteristics of neural progenitor cells during development and pattern formation

The neural tube is the embryonic tissue of the central nervous system, where a number of functional neurons are produced and precisely assigned. This pattern formation is mainly governed by a handful of extracellular molecules including BMP, Wnt and Sonic Hedgehog (Shh). These molecules are collectively called morphogens, and induce different neuronal subtypes in a graded manner. On the other hand, the intrinsic characteristics of neural progenitor cells change over time, and respond to the same inducing molecules differently. We are particularly interested in the relationship between the inducing activity and the cells' mode of response.

2. Detailed analysis of the Shh signalling pathway

There are many unique aspects of the intracellular signaling pathway induced by Shh. For instance, the Shh pathway is introduced into the cells through the protrusive structure on the surface of cells, called cilium. In addition, Shh target genes start to be expressed only after 6 hours, which is much slower than other signaling pathways. We attempt to identify the proteins that regulate the speed of the signal transduction, and further to reveal the relationship between the speed of the signal and the patterning of the neural tube.

3. Homeostasis of functional cells

How functional cells are maintained is also an important question. We recently demonstrated that the membrane protein Prominin-1 (Prom1) has an essential role in maintaining established photoreceptor cells, and that Prom1-deficient mice show severe retinal degeneration. In addition, our recent study suggests that Prom1 is involved in many more dystrophies in a number of other organs. We therefore aim to propose a novel therapeutic method by analysing these model mice.

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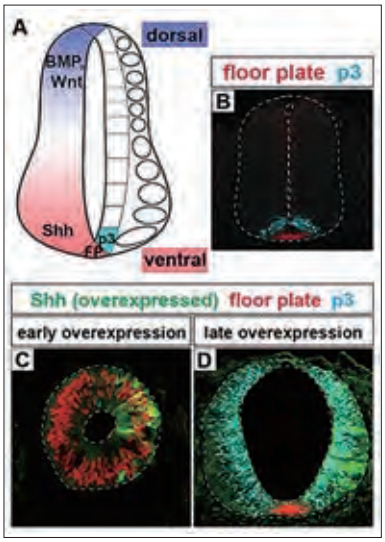

Fig. 1
(A) The cross section of the trunk neural tube. The neural tube is divided into at least 13 subdomains along the dorsal-ventral axis. (B) The floor plate and the p3 interneuron progenitor domains can be separated by immunohistochemistry. (C, D) The phenotype of the neural tube upon forced expression of Shh. The neural progenitor cells tend to differentiate into the floor plate cells (C), while they differentiate into the p3 cells when Shh is overexpressed at the late stage (D). This finding suggests that the neural progenitor cells respond to the same signal differently over time.

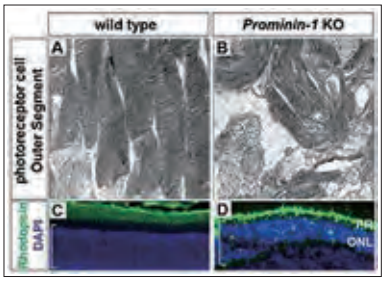

Fig. 2
Eye phenotype in the Prominin-1 (Prom1) deficient mice. The outer segments are degenerated (A, B), and Rhodopsin proteins are misplaced in the photoreceptor cells of the Prom1-knockout eyes (C, D).

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 (Fig. 1 and 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 injected 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).

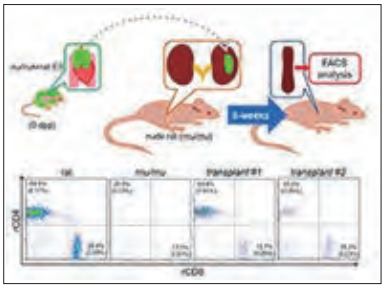

Fig. 3
The function of rat thymus in xenogeneic chimera
When rat thymus from a xenogeneic chimera was transplanted into renal subcutaneous tissues of nu/nu rat, rat T-cells were educated.

Microbial Molecular Genetics

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Outline of Research and Education

At our laboratory, we have been studying how genetic information is precisely transmitted from parent cells to daughter cells and, conversely, how mutation is induced by inaccurate transmission of genetic information. To approach these questions, it is important to understand molecular mechanisms of genomic stability and molecular functions of DNA replication machineries. We also put strong emphasis on the international education of young students who are highly interested in basic issues related to DNA transaction (3R: Replication, Repair and Recombination) and the molecular mechanisms of biological evolution. We want to assist our laboratory members in becoming globally active individuals who act and think independently.

Major Research Topics

1. Mechanisms of spontaneous mutation and its suppression (Fig. 1)
- Onset of DNA replication errors and their repair (References 1 & 4)
- Generation of DNA damage due to oxygen radicals and its repair (References 1 & 3)
- Spontaneous mutation induced by cellular growth environment

2. Molecular mechanisms for genetic stability (Fig. 2)
- Control mechanisms for genetic recombination
- Roles of DNA damage response and cell cycle checkpoint control (Reference 7)

3. Molecular functions of DNA replication machineries (Fig. 3)
- Biochemical activities of DNA polymerases (References 2, 5, 8, 10-12 &14)
- Replication fork arrest and its recovery processes (Reference 10)
- Dynamics of replication fork movement on genomes (References 6, 9,13, & 15)

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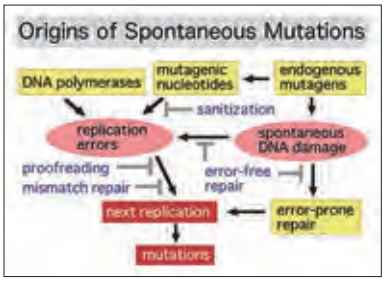

Fig. 1
Multiple mechanisms suppress mutations. However, spontaneous DNA lesions serve as major causes of mutation under normal growth conditions.

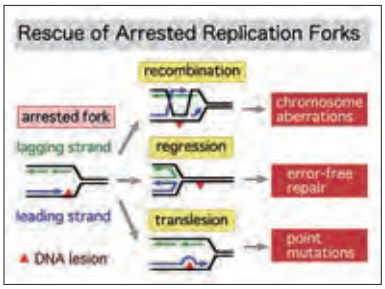

Fig. 2
When DNA replication occurs without repair of DNA lesions, replication fork progression is inhibited, potentially leading to genetic instability. Mechanisms to rescue arrested forks include recombination, regression of forks and translesion DNA synthesis.

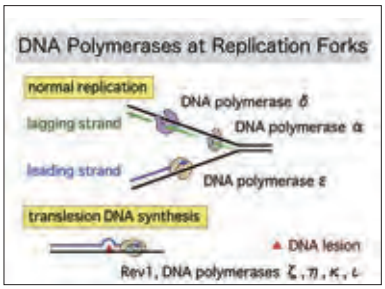

Fig. 3
Multiple DNA polymerases ordinarily work together for efficient DNA replication, thereby suppressing replication errors. Special DNA polymerases work in both eukaryote and bacteria to copy damaged DNA (translesion DNA synthesis).

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.

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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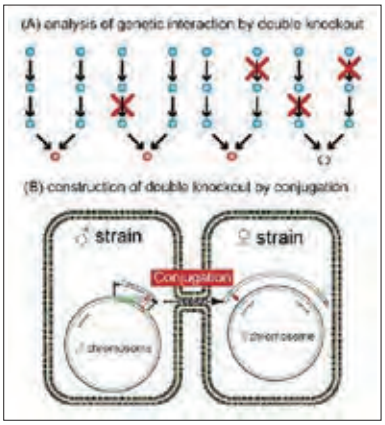

Fig. 1
(A) The concept of synthetic lethal/sickness analysis: Red circles represent essential metabolites for cells. If cells have redundant routes to produce essential metabolites, double deletion methods may identify such redundant steps of genes (enzymes). (B) The conjugation method to generate double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

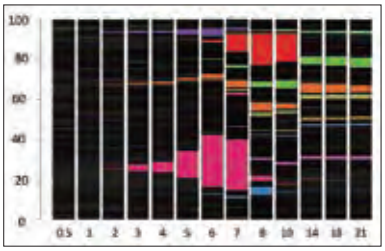

Fig. 2
The X axis shows time points of sampling and the Y axis represents population ration of all deletion strains.

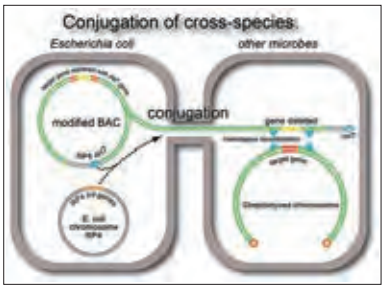

Fig. 3
Wide host-range incP family plasmid RP4 can deliver large DNA fragment by cross-species conjugation.

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.

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.

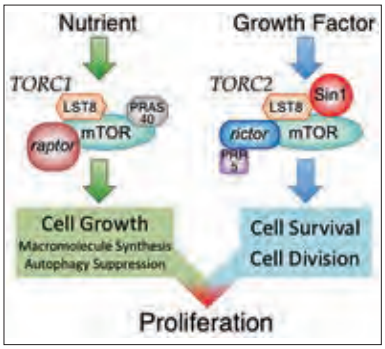

Fig. 1
The TORC1 and TORC2 signaling pathways integrate multiple stimuli to control cell proliferation.

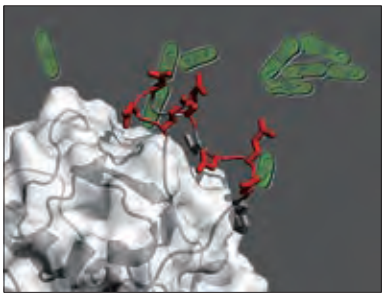

Fig. 2
The structure of the TORC2 subunit Sin1, whose function has been elucidated through genetic analysis in fission yeast (background).

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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.

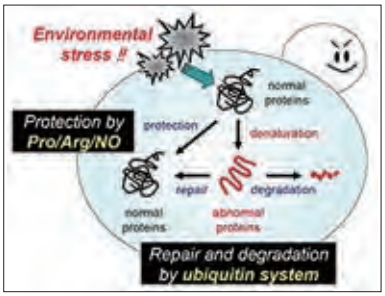

Fig. 1
Novel stress-tolerant mechanisms in *S. cerevisiae.*

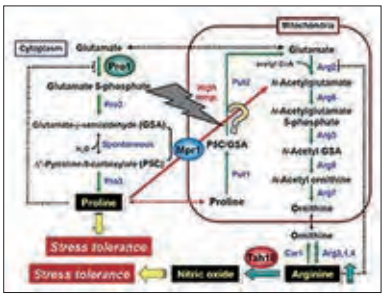

Fig. 2
Metabolic pathway of proline and arginine in *S. cerevisiae.*

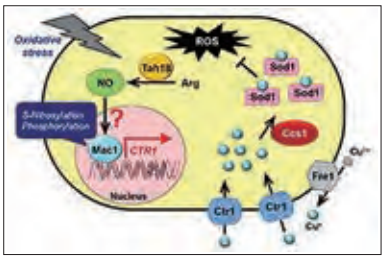

Fig. 3
NO-mediated antioxidative mechanism in *S. cerevisiae.*

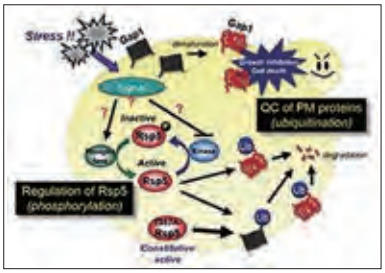

Fig. 4
Ubiquitin system under stress conditions in *S. cerevisiae.*

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Stress response and tolerance in yeast *Saccharomyces cerevisiae*

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ER stress and UPR

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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 fermentation

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.

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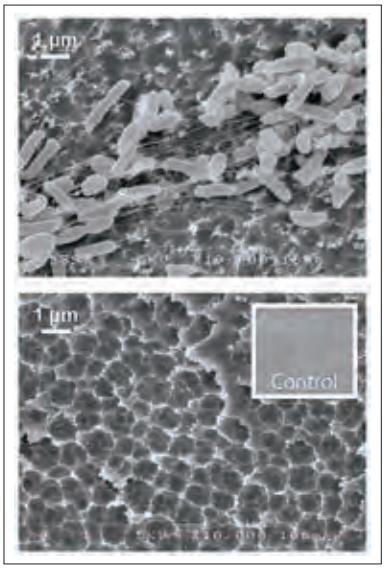

Fig. 1
A scanning electron microscopic image of *I. sakaiensis* cells grown on PET film (upper). The degraded PET film surface after washing out the adherent cells (lower).

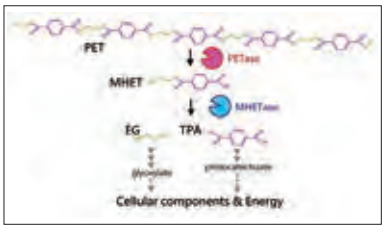

Fig. 2
Predicted PET metabolism by *I. sakaiensis*. Two unique enzymes, PETase and MHETase, are able to efficiently convert PET into its monomers.

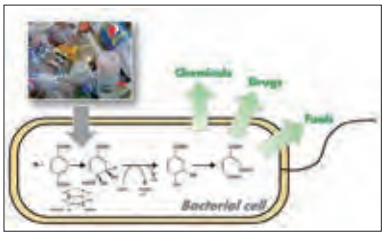

Fig. 3
Metabolic engineering to ferment waste plastic bottles into valued compounds.

Structural Biology

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Outline of Research and Education

Proteins are folded into specific three dimensional (3D) structures, which are essential for imparting functions such as molecular recognition and catalysis. Without precise knowledge of their 3D-structures, we are unable to understand how proteins execute their respective molecular functions and, in turn, unable to rationally design inhibitors or drugs. Thus, the experimental determination of protein 3D-structures represents the hallmark of structural biology. Structural biology in our laboratory is performed using X-ray crystallography to determine the 3D-structures of proteins and molecular complexes at atomic resolution, and biochemical/biophysical analyses are performed to delineate the mechanisms by which proteins function at the atomic, molecular, and cellular levels.

Our overall goal is to contribute to the understanding of the nature of life. Our long-term objective is to understand the molecular functions of proteins and other biological macromolecules and their complexes in terms of molecular structures. Our efforts are directed towards defining the manner by which protein interactions and 3D-structures determine specificity and how structural changes enable functional switches in living cells.

We expect our lab to be an international one and we welcome international students to study protein structures and functions with us.

Major Research Topics

1. Structural molecular medicine
Drug-target proteins and other proteins important in medical research, such as cancer, teratogenesis and infectious diseases

2. Structural cell biology
G proteins, and their regulators and effectors, which play central roles in intracellular signal transduction regulating cell motility, adhesion and morphogenesis

3. Structural molecular biology
Enzyme engineering in biodegradable plastic synthesis

4. Structural plant biology
Proteins that play pivotal roles in plant hormone signaling, such as receptors and master regulators

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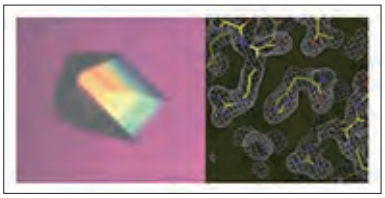

Fig. 1
A crystal of histidine protein phosphatase (left), crystallized in our laboratory and part of its electron density map at 1.9 Å resolution obtained from X-ray crystal structure analysis.

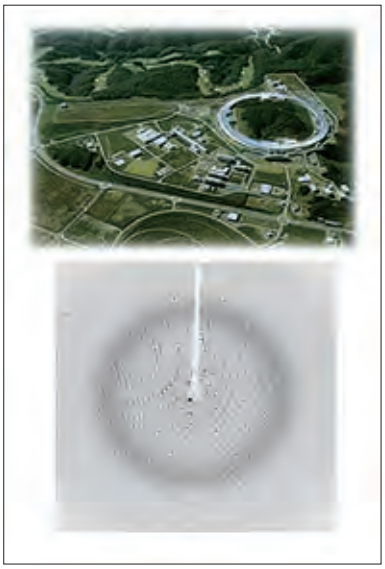

Fig. 2
The SPring-8 synchrotron radiation facilities at Harima, Hyogo. We perform X-ray intensity data collection at SPring-8 for structure.

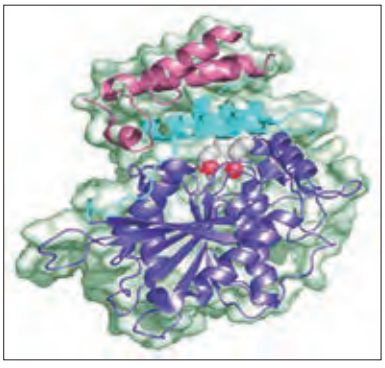

Fig. 3
The ternary complex of gibberellin (space-filled model in white and red)-bound receptor GID1 (blue and cyan) trapping its downstream effector protein DELLA protein (pink) from our recent Nature article [5].

Structural Life Science

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Outline of Research and Education

Various proteins in the cell are involved in a variety of fundamental biological phenomena. To understand living organisms, it is crucial to know how these proteins function in the cell. Unfortunately, most molecular mechanisms of proteins are still unclear. Our laboratory studies various proteins and, in particular, we are focusing on how proteins, small molecules, and ions are transported across membranes. This transportation is mediated by dedicated membrane proteins including transporters, channels, and translocases (Fig. 1, 2). Some of these membrane proteins can be drug targets. Our laboratory conducts fundamental research by structural biological analyses in combination with 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). When we obtain detailed structural information of target proteins, it provides much insight into how these proteins function. 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. Thus, we utilize several methods for our research. In short, it can be said that our studies will be those "published in textbooks".

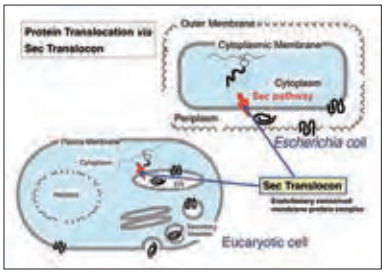

Fig. 1
Conserved protein translocation across the membrane via translocon

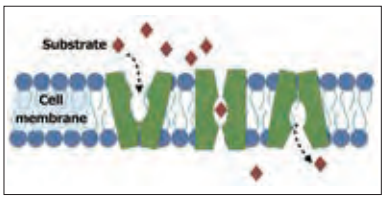

Fig. 2
Membrane transporter

Major Research Topics

1. Transportation across cell membranes
2. Molecular function and dynamics of proteins
3. X-ray crystallography

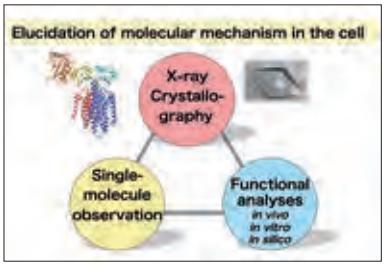

Fig. 3
Outline of our research

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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 (Fig. 2, Fig. 3). We are conducting studies to understand the biological clock in a comprehensive manner.

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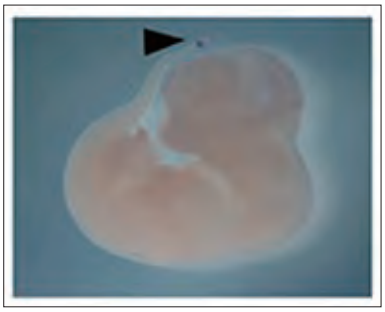

Fig. 1
Transcription factor Hes7, serving as a molecular clock, is specifically expressed in the primordium of somites.

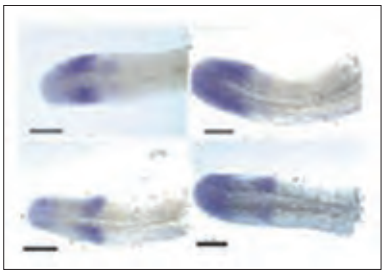

Fig. 2
The expression of Hes7 oscillates in the primordium of somites.

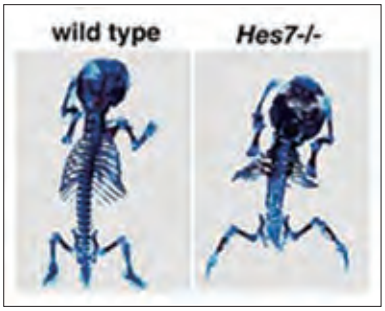

Fig. 3
In Hes7 knockout mice, somite segmentation does not occur cyclically and the metameric structures along the anteroposterior axis are lost.

Systems Neurobiology and Medicine

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Outline of Research and Education

Neurons extend long processes, axons, and form elaborate networks in our brain; all our brain activity depends on these neuronal networks. Axons decide their migratory route in response to gradients of chemical signals with extraordinary sensitivity. Such a paradigm was proposed over a century ago (1890) by the prominent neuroscientist Santiago Ramón y Cajal, but little is known about how axons are able to decide their migratory routes by reading subtle gradients of chemical signals and by translating them into directional driving force.

In addition to axons, various cells migrate within our body, thereby playing key roles in forming the body and organs as well as in immune responses, wound healing and regeneration. Disruption of cell migration is implicated in diseases, including birth abnormality, neuronal disabilities, immune disorders and cancer metastasis.

Our laboratory focuses on cell morphogenesis and the proteins Shootin1a, Shootin1b and Singar1, which we identified via proteome analyses. We analyze the molecular mechanisms for axon guidance, cell migration, neuronal polarization and synaptogenesis, using up-to-date methods including systems biology and mechanobiology. We also analyze actin waves which represent a new type of intracellular protein transport system for cell morphogenesis.

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

Major Research Topics

1. **Molecular mechanisms of neuronal network formation**
2. **Generation of mechanical forces for axon guidance and cell migration**
3. **Actin waves and novel mechanisms of protein transport**
4. **Brain morphogenesis and diseases**

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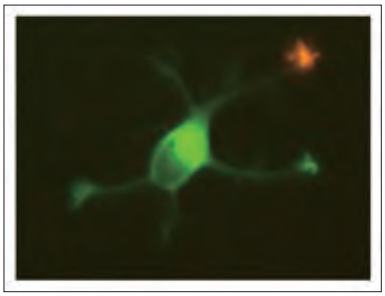

Fig. 1
Shootin1 is a key molecule involved in neuronal symmetry breaking.

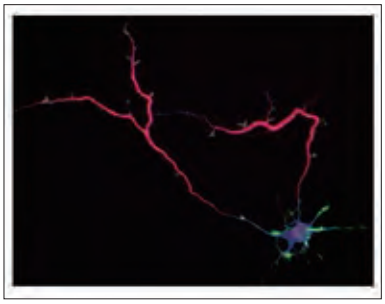

Fig. 2
Singar knockdown leads to formation of surplus axons.

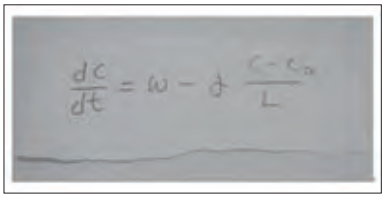

Fig. 3
An equation to describe neurite length sensing by shootin1.

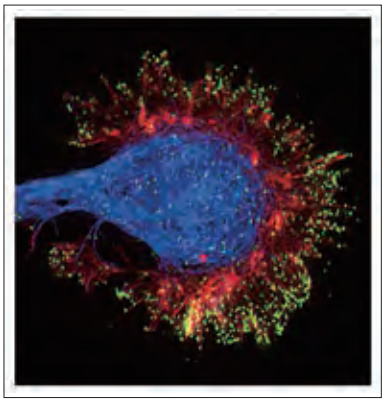

Fig. 3
Signal-force transduction through shootin phosphorylation at growth cones.

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.

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

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

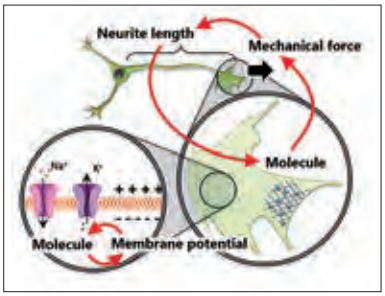

Fig. 1
Examples of system consisting of membrane potential and molecules, and system consisting of neurite length, mechanical force, and molecules. Signal transduction between various quantities are derived from experimental data. System can be reconstructed by integrating these signal transductions.

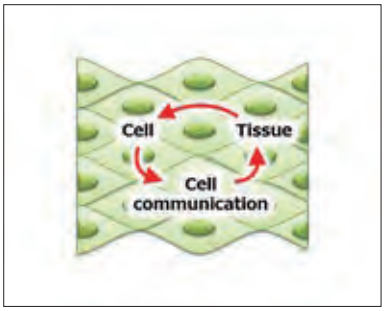

Fig. 2
Tissue formation can be regarded as the system consisting of cell, cell communication, and tissue itself. We aim to understand tissue formation as an aspect of such multimodal system.

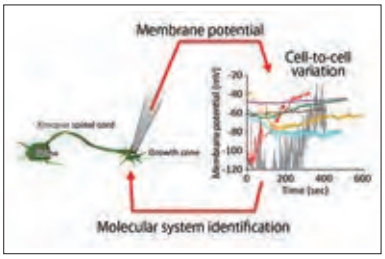

Fig. 3
Identification of molecular system from membrane potential time series. Measuring membrane potential is relatively easier than observing molecular interaction. Computation enables us to estimate intracellular molecular system from membrane potential.

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Humanophilic Innovation Project

Information Science

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Outline of Research and Education

We promote seminal research for the creation of human life support systems in the "Humanophilic Innovation Project". With this approach, we endeavor to create novel interdisciplinary research integrating the fields of material, biological and information science, and to produce researchers and engineers capable of solving the complicated problems facing the world and in the future. These achievements will be applied to develop new support systems for social activities such as agriculture and nursing care, in order to address the needs created by a low birth rate and an aging population.

Major Research Topics

1. Development of monitoring technology for biological activity
- Development of micro photonic device systems for organisms
- Application of monitoring technology with portable devices

2. Development of ecological device systems
- Fabrication of nano devices using organic super molecules
- Production of green materials using synthetic biology

3. Creation of human life support systems
- Application of ubiquitous computing systems
- Integration of achievements in monitoring technology and ecological device systems

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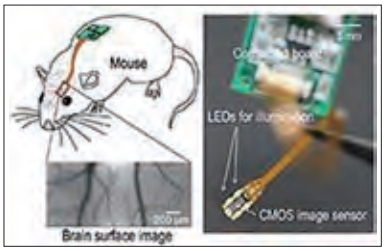

Fig. 1
Development of monitoring technology for biological activity. Monitoring brain activity and action of a mouse with a micro photonic device.

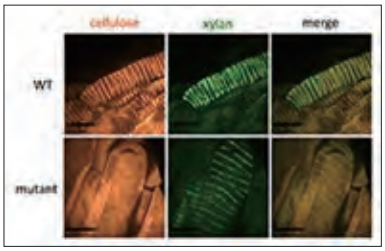

Fig. 2
Development of ecological device system. Micrographs of a cell wall of Arabidopsis mutant's modified production of cellulose as a green material by genome breeding.

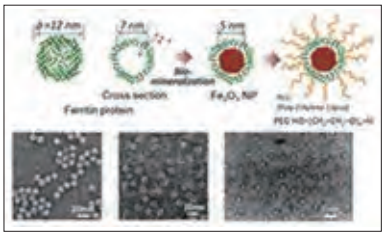

Fig. 3
Development of ecological device systems. Controlling density of the organic super molecule ferritin for development of new eco devices.

Fig.4
Creation of human life support systems. Demonstration of a context awareness system and monitoring of human activity in a "smart home".

Molecular Microbiology and Genetics *(with Research Institute of Innovative Technology for the Earth (RITE))*

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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.

References

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2. Hasegawa S et al., J Microbiol Methods, 146, 13-15, 2018
3. Kitade Y. et al., Appl Environ Microbiol, 84, e02587-17, 2018
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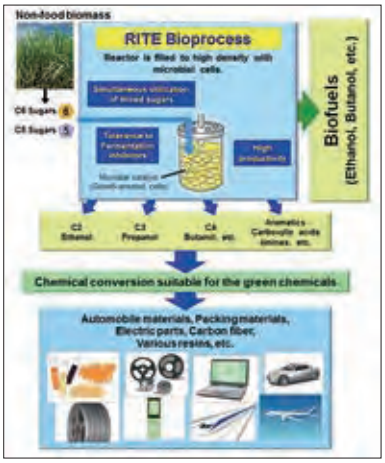

Fig. 1
The biorefinery concept

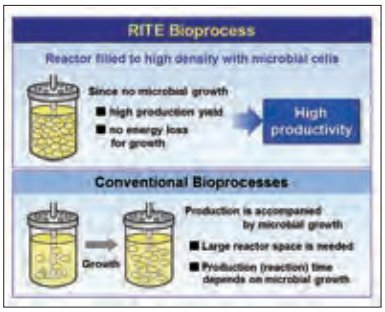

Fig. 2
Novel features of the RITE Bioprocess

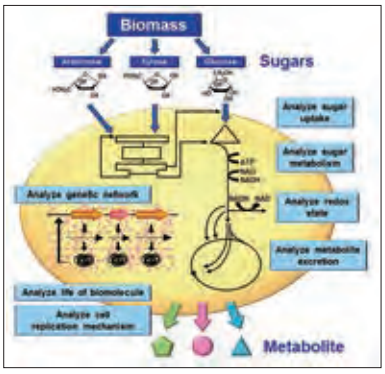

Fig. 3
Breeding of recombinant strains using system biology

Medical Genomics

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Outline of Research and Education

Our current research focus is circulating tumor DNA (ctDNA), which is cell-free DNA released from dying cancer cells (Fig. 1). Because ctDNA enables detection of cancer cell DNA of various lesions using only a small amount of blood (~1 ml), there are huge expectations for clinical applications including early detection. We use next-generation sequencing (NGS) to detect ctDNA. We offer students the opportunity to study experimental basics and bioinformatics of NGS.

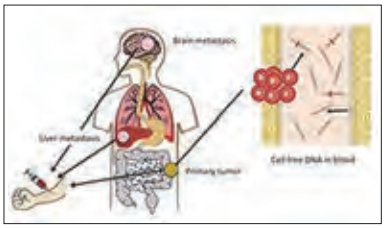

Fig. 1
Circulating tumor DNA

Major Research Topics

1. Noninvasive genotyping of *EGFR* for lung cancer therapy

Gefitinib (Iressa) is a molecular target agent for lung cancer to inhibit tyrosine kinase activity of *EGFR*. It is effective only for lung cancer with activating *EGFR* mutations, and patients are selected through a genetic test. Gefitinib is a good example of "personalized medicine" (Fig. 2), a new concept of medicine, i.e., choosing therapy based on genetic information of each patient. An important concern in clinical practice is that tumor samples are often difficult to obtain by biopsy. In particular, biopsy for advanced or resistant cases and repeated sampling is extremely difficult.

We developed a noninvasive detection system for *EGFR* mutation in ctDNA based on NGS (Kukita et al., 2013). The mutations are sought in more than 100,000 reads of the *EGFR* fragments. We conducted a multi-institute prospective study to evaluate the performance of the detection system, and demonstrated that the system was sufficient for practical use (Uchida et al., 2015). This study was done in collaboration with the Department of Thoracic Oncology, Osaka International Cancer Institute.

Fig. 2
Personalized medicine

2. Development of methodologies for cancer detection

The accuracy of current sequencing technologies has limitations when detecting rare mutations in multiple loci. To overcome this problem, we developed a new sequencing method named NOIR-SeqS (non-overlapping integrated read sequencing system) (Fig. 3) (Kukita et al, 2015). The system employs the barcode technology, and achieved 60-100 fold increase of accuracy from that of the standard NGS. We applied NOIR-SeqS to ctDNA, demonstrating its feasibility for practical use.

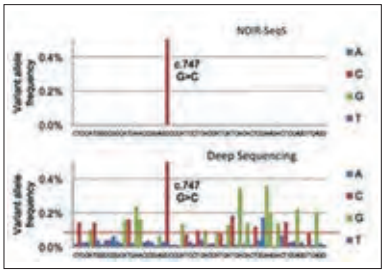

Fig. 3
Detection of a mutation in TP53. Top, NOIR-SeqS; bottom, conventional next-generation sequencing.

References

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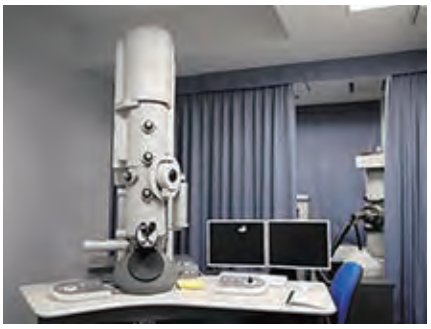
Abundant Research Facilities

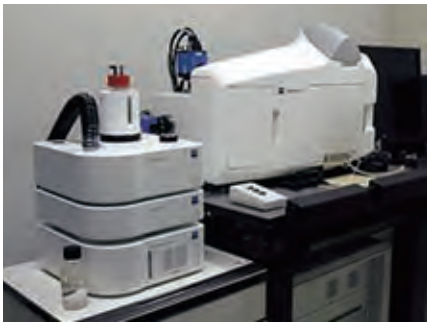
Each division is equipped with a variety of state-of-the-art equipment.
Shared equipment, among the most advanced available for biological science research in Japan, is provided at numerous locations within the division.



Transmission Electron Microscope

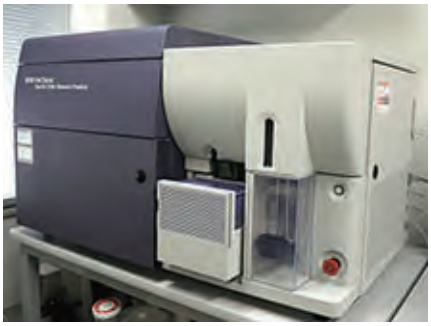
Scanning Electron Microscope

Confocal Laser Scanning Microscope

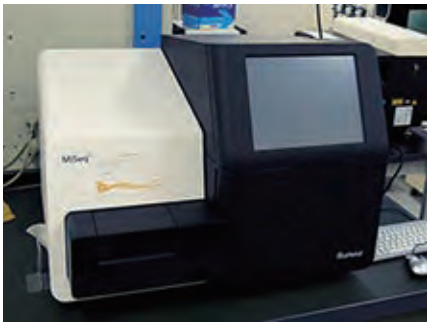


Light Sheet Fluorescence Microscopy

High Resolution Fluorescence Microscopy Imaging System

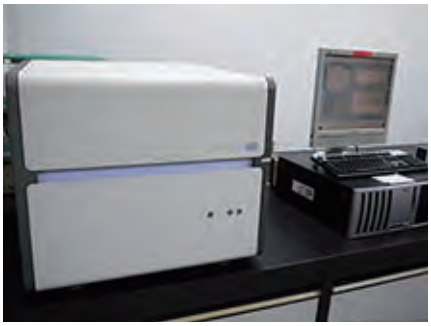


Flow Cytometer



Next Generation Sequencer

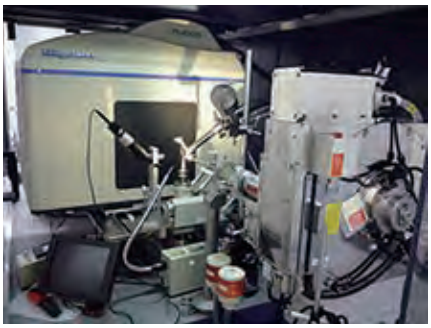
DNA Sequencer



Real-Time PCR System

Triple Quadrupole Mass Spectrometer

Protein Sequencer



Ultra High-Intensity Microfocus X-ray Generator • Macromolecular Crystallography Diffraction System

Cell Preservation Container

Botanical Greenhouse

Animal Experimentation Facility

Radioisotope Facility

Materials Science

Laboratories

List of Laboratories

Core Laboratories	Professor	Associate Professor	Assistant Professor	Page
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Ecomaterial Science (with Research Institute of Innovative Technology for the Earth)	Katsunori Yogo, Kazuya Goto	Hidetaka Yamada	106
Sensory Materials and Devices (with Shimadzu Corporation)	Keishi Kitamura, Masaki Kanai	Shigeyoshi Horiike	107
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Humanophilic Innovation Project	Jun Ohta, Yukiharu Uraoka		77

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.

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.

Recent Research Papers and Achievements

1. N. Kurahashi, V.-C. Nguyen, F. Sasaki, and H. Yanagi, *Appl. Phys. Lett*. **113**, 011107 (2018).
2. K. Torii, T. Higuchi, K. Mizuno, K. Bando, K. Yamashita, F. Sasaki, and H. Yanagi, *ChemNanoMat* **3**, 625 (2017).
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5. A. Ishizumi, S. Fujita, and H. Yanagi, *Opt. Mater*. **33**, 1116 (2011).

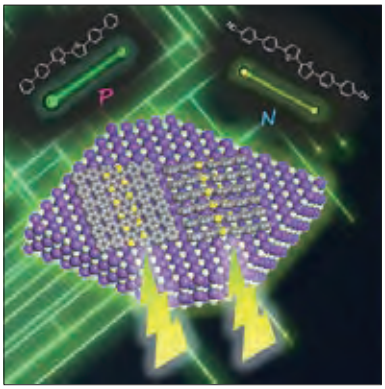

Fig. 1
A molecular crystal-based organic laser

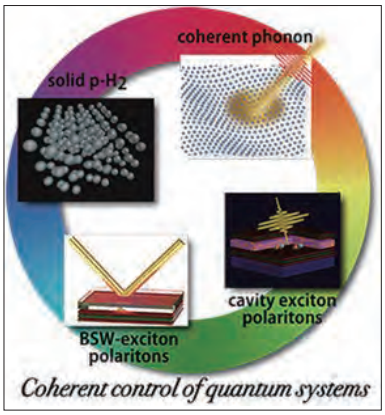

Fig. 2
Targets of coherent control

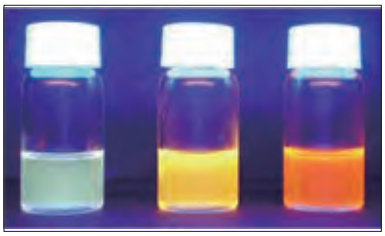

Fig. 3
Luminescence from impurity-doped semiconductor nanoparticles

Surface and Materials Science

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Education and Research Activities in the Laboratory

1. Research purpose and target

All materials, when smaller than one nanometer in size, begin to exhibit different properties from those under normal conditions as exemplified by iron and gold: iron becomes nonmagnetic, while gold becomes highly reactive. These materials are the new microscopic materials essential for resource saving, energy saving, element strategy, and nanotechnology. They can be manufactured and analyzed on the surface of a solid at the atomic and electron levels. Our laboratory studies atomic and electronic structures of surfaces and nanomaterials, and their functionalities such as electric conductivity and gas-molecule reaction using scanning tunneling microscopy (STM), Raman spectroscopy, reflection high-energy electron diffraction (RHEED), low-energy electron diffraction (LEED), angle-resolved photoelectron spectroscopy (ARPES), four-point probe method, desorption detection, and so on, working in ultra-high vacuum. The aim is to clarify the physical properties of nanomaterials and to create new functions from atomic and electron viewpoints. Our research targets include superstructures on semiconductor surfaces and magnetic thin-films, as well as organic and biological molecule adsorbing surfaces vital to catalysis and molecular electronics.

2. Educational policy

We provide education not only on experiments but also on what is important as a researcher and a professional engineer, including having an active attitude toward obtaining knowledge through research, originality training, acquisition of technical skills to enhance laboratory techniques (such as shop practices, machine control, and data analysis), and cooperation with laboratory members. 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 have contact with external researchers as well as the regular educational staff in the laboratory.

Research Themes

1. Atomic structural analysis of surface nano-materials by STM, LEED, and RHEED. Azimuth-scanning RHEED: three-dimensional reciprocal space mapping (3D-RSM)
2. Energy bands on surfaces studied with ARPES and their modification by electric field and strain
3. Adsorption and desorption of molecules from surfaces: atomic analysis of surface-molecular reactions
4. Surface nanomaterial physical property analysis
5. Density functional theoretical (DFT) calculations

Recent Research Papers and Achievements

1. N. Hirota, K. Hattori, *et al*., Appl. Phys. Express **9**, 047002 (2016).
2. O. Romanyuk, K. Hattori, *et al*., Phys. Rev. B **90**, 155305 (2014).
3. S. N. Takeda, *et al*., Phys. Rev. B **93**, 125418 (2016).
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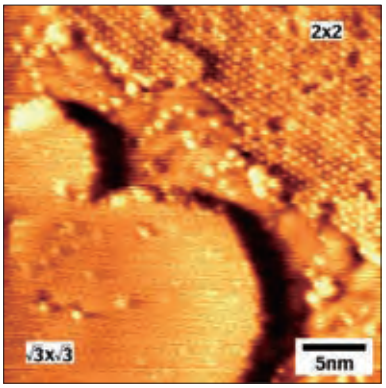

Fig. 1
Atomic-scale STM image of ultra-thin film and island of iron-silicides on a Si(111) surface.

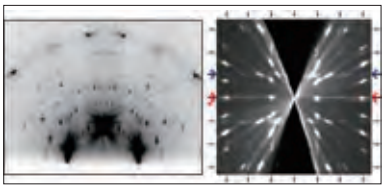

Fig. 2
RHEED pattern of Si(111)7x7 surface, and 3D-RSM of a 3D elongated island of α-$FeSi_2$(110) on Si(001).

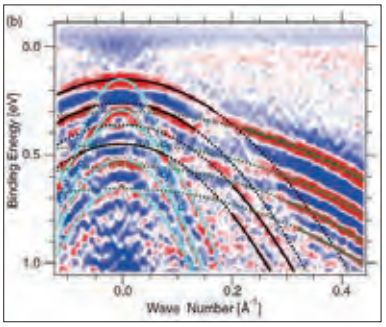

Fig. 3
Si valence subbands in p-type inversion layer.

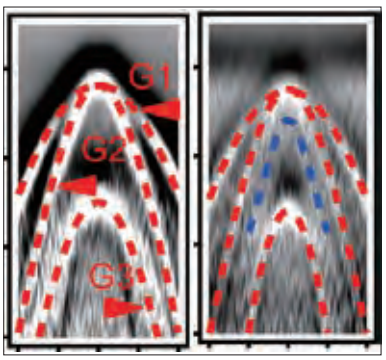

Fig. 4
Ge and Pb/Ge valence band dispersions.

Photonic Device Science




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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.

Fig. 1
Research fields of the Photonic Device Science Lab

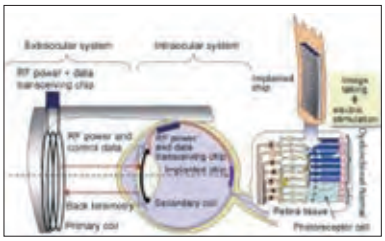

Fig. 2
Retinal prosthesis device

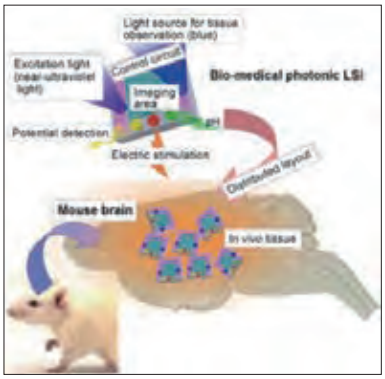

Fig. 3
Brain implantable microimager

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 mm^3-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).

Information Device Science


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Mutsunori Uenuma


Assist. Prof.
Mami Fujii


Assist. Prof.
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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.

Fig. 1

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

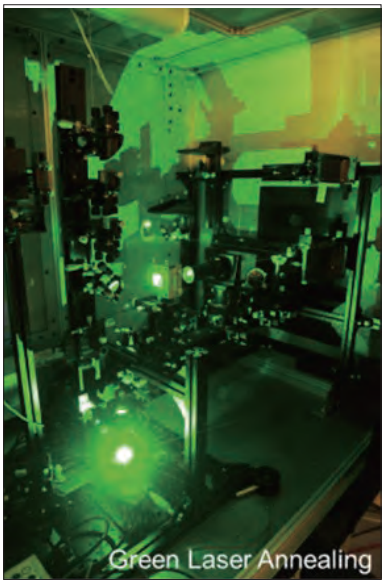

Fig. 2

Recent Research Papers and Achievements

1. 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).
2. 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).
3. 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).
4. Mutsunori Uenuma, Yasuaki Ishikawa and Yukiharu Uraoka, "Joule heating effect in nonpolar and bipolar resistive random access memory", Appl. Phys. Lett., **107**, 073503 (2015).
5. 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).

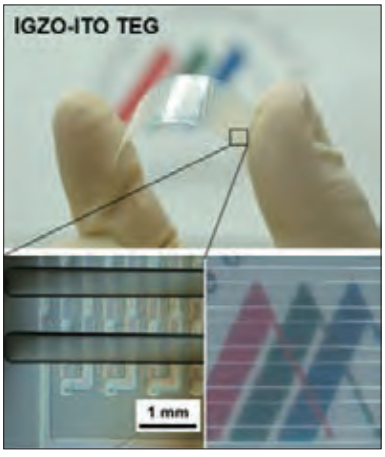

Fig. 3

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.

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).

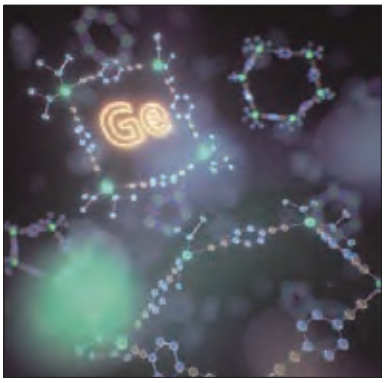

Fig. 1

Fig. 2

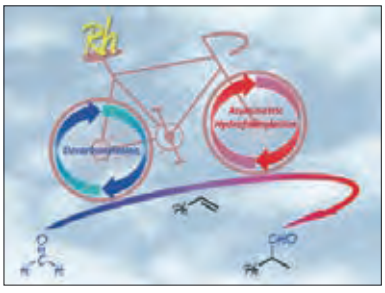

Fig. 3

Recent Research Papers and Achievements

1. H. Tanimoto, S. Ueda, T. Morimoto, K. Kakiuchi, *J. Org. Chem*. **2018**, *83*, 1614.
2. 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)
3. S. Hikage, Y. Nishiyama, Y. Sasaki, H. Tanimoto, T. Morimoto, K. Kakiuchi, *ACS Omega* **2017**, *2*, 2300.
4. T. Furusawa, H. Tanimoto, Y. Nishiyama, T. Morimoto, K. Kakiuchi, *Chem. Lett*. **2017**, *46*, 926.
5. T. Furusawa, H. Tanimoto, Y. Nishiyama, T. Morimoto, K. Kakiuchi, *Adv. Synth. Catal*. **2017**, *359*, 240.
6. M. Nakano, Y. Nishiyama, H. Tanimoto, T. Morimoto, K. Kakiuchi, *Org. Process Res. Dev*. **2016**, *20*, 1626.

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).

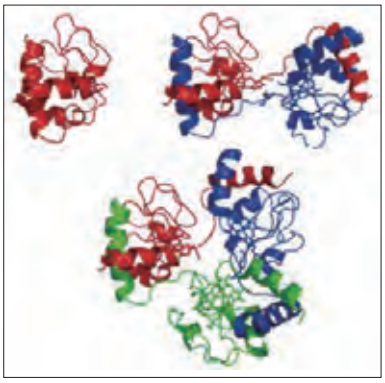
Fig. 1
Elucidated structures of cytochrome c supra -molecules

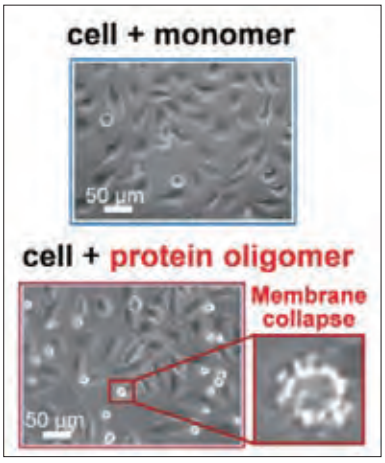

Fig. 2
Creation of antibacterial protein supramolecules

Recent Research Papers and Achievements

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

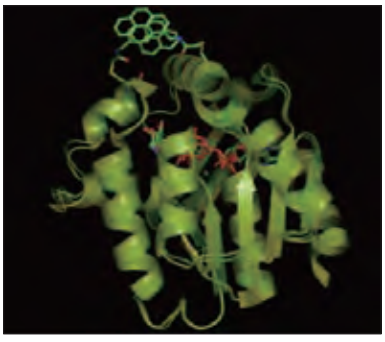
Fig. 3
X-ray crystallographic structure of an artificial fluorescent protein constructed by a combination of genetic and synthetic methods

Photonic Molecular Science




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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 accept students who have been educated in chemistry and chemistry-related field in Japanese and overseas universities. Small number of students may 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.

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

Research Themes

1. Photoresponsive molecules based on terarylene structures for photon quantitative reactions, photoacid generators (PAGs), ultra-efficient oxidative cycloreversion, and photoswitching of circularly polarized luminescence (CPL)
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

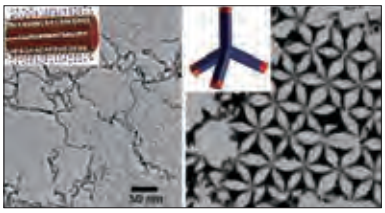

Fig. 2
TEM images of Self-assembling structures of amphiphilic semiconductor nanoparticles with rod-(left) and tetrapod-(right) shape.

Recent Research Papers and Achievements

1. 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)
2. 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)
3. T. Y. Bin, T. Kawai, J. Yuasa, "Ligand-to-Ligand Interactions Direct Formation of D_2-Symmetrical Alternating Circular Helicate", *J. Am. Chem. Soc*., 140, 3683-3689 (2018)
4. R. Sethy, J. Kumar, R. Métivier, M. Louis, K. Nakatani, N. M. T. Mecheri, A. Subhakumari. K. G. Thomas, T. Nakashima, "Enantioselective Light Harvesting with Perylenediimide Guests on Self-Assembled Chiral Naphthalenediimide Nanofibers", *Angew. Chem. Int. Ed*., 56, 15053-15057 (2017).
5. Y. Taniguchi, M. A. B. Sazali, Y. Kobayashi, N. Arai, T. Kawai, T. Nakashima, "Programmed Self-Assembly of Branched Nanocrystals with an Amphiphilic Surface Pattern", *ACS Nano*, 11, 9312-9320 (2017).
6. Y. Nonoguchi, S. Sudo, A. Tani, T. Murayama, Y. Nishiyama, R. M. Uda, T. Kawai, "Solvent Basicity Promotes the Hydride-mediated Electron Transfer Doping of Carbon Nanotubes", *Chem. Commun*., 53, 10259-10262 (2017)
7. Y. Nonoguchi, M. Nakano, T. Murayama, H. Hagino, S. Hama, K. Miyazaki, R. Matsubara, M. Nakamura, T. Kawai, "Simple Salt-coordinated n-Type Nanocarbon Materials Stable in Air", *Adv. Funct. Mater*., 26, 3021-3028 (2016).

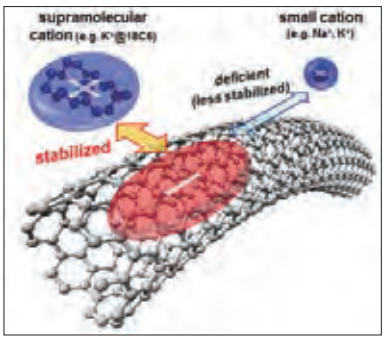

Fig. 3
A representative concept for supramolecular n-type doping of carbon nanotubes.

Photofunctional Organic Chemistry



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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.

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 solar cells. To this end, we employ a unique deposition technique called "precursor approach" (Fig. 1), and are preparing new compounds—typically derivatives of acenes and benzoporphyrin—that can be processed by this method (Fig. 2). We have been conducting joint research "3D Active-Site Science" (JSPS Grant-in-Aid for Scientific Research on Innovative Areas).

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. 3). Our group is currently involved in, among others, collaborative projects of "Tailor-Made Synthesis of Graphene Nanoribbons for Innovative Devices" (JST CREST).

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 (Fig. 4).

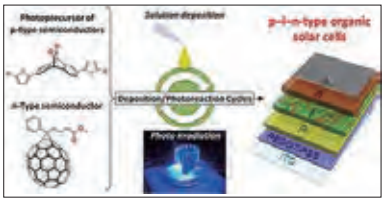

Fig. 1
A photoprecursor method for solution-processing of organic thin-film devices

Fig. 2
Photo-irradiation process on making of organic thin-film devices

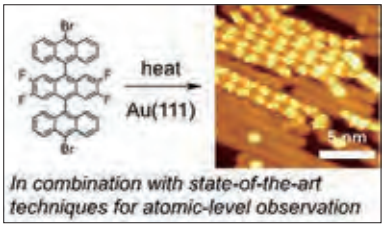

Fig. 3
On-surface synthesis of graphene nanoribbon (GNR)

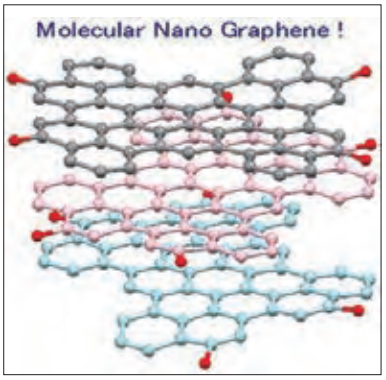

Fig. 4
Novel functional PAH

Recent Research Papers and Achievements

1. M. Suzuki, K. Nakayama, H. Yamada *et al*. A photochemical layer-by-layer solution process for preparing organic semiconducting thin films having the right material at the right place, *Chem. Sci*., **2018**, *9*, 6614.
2. K. Takahashi, M. Suzuki, K. Nakayama, H. Yamada et al., Side-chain engineering in a thermal precursor approach for efficient photocurrent generation, *J. Mater. Chem. A,* **2017**, *5,* 14003. (Selected as an Inside Front Cover)
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. A. Matsumoto, M. Suzuki, D. Kuzuhara, H. Hayashi, N. Aratani, H. Yamada, Tetrabenzoperipentacene: Stable Five-Electron Donating Ability and a Discrete Triple-Layered β-Graphite Form in the Solid State, *Angew. Chem. Int. Ed*., **2015**, *54,* 8175. (Selected as a Hot paper)

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, 4-800 K. 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

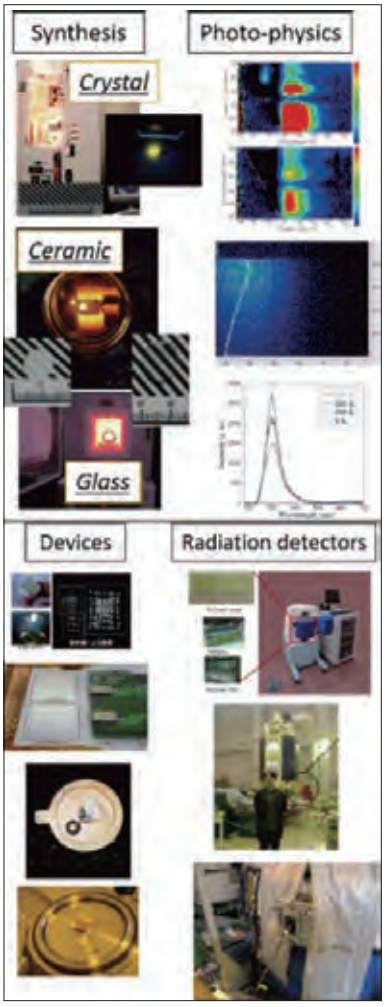

Fig. 2
Outline of studies in this group, from material synthesis to radiation detectors

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, CH3NH3SnI3: 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).

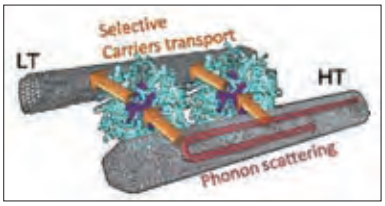

Fig. 1
A novel design of a thermoelectric nanocomposite using biomolecular junctions

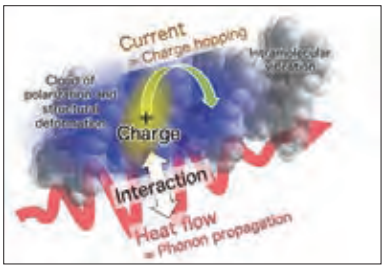

Fig. 2
Conceptual diagram of the *Giant Seebeck Effect*: a specific current-heat flow interaction in organic solids

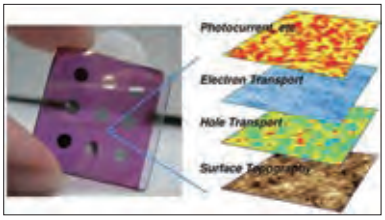

Fig. 3
Functional structures for photovoltaic conversion in plastic solar cells

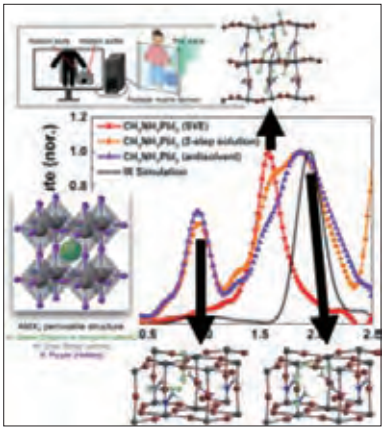

Fig. 4
AMX_3 perovskite structure and THz-absorption properties

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), micro-fluidic 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). Micro-fluidic 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 micro-fluidic 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), and created unique thin devices (World Class) (Ref. 2). These activities and devices aim to open new fields 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.

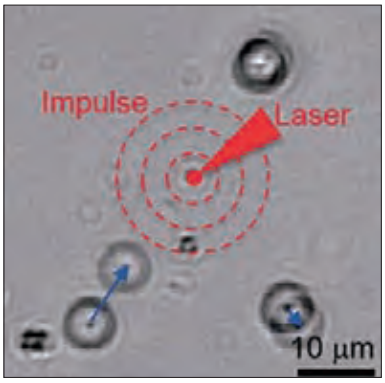

Fig. 1
Manipulation of microbeads by laser impulse

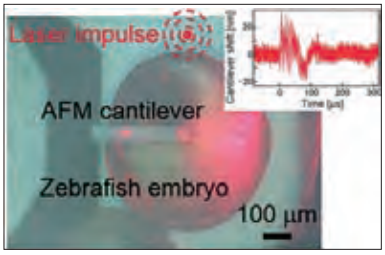

Fig. 2
Nanometer scale vibration of Zebrafish embryo induced by laser impulse and detected by AFM

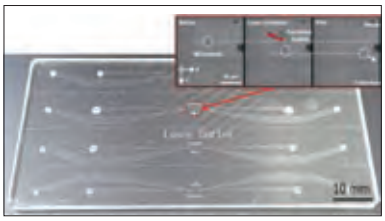

Fig. 3
High-speed laser manipulation in micro-fluidic chips

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 micro-fluidic 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. Y. Yalikun, Y. Hosokawa, T. Iino, and Y. Tanaka, "An all-glass 12 μm ultra-thin and flexible micro-fluidic chip fabricated by femtosecond laser processing," Lab Chip, 2016,16, 2427–2433.
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.

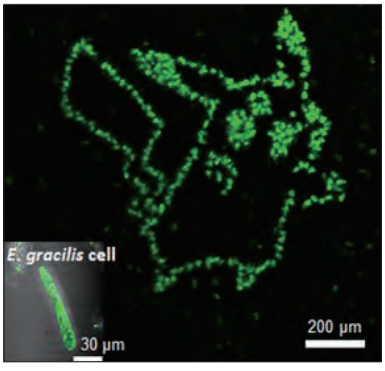

Fig. 4
Laser scanning photoporation of fluoresce probe molecules at single cell resolution

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

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

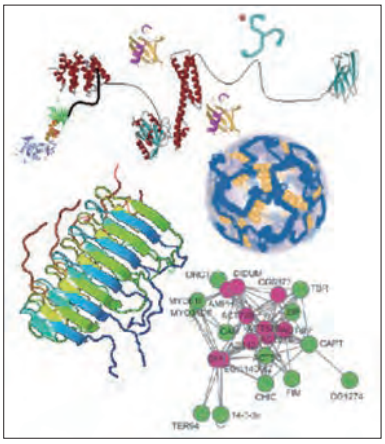

Fig. 2
Biological complex molecular systems

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).

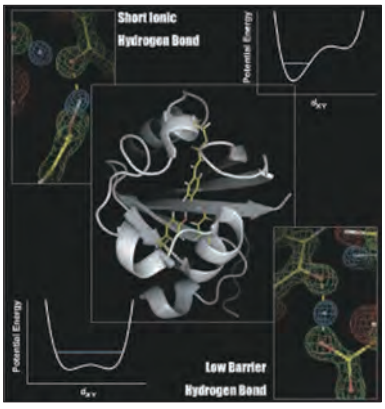

Fig. 3
Protonics in protein molecules

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 and/or 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.

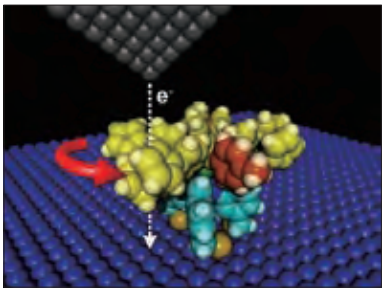

Fig. 1
A Molecular motor rotating clockwise or counterclockwise by request.[5]

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.

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.

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.

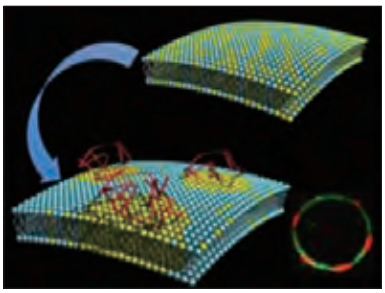

Fig. 2
Modulation of cell membrane structure by biomimetic molecular machines.

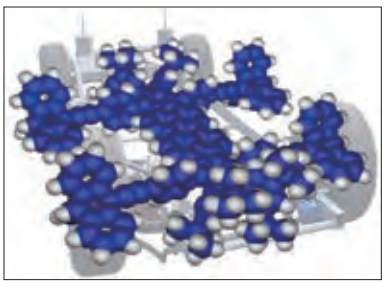

Fig. 3
Molecular nanovehicles which participated to the first Nanocar Race[1].

Recent Research Papers and Achievements

1. G. Rapenne, T. Kawai *et al., J. Phys. Chem. C* **122**, 5978 (2018).
2. G. Rapenne, C. Joachim, *Nature Rev. Mater.* **2**, 17040 (2017).
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).

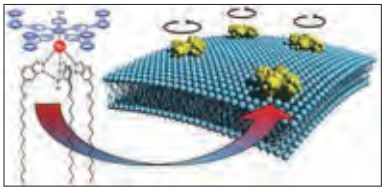

Fig. 4
A Hybrid molecular motor designed to be inserted in artificial or cell membrane.

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.

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 L_3 Absorption Edge ", *J. Phys. Soc. Jpn*. **84**, 064704-1-8 (2015).

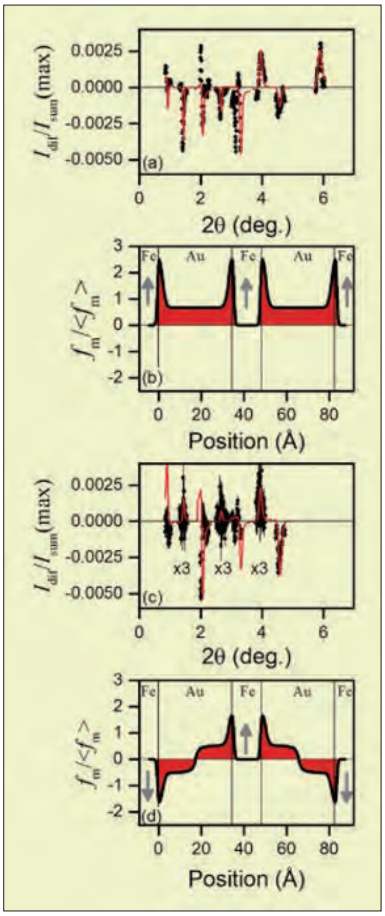

Fig. 1
Resonant X-ray magnetic scattering profiles in (a) parallel and (c) antiparallel states of Fe magnetizations measured near the Au L_3 absorption edge, and induced magnetic structures of Au layers in (b) parallel and (d) anti-parallel states of Fe magnetizations.

Precision Polymer Design and Engineering

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Education and Research Activities in the Laboratory

We educate students and conduct research to design and create new and novel functional materials based on precise synthesis of polymers. For example, we develop functional materials that will contribute to highly reliable medical devices which may be used in regenerative medicine, new therapeutic methods, new drugs, DDS, etc. Therefore, molecular design, synthesis, and evaluation of functional materials are conducted based on knowledge and technology from a wide range of disciplines such as organic chemistry, polymer science, molecular biology, medicine, and pharmaceutical science.

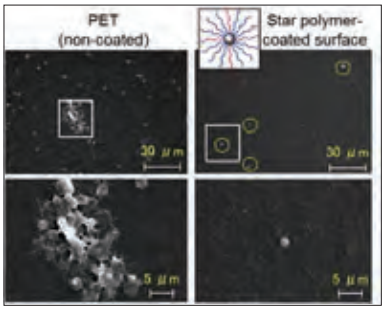

Fig. 1

Research Themes

1. Biocompatible coatings based on precisely designed polymers
2. Development of helical polymers for gene or drug carriers
3. Development of controlled polycondensation systems

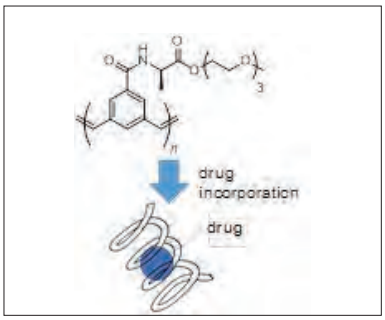

Fig. 2

Recent Research Papers and Achievements

1. Nurlidar F, Kobayashi M, Terada K, Ando T, Tanihara M; "Cytocompatible polyion complex gel of poly(Pro-Hyp-Gly) for simultaneous rat bone marrow stromal cell encapsulation" J Biomat Sci, Polym Ed. 2017 May 18. doi: 10.1080/09205063.2017.1331872
2. Kusumastuti Y, Shibasaki Y, Hirohara S, Kobayashi M, Terada K, Ando T, Tanihara M; "Encapsulation of rat bone marrow stromal cells using apolyion complex gel of chitosan and succinylated poly(Pro-Hyp-Gly)" J Tissue Eng Regen Med, 2015 Jan 28. doi: 10.1002/term.1987
3. Totani M, Ando T, Terada K, Terashima T, Kim I-Y, Ohtsuki C, Xi C, Kuroda K, Tanihara M; "Utilization of star-shaped polymer architecture in the creation of high-density polymer brush coatings for the prevention of platelet and bacteria adhesion" Biomat Sci 2(9), 1172-1185, 2014
4. Kusumaatmaja A, Ando T, Terada K, Hirohara S, Nakashima T, Kawai T, Terashima T, Tanihara M; "Synthesis and photoproperties of Eu(III)-bearing star polymers as luminescent materials" J Polym Sci Part A: Polym Chem 51(12), 2527-2535, 2013
5. Kumagai S, Chang C-Y, Jeong J, Kobayashi M, Shimizu T, Sasaki M; "Development of plasma-on-chip: Plasma treatment for individual cells cultured in media" Jap J Appl Phys 55, 01AF01, 20162.

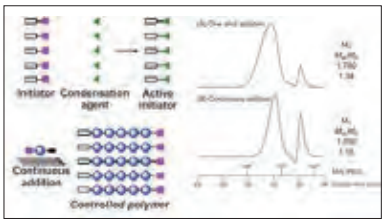

Fig. 3

Data-driven Chemistry

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Assoc. Prof.
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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., 56, 286-299, 2016

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 and nanomaterials 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. We offer a thorough education to prepare students to become researchers through discussions, presentations, and participation in academic conferences and meetings.

Fig. 1

Research Themes

We aim to create functional polymer materials through the application of "molecular technology". 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. For example, an oil gel using polystyrene and functional polyurethane through monomer design (Fig. 1).
2. **Biodegradable Polymers**
   Multi-functional Biodegradable polymers are designed. For example, the medical materials for circular organs, long-term release, and antithrombotic surface materials by poly (trimethylene carbonate) derivatives (Fig. 2).
3. **Amphiphilic Polymers**
   Functional materials are designed using amphiphilic polymers. For example, N-vinylamide derivatives for gas hydrate inhibitors and antibacterial materials (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 (Fig. 4).

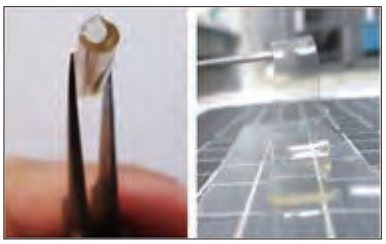

Fig. 2

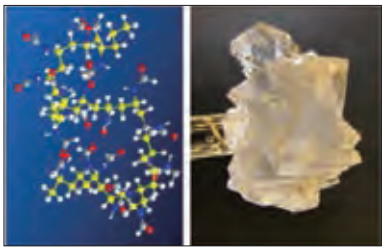

Fig. 3

Recent Research Papers and Achievements

1. D. Aoki, H. Ajiro*, *Macromol. Rapid Commun*. accepted **2018**.
2. P. Charoensumran, H. Ajiro*, *Polym. J*. accepted **2018**.
3. K. Kan, H. Ajiro*, *Chem. Lett*. **2018**, *47*, 591.
4. D. Aoki, H. Ajiro*, *Macromolecules* **2017**, *50*, 6529.
5. N. Chanthaset, Y. Takahashi, Y. Haramiishi, M. Akashi, H. Ajiro*, *J. Polym. Sci. Part A: Polym. Chem*. **2017**, *55*, 3466.
6. S. Seitz, M. Akashi, H. Ajiro*, *Colloid Polym. Sci*. **2017**, *295*, 1541.
7. R. Kawatani, Y. Nishiyama, H. Kamikubo, K. Kakiuchi, H. Ajiro*, *Nanoscale Res. Lett*. **2017**, *12*, 461.
8. S. Fujishiro, K. Kan, M. Akashi, H. Ajiro*, *Polym. Degrad. Stab*. **2017**, *141*, 69.
9. H. Ajiro*, K. Kan, M. Akashi*, *J. Nanosci. Nanotechnol*. **2017**, *17*, 837.
10. K. Kan, M. Akashi, H. Ajiro*, *Macromol. Chem. Phys*. **2016**, *217*, 2679 [Cover Picture].
11. K. Kan, M. Fujiki*, M. Akashi*, H. Ajiro*, *ACS Macro Lett*. **2016**, *5*, 1014.
12. H. Ajiro* T. Ueyama, M. Akashi*, *Colloids Surf. A* **2016**, *506*, 338.
13. Y. Haramiishi, N. Chanthaset, K. Kan, M. Akashi, H. Ajiro*, *Polym. Degrad. Stab*. **2016**, *130*, 78.
14. R. Kawatani, K. Kan, M.A. Kelland, M. Akashi, H. Ajiro*, *Chem. Lett*. **2016**, *45*, 589.
15. H. Ajiro*, S. Ito, K. Kan, M. Akashi*, *Macromol. Biosci*. **2016**, *16*, 694., etc.

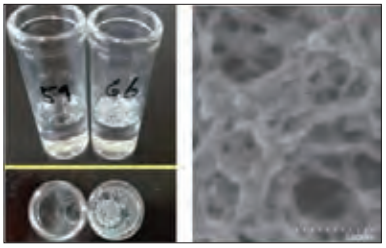

Fig. 4

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.

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. N. Hayakawa, K. Sadamori, S. Tsujimoto, M. Hatanaka, T. Wakabayashi, T. Matsuo, "Cleavage of a P=P Double Bond Mediated by N-Hetrocyclic Carbenes", *Angew. Chem. Int. Ed*. 56, 5765-5769 (2017).
2. M. Hatanaka, Y. Hirai, Y. Kitagawa, T. Nakanishi, Y. Hasegawa, K. Morokuma, "Organic linkers control the thermosensitivity of the emission intensities from Tb(III) and Eu(III) in a chameleon polymer", *Chem. Sci*. 8, 423-429 (2017).
3. W. M. C. Sameera, M. Hatanaka, T. Kitanosono, S. Kobayashi, K. Morokuma, "The Mechanism of Iron(II)-catalyzed Asymmetric Mukaiyama Aldol Reaction in Aqueous Media: Density Functional Theory and Artificial Force-Induced Reaction Study", *J. Am. Chem*. Soc. 137, 11085-11094 (2015).
4. M. Hatanaka, K. Morokuma, "How Can Fluctional Chiral Lanthanide (III) Complexes Achieve a High Stereoselectivity in Aqueous Mukaiyama-Aldol Reaction?", *ACS Catal*. 5, 3731-3739 (2015).

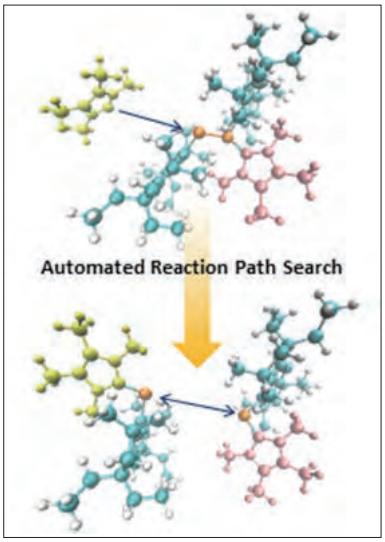

Fig. 1
Automated reaction path search by the "Global Reaction Route Mapping" strategy

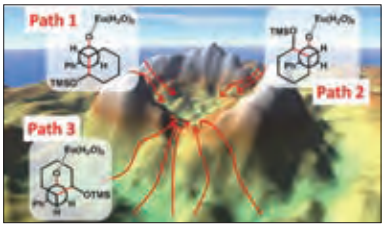

Fig. 2
Exhaustive sampling of the transition states of the stereo-determining step

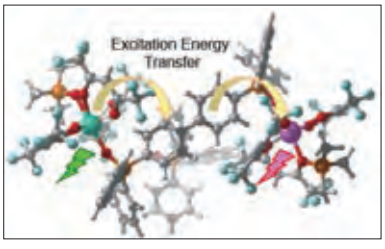

Fig. 3
Excitation energy transfer pathway of the thermometer using lanthanide luminescence

Mesoscopic Materials Science (with Panasonic Corporation)

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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.

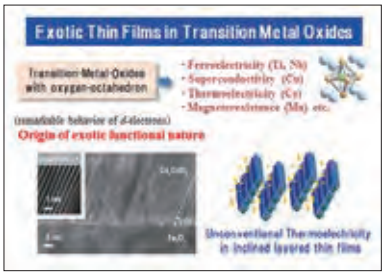

Fig. 1
A conceptual illustration of strongly correlated electronic materials and the layer-controlled thermoelectric thin film structure

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

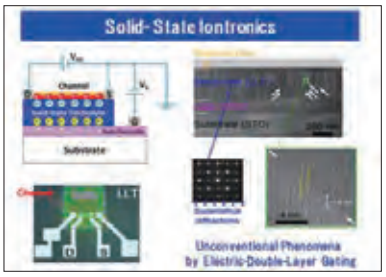

Fig. 2
A conceptual illustration of a solid-state iontronics device made of ion-conducting epitaxial thin film

Recent Research Papers and Achievements

1. K. Wasa, S. Yoshida, H. Hanzawa, H. Adachi, T. Matsunaga, and S. Tanaka, "Structure and ferroelectric properties of high T_c $BiScO_3$–$PbTiO_3$ epitaxial thin films", *IEEE Trans. UFFC* **63**, (10) 1636-1641 (2016).
2. 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).
3. 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).

Intelligent Materials Science Laboratory (with SHARP Corporation)

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Education and Research Activities in the Laboratory

The Intelligent Materials Science Laboratory has two faculty members who independently conduct research on new devices and materials in their own specialized fields, including research on nano-sized materials such as quantum dot compound semiconductors for light emitting diodes (LEDs) or new-type photovoltaic, and p-type oxide for transparent and flexible TFTs.

Fig. 1
Organic vacuum deposition apparatus

Fig. 2
Analytical equipment for power management system

Research Themes

1. Nano-sized materials

Electronic characteristics of semiconducting materials are entirely different from bulk materials due to quantum effects when crystal structures are controlled in a microscopic region ranging from atomic to several nanometers in size. We are studying functional materials that can sensitively show macroscopic responses to external stimuli such as light, electric fields, and magnetic fields through controlling electronic level or phase transition

2. Oxide semiconductors

Flexible semiconductor devices are widely expected for future displays, photovoltaics, and sensors. We are studying thin film amorphous oxide semiconductors with high carrier mobility based on the physical vapor deposition (PVD) method. The main topics here are the creation of transparent p-type semiconductors and investigations of organic-inorganic hybrid p-n junctions.

Recent Research Papers and Achievements

1. Signal equalization and reproduction from amplitude information through the use of the frequency response of an optical disc system
   • T. Okumura, T. Numata, J. Akiyama, S. Maeda, T. Yamaguchi, A. Takahashi, "Method for Evaluating Partial Response Maximum Likelihood System Performance Using Sequenced Amplitude Margin," Jpn. J. Appl. Phys. Vol.41, pp.1783-1784 (2002), T. Honda, et al., Bioorg. Med. Chem. 17, 699 (2009).
2. Super-resolution reproduction through the use of changes in optical characteristics due to temperature at the absorption edge of zinc oxide
   • M. Yamamoto, G. Mori, H. Tajima, N. Takamori, A. Takahashi, "Super-Resolution Optical Disc with High Readout Stability Using Zinc Oxide Thin Film," Jpn. J. Appl. Phys. Vol.43, pp.4959-4963 (2004).

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


Prof. Takahiro Honda


Prof. Hiroshi Enomoto


Assoc. Prof. Komei Okabe

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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 (Fig. 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).

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).

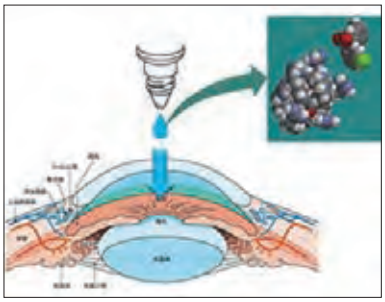

Fig. 1
DDS for eye disease (anterior chamber)

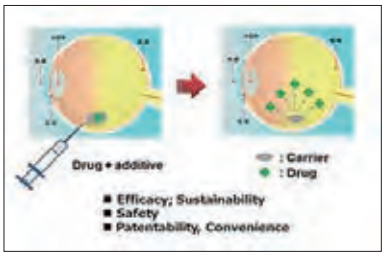

Fig. 2
DDS for eye disease (posterior chamber)

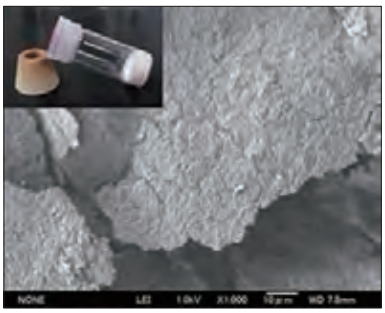

Fig. 3
Injectable gel for DDS using ascorbic acid ester derivative and its SEM image

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.

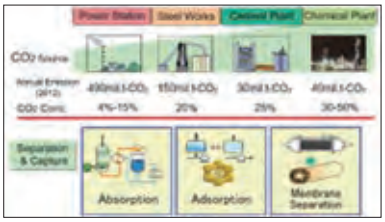

Fig. 1
CO_2 separation and capture technologies

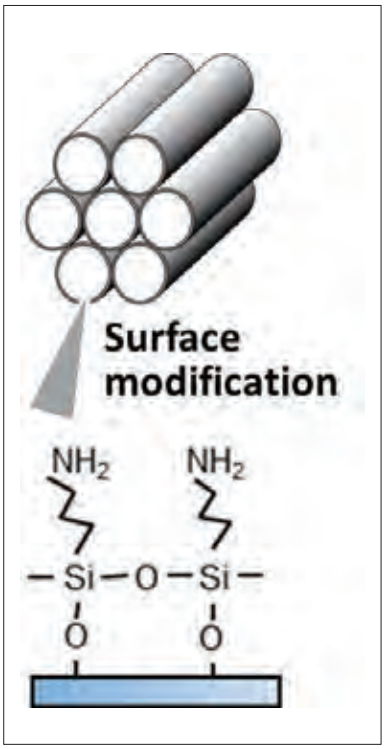

Fig. 2
Amine solid sorbent for CO_2 capture (amine-grafted mesoporous silica)

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).

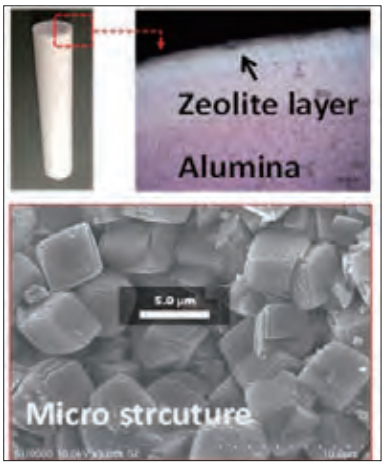

Fig. 3
Novel zeolite membrane for H_2 separation

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).

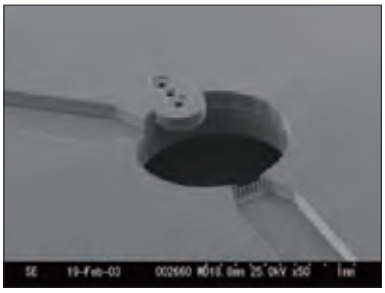

Fig. 1
Cell culture chips

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

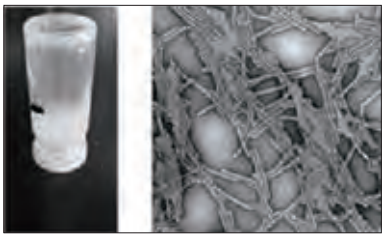

Fig. 2
A biocompatible polymer gel

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).

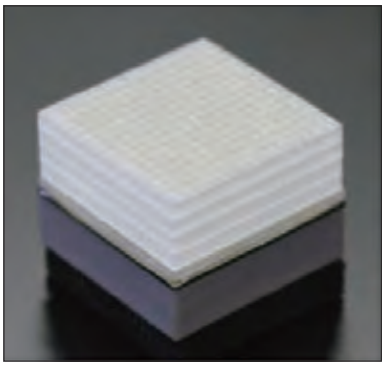

Fig. 3
A PET detector

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


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Prof. Yutaka Fujiwara


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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.

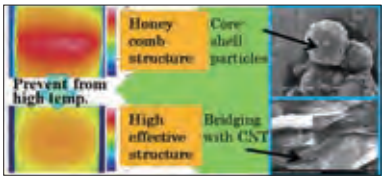


Fig. 1
Honeycomb structure of phenol resin particles with thermal conductive BN nanoparticles, or bridged structure of graphite plates with CNF has promoted thermal conductivity to increase immediately (two times).

Research Themes

1. Highly thermal conductive materials and transparent and highly thermal emissivitive 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.).

2. 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.

3. Highly reliable wiring fabrication on flexible polymer substrates

The core technology to fabricate wiring pattern is selective polymer metallization using plating. Along with plating technology, nanoparticle fabrication and the surface engineering of polymers are fully used to develop wiring with controlled nanostructures at the metal/polymer interface.

4. Lithium ion batteries fully composed of ceramics

Our research is aimed at the development of an all solid state lithium ion battery 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.

Fig. 2
Metallizing of Polymer Substrates

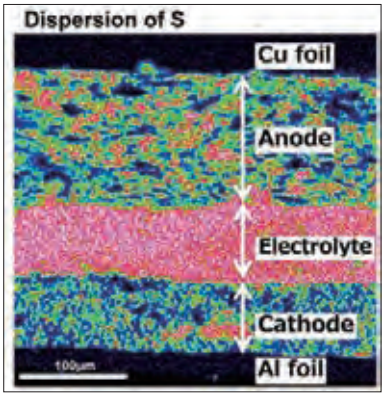


Fig. 3
A cross-section of an all solid state lithium ion battery. The layer by layer structure is composed of a cathode ($LiNi_{1/3}Co_{1/3}Mn_{1/3}O_2$ with Li_3PS_4 and acetylene black), a solid state electrolyte (Li_3PS_4), and an anode (carbon with Li_3PS_4 and acetylene black).

Recent Research Papers and Achievements

1. T. Nagayama, T. Yamamoto, T. Nakamura, Y. Fujiwara, "Properties of electrodeposited invar Fe–Ni alloy/SiC composite film", *Surface and Coatings Technology*, **322C**, 70-75 (2017).
2. Y. Agari, K. Uotani, K. Mizuuch, 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).
3. M. Takahashi, J. Tani, H. Kido, A. Hayashi, K. Tadanaga, and M. Tatsumisago, "Thin Film Electrode Materials $Li_4Ti_5O_{12}$ and $LiCoO_2$ Prepared by Spray Pyrolysis Method", 2011 IOP Conf. Ser. Mater. Sci. Eng., 18, 122004.

Research Instruments

Transmission Electron Microscope
(TEM)

Scanning Transmission Electron Microscope
(STEM)

Low Vacuum Scanning Electron Microscope
(LVSEM)

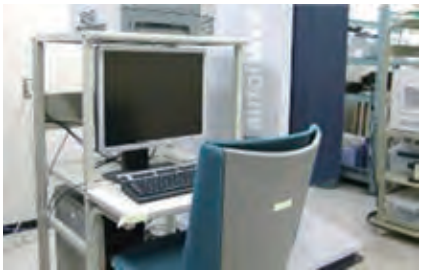
Nano-prober/EBAC

Scanning Probe Microscope
(SPM)

Focused Ion Beam
(FIB)

Double-focusing Mass Spectrometer

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

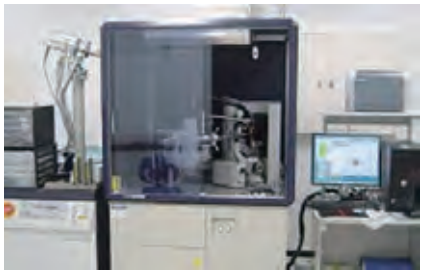


MALDI-TOF Mass Spectrometer

High Resolution MALDI-TOF Mass Spectrometer

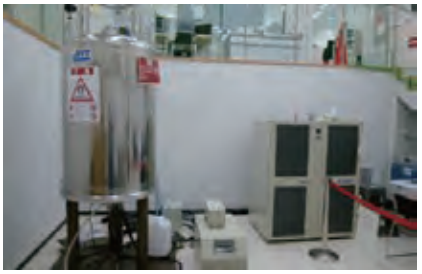
DART Mass Spectrometer

Wide-angle X-ray Diffractometer
(WAXD)



Single Crystal X-ray Diffractometer and Structure Analysis System

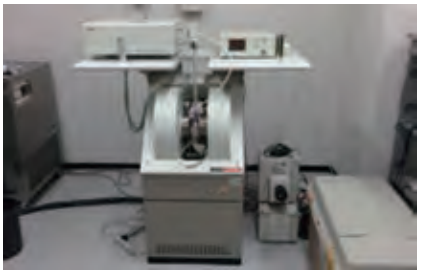
Small-angle X-ray Scattering Diffractometer
(SAXD)



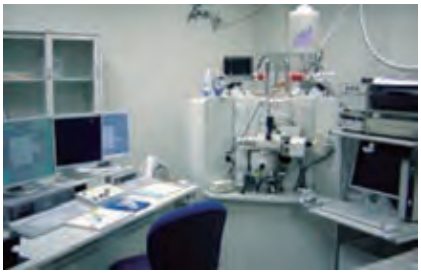
600MHz Nuclear Magnetic Resonance
(600MHz NMR)

500MHz Nuclear Magnetic Resonance
(500MHz NMR)

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



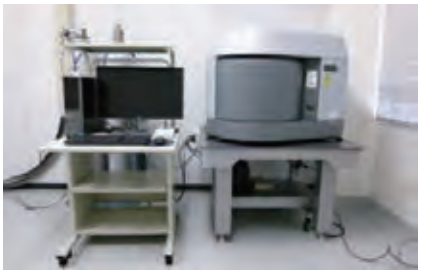
Electron Spin Resonance
(ESR)



Electron Probe MicroAnalyser
(EPMA)

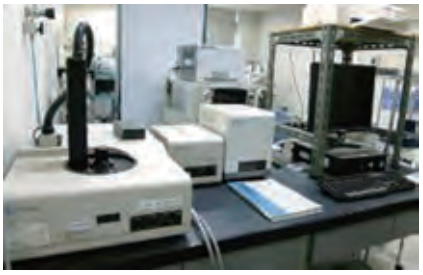
Secondary Ion Mass Spectrometer
(SIMS)

X-ray Photoelectron Spectroscope
(ESCA)



Micro Raman Spectrometer

Circular Dichroism Spectropolarimeter
(CD)

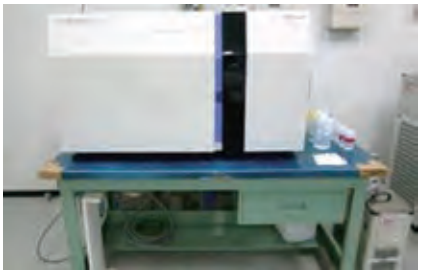


Dynamic Light Scattering Spectrometer
(DLS)

Spectroscopic Ellipsometer

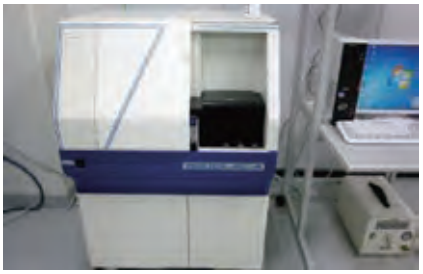
Photoluminescence Lifetime Measurement System

Elemental Analysis
(EA)



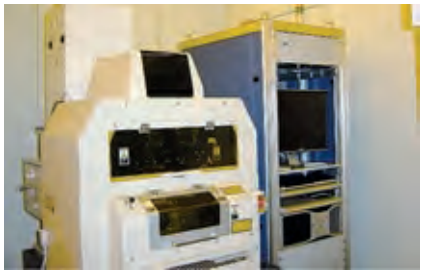
Inductively Coupled Plasma Mass Spectrometer
(ICP-MS)

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

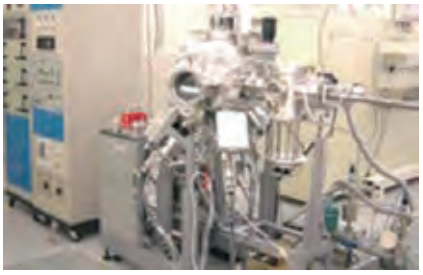


Photoelectron Yield Spectroscopy
(PYS)

Electron Beam Lithography Exposure



Projection Aligner



Oxide Complex Thin Film Coating Apparatus

High Purity Metal Sputter

Surface Profiler

NAIST