IROAST
International Research Organization for Advanced Science & Technology

Annual Report 2020

Kumamoto University

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International Research Organization for Advanced Science and Technology
Kumamoto University

He who loses wealth loses much; he who loses a friend loses more;
but he who loses courage loses all.

Miguel de CERVANTES

Contents

Preface

The International Research Organization for Advanced Science and Technology (IROAST), which opened in April of 2016, is one of the Centers of Excellence in Kumamoto University and promotes world class, cutting-edge research in science and technology.

We have been vigorously promoting our partnership with the International Collaborative Research Group for Science and Technology, which opened in Kumamoto University in 2013 and closed at the end of March 2018. All of the group members are still working as IROAST's adjunct researchers and are collaborating on international research projects with IROAST faculty and our visiting professors.

The aims of IROAST are the further promotion of international collaborations to establish international research networks in the following four advanced areas of science: Nano Material Science, Green Energy, Environmental Science and Advanced Green Bio, in parallel with the development of young excellent researchers, promotion of ongoing cutting-edge research projects, and initiation of innovative interdisciplinary research projects.

To achieve these goals, we have been promoting the international partnership with overseas universities and institutions. The ultimate goal of IROAST is to be fully and globally recognized as a hub of world-class, cutting-edge research networks through the international brain circulations.

Because of the pandemic outbreak of new Corona virus (COVID-19), our research supporting activities have limited in 2020. We should abandon the exchange of researchers. However, joint research activities have continued through on-line basis. We should give our sincere thanks to all the medical doctors and health care and associated workers, for their tremendous effort against the Corona. Definitely it takes some time to win the Corona, but we should do what we can do for all the other people including our family.

I will finish my job as the Director of IROAST at the end of March, 2021. I would like to give my sincere and deep thanks to all the people associated with the activities at IROAST.

Takashi Hiyama

Dr. Takashi HIYAMA, Professor Emeritus
Distinguished Professor
Director of International Research Organization for
Advanced Science and Technology (IROAST)
Kumamoto University, JAPAN
E-mail: hiyama@kumamoto-u.ac.jp
URL: http://www.cs.kumamoto-u.ac.jp/hiyama/

IROAST Members

Director / Vice-Director

Takashi Hiyama

Kazuki Takashima

Distinguished Professors

Konstantinos Kontis

László Pusztai

Yufeng Zheng

Tenure-track Professor / Associate Professors / Assistant Professor

Mitsuhiro Aida

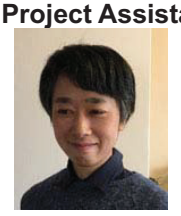
Takumi Higaki

Ruda Lee

Atsushi Sainoki

Takashi Ishida

Project Assistant Professor/ Postdoctoral Researchers



Akiko Nakamasu

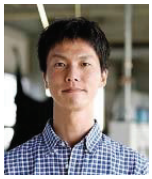
Sajid Fazal

Adam Karl Schwartzkopff

Mizuki Yamada

Young Faculty Members for International Joint Research

Takahiro Hosono
FAST



Kei Ishida
CWMD

Makoto Kumon
FAST

Mizue Munekata
FAST

Yuta Nakashima
FAST

Masayuki Tanabe
FAST

Visiting Professors

U Rajendra Acharya
Ngee Ann Polytechnic
Singapore

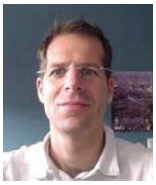
José E. Andrade
California Institute of Technology
USA

Josep-Lluís Barona-Vilar
University of Valencia
Spain

Pouyan Boukany
Delft University of Technology
Netherlands

Olivier Boutin
Aix Marseille University
France

Paul Bowen
The University of Birmingham
UK



Pierre Breul
University of
Clermont Auvergne
France

Maria Jose Cocero
The University of
Valladolid
Spain

Marc De Boissieu
CNRS, SiMAP
Université
Grenoble Alpes
France

Patrice Delmas
The University of
Auckland
New Zealand

Martin Dienwiebel
Karlsruhe
Institute for
Technology
Germany

Martino Di Serio
University of
Naples Federico II
Italy

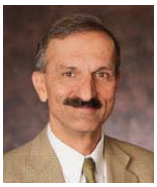
Derek Elsworth
The Pennsylvania
State University
USA

Carolina Escobar
University of
Castilla La Mancha
Spain

Amir A. Farajian
Wright State
University
USA

Etsuko Fujita
Brookhaven
National Laboratory
USA

Tomonari Furukawa
University of
Virginia
USA



Hamid Ghandehari
University of Utah
USA

Olivier Hamant
INRA, RDP
ENS Lyon
France

Christian Hardtke
University of
Lausanne
Switzerland

Jens Hartmann
Universität
Hamburg
Germany

Yang Kim
Kosin University
Republic of Korea

Alexei Kuzmin
Institute of Solid
State Physics
University of
Latvia
Latvia

Ick Chan Kwon
Dana Farber Cancer
Institute, Harvard
Medical School
USA/
Korea Institute of
Science and
Technology (KIST)
Republic of Korea

Youn-Woo Lee
Seoul National
University
Republic of Korea

Pavel Lejček
Academy of
Sciences of the
Czech Republic/
University of
Chemistry and
Technology, Prague
Czech Republic

Viren Ivor Menezes
Indian Institute of
Technology
Bombay
India

Matthieu Micoulaut
Sorbonne
University
France

Dmitri Aleks Molodov
RWTH Aachen
University
Germany

Rahul Raveendran Nair
The University of
Manchester
UK

Reiko Oda
CNRS, University
of Bordeaux
France

Shie-Ming Peng
National Taiwan
University
Taiwan

Ramesh S. Pillai
University of
Geneva
Switzerland

Zoran Ren
University of
Maribor
Slovenia

Christian Rentenberger
University of
Vienna
Austria

Stelios Rigopoulos
Imperial College
London
UK

Shirley Shen
Commonwealth Scientific and Industrial Research Organisation (CSIRO)
Australia

Gioacchino Viggiani
Université Grenoble Alpes
France

Thomas Waitz
University of Vienna
Austria

Andrew Whittle
Massachusetts Institute of Technology (MIT)
USA

Zhenghe Xu
Southern University of Science and Technology
China/
University of Alberta
Canada

Firuz Zare
The University of Queensland
Australia

Visiting Associate Professors

Tomoyasu Mani
University of Connecticut
USA

Daniel P. Zitterbart
Woods Hole Oceanographic Institution
USA/
University of Erlangen-Nuremberg
Germany

Distinguished Professors (3)

Name	Period of Appointment	Position/Affiliation
Konstantinos Kontis	November 1, 2018-	Professor /Head of the Aerospace Sciences Division /Sir Henry Mechan Chair of Engineering School of Engineering University of Glasgow, UK
László Pusztai	April 1, 2017-	Scientific Advisor Wigner Research Centre for Physics Hungary
Yufeng Zheng	May 1, 2017-	Professor Department of Materials and Engineering College of Engineering Peking University, China

Tenure-Track Professor/Associate Professors/Assistant Professor (5)

Name	Period of Appointment	Former Position/Affiliation
Mitsuhiro Aida Professor	July 1, 2017-	Postdoctoral Researcher Department of Applied Biological Science Tokyo University of Science PhD: Kyoto University (1999)
Takumi Higaki Associate Professor	August 1, 2017-	Research Associate Professor Graduate School of Frontier Sciences The University of Tokyo PhD: The University of Tokyo (2009)
Ruda Lee Associate Professor	January 1, 2017-	Postdoctoral Researcher Department of Drug Discovery and Development Instituto Italiano Di Technologia, Italy PhD: Korea University, Korea (2013)
Atsushi Sainoki Associate Professor	January 1, 2017- March 31, 2021	Postdoctoral Researcher Mine Design Laboratory, McGill University, Canada PhD: McGill University, Canada (2014)
Takashi Ishida Assistant professor	June 1, 2016-	Postdoctoral Researcher Graduate School of Science and Technology, Kumamoto University PhD: Nara Institute of Science and Technology (2007)

Project Assistant Professor (1)

Name	Period of Appointment	Former Position/Affiliation
Akiko Nakamasu Higaki Laboratory	November 1, 2019- (Postdoctoral Researcher December 1, 2017- October 30, 2019)	Research Assistant Professor Faculty of Medical Science, Kyushu University PhD: Ochanomizu University (2010)

Postdoctoral Researchers (3)

Name	Period of Appointment	Former Position/Affiliation
Sajid Fazal Lee Laboratory	December 1, 2020- March 31, 2021	Postdoctoral Research Associate Indian Institute of Technology Delhi PhD: Amrita Vishwa Vidyapeetham, India (2018)
Adam Karl Schwartzkopff Sainoki Laboratory	July 1, 2017- March 31, 2021	Casual Lecturer/ Course Coordinator The University of Adelaide, Australia PhD: The University of Adelaide, Australia (2016)
Mizuki Yamada Aida Laboratory	October 1, 2019-	Researcher Institute of Vegetable and Floriculture Science National Agriculture and Food Research Organization PhD: Niigata University (2014)

Young Faculty Members for International Joint Research (6)

Name	Period of Appointment	Partner University/Institution
Takahiro Hosono Associate Professor FAST	June 1, 2019- March 31, 2022	Department of Earth and Planetary Science University of California, Berkeley USA
Kei Ishida Associate Professor CWMD	June 1, 2019- March 31, 2022	McGill University Canada/ University of California, Davis USA
Makoto Kumon Associate Professor FAST	April 1, 2018- March 31, 2021	Virginia Polytechnic Institute and State University USA/ University of Virginia USA
Mizue Munekata Associate Professor FAST	April 1, 2019- March 31, 2022	German Aerospace Center Germany/ Institute of Aerodynamics and Flow Technology Germany
Yuta Nakashima Associate Professor FAST	December 1, 2019- March 31, 2022	The Children's Hospital of Philadelphia USA/ University of Pennsylvania USA
Masayuki Tanabe Assistant Professor FAST	June 1, 2019- March 31, 2021	Department of Biomedical Engineering and Radiology Columbia University USA/ School of Engineering, Ngee Ann Polytechnic Singapore

Visiting Professors (42)

Name	Position/Affiliation	Host Professor
U Rajendra Acharya	Senior faculty member Ngee Ann Polytechnic, Singapore	**Makiko Kobayashi** FAST
José E. Andrade	Professor California Institute of Technology, USA	**Jun Otani** FAST
Josep-Lluís Barona-Vilar	Professor University of Valencia, Spain	**Makoto Takafuji** FAST
Pouyan Boukany	Associate Professor Delft University of Technology, Netherlands	**Hamid Hosano** IINa
Olivier Boutin	Professor Deputy Director M2P2 Laboratory Director Master Chemical Engineering Aix Marseille University, France	**Mitsuru Sasaki** IINa
Paul Bowen	Deputy Pro-Vice-Chancellor/ Feeney Professor of Metallurgy The University of Birmingham, UK	**Kazuki Takashima** FAST
Pierre Breul	Professor University of Clermont Auvergne, France	**Jun Otani** FAST
Maria Jose Cocero	Professor The University of Valladolid, Spain	**Tetsuya Kida** FAST
Marc De Bossieu	Director CNRS, SIMaP, Université Grenoble Alpes, France	**Shinya Hosokawa** FAST
Patrice Delmas	Associate Professor The University of Auckland, New Zealand	**Toshifumi Mukunoki** FAST
Martin Dienwiebel	Professor Karlsruhe Institute for Technology, Germany	**Kazuki Takashima** FAST
Martino Di Serio	Professor University of Naples Federico II, Italy	**Shinya Hayami** FAST
Derek Elsworth	Professor The Pennsylvania State University, USA	**Atsushi Sainoki** IROAST

Carolina Escobar	Professor University of Castilla La Mancha, Spain	**Shinichiro Sawa** FAST
Amir A. Farajian	Professor Wright State University, USA	**Hamid Hosano** IINa
Etsuko Fujita	Senior Chemist Brookhaven National Laboratory, USA	**Yutaka Kuwahara** FAST
Tomonari Furukawa	Professor University of Virginia, USA	**Makoto Kumon** FAST
Hamid Ghandehari	Professor University of Utah, USA	**Hamid Hosano** IINa
Olivier Hamant	Research Director INRA in the Plant Reproduction and Development Laboratory, ENS Lyon, France	**Shinichiro Sawa** FAST
Christian Hardtke	Professor University of Lausanne, Switzerland	**Shinichiro Sawa** FAST
Jens Hartmann	Professor Universität Hamburg, Germany	**Takahiro Hosono** FAST
Yang Kim	Professor Emeritus Kosin University, Republic of Korea	**Shinya Hayami** FAST
Alexei Kuzmin	Leading Researcher/ Full Member of the Latvian Academy of Science Institute of Solid State Physics University of Latvia, Latvia	**Laszlo Pusztai** IROAST
Ick Chan Kwon	Presidential Scholar Dana Farber Cancer Institute Harvard Medical School, USA/ Principal Research Scientist Korea Institute of Science and Technology (KIST) Republic of Korea	**Takuro Niidome** FAST
Youn-Woo Lee	Professor Seoul National University, Republic of Korea	**Mitsuru Sasaki** IINa

Pavel Lejček	Professor Academy of Sciences of the Czech Republic/ University of Chemistry and Technology, Prague Czech Republic	**Sadahiro Tsurekawa** FAST
Viren Ivor Menezes	Professor Indian Institute of Technology Bombay, India	**Hamid Hosano** IINa
Matthieu Micoulaut	Professor Sorbonne University, France	**Shinya Hosokawa** FAST
Dmitri Aleks Molodov	Professor RWTH Aachen University, Germany	**Sadahiro Tsurekawa** FAST
Rahul Raveendran Nair	Professor The University of Manchester, UK	**Shinya Hayami** FAST
Reiko Oda	Senior Principal Investigator CNRS, University of Bordeaux, France	**Makoto Takafuji** FAST
Shie-Ming Peng	Distinguished Research Professor National Taiwan University, Taiwan	**Shinya Hayami** FAST
Ramesh S. Pillai	Professor University of Geneva, Switzerland	**Tokio Tani** FAST
Zoran Ren	Professor University of Maribor, Slovenia	**Kazuyuki Hokamoto** IINa
Christian Rentenberger	Associate Professor University of Vienna, Austria	**Mitsuhiro Matsuda** FAST
Stelios Rigopoulos	Reader (Associate Professor) Imperial College London, UK	**Hamid Hosano** IINa
Shirley Shen	Principal Research Scientist Commonwealth Scientific and Industrial Research Organisation (CSIRO), Australia	**Kazuki Takashima** FAST
Gioacchino Viggiani	Professor Université Grenoble Alpes, France	**Jun Otani** FAST
Thomas Waitz	Associate Professor University of Vienna, Austria	**Mitsuhiro Matsuda** FAST
Andrew Whittle	Professor of Civil & Environmental Engineering Massachusetts Institute of Technology (MIT), USA	**Jun Otani** FAST

Zhenghe Xu	Professor Southern University of Science and Technology China/ Professor University of Alberta, Canada	**Makoto Takafuji** FAST
Firus Zare	Professor The University of Queensland, Australia	**Hamid Hosano** IINa

Visiting Associate Professors (2)

Name	Position/Affiliation	Host Professor
Tomoyasu Mani	Assistant Professor University of Connecticut, USA	**Yutaka Kuwahara** FAST
Daniel P. Zitterbart	Assistant Professor Woods Hole Oceanographic Institution, USA/ University of Erlangen-Nuremberg Germany	**Kei Toda** FAST

*The names of each list are arranged alphabetically by last name.

Research Units (23)

Units of World-leading Researchers (13)

Unit Name	Unit Coordinator
Development of Nano and Supramolecular Materials	**Shinya Hayami** FAST
RNA Biology	**Tokio Tani** FAST
Plant Cell and Developmental Biology	**Shinichiro Sawa** FAST
Nano-Organics and Nano-Hybrids	**Makoto Takafuji** FAST
Nano-medicine and Drug Delivery System	**Hamid Hosano** IINa
Nano-medicine and Theranostics	**Takuro Niidome** FAST
Multiscale Modeling of Soil and Rock Materials Using X-ray CT	**Jun Otani** FAST
Medical Application of X-ray CT	**Toshifumi Mukunoki** FAST
-Quantification of Three Dimensional Vascular Network	
-MicroCT-based Quantification of Fibrosis and Vascularization in Pancreatic Tumor	
Advanced Structural Materials	**Kazuki Takashima** FAST
Microstructure Analysis and Grain Boundary Engineering	**Sadahiro Tsurekawa** FAST
Structure and Dynamics of Materials Using Quantum Beams and Data-Driven Sciences	**Shinya Hosokawa** FAST
Hydrological Environments	**Takahiro Hosono** FAST

Units of Young Researchers (10)

Unit Name	Unit Coordinator
Quantitative Bioimaging	**Takumi Higaki** IROAST
Development of novel therapeutic strategy using iron targeted upconversion nanoparticles for Parkinson's disease	**Ruda Lee** IROAST
Deep Learning for Hydrology	**Kei Ishida** CWMD
Environmental Impacts of Ionic Solutes	**Shin-Ichi Ohira** FAST
Radio Astronomy	**Keitaro Takahashi** FAST
Plant Stem Cells and Regeneration	**Mitsuhiro Aida** IROAST
Development of microbially-aided carbon sequestration technology	**Atsushi Sainoki** IROAST
Advanced Biomedical Evaluation System	**Makiko Kobayashi** FAST
Bio-inspired Functional Molecular System	**Yutaka Kuwahara** FAST
Nanomaterials processing for medical, cosmetic, and environmental applications	**Mitsuru Sasaki** IINa

FAST: Faculty of Advanced Science and Technology, Kumamoto University
IINa: Institute of Industrial Nanomaterials, Kumamoto University
CWMD: Center for Water Cycle, Marine Environment and Disaster Management, Kumamoto University

Operation and Management of IROAST

Operation and Management of IROAST

1. IROAST Steering Committee Activities

We held our IROAST Steering Committee meetings 10 times in the academic year of 2020 to discuss and determine varieties of regulations and agenda items required for successful operation and management of IROAST. We have enacted 13 regulations and rules so far. The committee has approved the adoption of many researchers participating in the IROAST research support programs below.

2. IROAST Research Support Programs

We have several research support programs running in parallel to promote internationally collaborated research programs with an aim to configure international joint research networks and offer/gain benefit from the brain circulation around the world.

IROAST Young Faculty Members for International Joint Research

We select young excellent faculty members from the Faculty of Advanced Science and Technology, the Institute of Industrial Nano Materials, the Magnesium Research Center and the Center for Water Cycle, Marine Environment and Disaster Management and invite them to IROAST for three or four years to give them opportunities to conduct international joint research at overseas universities and institutions for at least one year in total.

IROAST International Joint Research Travel Support

We select excellent faculty members from the Faculty of Advanced Science and Technology, the Institute of Pulsed Power Science, the Magnesium Research Center and the Center for Water Cycle, Marine Environment and Disaster Management and send them to overseas universities and institutions to conclude MOUs to promote their international joint research and/or to perform their joint research there. Unfortunately, we should stop this support because of pandemic outbreak of new Corona virus (COVID-19).

IROAST Visiting Professor and Visiting Professor Candidate Invitation

We invite our Visiting Professors and candidates for Visiting Professors to IROAST to promote the joint research with their host researchers toward the configuration of international joint research networks and to open international seminars to attract young researchers including graduate students into the cutting-age research activities. Because of the pandemic outbreak of COVID-19, we have postponed the invitation of visiting professors and the candidates.

IROAST Research Award (for IROAST faculty members only)

We select and award outstanding and promising IROAST faculty members at the end of every academic year to encourage their research activities.

IROAST Proofreading/Publication Support

We give financial support for proofreading/publication to IROAST-affiliated researchers to increase the number of publications from the Kumamoto University science and technology fields.

IROAST Research Internship Program

We provide hands-on research opportunities for highly motivated undergraduate/graduate students and young postdoctoral researchers who have interests in advanced scientific research. In 2020, we have just conducted one symposium online basis because of the pandemic outbreak of COVID-19.

IROAST Symposiums

We invite keynote speakers from overseas and domestic universities to hold international symposiums two to three times a year. Due to the COVID-19 outbreak, only one symposium was conducted in 2020, a joint symposium among the International Research Center for Medical Sciences (IRCMS) and IROAST of Kumamoto University and Korea Advanced Institute of Science and Technology (KAIST) in Korea, and this was conducted online, aiming to match up multidisciplinary research collaborations between Kumamoto University and KAIST. Indeed, discussions on joint research between researchers from both countries are ongoing.

IROAST Seminars

International researchers invited through the IROAST Visiting Professor and Visiting Professor Candidate Invitation program above give talks in the IROAST Seminars organized by their host professors. In 2020, due to the spread of COVID-19, no visiting professors visited Japan, but we were able to hold two seminars using online tools. One of the seminars was held in cooperation with the IRCMS. In this seminar, researchers from both organizations gave presentations and more than 30 participants engaged in active discussions. Collaborative researches between researchers from both organizations that stated with the previous joint seminars are also continuing and achieving successful results.

3. Statistics for IROAST Research Activities

The following tables indicate several indices to evaluate our research activities.

◆ Indices for Self-evaluation of IROAST Research Activities

Indices for Self-Evaluation **(Numerical Target)**	2016	2017	2018	2019	**2020**
Number of Papers **(30 papers per year)**	13	26	43	72	**112**
Rate of Internationally Collaborated Papers **(~80%~)**	84.6	88.5	79.1	81.9	**83.0**
Rate of Top 10% Papers **(~20%~)**	0	15.4	16.3	20.8	**23.2**
Field Weighted Citation Index **(>1.1)**	0.85	1.33	1.31	1.59	**2.41**

Indices for Self-Evaluation **(Numerical Target)**	2016	2017	2018	2019	**2020**
Number of Concluded MOU **(>20 for the first term)**	3	8	13	16	**16**
Number of Visiting Professors **(~40~)**	18	26	37	41	**44**
Number of Distinguished Professors **(4)**	0	2	3	4	**3**
Number of International Symposia including KU-KAIST Joint Symposium **(>1)**	1	1	5	3	**1**
Number of International Seminars including IROAST&IRCMS Joint Seminars **(~20~)**	8	20	23	20	**2**
Number of Invited Researchers **(~25~)**	9	25	28	22	–
Number of Researchers Visiting Overseas Universities and Institutions **(~20~)**	5	21	18	15	–
Number of Internship Students	–	–	3	13	–

Note) The number of papers and other paper-related data for 2018-2020 were obtained from the Web of Science by requesting the IR office in April 2021.

◆ Summary of Research Fund

FY2020

Categories	Number of Grants	Amount (x 1000 Yen)
JSPS Grant-in-Aid	8	32,560
Commissioned Research	1	1,300
Private Research Grant	2	1,000
Total	11	34,860

FY2019

Categories	Number of Grants	Amount (x 1000 Yen)
JSPS Grant-in-Aid	4	23,400
Commissioned Research	1	2,200
Private Research Grant	2	1,000
Donated Grant	1	950
Total	8	27,550

FY2018

Categories	Number of Grants	Amount (x 1000 Yen)
JSPS Grant-in-Aid	6	27,430
Commissioned Research	1	6,862
Private Research Grant	7	5,870
Donated Grant	1	6,000
Total	15	46,162

*Amended some numbers for the last three years based on a revised criterion.

Research Activities

1. IROAST Researchers

Research Activities

1. IROAST Researchers

No.	Name	Project Title
1-1	**Mitsuhiro Aida**	Plant developmental biology
1-2	**Takumi Higaki**	Quantitative Bioimaging
1-3	**Ruda Lee**	Overcoming multi-drug resistance cancer cells using multi-functional nanoconstructs
1-4	**Atsushi Sainoki**	Sustainable energy development
1-5	**Takashi Ishida**	Deciphering the molecular basis of the plant morphogenesis
1-6	**Akiko Nakamasu**	Theoretical modeling for the understanding of plant structure formations
1-7	**Adam Karl Schwartzkopff**	Prediction of induced seismicity from fluid injection into faults
1-8	**Mizuki Yamada**	Analysis of multilayered regulation of auxin signaling in the apical region development of the plant embryo

No.1-1	Plant developmental biology		
Name	Mitsuhiro Aida		
Affiliation	IROAST Email: m-aida@kumamoto-u.ac.jp	Title	Professor
Research Field	Advanced Green Bio		

1. Research Achievements

Our research aim is to elucidate molecular and genetic mechanisms that regulate the activity of shoot meristem, a group of dividing cells that is responsible for production of plant aerial organs, such as leaves, stems and floral organs, which are collectively called shoot organs. In dicotyledonous plants, the shoot meristem is initially formed during embryogenesis in a boundary region between the two cotyledon primordia, and after germination, it maintains a group of stem cells at its center and continuously provides new cells that give rise to shoot organs from its periphery.

We have been focusing on a set of transcription factor encoding genes called *CUC1*, *CUC2* and *CUC3*, which are expressed in the cotyledon boundary region and required for shoot meristem formation in *Arabidopsis thaliana*. We demonstrated that the CUC1 protein, together with the functionary redundant transcription factors, promotes expression of key regulatory downstream genes that are essential for maintaining postembryonic shoot meristem activity, and the mode of its transcriptional regulation on many of these downstream genes is possibly direct. Of note, a pair of the downstream genes, the *KNOX* gene *STM* and the cytochrome P450 gene *KLU*, have opposite effects on the shoot meristem activity, suggesting that a balancing mechanism for shoot meristem activity upon its initiation (ref. 3).

We also investigated involvement of these transcription factors in reproduction organ development. The gynoecium, or the female reproductive organ of flowering plants, has an elaborated structure suitable for fertilization and seed dispersal. We have shown that the *CUC* genes and its downstream gene *BLR* interact to ensure proper development of the medial tissues, which provide physical strength and the ability for efficient seed dispersal to the gynoecium (ref. 5). The medial tissues also undergo post-genital fusion to produce transmitting tract for pollen tubes and we described changes in the epidermal identity during this event (ref. 4).

Finally, we have also developed a technique to visualize 3D structure oof plant embryo. In collaboration with the Shinichiro Sawa from FAST and Takashi Ishida from IROAST, we optimized a tissue clearing method for embryos of the model plant *Arabidopsis thaliana*, enabling the collection of high-quality 3D morphological data, which is suitable for quantitative analyses (Figure). Our new method would facilitate analysis of developmental mechanisms that govern plant embryogenesis, in which a series of coordinated patterning and morphological events proceed to establish the basic body plan (ref. 2).

2. International Research Collaboration

International collaborative work was made between Michael Lenhard's group (University of Potsdam, Germany) and our group, and led to a publication of *CUC* downstream genes (ref. 3). Other collaborative work has been carried out with Jose Ireapan Reyes Olalde, a research fellow from Consejo Nacional de Ciencia y Tecnología (CONACYT) of Mexico, to elucidate hormonal control of gynoecium development, which led to an oral presentation in the 84th Annual Meeting of the Botanical Society of Japan (September 20th, 2020). A collaboration with Yoshihisa Ikeda from Palacký University (Czech Republic) has led to a publication of a review article about the role for the plant hormone cytokinin in intracellular signaling (ref 1) and details of this activity is described elsewhere (Research Unit "Plant Stem Cells and Regeneration" section).

3. Prospect for further research collaboration

The following collaborative research is planned in FY2021.

- ✓ Analysis of transcription factor-target gene interactions during shoot meristem formation with Simon Scofield in Cardiff University, UK.
- ✓ Mechanisms of fruit development with Stefan de Folter in CINVESTAV, LANGEBIO, Mexico.
- ✓ The role of mechanical signals in the regulation of gene expression with Olivier Hamant in INRA ENS de Lyon, France.
- ✓ The role of boundary specific signaling peptide in embryogenesis with Keiko U Torii in Howard Hughes Medical Institute and University of Texas at Austin, USA, and Rüdiger Simon in Heinrich-Heine University, Germany.

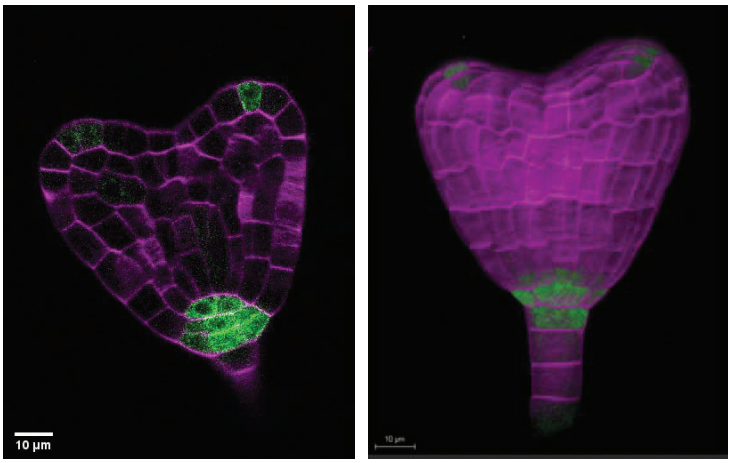
4. Other activities

- ✓ Chairperson of Public Relations Committee, The Japanese Society of Plant Physiologists (March 2020–present)
- ✓ Writing a short article for a scientific exhibition ("Plants: Mainstays of the Planet, National Museum of Nature and Science)
- ✓ Peer review of three papers
- ✓ Lectures (6 times in Faculty of Science, 4 times in Multidisciplinary Studies, 90 min/time)
- ✓ Host of a visiting lecture (Faculty of Science, Prof. Sachihiro Matsunaga from Univ. Tokyo)
- ✓ Supervision of three undergraduate students of Faculty of Science)
- ✓ Thesis reviewer for two master course students, Graduate School of Science and Technology

List of Publications (*Corresponding Author)

1. Ikeda Y, Zalabák D, Kubalová I, Králová M, Brenner WG, **Aida M** (2021). Interpreting cytokinin action as anterograde signaling and beyond. Front Plant Sci 12, 641257. doi: 10.3389/fpls.2021.641257.
2. Imoto A, Yamada M, Sakamoto T, Okuyama A, Ishida T, Sawa S, ***Aida M** (2021). A ClearSee-based clearing protocol for 3D visualization of *Arabidopsis thaliana* embryos. Plants 10, 190. doi: 10.3390/plants10020190
3. ***Aida M**, Tsubakimoto Y, Shimizu S, Ogisu H, Kamiya M, Iwamoto R, Takeda S, Karim MR, Mizutani M, Lenhard M, Tasaka M (2020). Establishment of the embryonic shoot meristem involves activation of two classes of genes with opposing functions for meristem activities. Int J Mol Sci 21, 5864. doi: 10.3390/ijms21165864.
4. Yokoi A, ***Aida M** (2021). Postgenital fusion and epidermal cell fate control during gynoecium development. Cytologia 86, 1-2. doi: 10.1508/cytologia.86.1.
5. Yamamoto K, Tasaka M, ***Aida M**. Genetic interactions between the *CUP-SHAPED COTYLEDON* and the *BELLRINGER* genes indicate their overlapping functions in carpel boundary development in *Arabidopsis thaliana*. Plant Morphol, in press.

Figure

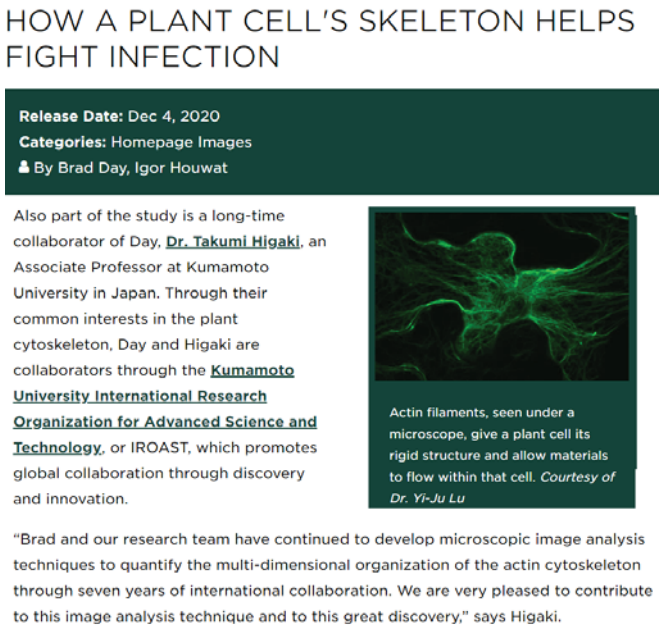


Confocal image of a cleared *Arabidopsis thaliana* embryo expressing the auxin response reporter *DR5* (ref 2). An optical section (left) and 3D reconstruction.

No.1-2	Quantitative Bioimaging		
Name	Takumi Higaki		
Affiliation	IROAST Email: thigaki@kumamoto-u.ac.jp	Title	Associate Professor
Research Field	Advanced Green Bio		

Details of activities

Recent advances in bioimaging equipment have enabled biological scientists to easily acquire large amounts of bioimage data within a short period of time. Following this influx of information, biologists are now engaging in bioimage informatics, an emerging area of bioinformatics. I am working on this interdisciplinary research area through the development of bioimage analysis tools and their application to cell biological problems. As great opportunities in FY2020, the outcome of my collaborative researches with the group of Professor Brad Day of Michigan State University was published in *Nature Communications* (Lu et al. 2020). In this collaboration, I contributed to quantitatively evaluate the actin cytoskeleton organization in plant cells during the immune response. This research topic including my interview was featured on the Michigan State University website (December 4, 2020) (https://mps.natsci.msu.edu/news-events/news/how-a-plant-cells-skeleton-helps-fight-infection/).


HOW A PLANT CELL'S SKELETON HELPS FIGHT INFECTION

Release Date: Dec 4, 2020
Categories: Homepage Images
By Brad Day, Igor Houwat

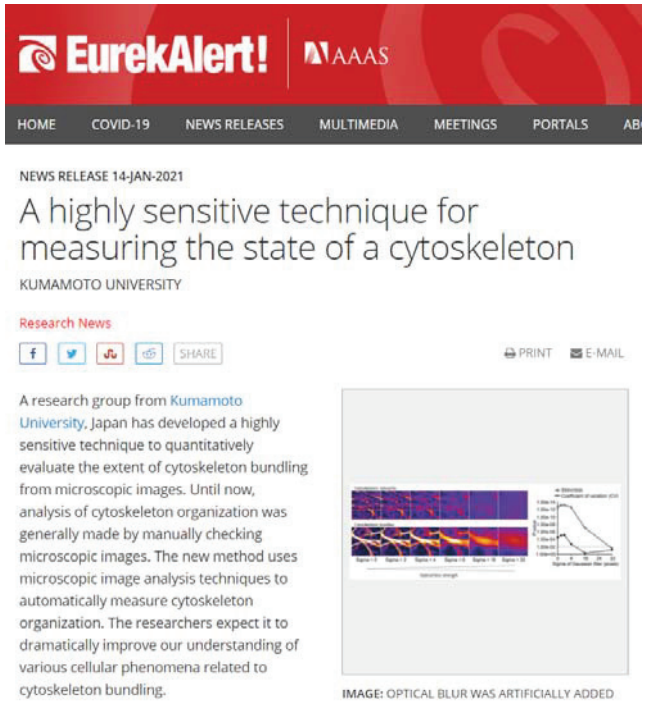
Also part of the study is a long-time collaborator of Day, **Dr. Takumi Higaki**, an Associate Professor at Kumamoto University in Japan. Through their common interests in the plant cytoskeleton, Day and Higaki are collaborators through the **Kumamoto University International Research Organization for Advanced Science and Technology**, or IROAST, which promotes global collaboration through discovery and innovation.

Actin filaments, seen under a microscope, give a plant cell its rigid structure and allow materials to flow within that cell. *Courtesy of Dr. Yi-Ju Lu*

"Brad and our research team have continued to develop microscopic image analysis techniques to quantify the multi-dimensional organization of the actin cytoskeleton through seven years of international collaboration. We are very pleased to contribute to this image analysis technique and to this great discovery," says Higaki.

URL:

I have also worked on the development of a highly sensitive technique to quantitatively evaluate the extent of cytoskeleton bundling from microscopic images as a collaboration with Drs Kaoru Katoh of AIST and Kae Akita of Japan Women's University, and published the works in *Scientific Reports* (Higaki et al. 2020). In this paper, we reported that the coefficient of variation of intensities in cytoskeleton pixels nicely reflected the bundle state in the images obtained by various types of light microscopes. These research highlights were featured on the Kumamoto University website (https://ewww.kumamoto-u.ac.jp/en/news/428/) and EurekAlert!


EurekAlert! AAAS

HOME COVID-19 NEWS RELEASES MULTIMEDIA MEETINGS PORTALS

NEWS RELEASE 14-JAN-2021

A highly sensitive technique for measuring the state of a cytoskeleton

KUMAMOTO UNIVERSITY

Research News

SHARE PRINT E-MAIL

A research group from Kumamoto University, Japan has developed a highly sensitive technique to quantitatively evaluate the extent of cytoskeleton bundling from microscopic images. Until now, analysis of cytoskeleton organization was generally made by manually checking microscopic images. The new method uses microscopic image analysis techniques to automatically measure cytoskeleton organization. The researchers expect it to dramatically improve our understanding of various cellular phenomena related to cytoskeleton bundling.

IMAGE: OPTICAL BLUR WAS ARTIFICIALLY ADDED

(https://www.eurekalert.org/pub_releases/2021-01/ku-ahs011421.php) (January 14, 2021).

In addition, I have published three papers as a corresponding author in FY2020. First, we determined the effect of the elevated CO_2 concentration on the stomatal distribution patterns in *Arabidopsis thaliana* cotyledons (Higaki et al. 2020 *Gene Cells*). Second, as a collaboration with Dr. Hidenobu Mizuno of IRCMS Kumamoto University, we developed the 4-D microscopic imaging system with virtual reality to quantitatively explore jigsaw puzzle-like morphogenesis of *Arabidopsis* cotyledon pavement cells (Higaki and Mizuno 2020 *Plant Biotech*). Lastly, we examined the effects of pharmacological disruption of actin filaments on the mitosis and cytokinesis in tobacco BY-2 cultured cells (Maeda and Higaki 2021 *Plant Sig Behav*).

As collaborative projects based on my image analysis techniques, I performed the quantitative evaluation of plant cell morphology in the cell wall mutants as a collaboration with Prof. Toshihisa Kotake od Saitama University (Yoshimi et al. 2020 *J Exp Bot*). I also quantitatively evaluated the distribution and morphology of mitochondria in plant zygote as a collaboration with Prof. Minako Ueda of Tohoku University (Kimata et al. 2020 *Quant Plant Biol*). In addition, I examined the effects of the novel chemical compound named ‘Kumamonamide’ using tobacco BY-2 cultured cells and microscopic image analysis techniques as a collaboration with the IROAST member Dr. Takashi Ishida (Ishida et al. 2021 *Sci Rep*).

Related to the research activities, my graduate student Mr. Keisho Maeda won the "Best Presentation Award" at the presentation of graduation theses of the Biological Sciences Course of the Graduate School of Science and Technology, Kumamoto University (February 12, 2020). Also, my undergraduate students Ms. Kotomi Kikukawa and Mr. Daichi Yoshida won the "Best Presentation Award" at the presentation of graduation theses of the Biological Sciences Course of the Faculty of Science, Kumamoto University (February 10, 2020).

I was very honored to receive The 6th CYTOLOGIA Encouragement Awards from The Japan Mendel Society” (December 28, 2020) and The Japanese Society of Plant Physiologists (JSPP) Young Investigator Award” from the JSPP (March 15, 2021). The former award ceremony and lecture were canceled due to COVID-19, but I gave the online award lecture concerning the latter award with the title "Quantitative bioimaging of plant cytoskeleton" (see also right panels). It was a wonderful opportunity for me to reflect on my research to date. I would like to express my sincere thanks for the continuous supports of the IROAST members and the administrative staff for these awards.

No.1-3	Overcoming multi-drug resistance cancer cells using multi-functional nanoconstructs		
Name	Ruda Lee		
Affiliation	IROAST Email: aeju-lee@kumamoto-u.ac.jp	Title	Associate Professor
Research Field	Advanced Green Bio		

1. Research achievements

Cancer is considered one of the most challenging health care problems. Despite promising and considerable advances in the discovery of the etiology and underlying mechanisms of cancer, as well as the design of novel and effective diagnostic and therapeutic strategies, there still is a highly increasing incidence and mortality of cancer. The failure of chemotherapy in the clinic is mainly due to different extents of multidrug resistance (MDR) results with approximately 90% of cancer patients died. MDR occurs when tumor cells develop resistance to structurally and functionally unrelated classes of chemotherapeutic agents leading to drug inactivation and/or drug efflux from cancer cells leading to obstacles to the treatment.

In FY2020, I was focused on 1) developed a smart drug delivery system, 2) preparation of MDR cell lines, and 3) set up for 3D organoid. Various types of NPs were successfully developed and evaluated *in vitro* and *in vivo*. Each NPs showed their own characteristics and properly worked under a specific environment (low pH, reactive oxygen species). The MDR cell lines are compared with parent cell lines for checking the differences. 3D organoid was set up in two different methods and confirmed the inner structure using confocal microscopy. The epithelial cells (blood vessel) and tumor cells are successfully built for co-culture immune cells. A better understanding of complex and dynamic system is essential to enable us to develop therapeutic strategies that bypass MDR, and also effective ways of inhibiting MDR components to increase the efficacy of our current extensively used chemotherapies. In further study, to get real-time MDR reactive information, I will build optimized customizable 3D microfluidic chips, set up natural conditions, and use super resolution imaging devices.

[Lee lab paper achievement]: First author (1), Corresponding author (2), Last author (1)

1. Yong Il Park, Seung-Hae Kwon, Gibok Lee, Keiichi Motoyama, Min Woo Kim, Min Lin, Takuro Niidome, Jung Hoon Choi, **Ruda Lee***. pH-sensitive multi-drug liposomes targeting folate receptor β for efficient treatment of non-small cell lung cancer. *Journal of Controlled Release*, 330, 1-14, February 2021.
2. Sho Ueno, Min Woo Kim, Gibok Lee, Yong Il Park, Takuro Niidome, and **Ruda Lee***. Development of

ErbB2-Targeting Liposomes for Enhancing Drug Delivery to ErbB2-Positive Breast Cancer. *Pharmaceutics*, 12, 585, June 2020.

3. Xiaoxue Xu, Hongxu Lu and **Ruda Lee**. Near Infrared Light Triggered Photo/Immuno-Therapy Toward Cancers. *Frontiers in Bioengineering and Biotechnology*, 8, 488. May 2020.
4. Song Yeul Lee*, **Ruda Lee***, Eunha Kim, Sanghee Lee and Yong Il Park. Near-Infrared Light-Triggered Photodynamic Therapy and Apoptosis Using Upconversion Nanoparticles with Dual Photosensitizers. *Frontiers in Bioengineering and Biotechnology*, 8, 275. Apr 2020.

2. International research collaboration

In FY2020, I focused on the development of nanomaterials. Because of COVID-19, no exchange collaborative research was performed for a year. Instead of joint work, we separately processed each part (Japan: Material, Korea: Animal/ Japan: Cell line, Australia: Material/ Japan: Sensor, US: Animal) and set up an optimized conditions for joint work. When the COVID-19 situation becomes better, we will make the best results based on collaborative work.

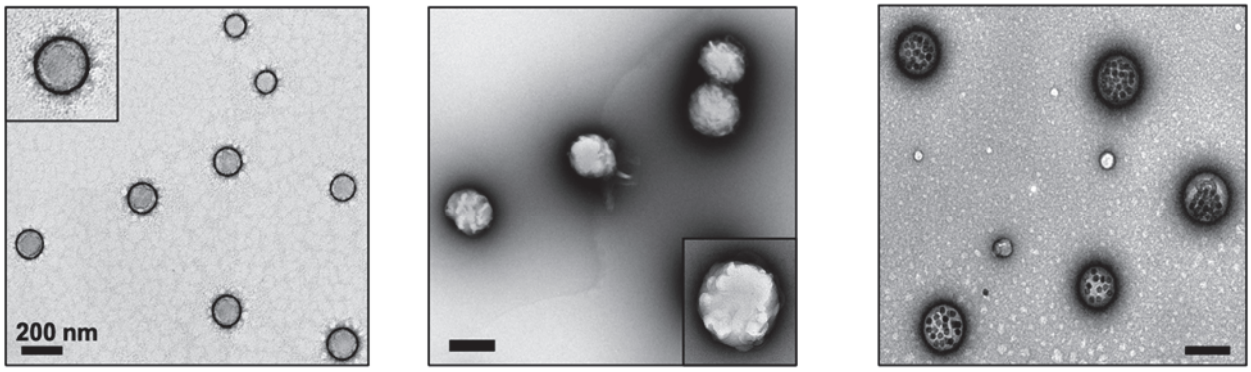
3. Prospect for further research collaboration

First, I and Yonsei University hospital team started to get patient-derived samples and will apply on imaging sensor to diagnosis disease severity. One of my graduate students succeeded in selecting the most specific sequence of peptides for targeting tumor margin. We prepare 20 patient and 5 normal tissues for clinical application. Furthermore, the IRCMS-IROAST research collaboration project used that selected peptide for tracking epithelial-mesenchymal transition (EMT). Three researchers(Biologist, Pharmacologist, and Nano scientist) focused on inhibition of EMT using the chemical drug and siRNA loaded nanoparticles, respectively. The materials will be confirmed in cells and chicken embryo model. We are expecting published two papers in FY2021.

Second, Yang Zheng (Claire) M.D., Ph.D., a new collaborator of Dana Faber Cancer Institute, and I submitted CRDF global research grant for young female researcher on April 1. We will be focusing on investigating DNA origami vaccine efficacy in infectious diseases. To expand my research, I was involved in immunology related project. After getting preliminary data in FY2021, we have plan to apply HFSP young researcher grant in FY2022.

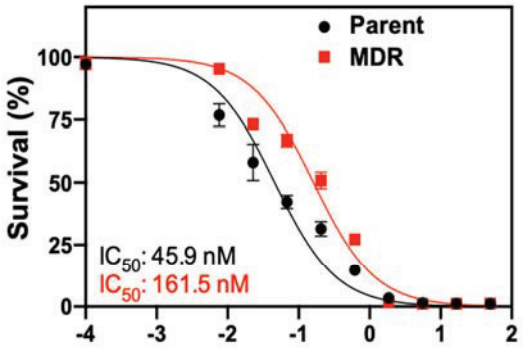
Third, Dr. Ick Chan Kwon, IROAST visiting Professor of Korea Institute of Science and Technology (KIST), and I started to organize new project for cell-mediated drug delivery. One of my undergraduate students involved in this project. Under my supervision, we will synthesis and evaluate the materials properties for *in vivo* application in FY2021. After confirmation, I and the student will perform collaborative experiments at KIST in FY2022.

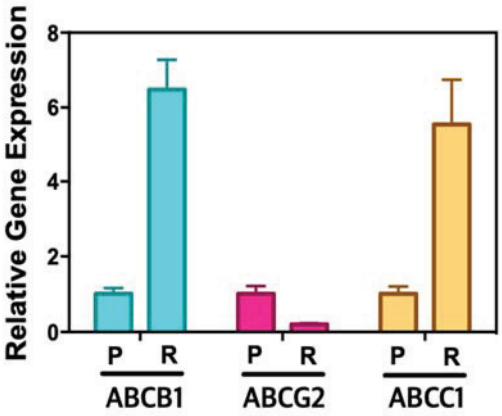
1. Set up a smart drug delivery system

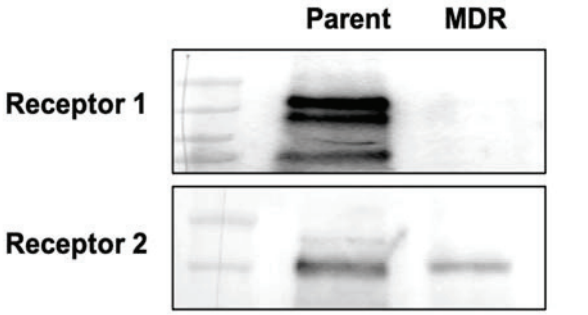


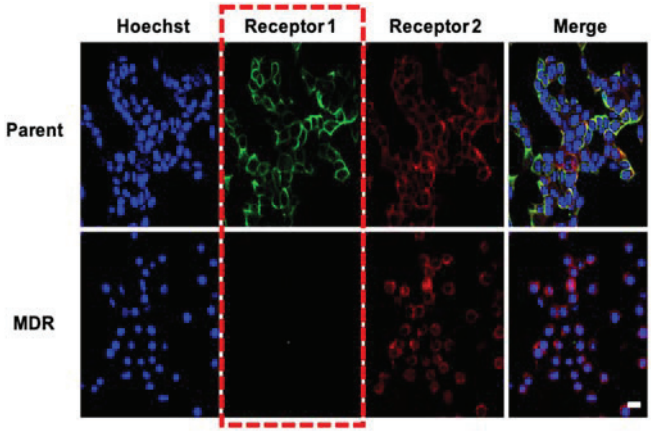
[Polymeric NPs] [Polymersome] [Polymer/inorganic NPs]

2. Set up and evaluation of anti-chemo drug treated MDR cell line



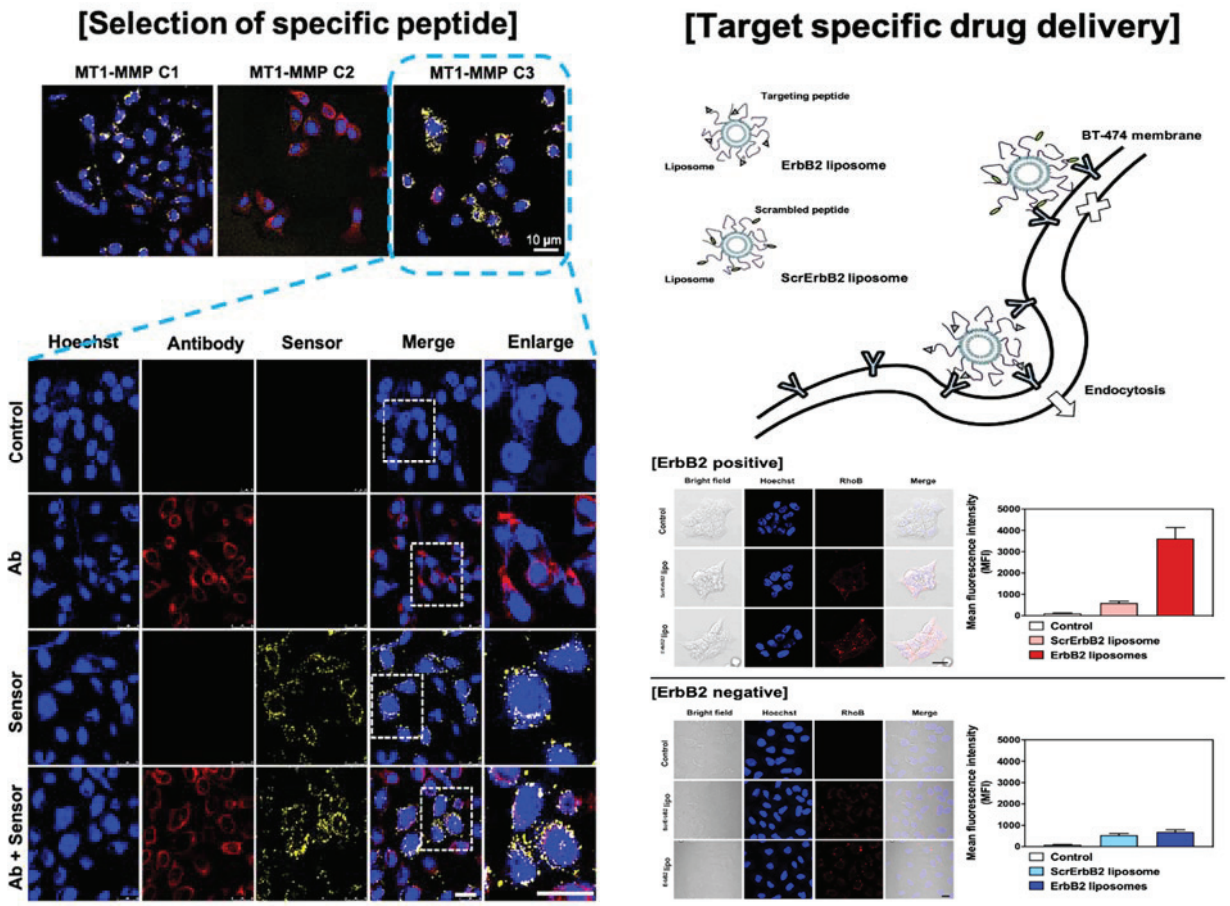






[MDR-induces cell line]

3. Stimuli-response nanomaterials



4. Supervising student

No.1-4	Sustainable energy development		
Name	Atsushi Sainoki		
Affiliation	IROAST Email: atsushi_sainoki@kumamoto-u.ac.jp	Title	Associate Prof.
Research Field	Green Energy		

Research collaboration with Pennsylvania State University

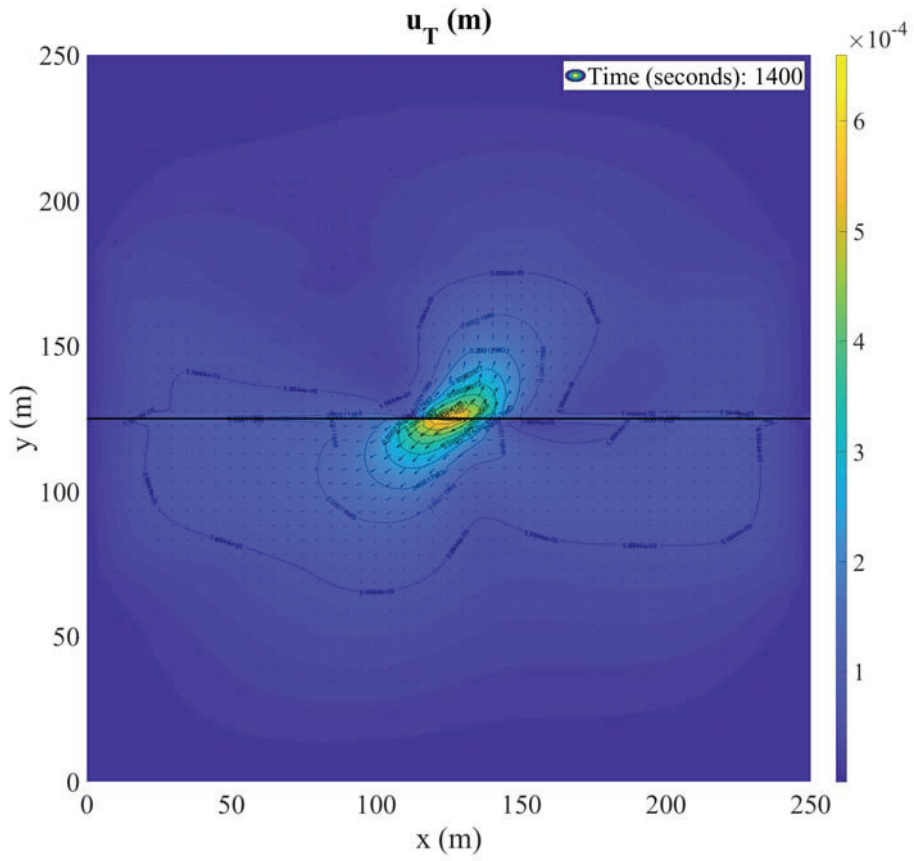
We have been developing a numerical simulation methodology for fluid injection into a natural fault, based on the Extended Finite Element Method, while collaborating with Prof. Derek Elsworth at Pennsylvania State University since 2019. The goal of this study is to predict the occurrence of induced seismicity caused by fluid injection related to various engineering projects, such as shale gas, oil, and geothermal energy development, and to estimate seismic source parameters of the induced seismic event. To this end, it is indispensable to develop a numerical simulation code that allows us to quantify the fluid injection-induced mechanical behaviour of the rock mass and fault that involves not only fluid flow within the fault but also fluid leak-off into the surrounding rock mass, which is known to be really complex.

Although many numerical simulations have been done with conventional numerical techniques, such as the finite element method and finite difference method, such methodologies cannot fully consider the complex mechanical behaviour. To overcome the limitation, we have applied the Extended Finite Element Method to the simulation of the mechanical behaviour of the fault and rock mass undergoing fluid injection-induced pore pressure change. The application of XFEM to fluid injection simulation while coupling fluid flow with rock mass behaviour has not yet been explored sufficiently and developed. To my knowledge, this is the first time that fluid injection-induced fault shear behaviour was successfully simulated with the XFEM and validated against experimental data obtained from a natural fault. The paper has been published in Rock Mechanics and Rock Engineering. At this moment, we are further developing the code to consider the dynamic behaviour of the fault during fluid injection with the purpose of quantifying seismic energy released during fluid injection so that it is possible to estimate the risk of induced seismicity.

Research collaboration with McGill University and The University of British Colombia

We are being required to reduce greenhouse gas emission significantly in the next decades, which has brought global attention to the use of sustainable energy. In Japan, to achieve the goal, green power is widely used for electricity generation, including solar system, wind-power generation, tidal power generation, and so on. As such, geothermal energy has been brought back into the spotlight. New geothermal power plants are being planned and developed with the aim of increasing the installed capacity. With the aim, our research group has been collaborating with Prof. Sasmito at McGill University and Prof. Madiseh at The University of British Colombia (UBC), regarding the development of co-axial heat exchanger for geothermal energy extraction. In 2020, based on experimental data obtained from a pilot site, Beppu, Japan, numerical simulations have been done using a workstation at UBC. The simulation precisely modelled the geothermal energy extraction system with the co-axial heat exchanger, and the result was validated against the temperature change of fluid that circulates in the pipe while extracting thermal energy from the surrounding hot rock mass.

The numerical simulation results were then summarized and submitted to a conference. A manuscript that includes more results has been prepared to submit the result to an international journal.



Example of fault shear behaviour caused by fluid injection simulated with the Extended Finite Element Method that couples fluid flow with the mechanical behaviour of the fault and the rock mass.

Research on microbially-aided carbon sequestration technology

This project entitled "development of microbially-aided carbon sequestration technology" can be divided into two parts: enhancement of carbon precipitation using anaerobic microbes and closure of rock fractures in an aquifer with a grout technology using aerobic microbes.

Experiments for anaerobic microbes

For the first one, this year was predominantly spent on preparing reagents and culture media in order to develop clusters of anaerobic microbes as well as on preparing experimental apparatus. We have finished preparing almost all culture media planned and broken one rock sample into small pieces under an anaerobic condition. In 2021, we will place the rock fragments on the culture media under an anaerobic condition and aim at observing clusters of microbes that contribute to the enhancement of carbon precipitation.

Experiments for aerobic microbes (grout technology)

Regarding the second one (application of the grout technology into carbon sequestration), during the fiscal year of 2020, we have performed the following two experiments: i) creation of a grout material with urease, ii) image analysis of grouted rock samples with an industrial X-ray CT scanner. Regarding the grout technology, we have investigated the effect of urease concentrations on the chemical reaction rate of calcium chloride and urea that results in calcium carbonate. It is found from Fig. 1 that as the urease concentration increases, more $CaCO_3$ is precipitated, giving an insight into the necessity of optimizing urease concentration when applying the grout technology to carbon sequestration. This is because extremely high reaction rates would prevent grouts from permeating a fractured rock mass, whilst low reaction rate does not effectively fill fractures in a rock mass.

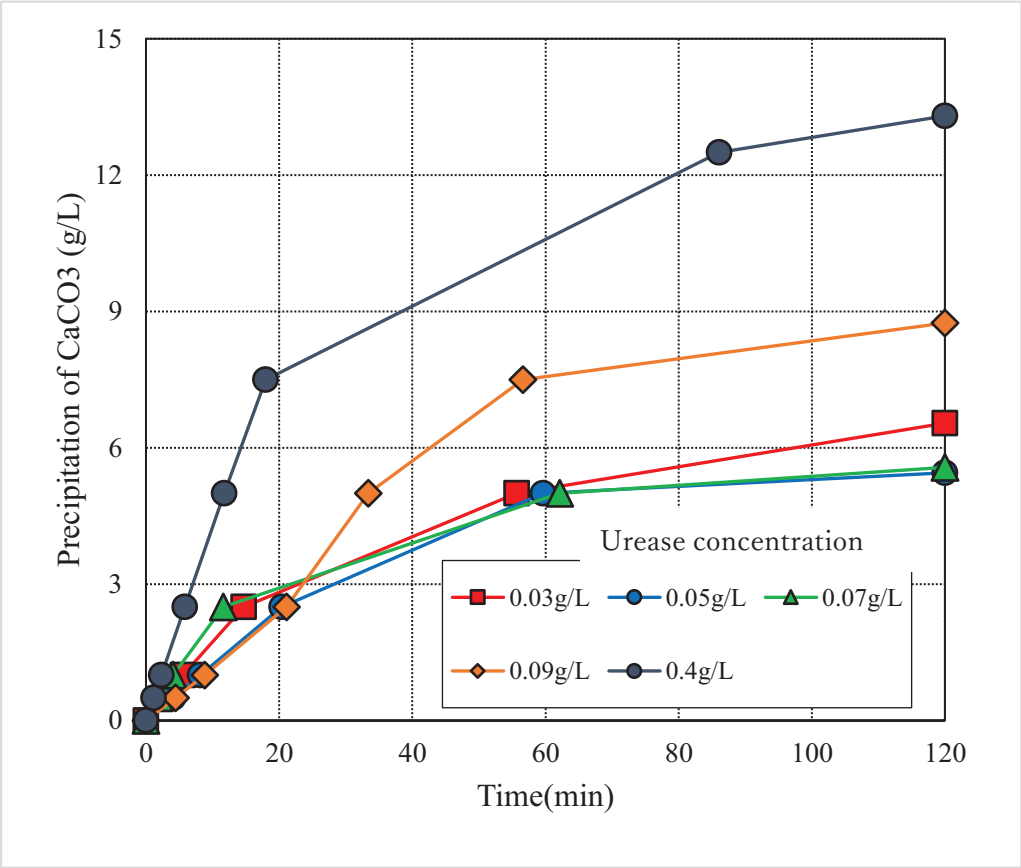


Fig. 1: Effect of urease concentration of the precipitation rate of $CaCO_3$

ii) Image analysis of grouted rock samples with an industrial X-ray CT scanner

X-ray CT images were taken for rock samples to which grouting was performed using urea, carbon chloride, and urease. Fig. 2 shows the difference in specific density between an original rock sample and grouted one. The warm color in the picture corresponds to a region with high specific density, indicating calcium carbonate precipitated as a result of grouting. As can be seen, the grouted region is spatially dotted in the rock sample. This indicates that calcium carbonate was effectively precipitated, thus contributing to the reduction of permeability.

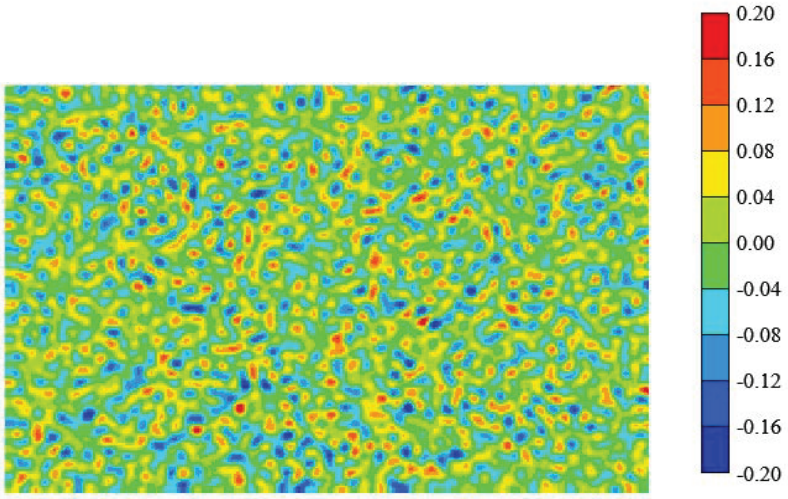


Fig. 2: Difference in specific density between an original rock and grouted samples

No.1-5	Deciphering the molecular basis of the plant morphogenesis		
Name	Takashi Ishida		
Affiliation	IROAST Email: ishida-takashi@kumamoto-u.ac.jp	Title	Assistant Professor
Research Field	Advanced Green Bio		

Details of activities

1. Research achievements

Coordinated cell proliferation and cell differentiation are essential processes in multicellular organisms. To achieve these functions, organisms have developed scrupulously designed cell-to-cell communication systems over the course of evolution. Plants have established unique ligand-receptor-based signaling modules, such as the CLAVATA (CLV) pathway, which comprises the CLV3 small signaling peptide and leucine-rich repeat (LRR) domain-containing receptors. In the shoot meristem of *Arabidopsis thaliana*, the CLV signaling modules play roles in the repression of cell proliferation. However, the molecular basis for the CLV-like signaling systems functioning in the root is to be elucidated. In order to decipher the molecular mechanisms revolving around the root CLV-like signaling modules, we have developed a series of mutants for the signaling modules as well as higher-order mutants with the CRISPR-Cas9-mediated genome editing. Resulted in the phenotypic analyses, we found that the lesion of some of the signaling mediators diminished the root growth, suggesting that they play roles in the promotive regulation of cell proliferation in root. In addition, the signaling mediator seems to be conserved in the land plants. These results would raise an attractive possibility that the signaling pathway is an invention of the rooting plants for the acquisition of the root.

Higher organisms have evolved sophisticated developmental regulation mechanisms. In the steady-state, they routinely develop various tissues based on the genetically encoded body plan. However, biotic stimuli sometimes trigger the formation of malformed organs. The gall formation induced by plant parasitic root-knot nematodes is representative of irregular organogenesis. However, little is known about the molecular mechanisms of gall formation. In this FY, we have conducted the nematode infection assays using various Arabidopsis mutants and evaluated the efficiencies to screen plant genes that are involved in the gall formation processes. Simultaneously, we observed various gene expression markers in the galls to select plant genes that are activated during the gall formation. Resulted in the screening described in manuscript **III**, we obtained many candidates of the genes that play some roles in the gall formation. In addition, we characterized an atypical E2F-type transcription factor DEL1 of *Arabidopsis thaliana* in the context of the gall formation. Growth–defense tradeoffs are essential for optimizing plant performance and adaptation under stress conditions. The lesion of DEL1 induced the excessive accumulation of defense hormone salicylic acid (SA) and *del1* mutant is more resistant to RKN infection while the root growth was severely affected. Based on the results, we proposed that DEL1 plays an important role in the balance between plant growth and defense responses to RKN infection in manuscript **IV**.

In this FY, I have conducted several interdisciplinary collaborative researches with chemists and microbiologists. The discovery and practical application of useful natural products and their derivatives are a means of improving the quality of human life. For example, herbicides that

suppress the growth of undesired weeds are essential agents for increasing the yield of crops in modern agriculture, and various types of natural products-derived compounds are used commercially. Among the herbicidal agents, compounds that inhibit microtubule function are a common class of herbicides that affect the growth of plants by affecting mitotic regulation. Streptomyces is aerobic, Gram-positive, filamentous bacteria and is well-recognized for their ability to produce diverse secondary metabolites. In the published manuscript **I**, we discovered a novel compound named kumamonamide from the secondary metabolite of *Streptomyces werraensis*. Kumamonamic acid, a synthetic intermediate of kumamonamide and its derivatives were found to inhibit the growth and germination of plants, suggesting the potency of the use as an herbicide. Based on the cell biological analyses, we found that these Kumamonamic acid derivatives would target microtubules. Furthermore, their effects were likely to differ from those of known microtubule inhibitors, suggesting a novel mode of action of kumamonamic acid, which represents an important lead for the development of new herbicides. In summary, we have discovered a novel, plant-specific growth inhibitor with a unique mode of action involving disruption of the microtubules.

Publications

I. Discovery, characterization and functional improvement of kumamonamide as a novel plant growth inhibitor that disturbs plant microtubules. **Ishida T**, Yoshimura H, Takekawa M, Higaki T, Ideue T, Hatano M, Igarashi M, Tani T, Sawa S, Ishikawa H, ***Scientific Reports***, 11, 6077, 2021, doi: 10.1038/s41598-021-85501-1 (Impact Factor: 3.998)

II. A ClearSee-Based Clearing Protocol for 3D Visualization of *Arabidopsis thaliana* Embryos. Imoto A, Yamada M, Sakamoto T, Okuyama A, **Ishida T**, Sawa S, Aida M, ***Plants***, 10(2), 190, 2021, doi: 10.3390/plants10020190 (Impact Factor: 2.762)

III. Identification of genes involved in *Meloidogyne incognita*-induced gall formation processes in *Arabidopsis thaliana*. Suzuki R, Ueda T, Wada T, Ito M, **Ishida T**, Sawa S, ***Plant Biotechnology***, 38(1), 1-8, 2021, doi: 10.1016/j.cub.2020.02.017 (Impact Factor: 0.901)

IV. The atypical E2F transcription factor DEL1 modulates growth–defense tradeoffs of host plants during root-knot nematode infection. Nakagami S, Saeki K, Toda K, **Ishida T**, Sawa S, ***Scientific Reports***, 10, 8836, 2020, doi: 10.1038/s41598-020-65733-3 (Impact Factor: 3.998)

Media

2021 年 3 月 23 日　熊本大と微化研、除草剤候補化合物クマモナミドを発見　日本経済新聞

Patents (国内移行)

2020 年 9 月 11 日　特許第 6744926 号 植物成長抑制剤、およびそれを用いた植物成長抑制方法
石川勇人，谷時雄，澤進一郎，**石田喬志**，福島悠介，稲垣準

2. International research collaboration

Part of the studies described in section 1 was done as international collaboration.
Although there is no publication accomplished by international collaboration in this FY, several international collaborative studies are ongoing.

3. Prospect for further research collaboration

In FY2020, I have started several international collaborations on genome editing in plants. Our pipeline for rapid generation of Arabidopsis mutant will provide us opportunities for further collaborations; in particular, generation of the higher-order loss-of-function mutants using the technique will solve the redundancy problem in the molecular genetic studies in the field of plant small signaling peptides.

No.1-6	Theoretical modeling for the understanding of plant structure formations		
Name	Akiko Nakamasu		
Affiliation	IROAST Email: nakamasu@kumamoto-u.ac.jp	Title	Project assistant professor
Research Field	Advanced Green Bio		

The year 2020, Japan was also suffering a disaster from COVID19 as in other countries, then I felt huge hindrance in my research. However, I could achieve the followings with supports from Associate professor T. Higaki, IROAST staffs, and so on. I'd like to thank them at first.

In 2020 FY, I conducted researches at following four main themes.

1) Morphological problems mainly in plant leaves.
2) Understandings of fish pigmentation pattern on a molecular level.
3) Dynamic network observed in plant endoplasmic reticulum.
4) Generalization of motile patterns.

As a feature of theoretical approaches, these themes covered a broad range of a hierarchy in plants and animals, i.e., on molecular, subcellular, tissue, and organ levels, then I treated targets with abstract to more concrete concepts.

About the theme 1), Grant-in-Aid for Scientific Research on Innovative Areas (The Japan Society for the Promotion of Science), Periodicity and its modulation in plant, "Theoretical understandings of leaf diversity caused by modulations of spatial periodicity on leaf peripherals." was adapted. Though modeling techniques for pattern formation phenomena were required in this aria, I could not handle any of these collaborative researches because of the incomplete of my research. Though interesting discussions and an experience of the attendance to an international symposium in this area activated my research motivation.

The variation observed in leaf shapes were explained by a model combined different types of positional information and growth modes. This was indeed "Periodicity and its modulation in plant." I had a short talk presentation and a poster session about this model titled "Theoretical model for leaf-shape variation in heterophyllous lake cress" at Japan society of developmental biology (JSDB) online trial meeting 2020 (This is an alternate meeting for cancelled 53rd annual JSDB meeting). This theme will expand to collaborative researches with in the area. Then I'm planning to conduct a research focused on the wavelength of pattern in plants with Jose Irepan Reyes-Olalde as international collaborative research.

I could not get to the points where publishments, though now I'm submitting two papers related to the themes 1) and 2), "Outreach lengths of repressive gradient determine tow-dimensional morphogenetic proportions in a combination of growth modes." and "Correspondences between parameters in a reaction-diffusion model and connexin functions during zebrafish stripe formation.". The former is a theoretical assumption of the mechanism which switch between robustness and variability in morphogenesis. Then the latter is an interpretation of a model on a molecular level to understand interactions required for pigment pattern formations in fish.

The theme 3) and 4) brought difficulties in my researches in 2020. These are collaborative researches with T. Higaki and H. Izuhara (Miyazaki Univ.), gained a research grant from Shimadzu Science Foundation, "Study on displacable effects of spatial inhomogeneity on Turing pattern." in last FY. I'd like to compile obtained results in several papers with improvements of the environment for numerical analyses.

Then I was invited to a contributed talk of a symposium in Pacifichem 2021 (December 16-17th, postponed from 2020). This may lead to (international) collaborative researches in the future.

No.1-7	Prediction of induced seismicity from fluid injection into faults		
Name	Adam Schwartzkopff		
Affiliation	IROAST Email: aschwartzkopff@kumamoto-u.ac.jp	Title	Postdoctoral Researcher
Research Field	Green Energy		

1. Research achievements

During this fiscal year, I have been developing the dynamic module of the cutting edge numerical simulation program. This has led to a method to switch between static and dynamic analysis during periods of instability according to earthquake nucleation theory. I have recalibrated the input parameters using this method to validate the code against an in-situ experiment. From this I conducted a parametric study to reveal the influence of the injection rate on the produced seismicity from the simulations. This associated manuscript was submitted to the International Journal of Rock Mechanics and Mining Sciences and has received minor revisions after peer review.

In addition, I have developed a method for generalization of the Mohr-Coulomb and Hoek-Brown failure criteria to account for the influence of the intermediate effective principal stress on rock strength. This generalization method produces a failure envelope that is closely aligned to the true-triaxial data. The associated manuscript was submitted to the Journal of Rock Mechanics and Geotechnical Engineering and is currently under review.

2. International research collaboration

Associate Professor Atsushi Sainoki and I have been collaborating with Professor Derek Elsworth from Pennsylvania State University, United States to write the manuscript associated with the numerical simulation program (mentioned above).

3. Prospect for further research collaboration

Not applicable.

No.1-8	Analysis of multilayered regulation of auxin signaling in the apical region development of the plant embryo		
Name	Mizuki Yamada		
Affiliation	IROAST Email: myamada@kumamoto-u.ac.jp	Title	Postdoctoral Researcher
Research Field	Advanced Green Bio		

Details of activities

1. Research achievements

The aerial organs of plants, such as leaves, stems and flowers, are generated from the shoot meristem. During embryogenesis of dicotyledonous plants, the apical region of the embryo is separated into two cotyledon primordia, and shoot meristem is formed in boundary region between cotyledon primordia. This tissue differentiation is regulated by the *CUP-SHAPED COTYLEDON* (*CUC*) genes. *CUC* genes are key factors of this differentiation and are required for it. On the other hands, auxin is a phytohormone that plays important roles in various developmental processes including embryogenesis in plants.

In FY 2020, I reported that the *CUC* genes affect the expression patterns of several auxin related genes in a multilayered manner to regulate the tissue differentiation in the apical region of embryo in *Arabidopsis thaliana* (the 84th annual meeting of BSJ and the 62nd annual meeting of JSPP). Previously, our research group has found that the three auxin related genes are positively regulated by *CUC* genes. During this FY, I investigated the role of these genes in the *CUC* regulated tissue differentiation. It was indicated that, among these genes, one auxin response gene acts the positive role in this differentiation. On the other hand, two auxin biosynthetic genes seem to have negative function in this differentiation. These results suggest that *CUC* genes affect multiply auxin signaling including additional unknown regulations, and that the tissue differentiation in plant embryo is orchestrated by the interaction of these regulations. I am further investigating genetic interaction of these auxin signaling and *CUC* genes. The results will be reported in FY 2021.

Besides the auxin related genes, it is also important to find the additional genes which work as *CUC* downstream factors. With a collaboration with Dr. Minoru Kubo (Kumamoto University in FY2020, NAIST in FY2021), I have started the transcriptome analysis of Arabidopsis embryos in FY 2020. High quality RNA was extracted from the embryos of *cuc* mutants, and RNA-seq library samples were prepared. The transcriptome data from these libraries will be analyzed in FY 2021, and then our group and I will start the investigation of new *CUC* downstream genes.

Publication

Imoto A, Yamada M, Sakamoto T, Okuyama A, Ishida T, Sawa S, Aida M (2021). A ClearSee-based clearing protocol for 3D visualization of *Arabidopsis thaliana* embryos. Plants 10, 190. doi: 10.3390/plants10020190

2. International research collaboration

NA

3. Prospect for further research collaboration

In the analysis of embryo transcriptome, the collaboration with Dr. Minoru Kubo will be continued.

And some additional collaboration will be necessary in FY 2021. From the results of embryo transcriptome analysis, I will find the various new candidate genes involved in the tissue differentiation in the apical region of embryo. I will have to collaborate with researchers who are expert in those genes.

Research Activities

2. Distinguished Professors

2. Distinguished Professors

No.	Name	Project Title
2-1	**László Pusztai**	Nanoscale assemblies in hydrogen-bonded liquids and in amorphous materials
2-2	**Yufeng Zheng**	Development and management of biomaterials

No. 2-1	Nanoscale assemblies in hydrogen-bonded liquids and in amorphous materials		
Name	PUSZTAI, László		
Affiliation (home)	Wigner Research Centre for Physics Hungary Email: pusztai.laszlo@wigner.hu	Title	Scientific advisor
Research Field	Nanomaterial Science		
Period of appointment	04, 2020- 03, 2021 (I was not able to show up in Japan)		
Host Professor	HOSOKAWA, Shinya		
Affiliation	FAST, KU Email: shhosokawa@kumamoto-u.ac.jp	Title	Professor

In FY 2020 my activities have been very much determined by the COVID-19 pandemic that prevented me from staying one single day at IROAST. What I can report below is (i) work that has been mostly done before FY 2020 but has been completed in FY 2020, and (ii) the very much retarded activities that has been possible to maintain remotely.

1. Research achievements

My primary research goal in general may be described in short as '**understanding disordered structures'.** Accordingly, my main activity (still, in general) is the investigation of the microscopic structure of liquids, amorphous materials and disordered crystals. We combine experimental data, such as total scattering structure factors (TSSF) from X-ray and neutron diffraction (XRD and ND, respectively) and EXAFS spectra, with computer modeling tools, such as Reverse Monte Carlo (RMC) and molecular dynamics (MD) simulations. As a result of such an approach, large sets (containing tens of thousands) of atomic coordinates ('particle configurations') in simulation boxes are provided that are consistent (within errors) with experimental data. These configurations are then subjected to various geometrical analyses, so that specific questions concerning the structure of a material may be answered. Below I describe some selected results from the year of 2020 (only publications where the name of IROAST appears).

(i) *Temperature dependent structure and dynamics of isopropanol-water (CH_3-CH(OH)-CH_3/H_2O) mixtures over a wide concentration range.* Synchrotron X-ray diffraction measurements have been conducted on aqueous mixtures of propan-2-ol (a.k.a. isopropanol, or 2-propanol), for alcohol contents between 10 and 90 mol%, from room temperature down to 230 K. Molecular dynamics simulations, by using an all-atom parametrization of the propan-2-ol molecule and the well-known TIP4P/2005 water model, were able to provide semi-quantitative descriptions of the measured total structure factors. Various quantities related to hydrogen bonding, like hydrogen bond numbers, size distribution of cyclic entities and cluster size distributions, have been determined from the particle co-ordinates obtained from the simulations. A clear tendency was observed towards that an increasing proportion of water molecules participate in hydrogen bonding with exactly 2 donor- and 2 acceptor sites as temperature decreases. The percolation threshold at room temperature could be estimated to be between isopropanol concentrations of 62 and 74 mol%, whereas at very low temperature, calculations yielded a value above 90 mol%. It was also demonstrated that, similarly to ethanol−water mixtures, the occurrence of 5-membered-hydrogen-bonded rings are significant, particularly at higher alcohol concentrations.

Related publication: Pothoczki, Sz; Pethes, I; **Pusztai, L**; Temleitner, L; Csókás, D; Kohara, S; Ohara, K; Bakó, I; Hydrogen bonding and percolation in propan-2-ol – Water liquid mixtures: X-ray diffraction experiments and computer simulations; *J. Mol. Liq.* **329** Paper:115592, 10 p. (2021)

(ii) Temperature-dependent structure of methanol—water liquid mixtures. — Our collaboration with Japanese scientists is in the midst of a long-term systematic investigation in this field; as a first step, experimental and simulated results have been published for methanol-water mixtures. Experimentally, these mixtures have been investigated by high-energy synchrotron X-ray and neutron diffraction at low temperatures. It was thus possible to report the first complete sets of both X-ray and neutron weighted total scattering structure factors over the entire composition range (at 12 different methanol concentrations (x_M) from 10 to 100 mol%) and at temperatures from ambient down to the freezing points of the mixtures. The new diffraction data may later be used as reference in future theoretical and simulation studies. Measured data were interpreted by molecular dynamics simulations, in which the all atom OPLS/AA force field model for methanol was combined with both the SPC/E and TIP4P/2005 water potentials. Both combinations provide at least semi-quantitative agreement with measured diffraction data. As a general trend, the average number of hydrogen bonds increases upon cooling. However, the number of hydrogen bonds between methanol molecules slightly decreases with lowering temperatures in the concentration range between ca. 30 and 60 mol % alcohol content. The same is valid for water-water hydrogen bonds above 70 mol % of methanol content, from room temperature down to 193 K.

Related publication: Pethes, I; **Pusztai, L**; Ohara, K; Kohara, S; Darpentigny, J; Temleitner, L; Temperature-dependent structure of methanol-water mixtures on cooling: X-ray and neutron diffraction and molecular dynamics simulations; *J. Mol. Liq.* **314**, Paper: 113664, 10 p. (2020)

(iii) Solvent-separated anion pairs in concentrated solutions. Hydrogen bonding to chloride ions in various aqueous environments has been discussed many times over the past more than 5 decades. Still, the possible role of such anion-to-water type hydrogen bonds (HB) in networks of HB-s has not been investigated in any detail. Here, computer models of concentrated aqueous LiCl solutions are considered and usual HB network characteristics, such as distributions of cluster sizes and of cyclic entities, are computed for the models by (1) taking and (2) not taking chloride ions into account. During the analysis of hydrogen bonded rings, a significant amount of ‘solvent separated anion pairs’ have been detected at high LiCl concentrations. It is demonstrated that including the halide anions into the network does make the interpretation of structural details significantly more meaningful than when considering water molecules only. Finally, simulated structures generated by ‘good’ and ‘bad’ potential sets have been compared on the basis of the tools developed here, and it is shown that the novel concept (1) is, indeed, helpful from this respect, too.

Related publication: Pethes, I; Bakó, I; **Pusztai, L**; Chloride ions as integral parts of hydrogen bonded networks in aqueous salt solutions: the appearance of solvent separated anion pairs; *Physical Chemistry Chemical Physics (PCCP)* **22**, pp. 11038-11044. (2020)

(iv) Pressure-Dependent Structure of Methanol–Water Mixtures up to 1.2 GPa. Total scattering structure factors of per-deuterated methanol and heavy water, CD_3OD and D_2O, have been

determined across the entire composition range as a function of pressure up to 1.2 GPa, by neutron diffraction. The largest variations due to increasing pressure were observed below a scattering variable value of 5 A^{-1}, mostly as shifts in terms of the positions of the first and second maxima. Molecular dynamics computer simulations, using combinations of all-atom potentials for methanol and various water force fields, were conducted at the experimental pressures with the aim of interpreting neutron diffraction results. The peak-position shifts mentioned above could be qualitatively reproduced by simulations, although in terms of peak intensities, the accord between neutron diffraction and molecular dynamics was much less satisfactory. However, bearing in mind that increasing pressure must have a profound effect on repulsive forces between neighboring molecules, the agreement between experiment and computer simulation can certainly be termed as satisfactory. In order to reveal the influence of changing pressure on local intermolecular structure in these "simplest of complex" hydrogen-bonded liquid mixtures, simulated structures were analyzed in terms of hydrogen bond-related partial radial distribution functions and size distributions of hydrogen-bonded cyclic entities. Distinct differences between pressure-dependent structures of water-rich and methanol-rich composition regions were revealed.

Related publication: Temleitner, L.; Hattori, T; Abe, J; Nakajima, Y; **Pusztai, L**; Pressure-Dependent Structure of Methanol–Water Mixtures up to 1.2 GPa: Neutron Diffraction Experiments and Molecular Dynamics Simulations; *Molecules* **26(5)**, 1218, 13 p. (2021)

(v) Detailed structural analysis of the metallic glass $Pd_{40}Cu_{40}P_{20}$. To clarify the relationship between the glass-forming ability (GFA) and local atomic structure of Pd-based metallic glasses, the structures of an amorphous $Pd_{40}Cu_{40}P_{20}$ (PCP) were investigated using the same methods as for $Pd_{40}Ni_{40}P_{20}$ (PNP) metallic glass, i.e., by a combination of anomalous X-ray scattering, X-ray and neutron diffraction, and reverse Monte Carlo modeling. From the comparison between the results of PNP with an excellent GFA and the PCP with a worse GFA, important features characteristic to the GFA are found in the hyper-ordered structures. Firstly, the compositional inhomogeneity of Cu in PCP is larger than Ni in PNP. Secondly, a Voronoi tessellation reveals that icosahedral arrangements are found with considerable probability around the Ni atoms in PNP, while a less existence around the Cu atoms in PCP. Thirdly, a persistent homology (PH) analysis shows smaller intermediate-size Cu PH rings in PCP than Ni PH rings in PNP.

Related publication: Hosokawa, S; Bérar, J-F; Boudet, N; Pilgrim, W-C; **Pusztai, L**; Hiroi, S; Kohara, S; Kato, H; Fischer, HE; Zeidler, A; Detailed structural analysis of amorphous $Pd_{40}Cu_{40}P_{20}$: Comparison with the metallic glass $Pd_{40}Ni_{40}P_{20}$ from the viewpoint of glass forming ability; *J.Non-Cryst. Solids*, **552** Paper: 120536 , 10 p. (2021)

(vi) Investigations of short- and intermediate-range structures of Ge-Se glasses. In order to improve the reliability of short- and intermediate-range atomic structures of Ge_xSe_{1-x} glasses, high quality neutron diffraction data, in both the real and reciprocal spaces, were added to the existing anomalous x-ray scattering and x-ray diffraction datasets [Hosokawa et al., Phys. Rev. B 84, 014201 (2011)] for reverse Monte Carlo modeling. This addition proved to be highly effective for obtaining well-refined structural data and for revealing a close relationship between the compositional stiffness transition occurring at about $x = 0.20–0.26$ and the partial structures. Although the $S_{ij}(Q)$ and $g_{ij}(r)$ functions gradually change with varying x, important indications on the stiffness transition are confirmed on the basis of the intermediate-range element-selective atomic structures (hyper-ordered structures) more clearly than it was possible by previous results. An abrupt decrease in terms of the pre-peak intensity of $S_{GeGe}(Q)$, a rapid disappearance of the

Ge–Ge homopolar bonds, anomalies in the ratio of edge- and corner-sharing $Ge(Se_{1/2})_4$ tetrahedra, and characteristic changes in the tetrahedral connections with decreasing x across the so-called intermediate phase have all been observed.

In *Ag-doped Ag-$GeSe_3$ glasses*, the coordination numbers around Ge and Se atoms follow (roughly) the $8 - N$ rule over all Ag concentrations if Ag ions are not taken into account. With increasing the Ag concentration, the number of Ge and Se atoms around Ag increase remarkably, while the Ag-Ag coordination number increases only slightly. This indicates that an Ag conducting path is formed through the second neighbor Ag-Ag correlations.

On the other hand, in Ga-Ge-Se glasses, total coordination numbers around Ga, Ge, and Se atoms are 3.80, 4.68, and 2.25, respectively, which contradict the $8 - N$ rule. The numbers of Ga-Ga, Ga-Ge, Ge-Ga, and Ge-Ge wrong bonds were found to be 0.71, 1.32, 0.76, and 1.12, respectively. In the three-dimensional atomic configurations, the structure looks inhomogeneous, in terms of both density and concentration.

Related publications:

Hosokawa, S; Kawakita, Y; **Pusztai, L**; Ikeda, K; Otomo, T; Detailed investigations on short- and intermediate-range structures of Ge-Se glasses near the stiffness transition composition; *J. Phys. Soc. Jpn*., **90** 024601, 12 p. (2021)

Hosokawa, S; Kawakita, Y; Stellhorn, JR; **Pusztai, L**; Blanc, N; Boudet, N; Ikeda, K; Otomo, T; Local- and Intermediate-Range Atomic Structures on Room-Temperature Superionic-Conducting Ag-GeSe3 Glasses; *J. Phys. Soc. Jpn. -- Conf. Proceedings (JPS Conf. Proc.), 3rd J-PARC Symposium (J-PARC2019)*, **33,** 011070 (2021)

Hosokawa, S; Stellhorn, JR; Onodera, Y; Kohara, S; Magome, E; **Pusztai, L**; Ikeda, K; Otomo, T; Krbal, M; Wagner, T; Local- and Intermediate-Range Atomic Order in $Ga_2Ge_3Se_9$ Glass: Complementary Use of X-Rays and Neutrons; *J. Phys. Soc. Jpn. -- Conf. Proceedings (JPS Conf. Proc.), 3rd J-PARC Symposium (J-PARC2019)*, **33**, 011069 (2021)

Talks at meetings, seminars:

No meetings, unfortunately, due to the virus situation.

2. Overview and significance of the research collaboration and lectures to the students

During FY 2020, I've collaborated mostly with my host professor, Dr. Hosokawa, and his co-worker at the Department of Physics, Dr. Nakajima, a young tenured-track fellow – with both of them, only remotely.

A number joint publications with Prof. Hosokawa have appeared during FY2020.

The joint research work with Dr. Nakajima, on high pressure diffraction measurements of alcohol-water liquid mixtures, has produced the first publications by the end of FY 2020.

3. Comments/suggestions for IROAST/Kumamoto University

I cannot add anything useful here, I'm afraid, as I haven't been able to come this fiscal year.

4. Prospect for further research collaboration with Kumamoto University

The high pressure work, for which I obtain vital help and assistance from Dr. Nakajima, is still expected to expand – provided that we can conduct proper joint research in the near future. Follow-up publications with Prof. Hosokawa on the structure of amorphous materials may continue to appear for a while.

5. Impressions of Kumamoto University/Kumamoto

I perhaps will be able to write about these in a year – with at least a few stays at completed IROAST by then…

No. 2-2	Development and management of biomaterials		
Name	Yufeng Zheng		
Affiliation (home)	Department of Materials Science and Engineering College of Engineering Peking University, China Email: yfzheng@pku.edu.cn yfzheng@kumamoto-u.ac.jp	Title	Professor
Research Field	Nanomaterial Science		
Period of appointment	—		
Host Professor	Kazuki Takashima		
Affiliation	Faculty of Advanced Science and Technology Email: takashik@gpo.kumamoto-u.ac.jp	Title	Professor

1. Research achievements

On February 22th, 2021, I gave a talk entitled “Nanostructured magnesium alloys processed for biomedical applications” on 3nd KAIST-KU workshop and joint symposium.

Publications

Hongtao Yang, Bo Jia, Zechuan Zhang, Xinhua Qu, Guannan Li, Wenjiao Lin, Donghui Zhu, Kerong Dai, Yufeng Zheng, Alloying design of biodegradable zinc as promising bone implants for load-bearing applications, Nature Communications 11 (2020) 401

Wei Yuan, Dandan Xia, Y.F. Zheng, Xiangmei Liu, Shuilin Wu, Bo Li, Yong Han, Zhaojun Jia, Donghui Zhu, Liqun Ruan, Kazuki Takashima, Yunsong Liu, Yongsheng Zhou, Controllable biodegradation and enhanced osseointegration of ZrO2 nanofilm coated Zn-Li alloy: in vitro and in vivo studies, Acta Biomaterialia 105 (2020) 290-303

Xinhua Qu, Hongtao Yang, Zhifeng Yu, Bo Jia, Han Qiao, Yufeng Zheng, Kerong Dai, Serum zinc levels and multiple health outcomes: Implications for zinc-based biomaterials, Bioactive Materials 5 (2020) 410-422

Guo Bao, Qianqian Fan, Dongfeng Ge, Kun Wang, Mingming Sun, Zechuan Zhang, Hui Guo, Hongtao Yang, Bin He, Yufeng Zheng, In vitro and in vivo studies to evaluate the feasibility of Zn-0.1Li and Zn-0.8Mg application in the uterine cavity microenvironment compared to pure zinc, Acta Biomaterialia 123 (2021) 393-406

2. Overview and significance of the research collaboration and lecture(s) to the students

Sorry, I had no chance to give lectures to students due to COVID-19. It is not applicable this year.

3. Comments/suggestions for IROAST/Kumamoto University

I wish IROST will keep growing rapidly and internationally under the leadership of Prof. Takashima Kazuki, and I will work hard as a member of IROAST in the coming years.

4. Prospect for further research collaboration with Kumamoto University

With the introduction of Prof. Takashima Kazuki, I will be happy to be hosted by Prof. Yoji Mine and do some collaboration research in the year 2021-2022. Moreover, future collaboration with other professors in KU will be considered.

5. Impressions of Kumamoto University/Kumamoto

Sorry, I had no chance to visit Kumamoto in this year.

Research Activities

3. Young Faculty Members for International Joint Research

3. Young Faculty Members for International Joint Research

No.	Name	Project Title
3-1	**Takahiro Hosono**	Coseismic hydro-environmental changes after the 2016 Kumamoto earthquake
3-2	**Kei Ishida**	Development of Hybrid Downscaling Method of Future Climate Projections
3-3	**Makoto Kumon**	Autonomous Control of Drones for Environment Monitoring
3-4	**Mizue Munekata**	Development and Application of Simultaneous Measurement Technique of Pressure and Temperature by Luminescent Paint Using Modulated Excitation Light
3-5	**Yuta Nakashima**	Bio-sensing and bio-imaging for cellular behavior
3-6	**Masayuki Tanabe**	Development of Medial Ultrasound Functional Sensor

No. 3-1	Coseismic hydro-environmental changes after the 2016 Kumamoto earthquake		
Name	Takahiro Hosono		
Affiliation	Faculty of Advanced Science and Technology Email: hosono@kumamoto-u.ac.jp	Title	Associate Professor
Research Field	Environmental Science		
Period of Travel	—		
Host Researcher	Michael Manga		
Affiliation	Department of Earth and Planetary Science University of California, Berkeley	Title	Professor

1. Overview and significance of the international research collaboration

I made two major international research collaborations during 2020. One is the joint research with a research team from Department of Earth and Planetary Science, University of California, Berkeley, and the other is promoting Journal Special Issue editing in high impact international journal of our research field, Journal of Hydrology. Both collaboration research achieved very good results.

2. Research achievements and progress of the international joint research

1.1. Joint research with a research team from Department of Earth and Planetary Science, University of California, Berkeley

I and Profs. Michael Manga and Chi-Yuen Wang from University of California, Berkeley corroborate on publishing our co-authoring paper in international journal which describes post seismic mountain water release due to permeability enhancement after the 2016 Kumamoto earthquake. We communicate tightly via email and succeed our publication on high impact journal *Nature Communications*. This finding was released by the American Association for the Advancement of Science (AAAS) through following link.
https://www.eurekalert.org/pub_releases/2020-07/ku-coa070120.php

Hosono, T., Yamada, C., Manga, M., Wang, C. -Y., Tanimizu, M., 2020. Stable isotopes show that earthquakes enhance permeability and release water from mountains. Nature Communications, 11, 2776. https://doi.org/10.1038/s41467-020-16604-y

1.2. Special Issue in Journal of Hydrology

Journal Special Issue 'Coseismic hydro-environmental changes: Insights from recent earthquakes' was published in the Journal of Hydrology, one of the major high impact international journals in our academic field. I was a head editor and published in total 23 papers submitted from various countries with a help of other international co-editors. I also published Editorial article of this Special Issue.

Hosono, T., Saltalippi, C., Jean, J.-S., 2020. Coseismic hydro-environmental changes: insights from recent earthquakes. Journal of Hydrology, 585, 124799.

The Special Issue include 8 other co-authoring papers as shown below.

Kawabata, K., Sato, T., Takahashi, H.A., Tsunomori, F., **Hosono, T.,** Takahashi, M., Kitamura, Y.,

2020. Changes in groundwater radon concentrations caused by the 2016 Kumamoto earthquake. Journal of Hydrology, 584, 124712. https://doi.org/10.1016/j.jhydrol.2020.124712

Tawara, Y., **Hosono, T.,** Fukuoka, Y., Yoshida, T., Shimada, J., 2020. Quantitative assessment of the changes in regional water flow systems caused by the 2016 Kumamoto Earthquake using numerical modeling. Journal of Hydrology, 583, 124559. https://doi.org/10.1016/j.jhydrol.2020.124559

Ide, K., **Hosono, T.,** Kagabu, M., Fukamizu, K., Tokunaga, T., Shimada, J., 2020. Changes of groundwater flow systems after the 2016 Mw 7.0 Kumamoto earthquake deduced by stable isotopic and CFC-12 compositions of natural springs. Journal of Hydrology, 583, 124551. https://doi.org/10.1016/j.jhydrol.2020.124551

Nakagawa, K., Yu, Z.-Q., Berndtsson, R., **Hosono, T.,** 2020. Temporal characteristics of groundwater chemistry affected by the 2016 Kumamoto earthquake using self-organizing maps. Journal of Hydrology, 582, 124519. https://doi.org/10.1016/j.jhydrol.2019.124519

Kagabu, M., Ide, K., **Hosono, T.,** Nakagawa, K., Shimada, J., 2020. Describing coseismic groundwater level rise using tank model in volcanic aquifers, Kumamoto, southern Japan. Journal of Hydrology, 582, 124464. https://doi.org/10.1016/j.jhydrol.2019.124464

Miyakoshi, A., Taniguchi, M., Ide, K., Kagabu, M., **Hosono, T.,** Shimada, J., 2020. Identification of changes in subsurface temperature and groundwater flow after the 2016 Kumamoto earthquake using long-term well temperature–depth profiles. Journal of Hydrology, 582, 124530. https://doi.org/10.1016/j.jhydrol.2019.124530

Morimura, S., Zeng, X., Noboru, N., **Hosono, T.,** 2020. Changes to the microbial communities within groundwater in response to a large crustal earthquake in Kumamoto, southern Japan. Journal of Hydrology, 581,124341. https://doi.org/10.1016/j.jhydrol.2019.124341

Hosono, T., Masaki, Y., 2020. Post-seismic hydrochemical changes in regional groundwater flow systems in response to the 2016 Mw 7.0 Kumamoto earthquake. Journal of Hydrology, 580,124340. https://doi.org/10.1016/j.jhydrol.2019.124340

1.3. Others

The research foundation from JSPS which allows me to enhance international research collaboration including travel abroad has activated. I will use this support for traveling in next 2 years to: University of Canterbury, New Zealand, University of Rome, Italy, and University of Iceland, Iceland, with a partial support from IROAST program.

T. Hosono, principle investigator, JSPS Fostering Joint International Research (A), 2020-2023, 19KK0291

3. Prospect for further research collaboration with the visited university/institution

I had a plan visiting University of Rome, Italy on 2020. However, currently this plan became suspended due to corona virus issue. I hope I can travel on 2021 when it's possible.

4. Comments/suggestions for IROAST (programs).

Thank you providing me good opportunities working within IROAST program. This is beneficial program for young researchers promoting ones' international research activity from both financial and phycological point of view.

This study was financially supported by IROAST for paying article processing charges on publishing paper in Nature Communications ($5,380). The study was also supported by IROAST research award (500,000 JPY). I wish to thank all these supports.

5. List of journal papers (with your IROAST affiliation) published between April 2020 and March 2021.

Shown above.

No. 3-2	Development of Hybrid Downscaling Method of Future Climate Projections		
Name	Kei Ishida		
Affiliation	Center for Water Cycle, Marine Environment and Disaster Management (CWMD) Email: keiishida@kumamoto-u.ac.jp	Title	Associate Professor
Research Field	Environmental Science		
Period of Travel	－		
Host Researcher	Van-Thanh-Van Nguyen		
Affiliation	McGill University	Title	Professor
Period of Travel	－		
Host Researcher	Ali Ercan		
Affiliation	University of California, Davis	Title	Assistant Research Professor

Details of Activities

1. Overview and significance of the international research collaboration

Climate change is a large concern in many countries in the world now. To investigate impacts of climate change, future climate projections are used. Future climate projections are basically simulated results by means of general circulation models based on future climate scenarios. However, the resolutions of future climate projections are generally too coarse for regional-scale analysis. Therefore, downscaling technique is frequently utilized to obtain the projections at a finer resolution. There are mainly two types of downscaling techniques: Dynamical downscaling and statistical downscaling. Both of them have pros and cons. Therefore, hybrid downscaling technique, which is combined approach of dynamical and statistical downscaling, is sometimes utilized. In this international joint research, we will develop a new hybrid downscaling technique to improve estimations of climate change impacts at regional-scale.

2. Research achievements and progress of the international joint research

Because of the COVID-19 pandemic, we could not go abroad this fiscal year at all. It was difficult to proceed the collaborative research. However, I had online meetings and meetings on phone with Dr. Ercan. We have done a study on the hybrid downscaling with dynamical downscaling and deep learning downscaling. We have just written a journal paper, and submitted based on the results.

3. Prospect for further research collaboration with the visited university/institution

I hope that we can go abroad again in the near future.

4. Comments/suggestions for IROAST (programs).

None

5. List of journal papers (with your IROAST affiliation) published between April 2020 and March 2021.

None

No. 3-3	Autonomous control of drones for environment monitoring		
Name	Makoto Kumon		
Affiliation	Faculty of Advanced Science and Technology Email: kumon@gpo.kumamoto-u.ac.jp	Title	Associate Professor
Research Field	Advanced Green Bio		
Period of Travel	April 1, 2020-May 8, 2020		
Host Researcher	Tomonari Furukawa		
Affiliation	University of Virginia	Title	Professor

1. Overview and significance of the international research collaboration:

Since June 2019, I stayed in Virginia, USA to conduct the collaborative research at Virginia Tech (VT) and University of Virginia (UVA) under the supervision of Professor Furukawa by the support of IROAST program. The stay was originally planned until the end of June, 2020, but it was unfortunate that the term was shortened till the mid-April because of the pandemic of COVID-19.

Although the stay was distorted, the on-site activity at the host researcher's lab allowed to have concentrated discussion on the research topics, and we have kept working on the human-drone system even after my return to Kumamoto through the regular remote meetings. The output of this work is under preparation for the publication, and we are discussing its potential for further extensions.

2. Research achievements and progress of the international joint research:

I have joined the international robotic competition (Mohamed Bin Zayed International Robotic Competition; MBZIRC) where robots demonstrated autonomous drones and mobile platforms to achieve in February, 2020 as a member of Team VICTOR (the team of VT and UVA). During this activity, the importance of the state-estimation and the prediction of the intelligent agents in the field was emerged, and I have been involved in the group to study on that topic. The prediction of another agents has been recently attracting attention for the autonomous robots as human-robot cooperation is getting more important, for example, autonomous driving cars need to predict human driving cars for safety.

As potential human operated robots / agents in the practical applications, we have selected as a human controlled drone as an example of the research project, and the group established a method to estimate the drone motion taking the operator's "intention" as a part of the internal state. The result is now under the preparation for the publication. This activity has been conducted by the remote meetings over the internet, and numerical simulation approach has been utilized to verify the effectiveness so far.

3. Prospect for further research collaboration with the visited university

We have on-going project, and the prospect for the further collaborative research activity is clear. Although the proposed approach of the human intention has been tested by the numerical methods, it is inevitable to evaluate by the real devices. In order to achieve this evaluation by the

experiment, the group is going to prepare international collaborative field tests after the pandemic will settle down. The group will share the data of the experiments to analyze internationally, but this may limit the effectiveness. Therefore, if the situation allows, exchange of researchers is one of the options to accelerate the project. It is also an option to involve graduate students, which can encourage students' international experience.

4. Comments/suggestions for IROAST

I sincerely acknowledge the support for my visit to Virginia in order to conduct the international collaborative research. I wish the further extending activity of IROAST to encourage the international researches.

5. Publication lists (referred):

1. Kotaro Hoshiba, Ryusuke Noda, Toshiyuki Nakata, Hao Liu, Kei Senda, Kazuhiro Nakadai, Makoto Kumon, Hiroshi G. Okuno, "Development of surface-processed low-noise propeller for search and rescue tasks with drone audition" Proceedings of Quiet Drones, Paris(online), 2020/11/20.
2. Makoto Kumon, Hiroshi G. Okuno, Kazuhiro Nakadai, Kotaro Hoshiba, Ryosuke Noda,"Proposal of Cognitive Drone Audition based on Cognitive Dynamic Systems," Proceedings of Quiet Drones, Paris(online), 2020/11/20.
3. M. Wakabayashi, H.G. Okuno and M. Kumon, " Drone Audition Listening from the Sky Estimates Multiple Sound Source Positions by Integrating Sound Source Localization and Data Association," Advanced Robotics, Vol. 34, No. 11, pp. 744-755, doi:10.1080/01691864.2020.1757506, 2020/5/5.
4. T. Kagawa, F. Ono, L. Shan, R. Miura, K. Nakadai, K. Hoshiba, M. Kumon, H. G. Okuno, S. Kato and F. Kojima, " Multi-hop wireless command and telemetry communication system for remote operation of robots with extending operation area beyond line-of-sight using 920 MHz/169 MHz," Advanced Robotics, Vol. 34, No. 11, pp. 755-766, doi:10.1080/01691864.2020.1760934, 2020/5/12.

No. 3-4	Development and Application of Simultaneous Measurement Technique of Pressure and Temperature by Luminescent Paint Using Modulated Excitation Light		
Name	Mizue Munekata		
Affiliation	Faculty of Advanced Science and Technology Email: munekata@kumamoto-u.ac.jp	Title	Associate Professor
Research Field	Green Energy/ Environmental Science		
Period of Travel	－		
Host Researcher	Christian Klein		
Affiliation	German Aerospace Center Institute of Aerodynamics and Flow Technology	Title	Team Leader TSP/PSP

Details of Activities

Pressure Sensitive Paint (PSP) measurement technique is based on the dependence of the intensity or decay time of its luminescence on pressure, brought about by oxygen quenching. PSP is usually exited by light at an appropriate wavelength (e.g. UV-Light) and its pressure dependent luminescence intensity or lifetime is detected by a camera system (CCD or CMOS). In the method based on the luminescent lifetime, two basic types of measurement exist: The first type is the time-domain lifetime method, which is mostly used in various PSP applications. For this method a pulsed light is used to excite the paint and the pressure dependent time constant is determined from decay curve of luminescence intensity. The second type is the frequency-domain fluorescence lifetime imaging (FLIM) where modulated light is used to excite the paint and the PSP luminescence is simultaneously detected to calculate pressure dependent phase shift or amplitude. Only few applications were reported using this method.

Recently, a new CMOS image sensor has been developed by CSEM and PCO for frequency-domain FLIM system and equipped in the pco.flim camera for fluorescence lifetime imaging in microscopy. In this study, the frequency-domain lifetime PSP technique (FLIM-PSP) is investigated using a larger model for industrial applications.

We planned to test the FLIM-PSP technique with the pco.flim camera for industrial models. However, we could not test it because of COVID-19.

As one of new challenges, we have investigated simultaneous measurement of temperature and pressure with FLIM-PSP technique. Since we succeeded in obtaining temperature and pressure calibration curves using a photomultiplier tube, we clarified that it is possible to measure simultaneously temperature and pressure at the calibration test level. Our next test is performed by a high speed camera (CMOS) at Kumamoto university. It was not trial by the FLIM camera in DLR. The calibration curves by some high speed cameras were obtained successfully. Demonstration tests are underway with simultaneous measurement of temperature and pressure distribution by this technique using a wall impinging jet model. However, in order to apply it to the industrial model, it is necessary to investigate to further increase the temperature sensitivity and temperature sensitivity.

We hope to have collaboration tests using the FLIM camera at DLR in Germany in 2021.

No. 3-5	Bio-sensing and bio-imaging for cellular behavior		
Name	Yuta Nakashima		
Affiliation	Faculty of Advanced Science and Technology Email: yuta-n@mech.kumamoto-u.ac.jp	Title	Associate Professor
Research Field	Advanced Green Bio		
Period of Travel	－		
Host Researcher	Dr. Douglas A. Coulter Dr. Hajime Takano		
Affiliation	The Children's Hospital of Philadelphia & University of Pennsylvania（UPenn）	Title	Professor Assistant Professor

The objective of this project is to develop the palm-size medical diagnostic devices apply to detection of disease and post-surgical management based by cell behavior. The development of the desired medical devices is need to fundamental technique shown below.

* Microfabrication technique for fabricating cell size and palm-size structure.
* Cell handling technique
* Sensing technique for cell produced signals such as protein, exosome, RNA, etc. on the devices.
* Imaging technique for detecting the morphology, movement, behavior, etc. of cells on the devices.

In my laboratory, microfabrication technique and cell handling technique are already possessed. Host researchers has a lot of knowledges about in vitro and in vivo sensing/detection/imaging techniques for cell and tissue evaluation. We will promote joint research to achieve the objective medical devices by integrating our technologies.
I had planned the starting collaborative research at host researcher laboratory in June 2020. However, I could not be achieved this plan by influence of COVID-19. In the next season, I would like to restart the discussion about our collaborative research with host researchers, and I will prepare to the collaborative research at USA.

List of journal papers

*Corresponding author

[1] Souichiro Fukuyama, Seitaro Kumamoto, Seiya Nagano, Shoma Hitotsuya, Keiichiro Yasuda, Yusuke Kitamura, Masaaki Iwatsuki, Hideo Baba, Toshihiro Ihara, Yoshitaka Nakanishi, and Yuta Nakashima*, “Detection of cancer cells in whole blood using a dynamic deformable microfilter and a nucleic acid aptamer,” Talanta, 2021. *in press*

[2] Yoshitaka Nakanishi, Hajime Yamaguchi, Yusuke Hirata, Yuta Nakashima, Yukio Fujiwara, “Micro-abrasive glass surface for producing microplastics for biological tests,” Wear, 2021. *in press*

[3] Hajime Yamaguchi, Katsunori Higuchi, Koshi Sakata, Tetsuya Akiyama, Keiji Kasamura, Yuta Nakashima, Yoshitaka Nakanishi, “Hydrophilic sealing material for live centers in machine tools,” Wear, 2021. *in press*

[4] Yoshitaka Nakanishi, Yuta Nakashima, Emile van der Heide, “Microstructuring Glass Surfaces Using a Combined Masking and Microslurry-Jet Machining Process,” Precision Engineering, 67, pp.172-177, 2021.

[5] **[Selected as an Editor’s Pick paper]** Seitaro Kumamoto, Kenshiro Nakatake, Souichiro Fukuyama, Keiichiro Yasuda, Yusuke Kitamura, Masaaki Iwatsuki, Hideo Baba, Toshihiro Ihara, Yoshitaka Nakanishi, and Yuta Nakashima*, “A dynamically deformable microfilter for selective separation of specific substances in microfluidics,” Biomicrofluidics, 14, 064113, 2020.

[6] Yoshitaka Nakanishi, Yuta Nakashima, Yukio Fujiwara, Yoshihiro Komohara, Kazunori Hino, Hiromasa Miura, Hidehiko Higaki, “Microfluidic Device used for the Secretion of Inflammatory Cytokines from Human Monocyte-Derived Macrophages Stimulated by Ultra-High Molecular Weight Polyethylene Particles,” Biotribology, 23, 100137, 2020.

List of awards

[1] Award a grand prize
TECH PLAN DEMO DAY　BIO-TECH GRAND PRIX
Sep. 19, 2020.
[2] Chiome Bioscience Award
TECH PLAN DEMO DAY　BIO-TECH GRAND PRIX
Sep. 19, 2020.
[3] Tomita Pharmaceutical Award
Kumamoto Tech Grand Prix
Jul. 18, 2020.
[4] Atsumaru Holdings Award
Kumamoto Tech Grand Prix
Jul. 18, 2020.

List of social contributions

[1] Member of the review committee
JSPS Research Fellowship for Young Scientists
Jul. 1, 2019 – Jun 30, 2020.
[2] Advisory Board of Ph.D. candidate
Graduate School and Faculty of Information Science and Electrical Engineering, Kyushu University
Jun 12, 2019 – Mar. 31, 2022.
[3] Member of the review committee
JSPS Research Fellowship for Young Scientists
Jul. 1, 2020 – Sep. 30, 2020.
[4] Editorial committee
37th Sensorsymposium, IEEJ (The Institute of Electrical Engineers of Japan)

List of international exchanges

[1] Faculty-level exchange agreement, Gazi University, Turkey
Oct. 6, 2020.
[2] Faculty-level exchange agreement, Universiteit Twente, Netherlands
Sep. 8, 2020.

No. 3-6	Development of Medial Ultrasound Functional Sensor		
Name	Masayuki Tanabe		
Affiliation	Faculty of Advanced Science and Technology Email: mtanabe@kumamoto-u.ac.jp	Title	Assistant Professor
Research Field	Nanomaterial Science/ Advanced Green Bio		
Period of Travel	－		
Host Researcher	Elisa E. Konofagou		
Affiliation	Department of Biomedical Engineering and Radiology, Columbia University	Title	Robert and Margaret Hariri Professor
Period of Travel	－		
Host Researcher	Rajendra Udyavara Acharya		
Affiliation	School of Engineering, Ngee Ann Polytechnic	Title	Senior Faculty Member

In February 2020, I flew to New York to start a joint research project with Columbia University, but the lab was shut down due to COVID-19 and I had to wait in a hotel room in Manhattan, New York. Unfortunately, I had to return to Japan the day after the emergency was declared without entering the lab. More than a year has passed since then, and even though effective vaccines have been developed, it is still impossible to travel abroad.
Nevertheless, our research team have continued our joint research with domestic companies to develop a flexible and thin patch-type ultrasound sensor, which is designed to constantly monitor the heart and detect abnormalities before they occur. I have also been continuing to discuss with researchers and medical doctors in Japan and Singapore, and am preparing for conducting clinical trials using our devices. We will complete fabrication of the prototype and conduct clinical trials with it by the end of 2021.
Thanks to the generous support of IROAST, we are able to continue the development of the device. We will continue our research for the development of innovative medical devices.

Shu Lih Oh, V. Jahmunaha Chui Ping Ooi, Ru-San Tan, Edward J Ciaccio, Toshitaka Yamakawa, Masayuki Tanabe, Makiko Kobayashi, U Rajendra Acharya "Classification of heart sound signals using a novel deep WaveNet model," Computer Methods and Programs in Biomedicine, Vol. 196, November 2020, 105604.

Research Activities

4. Visiting Professors

4. Visiting Professors

No.	Name	Project Title
4-1	**U Rajendra Acharya** HP: Makiko Kobayashi	Advanced Biomedical Evaluation System
4-2	**Paul Bowen** HP: Kazuki Takashima	Advanced Structural Materials
4-3	**Maria Jose Cocero** HP: Tetsuya Kida	Biomass to Green Energy Conversion Technologies
4-4	**Derek Elsworth** HP: Atsushi Sainoki	Development of a numerical simulation method for fluid injection into a natural fault
4-5	**Carolina Escobar** HP: Shinichiro Sawa	Analysis of plant parasitic nematode infection mechanisms.
4-6	**Tomonari Furukawa** HP: Makoto Kumon	Autonomous control of drones for environment monitoring
4-7	**Olivier Hamant** HP: Shinichiro Sawa	Plant Cell and Developmental Biology
4-8	**Yang Kim** HP: Shinya Hayami	Development of Nano and Supramolecular Materials
4-9	**Ick Chan Kwon** HP: Takuro Niidome	Nano-medicine and Theranostics
4-10	**Zoran Ren** HP:Kazuyuki Hokamoto	Fabrication of various porous materials through explosive and other processes and the evaluation of such porous materials under high-rate impact loading
4-11	**Shirley Shen** HP: Kazuki Takashima	Advanced Structural Materials ~3D Printing of Bio-degradable Implant Components~
4-12	**Daniel P. Zitterbart** HP: Kei Toda	Understanding the role of oceanic chemoattractants in marine animal navigation

HP: Host Professor

No.4-1	Advanced Biomedical Evaluation System		
Name	Rajendra Udyavara Acharya		
Affiliation	Ngee Ann Polytechnic Email: rajendra_udyavara_acharya@np.edu.sg	Title	Senior Research Fellow
Research Field	Nanomaterial Science/ Advanced Green Bio		
Host Professor	Makiko Kobayashi	Title	Associate Professor
Affiliation	Faculty of Advanced Science and Technology Email: kobayashi@cs.kumamoto-u.ac.jp		

1. Research achievements:
Ans:
(a) Discussed the project entitled "Automated system and method of monitoring anatomical structures". We filed a PCT application (PCT/SG2020/050538) on this topic.
(b) Published 2 papers "Classification of heart sound signals using a novel deep WaveNet model" and "Comprehensive electrocardiographic diagnosis based on deep learning"

2. Overview and significance of the research collaboration with Kumamoto University
Ans: Cardiovascular disease (CVD) is the leading cause of death worldwide, and coronary artery disease (CAD) is a major contributor. Early-stage CAD can progress if undiagnosed and left untreated, leading to myocardial infarction (MI) that may induce irreversible heart muscle damage, resulting in heart chamber remodeling and eventual congestive heart failure (CHF). Electrocardiography (ECG) can detect established MI and may also be helpful for early diagnosis of CAD. For the latter especially, the ECG perturbations can be subtle and potentially misclassified on manual interpretation and/or traditional algorithms found in ECG machines. For automated diagnostic systems (ADS), deep learning techniques are favored over conventional machine learning techniques, due to the automatic feature extraction and selection processes involved. This paper highlights various deep learning algorithms exploited for the classification of ECG signals into CAD, MI and CHF conditions. The Convolutional Neural Network (CNN), followed by combined CNN and Long Short-Term Memory (LSTM) models, appear to be the most useful architectures for classification. A 16-layer LSTM model was developed in our study and validated using 10-fold cross validation. A classification accuracy of 98.5% was achieved. Our proposed model has the potential to be a useful diagnostic tool in hospitals for the classification of abnormal ECG signals.

3. Comments or suggestions for IROAST/Kumamoto University
Ans: Better for the students to speak and write in English.

4. Prospect for further research collaboration with Kumamoto University
Ans: I shall continue to collaborate and write papers with Prof. Toshitaka Yamakawa, Prof. Masayuki Tanabe, and Prof. Makiko Kobayashi in the coming days.

5. Impressions of Kumamoto University/Kumamoto
Ans: Very good University and Professors are knowledgeable. Students are well behaved.

No.4-2	Advanced Structural Materials		
Name	Paul Bowen		
Affiliation	University of Birmingham Email: P.Bowen@bham.ac.uk	Title	Deputy Pro-Vice-Chancellor / Feeney Professor of Metallurgy
Research Field	Nanomaterial Science		
Host Professor	Kazuki Takashima	Title	Professor
Affiliation	Faculty of Advanced Science and Technology Email: takashik@gpo.kumamoto-u.ac.jp		

Since being appointed as a visiting professor at International Research Organisation for Advanced Science and Technology (IROAST) at Kumamoto University (KU) in late 2018, IROAST and the School of Metallurgy and Materials at the University of Birmingham (UoB) have:

(i) continued with long standing research collaborations (started originally in 1993 by the extended visit of Professor Takashima to UoB);

(ii) utilised the UoB-KU Exchange Programme (2018) to strengthen collaborative research through exchanging post-graduate students and to foster internationally renowned researchers to visit and carry out collaborative research;

(iii) started collaborative research for the synergetic development, specific to next generation energy materials used in auto-motive and aerospace components. This programme is partly funded by a grant from the Great Britain Sasakawa Foundation to facilitate a research exchange programme.

The Materials Science and Engineering Department at KU is prominent, for example, in the field of magnesium alloys for components of future automotive vehicles to achieve lighter body weight, as well as hydrogen embrittlement studies that are anticipated to contribute to challenges with hydrogen storage systems and transportation. At the School of Metallurgy and Materials in UoB, Professor Bowen directs a Rolls-Royce University Technology Centre (UTC) which carries out multiple projects for the development of future civil engines with improved fuel efficiency by developing new alloys and composites. The automotive and aerospace industries are large sources of carbon emissions, but they are the essential means of transportation. Our future collaborative research with IROAST will thus focus on opportunities for next generation materials to reduce the carbon footprints of these industries. Here, it is necessary to involve further academics to sustain and to grow our long-standing relationship. These will include: Dr Yu-Lung Chiu (Reader) and Dr Hiroto Kitaguchi (Senior Research Fellow) at UoB; and Professor Yoji Mine at KU. These researchers have already established informal research collaborations and routinely publish together. The collaboration with IROAST will also seek to expand the programme further with interactions to private companies such as IHI, Daido Steel and Honda.

In summary, although research visits have been postponed during 2020 and 2021 due to the ongoing pandemic, research collaboration continues and plans for future growth are in place. Such international interactions, with an excellent university in Japan and especially in view of its aspirations to become an even more influential global university (through such initiatives as IROAST), remain crucial to universities in the UK with similar ambition for advancement.

No.4-3	Biomass to Green Energy Conversion Technologies		
Name	Maria Jose COCERO		
Affiliation	High Pressure Research Group Department of Chemical Engineering and Environmental Technology Valladolid University, Spain Email: mjcocero@iq.uva.es	Title	Professor
Research Field	Green Energy/ Advanced Green Bio		
Host Professor	1. Tetsuya KIDA	Title	1.Professor
	2. Armando QUITAIN		2.Professor
Affiliation	1. Faculty of Advanced Science and Technology Email: tetsuya@kumamoto-u.ac.jp		
	2. Center for International Education, Kumamoto University Email: quitain@kumamoto-u.ac.jp		

Details of Activities

1. Research achievements

Due to coronavirus-related pandemic, I was not able to visit Kumamoto University as an IROAST Visiting Professor this year. Student mobility was also not possible this time. However, I have followed up online on the research activities carried out by Dr. Armando T. Quitain, during his stay in my laboratory in Valladolid University (Spain).

The following research-related and academic activities were carried out:

①Acceptance of an alumnus from Kumamoto University, Dr. Elaine G. Mission, under the Marie-Curie Individual Fellowship Program. She was a doctoral student under the supervision of Prof. Tetsuya Kida and Prof. Armando Quitain. She will carry out research related to biomass utilization using microwave and supercritical fluid technologies in my laboratory for 2 years starting October 2020.

②Gave an online lecture in the Global Team Teaching subject on “Perspectives on Biomass Utilization”, being offered at the Center for International Education and participated by a total of about 180 undergraduate students from Kumamoto University and Sepuluh Nopember Institute of Technology (ITS, Indonesia).

③Publication of a joint article with Kumamoto University team in reputable journal in this field: “Supercritical CO2–subcritical H2O system: A green reactive separation medium for selective conversion of glucose to 5-hydroxymethylfurfural” including the previous research outcomes of Prof. Quitain and his students in my laboratory.

2. Overview and significance of the research collaboration with Kumamoto University

The research collaboration on the use of green technologies (supercritical fluid and microwave) for biomass utilization with Kumamoto University (KU) started more than a decade ago with Prof. Motonobu Goto, and was renewed by Dr. Armando T. Quitain when he visited as an IROAST Young Researcher in 2017 for half a year. This collaboration also supported visits of 8 promising young students from Kumamoto under TOBITATE Ryugaku Japan Program or IJEP Scholarship, significantly broadening the global perspectives of participating students to the

science and technology of this promising environment-related topic on biomass utilization.

My consultation and discussion with the students significantly helped them improved their research capability. My expertise on the research topic guided them in carrying out the right direction for their respective research topics. This also gave them rare opportunity to have a discussion with prominent and leading scientists/international researchers in this field, thereby improving their research capability and global mindset.

3. Comments or suggestions for IROAST/Kumamoto University

IROAST is doing a good job in globalizing cutting-edge research of Kumamoto University.

4. Prospect for further research collaboration with Kumamoto University

I wish to further strengthen the research collaboration with Kumamoto University by continuously accepting students to my laboratory, and also by sending our students to Kumamoto University. There are also some interests from our students here in Valladolid University to study in Kumamoto University. With subsequent visits in the future, it is expected that a new set of students will benefit from it, and more research papers will be jointly published from this extended collaboration.

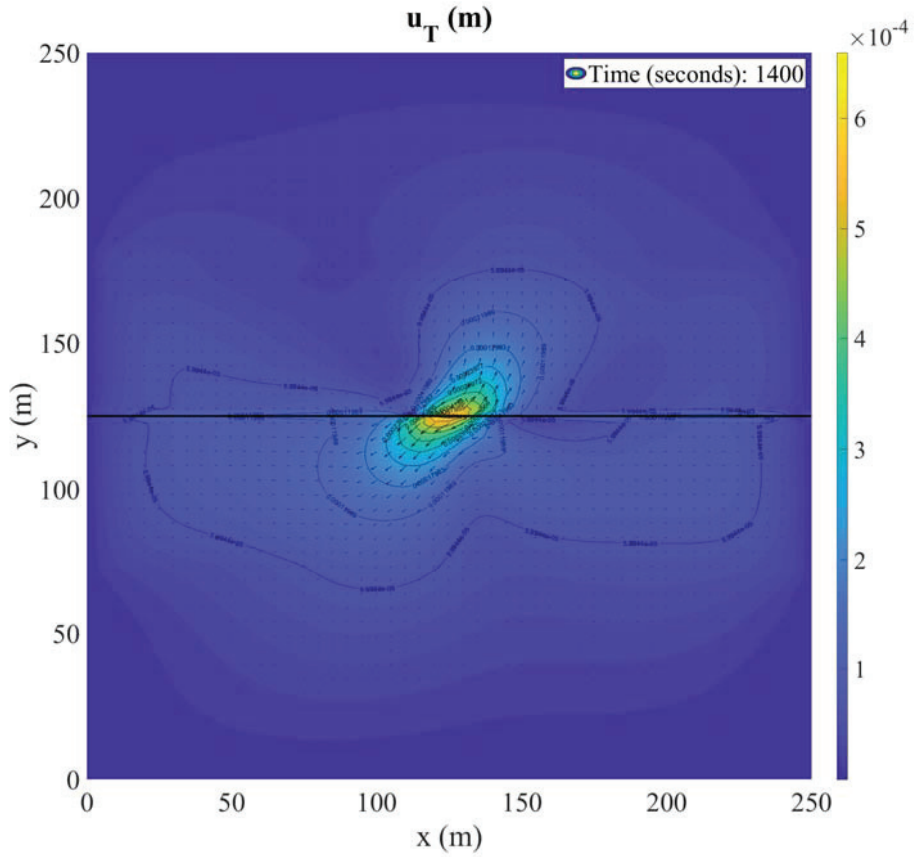
5. Impressions of Kumamoto University/Kumamoto

In my opinion, the integration of student mobility programs with research collaboration is a strength of Kumamoto University. It could make a big difference to Kumamoto University students compared to those from other universities in Japan.

No.4-4	Development of a numerical simulation method for fluid injection into a natural fault		
Name	Derek Elsworth		
Affiliation	Department of Energy and Mineral Engineering Pennsylvania State University Email: elsworth@psu.edu	Title	Prof.
Research Field	Green Energy		
Host Professor	Atsushi Sainoki	Title	Associate Professor
Affiliation	International Research Organization for Advanced Science and Technology Email: atsushi_sainoki@kumamoto-u.ac.jp		

We have been developing a numerical simulation methodology for fluid injection into a natural fault, based on the Extended Finite Element Method with Dr. Sainoki's research team at Kumamoto University. The goal of this study is to predict the occurrence of induced seismicity caused by fluid injection related to various engineering projects, such as shale gas, oil, and geothermal energy development, and to estimate seismic source parameters of the induced seismic event. To this end, it is indispensable to develop a numerical simulation code that allows us to quantify the fluid injection-induced mechanical behaviour of the rock mass and fault that involves not only fluid flow within the fault but also fluid leak-off into the surrounding rock mass.

Although many numerical simulations have been performed with conventional numerical techniques, such as the finite element method and finite difference method, such methodologies cannot fully consider the complex mechanical behaviour. To overcome this limitation, we have applied the Extended Finite Element Method to the simulation of the mechanical behaviour of the fault and rock mass undergoing fluid injection-induced pore pressure change. The application of XFEM to fluid injection simulation while coupling fluid flow with rock mass behaviour has not yet been explored sufficiently and developed. To my knowledge, this is the first time that fluid injection-induced fault shear behaviour was successfully simulated with the XFEM and validated against experimental data obtained from a natural fault. The paper has been published in Rock Mechanics and Rock Engineering. At this moment, we are further developing the code to consider the dynamic behaviour of the fault during fluid injection with the purpose of quantifying seismic energy released during fluid injection so that it is possible to estimate the risk of induced seismicity.



Example of fault shear behaviour caused by fluid injection simulated with the Extended Finite Element Method that couples fluid flow with the mechanical behaviour of the fault and the rock mass.

No.4-5	Analysis of plant parasitic nematode infection mechanisms.		
Name	Carolina Escobar		
Affiliation	UNIVERSIDAD DE CASTILLA LA MANCHA Email: Carolina.Escobar@uclm.es	Title	Professor
Research Field	Advanced Green Bio		
Host Professor	Shinichiro Sawa	Title	Professor
Affiliation	Faculty of Advanced Science and Technology Email: sawa@kumamoto-u.ac.jp		

Details of Activities

1. Research achievements
We have identified that RKN induce gall formation by recruiting plant developmental pathways by collaboration.

2. Overview and significance of the research collaboration with Kumamoto University
Kumamoto University has launched IRCAEB in GSST for agricultural research. Our collaboration is related to agricultural perspective, and this collaboration is quite important for the development of Agricultural Research Activity in KU.

3. Comments or suggestions for IROAST/Kumamoto University
Nothing.

4. Prospect for further research collaboration with Kumamoto University
We will continue about the agricultural collaboration.

5. Impressions of Kumamoto University/Kumamoto
Nothing.

No.4-6	Autonomous control of drones for environment monitoring		
Name	Tomonari Furukawa		
Affiliation	University of Virginia, USA Email: tomonari@virginia.edu	Title	Professor
Research Field	Advanced Green Bio		
Host Professor	Makoto Kumon	Title	Associate Professor
Affiliation	Faculty of Advanced Science and Technology / IROAST Email: kumon@gpo.kumamoto-u.ac.jp		

1. Research achievement

I have accepted A. Prof. Kumon from Kumamoto University for the international collaborative research since June, 2019 until April 2020 while his original plan was until the end of June, 2020 because of the pandemic of CoVID-19. During his stay, we have discussed about a human-robot interaction system taking the humans' intention into account to realize safe and reliable intelligent agents. After his return to Kumamoto, we have kept discussing on the topic, and formalized the problem to establish a novel framework. The first report is now under preparation, and we are discussing to extend it for more applications.

2. Overview and significance of the research collaboration with Kumamoto University

I have a long history to work with the host researcher since his visit to my lab in 2007. Both of us uniquely work on autonomous drones and auditory robotics, so we can explore and collaborate on multiple projects. The past collaboration has produced many co-authored papers. The collaboration is important also because we also exchanged students.

3. Comments or suggestions for IROAST/Kumamoto University

I believe that supports for visiting scholars by IROAST are meaningful both for the visitors and Kumamoto University, and I expect that such activities will last for a long time.

4. Prospect for further research collaboration with Kumamoto University

The host researcher and I will keep working on the project of the robot systems to cope with human intention. We start thinking about the physical exchange once the pandemic settles down.

5. Impressions of Kumamoto University/Kumamoto

Kumamoto is my hometown where I lived until 18 years old, so I have been to Kumamoto University many times. I have more reasons to like and support Kumamoto and Kumamoto University. Kumamoto has suffered from earthquakes whereas I primarily work on disaster robotics. Having been in a faculty position overseas for over 20 years, I keep thinking what I can do for my hometown.

No.4-7	Plant Cell and Developmental Biology		
Name	Olivier Hamant		
Affiliation	INRAE, CNRS Email: olivier.hamant@ens-lyon.fr	Title	Professor
Research Field	Advanced Green Bio		
Host Professor	Sinichiro Sawa	Title	Professor
Affiliation	Faculty of Advanced Science and Technology Email: sawa@kumamoto-u.ac.jp		

Details of Activities

1. Research achievements
We have identified taht stem integrity in plant requires a load-bearing epidermis as collaboration.

2. Overview and significance of the research collaboration with Kumamoto University
Kumamoto University has launched IRCAEB in GSST for agricultural research. Our collaboration is related to agricultural perspective, and this collaboration is quite important for the development of Agricultural Research Activity in KU.

3. Comments or suggestions for IROAST/Kumamoto University
Nothing.

4. Prospect for further research collaboration with Kumamoto University
We will continue about the agricultural collaboration.

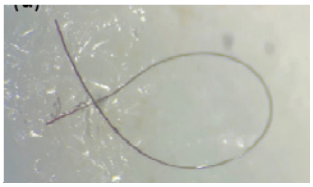
5. Impressions of Kumamoto University/Kumamoto
Nothing.

No.4-8	Development of Nano and Supramolecular Materials		
Name	Yang Kim		
Affiliation	Kosin University Email: ykim@kumamoto-u.ac.jp	Title	Professor
Research Field	Nanomaterial Science		
Host Professor	Shinya Hayami	Title	Professor
Affiliation	Faculty of Advanced Science and Technology Email: hayami@kumamoto-u.ac.jp		

Details of Activities

1. Research achievements

Novel elastic crystalline fibres composed of metal complex are demonstrated. The plate-like crystal of Ni(II)(salophen) complex (H_2(salophen) = N,N'-bis(salicylidene)-o-phenylenediamine) (**1**) can be mechanically-stimuli shaping into crystal fibres. This fibril-like crystal could be made into a loop shape, suggesting its high elasticity. Controlling the stiffness of a crystal was also achieved by inducing recrystallization solvent in the crystal lattice.



2. Overview and significance of the research collaboration with Kumamoto University

Soft materials, such as elastomers, organic polymers, liquid crystal and flexible crystal, have been attracted considerable attention due to their potential applications for flexible electronics, optical devices, sensors, artificial muscles and smart nanomaterials. Of these, highly ordered soft material, flexible molecular crystal, is expected as a new platform for soft materials comparable to that of elastomers and polymers in recent years. The examples of the flexible (elastic/plastic) bending in an organic crystal were increasing observation in recent years, however, examples of metal complexes are still limited. Flexible crystal composed of metal complex has been expected for new functional crystalline soft materials reflecting their physical properties.

We have succeeded to develop the elastic crystalline fibres composed of a metal complex. The plate-like crystal of a Ni(II) (salophen) complex (H_2salophen= N,N'-bis(salicylidene)-o-phenylenediamine) (1) can be shaped into crystal fibres by mechanical stimuli.

3. Comments or suggestions for IROAST/Kumamoto University

We have thank IROAST for some supports and we hope IROAST will continuously support for us.

4. Prospect for further research collaboration with Kumamoto University

We expect our research opens up the further exploration to develop the functional crystalline fibres composed of metal complex. In order to explore the functional crystalline fibres composed of metal complex, further investigation using other metal ion with π-conjugated ligand based on salen type are now in progress.

5. Impressions of Kumamoto University/Kumamoto

It is also important to remark the decisive contribution to this research project from IROAST at Kumamoto University that allowed my visit to be possible. I am planning to start to develop at

Professor Hayami research facilities a project on advanced nanomaterials.

Publication List

1. P. Thuery, Y. Atoini, S. Kusumoto, S. Hayami, Y. Kim, J. Harrowfield, Optimizing Photoluminescence Quantum Yields in Uranyl Dicarboxylate Complexes: Further Investigations of 2,5-, 2,6- and 3,5-Pyridinedicarboxylates and 2,3-Pyrazinedicarboxylate, Eur. J. Inorg. Chem., 46, 4391-4400 (2020). DOI: 10.1002/ejic.202000803
2. S. Kusumoto, A. Saso, H. Ohmagari, M. Hasegawa, Y. Kim, M. Nakamura, L. F. Lindoy, S. Hayami, Solvent-Dependent Bending Ability of Salen-Derived Organic Crystals, ChemPlusChem, 85(8), 1692-1696 (2020). DOI: 10.1002/cplu.202000362
3. Y. Hirano, J. N. Beltramini, A. Mori, M, Nakamura, M. R. Karim, Y. Kim, M. Nakamura, S. Hayami, Microwave-assisted catalytic conversion of glucose to 5-hydroxymethylfurfural using "three dimensional" graphene oxide hybrid catalysts, RSC Adv., 10, 11727-11736 (2020). DOI: 10.1039/D0RA01009J
4. S. Kusumoto, Y. Kim, M. Nakamura, L. F. Lindoy, S. Hayami, Ferromagnetically coupled hydroxo-bridged heptanuclear Ni(II) wheel cluster with S= 7 ground spin state, Chem. Lett., 49, 24-27 (2020). DOI: 10.1246/cl.190765

No.4-9	Nano-medicine and Theranostics		
Name	Ick Chan KWON		
Affiliation	Biomedical Research Institute Korea Institute of Science and Technology (KIST) Republic of Korea/ Dana-Farber Cancer Institute, USA Email: ikwon@kist.re.kr	Title	Principal Research Scientist
Research Field	Nanomaterial Science		
Host Professor	Takuro NIIDOME	Title	Professor
Affiliation	Faculty of Advanced Science and Technology Email: niidome@kumamoto-u.ac.jp		

In the last decades, the development of nanocarriers for the efficient delivery of drugs offers a wide range of biotechnology applications. Due to the advantage of the size, nanomaterials have been shown to be robust drug delivery systems and may be useful for encapsulating drugs and enabling more precise targeting with a controlled release by various external stimulation (ex. pH, ROS, Temperature and so on). Nanomedicine has revolutionized existing cancer therapies through the improvement of pharmacological kinetics and dynamics. As well as, image-guided drug delivery can be used for various different purposes, ranging from simple and straightforward biodistribution studies to extensive and elaborate experimental setups aiming to enable “personalized medicine”, and to improve the efficacy of combined modality anticancer therapy. Despite the enormous progress in the field of nanotherapeutics, the use of artificially synthesized nanocarriers still faces several challenges, including rapid clearance from blood circulation, off-target effects, and ineffective nanoparticles (NPs) transfer in patients with advanced forms of cancer. Furthermore, NPs will encounter multiple physiological barriers that influence their effectiveness, such as blood circulation, NPs-protein interaction, extravasation into tumor tissue or the tumor microenvironment (TME), phagocytic sequestration, and renal clearance.

Prof. Kwon is an expert of smart nanomaterials for bioimaging. He gave us information for state-of-art diagnosis and drug delivery systems and lots of advices for our research unit. His supports will be a great basis of our research activities for the development of novel therapeutic approaches. Although he could not come to IROAST and have a chance to talk together due to the pandemic of COVID-19 in 2020, in 2021, we are going to have chances to talk through web system, and exchange information of our research work and progress of this research field in the world.

No.4-10	Fabrication of various porous materials through explosive and other processes and the evaluation of such porous materials under high-rate impact loading		
Name	Zoran Ren		
Affiliation	Faculty of Mechanical Engineering University of Maribor, Slovenia Email: zoran.ren@um.si	Title	Professor
Research Field	Other (Materials Processing)		
Host Professor	Kazuyuki Hokamoto	Title	Professor
Affiliation	Institute of Industrial Nanomaterials Email: hokamoto@mech.kumamoto-u.ac.jp		

Details of Activities

1. Research achievements

It is my distinct pleasure to collaborate with prof. Kazuyuki Hokamoto and his team at the Institute of Industrial Nanomaterials of the Kumamoto University for many years now. I am very honored and grateful for my continuing appointment as the IROAST Visiting Professor, which is further strengthening a bond to Kumamoto University. My research team members and I have been regular visitors to Kumamoto before the pandemic, which resulted in many joint publications in high-quality scientific journals due to outstanding collaborative research effort in developing new cellular structures in previous years. I was also happy to host prof. Hokamoto and his colleagues and students at the University of Maribor in Slovenia.

The year 2020 was different. Due to the pandemic, we could not realize the planned exchanges, which was reflected on somewhat slower combined research activities. Nevertheless, we have taken advantage of new ways of online communication to keep in touch, which led to the successful publication of three joint articles in high-ranked international journals. We are hopeful that we will return to regular research exchanges again in the second half of 2021.

2. Overview and significance of the research collaboration with Kumamoto University

The joint research work objective is to continue to perform frontier research of cellular structure designs on different length scales for their broader use in the next generation of engineering (lightweight structures, energy absorbers), medical (vascular stents and scaffolds), sports (cellular textiles, vibration mitigation) and other products. The collaborative research effort provides for significant advances in design, production technology, geometrical and mechanical characterization of new metamaterials with cellular structures at micro and subsequently nano-level shortly with the efficient application of theoretical, analytical, experimental, and computational research methods. The research focuses on developing new cellular metamaterials designs with specifically tailored (individualized) mechanical properties (stiffness, damping, energy absorption, etc.) by a careful combination of cell topology and morphology with efficient use of (multi)material combinations to achieve their best structural and functional performance in new products with advanced multifunctional properties. We adapt, upgrade, and propose new characterization methodologies using improved testing rigs supported by advanced computational capabilities and an AI-supported analysis system throughout the entire research process.

3. Comments or suggestions for IROAST/Kumamoto University

Perhaps a possibility to visit Kumamoto University through the IROAST visiting professorship

once every year would be an excellent opportunity to strengthen and expand the collaboration further.

4. Prospect for further research collaboration with Kumamoto University

Research groups at both partner institutions have significant and complementary experiences in fabrication, characterization and computer modelling of novel engineering materials. The cooperation contributes to the effective transfer of knowledge between the partner institutions. Since the undertaken research effort is scientifically and industrially significant for both partner institutions, it is safe to assume that future research collaboration will result in important scientific findings, published in high ranking reviewed scientific journals and possibly some new patents for industrial application.

5. Impressions of Kumamoto University/Kumamoto

Kumamoto University is a very friendly academic and research institution with great facilities and excellent professors and students. Many excellent specialist work at the Institute of Industrial Nanomaterials, covering the fields essential for developing and characterizing new metamaterials. The Institute also has at its disposal some excellent and unique research equipment, like the powder gun and 2 explosion pits together with the measuring equipment, which together enables quality observations of materials behaviour at very high strain rates.

List of Publication:

Novak, N., Vesenjak, M., Tanaka, S., Hokamoto, K., Ren, Z., "Compressive behaviour of chiral auxetic cellular structures at different strain rates," International Journal of Impact Engineering, 141, art. no. 103566, 2020. https://doi.org/10.1016/j.ijimpeng.2020.103566

Vesenjak M., Nishi M., Nishi T., Marumo Y., Krstulović-Opara L., Ren Z., Hokamoto K., "Fabrication and mechanical properties of rolled aluminium unidirectional cellular structure", Metals, 10, 6, 770, 1-12, 2020. https://doi.org/10.3390/met10060770

Borovinšek, M., Vesenjak, M., Hokamoto, K., Ren, Z., "An experimental and computational study of the high-velocity impact of low-density aluminum foam," Materials, 13 (8), art. no. 1949, 2020. https://doi.org/10.3390/ma13081949

Nishi M., Tanaka S., Vesenjak M., Ren Z., Hokamoto K., "Fabrication of composite unidirectional cellular metals by using explosive compaction", Metals, 10, 2, 193, 2020. https://doi.org/10.3390/met10020193

Nishi M., Tanaka S., Vesenjak M., Ren Z., Hokamoto K., "Experimental and computational analysis of the uni-directional porous (UniPore) copper mechanical response at high-velocity impact", International Journal of Impact Engineering, 136, 103409, 2020. https://doi.org/10.1016/j.ijimpeng.2019.103409

No.4-11	Advanced Structural Materials ~3D Printing of Bio-degradable Implant Components~		
Name	Shirley Shen		
Affiliation	CSIRO Manufacturing, Australia Email: Shirley.Shen@csiro.au	Title	Principal Research Scientist
Research Field	Nanomaterial Science		
Host Professor	Kazuki Takashima	Title	Professor
Affiliation	Faculty of Advanced Science and Technology Email: takashik@gpo.kumamoto-u.ac.jp		

1. Overview and significance of the research collaboration with Kumamoto University
Biodegradable metals, generally alloys of magnesium, calcium, and/or zinc, that exhibit both good initial strength and bio-resorption can be used as medical implants. These alloys, however, have low boiling point and high vapour pressure making it very challenging to fabricate using Additive Manufacturing, also known as 3D printing. A team of researchers from CSIRO Australia and Kumamoto University, Japan, with funding from FAJS, have successfully fabricated several magnesium alloys using Additive Manufacturing. This initial success will allow the researchers to take advantage of the design flexibility of Additive Manufacturing and print patient-specific and geometrically complex designs. The successful 3D printing of biodegradable magnesium alloys opens the way for widespread use of these alloys, minimising surgical intervention and patient trauma in case of a change in management plan or adverse clinical outcome. Elimination of second surgery also leads to significant cost savings and the availability of the operating theatres for more important patient care. The researchers are currently negotiating with commercial partners to take the technology for further development leading to commercialisation.
The active approaches and high-quality research ability at IROAST/Kumamoto University also facilitated greater achievements with planned publications and additional development projects between the two institutions in the pipeline.

2. Comments or suggestions for IROAST/Kumamoto University
I really appreciate what IROAST/Kumamoto University has been doing for our collaborations, particularly under the COVID-19 breakout challenges. We are keen to collaborate further with IROAST/Kumamoto University in the collaborated area as well as to explore broader and deeper collaborations in other research areas where both parties are interested in work together.

3. Prospect for further research collaboration with Kumamoto University
We are working together on publications planned to disseminate the results to the medical community. We are also discussing with potential partners for next stage of funding to develop the technology further.
We have attracted post-graduate students from universities in Melbourne to develop the technology further. Two new students have started working in the area since February 2021. It is expected that we will have some more students to work with us in the future, including students from Kumamoto University.

4. Impressions of Kumamoto University/Kumamoto

I have had an excellent impression of KU and Kumamoto and we are more than happy to visit KU in near future. If there is no COVID-19, my colleagues and I would have visited KU in March last year.

Through our FAJS project collaboration, we have deepened our relationships with IROAST/KU and impressed by the integrity of an open mind with a broad view, a creative imagination, the ability to solve problems, and the aptitude to communicate internationally.
I believe that KU will have educated many competent professionals and leaders of future societies. I do hope CSIRO and KU will continue our collaboration further, stronger and closer in the future.

No.4-12	Understanding the role of oceanic chemoattractants in marine animal navigation		
Name	Daniel P. Zitterbart		
Affiliation	Woods Hole Oceanographic Institution, USA / University of Erlangen-Nuremberg, Germany Email: dpz@whoi.edu	Title	Assistant Scientist / Lecturer
Research Field	Environmental Science		
Host Professor	Kei Toda	Title	Professor
Affiliation	Faculty of Advanced Science and Technology Email: todakei@kumamoto-u.ac.jp		

1. Research achievements

Dr. Zitterbart could not visit Kumamoto University in 2020 due to situation of COVID-19. However, we have had a great field survey in Antarctic in February. Dr. Zitterbart developed a new device to measure dimethyl sulfide (DMS) in seawater based on knowledge and technique he learned at Kumamoto University in 2019. The developed device was small and tough to conduct measurement on a rigid hull inflatable boat. He accepted a team member from Kumamoto University and doctor course student, Kentaro Saeki, joined the field measurement. We could demonstrate DMS measurement and whale observation in Antarctic. We will solve issues found in the first survey and prepare for the next expedition in Antarctic in 2022.


Joint field measurement of seawater chemicals and observation of whale behavior in Antarctic.

2. Overview and significance of the research collaboration with Kumamoto University

This is the international collaboration among USA, Japan, Germany and Sweden. World top researchers joined from the field of physical remote monitoring, chemical analysis, acoustical oceanography, and ocean animal behavior.

4. Prospect for further research collaboration with Kumamoto University

Dr. Zitterbart and Dr. Toda are actively working on extending the collaboration. This is expressed in jointly planned field experiments (up to 6 in the next 3 years) and in coordinated Research proposals across Japanese and US funding agencies to fund our field experiments. After initiation of a student exchange program, we plan to have concurrent PhD students in this research fields at both institutions.

Research Activities

5. Research Units

5. Research Units

No.	Unit Name	Unit Coordinator
5-1	**Development of Nano and Supramolecular Materials**	Shinya Hayami
5-2	**RNA Biology**	Tokio Tani
5-3	**Plant Cell and Developmental Biology**	Shinichiro Sawa
5-4	**Nano-Organics and Nano-Hybrids**	Makoto Takafuji
5-5	**Nano-medicine and Drug Delivery System**	Hamid Hosano
5-6	**Nano-medicine and Theranostics**	Takuro Niidome
5-7 5-8	**Medical Application of X-ray CT** **-Quantification of Three Dimensional Vascular Network** **-MicroCT-based Quantification of Fibrosis and Vascularization in Pancreatic Tumor**	Toshifumi Mukunoki
5-9	**Advanced Structural Materials**	Kazuki Takashima
5-10	**Microstructure Analysis and Grain Boundary Engineering**	Sadahiro Tsurekawa
5-11	**Structure and Dynamics of Materials Using Quantum Beams and Data-Driven Sciences**	Shinya Hosokawa
5-12	**Hydrological Environments**	Takahiro Hosono
5-13	**Quantitative Bioimaging**	Takumi Higaki
5-14	**Development of novel therapeutic strategy using iron targeted upconversion nanoparticles for Parkinson's disease**	Ruda Lee
5-15	**Deep Learning for Hydrology**	Kei Ishida
5-16	**Environmental Impacts of Ionic Solutes**	Shin-Ichi Ohira
5-17	**Radio Astronomy**	Keitaro Takahashi
5-18	**Plant Stem Cells and Regeneration**	Mitsuhiro Aida
5-19	**Development of microbially-aided carbon sequestration technology**	Atsushi Sainoki
5-20	**Advanced Biomedical Evaluation System**	Makiko Kobayashi
5-21	**Bio-inspired Functional Molecular System**	Yutaka Kuwahara
5-22	**Nanomaterials processing for medical, cosmetic, and environmental applications**	Mitsuru Sasaki

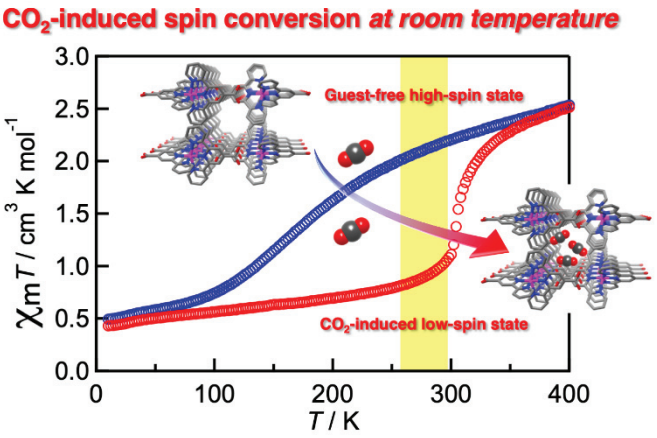
No. 5-1	Development of Nano and Supramolecular Materials		
Research Field	Nano Material Science		
Unit Coordinator			
Name	Shinya HAYAMI		
Affiliation	Faculty of Advanced Science and Technology Email: hayami@kumamoto-u.ac.jp	Title	Professor

Unit Members	
Name	Affiliation/Title
Shintaro IDA	Institute of Industrial Nanomaterials (IINa), Kumamoto University Professor
Jorge BELTRAMINI	Nanomaterials Centre (NANOMAC); Australian Institute for Bioengineering and Nanotechnology (AIBN), The University of Queensland, Australia Associate Professor-Senior Research Fellow
Yang KIM	Kosin University, Korea Professor, IROAST Visiting Professor
Rahul Raveendran NAIR	Materials Physics National GrapheneInstitute & School of Chemical Engineering and Analytical Science, The University of Manchester, UK Professor, IROAST Visiting Professor
Martino DI SERIO	University of Naples Federico II, Italy Professor, IROAST Visiting Professor
Masaaki NAKAMURA	Faculty of Advanced Science and Technology (FAST), Kumamoto University Associate Professor
Michio KOINUMA	Institute of Industrial Nanomaterials (IINa), Kumamoto University Associate Professor

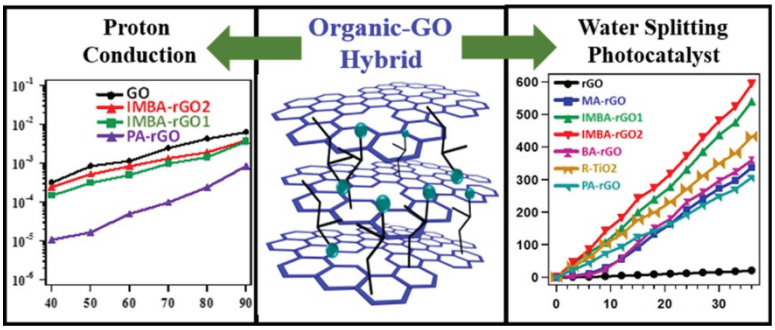
1. Overview of achievements

Graphene oxide (GO) has been considered as only a precursor for graphene but also one of the most promising materials because of its excellent properties such as photoluminescence, ferromagnetism, electrodes and water permeation. As it is now, it is said that GO has wider range of applications than graphene. GO has two important advantages: (1) it can be produced using inexpensive graphite as stating material by cost-effective chemical methods with a high yield, and (2) it is highly hydrophilic and can form stable aqueous colloids to facilitate the assembly of macroscopic structures by simple and cheap solution processes. These advantages indicate that GO can be easily applicate and scale up to industrial level. Therefore, it is important for industrial development to study GO. Recently, we focused on (i) gas adsorption material, (ii) photocatalyst, (iii) anti-corona by using GO nanosheet and its derivatives. Detail achievements are following.

(i) CO_2-responsive spin-state conversion between high-spin (HS) and low-spin (LS) states at room temperature was achieved in a monomeric cobalt(II) complex. A neutral cobalt(II) complex, $[Co^{II}(COO\text{-}terpy)_2]\cdot 4\,H_2O$ (**1**·**4 H₂O**), stably formed cavities generated via π–π stacking motifs and hydrogen bond networks, resulting in the accommodation of four water molecules. Crystalline **1**·**4 H₂O** transformed to solvent-free **1** without loss of porosity by heating to 420 K. Compound **1** exhibited a selective CO_2 adsorption via a gate-open type of the structural modification. Furthermore, the HS/LS transition temperature ($T_{1/2}$) was able to be tuned by the CO_2 pressure over a wide temperature range. Unlike **1** exhibits the HS state at 290 K, the CO_2-accomodated form **1**⊃**CO₂** (P_{CO2} =110 kPa) was stabilized in the LS state at 290 K, probably caused by a chemical pressure effect by CO_2 accommodation, which provides reversible spin-state conversion by introducing/evacuating CO_2 gas into/from **1**.



(ii) Multifunctionalities including the solid electrolytic property, electron conductivity (EnC), and photocatalytic water splitting (PWS) ability of organic-only hybrids obtained by intercalating short and branched-chain alkylamines including methylamine (MA), butylamine (BA), pentylamine (PA), and isomethylbytylamine (IMBA) in reduced graphene oxide (rGO) were reported. The alkylamine–rGO hybrids were synthesized by a facile solid-state reduction process. Within the series, IMBA–rGO exhibited high proton conductivity (PrC), EnC, and optimized PWS capacity. The PrC of IMBA–rGO was from 10^{-4} to 10^{-3} S cm^{-1}, which is only half an order less than that for pristine GO. The EnC was 1.25 μA/V. Though the PWS performances of MA–rGO, BA–rGO, and PA–rGO were comparatively lower, IMBA–rGO could generate about 1.5 times H_2 compared with that for R–TiO_2. The IR spectra indicate the association of IMBA and GO by chemical bonds. The Raman spectra show the transformation of GO's nonconductive sp^3 carbon sites into electron-conductive sp^2 carbon centers. The thermogravimetric analysis show improved water adsorbing capacity of IMBA–rGO, which resulted in higher PrC. Doping of the nitrogen atom at the graphitic sp^2 system was confirmed from the presence of pyrrolic N in X-ray photoelectron spectroscopy spectra. The resultant N-type semiconducting behavior is majorly responsible for the PWS process. The powder X-ray diffraction analysis indicates a more flexible interlayer space in IMBA–rGO, which facilitates both the reformation of hydrogen bonds during proton conduction and water dynamics during photocatalysis. The material indicates the possibility of devising graphene-based organic-only multifunctional hybrids.



(iii) Graphene oxide (GO) nanosheet has been focused on antiviral effect, and the effect on Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in Chinese, UK, and Brazilian has been investigated. SARS-CoV-2 was suppressed by 50% when the virus was incubated with GO for 1 minute, and 98% for 60 minutes in RT-PCR or plaque assay test. It is thought there are two process in this high anti SARS-CoV-2. The first is adsorption between GO and SARS-CoV-2

because GO surface has negative charge, and the spike of SARS-CoV-2 has positive charge. The second is oxidation in GO, and SARS-CoV-2 can be decomposed by GO. Furthermore, TEM images of SARS-CoV-2 was also observed on GO, and the image shows that SARS-CoV-2 was adsorbed on GO. The number of the spikes tend to decrease depending on incubation time. GO is carbon material, and can be easy to fabricate for fibers, non-woven cloths and so on. We should develop the GO mask and GO filter for SARS-CoV-2 as soon as possible, and it is thought that it can greatly contribute to the prevention of the spread of SARS-CoV-2 infection.

2. Presentations & Publications

1. P. Thuery, Y. Atoini, S. Kusumoto, S. Hayami, Y. Kim, J. Harrowfield, Optimizing Photoluminescence Quantum Yields in Uranyl Dicarboxylate Complexes: Further Investigations of 2,5-, 2,6- and 3,5-Pyridinedicarboxylates and 2,3-Pyrazinedicarboxylate, ***Eur. J. Inorg. Chem.***, 46, 4391-4400 (2020). DOI: 10.1002/ejic.202000803
2. M. Nakaya, R. Ohtani, S. Hayami, Guest Modulated Spin States of Metal Complex Assemblies, ***Eur. J. Inorg. Chem.***, 39, 3709-3719 (2020). DOI: 10.1002/ejic.202000553
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10. S. Ogo, T. Kishima, T. Yatabe, K. Miyazawa, R. Yamasaki, T. Matsumoto, T. Ando, M. Kikkawa, M. Isegawa, K. Yoon, S. Hayami, [NiFe],[FeFe],and [Fe] hydrogenase models from isomers, ***Sci. Adv.***, 6, eaaz8181 (2020). DOI: 10.1126/sciadv.aaz8181

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22. J. W. Shin, A. R. Jeong, J. H. Jeong, H. Zenno, S. Hayami, K. S. Min, Two-dimensional square-grid iron(II) coordination polymers showing anion-dependent spin crossover behavior, ***RSC Adv.***, 10, 5040-5049 (2020). DOI: 10.1039/c9ra09782a
23. S. Kusumoto, Y. Kim, M. Nakamura, L. F. Lindoy, S. Hayami, Ferromagnetically coupled hydroxo-bridged heptanuclear Ni(II) wheel cluster with S= 7 ground spin state, ***Chem. Lett.***, 49, 24-27 (2020). DOI: 10.1246/cl.190765

3. Application & acquisition status of KAKENHI and other external grants

I got KAKENHI Grant-in-Aid for Scientific Research (A) JP17H01200 for 2017-2021 and Grant-

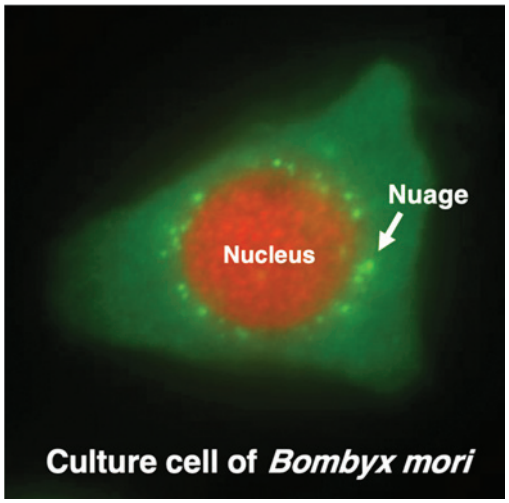
in-Aid for Challenging Exploratory Research 20K21213 for 2020-2021.
I have applied for Grant-in-Aid for Scientific Research on Innovative Areas.

4. Application & acquisition status of industrial property rights
I have not applied for PATENT in 2020.

No. 5-2	RNA Biology		
Research Field	Advanced Green Bio		
Unit Coordinator			
Name	Tokio TANI		
Affiliation	Faculty of Advanced Science and Technology Email: ttani@kumamoto-u.ac.jp	Title	Professor
Unit Members			
Name	Affiliation/Title		
Ramesh Shanmughom PILLAI	Department of Molecular Biology, University of Geneva, Switzerland Professor, IROAST Visiting Professor		
Takashi IDEUE	Faculty of Advanced Science and Technology (FAST), Kumamoto University Assistant Professor		

Details of activities

1. Overview of achievements



The scientific goal of the collaborative project with Prof. Ramesh Pillai is to understand how germline-specific RNA-protein granules called nuage are assembled in a cell. Nuage is non-membrane cytoplasmic electron-dense structure localized near nuclear membrane (a left picture). Nuage is a French word that means “cloud”, as the shape of Nuage is similar to a cloud in the sky under the microscopic observation. Nuage is implicated in the biogenesis of small RNAs called Piwi-interacting RNAs (piRNAs) involved in suppression of transposon induction in germline cells. Using the cultured germline cells established from silk worm *Bombyx mori*, we have screened for compounds that can either enhance or decrease nuage formation, and have identified Borrelidin that enlarged Nuage and NSC95397 that inhibit Nuage formation. In 2020, as the collaborative work with Prof. Pillai, we analyzed the action mechanisms of these compounds to understand the function of Nuage in piRNA biogenesis. As a result, we revealed that Borrelidin and NSC95397 are kinase and phosphatase inhibitors, respectively, and demonstrated that Nuage formation is regulated by phosphorylation of factors in Nuage. Also, Pillai’s laboratory has developed a systematic imaging-based screen for such Nuage-localizing signals (NuLS). Identification of NuLS peptides will allow the two studies to come together and synergize, as Ramesh group will be able to look for phosphorylation site motifs in the NuLS that might modulate its activity. Knowledge of the NuLS peptides might help us screen for putative kinase and phosphatase regulators of nuage formation. Thus, the collaboration between University of Geneva and Kumamoto University is critical for a complete success of this project.

For the smooth progress of the collaborative project, we did online discussion using the Zoom system several times. I think that discussion on the Zoom was nicely done. We will continue the collaborative project on Nuage formation and its function also in 2021. We are now preparing the manuscript on our collaborative work on Nuage inhibitors.

2. Presentations & publications
A paper on this project is now under preparation with Prof. Pillai.

3. Application & acquisition status of KAKENHI and other external grants
KAKENHI: Grant-in-Aid for Scientific Research (B) (3,200,000 yen)
Other external grants: HIGIN Gap Grant (3,000,000 yen)

4. Application & acquisition status of industrial property rights
(1) Application 19036AA08: Novel anti-bacterial agent
(2) Application 2020-067255: Novel fission yeast strain for shochu brewing
(3) Application 2021-11906: Novel Iridoido glycoside
(4) Acquisition Patent 6744926: Novel plant growth inhibitor Kumamonamide

No. 5-3	Plant Cell and Developmental Biology		
Research Field	Advanced Green Bio		
Unit Coordinator			
Name	Shinichiro SAWA		
Affiliation	Faculty of Advanced Science and Technology Email: sawa@kumamoto-u.ac.jp	Title	Professor
Unit Members			
Name	Affiliation/Title		
Olivier HAMANT	INRA, RDP, ENS Lyon, France Research Director, IROAST Visiting Professor		
Carolina ESCOBAR	Department of Environmental Sciences, School of Environmental Sciences and Biochemistry, University of Castilla La Mancha, Spain Professor, IROAST Visiting Professor		
Christian Siegfried HARDTKE	Department of Plant Molecular Biology, University of Lausanne, Switzerland Professor, IROAST Visiting Professor		
Mitsuhiro AIDA	IROAST Professor		
Takumi HIGAKI	IROAST Associate Professor		
Takashi ISHIDA	IROAST Assistant Professor		
Chihiro FURUMIZU	Faculty of Advanced Science and Technology (FAST), Kumamoto University Project Assistant Professor		
Yuki YOSHIDA	Faculty of Advanced Science and Technology (FAST), Kumamoto University Project Assistant Professor		
Hidehiko SUNOHARA	Faculty of Advanced Science and Technology (FAST), Kumamoto University Visiting Assistant Professor		

Details of activities

Please include the following points (1-4) regarding this project.

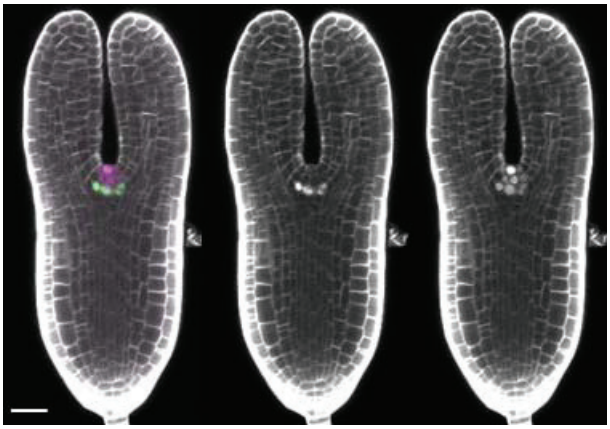
1. Overview of achievements

In this Research Unit, Plant Cell and Developmental Biology, we characterize the molecular and physical mechanisms that contribute to plant development and plant–parasitic nematodes interactions using genetic, biochemical, physiological approaches.

Olivier Hamant, a unit member, has analyzed mechanical stress of epidermal cell of Arabidopsis, together with Shinichiro Sawa and published a paper in Development. This international collaboration was performed in this Research Unit.

Takumi Higaki, a unit member, contributed to the work on the potential herbicide together with Shinichiro Sawa and we published the report in Scientific Reports. He analyzed the effects of the drug on cytoskeleton rearrangement and cell viability using microscopic image analysis.

Mitsuhiro Aida, together with Shinichiro Sawa and Takashi Ishida, analyzed mechanisms regulating shoot meristem formation during plant embryogenesis and established a protocol suitable for capturing high-quality confocal images of *Arabidopsis thaliana* embryos.



2. Presentations & Publications

Proveda, J., Abril-Urias, P., Escobar, C. (2020) Biological Control of Plant-Parasitic Nematodes by Filamentous Fungi Inducers of Resistance: Trichoderma, Mycorrhizal and Endophytic Fungi. Frontiers in Microbiology. 11. doi: 10.3389/fmicb.2020.00992

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Maeda K, Higaki T (2021) Disruption of actin filaments delays accumulation of cell plate membranes after chromosome separation. Plant Sig Behav 16: 1873586.

Higaki T, Akita K, Katoh K (2020) Coefficient of variation as an image-intensity metric for cytoskeleton bundling. Sci Rep 10: 22187.

Lu YJ, Li P, Shimono M, Corrion A, Higaki T, He SY, Day B (2020) Arabidopsis calcium-dependent protein kinase 3 regulates actin cytoskeleton organization and immunity. Nat Commun 11:6234.

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Higaki T, Akita K, Hasezawa S (2020) Elevated CO_2 promotes satellite stomata production in young cotyledons of *Arabidopsis thaliana*. Genes Cells 25: 475-482.

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Yuan, N., Furumizu, C., Zhang, B., and Sawa, S. (2021) Database mining of plant peptide homologues. Plant Biotech. In Press.

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Imoto, A., Yamada, M., Sakamoto, T., Okuyama, A., Ishida, T., Sawa, S., and Aida, M. (2021) A ClearSee-based clearing protocol for 3D visualization of Arabidopsis tahaliana embryos. Plants. 10, 190; https://doi.org/10.3390/plants10020190

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メ科）の DNA シーケンスによる種同定, Botany, 70, 8-10.

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Suetsugu K., Kaida, S., Fukunaga, H., and Sawa, S. (2020). A New Form of the Mycoheterotrophic Plant Lecanorchis japonica (Orchidaceae) from Japan. 71, 243-248. doi: 10.18942/apg.201924

Sawa, S., Sato, M. H., and Favery, B. (2020). Developmental Modification under Biotic Interactions in Plants. Frontiers in Plant Science. doi: 10.3389/fpls.2020.619804

Furumizu, C., and Sawa, S. (2021) Insight into early diversification of leucine-rich repeat receptor-like kinases provided by the sequenced moss and hornwort genomes. Plant Mol. Biol. https://doi.org/10.1007/s11103-020-01100-0

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Nakai, R., Azuma, T., Nakaso, Y., Sawa, S., and Demura, T. (2020) Development of a dynamic imaging method for gravitropism in pea sprouts using clinical magnetic resonance imaging system. Plant Biotech. 37. 437-442.

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岡本竜弥、相田光宏、石川勇人、澤進一郎 (2020) 熊本におけるアイラトビカズラ（マメ科）の DNA シーケンスによる種同定, Botany, 70, 8-10.

Hirakawa, Y., Fujimoto, T., Ishida, S., Uchida, N., Sawa, S., Kiyosue, T., Ishizaki, K., Nishihama, R., Kohchi, T., and Bowman, J.L., (2020). Induction of multichotomous branching by CLAVATA peptide in Marchantia polymorpha. Curr. Biol. 30, 3833-3840.

佐古隆太朗，澤進一郎，古水千尋，神野伊策，肥田博隆 (2020) ポアメンブレンを用いた植物寄生性線虫の化学走性分析デバイス.第37回センサ・マイクロマシンと応用システム（センサ・マイクロマシン部門大会）2020年10月26-28日、熊本

Tsai, A, Y-L., Oota, M., and Sawa, S. (2020) Chemotactic host-finding strategies of plant endoparasites and endophytes. Frontiers in Plant Science. https://doi.org/10.3389/fpls.2020.01167

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3. Application & acquisition status of KAKENHI and other external grants

Mitsuhiro Aida, Grant-in-Aid for Scientific Research on Innovative Areas (The Japan Society for the Promotion of Science), Principles of pluripotent stem cells underlying plant vitality, Establishment of plant hormone microenvironment during shoot stem cell formation, April 2020-March 2022.

Takumi Higaki, Grant-in-Aid for Scientific Research (B) (The Japan Society for the Promotion of Science), "Multi-dimensional bioimage analyses with machine learning to reveal the dynamics of membrane vesicles and microtubules in stomatal guard cells," April 2020-March 2023.

Takumi Higaki, Grant-in-Aid for Scientific Research on Innovative Areas (The Japan Society for the Promotion of Science), Elucidation of the strategies of mechanical optimization in plants toward the establishment of the bases for sustainable structure system, "Imaging analysis on cell geometry during mechanical optimization in leaves," June 2018-March 2023.

Takumi Higaki, Grant-in-Aid for Scientific Research on Innovative Areas (The Japan Society for the Promotion of Science), Platforms for Advanced Technologies and Research Resources "Advanced Bioimaging Support," "Consultation and technical support for bioimage analysis," April 2018-March 2022.

Shinichiro Sawa, Grant-in-Aid for Scientific Research on Innovative Areas (The Japan Society for the Promotion of Science), Elucidation of the strategies of mechanical optimization in plants toward the establishment of the bases for sustainable structure system, June 2018-March 2023.

Shinichiro Sawa, Grant-in-Aid for Scientific Research on Innovative Areas (Research in a proposed research area), April 2018-March 2023.

Shinichiro Sawa, Grant-in-Aid for Scientific Research on Innovative Arias (A), April 2020-March 2025.

Shinichiro Sawa, Grant-in-Aid for Fostering Joint International Research（B）, October 2020-March 2024.

4. Application & acquisition status of industrial property rights
Patent application number; 2021-024793
Title of invention; Plant parasitic nematode control agent.
Application day; 2013/2/29
Patent applicant; Kumamoto University
Inventors; Shinichiro Sawa, Hidehiko Sunohara, Yutaka Sato, and Kazuyuki Doi.

No. 5-4	Nano-Organics and Nano-Hybrids		
Research Field	Nano Material Science, Green Energy, Next-generation Technology		
Unit Coordinator			
Name	Makoto TAKAFUJI		
Affiliation	Faculty of Advanced Science and Technology Email: takafuji@kumamoto-u.ac.jp	Title	Professor

Unit Members	
Name	Affiliation/Title
Tetsuya KIDA	Faculty of Advanced Science and Technology (FAST), Kumamoto University Professor
Armando T. QUITAIN	Center for International Education, Kumamoto University Professor
Yutaka KUWAHARA	Faculty of Advanced Science and Technology (FAST), Kumamoto University Assistant Professor
Hirotaka IHARA	Faculty of Advanced Science and Technology (FAST), Kumamoto University Visiting Professor / National Institute of Technology, Okinawa College President
Reiko ODA	CNRS, Université de Bordeaux, France Research Director *IROAST Visiting Professor*
Josep-Lluis BARONA-VILAR	Instituto de Historia de la Medicina y de la Ciencia López Piñero (IHMC) Universidad de Valencia, Spain Professor *IROAST Visiting Professor*
Zhenghe XU	College of Engineering, Southern University of Science and Technology, China Dean / Department of Chemical and Materials Engineering, University of Alberta, Canada Teck Professor *IROAST Visiting Professor*
Etsuko FUJITA	Chemistry Division, Brookhaven National Laboratory, USA Senior Chemist *IROAST Visiting Professor*
Maria Jose COCERO	Chemical Engineering & Environmental Technology, Universidad de Valladolid, Spain Professor *IROAST Visiting Professor*

Details of activities

1. Overview of achievements

1-1. Enhancement of International Collaboration with University of Bordeaux, France

The second term of joint research project of University of Bordeaux (UB) with Kumamoto University (KU) and Kyoto University since 2015, which has been called as Laboratoire international associé (LIA) - “Chiral Nanostructures for Photonic Applications” (CNPA) approved as by Agence Nationale de la Recherche (ANR), France, is proceeding. In this project, Prof. Ihara and Dr. Oda (Visiting Professor of IROAST) are co-PIs in Japan and French sides, respectively, and Prof. Takafuji and Dr. Kuwahara have associated as core members. In 2020, Japanese and French members could not visit each other because of COVID-19 pandemic.

The joint KAKEN research project with Dr. Oda of Grants-in-Aid for Fostering Joint International Research (B) funded by JSPS since 2017 has continued. In this project, Prof. Takafuji and Prof. Ihara are a PI and a core member, respectively, of Japan side.

The project with Dr. Y. Ferrand and Dr. C. Olivier, who are the LIA members of the French side is ongoing from 2018. We received mixed compounds from the French side and send back essential compounds purified by our special technique.

The four joint papers have been published with researchers of UB in international journals in 2020.

1-2. Maintaining International Collaboration with Universitat de València, Spain

Japanese and Spanish members could not alternately visit this year.

1-3. Enhancement of International Collaboration with University of Valladolid, Spain

Due to coronavirus-related pandemic, mobility of researchers and students was not possible this academic year. However, the following research-related and academic activities were carried out with Valladolid University:

① Mobility of an alumnus from Kumamoto University, Dr. Elaine G. Mission, under the Marie-Curie Individual Fellowship Program (Research Title: "Cascade Hydrolytic Recovery and Conversion of Suberin in High Pressure Media."). She was a doctoral student under the supervision of Prof. T Kida and Prof. AT Quitain. She will carry out research related to biomass utilization using microwave and supercritical fluid technologies in Valladolid University for 2 years starting October 2020.

② Online lecture by Prof. MJ Cocero in the Global Team Teaching subject on “Perspectives on Biomass Utilization”, being offered at the Center for International Education and participated by a total of about 180 undergraduate students from Kumamoto University and Sepuluh Nopember Institute of Technology (ITS, Indonesia).

③ Publication of a joint article in reputable journal in this field: “Supercritical CO_2-subcritical H_2O system: A green reactive separation medium for selective conversion of glucose to 5-hydroxymethylfurfural” that consolidates previous research outcomes of Prof. AT Quitain and his students in Valladolid University.

1-4. Maintaining International Collaboration with University of Geneva, Switzerland

Japanese and Swiss members could not alternately visit this year.

1-5. Maintaining International Collaboration with Brookhaven National Laboratory, USA

Japanese and American members could not alternately visit this year.

1-6. Maintaining International Collaboration with University of Connecticut, USA

Japanese and American members could not alternately visit this year. Dr. Kuwahara had several discussions about our recent research results with Prof. Mani (Visiting Associate Professor of IROAST) online.

1-7. Enhancement of International Collaboration with Lanzhou Institute of Chemical Physics, Chinese Academy of Sciences, China

After the Bilateral Joint Research Project of JSPS, we have continued the collaboration with Prof. H. Qiu’s group of Lanzhou Institute of Chemical Physics (LICP), Chinese Academy of Sciences (CAS), China. Prof. Ihara has been selected as a President's International Fellowship Initiative Visiting Scientist from Chinese Academy of Sciences from 2019, associated with this collaboration with the LICP. However, Japanese and Chinese members could not alternately visit this year. The two joint papers have been published with researchers of the LICP, CAS, in international journals in 2020.

1-8. Maintaining International Collaboration with Beijing University of Chemical Technology

Japanese and Chinese members could not alternately visit this year.

1-9. Enhancement of International Collaboration with University of Dhaka, Bangladesh

Japanese and Bangladeshi members could not alternately visit this year. Prof. Takafuji and Prof. Ihara discussed with Dr. Shahruzzaman, Prof. Rahman and other collaborators, the University of Dhaka (UD), about the joint research project by e-mails.

The two joint papers have been published with researchers of UD in international journals in 2020.

1-10. Maintaining International Collaboration with Noakhali Science and Technology University, Bangladesh

Japanese and Bangladeshi members could not alternately visit this year.

1-11. Maintaining International Collaboration with Baku State University, Azerbaijan

Japanese and Azerbaijani members could not alternately visit this year.

1-12. Enhancement of International Collaboration with Kyrgyz-Turkish Manas University, Kirgiz

Japanese and Kirgiz members could not alternately visit this year. The collaboration with the Kyrgyz-Turkish Manas University (KTMU) have started from 2020. The researcher, who participated the Sakura Science Plan (A) supported by JST from the KTMU in 2019, was selected the Matsumae International Foundation in 2020. However, the visiting plan to our group using the foundation have been postponed due to the COVID-19.

1-13. Establishment of International Collaboration with Vytautas Magnus University, Lithuania

The Bilateral Joint Research Project of JSPS with Lithuania conducted by Prof. Ihara has been selected this year. The collaboration with Prof. A. S. Maruska, Vytautas Magnus University, for two year will start from next year, 2021. We believe that the invitation as an invited speaker in the 4th IROAST symposium at KU held in January 2019 could contributed the grant selection.

2. Presentations & Publications

2-1. Polymer encapsulation and stabilization of molecular gel-based chiroptical information for strong, tunable circularly polarized luminescence film.
Journal of Materials Chemistry C, Vol.8, pp.8732-8735, 2020.
H. Oishi, S. Mashima, **Y. Kuwahara**, **M. Takafuji**, K. Yoshida, **R. Oda**, H. Qiu, **H. Ihara**

2-2. Extreme enhancement of secondary chirality through coordination-driven steric changes of terpyridyl ligand in glutamide-based molecular gels.
RSC Advances, Vol.10, pp. 29627-29632, 2020.
M. Takafuji, T. Kawahara, N. Sultana, N. Ryu, K. Yoshida, **Y. Kuwahara**, **R. Oda**, **H. Ihara**

2-3. Chirality induction on non-chiral dye-linked polysilsesquioxane in nanohelical structures.
Chemical Communications, Vol.56, pp.7241-7244, 2020.
N. Ryu, T. Kawaguchi, H. Yanagita, Y. Okazaki, T. Buffeteau, K. Yoshida, T. Shirosaki, S. Nagaoka, **M. Takafuji**, **H. Ihara**, **R. Oda**

2-4. Fabrication of carbon-like, π-conjugated organic layer on a nano-porous silica surface.
Nanomaterials, Vol. 10, 1882, 2020.
H. Noguchi, M. Sultana, N. Hano, **Y. Kuwahara**, **M. Takafuji**, S. Nagaoka, H. Qiu, **H. Ihara**

2-5. Multi-chiro-informative system created by a porphyrin-functionalized chiral molecular assembly.
Chemistry Letters, Vol.49, pp.368-371, 2020.
S. Mashima, N. Ryu, **Y. Kuwahara**, **M. Takafuji**, H. Jintoku, **R. Oda**, **H. Ihara**

2-6. Calcium ion mediated rapid wound healing by nano-ZnO doped calcium phosphate-chitosan-alginate biocomposites.
Materialia, Vol. 13, 100839, 2020.
M. A. Rahman, M. S. Islam, P. Haque, M. N Khan, **M. Takafuji**, M. Begum, G. W. Chowdhury, M. Khan, M. M. Rahman

2-7. Preparation of novel chitosan/poly (ethylene glycol)/ZnO bionanocomposite for wound healing application: Effect of gentamicin loading.
Materialia, Vol. 12, 100785, 2020.
R. A. Masud, M. S. Islam, P. Haque, M. N. I. Khan, M. Shahruzzaman, M. Khan, **M. Takafuji**, M. M. Rahman

2-8. Spherical filler-promoting thermally conductive pathway in graphite-containing polymer composites for high heat radiation.

Journal of Polymer Science, Vol.58, pp.607-615, 2020.
M. Takafuji, N. Kawamoto, N. Hano, K. Sasahara, S. Nagaoka, **H. Ihara**

2-9. Supercritical CO_2–subcritical H_2O system: A green reactive separation medium for selective conversion of glucose to 5-hydroxymethylfurfural.
Journal of Supercritical Fluids, Vol 168, 105079-105090, 2021.
R. Inoue, JKC N. Agutaya, **A. T. Quitain**, M. Sasaki, **M. J. Cocero, T. Kida**

2-10. Metal-Free Synthesis of HMF from Glucose Using the Supercritical CO2–Subcritical H2O–Isopropanol System.
Ind. Eng. Chem. Res., Vol 59, 16527-16538, 2020.
J. K. C. N. Agutaya, R. Inoue, S. S. V. Tsie, **A. T. Quitain**, J. de la Peña-García, H. Perez-Sanchez, M. Sasaki, **T. Kida**

2-11. Synergizing Sulfonated Hydrothermal Carbon and Microwave Irradiation for Intensified Esterification Reaction,
ACS Omega**,** 5, 23542-23548 (2020).
L. Tumkot, **A. T. Quitain**, P. Boonnoun, N. Laosiripojana, **T. Kida,** A. Shotipruk

2-12. Green synthesis of sulfonated organosilane functionalized multiwalled carbon nanotubes and its catalytic activity for one-pot conversion of high free fatty acid seed oil to biodiesel,
Journal of Cleaner Production, Vol 275, 123146, 2020
MC Macawile, **AT Quitain, T Kida**, R Tan, J Auresenia

3. Application & acquisition status of KAKENHI and other external grants

3-1. FY 2017 - 2021: KAKEN, Fund for the Promotion of Joint International Research (Fostering Joint International Research (B)), JSPS, PI: **M. Takafuji**, Co-PI: **H. Ihara,** N. Ryu, 13,800,000 yen.

3-2. FY 2020 - 2022: KAKEN, Grant-in-Aid for Scientific Research (B), JSPS, PI: **H. Ihara**, Co-PI: **M. Takafuji**, S. Nagaoka, 13,700,000 yen.

3-3. FY 2020 - 2022: KAKEN, Grant-in-Aid for Challenging Research (Exploratory), JSPS, PI: **H. Ihara**, Co-PI: **Y. Kuwahara**, S. Nagaoka, 5,000,000 yen.

3-4. FY 2020 - 2022: KAKEN, Grant-in-Aid for Scientific Research (C), JSPS, PI: **Y. Kuwahara**, Co-PI: **H. Ihara**, N. Ryu, 3,300,000 yen.

3-5. FY 2019 - 2021: KAKEN, Grant-in-Aid for Scientific Research (C), JSPS, PI: T. Shirosaki, Co-PI: **M. Takafuji,** N. Ryu, 3,500,000 yen.

3-6. FY 2020 - 2022: KAKEN, Grant-in-Aid for Scientific Research (C), JSPS, PI: N. Ryu, Co-PI: **M. Takafuji**, 3,400,000 yen.

3-7. FY 2020 - 2022: KAKEN, Grant-in-Aid for Scientific Research (C), JSPS, PI: K. Nishiyama, Co-PI: **M. Takafuji**, S. Yoshimoto, 3,400,000 yen.

3-8. FY 2018 - 2020: Open Partnership Joint Research Projects with Spain, JSPS, PI: **M. Takafuji**, 5,000,000 yen.

3-9. FY 2020 - 2021: Bilateral Joint Research Projects with Lithuania, JSPS, PI: **H. Ihara**, 5,000,000 yen.

3-10. FY 2018 - 2020: KAKEN Grant-in-Aid for Scientific Research (C), JSPS, PI: **A. T. Quitain**, 3,400,000 yen.

3-11. FY 2018 - 2021: KAKEN Fund for the Promotion of Joint International Research, Fostering Joint International Research, JSPS, PI: **A. T. Quitain**, 11,700,000 yen.

3-12. FY 2019 - 2020: KAKEN Grant-in-Aid for Scientific Research (Exploratory Research), JSPS, PI: **T. Kida**, 5,000,000 yen.

3-13. FY 2019 - 2021: Open Partnership Joint Research Projects with Malaysia, JSPS, PI: **A. Quitain**, 4,000,000 yen.

3-14. FY 2019 - 2021: e-ASIA Joint Research Project with Thai, Indonesia, Philippines, Malaysia, Vietnam and Myanmar, JST, PI: **A. Quitain**, Co-I: **T. Kida**, 27,000,000 yen

4. Application & acquisition status of industrial property rights

4-1. Patent Acquisition: Malaysian Patent Office
Patent Number: MY-178358-A
Date of Grant/Publication: 9 October 2020
Title: Natural Low Transition Temperature Mixtures (LTTMs) and Processes for Making the Same
Inventors: Suzana Yusup, Yoshimitsu Uemura, **Armando T. Quitain**, Mitsuru Sasaki, **Tetsuya Kida**, Yiin Chung Loong

No. 5-5	Nano-medicine and Drug Delivery System		
Research Field	Nano Material Science, Advanced Green Bio		
Unit Coordinator			
Name	Hamid HOSANO		
Affiliation	Institute of Industrial Nanomaterials Email: hamid@kumamoto-u.ac.jp	Title	Professor

Unit Members	
Name	Affiliation/Title
Nushin HOSANO	Biomaterials and Bioelectrics Division, Institute of Industrial Nanomaterials Visiting Associate Professor
Konstantinos KONTIS	School of Engineering, University of Glasgow, UK / IROAST Professor/ Dean for Global Engagement-East Asia & China / Distinguished Professor
Firus ZARE	The University of Queensland, Australia Professor/ Discipline Leader of Power of Energy and Control Engineering / IEEE Fellow / IROAST Visiting Professor
Viren Ivor MENEZES	Department of Aerospace Engineering, Indian Institute of Technology Bombay, India Professor/ IROAST Visiting Professor
Hamid GHANDEHARI	Director of Utah Center for Nanomedicine/ Chair of Department of Pharmaceutics and Pharmaceutical Chemistry and Bioengineering, University of Utah, USA Professor/ IROAST Visiting Professor
Amir A. FARAJIAN	Department of Mechanical and Materials Engineering, Wright State University, USA Professor/ IROAST Visiting Professor

Details of activities

We have been studying the use of physical delivery of drug or reprogramming factors into the cells and tissue, as a safe and reliable method. We have also been exploring integrated diagnostic and therapeutic (theranostics) modalities/nanoparticles/agents, as a unique approach in nanomedicine. The research has potential to be used in a wide range of medical applications.
Our physical delivery approaches are based on applying electrical/mechanical stresses to the cells. In this respect, attention has been made to understand biophysical reactions to reversibly manipulate the cells by the external stress. We have been investigating promising physical delivery methods including: electroporation with nanosecond pulsed electric fields, needle-free painless microinjection, micro/nano-particle carrier laser-biolistic delivery, sonoporation with microfluidics, and shock waves; which are shown to be appropriate for clinical applications.

During year 2020, due to travel and other restrictions brought by the COVID-19 pandemic, we could not have presence of our Visiting Professors in Kumamoto University.
The Research Unit has welcomed two distinguished scientists as IROAST Visiting Professors, Prof. Stelios Rigopoulos, from Department of Mechanical Engineering, Imperial College London, UK; and Prof. Pouyan Boukany, from Delft University of Technology, Netherlands. Their presence will promote our projects and will help the Research Unit to further achieve its goals.

Joint publication with Prof. Menezes's group:

M. Thorat, S. Sahu, V. Menezes, A. Gokhale, H. Hosano, Shock loading of closed cell aluminum foams in the presence of an air cavity, Applied Sciences, 10(12), 4128, June 2020
DOI: 10.3390/app10124128

Joint publication with Internship student from the University of Queensland (Prof. Zare's group):

F. Zare, N. Ghasemi, N. Bansal, G. Abhishek, H. Hosano, Increasing the production yield of white oyster mushrooms with pulsed electric fields, IEEE Trans. Plasma Science, 49(2), 805-812, February 2021
DOI: 10.1109/TPS.2021.3053071

Other publications:

M. Sato, T. Sakugawa, T. Yamashita, N. Hosano, H. Hosano, Effects of Voltage and Current Waveforms on Pulse Discharge Energy Transfer to Underwater Shock Waves for Medical Applications, IEEE Trans. Plasma Science, 48(7): 2639 – 2645, July 2020
DOI: 10.1109/TPS.2020.2992638

Z. Yang ; H. Cao ; J. Hao ; H. Hosano ; S. Katsuki ; H. Akiyama ; C. Zhang, Post-breakdown dielectric recovery characteristics of water for high-repetition-rate switch, IEEE Transactions on Dielectrics and Electrical Insulation 27(3):909-914, June 2020
DOI: 10.1109/TDEI.2020.008507

No. 5-6	Nano-medicine and Theranostics		
Research Field	Nano Material Science		
Unit Coordinator			
Name	Takuro NIIDOME		
Affiliation	Faculty of Advanced Science and Technology Email: niidome@gpo.kumamoto-u.ac.jp	Title	Professor
Unit Members			
Name	Affiliation/Title		
Ick Chan KWON	Biomedical Research Institute, Korea Institute of Science and Technology (KIST), Korea/ Dana Faber Cancer Center, Harvard Medical School, USA Principal Research Scientist / Presidential Scholar IROAST Visiting Professor		
Ruda LEE	IROAST Associate Professor		
Keiichi MOTOYAMA	Faculty of Life Sciences, Kumamoto University Associate Professor		
Taishi HIGASHI	Priority Organization for Innovation and Excellence (POIE), Kumamoto University Associate Professor		

Details of activities

1. Overview of achievements

In the last decades, the development of nanocarriers for the efficient delivery of drugs offers a wide range of biotechnology applications. Due to the advantage of the size, nanomaterials have been shown to be robust drug delivery systems and may be useful for encapsulating drugs and enabling more precise targeting with a controlled release by various external stimulation (ex. pH, ROS, Temperature and so on). Nanomedicine has revolutionized existing cancer therapies through the improvement of pharmacological kinetics and dynamics. As well as, image-guided drug delivery can be used for various different purposes, ranging from simple and straightforward biodistribution studies to extensive and elaborate experimental setups aiming to enable “personalized medicine”, and to improve the efficacy of combined modality anticancer therapy. Despite the enormous progress in the field of nanotherapeutics, the use of artificially synthesized nanocarriers still faces several challenges, including rapid clearance from blood circulation, off-target effects, and ineffective nanoparticles (NPs) transfer in patients with advanced forms of cancer. Furthermore, NPs will encounter multiple physiological barriers that influence their effectiveness, such as blood circulation, NPs-protein interaction, extravasation into tumor tissue or the tumor microenvironment (TME), phagocytic sequestration, and renal clearance.

This research unit focus on the development of diagnosis and drug delivery smart nanomaterial system for overcoming challenges. The research unit’s interdisciplinary research collaboration with engineer, pharmacist, and clinician can improve a deeper knowledge and understanding of

the real interactions involved in the diseased tissues is fundamental for the development of novel therapeutic approaches.

2. Presentations & Publications

Takuro NIIDOME

[Presentations]

1. A. Harada, H. Tsutsuki, T. Zhang, R. Lee, K. Yahiro, T. Sawa, T. Niidome, Delivery of an Anti-inflammatory Bacterial Toxin to Macrophages Using Biodegradable PLGA-Nanoparticles, Society for Biomaterials, The 15th International Student Conference on Advanced Science and Technology（ICAST 2020 Kumamoto, Dec 3-4 (2020), Kumamoto, Japan (Online)
2. R. Yamashita, T. Niidome, Controlled drug release from gold nanorods-encapsulated PLGA nanoparticles responding to NIR irradiation, 11th World Biomaterials Congress, Dec 11-15 (2020), Scotland, UK (Online)
3. W. Xu, K. Yuki, S. Makoto, T. Niidome, Improved efficacy of Mg stents in sirolimus-eluting and corrosion resistance through polymer coating, 11th World Biomaterials Congress, Dec 11-15 (2020), Scotland, UK (Online)
4. T. Niidome, Surface coating of bioresorbable coronary stents and their corrosion behaviors, 4th KAIST-KU workshop and joint symposium, Feb 22 (2021), Kumamoto, Japan (Online)

[Publications]

1. Y. Xiao, W. Xu, Y. Komohara, Y. Fujiwara, H. Hirose, S. Futaki, T. Niidome, Effect of surface modifications on cellular uptake of gold nanorods in human primary cells and established cell lines, *ACS Omega,* **5**, 32744-32752 (2020)
2. S. Ueno, M. W. Kim, G. Lee, Y. I. Park, T. Niidome, R. Lee, Development of ErbB2-targeting liposomes for enhancing drug delivery to ErbB2-positive breast cancer, *Pharmaceutics,* **12**, 585 (2020)
3. T. Taharabaru, R. Yokoyama, T. Higashi, A. F. A. Mohammed, M. Inoue, Y. Maeda, T. Niidome, R. Onodera, K. Motoyama, Genome editing in a wide area of brain using dendrimer-based ternary polyplex of Cas9 ribonucleoprotein, *ACS Appl. Mater. Interfaces*, **12**, 21386–21397 (2020)
4. H. Tsutsuki, T. Zhang, A. Harada, A. Rahman, K. Ono, K. Yahiro, T. Niidome, T. Sawa, Involvement of protein disulfide isomerase in Subtilase cytotoxin-induced cell death in HeLa cells, *Biochem. Biophys. Res. Co.*, **525**, 1068-1073 (2020)
5. M. W. Kim, G. Lee, T. Niidome, Y. Komohara, R. Lee, Y. I. Park, Platelet-like gold nanostars for cancer therapy: the ability to treat cancer and evade immune reactions, *Front. Bioeng. Biotechnol.,* **8**, 133 (2020)
6. A. Harada, H. Tsutsuki, T. Zhang, R. Lee, K. Yahiro, T. Sawa, T. Niidome, Preparation of biodegradable PLGA-nanoparticles used for pH-sensitive intracellular delivery of an anti-inflammatory bacterial toxin to macrophages, *Chem. Pharm. Bull.*, **68**, 363–368 (2020)
7. W. Xu, K. Yagoshi, T. Asakura, M. Sasaki, T. Niidome, Silk fibroin as a coating polymer for sirolimus-eluting magnesium alloy stents, *ACS Applied Bio Materials,* **3**, 531-538 (2020)
8. W. Xu, K. Sato, Y. Koga, M. Sasaki, T. Niidome, Corrosion resistance of HF-treated Mg alloy stent following balloon expansion and its improvement through biodegradable polymer coating, *J. Coat. Technol. Res.* **17**, 1023-1032 (2020)

Ruda LEE

[Presentations]

1. Ueno Sho, Takuro Niidome, Ruda Lee. Development of ErB2-targeting Liposomes for Enhancing Delivery to ErbB2- positive Breast cancer. The 15th International Student Conference on Advanced Science and Technology（ICAST 2020 Kumamoto, Dec 3-4 (2020), Kumamoto, Japan (Online)
2. Seung-Hae Kwon, Ji Hoon Kim, Jung Hoon Choi, Ruda Lee. Non-invasive early detection of calpain 2-enriched non-small cell lung cancer using a human serum albumin-based calpain-2 nanosensor. 7th International Conference on Bio-Sensing Technology, Busan, Korea (Online)

[Publications]

1. Yong Il Park, Seung-Hae Kwon, Gibok Lee, Keiichi Motoyama, Min Woo Kim, Min Lin, Takuro Niidome, Jung Hoon Choi, Ruda Lee*. pH-sensitive multi-drug liposomes targeting folate receptor β for efficient treatment of non-small cell lung cancer. *Journal of Controlled Release*, 330, 1-14, February 2021.
2. Sho Ueno, Min Woo Kim, Gibok Lee, Yong Il Park, Takuro Niidome, and Ruda Lee*. Development of ErbB2-Targeting Liposomes for Enhancing Drug Delivery to ErbB2-Positive Breast Cancer. Pharmaceutics, 12, 585, June 2020.
3. Song Yeul Lee*, Ruda Lee*, Eunha Kim, Sanghee Lee and Yong Il Park. Near-Infrared Light-Triggered Photodynamic Therapy and Apoptosis Using Upconversion Nanoparticles with Dual Photosensitizers. Frontiers in Bioengineering and Biotechnology, 8, 275. Apr 2020.
4. Seung-Hae Kwon, Taemin Wi, Yong Il Park, Min Woo Kim, Gibok Lee, Takumi Higaki, Jung Hoon Choi*, and Ruda Lee*. Noninvasive Early Detection of Calpain 2-Enriched Non-Small Cell Lung Cancer Using a Human Serum Albumin-Bounded Calpain 2 Nanosensor. Bioconjugate Chemistry, 31, 3, 803-812, Mar 2020.
5. Min Woo Kim, Gibok Lee, Takuro Niidome, Yoshihiro Komohara, Ruda Lee* and Yong Il Park*. Platelet-Like Gold Nanostars for Cancer Therapy: The Ability to Treat Cancer and Evade Immune Reactions. Frontiers in Bioengineering and Biotechnology, 8, 133. Feb 2020.
6. Sofiane Hamidi, Yukiko Nakaya, Hiroki Nagai, Cantas Alev, Takeya Kasukawa, Sapna Chhabra, Ruda Lee, Hitoshi Niwa, Aryeh Warmflash, Tatsuo Shibata, Guojun Sheng. Mesenchymal-epithelial transition regulates initiation of pluripotency exit before gastrulation. Development, 147, dev184960. Feb 2020.
7. Ruda Lee, Yu Jin Choi, Myeong Seon Jeong, Yong Il Park, Keiichi Motoyama, Min Woo Kim, Seung-Hae Kwon*, and Jung Hoon Choi*. Hyaluronic Acid-Decorated Glycol Chitosan Nanoparticles for pH-Sensitive Controlled Release of Doxorubicin and Celecoxib in Nonsmall Cell Lung Cancer. Bioconjugate Chemistry, 31, 3, 923-932, Feb 2020.
8. Ayaka Harada, Hiroyasu Tsutsuki, Tianli Zhang, Ruda Lee, Kinnosuke Yahiro, Tomohiro Sawa, Takuro Niidome, Preparation of biodegradable PLGA-nanoparticles used for pH-sensitive intracellular delivery of an anti-inflammatory bacterial toxin to macrophages. Chemical and Pharmaceutical Bulletin**,** 68, 4, 363-368, Jan 2020.

Ick Chan KWON

[Presentations]

N/A

[Publications]

1. Han Young Kim, Sang Hoon Um, Yejin Sung, Man Kyu Shim, Suah Yang, Jooho Park, Eun Sun Kim, Kwangmeyung Kim, Ick Chan Kwon*, Ju Hee Ryu. Epidermal growth factor (EGF)-based activatable probe for predicting therapeutic outcome of an EGF-based doxorubicin prodrug. *Journal of Controlled Release* 328, 222-236, December 2020.

2. Yongwhan Choi, Hong Yeol Yoon, Jeongrae Kim, Suah Yang, Jaewan Lee, Ji Woong Choi, Yujeong Moon, Jinseong Kim, Seungho Lim, Man Kyu Shim, Sangmin Jeon, Ick Chan Kwon*, Kwangmeyung Kim. Doxorubicin-Loaded PLGA Nanoparticles for Cancer Therapy: Molecular Weight Effect of PLGA in Doxorubicin Release for Controlling Immunogenic Cell Death. *Pharmaceutics* 12, 1165, December 2020.
3. Ju Hee Ryu, Hong Yeol Yoon, In-Cheol Sun, Ick Chan Kwon*, Kwangmeyung Kim. Tumor-Targeting Glycol Chitosan Nanoparticles for Cancer Heterogeneity. *Advanced Materials* 32, 2002197, December 2020.
4. Yongwhan Choi, Hyounkoo Han, Sangmin Jeon, Hong Yeol Yoon, Hyuncheol Kim, Ick Chan Kwon*, Kwangmeyung Kim. Deep Tumor Penetration of Doxorubicin-Loaded Glycol Chitosan Nanoparticles Using High-Intensity Focused Ultrasound. *Pharmaceutics* 12, 974, October 2020.
5. Young Ji Ko, Jong Won Lee, Hyosuk Kim, EunJi Cho, Yoosoo Yang, In-San Kim, Sun Hwa Kim, Ick Chan Kwon*. Versatile activatable vSIRPα-probe for cancer-targeted imaging and macrophage-mediated phagocytosis of cancer cells. *Journal of Controlled Release* 323,376-386, July 2020.
6. Gi Beom Kim, Gi-Hoon Nam, Yeonsun Hong, Jiwan Woo, Yakdol Cho, Ick Chan Kwon, Yoosoo Yang, In-San Kim. Xenogenization of tumor cells by fusogenic exosomes in tumor microenvironment ignites and propagates antitumor immunity. *Science Advances* 2, eaaz2083, July 2020.
7. Jiwon Kim, Hee Jeong Jang, Dawid Schellingerhout, Jeong Wook Kang, Seungbum Choi, Hyerin Oh, Eo Jin Kim, Su-Kyoung Lee, Ji Sung Lee, Ick Chan Kwon, Kwangmeyung Kim, Young Jun Koh, Wi-Sun Ryu, Dong-Eog Kim. Effects of exercise training and detraining on atheromatous matrix metalloproteinase activity in mice. *Atherosclerosis* 299, 15023, April 2020.
8. Min Ju Kim, So Jin Lee, Ju Hee Ryu, Sun Hwa Kim, Ick Chan Kwon*, Thomas M Roberts. Combination of KRAS gene silencing and PI3K inhibition for ovarian cancer treatment. *Journal of Controlled Release* 318, 98-108, February 2020.
9. Sun Young Wang, Hyosuk Kim, Gijung Kwak, Sung Duk Jo, Daeho Cho, Yoosoo Yang, Ick Chan Kwon, Ji Hoon Jeong, Sun Hwa Kim. Development of microRNA-21 mimic nanocarriers for the treatment of cutaneous wounds. *Theranostics* 10, 3240, January 2020.
10. Manse Kim, Abhishek Sahu, Youngmin Hwang, Gi Beom Kim, Gi Hoon Nam, In-San Kim, Ick Chan Kwon*, Giyoong Tae. Targeted delivery of anti-inflammatory cytokine by nanocarrier reduces atherosclerosis in Apo E−/-mice. *Biomaterials* 226, 119550, January 2020.
11. Young Ji Ko, Jae-Won Lee, Eun-Jeong Yang, Nayoon Jang, Jooho Park, Yoon Kyung Jeon, Je-Wook Yu, Nam-Hyuk Cho, Hye-Sun Kim, Ick Chan Kwon*. Non-invasive in vivo imaging of caspase-1 activation enables rapid and spatiotemporal detection of acute and chronic inflammatory disorders. *Biomaterials* 226, 119534, January 2020.

Keiichi MOTOYAMA & Taishi HIGASHI

[Presentations]

N/A

[Publications]

1. Lactose-appended β-cyclodextrin as an effective nanocarrier for brain delivery. R. Yokoyama, T. Taharabaru, T. Nishida, Y. Ohno, Y. Maeda, M. Sato, K. Ishikura, K. Yanagihara, H. Takagi, T. Nakamura, S. Ito, S. Ohtsuki, H. Arima, R. Onodera, T. Higashi, K. Motoyama, J. Control. Release, 328, 722-735 (2020).
2. Improvement of pharmaceutical properties of Zerumbone, a multifunctional compound, using cyclodextrin derivatives. Md. M. Hassan, A.F.A. Mohammed, K.M. Elamin, H.P.

Devkota, Y. Ohno, K. Motoyama, T. Higashi, T. Imai, Chem. Pharm. Bull., 68, 1117-1120 (2020).

3. Efficient anticancer drug delivery for pancreatic cancer treatment utilizing supramolecular polyethylene-glycosylated bromelain. T. Higashi, T. Kogo, N. Sato, T. Hirotsu, S. Misumi, H. Nakamura, D. Iohara, R. Onodera, K. Motoyama, H. Arima, ACS Appl. Bio Mater., 3, 3005-3014 (2020).
4. Folate-appended cyclodextrin improves the intratumoral accumulation of existing boron compounds. Y. Matsumoto, K. Hattori, H. Arima, K. Motoyama, T. Higashi, H. Ishikawa, N. Fukumitsu, T. Aihara, K. Nakai, H. Kumada, H. Sakurai, Appl. Radiat. Isot., 163, 109201 (2020).
5. Genome editing in a wide area of the brain using dendrimer-based ternary polyplexes of Cas9 ribonucleoprotein. T. Taharabaru, R. Yokoyama, T. Higashi, A.F.A. Mohammed, M. Inoue, Y. Maeda, T. Niidome, R. Onodera, K. Motoyama, ACS Appl. Mater. Interfaces, 12, 21386-21397 (2020).
6. Differential effects of 2-hydroxypropyl-cyclodextrins on lipid accumulation in Npc1-null cells. S. Hoque, Y. Kondo, N. Sakata, Y. Yamada, M. Fukaura, T. Higashi, K. Motoyama, H. Arima, K. Higaki, A. Hayashi, T. Komiya, Y. Ishitsuka, T. Irie, Int. J. Mol. Sci., 21, 898 (2020).
7. Nanoparticle drug delivery systems for α-mangostin. N. Wathoni, A. Rusdin, K. Motoyama, I.M. Joni, R. Lesmana, M. Muchtaridi, Nanotechnol. Sci. Appl., 13, 23-36 (2020).
8. Hyaluronic Acid-Decorated Glycol Chitosan Nanoparticles for pH-Sensitive Controlled Release of Doxorubicin and Celecoxib in Nonsmall Cell Lung Cancer. R. Lee, Y.J Choi, M.y.S Jeong, Y.Il. Park, K. Motoyama, M.W. Kim, S.H. Kwon, J.H. Choi, Bioconjug. Chem., 31, 923-932 (2020).
9. A thermoresponsive hydrophobically modified hydroxypropylmethyl cellulose/cyclodextrin injectable hydrogel for the sustained release of drugs. M. Okubo, D. Iohara, M. Anraku, T. Higashi, K. Uekama, F. Hirayama, Int. J. Pharm., 575, 118845 (2020).

3. Application & acquisition status of KAKENHI and other external grants

Takuro NIIDOME
: JST, CREST
Ruda Lee
: FY2020 JSPS Early Career Research Grant
Ick Chan KWON
: N/A
Keiichi MOTOYAMA & Taishi HIGASHI
: Mochida Memorial Foundation for Medical and Pharmaceutical Research Grant (Keiichi MOTOYAMA)
: A-STEP (Adaptable and Seamless Technology Transfer Program through Target-driven R&D) (Taishi HIGASHI)

4. Application & acquisition status of industrial property rights

Takuro NIIDOME
: N/A
Ruda Lee
: N/A
Ick Chan Kwon

1. Kim Kwangmeyung, Ick Chan Kwon, Juho Park. Tumor cell-specific responsive self-assembling drug nanoconjugate. Publication of US10610602B2, April 2020.
2. Ick Chan Kwon, Ju Hee Ryu, Young-ji KO, Hye-Sun Kim, Nam-Hyuk Cho, Eun-Jeong Yang, Jae Won Lee. Probe for measuring activity of caspase-1 and composition for diagnosis of inflammatory diseases containing same. Publication of US20200087705A1, March 2020.
3. Sun Hwa Kim, Ick Chan Kwon, KIM Kwangmeyung, Hong Yeol Yoon, KWAK Gi-Jung, Juho Park. Therapeutic agent for treating cancer comprising anti-mirna-albumin composite. Publication of US20200071698A1, March 2020.
4. Hak Suk Chung, Yu Hyun Ji, Jin Su An, Ick Chan Kwon, Eun Gyeong Yang. Bacterium constitutively producing monophosphoryl lipid A and method of producing monophosphoryl lipid A by using bacterium. Publication of US10557156B2, February 2020.
5. Ick Chan Kwon, Sun Hwa Kim, YANG Yoosoo, Hyosuk Kim. Method for inducing trans-differentiation of cardiomyocytes based on exosome. Publication of US20200002677A1, January 2020.

Keiichi MOTOYAMA & Taishi HIGASHI

: N/A

No. 5-7, 5-8	Medical Application of X-ray CT -Quantification of Three Dimensional Vascular Network -MicroCT-based Quantification of Fibrosis and Vascularization in Pancreatic Tumor		
Research Field	Advanced Green Bio		
Unit Coordinator			
Name	Toshifumi MUKUNOKI		
Affiliation	Faculty of Advanced Science and Technology Email: mukunoki@kumamoto-u.ac.jp	Title	Professor

Unit Members - Quantification of Three Dimensional Vascular Network	
Name	Affiliation/Title
Yuichiro ARIMA	International Research Center for Medical Sciences (IRCMS), Kumamoto University Assistant Professor
Jun OTANI	Faculty of Advanced Science and Technology (FAST), Kumamoto University Professor
Patrice DELMAS	The University of Auckland, New Zealand Associate Professor

Unit Members - Micro-CT-based Quantification of Fibrosis and Vascularization in Pancreatic Tumor	
Name	Affiliation/Title
Takatsugu ISHIMOTO	International Research Center for Medical Sciences (IRCMS), Kumamoto University Associate Professor
Jun OTANI	Faculty of Advanced Science and Technology (FAST), Kumamoto University Professor
Patrice DELMAS	The University of Auckland, New Zealand Associate Professor

Unit- Quantification of Three Dimensional Vascular Network

1. Overview of achievements
   1） Using the joint research budget, we prepared gold colloid for use in the newly introduced nano x-ray CT. We are trying to make the CT immunostaining, in which a gold colloid-labeled antibody is photographed by CT.

   2） In addition, we are preparing to summarize the x-ray CT protocol so far and submit it to journal of visualized experiments (JoVE).

   3） Daiki Seya, Yuichiro Arima*, Yu Yuquing, Toshifumi Mukunoki, Kenichi Tsujita and Osamu Nakagawa. Computed-tomography based three-dimensional visualization of murine hind-limb vessels. (in preparation) *Corresponding author.

2. Presentations & Publication
   none
3. Application & acquisition status of KAKENHI and other external grants
   Arima and Mukunoki submitted the joint-research grant of Japan Agency for Medical Research and Development (AMED)

4. Application & acquisition status of industrial property rights

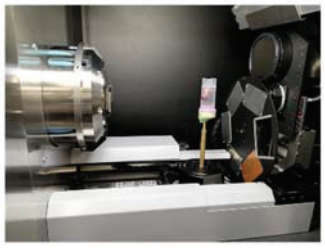
none

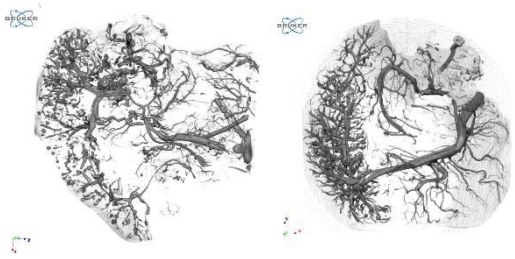
Unit- Micro-CT-based Quantification of Fibrosis and Vascularization in Pancreatic Tumor

1. Overview of achievements

Inflammation and cancer are closely related and favor each other mutually. We are aiming to find the connection between pancreatic cancer and arachidonic cascade, in which we knocked out the key enzyme15pgdh in mice and established an inflammatory syngeneic mouse model. Arachidonate cascade is a major inflammatory pathway that produces prostaglandin E2 (PGE2). We have reported that accumulation of PGE2 in 15pgdh KO mouse promoted cancer stem cell fraction and tumor formation (Arima et al. *Oncogene*). At present we focus on angiogenesis in 15pgdh depleted tumor microenvironment, and have already confirmed enhancement of vascular structure in 15pgdh+/- mouse comparing to wildtype mouse by NanoCT (Figure 1)

Figure 1





Nano-focused X-ray CT scanning of mouse pancreas **15pgdh+/-** **WT**

2. Presentations & Publication

We are preparing the manuscript and planning to submit the article in April.

3. Application & acquisition status of KAKENHI and other external grants

Ishimoto got the grant of “Fusion Oriented Research for disruptive Science and Technology” from 2021-2028.

4. Application & acquisition status of industrial property rights

none

No. 5-9	Advanced Structural Materials		
Research Field	Nano Material Science		
Unit Coordinator			
Name	Kazuki TAKASHIMA		
Affiliation	Faculty of Advanced Science and Technology Email: takashik@gpo.kumamoto-u.ac.jp	Title	Professor
Unit Members			
Name	Affiliation/Title		
Yufeng ZHENG	Department of Materials Science and Engineering, College of Engineering, Peking University, China/IROAST Professor, IROAST Distinguished Professor		
Paul BOWEN	School of Metallurgy and Materials, University of Birmingham, UK Professor, IROAST Visiting Professor		
Yu-Lung CHIU	School of Metallurgy and Materials, University of Birmingham, UK Reader		
Hiroto KITAGUCHI	School of Metallurgy and Materials, University of Birmingham, UK Senior Research Fellow		
Martin DIENWIEBEL	Applied Nanotribology, Karlsruhe Institute for Technology (KIT), Germany Heisenberg-Professor, IROAST Visiting Professor		
Shirley SHEN	CSIRO, Australia Principal Research Scientist, IROAST Visiting Professor		
Yoji MINE	Faculty of Advanced Science and Technology (FAST), Kumamoto University Professor		
Kwangsik KWAK	Faculty of Advanced Science and Technology (FAST), Kumamoto University Assistant Professor		

1. Overview of achievements

The mechanical properties of materials are dominated by their microstructures such as grain size, precipitates, phase boundary, grain boundary, etc. In our research group, we aim to clarify the mechanical properties at microscopic level, including tensile properties, fracture and fatigue properties, using the micromechanical testing technology that we have developed. Furthermore, in conjunction with crystal plasticity finite element simulation, we aim to predict the mechanical properties of bulk materials based on those at microscopic scale. Unfortunately, due to the pandemic of COVID-19, mutual exchanges were not possible in FY2020, and results were limited. In spite of this situation, some new and valuable results were obtained, which are outlined below.

1) Mechanical Properties of Biomaterial

This research has been conducted in collaboration with Professor Zheng, Distinguished Professor of IROAST. In the development of biomaterials, it is important to evaluate the mechanical properties in a shape close to the final shape and size. As the stents are used intravascularly, the effects of fatigue associated with cyclic loading by the pulse must be considered in addition to the effects of material corrosion in the in vivo environment. Previously, corrosion fatigue has been studied using bulk-sized specimens made from the same material as the stent. However, stents are usually several mm thick and are microfabricated using lasers and other processes. Therefore, in order to evaluate the actual mechanical properties of the stent, it is necessary to evaluate the mechanical properties for the miniature-sized specimens prepared from the stent fabricated by actual processes. Therefore, we have developed a testing machine that can measure the environmental fatigue properties in the same size as a stent.

In this year, Prof. Zhen was not able to visit Kumamoto for COVID-19, so there was no progress in our research. However, we have improved the corrosion fatigue test using miniature ring specimens at Kumamoto University, and made preparations to resume our research in the next year. In the next year, we plan to conduct research on the corrosion fatigue properties of Zn-Li-based biometallic materials developed by Prof. Zhen.

2) Elucidation of Fatigue Crack Growth Mechanism in Ti-Based Alloys

Ti alloys are expected to be used as aerospace materials, and improvement of fatigue properties is required from the viewpoint of long-term durability and reliability. In the fatigue of metallic materials, it is important to know the fundamental mechanism of crack propagation in order to improve their lifetime. Fatigue crack propagation is based on cyclic plastic deformation at the crack tip, and the crack propagation length per cycle is on the order of submicron. Therefore, it is necessary to directly observe the propagation process at the crack tip in the sub-micron order. We have collaborated with Professor Bowen, visiting professor at IROAST and researchers (Dr Yu-Lung Chiu and Dr Hiroto Kitaguchi) at the University of Birmingham to elucidate the mechanism of fatigue crack propagation using the micro-fatigue testing technique developed in our research group.

I Until last year, researchers and graduate students had been exchanging their research, but due to COVID-19, we were not able to do so this year. Therefore, we held web meetings to exchange information on the progress of our research. Based on the results of the web meetings, we plan to write an international joint paper.

3) Nanotribology of Metals

We have collaborated with Prof. Dienwiebel, visiting professor at IROAST and professor at Karlsruhe Institute of Technology, on the tribological properties of Mg alloys. This year we had planned to invite professors and send students, but due to COVID-19 this was cancelled, so unfortunately there was no progress in our research. However, we are planning to publish a co-authored paper in the next fiscal year.

4) Evaluation of Mechanical Properties of Additive Manufacturing Materials

From FY2019, we started a joint research on the mechanical properties of additive manufacturing materials with Dr. Shen of CSIRO Australia, who is a visiting professor at IROAST. Although mutual visits were not possible this year due to COVID-19, we were able to advance our research by sending samples from both institutions for analysis and by holding several web

meetings.

At CSIRO, the fabrication conditions to produce excellent compacts from two biodegradable Mg alloy powders by 3D additive manufacturing technology were investigated. At Kumamoto University, microstructural analysis and evaluation of fatigue properties of the fabricated compacts were carried out. The results obtained will greatly contribute to the practical application of this technology in the future. We have agreed to write co-authored papers on the results of this investigation and to promote our collaborative research.

2. Publications

International co-authored paper with a visiting professor.

J. Wu, S. Si, K. Takagi, T. Li, Y. Mine, K. Takashima, Y. L. Chiu: "Study of basal <a> and pyramidal <c + a> slips in Mg-Y alloys using micro-pillar compression", Phil. Mag., **100** (2020) pp. 1454-1475.

In addition to the above, we have published the following paper.

S. Ueki, R. Oura, Y. Mine, K. Takashima: "Micro-mechanical characterisation of hydrogen embrittlement in nano-twinned metastable austenitic stainless steel", Int. J. Hydrogen Energy, **45** (2020) pp. 27950-27957.

3. Application & acquisition status of KAKENHI and other external grants

Elucidation of Fatigue Crack Growth Mechanism using Microtesting Technique and Application to Fatigue Strengthening Design, KAKENHI Grant-in-Aid for Scientific Research (A) 2020-2024, (Continuing)

Exploration of Guiding Principles for Hydra Toughening Design by Multiscale Mechanical Tests, KAKENHI Grant-in-Aid for Scientific Research (B) 2019-2021 (Continuing)

3D Printing of Novel High Vapour Pressure Metals and Metal Matrix Composites as Bio-degradable Implant Components, Foundation for Australia-Japan Studies (FAJS) Grant, 2019-2020

No. 5-10	Microstructure Analysis and Grain Boundary Engineering		
Research Field	Nano Material Science		
Unit Coordinator			
Name	Sadahiro TSUREKAWA		
Affiliation	Faculty of Advanced Science and Technology Email: turekawa@kumamoto-u.ac.jp	Title	Professor
Unit Members			
Name	Affiliation/Title		
Dmitri Aleks MOLODOV	Institute of Physical Metallurgy and Metal Physics, RWTH Aachen University, Germany Professor, IROAST Visiting Professor		
Pavel LEJČEK	Institute of Physics, Academy of Sciences of the Czech Republic /University of Chemistry and Technology, Prague, Czech Republic Professor, IROAST Visiting Professor		
Mitsuhiro MATSUDA	Faculty of Advanced Science and Technology (FAST), Kumamoto University Associate Professor		
Thomas WAITZ	Faculty of Physics, University of Vienna, Austria Associate Professor, IROAST Visiting Professor		
Christian RENTENBERGER	Faculty of Physics, University of Vienna, Austria Associate Professor, IROAST Visiting Professor		
Yoshitaka MATSUKAWA	Faculty of Advanced Science and Technology (FAST), Kumamoto University Associate Professor		

Overview of achievements

S. Tsurekawa's (ST) group: Tsurekawa's group has collaborated with Prof. Dmitri A. Molodov (RWTH Aachen University) and Prof. Pavel Lejček (Institute of Physics, Czech Academy of Sciences), who are vising professors of IROAST, in the research field of grain boundary engineering over many years. Due to the covid19 pandemic, their stay at Kumamoto University in FY2020 was cancelled, unfortunately. However, with Prof. D. A. Molodov, we made efforts to prepare the manuscripts of our common papers on "influence of high-angle grain boundaries on the local mechanical properties of magnesum bicrystals" and "On incipient plasticity in the vicinity of grain boundaries in aluminum bicrystals: Experimental and simulation nanoindentation study", and submitted the papers to Acta Materialia. In addition, ST group also started to study the segregation of tungsten to grain boundary in molybdenum with Prof. P. Lejček.

M. Matsuda's (MM) group: Many of functional materials, such as semiconductor, super conductor, solar cell, magnetic materials and shape memory alloys, contains numerous interfaces and domains. Functional properties are greatly affected by the interfaces and boundaries between domains. The

structural and mechanical properties of nanocrystalline materials was discussed with Vienna's Group (Prof. T. Waitz and Prof. C. Rentenberger) by e-mail and web meeting. Also, our research team acquired "Promotion of Joint International Research (Fostering Joint International Research(B)) of KAKENHI", and the "Scientific Research B" to collaborate the research more strongly.

Publications

1. J-E Brandenburg, J. Seo, K. Eto, D. A. Molodov, S. Tsurekawa, Influence of symmetrical <$10\bar{1}0$> high-angle tilt grain boundaries on the local mechanical properties of magnesium bicrystals, Submitted to Acta Mater.
2. L. A. Barrales-Mora, Yoshiyiku Tokuda, D. A. Molodov, S. Tsurekawa, On incipient plasticity in the vicinity of grain boundaries in aluminum bicrystals: Experimental and simulation nanoindentation study, submitted to Acta Mater.
3. S. Ii, T. Enami, T. Ohmura and S. Tsurekawa, Direct characterization in relation between mechanical response and microstructure evolution in Aluminium by transmission electron microscope in-situ straining, Materials, 14(2021), 1431. DOI: 10.3390/ma14061431
4. M. Berahmand, M. Ketabchi, M. Jamshidian, S. Tsurekawa, Investigation of Microstructure Evolution and Martensite Transformation Developed in Austenitic Stainless Steel Subjected to a Plastic Strain Gradient: A Combination Study of Mirco-XRD, EBSD, and ECCI Techniques, Micron, 143 (2021), 103014. DOI: 10.1016/j.micron.2021.
5. S. Kobayashi, W.T. Yang, Y. Tomobe, R. Okada, S. Tsurekawa, Low-angle boundary engineering for improving high-cycle fatigue property of 430 ferritic stainless steel, J. Mater. Sci. 55 (2020), 9273. DOI: 10.1007/s10853-020-04555-0

Acquisition status of KAKENHI and other external grants

1. M. Matsuda: Promotion of Joint International Research (Fostering Joint International Research(B)), *Development of innovative functional materials based on the evaluation and control for interface dynamics*, Grant Number JP19KK0125.
2. M. Matsuda: Grant-in-Aid for Scientific Research (B), *Development of innovative functional materials based on the evaluation and control for interface dynamics*, Grant Number JP19KK0125
3. S. Tsurekawa: Grant-in-Aid for Scientific Research (S), *Breakthrough toward "second-generation" grain boundary engineering*, Grant Number 16H06366.

No. 5-11	Structure and Dynamics of Materials Using Quantum Beams and Data-Driven Sciences		
Research Field	Nano Material Science		
Unit Coordinator			
Name	Shinya HOSOKAWA		
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Unit Members	
Name	Affiliation/Title
Marc De BOISSIEU	CNRS, SIMaP, Université Grenoble Alpes, France Director, IROAST Visiting Professor
Matthieu MICOULAUT	Sorbonne Université, France Professor, IROAST Visiting Professor
Anita ZEITLER	Department of Physics, University of Bath, UK Lecturer
László PUSZTAI	Wigner Research Centre for Physics, Hungary/ IROAST Scientific Advisor, Distinguished Professor
Alexei KUZMIN	Laboratory of Materials Morphology and Structure Investigations, Institute of Solid State Physics, University of Latvia, Riga, Latvia Head of Laboratory, IROAST Visiting Professor
Ichiro AKAI	Institute of Industrial Nanomaterials (IINa), Kumamoto University Professor
Masaru ANIYA	Faculty of Advanced Science and Technology (FAST), Kumamoto University Professor
Masahiro HARA	Faculty of Advanced Science and Technology (FAST), Kumamoto University Associate Professor
Yoichi NAKAJIMA	Priority Organization for Innovation and Excellence (POIE), Kumamoto University Assistant Professor

Details of activities

1. Overview of achievements

The aim of this research group is to investigate structure and dynamics of materials using quantum beam facilities in combination with data-driven sciences and computer simulations. Recent developments of quantum beam facilities, such as synchrotron radiation, x-ray free electron laser, and intense neutron sources, lead remarkable progresses in the quality of experimental data. In conjunction with them, new varieties of the data sets appear, such as two-dimensional images

etc. and the corresponding data volumes explosively increase. The present task for researchers is how to extract scientifically valuable information from the experimental data of huge size in quantity but of still insufficient in quality. In this research unit, thus, we carry out state-of-art experiments such as scattering and imaging using quantum beam facilities, and analyze the data using, e.g., Inverse problem, Bayesian inference with Metropolis' algorithm (reverse Monte Carlo modeling) and some others. Furthermore, the data-driven science such as Sparse modeling is a very promising tool for handling the data. To support the experimental results, first principles computer simulations are also indispensable.

At the beginning of the 2019 fiscal year, we started this research unit. In this fiscal year, due to the COVID-19 calamity, the activities are very limited to the publication of 4 papers. Several publications concerning the topics of this unit are on going to international journals with impact factors.

2. Presentations & Publications (incl. submitted papers)

1) S. Hosokawa, Y. Kawakita, L. Pusztai, K. Ikeda, and T. Otomo, Detailed investigations on short- and intermediate-range structures of Ge-Se glasses near the stiffness transition composition, *Journal of Physical Society of Japan* **90**, 024601-1-12 (2021).
2) S. Hosokawa, J.-F. Bérar, N. Boudet, W.-C. Pilgrim, L. Pusztai, S. Hiroi, S. Kohara, H. Kato, H. E. Fischer, and A. Zeidler, Detailed structural analysis of amorphous $Pd_{40}Cu_{40}P_{20}$: Comparison with the metallic glass $Pd_{40}Ni_{40}P_{20}$ from the viewpoint of glass forming ability, *Journal of Non-Crystalline Solids* **555**, 120536-1-10 (2021).
3) S. Hosokawa, Y. Kawakita, J. R. Stellhorn, L. Pusztai, N. Blanc, N. Boudet, K. Ikeda, and T. Otomo, Local- and Intermediate-Range Order in Room Temperature Superionic Conducting Ag-$GeSe_3$ Glasses, *JPS Conference Proceedings* **33**, 011069-1-6 (2021).
4) S. Hosokawa, J. R. Stellhorn, Y. Onodera, S. Kohara, H. Tajiri, E. Magome, L. Pusztai, K. Ikeda, T. Otomo, M. Krbal, and T. Wagner, Local- and Intermediate-Range Atomic Order in $Ga_2Ge_3Se_9$ Glass: Complementary Use of X-Rays and Neutrons, *JPS Conference Proceedings* **33**, 011069-1-6 (2021).

3. Application & acquisition status of KAKENHI and other external grants

1) JST CREST (Continued), Main Proposer: I. Akai, 10,950,000 JPY
2) JSPS Grant-in-Aid for Scientific Research (C) (Continued), Main Proposer: Y. Nakajima, 1,200,000 JPY

4. Application & acquisition status of industrial property rights

None.

No. 5-12	Hydrological Environments		
Research Field	Environmental Science		
Unit Coordinator			
Name	Takahiro HOSONO		
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Unit Members			
Name	Affiliation/Title		
Kimpei ICHIYANAGI	Associate Professor Faculty of Advanced Science and Technology (FAST), Kumamoto University, Japan		
Jens HARTMANN	Professor Institute for Geology, University of Hamburg, Germany		
Rusmawan SUWARMAN	Assistant Professor Faculty of Earth Science and Technology Bandung Institute of Technology (ITB), Indonesia		
Pascale LOUVAT	CNRS research engineer, Institut de Physique du Globe de Paris, France		

Details of activities

1. Overview of achievements

1.1. Discussing a new publication about the joint research on water from the Aso-caldera

The study of controls on the water quality in tectonically active areas like Japan is of relevance as several under-researched processes control the water quality and the mobilization of matter and transport to the ocean. This includes seismotectonic processes causing deep water upwelling into the shallow groundwater and hydrothermal processes affecting the water quality directly at a local level. To be able to understand the regional controls on these fluxes, a research area like the Aso caldera or Kirishima represent unique opportunities due the given infrastructure. Unit members Drs. J. Hartmann and T. Hosono have conducted surveys for the past six years due this infrastructure and have now a set of samples and data partly with a help of geochemical analysis by Dr. P. Louvat, which allows us to analyses in depth the diverse processes controlling the water quality, also using novel isotope approaches, which were not combined in the way as it is now down. Drs. J. Hartmann and T. Hosono with other co-authors discussed through email the contents of paper which is under submission.

1.2. Discussing on a global water quality database, considering a long-term plan and strategy building on the previous GLORICH database.

Dr. J. Hartmann is trying to develop a global water quality database, GLORICH database, https://www.geo.uni-hamburg.de/geologie/forschung/geochemie/glowachem.html, with several

key scientists over the world. Dr. T. Hosono is in charge of data collection from southeast Asian division. Dr. T. Hosono has collected database from whole Japanese islands and some southeastern countries that were added in the database.

1.3. Financial supports

Dr. T. Hosono was financially supported by IROAST for paying article processing charges on publishing paper in Nature Communications ($5,380). The study was also supported by IROAST research award (500,000 JPY). T.H. wishes to thank all these supports.

2. Presentations & Publications

Presentations

Ichiyanagi, K., Uesugi, T., Suwarman R., Belgaman, H. A., Tanoue, M., 2020, Seasonal variability of stable isotopes in precipitation over Indonesia observed for 2010-2018. AHW30-P07, JpGU-AGU Joint Meeting 2020: Virtual. (poster)

Books

細野高啓. 地震が起こると地下水や湧水に影響がありますか？ In: 地下水・湧水の疑問50（公益社団法人 日本地下水学会 編）, 2020, 成山堂書店, 194-198.

細野高啓, 井手　浄, 嶋田　純. 水道水源井や地下水観測井の水質に見えた地震に伴う変化. In: 巨大地震が地下水環境に与えた影響（嶋田　純, 細野高啓 編）, 2020, 成文堂, 107-133.

細野高啓, 田原康博. 水前寺成趣園湧水池の枯渇とその原因究明. In: 巨大地震が地下水環境に与えた影響（嶋田　純, 細野高啓 編）, 2020, 成文堂, 35-52.

Publications

Hosono, T., Hossain, S., Shimada, J., 2020. Hydrobiogeochemical evolution along the regional groundwater flow systems in volcanic aquifers in Kumamoto, Japan. Environmental Earth Sciences, 79(18), 410. https://doi.org/10.1007/s12665-020-09155-4

Hosono, T., Masaki, Y., 2020. Post-seismic hydrochemical changes in regional groundwater flow systems in response to the 2016 Mw 7.0 Kumamoto earthquake. Journal of Hydrology, 580,124340. https://doi.org/10.1016/j.jhydrol.2019.124340

Hosono, T., Saltalippi, C., Jean, J.-S., 2020. Coseismic hydro-environmental changes: insights from recent earthquakes. Journal of Hydrology, 585, 124799.

Hosono, T., Yamada, C., Manga, M., Wang, C. -Y., Tanimizu, M., 2020. Stable isotopes show that earthquakes enhance permeability and release water from mountains. Nature Communications, 11, 2776. https://doi.org/10.1038/s41467-020-16604-y

Ichiyanagi, K., Ide, K., Tanoue, M., 2020. Seasonal variability of stable isotopes in precipitation and spring water around Mt Kimpo, Kumamoto, southwestern Japan. Isotopes in Environmental and Health Studies, 56(2), 149-157. https://doi.org/10.1080/10256016.2020.1745203

Ichiyanagi, K., Imatsu, M., Ide, K., Shimada, J., 2020. Effects on fluvial discharges of the 2016 Kumamoto earthquakes, Japan. Journal of Hydrology, 583, 124600. https://doi.org/10.1016/j.jhydrol.2020.124600

Ide, K., Hosono, T., Kagabu, M., Fukamizu, K., Tokunaga, T., Shimada, J., 2020. Changes of groundwater flow systems after the 2016 Mw 7.0 Kumamoto earthquake deduced by stable isotopic and CFC-12 compositions of natural springs. Journal of Hydrology, 583, 124551. https://doi.org/10.1016/j.jhydrol.2020.124551

Ishii, E., Watanabe, Y., Agusa, T., Hosono, T., Nakata, H., 2021. Acesulfame as a suitable sewer tracer on groundwater pollution: A case study before and after the 2016 Mw 7.0 Kumamoto earthquakes. Science of the Total Environment, 754, 142409. https://doi.org/10.1016/j.scitotenv.2020.142409
Kagabu, M., Ide, K., Hosono, T., Nakagawa, K., Shimada, J., 2020. Describing coseismic groundwater level rise using tank model in volcanic aquifers, Kumamoto, southern Japan. Journal of Hydrology, 582, 124464. https://doi.org/10.1016/j.jhydrol.2019.124464
Kawabata, K., Sato, T., Takahashi, H.A., Tsunomori, F., Hosono, T., Takahashi, M., Kitamura, Y., 2020. Changes in groundwater radon concentrations caused by the 2016 Kumamoto earthquake. Journal of Hydrology, 584, 124712. https://doi.org/10.1016/j.jhydrol.2020.124712
Miyakoshi, A., Taniguchi, M., Ide, K., Kagabu, M., Hosono, T., Shimada, J., 2020. Identification of changes in subsurface temperature and groundwater flow after the 2016 Kumamoto earthquake using long-term well temperature–depth profiles. Journal of Hydrology, 582, 124530. https://doi.org/10.1016/j.jhydrol.2019.124530
Mizota, C., Khanthavong, P., Hosono, T., Okumura, A., Yamanaka, T., Murano, H., 2021. Reworking saltpetre manufacture in Lao PRD: Implications for isotopic fractionation during the historic processes. Journal of Archaeological Science: Reports, 35, 102747. https://doi.org/10.1016/j.jasrep.2020.102747
Mizota, C., Khanthavong, P., Okumura, A., Hosono, T., 2020. Dual isotopic (δ15N-δ18O) characterization of saltpetre currently prevailing in Lao PDR and its global compilation: new insight into isotope fractionation during production processes. Isotopes in Environmental and Health Studies, 56(1), 1-13. https://doi.org/10.1080/10256016.2020.1717486
Morimura, S., Zeng, X., Noboru, N., Hosono, T., 2020. Changes to the microbial communities within groundwater in response to a large crustal earthquake in Kumamoto, southern Japan. Journal of Hydrology, 581,124341. https://doi.org/10.1016/j.jhydrol.2019.124341
Nakagawa, K., Yu, Z.-Q., Berndtsson, R., Hosono, T., 2020. Temporal characteristics of groundwater chemistry affected by the 2016 Kumamoto earthquake using self-organizing maps. Journal of Hydrology, 582, 124519. https://doi.org/10.1016/j.jhydrol.2019.124519
Rahman, A.T.M.S., Hosono, T., Kisi, O., Dennis, B., Imon, A.H.M.R., 2020. A minimalistic approach for evapotranspiration estimation using the Prophet model. Hydrological Sciences Journal, 65(12), 1-13. https://doi.org/10.1080/02626667.2020.1787416
Rahman, A.T.M.S., Hosono, T., Quilty, J.M., Das, J., Basak, A., 2020. Multiscale groundwater level forecasting: Coupling new machine learning approaches with wavelet transforms. Advances in Water Resources. 141,103595. https://doi.org/10.1016/j.advwatres.2020.103595
Tawara, Y., Hosono, T., Fukuoka, Y., Yoshida, T., Shimada, J., 2020. Quantitative assessment of the changes in regional water flow systems caused by the 2016 Kumamoto Earthquake using numerical modeling. Journal of Hydrology, 583, 124559. https://doi.org/10.1016/j.jhydrol.2020.124559
一柳 錦平, 井手 淨, 嶋田 純, 市川 勉, 2020. 熊本市江津湖周辺における地下水湧出量の再考察. 日本水文科学会誌, 50(1), 3-11. https://doi.org/10.4145/jahs.50.3

3. Application & acquisition status of KAKENHI and other external grants

T. Hosono, principle investigator, JSPS Fostering Joint International Research (A), 2020-2023, 19KK0291
T. Hosono, principle investigator, JSPS Grant-in-Aid for Scientific Research (B), 2017-2020, 17H01861

4. Application & acquisition status of industrial property rights

non

No. 5-13	Quantitative Bioimaging		
Research Field	Advanced Green Bio		
Unit Coordinator			
Name	Takumi HIGAKI		
Affiliation	International Organization for Advanced Science and Technology Email: thigaki@kumamoto-u.ac.jp	Title	Associate Professor
Unit Members			
Name	Affiliation/Title		
Fei DU	Chinese Academy of Sciences, China Postdoctoral Fellow		
Masaki SHIMONO	Michigan State University, USA Research Associate		
Kae AKITA	Japan Women's University, Japan Assistant Professor		

Recent advances in bioimaging equipment have enabled scientists to acquire large amounts of bioimage data within a short period of time. Following this influx of bioimage information, biologists are now engaging in bioimage informatics, an emerging area of bioinformatics. In this Quantitative Bioimaging Unit, we focus on microscopic image analysis on cytoskeleton. Cytoskeleton relates cell dynamics including cell division, growth, and differentiation. Its higher-order structures (e.g. bundles or meshworks) dynamically change in response to developmental or environmental cues. We are working on the development of a bioimage analysis framework to quantitatively evaluate multi-dimensional cytoskeletal organizations (i.e. XYZTN images) based on tight collaboration among experts in cell biology (F. Du and M. Shimono) and bioimage informatics (T. Higaki and K. Akita). Specifically, we are now trying to make a new image analysis system that (1) does not need manual segmentation, (2) provides multi-dimensional features without laborious pre-processing, and (3) makes results visualization based on multi-dimensional features by multivariate analysis and image clustering method. In FY2020, we worked on a collection of various types of cytoskeletal images and the development of the image analysis framework to quantitatively evaluate multidimensional cytoskeletal organizations. Notably, we published a paper on changes in actin filament organization during plant immunity in *Nature Communication* (Lu et al. 2020). This work was performed as a part of this Research Unit with Dr. Masaki Shimono and Prof. Brad Day Laboratory of Michigan State University. We also published a paper about the development of the bioimage analysis framework to quantitatively evaluate the cytoskeleton bundling in *Scientific Reports* (Higaki et al. 2020). This work was performed as a part of this Research Unit with Dr. Kae Akita of Japan Women's University and featured on the Kumamoto University website (https://ewww.kumamoto-u.ac.jp/en/news/428/) and EurekAlert! (https://www.eurekalert.org/pub_releases/2021-01/ku-ahs011421.php). Furthermore, our image analysis techniques were used for quantitative evaluations of various plant cell biological phenomena including cell division in tobacco BY-2 cultured cells (Maeda and Higaki 2021 *Plant*

Sig Behav), chemical response in BY-2 cells (Ishida et al. 2021 *Sci Rep*), and pavement cell growth in *Arabidopsis thaliana* cotyledons (Higaki and Mizuno 2020 *Plant Biotech*). In addition, as a spin-off project, image analyst group (T. Higaki and K. Akita) analyzed wide-range confocal images in order to reveal the relationship between the spatial distribution pattern of stomatal development and atmospheric CO_2 concentrations in young cotyledons of *Arabidopsis thaliana* (Higaki et al. 2020). Based on the progress in the Research Unit, the unit coordinator applied for FY2021 KAKEN Grant-in-Aid for Scientific Research.

Publications

Ishida T, Yoshimura H, Takekawa M, Higaki T, Ideue T, Hatano M, Igarashi M, Tani T, Sawa S, Ishikawa H (2021) Discovery, characterization and functional improvement of kumamonamide as a novel plant growth inhibitor that disturbs plant microtubules. *Sci Rep* 23: 6077. http://doi.org/10.1038/s41598-021-85501-1

Maeda K, Higaki T (2021) Disruption of actin filaments delays accumulation of cell plate membranes after chromosome separation. *Plant Sig Behav* 16: 1873586. https://doi.org/10.1080/15592324.2021.1873586

Higaki T, Akita K, Katoh K (2020) Coefficient of variation as an image-intensity metric for cytoskeleton bundling. *Sci Rep* 10: 22187. https://doi.org/10.1038/s41598-020-79136-x

Lu YJ, Li P, Shimono M, Corrion A, Higaki T, He SY, Day B (2020) Arabidopsis calcium-dependent protein kinase 3 regulates actin cytoskeleton organization and immunity. *Nat Commun* 11:6234. https://doi.org/10.1038/s41467-020-20007-4

Higaki T, Mizuno H (2020) Four-dimensional imaging with virtual reality to quantitatively explore jigsaw puzzle-like morphogenesis of *Arabidopsis* cotyledon pavement cells. *Plant Biotech* 37: 429-435. http://doi.org/10.5511/plantbiotechnology.20.0605a

Higaki T, Akita K, Hasezawa S (2020) Elevated CO_2 promotes satellite stomata production in young cotyledons of *Arabidopsis thaliana*. *Genes Cells* 25: 475-482. https://doi.org/10.1111/gtc.12773

No. 5-14	Development of novel therapeutic strategy using iron targeted upconversion nanoparticles for Parkinson's disease		
Research Field	Advanced Green Bio		
Unit Coordinator			
Name	Ruda Lee		
Affiliation	International Organization for Advanced Science and Technology Email: aeju-lee@kumamoto-u.ac.jp	Title	Associate Professor
Unit Members			
Name	Affiliation/Title		
Yong Il PARK	Chonnam National University, Republic of Korea/ Associate Professor		
Jung Hoon CHOI	Kangwon National University, Republic of Korea/ Associate Professor		
Xiaoxue XU	University of Technology Sydney, Australia/ Chancellor Postdoctoral Research Fellow		

Details of activities

1. Overview of achievements

FY 2020, we focused on material evaluation under cellular condition. Approximately, 10-12 of upconversion nanoparticles (UCNPs) were loaded on the hybrid nanoconstructs. The cellular behaviors were confirmed using substantia nigra (SN) cell lines. Furthermore, various gene and protein expressions were evaluated after the nanoconstructs treatment. Based on these achievements, we will work on *in vivo* Parkinson's disease model treatment in FY2021.

2. Presentations & Publications (incl. submitted papers)

[Presentations]

Ruda LEE

1. Ueno Sho, Takuro Niidome, Ruda Lee. Development of ErB2-targeting Liposomes for Enhancing Delivery to ErbB2- positive Breast cancer. The 15th International Student Conference on Advanced Science and Technology (ICAST 2020 Kumamoto, Dec 3-4 (2020), Kumamoto, Japan (Online)
2. Seung-Hae Kwon, Ji Hoon Kim, Jung Hoon Choi, Ruda Lee. Non-invasive early detection of calpain 2-enriched non-small cell lung cancer using a human serum albumin-based calpain-2 nanosensor. 7th International Conference on Bio-Sensing Technology, Busan, Korea (Online)

Yong Il PARK

1. Song Yeul Lee, Yoongu Lim, Dohun Kim, Uk Sim, **Yong Il Park**. The Effect of $NaYF_4$ Upconversion Nanoparticles for the Enhancement of $ZnFe_2O_4/TiO_2$ Photoanode, KIChE Fall Meeting and International Symposium, Oct 14-16, Korea (Online).

2. Song Yeul Lee, **Yong Il Park**. Enhanced Cyclic Performance of Sodium-Ion Capacitor via Surface Modification, 2020 KSIEC Annual Meeting in Celebration of the 30th Anniversary, Oct 28-30, Gwangju, Korea.
3. Yoongu Lim, Song Yeul Lee, Dohun Kim, Uk Sim, **Yong Il Park**. Enhancement of $ZnFe_2O_4/TiO_2$ Photoanode Through the Effect of NaYF4 Upconversion Nanoparticles, The 16th International Symposium on Novel and Nano Materials Incorporating the Conference of Korean Powder Metallurgy Institute, Nov 3-6, Jeju, Korea.
4. Panju Kim, Eun Young Lee, Byung Joon Moon, Song Yeul Lee, **Yong Il Park**, Sang Hyun Lee. Synthesis and Applications of Lead-Free Perovskite Cesium Ytterbium Halide Nanocrystals. The 30th International Photovoltaic Science and Engineering Conference, Nov 9-13 (2020), Jeju, Korea.

Jung Hoon CHOI

1. Yoon-Hwan Kim, Min Soo Kang, Tae Hyeong Kim, Yunho Jeong, Jin-Ok Ahn, Jung Hoon Choi, Jin-Young Chung. Development of Synbio-glucan Functional Spray for Canine Atopic Dermatitis. 2020 KSVS symposium (Korea, Hongchun 19~20 NOV 2020)
2. Min Soo Kang, Woosuk Kim, Tae Hyeong Kim, Hyo Young Jung, Hyun Jung Kwon, Dae Won Kim,In Koo Hwang and Jung Hoon Choi. High fat diet accelerates and exacerbates microgliosis and neuronal damage/death in the somatosensory cortex after transient forebrain ischemia in gerbils. 2020 KALAS International symposium (Korea, Pyeongchang 15~18 Jul 2020)

Xiaoxue XU

N/A

[Publications]

Ruda Lee

1. Yong Il Park, Seung-Hae Kwon, Gibok Lee, Keiichi Motoyama, Min Woo Kim, Min Lin, Takuro Niidome, Jung Hoon Choi, **Ruda Lee***. pH-sensitive multi-drug liposomes targeting folate receptor ß for efficient treatment of non-small cell lung cancer. *Journal of Controlled Release*, 330, 1-14, February 2021.
2. Sho Ueno, Min Woo Kim, Gibok Lee, Yong Il Park, Takuro Niidome, and **Ruda Lee***. Development of ErbB2-Targeting Liposomes for Enhancing Drug Delivery to ErbB2-Positive Breast Cancer. Pharmaceutics, 12, 585, June 2020.
3. Xiaoxue Xu, Hongxu Lu and **Ruda Lee**. Near Infrared Light Triggered Photo/Immuno-Therapy Toward Cancers. *Frontiers in Bioengineering and Biotechnology*, 8, 488, 2020.
4. Song Yeul Lee*, **Ruda Lee***, Eunha Kim, Sanghee Lee and Yong Il Park. Near-Infrared Light-Triggered Photodynamic Therapy and Apoptosis Using Upconversion Nanoparticles with Dual Photosensitizers. Frontiers in Bioengineering and Biotechnology, 8, 275. Apr 2020.

Yong Il PARK

1. **Yong Il Park**, Seung-Hae Kwon, Gibok Lee, Keiichi Motoyama, Minwoo Kim, Min Lin, Takuro Niidome, Jung Hoon Choi, Ruda Lee. pH-Sensitive Multi-Drug Liposomes Targeting Folate Receptor ß for Efficient Treatment of Non-Small Cell Lung Cancer. *Journal of Controlled Release*, 330, 1-14, Feb 2021.
2. Da Hwi Gu, Jungsoo Lee, Hyeong Woo Ban, Gibok Lee, Minju Song, Wooyong Choi, Seongheon Baek, Hyewon Jeong, Song Yeul Lee, Yonghoon Choi, Jongnam Park, **Yong Il Park**,* Jae Sung Son*. Colloidal Suprastructures Self-Organized from Oppositely Charged All-Inorganic Nanoparticles. *Chemistry of Materials,* 32, 8662-8671, Oct 2020.
3. Sho Ueno, Min Woo Kim, Gibok Lee, **Yong Il Park**, Takuro Niidome, Ruda Lee. Development of ErbB2-Targeting Liposomes for Enhancing Drug Delivery to ErbB2-

Positive Breast Cancer. *Pharmaceutics*, 12, 585, Aug 2020.

4. Jinyue Zhang, Mingshi Jin, **Yong Il Park**, Longyi Jin, Bo Quan. Facile Synthesis of Ultra-Small Hollow Manganese Silicate Nanoparticles as pH/GSH-Responsive T1-MRI Contrast Agents. *Ceramics International*, 46, 18632–18638, Jun 2020.
5. Song Yeul Lee, Ruda Lee, Eunha Kim, Sanghee Lee,* **Yong Il Park***. Near-Infrared Light-Triggered Photodynamic Therapy and Apoptosis using Upconversion Nanoparticles with Dual Photosensitizers. *Frontiers in Bioengineering and Biotechnology*, 8, 275, Apr 2020.
6. Song Yeul Lee, Gibok Lee, Young-Si Jun, **Yong Il Park***. Visible/Near-Infrared Driven Highly Efficient Photocatalyst Based on Upconversion Nanoparticles/g-C_3N_4 Nanocomposite. *Applied Surface Science*, 508, 144839, Apr 2020.

Jung Hoon CHOI

1. Yong Il Park, Seung-Hae Kwon, Gibok Lee, Keiichi Motoyama, Min Woo Kim, Min Lin, Takuro Niidome, **Jung Hoon Choi**, Ruda Lee. pH-sensitive multi-drug liposomes targeting folate receptor ß for efficient treatment of non-small cell lung cancer. Journal of Controlled Release, 330, 1-14, February 2021.
2. Yoon-Hwan Kim, Min Soo Kang, Tae Hyeong Kim, Yunho Jeong, Jin-Ok Ahn, **Jung Hoon Choi***, Jin-Young Chung. Anti-Inflammatory and Immune Modulatory Effects of Synbio-Glucan in an Atopic Dermatitis Mouse Model Nutrients. 2021 Apr; 13(4): 1090.
3. Yoon-Hwan Kim, Tae Hyeong Kim, Min Soo Kang, Jin-Ok Ahn, **Jung Hoon Choi***, Jin-Young Chung. Comparison of the presentation of atopic dermatitis induced by trinitrochlorobenzene and house dust mite in NC/Nga mice J Vet Sci. 2020 Jul; 21(4): e59.
4. Sumin Yun, Woosuk Kim, Min Soo Kang, Tae Hyeong Kim, Yoonhwan Kim, Jin-Ok Ahn, **Jung Hoon Choi**, In Koo Hwang, Jin-Young Chung. Neuropathological changes in dorsal root ganglia induced by pyridoxine in dogs. BMC Neurosci. 2020; 21: 11.

Xiaoxue XU

1. Deming Liu, **Xiaoxue Xu**, Yi Du, Jiayan Liao, Shihui Wen, Xiaotong Dong, Yan Jin, Lei Liu, Dayong Jin, John A. Capobianco, Dezhen Shen. Reconstructing the Surface Structure of NaREF4 Upconversion Nanocrystals with a Novel K+ Treatment. *Chem. Mater.* 2021, 33, 7, 2548–2556 March 2021.
2. Yongliang Chen, **Xiaoxue Xu**, Chi Li, Avi Bendavid, Mika Westerhausen, Carlo Bradac, Milos Toth, Igor Aharonovich, Toan Trong Tran. Bottom-Up Synthesis of Hexagonal Boron Nitride Nanoparticles with Intensity-Stabilized Quantum Emitters. Small. In press March 2021.
3. Hongfang Li, Yahui Li, Kai Wang, Liyan Lai, **Xiaoxue Xu**, Bin Sun, Zhuoqing Yang, Guifu Ding. Ultra-high sensitive micro-chemo-mechanical hydrogen sensor integrated by palladium-based driver and high-performance piezoresistor. International Journal of Hydrogen Energy. 2021, 46, 1, 1434-1445. January 2021.
4. ZX Deng, JW Tao, W Zhang, HJ Mu, HJ Wu, YB Wang, **XX Xu**, W Zheng. Effect of protein adsorption on electrospun hemoglobin/gelatin-MWCNTs microbelts modified electrode: Toward electrochemical measurement of hydrogen peroxide. 2021, 257, 123827. January 2021.
5. Guohua Jia and Bing-Jie Ni Derek Hao, Chuangwei Liu, **Xiaoxue Xu**, mehran kianinia, Igor Aharonovich, Xiaojuan Bai, Xiaoqing Liu, Zhijie Chen, Wei Wei. Surface defect-abundant one-dimensional graphitic carbon nitride nanorods boost photocatalytic nitrogen fixation. New J. Chem., 2020, 44, 20651-20658. November 2020.
6. Sarah Meyer, Raquel Gonzalez de Vega, **Xiaoxue Xu**, Ziqing Du, Philip A Doble, David Clases. Characterization of Upconversion Nanoparticles by Single-Particle ICP-MS Employing a Quadrupole Mass Filter with Increased Bandpass. Analytical chemistry 2020,

92, 22, 15007-15016. November 2020.

7. Christian Clarke, Mandeep Singh, Sherif Abdulkader Tawfik, **Xiaoxue Xu**, Michelle JS Spencer, Rajesh Ramanathan, Philipp Reineck, Vipul Bansal, Cuong Ton-That. Mono-to few-layer non-van der Waals 2D lanthanide-doped NaYF4 nanosheets with upconversion luminescence. 2D Materials 2020, 8, 1, 015005. October 2020.
8. Laixu Gao, Xuchen Shan, **Xiaoxue Xu**, Yongtao Liu, Baolei Liu, Sonquan Li, Chenshuo Ma, Dayong Jin, Fan Wang. Video-rate upconversion display from optimized lanthanide ion doped upconversion nanoparticles. Nanoscale, 2020,12, 18595-18599. June 2020.
9. ZX Deng, JW Tao, LJ Zhao, W Zhang, YB Wang, HJ Mu, HJ Wu, **XX Xu**, W Zheng. Effect of protein adsorption on bioelectrochemistry of electrospun core-shell MWCNTs/gelatin-Hb nanobelts on electrode surface. Process Biochemistry, 2020, 96, 73-79. June 2020.
10. Ziqing Du, Abhishek Gupta, Christian Clarke, Matt Cappadona, David Clases, Deming Liu, Zhuoqing Yang, Shawan Karan, William S Price, **Xiaoxue Xu***. Porous upconversion nanostructures as bimodal biomedical imaging contrast agents. The Journal of Physical Chemistry C 124 (22), 12168-12174. May 2020.

3. Application & acquisition status of KAKENHI and other external grants

Ruda LEE

1. CRDF Global female young researcher grant, Applied (Principal Investigator)
2. Mitsubishi young researcher grant, Applied (Principal Investigator)

Yong Il PARK

1. National Research Foundation of Korea (NRF), Basic Science Research Program, 2020.06.01~2021.05.31 (Principal Investigator)
2. National Research Foundation of Korea (NRF), Korea Research Fellowship (KRF) for Postdoctoral Researchers, 2020.08.01~2022.12.31 (Principal Investigator)
3. Korea Basic Science Institute, 2021 Research Facility Council Development Support Project, 2021.04.01~2021.11.30 (Principal Investigator)
4. National Research Foundation of Korea (NRF), Basic Science Research Program, Applied (Principal Investigator)

Jung Hoon CHOI

1. National Research Foundation of Korea funded by the Ministry of Education (NRF-2019R1I1A3A01061857) (Principal Investigator)

Xiaoxue XU

N/A

4. Application & acquisition status of industrial property rights

Ruda LEE

N/A

Yong Il PARK

N/A

Jung Hoon CHOI

N/A

Xiaoxue XU

N/A

No. 5-15	Deep Learning for Hydrology		
Research Field	Environmental Science		
Unit Coordinator			
Name	Kei ISHIDA		
Affiliation	Center for Water Cycle and Marine Environmental and Disaster Management Email: keiishida@kumamoto-u.ac.jp	Title	Associate Professor
Unit Members			
Name	Affiliation/Title		
Motoki AMAGASAKI	Faculty of Advanced Science and Technology (FAST), Kumamoto University Associate Professor		
Masato KIYAMA	Faculty of Advanced Science and Technology (FAST), Kumamoto University Assistant Professor		
Ali ERCAN	University of California, USA Assistant Professor		
Tonbi TU	Sun Yat-Sen University Associate Professor		

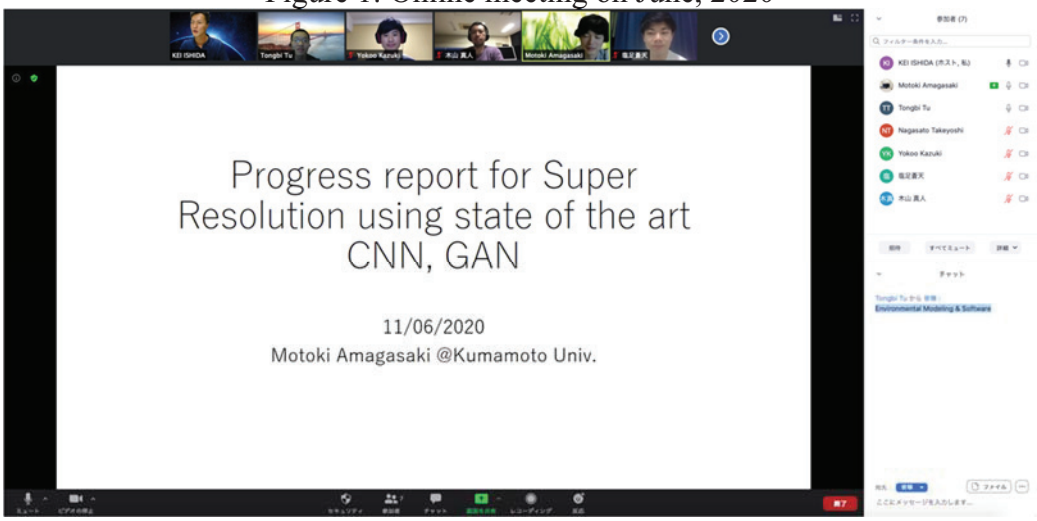
Details of activities

1. Overview of achievements

The objectives of this study are to apply new machine learning techniques to hydrological issues, and meanwhile develop new machine learning techniques with hydrological data. In this fiscal year (second year), because of the situation of COVID-19, we could not go abroad, and then we could not meet together. However, we had online meetings. For example, we had an online meeting with all the research unit members and our students in June, 2020. Then, we had online meetings with some of the members in December, 2020 and in January and February, 2021. In addition, we had discussions on phone several times.

We worked on several topics. First, we used recurrent neural networks to implement rainfall-runoff models in Japan. We had presentations based on the results at 2020 AGU Fall Meeting. The conference paper based on the results was accepted by ICGOES 2021. Second, we used convolutional neural network (CNN) to estimate precipitation from three-dimensional atmospheric data. We had presentations based on the results at 2020 AGU Fall Meeting. A conference paper was accepted by ICGOES 202, and a conference paper was published on IEICE. Then, a journal paper in Japanese was published on Annual journal of Hydraulic Engineering, JSCE. In addition, we used Generative Adversarial Network (GAN) to increase the resolution of sea surface temperature data. A conference paper was published on IEICE. We are now preparing to submit several papers based on these results.

Figure 1: Online meeting on June, 2020



2. Presentations & Publications

Poster Presentations:

1. Kazuki Yokoo, Kei Ishida , Takeyoshi Nagasato, Masato Kiyama and Motoki Amagasaki: Behavior of International Valiables Long and Short-Term Memory Neural Network for Rainfall-Runoff Modeling, 2020 AGU Fall Meeting, Dec. 2020, San Francisco, California.
2. Takeyoshi Nagasato, Kei Ishida , Kazuki Yokoo, Masato Kiyama and Motoki Amagasaki: Comparison between 2D-CNN a 3D-CNN for precipitation downscaling, 2020 AGU Fall Meeting, Dec. 2020, San Francisco, California.

Conference Papers:

1. Kazuki Yokoo, Kei Ishida, Takeyoshi Nagasato, Ali Ercan, and Tongbi Tu : Camparison of three recurrent neural networks for rainfall-runoff modelling at a snow-dominated watershed, International Conference on Geological Engineering And Geosciences (ICGOES 2021), Mar. 2021(accepted)
2. Takeyoshi Nagasato, Kei Ishida , Kazuki Yokoo, Masato Kiyama and Motoki Amagasaki: Effects of the spatial and temporal resolution of meteorological data on the accuracy of precipitation estimation by means of CNN, International Conference on Geological Engineering And Geosciences (ICGOES 2021), Mar. 2021(accepted)
3. Tomoki Izumi, Motoki, Amagasaki, Kei Ishida, and Masato Kiyama: Super resolution for sea surface temperature with CNN and GAN, IEICE, vol. 120, no. 302, NC2020-28, pp. 1-6, 2020. (In Japanese)
4. Takanori Ito, Motoki, Amagasaki, Kei Ishida, Masato Kiyama, and Masahiro Iida: Examination of precipitation estimation using atmospheric variables, IEICE, vol. 120, no. 331, NC2020-34, pp. 13-17, 2021(in Japanese)

Journal Papers:

1. Takeyoshi Nagasato, Kei Ishida, Makoto Ueda, Kazuki Yokoo, Masato Kiyama and Motoki Amagasaki: Characteristics of precipitation downscaling by means of deep learning method, Annual journal of Hydraulic Engineering, JSCE 65, I_373-378, 2020. (In Japanese)

3. Application & acquisition status of KAKENHI and other external grants

None

4. Application & acquisition status of industrial property rights

None

No. 5-16	Environmental Impacts of Ionic Solutes		
Research Field	Environmental Science		
Unit Coordinator			
Name	Shin-Ichi OHIRA		
Affiliation	Faculty of Advanced Science and Technology Email: ohira@kumamoto-u.ac.jp	Title	Associate Professor
Unit Members			
Name	Affiliation/Title		
C. Phillip SHELOR	Department of Chemistry, University of Texas at Arlington, USA Assistant Research Professor		
Jian MA	College of the Environment and Ecology, Xiamen University, CHINA Professor		
Yuta NAKASHIMA	Faculty of Advanced Science and Technology (FAST), Kumamoto University Associate Professor		

Details of activities

1. Overview of achievements

This research unit is targeted “ion” especially in environment. Ions plays an important role in the environment. Ions are one of the key chemical form of the global cycles and observed in marine, soil, river/lake, atmosphere, and living cells. In the research unit, the specialists of analytical chemistry, marine chemistry, and cell science are gathered worldwide. In 2020, we could not meet face to face, but we had several on-line meetings. The on-line meetings are following:

1) Drs Ohira and Ma (July 6, 2020): They discussed about the research progress and grant applications
2) Drs Ohira and Ma (Nov. 29, 2020): They discussed about the new research topic, arsenic speciation analysis.
3) Drs Ohira and Shelor (Feb. 1, 2020): They discussed about the computational approach for universal detection.

The members obtained research progresses. Drs. Ohira and Shelor developed universal detection system targeted organic acids. The method can obtain the sample concentration not by conventional calibration procedure but theoretical calculation. Now, they are preparing the manuscript. Drs. Ma and Ohira targeted ionic solutes in marine. Presently they studied for the determination methods to determine phosphate, Fe(II), and arsenic species. Also, they are preparing grants application for collaborative study.

Dr. Nakashima developed the method to determine the cancer cell in blood. The method can detects 1 of cancer cell from 10^8 of blood cells selectively. The collaborative study with company is also going.

2. Presentations & Publications

Presentations Total 15 and invited lecture 1

Publications Total 14

- K. Owen, K. Saeki, J.D. Warren, A. Bocconcelli, D. Wiley, S. Ohira, A. Bombosch, K. Toda*, D.P. Zitterbart*, Natural Dimethyl Sulfide Gradients would Lead Marine Predators to Higher Prey Biomass, *Communications Biology*, 4, accepted on Jan. 6, 2021.
- Y. Sugo, R. Miyachi, Y. Maruyama, S. Ohira*, M. Mori*, N.S. Ishioka, K. Toda, Electrodialytic Handling of Radioactive Metal Ions for Preparation of Tracer Reagents, *Analytical Chemistry*, **92**, 14953−14958 (2020). [Cover page]
- K. Abe, K. Shimohira, Y. Miki, Y. Hirose, S. Ohira, Kei Toda*, Measurement Device for Ambient Carbonyl Sulfide by Means of Catalytic Reduction Followed by Wet Scrubbing/Fluorescence Detection, *ACS Omega*, **5**, 25704–25711 (2020).
- S. Ohira*, T. Sakaki, R. Miyachi, A. Otsubo, A. Umemoto, Y. Kuwahara, K. Toda, Miniaturized Crossflow Ion Transfer Device for Post-column Enrichment in Ion Chromatography, *Talanta*, **216**, 120989 (2020).
- M. Taira, K. Sakakibara, K. Saeki, S. Ohira, K. Toda*, Determination of Oxoanions and Water-soluble Species of Arsenic, Selenium, Antimony, Vanadium, and Chromium Eluted in Water from Airborne Fine Particles (PM2.5): Effect of Acid and Transition Metal Content of Particles on Heavy Metal Elution, *Environmental Science: Processes and Impacts*, **22**, 1514–1524 (2020).
- W.C. Nugraha, H. Nagai, S. Ohira*, K. Toda, Semi-Continuous Monitoring of Cr(VI) and Cr(III) during a Soil Extraction Process by Means of an Ion Transfer Device and Graphite Furnace Atomic Absorption Spectroscopy, *Analytical Sciences*, **36**, 617–620 (2020).
- S. Kumamoto, K. Nakatake, S. Fukuyama, K. Yasuda, Y. Kitamura, M. Iwatsuki, H. Baba, T. Ihara, Y. Nakanishi, Y. Nakashima*, A dynamically deformable microfilter for selective separation of specific substances in microfluidics, *Biomicrofluidics*, **14**, 064113, 2020.

3. Application & acquisition status of KAKENHI and other external grants

Total 15 grants

- S. Ohira, Grant-in-Aid for Scientific Research (C) as representative, 2017 – 2020FY 400kJPY for 2020
- S. Ohira, Grant-in-Aid for Scientific Research (B), 2020 – 2023FY 1,400k JPY for 2020
- S. Ohira, Adaptable and Seamless Technology transfer Program through targetdriven R&D (A-STEP), 2019 – 2020FY 775k JPY for 2020
- S. Ohira, Collaborative study with two companirs, total 1,600kJPY for 2020.
- Y. Nakashima, Grant-in-Aid for Challenging Research (Exploratory) as representative, 2020 – 2021FY 2,990k JPY for 2020
- Y. Nakashima, Grant-in-Aid for Scientific Research (B) as representative, 2019 – 2022FY 2,200k JPY for 2020
- Y. Nakashima, Strategic Foundational Technology Improvement Support Operation
- Y. Nakashima, Environment Research and Technology Development Fund of the Ministry, 2019–2022FY

4. Application & acquisition status of industrial property rights

One patent was registered. (Dr. Ohira, Patent JP 6836028).

Two patents are under preparation.

No. 5-17	Radio Astronomy		
Research Field	Next-generation Technology		
Unit Coordinator			
Name	Keitaro TAKAHASHI		
Affiliation	Faculty of Advanced Science and Technology Email: keitaro@kumamoto-u.ac.jp	Title	Associate Professor
Unit Members			
Name	Affiliation/Title		
Rachel WEBSTER	The University of Melbourne, Australia Professor		
Bart PINDOR	The University of Melbourne, Australia Academic		
Shintaro YOSHIURA	National Astronomical Observatory of Japan JSPS Researcher		
Takuya AKAHORI	National Astronomical Observatory of Japan Researcher		
Takeshi FUKUSAKO	Faculty of Advanced Science and Technology (FAST), Kumamoto University Professor		

Details of activities

1. Overview of achievements

The purpose of our project is to detect radio waves, 21cm line, from neutral hydrogen in inter-galactic space during the Epoch of Reionization. Our group consists of Kumamoto University, National Astronomical Observatory of Japan and the University of Melbourne and we are operating a radio telescope named Murchison Widefield Array (MWA) to observe radio waves from the universe. However, the radio-wave signal we are interested in is so weak that we need to remove very bright foreground emission from our Galaxy to detect the signal.

This year, we continued to observations of 21cm line from the Epoch of Reionization with a radio telescope, Murchison Widefield Array. It is very important to conduct a precise calibration in order to detect the weak signal. We studied a detailed method of calibration for redundant array, which has multiple baselines with the same baseline vector. Further, we investigated the detectability of 21cm-line signal by cross-correlation with Lyman-alpha emitter and compared several models of Lyman-alpha emitter distribution.

Another important factor of radio astronomy is the reduction of RFI (radio frequency interference). We conducted an experiment on the measurement of RFI with two different types of antennas and discussed a possible method for RFI mitigation by cancelling it by the cross correlation between the outputs of the two antennas.

2. Presentations & Publications

H. Kumamoto, S. Dai, S. Johnston, M. Kerr, R. M. Shannon, P. Weltevrede, C. Sobey, R. N. Manchester, G. Hobbs, and K. Takahashi,
“Flux density variability of 286 radio pulsars from a decade of monitoring”
Monthly Notices of the Royal Astronomical Society 501 (2021) 4490-4513, 03/2021

N. Yonemaru, S. Kuroyanagi, G. Hobbs, K. Takahashi, X.-J. Zhu, W. A. Coles, S. Dai, E. Howard, R. Manchester, D. Reardon, C. Russell, R. Shannon, N. Thyagarajan, R. Spiewak, J.-B. Wang,
“Searching for gravitational wave bursts from cosmic string cusps with the Parkes Pulsar Timing Array”
Monthly Notices of the Royal Astronomical Society 501 (2021) 701-712, 02/2021

Suchetha Cooray, Tsutomu T. Takeuchi, Takuya Akahori, Yoshimitsu Miyashita, Shinsuke Ideguchi, Keitaro Takahashi and Kiyotomo Ichiki,
“An Iterative Reconstruction Algorithm for Faraday Tomography”
Monthly Notices of the Royal Astronomical Society 500 (2021) 5129-5141, 01/2021

Zhang, Zheng; Pober, Jonathan C.; Li, Wenyang; Hazelton, Bryna J.; Morales, Miguel F.; Trott, Cathryn M.; Jordan, Christopher H.; Joseph, Ronniy C.; Beardsley, Adam; Barry, Nichole; Byrne, Ruby; Tingay, Steven J.; Chokshi, Aman; Hasegawa, Kenji; Jacobs, Daniel C.; Lanman, Adam; Line, Jack L. B.; Lynch, Christene; McKinley, Benjamin; Mitchell, Daniel A. Murray, Steven; Pindor, Bart; Rahimi, Mahsa; Takahashi, Keitaro; Wayth, Randall B.; Webster, Rachel L.; Wilensky, Michael; Yoshiura, Shintaro; Zheng, Qian,
“The Impact of Tandem Redundant/Sky-Based Calibration in MWA Phase II Data Analysis”
Publications of the Astronomical Society of Australia 37 (2020) article id. e045, 11/2020

Yoshiura, Shintaro; Oguri, Masamune; Takahashi, Keitaro; Takahashi, Tomo,
“Constraints on Primordial Power Spectrum from Galaxy Luminosity Functions”
Phys. Rev. D 102 (2020) 083515, 10/2020

Haruya Eguchi, Masaki Suzuki, Yoshimitsu Miyashita, Shinsuke Ideguchi, Keitaro Takahashi,
“Faraday dispersion function of disk galaxies with axisymmetric global magnetic fields I”
Astrophys. J. 899 (2020) id.122, 08/2020

Yuta Shiohira, Yuka Terada, Den Mukuno, Yuka Fujii, Keitaro Takahashi,
“Microlensed Radio Emission from Exoplanets”
Monthly Notices of the Royal Astronomical Society 495 (2020) 1934-1942, 05/2020

Yoshiura, Shintaro; Takahashi, Keitaro; Takahashi, Tomo,
“Probing Small Scale Primordial Power Spectrum with 21cm Line Global Signal”
Phys. Rev. D 101 (2020) 083520, 04/2020

Kenji Kubota, Akio. K. Inoue, Kenji Hasegawa, Keitaro Takahashi,
“Detectability of 21cm signal during the Epoch of Reionization with 21cm-Lyman-α emitter cross-correlation. III. Model dependence”
Monthly Notices of the Royal Astronomical Society 494 (2020) 3131–3140, 04/2020

Naoyuki Yonemaru, Keitaro Takahashi, Hiroki Kumamoto, Shi Dai, Shintaro Yoshiura and Shinsuke Ideguchi,

“Artificial neural networks for selection of pulsar candidates from the radio continuum surveys” Monthly Notices of the Royal Astronomical Society 494 (2020) 1035–1044, 04/2020

3. Application & acquisition status of KAKENHI and other external grants

Kiban B (rep: Keitaro Takahashi), accepted (2021-2024)
Kiban B (rep: Hideyuki Kobayashi (National Astronomical Observatory of Japan)), rejected
Kiban A (rep: Naoshi Sugiyama (Nagoya University)), accepted (2021-2025)

4. Application & acquisition status of industrial property rights

N/A

No. 5-18	Plant Stem Cells and Regeneration		
Research Field	Advanced Green Bio		
Unit Coordinator			
Name	Mitsuhiro AIDA		
Affiliation	International Organization for Advanced Science and Technology Email: m-aida@kumamoto-u.ac.jp	Title	Professor
Unit Members			
Name	Affiliation/Title		
Yoshihisa IKEDA	Centre of the Region Haná for Biotechnological and Agricultural Research Czech Advanced Technology and Research Institute (CATRIN) Palacký University Olomouc /Junior Researcher		

1. Overview of achievements

During a period of the second year of this research unit, we proceeded researches according to our previously proposed plan, that is, to corroborate the underlying regulatory mechanism of the *CUP-SHAPED COTYLEDON 1* (*CUC1*) gene expression at the transcriptional level by two distinct classes of AP2/ERF transcription family members; one class is B1b subfamily comprised of members encoding the transcription activator that involves *ENHANCER OF SHOOT REGENERATION1 (ESR1)* and *ESR2* and the second is B1a comprised of 6 members encoding the transcriptional repressor that encompasses *ETHYLENE RESPONSE FACTOR 4 (ERF4), ERF8, ERF9, ERF10, ERF11,* and *ERF12*. During the second term, we transformed the wild type Col plants with the two fluorescent reporter constructs *CUC1p:CUC1-GFP* and *CUC1p:CUC1m7-GFP*, each expressing the microRNA164 sensitive and resistant transcripts of CUC1-GFP fusions, respectively, and several independent lines were obtained to analyze CUC1 expression in mutant backgrounds of *ESR* and *ERF* genes. In addition, another reporter line, M0233, which reflects promoter activity of *CUC1* (Cary et al, 2002 Plant J. 32. 867-877) was used to edit *ESR1* and *ESR2* coding regions by CRISPR/Cas9. In the T2 generation, we were able to obtain individual lines containing different mutations: two versions of single-base-pair insertions (A:T and T:A) in *ESR2* at 175 bp downstream from ATG and a single-base pair insertion of A:T in *ESR1* at 170 bp downstream from ATG. Hereafter, they are termed *esr2-175* or *esr1-170*, respectively. All mutations resulted in the production of a premature stop codon immediately after the insertion, suggesting that these mutant alleles were null. The original M0223 reporter line is in the C24 accession background. We noticed that *esr2-175* homozygous mutant plants without *pDe-Cas9* transgene, exhibited substantially delayed flowering phenotype, which resembled that of *esr1-1;esr2-2* double mutant in the Col-0 accession background, but not in the *esr2-2* single mutant (our unpublished data). We are going to make a cross to obtain the *esr1-170;esr2-175* double mutant to compare *CUC1* expression with that in the wild-type background.

To gain insight into the role of subclass B1a *ERF* repressor in shoot meristem development, translational *GFP* fusion reporter lines were made and more than 20 individual lines for *ERF4, ERF9,* and *ERF12* were obtained. We intend to analyze the expression pattern in the near future. At last, we were able to publish a perspective article in Frontiers in Plant Science. The majority of

the allocated budget for the second year was used for the article processing fee for this publication.

2. Presentations & Publications
Ikeda, Y., Zalabák, D., Kubalová, I., Králová, M., Brenner WG., Aida M. (2021) Interpreting Cytokinin Action as Anterograde Signaling and Beyond. Front. Plant Sci. 12:641257. doi: 10.3389/fpls.2021.641257

3. Application & acquisition status of KAKENHI and other external grants
Mitsuhiro Aida, Grant-in-Aid for Scientific Research on Innovative Areas (The Japan Society for the Promotion of Science), Principles of pluripotent stem cells underlying plant vitality, "Establishment of plant hormone microenvironment during shoot stem cell formation," April 2020-March 2022.

4. Application & acquisition status of industrial property rights
N/A

No. 5-19	Development of microbially-aided carbon sequestration technology		
Research Field	Green Energy		
Unit Coordinator			
Name	Atsushi SAINOKI		
Affiliation	International Organization for Advanced Science and Technology Email: atsushi_sainoki@kumamoto-u.ac.jp	Title	Associate Professor
Unit Members			
Name	Affiliation/Title		
Kazunori NAKASHIMA	Hokkaido University, Japan Associate Professor		
Murat KARAKUS	Adelaide University, Australia Associate Professor		
Akira SATO	Faculty of Advanced Science and Technology (FAST), Kumamoto University Associate Professor		
Hiroaki ITO	Faculty of Advanced Science and Technology (FAST), Kumamoto University Assistant Professor		

This project entitled “development of microbially-aided carbon sequestration technology” can be divided into two parts: enhancement of carbon precipitation using anaerobic microbes and closure of rock fractures in an aquifer with a grout technology using aerobic microbes.

Experiments for anaerobic microbes

For the first one, this year was predominantly spent on preparing reagents and culture media in order to develop clusters of anaerobic microbes as well as on preparing experimental apparatus. We have finished preparing almost all culture media planned and broken one rock sample into small pieces under an anaerobic condition. In 2021, we will place the rock fragments on the culture media under an anaerobic condition and aim at observing clusters of microbes that contribute to the enhancement of carbon precipitation.

Experiments for aerobic microbes (grout technology)

Regarding the second one (application of the grout technology into carbon sequestration), during the fiscal year of 2020, we have performed the following two experiments: i) creation of a grout material with urease, ii) image analysis of grouted rock samples with an industrial X-ray CT scanner.

i) Creation of a grout material with urease

We have investigated the effect of urease concentrations on the chemical reaction rate of calcium chloride and urea that results in calcium carbonate. It is found from Fig. 1 that as the urease concentration increases, more $CaCO_3$ is precipitated, giving an insight into the necessity of optimizing urease concentration when applying the grout technology to carbon sequestration. This is because extremely high reaction rates would prevent grouts from permeating a fractured

rock mass, whilst low reaction rate does not effectively fill fractures in a rock mass.

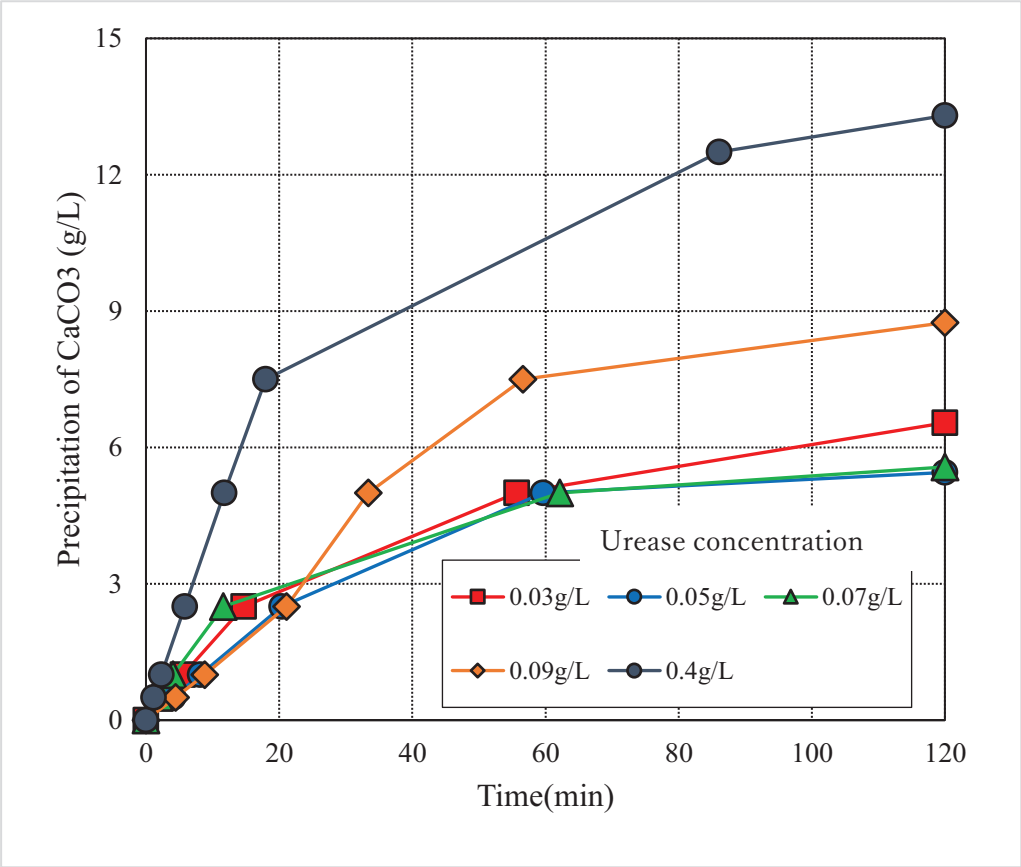


Fig. 1: Effect of urease concentration of the precipitation rate of $CaCO_3$

ii) Image analysis of grouted rock samples with an industrial X-ray CT scanner

X-ray CT images were taken for rock samples to which grouting was performed using urea, carbon chloride, and urease. Fig. 2 shows the difference in specific density between an original rock sample and grouted one. The warm color in the picture corresponds to a region with high specific density, indicating calcium carbonate precipitated as a result of grouting. As can be seen, the grouted region is spatially dotted in the rock sample. This indicates that calcium carbonate was effectively precipitated, thus contributing to the reduction of permeability.

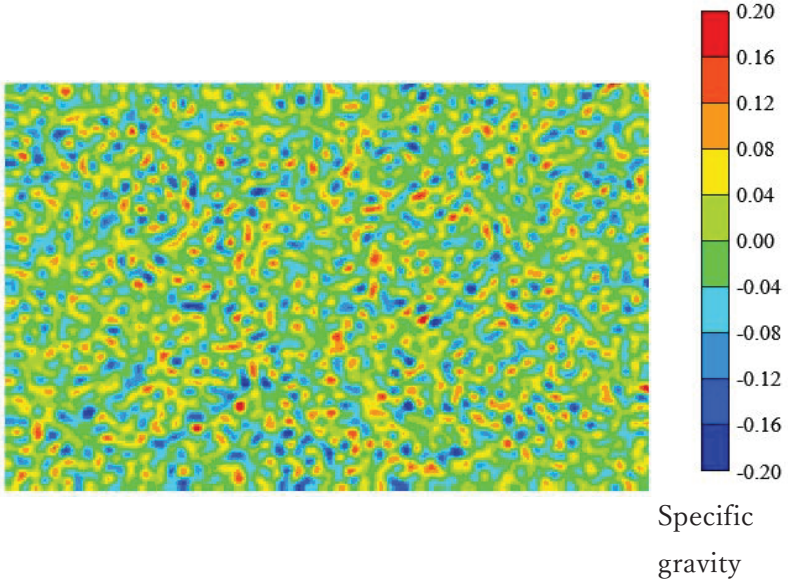


Fig. 2: Difference in specific density between an original rock and grouted samples

Plan to apply for Kakenhi

As shown, preliminary experiments were conducted for this research project in 2020. In the fiscal year of 2021, we will continue to conduct preliminary experiments. Specifically, regarding the experiment for anaerobic microbes, we will obtain further rock samples from a deep underground coal mine located in Hokkaido, with which we will try to find a new type of microbes that contributes to the generation of calcium carbonate under an anaerobic condition. In addition, rock samples will be also collected from mountain tunnels. As for the experiment of grouting, new types of urease will be tested in 2021 because the urease used in 2020 was found to have a very high enzyme activity that may not be suitable for filling rock fractures in an aquifer to which CO_2 is injected. As such, we have purchased several types of urease with various enzyme activities. Using the different ureases, we aim to select a urease with the most appropriate enzyme activity. Based on the result, we aim to apply for Kakenhi in 2022.

No. 5-20	Advanced Biomedical Evaluation System		
Research Field	Nano Material Science		
Unit Coordinator			
Name	Makiko KOBAYASHI		
Affiliation	Faculty of Advanced Science and Technology Email: kobayashi@cs.kumamoto-u.ac.jp	Title	Associate Professor
Unit Members			
Name	Affiliation/Title		
Toshitaka YAMAKAWA	Faculty of Advanced Science and Technology (FAST), Kumamoto University Associate Professor		
Masayuki TANABE	Faculty of Advanced Science and Technology (FAST), Kumamoto University Assistant Professor		
Rajendra Udyavara ACHARY	Ngee Ann Polytechnic, Singapore Senior Research Fellow		
OH SHU Liu	Ngee Ann Polytechnic, Singapore Project Engineer		
RU TAN San	National Heart Centre, Singapore Doctor		

1. Overview of achievements
   Prototype ultrasonic sensors for Cardiovascular disease (CVD) have been manufactured and feasible measurements were operated by Research unit members in Kumamoto University as shown in Fig. 1. M mode images were successfully obtained. Research unit members in Ngee Ann Polytechnique carried out 2kinds of signal processing as shown in Fig. 2. As a result, there are clear differences between normal, occlusion, and release conditions as shown in Fig. 3.

Fig. 1 Ultrasonic sensor and measurement setup.

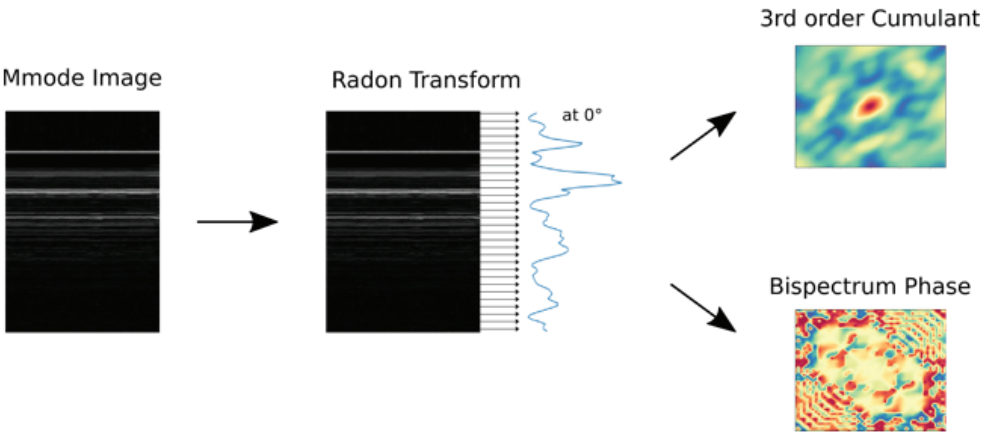


Fig. 2 Proposed signal processing system

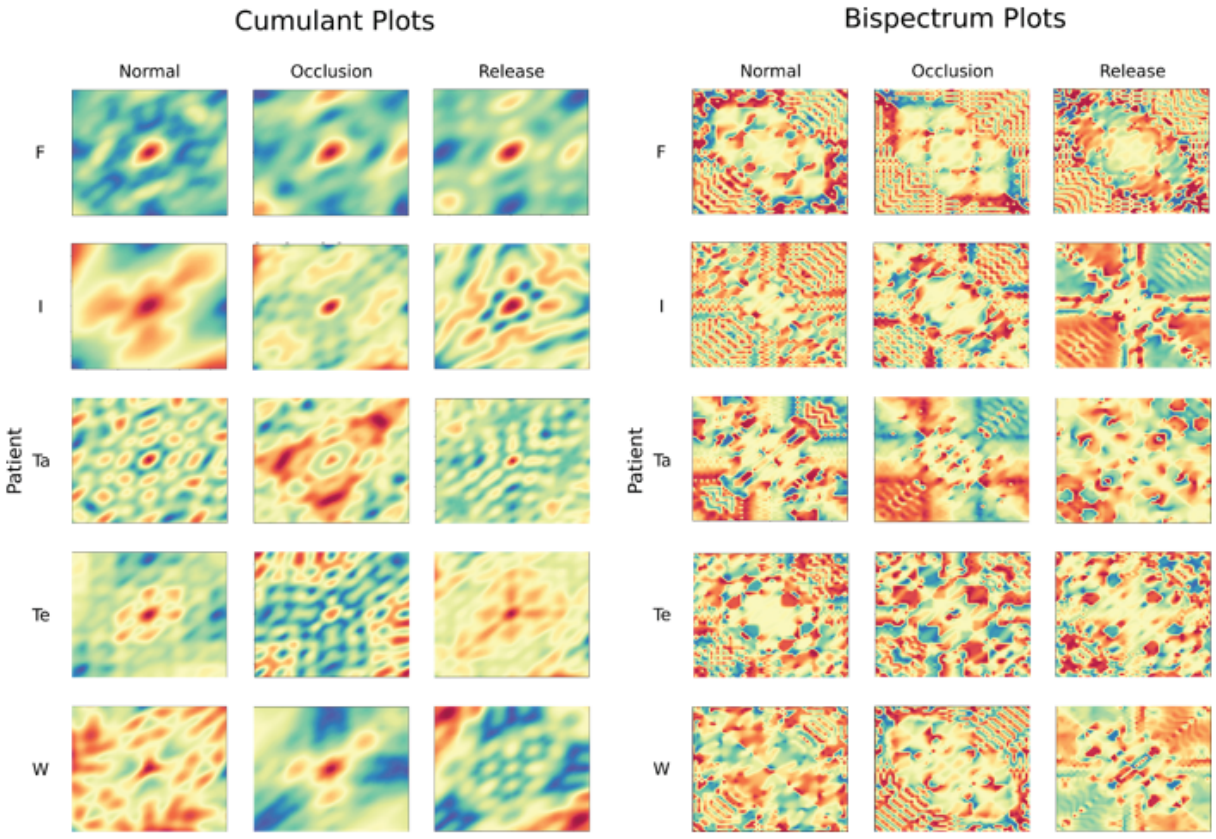


Fig. 3 Measurement results

2. Presentations & Publications
O. S. Lih, V. Jahmunah, C. P. Ooi, R. S. Tan , E. J Ciaccio, T. Yamakawa, M. Tanabe, M. Kobayashi, U. R. Acharya*, "Classification of heart sound signals using a novel deep WaveNet model," Computer Methods and Programs in Biomeducune, 196, 105604, 2020. (*corresponding)

3. Application & acquisition status of KAKENHI and other external grants
N/A

4. Application & acquisition status of industrial property rights
PCT application (PCT/SG2020/050538)

No. 5-21	Bio-inspired Functional Molecular System		
Research Field	Nano Material Science		
Unit Coordinator			
Name	Yutaka KUWAHARA		
Affiliation	Faculty of Advanced Science and Technology Email: kuwahara@kumamoto-u.ac.jp	Title	Assistant Professor
Unit Members			
Name	Affiliation/Title		
Tomoyasu MANI	University of Connecticut, USA / Assistant Professor		
Yann FERRAND	University of Bordeaux, France / Research Director, Group Leader		
Céline OLIVIER	University of Bordeaux, CNRS, France / Research Associate		
Etsuko FUJITA	Brookhaven National Laboratory, USA / Senior Chemist		

Details of activities

1. Overview of achievements

In this unit, we have developed bio-inspired functional molecular systems with chirality for controlling of their function. Three projects for applications of photonic (P1), electronic and magnetic (P2), catalytic reaction in artificial photosynthesis (P3) are conducted by the members from Kumamoto University (KU), Brookhaven National Laboratory (BNL), USA, University of Connecticut (UC), USA, and University of Bordeaux (UB), France.

1-1. Collaboration with the BNL, USA, related with the project P3

The unit members of the BNL and the KU could not alternately visit this year. We communicated with Dr. Fujita, Visiting Professor of IROAST, and other collaborators about research results to submit for an international journal.

1-2. Collaboration with the UC, USA, related with the projects P1 and P2

The KU and UC members could not alternately visit this year. Dr. Kuwahara had several discussions about our recent research results with Prof. Mani, Visiting Associate Professor of IROAST, online.

1-3. Collaboration with the UB, France, related with the project P1

The KU members could not visit and invite French collaborators, Dr. Ferrand and Dr. Olivier, of the UB this year. The KU group received mixed compounds from UB and purified the compounds by a special technique of the KU group. We applied to a research grant for international collaboration, Open Partnership Joint Research Projects, JSPS, with Y.F. and C.O. of the France group (*rejected*).

2. Presentations & Publications

Presentations

(i) M. Matsunaga, Y. Kuwahara, T. Iwamoto, S. Hamada, H. Ihara, M. Takahuji, Fabrication and evaluation for supramolecular assemblies of metal complexes induced by cationic glutamide derivatives as templates, The 69th SPSJ Annual Meeting (Japanese), May 28, 2020.
(ii) S. Mashima, N. Ryu, Y. Kuwahara, M. Takafuji, H. Jintoku, R. Oda, H. Ihara, Porphyrin-functionalized chiral molecular assembly for multi-chiro-informative system, The 69th SPSJ Annual Meeting (Japanese), May 28, 2020.

Publication
(iii) E. Fujita, B. Dimarco, D. Polyansky, D. Grills, P. Wang, Y. Kuwahara, X. Zhao, *submitted.*
(iv) H. Ihara, M. Takafuji, Y. Kuwahara, Chiroptical Polymer Functionalized by Chiral Nanofibrillar Network, *web-published as a book chapter*, DOI: 10.5772/intechopen.96853.

3. Application & acquisition status of KAKENHI and other external grants

Granted (Ongoing in 2020)
(i) KAKEN Grant-in-Aid for Scientific Research (C), JSPS, as a PI, Direct cost (total): 3,300,000 yen, FY: 2020 – 2022.
(ii) KAKEN Grant-in-Aid for Challenging Research (Exploratory), JSPS, as a Co-I, Direct cost (total as Co-I): 1,100,000 yen, FY: 2020 – 2022.
(iii) KAKEN Fund for the Promotion of Joint International Research (Fostering Joint International Research), JSPS, as a PI, Direct cost (total): 9,200,000 yen, FY: 2017 – 2019 (extended until 2020).

No. 5-22	Nanomaterials processing for medical, cosmetic, and environmental applications		
Research Field	Nano Material Science, Green Energy, Environmental Science		
Unit Coordinator			
Name	Mitsuru SASAKI		
Affiliation	Institute of Industrial Nanomaterials (IINa) Kumamoto University Email: msasaki@kumamoto-u.ac.jp	Title	Associate Professor

Unit Members	
Name	Affiliation/Title
Olivier BOUTIN	Aix Marseille University, France Professor
Bushra AL-DURI	The University of Birmingham, UK Professor
Hosano HAMID	Institute of Industrial Nanomaterials (IINa), Kumamoto University Professor
Marleny D.A. SALDAÑA	University of Alberta, Canada Professor
M. J. COCERO	Valladolid University, Spain Professor
Elisabeth BADENS	Aix Marseille University, France Professor
Rodolfo M. IBARRA	Universidad Autonoma de Nuevo León, Mexico Associate Professor
Cinthya ISSAI	Graduate School of Science and Technology (GSST), Kumamoto University Ph.D. candidate

Details of activities

1. Overview of achievements

1.1. Quick degradation of nitrogen- or sulfur-containing organic compounds in water.

Pulsed arc discharge was experimentally investigated as a rapid decomposition method for persistent substances in water. We used the following substances as starting materials in this study: (1) bisphenol-A, (2) dimethyldisulfide (DMDS) and (3) dimethyltrisulfide (DMTS). As a result, it was found that bisphenol A was almost decomposed within a couple of minutes to form phenol, hydroquinone,and a small amount of organic acids. It was also found that both DMDS and DMTS almost decomposed by the pulsed arc discharge. Next fiscal year we will try to do additional experiments of the substances to understand possible reaction pathways and to explore optimum operating conditions, and also try to compare reaction behavior with the other methods, especially

wet air oxidation. For clarifying the reaction pathway and mechanisms, we will continue systematic experiments and analyses with partner professors in this group.

1.2. Efficient biomass liquefaction and value-added component production with subcritical water

We tried to confirm possibility that food processing waste and nutrients in non-edible biomass can convert to value-added chemicals and functional materials using subcritical water. In this study, we aim to liquefy a food processing waste (sake lees) in subcritical water to produce aqueous solution with high contents of amino acids, ammonia, and minerals. As a result, it was found that about 40-50% of sake lees liquefied and relatively high concentration of amino acids and minerals in subcritical water at 120-140^{o}C for 4 hours by using a batch-type reactor (Yamato *et al.*, *SN Applied Sciences*, 2020). As a next step, we would like to conduct an acetic acid fermentation test using the liquefied samples to investigate the possibility of producing edible vinegars.

1.3. Nanomaterials production processes for medical and industrial fields.

We aimed to develop and establish an efficient, environmentally-friendly and feasible method for the synthesis of poly-(*N*-isopropylacrylamide) by using the gas-liquid interfacial pulsed arc discharge in water (Unpublished data). Also, we prepared a biomass-based solid acid catalyst using hydrothermal treatment. In this study, wakame, a kind of macroalgae, was employed and prepared the catalyst by the hydrothermal carbonization, gas-phase carbonization and sulfonation methods. As a result, it was found that the reactivity of the catalyst prepared from wakame was higher than that of typical solid acid catalyst Amberlyst-15 in the case of the esterification of ethanol and acetic acid (Shamala *et al.*, 2020).

2. Presentations & Publications (incl. submitted papers)

Publications

Shamala Balasubramaniam, Shohei Ninomiya, Mitsuru Sasaki*, Armando T. Quitain, Tetsuya Kida, Marleny D. A. Saldana, "Carbon-based solid acid catalyst derived from Undaria pinnatifida and its application in esterification", *Algal Research*, 55 (2021).

Kazuharu Yamamo, Katsuya Minami, Shoji Hirayama, Yuriko Hoshino, Munehiro Hoshino, Tetsuya Kida, Mitsuru Sasaki*, Yukihiro Mtsumori, "Recovery and liquefaction of nitrogen-containing component and minerals from food processing wastes of vinegar using subcritical water", *SN Applied Sciences*, 2(12) (2020).

Presentations

Shamala Balasubramaniam, Mitsuru Sasaki*, Quitain Armando, Tetsuya Kida, Marleny Saldaña, "Production of pyro-hydrochar from marine biomass, Undaria pinnatifida and its application as solid acid catalyst" (#AA999), The 51st SCEJ Fall R & D conference (online), September 2020.

Koki Nonaka, Armando T. Quitain, Tetsuya Kida, Mitsuru Sasaki*, Kunio Kawamura, Tomohiro Furusato, Tetsuo Homma, "Influence of operating parameters on the linear oligopeptides production from DKP with pulsed discharge" (#M206), The 51st SCEJ R&D conference (online), September 2020.

Koki Nonaka, Armando T. Quitain, Tetsuya Kida, Mitsuru Sasaki*, Kunio Kawamura, Tomohiro Furusato, Tetsuo Honma, "Effect of Some Parameters on The Conversion of Ala-DKP to Linear Oligopeptides Using Pulsed Discharge" (#6-17), The 15th International Student Conference on Advanced Science and Technology (ICAST) 2020 Kumamoto (online), December 2020.

Ippei Yamashina, Mitsuru Sasaki*, "Elution Behavior of Aromatic Components from Oak Surface

Treated by Pulsed Arc Discharge" (#6-23), The 15th International Student Conference on Advanced Science and Technology (ICAST) 2020 Kumamoto (online), December 2020.

Ramma Kamogawa, Hiras T. Manalu, Mitsuru Sasaki*, Armando T. Quitain, Tetsuya Kida, "Hydrolysis of Rutin using solid acid catalyst under hydrothermal conditions" (#6-19), The 15th International Student Conference on Advanced Science and Technology (ICAST) 2020 Kumamoto (online), December 2020.

Ryohei Mori, Mitsuru Sasaki*, Olivier Boutin, "Decomposition of Bisphenol A Using Gas-liquid Interface Pulsed Discharge Plasma" (#6-22), The 15th International Student Conference on Advanced Science and Technology (ICAST) 2020 Kumamoto (online), December 2020.

3. Application & acquisition status of KAKENHI and other external grants

Study on chemical evolution by simulation experiments regarding the plasma processes and hydrothermal conditions with minerals under the Hadean Earth environments, KAKENHI Grant-in-Aid for Scientific Research (B) 2019-2022 (Ongoing).

Research on the aging of rice shochu using locally produced wood and its utilization, Project Research at Japan Sake and Syochu Makers Association 2021 (Ongoing).

Publications Supported by IROAST Publication Support Program

Publications Supported by IROAST Publication Support Program

No.	Name	Publication Information
1	**Takahiro Hosono** FAST	Hosono, T., Yamada, C., Manga, M. et al., "Stable isotopes show that earthquakes enhance permeability and release water from mountains," Nature Communications, 11, 2776, 2020.
2	**Hamid Hosano** IINa	Thorat, M., Sahu, S., Menezes, V., Gokhale, A., Hosano, H., "Shock Loading of Closed Cell Aluminum Foams in the Presence of an Air Cavity," Applied Sciences, 10(12), 4128, 2020.
3	**Ruda Lee** IROAST	Ueno, S., Kim, M.W., Lee, G., Park, Y.I., Niidome, T., Lee, R., "Development of ErbB2-Targeting Liposomes for Enhancing Drug Delivery to ErbB2-Positive Breast Cancer," Pharmaceutics, 12(6), 585, 2020.
4	**Ruda Lee** IROAST	Yong Il Park, Seung-Hae Kwon, Gibok Lee, Keiichi Motoyama, Min Woo Kim, Min Lin, Takuro Niidome, Jung Hoon Choi, Ruda Lee*, "pH-sensitive multi-drug liposomes targeting folate receptor β for efficient treatment of non-small cell lung cancer," Journal of Controlled Release, 330, 1-14, 2021
5	**Shinya Hosokawa** FAST	Hosokawa S., Kawakita Y., Pusztai L., Ikeda K., Otomo T., "Detailed investigations on short- and intermediate-range structures of Ge-Se glasses near the stiffness transition composition," J. Phys. Soc. Jpn., 90 024601, 12 p. 2021

Winning Awards

Winning Awards

No.	Name	Name of award/Institute /Date of receiving award
1	**Takumi Higaki** IROAST	The 6th CYTOLOGIA Encouragement Award The Japan Mendel Society December 28, 2020
2	**Takumi Higaki** IROAST	28th JSPP Young Investigator Award (2021) The Japanese Society of Plant Physiologists (JSPP) March 15, 2021
3	**Yuta Nakashima** FAST	Grand Prize TECH PLAN DEMO DAY　The 7th BIO-TECH GRAND PRIX Sep. 19, 2020
4	**Yuta Nakashima** FAST	Chiome Bioscience Award TECH PLAN DEMO DAY　The 7th BIO-TECH GRAND PRIX Sep. 19, 2020
5	**Yuta Nakashima** FAST	Tomita Pharmaceutical Award Kumamoto Tech Grand Prix Jul. 18, 2020
6	**Yuta Nakashima** FAST	Atsumaru Holdings Award Kumamoto Tech Grand Prix Jul. 18, 2020

IROAST Symposium

KU-KAIST Joint Symposium

No.	Title	Organizer	Date
1	Facilitating Collaboration in Biomedical Engineering Research The 4th KASIT-KU Workshop and Joint Symposium	**Toshio Suda** Director, IRCMS **Takashi Hiyama** Director, IROAST	Feb. 22, 2021

IRCMS: International Research Center for Medical Sciences, Kumamoto University

KU-KAIST Joint Symposium Report 1

Organizer 1	Name	Toshio Suda		
	Affiliation	IRCMS, Kumamoto University	Title	Director
Organizer 2	Name	Takashi Hiyama		
	Affiliation	IROAST, Kumamoto University	Title	Director
Symposium Title	Facilitating Collaboration in Biomedical Engineering Research The 4th KAIST-KU Workshop and Joint Symposium			
Venue	Hybrid Symposium via Zoom and at sites; KAIST IRCMS Meeting Lounge, IRCMS Kurokami South C2 (Faculty of Engineering Bldg. I), 2F Meeting room B, IROAST			
Time & Date	10:00-17:15, February 22, 2021			
Speaker's Name/ Title/Affiliation	Kobayashi Akio (KU-IMEG) Jessie Sungyun Jeon (KAIST-Department of Mechanical Engineering) Sawa Shinichiro (KU- Faculty of Advanced Science and Technology) Kurotaki Daisuke (Yokohama City University / KU-IRCMS) Jong-Eun Park (KAIST-Graduate School of Medical Science and Engineering) Tani Tokio (KU- Faculty of Advanced Science and Technology) Jinkuk Kim (KAIST-Graduate School of Medical Science and Engineering) Pilhan Kim (KAIST-Graduate School of Medical Science and Engineering) Mizuno Hidenobu (KU-IRCMS) Won-Il Jeong (KAIST-Graduate School of Medical Science and Engineering) Muramatsu Masashi (KU-IRDA) Ji Eun Oh (KAIST-Graduate School of Medical Science and Engineering) Ishiguro Kei-ichiro (KU-IMEG) Niidome Takuro (KU-Faculty of Advanced Science and Technology) Hyun Jung Chung (KAIST-Department of Biological Science) Zheng Yufeng (KU-IROAST) —Flash Talk— 1. Takizawa Lab. (KU-IRCMS) 2. Won-Il Jeong Lab. (KAIST- Graduate School of Medical Science and Engineering) 3. Kobayashi Lab. (KU- Faculty of Advanced Science and Technology)			

<table>
<tr><td></td><td colspan="4">4. Injune Kim Lab. (KAIST- Graduate School of Medical Science and Engineering)
5. Mizuno Lab. (KU-IRCMS)
6. Sada Lab. (KU-IRCMS)
7. Jae Myoung Suh Lab. (KAIST- Graduate School of Medical Science and Engineering)
8. Hayami Lab. (KU-Faculty of Advanced Science and Technology)
9. Baba Lab. (KU-IRCMS)
10. Young Seok Ju Lab. (KAIST- Graduate School of Medical Science and Engineering)
11. Ruda Lee Lab. (KU-IROAST)
12. Pilhan Kim Lab. (KAIST- Graduate School of Medical Science and Engineering)</td></tr>
<tr><td rowspan="4">Number of Participants</td><td rowspan="2">From KU</td><td>Faculty: 35 (Int'l participants: 8)</td><td rowspan="4">Total</td><td rowspan="4">75</td></tr>
<tr><td>Students: 3 (Int'l participants: 2)</td></tr>
<tr><td rowspan="2">From outside KU</td><td>Faculty: 17 (Int'l participants: 16)</td></tr>
<tr><td>Students: 20 (Int'l participants: 19)</td></tr>
</table>

(Written by Kazuki Takashima, IROAST Vice Director)

On February 22, 2021, IRCMS and IROAST of Kumamoto University held the 4th Joint Symposium with KAIST in Korea. This joint symposium was held online this time due to the spread of COVID-19 infection. The theme of the symposium was “Facilitating Collaboration in Biomedical Engineering Research”, and it aimed to create a new interdisciplinary collaboration between life sciences and engineering that has not been done before between our university and KAIST.

The symposium started with an opening address by Professor Toshio Suda, Director of IRCMS. The symposium consisted of four sessions: “Communication Biology and Engineering”, “Nucleic Acids and Bioinformatics”, “Homeostasis and Disease”, and “Biomaterials & Biotechnology”. In addition, a session entitled "My Collaboration Experience" was set up for participants to share their experiences in international collaborative research. 2 people, 1 from Kumamoto University and 1 from KAIST, gave talks about their experiences in international collaborative research. In each lecture, each researcher introduced his or her research project, and there was a lively discussion. In addition to these sections, a "flash talk" was held in which young researchers gave a brief introduction of their laboratories. A total of 12 speakers, 7 from Kumamoto University and 5 from KAIST, gave talks.

From IROAST and Faculty of Advanced Science and Technology, Prof. Sawa talked about identification of plant attractant of plant parasitic nematodes, M. incognita, Prof. Tani talked about Shaping the nucleus: mechanisms and diseases, and Prof. Niidome talked about surface coating of bioresorbable coronary stents and their corrosion behaviors, and Prof. Zheng of IROAST talked on Nanostructured magnesium alloys processed for biomedical applications. In addition, Prof. Kobayashi, Prof. Lee, and Prof. Sekine (Hayami Lab) introduced their laboratories at the Flash Talk session.

Finally, Dr. Injune Kim of KAIST gave a closing address and expressed his vision for future collaboration.

The symposium was attended by 75 participants, including the speakers, and there was a very active discussion and exchange of ideas. This will lead to our future cooperative research.

Presenter from IROAST

Distinguished Professor Zhen

Presenters from FAST

Professor Sawa

Professor Tani

Professor Niidome

The 4th KAIST-KU Workshop and Joint Symposium

February 22 (Mon.), 2021

Time	Speaker	Affiliation	Title
10:00-10:05			Opening Remarks
Symposium 1		**"Communication biology and engineering"**	
10:05-10:25	Akio KOBAYASHI	IMEG, KU	Genetic regulation of cellular lineages in the kidney
10:25-10:45	Jessie Sungyun JEON	DME, KAIST	Lab on a chip in disease modeling and drug screening
10:45-11:05	Shinichiro SAWA	FAST, KU	Identification of Plant attractant of Plant parasitic nematodes, M. incognita.
11:05-11:10	**Break**		
Symposium 2		**"Nucleic acids and Bioinformatics"**	
11:10-11:30	Daisuke KUROTAKI	YCU/ IRCMS, KU	3D chromatin structure dynamics during dendritic cell differentiation and activation
11:30-11:50	Jong-Eun PARK	GSMSE, KAIST	Towards integrated atlas of human immunity
11:50-12:10	Tokio TANI	FAST, KU	Shaping the nucleus: mechanisms and diseases
12:10-12:30	Jinkuk KIM	GSMSE, KAIST	ASO therapy for neurological diseases
12:30-13:30	**Break**		
"My Collaboration experience"			
13:30-13:45	Pilhan KIM	GSMSE, KAIST	Integrating cutting-edge intravital imaging technology for biomedical research
13:45-14:00	Hidenobu MIZUNO	IRCMS, KU	A versatile vector system for in vivo single-cell labeling and gene manipulation
Flash Talks			
14:00-14:30	Laboratories from KAIST and KU		
14:30-14:40	**Break**		
Symposium 3		**"Homeostasis and Disease"**	
14:40-15:00	Won-Il JEONG	GSMSE, KAIST	Glutamate signaling drives alcoholic steatosis
15:00-15:20	Masashi MURAMATSU	IRDA, KU	NFAT signal for maintaining vascular integrity through controlling endothelium cell competition
15:20-15:40	Ji Eun OH	GSMSE, KAIST	Memory B cell recruitment to the vaginal mucosa is required for luminal antibody secretion
15:40-16:00	Kei-ichiro ISHIGURO	IMEG, KU	MEIOSIN directs the switch from mitosis to meiosis
16:00-16:10	**Break**		
Symposium 4		**"Biomaterials & Biotechnology"**	
16:10-16:30	Takuro NIIDOME	FAST, KU	Surface coating of bioresorbable coronary stents and their corrosion behaviors
16:30-16:50	Hyun Jung CHUNG	DBS, KAIST	Diagnostics at point-of-care: nanoengineering approaches
16:50-17:10	Yufeng ZHENG	IROAST, KU	Nanostructured magnesium alloys processed for biomedical applications
17:10-17:15			Closing Remarks

Affiliation
KU: Kumamoto University, Japan
IRCMS: International Research Center for Medical Sciences, Kumamoto University
IROAST: International Research Organization for Advanced Science & Technology, Kumamoto University
FAST: Faculty of Advanced Science and Technology, Kumamoto University
IMEG: Institute of Molecular Embryology and Genetics, Kumamoto University
IRDA: Institute of Resource Development and Analysis, Kumamoto University
YCU: Yokohama City University, Japan
KAIST: Korea Advanced Institute of Science and Technology, Korea
GSMSE: Graduate School of Medical Science and Engineering, KAIST
DME: Department of Mechanical Engineering, KAIST
DBS: Department of Biological Science, KAIST


Facilitating Collaboration in Biomedical Engineering Research
The 4th KAIST-KU Workshop and Joint Symposium
February 22nd (Mon.), 2021
10:00-17:15
Hybrid Symposium via Zoom and at sites
Kumamoto University (IRCMS, IROAST) and KAIST
Speakers
Akio KOBAYASHI
Jessie Sungyun JEON
Shinichiro SAWA
Daisuke KUROTAKI
Jong-Eun PARK
Tokio TANI
Jinkuk KIM
Pilhan KIM
Hidenobu MIZUNO
Won-Il JEONG
Masashi MURAMATSU
Ji Eun OH
Kei-ichiro ISHIGURO
Takuro NIIDOME
Hyun Jung CHUNG
Yufeng ZHENG
Registration is required to join.
See website for details.
ircms.kumamoto-u.ac.jp
Contact:
ircms@jimu.kumamoto-u.ac.jp
KAIST
Kumamoto University
IRCMS
IROAST

IROAST Seminars

IROAST Seminars

No.	Title	Organizer	Date
1	The 7th IROAST-IRCMS Joint Seminar “Creation of joint researches which develops interdisciplinary research fields” - The 75th IROAST Seminar/The 67th IRCMS Seminar	**Toshio Suda** Director, IRCMS **Takashi Hiyama** Director, IROAST	Aug. 25, 2020
2	The 1st IROAST Research Unit Progress Report Seminar -The 76th IROAST seminar-	**Takashi Hiyama** Director, IROAST	Sep. 28, 2020

IROAST Seminar Report

<table>
<tr><td rowspan="2">Organizer 1</td><td>Name</td><td colspan="3">Toshio Suda</td></tr>
<tr><td>Affiliation</td><td>IRCMS</td><td>Title</td><td>Director</td></tr>
<tr><td rowspan="2">Organizer 2</td><td>Name</td><td colspan="3">Takashi Hiyama</td></tr>
<tr><td>Affiliation</td><td>IROAST</td><td>Title</td><td>Director</td></tr>
<tr><td>Seminar Title</td><td colspan="4">The 7th IROAST-IRCMS Joint Seminar “Creation of joint researches which develops interdisciplinary research fields”
（The 75th IROAST Seminar/The 67th IRCMS Seminar）</td></tr>
<tr><td>Venue</td><td colspan="4">Online Seminar</td></tr>
<tr><td>Time & Date</td><td colspan="4">August 25, 2020 14:00-15:55</td></tr>
<tr><td>Speaker’s Name/ Title/Affiliation</td><td colspan="4">1) Hidenobu Mizuno, Associate Professor, IRCMS
2) Koichi Nishiyama, Associate Professor, IRCMS
3) Tokio Tani, Professor, FAST
4) Buluke, Doctoral Student, IRCMS
5) Sheng Guojun, Professor, IRCMS</td></tr>
<tr><td rowspan="4">Number of Participants</td><td rowspan="2">From KU</td><td>Faculty: 30
(Int'l participants: 2)</td><td rowspan="4">Total</td><td rowspan="4">34</td></tr>
<tr><td>Students: 4
(Int'l participants: 4)</td></tr>
<tr><td rowspan="2">From outside KU</td><td>Faculty:
(Int'l participants: 0)</td></tr>
<tr><td>Students:
(Int'l participants: 0)</td></tr>
</table>

The 7th IROAST-IRCMS Joint Seminar "Creation of joint researches which develops interdisciplinary research fields" (the 75th IROAST Seminar and the 67th IRCMS Seminar) was held from 14:00 to 16:00 on August 25th, 2020.

The seminar was jointly organized by Dr. Toshio Suda, Director of the International Research Center for Medical Sciences (IRCMS) and Dr.Takashi Hiyama, the director of International Research Organization for Advanced Science and Technology (IROAST).

In addition to the researchers from IRCMS, IROAST, the others researchers from the Faculty of Advanced Science and Technology (FAST) joined as presenters. This seminar was composed of two parts: the first part was the progress report by IRCMS-IROAST collaboration research groups and the second one was the self-making short research reports to introduce their own research to find their new joint research counterparts. This seminar gave us a good opportunity to put more emphasis on our joint research between IRCMS, IROAST, and adjunct researchers from FAST, and also to initiate new joint research activities through the varieties of discussions.

Due to the COVID-19 situation, the presentations and the Q&A sessions were held online, using the ZOOM conference system.

The 7th IROAST-IRCMS Joint Seminar

- The 75th IROAST Seminar/The 67th IRCMS Seminar -

"Creation of joint researches which develops interdisciplinary research fields"

August 25, 2020 (Tue.) 14:00-15:55

※ Zoom online seminar

Please pre-register to receive the Zoom meeting information.

http://ircms.kumamoto-u.ac.jp/symposium_reserve/symposium/reservation/

Progress Reports by IRCMS-IROAST Research Collaboration Groups

Quantitative bioimage analysis to elucidate dynamics of hematopietic stem cells (HSCs) in living animals

- Takumi Higaki, IROAST / Yuji Takihara, Univ. Hospital / Hidenobu Mizuno, IRCMS

in silico analyses to dissect roles of blood flow-derived mechancial stimuli in biological phenomena: vascular development and cancer metastasis

- Koichi Nishiyama, IRCMS / Toshifumi Mukunoki, FAST-IROAST

Development of the novel drugs for Adult T-cell Leukemia based on the modifications of nuclear morphology

- Tokio Tani, FAST / Yorifumi Sato, Joint Research Center for Human Retrovirus Infection – IRCMS / Takashi Ideue, FAST / Ramesh Pillai, IROAST

Micro CT-based quantification of angiogenesis in tumor microenvironment

- Takatshugu Ishimoto, IRCMS / Toshifumi Mukunoki, FAST-IROAST / Jun Otani, FAST-IROAST / Buluke, IRCMS

Targeted inhibition of epithelial to mesenchymal transition (EMT) in MT1-MMP-expressing cancer cells in vivo.

- Sheng Guojun, IRCMS / Ruda Lee, IROAST

Short Research Self-marketing

- Introduce own research to find new joint research counterparts

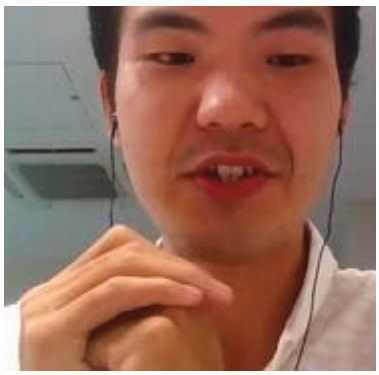
Inquiry: International Research Center for Medical Sciences (IRCMS)
TEL:096-373-6847 ircms@jimu.kumamoto-u.ac.jp
International Research Organization for Advanced Science and Technology (IROAST)
TEL: 096-342-3303, 3362 szk-kiko@jimu.kumamoto-u.ac.jp

Opening Remarks:
Dr. Suda, Director of IRCMS

Research Progress Report Group 1:
Dr. Mizuno, IRCMS

Research Progress Report Group2:
Dr. Nishiyama, IRCMS

Research Progress Report Group 3:
Dr. Tani, FAST



Research Progress Report Group 4:
Mr. Buluke, IRCMS

Research Progress Report Group 5:
Dr. Sheng, IRCMS

Short Research Self-Marketing:
Dr. Takashima, IROAST/FAST

Short Research Self-Marketing:
Dr. Kobayashi, FAST

Closing Remarks:
Dr.Hiyama, Director of IROAST

IROAST Seminar Report 2

<table>
<tr><td rowspan="2">Organizer</td><td>Name</td><td colspan="3">Takashi Hiyama</td></tr>
<tr><td>Affiliation</td><td>IROAST, Kumamoto University</td><td>Title</td><td>Director</td></tr>
<tr><td>Seminar Title</td><td colspan="4">The 1st IROAST Research Unit Progress Report Seminar
-The 76th IROAST seminar-</td></tr>
<tr><td>Venue</td><td colspan="4">Online seminar by Zoom</td></tr>
<tr><td>Time & Date</td><td colspan="4">13:30-16:45, September 28, 2020</td></tr>
<tr><td>Speaker’s Name/
Title/Affiliation</td><td colspan="4">Keitaro Takahashi, Associate Professor, FAST
Kei Ishida, Assistant Professor, FAST
Shin-Ichi Ohira, Associate Professor, FAST
Atsushi Sainoki, Associate Professor, IROAST
Makiko Kobayashi, Associate Professor, FAST
Yutaka Kuwahara, Assistant Professor, FAST
Ruda Lee, Associate Professor, IROAST
Takumi Higaki, Associate Professor, IROAST
Mitsuhiro Aida, Professor, IROAST
Shunko A. Inada, Assistant Professor, FAST
IROAST: International Organization for Advanced Science and Technology
FAST: Faculty of Advanced Science and Technology</td></tr>
<tr><td rowspan="4">Number of
Participants</td><td rowspan="2">From KU</td><td>Faculty: 22
(Int'l participants: 1)</td><td rowspan="4">Total</td><td rowspan="4">23</td></tr>
<tr><td>Students: 0
(Int'l participants: 0)</td></tr>
<tr><td rowspan="2">From outside KU</td><td>Faculty: 1
(Int'l participants: 1)</td></tr>
<tr><td>Students: 0
(Int'l participants: 0)</td></tr>
</table>

The 1st IROAST Research Unit Progress Report Seminar, and the 76th IROAST seminar, was held from 13:30 on September 28th in 2020 with the participants of around 30.

Due to the COVID-19 situation, both presentations and the discussions were held online using the ZOOM conference system.

Following the opening address by Kazuki Takashima, IROAST Vice Director, we welcomed nine speakers from each one of our Young Researchers’ Research Units to present their progress through the research activities in their own research units.

We also welcomed a new researcher, Assistant Prof. Shunko A. Inada from the Dept. of Computer Science and Electrical Engineering, who introduced his research targeting the additional set up of a research unit.

Before concluding this seminar, Takashi Hiyama, IROAST Director, introduced the guidelines how to set up a Young Researchers’ Research Unit, and ended this seminar by delivering the closing address.

The 1st IROAST Research Unit Progress Report Seminar

-The 76th IROAST seminar-

Mon, September 28, 2020 13:30～17:00

STYLE **Online seminar by Zoom** **The seminar is held in English**

PROGRAM

Opening address

13:30-13:35 Kazuki TAKASHIMA, IROAST Vice Director

Presentation **Unit name (Unit coordinator, affiliation)**

13:35-13:45 Radio Astronomy (Keitaro TAKAHASHI, FAST)
13:45-13:55 Deep Learning for Hydrology (Kei ISHIDA, FAST)
13:55-14:05 Q&A
14:05-14:15 Environmental Impacts of Ionic Solutes (Shin-Ichi OHIRA, FAST)
14:15-14:25 Development of microbially-aided carbon sequestration technology (Atsushi SAINOKI, IROAST)
14:25-14:35 Advanced Biomedical Evaluation System (Makiko KOBAYASHI, FAST)
14:35-14:45 Q&A
Break
15:00-15:10 Bio-inspired Functional Molecular System (Yutaka KUWAHARA, FAST)
15:10-15:20 Development of novel therapeutic strategy using iron targeted upconversion nanoparticles for Parkinson's disease (Ruda LEE, IROAST)
15:20-15:30 Nanomaterials processing for medical, cosmetic, and environmental applications (Mitsuru SASAKI, IINa)
15:30-15:40 Quantitative Bioimaging (Takumi HIGAKI, IROAST)
15:40-15:50 Plant Stem Cells and Regeneration (Mitsuhiro AIDA, IROAST)
15:50-16:00 Q&A

Free Discussion

16:00-16:55 Discussion session for exchange of ideas between participants and young researchers aiming for creating a new international research collaboration, etc.

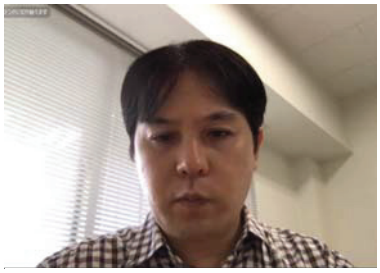
Closing address

16:55-17:00 Takashi HIYAMA, IROAST Director

IROAST International Research Organization for Advanced Science & Technology

Inquiry
International Research Organization for Advanced Science and Technology (IROAST)
Sato (ext. 3362)
E-mail: szk-kiko@jimu.kumamoto-u.ac.jp

Speakers and Discussers



Associate Professor
Keitaro Takahashi

Assistant Professor
Kei Ishida

Associate Professor
Shin-Ichi Ohira

Vice Director, Professor
Kazuki Takashima

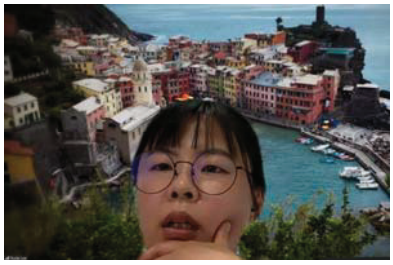
Associate Professor
Atsushi Sainoki

Associate Professor
Makiko Kobayashi

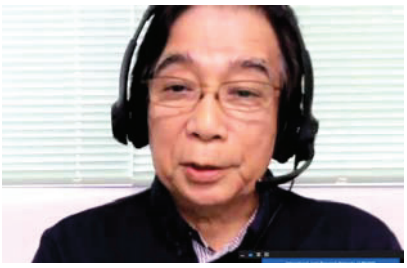
Associate Professor
Takumi Higaki

Professor
Mitsuhiro Aida

Assistant Professor
Yutaka Kuwahara



Associate Professor
Ruda Lee



Director, Professor
Takashi Hiyama

Published Papers by IROAST Researchers

Published Papers by IROAST Researchers

Jorge Norberto Beltramini

S. Mukundan, D. C. Boffito, A. Shrotri, L. Atanda, J. N. Beltramini, and G. S. Patience, "Thermocatalytic hydrodeoxygenation and depolymerization of waste lignin to oxygenates and biofuels in a continuous flow reactor at atmospheric pressure," ACS Sustainable Chemistry & Engineering, 8, 35, 13195, 2020.

S. Mukundan, R. K. Chowdari and J. Beltramini, "External Solvent-Free Catalytic Hydrodeoxygenation of Softwood Lignin to Aromatics over Carbon–ZrO2 Supported Ni/MoS2 Catalysts," Advances Sustainable Systems, 2000243, 2021.

H. K. Wyn, M. Konarova, J. N. Beltramini, G. Perkins and L. Yermán, "Self-sustaining smoldering combustion of waste: A review on applications, key parameters and potential resource recovery," Fuel Processing Technology, 205, 106425, 2020.

Swathi Mukundan, Jorge Beltramini, Krishnapillai Girish Kumar, Devika Sudha Ravindran, "Surface engineering of carbon supported CoMoS– an effective nanocatalyst for selective deoxygenation of lignin derived phenolics to arenes," Applied Catalysis A, 606, 117811, 2020.

Waqas Aslam, Jorge Beltramini, Luqman Atanda, Nundo Batalha, Tobias Schull and Muxina Konarova, "The catalytic activity of KMoCo carbon spheres for higher alcohols synthesis from syngas," Applied Catalysis, 605, 117803, 2020.

Athukoralalage Don K. Deshan, Luqman Atanda, Lalehvash Moghaddam, Darryn W. Rackemann, Jorge Beltramini and William O. S. Doherty, "Heterogeneous Catalytic Conversion of Sugars into 2,5 Furandicarboxylic Acid," Frontiers in Chemistry, 8, 659, 2020.

László Pusztai

Pothoczki Sz., Pethes I., Pusztai L., Temleitner L., Csókás D., Kohara S., Ohara K., Bakó I., "Hydrogen bonding and percolation in propan-2-ol – Water liquid mixtures: X-ray diffraction experiments and computer simulations," J. Mol. Liq., 329 Paper:115592, p10, 2021.

Pethes I., Pusztai L., Ohara K., Kohara S., Darpentigny J., Temleitner L., “Temperature-dependent structure of methanol-water mixtures on cooling: X-ray and neutron diffraction and molecular dynamics simulations,” J. Mol. Liq., 314, Paper: 113664, p.10, 2020.

Pethes I., Bakó I., Pusztai L., “Chloride ions as integral parts of hydrogen bonded networks in aqueous salt solutions: the appearance of solvent separated anion pairs,” Physical Chemistry Chemical Physics (PCCP), 22, pp.11038-11044, 2020.

Temleitner L., Hattori T., Abe J., Nakajima Y., Pusztai L., “Pressure-Dependent Structure of Methanol–Water Mixtures up to 1.2 GPa: Neutron Diffraction Experiments and Molecular Dynamics Simulations,” Molecules, 26(5), 1218, p.13, 2021.

Hosokawa S., Bérar J-F., Boudet N., Pilgrim W-C., Pusztai L., Hiroi S., Kohara S., Kato H., Fischer HE., Zeidler A, “Detailed structural analysis of amorphous Pd40Cu40P20: Comparison with the metallic glass Pd40Ni40P20 from the viewpoint of glass forming ability,” J. Non-Cryst. Solids, 552 Paper: 120536, p.10, 2021.

Hosokawa S., Kawakita Y., Pusztai L., Ikeda K., Otomo T., “Detailed investigations on short- and intermediate-range structures of Ge-Se glasses near the stiffness transition composition,” J. Phys. Soc. Jpn., 90 024601, p.12, 2021.

Yufeng Zheng

Xinhua Qu, Hongtao Yang, Zhifeng Yu, Bo Jia, Han Qiao, Yufeng Zheng, Kerong Dai, “Serum zinc levels and multiple health outcomes: Implications for zinc-based biomaterials,” Bioactive Materials, 5, 2, 410-422, 2020.

Guo Bao, Qianqian Fan, Dongfeng Ge, Kun Wang, Mingming Sun, Zechuan Zhang, Hui Guo, Hongtao Yang, Bin He, Yufeng Zheng, “In vitro and in vivo studies to evaluate the feasibility of Zn-0.1Li and Zn-0.8Mg application in the uterine cavity microenvironment compared to pure zinc,” Acta Biomaterialia, 123, 393-406, 2021.

Mitsuhiro Aida

Ikeda Y, Zalabák D, Kubalová I, Králová M, Brenner WG, Aida M. "Interpreting cytokinin action as anterograde signaling and beyond," Front Plant Sci 12, 641257. 2021.

Imoto A, Yamada M, Sakamoto T, Okuyama A, Ishida T, Sawa S, *Aida M., "A ClearSee-based clearing protocol for 3D visualization of Arabidopsis thaliana embryos," Plants 10, 190, 2021.

*Aida M, Tsubakimoto Y, Shimizu S, Ogisu H, Kamiya M, Iwamoto R, Takeda S, Karim MR, Mizutani M, Lenhard M, Tasaka M. "Establishment of the embryonic shoot meristem involves activation of two classes of genes with opposing functions for meristem activities," Int J Mol Sci 21, 5864, 2020.

Yokoi A, *Aida M., "Postgenital fusion and epidermal cell fate control during gynoecium development," Cytologia 86, 1-2, 2021.

Takumi Higaki

Ishida T, Yoshimura H, Takekawa M, Higaki T, Ideue T, Hatano M, Igarashi M, Tani T, Sawa S, Ishikawa H, "Discovery, characterization and functional improvement of kumamonamide as a novel plant growth inhibitor that disturbs plant microtubules," *Sci Rep* 23: 6077, 2021.

Maeda K, Higaki T, "Disruption of actin filaments delays accumulation of cell plate membranes after chromosome separation," *Plant Sig Behav* 16: 1873586, 2021.

Higaki T, Akita K, Katoh K, "Coefficient of variation as an image-intensity metric for cytoskeleton bundling," *Sci Rep* 10: 22187, 2020.

Lu YJ, Li P, Shimono M, Corrion A, Higaki T, He SY, Day B, "Arabidopsis calcium-dependent protein kinase 3 regulates actin cytoskeleton organization and immunity," *Nature Commun* 11:6234, 2020.

Kimata Y, Higaki T, Kurihara D, Ando N, Matsumoto H, Higashiyama T, Ueda M, "Mitochondrial dynamics and segregation during the asymmetric division of *Arabidopsis* zygotes. *Quant Plant Biol* 1: e3, 2020.

Higaki T, Mizuno H, “Four-dimensional imaging with virtual reality to quantitatively explore jigsaw puzzle-like morphogenesis of *Arabidopsis* cotyledon pavement cells,” *Plant Biotech* 37: 429-435, 2020.

Yoshimi Y, Hara K, Yoshimura M, Tanaka N, Higaki T, Tsumuraya Y, Kotake T, “Expression of a fungal exo-β-1,3-galactanase in *Arabidopsis* reveals a role of type II arabinogalactans in the regulation of cell shape,” *J Exp Bot* 71: 5414-5424, 2020.

Higaki T, Akita K, Hasezawa S, “Elevated CO_2 promotes satellite stomata production in young cotyledons of *Arabidopsis thaliana*,” *Genes Cells* 25: 475-482, 2020.

Ruda Lee

Yong Il Park, Seung-Hae Kwon, Gibok Lee, Keiichi Motoyama, Min Woo Kim, Min Lin, Takuro Niidome, Jung Hoon Choi, Ruda Lee*, “pH-sensitive multi-drug liposomes targeting folate receptor β for efficient treatment of non-small cell lung cancer,” Journal of Controlled Release, 330, 1-14, 2021.

Sho Ueno, Min Woo Kim, Gibok Lee, Yong Il Park, Takuro Niidome, and Ruda Lee*, “Development of ErbB2-Targeting Liposomes for Enhancing Drug Delivery to ErbB2-Positive Breast Cancer,” Pharmaceutics, 12, 585, 2020.

Xiaoxue Xu, Hongxu Lu and Ruda Lee, “Near Infrared Light Triggered Photo/Immuno-Therapy Toward Cancers,” Frontiers in Bioengineering and Biotechnology, 8, 488, 2020.

Song Yeul Lee*, Ruda Lee*, Eunha Kim, Sanghee Lee and Yong Il Park,”Near-Infrared Light-Triggered Photodynamic Therapy and Apoptosis Using Upconversion Nanoparticles with Dual Photosensitizers,” Frontiers in Bioengineering and Biotechnology, 8, 275, 2020.

Atsushi Sainoki

Schwartzkopff, A.K., Sainoki, A. and Elsworth, D., “Numerical simulation of an in-situ fluid injection experiment into a fault using coupled X-FEM analysis,” Rock Mechanics and Rock Engineering, 54(3), pp.1027-1053, 2021.

Sono, T., Tanikura, I., Sainoki, A., Schwartzkopff, A.K. and Obara, Y., “Optimization of chipping parameters to mitigate the damage in a concrete substrate using a discontinuum modelling approach,” Construction and Building Materials, 258, p.119658, 2020.

Takashi Ishida

Takashi Ishida, Haruna Yoshimura, Masatsugu Takekawa, Takumi Higaki, Takashi Ideue, Masaki Hatano, Masayuki Igarashi, Tokio Tani, Shinichiro Sawa, Hayato Shikawa, "Discovery, characterization and functional improvement of kumamonamide as a novel plant growth inhibitor that disturbs plant microtubules," Scientific Reports, 11, 6077, 2021.

Ayame Imoto, Mizuki Yamada, Takumi Sakamoto, Airi Okuyama, Takashi Ishida, Shinichiro Sawa, Mitsuhiro Aida, "A ClearSee-Based Clearing Protocol for 3D Visualization of *Arabidopsis thaliana* Embryos," Plants, 10(2), 190, 2021.

Reira Suzuki, Takashi Ueda, Takuji Wada, Masaki Ito, Takashi Ishida, Shinichiro Sawa, "Identification of genes involved in *Meloidogyne incognita*-induced gall formation processes in *Arabidopsis thaliana*," Plant Biotechnology, 38(1), 1-8, 2021.

Satoru Nakagami, Kentaro Saeki, Kei Toda, Takashi Ishida, Shinichiro Sawa, "The atypical E2F transcription factor DEL1 modulates growth–defense tradeoffs of host plants during root-knot nematode infection," Scientific Reports, 10, 8836, 2020.

Takashi Ishida, Reira Suzuki, Satoru Nakagami, Takeshi Kuroha, Shingo Sakamoto, Miyuki T. Nakata, Ryusuke Yokoyama, Seisuke Kimura, Nobutaka Mitsuda, Kazuhiko Nishitani, Shinichiro Sawa, "Root-knot nematodes modulate cell walls during root-knot formation in Arabidopsis roots," Journal of Plant Research, 133, 419–428, 2020.

Rocío Olmo, Javier Cabrera, Fernando E. Díaz-Manzano, Virginia Ruiz-Ferrer, Marta Barcala, Takashi Ishida, Alejandra García, María Fe Andrés, Simón Ruiz-Lara, Isabel Verdugo, Mónica Pernas, Hidehiro Fukaki, Juan Carlos del Pozo, Miguel Ángel Moreno-Risueno, Tina Kyndt, Godelieve Gheysen, Carmen Fenoll, Shinichiro Sawa and Carolina Escobar, "Root-knot nematodes induce gall formation by recruiting developmental pathways of post-embryonic organogenesis and regeneration to promote transient pluripotency," New Phytologist, 227(1), 200-215, 2020.

David S Favero, Ayako Kawamura, Michitaro Shibata, Arika Takebayashi, Jae-Hoon Jung, Takamasa Suzuki, Katja E Jaeger, Takashi Ishida, Akira Iwase, Philip A Wigge, Michael M Neff, Keiko Sugimoto, "AT-hook transcription factors restrict petiole growth by antagonizing PIFs," Current Biology, 30(8), 1454-1466. e6, 2020.

Minwoo Kim

Yong Il Park, Seung-Hae Kwon, Gibok Lee, Keiichi Motoyama, Min Woo Kim, Min Lin, Takuro Niidome, Jung Hoon Choi, Ruda Lee*, "pH-sensitive multi-drug liposomes targeting folate receptor β for efficient treatment of non-small cell lung cancer," Journal of Controlled Release, 330, 1-14, 2021.

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Adam Karl Schwartzkopff

Schwartzkopff, A.K., Sainoki, A. and Elsworth, D., "Numerical simulation of an in-situ fluid injection experiment into a fault using coupled X-FEM analysis," Rock Mechanics and Rock Engineering, 54(3), pp.1027-1053, 2021.

Schwartzkopff, A.K., Melkoumian, N.S. and Xu, C., "Breakdown pressure and propagation surface of a hydraulically pressurized circular notch within a rock material," Rock Mechanics and Rock Engineering, 54(1), pp.191-218, 2021.

Sono, T., Tanikura, I., Sainoki, A., Schwartzkopff, A.K. and Obara, Y., "Optimization of chipping parameters to mitigate the damage in a concrete substrate using a discontinuum modelling approach," Construction and Building Materials, 258, p.119658, 2020.

Mizuki Yamada

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Takahiro Hosono

Hosono, T., Yamada, C., Manga, M., Wang, C. -Y., Tanimizu, M., "Stable isotopes show that earthquakes enhance permeability and release water from mountains," Nature Communications, 11, 2776, 2020.

Hosono, T., Saltalippi, C., Jean, J.-S., "Coseismic hydro-environmental changes: insights from recent earthquakes," Journal of Hydrology, 585, 124799, 2020.

Makoto Kumon

M. Wakabayashi, H.G. Okuno and M. Kumon, "Drone Audition Listening from the Sky Estimates Multiple Sound Source Positions by Integrating Sound Source Localization and Data Association," Advanced Robotics, Vol. 34, No. 11, pp.744-755, 2020.

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Internationally Collaborated Papers

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Internationally Collaborated Papers by IROAST Internship Students/Researchers and their Host Professors

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