World Premier International Research Center Initiative (WPI)
FY 2019 WPI Project Progress Report

Host Institution	Hokkaido University	Host Institution Head	Toyoharu Nawa
Research Center	Institute for Chemical Reaction Design and Discovery (ICReDD)		
Center Director	Satoshi Maeda	Administrative Director	Yasunori Yamamoto

Common instructions:
* Unless otherwise specified, prepare this report based on the current (31 March 2020) situation of your WPI center.
* So as to execute this fiscal year's follow-up review on the "last" center project plan, prepare this report based on it.
* Use yen (¥) when writing monetary amounts in the report. If an exchange rate is used to calculate the yen amount, give the rate.

- Prepare this report within 10-20 pages (excluding the appendices, and including Summary of State of WPI Center Project Progress (within 2 pages)).

Summary of State of WPI Center Project Progress (write within **2 pages**)

1. Advancing Research of the Highest Global Level

The mission of ICReDD is not to leave the discovery and design of chemical reactions to serendipity or experience-guided intuition, but to purposefully craft chemical reactions. Therefore, ICReDD has defined its four flagship research areas as: **(1) Development and integration of state-of-the-art computational & informatics techniques**, **(2) Design and discovery of new synthesis methods**, and **(3) Design and discovery of new materials**, **(4) Creation of innovative measurement and diagnosis methods**. Through these efforts, ICReDD will *revolutionize Chemical Reaction Design and Discovery* (**ICReDD's slogan**).

The achievements for FY2019 are as follows: 87 papers were published in peer-reviewed journals (18 papers in journals with an IF > 10). Three papers were published in *Science* (IF: 41.063) and one in *Advanced Materials* (IF: 25.809). We reported the first successful case in which a path suggested by quantum chemical calculations led a discovery of a new synthetic method (see 1-2-1). ICReDD's members have presented their research in 75 invited lectures at international conferences and 13 awards have been granted. The total amount of research funding was 668 million JPY. Representative grants are 1 JST-ERATO, 7 JST-CREST, 1 AMED-CREST, 2 JST-PRESTO, 1 JST-ImPACT, 1 Grant-in-Aid for Scientific Research on Innovative Areas, 1 Grant-in-Aid for Scientific Research (S), 2 Grant-in-Aid for Scientific Research (A) projects. ICReDD faculty members, despite being 1.5% of the faculty members of Hokkaido University, produce 10% in papers and 5% in research funding.

2. Generating Fused Disciplines

To realize ICReDD's vision and mission, the following facilities, systems, and research themes were established with promotion of research in four priority areas that integrate computational, information, and experimental science. The specific activities are as follows.

(1) **Incubation space for fusion researches**: Establishment of mix-office (307 m^2), mix-labs (608 m^2), facility rooms (159 m^2), the ICReDD salon (182 m^2) and administration office (138 m^2).

(2) **ICReDD seminar system**: Seminar system toward fusion researches.
Fusion Seminar: Idea generation among researchers in different fields.
Stirring Seminar: Cross-disciplinary exchange seminar for researchers from different fields to understand each other's research.
Tutorial Seminar: Learning seminars in which researchers from different disciplines explain the basics of each other's areas of expertise.
Seeds/Needs Seminar: a seminar oriented towards collaboration with researchers in different fields (in preparation).

(3) **Interdisciplinary research start-up support**: 8 research projects in total 37.5 million JPY to support challenging bottom-up fusion projects.

(4) **Setup of flagship research projects**: Computation/informatics-guided challenging research. i) Integration of Theory-driven and Data-driven Reaction Prediction, ii) New Chemical Reaction Discovery, iii) Designing Cavity in Supramolecular Catalyst, iv) Bridge between Micro- and Macro-Worlds, v) Reaction Discovery by Artificial Enzyme Design, vi) Stimuli-Degradable Polymer Material, vii) Development of Cancer Diagnosis Method.

3. Realizing an International Research Environment

(1) Active recruitments of foreign and female researchers: 22 (37%) of 59 researchers are foreign nationals and 6 (10%) are female.

(2) Domestic and international collaborations: We plan the collaboration agreements with leading domestic and international research institutions (4 institutions) and to add an information PI (The University of Tokyo).
(3) International symposia (internationalization of young researchers): Proactively held international symposia and supported young researchers (2nd international symposium: 403 participants).
(4) Suzuki Akira Award and ICReDD Award: To contribute to the international recognition of ICReDD.
(5) MANABIYA system (internationalization of young researchers): Implementation of ICReDD's unique human resource development system (MANABIYA(ACADEMIC) international/total: 21/36).
(6) International public relations and outreach activities: Implementation and planning of strategic public relations strategies with a clear target community.

4. Making Organizational Reforms

(1) Improvement of management structure: Establishment of Executive Director, Establishment of Advisory Board, Strengthening of governance by the Center Director.
(2) Revision of organizational structure: Flexible coordination of the steering committee, executive committee, and PI meetings.
(3) Revision of the university's rules of employment and salary system: Clarification of responsibility for the formation of the institute

5. Efforts to Secure the Center's Future Development over the Mid- to Long-term

(1) Research plan, composition of researchers, and final composition of personnel
a) Research plan: Four research areas to establish computation/informatics driven strategies.
b) ICReDD currently consists of 46% computational/information, and 54% experimental scientists.
- At the end of March 2020/2023, 22/28 of 59/70 researchers (37/40%) were foreign nationals and 6/10 (10/14%) were female (14/15 PIs, 20/24 faculty members, 15/20 researchers, and 10/11 research collaborators).

(2) Buildings and facilities
- In addition to 1,400 m^2 of CRIS building renovation, we have received funding of 189 million JPY from the University's headquarters to provide an additional 1,200 m^2 of research space. A request for a new building (5,500m^2) is planned as the most important project for FY2021.
- The new building will provide "*Super Mix-lab.*" in which researchers of three fields (75 researchers) can interact on a daily basis to accelerate fusion research further.

(3) Form of organization
- Establishment of a future planning working group to consider the organizational structure of ICReDD during and after the subsidy period.
- We have started considering the graduate school concept with Graduate School of Chemical Sciences and Engineering.
- Design of new buildings according to the future organizational structure.

(4) Finance (external funds, joint research funds with companies)
339 million JPY in University Top-down Financial Support and 668 million JPY in External Funds.
a) Measures to improve the acquisition of external funds: Support for integrated research, seminars for acquiring research funds, and promotion of corporate joint research.
b) Establishing a funding plan: 100 million JPY for indirect expenses (600 million JPY for Grants-in-Aid for Scientific Research, etc. and 100 million JPY for corporate joint research).

(5) Human resources development
- Utilization of MANABIYA and collaboration with researches in other institutions within the university
- Exchange seminars in each department and promote the recruitment of young faculty members in the department.

(6) Graduate school
- Plan to establishment of new graduate school with 15 to 20 students per year (FY2027 -).
- Installation of educational facilities in the new building.
- Linking with the WISE Program "Advanced Training Course for Smart Materials Science".

6. Others

(1) Press release: 7 press releases and 1 research news were issued; 1 press conference was hosted. Publishing of a magazine, newsletters and news-postcards with a clear target community.
(2) Web-based activities: The website has been revamped, and a presence on social media has been established (Facebook (113 posts), Twitter (134 posts), YouTube (12 videos)). We created a promotion video as well as a video series aiming at introducing all our PIs, all posted on social media and the website.
(3) International recruitment: We created and distributed an English-language recruitment brochure, and posted job openings on the website of Asia Research News, JREC-IN and other media.
(4) Outreach activities: We participated in and exhibited at nine international events, including the WPI Science Symposium, World Conference of Science Journalists, and the AAAS Annual Meeting.

* Describe clearly and concisely the progress being made by the WPI center project from the viewpoints below.
- In addressing the below-listed 1-6 viewpoints, place emphasis on the following:
  (1) Whether research is being carried out at a top world-level (including whether research advances are being made by fusingdisciplines).
  (2) Whether a proactive effort continues to be made to establish itself as a "truly" world premier international research center.
  (3) Whether a steadfast effort is being made to secure the center's future development over the mid- to long-term.

1. Advancing Research of the Highest Global Level

* Among the research results achieved by the center, concretely describe those that are at the world's highest level. In Appendix 1, list the center's research papers published in 2019.
* Regarding the criteria used when evaluating the world level of center, note any updated results using your previous evaluation criteria and methods or any improvements you have made to those criteria and methods.

ICReDD scientific mission

For the achievement of sustainable development goals through realization of Society 5.0, new chemical reactions are required for creation of novel functional molecules and high-performance materials, and even for medical treatments for intractable diseases. However, the design and discovery of new chemical reactions have depended on serendipity or experience-guided intuition, which was a bottleneck in the innovation for the new society. The mission of ICReDD is to enable humanity to purposefully craft chemical reactions to any design, not to leave serendipity or experience -guided intuition, accelerating the innovation. At ICReDD, we combine **computational science**, **information science**, and **experimental science** to develop new synthesis methods, new materials, and new applications across all fields in our society. The key to achieving this mission is the development of computational and informatics techniques for predicting chemical reactions. In ICReDD, the top computational research team directed by Maeda tackles the development of practically useful chemical reaction design techniques through close cooperation with information and experimental teams. Therefore, we first establish **(1) Development and integration of state-of-the-art computational & informatics techniques** as the flagship research area.

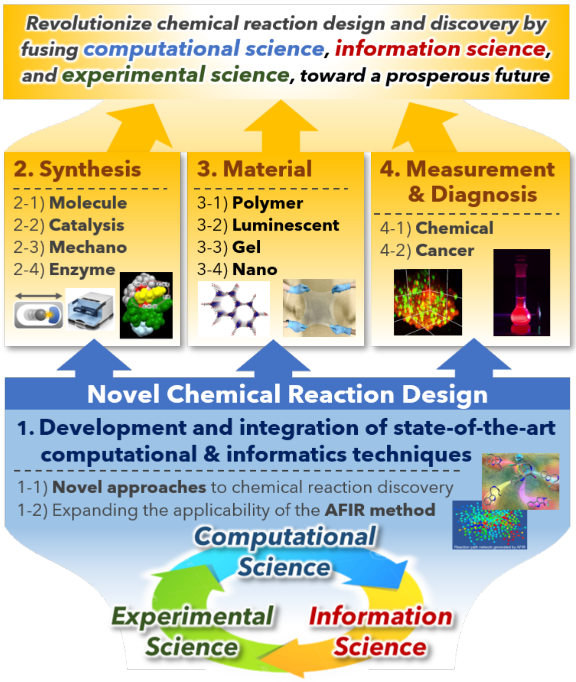


Figure 1. The overview of ICReDD's mission and research subjects.

For the innovation to the sustainable development goals in Society 5.0, new chemical reactions are essential for synthesizing novel functional molecules to support the innovation. In ICReDD, we set **(2) Design and discovery of new synthesis methods (Synthesis)** as one of the four flagship research areas. The most advanced researches in synthetic and catalytic chemistry have been made in our university, as symbolized by Nobel Prize laureate Akira Suzuki, emeritus professor of Hokkaido University. Top organic chemists join ICReDD to be working on design and discovery of new synthesis methods utilizing the chemical reaction design techniques. The design and creation of new high-performance materials would be the next stage: **(3) Design and discovery of new materials (Material)**, which also need new chemical reactions. The researchers in ICReDD have already developed unique polymer-, luminescent-, and gel-materials, and, based on their results, the chemical reaction design techniques will open new strategies for materials that could never be imagined. Finally, **(4) Creation of innovative measurement and diagnosis methods (Measurement & Diagnosis)** is also set to the flagship research area in ICReDD. Measurement and diagnosis methods are highly integrated techniques based on chemical reactions, and new chemical reactions will, therefore, break new ground for measurements and diagnosis. Information and medical scientists who can utilize chemical reactions in their research fields join ICReDD to work on the fusion researches. In ICReDD, putting "chemical reaction" as a common term, we tackle the development of chemical reaction design and discovery strategies for these three subjects (2) – (4) in parallel; there are further hierarchies in the three subjects as described in subsections 2-1 – 2-4, 3-1 – 3-4, and 4-1 – 4-2. Through these efforts, ICReDD will ***revolutionize Chemical Reaction Design and Discovery*** (ICReDD's slogan).

Our achievements such as journal publications, invited lectures, awards, funds, press releases and media coverage in FY2019

The following data supports that the research outcome from ICReDD is at the world's highest level. ICReDD faculty members, despite being 1.5% of the faculty members of Hokkaido University, produce 10% in papers and 5% in research funding. In 2019, 87 papers were published in peer-reviewed journals (18 papers in journals with an IF > 10). Notably, three papers were published in *Science* (IF: 41.063) and one in *Advanced Materials* (IF: 25.809). ICReDD's members have presented their research in a total of 75 invited lectures at international conferences and 13 awards have been granted. ICReDD has been making marked progress in its research, which is evident from the record of competitive research funds granted to ICReDD's researchers. In FY2019, the total amount of research funding obtained was 668 million JPY. Representative grants are 1 JST-ERATO, 7 JST-CREST, 1 AMED-CREST, 2 JST-PRESTO, 1 JST-ImPACT, 1 Grant-in-Aid for Scientific Research on Innovative Areas, 1 Grant-in-Aid for Scientific Research (S), 2 Grant-in-Aid for Scientific Research (A).

ICReDD held 1 press conference and issued 7 national and international press releases on its research achievements. In addition, ICReDD's research and researchers were featured 49 times in a range of national and international media, including newspapers, TV, magazines, and news websites. ICReDD researchers gave 11 lectures and seminars for general public, elementary, secondary and high school students and exhibit in 9 outreach events.

Below, preliminary reports and interdisciplinary collaborations are marked as follows.

- *** Preliminary report (confidential)**
- **† Interdisciplinary collaboration within ICReDD**
- **‡ Interdisciplinary collaboration with groups outside ICReDD**

(1) Development and integration of state-of-the-art computational & informatics techniques

The development and integration of fundamental computational and informatics methods for predicting chemical reactions are key issues in creating strategies for the **computation-** and **informatics**-driven chemical reaction development. In FY2019, we developed new computation and informatics technologies for chemical reaction discovery (**1-1**), and generalization and acceleration of reaction path search methods were examined (**1-2**).

1-1) Computational and Informatics Approaches to Chemical Reaction Discovery

We created a technique called QCaRA based on the AFIR method, which has made possible for the first time in the world to systematically predict the reaction path to give a desired product (**a**) (see **2-1** for an actual synthesis method discovery by QCaRA). By integrating multiple methods from information science and technology, we have also successfully developed a chemical reaction prediction artificial intelligence that predicts new reactions based on existing chemical reaction databases (**b**). Furthermore, by systematically applying the AFIR method to various molecules, we set out to construct a database of chemical reactions by quantum chemical calculations (**c**).

†a) Quantum Chemistry aided Retrosynthetic Analysis (QCaRA)

It remains unclear whether it is feasible to propose a synthesis method from scratch using quantum chemical calculations. To realize such predictions, the **Maeda group** proposed "Quantum Chemistry-aided Retrosynthetic Analysis" (QCaRA) method. QCaRA applies quantum chemical calculations to search systematically for the decomposition paths of a target molecule and suggest a synthesis method corresponding to the reverse reaction of the obtained path. QCaRA requires an automated reaction path search method as its reaction path exploration engine, for which we used the AFIR method. An application of QCaRA to α,α-difluoroglycine generated 30 reactant candidates as terminals of its isomerization and dissociation paths. Among these 30, a set CF_2 + NH_3 + CO_2 was chosen and further verified **computationally** and **experimentally** in collaboration with the **experimental scientist Mita** of ICReDD's mix-lab (see **2-1** for details on the experimental confirmation of the reaction). This **computational technique** will be used to discover new chemical reactions (*Chem. Sci.* 2020).

†b) Artificial Intelligence techniques to generate novel chemical reactions using chemical reaction databases

The discovery of new types of chemical reactions using the conventional trial-and-error approach is highly inefficient and slow. To generate novel chemical reactions automatically based on available chemical reaction databases, the **Varnek group** has developed artificial intelligence techniques using a combination of three computational technologies – "Condensed Graphs of

Reaction" (CGR), "Generative Topographic Maps" (GTM) and a special architecture of Deep Neural Networks – Autoencoders. CGR provided a way to represent a given reaction as a pseudo-molecule with a unique encoding in a SMILES string. An ensemble of specially designed SMILES/CGR strings prepared for the USPTO reactions database was used as an input for the autoencoder. GTM was used to focus on a particular zone of the chemical reaction space populated by a specific type of chemical transformations. A special approach and related tool of novelty detection for chemical reactions have been developed. The approach discovered several reactions with novel reaction centers and their environments compared to those used for the modelbuilding (preprint available on *ChemRxiv*).

The proposed approach can be used in combination with any chemical reaction database. Therefore, two collaborative projects have been initiated with the **Ito group** and the **Maeda group**, respectively. In the first, the US patent database which contains 3.5 million experimentally verified chemical reactions are used, and novel types of C-C coupling reactions are the target to be focused. In the latter, AFIR^{3}M-DB which includes computationally predicted chemical reactions is used (see **1-1-c** for details on AFIR^{3}M-DB). AFIR^{3}M-DB is a new database which is under development in the **Maeda group**, and the **Varnek group** will contribute to the development of analysis and visualization tools for AFIR^{3}M-DB. Besides, Furthermore, this reaction generation approach will be further strengthened by contributions to its deep neural network aspects by the **Takigawa group**.

*†c) AFIR-generated reaction route map database (AFIR^{3}M-DB)

In the FY2019, toward establishing a useful chemical reaction analysis and prediction platform, the **Maeda group** initiated the construction of a database using the AFIR method. The resulting database, referred to as "AFIR-generated reaction route map database" (AFIR^{3}M-DB) will be used at the ICReDD for the design and discovery of chemical reactions. **Informatics tools** will also be developed to extract useful information from AFIR^{3}M-DB and also to further develop the database efficiently.

Currently, it is partially shared with the **Komatsuzaki group**, **Varnek group**, and **Iwata** of The University of Tokyo (Iwata is expected to join ICReDD in FY2020 as a PI in information science), and we will pursue research to predict new reactions from AFIR^{3}M-DB. We will also cooperate with the **Yoshioka group** for comparing AFIR^{3}M-DB with experimental databases and the literature.

*†1-2) Expanding the applicability of the AFIR method

The **Maeda group** updated the GRRM program, which implements the AFIR method, and developed a tool that allows members of other groups to easily participate in the development. With this tool, researchers can participate in the development without first having to master the whole of the complex GRRM program, a process that usually can take several years. With this new tool, researchers can avoid this process altogether by assembling a simple external program. Normally, it takes years of skill to understand the contents and participate in the development, but with this tool, one can to avoid that step. We have already shared the tool with the **Taketsugu group**, **Komatsuzaki group**, **Varnek group**, and **Iwata** of The University of Tokyo. This approach is expected to be faster and more generalizable, for example, enabling the application of information science tools to narrow down the results of proposal pathway.

(2) Design and discovery of new synthesis methods

At ICReDD, chemical reactions of varying complexity are viewed in a hierarchical manner and effective strategies are being developed for different hierarchies in parallel. In small molecule transformations that lies at the lowest hierarchy of the complexity, the dream of quantum chemists to create ideas for chemical synthesis methods from quantum chemical calculations is becoming a reality (**2-1**). In the next stage of the hierarchy for the complexity, we are exploring new catalytic functions for catalytic chemical reactions using quantum chemical calculations and information science techniques (**2-2**). The chemical reactions driven by mechanical stimuli, which have hitherto been difficult to understand, would be the more complexed system, but they have already been explored experimentally and collaborative research for understanding and design those reactions has been started (**2-3**). Furthermore, as one example from the most complex hierarchy, we are developing a computational method to screen enzymatic reactions from the process of substrate binding, which has been difficult to compute, to the chemical transformation at the reaction site. As part of this endeavor, we also started to design reactions using artificial enzymes (**2-4**).

2-1) Small molecule activation and utilization

Here, we describe our efforts to generate chemical reactions from quantum chemical calculations. As described in 1-1-a, we built a theory called "Quantum Chemistry-aided Retrosynthetic Analysis" (QCaRA), based on the AFIR method. Based on the resulting reaction pathway, we found a chemical reaction to synthesize difluoroglycine derivatives from CO_2.

† Establishment of quantum chemistry-aided retrosynthetic analysis

Mita, the chief of ICReDD's mix-lab, and the **Maeda group** discovered a chemical reaction which activated CO_2 and produced a difluoroglycine derivative. This was the first successful case of discovering a new synthetic method based on QCaRA. QCaRA searches for dissociation paths of a target molecule systematically using the AFIR method and proposes synthetic paths of the target molecule as inverse processes of these dissociation paths.

In this study, to demonstrate the power of QCaRA, we chose a target molecule for which no facile synthesis methods exist, i.e., α,α-difluoroglycine (NH_2-CF_2-CO_2H). The replacement of a hydrogen atom with a fluorine atom in bioactive molecules such as α-amino acids is a promising strategy for enhancing the biological activity and bioavailability via increased lipophilicity and improved stability against enzymatic degradation. From a large number of paths obtained by QCaRA (see 1-1-a for details on the computational prediction), one in which multiple components, i.e., difluorocarbene, carbon dioxide, and amine, react to give a difluoroglycine derivative in a one-pot reaction was selected. Then, reaction conditions, etc. were examined by quantum chemical calculations and experiments. As a result, a difluoroglycine derivative was successfully synthesized through a multicomponent reaction among the three reagents.

This is the first successful case in which a path suggested by quantum chemical calculations led to the discovery of a new synthetic method (*Chem. Sci.* 2020). We proved that QCaRA opens the door to the systematic design and discovery of unexplored chemical reactions. **Mita** and **Maeda** are working on further successful cases of QCaRA. Besides, Tsuji of the **List group**, Harabuchi of the **Maeda group**, and Ono of the **Taketsugu group** are tackling a highly efficient amino acid synthesis which has been considered as one of dream chemical transformations, through QCaRA and an iterative catalyst design.

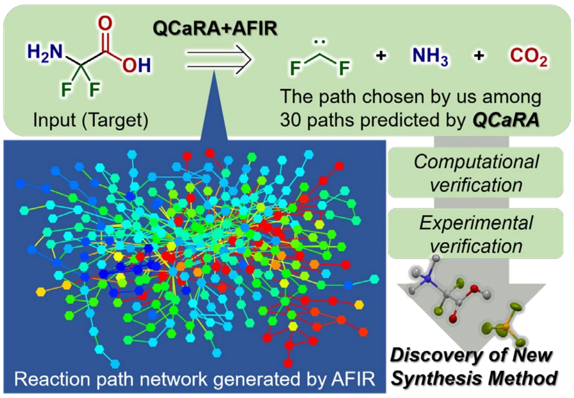


Figure 2. The flow of discovery of the difluoroglycine derivative synthesis method by QCaRA. A theoretical path found in a reaction path network generated by AFIR was verified computationally and experimentally to discover the synthesis method.

2-2) Catalyst design and discovery

Here, we describe our efforts to search for new catalytic functions. At the end of FY2019, we ventured into the challenge of a dream technique to cleave a C-H bond at an arbitrary position and replace it with another substituent in a linear alkyl chain R^1-$(CH_2)_n$-R^2. We describe the **experimental** breakthroughs that underlie the approach of designing the necessary catalysts on demand using computation and informatics (**a**). In several examples, the attempt to maximize the enantioselectivity of a particular chemical reaction by alternating between **experimental** demonstration and **computation**-based design was successful (**b**). In addition, our catalytic discovery strategies are working to realize innovative but largely unrealized catalytic reactions, such as catalysts that promote peptide hydrolysis in solution (**c**). Although the chemical transformations these examples target are diverse, we would like to establish a generalized catalyst discovery strategy by integrating the discovery strategies of the different catalysts created in each of them.

†a) Asymmetric Borylation of Unactivated Methylene C(sp^3)–H Bonds

The **Sawamura group** and the **Maeda group** have developed the highly enantioselective borylation of unactivated methylene C(sp^3)–H bonds in 2-alkylpyridines and related compounds using an iridium-BINOL-based chiral monophosphite catalyst system (*J. Am. Chem. Soc.* 2019). Quantum chemical calculations using the AFIR method indicated that the catalyst generates an enzyme-like narrow chiral reaction pocket where the differentiation of the enantiotopic methylene C–H bonds is accomplished through an assembly of multiple noncovalent interactions.

The **Sawamura group** extended the study to a Rh-monophosphite chiral catalytic system, which enabled a highly efficient enantioselective borylation of *N*-adjacent C(sp^3)–H bonds for a range of substrate classes including 2-(*N*-alkylamino)heteroaryls and N-alkanoyl or aroyl-based secondary or tertiary amides, some of which are pharmaceutical agents or related compounds (*J. Am. Chem. Soc.* 2020) This reaction demonstrated various stereoselective synthesis of enantioenriched α-aminoboronates, important building blocks contained in many compounds exhibiting biomedical implications. The borylation protocol was successfully applied to the catalyst-controlled site- and stereoselective C(sp^3)–H borylation of an unprotected dipeptidic compound allowing the remarkably streamlined synthesis of the anti-cancer drug molecule bortezomib.

The scope of the research has been greatly expanded through collaborations among Reyes of the **Sawamura group**, Ono, Kobayashi, Lyalin, and Kumar of the **Taketsugu group**, Nagahata, Tsitsvero, and Tabata of the **Komatsuzaki group**, and Sidorov of the **Varnek group**. Through the interdisciplinary collaboration, we are targeting the "on-demand design" of an effective catalyst for the selective activation of a targeted C(sp^3)–H bond in an arbitrary aliphatic carboxylic compound. Such a strategy, once established, will dramatically increase the diversity of molecular structures that can be synthesized through organic synthesis and contribute to creating of a variety of compounds that are useful in various purposes such as for pharmaceuticals and in devises.

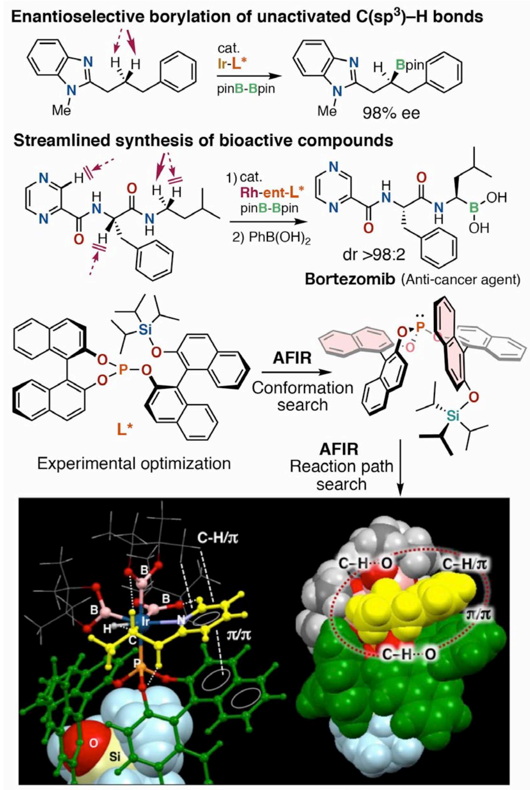


Figure 3. Experimental development of metal-catalyzed enantioselective C(sp^3)–H borylation reactions and computational AFIR/DFT exploration of the reaction paths and the enantioselection mechanism.

†b) Calculation-guided Catalyst Design for Asymmetric Synthesis

Asymmetric synthesis is an important technique that can selectively produce one of two enantiomers of the chiral molecules, which has previously been very difficult because the two enantiomers of chiral molecules have the same thermodynamic formation energy. The development of an asymmetric catalyst enabled this synthesis by selectively accelerating the reaction that can form the desired enantiomer. The design of the catalyst was still difficult and highly dependent on the trial-and-error approach based on **experimental** experiences of researchers. The **Ito group** has studied asymmetric copper-catalyzed borylations, mainly relying on the conventional **experimental** approach for 20 years, but is now investigating new ways to design catalysts that make good use of **computational** chemistry and **machine learning** tools (*Nature Comm*. 2018). We have successfully designed a catalyst that takes strong advantage of the non-covalent interactions between catalysts and substrates (*Angew. Chem. Int. Ed.* 2019). Because the non-covalent bond interactions are weak and difficult to predict based on **experimental experience**, it is crucial to utilize the **computer-aided procedure**. In addition, we also utilized a machine-learning technique [t-distributed stochastic neighbor embedding (t-SNE)] for categorizing the transition state structures, which are critical for the catalyst selectivity (*under submission*).

These studies are the successful results of a fusion research between **experiment** and **calculation**. The further collaboration with the researchers of **information science** can make this computer-aided design more effective and less time-consuming.

*†c) Peptide degradation catalyst

Kubota of the **Ito group** and Okada (a master course student) of the **Maeda group** are working on the development of a catalyst which can promote the hydrolysis of amides. In solution, the hydrolysis of amides requires extreme conditions such as high temperature and/or high pH. In this project, a catalyst which avoids such conditions are explored by **computational** catalyst screening (*under preparation*). Such a catalyst, once discovered, will make artificial modifications of peptides easy and will be used in many pharmaceutical developments.

2-3) Chemical reactions driven by mechanical stimuli

†a) Development of Mechanochemical Reactions for Revolution of Organic Chemistry

Conventional organic reactions use solvents to dissolve substrates and reagents. Researchers believe that solvents are necessary to promote and control the organic reactions; however, the use of solvents causes a significant environmental load through waste treatment as well as an increase in the production cost of the target materials. In addition, because modern organic chemistry has developed on the assumption that reactants are dissolved in solution, the transformations of organic molecules that are difficult to dissolve in organic solvents remine undeveloped. As a result, the availability of potentially useful materials is limited. The **Ito group** recently focused on the mechanochemical synthesis of organic compounds using a ball mill technique. Palladium-catalyzed cross-coupling reactions, which are essential tools for the production of pharmaceutical compounds and organic materials, were found to proceed very effectively in a ball mill when alkene additives were used as the stabilizer of the catalyst (*Nature Comm*. 2019; *Chem. Sci.* 2019). The **Ito group** further developed an efficient synthesis method for air-sensitive transition-metal complexes by taking advantage of the fact that oxygen cannot easily difficult to penetrate into solids (*Chem Sci.* 2019). Moreover, the redox reaction in a ball mill was first developed with piezoelectric materials ($BaTiO_3$), where the electricity generated by the piezoelectric material powder promotes the redox reactions (*Science* 2019).

The further reaction design based on calculation and theoretical simulation is currently in progress in collaboration with the **Maeda group** and Yamamoto of the **Rubinstein group**. The collaboration with information science groups in the view of "design of experiments" are also being planned in order to accelerate the reaction development. The mechano-chemical synthesis research being conducted at ICReDD is currently the world's leading research, and further fusion research will greatly develop this technology.

†b) Bridge between Macro- and Micro Scale World in Material Science

The gap between the macroscopic and microscopic worlds needs to be better understood in science. Although the molecules themselves are not visible, but there is no doubt that the assembly of molecules produces materials that function in the real world. We study luminescent materials sensitive to macroscopic stimulation, including mechanical stress. A study of a **computational** approach to understand how mechanical stress changes material properties was reported in collaboration with theoreticians (*J. Phys. Chem. C* 2019). The **Ito group** also studies the salient effect where molecular scale structural strain in crystals causes jumps or migration at the macro level. Analysis revealed that the anisotropic structure strain of the crystal was generated by the accumulation of changes in the molecular structure. In collaboration with the group of Prof. Garcia-Garibay at UCLA in the US, the **Ito group** found that the macroscopic migration was clearly explained by the molecular-level structure rearrangements (*Angew. Chem. Int. Ed.* 2019; *Chem. Sci.* 2019). New molecular-rotor material studies including AFIR analyses are currently underway, in collaboration with the **Maeda group**. We have also started new research into the visualization of polymer degradation due to mechanical stress in ball mill agitation (manuscript in preparation). This research is conducted in collaboration with the **Maeda group** and the **Gong group**.

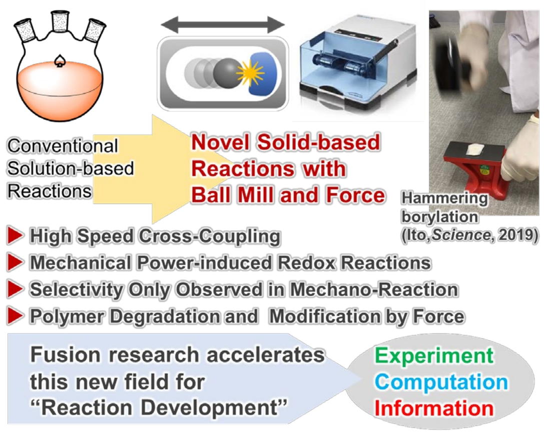


Figure 4. The research overview for mechanical force-induced reaction with ball mill and hammering. The fusion research is a key for the rapid development in this very new field.

*†2-4) Chemical Reaction Discovery by Artificial Enzyme Design

Imajo, Tsuda, Tanaka, Hirota, et al. of the **Tanaka group**, Suzuki of the **Maeda group**, the **Takigawa group**, as well as **Hayashi** and **Mita** of ICReDD's mix-lab, are working on chemical reaction discovery by artificial enzyme design. Chemical reactions utilizing artificial enzymes have been developed through **experimental** trial and error approaches or through screenings. However, the complexity of the mechanism of enzymatic reactions has prevented rational the design of such reactions. The goal of this research is to establish a chemical reaction design and discovery strategy for enzyme reactions. Therefore, the substrate binding paths were systematically searched using the AFIR method combined with the QM/MM-ONIOM method. Such a path search is performed for enzymes with different mutations to identify good mutations that increase reactivity and selectivity. We try to reduce the amount of **computational** trials using **informatics** techniques. Once a mutant showing sufficient **computational** selectivity and reactivity scores is identified, its catalytic ability for the target chemical reaction is **experimentally** verified.

(3) Design and discovery of new materials

The control over chemical reactions is an essential prerequisite in the production of modern and functional materials. In other words, ICReDD should also tackle to find out new chemical reactions and regulate them to produce novel high-performance materials. Nonetheless, because the number of atoms involved in material systems is large and the degree of complexity is different from that of molecular systems by an order of magnitude, there are many objects for which even theoretical analysis cannot be performed satisfactorily. Based on the recent results of the experimental researchers in ICReDD, we are currently conducting exploratory studies on polymeric- (**3-1**), luminescent- (**3-2**), gel- (**3-3**), and nano-materials (**3-4**) to see what kind of computation- and informatics-guided design strategies can be adopted. Among them, for nano-materials, we succeeded in designing useful materials in (**3-4-b**) and (**3-4-c**) with computation-driven approaches. On the other hand, for polymeric, luminescent, and gel-materials, we are still in the phase of analyzing available experimental results. To proceed beyond this phase, we initiated an attempt to implement a computation- and informatics-driven design for polymer materials that respond to special stimuli (**3-1-b**).

3-1) Polymer materials

†a) Exploration of reactivities of aliphatic polyketones

Functional molecular materials based on aliphatic polyketones have been developed, such as π-conjugated chromophores, lithium ion-conducting materials, and metal-ion absorbers. A new photochemical rearrangement reaction that cleave and reorient π-conjugation has been found. The excitonic interactions of π-conjugated materials generated from polyketones were experimentally and theoretically analyzed by Miyata (Kyushu University). In addition, the prediction of the preferred conformations of polyketones is being investigated in collaboration with Kobayashi of the **Taketsugu group** using conformational searching techniques.

*†b) Stimuli-degradable polymer material

Nakajima of the **Gong group**, Kubota and Jin of the **Ito group**, Harabuchi of the **Maeda group**, Yamamoto of the **Rubinstein group**, the **Takigawa group**, and **Hijikata** and **Pirillo** of ICReDD's mix-office, are working on the development of stimuli-degradable polymer materials. Considering the global environmental problems associated with microplastic pollution, there is an urgent need to develop polymers that are strong under normal conditions but are easily degraded by special stimuli. In this project, changes in the bond strength in the main chain induced by external stimuli are screened **computationally** for a variety of polymer candidates in order to identify the polymer most responsive to external stimuli. To reduce the number of required **computational** trials, **informatics** techniques will be applied. Once a good candidate is suggested **computationally**, its performance will be verified **experimentally**.

3-2) Luminescent materials

a) Effective photosensitizer for bright-luminescent Eu(III) complex

Photosensitizers are molecules that become excited by adsorption of light and transfer this excitation energy to another molecule. Photosensitizers are attractive for use in photochemical reactions, energy conversion systems and luminophores. Kitagawa of the **Hasegawa group** designed a photosensitizer based on extending the lifetime in the triplet excited state and reducing the gap between energy levels in the photosensitizer molecule. The effective photosensitizer is composed of a nanocarbon "antenna" made of coronene, a polycyclic aromatic hydrocarbon containing six benzene rings. Two nanocarbon antennas are stacked one on top of the other and then connected on either side to the red-luminescent europium. Extra connectors are added to strengthen the bonds between the nanocarbon antennas and europium. When the Eu(III) complex was irradiated with blue LED (light-emitting diode) light, it glowed more than five times brighter than the Eu(III) complex which showed the strongest emission under blue light reported so far. Kitagawa of the **Hasegawa group** also demonstrated that the Eu(III) complex can bear high temperatures above 300°C based on its rigid structure (*Commun. Chem.* 2020, *press release*, applied to international patents in Europe, China, USA). This study provides insight into the photosensitizer design for the development of photofunctional materials utilizing low-energy light.

3-3) Gel materials

†a) Controlling monomer sequences of copolymerization for supra-functions of hydrogels

The function of a hydrogel material depends not only on the chemical structure of the constituent monomers, but also on the monomer sequences. A few efforts have been made on the sequence control of monomers in hydrogel research. Fan of the **Gong group** has discovered that copolymers with adjacent cation–aromatic sequences can be synthesized through cation–π complex-aided free-radical polymerization (*Nat. Commun.* 2019). Based on this discovery, sequence-controlled hydrogels from diverse cation/aromatic monomers have been developed. These hydrogels exhibited unique functions that could not be achieved by the corresponding hydrogels without sequence control. Specifically, common poly(cation–π) networks having no controlled sequence hardly swell and are not adhesive to negatively charged surfaces in seawater since the electrostatic interaction is screened by the high ionic-strength environments. However, the newly developed poly(cation–adj-π) gels having controlled sequence exhibit fast, strong, but reversible adhesion to negatively charged surfaces in seawater. Aromatics on copolymers are found to enhance the electrostatic interactions of their adjacent cationic residues to the counter surfaces even in a high ionic-strength medium that screens for electrostatic interactions for common polyelectrolytes. This work opens a pathway to developing adhesives that work in saline water. This research giving insight into the molecular mechanism of adhesive proteins that contain rich adjacent cationic–aromatic amino acids sequences was rated as one of the most-read Nature Communications articles in chemistry and materials science in 2019 and was reported on by various international media outlets. Through a collaboration between the **Gong group** and the **Maeda group**, the initial stage of the polymer growth has been studied theoretically to gain atomistic understanding of the sequence control achieved in this material.

3-4) Nano-materials

‡a) Single-molecule resonance Raman effect in a plasmonic nanocavity

In collaboration with an **experimental group** at RIKEN led by Kim, Iwasa of the **Taketsugu group** contributed the theory parts to the study of a single molecule adsorbed onto NaCl/Ag(111) using scanning tunneling microscope tip-enhanced Raman spectroscopy (TERS) imaging. **Experimental** results together with **theoretical** analysis reveal that under resonance excitation conditions, the TERS imaging patterns depend on the molecular vibrational symmetries and that the perpendicular components of the electric near-field can play a substantial role in the enhancement. This single-molecule study in a well-defined environment provides insights into the Raman process at the plasmonic nanocavity, which may be useful in the nanoscale metrology of various molecular systems (*Nature Nanotech***.** 2020).

‡b) Synthesis of stable single-phase borophene on an Ir(111) surface

Lyalin of the **Taketsugu group** reported several significant findings on the properties of nanomaterials as a result of collaborations with international **experimental groups**. A novel single-phase structure of borophene (a two-dimensional layer of boron atoms) on an Ir(111) surface has been discovered via a combination of large-scale **computational** simulations and **experiments** in the groups of Preobrajenski (Sweden) and Vinogradov (Russia). Discovered experimentally in 2015, borophene was mainly studied on Ag(111) where it can be formed as a mixture of several different phases. As the physical properties of these phases are intrinsically different, their co-existence hindered the practical implementation of this material, and thus, the discovery of stable single-phase borophene on Ir(111) is a major step towards unleashing the borophene's potential (*ACS Nano* 2019). In collaboration with the **experimental group** of Huang (Australia), Lyalin and Kumar of the **Taketsugu group** have demonstrated that highly defective boron nitride possesses performs outstandingly at the oxidative dehydrogenation of ethylbenzene. Using **computations**, the enhancement in catalytic activity was explained by the formation of a large number of active BN edge sites in the catalyst (*J. Ene. Chem.* 2020).

‡c) Carbon material exhibiting very high Seebeck coefficient

The **Maeda group** contributed to a discovery of a carbon material showing an extremely high Seebeck coefficient. The **experimental** parts of this study were done by Hada of the University of Tsukuba and coworkers. We first conducted theoretical searches for annealing paths of amorphous carbon using the AFIR method. The searches were done for cases with and without carbon nanotubes around the amorphous carbon. As a result, it was found that in the case where a carbon nanotube is present, a structural transition from a sp^3-bond-rich state to a sp^2-bond-rich one takes place at a lower temperature in a shorter time than in the case where a carbon nanotube is not present. It is expected that carbon materials with few defects can be synthesized if the structural transition occurs at a low temperature in a short time. Therefore, the annealing experiment was conducted in the presence of carbon nanotube yarn. This resulted in a carbon material with few defects, and it was found to show an extremely high Seebeck coefficient (*ACS Appl. Energy Mater.* 2019).

(4) Creation of innovative measurement and diagnosis methods

Many measurement technologies in chemistry is based on a series of chemical reactions. The improvements of the scope of application and efficiency of the measurements also have a significant impact on the design and discovery of chemical reactions. Therefore, we ventured to create innovations in the measurement technologies by using combined approaches of experimental, computational and information science. ICReDD is also challenging innovation in one of the most complex measurements, diagnosis, a clinical measurement. In FY2019, we engaged in a fusion research to expand the gel materials from **Gong group** into an innovative cancer diagnosis technology.

4-1) Novel measurement techniques for chemical systems

*†a) Prediction of Chirality with Computer and Information Sciences

The **Ito** and **Takigawa** groups started a collaboration study for predicting the compound properties generated by chirality. Organic compounds with chirality can be formed as either one of a pair of enantiomers with similar chemical and physical properties. However, the biological activity of one enantiomer is often very different from that of the other enantiomer. The composition of enantiomers can be analyzed by the HPLC technique. Still, it has been impossible to predict which of the two enantiomers would have the shorter retention time and be eluted faster by HPLC with a chiral phase. We are studying a method for predicting of this essential information in chirality analysis by the combination of **experimental**, **computational**, as well as **information** science.

4-2) Cancer diagnosis

†a) Successful rapid induction of cancer stem cells by hydrogel

The **Tanaka** and **Gong** groups established a novel technique for rapidly and efficiently inducing cancer stem cells using a double network hydrogel (DN gel) developed by the **Gong group**. This phenomenon is referred to as the HARP (hydrogel activated reprogramming) phenomenon, and patent on its discovery is pending (Japan 2017-028833:PCT/JP2018/005884:US 16/487,247). For a complete cure of cancer patients, eradication of cancer stem cells (CSCs) is required. CSCs are resistant to chemo- and radiotherapies and are a source of cancer recurrence. However, detection of CSCs is extremely difficult. Here, we found the presented the novel potential of a DN gel to rapidly generate CSCs. By placing cancer cells onto DN hydrogels, formation of spheres that expressed stemness markers was observed within 24 hours. These DN gel-induced CSCs were highly tumorigenic in SCID mice, indicating the presence of functional CSCs. This rapid detection of CSCs can be used for CSC diagnosis directly predicting the therapeutic reagents for individual cancer patients. In addition, DN gels may become a powerful tool for detecting CSCs promising to contribute to the discovery of reagents for the complete eradication of CSCs. We have elucidated the mechanism of induction of CSC by DN gel in the HARP phenomenon and found that DN gels rapidly modulated the cellular gene expression and facilitated the reprogramming of differentiated cancer cells towards CSCs via the calcium channel TRP/osteopontin/tyrosine kinase signaling axis. This may become an epoch-making result that leads to the development of a new method for diagnosis and treatment of cancer stem cells using hydrogels (accepted by *Nat. Biomed. Eng.* 2020).

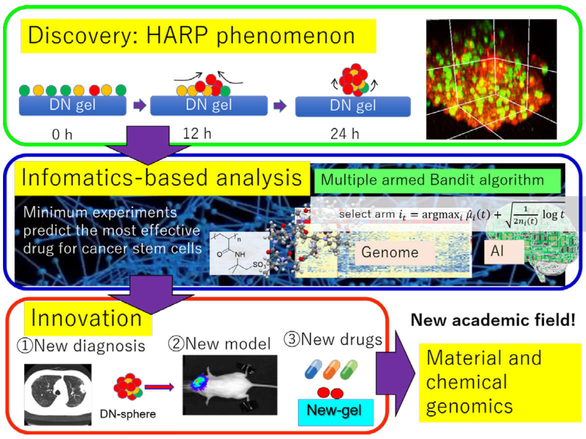


Figure 5. Based on the discovery of HARP phenomenon, informatics-based analysis, multiple-armed Bandit algorithm can predict the most efficient drugs to eradicate CSCs by minimal numbers of the experiments. The goal of this project is to bring three types of innovation as 1) new cancer diagnostic system, 2) new cancer model for therapy, and 3) new drugs for CSCs. Entire process creates the new academic field, material and chemical genomics.

2. Generating Fused Disciplines

* Describe the content of measures taken by the center to advance research by fusing disciplines. For example, measures that

facilitate doing joint research by researchers in differing fields. If any, describe the interdisciplinary research/fused discipline that have resulted from your efforts to generate fused disciplines. You may refer to the research results described concretely in "1. Advancing Research of the Highest Global Level."

ICReDD scientific mission

ICReDD's slogan, "*Revolutionize Chemical Reaction Design and Discovery*" expresses our vision to renew the way chemical reactions are developed by fusing **computational science**, **information science**, and **experimental science**, and to tackle current and future challenges for humanity. To achieve the scientific mission by **computation/informatics**-driven research, we established various built facilities and social institutions, such as (1) Incubation space for fusion research, (2) ICReDD seminar system, (3) Interdisciplinary research start-up support, and (4) Setup of flagship research projects.

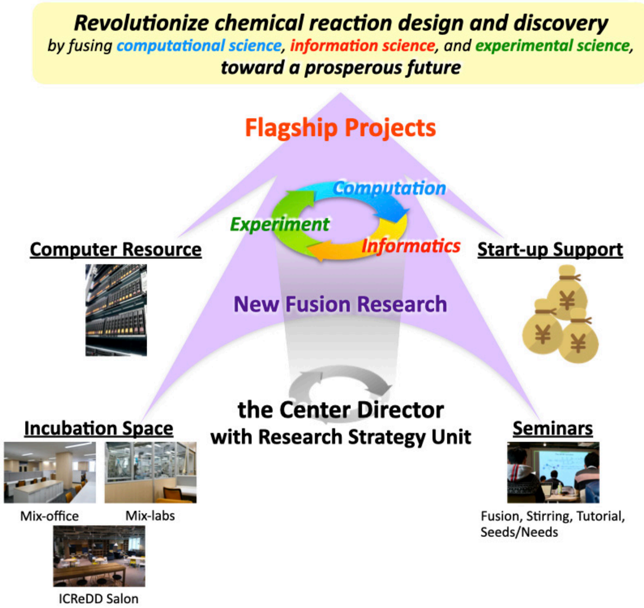


Figure 6. The overview of measures by ICReDD taken to advance research by fusing disciplines.

(1) Incubation space for fusion research: Establishment of the mix-office, the mix-labs, and the ICReDD salon

To accelerate the emergence of true fusion research, a new mix-office and two new mix-labs, have been launched, which catalyze spontaneous, every-day scientific communication across disciplines. In these 3 rooms, researchers from the three fields are seated in a mixed fashion. In the mix-office, the establishment of PI rooms enables low-threshold communication to PIs and their mingling with members of other groups. The cross-disciplinary interaction picked up right after the establishment of these mix-rooms and even across different rooms. Indeed, many experimental scientists have started to use calculations by themselves in their projects on a daily basis with strong support from computational scientists in these mix-rooms. In order to support computational environment, we additionally installed a new computational cluster machine that have 4,000 CPU-cores in total. In addition, we furnished a separate room, ICReDD Salon, where researchers can spend time together for various purpose, from a leisurely talk or coffee break to a scientific discussion, a seminar, a meeting, etc. The newly established environment is a strong support in the spirit of our slogan for all of the members to integrate the knowledge and skills of each group, which is important to initiate fusion research with new ideas. In addition, we submitted a budget request for a new building to enable us to share even more space and time with each other under one roof.

(2) ICReDD seminar system: We set up seminars toward fusion researches to find research seeds and to accelerate research activities. The Center Director and the Research Strategy Unit Manager attended all seminars to support their challenges.

Fusion Seminar

Bi-weekly and monthly seminars were held a total 14 times over half a year after many new faculty members joined ICReDD in April 2019 to learn what kinds of backgrounds, knowledge and skills our members have. The seminars were helpful not only to learn about the expertise of the researchers but also to understand differences in standard practice and style in each field.

Stirring Seminar

We recognized that we need a more fundamental understanding of each other's work to come up with new ideas during the fusion seminars. For example, even though both computational and information scientists use computers, it was sometimes difficult to find common terminologies. We started the stirring seminars (held 5 times in FY2019) led by pairs of researchers from two different fields, in which one researcher prepares a presentation on his/her research and the other researcher presents it to the audience with an even more diverse background. During the preparation for the presentation, the presenters can learn about a field outside of their expertise more deeply than by just listening to presentations, while the researcher who prepared the presentation has an opportunity to understand what researchers in other fields do not understand. In addition, it is also easier for audiences to follow such presentations because of the easier explanations by non-experts.

Tutorial Seminar

The tutorial type seminar has been started to share an overview of one approach, one topic, one technique, etc. with a broader perspective. The tutorial seminar is held irregularly upon requests from researchers (topics in FY2019: Cheminformatics. In FY2020, 3 topics)

Seeds/Needs Seminar

Our seminars are not only an opportunity to learn but we also started to prepare seminars aimed more directly at common research, namely the Seeds/Needs seminar, in which researchers explain their ongoing research projects to get ideas from other fields for their stumbling blocks or researchers introduce their techniques and ideas for fusion researches that might be of interest to researchers in other fields.

(3) Interdisciplinary research start-up support:

We assigned start-up budgets to 8 research projects for a total 37.5 million JPY to encourage and support their challenging bottom-up fusion projects, and successfully started research collaboration toward realizing true fusion research. We revise our selection process for the start-up budget to become able to more flexibly assign it to bottom-up research projects coming out of the ICReDD seminars and daily spontaneous discussion, and to encourage young faculty members to initiate fusion research among the three fields.

(4) Setup of flagship research projects:

ICReDD set challenging and long-term targets of high significance as mentioned in section 1. To decide such targets, the Center Director called for proposals of new fusion research to PIs and young researchers in ICReDD. As a result, 23 research proposals were received. After careful discussions with them, the Center Director selected five themes as new flagship projects (projects i - iii, v and vi in Table 1). In addition to these five, two additional projects that have been proceeding were also set as flagship projects (projects iv and vii in Table 1). These seven are thus flagship projects of ICReDD, and ICReDD will focus on them most in FY2020. It is noted that all these seven are challenging and long-term targets of high significance, and the themes could revolutionize current scientific concepts. To pursue the newly launched flagship projects smoothly, these projects hold a project meeting monthly among all involved members together with the Center Director and the Research Strategy Unit Manager.

Table 1. Flagship projects in ICReDD.

Project		Member	Area	Related description in section 1
i)	Integration of Theory-driven and Data-driven Reaction Prediction	Varnek, Komatsuzaki, Takigawa, Taketsugu, Maeda	Informatics technique	1-1
ii)	New Chemical Reaction Discovery [a]	List, Ito, Mita (Mix-lab), Inokuma, Hasegawa, Maeda, Taketsugu	Synthesis	2-1, 2-2-c
iii)	Designing Cavity in Supramolecular Catalyst	Sawamura, Taketsugu, Komatsuzaki, Varnek	Synthesis	2-2-a
iv)	Bridge between Micro- and Macro-Worlds	Ito, Gong, Hasegawa, Rubinstein, Maeda	Synthesis	2-3
v)	Reaction Discovery by Artificial Enzyme Design	Tanaka, Mita (Mix-lab), Maeda, Takigawa	Synthesis	2-4
vi)	Stimuli-Degradable Polymer Material	Gong, Ito, Rubinstein, Maeda, Hijikata (Mix-office), Takigawa	Material	3-1-b
vii)	Development of Cancer Diagnosis Method	Tanaka, Gong, Hasegawa, Komatsuzaki	Diagnosis	4-2

[a] This project focuses on multiple chemical reactions such as amino acid synthesis from CO or CO_2, exploring catalysts for peptide bond activation, and so forth, and three target reactions were newly set as focus through this initiative.

3. Realizing an International Research Environment

* Describe what's been accomplished in the efforts to raise the center's recognition as a genuine globally visible research institute, along with innovative efforts proactively being taken in accordance with the development stage of the center, including the following points, for example:

- Efforts being developed based on the analysis of number and state of world-leading, frontline researchers (in Appendix 2); exchanges with overseas entities (in Appendix 4); number and state of visiting researchers (in Appendix 5)
- Proactive efforts to raise the level of the center's international recognition
- Efforts to make the center into one that attracts excellent young researchers from around the world (such as efforts fostering young researchers and contributing to advancing their career paths)

ICReDD has rapidly advanced the formation of an international research environment in FY2019. To raise the center's recognition as a highly visible research institute of genuinely global rank, ICReDD continued its efforts on **Human resources internationalization**, **organizational internationalization**, **internationalization of young researchers**, and **international public relations**.

Human resources and organizational internationalization

(1) Strategy of recruiting international researchers

As a result of refining our recruitment process, in the last stage of the interview process all final candidates are interviewed by the Center Director directly to ensure that they share the mission of ICReDD. We received a large number of domestic and international applications (225) for 33 positions, 18 of which were filled with foreign nationals. As of March 31, 2020, 22 among the total of 59 researchers (37%) are foreign nationals, and 6 researchers (10%) are female. Co-PIs and postdoctoral researchers were also appointed to work under the three overseas PIs. After recruitment, ICReDD provided start-up support, and gave guidance in applying for external funding, to help the newly hired researchers achieve outstanding results during their tenure, and to become prime candidates for faculty and postdoctoral positions at other international research institutions.

(2) Establishment of relationships with domestic and international sites

Overseas PI's host institutions are important partners of ICReDD. The University of Strasbourg (France), the Max-Planck-Institute (Germany), and Duke University (USA). We have started planning for international symposia to be held at each of these institutions every few years and are aiming to conclude inter-university agreements or MOUs with the Max-Planck-Institute, and Duke University. ICRDD has also conducted joint research with ESPCI, ETH-Zurich, Peking University, the Graduate School of Informatics, Kyoto University, and Chubu University, and active exchanges are taking place between their members and ICReDD. We have already concluded inter-university agreements with these institutions (ESPCI, ETH-Zurich, and Peking University) and are planning to conclude MOUs in the future. Collaborations with the University of Oslo and with Stockholm University focusing on computational and information science are ongoing and a joint symposium is planned for in FY2020. Moreover, in order to deepen ties with domestic and overseas research institutes, ICReDD has agreed to sign agreements with Chubu University, the University of Strasbourg and Stockholm University.

To further deepen our work in information science, it was decided to add Professor Satoru Iwata from the Graduate School of Information Science and Technology at the University of Tokyo, as a PI in FY2020 and to conclude a partnership agreement with the institution. Professor Iwata will develop an informatics tool to extract useful information for chemical reaction design and discovery from the AFIR reaction path map database used at ICReDD.

Figure 7. Institutions planning to enter into international agreements with ICReDD.

(3) Rhythm of international symposia (Internationalization of young researchers)

We held the second International Symposium with 8 overseas and 4 domestic lecturers, and a total of 403 participants attended the symposium, discussing the fusion of computational science, information science, and experimental science, and establishing exchange relationships among the participants. This contributed to realizing an international research environment and to fostering the internationalization of our young researchers through providing them with opportunities to present (25 poster presentations) before an audience of young faculty members and postdoctoral fellows (162 participants). A series of symposia is being planned to be held in FY2020, including at university of Oslo, Stockholm University, TACC2020, Pacifichem, and Strasbourg University. We have already decided lecturers for the symposium at the University of Strasbourg (February 2021). It was decided that each PI will organize an international symposium at least once in the future.

(4) Establishment of Akira Suzuki Award and ICReDD Award

In order for ICReDD to be recognized by excellent researchers around the world, we have decided to establish two awards. One is called the Akira Suzuki Award, which will reward researchers who have made outstanding achievements in the development of chemical reactions. Another is the ICReDD Award, which will be given to researchers who have made distinguished achievements in the development of chemical reactions in computational (theoretical) and information science. The award winners have been selected and preparations for the award ceremony and the award lecture at the International Symposium are underway for both awards.

(5) Development of the MANABIYA system (Internationalization of young researchers)

We have established the "MANABIYA (ACADEMIC)" and "MANABIYA (INDUSTRY)" as a part of a strategic framework that enables us to develop an international collaborative research environment and foster highly skilled world-class researchers, and to help us build collaborative relationships with research centers in Japan and overseas. The MANABIYA system will be the basis of our new graduate school, the "Graduate School of Chemical Reaction Design and Discovery". Young researchers and graduate-level students from domestic and international research centers, universities and companies are invited to stay at ICReDD from 2 weeks to 3 months. The purpose of this system is to help the researchers acquire ICReDD's techniques for developing new chemical reactions.

To promote awareness of the MANABIYA system among external researchers, the MANABIYA AFIR Workshop was held during the 2nd International Symposium in November 2019. 36 researchers were accepted to participate in MANABIYA (ACADEMIC) on a trial basis. 22 corporate researchers were recruited as part of the MANABIYA (INDUSTRY) trial through joint research contracts and academic consultancy agreements, etc. We began accepting applications for MANABIYA (ACADEMIC) in March 2020 and are planning to accept 20 students in FY2020.

(6) International public relations and outreach activities

Members of ICReDD participated in various international conferences, including WCSJ2019 (Lausanne) and AAAS (Seattle), to publicize ICReDD's activities in front of an international academic and journalistic audience. We published a recruitment booklet entitled "REACT WITH US" introducing the research facilities and the views of actual researchers at ICReDD to attract international talent to ICReDD and disseminated it widely in Japan and overseas. The website of ICReDD was revised to make frequently posted news updates more visible, and we use a variety of channels to target different audiences (international vs. domestic audiences, established vs. young researchers, academic vs. non-academic audiences, etc.). ICReDD decided to publish an annual magazine, quarterly newsletters and monthly news-postcards in addition to regular digital research and researcher highlights starting from FY2020.

4. Making Organizational Reforms

* Describe the system reforms made to the center's research operation and administrative organization, along with their background and results.
* If innovated system reforms generated by the center have had a ripple effect on other departments of the host institutions or on other research institutions, clearly describe in what ways.
* Describe the center's operation and the host institution's commitment to the system reforms.

We implemented measures to ensure that the vision and mission of ICReDD is shared among all members of the center and so that the Center Director has the final decision in all matters related to the operation and management of ICReDD. The measures are as follows: (1) <u>Improvement of the management structure</u>, (2) <u>revision of the organizational structure,</u> and (3) <u>revision of the University's rules of employment and salary system</u>.

(1) Improvement of the management structure

In order to realize the mission of the center and to contribute to its further development, we added the following two professors; Professor Kuniharu Ijiro, Vice Director of the Research Institute for Electronic Science, as advisor, and Professor Koichiro Ishimori from the Faculty of Science, who has experience as dean of the department, as Executive Director (ED). With the ED devoting 50% of his effort to be directly involved in the operations, ICReDD is becoming an organization that supports the strong governance of the Center Director. The ED also plans to evaluate faculty members' achievements and have face-to-face conversations to share ICReDD's vision and mission, in an effort to increase the researcher's motivation and to encourage the discovery of new research seeds. The advice received from the advisory board of domestic and international experts will further strengthen the management system.

(2) Revision of organizational structure

The following committees and meetings have been established to ensure the smooth operation and to share the vision and mission among all members.

Steering Committee: The Center Director, Vice Director, Administrative Director, Executive Director and three principal investigators appointed by the Center Director, one from each of the three fields, met 12 times in FY2019 to discuss matters related to the center.

Executive Committee: 41 Meetings were held between the Center Director, Vice Director, Administrative Director, Executive Director, Advisor, Research Strategy Unit Manager, Mix-lab Chief and Management Planning Unit Manager to assist the Center Director in his decision-making.

PI Meeting: The meeting was held every month as a place for young researchers to exchange opinions among each other. However, from July, it was changed to a PI meeting as a place for PIs to exchange opinions and for sharing ICReDD's vision, mission and research & management strategy.

Advisory Board: Five foreign and three domestic researchers will be appointed as members of the Advisory Board to advise on the operation and research of ICReDD for the enhancement of our international presence.

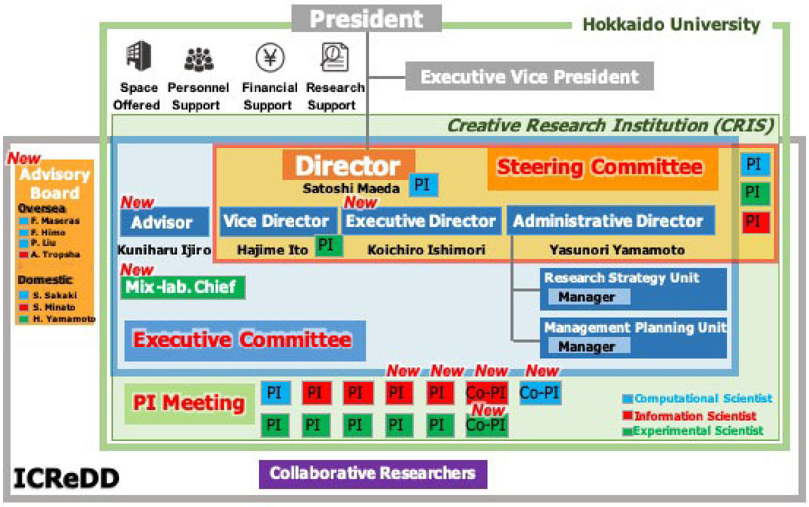


Figure 8. Revision of management and organizational structure.

(3) Revision of the University's rules of employment and salary system

The University's rules of employment were revised to emphasize the responsibility to the formation of the institute, including the establishment of a provision of allowances for those who devote their effort to engage in ICReDD's management and fusion research (Center Director, Vice Director, Executive Director, Administrative Director, and PIs).

5. Efforts to Secure the Center's Future Development over the Mid- to Long-term

* Address the following items, which are essential to mid- to long-term center development:
- Future prospects with regard to the research plan, research organization and PI composition; prospects for fostering and securing of next-generation researchers
- Prospects for securing resources such as permanent positions and revenues; plan and/or implementation for defining the center's role and/or positioning the center within the host institution's institutional structure
- Measures to sustain the center as a world premier international research center after program funding ends
- Host institution's organizational reforms carried out for the center's autonomous administration simultaneously with the creation of the center.

In the following, medium- and long-term organizational developments are discussed in highlighting the initiatives taken by the Executive Committee, the New Building Working Group, the Future Planning Working Group, and the Institute for the Promotion of Business-Regional Collaboration, Hokkaido University.

(1) Research plan, researcher composition and the final personnel composition

a) Research plan: ICReDD defined its four flagship research areas to establish computation/informatics-driven strategies for the development of chemical reactions and the creation of new chemical reactions and materials as: **(1) Development and integration of state-of-the-art computational & informatics techniques**, **(2) Design and discovery of new synthesis methods**, **(3) Design and discovery of new materials**, and **(4) Creation of innovative measurement and diagnosis methods**.

b) Researcher composition to carry out the research plans:

Currently, 46% of ICReDD researchers are from computational/informatics, and 54% are experimental scientists, for FY2023, we aim for a researcher composition of 50% from computational/informatics, and 50% experimental scientists.

- At the end of March 2020, 22 among a total of 59 researchers (37%) are foreign nationals, and 6 researchers (10%) are female (PIs: 14 [3 computational, 4 information and 7 experimental scientists], faculty members: 20, researchers: 15, research collaborators: 10).
- At the end of March 2023, 28 among a total of 70 researchers (40%) to be foreign nationals, and 10 researchers (14%) to be female (PIs: 15 [3 computational, 5 information and 7 experimental

scientists], faculty members: 24, researchers: 20, research collaborators: 11).

(2) Buildings and Facilities

Improvement of the environment for promoting integrated research and the future of the mix office and labs:

The currently developed research space (about 1,400 m^2) in the University's CRIS building comprises an analytical instrument room, a large computer server room, a dry Mix-office for a focus on computational and information science and a wet Mix-lab for experimental science. An additional 1,200 m^2 of research space in the CRIS building was secured with top-down financial support of 189 million JPY from the university's executive department. A new building (5,500 m^2) connected to the CRIS building is planned to be built. The budget request to the government is planned as a top priority project for FY2021, and the university has committed to contributing half of the building cost of the new building (up to 1,220 million JPY). The new building will prominently feature a "*Super Mix-lab.*" where 75 researchers from all three fields can mingle on an every-day basis, further accelerating research fusion.

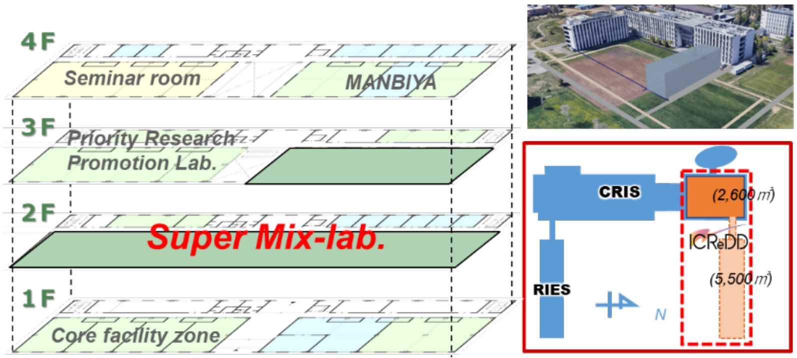


Figure 9. The conceptional drawing of the new building (5,500m^2) that will be connected to the CRIS building.

(3) Form of organization

New institute organization:

The Future Planning Working Group launched discussions on the re-organization of the institute for the establishment of our new graduate school, on the space management for the new building and facilities in the CRIS building, financial plans, on the system of cooperation with other research institutes in the university, and etc. ICReDD is a special organization under the direct control of the President and operates under a fast-track decision-making system, and will contribute to the organizational reform of CRIS.

(4) Finance (external funds and joint research funds with companies)

The financial outlook for the institute is being discussed in the Future Planning Working Group, and the composition of the sites' operating expenses for FY 2019 is as follows.

・Support from the host institution (339 million JPY Top-down Financial Support: relocation and renovation funding, operational funding (including laboratory costs for PIs and research space) and reducing the educational duties of PIs, etc.

・668 million JPY in external funding (FY2019).

To expand the acquisition of external funds, we are also considering (a) measures to promote the acquisition of external funds, and (b) the development of a financial plan for the end of the grant period.

a) Measures to increase fund acquisition

・Start-up support for fusion research
・Seminar for the improvement of application writing skills
・Direct support of young faculty members who have not acquired external funding.
・Promotion of joint research with companies.

b) Future financial planning

We drew up a plan to obtain 700 million JPY (100 million JPY in indirect expenses) in external funding to operate ICReDD after the support period.

・Grants-in-Aid for Scientific Research, etc.: 600 million JPY (90 million JPY in indirect expense) and joint research funds with companies: 100 million JPY (15 million JPY in indirect expense).

(5) Human resource development

MANABIYA and the promotion of the recruitment of specially appointed faculty:

Through MANABIYA, ICReDD fosters the next generation of international researchers are well versed in the three fields of computational science, information science, and experimental science. In cooperation with other faculties at the university, the university provides a wide range of opportunities to attend education and presentations at graduate schools, summer institutes, MANABIYA lecturers, symposia, and seminars to boost the skill of young faculty members. In addition, we integrate international researchers through the MANABIYA, ICReDD's seminars and symposia, in collaboration with the Hokkaido Summer Institute, the Learning Satellite (a range of international education programs at the University), the World-leading Innovative & Smart Education (WISE) program and the Ambitious Leader's Program (ALP) (a program for leading graduate school).

(6) Graduate School

We are currently discussing the establishment of a new graduate school (15-20 students per year in a doctoral course) with the Graduate School of Chemical Sciences and Engineering. The new building will have two IT-equipped 30-person lecture rooms to prepare a state-of-the-art educational environment that integrates computational, information, and experimental science for graduate education. The host institution also drew up a concept for the WISE Program focusing on mathematical science, computational chemistry, and data science, which will start in FY2020. MANABIYA, in conjunction with the WISE Program, will actively contribute to the graduate education of the University and become the foundation for the establishment of ICReDD's own graduate school. We will establish our new graduate school by utilizing the MANABIYA system, ICReDD's seminars and symposium, and in collaboration with the Hokkaido Summer Institute and Learning Satellite, as well as taking advantage of the results of the interdisciplinary education in the Ambitious Leader's Program (ALP).

6. Others

* Describe what was accomplished in the center's outreach activities last year and how the activities have contributed to enhancing the center's "globally visibility." In Appendix 6, describe concretely the contents of these outreach activities. In Appendix 7, describe media reports or coverage, if any, of the activities.
* In addition to the above 1-5 viewpoints, if there is anything else that deserves mention regarding the center project's progress, note it.

Outreach activities headed by research strategy unit

The main goal of ICReDD's public relations strategy is to increase the institute's international visibility among the academic, scientific and industrial communities. In conjunction with the university's international public relations team and Institute for International collaboration, we device and implement a strategic public relations strategy with a clear target community and annual goals. In FY2019, ICReDD's Research Strategy Unit put special effort into advertising the institute as an attractive career development opportunity for talented young researchers. We executed this strategy by relying on the following tools: **(1) Press release**, **(2) Web-based activities**, **(3) International recruitment**, **(4) Outreach activities**.

(1) Press release:

We issued 7 research press releases and 1 research news article as well as hosted 1 press conference.

(2) Web-based activities:

To raise awareness of ICReDD, the website has been revamped to emphasize new developments, and a presence on social media has been established (Facebook (113 posts), Twitter (134 posts), YouTube (12 videos)). We created a promotion video as well as a video series aiming at introducing all our PIs, all posted on social media and the website. The average reach of SNS posts containing videos (2,175 per post) is on average 9 times higher than those containing only links (246 per post) and still 5 times higher than posts containing photos (435 per post). In addition, we started posting job openings on the internationally well-regarded website of Asia Research News.

(3) International recruitment:

A recruitment brochure was created and distributed by foreign PIs, by the PR team at conferences and online, both on our social media platforms and through the university's Ambassadors and Partners network. An advertisement for the center's jobs has started to appear on the website of "Asia Research News", and indeed, comparing similar time frames this and last year, the number of applications increased by 38%.

(4) Outreach activities:

We participated in 9 events (with ICReDD-focused booths at the WPI Science Symposium, the 2020 AAAS Annual Meeting, and the 2019 World Conference of Science Journalists, etc.), gave five general public lectures, three lectures for elementary, junior high and high school students, and three public lectures at Hokkaido University.

7. Center’s Response to Results of Last Year’s Follow-up

* Transcribe the item from the “Actions required and recommendations” section in the site visit report and the Follow-up report, then note how the center has responded to them.
* If you have already provided this information, indicate where in the report.

(1) The Program Committee urges ICReDD to establish a strong administrative/scientific team to support the director. Setting up of an advisory board is also recommended.

As stated in Section 4-(1), important matters are decided by the Executive Committee, and we have appointed an Advisor and an Executive Director (ED), who are directly involved in the development of operation and research strategies to reinforce the center's speedy, the Center Director-led operation and research support system, and have decided to set up an advisory board. The Advisory Board advises on the center's goals and strategies, as well as on matters related to fusion research and internationalization, in response to the Center Director's consultation. In addition, the Center Director started to interview final candidates for new faculty members and researchers.

(2) The center does not have competence in information science sufficient for the area to be fully integrated into the center. This problem should be solved promptly. The gender issue should also be addressed for the activity of ICReDD.

We had a change in information science PIs from Prof. Arimura to Prof. Yoshioka (Director of Global Stations for Big Data and Cybersecurity, GI-CoRE) to realize an efficient information retrieval from experimental databases and literature (section 1-1-1-c). Furthermore, as stated in section 3-(2), it was decided to add Professor Satoru Iwata from the Graduate School of Information Science and Technology at the University of Tokyo, as a PI in FY2020 and to enter in a partnership agreement with the institution. Professor Iwata will develop an informatics tool to extract useful information for chemical reaction design and discovery from the AFIR reaction path map database (AFIR^{3}M-DB) used at ICReDD, supporting the development of an efficient database (section 1-1-1-c). We will also address the gender issues. We are considering openings for women only and will encourage all PIs to hire female researchers.

(3) ICReDD’s vision and mission should be appropriately shared by all the center’s members.

To share the vision and mission, Executive Director Prof. Ishimori met with PIs and faculty members. PI meetings were held as an opportunity for the Center Director to exchange opinions with PIs, sharing the vision, mission, and research as well as operational strategies. As stated in section 3-(1), we reinforced the final hiring process, so that the Center Director can directly participate in interviews and share the mission of ICReDD.

(4) To realize the scientific goal(s) set by ICReDD, concrete and specific scientific targets should be promptly set. At the same time, challenging, long-term targets of high significance should be set, targets that could revolutionize current scientific concepts.

As stated in sections 1 and 2, to realize the scientific goals, ICReDD has defined its four flagship research areas as: **(1) Development and integration of state-of-the-art computational & informatics techniques, (2) Design and discovery of new chemical reactions**, **(3) Design and discovery of new materials**, and **(4) Creation of innovative measurement and diagnosis methods**. After the end of the fusion seminar series, we collected 23 proposals by PIs for new interdisciplinary research projects which differ from their own current trends/topics and were inspired by the fusion seminars. The Center Director selected the following 7 projects as “ICReDD interdisciplinary computation/informatics-guided initiative research themes” to aim for the discovery of a new chemical reactions that without aid from computational and information science cannot be found within 10 years.

(1) Development and integration of state-of-the-art computational & informatics techniques.

- <u>Integration of Theory-driven and Data-driven Reaction Prediction.</u>

(2) Design and discovery of new synthesis methods.

(a) <u>Designing Cavity in Supramolecular Catalyst.</u>
(b) <u>New Chemical Reaction Discovery.</u>
1. Amino acid synthesis from CO or CO_2; 2. Exploring catalysts for peptide bond activation; and three others

(c) Bridge between Micro- and Macro-Worlds.
1. Visualizing molecular breaking at the nanoscale.
2. Synthesis revolution by mechanochemistry.
(d) Reaction Discovery by Artificial Enzyme Design.

(3) Design and discovery of new materials.
- Stimuli-Degradable Polymer Material.

(4) Creation of innovative measurement and diagnosis methods.
- Development of Cancer Diagnosis Methods.

(5) Attention needs to be directed on identifying joint projects that achieve defined strategic objectives and on how working together and integrating skills across ICReDD can best be achieved.

Several new computational and information-driven projects have been started that involve four or more groups. Through these projects, we aim to integrate ICReDD's computational and information knowledge and technology to strategically realize the goals of ICReDD. A range of ICReDD seminar system (Fusion, Stirring, Tutorial and Seeds/Needs seminars) were held to find seeds of fusion research, to support their launch and to assign the start-up budget. The Center Director and the Research Strategy Unit (RSU) Manager attended all meetings about the projects proposed by PIs to support their initiation. Furthermore, the RSU Manager started to work in the mix-office to bridge computational, information, and experimental science. In addition, the RSU Manager interacts with the ICReDD members on a daily and during various events (ICReDD lunch, mixing events) to break down walls between scientific fields, nationality, and languages.

(6) There are a handful of good examples of international networking carried out on an individual basis among the PIs. The scope of these individual networkings should be expanded to an institutional level.

As stated in Section 3-(2), (3) and (4), the collaborations with the University of Oslo and the Stockholm University focusing on computational and information science are ongoing and a symposium is planned to be held in FY2020. In order to strengthen the ties with domestic and overseas research institutes, ICReDD has agreed to sign agreements (AEA or MOU) with the University of Strasbourg in France and Stockholm University in Sweden. We are also planning to establish agreements with the Max Planck institute and Duke university, etc. PIs will further organize ICReDD symposia at leading overseas research institutions to raise international visibility, after which we will pursue the conclusion of agreements with these institutions.

(7) Plan to publish booklet(s) and periodical(s). It is also suggested that an immediate effort be made to correct any broken links and to urgently improve ICReDD’s current website.

The broken links were corrected. We published a recruitment booklet entitled "REACT WITH US" introducing the research facilities and the views of actual researchers at ICReDD to attract international talent to ICReDD and disseminated it widely in Japan and overseas. The website of ICReDD was revised to make frequently posted news updates more visible, and we use a variety of channels to target different audiences (international vs. domestic audiences, established vs. young researchers, academic vs. non-academic audiences, etc.). ICReDD decided to publish an annual magazine, quarterly newsletters and monthly news-postcards in addition to regular digital research and researcher highlights starting from FY2020. As stated in Section 6, videos were produced to introduce the center and portray all PIs, which have been received very positively.

(8) It is urgent that additional lab space is secured, to do which the construction of a newbuilding is the key. HU should, as quickly as possible, take aggressive action to provide ICReDD with an expanded working environment.

ICReDD submitted a request to the university while liaising with both the university and MEXT. As a result, a new building (5,500 m^2) connected the CRIS building is planned to be built. The budget request to the government is planned as a top priority project for Hokkaido University in FY2021, and the university has committed to contributing half of the building cost of the new building (up to 1,220 million JPY).

Appendix 1　FY 2019 List of Center's Research Results and Main Awards

1. Refereed Papers

- List only the Center's papers published in 2019. (Note: The list should be for the calendar year, not the fiscal year.)

(1) Divide the papers into two categories, A and B.
A. WPI papers
List papers whose author(s) can be identified as affiliated with the WPI program (e.g., that state "WPI" and the name of the WPI center (WPI-center name)). (Not including papers in which the names of persons affiliated with the WPI program are contained only in acknowledgements.)
B. WPI-related papers
List papers related to the WPI program but whose authors are not noted in the institutional affiliations as WPI affiliated. (Including papers whose acknowledgements contain the names of researchers affiliated with the WPI program.)

Note: On 14 December 2011, the Basic Research Promotion Division in MEXT's Research Promotion Bureau circulated an instruction requiring paper authors to include the name or abbreviation of their WPI center among their institutional affiliations. From 2012, the authors' affiliations must be clearly noted.

(2) Method of listing paper
- List only refereed papers. Divide them into categories (e.g., original articles, reviews, proceedings).
- For each, write the author name(s); year of publication; journal name, volume, page(s), and article title. Any listing order may be used as long as format is consistent. (The names of the center researchers do not need to be underlined.)
- If a paper has many authors (say, more than 10), all of their names do not need to be listed.
- Assign a serial number to each paper to be used to identify it throughout the report.
- If the papers are written in languages other than English, underline their serial numbers.
- Order of Listing
A. WPI papers
1. Original articles
2. Review articles
3. Proceedings
4. Other English articles

B. WPI-related papers
1. Original articles
2. Review articles
3. Proceedings
4. Other English articles

(3) Submission of electronic data
- In addition to the above, provide a .csv file output from the Web of Science (e.g.) or other database giving the paper's raw data including Document ID. (Note: the Document ID is assigned by paper database.)
- These files do not need to be divided into paper categories.

(4) Use in assessments
- The lists of papers will be used in assessing the state of WPI project's progress.
- They will be used as reference in analyzing the trends and whole states of research in the said WPI center, not to evaluate individual researcher performance.
- The special characteristics of each research domain will be considered when conducting assessments.

(5) Additional documents
- After all documents, including these paper listings, showing the state of research progress have been submitted, additional documents may be requested.

A. WPI papers

1. Original articles

1. A Polystyrene-Cross-Linking Tricyclohexylphosphine: Synthesis, Characterization and Applications to Pd-Catalyzed Cross-Coupling Reactions of Aryl Chlorides. J. Arashima, T. Iwai, M. Sawamura, *Chem. Asian J.*, **2019**, 14, 411-415

2. A Theoretical Study on the Mechanism of the Oxidative Deborylation/C-C Coupling Reaction of Borepin Derivatives. C. Ozen, Y. Shoji, T. Fukushima, S. Maeda, *J. Org. Chem.*, **2019**, 84, 1941-1950

3. Ab Initio Surface Hopping Molecular Dynamics on the Dissociative Recombination of CH_3^+. T. Taketsugu, Y. Kobayashi, *Comput. Theor. Chem*, **2019**, 1150, 1-9

4. Additive-Dependent Iptycene Incorporation in Polyanilines: Insights into the Pentiptycene Clipping Effect and the Polymerization Mechanism. WS. Tan, TY. Lee, SF. Tseng, YF. Hsu, M. Ebina, T. Taketsugu, SJ. Huang, JS. Yang, *J. Chin. Chem. Soc.*, **2019**, 66, 1141-1156

5. Adjacent Cationic–aromatic Sequences Yield Strong Electrostatic Adhesion of Hydrogels in Seawater. HL. Fan, JH. Wang, Z. Tao, JC. Huang, P. Rao, T. Kurokawa, JP. Gong, *Nat. Commun.*, **2019**, 10, 5127

6. Anharmonic Vibrational Computations with a Quartic Force Field for Curvilinear Coordinates. Y. Harabuchi, R. Tani, N. De Silva, B. Njegic, MS. Gordon, T. Taketsugu, *J. Chem. Phys*., **2019**, 151, 064104

7. Anisotropic Strain Release in a Thermosalient Crystal: Correlation Between the Microscopic Orientation of Molecular Rearrangements and the Macroscopic Mechanical Motion. T. Seki, T. Mashimo, H. Ito, *Chem. Sci*., **2019**, 10, 4185-4191

8. Anisotropic Thermal Expansion as the Source of Macroscopic and Molecular Scale Motion in Phosphorescent Amphidynamic Crystals. M. Jin, S. Yamamoto, T. Seki, H. Ito, MA. Garcia-Garibay, *Angew. Chem., Int. Ed*., **2019**, 58, 18003-18010

9. Asymmetric Synthesis of α-Alkylidene-β-Lactams Through Copper Catalysis with a Prolinol-Phosphine Chiral Ligand. K. Imai, Y. Takayama, H. Murayama, H. Ohmiya, Y. Shimizu, M. Sawamura, *Org. Lett*., **2019**, 21, 1717-1721

10. Autopsy Findings in the Early Stage of Amyotrophic Lateral Sclerosis with "Dropped Head" Syndrome. S. Tanikawa, M. Tanino, L. Wang, M. Ishikawa, M. Miyazaki, M. Tsuda, Y. Orba, H. Sawa, K. Matoba, N. Nakamura, K. Nagashima, WW. Hall, S. Tanaka, *Neuropathology*, **2019**, 39, 374-377

11. Boron-Catalyzed Alpha-Amination of Carboxylic Acids. T. Morisawa, M. Sawamura, Y. Shimizu, *Org. Lett*., **2019**, 21, 7466-7469

12. Catalytic Enantioselective Synthesis of Allylic Boronates Bearing a Trisubstituted Alkenyl Fluoride and Related Derivatives. S. Akiyama, K. Kubota, MS. Mikus, PHS. Paioti, F. Romiti, QH. Liu, YB. Zhou, AH. Hoveyda, H. Ito, *Angew. Chem., Int. Ed*., **2019**, 58, 11998-12003

13. CO_2 Adsorption on $Ti_3O_6^-$: A Novel Carbonate Binding Motif. S. Debnath, XW. Song, MR. Fagiani, ML. Weichman, M. Gao, S. Maeda, T. Taketsugu, W. Schollkopf, A. Lyalin, DM. Neumark, KR. Asmis, *J. Phys. Chem. C*, **2019**, 123, 8439-8446

14. Combined Automated Reaction Pathway Searches and Sparse Modeling Analysis for Catalytic Properties of Lowest Energy Twins of Cu_{13}. T. Iwasa, T. Sato, M. Takagi, M. Gao, A. Lyalin, M. Kobayashi, K. Shimizu, S. Maeda, T. Taketsugu, *J. Phys. Chem. A*, **2019**, 123, 210-217

15. Concise Synthesis of Potassium Acyltrifluoroborates from Aldehydes Through Copper(I)-Catalyzed Borylation/Oxidation. J. Taguchi, T. Takeuchi, R. Takahashi, F. Masero, H. Ito, *Angew. Chem., Int. Ed*., **2019**, 58, 7299-7303

16. Conjugated Quantitative Structure-Property Relationship Models: Application to Simultaneous Prediction of Tautomeric Equilibrium Constants and Acidity of Molecules. DV. Zankov, TI. Madzhidov, A. Rakhimbekova, TR. Gimadiev, RI. Nugmanov, MA. Kazymova, II. Baskin, A. Varnek, *J. Chem. Inf. Model*., **2019**, 59, 4569-4576

17. Control over Coordination Self-Assembly of Flexible, Multidentate Ligands by Stepwise Metal Coordination of Isopyrazole Subunits. Y. Ashida, Y. Manabe, S. Yoshioka, T. Yoneda, Y. Inokuma, *Dalton Trans*., **2019**, 48, 818-822

18. Copper(I)-Catalyzed Enantioconvergent Borylation of Racemic Benzyl Chlorides Enabled by Quadrant-by-Quadrant Structure Modification of Chiral Bisphosphine Ligands. H. Iwamoto, K. Endo, Y. Ozawa, Y. Watanabe, K. Kubota, T. Imamoto, H. Ito, *Angew. Chem., Int. Ed*., **2019**, 58, 11112-11117

19. Damage Cross-Effect and Anisotropy in Tough Double Network Hydrogels Revealed by Biaxial Stretching. TT. Mai, T. Matsuda, T. Nakajima, JP. Gong, K. Urayama, *Soft Matter*, **2019**, 15, 3719-3732

20. Dependence of Absorption and Emission Spectra on Polymorphs of Gold(I) Isocyanide Complexes: Theoretical Study with QM/MM Approach. S. Aono, T. Seki, H. Ito, S. Sakaki, *J. Phys. Chem. C*, **2019**, 123, 4773-4794

21. Direct Dimesitylborylation of Benzofuran Derivatives by an Iridium-Catalyzed C-H Activation with Silyldimesitylborane. R. Shishido, I. Sasaki, T. Seki, T. Ishiyama and H. Ito, *Chem. Eur. J*., **2019**, 25, 12924-12928

22. Divergent Dynamics and Functions of ERK MAP Kinase Signaling in Development, Homeostasis and Cancer: Lessons from Fluorescent Bioimaging. Y. Muta, M. Tsuda, M. Imajo, *Cancers*, **2019**, 11, 513

23. Double Network Hydrogels Based on Semi-Rigid Polyelectrolyte Physical Networks. R. Takahashi, T. Ikai, T. Kurokawa, DR. King, JP. Gong, *J. Mater. Chem. B*, **2019**, 7, 6347-6354

24. Dynamic Topochemical Reaction Tuned by Guest Molecules in the Nanospace of a Metal-Organic Framework. S. Kusaka, A. Kiyose, H. Sato, Y. Hijikata, A. Hori, YS. Ma, R. Matsuda, *J. Am. Chem. Soc*., **2019**, 141, 15742-15746

25. Effect of Structure Heterogeneity on Mechanical Performance of Physical Polyampholytes Hydrogels. K. Cui, YN. Ye, TL. Sun, L. Chen, X. Li, T. Kurokawa, T. Nakajima, T. Nonoyama, JP. Gong, *Macromolecules*, **2019**, 52(19), 7369-7378

26. Exosomes Containing ErbB2/CRK Induce Vascular Growth in Premetastatic Niches and Promote Metastasis of Bladder Cancer. K. Yoshida, M. Tsuda, R. Matsumoto, S. Semba, L. Wang, H. Sugino, M. Tanino, T. Kondo, K. Tanabe, S. Tanaka, *Cancer Sci*., **2019**, 110, 2119-2132

27. Fabrication of Tough and Stretchable Hybrid Double-Network Elastomers Using Ionic Dissociation of Polyelectrolyte in Nonaqueous Media. T. Matsuda, T. Nakajima, JP. Gong, *Chem. Mater*., **2019**, 31, 3766-3776

28. Fabrication of Tough Hydrogel Composites from Photoresponsive Polymers to Show Double-Network Effect. Z. Tao, HL. Fan, JC. Huang, TL. Sun, T. Kurokawa, JP. Gong, *ACS Appl. Mater. Interfaces*, **2019**, 11, 37139-37146

29. Facile Synthesis of Novel Elastomers with Tunable Dynamics for Toughness, Self-Healing and Adhesion. L. Chen, TL. Sun, KP. Cui, DR. King, T. Kurokawa, Y. Saruwatari, JP. Gong, *J. Mater. Chem. A*, **2019**, 7, 17334-17344

30. Heterogeneous Nickel-Catalyzed Cross-Coupling Between Aryl Chlorides and Alkyllithiums Using a Polystyrene-Cross-Linking Bisphosphine Ligand. Y. Yamazaki, N. Arima, T. Iwai, M. Sawamura, *Adv. Synth. Catal*., **2019**, 361, 2250-2254

31. High-Resolution Raman Microscopic Detection of Follicular Thyroid Cancer Cells with Unsupervised Machine Learning. JN. Taylor, K. Mochizuki, K. Hashimoto, Y. Kumamoto, Y. Harada, K. Fujita, T. Komatsuzaki, *J. Phys. Chem. B*, **2019**, 123, 4358-4372

32. Hydrogel/Elastomer Laminates Bonded via Fabric Interphases for Stimuli-Responsive Actuators. AM. Hubbard, W. Cui, Y. Huang, R. Takahashi, MD. Dickey, J. Genzer, DR. King, JP. Gong, *Matter*, **2019**, 1(3), 674-689

33. Hydrophobic Hydrogels with Fruit-Like Structure and Functions. H. Guo, T. Nakajima, D. Hourdet, A. Marcellan, C. Creton, W. Hong, T. Kurokawa, JP. Gong, *Adv. Mater*., **2019**, 31, 1900702

34. Internal Damage Evolution in Double-Network Hydrogels Studied by Microelectrode Technique. HL. Guo, W. Hong, T. Kurokawa, T. Matsuda, ZL. Wu, T. Nakajima, M. Takahata, TL. Sun, P. Rao, JP. Gong, *Macromolecules*, **2019**, 52, 7114-7122

35. Iridium-Catalyzed Alkene-Selective Transfer Hydrogenation with 1,4-Dioxane as Hydrogen Donor. DL. Zhang, T. Iwai, M. Sawamura, *Org. Lett*., **2019**, 21, 5867-5872

36. Iridium-Catalyzed Asymmetric Borylation of Unactivated Methylene $C(sp^3)$-H Bonds. RL. Reyes, T. Iwai, S. Maeda, M. Sawamura, *J. Am. Chem. Soc*., **2019**, 141, 6817-6821

37. Iridium(I)-Catalyzed C-H Borylation in Air by Using Mechanochemistry. YD. Pang, T. Ishiyama, K. Kubota, H. Ito, *Chem. Eur. J*., **2019**, 25, 4654-4659

38. Lifetimes of Lanthanide(III) Triboluminescence Excited by Aerodynamic Shock Waves. Y. Hirai, A. Kotani, H. Sakaue, Y. Kitagawa, Y. Hasegawa, *J. Phys. Chem. C*, **2019**, 123, 27251-27256

39. Linear Correlations Between Adsorption Energies and HOMO Levels for the Adsorption of Small Molecules on TiO_2 Surfaces. T. Kamachi, T. Tatsumi, T. Toyao, Y. Hinuma, Z. Maeno, S. Takakusagi, S.

Furukawa, I. Takigawa, K. Shimizu, *J. Phys. Chem. C*, **2019**, 123, 20988-20997

40. Low-Lying Excited States of HqxcH and Zn-Hqxc Complex: Toward Understanding Intramolecular Proton Transfer Emission. M. Ebina, Y. Kondo, T. Iwasa, T. Taketsugu, *Inorg. Chem*., **2019**, 58, 4686-4698

41. Luminescent Mechanochromism of Gold N-Heterocyclic Carbene Complexes with Hypso- and Bathochromic Spectral Shifts. T. Seki, K. Kashiyama, H. Ito, *Dalton Trans*., **2019**, 48, 7105-7109

42. Macroscale Double Networks: Design Criteria for Optimizing Strength and Toughness. DR. King, T. Okumura, R. Takahashi, T. Kurokawa, JP. Gong, *ACS Appl. Mater. Interfaces*, **2019**, 11, 35343-35353

43. Mechanochemistry Allows Carrying out Sensitive Organometallic Reactions in Air: Glove-Box-and-Schlenk-Line-Free Synthesis of Oxidative Addition Complexes from Aryl Halides and Palladium(0). K. Kubota, R. Takahashi, H. Ito, *Chem. Sci*., **2019**, 10, 5837-5842

44. Mechanoresponsive Self-growing Hydrogels Inspired by Muscle Training. T. Matsuda, R. Kawakami, R. Namba, T. Nakajima, JP. Gong, *Science*, **2019**, 363(6426), 504-508

45. Microphase Separation of Carbohydrate-Based Star-Block Copolymers with Sub-10 nm Periodicity. T. Isono, N. Kawakami, K. Watanabe, K. Yoshida, I. Otsuka, H. Mamiya, H. Ito, T. Yamamoto, K. Tajima, R. Borsali, T. Satoh, *Polym. Chem*., **2019**, 10, 1119-1129

46. Modulation and Characterization of the Double Network Hydrogel Surface-Bulk Transition. M. Frauenlob, DR. King, HL. Guo, S. Ishihara, M. Tsuda, T. Kurokawa, H. Haga, S. Tanaka, JP. Gong, *Macromolecules*, **2019**, 52, 6704-6713

47. Near-IR Luminescent Yb^{III} Coordination Polymers Composed of Pyrene Derivatives for Thermostable Oxygen Sensors. Y. Hasegawa, T. Matsui, Y. Kitagawa, T. Nakanishi, T. Seki, H. Ito, Y. Nakasaka, T. Masuda, K. Fushimi, *Chem. Eur. J*., **2019**, 25, 12308-12315

48. Nickel-Catalyzed Decarboxylation of Aryl Carbamates for Converting Phenols into Aromatic Amines. A. Nishizawa, T. Takahira, K. Yasui, H. Fujimoto, T. Iwai, M. Sawamura, N. Chatani, M. Tobisu, *J. Am. Chem. Soc*., **2019**, 141, 7261-7265

49. Nickel-Copper-Catalyzed Hydroacylation of Vinylarenes with Acyl Fluorides and Hydrosilanes. Y. Ueda, T. Iwai, M. Sawamura, *Chem. Eur. J*., **2019**, 25, 9410-9414

50. Olefin-Accelerated Solid-State C-N Cross-Coupling Reactions Using Mechanochemistry. K. Kubota, T. Seo, K. Koide, Y. Hasegawa, H. Ito, *Nat. Commun*., **2019**, 10,

51. On Benchmarking of Automated Methods for Performing Exhaustive Reaction Path Search. S. Maeda, Y. Harabuchi, *J. Chem. Theory Comput*., **2019**, 15, 2111-2115

52. One-Minute Joule Annealing Enhances the Thermoelectric Properties of Carbon Nanotube Yarns via the Formation of Graphene at the Interface. M. Hada, T. Hasegawa, H. Inoue, M. Takagi, K. Omoto, D. Chujo, S. Iemoto, T. Kuroda, T. Morimoto, T. Hayashi, T. Iijima, T. Tokunaga, N. Ikeda, K. Fujimori, C. Itoh, T. Nishikawa, Y. Yamashita, T. Kiwa, S. Koshihara, S. Maeda, Y. Hayashi, *ACS Appl. Energy Mater*., **2019**, 2, 7700-7708

53. One-Step Synthesis of an Adaptive Nanographene MOF: Adsorbed Gas-Dependent Geometrical Diversity. S. Suginome, H. Sato, A. Hori, A. Mishima, Y. Harada, S. Kusaka, R. Matsuda, J. Pirillo, Y. Hijikata, T. Aida, *J. Am. Chem. Soc*., **2019**, 141, 15649-15655

54. Photoluminescence Properties of [Core plus exo]-Type Au-6 Clusters: Insights into the Effect of Ligand Environments on the Excitation Dynamics. Y. Shichibu, MZ. Zhang, T. Iwasa, Y. Ono, T. Taketsugu, S. Omagari, T. Nakanishi, Y. Hasegawa, K. Konishi, *J. Phys. Chem. C*, **2019**, 123, 6934-6939

55. Polyelectrolyte Complexation via Viscoelastic Phase Separation Results in Tough and Self-Recovering Porous Hydrogels. K. Murakawa, DR. King, TL. Sun, HL. Guo, T. Kurokawa, JP. Gong, *J. Mater. Chem. B*, **2019**, 7, 5296-5305

56. Programmed Diffusion Induces Anisotropic Superstructures in Hydrogels with High Mechano-Optical

Sensitivity. LC. Qiao, C. Du, JP. Gong, ZL. Wu, Q. Zheng, *Adv. Mater. Technol.*, **2019**, 4, 1900665

57. Raman spectroscopic histology using machine learning for nonalcoholic fatty liver disease. KM. Helal, JN. Taylor, H. Cahyadi, A. Okajima, K. Tabata, Y. Itoh, H. Tanaka, K. Fujita, Y. Harada, T. Komatsuzaki, *Febs Letters*, **2019**, 593, 2535-2544

58. Redox Reactions of Small Organic Molecules Using Ball Milling and Piezoelectric Materials. K. Kubota, YD. Pang, A. Miura, H. Ito, *Science*, **2019**, 366, 1500-1504

59. Relaxation Dynamics and Underlying Mechanism of a Thermally Reversible Gel from Symmetric Triblock Copolymer. YN. Ye, KP. Cui, T. Indei, T. Nakajima, D. Hourdet, T. Kurokawa, JP. Gong, *Macromolecules*, **2019**, 52, 8651-8661

60. Roles of Closed-and Open-Loop Conformations in Large-Scale Structural Transitions of L-Lactate Dehydrogenase. K. Suzuki, S. Maeda, K. Morokuma, *Acs Omega*, **2019**, 4, 1178-1184

61. Roles of Silver Nanoclusters in Surface-Enhanced Raman Spectroscopy. T. Tsuneda, T. Iwasa, T. Taketsugu, *J. Chem. Phys.*, **2019**, 151, 094102

62. Shearing-Induced Contact Pattern Formation in Hydrogels Sliding in Polymer Solution. S. Yashima, S. Hirayama, T. Kurokawa, T. Salez, H. Takefuji, W. Hong, JP. Gong, *Soft Matter*, **2019**, 15, 1953-1959

63. Single-Phase Borophene on Ir(111): Formation, Structure, and Decoupling from the Support. NA. Vinogradov, A. Lyalin, T. Taketsugu, AS. Vinogradov, A. Preobrajenski, *Acs Nano*, **2019**, 13, 14511-14518

64. Soft X-Ray Li-K and Si-$L_{2,3}$ Emission from Crystalline and Amorphous Lithium Silicides in Lithium-Ion Batteries Anode. A. Lyalin, VG. Kuznetsov, A. Nakayama, IV. Abarenkov, II. Tupitsyn, IE. Gabis, K. Uosaki, T. Taketsugu, *J. Electrochem. Soc.*, **2019**, 166, A5362-A5368

65. Solid-State Suzuki-Miyaura Cross-Coupling Reactions: Olefin-Accelerated C-C Coupling Using Mechanochemistry. T. Seo, T. Ishiyama, K. Kubota, H. Ito, *Chem. Sci.*, **2019**, 10, 8202-8210

66. Statistical Analysis and Discovery of Heterogeneous Catalysts Based on Machine Learning from Diverse Published Data. K. Suzuki, T. Toyao, Z. Maeno, S. Takakusagi, K. Shimizu, I. Takigawa, *Chemcatchem*, **2019**, 11, 4537-4547

67. Superior Fracture Resistance of Fiber Reinforced Polyampholyte Hydrogels Achieved by Extraordinarily Large Energy-Dissipative Process Zones. YW. Huang, DR. King, W. Cui, TL. Sun, HL. Guo, T. Kurokawa, HR. Brown, CY. Hui, JP. Gong, *J. Mater. Chem. A*, **2019**, 7, 13431-13440

68. Synthesis of 2-Alkyl-2-Boryl-Substituted-Tetrahydrofurans via Copper(I)-Catalysed Borylative Cyclization of Aliphatic Ketones. K. Kubota, M. Uesugi, S. Osaki, H. Ito, *Org. Biomol. Chem.*, **2019**, 17, 5680-5683

69. The Direct Observation of the Doorway $^1n\pi^*$ State of Methylcinnamate and Hydrogen-Bonding Effects on the Photochemistry of Cinnamate-Based Sunscreens. S. Kinoshita, Y. Inokuchi, Y. Onitsuka, H. Kohguchi, N. Akai, T. Shiraogawa, M. Ehara, K. Yamazaki, Y. Harabuchi, S. Maeda, T. Ebata, *Phys. Chem. Chem. Phys.*, **2019**, 21, 19755-19763

70. Thermal and Crystallographic Investigation of Luminescent Eu(III) Coordination Polymers with Dithiane and Dioxane Hexyl Rings. Y. Hirai, PPF. da Rosa, Y. Kitagawa, Y. Hasegawa, *Chem. Lett.*, **2019**, 48, 1544-1546

71. Topological Molecular Nanocarbons: All-Benzene Catenane and Trefoil Knot. Y. Segawa, M. Kuwayama, Y. Hijikata, M. Fushimi, T. Nishihara, J. Pirillo, J. Shirasaki, N. Kubota, K. Itami, *Science*, **2019**, 365, 272-276

72. Tough Double Network Elastomers Reinforced by the Amorphous Cellulose Network. J. Murat, T. Nakajima, T. Matsuda, K. Tsunoda, T. Nonoyama, T. Kurokawa, JP. Gong, *Polymer*, **2019**, 178, 121686

73. Tough Double-Network Gels and Elastomers from the Nonprestretched First Network. T. Nakajima, Y. Ozaki, R. Namba, K. Ota, Y. Maida, T. Matsuda, T. Kurokawa, JP. Gong, *ACS Macro Lett.*, **2019**, 8,

1407-1412

74. Tough Triblock Copolymer Hydrogels with Different Micromorphologies for Medical and Sensory Materials. HJ. Zhang, F. Luo, Y. Ye, TL. Sun, T. Nonoyama, T. Kurokawa, T. Nakajima, *ACS Applied Polymer Materials*, **2019**, 1, 1948-1953

75. Two-Step Transformation of Aliphatic Polyketones into π-Conjugated Polyimines. Y. Manabe, M. Uesaka, T. Yoneda, Y. Inokuma, *J. Org. Chem*., **2019**, 84, 9957-9964

76. Understanding CO Oxidation on the Pt(111) Surface Based on a Reaction Route Network. K. Sugiyama, Y. Sumiya, M. Takagi, K. Saita, S. Maeda, *Phys. Chem. Chem. Phys*., **2019**, 21, 14366-14375

77. Understanding the Acetalization Reaction Based on its Reaction Path Network. Y. Sumiya, Y. Tabata, S. Maeda, *ChemSystemsChem*, **2019**, 1, e190002

78. $Zn(OTf)_2$-Mediated Annulations of N-Propargylated Tetrahydrocarbolines: Divergent Synthesis of Four Distinct Alkaloidal Scaffolds. S. Yorimoto, A. Tsubouchi, H. Mizoguchi, H. Oikawa, Y. Tsunekawa, T. Ichino, S. Maeda, H. Oguri, *Chem. Sci*., **2019**, 10, 5686-5698

2. Review articles

79. Aliphatic Polyketones as Shapable Molecular Chains. Y. Inokuma, J. *Syn. Org. Chem. Jpn*., **2019**, 77, 1078-1085

80. Thermo-sensitive luminescence of lanthanide complexes, clusters, coordination polymers and metal–organic frameworks with organic photosensitizers. Y. Hasegawa, Y. Kitagawa, *J. Mater. Chem. C*, **2019**, 7, 7494-7511

81. 【病理医育成の新時代】分子病理専門医の育成について. 田中伸哉, *病理と臨床*, **2019**, 37巻1号, 67-72

82. Tough and Self-healing Supramolecular Hydrogels Composed of Polyampholytes. 崔 昆朋, 孫 桃林, 龔 剣萍, *高分子通報（Polymer Bulletin）*, **2019**, 創刊30周年記念号, 3, 1-16

83. Glioma：統合診断への道しるべ. 田中伸哉, *病理と臨床*, **2019**, 37巻7号, 654-656

84. ダブルネットワークゲルのタフ化機構とその最新の研究動向/Toughening Mechanism of Double Network Gels and New Research Trends. 木山竜二, 龔剣萍, *日本ゴム協会誌/Journal of Society of Rubber Science and Technology, Japan*, **2019**, 第92巻, 第9号, 352-356

85. 受容体型チロシンキナーゼRTKがんの特徴と治療戦略. 津田真寿美, 田中伸哉, *医学のあゆみ*, **2019**, 269巻3号, 203-206

86. 生体内におけるERK MAPキナーゼ活性の動態と生理的意義. 今城正道, 牟田優, 松田道行, *生化学*, **2019**, 91, 4, 546-550

87. 鍛えて成長するゲル―破壊による創造の材料科学―. 松田昂大, 中島祐, 龔剣萍, *現代化学*, **2019**, 2019年8月号, No.581, 53-57

3. Proceedings

NA

4. Other English articles

NA

B. WPI-related papers

1. Original articles

NA

2. Review articles

NA

3. Proceedings

NA

4. Other English articles

NA

2. Invited Lectures, Plenary Addresses (etc.) at International Conferences and International Research Meetings

- List up to 10 main presentations during FY 2019 in order from most recent.
- For each, write the date(s), lecturer/presenter's name, presentation title, and conference name.

Date(s)	Lecturer/Presenter's name	Presentation title	Conference name
2019/12/12	Yasuhide INOKUMA	Aliphatic Polyketones for Clay-Play Like Molecular Synthesis	The 18th Asian Chemical Congress
2019/12/10	Jian Ping GONG	Self-growing hydrogels by repetitive mechanical training	CEMS International Symposium on Supramolecular Chemistry and Functional Materials 2019 (CEMSupra2019)
2019/11/22	Hajime ITO	Mechanochemistry: Luminescent Materials and Organic Synthesis	12th International Symposium on Integrated Synthesis
2019/10/02	Michael RUBINSTEIN	Mysteries of Mucus Physical Properties	5th International Symposium on "Multivalency in Chemistry and Biology"
2019/07/15	Satoshi MAEDA	Systematic Generation and Analysis of Reaction Path Networks by the Artificial Force Induced Reaction Method	10th Triennial Congress of the International Society for Theoretical Chemical Physics (ISTCP 2019)
2019/07/2-5	Masaya SAWAMURA	Enantioselective Methylene $C(sp^3)$–H Borylation	The 47th Naito Conference on "C-H Activation and Transformation"
2019/07/11-13	Shinya TANAKA	Engineered hydrogels for rapid induction of cancer stem cells	The 38th Sapporo International Cancer Symposium
2019/05/23-24	Yasuchika HASEGAWA	Eu(III) and Tb(III) Coordination polymers with strong luminerscence and photo-functional properties	International Conference on Photocatalysis and Photoenergy 2019 (ICoPP2019)
2019/05/04	Tamiki KOMATSUZAKI	Deciphering hierarchical features in reaction network and energy landscape	CECAM conference on Network analysis to elucidate natural system dynamics, diversity and performances
2019/04/22	Benjamin LIST	Very Strong and Confined Acids Enable a General Approach to Asymmetric Lewis Acid Catalysis	Fifth International Scientific Conference: Advances in Synthesis and Complexing

3. Major Awards

- List up to 10 main awards received during FY 2019 in order from the most recent.
- For each, write the date issued, the recipient’s name, and the name of award.
- In case of multiple recipients, underline those affiliated with the center.

Date	Recipient's name	Name of award
2020/03/23	Tomohiro SEKI	The CSJ Award for Young Chemists
2020/01/14	Yohei SHIMIZU	Thieme Chemistry Journals Award
2019/12/12	Yasuhide INOKUMA	Asian Rising Stars Lectureship
2019/12/12	Mingoo JIN	Inoue Research Award for Young Scientists
2019/09/11	Tomohiro SEKI	The Japanese Photochemistry Association Award for Young Scientist for 2019
2019/04/17	Jian Ping GONG	The 2019 Commendation for Science and Technology by the Minister of Education, Culture, Sports, Science and Technology: Prizes for Science and Technology
2019	Benjamin LIST	Nankai Organic Lectureship, Nankai University, Tianjin, China
2019	Benjamin LIST	Herbert C. Brown Lecture, Purdue University, Indiana, USA
2019	Michael RUBINSTEIN	Soft Matter and Biological Physical Chemistry Award, Royal Society of Chemistry
2019	Michael RUBINSTEIN	Fellow, Royal Society of Chemistry

Appendix 2 FY 2019 List of Principal Investigators

NOTE:

*Underline names of principal investigators who belong to an overseas research institution.

*In the case of researcher(s) not listed in the latest report or, for centers selected in FY2012 in the progress report for Extension application screening, attach a "Biographical Sketch of a New Principal Investigator"(Appendix 2a).

<Results at the end of FY2019> **Principal Investigators Total: 15**

Name	Age	Affiliation (Position title, department, organization)	Academic degree, specialty	Effort (%)*	Starting date of project participation	Status of project participation (Describe in concrete terms)	Contributions by PIs from overseas research institutions
Center Director Satoshi MAEDA	40	Professor, Institute for Chemical Reaction Design and Discovery / Faculty of Science, Hokkaido University	Ph.D., computational chemistry	80	October 2018	Usually stays at the center	
Tetsuya TAKETSUGU	55	Professor, Institute for Chemical Reaction Design and Discovery / Faculty of Science, Hokkaido University	Ph.D., quantum chemistry	80	October 2018	Usually stays at the center	
<u>Michael RUBINSTEIN</u>	63	Professor, Duke University	Ph.D., polymer physics	20	October 2018	- Primarily stays at Partner institution - attends meeting (by online)	- Conducting interdisciplinary research - Recruitment of young researchers
Hiroki ARIMURA	54	Professor, Institute for Chemical Reaction Design and Discovery / Global Institution for Collaborative Research and Education / Faculty of Information Science and Technology, Hokkaido University	Ph.D., data mining	80	October 2018	Usually stays at the center	
Masaharu YOSHIOKA	51	Professor, Institute for Chemical Reaction Design and Discovery / Global Institution for Collaborative Research and Education / Faculty of Information Science and Technology, Hokkaido University	Doctor of Engineering, knowledge engineering	20	January 2020	Usually stays at the center	
<u>Alexandre VARNEK</u>	64	Professor, University of Strasbourg	Ph.D. chemoinformatics	20	October 2018	- Primarily stays at Partner institution - attends meeting (by online)	- Conducting interdisciplinary research - Recruitment of young researchers
Ichigaku TAKIGAWA	43	Specially Appointed Associate Professor, Institute for Chemical Reaction Design and Discovery, Hokkaido University Researcher, Center for Advanced Intelligence Project, RIKEN	Ph.D., machine learning	30	October 2018	- Stays at the center once a month - attend meeting (by online)	

Tamiki KOMATSUZAKI	55	Professor, Institute for Chemical Reaction Design and Discovery / Research Center of Mathematics for Social Creativity・Research Institute for Electronic Science, Hokkaido University	Ph.D., mathematical science	80	October 2018	Usually stays at the center	
Hajime ITO	52	Professor, Institute for Chemical Reaction Design and Discovery / Faculty of Engineering, Hokkaido University	Doctor of Engineering, synthetic chemistry	80	October 2018	Usually stays at the center	
Masaya SAWAMURA	58	Professor, Institute for Chemical Reaction Design and Discovery / Faculty of Science, Hokkaido University	Doctor of Engineering, catalysis	80	October 2018	Usually stays at the center	
Benjamin LIST	52	Professor and Director, Max Planck Institute for Coal Research	Ph.D., Reaction design	20	October 2018	- Primarily stays at Partner institution - attends meeting (by online)	- Conducting interdisciplinary research - Recruitment of young researchers
Yasuchika HASEGAWA	51	Professor, Institute for Chemical Reaction Design and Discovery / Faculty of Engineering, Hokkaido University	Ph.D., optical materials science	80	October 2018	Usually stays at the center	
Yasuhide INOKUMA	38	Associate Professor, Institute for Chemical Reaction Design and Discovery / Faculty of Engineering, Hokkaido University	Ph.D., structural chemistry	80	October 2018	Usually stays at the center	
Jian Ping GONG	58	Professor, Institute for Chemical Reaction Design and Discovery / Global Institution for Collaborative Research and Education / Faculty of Advanced Life Science, Hokkaido University	Doctor of Science, Doctor of Engineering, polymer chemistry	80	October 2018	Usually stays at the center	
Shinya TANAKA	55	Professor, Institute for Chemical Reaction Design and Discovery / Global Institution for Collaborative Research and Education / Faculty of Medicine, Hokkaido University	MD, Ph.D., tumor pathology	80	October 2018	Usually stays at the center	

*Percentage of time that the principal investigator devotes to working for the center vis-à-vis his/her total working hours.

Principal investigators unable to participate in project in FY 2019

Name	Affiliation (Position title, department, organization)	Starting date of project participation	Reasons	Measures taken
Hiroki ARIMURA	Professor, Global Institution for Collaborative Research and Education / Graduate School of Information Science and Technology, Hokkaido University	October 2018	To concentrate on the research at Graduate School of Information Science and Technology	Appointment of the new PI (Masaharu YOSHIOKA)

Appendix 2a Biographical Sketch of a New Principal Investigator

(within 3 pages per person)

Name (Age) **Masaharu YOSHIOKA (51)**

Affiliation and position (Position title, department, organization, etc.)

Professor

Faculty of Information Science and Technology, Hokkaido University, Japan

Graduate School of Information Science and Technology, Hokkaido University, Japan

GI-CoRE Global Station for Big Data and Cybersecurity, Hokkaido University, Japan

Academic degree and specialty

Academic degree : Doctor (Engineering) at University of Tokyo

specialty : Knowledge Engineering

Effort **20 %**

* Percentage of time that the principal investigator devotes to working for the center vis-à-vis his/her total working hours.

Research and education history

1991.3	B.E. Department of Precision Machinery Engineering, Faculty of Engineering, The University of Tokyo
1993.3	M.E. Department of Precision Machinery Engineering, Graduate School of Engineering, The University of Tokyo
1996.3	Doctor (Engineering) Department of Precision Machinery Engineering, Graduate School of Engineering, The University of Tokyo
1996.4-2000.3	Research Associate, The National Center for Science Information Systems
2000.4-2001.5	Research Associate, The National Institute of Informatics
2001.6-2004.3	Associate Professor, Graduate School of Engineering, Hokkaido University
2004.4-2017.12	Associate Professor, Graduate School of Information Science and Technology, Hokkaido University
2018.1-	Professor, Graduate School of Information Science and Technology, Hokkaido University
2004.12-2010.3	Visiting Associate Professor, The National Institute of Informatics
2010.1-2011.3	Special appointed fellow: Center for Research and Development Strategy Japan Science and Technology Agency
2017.1-	Visiting researcher, Center for Advanced Intelligence Project, RIKEN

Achievements and highlights of past research activities

He started his research in the field of knowledge engineering for computer aided design. He proposed physical concept-based ontology for knowledge intensive engineering to support design process. After his graduation of the university, he started the research on information access using documents including information retrieval, knowledge management using documents, information/knowledge extraction from the documents. He joined as a program member of The 21st Century Center of Excellence program and Global Center of Excellence program at the graduate school of information science and technology, Hokkaido University. In these programs he started knowledge exploratory project for nanocrystal device development as a part of the interdisciplinary collaborative research between nanodevice development and computer science. He proposed a framework for extracting experiment related information from the nanocrystal research papers and recognized as a first approach to this domain. He also serves as a vice director of Global Station for Big Data and Cybersecurity for promoting international research and educational collaboration.

Achievements

(1) International influence * Describe the kind of attributes listed below.

a) Recipient of international awards

NA

b) Member of a scholarly academy in a major country

A member of Asian Information Retrieval Societies Steering Committee

c) Guest speaker or chair of related international conference and/or director or honorary member of a major international academic society in the subject field

NA

d) Editor of an international academic journal

NA

e) Peer reviewer for an overseas competitive research program (etc.)

NA

(2) Receipt of major large-scale competitive funds (over the past 5 years)

Principal Investigator
Grant-in-Aid for Scientific Research(B) 18H03338 (2018-2021)
Grant-in-Aid for Challenging Research (Exploratory) 19K22888 (2019-2020)
Grant-in-Aid for Scientific Research(B) 25280035 (2013-2015)
Grant-in-Aid for Challenging Exploratory Research 26540165 (2014-2015)

(3) Major publications (Titles of major publications, year of publication, journal name, number of citations)

1. Yoshinobu Kan, Mi-Young Kim, Masaharu Yoshioka, Yao Lu, Juliano Rabelo, Naoki Kiyota, Randy Goebel, and Ken Satoh : COLIEE-2018: Evaluation of the Competition on Legal Information Extraction and Entailment. In New Frontiers in Artificial Intelligence. JSAI-isAI 2018. Lecture Notes in Computer Science, pp. 177-192, Springer International Publishing, Cham, LNCS11717, 2019.
2. Masaharu Yoshioka, and Shinjiro Hara: Construction of an In-House Paper/Figure Database System Using Portable Document Format Files. In Information Search, Integration, and Personalization: 10th International Workshop, ISIP 2018, Dimitris Kotzinos, Dominique Laurent, Nicolas Spyratos, Yuzuru Tanaka, and Rin-ichiro Taniguchi (eds), pp. 142-156, Springer-Verlag GmbH, CCIS 1040, 2019.
3. Masaharu Yoshioka: Analysis of COLIEE Information Retrieval Task Data. In New Frontiers in Artificial Intelligence. JSAI-isAI 2017. Lecture Notes in Computer Science, pp. 5-19, Springer International Publishing, Cham, LNCS10838, 2018
4. Masaharu Yoshioka: WC3: Analyzing the style of metadata annotation among Wikipedia articles by using Wikipedia category and the DBPedia metadata database. In Knowledge Graphs and Language Technology: ISWC 2016 International Workshops: KEKI and NLP&DBpedia, Kobe, Japan, October 17-21, 2016, Revised Selected Papers, pp. 119-136, 2017.
5. Masaharu Yoshioka, Masahiko Itoh and Michele Sebag: Interactive Metric Learning-Based Visual Data Exploration: Application to the Visualization of a Scientific Social Network. In Information Search, Integration, and Personalization: 10th International Workshop, ISIP 2015, Grand Forks, ND, USA, October 1-2, 2015, Revised Selected Papers, Emanuel Grant, Dimitris Kotzinos, Dominique Laurent, Nicolas Spyratos, and Yuzuru Tanaka (eds), pp. 142-156, Springer-Verlag GmbH, CCIS 622, 2016.
6. Thaer M. Dieb, Masaharu Yoshioka, and Shinjiro Hara: NaDev: An Annotated Corpus to Support Information Extraction from Research Papers on Nanocrystal Devices. Journal of Information Processing, Vol. 24, No. 3, pp. 554-564, 2016.
7. Thaer M. Dieb and Masaharu Yoshioka: Extraction of Chemical and Drug Named Entities by Ensemble Learning Using Chemical NER Tools Based on Different Extraction Guidelines. Transactions on Machine Learning and Data Mining, Vol. 8, No. 2, pp. 61-76, 2015.
8. Thaer M. Dieb, Masaharu Yoshioka, Shinjiro Hara, and Marcus C. Newton: Framework for automatic information extraction from research papers on nanocrystal devices. Beilstein Journal of Nanotechnology, Vol. 6, pp. 1872-1882, 2015.
9. Martin Krallinger, Obdulia Rabal, Florian Leitner, Miguel Vazquez, David Salgado, Zhiyong Lu, Robert Leaman, Yanan Lu, Donghong Ji, Daniel M Lowe, Roger A Sayle, Riza Theresa Batista-Navarro, Rafal Rak, Torsten Huber, Tim Rocktäschel, Sérgio Matos, David Campos, Buzhou Tang, Hua Xu, Tsendsuren Munkhdalai, Keun Ho Ryu, SV Ramanan, Senthil Nathan, Slavko Žitnik, Marko Bajec, Lutz Weber, Matthias Irmer, Saber A Akhondi, Jan A Kors, Shuo Xu, Xin An, Utpal Kumar Sikdar, Asif Ekbal, Masaharu Yoshioka, Thaer M Dieb, Miji Choi, Karin Verspoor, Madian Khabsa, C Lee Giles, Hongfang Liu, Komandur Elayavilli Ravikumar, Andre Lamurias, Francisco M Couto, Hong-Jie Dai, Richard Tzong-Han Tsai, Caglar Ata, Tolga Can, Anabel Usié, Rui Alves, Isabel Segura-Bedmar, Paloma Martínez, Julen Oyarzabal and Alfonso Valencia: The CHEMDNER corpus of chemicals and drugs and its annotation principles. Journal of Cheminformatics, Vol. 7, No. Suppl 1, pp. S2, 2015.
10. Masaharu Yoshioka: On a Combination of Probabilistic and Boolean IR Models for Question Answering. In Information Retrieval Technology 6th Asia Information Retrieval Symposium, AIRS 2010, Taipei, Taiwan, December 2010 Proceedings, pp. 588-598, LNCS6458, 2010.
11. Masaharu Yoshioka: IR Interface for Contrasting Multiple News Sites. In Information Retrieval Technology 4th Asia Information Retrieval Symposium, AIRS 2008, Harbin, China, January 15-18, 2008 Revised Selected Papers, pp. 508-513, LNCS4993, 2008.
12. Hideaki Takeda, Yutaka Fujimoto, Masaharu Yoshioka, Yoshiki Shimomura, Kengo Morimoto and Wataru Oniki: Tagging for Intelligent Processing of Design Information. In New Frontiers in Artificial Intelligence: JSAI 2003 and JSAI 2004 Conferences and Workshops, A. Sakurai, K. Hasida and K. Nitta (eds), pp. 216-225, Springer-Verlag GmbH, LNCS3069, 2007.
13. Masaharu Yoshioka and Makoto Haraguchi: On a Combination of Probabilistic and Boolean

IR Models for WWW Document Retrieval. ACM Transactions on Asian Language Information Processing (TALIP), Vol. 4, No. 3, pp. 340-356, 2005.
14. Masaharu Yoshioka, Yasushi Umeda, Hideaki Takeda, Yoshiki Shimomura, Yutaka Nomaguchi, Tetsuo Tomiyama: Physical Concept Ontology for the Knowledge Intensive Engineering Framework. Advanced Engineering Informatics, Vol. 18, No. 2, pp. 95-113, 2004.

(4) Others (Other achievements indicative of the PI's qualification as a top-world researcher, if any.)

He started research on extracting information from documents for nanoinformatics.

Appendix 3-1 FY 2019 Records of Center Activities

1. Researchers and center staff, satellites, partner institutions

1-1. Number of researchers in the "core" established within the host institution

- Regarding the number of researchers at the Center, fill in the table in Appendix 3-1a.

Special mention

- Enter matters warranting special mention, such as concrete plans for achieving the Center's goals, established schedules for employing main researchers, particularly principal investigators.
- As background to how the Center is working on the global circulation of world's best brains, give good examples, if any, of how career paths are being established for the Center's researchers; that is, from which top-world research institutions do researchers come to the Center and to which research institutions do the Center's researchers go, and how long are their stays at those institutions.

1-2. Satellites and partner institutions

- List the satellite and partner institutions in the table below.
- Indicate newly added and deleted institutions in the "Notes" column.
- If satellite institutions have been established overseas, describe by satellite the Center's achievements in coauthored papers and researcher exchanges in Appendix 4.

<Satellite institutions>

Institution name	Principal Investigator(s), if any	Notes

< Partner institutions>

Institution name	Principal Investigator(s), if any	Notes
University of Strasbourg	Alexandre Varnek	
Max Planck Institute for Coal Research	Benjamin List	
Duke University	Michael Rubinstein	
ESPCI		
Swiss Federal Institute of Technology in Zurich		
Peking University		
Kyoto University, Graduate School of Informatics		
Chubu University, Molecular Catalyst Research Center		

2. Holding international research meetings

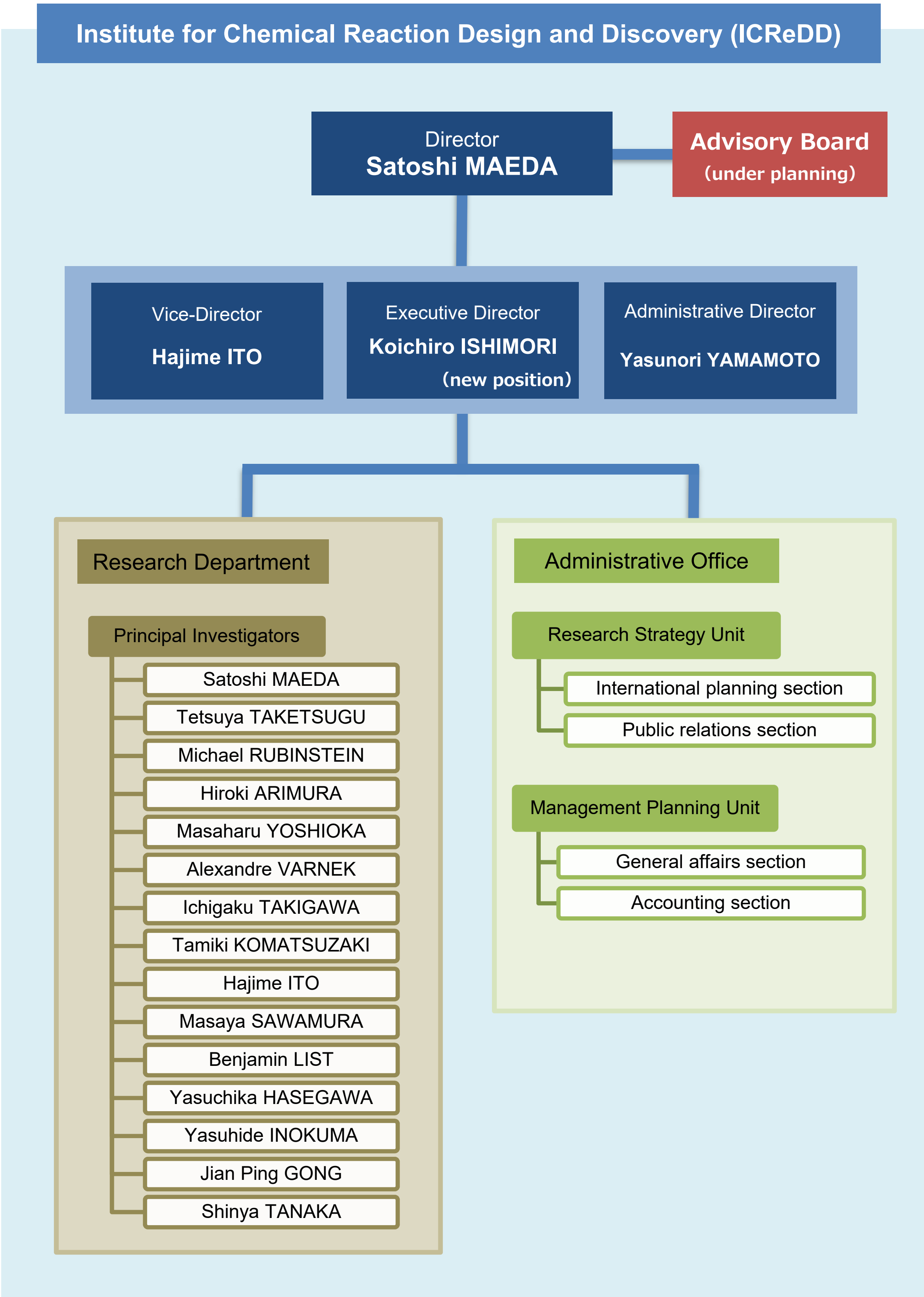
- Indicate the number of international research conferences or symposiums held in FY2019 and give up to three examples of the most representative ones using the table below.

FY 2019: 1 meeting

Major examples (meeting titles and places held)	Number of participants
The 2nd ICReDD International Symposium FMI Hall, Hokkaido University (Sapporo) November 27-29, 2019	From domestic institutions: 379 From overseas institutions: 24

3. Diagram of management system

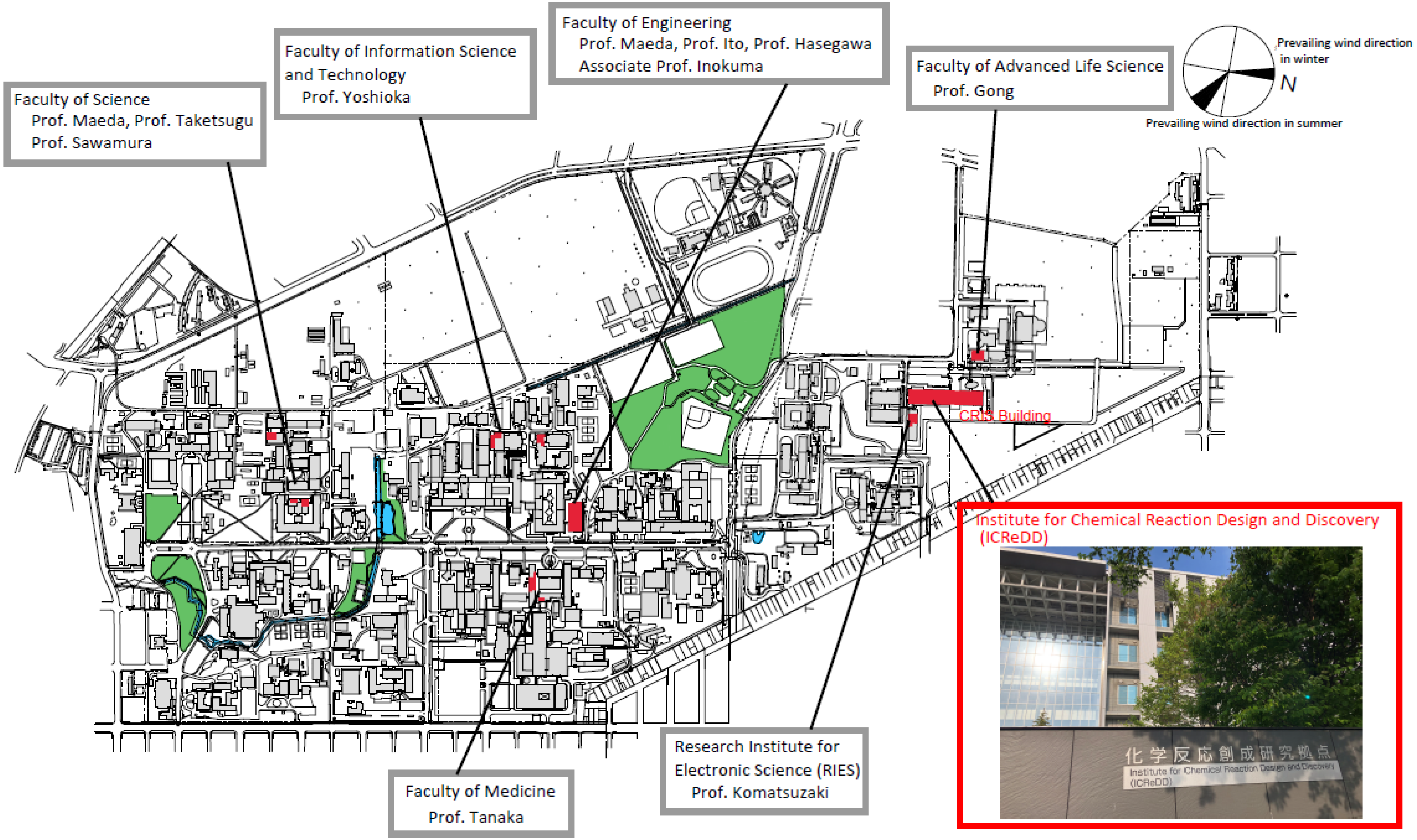
- Diagram the center's management system and its position within the host institution in an easily understood manner.
- If any new changes have been made in the management system from that in the latest "center project" last year, describe them. Especially describe any important changes made in such as the center director, administrative director, head of host institution, and officer(s) in charge at the host institution (e.g., executive vice president for research).



4. Campus Map

- Draw a simple map of the campus showing where the main office and principal investigator(s) are located.

As of March 31, 2020



5. Securing external research funding*

External research funding secured in FY2019

Total: 342,237,155 yen

- Describe external funding warranting special mention. Include the name and total amount of each grant.

* External research funding includes "KAKENHI," funding for "commissioned research projects," "joint research projects," and for others. (donations, etc.)

Name	Provider	Project	Period	Total （ in units of 1,000 yen）
Satoshi MAEDA	Japan Science and Technology Agency	Strategic Basic Research Programs（ERATO）	2019 - 2024	1,200,000
Satoshi MAEDA	Japan Science and Technology Agency	Strategic Basic Research Programs（CREST）	2014 - 2019	245,180
Hajime ITO	Japan Science and Technology Agency	Strategic Basic Research Programs（CREST）	2019 - 2024	150,000
Hajime ITO	Japan Society for the Promotion of Science	Grant-in-Aid for Scientific Research on Innovative Areas（Research in a Proposed Research Area）	2017 - 2021	84,110
Hajime ITO	Japan Society for the Promotion of Science	Grant-in-Aid for Scientific Research（A）	2018 - 2021	44,200
Masaya SAWAMURA	Japan Society for the Promotion of Science	Grant-in-Aid for Scientific Research（A）	2018 - 2021	43,810
Jian Ping GONG	Japan Society for the Promotion of Science	Grant-in-Aid for Scientific Research（S）	2017 - 2021	204,100
Tamiki KOMATSUZAKI	Japan Society for the Promotion of Science	Grant-in-Aid for Scientific Research on Innovative Areas（Research in a Proposed Research Area）	2018 - 2022	98,280
Tamiki KOMATSUZAKI	Japan Science and Technology Agency	Strategic Basic Research Programs（CREST）	2016 - 2021	126,263
Tamiki KOMATSUZAKI	Hitachi, Ltd.	Joint Research Funding	2016 – 2021	37,802
Shinya TANAKA	Japan Society for the Promotion of Science	Grant-in-Aid for Scientific Research（A）	2019 - 2022	45,110

Appendix 3-1a FY 2019 Records of Center Activities

Researchers and other center staff

Number of researchers and other center staff

* Fill in the number of researchers and other center staff in the table blow.
* Describe the final goals for achieving these numbers and dates when they will be achieved described in the last "center project."

a) Principal Investigators

(full professors, associate professors or other researchers of comparable standing)

(number of persons)

	At the beginning of project	At the end of FY 2019	Final goal (Date: March, 2023)
Researchers from within the host institution	11	11	11
Researchers invited from overseas	3	3	3
Researchers invited from other Japanese institutions	0	0	1
Total principal investigators	14	14	15

b) Total members

			At the beginning of project		At the end of FY2019		Final goal (Date: March, 2023)	
			Number of persons	%	Number of persons	%	Number of persons	%
Researchers			14		59		70	
	Overseas researchers		3	21.4	22	37.3	28	40.0
	Female researchers		1	7.1	6	10.2	10	14.3
	Principal investigators		14		14		15	
		Overseas PIs	3	21.4	3	21.4	3	20.0
		Female PIs	1	7.1	1	7.1	1	6.7
	Other researchers		0		30		35	
		Overseas researchers	0	0	8	26.7	10	28.6
		Female researchers	0	0	3	10	5	14.3
	Postdocs		0		15		20	
		Overseas postdocs	0	0	11	73.3	16	80.0
		Female postdocs	0	0	2	13.3	4	20.0
Research support staffs			0		1		5	
Administrative staffs			6		16		16	
Total number of people who form the "core" of the research center			20		76		91	

Appendix 3-2 Project Expenditures

1) Overall project funding

* In the "Total costs" column, enter the total amount of funding required to implement the project, without dividing it into funding sources.
* In the "Amount covered by WPI funding" column, enter the amount covered by WPI within the total amount.
* In the "Personnel," "Project activities," "Travel," and "Equipment" blocks, the items of the "Details" column may be changed to coincide with the project's actual content.

(Million yen)

Cost items	Details (For Personnel - Equipment please fill in the breakdown of fiscal expenditure, and the income breakdown for Research projects.)	Total costs	Amount covered by WPI funding
Personnel	Center Director, Executive Director, Administrative Director	15	0
	Principal investigators (no. of persons): 11	83	4
	Part-time faculty members (no. of persons): 10	80	0
	Specially appointed faculty members (no. of persons): 20	120	120
	Postdoctoral fellows (no. of persons): 15	52	52
	Research support staff (no. of persons): 7	11	11
	Administrative staff (no. of persons): 13	77	26
	Center allowance	19	19
	Subtotal	457	232
Project activities	Startup research project costs	51	51
	Outreach-related costs	6	6
	Center operating costs	27	27
	Relocation costs	9	1
	Environmental improvement costs	33	19
	Facility rental fees	24	0
	Utility costs	4	0
	Others	61	0
	Subtotal	215	104
Travel	Domestic travel costs	4	4
	Overseas travel costs	11	11
	Travel costs for scientists on transfer (no. of domestic scientists/overseas scientists): 5/3	3	3
	Subtotal	18	18
Equipment	Facility improvement costs	118	100
	Facility/equipment procurement costs	250	246
	Subtotal	368	346
Research projects (Detail items must be fixed)	Project supported by other government subsidies, etc. *1	325	0
	KAKENHI	122	0
	Commissioned research projects, etc.	109	0
	Joint research projects	29	0
	Others (donations, etc.)	83	0
	Subtotal	668	0
Total		1,726	700

Costs (Million yen)

WPI grant in FY 2019

Costs of establishing and maintaining facilities	100
- Renovation of CRIS Building (Renovated floor area: 671 m²)	100
Costs of equipment procured	246
- High performance computer system (Number of units: 1)	99
- Circularly polarized luminescence spectrometer (Number of units: 1)	26
- Others	121

*1. Management Expenses Grants (including Management Enhancements Promotion Expenses (機能強化経費)), subsidies including National university reform reinforcement promotion subsidy (国立大学改革強化推進補助金) etc., indirect funding, and allocations from the university's own resources.
*2 When personnel, travel, equipment (etc.) expenses are covered by KAKENHI or under commissioned research projects or joint research projects, the amounts should be entered in the

*1 運営費交付金(機能強化経費を含む)、国立大学改革強化推進補助金等の補助金、間接経費、その他大学独自の取組による学内リソースの配分等による財源
*2 科研費、受託研究費、共同研究費等によって人件費、旅費、設備備品等費を支出している場合も、その額は「研究プロジェクト費」として計上すること

Appendix 4 FY 2019 Status of Collaboration with Overseas Satellites

1. Coauthored Papers

- List the refereed papers published in FY 2019 that were coauthored between the center's researcher(s) in domestic institution(s) (include satellite institutions) and overseas satellite institution(s). List them by overseas satellite institution in the below blocks.
- Transcribe data in same format as in Appendix 1. Italicize the names of authors affiliated with overseas satellite institutions.
- For reference write the Appendix 1 item number in parentheses after the item number in the blocks below. Let it free, if the paper is published in between Jan.-Mar. 2020 and not described in Appendix 1.

Overseas Satellite 1 Name (Total: OO papers)

1)
2)
3)
4)

Overseas Satellite 2 Name (Total: OO papers)

1)
2)
3)
4)

Not applicable.

2. Status of Researcher Exchanges

- Using the below tables, indicate the number and length of researcher exchanges in FY 2019. Enter by institution and length of exchange.
- Write the number of principal investigator visits in the top of each space and the number of other researchers in the bottom.

Overseas Satellite 1:

<To satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2019					

<From satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2019					

Overseas Satellite 2:

<To satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2019					

<From satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2019					

Appendix 5 FY 2019 Visit Records of Researchers from Abroad

* If researchers have visited/ stayed at the Center, provide information on them in the below table.

Total: 24

	Name	Age	Affiliation: Position title, department, organization	Affiliation: Country	Academic degree, specialty	Record of research activities (Awards record, etc.)	Time, duration	Summary of activities during stay at center (e.g., participation as principal investigator; short-term stay for joint research; participation in symposium)
1	Benjamin LIST	52	Max-Planck-Institute Professor	Germany	Ph.D. in Chemistry, Organic Chemistry and Organocatalysis	Herbert C. Brown Lecture (2019) Member of the German National Academy of Science Leopoldina, Gottfried Wilhelm Leibniz-Prize (2016), Thomson Reuters Highly Cited Researcher (2014, 2016) Arthur C. Cope Scholar Award, ACS (2014)	2019/08/07- 2019/08/08 2 days	Attended the site visit, gave a presentation on research achievements and played a part in the meeting; had a discussion with the Director of ICReDD, Prof. Maeda, and other members about ICReDD.
2	Michael RUBINSTEIN	63	Duke University Professor	USA	Ph.D. in Physics, theoretical polymer science and soft matter	Soft Matter and Biological Physical Chemistry Award, Royal Society of Chemistry (2019), Bingham Medal, Society of Rheology(2018), American Physical Society Polymer Physics Prize (2010)	2019/08/06- 2019/08/09 4 days	Attended the site visit, gave a presentation on research achievements and played a part in the meeting; had a discussion with the Director of ICReDD, Prof. Maeda, and other members about ICReDD.
3	Alexandre VARNEK	64	University of Strasbourg Professor	France	Ph.D. in Physical Chemistry, Chemoinformatics	Member of Advisory Board and Guest Editor in "Molecular Informatics" Director of French national network in chemoinformatics (2011-2014)	2019/08/07- 2019/08/08 2 days	Attended the site visit, gave a presentation on research achievements and played a part in the meeting; had a discussion with the Director of ICReDD, Prof. Maeda, and other members about ICReDD.
4	Mu-Hyun BAIK	49	Korea Advanced Institute of Science and Technology Professor	Korea	Ph.D. in Chemistry, Organometallic Catalysis and Computational	Friedrich Wilhelm Bessel Award (2018) Alfred P. Sloan Research Fellow (2007) NSF-CAREER Award (2007) Cottrell Scholar Award (2006)	2019/11/27- 2019/11/29 3 days	Attended the 2nd ICReDD International Symposium and delivered a lecture.
5	Luisa DE COLA	59	University of Strasbourg Professor	France	Ph.D. in Chemistry, Supularmolecular Chemisty and Photo Chemistry	IUPAC award (2011) Editorial board of Material Horizons (RSC) Editorial board of Angewandte Chemie (Wiley)	2019/11/27- 2019/11/29 3 days	Attended the 2nd ICReDD International Symposium and delivered a lecture.
6	Vladimir GEVORGYAN	63	University of Texas Professor	USA	Ph.D. in Chemistry, Organometal catalysis	UIC Researcher of the Year (2008) Foreign member of Latvian Academy of Sciences (2016) Markovnikov medal (2018)	2019/11/27- 2019/11/29 3 days	Attended the 2nd ICReDD International Symposium and delivered a lecture.
7	Fahmi HIMO	46	Stockholm University Professor	Sweden	Ph.D. in Physics, Quantum Chemisty	Göran Gustafsson Award (2011) The Sven & Ebba-Christina Hagberg Prize (2003)	2019/11/27- 2019/11/29 3 days	Attended the 2nd ICReDD International Symposium and delivered a lecture.

	Name	Age	Affiliation		Academic degree, specialty	Record of research activities (Awards record, etc.)	Time, duration	Summary of activities during stay at center (e.g., participation as principal investigator; short-term stay for joint research; participation in symposium)
			Position title, department, organization	Country				
8	Djamaladdin Gashim MUSAEV	63	Emory University Director	USA	Ph.D. in Chemistry, Quantum Chemisty	Director, Cherry L. Emerson Center, Emory University Editorial Board Member of Organometallics	2019/11/27-2019/11/29 3 days	Attended the 2nd ICReDD International Symposium and delivered a lecture.
9	Jianbo WANG	57	University of Peking Professor	China	Ph.D. in Chemistry, Catalytic Reaction	Baeyer Investigator Award (2016) CCS-BASF Award (2008) Editorial Advisory Board for Organic Letters	2019/11/27-2019/11/29 3 days	Attended the 2nd ICReDD International Symposium and delivered a lecture.
10	Andrei YUDIN	49	University of Toronto Professor	Canada	Ph.D. in Chemistry, Organic Chemsitry	Rutherford Medal of the Royal Society of Canada (2011) Bernard Belleau Award (2015) Associate Editor for Chemical Science	2019/11/27-2019/11/29 3 days	Attended the 2nd ICReDD International Symposium and delivered a lecture.
11	Peng LIU	38	University of Pittsburgh Associate Professor	USA	Ph.D. in Chemistry, Quantum Chemisty	NIH Maximizing Investigators' Research Award for Early Stage Investigators (ESI-MIRA) (2018) NSF CAREER award (2017)	2019/11/27-2019/12/03 7 days	Attended the 2nd ICReDD International Symposium and delivered a lecture; had discussions with the Director of ICReDD, Prof. Maeda, about the operation of ICReDD.
12	Ramil NUGMANOV	32	Kazan Federal University Senior Researcher	Russia	Ph.D. in Chemistry, Quantum Chemisty	n/a	2020/02/16-2020/03/12 26 days	Visited ICReDD at Hokkaido University and had discussions with Specially Appointed Assistant Prof. Pavel Sidorov about the research project.
13	Md. Anamul HAQUE	37	University of Dhaka Associate Professor	Bangladesh	Ph.D. in Material Science, materials chemistry	JSPS postdoctoral felloship (2015) Deans Award, Faculty of Science, University of Dhaka (2014)	2019/05/07-2019/06/29 54 days, 2019/12/01-2019/12/27 27 days	Had discussions about research projects
14	Alba MARCELLAN	42	ESPCI Paris	France	Ph.D. in Material Science and Engineering	Award from the Group France des Polymers(2014)	2019/05/05-2019/05/17 13 days	Delivered a GSS seminar; had discussions about research projects
15	Cecile MONTEUX	42	ESPCI Paris Professor	France	Ph.D. in Physics	PMSE young investigator award, for the Polymer Materials Science and Engineering division of the ACS(2017);TA instrument Young reology award(2013); Prix Jean Langlois(2009)	2019/06/23-2019/06/29 7 days	Taught a Hokkaido Summer Institute course; had discussions about research projects
16	Wei HONG	42	Southern University of Science and Technology Professor	China	Ph.D. in Engineering Science, Mechanics of soft materials	Early-Career Engineering Faculty Research Award, Iowa State University(2015); Bailey Research Career Development Award(2015); Award of Distinction in Teaching, Harvard University(2006); Chinese Government Outstanding Student Abroad(2005)	2019/06/30-2019/08/01 33 days, 2020/01/06-2020/01/16 11 days	Taught a Hokkaido Summer Institute course; gave GSS mini-symposium presentation; delivered a GSS seminar; had discussions about research projects

	Name	Age	Affiliation		Academic degree, specialty	Record of research activities (Awards record, etc.)	Time, duration	Summary of activities during stay at center (e.g., participation as principal investigator; short-term stay for joint research; participation in symposium)
			Position title, department, organization	Country				
17	Bryan COUGHLIN		University of Massachusetts Amherst Department of Polymer Science and Engineering Head	USA	Ph.D. in Chemistry, Polymer Synthesis	Dean of the University of Massachusetts Amherst Polymer Science and Engineering department; NSF Career Award (2007)	2019/06/17 1 day	Gave 1st Dr. Clark Research Symposium presentation; met with students to discuss research
18	Herbert HUI	68	Cornell University Professor	USA	Ph.D. in Mechanical Engineering, Theoretical and Applied Mechanics	Michelin Visiting Professor Award, ESPCI Paris Tech (2010) Chairman of Gordon Conference on Adhesion (2010)	2019/07/08-2019/07/31 24 days, 2020/01/06-2020/01/17 12 days	Gave GSS mini-symposium presentation; delivered a GSS seminar; had discussions about research projects
19	Alfred CROSBY	46	University of Massachusetts Amherst Professor	USA	Ph.D. in Materials Science and Engineering, Mechanics	Adhesion Society Excellence in Adhesion Award (2019); Fellow of the American Physical Society (2015); National Academy of Inventors (2015)	2019/07/15-2019/07/20 6 days	Gave 2nd Dr. Clark Research Symposium presentation; met with students for research discussions; worked to develop new collaborative research projects
20	Huijie ZHANG	33	Shaanxi University of Science and Technology	China	Ph.D. in Life Science	n/a	2019/08/04-2019/08/07 4 days	Met with faculties and students to discuss research
21	Xuechuan WANG	57	Shaanxi University of Science and Technology Professor	China	Ph.D. in Engineering	n/a	2019/08/04-2019/08/07 4 days	Met with faculties and students to discuss research
22	Jun YIN	38	Zhejiang University	China	Ph.D. in Mechanical Engineering	Chinese Government One Thousand Program for Young Talents (2013)	2019/08/06-2019/08/07 2 days	Met with faculties and students to discuss research
23	Tetsuharu NARITA	46	ESPCI Paris	France	Ph.D. in Polymer Science	n/a	2020/01/20-2020/01/29 10 days	Delivered a GSS seminar; had discussions about research projects
24	Costantino CRETON	57	ESPCI Paris Professor	France	Ph.D. in Materials Science and Engineering, Polymer Science	Prix Dédale of the French Adhesion Society (2007) Wake Medal from the UK Society of Adhesion and Adhesives (2011)	2020/02/09-2020/02/15 7 days	Delivered a GSS seminar; had discussions about research projects

Appendix 6 FY2019 State of Outreach Activities

* Fill in the numbers of activities and times held during FY2019 by each activity.
* Describe the outreach activities in the "6. Others" of Progress Report, including those stated below that warrant special mention.

Activities	FY2019 (number of activities, times held)
PR brochure, pamphlet	2: ICReDD pamphlet JP, recruitment brochure
Lectures, seminars for general public	4: Public Lectures (Maeda), HU LS Forum (Gong), Dream-Chemistry 21 (Inokuma), JST workshop (Komatsuzaki), Hitachi competition (Komatsuzaki)
Teaching, experiments, training for elementary, secondary and high school students	3: Trial enrolment (Gong), Lecture at Sapporo Intercultural and Technological HS (Ito), Lecture at Ishikawa Kanazawa Fushimi HS (Ito)
Science café	1: Science Café Sapporo (Inokuma)
Open houses	3: Hokkaido University CRIS (PR), Hokkaido University Festival (Gong), HU Open Campus (Gong)
Participating, exhibiting in events	9: Japan SciCom Forum 2019 (PR), WCSJ 2019 (PR), SSH Event 2019 (PR), Japan PIO Summit 2019 (PR), WPI Science Symposium 2020 (PR), AAAS Annual Meeting 2020 (PR), Science Agora (Gong), Sapporo Science Festa (Gong, Hasegawa), Osaka Science Show (Gong)
Press releases	9: 7 press releases, 1 press conference, 1 research news
Others（Videos）	12: 10 PIs, 2 institute
Others (Social Media)	2: Twitter (134 posts), Facebook (113 posts)
Others (Original goods)	2: Pen, Notepad

*If there are any rows on activities the center didn't implement, delete that (those) row(s). If you have any activities other than the items stated above, fill in the space between parentheses after "Others" on the bottom with the name of those activities and state the numbers of activities and times held in the space on the right. A row of "Others" can be added, if needed.

Outreach Activities and Their Results

List the Center's outreach activities carried out in FY 2019 that have contributed to enhancing the brand or recognition of your Center and/or the brand of the overall WPI program, if any, and describe its concrete contents and effect in narrative style. (Where possible, indicate the results in concrete numbers.)

Examples:
- As a result of using a new OO press-release method, a OO% increase in media coverage was obtained over the previous year.
- By holding seminars for the public that include people from industry, requests for joint research were received from companies.
- We changed our public relations media. As a resulting of using OO to disseminate information, a OO% increase in inquiries from researchers was obtained over the previous year.
- As a result of vigorously carrying out OO outreach activity, ¥OO in external funding was acquired.

We focused this year's outreach activities on ICReDD's recruitment efforts, advertising the center as an attractive place for early-career researchers' career development. We produced a dedicated recruitment brochure and distributed it at conferences and online, both on our social media platforms and through the university's Ambassadors and Partners network. We also started to advertise our openings on the website of Asia Research news, an international research-focused magazine. Comparing similar time frames within this and past year, the number of applications increased by up to 38%, although the causality is uncertain.

Very early we also started to produce a video introduction of the center and video portraits of all our PIs which have been received very positively. The attention our social media posts containing videos receive (2175 reach/121 engagements) is on average 9x higher the attention of posts containing only links (246 reach/31 engagements) and on average 5x higher than the attention of posts containing photos (435 reach/84 engagements).

At our booth presentation at the 2020 AAAS Annual Meeting, we exhibited research samples and interactive physical models in our booth as well as advertised our presence with flyers inserted into give-away notepads placed on tables in the press room. As a result, around 60 people actively engaged with us at our booth in detailed conversations, around 10 of which stayed in touch with us after the event. This is up from about 20 long interactions at the 2019 World Conference of Science Journalists where we focused on exhibiting visual material (banners, videos).

Appendix 7 FY 2019 List of Project's Media Coverage

* List and describe media coverage (e.g., articles published, programs aired) in FY2019.

	Date	Types of Media (e.g., newspaper, magazine, television)	Description
1	2019/05/27	Magazine	Article on ICReDD in QS Wow News print edition
2	2019/07/01	Magazine	Interview with Satoshi Maeda in 化学
3	2019/12/19	Magazine	Article on ICReDD research press release (12/11/2019) about seawater glue gel in Asia Research News print edition
4	2019/12/03	Scientific journal	Article on ICReDD research (10.1002/adma.201905878) on rigidity-switching hydrogel in Nature Reviews Materials
5	2019/11/25	TV	TV segment on ICReDD research on NHK Sapporo
6	2019/12/08	TV	TV segment on ICReDD research on NHK Sapporo
7	2019/12/27	TV	TV segment on ICReDD research (10.1126/science.aay8224) on redox mechanochemistry on NHK
8	2020/02/15	TV	TV segment on ICReDD research on TV-Hokkaido
9	2019/06/01	Pamphlet	Article on ICReDD research in Intelligent Measurement Analysis (issued by JST)
10	2020/02/01	Pamphlet	Article on ICReDD research in Japanese Scientists in Science 2019 サイエンス誌に載った日本人研究者
11	2019/04/24	Newspaper	Article on ICReDD research press release (01/02/2019) about self-toughening hydrogel in Hokkaido Shimbun
12	2019/07/19	Newspaper	Article on ICReDD-organised symposium in Hokkaido Iryou Shimbun
13	2019/10/28	Newspaper	Article on ICReDD in Yomiuri Shimbun
14	2019/11/15	Newspaper	Article on ICReDD research press release (12/11/2019) about seawater glue gel in Yomiuri Shimbun

15	2019/12/23	Newspaper	Article on ICReDD research (10.1126/science.aay8224) on redox mechanochemistry in Hikkan Kogyo Shimbun
16	2019/12/27	Newspaper	Article on ICReDD research press release (01/02/2019) about self-toughening hydrogel in Yomiuri Shimbun
17	2020/01/08	Newspaper	Article on ICReDD research press release (12/11/2019) about seawater glue gel in Hokkaido Shimbun
18	2020/01/15	Newspaper	Article on ICReDD research press release (14/01/2020) about high-efficiency photosensitizer in Zaikei shimbun
19	2020/01/28	Newspaper	Article on ICReDD research press release (14/01/2020) about high-efficiency photosensitizer in Nikkei Sangyo Shimbun
20	2020/02/07	Newspaper	Article on ICReDD research press release (14/01/2020) about high-efficiency photosensitizer in Nikkei Sangyo Shimbun
21	2019/03/28	Online news	Interview with Tamiki Komatsuzaki on Hitachi Website
22	2019/07/30	Online news	Article on ICReDD research press release (24/05/2019) about flexible alkaloidal scaffold synthesis in Phys.org (reach: 5,102,926)
23	2019/07/31	Online news	Article on ICReDD research press release (24/05/2019) about flexible alkaloidal scaffold synthesis in ScienceDaily (reach: 7,093,051)
24	2019/07/31	Online news	Article on ICReDD research press release (24/05/2019) about flexible alkaloidal scaffold synthesis in The Medical News (reach: 1,652,128)
25	2019/08/06	Online news	Article on ICReDD research press release (24/05/2019) about flexible alkaloidal scaffold synthesis in Technology Networks (reach: 315,028)
26	2019/10/07	Online news	Article on ICReDD research press release (19/07/2019) about all-benzene catenane and trefoil knot in Nanowerk (reach: 75,074)
27	2019/10/07	Online news	Article on ICReDD research press release (19/07/2019) about all-benzene catenane and trefoil knot in Phys.org (reach: 5,523,020)
28	2019/10/07	Online news	Article on ICReDD research press release (19/07/2019) about all-benzene catenane and trefoil knot in ScienceDaily (reach: 6,914,300)
29	2019/10/26	Online news	Article on ICReDD research press release (01/02/2019) about self-toughening hydrogel in Diamon Weekly
30	2019/11/12	Online news	Article on ICReDD research press release (12/11/2019) about seawater glue gel in Daily Mail (reach: 59,623,497)
31	2019/11/12	Online news	Article on ICReDD research press release (12/11/2019) about seawater glue gel in SciTech Daily (reach: 1,419,752)

32	2019/11/13	Online news	Article on ICReDD research press release (12/11/2019) about seawater glue gel in Phys.org (reach: 4,985,649)
33	2019/11/13	Online news	Article on ICReDD research press release (12/11/2019) about seawater glue gel in ScienceDaily (reach: 7,255,533)
34	2019/11/19	Online news	Article on ICReDD research press release (12/11/2019) about seawater glue gel in 環境情報メディア「環境展望台」
35	2019/11/26	Online news	Article on ICReDD research in Jiji.com
36	2019/12/06	Online news	Article on ICReDD research on New Atlas
37	2019/12/20	Online news	Article on ICReDD research press release (20/12/2019) about redox mechanochemistry in Phys.org (reach: 6,014,128)
38	2019/12/20	Online news	Article on ICReDD research press release (20/12/2019) about redox mechanochemistry in ScienceDaily (reach: 6,825,295)
39	2019/12/21	Online news	Article on ICReDD research press release (20/12/2019) about redox mechanochemistry in Chemical & Engineering News (reach: 282,868)
40	2020/01/15	Online news	Article on ICReDD research press release (14/01/2020) about high-efficiency photosensitizer in Optronics
41	2020/01/21	Online news	Article on ICReDD research press release (14/01/2020) about high-efficiency photosensitizer in Nanowerk (reach: 165,628)
42	2020/01/21	Online news	Article on ICReDD research press release (14/01/2020) about high-efficiency photosensitizer in Technology (reach: 98,439)
43	2020/01/22	Online news	Article on ICReDD research press release (14/01/2020) about high-efficiency photosensitizer in eeNews Europe (reach: 65,958)
44	2020/01/22	Online news	Article on ICReDD research press release (14/01/2020) about high-efficiency photosensitizer in Phys.org (reach: 6,014,128)
45	2020/01/24	Online news	Article on ICReDD research press release (14/01/2020) about high-efficiency photosensitizer in Photonics.com (reach: 91.919)
46	2020/01/28	Online news	Article on ICReDD research in Innovation News Network
47	2020/02/26	Online news	Article on ICReDD research press release (05/02/2020) about MOF carbohydrate gas separation in Nanowerk (reach: 103,525)
48	2020/02/26	Online news	Article on ICReDD research press release (05/02/2020) about MOF carbohydrate gas separation in Phys.org (reach: 5,078,145)

49	2020/02/27	Online news	Article on ICReDD research press release (05/02/2020) about MOF carbohydrate gas separation in ScienceDaily (reach: 6,547,254)