World Premier International Research Center Initiative (WPI)
FY 2023 WPI Project Progress Report (The center selected in and before FY2020)

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Research Center	Institute for Chemical Reaction Design and Discovery (ICReDD)		
Center Director	Satoshi Maeda	Administrative Director	Koichiro Ishimori

Common instructions:
* Unless otherwise specified, prepare this report based on the current (31 March 2024) 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

To achieve sustainable development goals through the realization of Society 5.0, new chemical reactions are needed to create novel functional molecules and high-performance materials, and even medical treatments for intractable diseases. However, the design and discovery of new chemical reactions has relied on serendipity or experience-guided intuition, which has been a bottleneck in innovation for the new society. In the center, the computational research team, which is capable of simulating various types of chemical reactions, is engaged in the development of practical chemical reaction design techniques through close cooperation with information and experimental teams. To address various problems in highly complex chemical processes, the information team, which covers diverse fields ranging from chemical and materials informatics to combinatorial optimization, knowledge engineering, and mathematical modeling, was established by bringing together top information scientists in these fields. The experimental team also consists of top scientists from diverse backgrounds, such as organic synthesis, materials chemistry, polymer physics, and medical science. The center is engaged in developing "chemical reaction design and discovery" strategies for various application fields through high-level fusion research combining computational, informatics, and experimental techniques owned by these teams. Through these efforts, the center will revolutionize chemical reaction design and discovery. The achievements for FY2023 are as follows: 166 papers were published in peer-reviewed journals (47 papers in journals with an IF > 10). One paper was published in *Science* (IF: 56.9), two in *Nature Chemistry* (IF: 21.8), two in *ACS Nano* (IF: 17.1).. The center members have presented their research in 84 invited lectures at international conferences and 10 awards have been granted. The total amount of research funding was 1,273 million JPY. Representative grants are JST-ERATO, JST-CREST, AMED-P-PROMOTE, etc.

2. Generating Fused Disciplines

Promotion of fusion research: The center was working on several flagship projects and bottom-up projects. These projects are evaluated yearly, and then, promising ones were expanded or promoted from bottom-up to flagship project. These projects were carried out under the Center Director's initiative with the Fusion Research Coordinator leading the project together with project leader.

Fusion research achievements in FY2023: There was progress in computation-informatics fusion research across multiple projects (*J. Chem. Phys. A*, *J. Chem. Inf. Model.*, Mol. Inf.). The Gong group and Maeda group investigated the efficiency and selectivity of mechanophore activation in double network hydrogels as a function of relative bond rupture force (J. Am. Chem. Soc., Nat. Chem.). Additionally, fusion research was incorporated into bottom-up projects on a Cancer GPS method for evaluating tumor malignancy, chemical mixture composition analysis from image data, and crystalline molecular machines (Sci. Rep., Industrial & Engineering Chemical Research, J. Am. Chem. Soc.).

Start-up support for fusion research: In FY2023, start-up support for new appointments (8 million yen for 3 new positions) and start-up support for fusion research to take on challenging bottom-up fusion projects (18 projects (16.62 million yen) and 1 group project (10 million yen) for a total of 26.62 million yen) were awarded. These projects led to the acquisition of Grants-in-Aid for Scientific Research, 5 projects (59.6 million yen) were granted.

Pre-checking system for the grant application: The center conducted a pre-checking system to review and revise the applications for Grants-in-Aid for Scientific Research, etc. before submission. 36.0% of the applications for Grants-in-Aid for Scientific Research were granted for FY2024 (university average 34.7%). The amounts of Grants-in-Aid for Scientific Research obtained have been increasing every year. FY2023: 288 million yen, and overseas PIs and Jr-PIs have also succeeded in obtaining Grants-in-Aid for Scientific Research.

3. Realizing an International Research Environment

Number of researchers: The center conducted an international call for applications for new specially appointed faculty members and postdoctoral researchers to be hired at the center and received 90 applications for 16 positions from Japan and abroad in FY2023. As of March 31, 2024,

the number of PIs was 15 including 3 foreign PIs, 48% of all researchers were foreign nationals, and 19% were female researchers (total of 84 researchers, including 40 foreign nationals and 16 female researchers, split between the fields of Computation the fields of Computation (16 researchers, 19%), Information (19 researchers, 23%), and Experiment (49 researchers, 58%).

Symposiums and seminars: The center has held the ICReDD international symposium, inviting researchers from Japan and overseas to introduce them to the vision and research of the center. The sixth ICReDD international symposium was held on September 10th and 11th, 2023 and had 350 total participants (222 on-site and 128 online), 17 actual participants from overseas (9 countries), and 38 poster sessions. The "List Platform" Kick-off Symposium was held on October 5th, and had 95 participants. Furthermore, the 7th ICReDD International Symposium under the title of the "Rising Star Program", was held on January 18th and 19th, 2024, and was attended by 165 researchers (100 on-site and 65 online). In FY2023, the center held eighteenth international seminars. These events include seven co-organized symposiums, and seven ICReDD seminars (two research ethics seminar, two diversity seminars, NNP-AFIR tutorial seminar, and two Japanese seminars).

Fostering young researchers by MANABIYA: Researchers were accepted through the MANABIYA system. "MANABIYA (ACADEMIC)" invited applications from April 2023 and accepted 21 researchers (13 were accepted from Japan and 8 were accepted from abroad) out of 22 applicants, who were trained in the center's techniques. With the removal of Covid travel restrictions, the number of applicants from overseas increased in FY2023.

4. Making Organizational Reforms

Evaluation system of center faculty members: The results of the self-performance evaluation, and discretionary performance evaluation based on annual interview with the Center Director are used to determine the salary increase or decrease by one or two steps from the base annual salary for the following year, which has not yet been done in any other departments in the University. Performance evaluations (S, A, B, C and D) were conducted for 15 of 16 faculty members, excluding those who arrived and left during FY2023. One faculty member received a two-level salary increase for evaluation grade S, 7 faculty members received a one-level salary increase for evaluation grade A, 7 faculty members received no revision salary for evaluation grade B and no faculty member received a one or two-level salary decrease for evaluation grade C or D.

Establishment of ICReDD fellow system: In FY2023, the center established a new position called the ICReDD fellow to expand ICReDD's research activities inside and outside the university and to serve as an incubation system for new PIs and five professors were appointed.

Establishment of Equipment Management Center: The Equipment Management Unit, which was established by hiring a researcher holding a PhD with expertise in the field, developed a system to manage data on equipment at the center and check all figures for submission against the raw data.

Establishment of Human Resource Development Unit: "Chemical Reaction Design and Discovery" and "MANABIYA" will be firmly rooted in the university's organizational structure via the establishment of the "Graduate School of Chemical Reaction Design and Discovery". The center will have its own graduate school, which is different from the current graduate school, and attractive content such as MANABIYA, which is short-term research exchange with a laboratory in a different field, to the regular graduate school curriculum.

Prevention of research misconduct: The Equipment Management Center developed a system to manage data on equipment at the center and check all figures for submission against the raw data. In addition, by facilitating an environment in which research results can be openly discussed, periodical social gathering events, so-called "ICReDD get togethers" were held 6 times, where young researchers, students and PIs communicated and exchanged their opinions.

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

The University has strongly supported the center and has secured funds equal to or more than the WPI grant for its operation (FY2023: 1,830 million yen). The center will be made a permanent research center that always promotes cutting-edge, world-class research based on a new adaptive research strategy involving periodically changing researchers and research themes. The center launched the "List-DX Catalyst Collaboration Research Platform (List-Platform)" and the "Mitsui Chemicals-ICReDD Innovative Chemical Reaction Design Laboratory (Mitsui Chemicals-ICReDD Laboratory)" in FY2023. The university highly evaluates the center's achievements, such as a management system that clearly separates research and administrative organization, like a Center Director and Administrative Director, a careful performance evaluation system, a hospitality system, the assignment of faculty members specializing in fusion research (Fusion Research Coordinator), and instrument management faculty to prevent research misconduct, and ICReDD fellow system.

6. Others

In FY 2023, an updated institutional pamphlet was created to convey the current direction of ICReDD as well as a pamphlet highlighting the design philosophy and architectural features of the new ICReDD building. Novelty goods with ICReDD branding were created to attract attention to our booth at events. The center published 24 research-related articles on the web, including 18 research press releases and 6 research news articles. Focusing on research-related posts on SNS and regularly mentioning scientific journals through the @ function on X (formerly Twitter) when tweeting new publications, so that journals retweet our posts, has contributed to a 52% increase (to 1,093) over last year in the traffic driven to research news articles on the ICReDD website through posts on X. This also contributed to a 35% increase (to 6743) in the number of unique visitors that viewed research news articles on the ICReDD website. The center hosted the 12th WPI Science Symposium for the general public, with a focus on middle and high school students on November 23rd. The theme of the symposium was "Frontier Research Driven by Informatics" and had 270 participants (117 on-site and 153 online). By holding a variety of other outreach events, such as a joint open campus event, a hands-on lab experience, a tour, a special class, among other activities, ICReDD increased its presence among the local community.

* 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 fusing disciplines).
  (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 2023.
* 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.

I. The center's scientific mission

To achieve sustainable development goals through the realization of Society 5.0, new chemical reactions are needed to create novel functional molecules and high-performance materials, and even medical treatments for intractable diseases. However, the design and discovery of new chemical reactions has relied on serendipity or experience-guided intuition, which has been a bottleneck in innovation for the new society. The center's mission is to establish "chemical reaction design and discovery" strategies and to enable humanity to purposefully design chemical reactions without relying on serendipity or experience-guided intuition. The center combines computational science, information science, and experimental science to develop new synthetic methods, new materials, and new applications in all areas of our society. In the center, the computational research team, which is capable of simulating various types of chemical reactions, is engaged in the development of practical chemical reaction design techniques through close cooperation with information and experimental teams. To address various problems in highly complex chemical processes, the information team, which covers diverse fields ranging from chemical and materials informatics to combinatorial optimization, knowledge engineering, and mathematical modeling, was established by bringing together top information scientists in these fields. The experimental team also consists of top scientists from diverse backgrounds, such as organic synthesis, materials chemistry, polymer physics, and medical science. In the center, we are engaged in developing "chemical reaction design and discovery" strategies for various application fields through high-level fusion research combining computational, informatics, and experimental techniques developed by these teams. Through these efforts, the center will revolutionize chemical reaction design and discovery.

II. Overview of the center's research

In FY2023, we decided to continue six flagship projects which were decided by the internal evaluation held at the end of FY2021. Among them, Project I is the most important project in ICReDD. It is closely related to all the other projects and provides computational acceleration tools for them. During monthly meetings, all computational and informatics groups come together to share successes and failures based on their contributions to the other flagship projects. This feedback loop allows us to stay abreast of the latest state-of-the-art computational and informatics tools being used in these projects and helps us to further develop these tools. The other projects have a hierarchical complexity. The complexity increases in the order of the project number. In other words, the number of atoms involved in the reaction treated in each project increases in that order. Working simultaneously on these projects of varying complexity will allow us to build a comprehensive set of tools that can be applied to a wide range of problems in the chemical and materials sciences.

The list of these projects is shown below:

Project-I: **Computational and informatics tools development**. We consistently make Project I the cornerstone of all our projects. All computational and informatics PIs work with Project I and provide feedback on the application of their tools to other projects. This feedback loop strengthens our foundation and helps accelerate all of our projects. The goal of this project is to create a set of *in silico* reaction design strategies that can be tailored to individual cases. In the first half of the WPI period, Project I contributed to the development of the QCaRA/AFIR approach, which combines the AFIR method with a graph-theory-based method for calculating reaction yields, leading to the first-principle discovery of previously unexplored chemical reactions. In addition, a cheminformatics-based approach to predicting the enantioselectivity of organocatalysis has contributed to the discovery of new catalysis. Two goals for the second half of the WPI period are the development of a method for designing an appropriate organometallic catalyst for a given chemical transformation (related to Project II) and the design of a high performance organocatalyst that achieves asymmetric activation of unfunctionalized molecules (related to Project III).

Project-II: New reaction design and discovery from scratch. We continue to work on a

project to predict new reactions from scratch using reaction path networks based on quantum chemical calculations (former Project II). So far, we have demonstrated several successful examples of (non-catalytic) small molecule synthesis. In the future, we will focus our efforts on the discovery of catalysis. This can be done in part on the basis of the achievements in non-catalytic reactions made in the first half of the WPI period, but is a much more complex matter requiring the further development of computational and informatics tools. The goal of this project is to establish a systematic design framework for discovering an organometallic catalyst that can achieve previously unexplored chemical transformations.

Project-III: Catalyst design and discovery through screening. Project III replaces the Supramolecular Catalytic Reaction Space Design project (former Project III) that we were working on. In its current form, the project involves finding the optimal substituents for certain transformations in molecular catalysts. For example, we aim to improve the enantioselectivity of List's IDPi catalyst for various chemical transformations by using a computational and informatics based approach to screen and optimize the substituents of the catalyst. The goal of this project is to achieve an asymmetric activation of unfunctionalized molecules with the assistance of a computational and informatics approach. Such a transformation is highly difficult to achieve by an organocatalyst and is an appropriate target for the second half of the WPI period.

Project-IV: Exploration of mechanochemical synthesis. Project IV is related to the Bridging Micro- and Macro-World project (former Project IV), but focuses exclusively on mechanochemical synthesis using ball mills. It is an ideal target for our computational and informatics tools because of its rapidly growing importance and the large amount of unexplored knowledge that remains. This synthetic method has proven to be a promising tool in organic synthesis. However, its applicability and understanding have not yet been sufficiently explored. The goal of this project is to expand its applicability, elucidate unexpected species unique to this synthesis, and construct a theory for modeling the effects of mechanical impact. Based on the rational design of mechanochemical reactions we will investigate target reactions such as the cross-coupling of solid materials, synthesis of new organometallic reagents like Grignard reagents in the solid state, and the decomposition and recycling of polymer materials.

Project-V: Understanding and controlling polymer property, formation, and degradation. Project V is an extension of the Polymer Degradation Project (former Project VI) that we have been working on. The project, in its current form, involves the design of polymer properties through simulation, the visualization of polymer mechanoradicals, the exploitation of polymer mechanoradicals, the design of polymer sequences to maximize desired properties, and more. Two goals of this project are to improve the performance of muscle-like double network hydrogels and to utilize plastic materials in the synthesis of useful materials.

Project-VI: Cancer diagnosis utilizing new materials and measurement techniques. We will continue our work on developing cancer diagnostic methods using new materials and measurement techniques (former Project VII). In particular, we will further investigate the hydrogel-activated reprogramming phenomenon (HARP) that was discovered during the first half of the WPI period. Two goals of this project are to understand HARP properly and to achieve its clinical applications by a fusion team of materials scientists, information scientists, and medical scientists.

In addition, in partnership with the School of Medical Science, we have launched a consortium called the Clinical Platform for Chemical Reaction Collaboration. Through this consortium, we aim to accelerate the use of our chemical products in medical diagnosis and treatment.

Bottom-up project: Furthermore, we have provided opportunities for young researchers to propose new ideas and launch related bottom-up projects. The launch of each bottom-up project is supported by an internal budget called Fusion Research Start-up. Based on their results, successful bottom-up projects are promoted as flagship projects, while underperforming flagship projects are evaluated and may be discontinued. This approach allows us to consistently deliver high-impact results while encouraging the activities of our young researchers.

III. Achievements and progress on the center research

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

* Preliminary report (confidential)

† Interdisciplinary collaboration within the center

‡ Interdisciplinary collaboration with groups outside the center

Below, achievements and progress on the above six flagship projects I-VI and two bottom-up projects are showcased.

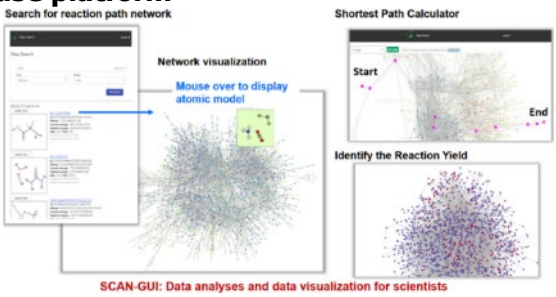
(1) Achievements and progress on Project-I: Computational and informatics tools development

The development and integration of fundamental computational and informatics methods are key issues in developing strategies for computational and informatics driven chemical reaction design and discovery. In FY2023, the achievements and progress are on five topics: a theoretical reaction database platform based on the quantum chemistry aided retrosynthetic analysis (QCaRA) and artificial force induced reaction (AFIR) methods (**1-1**), a yield derivative method for mathematically identifying elementary steps that control reactivity within a reaction path network (**1-2**), generative topographic mapping (GTM) for visualizing reaction path networks (**1-3**), computer-aided synthesis

planning (CASP) (**1-4)** and automated extraction of detailed synthesis procedures (**1-5**).

†1-1) QCaRA-based theoretical reaction database platform

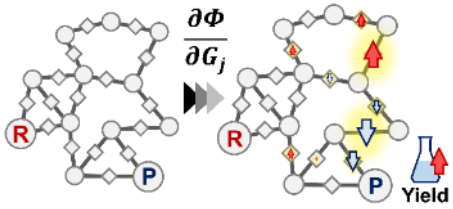
The **Maeda group** and **Takahashi group (ICReDD Research Collaborator)** have developed the Searching Chemical Action and Network (SCAN) platform, which is a centralized, interactive, and user-friendly platform for exploring reaction pathways generated by computational chemistry. Advances in computational chemistry, such as the AFIR method used at ICReDD, have led to the discovery of new reaction pathways. However, these methods generate immense amounts of data, and tools are needed to explore and visualize this data to make it useful for future research. The SCAN platform is one such tool, enabling the sharing, visualization and analysis of reaction path data stored in the database. Massive amounts of AFIR raw data are put through a pre-processing step to extract only the key information needed for the SCAN platform. The SCAN platform then uses this information to make interactive reaction pathway maps that can be searched and viewed by the user. SCAN is accessible on the internet at https://scan.sci.hokudai.ac.jp/. The source code for SCAN is also publicly available on git-hub. SCAN is being accessed by users from around the world and we anticipate the platform will become a foundational tool that will be used to inspire new research directions (*Digital Discovery* 2023).



SCAN-GUI: Data analyses and data visualization for scientists

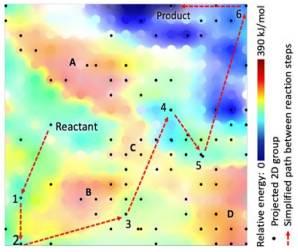
*†1-2) Differentiating the yield of chemical reactions to identify elementary steps that control reactivity

The **Iwata group** and **Maeda group** proposed an approach for differentiating yields to identify elementary reaction steps that control reactivity. The yield derivative for a specific reactant and product pair is derived by employing the rate constant matrix contraction method, which is a simple mathematical method for kinetic analysis. The Gibbs energies of the intermediates and transition states in the reaction path network are used as parameters to formulate the rate equation, which is expressed as a first-order linear differential equation. This approach for differentiating the yield allows numerical evaluation of the contribution of energy variation to the yield for each intermediate and transition state in the reaction path network. In other words, a comparison of these values automatically extracts the factors affecting the yield from a complicated reaction path network consisting of numerous reaction paths and intermediates. This study verifies the behavior of the proposed approach through numerical experiments on the reaction path networks of a model system and the Rh-catalyzed hydroformylation reaction. This approach may potentially be used for designing ligands for organometallic catalysts.

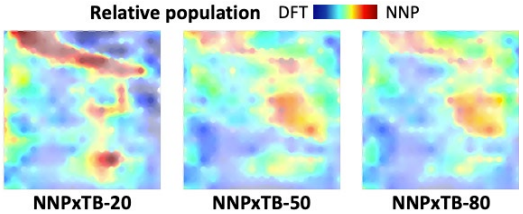


†1-3) GTM to visualize reaction path networks

The AFIR method allows scientists to elucidate the mechanism of chemical reactions by exploring many reaction paths and therefore creating large reaction path networks. Visualization and analysis of the generated chemical reaction networks becomes rather challenging when conventional graph-based approaches are used, due to the sheer size of the networks. As an alternative, the **Varnek group** and the **Maeda group** explored the capabilities of Generative Topographic Mapping (GTM) to intuitively represent large reaction path networks and describe the data distribution on a 2-dimensional map. In this context, new descriptors encoding 3D geometries were proposed. They preserve the fundamental symmetries and neighborhood behavior: similar 3D structures have similar descriptions. Using these new descriptors, GTM based on the new descriptors has been built for the reaction path network of a simplified Wilkinson's catalyst-catalyzed hydrogenation (containing some 10^5 structures generated with AFIR) using either Density Functional Theory or Neural Network Potential (NNP) to evaluate potential energy surface. This analysis demonstrated ability of GTM to cluster structures sharing the same 2D representation; to visualize potential energy surface; to provide insights on the reaction path exploration as a function of time and to compare reaction path networks obtained with different methods of energy assessment (*Mol. Inf.* submitted).



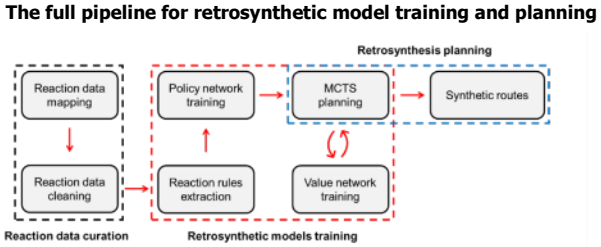
GTM energy representation of ~10^5 geometries explored during AFIR search on catalyzed hydrogenation.

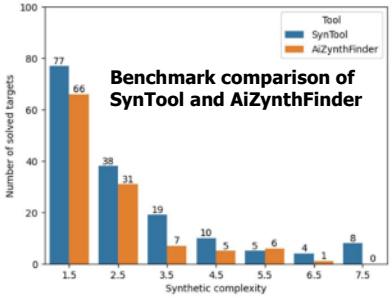


Comparison of reaction paths obtained using different PES evaluation methods.

***1-4) Predicting reaction routes**

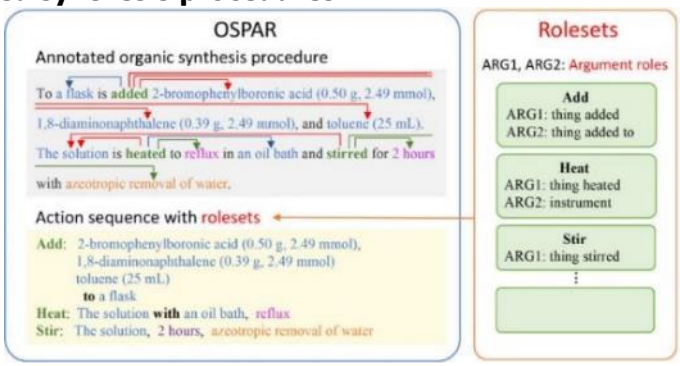
Computer-aided synthesis planning (CASP) tools leverage artificial intelligence and machine learning to assist chemists in designing efficient and cost-effective pathways for the synthesis of complex organic molecules. By analyzing vast databases of chemical reactions, CASP algorithms can suggest optimized synthesis strategies, leading to an accelerated discovery of molecules with desired properties. The **Varnek group** developed a novel open-source tool for synthesis planning, SynTool, which combines Monte-Carlo Tree Search (MCTS) with graph neural networks for the prediction of applicable reaction rules and synthesizability of intermediate products. SynTool is an end-to-end solution that includes three main modules: (1) reaction data curation (reaction database development part), (2) retrosynthetic model training, and (3) retrosynthesis planning, extraction, and visualization of the found retrosynthetic routes. As such, this tool can be directly used for retrosynthesis planning with pre-trained policy/value neural networks (planning mode) or can be fine-tuned to the custom data using an automated end-to-end training pipeline (training mode).
SynTool is an original software implemented in Python 3. Compared to state-of-the-art open-source tools, SynTool demonstrates similar performance but more flexible functionalities for standardizing and filtering reaction data, making it applicable to the variety of reaction data sources and reaction types that are explored in ICReDD.





†1-5) Automatically extracting detailed synthesis procedures

The **Yoshioka group** and **Nagata** (**experimental scientist**) developed a framework to extract detailed synthesis procedures form organic chemistry articles.



Many scientific papers in organic chemistry propose a new chemical reaction process and this new reaction is registered in a chemical reaction database such as Reaxys. Although the information included in the database consists of information such as reactants, catalysts and products, details regarding the synthetic procedure must be looked up in the original paper.

In order to extract such information using machine learning techniques, it is important to have a corpus that includes annotated information about the detailed reaction procedures for the training. For this purpose, the corpus OSPAR (Organic Synthesis Procedures with Argument Roles) was constructed, which includes annotated information about operational procedures using rolesets that explain the relationship between verbs and other terms (i.e., arguments). This corpus was constructed using articles from Organic Syntheses, a trusted journal within the field of organic chemistry.

This argument structure allows for the distinction between the operations "add A to B" and "add B to A". Additionally, by utilizing deep learning analysis with this corpus, it was demonstrated that such additional procedural details could be extracted from scientific papers that were not included in the training data.

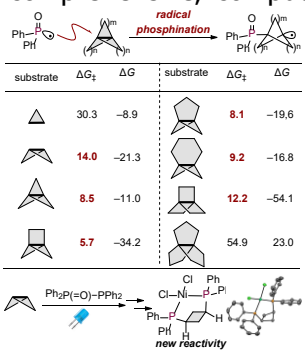
Using this foundational technology will enable chemical reaction databases to provide additional details regarding synthetic procedure, rather than ambiguous "A+B" instructions. This additional information is expected to be useful for scientists when planning follow-up experiments and detailed experimental procedures. (*J. Chem. Inf. Model.* 2023)

(2) Achievements and progress on Project-II: New reaction design and discovery from scratch

We continue to utilize reaction path networks calculated by AFIR to realize small molecule activation reactions. In FY2023, a novel CO_2 incorporation reaction transforming allylic alcohols into γ-lactones was discovered and radical phosphonylation pathways were calculated for creating strained molecules, from which a *cis*-coordinated diphosphine and corresponding nickel complex were synthesized (**2-1**). Additionally, silicon-stereogenic nucleophiles were synthesized and the oxyboration of arynes was achieved (**2-2**).

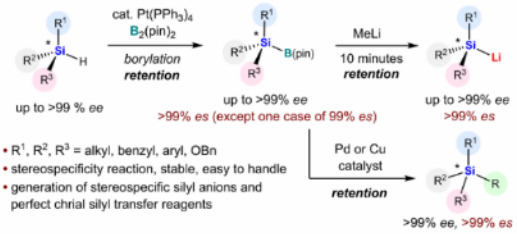
*†2-1) CO_2 and small strained molecule incorporation reactions

Mita (**mix-lab chief**) and the **Maeda group** have developed a method to γ-lactone synthesis from allylic alcohols. γ-lactones are structural motifs widely present in natural organic compounds and pharmaceuticals, and various synthetic methods have been developed for their construction. **Mita** (**mix-lab chief**) has developed a method that uses light irradiation to enable the building of γ-lactones from inexpensive formate salts and allylic alcohols, both of which are very simple starting materials. This is the first reported one-step synthesis of γ-lactones from allylic alcohols, and the reaction was successful for a variety of differently substituted allylic alcohols. To understand the mechanism of this novel rearrangement, the artificial force induced reaction (AFIR) method was used to perform a comprehensive, computational reaction path search, identifying all possible reaction pathways from a single starting molecular structure. The pathway of the main reaction was found to be both kinetically and thermodynamically favorable compared to other side reactions, thus clarifying the overall reaction mechanism (***Precis. Chem.*** 2024). In a separate study, the AFIR method was used to calculate radical phosphonylation pathways toward strained molecules. Promising substrates among them included bicyclo[1.1.0]butane, [n.1.1]propellane (n = 1-4), and [2.2.2]propellane. Following experimentation, a *cis*-coordinated diphosphine was successfully derived from bicyclo[1.1.0]butane under light irradiation conditions. This compound was subsequently transformed into the corresponding Ni-complex with a cyclobutane backbone. Interestingly, the bite angle in this complex was wider than that in the structurally closely related complex $NiCl_2$(dppp), suggesting potential for future applications in catalysis (***submitted*** 2024).

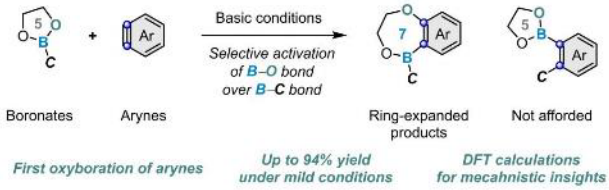


†2-2) Silicon-stereogenic nucleophiles and oxyboration of arynes

The **Ito group** and **Maeda group** have reported the synthesis of silicon-stereogenic optically active silylboranes via a stereospecific $Pt(PPh_3)_4$-catalyzed Si–H borylation of chiral hydrosilanes, which are synthesized by stoichiometric and catalytic asymmetric synthesis, in high yield and very high or perfect enantiospecificity (99% es in one case, and >99% es in the others) with retention of the configuration. Furthermore, a practical approach to generate silicon-stereogenic silyl nucleophiles with high enantiopurity and configurational stability using MeLi activation was reported. This protocol is suitable for the stereospecific and general synthesis of silicon-stereogenic trialkyl-, dialkylbenzyl-, dialkylaryl-, diarylalkyl-, and alkylary benzylo xy-substituted silylboranes and their corresponding silyl nucleophiles with excellent enantiospecificity (>99% es except one case of 99% es). Transition-metal-catalyzed C–Si bond-forming cross-coupling and conjugate-addition reactions are also demonstrated. The mechanisms underlying the stability and reactivity of such chiral silyl anions were investigated by DFT calculations conducted by the **Maeda group** (***Nat. Commun.*** 2023).



The **Ito group** and **Maeda group** have reported the oxyboration of arynes. A series of 2-aryl-1,3,2-dioxaborolane derivatives were reacted with aryne precursors in the presence of CsF to give the corresponding ring-expanded seven-membered borinic acid esters via selective boron–oxygen bond activation. Density functional theory (DFT) calculations conducted by the **Maeda group** suggest that this unprecedented aryne oxyboration proceeds through the formation of boron ate complexes of arylboronates with CsF, followed by aryne insertion into the boron–oxygen bond (***J. Am. Chem. Soc.*** 2024).

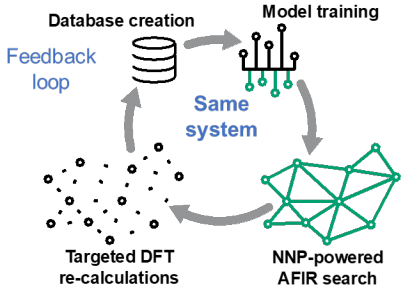


(3) Achievements and progress on Project-III: Catalyst design and discovery through screening

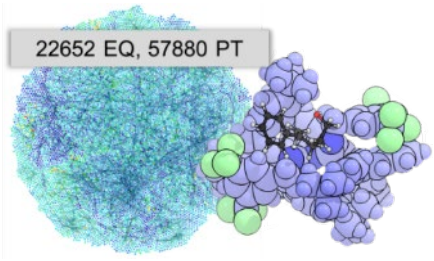
Project III involves finding the optimal substituents and conditions for catalysts through a computational screening process. In FY2023, we made progress in applying AFIR to larger systems such as the IDPi catalyst, which were previously inaccessible, by utilizing a neural network potential(NNP)-aided method (**3-1**) and in employing multi-instance machine learning for catalyst enantioselectivity prediction (**3-2**)

*†3-1) Predicting enantioselectivity using NNP-AFIR

The Neural-Network Potential (NNP)-aided AFIR approach has already been developed in ICReDD in the last fiscal year. This year, the **List group**, **Varnek group**, **Gao group**, and **Maeda group** jointly developed the iterative version of the NNP-aided AFIR approach, applying it to IDPi catalysis. The approach was employed for the intramolecular hydroalkoxylation reaction, and, indeed, NNP accelerated the calculation by approximately 10^4 times, allowing the preparation of a reaction map for such a massive molecular system (228 atoms), which was not practically achievable with conventional DFT methods. Now, more than 50,000 paths have been calculated, and the error is below 0.5 kcal/mol despite the cost.

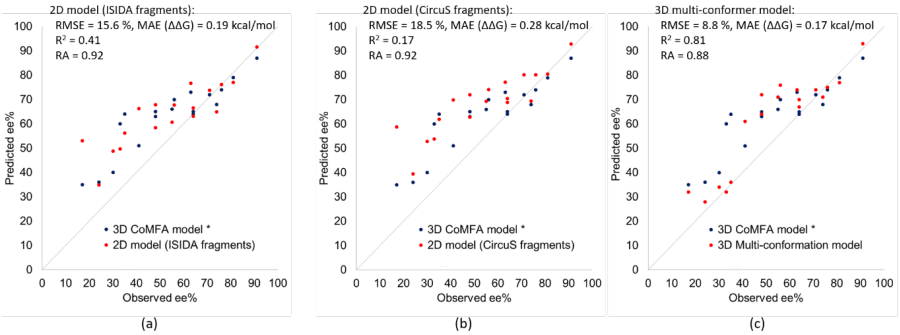


The obtained reaction map provides stable transition states leading to major and minor products. Compared to the transition state structures described in the previous literature, more stable conformers were found for transition states leading to both major and minor enantiomers. Additionally, the reaction mechanism leading to each enantiomer was expected to be identical; however, it appears to proceed through different mechanisms. Namely, the reaction map suggests the major enantiomer is obtained by an asynchronous concerted mechanism, while the minor enantiomer is generated by a stepwise mechanism. This study demonstrates the significance of the AFIR method accelerated by NNP.



‡3-2) Catalyst enantioselectivity prediction using MIL

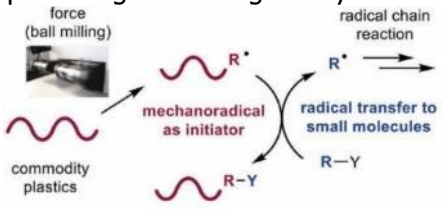
Traditional machine learning approaches for Quantitative Structure-Property Relationship (QSPR) analysis usually rely on a single molecular form/structure for predicting a target property. However, in some cases, such as conformations, different molecular forms can have very different properties, and it is often not known which molecular form is responsible for the observed physicochemical and biological properties of a given molecule. Multi-instance machine learning (MIL) is an efficient approach for solving problems where objects under study cannot be uniquely represented by a single instance, but rather by a set of multiple alternative instances. The **Varnek group** demonstrated the advantages of MIL over the traditional single-instance learning (SIL) in the case of enantioselectivity prediction, where 3D multi-conformation models outperformed 3D single-conformation models and traditional 2D models (***WIREs Comput. Mol. Sci.*** 2023).



Observed and predicted ee % for 18 test catalysts from the asymmetric phase-transfer catalysts comparing the performance of the 3D-CoMFA model: (a) 2D model (ISIDA fragments), (b) model (CircuS fragments), and (c) 3D multi-conformer model (atom triplets).

(4) Achievements and progress on the Project-IV: Exploration of mechanochemical synthesis

Ball mill-based mechanochemical synthesis has emerged as a promising tool in organic synthesis. However, despite its growing importance, little is understood about this new method. In FY2023, we uncovered novel tools and strategies related to ball mill synthesis, including a method that reuses common plastic to initiate radical chain reactions, and a simplified method for performing the Birch reduction that can be completed in an incredibly quick one minute.

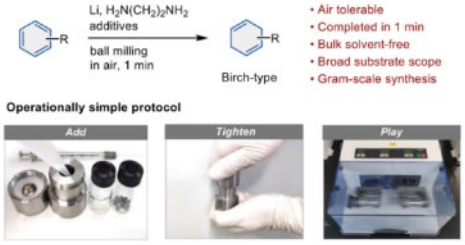


†4-1) Mechanochemical synthesis with the ball mill technique

The **Ito group** and **Maeda group** have developed a method that uses common plastic materials instead of potentially explosive compounds to initiate radical chain reactions. This approach significantly increases the safety of

the process while also providing a way to reuse common plastics such as polyethylene and polyvinyl acetate. When the ball slams into the plastic, the mechanical force breaks a chemical bond to form radicals, which have a highly reactive, unbonded electron. These radicals facilitated a self-sustaining chain reaction that promotes dehalogenation– i.e. the replacement of a halogen atom with a hydrogen atom—of organic halides. The reuse of waste plastic was demonstrated by adding plastic shreds of a common grocery bag to the ball mill jar and successfully carrying out the reaction. The method was shown to be applicable to the treatment of highly toxic polyhalogenated compounds, which are widely used in industry. The proposed force-induced mechanism was validated computationally by the **Maeda group** via the artificial force-induced reaction (AFIR) method (***J. Am. Chem. Soc.*** 2024).

The **Ito group** demonstrated a simplified method for performing the Birch reduction that avoids the use of ammonia, can be done at room temperature and in ambient air, and is 20-150 times faster than conventional methods. The process proved versatile, showing compatibility with a wide variety of organic compounds, including pharmaceutical intermediates and other bioactive molecules. In most cases, the Birch reduction was completed in an astonishingly quick one minute. This technique could potentially enable the simplified synthesis of a wide variety of molecules, while also marking an important advance in mechanochemistry (***Angew. Chem. Int. Ed.*** 2023).



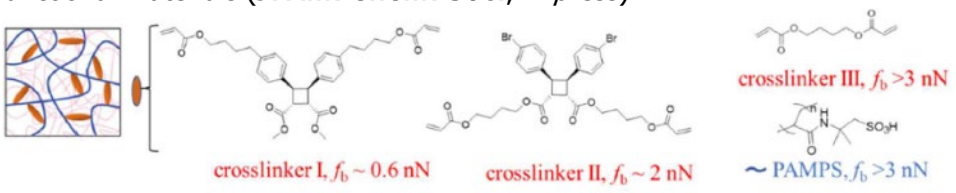
(5) Achievements and progress on the Project-V: Understanding and controlling polymer property, formation, and degradation

This project includes the design of polymers to exhibit unique properties through AFIR simulation, machine learning, the use of polymer mechanoradicals, and the control of polymer network structures to maximize desired properties. In FY2023, we had progress in clarifying bond activation efficiency and accuracy of the mechanophores through a double network method (**5-1**) and controlling the polymer structure using solvents to synthesize functional gels (**5-2**).

***†‡5-1) Clarifying bond activation efficiency and accuracy of the mechanophores through a double network method.**

In recent decades, more than 100 different mechanophores with a broad range of bond rupture forces have been developed. For various applications in polymer materials, it is crucial to selectively activate the mechanophores with high efficiency without causing non-specific bond scission of the materials. The **Gong group** and **Maeda group**, in collaboration with the Craig goup at Duke University, performed a comprehensive investigation into the integration of cyclobutane based weak mechanophore crosslinkers within the PAMPS/PAAm double network hydrogel system, employing varied crosslinker densities, activation forces, and mechanophores. By quantitatively measuring the concentration of force-activated bond breaking of the mechanophores and of non-specific bonds in the DN gels, we clarified the efficiency and selectivity of activation of these mechanophores in competition with backbone scission and/or other mechanophores. We discovered that weak mechanophores having 1/4 the bond rupture force relative to that of the network strand backbone and/or other mechanophores are activated with 100% selectivity. An increase of the relative bond rupture force of the mechanophore led to a decrease of its activation selectivity, due to concomitant scission of a large number of non-specific bonds. These findings provide insights into the prevention of non-specific bond rupture during mechanophore activation and enhance our understanding of the damage mechanism within polymer networks when using mechanophores as detectors. Additionally, it establishes a principle for combining different mechanophores to design multiple mechanoresponsive functional materials (***J. Am. Chem. Soc.***, *in press*).

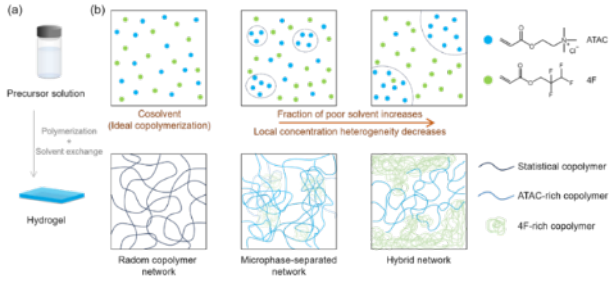
The **Gong group** and **Maeda group**, in collaboration with the Cao goup at Nanjing University showed that the light-induced structural change of azobenzene can also alter its rupture forces, making it an ideal light-responsive mechanophore. The use of light-induced conformational changes to alter the mechanical response of mechanophores provides an attractive way to engineer polymer networks with light-regulatable mechanical properties (***Nat. Chem.*** 2023).



***†5-2) Solvent-controlled synthesis of amphiphilic copolymer hydrogels with varied functions**

Amphiphilic copolymer hydrogels are promising for functional applications. The **Gong group** and **Rubinstein group** developed a facile solvent-controlled method to synthesize amphiphilic copolymer hydrogels with various functions at the same chemical composition. By varying the fractions of a cosolvent and a poor solvent in the reaction solution, amphiphilic hydrogels were

prepared via the copolymerization of cationic and fluorous monomers in the presence of crosslinkers. The fabricated hydrogels show diverse network structures (from disordered to phase-separated) under the same monomer compositions. The structure of hydrogels significantly affects their swelling in various solvents, their mechanical properties, and their fracture behaviors. The effect of solvent on copolymerization and network formation was examined by coarse-grained molecular dynamics simulations. These findings underscore the critical role of monomer distribution in controlling copolymer hydrogel properties, offering an avenue for hydrogel materials design (***Submitted.*** 2023).

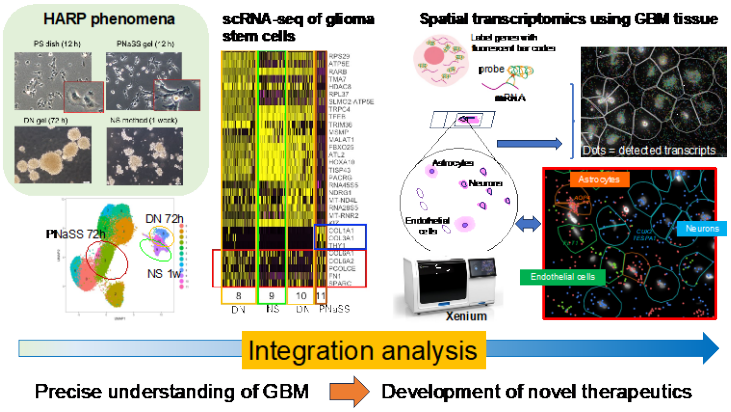


(6) Achievements and progress on the Project-VI: Cancer diagnosis utilizing new materials and measurement techniques

We have continued to investigate the hydrogel-activated reprogramming phenomenon (HARP), which was discovered during the first half of the WPI period. Understanding HARP and its potential clinical applications are pressing issues to be addressed in this project. In FY2023, we verified the presence of cancer stem cells (CSCs) in glioblastoma (GBM) samples using scRNA-seq and spatial transcriptomics techniques (**6-1**), discovered that culture on a positively charged hydrogel (co-APTMA-AMPS gel) triggers the reprogramming of adult intestinal stem cells (ISCs) into a fetal intestine-like state (**6-2**), and developed a new cancer grade probing system (cancer GPS) for evaluating the malignancy grade of model glioma tumor cells using a water-soluble and structure-changeable luminescent europium complex (**6-3**).

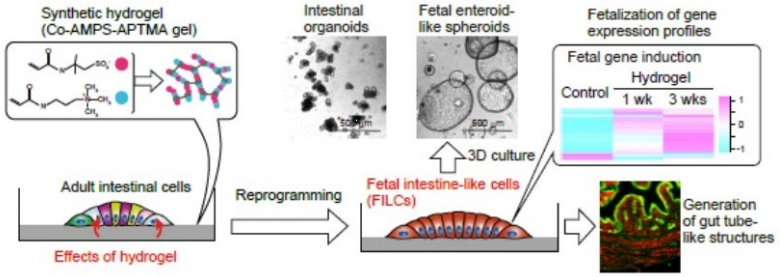
***†6-1) Spatial transcriptomics of glioblastoma and reprogramming of intestinal stem cells**

The **Tanaka group** and **Gong group** previously reported the rapid reprogramming of cancer cells to cancer stem cells (CSCs) using hydrogels, which was named the hydrogel activated reprogramming (HARP) phenomenon (***Nat. Biomed. Eng.***, 2021). The HARP phenomenon is a valuable method to understand the characteristics of CSCs and develop novel therapeutic strategy targeting CSCs. We recently found that the PNaSS (poly(sodium p-styrene sulfonate)) gel can induce CSCs more efficiently. The gene expression profile based on single-cell RNAseq (scRNA-seq) analysis clarified that glioblastoma (GBM) cells cultured on the PNaSS gel were distributed in specific clusters, which include the extracellular matrix collagens. To verify these findings, we performed spatial transcriptomics Xenium using patient-derived GBM tissues, and demonstrated these cells certainly exist in the special CSC niche such as the perivascular region. Thus, integrated analysis using HARP, the scRNA-seq, and spatial transcriptomics will provide a precise understanding of the GBM properties and the interactions between the glioma stem cells and tumor microenvironment, which might contribute to the development of novel therapeutics that can overcome therapy resistance and recurrence.



***†6-2) Reprogramming of adult intestinal stem cells (ISCs) into a fetal intestine-like state**

Given the strong ability of hydrogels to reprogram cancer cells into CSCs, the **Tanaka group** and **Gong group** have also investigated the effects of hydrogels on normal tissue-resident stem cells. This collaborative study has unveiled that culture on a positively charged hydrogel (co-APTMA-AMPS gel) triggers the reprogramming of adult intestinal stem cells (ISCs) into a fetal intestine-like state characterized by unique gene expression profiles, the ability to form fetal enteroid-like structures under 3D culture conditions, and the ability to induce generation of intestinal tube-like structures after



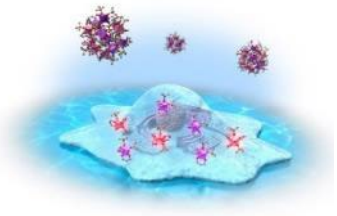
transplantation into immunodeficient mice. This hydrogel-induced reprogramming of ISCs was found to be mediated by activation of Src-Yap and Src-Erk5 signaling pathways. These findings demonstrate the usefulness of hydrogels in reprogramming normal tissue stem cells and suggest that reprogramming of normal stem cells into a fetal-like state may pave the way for organ neogenesis, a key goal in regenerative medicine.

†6-3) Cancer GPS

The **Tanaka group** and **Hasegawa group** developed a new cancer grade probing system (cancer GPS) for evaluating the malignancy grade of model glioma tumor cells using a water-soluble and structure-changeable luminescent europium complex. This method could lead to activity grade tests for the determination of tumor malignancy in patients.

Tumor malignancy was evaluated by introducing the europium complex to model cells that mimic glioma, a common type of tumor that accounts for 26.3% of brain cancers. Three different model cells that mimic different grades of malignancy were tested by measuring changes in the lifetime of the europium complex's characteristic red-light emission. It was found that during the first three hours after adding the europium complex, larger changes in the radiative rate constant of the light emission occurred in the more malignant cells.

To achieve this result, the europium complex was modified to be water soluble and stable among the amino acids in the cell culture medium. Upon addition to the cell culture medium, the europium complex initially forms an aggregate with itself. Interaction with model tumor cells results in the aggregates breaking into single molecules, which are then rapidly taken up by the cells. This process promotes structural changes in the europium complex, which cause changes in the radiative rate constant of the complex's red-light emission. This cancer GPS, which uses a structure-changeable luminescent Eu(III) complex, provides a new diagnostic method for determining human brain tumor malignancy. (***Sci. Rep.*** 2024).

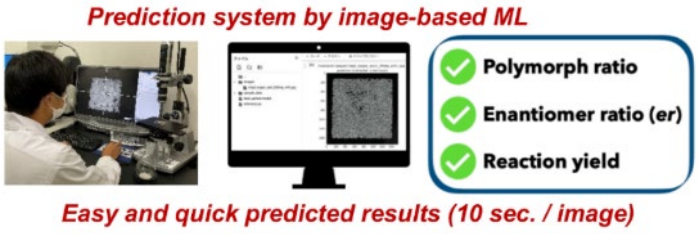


(7) Achievements and progress on Bottom-up projects

Bottom-up projects are initiatives led by our young researchers, and three outstanding projects from FY2023 are highlighted below. Inokuma, the youngest PI, collaborated with Takigawa on the first project, which developed a machine learning model for evaluating chemical composition from images. The second project, led by ICReDD Junior PI Jin, designed a clutch-stack arrangement of triaryltriazines, enabling correlated rotational motion and a thermo-responsive gearshift function in crystalline media. Finally, Ogawa collaborated with computational groups on multiple projects to design functional molecules using quantum chemical calculations .

†7-1) Machine learning model provides quick method for determining the composition of solid chemical mixtures using only photographs of the sample.

As an approach to rapidly reproduce the experience and intuition of experimental researchers, the **Inokuma group** and **Takigawa group** have developed a machine learning model that can distinguish the composition ratio of solid mixtures of chemical compounds based solely on photographs of the samples.



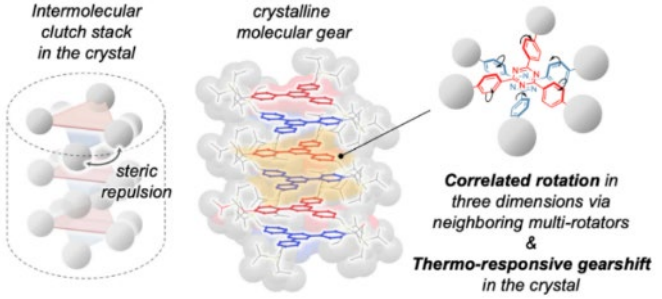
The model was designed and developed using mixtures of sugar and salt as a test case, and the format was also optimized for sample image photography. A combination of random cropping, flipping and rotating of the original photographs was employed in order to create a larger number of sub images for training and testing. This enabled the model to be developed with only 300 original images for training. The trained model was roughly twice as accurate as the naked eye of even the most expert member of the team. Following this successful test case, the model was applied to evaluate various chemical mixtures. The model successfully distinguished different polymorphs and enantiomers, both of which are extremely similar versions of the same molecule with subtle differences in atomic or molecular arrangement. Distinguishing these subtle differences is important in the pharmaceutical industry and normally requires a more time-consuming process.

The model was also able to handle more complex mixtures, accurately predicting the ratio of a target molecule in a four-component mixture. It was also applied to actual reaction yield analysis to predict the progress of the thermal decarboxylation of *p*-aminosalicylic acid to *m*-aminophenol as the reaction was carried out under different heating profiles.

The versatility of the model was further demonstrated by showing that it could accurately analyze images taken with a mobile phone, after supplemental training was performed. This system is anticipated to have a wide range of applications both in the laboratory and in industry, as it can be used to quickly make quantitative predictions from image data alone (***Industrial & Engineering Chemical Research,*** 2024).

†7-2) Steric-repulsion-driven clutch stack of triaryltriazines: Correlated molecular rotational motions and a thermo-responsive gearshift function in crystalline media

Designing molecular motion is known as one of the important subjects for developing nano-scale machinery. Most examples have been studied in solution or polymer media to afford free volume that enables the molecular dynamics. However, these examples have clear limitations on the utilization of molecular dynamics to affect general physical properties due to their isolated manner. To overcome this general issue, crystalline molecular machinery has attracted much interest because it can take advantage of highly ordered molecular packing to integrate molecular motion. The **Jin group, Ito group** and **Taketsugu group** developed a new crystalline molecular gear system via novel design of intermolecular packing arrangement of triphenyl triazine. By attaching bulky, stationary molecules to the phenylene rings, researchers induced a "clutch stack" arrangement, where adjacent triaryltriazine molecules are rotated 60° from each other, rather than stacking in the same orientation. The attached stationary molecules also created enough space for the three phenylene rings to rotate between two positions in a flapping motion. The clutch stack arrangement of the triaryltriazine molecules enabled adjacent molecules to hook on to each other as the phenylene rings rotated, much like interlocking gears. This resulted in the correlated motion of all the molecules in the stack.



When the temperature was raised above a certain threshold, a different correlated motion was observed, in which phenylene rings underwent a 180° rotation. This change in motion was attributed to a phase transition in the crystal that created more space between adjacent molecules, giving the phenylene rings more room to rotate. This change in motion could be reversed by cooling the crystal, marking the first time such controllable molecular motion has been observed in a solid. The effect of the molecular gearshift could be fine-tuned by adjusting the size and structure of the stationary molecule attached to the gear molecule. This adjustability opens the door to the development of new functional materials that leverage crystalline molecular machines. (***J. Am. Chem. Soc.*** 2023).

†7-3) Functional molecular design and reaction analysis using quantum chemical calculations.

The **Ogawa group** and **Taketsugu group** developed X-ray activatable caged compounds based on azo bond cleavage. Hard X-rays can ionize water generating radical species such as hydrated electrons (e^-_{aq}). If molecules can be created that react easily with these radicals, it would be possible to activate compounds in deep tissue without reacting with biomolecules.

Thus, AZO-Rhodamines containing azo moieties with a positive charge and long π-conjugated system to increase the reaction efficiency with e^-_{aq} were designed and synthesized. The azo bonds were selectively cleaved by X-ray, and the fluorescent substance was released. Based on the experimental results and quantum chemical calculations, it was assumed that the azo bond cleavage occurred via a two-electron reduction of the azo bond followed by N—N bond cleavage. Furthermore, azo bonds were cleaved in the cultured cells. The proof-of-concept showed in this study encourages the development of molecules that release anti-cancer drugs triggered by azo bond cleavage upon X-ray irradiation. (***Adv. Sci.***, 2023).

The **Ogawa group** and **Taketsugu group** developed a red-shifted photosensitizer, KA800, with a destabilized HOMO energy level by introducing an ethoxy group for more effective near-infrared photoimmunotherapy. KA800 showed a red-shift of 84nm compared to the conventional IR700 photosensitizer, however, KA800 has low reactivity with ligand cleavage, which is required to induce cell death. Based on the experimental results and quantum chemical calculations, it was found that the low reactivity of KA800 is due to its low efficiency of receiving electrons, which resulted from the destabilization of the HOMO energy level. These results suggested that stabilizing the LUMO energy level would be better than destabilizing the HOMO energy level when developing a red-shifted photosensitizer for NIR-PIT (***J. Photochem. Photobiol.***, 2024).

The **Ogawa group** and **Komatsuzaki group** are investigating the reaction condition optimization of nucleophilic astatination reactions from spirocyclic aryliodonium ylides using an informatics-aided framework. The goal of this research is to produce an At-labeled compound efficiently and with little byproduct.

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."

Promotion of fusion research: The center is working on several flagship projects. Each project involves groups from two or more disciplines. Setting and working on such flagship projects together has been a strong driving force to promote interdisciplinary fusion in the center. In addition, the center holds a call for ideas from young researchers in the center and provides them with an opportunity to lead a bottom-up project. These flagship and bottom-up projects are evaluated yearly. Then, promising ones are expanded or promoted from bottom-up to flagship projects. Conversely, ones that are not proceeding well are terminated or restarted as a bottom-up project. These projects are carried out under the Center Director's initiative. To do that, the center set up a position called "Fusion Research Coordinator" in 2022. They join periodic meetings of all these projects and report their progress to the Center Director. Additionally, the Fusion Research Coordinator participates as a computational scientist in a project themselves and leads the project together with the project's leader. Moreover, all researchers in the center have an opportunity to report their progress, including interactive discussions, once every year to the Center Director, the Administrative Director, and the Fusion Research Coordinator. In FY2023, periodical social gathering events, so-called "ICReDD get togethers" were held 6 times, where young researchers, students and PIs communicated and exchanged their opinions. As for start-up support, a presentation event was held on March 1, 2024 to introduce the annual report directly to the director. At this event, 19 bottom-up projects presented their progress, followed by discussion on research directions for the next fiscal year. The following outputs demonstrate the effectiveness of our strategy for achieving our goal of "revolutionizing chemical reaction design and discovery".

Fusion research achievements in FY2023: In FY2023 there was progress in computation-informatics fusion research across multiple projects, including development of a theoretical reaction database platform, the visualization of reaction path networks, and the identification of reaction steps that control reactivity (***J. Chem. Phys. A*** 2024, ***J. Chem. Inf. Model.*** 2023, ***Mol. Inf.*** Submitted). The Gong group (experiment) and Maeda group (computation) investigated the efficiency and selectivity of mechanophore activation in double network hydrogels as a function of relative bond rupture force (***J. Am. Chem. Soc.*** *under revision*, ***Nat. Chem.*** 2023). Additionally, fusion research was incorporated into bottom-up projects on a Cancer GPS method for evaluating tumor malignancy, chemical mixture composition analysis from image data, and crystalline molecular machines (***Sci. Rep.*** 2024, ***Industrial & Engineering Chemical Research*** 2024, ***J. Am. Chem. Soc.*** 2023).

Papers in collaborations: In 2023, the center has achieved outstanding research achievements. 166 papers including 18 TOP 10% papers (11% of 166 total papers, university average 9%) and 50 highly cited papers (IF 9 or more) were published in peer-reviewed journals which is 3.6 times (11 papers per PI) the number of papers published by professors of the University per year (3 papers). 3 papers were in journals with IF > 20, and 44 papers were in journals with 20 > IF >10. One paper was published in *Science* (IF: 56.9), two in *Nature Chemistry* (IF: 21.8), and two in ACS Nano (IF: 17.1). Since the establishment of the center, the center has been actively collaborating with domestic and international researchers as well as promoting fusion research within the center, leading to collaborative papers within Hokkaido University (41), with domestic collaborators (79), and with international collaborators (48; 28% of papers from the center) in 2023.

Interdepartmental joint symposiums: The 9th Hokkaido University Cross-Departmental Symposium was held on October 11th, 2023, which aims to promote exchange among young researchers within Hokkaido University and the creation of fusion research. This symposium had 700 participants (200 on-site and 500 online). Professor List made a special lecture, 10 center-related faculty members presented four oral and six poster presentations. Six center-related faculty members received awards at the symposium, including the 2023 Hokkaido University Research Encouragement Award (4 faculty members), Best Presentation Award (1 faculty members) and Best Poster Award (1 faculty members).

Start-up support for new appointments and fusion research: In FY2023, start-up support for new appointments (8 million yen for 3 new positions) and start-up support for fusion research to take on challenging bottom-up fusion projects (18 projects (16.62 million yen) and 1 group project (10 million yen) for a total of 26.62 million yen) were awarded. These projects led to the acquisition of Grants-in-Aid for Scientific Research, 5 projects (59.6 million yen) were granted.

Pre-checking system for the grant application: The center conducted a pre-checking system to review and revise the applications for Grants-in-Aid for Scientific Research, etc. before submission. 36% of the applications for Grants-in-Aid for Scientific Research, including "Transformative Research Areas B", were granted for FY2024 (see below). The amounts of Grants-in-Aid for Scientific Research obtained have been increasing every year. FY 2018: 78 million yen, FY 2019: 159 million yen, FY 2020: 148 million yen, FY 2021: 182 million yen, FY2022: 219 million yen, FY2023: 288 million yen and overseas PIs, Jr-PIs, and young researchers have also succeeded in obtaining Grants-in-Aid for Scientific Research.

	Scientific Research A	Scientific Research B	Scientific Research C	Scientific Research on Innovative Areas	Transformative Research Areas A	Transformative Research Areas B	Early-Career Scientists	Total	Average of adoptions for the center	Average of adoptions for the university
FY2024 number of adoptions / applications	0/0	0/3	1/5	0/0	3/9	0/1	5/7	9/25	36.0%	34.7%
FY2023 number of adoptions / applications	0/0	0/4	0/4	0/0	0/0	4/4	7/15	11/27	40.7%	38.3%
FY2022 number of adoptions / applications	0/0	1/4	1/4	0/0	1/3	0/3	4/9	7/23	30.4%	37.1%
FY2021 number of adoptions / applications	0/1	2/6	3/5	1/1	-	-	6/14	12/27	44.4%	38.0%
FY2020 number of adoptions / applications	0/1	1/3	0/1	1/3	-	-	3/7	5/15	33.3%	37.1%

Securing research funding: The center's PIs and other researchers have continued to receive competitive research funding steadily since its inception. The total amount of these funds was 203 million yen in 2018, 668 million yen in 2019, 934 million yen in 2020, 655 million yen in 2021, 843 million yen in FY2022, and 1,273 million yen in FY2023. Representative competitive research funds in FY2023 are Grants-in-Aid for Scientific Research "Fund for the Promotion of Joint International Research (International Leading Research)" (1) and "Scientific Research S" (1), JST-ERATO (1), JST-CREST (9), JST-FOREST (3), JST-PRESTO (3), JST-START (1), JST-MIRAI (1), AMED-P-PROMOTE (1) etc.

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)

(1) **Number of researchers**: The center conducted an international call for applications for new specially appointed faculty members and postdoctoral researchers to be hired at the center and received many applications from Japan and abroad in FY2023 (90 applications for 16 positions). As of March 31st, 2024, the number of PIs was 15 including 3 foreign PIs, 48% of all researchers were foreign nationals, and 19% were female researchers (total of 84 researchers, including 40 foreign nationals and 16 female researchers, split between the fields of Computation (16 researchers, 19%), Information (19 researchers, 23%), and Experiment (49 researchers, 58%)). The ratio of research fields is 4:6 for computational/information to experimental science, which sufficiently covers all research fields to strengthen the center's mission.

(2) **ICReDD International symposium**: Since 2021, the center established the Akira Suzuki and ICReDD Awards, which honor prominent chemists in both experimental chemistry and computational chemistry or information science. The 3rd annual awards were given to Professor Erick M. Carreira from the Swiss Federal Institute of Technology in Zurich and Professor Frank Neese from the Max Planck Institute for Coal Research, strengthening the center's connection with these two prominent scientists and their institutions. Each fiscal year, the center has held the ICReDD international symposium, inviting researchers from Japan and overseas to introduce them to the vision and research of the center. The sixth ICReDD international symposium was held on September 10th and 11th, 2023. The symposium had 350 total participants (222 on-site and 128 online), 17 actual participants from overseas (9 countries), and 38 poster sessions. Speakers were Erick M. Carreira (ETH Zürich, Akira Suzuki Award winner), Frank Neese (MPI Kofo, ICReDD Award winner), Koji Tsuda (Univ. Tokyo), Kazunari Yoshizawa (Kyushu Univ.), Takashi Ooi (Nagoya Univ.), Lutz Ackermann (Univ. of Göttingen), Abigail G. Doyle (UCLA), Timothy Newhouse (Yale Univ.), Sarah E. Reisman (Caltech), Yi Cao (Nanjing Univ.) and ICReDD's Yasuhide Inokuma and Jian Ping Gong. The "List Sustainable DX Catalyst Collaboration Platform (List-PF)" Kick-off Symposium was held on October 5th, where professors List, Maeda, Ito, and Sidorov (Junior PI) from ICReDD and two invited speakers (Professors Maruoka and Gatzenmeier) gave lectures. The symposium had 95 participants, including five distinguished leading researchers in the field of organocatalytic chemistry (Platform Fellows). Furthermore, the 7th ICReDD International Symposium, was held on January 18th and 19th, 2024, differed from the regular international symposia held in the past in that it was organized and managed by Junior PIs under the title of the "Rising Star Program." Thirteen young researchers (8 from Japan and abroad (David Bryce (Univ. of Ottawa), Nong Artrith (Utrecht Univ.), Julia Kalow (Northwestern Univ.), Ramil Nugmanov (Johnson & Johnson), Philippe Schwaller (Ecole Polytechnique Fédérale de Lausanne), Nobuhiro Yanai (Kyushu Univ.), Midori Akiyama (Kyoto Univ.), Yoichi Hoshimoto (Osaka Univ.) and 5 from ICReDD (Professors Tsuji, Kubota, Harabuchi, Staub, and Nath)) who are active in the fields of experimental science, computational science, and information science gave talks on the development of new chemical reactions and materials using mechanical forces, light, and artificial intelligence. 22 posters were presented at the poster

sessions, and the symposium was attended by 165 researchers (100 on-site and 65 online).

(3) **International seminars**: In FY2023, the center held eighteenth international seminars. Speakers for the seminars were Hung-Jue Sue (Texas A&M Univ., April 27), David Liptrot (Univ. Bath, June 14), Marek J. Wójcik (Jagiellonian Univ., July 3), Jeung Gon Kim (Chonbuk National Univ, July 18), Thanyada Rungrotmongkol (Chulalongkorn Univ., Sept. 4), Supawadee Namuangruk (NANOTEC, Sept. 4), Xueyu Li (Hokkaido Univ., Sept. 4), Kanokwan Kongpatpanich (VISTEC, Sept. 4), Daniel J. Mindiola (Univ. of Pennsylvania, Sept. 8), Stefan Hecht (Humboldt-Universität zu Berlin, Nov. 13), Liang-Yan Hsu (Academia Sinica, November 30), Kaking Yan (Shanghai Tech Univ., Feb. 5), Petra Hellwig (seminar on diversity (Univ. Strasbourg, Feb. 5)), Ram Kinkar Roy (Birla Inst. Tech. Sci. Pilani, Feb. 19), Katsunori Tanaka (Tokyo Inst. Tech./RIKEN, Feb. 21), Panida Surawatanawong (Mahidol Univ., March 11), Erli Lu (Newcastle Univ., March 15) and Eric N. Jacobsen (Harvard Univ., March 22). Such seminars will be held regularly in the future.

(4) **Other seminars and symposia**: A number of seminars and symposia were held in order to ensure opportunities for regular and active communication in a cross-disciplinary manner among the center's young researchers, to advance future fusion research, and to solicit and propose new collaborative research. These events include seven co-organized symposiums (Low Entropy Polymer Network Materials (June 9), Molecular Pathology Research Society (July 14), Chemical Applications of Quantum Info. Process. (Aug. 1), 26th SCF forum (Aug. 25), 23rd Annual Meeting for Neutron Science (Sept. 13-14), 9th HU Cross-Departmental Symposium (Oct. 11), 14th ISAJ (Integrated Science for a Sustainable Society) Annual Symposium (Nov. 10)), and seven ICReDD seminars (two research ethics seminars (Robert J Gellar (Oct. 12) and Koji Okabayashi (Oct. 13)), two diversity seminars (Petra Hellwig (Univ. Strasbourg, Feb. 5), female researcher lectures (Sept. 4)), NNP-AFIR tutorial seminar (Ruben Staub and Carine Seraphim (ICReDD, Oct. 18)), two Japanese seminars (Ryoji Tanaka (Sagami Chem. Res. Inst., July 6) and Hironao Sajiki (Gifu Pharmaceutical Univ., July 19)).

(5) **Fostering young researchers by MANABIYA**: Researchers were accepted through the MANABIYA system. "MANABIYA (ACADEMIC)" invited applications from April 2023 and accepted 21 researchers (13 were accepted from within Japan and 8 were accepted from abroad) out of 22 applicants, who were trained in the center's techniques.

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.

(1) **Evaluation system of center faculty members**: In FY2022, a new regulation was established to provide incentives based on the research performance and discretionary evaluation by annual interview of center faculty members, for whom no evaluation system was previously in place. The results of the self-performance evaluation, and discretionary performance evaluation based on annual interview with the Center Director are used to determine the salary increase or decrease by one or two steps from the base annual salary for the following year, which has not yet been done in any other departments in the University. Performance evaluations (S, A, B, C and D) were conducted for 15 of 16 faculty members, excluding those who arrived and left during FY2023. One faculty member received a two-level salary increase for evaluation grade S, 7 faculty members received a one-level salary increase for evaluation grade A, 7 faculty members received no revision salary for evaluation grade B and no faculty member received a one or two-level salary decrease for evaluation grade C or D.

(2) **Establishment of ICReDD fellow system**: In FY2023, the center established a new position called the ICReDD fellow to expand ICReDD's research activities inside and outside the university and to serve as an incubation system for new PIs and five professors were appointed. The center provides ICReDD fellows with our resources and we collaborate with them. When a senior PI is replaced or new developments in research are needed, the most suitable ICReDD fellow is selected. ICReDD fellows are potential candidates for future senior PIs. The center will be made a permanent research center that always promotes cutting-edge, world-class research based on a new adaptive research strategy involving periodically changing researchers and research themes.

(3) **The decision-making system**: The mission of the center is communicated to all members through interviews at hiring and annually with researchers conducted by the center director. Laboratory chiefs were appointed in mixed laboratories and mixed offices, and laboratory management is conducted so that the Center Director's policies are promptly communicated. Under the direct supervision of the Center Director, the "Fusion Research Coordinator," established since FY2022 and directly connected to the research division, actively promotes and plans fusion research and advises on the progress of the research. Authority had been delegated to the Future Plan Working Group and Equipment Management Working Group, so that they can manage the center by the direction of the center director. The regularly scheduled Advisory Board Meetings were established to obtain advice, recommendations, and evaluations from

experts on future prospects, strategies, and approaches to solving problems in order to realize the center's vision and create a world-class research center, thereby contributing to the future management of the center. The Advisory Board online meetings were held on March 7th (with European members) and 28th (with U.S. and Canadian members). The board members reviewed the progress and follow-up reports from an international perspective and made recommendations on the future direction of the center and provided advice on how to promote research. Specifically, the members suggested that (1) there is a large gap in cancer diagnosis from small molecules, and efforts should be made in stages from small molecules, macromolecules, enzymes, and proteins; (2) a system should be established to dispatch young researchers to international conferences and overseas research institutions; (3) applications should be encouraged not only for funding in Europe but also for funding in North America, such as NSF; (4) it is recommended that a goal be set for the number of female lecturers., etc.

(4) **Strengthen the research support system**: The management organization was reorganized into the Research Support Division to better clarify research support and administration. The "Executive Director" was already appointed as the "Administrative Director" to ensure stronger cooperation with the University Executive Office and to ensure that decisions made by the University are promptly reflected in the center's projects, which steadily strengthened the governance of the center. The Research Support Division was reorganized into the following four units: the "Administrative Affairs Unit", which is responsible for general affairs and accounting; the "International Planning Unit", which invites outstanding overseas researchers and students and conducts international outreach beyond the academic community in cooperation with the Institute for International Collaboration; the "Research Strategy Unit", which works with the URA and the Institute for the Promotion of Business-Regional Collaboration to obtain large-scale funds, promotes collaboration agreements with other institutions, and establishes joint research projects with companies; and the "Human Resource Development Unit", which is a new unit in charge of fostering researchers, graduate students, and industrial researchers using MANABIYA, as well as creating strategies and roadmaps for the center's graduate and recurrent education. The center established this "Human Resource Development Unit" with an aim to establish a graduate school in the future. "Chemical Reaction Design and Discovery" and "MANABIYA" will also be firmly rooted in the university's organizational structure via the establishment of the "Graduate School of Chemical Reaction Design and Discovery". Since the center will have its own graduate school, which is different from the current graduate school, the ICReDD graduate school will have an influence on the development of young researchers at other research institutes, etc., and add new and attractive content such as MANABIYA, which is short-term research exchange with a laboratory in a different field, to the regular graduate school curriculum. Additionally, the "Fusion Research Coordinator" and "Equipment Management Center" is directly connected to the research division, so that the Center Director's policies are managed, and progress is monitored in close concert with researchers.

(5) **Prevention of research misconduct**: In the second half of the WPI funding period, in addition to thorough ethics education within the center (attending the center's own research ethics education seminars is required upon hiring and once a year thereafter), the Equipment Management Unit, which was established by hiring a researcher holding a PhD with expertise in the field, developed a system to manage data on equipment at the center and check all figures for submission against the raw data. In addition, by facilitating an environment in which research results can be openly discussed, the center will achieve a global standard in terms of research transparency, misconduct prevention, and further acceleration of fusion research.

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.

The university highly evaluates the center's achievements and plans to expand these achievements to other departments of the university, such as a management system that clearly separates research and administrative organization, like a Center Director and Administrative Director, a careful performance evaluation system that provides incentives to faculty members, a hospitality system that supports the daily life of foreign researchers, and the assignment of faculty members specializing in fusion research (Fusion Research Coordinator) and an instrument management faculty member to prevent research misconduct.

(1) **Financial support**: Since the establishment of the center, Hokkaido University has strongly supported the center and has secured funds equal to or more than the WPI grant for its operation (FY2018: 358 million yen, FY2019: 1,026 million yen, FY2020: 1,388 million yen, FY2021: 1,904 million yen, FY2022: 2,620 million yen, FY2023: 1,830 million yen). The university also provides the center with full access to its financial infrastructure, i.e., the

opportunity to request budget estimates and to apply for competitive cross-departmental funding. The List-DX Catalyst Collaboration Research Platform (List-Platform) was launched in FY2023 for the further development of research and enhancement of domestic and international research hub functions. The university supported the formation of consortia that involve companies that collaborate with the center in order to promote industrial collaborations and established a system to attract independent funding for the center. Since June 2021, GRRM20 was launched by HPC Systems, Inc. under a program license agreement with the University, and license income has been increasing year by year. From FY2023, a five-year large-scale joint research project (250 million yen in total) with Mitsui chemicals was launched. The center will conduct recurrent education by using MANABIYA (INDUSTRY) to attract companies in related fields and expand its network in order to best match the center's research with these industries. In FY2023, a start-up (MECHANOCROSS Co., Ltd.) associated with Flagship Project IV was launched. In this way, from FY2023, the center plans to gradually become independent and secure continuous research funding by increasing the proportion of the university's voluntary cost burden.

(2) **Personnel support**: In order to ensure that the center sustainably continues its research activities independently, the university provided financial support starting for tenure-track positions that were offered to outstanding WPI researchers. These were appointed following a rigorous selection process based on research activities such as high-impact publications and receipt of competitive funds. Based on this plan, 4 tenure-track associate professors and 1 assistant professor have already been assigned to the center as of April 2023. Furthermore, two specially appointed faculty members were secured in FY2023 with the establishment of the List Platform. The university also decided to secure one associate professor as a young PI for the center in FY2024. In the future, one regular associate professor and one post-doctoral researcher will be assigned to each senior PI of the center. Six young PIs will be assigned one post-doctoral fellow each. Starting in FY2024, the university will take measures to hire necessary faculty members by utilizing various financial resources such as budget requests, making a gradual increase to ten associate professors (one assigned to each senior PI), and 6 young PIs.

(3) **Participation of female researchers**: The future vision of the center aims to achieve a gender balance of 25% (19% as of March 2024). The university also developed a policy for improving gender balance (23% female by 2028) based on the university's program "Accelerate Ambitious of All" adopted as the MEXT subsidy program "The Initiative for Realizing Diversity in the Research Environment (leadership training for women)". All PI-groups are asked to have at least one female. The university secured positions for a female assistant professor and a tenure-track associate professor. Through these positions, a career path system for female researchers from student, postdoctoral researcher, assistant professor, and associate professor (Jr. PI) to professor (PI) was established and role models were shown. Finally, they will be established as PIs of the center and inject a fresh, young perspective into the center's research direction and leadership. The center will also actively recruit female students using the University Fellowship System, and establish a strong, collaborative relationship with the Office of Diversity, Equity, and Inclusion.

(4) **Technical support**: The university established an integrated technical staff organization, the Office for Technical Support, to which technical staff members from various departments in the university were dually appointed, and the consolidation of the centralized administrative system within its operating structure strengthens the support system for cross-divisional education and research activities. In response to a request from the center, the Office for Technical Support dispatched technical staff, performing duties in cooperation with the equipment management faculty members to assist in the maintenance and management of the center's equipment (nuclear magnetic resonance equipment) under the coordination with the Equipment Management Unit. The university provided the fees required to analyze synthesized samples in research projects of the center, as well as the usage fees for the open facility system, which provides access to cutting-edge equipment such as high-resolution NMR spectrometers that are managed by the university (FY2019: 850,000 yen; FY2020: 1 million yen; FY2021: 2.5 million yen; FY2022: 2.3 million yen, FY2023: 4.3 million yen).

(5) **Establishment of graduate school**: From FY2023, the reorganization and integration of existing graduate schools in order to establish a graduate school of "Chemical Reaction Design and Discovery" will be implemented, with plans to cement "Chemical Reaction Design and Discovery" and "MANABIYA" as educational organizations of the university. In order to incorporate the world's most advanced research back into educational programs, the university plans to establish a system for cross-disciplinary and interdisciplinary education that is not bound by the framework of existing research institutes and graduate schools. The center established the "Human Resource Development Unit" to design a human resource development framework that will function as a model case for next-generation higher education through a multilateral approach for students and working people regardless of national or international affiliation. From FY2023, the university already hired a full professor and specialized faculty with extensive teaching and research experience for the Human Resource Development Unit. No other international research institute in the university has such a human resource development unit, and this organizational reform will also lead to the center's further development as a research center to foster young researchers, which would contribute to the reformation of the

entire university. Furthermore, the educational reform of a research institution having its own graduate school is worthy of attention not only for its impact within the university but also outside the university, and as an attempt to foster human resources to take responsibility for the world-leading-edge research.

(6) **Research space**: The university already provided 2,600 m^2 of ICReDD space in the CRIS building and pays for the use of the space, including utilities. The center's research space was expanded from 2,600m^2 to 8,100m^2 in February 2023. The university provided land on the north side of the campus, where the CRIS building and industry-academia collaboration research facilities are concentrated, and supported half of the construction cost of a new research building (4 floors, 5,500 m^2), creating an environment where a total of over 100 researchers can conduct research under one roof. This includes an animal laboratory, an industry-academia collaboration laboratory and a fusion research office where 90 researchers can research in a single space.

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.

(1) Each fiscal year, the center has held the ICReDD international symposium, inviting researchers from Japan and overseas to introduce them to the vision and research of the center. In FY2021, the center established the Akira Suzuki and ICReDD Awards, which honor prominent scientists in both experimental chemistry and computational chemistry or information science. The 3rd annual awards were given to Professor Erick M. Carreira from the Swiss Federal Institute of Technology in Zurich and Professor Frank Neese from the Max Planck Institute for Coal Research. The 3rd Akira Suzuki Awards Ceremony & the 6th ICReDD International Symposium, the first in-person meeting in three years since 2020, had 350 total participants (222 on-site and 128 online), 17 participants from overseas (9 countries), and 38 poster sessions. The "List-PF Kick-off Symposium" was held on October 5th, and had 95 participants. Furthermore, the 7th ICReDD International Symposium "Rising Star Program" was held on January 18th and 19th, 2024, and had 165 researchers (100 on-site and 65 online) and 22 poster sessions. Moving forward, ICReDD plans to periodically hold Rising Star Program events under the organization of the Junior PIs. The center hosted the 12th WPI Science Symposium for the general public, with a focus on middle and high school students on November 23rd. The theme of the symposium was "Frontier Research Driven by Informatics" and had 270 participants (117 on-site and 153 online).

(2) The center has world-class researchers as Principal Investigators (PIs) and has received outstanding awards such as ACS Div. Chem. Info. 2024 Herman Skolnik Award (Varnek). In FY2023, the center members have presented their research in 84 invited lectures at international conferences and received 10 awards.

(3) Since 2018, the center has created a number of promotional materials, including an institute pamphlet and a recruiting brochure targeted at overseas researchers. An English language Annual Report brochure for FY2023 was created to convey the vision and recent progress of the center to domestic and international audiences. In FY 2023, an updated institutional pamphlet was created to convey the current direction of ICReDD as well as a pamphlet highlighting the design philosophy and architectural features of the new ICReDD building. Novelty goods with ICReDD branding were created to attract attention to our booth at events, including pens, clear files, notepads, lab coats, calendars, a stuffed toy mascot, and tote bags, as well as outreach-focused handouts like our unique custom label packaged bath salts and tea. These items have been handed out at many events such as outreach events like the WPI Science Symposium to inspire high school students.

(4) The center has published a "Monthly Research News Postcard" that provides monthly research highlights, a "Quarterly News Poster" that presents research content in an easy-to-understand manner, and an "Annual Report" to provide information on the center's annual research activities. Information was widely disseminated domestically and internationally. Our monthly research news postcard series promote our latest research to a mailing list of hundreds of people, including over 70 international addresses. A unique endeavor at the center is our quarterly news poster "The CATALYST", which explains concepts of chemistry in an easy-to-understand manner, while also introducing the center's research to a high school level, non-scientist audience via a mailing list of 220. In FY2023, 4 issues have been issued, including "The many combinations of computational chemistry", "Machine Learning for Chemical Reaction Design", "Neural Networks for Distinguishing Chemical Compounds", and "Going beyond the frontier with information science".

(5) The center also promotes itself on social media, including Facebook, X, LinkedIn and Instagram. In FY2023, the center published 24 research-related articles on the web, including 18 research press releases and 6 research news articles. Focusing on research-related posts on SNS and regularly mentioning scientific journals through the @ function on X (formerly Twitter) when

tweeting new publications, so that journals retweet our posts, has contributed to a 52% increase (to 1,093) over last year in the traffic driven to research news articles on the ICReDD website through posts on X. This also contributed to a 35% increase (to 6743) in the number of unique visitors that viewed research news articles on the ICReDD website.

(6) By holding a variety of other outreach events, ICReDD increased its presence among the local community. ICReDD held a joint open campus event, with over 250 people trying activities at our booth, and approximately 50 people attending a public lecture by an ICReDD PI. ICReDD also hosted 13 high school students for a hands-on lab experience, held a tour for 16 students from neighboring Ishikari city, and held a special class for 15 high school students through the Academic Fantasista program, among other activities.

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) Continue the efforts to achieve the top-level science through fusion research of theoretical/ informational/experimental sciences. The flagship projects as well as the bottom-up projects have been a very effective promoters for this purpose.

Project I is the most important project in the center because it is closely related to all the other projects and provides computational acceleration tools for them. All computational and informatics groups come together to share successes and failures based on their contributions to the other flagship projects. This feedback loop allows us to stay abreast of the latest state-of-the-art computational and informatics tools being used in these projects and helps us to further develop these tools.

The other projects have a hierarchical complexity. The complexity increases in the order of the project number. In the second half of the WPI period, the center will focus more on systems of higher complexity.

Project-II: New reaction design and discovery from scratch. So far, the center has demonstrated multiple successful examples of (non-catalytic) small molecule synthesis. Going forward, the center will be focusing our efforts on discovering organometallic catalysts that can achieve previously unexplored chemical transformations within this framework.

Project-III: Catalyst design and discovery through screening. The project entails finding the optimal catalyst ligands and substituents through a computation-aided screening process. For example, the center aims to enhance the enantioselectivity of Prof. List's IDPi catalyst for various chemical transformations by utilizing a computation- and informatics-based approach to screen and optimize the catalyst's substituents.

Project-IV: Exploration of mechanochemical synthesis. Project IV focuses on mechanochemical synthesis using ball mills. This synthetic method has emerged as a highly promising tool in organic synthesis. However, its applicability and understanding have not been sufficiently explored yet. The goal of this project is to broaden its applicability, elucidate unexpected species unique to this synthesis method, construct a theory for modeling the influences of mechanical impacts, and more.

Project-V: Understanding and controlling polymer properties, formation, and degradation. The project involves the design of polymer properties through simulation, visualization of polymer mechanoradicals, utilization of polymer mechanoradicals, the design of polymer sequences to maximize desired properties, and more.

Project-VI: Cancer diagnosis utilizing new materials and measurement techniques. This project focuses on developing cancer diagnosis methods that utilize new materials and measurement techniques. Specifically, the center will be conducting further research on the hydrogel-activated reprogramming phenomenon (HARP), which was discovered during the first half of the WPI period. Understanding HARP and its potential clinical applications are urgent topics to be addressed in this project, through a fusion team among materials scientists, informaticians, and medical doctors.

Bottom-up projects: Additionally, fusion research was incorporated into bottom-up projects on a Cancer GPS method for evaluating tumor malignancy, chemical mixture composition analysis from image data, and crystalline molecular machines.

2) Continue the efforts to fulfill the gender balance at every level in line with the policy of Hokkaido University.

The university developed a policy for improving gender balance (23% female by 2028) based on the university's program "Accelerate Ambitious of All", adopted as the MEXT subsidy program "The Initiative for Realizing Diversity in the Research Environment (leadership training for women)". The future vision of the center aims to achieve a gender balance of 25% (19% as of March 2024). The center will tackle this issue with an awareness of the significance of improving the gender balance as well as the numerical target.

3) Continue the efforts to establish the staffing plan to guarantee that ICReDD will maintain 10 PI positions of its own.

After the funding period from WPI, the center will be established as a permanent research institute at Hokkaido University. Unlike conventional research institutes, the center will implement a dynamic personnel appointment system. This means that senior PIs at the center will have two laboratories: one at the center and the other in a different department of Hokkaido University or a top institute outside of Hokkaido University. The university will provide one associate professor and one postdoctoral fellow to each senior PI's laboratory and support their activities at the center. Ten senior PI laboratories will be created in the center, and the budget to hire additional staffs (ten associate professors and ten postdoctoral fellows in total) will be covered by Hokkaido University. These ten senior PIs are top-level researchers who undergo annual evaluations and may be replaced based on their performance to ensure that the center maintains the highest level of excellence. From FY2023, the center established a new position called the ICReDD Fellow as an incubation system for future PIs. When a senior PI is replaced or new research areas need to be developed, the most suitable ICReDD fellow will be selected. In addition, the center plans to establish approximately six junior PI groups, led by rising stars in related fields. These junior PIs will be recruited from top institutes abroad and appointed as tenure-track associate professors. After several years, they are expected to become full professors in Hokkaido University after obtaining tenure, or to secure tenured positions at top institutes abroad. Hokkaido University will cover the costs required to establish the junior PI groups, including the employment costs of the junior PIs and each junior PI group with one postdoctoral fellow. The university will also provide expense for hiring a postdoctoral fellow dedicated to each flagship project. With this dynamic personnel circulation system, the center will maintain the highest level of scientific excellence always.

4) It is recommended that ICReDD and Hokkaido University aid "List DX Catalyst Collaboration Research Platform" to promote additional funds from funding agencies both in Japan and in Germany, e.g. JSPS and DFG.

The center has already made contact with DFG and the Delegation of the European Union and have begun discussions. In addition, the center will actively apply for funding not only in Europe, but also in North America, such as from the NSF.

5) ICReDD is recommended to bring in more researchers and students from established top-institutes abroad, e.g., those in Europe and in the USA.

The center will establish a program to dispatch young researchers to international conferences and overseas research institutions in order to increase ICReDD's international visibility and to accelerate recruitment from top research institutions in Europe and the United States.

6) mission of MANABIYA for spreading the methods of "computation-aided chemical reaction design" is fine, but the planning and setting-up for MANABIYA-based new graduate school needs to be much accelerated.

From FY2024, the reorganization and integration of existing graduate schools in order to establish of the graduate school of "Chemical Reaction Design and Discovery" will be accelerated, with plans to cement "Chemical Reaction Design and Discovery" and "MANABIYA" as educational organizations of the university. In order to incorporate the world's most advanced research back into educational programs, the university plans to establish a system for cross-disciplinary and interdisciplinary education that is not bound by the framework of existing research institutes and graduate schools. The center established the "Human Resource Development Unit" to design a human resource development framework that will function as a model case for next-generation higher education through a multilateral approach for students and working people regardless of national or international affiliation. The educational reform of a research institution having its own graduate school is worthy of attention not only for its impact within the university but also outside the university, and as an attempt to foster human resources to take responsibility for the world-leading, cutting-edge research.

7) Hokkaido University is asked to conduct reforms in order to prevent reoccurrences of the scientific misconduct that occurred at ICReDD, and the members at the center are asked to share deep understanding on research ethics and proper scientific conduct.

In addition to thorough ethics education within the center (attending the center's own research ethics education seminars is required upon hiring and once a year thereafter), the Equipment Management Unit, which was established by hiring a researcher holding a PhD with expertise in the field, developed a system to manage data on equipment at the center and check all figures for submission against the raw data. From FY2023, regular "ICReDD get-togethers" were held to promote exchange and open discussion among young researchers, students, and PIs. The center aims to set a global standard in terms of research transparency, prevention of misconduct, and further acceleration of fusion research.

Appendix 1 FY 2023 List of Center's Research Results and Main Awards

1. Refereed Papers

- List only the Center's papers published in 2023. (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 (the Basic and Generic Research Division at present) 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) (or DOI number), 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.)
   - The papers should be divided into A or B categories on separate sheets, not divided by 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

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2. Review articles

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3. Proceedings

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4. Other English articles

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B. WPI-related papers

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(183) Yasumura, S.; Kato, T.; Toyao, T.; Maeno, Z.; Shimizu, K. An automated reaction route mapping for the reaction of NO and active species on Ag_4 clusters in zeolites. *Physical Chemistry Chemical Physics* **2023**, 25 (12), 8524-8531, Article. DOI: 10.1039/d2cp04761f.

2. Review articles
3. Proceedings
4. Other English articles

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

- List up to 10 main presentations during FY 2023 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
Dec. 4, 2023	Michael Rubinstein	Mysteries of Airway Mucus Layer: From Scattering to Rheology	Pacific Polymer Congress 18, Puerto Vallarta, Mexico
Nov. 15, 2023	Tetsuya Taketsugu	A combined reaction path network and ab initio MD approach to understand the reaction mechanism and dynamics	The International Conference on Molecular Energy Transfer in Complex Systems (iCOMET) 2023 in Jaipur, India
Oct. 17, 2023	Alexandre Varnek	Chemical libraries space – a new library design paradigm	Conference "Exploring Chemical Space", London
Oct. 16, 2023	Benjamin List	Universal Organocatalysts for our World (Plenary lecture)	The 23rd International Conference on Organic Synthesis (23-ICOS) Shanghai, China
Sep. 6, 2023	Jian Ping Gong	Bioinspired Soft Matter Design	The 7th International Soft Matter Conference (ISMC2023)
Aug. 29, 2023	Hajime Ito	Mechanically Induced Structural Transformations in Luminescent Gold Complexes	26TH CONGRESS AND GENERAL ASSEMBLY OF THE INTERNATIONAL UNION OF CRYSTALLOGRAPHY
Jul. 24, 2023	Mikako Ogawa	Targeted cancer therapy using photochemical reactions	The 31st International Conference on Photochemistry (ICP 2023)

July 20, 2023	Toshifumi Satoh	One-step synthesis of sequence-controlled multiblock polymers from monomer mixture	The 13th SPSJ International Polymer Conference (IPC2023), Sapporo
July 8-14, 2023	Satoshi Maeda	Reactivity Prediction through Quantum Chemical Calculations. (Keynote lecture)	Asiachem – 19th Asian Chemical Congress, Istanbul Technical University, Turkey,
Jun. 25 2023	Yasuhide Inokuma	"From Polyketone to Calix[3]pyrrole-type Macrocycles"	The 17th International Symposium on Macrocyclic and Supramolecular Chemistry (ISMSC) Harpa Conference and Concert Centre, Reykjavík, Iceland

3. Major Awards

- List up to 10 main awards received during FY 2023 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
Mar. 18, 2024	Shin Mukai	The Society of Chemical Engineers, Japan, Fellow
Feb. 20, 2024 (Announced)	Toshifumi Satoh	The Award of the Society of Polymer Science, Japan (2023), "Precise Synthesis and Characterization of Architecturally Complex Polymers".
Dec. 21, 2023	Yasuhide Inokuma	The Chemical Society of Japan for Creative Work for 2023, for the research on "Development of Functional Organic Molecules Based on Discrete Polyketones"

Dec. 4, 2023	Hiroki Hayashi	The Asian Core Program (ACP) Lectureship Award, the 16th International Conference on Cutting Edge Organic Chemistry in Asia (ICCEOCA-16), Singapore
Sep. 19, 2023 (Announced)	Alexandre Varnek	The 2024 Skolnik Award, the American Chemical Society's Division of Chemical Information
Sep. 12, 2023	Benjamin List	Friedrich Bergius Lecture, Germany
Sep. 7, 2023	Benjamin List	Silver Jubilee Lecture, Shanghai, China
Sep. 6, 2023	Yu Harabuchi, Yuuya Nagata, and Satoshi Maeda	The inaugural JACS Au Outstanding Paper Award for the paper "Quantum Chemical Calculations to Trace Back Reaction Paths for the Prediction of Reactants"
Apr. 14, 2023	Shinya Tanaka	The Japan Pathology Award for the research on "Analysis of the regulatory factors for cancer therapy resistance – Pathology creates basic science", the Japanese Society of Pathology, the 112th General Meeting of The Japanese Society of Pathology
Apr. 14, 2023	Benjamin List	Purdue Brown Lecture, USA

Appendix 2　FY 2023 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, attach a "Biographical Sketch of a New Principal Investigator"(Appendix 2a).

*Enter the host institution name and the center name in the footer.

<Results at the end of FY2023> **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	44	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	59	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	
Michael RUBINSTEIN	67	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
Masaharu YOSHIOKA	55	Professor, Institute for Chemical Reaction Design and Discovery / Graduate School of Information Science and Technology, Hokkaido University	Doctor of Engineering, Knowledge Engineering	20	January 2020	Usually stays at the center	
Alexandre VARNEK	68	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	47	Specially Appointed Professor, Institute for Chemical Reaction Design and Discovery, Hokkaido University Program-Specific Professor,Center for Innovative Research and Education in Data Science, Institute for Liberal Arts and Sciences, Kyoto University	Ph.D., Machine Learning	20	October 2018	- Primarily stays at Partner institution - attends meeting (by online)	
Tamiki KOMATSUZAKI	59	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	
Satoru IWATA	55	Specially Appointed Professor, Institute for Chemical Reaction Design and Discovery, Hokkaido University Professor, Graduate School of Information Science and Technology, The University of Tokyo	Doctor of Science, Mathematical Engineering	20	November 2020	- Primarily stays at Partner institution - attends meeting (by online)	
Hajime ITO	56	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	
Benjamin LIST	56	Specially Appointed Professor, Institute for Chemical Reaction Design and Discovery, Hokkaido University 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	55	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	42	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	62	Professor, Institute for Chemical Reaction Design and Discovery / Faculty of Advanced Life Science, Hokkaido University	Doctor of Science, Doctor of Engineering, Polymer Chemistry	80	October 2018	Usually stays at the center	
Mikako OGAWA	50	Professor, Institute for Chemical Reaction Design and Discovery / Graduate School of Pharmaceutical Sciences, Hokkaido University	Doctor of Pharmaceutical Sciences, Life sciences	80	April 2023	Usually stays at the center	
Shinya TANAKA	59	Professor, Institute for Chemical Reaction Design and Discovery / Global Institution for Collaborative Research and Education / Faculty of Medicine, Hokkaido University	M.D., 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 2023

Name	Affiliation (Position title, department, organization)	Starting date of project participation	Reasons	Measures taken
N/A				

Appendix 3-1 FY 2023 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.

N/A

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
N/A	N/A	N/A

< Partner institutions>

Institution name	Principal Investigator(s), if any	Notes
University of Strasbourg	Alexandre Varnek	N/A
Max Planck Institute for Coal Research	Benjamin List	N/A
Duke University	Michael Rubinstein	N/A
ESPCI	-	N/A
Swiss Federal Institute of Technology in Zurich	-	N/A
Peking University	-	N/A
Kyoto University, Graduate School of Informatics	-	N/A
Chubu University, Molecular Catalyst Research Center	-	N/A
The University of Tokyo, Graduate School of Information Science and Technology	Satoru Iwata	N/A
Stockholm University	-	N/A
University of Oslo	-	N/A

2. Holding international research meetings

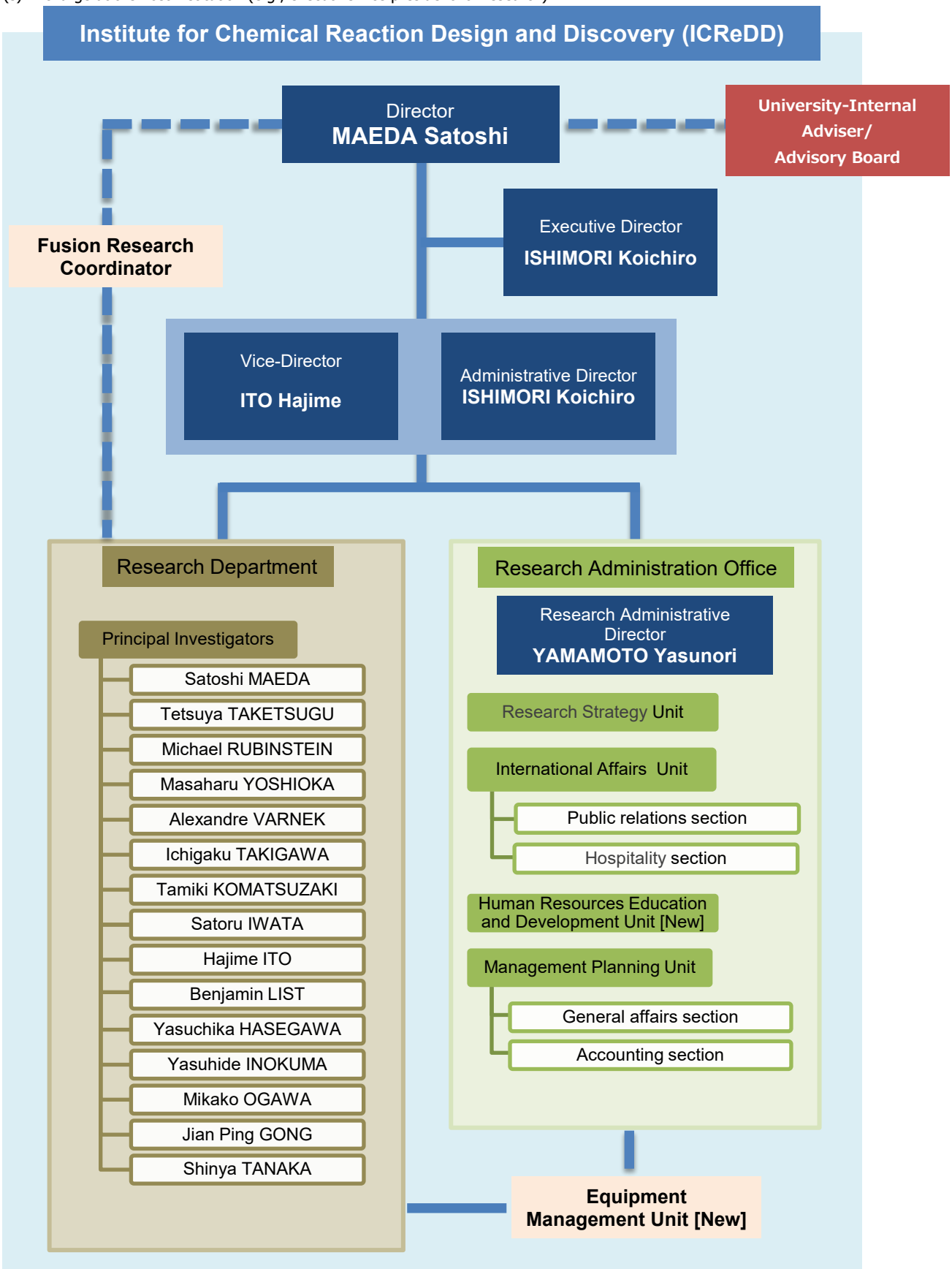
- Indicate the number of international research conferences or symposiums held in FY2023 and give up to three examples of the most representative ones using the table below.

FY 2023: 3 meetings	
Major examples (meeting titles and places held)	Number of participants
The 3rd Akira Suzuki Awards Ceremony & the 6th ICReDD International Symposium (September 10th -11th, on-site and online)	(Total attendance: 350) On-site From domestic institutions: 196 From overseas institutions: 26 Online From domestic institutions: 122 From overseas institutions: 6

List Sustainable Digital Transformation Catalyst Collaboration Research Platform Kickoff Symposium (October 5th, 2023, on-site)	(Total attendance:95) From domestic institutions: 93 From overseas institutions: 2
The 7th International Symposium "The Rising Star Program" (January 18th -19th, 2024, on-site and online)	(Total attendance: 165) On-site From domestic institutions: 95 From overseas institutions: 5 Online From domestic institutions: 40 From overseas institutions: 25

3. Diagram of management system

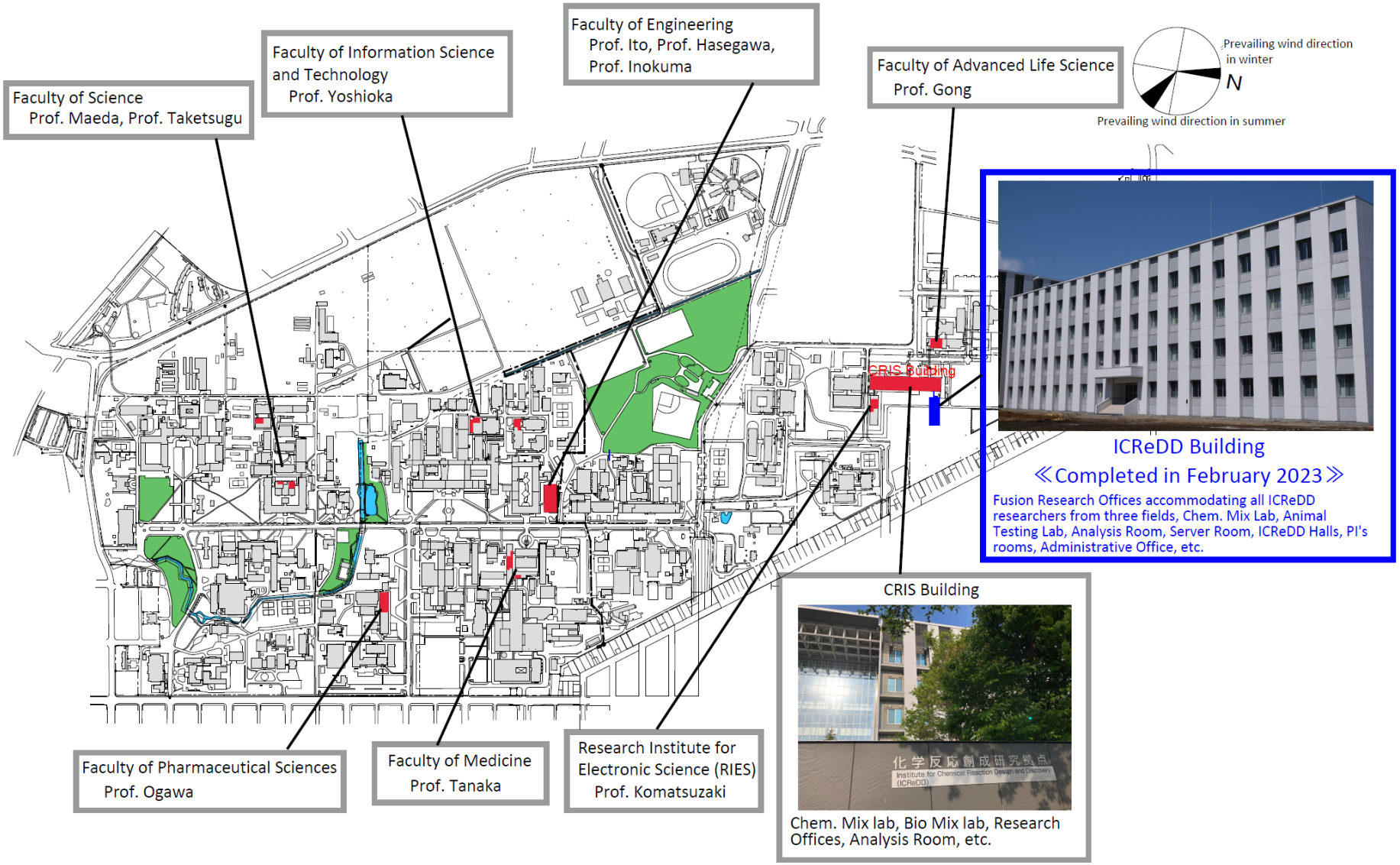
- Diagram the center's management system and its position within the host institution in an easily understood manner.
- If any new changes have been made in the management system from that in the latest "center project" last year, describe them. Especially describe any important changes made in such 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, 2024



5. Securing external research funding*

External research funding secured in FY2023

Total: 858,505,927 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.) as listed under "Research projects" in Appendix 3-2, Project Expenditures.

・Name: Strategic Basic Research Programs (ERATO), JST
Total Amount: 212,538,400 JPY (acquired by Satoshi Maeda)

・Name: International Leading Research, JSPS
Total Amount: 84,760,000 JPY (acquired by Jian Ping Gong)

・Name: Medical Devices Research Results Development Project, AMED
Total Amount: 59,990,000 JPY (acquired by Mikako Ogawa)

Appendix 3-1a FY 2023 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 2023	Final goal (March, 2028)
Researchers from within the host institution	11	12	12
Researchers invited from overseas	3	3	3
Researchers invited from other Japanese institutions	0	0	0
Total principal investigators	14	15	15

b) Total members

	At the beginning of project		At the end of FY 2023		Final goal (March, 2028)	
	Number of persons	%	Number of persons	%	Number of persons	%
Researchers	14		84		85	
Overseas researchers	3	21	40	48	38	45
Female researchers	1	7	16	19	21	25
Principal investigators	14		15		15	
Overseas PIs	3	21	3	20	7	47
Female PIs	1	7	2	13	2	13
Other researchers	0		42		45	
Overseas researchers	0	0	13	31	13	29
Female researchers	0	0	6	14	10	22
Postdocs	0		27		25	
Overseas postdocs	0	0	24	89	18	72
Female postdocs	0	0	8	30	9	36
Research support staffs	0		3		4	
Administrative staffs	6		20		19	
Total number of people who form the "core" of the research center	20		107		108	

	At the beginning of project		At the end of FY 2023		Final goal (March, 2028)	
	Number of persons	%	Number of persons	%	Number of persons	%
Doctoral students	67		64		80	
Employed	17	25.4	16	25.0	48	60.0

※b) The number of doctoral students in the lower table can be duplicated in the upper table of overall composition.

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" culumn may be changed to coincide with the project's actual content.

(Million yens)

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, Administrative Director, Research Administrative Director	26	12
	Principal investigators (no. of persons):9	80	0
	Full-time faculty members (no. of persons): 6	54	0
	Part-time faculty members (no. of persons): 16	85	0
	Specially appointed faculty members (no. of persons): 25	176	176
	Postdoctoral fellows (no. of persons): 21	80	62
	Other researchers (no. of persons): 2	3	3
	Research support staff (no. of persons): 6	2	2
	Administrative staff (no. of persons): 17	71	26
	Center allowance	20	20
	Subtotal	597	301
Project activities	Startup research project costs	31	22
	Outreach costs	9	9
	Center operating costs	14	14
	Environmental improvement costs	117	9
	Facility rental fees	16	0
	Utility costs	93	58
	Puclic equipments usage fees	4	0
	Others	71	0
	Subtotal	355	112
Travel	Domestic travel costs	4	4
	Overseas travel costs	8	8
	Travel cost for scientists on transfer (no. of domestic scientists):1	1	1
	Subtotal	13	13
Equipment	Depreciation of equipment	292	274
	Subtotal	292	274
Research projects (Detail items must be fixed)	Project supported by other government subsidies, etc. *1	415	0
	KAKENHI	191	0
	Commissioned research projects, etc.	467	0
	Joint research projects	97	0
	Ohers (donations, etc.)	103	0
	Subtotal	1273	0
Total		2530	700

Costs (Million yens)

WPI grant in FY 2023	700
Costs of equipment procured	274
System for Spatial Omics Analysis (Number of units:1)	68
High Performance Computer System (Number of units:1)	79
Organic Solvent Purification System (Number of units:1)	10
Others	117

*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 "Research projects" block.

*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 2023 Status of Collaboration with Overseas Satellites

1. Coauthored Papers

- List the refereed papers published in FY 2023 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. 2024 and not described in Appendix 1.

Overseas Satellite 1 **Name** (Total: OO papers)

1) N/A
2) N/A
3) N/A
4) N/A

Overseas Satellite 2 **Name** (Total: OO papers)

1) N/A
2) N/A
3) N/A
4) N/A

2. Status of Researcher Exchanges

- Using the below tables, indicate the number and length of researcher exchanges in FY 2023. 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
FY2023	N/A	N/A	N/A	N/A	N/A
	N/A	N/A	N/A	N/A	N/A

<From satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2023	N/A	N/A	N/A	N/A	N/A
	N/A	N/A	N/A	N/A	N/A

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
FY2023	N/A	N/A	N/A	N/A	N/A
	N/A	N/A	N/A	N/A	N/A

<From satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2023	N/A	N/A	N/A	N/A	N/A
	N/A	N/A	N/A	N/A	N/A

Appendix 5　FY 2023 Visit Records of Researchers from Abroad

* If researchers have visited/ stayed at the Center, provide information on them in the below table.
* Enter the host institution name and the center name in the footer.

Total: 34

	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				
1	LIPTROT, David	34	Lecturer and Royal Society University Research Fellow, University of Bath	UK	Ph.D., Catalysis, Organometallic Chemistry, Reaction Monitoring	Secured a 5-year research fellowship, adopted as a 50th Anniversary Prize Fellow in University of Bath	2023/6/5-7/7, 1 month	Participation in the MANABIYA (Academic) program
2	LEE, Gueseon	28	Ph.D. candidate, Jeonbuk National University	South Korea	Ph.D. candidate, Mechanochemical Polymer Synthesis	Selected for the Basic Science Research Program through the National Research Foundation (NRF)	2023/7/2-8/30, 2 months	Participation in the MANABIYA (Academic) program
3	NOZICKOVA, Anna	23	M1 student, University of Chemistry and Technology, Prague	Czechia	M1 student, Indigo-Acylhydrazone Hybrid Photoswitches	Bachelor degree in General chemistry with honors	2023/8/1-9/28, 2 months	Participation in the MANABIYA (Academic) program
4	LIKHIT, Oranit	28	Research Assistant, Faculty of Medicine Siriraj Hospital, Mahidol University	Thailand	Master's degree, Immunology and Virology	Completed Master's thesis on immune activation in Systemic sclerosis (SSc) patients	2023/9/1-9/29 1 month	Participation in the MANABIYA (Academic) program
5	IBRAGIMOV, Sapajan	31	Ph.D. candidate, Gdansk University of Technology	Poland	Ph.D. candidate, Quantum Chemistry	Conference presentations in Poland and overseas	2023/9/11-11/30 2.5 months	Participation in the MANABIYA (Academic) program
6	HALIM, Abdul	35	Assistant Professor, Universitas Internasional Semen Indonesia	Indonesia	Ph.D., Engineering of Biomaterials	Conducting research on engineering biomaterials	2023/12/1-2024/1/31 2 months	Participation in the MANABIYA (Academic) program
7	KIM, Namhee	26	Integrated MS-Ph.D., Yonsei University	South Korea	Integrated M.S. Ph.D. student, Chiral Supramolecular Crystallization	Ph.D. Fellowship from National Research Foundation (NRF), Outstanding Teaching Assistant Award from Yonsei University	2023/12/4-2024/2/28 3 months	Participation in the MANABIYA (Academic) program
8	KOOLATH, Sajeer	38	Research Scientist, Anticancer Bioscience	India	Ph.D., Small Molecules Drug Discovery	Conducting research on small molecules drug discovery and biological studies	2024/1/9-2/9 1 month	Participation in the MANABIYA (Academic) program
9	CARREIRA, Erick Moran	60	Professor, ETH Zürich	USA	Ph.D., Asymmetric Synthesis	Member of the U.S. National Academy of Sciences and the American Academy of Arts and Sciences, lectureships in Europe and North America, editor-in-chief of Organic Letters	2023/9/10 1 day	Participation in the 6th ICReDD International Symposium & 3rd Akira Suzuki Awards Ceremony

10	NEESE, Frank	55	Professor, Max-Planck-Institut für Kohlenforschung	Germany	Ph.D., Magnetic Spectroscopies	Gottfried Wilhelm Leibniz Award, Member of the German National Academy of Sciences and the Academia Europaea	2023/9/10-9/11 2 days	Participation in the 6th ICReDD International Symposium & 3rd Akira Suzuki Awards Ceremony
11	ACKERMANN, Lutz	50	Professor, University of Göttingen	Germany	Ph.D., Sustainable Catalysis	AstraZeneca Excellence in Chemistry Award, ERC Consolidator Grant, Gottfried Wilhelm Leibniz-Preis, ERC Advanced Grant	2023/9/10-9/11 2 days	Participation in the 6th ICReDD International Symposium & 3rd Akira Suzuki Awards Ceremony
12	REISMAN, Sarah E.	44	Professor, California Institute of Technology	USA	Ph.D., Chemical Synthesis	Alfred P. Sloan Research Fellowship, Cottrell Scholar Award, the Arthur C. Cope Scholar Award, editorial board member at Organic Syntheses	2023/9/10-9/11 2 days	Participation in the 6th ICReDD International Symposium & 3rd Akira Suzuki Awards Ceremony
13	CAO, Yi	44	Professor, Nanjing University	China	Ph.D., Synthetic Soft Materials	National Science Fund for Distinguished Young Scholars, 2019 Young Scientist Award, editor-in-Chief of the journal Materials Research Express	2023/9/10-9/11 2 days	Participation in the 6th ICReDD International Symposium & 3rd Akira Suzuki Awards Ceremony
14	NEWHOUSE, Timothy	40	Associate Professor, Yale University	USA	Ph.D., Step-efficient Synthesis	Boehringer Ingelheim Scientific Advancement Grant, Genentech Research Innovation Award, Arthur C. Cope Scholar Early Career Award	2023/9/10-9/11 2 days	Participation in the 6th ICReDD International Symposium & 3rd Akira Suzuki Awards Ceremony
15	LIST, Benjamin	56	Principal Investigator & Professor, ICReDD, Director & Professor, Max-Planck-Institut fuer Kohlenforschung	Germany	Ph.D., Chemical Synthesis and Catalysis	The Nobel Prize in Chemistry, Herbert C. Brown Award 2022 for Creative Research in Synthetic Methods, Member of the German National Academy of Science Leopoldina	2023/10/1-10/12 12 days	Visit as principal investigator, giving a lecture in Platform Kickoff Symoposium
16	NUGMANOV, Ramil	35	Senior Scientist, Janssen Pharmaceuticals	Belgium	Ph.D., Organic Chemistry	Associate Professor of Kazan Federal University	2024/1/16-1/20 5 days	Participation in the 7th ICReDD International Symposium
17	BRYCE, David	49	Professor, Universtity of Ottawa	Canada	Ph.D., Physical and Theoretical Chemistry	Gerhard Herzberg Award, Member of the International Society of Magnetic Resonance Council, Member of Sigma Xi Honor Society, Amazing Hillcrest High School Alumni recognition	2024/1/16-1/20 5 days	Participation in the 7th ICReDD International Symposium
18	KALOW, Julia	39	Associate Professor, Northwestern University	USA	Ph.D., Organic Synthesis	DOE Early Career Award, American Chemical Society Pure Chemistry Award, Marion Milligan Mason Award for Women in the Chemical Sciences	2024/1/19 1 day	Online participation in the 7th ICReDD International Symposium
19	NONG, Artrith	N/A	Assistant Professor, Utrecht University	Netherland	Ph.D., Computational Materials Chemistry	Member of the Editorial Board for JPhys, Judge for the ENVISION High School Science Competition, Guest Editor for JPhys	2024/1/18 1 day	Online participation in the 7th ICReDD International Symposium
20	SCHWALLER, Philippe	N/A	Assistant Professor, EPFL (Ecole polytechnique fédérale de Lausanne)	Switzerland	Ph.D., Artificial Chemical Intelligence	Best presentation in the Chemical Information session at ACS Spring meeting, Best chemistry poster award, IOP Publishing twitter poster conference	2024/1/19 1 day	Online participation in the 7th ICReDD International Symposium
21	HECHT, Stefan	49	Professor, Humboldt-Universität zu Berlin	Germany	Ph.D., Organic Chemistry and Functional Materials	UNIPRENEUR Award, Einstein Professorship of the Einstein Foundation Berlin, Fellow of the European Academy of Sciences (EurASc), Fellow of the Max Planck School Matter to Life	2023/11/12-11/15 4 days	Participation in the ICReDD International Seminar
22	HSU, Liang-Yang	40	Associate Research Fellow, Institute of Atomic and Molecular Sciences, Academia Sinica	Taiwan	Ph.D., Quantum Electrodynamical Chemistry	Center Scientist and Coordinator of National Center for Theoretical Sciences, Joint Associate Professor of National Taiwan University	2023/11/29-12/8 10 days	Participation in the ICReDD International Seminar

23	WOJCIK, Marek J.	77	Distinguished Professor, Jagiellonian University	Poland	Ph.D., Molecular Spectroscopy	Doctor of Science in Physcial Chemistry (Habilitation), Visiting Professor (RIKEN, University of Oklahoma, University of Illinois)	2023/7/3-7/6 4 days	Participation in the ICReDD International Seminar
24	KIM, Jeung Gon	N/A	Associate Professor, Chonbuk National University	Korea	Ph.D., Organic and Polymer Chemistry	Research Fellow (KAIST), Principle Research Engineer (Samsung Chiel Industries), Posdoctoral Scholar (Cornell University)	2023/7/18 1 day	Participation in the ICReDD/FCC International Seminar
25	KONGPATPANICH, Kanokwan	37	Assistant Professor, VISTEC	Thailand	Ph.D., Inorganic and Materials Chemisty	New Technologist Award 2023, Monbukagakusho Scholarship, Professor Tab Nilaniti Foundation Outstanding Graduate Award	2023/9/4 1 day	Participation in ICReDD International Seminar Female Researcher Series
26	RUNGROTMONGKOL, Thanyada	45	Associate Professor, Chulalongkorn University	Thailand	Ph.D., Molecular Modeling	International consultant (International Centre for Science and High Technology, United Nations), Postdoctoral Fellow (Chulalongkorn University)	2023/9/4 1 day	Participation in ICReDD International Seminar Female Researcher Series
27	NAMUANGRUK, Supawadee	45	Principal Researcher, National Nanotechnology Center	Thailand	Ph.D., Nanocatalysis and Molecular Simulation	Wiley-CST Green Chemistry Award, The UNESCO-L'Oreal Award for Women in Science, President of Computational Science and Engineering Association (CSEA), Thailand	2023/9/4 1 day	Participation in ICReDD International Seminar Female Researcher Series
28	MINDIOLA, Daniel J.	N/A	Professor, University of Pennsylvania	USA	Ph.D., Inorganic and Organometallic Synthesis	Fellow of the Royal Society of Chemistry, Fellow of the American Association for the Advancement of Science, Associate Editor for Organometallics	2023/9/8 1 day	Participation in the ICReDD/FCC International Seminar
29	HELLWIG, Petra	53	Professor, Universtity of Strasbourg	France	Ph.D., Bioelectrochemistry and Spectroscopy	Senior member (Institut Universitaire de France), President of the French Bioenergetic Group, French Research Council Chair d'excellence	2024/2/5 1 day	Participation in the ICReDD International Seminar
30	YAN, Kaking	N/A	Assistant Professor, Shanghai Tech University	China	Ph.D., Supramolecular Chemistry	Postdoctoral Scholar (The University of Tokyo; University of California-Berkeley)	2024/2/5 1 day	Participation in the ICReDD/FCC International Seminar
31	ROY, Ram Kinkar	59	Senior Professor, Birla Institute of Technology and Science Pilani	India	Ph.D., Computational Chemistry	Senior JSPS Fellow (Hokkaido University), Visiting Researcher (Advanced Institute for Computational Science, RIKEN)	2023/10/1- 2024/7/31 10 months	JSPS Visiting Researcher, ICReDD International Seminar
32	SURAWATANAWONG, Panida	40	Associate Professor, Mahidol University	Thailand	Ph.D., Computational Chemistry	National Research Council Award, L'Oreal Thailand "For Women in Science" Grant, TRF-OHEC-Scopus Young Researcher Award	2024/3/11 1 day	Participation in the ICReDD International Seminar
33	LU, Erli	N/A	Lecturer, Newcastle University	UK	Ph.D., Alkali Metal Chemistry	Marie Curie International Incoming Fellowship (University of Nottingham), M. Braun Scholarship, Professor You Wang Memorial Award	2024/3/15 1 day	Participation in the ICReDD/FCC International Seminar
34	JACOBSEN, Eric N.	64	Professor, Harvard University	USA	Ph.D., Asymmetric Catalysis	Tetrahedron Chair Award, Humboldt Research Award, Arthur C. Cope Award, Remsen Award, Chirality Medal, Nagoya Gold Medal Award, Noyori Prize, NIH Merit Award	2024/3/22 1 day	Participation in the ICReDD International Seminar

Appendix 6 FY2023 State of Outreach Activities

* Fill in the numbers of activities and times held during FY2023 by each activity.
* Describe the outreach activities in the "6. Others" of Progress Report, including those stated below that warrant special mention.

Activities	FY2023 (number of activities, times held)
PR brochure, pamphlet	5: Monthly post card J/E, Quarterly news poster J/E, Annual report J/E ICReDD pamphlet J/E, ICReDD building pamphlet
Lectures, seminars for general public	4: -Lecture on luminescent materials by Prof. Hasegawa (June 3rd, 2023) -Seminar series for high school teachers (6) "The WPI's latest research" (Aug. 1st, 2023 [Co-hosted] -The 12th WPI Science Symposium (Nov. 23rd, 2023) -Seminar series for high school teachers (7) "The WPI's latest research" (March 28th, 2024 [Co-hosted])
Teaching, experiments, training for elementary, secondary and high school students	5: -ICReDD's 3 laboratories participated in "Dream Chemistry 21" program of the Hokkaido Branch of the Chemical Society of Japan (Hands-on lab experience for high school students, Aug. 3-4th, 2023), -Science tour led by "Science Eye" (Lecture and lab tour for students from elementary to high school, Aug. 10th, 2023), - "Academic Fantasista" (Lecture and lab tour for high school students, Dec. 22nd, 2023)
Open houses	1: Joint open campus event (June 3rd, 2023)
Participating, exhibiting in events	1: Exhibition booth (The 12th WPI Science Symposium, Nov. 23rd, 2023)
Press releases	18: Press releases (research)
Others（Research News Articles on ICReDD Web）	6
Others（SNS）	6: X (Twitter), Facebook, YouTube, Instagram, Instagram 2nd account, LinkedIn
Others（ICReDD Goods）	5: Lab coat, Calendar, Stuffed toy, Bath salt, Tea bag

*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 up to three of the Center's outreach activities carried out in FY 2023 that have contributed to enhancing the brand or recognition of your Center and/or the brand of the overall WPI program, 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.

1) Focusing on research-related posts on SNS and regularly mentioning scientific journals through the @ function on X (formerly Twitter) when tweeting new publications, so that journals retweet our posts, has contributed to a 52% increase over last year in the traffic driven to research news articles on the ICReDD website through posts on X. This also contributed to a 35% increase in the number of unique visitors that viewed research news articles on the ICReDD website.

2) ICReDD hosted the WPI Science Symposium for middle/high school students and the general public, which introduced WPI fusion research projects that incorporate information science to non-scientists. The hybrid event attracted 270 participants (117 in-person participants, 153 online participants) and increased the recognition of ICReDD and the overall WPI program (42% of questionnaire respondents had not heard of ICReDD, 23% had not heard of WPI) both within Sapporo and throughout Japan.

3) By holding a variety of other outreach events, ICReDD increased its presence among the local community. ICReDD held a joint open campus event, with over 250 people trying activities at our booth, and approximately 50 people attending a public lecture by an ICReDD PI. ICReDD also hosted 13 high school students for a hands-on lab experience, held a tour for 16 students from neighboring Ishikari city, and held a special class for 15 high school students through the Academic Fantasista program, among other activities.

Appendix 7 FY 2023 List of Project's Media Coverage

* List and describe media coverage (e.g., articles published, programs aired) in FY2023.

* Enter the host institution name and the center name in the footer.

1) Japan

	Date	Types of Media (e.g., newspaper, magazine, television)	Description
1	2023/6/17	Newspaper	Article on the opening ceremony of the new ICReDD building, Hokkaido Shimbun
2	2023/6/21	Newspaper	Article on the opening ceremony of the new ICReDD building, Yomiuri Shimbun
3	2023/7/5	Newspaper	Feature article on the development of hydrogels for artificial bone applications, NIKKEI Shimbun
4	2023/7/6	Newspaper	Article on ICReDD Research press release about "Searching Chemical Action and Network (SCAN): Interactive Chemical Reaction Path Network Platform", Nikkei Press Release
5	2023/7/8	Newspaper	Article on the 3rd Akira Suzuki Awards recipients, Yomiuri Shimbun
6	2023/7/11	Magazine	Article on ICReDD Research press release about "Searching Chemical Action and Network (SCAN): Interactive Chemical Reaction Path Network Platform", Nikkan Chemical News
7	2023/9/20	Newspaper	Article on the reports of research misconduct at HU by the investigation committee, Sankei Shimbun
8	2023/9/21	Newspaper	Article on the investigations into the research misconduct found in 4 research papers, Asahi Shimbun
9	2023/9/21	Newspaper	Article summarizing the result of the investigations into research misconduct, Hokkaido Shimbun
10	2023/9/21	Newspaper	Article on the number of cases of research misconduct found in research papers, Hokkaido Shimbun
11	2023/9/21	Newspaper	Article on the research misconduct by a former specially appointed assistant professor, Yomiuri Shimbun
12	2023/9/21	Newspaper	Article on the research misconduct by a former specially appointed assistant professor whose Ph. D. retraction is being considered, Yomiuri Shimbun
13	2023/9/21	Newspaper	Article on the background of the research misconduct and the management system to prevent it, Hokkaido Shimbun

14	2023/9/21	Newspaper	Article on "Hokkaido University admits misconduct by chemistry research team", The Japan Times
15	2023/9/22	Newspaper	Editorial article on the cases of research misconduct in Hokkaido University, Hokkaido Shimbun
16	2023/9/22	Newspaper	Article on the comments of the executive vice presidents of Hokkaido University, research misconduct is a "Serious problem", Yomiuri Shimbun
17	2023/9/29	Newspaper	Article on research misconduct - 519 cases of fabrications, 317 cases of falsifications-, The Science News
18	2023/10/7	Newspaper	Article on uniform database management as a countermeasure to prevent research misconduct, Hokkaido Shimbun
19	2023/11/8	Newspaper	Feature article on the innovative research on hydrogels at Prof. Gong's laboratory, NIKKEI Shimbun
20	2023/11/21	Newspaper	Article on increasing demands for DX management personnel at research institutions, Nikkan Kogyo Shimbun
21	2023/11/29	Online news	Article on increasing demands for research data management at research institutions, Newswitch (by Nikkan Kogyo Shimbun)
22	2023/12/7	Newspaper	Featured article on the innovative development of double network gels at Prof. Gong's laboratory, NIKKEI Business Daily
23	2024/1/8	Newspaper	Feature Article on the latest research topics in information science introduced to a public audience at the 12th WPI Science Symposium organized by ICReDD, Hokkaido Shimbun
24	2024/3/20	Newspaper	Article on ICReDD Research press release about "Artificial intelligence-based, on-the-fly Raman spectroscopy method shows promise for rapid medical diagnosis", Nikkan Kogyo Shimbun

2) Overseas

	Date	Types of Media (e.g., newspaper, magazine, television)	Description
1	2023/4/7	Online News	Article on ICReDD research press release (EN): "Birch reduction simplified to a one-minute mechanochemical process" Phys.org; https://phys.org/news/2023-04-birch-reduction-one-minute-mechanochemical.html; Reach: 4,346,307
2	2023/4/7	Online News	Article on ICReDD research press release (EN): "Birch reduction simplified to a one-minute mechanochemical process" EurkeAlert!; https://www.eurekalert.org/news-releases/985409; Reach: 597,552
3	2023/4/8	Online News	Article on ICReDD research press release (EN): "Birch reduction simplified to a one-minute mechanochemical process" NewsBeezer; https://newsbeezer.com/singapore/birch-reduction-simplified-to-a-one-minute-i/; Reach: 226,995
4-15	Various	Online News	12 other articles on ICReDD research press release (EN): "Birch reduction simplified to a one-minute mechanochemical process" Various Websites; Reach: 401,780
16	2023/7/3	Online News	Article on ICReDD research press release (EN): "Virtual exploration of chemical reactions" Phys.org; https://phys.org/news/2023-06-user-friendly-platform-virtual-exploration-chemical.html; Reach: 4,247,714
17	2023/7/5	Online News	Article on ICReDD research press release (EN): "Virtual exploration of chemical reactions" Chemie; https://www.chemie.de/news/1180983/virtuelle-erkundung-chemischer-reaktionen.html; Reach: 731,552
18	2023/7/7	Online News	Article on ICReDD research press release (EN): "Virtual exploration of chemical reactions" Science Daily; https://www.sciencedaily.com/releases/2023/07/230703133113.htm; Reach: 2,318,611
19-33	Various	Online News	15 other articles on ICReDD research press release (EN): "Virtual exploration of chemical reactions" Various Websites; Reach: 1,616,271
34	2023/8/31	Online News	Article on ICReDD research press release (EN): "Surpassing the human eye: Machine learning image analysis rapidly determines chemical mixture composition" Phys.org; https://phys.org/news/2023-08-surpassing-human-eye-machine-image.html; Reach: 7,634,103
35	2023/8/31	Online News	Article on ICReDD research press release (EN): "Surpassing the human eye: Machine learning image analysis rapidly determines chemical mixture composition" Science Daily; https://www.sciencedaily.com/releases/2023/08/230830131922.htm; Reach: 2,378,197
36	2023/9/1	Online News	Article on ICReDD research press release (EN): "Surpassing the human eye: Machine learning image analysis rapidly determines chemical mixture composition" 0XZX; https://0xzx.com/2023090101383700232.html; Reach: 608,006
37-47	Various	Online News	11 other articles on ICReDD research press release (EN): "Surpassing the human eye: Machine learning image analysis rapidly determines chemical mixture composition" Various Websites; Reach: 2,048,654
48	2023/9/29	Online News	Article on ICReDD research press release (EN): "Making elbow room: Giant molecular rotors operate in solid crystal" Phys.org; https://phys.org/news/2023-09-concave-umbrella-like-metal-complexes-space.html; Reach: 6,846,867
49	2023/9/30	Online News	Article on ICReDD research press release (EN): "Making elbow room: Giant molecular rotors operate in solid crystal" Science Daily; https://www.sciencedaily.com/releases/2023/09/230929170953.htm; Reach: 2,327,983
50	2023/10/2	Online News	Article on ICReDD research press release (EN): "Making elbow room: Giant molecular rotors operate in solid crystal" 0XZX; https://0xzx.com/2023100207353774327.html; Reach: 720,979

51-69	Various	Online News	19 other articles on ICReDD research press release (EN): "Making elbow room: Giant molecular rotors operate in solid crystal" Various Websites; Reach: 1,554,169
70	2023/12/25	Online News	Article on ICReDD research press release (EN): "Turning plastic trash into chemistry treasure" KPACHAR BECHA; https://rossaprimavera.ru/news/a29abf52; Reach: 911,137
71	2023/12/28	Online News	Article on ICReDD research press release (EN): "Turning plastic trash into chemistry treasure" Phys.org; https://phys.org/news/2023-12-reusing-plastic-kickstart-radical-chain.html; Reach: 7,686,494
72	2023/12/30	Online News	Article on ICReDD research press release (EN): "Turning plastic trash into chemistry treasure" Interesting Engineering; https://interestingengineering.com/science/catalysts-plastic-waste-detoxify-chemicals; Reach: 2,671,638
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