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

Host Institution	Kanazawa University	Host Institution Head	Koetsu Yamazaki
Research Center	Nano Life Science Institute (NanoLSI)		
Center Director	Takeshi Fukuma	Administrative Director	Yoshihiro Fukumori

Common instructions:
* Unless otherwise specified, prepare this report based on the current (31 March 2020) situation of your WPI center.
* So as to execute this fiscal year's follow-up review on the "last" center project plan, prepare this report based on it.
* Use yen (¥) when writing monetary amounts in the report. If an exchange rate is used to calculate the yen amount, give the rate.
➢ Prepare this report within 10-20 pages (excluding the appendices, and including Summary of State of WPI Center Project Progress (within 2 pages)).

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

1. Research Progress

At NanoLSI, we have been working on three major projects: (1) development of novel nanoprobe technologies especially for live cell imaging, (2) nano-level understanding of basic cellular functions and cancer, and (3) establishment of a new research field "nanoprobe life science" (Fig. 1). Since the launch of NanoLSI, the applications of our world's top-level bio-SPM technologies to life science research have been actively explored in projects (2) and (3), and some of them have already resulted in impactful publications (***Nature 2019*** **(x2),** ***2020***). Meanwhile, the progress in project (1) enabled us to visualize some of the nanoscale structures and dynamics at the surfaces or inside live cells, and stimulated intensive discussions on the target cellular functions and phenomena to be investigated as summarized in Fig. 2. Now, projects (1) and (2) are closely linked to each other.

(1) Development of novel nanoprobe technologies

- **Scanning probe microscopists** established the basic fabrication methods of the special nanoprobes; the exploration of various methods for the probe scanning and the interaction detection has been started. **Fukuma** improved the fabrication method for a long nanoprobe and enabled 3D imaging of intracellular structures such as the nucleus and actin fibers without killing the cell. In addition, intracellular 2D imaging at the internal surfaces of the cellular and nuclear membranes of a live cell was demonstrated for the first time. **Ando** established a method to fabricate a nanopipette with a 2-5 nm hole and a 3-6 nm wall and developed a novel method to detect the probe-sample interaction as a potential way of achieving high spatio-temporal resolution. **Korchev** developed a nanopipette pH sensor and succeeded in mapping the 3D distribution of pH around a living melanoma cell (***Nat. Commun. 2019***).
- **Supramolecular chemists** had intensive discussions with life scientists and selected some molecules including chiral molecules, oligosaccharides, ions with different charges, and metabolites, whose design and synthesis can be effectively performed by their unique expertise in host-guest chemistry. They have already synthesized several kinds of host molecules including macrocyclic compounds (**Ogoshi** & **MacLachlan**) and metal complexes (**Akine**), but their specificity and sensitivity have to be further improved. They are now exploring various possibilities for their design and synthesis. This is a relatively long-term project. As a shorter-term project, they started to integrate a polymer gel at the opening of a nanopipette (**Maeda**) for SICM technology (**Korchev** & **Takahashi**). The overall sensitivity and the size of the molecules that interact with the sensor molecules can be modified and controlled by functionalizing the polymer with many sensor molecules and adjusting the pore size of the polymer gel, respectively. In order to manipulate the local concentration of metabolites and signaling molecules at the nanoscale, a light-modulated nanodevice that allows the on-demand release of small chemicals at a subcellular level has also been developed (**Arai**).
- **Computational scientists** continued to work on modeling and simulations of biological systems. In addition, they extended their work to develop software and database systems for Bio-SPM analysis. **Foster** extended functionality of the SPM image database that he had introduced in 2018. In addition, he developed machine learning methods to predict a molecular structure from AFM images (***Sci. Adv. 2020***), and to classify different cancer cells. He also performed simulations of several systems to interpret AFM images. **Mikhailov** developed an SPM simulator to convert a PDB file to a simulated AFM image. He also performed simulations of various proteins (myosin V, ABC transporter, MET receptor, MeCP2, dynamin) for the interpretation of AFM images. In addition, he also worked on simulations of larger-scale biological systems such as bacterial cytoplasm.

(2) Nano-level understanding of cellular functions and cancer

- **Cell biologists** have started to address basic principles of cellular functions by observing nanostructures and nanodynamics of cells using BioSPM. Several collaborative projects are now on track. **Matsumoto** proposed a novel model of HGF-induced cell signaling, which was uncovered by HS-AFM (***Nature Chem. Biol., 2019***), and is now focusing on single-molecule imaging in live cells to validate this model. **Wong** visualized the native nuclear pore by HS-AFM, and further revealed the role of the nuclear pore component TPR in ependymoma (***Autophagy, 2020***). **Hanayama** found that large extracellular vesicles (EVs) in thymus strongly express tissue antigens on MHC molecules and discovered a novel type of immune cell that presents tissue antigens to T cells (***J Exp Med, 2019***). **Nakajima** found novel regulation mechanisms of cytochrome P450, a major drug-metabolizing enzyme superfamily, by two post-transcriptional regulation mechanisms, A-to-I RNA editing and RNA methylation (***Biochem Pharmacol, 2020; Drug Metab Dispos, 2019***). **Toda has** just joined the institute and set up his lab. He plans to make cellular sensing and responding systems for molecular-level manipulation of protein activities to allow the engineering of customized cell-cell communication.
- **Cancer researchers** performed cross-disciplinary research using SICM, HS-AFM and supramolecular chemistry to reveal changes in cancer stem cell metabolism and characteristics, oncogene-regulated physical and dynamic changes in cancer cells, and mechanisms of drug resistance. **Hirao** identified 1-methylnicotinamide (1-MNA) as a specific metabolite in therapy-resistant leukemia stem cells and validated the sensitivity and selectivity of a newly developed method for 1-MNA measurement by using supramolecular technology. **Oshima** revealed oncogene-related changes in stiffness and dynamic physical properties of cancer cells by SICM analysis, using genetically engineered cancer model mice and organoid cultures of the mouse-derived cancer cells. **Yano** newly identified miR-449a microRNA as a key player in the acquisition of resistance to the inhibitor of driver oncoprotein ALK (***J Thorac Oncol, 2020***), and established an AFM approach to study the dynamics/oligomerization of oncoprotein EML4-ALK.

(3) Establishment of the novel research field "Nanoprobe Life Science"

We aim to establish the new research field, "Nanoprobe Life Science" by combining the four research fields(①Nanometrology, ②Life Science, ③Supramolecular Chemistry and ④Computational Science). In FY2017, we started to work on many transdisciplinary subjects combining two or three disciplines. In FY2019, we continued this effort and started to summarize the results for publication of many of the projects. Some examples of the published papers are highlighted below:

①×② HS-AFM imaging of nanodynamics of various proteins such as Atg (***Nature, 2020***), TOM complex (***Nature, 2019***), heliorhodopsin (***Nature, 2019***) and Mre11/Rad50 complex (***Nat. Commun.*, 2020**). 3D pH mapping around a live cell by SICM (***Nat. Commun., 2019***).

①×③×④ Predicting molecular structure from AFM images by ML (***Sci. Adv.*, 2020**), experiments and simulation of tip-induced chemical reactions (***Sci. Adv., 2020***).

①×②×③ Visualization by HS-AFM of the regulation of HGF dynamics by Hip-8 (***Nat. Chem. Biol., 2019***).

①×②×④ Visualization by HS-AFM of Agitoxin-2 binding to K+ channel by induced fit (***Sci. Adv., 2019***).

2. Generating Fused Disciplines

Measures to advance research by fusing disciplines: NanoLSI organized 31 T-meetings for intensive discussion between two research groups from different fields, and 2 colloquia for all members to inform one another of the progress of their projects. An advisory board meeting was held to discuss the promotion of interdisciplinary research involving nanometrology, life science, supramolecular chemistry and computational science, which had been particularly remarked upon in the FY2019 Site Visit report. Furthermore, NanoLSI started a luncheon meeting once a week that enables young researchers to introduce themselves for about 10 minutes and then talk about their research topics, followed by a free exchange. A retreat in the form of a training camp is planned with about 80 participants for the mixing of young researchers, in particular students.

3. Realizing an International Research Environment

Overseas satellite research sites: NanoLSI renewed bilateral Agreements with Imperial College London, UK and the University of British Columbia (UBC), Canada for long-term research cooperation.

4. Making Organizational Reforms

Ripple effect: Details of the support program for non-Japanese researchers voluntarily made by NanoLSI administrative staff were compiled into a PowerPoint presentation, which was shared within the University.

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

Education unit of NanoLSI: The graduate school, "Division of Nano Life Science," started in FY2020 with 9 master course students and 7 doctorate students. Various measures were taken in order to promote interdisciplinary research in the Division and to secure the operational autonomy of the Division.

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

1. Advancing Research of the Highest Global Level

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

[Outline]

At NanoLSI, we have been working on three major research projects as summarized in Fig. 1. In each research project, many interdisciplinary research subjects involving nanometrology, supramolecular chemistry, life science and computational science, have been promoted. Soon after the launch of NanoLSI, we started to explore applications of our world-leading bio-SPM technologies to life science research. These efforts have already resulted in impactful publications, and now many papers are being prepared. Moreover, some of the transdisciplinary studies across not only two, but also three disciplines have reached publication stage.

Meanwhile, we have made huge efforts to develop novel nanoprobe technologies and have already obtained preliminary results showing their potential. The nanoendoscopic technology is beginning to visualize intracellular structures such as the nucleus and cytoskeleton. In addition, we have succeeded in visualizing dynamic changes in the elasticity of the cell surface by high-speed SICM, as well as pH distribution near the cell surface by SICM. Based on these achievements, we have started to explore possible applications of the newly developed technologies to the life science research as summarized in Fig. 2. Therefore, projects 1 and 2 are now very closely integrated.

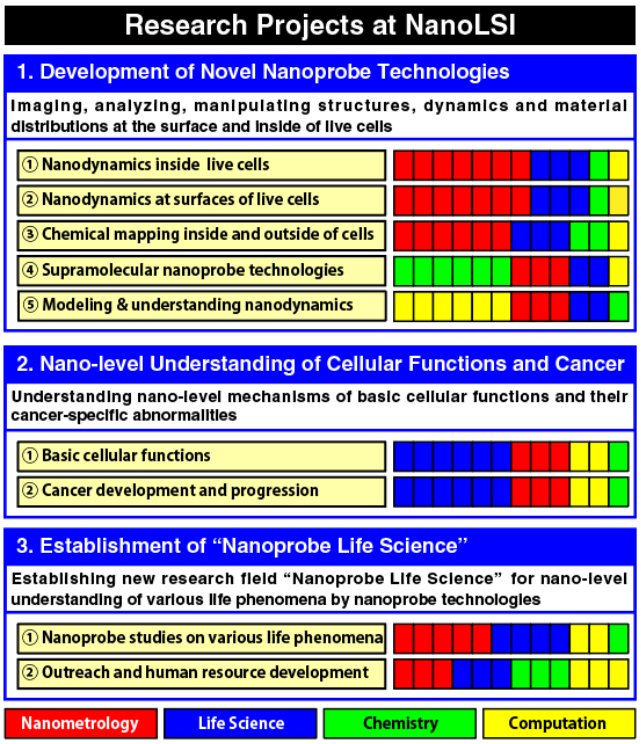


Fig. 1: Research projects at NanoLSI and contributions from the four major disciplines to each project.

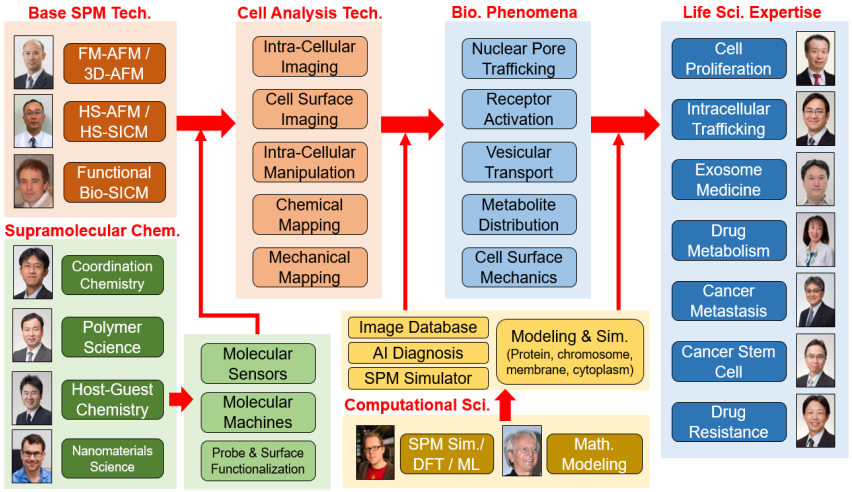


Fig. 2: Strategy for the development of new nanoprobe technologies and their applications to life science research.

Achievements in FY2019 include
- Papers: 91 (51% internationally co-authored; 24 with an IF > 10; 28 with an IF > 7),
- Invited talks in int'l meetings: 44,
- Funding: ¥767,479,979 overall (20 grants > ¥10,000,000).

These achievements are of the highest global level for an institute with 74 researchers (as of March 2020).

[Outline, plan, and progress of each research subject]

(1) Development of Novel Nanoprobe Technologies

Here, we will develop a nanoprobe technique to visualize nanodynamics at the surface and inside of live cells. In addition, we will also develop a technique to measure the nanoscale distribution of specific molecules or ions using a chemically functionalized probe. Furthermore, we will develop a method for analyzing the measured data and understanding the nanoscale mechanisms of the molecular or cellular functions as well as the measurement principle of the newly developed nanoprobe technologies.

① Visualizing nanodynamics inside live cells (Main PI: Fukuma)

(Objective)

We aim to develop a nanoendoscopic imaging technique to visualize nanoscale structures and dynamics inside live cells.

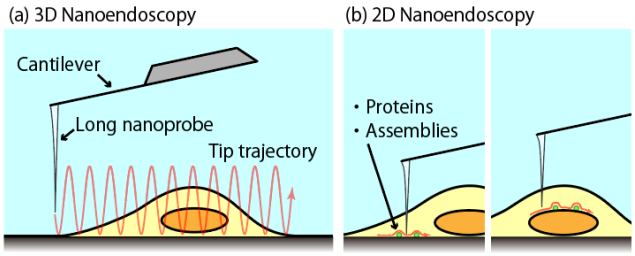


Fig. 3: 2D & 3D nanoendoscopic imaging of a live cell.

(Background and Methods)

We will develop 2D/ 3D nanoendoscopic imaging techniques. By scanning a long nanoprobe in a 3D space, including the inside of a live cell, we will visualize intra-cellular nanostructures. In addition, by controlling the tip position inside a cell, we will perform a 2D imaging on the cytoplasmic side of the cell membrane or on an organelle surface (Fig. 3).

(Subjects and Plans)

Table 1: Research subjects and plans for the development of nanoendoscopic imaging technique

Subjects	FY2017-2019	FY2020	FY2021	FY2022	FY2023
Long Nanoprobe	**Fabrication** (EBD, FIB-milling, Nanopillars)	**Functionalization** (surface modification with living polymerization (Prof. Maeda), molecular sensors (Profs. Arai & Hirata))		**Improvements** (optimization for individual applications)	
Imaging & Analysis	**Fundamentals** (imaging parameters; tip position control; image analysis)	**Advanced** (combination with confocal and super-res. OM; improvements in spatial and temporal res.)		**Improvements** (usability, analysis software, quantitative capability)	
Intracellular Imaging	**Proof of Concept** (membrane penetration; 3D imaging of nucleus, actin fibers; cell viability)	**Proof of Concept** (3D imaging of mitochondria; 2D imaging on actin fibers, nucleus, mitochondria; comparison with super-res. OM)		**Biological Applications**: NPCs (Prof. Wong); bone formation (Prof. Ishii); cell-cell adhesion (Prof. Okuda); magnetosomes (Prof. Taoka)	

(Research Progress)

・Improvement in nanoprobe fabrication

In 2018, we succeeded in the fabrication of a long nanoprobe by milling an AFM probe by focused ion beam (FIB). Since then, we have improved the process and enabled the fabrication of a sharper nanoprobe. This has greatly improved the membrane penetration success rate.

・2D/3D imaging inside a live cell

With the improved nanoprobe, we succeeded in 3D intra-cellular imaging of live cells. In the images, membranes, nucleus and actin fibers are visualized. In addition, we also succeeded in 2D imaging of the interior of live HeLa cells. In the images, fibrillar structures at the cytoplasmic side of a basal membrane and mesh-like features presumably corresponding nuclear lamina are visualized. Furthermore, we confirmed by fluorometric assay that such 2D/3D measurements do not kill the cells.

(World-leading Achievements)

So far, many AFM researchers tried to image inside live cells using an ultrasound wave or elasticity mapping. However, these previous methods did not provide a nanoscale 3D view but only a 2D projection of internal structures. Importantly, these methods do not allow direct access of a probe to intracellular components, which has hindered improvements in the spatial resolution and measurements of intracellular mechanics. In this study, we succeeded in the 2D/3D imaging of the intra-cellular structures by directly inserting a probe into a live cell for the first time. In contrast to the previous techniques, this method allows us to perform high-resolution 2D/3D imaging at the surfaces of intracellular components such as the cytoskeleton and organelles. Thus, this method has the potential to provide nanoscale structural and mechanical information that have not been accessible using existing measurement tools.

② Measuring nano-dynamics at the surfaces of live cells (Main PI: Ando)

(Objective)

We aim to develop high-speed scanning probe microscopy techniques: (i) HS-SICM enabling *in-situ* observation of protein molecules in action on the surfaces of live cells and intracellular organelles, and in the interior of de-roofed cells, (ii) assay systems enabling observations of purified membrane proteins in asymmetric environments across the membrane, and (iii) devices for even faster HS-AFM. Further, we will reveal the functional mechanisms of proteins by HS-AFM imaging.

(Background and Methods)

We have established HS-AFM, thus enabling real-time and high-resolution imaging of biological nano-machines during their functional activity. This has been successfully used for many purified protein systems. Nevertheless, there are still many interesting targets and phenomena that cannot be imaged with the current HS-AFM. We will break through this limitation by developing various techniques.

(Subjects and Plans)

Table 2: Research subjects and plans for developing HS-AFM/HS-SICM capable of *in-situ* imaging

Subjects	FY2017-2019	FY2020	FY2021	FY2022	FY2023
Nanoprobes	Nanopipette f fabrication methods for high-speed/high-resolution SICM	**Optimization of SICM nanoprobes** (surface charge neutralization, electrolytes for larger diffusion potential and faster response)		**Optimization of SICM nanoprobes** (adaptation for individual functional measurements)	
Microscope	**HS-SICM I** (higher spatiotemporal resolution) **HS-AFM I** (extended functionality)	**HS-SICM II** (compatibility between high speed and high resolution, and functional extension) **HS-AFM II** (further faster and less invasive performances)		**HS-SICM III** (development into a commercial product) **HS-AFM III** (establishment of faster and less invasive imaging)	
Imaging	**HS-SICM** (test imaging of cells and proteins) **HS-AFM** (membrane proteins embedded in suspended membranes and de-roofed cells)	**HS-SICM** (intracellular architectures in de-roofed cells, surfaces of cancer (Prof. Oshima) and other cells and intracellular organelles, and property mapping) **HS-AFM** (membrane proteins, de-roofed cells, faster dynamic molecular processes, protein molecules under external force)		**SICM** (various biological samples, sub-molecular resolution, faster imaging, truly non-invasive imaging, property mapping) **HS-AFM** (*in-situ* imaging of biological samples in various environments, and imaging of faster molecular processes)	

(Research Progress)

・Development of nanoprobes for SICM

To increase the spatial resolution of SICM, we have been testing several methods to fabricate probes with smaller pore and thinner wall. We established parameters for the laser puller that can produce a pore diameter of 2-5 nm and a wall thickness of 3-6 nm. This results in a lateral resolution of 3-4 nm (Fig. 4).

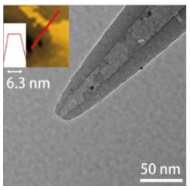


Fig. 4: Glass nanopipette with a small pore and its use for imaging.

・Development of high-resolution HS-SICM

We have already established HS-SICM capable of fast imaging. However, this capability is not compatible with high-resolution imaging. We have probably found a solution for this.

・Development of property mapping with HS-SICM

We developed a HS-SICM method to quickly capture 2D maps of the softness of live cell surfaces, using electroosmotic flow, and a method to capture 2D maps of electric charge density.

・Development of faster/less invasive HS-AFM and optical tweezers-combined HS-AFM

The imaging rate will likely increase to 100 fps when this method is combined with the recently developed Z-scanner and amplitude detector. Further, we succeeded in imaging a DNA hairpin being unfolded and refolded by optical tweezers (OT).

・Development of assay systems for membrane proteins

HS-AFM imaging of membrane proteins under physiological conditions is difficult, due to the membrane softness and the absence of assay systems with asymmetric environments across the membrane. To solve this problem, we have been developing several methods including the use of protein 2D crystals with many point defects, a glass capillary and nanoparticle-deposited surfaces (Fig.5a, b). For example, lipid bilayers were formed on a nanoparticle-deposited surface (Fig.5c) and membrane protein MsbA (lipid A transporter) (Fig.5d–f) was successfully imaged.

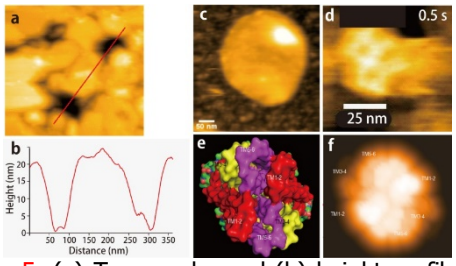


Fig.5: (a) Topography and (b) height profile of a nanoparticle-deposited surface. (c,d) HS-AFM images of membrane placed on the surface (c) and MsbA (d). (e) Atomic structure and (f) pseudo AFM image of MsbA.

・De-roofing cells and imaging the cell interior

To accomplish HS-AFM/HS-SICM imaging of the exposed interior of de-roofed cells, gentle removal of a part of the cell membrane is essential. We tested two methods based on detergents or amphiphilic polymers. Both methods could remove the membrane while the intracellular architectures were retained, enabling imaging of stress fibers and clathrin-coated vesicles with HS-AFM.

(World-leading Achievements)

We have established the world's fastest HS-AFM and HS-SICM for biological studies. Using these microscopes, we have been observing interesting biological phenomena inaccessible with other approaches. We are now adding a high-resolution imaging capability to HS-SICM and further adding faster and less invasive performances to HS-AFM, which will materialize in-situ observations of dynamic events occurring on higher order cellular architectures.

③Material distribution measurement inside and outside of cells (Main PI: Korchev)

(Objective)

We aim to develop a nanopipette-based measurement method that visualizes the distribution of

biomolecules inside and outside cells.

(Methods)

We are developing a chemical sensor based on a scanning ion conductance microscope (SICM). With SICM, voltage is applied between two electrodes—one placed inside and one outside a probe—and the ionic current is recorded while scanning the sample surface, which allows the nanoscale surface shape of live cells to be visualized. Through regulation of the applied voltage and chemical modification of the nanopipette tip, SICM can be used as a sensor to measure chemical distribution near the cell surface (Fig. 3).

(Subjects and plans)

Table 3: Research subjects and plans for the development of material distribution measurement

Subjects	FY2017-2019	FY2020	FY2021	FY2022	FY2023
Chemical sensor	**Nanopore sensor** (modification, method, principle)	**Multi-barrel probe** measurement of different cancer metabolites simultaneously)		**Nanobiopsy technique** (part of cell, tissue)	
Cell function mapping	**Nanoparticle uptake, cell interaction, lipid imaging**	**Cell metabolite measurement using microelectrodes and ISFETs** **Signal molecule measurement using nanopore chemical sensors**		**Improvements** (temperature control during imaging, Scan speed)	
mRNA evaluation	**System for picking up a small amount of cytosol**	**Development of high-throughput cytosol collection system for PCR in a nanopipette**		**Improvements** (time-dependence, automation, quantitative capability)	

(Research progress)

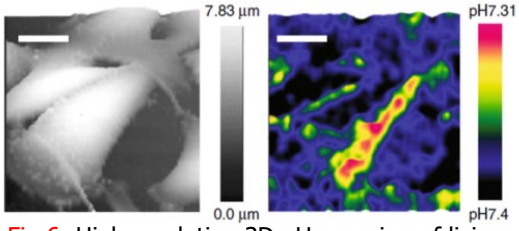


Fig.6: High-resolution 3D pH mapping of living melanoma cells.

・Development of a nanopipette based pH sensor

We developed a zwitterionic label-free nanoprobe pH sensor to perform dynamic mapping of extracellular pH at the single-cell level. This platform allows SICM feedback-controlled precise positioning of the nanoprobe to the cell surface to monitor the local pH with high spatiotemporal resolution and high sensitivity. Furthermore, we fabricated double-barrel SICM-pH nanoprobes to combine the advantages of high-resolution SICM feedback-controlled scanning with high-sensitivity pH-sensing. We succeeded in real-time high spatiotemporal resolution pH mapping at the subcellular level and revealed tumour heterogeneity of the peri-cellular environments of melanoma and breast cancer cells. (Fig.6, ***Nat. Commun 2019***).

・Visualization of cargo transport using SICM

To improve the scanning speed of time-lapse imaging, we developed a new scanning method, automation region of interest (AR)-mode SICM to select the next imaging region by predicting the location of a cell (Fig.7, ***Anal. Chem 2020***). Using the AR-mode SICM, we succeeded in time-lapse imaging of the nanoscale structural changes on the dendritic spine and synaptic bouton, which are closely related to memory. Furthermore, translocation of plasmalemmal precursor vesicles (ppvs), for which fluorescent labeling has not been established, was also visualized along with the rearrangement of the cytoskeleton at the growth cone.

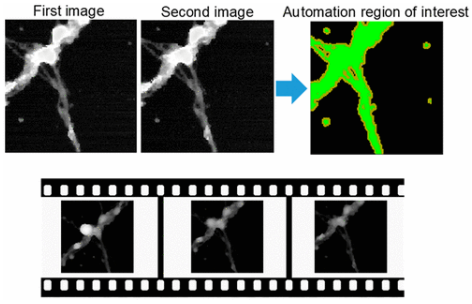


Fig.7: Principles of AR-mode SICM.

(World-leading Achievements)

A nanopipette-based chemical sensor is effective in characterizing the metabolite state of cancer cells. We focused on developing nanopipette-based glucose, lactate, glutamate, and ATP sensors to elucidate their local function in cancer cells at the nanoscale. These nanopipette sensors are able to detect cell surface and intracellular chemical sensing. Study of these phenomena would be facilitated with our newly developed technologies, an achievement at the highest international level in nanometrology and life sciences.

④Supramolecular nanoprobe development (Main PIs: Akine, Maeda, Ogoshi, MacLachlan)

(Objective)

We aim to develop new probes for high-performance nano-endoscopy, which are functionalized with the latest supramolecular technology.

(Methods)

In this study, we develop highly selective probe molecules based on recent advances in supramolecular

chemistry and molecular recognition chemistry. Further, we aim to develop nanoprobes with enhanced performance. We develop dual-mode probes functionalized with responsive molecules and probes for molecular observations and manipulations with nanoscale precision.

(Subjects and plans)

Table 4: Research subjects and plans for the development of supramolecular nanoprobes

Subjects	FY2017-2019	FY2020	FY2021	FY2022	FY2023
Supramolecular nanoprobe	**Design and synthesis of new probe molecules** (responsive helical polymer, photoswitching receptor, surface analysis, bioconjugate probes, etc.)	**Improvement of new probe molecules** (highly sensitive and selective probes, reactive probes, switching of dual-mode probes, etc.) **Development of nano- and molecular devices** (manipulation of cellular activities) (Profs. Frantz, Okuda, & Miyata)		**Improvements and applications** (sensing and control of cellular functions such as energy metabolism, cell motility, signaling, etc.)	
Nanolevel cancer research	**Molecular sensors for biomolecules** (glucose, pH, oxygen, lactate, oncometabolites, etc.)	**Molecular sensors for biomolecules** (temperature, pH, oxygen, ATP, chiral molecules, oligosaccharides, ions with different charges, and oncometabolites, etc.) **Development of new probes modified with sensors** (chemically modified gel-filled SICM nanopipette) (Profs. Takahashi & Hirao)		**Improvements and applications** (investigation of sensing ability in cellular environments and quantification of intracellular elements)	

(Research progress)

・Development of fundamental supramolecular nanoprobe technology

To gain a deeper understanding of proteins and biomembrane surfaces, analysis of chemical information in addition to morphological information at the nanometer scale is needed. To this end, specialized probe molecules that can detect specific chemical information are necessary. Therefore, our goal is to identify surface functional groups with high selectivity, sensitivity and nanometer-scale accuracy. It is effective to introduce cyclic molecules, helical polymers, metal complexes, peptides, and proteins with highly selective recognition abilities for each target molecule. We have successfully developed a host molecule that can selectively bind a fluoride ion (***Inorg. Chem., 2019***), a novel cobalt(III)-based host molecule in which Na^+-binding causes chemical reactions with changes in the electric charge (***J. Am. Chem. Soc., 2019***), and a cyclic host molecule exhibiting reversible state changes between solid and liquid in response to specific molecules (***J. Am. Chem. Soc., 2019***). We also developed fluorescent one-handed helical polymers (***J. Am. Chem. Soc., 2020***), which can be used as functional nanoprobes because they are very rigid and can present significant changes in helical pitch in response to various external stimuli such as ions and temperature. Moreover, we have succeeded in developing an easy and versatile living polymerization method to immobilize helical polymers on the substrates and probes (***Angew. Chem., Int. Ed., 2020***). Therefore, we will introduce these molecules to a probe tip to study the substrate surfaces. We are also trying to develop new host molecules that can switch the recognition ability toward biofunctional molecules, which activate their function only when needed. We developed a switchable molecule in which its molecular recognition ability can be disabled by a molecular machine mechanism using a rotaxane structure (***Org. Lett., 2019***). We further attempt to manipulate the local concentration of metabolites and signaling molecules at the nanoscale. To achieve this, we have developed a light-modulated nanodevice that allows an on-demand release of small chemicals at a subcellular level.

・Development of application technology for nanoscale cancer research

The region around cancer cells has chemical properties different from those around normal cells. Therefore, it is important to accurately determine the concentration distributions in real time at the nanometer scale. We are now designing selective sensors for oxygen, pH, temperature, ATP, chiral molecules (D-amino acids), oligosaccharides, ions with different charges (Fe^{2+} and Fe^{3+} ions), and the other oncometabolites (1-methylnicotinamide: 1-MNA) and will evaluate the local concentrations at the nanometer scale by combining these sensors with the nanoprobe technology. We have succeeded in the selective recognition of 1-MNA in urine samples using the water soluble pillar[6]arene derivative. We have started to develop new receptors for lactate ion and molecular oxygen, whose concentrations around cancer cells are known to be different from those of normal cells, or measure the temperature and intracellular ATP to elucidate the environment of cancer cells using the nanoprobe technology. We have also started to integrate a polymer gel at the opening of a nanopipette for SICM technology (Fig.8). By functionalizing the polymer with many sensor molecules, we can improve the overall sensitivity. In addition, by adjusting the pore size of the polymer gel, we can control the size of the molecules that interact with the sensor molecules and thereby improve the selectivity. This approach is applicable to a wide range of molecular binders. In contrast to a fluorescent probe design, we do not need to combine the binder to a fluorescent part, which allows us to explore a wider range of binder design.

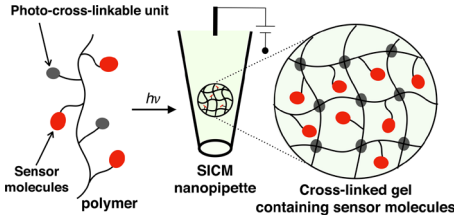


Fig.8: SICM nanopipette filled with chemically modified gel.

(World-leading Achievements)

If we achieve the above objectives, we will be able to determine the local concentrations of various substances at high spatial resolutions, which has not been possible using any existing technology. Clarification of these concentration distributions will contribute to a greater understanding of nanoscale substance transport in cancer cells. By comparing cancer cells to normal cells, advances could be made in our understanding of substance transport in cancer cells and the abnormalities of metabolite production. Further, our technology enables us to address the concentration gradient of chemicals or physicochemical elements near cell membranes, which has never been demonstrated experimentally. This imaging study has only been made possible by combining our supramolecular chemistry with nanoprobe technology, consistent with the highest international standards in nanometrology and life sciences.

⑤ Computational Analysis of Biological Phenomena and Bio-SPM Measurement Principles (Main PIs: Foster, Mikhailov)

(Objective)

We aim to elucidate nanoscale structures and dynamics of biological systems by computational approaches such as mathematical modeling, simulation and machine learning. We also use these approaches to understand the mechanism of bio-SPM measurements.

(Background and Methods)

Bio-SPM provides direct information of the structures and dynamics of proteins and cells. However, due to the complexity of the biological phenomena, it is not always straightforward to understand the mechanisms from the observed bio-SPM images. In this study, we address this issue by using computational approaches. We will perform mathematical modeling of the complicated biological systems. With the developed models, we will simulate the biological phenomena and their bio-SPM measurements. Meanwhile, the images and movies obtained by the bio-SPM measurements will be analyzed by the advanced image processing or machine learning approaches.

(Subjects and Plans)

Table 5: Research subjects and plans for analyses of real models from measured data

Subjects	FY2017-2019	FY2020	FY2021	FY2022	FY2023
Database, ML, SPM Simulation (Foster, Yang)	Development of analysis infrastructure and deployment in Kanazawa (NanoLSI). Simulations of solid-liquid interfaces (Fukuma). Machine learning (ML) prediction of AFM imaging of molecules.	Machine learning integration and features based on user feedback (NanoLSI). Interpretation of imaging of cellulose, chitin and polymer systems. ML classification of cancer cell imaging. Cell membrane penetration simulations. ML prediction of AFM imaging of systems in solution. (Fukuma).		Features based on user feedback (NanoLSI). ML prediction of AFM imaging of biological systems in solution.	
Biomolecular Simulation (Mikhailov, Flechsig)	Simulation of the dynamics of myosin V (Ando, Kodera), F1-ATPase, ABC transporter MsbA (Ando, Ngo), MET receptor (Matsumoto, Shibata, Sakai), protein kinase CaMKII (Shibata), dynamin filaments, crowded active colloids, and hydrodynamics of proteins. Development of BioAFMViewer (Kodera)	Improvement of BioAFMViewer - Data analysis: MET receptor (Matsumoto, Shibata), CaMKII (Shibata). MD simulations: MeCP2 protein (Ando, Kodera), ABC transporters (Ando, Dr. Ngo), motor domains of dynamin. Kinetic models: ATP-driven translocation of myosin V (Ando, Kodera), motor operation of dynamin. Design: hybrid light-powered molecular machines (Kodera, Cotti). Computational microrheology: active crowded colloids as models of cytoplasm.		Analysis and interpretation of novel HS-AFM data for protein machines. Advanced functions in BioAFMViewer. Design and implementation of hybrid light-powered molecular motors and machines. Stochastic thermodynamics of nanomachines. Computational studies of non-equilibrium transport phenomena in active colloids and in biomembranes with active protein inclusions.	
Chromosome structures (Sumikama)	Development of programs to simulate chromosomes both in the interphase and mitotic phase. Established theories to compute topographies and 3D-AFM images.	Developing more realistic chromosomes models to compare with relevant 3D-AFM experiments (Miyazawa). Establishing methods for analyzing molecular dynamics obtained by HS-AFM (Shibata and Sumino).		Computing of 3D-AFM images of organelles and cytoskeletons (Penedo). Establishing theories to obtain molecular dynamics at microseconds by AFM.	

(Research progress)

・Database and ML Analysis for AFM Image Data (Foster):

The development of the NanoLSI machine learning infrastructure (cassandra.nanolsi.kanazawa-u.ac.jp) has continued and it now includes a wide variety of analysis tools, parsing options and interface updates. We continued joint experimental and simulation studies of AFM imaging in solution (***Phys. Rev. B, 2019, J. Phys. Chem. C, 2019***). We further established important references for the management and analysis of data from simulations (***Adv. Sci., 2019, Comp. Phys. Comm., 2020***) (see Fig.9) and explored the limits of molecular analysis in high-resolution AFM (***Sci. Adv., 2020, Sci. Adv., 2020***).

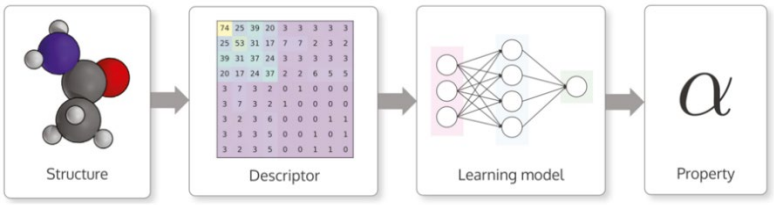


Fig.9: Typical workflow for making machine learning based property predictions for molecular structures.

・Modeling and Simulations of Biological Systems (Mikhailov and Flechsig):

The focus was on providing theoretical support for HS-AFM experiments with biomolecules. The

interactive BioAFMViewer software platform for visualization and analysis of protein structures has been developed. Transdisciplinary Research Projects (TDRP) were (1) *Modeling of ATP-less myosin V translocation under interactive HS-AFM* (with T. Ando, N. Kodera), (2) *Structural dynamics of ABC transporter MsbA* (with T. Ando, K. Ngo), (3) *Dynamic structural basis of MET receptor activation* (with K. Matsumoto, K. Sakai, M. Shibata). A new TDRP on *Design and implementation of hybrid light-powered molecular machines* (with N. Kodera, L. Cotti) has been planned to start in FY2020. Structure-based coarse-grained MD simulations of unfolding of the intrinsically disordered MeCP2 protein and all-atom MD simulations for dynamin were performed (with J. Noel, Max Delbrück Center for Molecular Medicine, Berlin). Multiparticle simulations of active crowded colloids as models for bacterial cytoplasm were performed (with H. Kitahata, Chiba University, and Y. Koyano, Tohoku University) and hydrodynamic effects of protein machines were analyzed (with S. Komura, Tokyo Metropolitan University). Three invited reviews (***J. Royal Soc. Interface, Biophys. Rev., Butsuri***) and three research articles (***Biophys. J., Biomolecules, Europhysics Lett.***) appeared in press. Together with the Universal Biology Institute of the University of Tokyo, a three-day theoretical and experimental workshop *Trends in Molecular Biophysics of Living Cells* (Kanazawa, November 2019) was organized.

・3D-AFM Simulation of Chromosomes (Sumikama):

A theoretical method to compute topographic images of chromosomes using a polymer simulation was established and published as a cover paper. A program to produce the x-shaped form of chromosomes was developed, in which dominant proteins for the x-shape formation such as condensin were included. A method to compute 3D-AFM images using the Jarzynski equality was established and applied to the structure. It was found that a dense part of the chromosome such as chromosome axis would be resolved as a higher force region, whereas a loose packing part such as loops would appear as a lower force in the 3D-AFM image.

(World-leading Achievements)

Computational approaches such as simulation and machine learning have been powerful tools for analyzing SPM data. However, their applications have been mostly limited to relatively simple systems consisting of atoms or small organic molecules. By combining these computational approaches with mathematical modeling techniques, we aim to analyze more complicated biological systems, which will lead to a significant development of the interdisciplinary research field "Nanoprobe Computational Science". As this research is only possible by combining expertise from three different fields — nanometrology, life science and computational science—, we expect results at a high level of international competitiveness.

(2) Nano-level understanding of cellular functions and cancer

Fundamental understanding of the basic functions of cells and cancer-specific abnormalities at the nano level.

① Basic cellular functions (Main PIs: Matsumoto, Wong, Hanayama, Nakajima, Toda)

(Objective)

Understanding the basic principles of cellular functions by observing nanostructures and dynamics inside cells.

(Background and Methods)

NanoLSI has decided to engage in this project with a high priority by integrating it into its flagship research areas of SPM and molecular cell biology. We have set out five aims to further understand the basic principles of various cellular functions such as cell proliferation, intracellular trafficking (nuclear pore complex/NPC, vesicular communication, and the post-transcriptional regulation of enzymes and cell morphogenesis (synthetic biology approach). We also plan to apply the crowding analytical scanning probe technologies to several cellular nanostructures and dynamics imaging.

(Subjects and Plans)

Table 6: Research subjects and plans for studying fundamental cellular functions

Subjects	FY2017-2019	FY2020	FY2021	FY2022	FY2023
Cell proliferation	**· Validation of the receptor activation mechanism by dynamic molecular imaging and simulation**	**· Dynamic mechanism and direct observation of membrane receptor activation** (Profs. Shibata & Fukuma) **· Receptor imaging using chemically manipulated AFM tips** (Prof. Shibata)		**· Dynamic mechanism and direct observation of membrane receptor activation** (Profs. Shibata & Fukuma) **· Receptor imaging using manipulated AFM tips in living cells** (Prof. Shibata)	
Intracellular trafficking (nuclear pore)	**· Nanoscopy imaging of Nanoscopy imaging of the nuclear pore complex (NPC) and its transport pathway (STED, HS-AFM)**	**· NPC inner FG filament measurement** (Profs. Ando, Kodera, Nakayama) **· STED nanoscopy imaging of NPC in a clinical study/brain t tumor cells** **· Influenza proteins intracellular trafficking** (Profs. Ando, Kodera, Yano, Hanayama)		**· Visualization of dynamics of NPC proteins** (Profs. Ando, Kodera, Nakayama) **· Visualization of intracellular trafficking dynamics of viral proteins** (Profs. Ando, Kodera)	

Vesicular communication	· **Characterization of nanostructures and stiffness of exosomes using 2D/3D FM-AFM** (Prof. Fukuma)	· **Development of a method to analyze the nano-dynamics of exosome transfer with the combination of SICM and confocal microscopy** (Prof. Takahashi)	· **Manipulation of nanostructures and nano-dynamics of exosomes both inside and outside of cells** (Profs. Fukuma, Takahashi, Ogoshi)
Post-transcriptional regulation of enzymes	· **Functional analysis of post-transcriptional regulators of enzymes**	· **Visualization of interaction between (post-) transcriptional regulators and/or RNA or DNA using HS-AFM** (Prof. Kodera)	· **Identification of peptide aptamer inhibitors for post-transcriptional regulators and visualization of their interaction using AFM**(Prof. Kodera)
Cell morphogenesis		· **Development of synthetic receptor platforms to control cytoskeletal dynamics and cell morphology** · **Mechanisms of cell cortical tension with AFM measurement** (Prof. Okuda)	· **Nano-manipulation of cytoskeletal dynamics inside cells using AFM** · **Designing synthetic cell-cell communication to reconstitute tissue morphogenesis**

(Research Progress)

· Cell Proliferation (Matsumoto)

Matsumoto et al. have been investigating cell membrane growth factor receptor activation, a fundamental process of cell signal activation. The HS-AFM analysis revealed allosteric MET receptor activation (dimerization) by HGF. MET dimerization was proved by molecular dynamics (MD) simulation, and the model was proved experimentally by a split luciferase assay using mutant MET proteins. A new model provided by AFM will facilitate reconsideration of the mechanism of receptor activation.

· Intracellular trafficking (Wong)

The control of intracellular traffic is vital for cell growth and differentiation. Nuclear pore complexes (NPCs) are multi-protein turnstiles that regulate nucleo-cytoplasmic traffic. Recently, Wong et al. visualized the native NPC and further succeeded in the observation of single filament inside the inner ring of nuclear pore by HS-AFM. NPC protein TPR regulated autophagy induction in a brain tumor-ependymoma (***Autophagy 2020***, IF 11.10). Deletion of the TPR protein is known to induce a process called autophagy within cells. Autophagy is initiated when a cell is under undue stress and results in the death of damaged cells. The patient tumor samples, with their high levels of TPR protein, showed little or no presence of autophagy. The high TPR levels were also accompanied by an increase in HSF-1 and MTOR, molecules which are responsible for cell growth and differentiation. Further, treatment of mice having tumors with the drug, rapamycin which inhibits MTOR, led to decreased TPR levels and a shrinking of the brain tumors (Fig.10). Besides, Wong et al. also found that nuclear transport protein KPNA4 established a feed-forward signaling in head and neck squamous cell carcinoma (***Oncogene 2020***, IF 6.85). Interestingly, human influenza virus infects differentiated epithelial cells in the respiratory tract. In a pilot experiment, using HS-AFM, we captured the nanoscopic conformation dynamics of influenza protein hemagglutinin (HA) precursor using HS-AFM (***BBA 2019***). We have further initiated interdisciplinary research with the Ando group, Yano group and the Hanayama group to further visualize conformation dynamics of HA binding to liposomes/exosomes in differentiated epithelial lung cells.

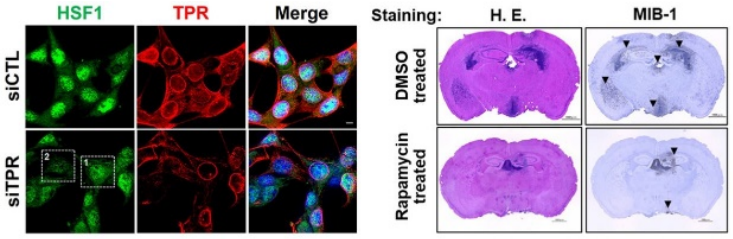


Fig.10: Deletion of the TPR gene led to lower levels of TPR and its associated protein HSF1 (left; lower panel) whereas rapamycin treatment reduced the size of tumor cells (dark blue cells) in the brains of mice (right, lower panel).

· Vesicular communication (Hanayama)

Hanayama et al. have been working on the molecular mechanisms of cell-cell communications in immune systems. In FY2019, we discovered a novel type of immune cells that present tissue antigens to T cells (*J Exp Med* **2019**, IF 10.892). We also found that large extracellular vesicles (EVs) in thymus strongly express tissue antigens on MHC molecules. We are currently trying to clarify how these EVs control T cell responses with an analytical method that combines confocal microscopy and SICM in collaboration with the Takahashi group. To understand the differences in the characteristics of cancer-derived exosomes, we analyzed them with a high-resolution AFM by working with Fukuma group. We found that cancer-derived exosomes are significantly stiffer than normal ones, which may underlie the mechanisms of cancer progression.

· Post-transcriptional regulation of biotransformation enzymes (Nakajima)

Nakajima et al. found novel regulation mechanisms of cytochrome P450, a major drug-metabolizing enzyme superfamily, by two post-transcriptional regulation mechanisms, A-to-I RNA editing and RNA methylation (***Biochem Pharmacol, 2020***, IF 5.01; ***Drug Metab Dispos, 2019***). In addition, they are now attempting to observe Nrf2-Keap1 interaction, which is an important transcriptional regulation system for the oxidative stress response- and for drug detoxification-enzymes, by using HS-AFM.

· Morphogenesis-bottom up & mechanical approach (Toda)

Toda et al. established a synthetic biology research group in October, 2019. In FY2019, they engineered cellular sensing and responding systems that enable us to design customized cell-cell communication. They are now developing synthetic receptor platforms that can control specific protein activity. They aim to activate the synthetic receptor using a ligand-conjugated AFM cantilever for molecular-level manipulation of specific protein activity inside cells to understand the principles of how nanoscale molecular dynamics can lead to macroscale cell behaviors. Toda group also started collaborating with Okuda group to study how cell adhesion molecules control cell cortical tension with direct measurement of the tension by AFM.

(Expected World's Top-level Achievements)

By using an integrated approach with cutting-edge nanoscale imaging technology, they expect to obtain highly valuable information for these cellular studies, such as dynamic protein-receptor interaction, post-transcriptional regulation of enzymes, nanoscopic trafficking within organelles (NPC), nanoparticles (exosomes)/vesicular communication and the development of synthetic receptor platforms inside cells. These data will provide novel insights to identify core machinery regulating cellular functions at the nanoscale. Therefore, they are confident that the outcome of these interdisciplinary projects will be competitive at the international level.

② Development of innovative therapeutic technology based on the understanding of cancer progression mechanisms (Main PIs: Oshima, Yano, Hirao)

(Objective)

Through interdisciplinary studies with scanning probe microscopy, supramolecular chemistry, and computational sciences, we aim to elucidate the nanostructures and dynamic changes in molecules, metabolism, and cells associated with cellular transformation, stem cell fate, and malignant progression. Based on these findings, we are developing novel cancer diagnostic and therapeutic methods as well as precision medicine.

(Background and methods)

Our basic experimental systems are molecular cell biology, biochemistry, and genetically engineered mouse models; these systems are combined with nano-level techniques using AFM, SICM, and supramolecular chemistry. We also promote metabolite measurement with a newly developed nanoprobe. Based on the novel information obtained, we will develop applied studies that will contribute to the development of new diagnostic and therapeutic methods.

(Subjects and Plans)

Table 7: Research subjects and plans for cancer progression and diagnosis/treatment

Subjects	FY2017-2019	FY2020	FY2021	FY2022	FY2023
Cancer Progression	· **Oncogene-induced progression and cancer cell dynamics** (SICM) · **Metabolite discovery in stem cells** (supramolecular chemistry) · **Oncogenic fusion-protein dynamics and distribution** (AFM)	· **Oncogene-induced progression and cancer cell dynamics** (Prof. Watanabe) · **Chemical detection of metabolic changes in cancer stem cells (Profs. Akine & Arai)** · **Oncogenic fusion-protein dynamics and distribution** (Prof. Kodera)		· **Cancer progression and cellular dynamics** (Profs. Watanabe & Fukuma) · **Metabolic changes in cancer stem cells** (Profs. Akine & Arai)	
Cancer Diagnosis	· **Cyclic peptides for PET imaging** (peptide chemistry, AFM)	· **Cancer metabolite measurement** (Profs. Ogoshi, Maeda, & Takahashi) · **PET imaging in a clinical study**		· **Cancer prognosis by cellular dynamics** (Prof. Watanabe) · **Cancer diagnosis by metabolite measurement** (Profs. Ogoshi, Maeda, & Takahashi) · **PET imaging in a clinical study** · **Fusion oncoprotein structures and drug resistance (Prof. Kodera)**	
Cancer Treatment	· **Cyclic peptide application for growth factor inhibition** (AFM)	· **Protein-drug interaction** (cryoSEM, nanoprobe) · **Oncogenic fusion-protein structures and drug resistance** (Prof. Kodera)			
Precision Medicine	· **Function and regulation mechanisms of drug-metabolizing enzymes**	· **Nano-imaging of drug-metabolizing enzymes/related proteins** (Prof. Kodera)		· **Proof of concept for drug predisposition** (Prof. Kodera)	

(Research progress)

・Stem Cell Fate (Hirao)

Hirao et al. have been investigating molecular mechanisms of stem cell fate decision by metabolic regulation. By functional screening based on CRISPR/Cas9 library, they identified a vitamin B3 metabolic enzyme, N-nicotinamide methyl transferase (NNMT), and its metabolite, 1-methylnicotinamide (1-MNA), as a unique pathway for control of cancer stem cell properties, including therapy resistance (Fig.11). In addition, they found that this metabolite is up-regulated in cancer tissues from patients, indicating that the vitamin metabolism is a possible diagnostic indicator of malignant progression. Collaborative research on metabolite sensing with Ogoshi group revealed that a pillar[6]arene derivative, binds to 1-MNA with high affinity. To investigate the specificity, they generated NNMT deficient mice and found that the

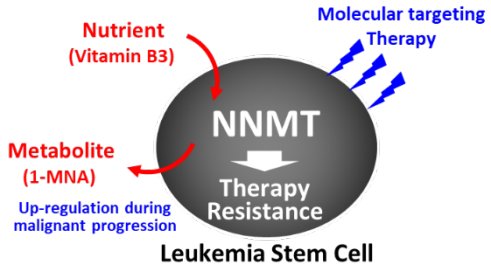


Fig.11: Critical metabolism for drug resistance of cancer (leukemia) stem cells.

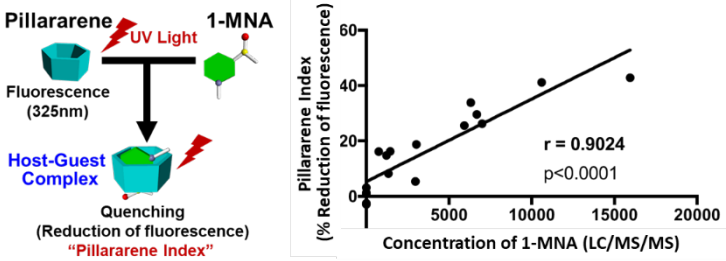


Fig.12: Quantification of 1-MNA by Pillararene. Quenching of fluorescence by Host-Guest complex (left). Significant correlation of "Pillararene Index" with 1-MNA of mouse urine samples (right).

pillararene specifically recognizes 1-MNA, but not other metabolites, through Host-Guest interaction (Fig.12). Based on these results, they have started further collaborations with the Maeda and Takahashi groups for SCIM imaging. These interdisciplinary collaborations will lead to the development of a unique metabolite imaging system at the single cell level, contributing to a deep understanding of cancer malignancy and establishment of novel methods for clinical cancer diagnosis.

・Oncogenes and Cancer Cell Dynamics (Oshima)

Oshima et al. previously established intestinal cancer-derived organoid lines that carried driver mutations for colon cancer including APC (A), KRAS (K), TGFBR2 (T), FBXW7 (F), and TP53 (P) genes in various combinations (Cancer Res, 2018, IF 9.130). Using these organoid systems, they have performed CRISPR screening and identified activin receptor as a novel tumor suppressor (Proc Natl Acad Sci USA, 2019, IF 9.580). Furthermore, in collaboration with Watanabe group at Bio-SPM, they have examined physical properties of these organoids using SICM (Fig.13). Although SEM images of the respective organoid surfaces did not show morphological differences, SICM images indicated certain differences according to malignancies. Importantly, each physical property showed significant changes according to the accumulation of mutations, i.e. dependent on increased malignancy. This is the first evidence that links genotype/phenotype of cancer cells and physical properties, which expands our knowledge of the mechanisms of cancer progression.

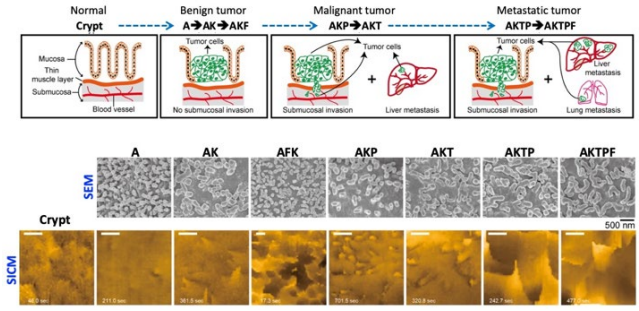


Fig.13: Genotypes and phenotypes of organoids (top) and their SEM and SICM images (bottom).

・Development of Cancer Therapeutic Technology (Yano and Ando)

Yano et al. discovered that downregulation of miR-449a induced ALK inhibitor resistance, via increased expression of EGFR ligand amphiregulin which caused EGFR mediated survival signal. Moreover, combined use of EGFR inhibitor with ALK inhibitor circumvents the resistance (Fig.14) (*J Thorac Oncol 2020,* IF 12.460).

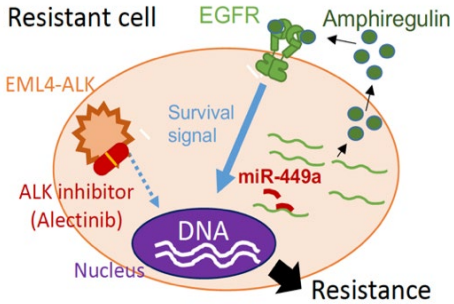


Fig.14: Downregulation of miR-449a induced ALK inhibitor resistance via increased expression of EGFR ligand amphiregulin which induced an EGFR-mediated survival signal.

(World-leading Achievements)

Changes in cancer metabolism are a hot topic. We have identified that the metabolic enzyme NNMT participates in drug resistance in cancer stem cells and that 1-MNA generated via NNMT can be trapped and quantified using a pillararene designed and synthesized by supramolecular chemistry. Basically, cancer development and progression occur though an accumulation of oncogenic mutations. Unique changes in dynamic structures and stiffness of cancer cells were first discovered using genetically engineered mouse models and SPM technology. Cancer drug resistance is a key issue that needs to be overcome in cancer treatment. We have identified down-regulation of microRNA as a new mechanism of drug resistance. Together with published and ongoing unpublished findings, our understanding of changes in the dynamic structures and physical properties of molecules, metabolites, and cell behaviors, using world-leading SPM technologies show distinguishing features at the highest international standard.

(3) Establishment of New Research Field: Nanoprobe Life Science

We aim to establish a new research field "nanoprobe life science" by integrating knowledge from the four research fields: nanometrology, life science, supramolecular chemistry, and computational science. In FY2017, we started to work on various transdisciplinary subjects combining two or three disciplines. In FY2019, we continued this effort and started to summarize the results for publication in many of the projects. Some examples of the published works are highlighted below.

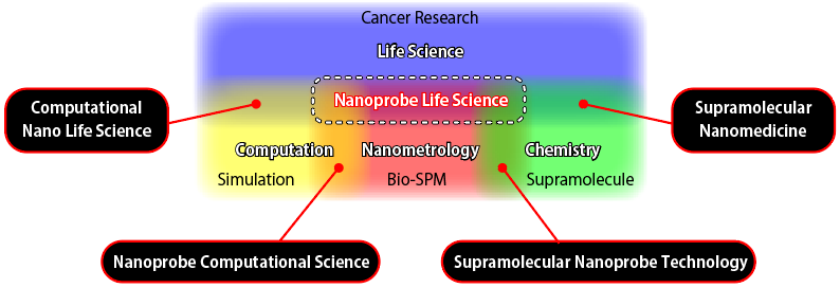


Fig.15: Relationship between the four major research disciplines.

① Nanometrology x Life Science

Phase separation organizes the site of autophagosome formation (*Nature, 2020,* IF: 43.070)

Autophagosomes, double-membrane vesicles formed *de novo* upon starvation, deliver cytoplasmic components to lysosomes or vacuoles for their degradation. The formation of the autophagosome precursor (called PAS) comprising cytosolic Atg proteins (Atg1, Atg13, and Atg17- Atg29-Atg31 complex) is triggered by dephosphorylation (de-Pi) of Atg13 upon starvation. Yet, early PAS formation processes and its physicochemical and functional properties have been elusive, mainly because these Atg proteins are intrinsically disordered proteins (IDPs), except for dimeric Atg17. HS-AFM first revealed that the disordered region of Atg13 folded into a globule upon phosphorylation (+Pi), suggesting blocking of the Atg17-binding sites of Atg13. Next, HS-AFM showed a network-like structure formed by crosslinking of Atg17 by de-Pi Atg13. Upon long incubation of the mixture of de-Pi Atg13 and the Atg17-Atg29-Atg31 complex, a droplet-like structure developed on mica. The liquid droplet formation was also observed *in vivo*. Thus, the PAS is formed by liquid-liquid phase separation through a weak multivalent binding among the Atg proteins.

Fujioka Y., Alam J.M., Noshiro D., Mouri K., Ando T., Okada Y., May A.I., Knorr R.L., Suzuki K., Ohsumi Y., Noda N.N., *Nature*, vol.578, 301-305

Structure of the mitochondrial import gate reveals distinct preprotein paths (*Nature, 2019,* IF: 43.070)

Mitochondria are composed of ~1000 different proteins, ~99% of which are synthesized as preproteins in the cytosol, and imported into mitochondria with the aid of translocator complexes. The translocase of the outer mitochondrial membrane (TOM) complex functions as the major entry gate for passage of >90% of the mitochondrial proteins across the outer membrane. TOM is a large protein complex comprising the channel-forming β-barrel protein Tom40 and six other α-helical membrane-integrated subunits, the receptor subunits Tom20, Tom22, and Tom70, and regulatory Tom5, Tom6, and Tom7. This study determined the atomic structure of this intricate TOM complex at 3.8 Å resolution, using cryo-EM and detergent solubilized TOM in dimeric form. HS-AFM contributed to the starting point of this study by showing that TOM exists as both dimers and trimers, which are interconvertible.

Araiso Y., Tsutsumi A., Qiu J., Imai K., Shiota T., Song J., Lindau C., Wenz L.-S., Sakaue H., Yunoki K., Kawano S., Suzuki J., Wischnewski M., Schütze C., Ariyama H., Ando T., Becker T., Lithgow T., Wiedemann N., Pfanner N., Kikkawa M., Endo T., *Nature,*vol.575(7782),395-401

Crystal structure of heliorhodopsin (*Nature, 2019*, IF: 43.070)

Heliorhodopsins (HeR) are a distinct, abundant group of microbial rhodopsins discovered by functional metagenomics. HeRs have a long-lived photo-activated state ($\tau > 1$ s), suggesting that HeRs function as light-sensors through interaction with partners. Here, we present the crystal structure and high-speed AFM images of a HeR. HS-AFM revealed that HeRs form stable dimers in the lipid membrane. The HeR structure has seven transmembrane helices and an all-trans retinal chromophore, linked to lysine at the seventh transmembrane helix through a protonated Schiff base linkage. The lateral fenestration in the HeR plays a critical role in capturing the retinal from the environment. Our study deepens the understanding of the functions of HeRs, and the structural diversity of microbial rhodopsins.

Shihoya W., Inoue K., Singh M., Konno M., Hososhima S., Yamashita K., Ikeda K., Higuchi A., Izume T., Okazaki S., Hashimoto M., Mizutori R., Tomida S., Yamauchi Y., Abe-Yoshizumi R., Katayama K., Tsunoda S.P., Shibata M., Furutani Y., Pushkarev A., Béjà O., Uchihashi T., Kandori H., Nureki O., *Nature*, vol.574(7776), 132-136

Rad50 zinc hook functions as a constitutive dimerization module interchangeable with SMC hinge (*Nat. Commun., 2020*, IF: 11.878)

The human Mre11/Rad50 complex is one of the key factors in genome maintenance pathways. Imaging

of the human Mre11/Rad50 complex by high-speed AFM shows that the Rad50 coiled-coil arms are consistently bridged by the dimerized hooks while the Mre11/Rad50 ring opens by disconnecting the head domains, resembling other SMC (Structural Maintenance of Chromosomes) proteins such as cohesin or condensing. These architectural features are conserved in the yeast and bacterial Mre11/Rad50 complexes. We propose that the basic role of the Rad50 hook is similar to that of the SMC hinge, which serves as a rather stable dimerization interface.

Tatebe H., Lim C.T., Konno H., Shiozaki K., Shinohara A., Uchihashi T., Furukohri A., *Nature Communications*, vol.11(1), 370

High-resolution label-free 3D mapping of extracellular pH of single living cells (*Nat. Commun., 2019*, IF: 11.878)

Dynamic mapping of extracellular pH (pHe) at the single-cell level is critical for understanding the role of H^+ in cellular and subcellular processes, with particular importance in cancer heterogeneity and progression. We developed a novel zwitterionic label-free pH nanoprobe that has a sensitivity >0.01 units, 2 ms response time, and 50 nm spatial resolution. This high spatiotemporal resolution pH sensing nanoprobe can be easily combined with Scanning Ion Conductance Microscopy (SICM), which has allowed simultaneous 3D topographical imaging and label-free pHe mapping of living melanoma A375M cells at real-time.

Zhang Y., Takahashi Y., Hong S.P., Liu F., Bednarska J., Goff P.S., Novak P., Shevchuk A., Gopal S., Barozzi I., Magnani L., Sakai H., Suguru Y., Fujii T., Erofeev A., Gorelkin P., Majouga A., Weiss D.J., Edwards C., Ivanov A.P., Klenerman D., Sviderskaya E.V., Edel J.B., Korchev Y., *Nature Communications*, vol.10(1), 5610

② Nanometrology x Supramolecular Chemistry

One-step synthesis of one-dimensional supramolecular assemblies composed of helical macromolecular building blocks (*J. Am. Chem. Soc., 2019*, IF: 14.695)

This study was supported by the NanoLSI transdisciplinary research promotion grant. De novo design of biomimetic molecular systems having sophisticated functions is still challenging. To obtain a guideline for de novo design, transdisciplinary research combining supramolecular chemistry and molecular-resolution analysis technology is required. In this study, the supramolecular chemistry group (Ikai et al.) and the AFM group (Asakawa et al.) revealed a novel molecular design that can achieve one-dimensional (1D) supramolecular assemblies like the cytoskeleton of eukaryotic cells. The helical constituent polymers of 1D supramolecular assemblies were linked end-to-end through multiple hydrogen bonds.

Wada Y., Shinohara K.-I., Asakawa H., Matsui S., Taima T., Ikai T., *Journal of the American Chemical Society*, vol.141(35), 13995-14002

High resolution electrochemical mapping of hydrogen evaluation reaction site (*Angew. Chem. Int. Ed., 2020*, IF: 12.257)

Electrochemical detection is useful for chemical detection around the sample surface. Owing to a recent increase in interest of two-dimensional (2D) layered transition-metal dichalcogenides, molybdenum disulfide (MoS_2) has received a great amount of research attention. Scanning electrochemical cell microscopy (SECCM), which uses a nanopipette as a probe in a local and movable electrochemical cell, is an effective tool for characterizing surface structures electrochemically at a submicroscale spatial resolution. We have visualized inhomogeneous hydrogen evaluation reaction (HER) activity on a triangular 1H-MoS_2 monolayer nanosheet and unveiled heterogeneous reactivity, relationship of layer number and HER activity, and aging effect.

Takahashi Y., Kobayashi Y., Wang Z., Ito Y., Ota M., Ida H., Kumatani A., Miyazawa K., Fujita T., Shiku H., Korchev Y.E., Miyata Y., Fukuma T., Chen M., Matsue T., *Angewandte Chemie* - International Edition, vol.59, 3601 – 3608

③ Nanometrology x Computational Science

Automated Structure Discovery in Atomic Force Microscopy (*Sci. Adv., 2020*, IF: 12.53)

AFM with molecule-functionalized tips has emerged as the primary experimental technique for probing the atomic structure of organic molecules on surfaces. Most experiments have been limited to nearly planar aromatic molecules due to difficulties with interpretation of highly distorted AFM images originating from nonplanar molecules. Here, we develop a deep learning infrastructure that matches a set of AFM images with a unique descriptor characterizing the molecular configuration, allowing us to predict the molecular structure directly. This approach will open the door to applying high-resolution AFM to a large variety of systems, including biomolecular ones, for which routine atomic and chemical structural resolution on the level of individual objects/molecules would be a major breakthrough.

Alldritt B., Hapala P., Oinonen N., Urtev F., Krejci O., Canova F.F., Kannala J., Schulz F., Liljeroth P., Foster A.S, *Science Advances*, vol.6(9),eaay6913

Three-dimensional Graphene Nanoribbons as a Framework for Molecular Assembly and Local Probe Chemistry (*Sci. Adv., 2020*, IF: 12.53)

Recent advances in state-of-the-art probe microscopy allow us to conduct single molecule chemistry via tip-induced reactions and direct imaging of the inner structure of the products. Here, we synthesize three-dimensional graphene nanoribbons via on-surface chemical reactions and take advantage of tip-induced assembly to demonstrate their capability as a playground for local probe chemistry. The experimental

results combined with theoretical calculations pave the way for tailoring interactions by a local probe at the single-molecule level, allowing wide application for the characterization of complex molecular systems.
Kawai S., Krejčí O., Nishiuchi T., Sahara K., Kodama T., Pawlak R., Meyer E., Kubo T., Foster A.S., *Science Advances*, vol.6(9), eaay8913

④ Nanometrology x Life Science x Supramolecular Chemistry

Molecular dynamics suppressed by novel macrocyclic peptide (*Nat. Chem. Biol.*, *2019*, IF:13.843)

Through a cross-disciplinary approach, Matsumoto et al. found that HiP-8 (HGF-inhibitory peptide-8), a macrocyclic peptide consisting of 12 amino acids, specifically binds to HGF (***Nat. Chem. Biol., 2019***). Biochemical analysis indicated that HiP-8 binds to HGF through multivalent binding interfaces. High-speed AFM analysis indicated that HiP-8 restricted the dynamic domain movement of HGF into static closed conformations. This study established the novel concept that a small macrocyclic peptide can inhibit the molecular dynamics of a target protein.

Macrocyclic peptide-based inhibition and imaging of hepatocyte growth factor, Sakai K., Passioura T., Sato H., Ito K., Furuhashi H., Umitsu M., Takagi J., Kato Y., Mukai H., Warashina S., Zouda M., Watanabe Y., Yano S., Shibata M., Suga H., Matsumoto K., *Nature Chemical Biology*, vol.15(6), 598-606

⑤ Nanometrology x Life Science x Computational Science

HS-AFM revealed accelerated binding of agitoxin-2 to a K^+ channel by induced fit (*Sci. Adv., 2019*, IF: 12.804)

Agitoxin-2 (AgTx2) from scorpion venom is a potent blocker of K^+ channels. The docking model has been elucidated, but it remains unclear whether binding dynamics are described by a two-state model (AgTx2-bound and AgTx2-unbound) or a more complicated mechanism. Here, we analyzed the binding dynamics of AgTx2 to the KcsA channel using HS-AFM. From images of repeated binding and dissociation of AgTx2 to the channel, single-molecule kinetic analyses using a supercomputer revealed that the affinity of the channel for AgTx2 increased during persistent binding and decreased during persistent dissociation. We propose a four-state model, including high- and low-affinity states of the channel, with rate constants. An induced-fit pathway was dominant and accelerated binding 400-fold. This is the first analytical imaging of scorpion toxin binding in real time, which is applicable to various biological dynamics.
Sumino A., Sumikama T., Uchihashi T., Oiki S., *Science Advances*, vol.5(7), eaax0495

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."

We have made various efforts to promote interdisciplinary research among the four fields, i.e.nanometrology, life science, supramolecular chemistry, and computational science. So far, in addition to open academic meetings such as international symposia and seminars, closed meetings such as colloquia (but open to whole NanoLSI) and "T-meetings" (by two research groups) have been held regularly. In addition, the Advisory Board Meeting had an intensive discussion focused on issues that are particularly important in promoting interdisciplinary research. We also started weekly luncheon meetings FY 2019, based on the recommendations from the Site Visit and those from the Advisory Board Meeting of the FY 2018. Furthermore, we decided to implement a retreat involving students in deciding its content. In the following, important points of these activities remarked for FY 2019 will be described.

- International Symposium

The third International Symposium was held in Vancouver, Canada, with the central theme of interdisciplinary research in supramolecular chemistry, life sciences and nanometrology. Prof. MacLachlan of UBC, where the satellite research site of NanoLSI has been established, took the lead in the preparation of the Symposium. At the Symposium, several renowned researchers were invited, primarily from North America, to give lectures and to actively discuss interdisciplinary research. Various ripple effects are being seen thanks to this Symposium. For example, Prof. Leonenko (Univ. of Waterloo), the chair of the Biophysical Society of Canada, was nominated as a Fellow of the NanoLSI Fellow Program to visit Kanazawa University, Japan. Prof. Bruke (UBC), one of the invited speakers, has invited Prof. Fukuma of NanoLSI to ICNT, a big international conference, which will be held in July 2020.

- Advisory Board Meeting

The Advisors intensively discussed selected issues of importance in promoting interdisciplinary research. This fiscal year, several prominent scientists were invited to a one-day seminar to discuss the promotion of interdisciplinary research involving supramolecular chemistry, life science, and nanometrology, which had been particularly remarked upon in the Site Visit report. Afterwards, an intensive discussion was held between the Advisor, Prof. Suga (Univ. Tokyo), and researchers from NanoLSI, which was very fruitful for considering the policy direction of NanoLSI. (For the policy, see the response to Comment 4 in 7. Center's Response to Results of Last Year's Follow-up)

- Luncheon meeting and retreat

NanoLSI started a luncheon meeting once a week in FY 2019. At a luncheon meeting, young researchers introduced themselves for about 10 minutes and then talked about their research, followed by a free exchange. This deepened their understanding of each other's backgrounds and should greatly contribute to the promotion of interdisciplinary research. A further recommendation was appreciated that opportunities should be provided for the mixing of young researchers, students in particular. In response to this recommendation, a retreat in the form of a training camp is planned with an expectation of about 80 participants including students. Unfortunately, the retreat has been postponed to prevent spreading of the new coronavirus, SARS-CoV-2, but will be held once the situation has settled down.

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)

- Achievements of 16 PIs: 564 papers were published during the period 2014-2018, of which 7 (1.2%) were rated within the top 1% cited publications and 95 (16.8%), within the top 10%. The number of international co-authored papers is 212 (37.6%) of the total. These percentages of the top 10% and international co-authored papers are higher than those of 16 other Japanese national universities that aim to promote excellence in education and research.

- Enhanced international recognition of NanoLSI: NanoLSI organized the "Bio-AFM Summer School" for young researchers, the "Bio-SPM Collaborative Research" for established researchers, and the "NanoLSI Fellow Program" for PI-level researchers. A total of 29 overseas researchers participated from 13 countries out of 70 participants in total. The Bio-AFM Summer School contributed to the establishment of 45 research collaborations including 9 international research collaborations and the publication of 35 co-authored papers including 2 international co-authored papers accumulatively.

- Overseas satellite research sites: NanoLSI renewed bilateral Agreements with Imperial College London, UK and the University of British Columbia (UBC), Canada for long-term research cooperation. The Agreements stipulate (1) the specifications of research conducted by the PIs at these satellite research sites, (2) the financial support for research personnel at the satellites, and (3) the joint patents resulted from the joint research, the mutual recognition of use of the results, and profit sharing. As a result of the international collaboration, three international co-authored papers were produced between NanoLSI and the satellite at Imperial College London. In addition, the NanoLSI 3rd International Symposium was co-hosted at UBC with the participation of 72 researchers (54 non-Japanese, 18 Japanese), including 7 invited speakers from Canada and the United States.

- Number of non-Japanese researchers: NanoLSI has 74 researchers, of which 23 (31.1%) are from abroad.

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.

- Research Professorship and evaluation-dependent allowance: NanoLSI has continued to award Research Professorships with reduced university obligations outside NanoLSI as well as the evaluation-dependent allowance. The evaluation was conducted by the Director of NanoLSI on the basis of various evaluation criteria, i.e. research performance and contribution to activities related to establishing NanoLSI.

- Executive meetings: The University President, the Vice President in charge of general affairs, finance, and facilities and the Director of the NanoLSI discuss matters relating to NanoLSI and the direction of its medium- to long-term development on a regular basis (once a month for about one hour).

- Ripple effect: Details of the support program for non-Japanese researchers voluntarily made by NanoLSI administrative staff were compiled into a PowerPoint presentation, including resident registration, long-term visa acquisition, driver's license registration, bank account opening, housing/parking/credit card contracts, pensions/medical insurance, hospital consultation, nursery school introduction, and family member employment support. This presentation was shared within the University. This effort has turned out to be important for staff development in support of the top international research site of NanoLSI. This encourages the University as a whole to consider using these measures as a guide and strengthening the educational support for non-Japanese students at schools attached to the University.

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.

- Commitment from the University: Kanazawa University has made a major commitment to further development of NanoLSI, providing research funds of ¥60 million, covering the salary for researchers who had been employed before the inauguration of NanoLSI, and securing 3,000 m^2 for future NanoLSI research facility.

- New NanoLSI Building: A new building with 4 floors and a basement having a total area of 6,800 m^2 is under construction with a total budget of ¥2.2 billion including the University's own expenses of ¥700 million(edit: settled amount of ¥650 million as of January 2021). It will be completed at the end of September 2020.

- Independence of NanoLSI: The University has decided that NanoLSI will be an autonomous institute from FY2020 in terms of its independence; the institute’s responsibility for budget and personnel has been reinforced.

- Fostering next-generation researchers: NanoLSI has recruited four more junior PIs in FY2019 to complete the plan of having 6 junior PIs. Each junior PI is expected to play an important role in conducting interdisciplinary research. The tenure track system is applied to the junior PIs, and the tenure posts are secured at the President's discretion.

- Acquisition of external research funds: Two PIs were newly successful in each acquiring a KAKENHI Grant-in-Aid (A). Four PIs have been adopted by CREST. A total of 11 AMED grants by 8 PIs have been approved. The amount of external funds acquired in FY2019 is ¥1,044,068,024 in total, of which ¥701,070,767 are calculated as part of the NanoLSI budget by applying the effort rates of all the NanoLSI researchers.

- Education unit of NanoLSI: The graduate school, “Division of Nano Life Science,” started in FY2020 with 9 master course students (the fixed number of 6 students) and 7 doctorate students (the fixed number of 6 students). To promote interdisciplinary research in the Division of Nano Life Science, all 27 full-time researchers of NanoLSI who have an educational assignment become engaged as educators in the Division of Nano Life Science. Two mentors selected from different research fields supervise each student as dual mentors. Interdisciplinary research training courses are to be set up along with the NanoLSI research activities such as the Bio-AFM Summer School (renamed "Bio-SPM Summer School" from FY2020) and interdisciplinary research promotion grants. Graduate students in the Division, including master course students, participate in the research of NanoLSI PIs as research assistants. In addition, in order to ensure the operational autonomy of the Division, (1) a NanoLSI PI is assigned to the Head of Division of Nano Life Science, (2) the NanoLSI administrative director supports the Head and acts as the manager of the Division, and (3) the NanoLSI administrative office is in charge of managing this Division together with the Student Affairs Department of the University headquarters.

6. Others

* Describe what was accomplished in the center’s outreach activities last year and how the activities have contributed to enhancing the center’s “globally visibility.” In Appendix 6, describe concretely the contents of these outreach activities. In Appendix 7, describe media reports or coverage, if any, of the activities.

* In addition to the above 1-5 viewpoints, if there is anything else that deserves mention regarding the center project’s progress, note it.

- Outreach activities: The website of the Institute contains sections on “Education,” introducing the Division of Nano Life Science, its PIs and financial support and “Diversity in NanoLSI,” introducing the research activities of female researchers. In addition, NanoLSI researchers have collaborated with JSPS and publishers to create “World of Nanoscale: Do Life Scientists see Dancing Protein in Their Dreams?” (Japanese only), which introduces the life science research performed by Bio-SPM. Documents are also available on “Open Facility Programs at NanoLSI” and “Recruiting Flyer for the Graduate School Course of NanoLSI”.

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.

Responses to Site Visit Report

Comment 1 *"Indicate the activities of the foreign PIs at NanoLSI more explicitly. Internationality is one of WPI's key aspects, and NanoLSI has strong foreign members including those from its two satellites in England and Canada. However, their presence and their research activities at NanoLSI were obscure during this site visit. The physical presence of foreign PIs is requested at the next site visit, and their activities should be explained in detail."*

Attendance of all foreign PIs at the next site visit: We seriously apologize for the absence of some of the foreign PIs in the Site Visit FY2019. After the last site visit, we immediately made sure that all of the foreign PIs can attend the next site visit. However, due to the outbreak of the new coronavirus, some of the members may not be able to travel to Japan. If that is the case, we would like to make sure that all of them can attend the meeting through a WEB meeting system.

Explicit presentation of foreign PIs' activities: We plan to have presentations by individual foreign PIs in the next site visit even if it is held in a web meeting style. In these presentations, we believe that we can present their great contributions to our projects. In addition, we made several efforts to enhance their presence and activities at NanoLSI. First, we updated the contracts with their institutions to enable their longer stay at NanoLSI than before. Secondly, we hired new members for Prof. Korchev and Prof. MacLachlan to accelerate their activities at NanoLSI. Finally, we organized meetings between these members and individual domestic PIs' groups as many as possible during their stay at NanoLSI.

Comment 2 *"Improve the gender balance. The WG recognized that there were few presentations by female researchers of the institute. It may be a social and/or structural problem of Japan but NanoLSI is encouraged to improve it."*

Although there were no oral presentations from female researchers in the site visit, they are actively contributing to the works at NanoLSI in every discipline. In response to this comment, we made efforts to collect information from other WPI centers and took a few measures to improve the gender balance.

Improve Visibility of Female Researchers' Activities: We set up a new WEB page, where we highlight research activities of female researchers at NanoLSI in all disciplines. This information should reduce the barrier for a female to join our institute.

Explicit Description of Our Support in Job Advertisements: At Kanazawa Univ. we have a few attractive support systems for female researchers. For example, we support hiring a research assistant for a researcher who is restarting their research activities after raising children or nursing care. However, we have not made efforts to appeal it to job applicants. Thus, we changed our format for the job advertisement so that these systems are more explicitly described.

Comment 3 *"Hold meetings more often. T-meetings are being held to facilitate communications between young researchers, but the frequency of once per month is too low. Deep discussions between the SPM and other fields are essential. Seminars/meetings would enhance interaction among the members, pro-mote collaboration, and help to build a more cohesive structure along with a "sense of belonging" to the institute. Holding a retreat involving all the members of NanoLSI may also be a good idea."*

We have been organizing many meetings in different scales. In FY2019, we had symposiums (6), Open seminars (28), NanoLSI colloquiums (2), and T-meetings (31). In addition, we introduced the following events;

Luncheon Meetings: We have started to have an hour luncheon meeting every week, where one of the young researchers give a short presentation to introduce their backgrounds and research interests. These events give us an opportunity to learn more about individual members and to have a chat.

NanoLSI Retreat: We decided to have a retreat event every year. Participants to the event include not only staff members but also students in each lab. We planned to have the first event on 17-18 April, 2020 at Hotel Arrowle at Kaga Area of Ishikawa Prefecture with ~80 participants. Although this event was postponed due to the new coronavirus outbreak, we plan to have it as soon as the situation is recovered.

Comment 4 *"Consider in a realistic way a goal-oriented strategy for the fusion between BioSPM and supramolecular chemistry. Development of new sensors to be installed into the nanoprobes would be a key to creating innovative methodology. It is important to consider how such technologies enable analyses that are not possible with other tools."*

Active Discussions: We have been seriously considering this point since the start of NanoLSI. In particular, in the last FY, we had intensive discussions by having symposium specifically focusing on bio-chem collaborations, joint symposium with iCeMS, an Advisory Board meeting with Prof. Suga at Univ. Tokyo, and many meetings within NanoLSI. Through these discussions, we summarized the following

strategies:

Target Molecules: While many fluorescent probes have been developed so far, there remain molecules whose functions are not fully understood and whose binder proteins are difficult to explore. Among them, we select molecules whose design and synthesis can be effectively performed by our unique expertise in complex chemistry and host-guest chemistry. Several examples are shown below.

(1) Chiral molecules: D-amino acids (Prof. Akine)
(2) Oligosaccharides: disaccharides and trisaccharides (Prof. MacLachlan & Prof. Akine)
(3) Ions with different charges: Fe^{2+} and Fe^{3+} ions (Prof. Akine)
(4) Metabolites: 1-MNA (Prof. Ogoshi)

While (1) is important for neurodegenerative diseases, (2)-(4) are for cancer metabolism.

Integration into Nanoprobes: One of the major issues of the synthesized molecular sensors is their specificity and sensitivity. To overcome these difficulties, we plan to use our expertise in polymer science (Prof. Maeda) and SICM technology (Prof. Korchev). Here, we integrate a polymer gel at the end of a nanopipette. By functionalizing the polymer with many sensor molecules, we can improve the overall sensitivity. In addition, by adjusting the pore size of the polymer gel, we can control the size of the molecules that interact with the sensor molecules and thereby improve the selectivity. This approach is applicable to a wide range of molecular binders. In contrast to a fluorescent probe design, we do not need to combine the binder to a fluorescent part, which allows us to explore a wider range of binder design.

Responses to Follow-Up Report

Comment 1 *"Define the activities of the foreign PIs at NanoLSI more explicitly."*
Comment 2 *"Improve the gender balance."*
Comment 3 *"Hold meetings more often. What is important here is to provide an environment where people, young researchers in particular, meet naturally and automatically."*
Comment 4 *"Consider in a realistic way a goal-oriented strategy for fusion between BioSPM and supramolecular chemistry."*

Responses to these comments have been described in the above responses to the site visit report.

Comment 5 *"As for the formation of a new graduate course, care should be taken to secure more autonomous and fusion science than in old departments."*

A response to this comment has been included in "5. Efforts to Secure the Center's Future Development over the Mid- to Long-term."

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

1. Refereed Papers

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

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

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

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

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

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

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

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

A. WPI papers

1. Original articles

1) Araiso Y, Tsutsumi A, Qiu J, Imai K, Shiota T, Song J, Lindau C, Wenz L-S, Sakaue H, Yunoki K, Kawano S, Suzuki J, Wischnewski M, Schütze C, Ariyama H, Ando T, Becker T, Lithgow T, Wiedemann N, Pfanner N, Kikkawa M, Endo T "Structure of the mitochondrial import gate reveals distinct preprotein paths", Nature 575 (2019) 395-401 (IF=43.07)
2) Shihoya W, Inoue K, Singh M, Konno M, Hososhima S, Yamashita K, Ikeda K, Higuchi A, Izume T, Okazaki S, Hashimoto M, Mizutori R, Tomida S, Yamauchi Y, Abe-Yoshizumi R, Katayama K, Tsunoda SP, Shibata M, Furutani Y, Pushkarev A, Béjà O, Uchihashi T, Kandori H, Nureki O "Crystal structure of heliorhodopsin", Nature 574 (2019) 132-136 (IF=43.07)
3) Cao Y, Lewis L, Hamad WY, MacLachlan MJ "Pressure-Responsive Hierarchical Chiral Photonic Aerogels", Adv Mater 31 (2019) 1808186 (IF=25.809)

4) Hasegawa T, Kikuta J, Sudo T, Matsuura Y, Matsui T, Simmons S, Ebina K, Hirao M, Okuzaki D, Yoshida Y, Hirao A, Kalinichenko VV, Yamaoka K, Takeuchi T, Ishii M "Identification of a novel arthritis-associated osteoclast precursor macrophage regulated by FoxM1", Nat. Immunol. 20 (2019) 1631-1643 (IF=23.53)
5) Han T-S, Voon DC-C, Oshima H, Nakayama M, Echizen K, Sakai E, Yong ZWE, Murakami K, Yu L, Minamoto T, Ock C-Y, Jenkins BJ, Kim S-J, Yang H-K, Oshima M "Interleukin 1 Up-regulates MicroRNA 135b to Promote Inflammation-Associated Gastric Carcinogenesis in Mice", Gastroenterology 156 (2019) 1140-11550000 (IF=19.809)
6) Nguyen T-D, Li J, Lizundia E, Niederberger M, Hamad WY, MacLachlan MJ "Black Titania with Nanoscale Helicity", Adv. Funct. Mater. 29 (2019) 1904639 (IF=15.621)
7) Sakata Y, Tamiya M, Okada M, Akine S "Switching of Recognition First and Reaction First Mechanisms in Host-Guest Binding Associated with Chemical Reactions", J. Am. Chem. Soc. 141 (2019) 15597-15604 (IF=14.695)
8) Wada Y, Shinohara K-I, Asakawa H, Matsui S, Taima T, Ikai T "One-Step Synthesis of One-Dimensional Supramolecular Assemblies Composed of Helical Macromolecular Building Blocks", J. Am. Chem. Soc. 141 (2019) 13995-14002 (IF=14.695)
9) Hirose D, Isobe A, Quiñoá E, Freire F, Maeda K "Three-State Switchable Chiral Stationary Phase Based on Helicity Control of an Optically Active Poly(phenylacetylene) Derivative by Using Metal Cations in the Solid State", J. Am. Chem. Soc. 141 (2019) 8592-8598 (IF=14.695)
10) Ishidate R, Markvoort AJ, Maeda K, Yashima E "Unexpectedly Strong Chiral Amplification of Chiral/Achiral and Chiral/Chiral Copolymers of Biphenylylacetylenes and Further Enhancement/Inversion and Memory of the Macromolecular Helicity", J. Am. Chem. Soc. 141 (2019) 7605-7614 (IF=14.695)
11) Ogoshi T, Maruyama K, Sakatsume Y, Kakuta T, Yamagishi T-A, Ichikawa T, Mizuno M "Guest Vapor-Induced State Change of Structural Liquid Pillar[6]arene", J. Am. Chem. Soc. 141 (2019) 785-789 (IF=14.695)
12) An C, Xu Z, Shen W, Zhang R, Sun Z, Tang S, Xiao Y-F, Zhang D, Sun D, Hu X, Hu C, Yang L, Liu J "The Opposite Anisotropic Piezoresistive Effect of ReS 2", ACS Nano 13 (2019) 3310-3319 (IF=13.903)
13) Maruyama S, Suzuki K, Imamura M, Sasaki H, Matsunami H, Mizutani K, Saito Y, Imai FL, Ishizuka-Katsura Y, Kimura-Someya T, Shirouzu M, Uchihashi T, Ando T, Yamato I, Murata T "Metastable asymmetrical structure of a shaftless V 1 motor", Sci. Adv. 5 (2019) eaau8149 (IF=12.804)
14) Sumino A, Sumikama T, Uchihashi T, Oiki S "High-speed AFM reveals accelerated binding of agitoxin-2 to a K+ channel by induced fit", Sci. Adv. 5 (2019) eaax0495 (IF=12.804)
15) Shimoi M, Maeda K, Geib SJ, Curran DP, Taniguchi T "Esters as Radical Acceptors: β-NHC-Borylalkenyl Radicals Induce Lactonization by C–C Bond Formation/Cleavage on Esters", Angew. Chem. Int. Ed. 58 (2019) 6357-6361 (IF=12.257)
16) Sakai K, Passioura T, Sato H, Ito K, Furuhashi H, Umitsu M, Takagi J, Kato Y, Mukai H, Warashina S, Zouda M, Watanabe Y, Yano S, Shibata M, Suga H, Matsumoto K "Macrocyclic peptide-based inhibition and imaging of hepatocyte growth factor", Nat. Chem. Biol. 15 (2019) 598-606

(IF=12.154)

17) Ogoshi T, Sueto R, Yagyu M, Kojima R, Kakuta T, Yamagishi T-A, Doitomi K, Tummanapelli AK, Hirao H, Sakata Y, Akine S, Mizuno M "Molecular weight fractionation by confinement of polymer in one-dimensional pillar[5]arene channels", Nat. Commun. 10 (2019) 479 (IF=11.878)
18) Owa M, Uchihashi T, Yanagisawa H-A, Yamano T, Iguchi H, Fukuzawa H, Wakabayashi K-I, Ando T, Kikkawa M "Inner lumen proteins stabilize doublet microtubules in cilia and flagella", Nat. Commun. 10 (2019) 1143 (IF=11.878)
19) Taniguchi H, Yamada T, Wang R, Tanimura K, Adachi Y, Nishiyama A, Tanimoto A, Takeuchi S, Araujo LH, Boroni M, Yoshimura A, Shiotsu S, Matsumoto I, Watanabe S, Kikuchi T, Miura S, Tanaka H, Kitazaki T, Yamaguchi H, Mukae H, Uchino J, Uehara H, Takayama K, Yano S "AXL confers intrinsic resistance to osimertinib and advances the emergence of tolerant cells", Nat. Commun. 10 (2019) 259 (IF=11.878)
20) Zhang Y, Takahashi Y, Hong SP, Liu F, Bednarska J, Goff PS, Novak P, Shevchuk A, Gopal S, Barozzi I, Magnani L, Sakai H, Suguru Y, Fujii T, Erofeev A, Gorelkin P, Majouga A, Weiss DJ, Edwards C, Ivanov AP, Klenerman D, Sviderskaya EV, Edel JB, Korchev Y "High-resolution label-free 3D mapping of extracellular pH of single living cells", Nat. Commun. 10 (2019) 5610 (IF=11.878)
21) Yamano T, Dobeš J, Vobořil M, Steinert M, Brabec T, Zietara N, Dobešová M, Ohnmacht C, Laan M, Peterson P, Benes V, Sedláček R, Hanayama R, Kolář M, Klein L, Filipp D "Aire-expressing ILC3-like cells in the lymph node display potent APC features", J. Exp. Med. 216 (2019) 1027-1037 (IF=10.892)
22) Nguyen T-D, Lizundia E, Niederberger M, Hamad WY, Maclachlan MJ "Self-Assembly Route to TiO2 and TiC with a Liquid Crystalline Order", Chem. Mater. 31 (2019) 2174-2181 (IF=10.159)
23) Takeda H, Kataoka S, Nakayama M, Ali MAE, Oshima H, Yamamoto D, Park J-W, Takegami Y, An T, Jenkins NA, Copeland NG, Oshima M "CRISPR-Cas9-mediated gene knockout in intestinal tumor organoids provides functional validation for colorectal cancer driver genes", Proc. Natl. Acad. Sci. U. S. A. 116 (2019) 15635-15644 (IF=9.58)
24) Soto MA, Lelj F, MacLachlan MJ "Programming permanent and transient molecular protection: Via mechanical stoppering", Chem. Sci. 10 (2019) 10422-10427 (IF=9.556)
25) Umeda K, Kobayashi K, Minato T, Yamada H "Atomic-Level Viscosity Distribution in the Hydration Layer", Phys Rev Lett 122 (2019) 116001 (IF=9.227)
26) Marino A, Camponovo A, Degl'Innocenti A, Bartolucci M, Tapeinos C, Martinelli C, De Pasquale D, Santoro F, Mollo V, Arai S, Suzuki M, Harada Y, Petretto A, Ciofani G "Multifunctional temozolomide-loaded lipid superparamagnetic nanovectors: Dual targeting and disintegration of glioblastoma spheroids by synergic chemotherapy and hyperthermia treatment", Nanoscale 11 (2019) 21227-21248 (IF=6.97)
27) Echizen K, Horiuchi K, Aoki Y, Yamada Y, Minamoto T, Oshima H, Oshima M "NF-κB-induced NOX1 activation promotes gastric tumorigenesis through the expansion of SOX2-positive epithelial cells", Oncogene 38 (2019) 4250-4263 (IF=6.634)
28) Soto MA, Maclachlan MJ "Disabling Molecular Recognition through Reversible Mechanical Stoppering", Org. Lett. 21 (2019) 1744-1748 (IF=6.555)

29) Sun L, Shigyou K, Ando T, Watanabe S "Thermally Driven Approach to Fill Sub-10-nm Pipettes with Batch Production", Anal. Chem. 91 (2019) 14080-14084 (IF=6.35)
30) Fukuda M, Rodríguez R, Fernández Z, Nishimura T, Hirose D, Watanabe G, Quiñoá E, Freire F, Maeda K "Macromolecular helicity control of poly(phenyl isocyanate)s with a single stimuli-responsive chiral switch", Chem. Commun. 55 (2019) 7906-7909 (IF=6.164)
31) Inomata H, Takahashi Y, Takamatsu D, Kumatani A, Ida H, Shiku H, Matsue T "Visualization of inhomogeneous current distribution on ZrO 2 -coated LiCoO 2 thin-film electrodes using scanning electrochemical cell microscopy", Chem. Commun. 55 (2019) 545-548 (IF=6.164)
32) Hirao T, Hisano N, Akine S, Kihara S-I, Haino T "Ring-Chain Competition in Supramolecular Polymerization Directed by Molecular Recognition of the Bisporphyrin Cleft", Macromolecules 52 (2019) 6160-6168 (IF=5.997)
33) Kose O, Boott CE, Hamad WY, Maclachlan MJ "Stimuli-Responsive Anisotropic Materials Based on Unidirectional Organization of Cellulose Nanocrystals in an Elastomer", Macromolecules 52 (2019) 5317-5324 (IF=5.997)
34) Lewis L, Hatzikiriakos SG, Hamad WY, Maclachlan MJ "Freeze-Thaw Gelation of Cellulose Nanocrystals", ACS Macro Lett. (2019) 486-491 (IF=5.775)
35) Aalbers GJW, Boott CE, D'Acierno F, Lewis L, Ho J, Michal CA, Hamad WY, MacLachlan MJ "Post-modification of Cellulose Nanocrystal Aerogels with Thiol-Ene Click Chemistry", Biomacromolecules 20 (2019) 2779-2785 (IF=5.667)
36) Cirillo F, Lappano R, Bruno L, Rizzuti B, Grande F, Guzzi R, Briguori S, Miglietta AM, Nakajima M, Di Martino MT, Maggiolini M "AHR and GPER mediate the stimulatory effects induced by 3-methylcholanthrene in breast cancer cells and cancer-associated fibroblasts (CAFs)", J. Exp. Clin. Cancer Res. 38 (2019) 335 (IF=5.646)
37) Yasumoto T, Takamura Y, Tsuji M, Watanabe-Nakayama T, Imamura K, Inoue H, Nakamura S, Inoue T, Kimura A, Yano S, Nishijo H, Kiuchi Y, Teplow DB, Ono K "High molecular weight amyloid β1-42 oligomers induce neurotoxicity via plasma membrane damage", FASEB J. 33 (2019) 9220-9234 (IF=5.391)
38) Oshima H, Kok S-Y, Nakayama M, Murakami K, Voon DC-C, Kimura T, Oshima M "Stat3 is indispensable for damage-induced crypt regeneration but not for Wnt-driven intestinal tumorigenesis", FASEB J. 33 (2019) 1873-1886 (IF=5.391)
39) Sakata Y, Chiba S, Miyashita M, Nabeshima T, Akine S "Ligand Exchange Strategy for Tuning of Helicity Inversion Speeds of Dynamic Helical Tri(saloph) Metallocryptands", Chem. Eur. J. 25 (2019) 2962-2966 (IF=5.16)
40) Ogoshi T, Hamada Y, Sueto R, Sakata Y, Akine S, Moeljadi AMP, Hirao H, Kakuta T, Yamagishi T-A, Mizuno M "Host–Guest Complexation Using Pillar[5]arene Crystals: Crystal-Structure Dependent Uptake, Release, and Molecular Dynamics of an Alkane Guest", Chem. Eur. J. 25 (2019) 2497-2502 (IF=5.16)
41) Akine S, Miyashita M, Nabeshima T "A Closed Metallomolecular Cage that can Open its Aperture by Disulfide Exchange", Chem. Eur. J. 25 (2019) 1432-1435 (IF=5.16)
42) Cametti M, Sakata Y, Martí-Rujas J, Akine S "ON/OFF Control of the Flipping Motion of Diuranyl

Bis(Salophen) Macrocycle by Extremely Strong Binding with Fluoride Ion", Inorg. Chem. 58 (2019) 14871-14875 (IF=4.85)

43) Ishidate R, Sato T, Ikai T, Kanoh S, Yashima E, Maeda K "Helicity induction and memory effect in poly(biphenylylacetylene)s bearing various functional groups and their use as switchable chiral stationary phases for HPLC", Polym. Chem. 10 (2019) 6260-6268 (IF=4.76)
44) Kita K, Fukuda K, Takahashi H, Tanimoto A, Nishiyama A, Arai S, Takeuchi S, Yamashita K, Ohtsubo K, Otani S, Yanagimura N, Suzuki C, Ikeda H, Tamura M, Matsumoto I, Yano S "Patient-derived xenograft models of non-small cell lung cancer for evaluating targeted drug sensitivity and resistance", Cancer Sci. 110 (2019) 3215-3224 (IF=4.751)
45) Miao W, Sakai K, Sato H, Imamura R, Jangphattananont N, Takagi J, Nishita M, Minami Y, Matsumoto K "Impaired ligand-dependent MET activation caused by an extracellular SEMA domain missense mutation in lung cancer", Cancer Sci. 110 (2019) 3340-3349 (IF=4.751)
46) Maekawa K, Ri M, Nakajima M, Sekine A, Ueda R, Tohkin M, Miyata N, Saito Y, Iida S "Serum lipidomics for exploring biomarkers of bortezomib therapy in patients with multiple myeloma", Cancer Sci. 110 (2019) 3267-3274 (IF=4.751)
47) Amyot R, Togashi Y, Flechsig H "Analyzing fluctuation properties in protein elastic networks with sequence-specific and distance-dependent interactions", Biomolecules 9 (2019) 549 (IF=4.694)
48) Inoue Y, Ogawa Y, Kinoshita M, Terahara N, Shimada M, Kodera N, Ando T, Namba K, Kitao A, Imada K, Minamino T "Structural Insights into the Substrate Specificity Switch Mechanism of the Type III Protein Export Apparatus", Structure 27 (2019) 965-976000000 (IF=4.576)
49) Kori S, Ferry L, Matano S, Jimenji T, Kodera N, Tsusaka T, Matsumura R, Oda T, Sato M, Dohmae N, Ando T, Shinkai Y, Defossez P-A, Arita K "Structure of the UHRF1 Tandem Tudor Domain Bound to a Methylated Non-histone Protein, LIG1, Reveals Rules for Binding and Regulation", Structure 27 (2019) 485-4960000000 (IF=4.576)
50) Haruyama T, Sugano Y, Kodera N, Uchihashi T, Ando T, Tanaka Y, Konno H, Tsukazaki T "Single-Unit Imaging of Membrane Protein-Embedded Nanodiscs from Two Oriented Sides by High-Speed Atomic Force Microscopy", Structure 27 (2019) 152-160000 (IF=4.576)
51) Miyata K, Kawagoe Y, Tracey J, Miyazawa K, Foster AS, Fukuma T "Variations in Atomic-Scale Step Edge Structures and Dynamics of Dissolving Calcite in Water Revealed by High-Speed Frequency Modulation Atomic Force Microscopy", J. Phys. Chem. C 123 (2019) 19786-19793 (IF=4.309)
52) Xu Y-T, Wang P-X, Maclachlan MJ "Self-Assembly of Two-Dimensional Colloids in Spherical Space", J. Phys. Chem. C 123 (2019) 17049-17055 (IF=4.309)
53) Sun K, Krejči O, Foster AS, Okuda Y, Orita A, Kawai S "Synthesis of Regioisomeric Graphene Nanoribbon Junctions via Heteroprecursors", J. Phys. Chem. C 123 (2019) 17632-17638 (IF=4.309)
54) Jangphattananont N, Sato H, Imamura R, Sakai K, Terakado Y, Murakami K, Barker N, Oshima H, Oshima M, Takagi J, Kato Y, Yano S, Matsumoto K "Distinct localization of mature hgf from its precursor form in developing and repairing the stomach", Int. J. Mol. Sci. 20 (2019) 2955 (IF=4.183)
55) Hartono, Hazawa M, Lim KS, Dewi FRP, Kobayashi A, Wong RW "Nucleoporin Nup58 localizes to centrosomes and mid-bodies during mitosis", Cell Div. 14 (2019) 7 (IF=4.056)
56) Saga Y, Kawano K, Otsuka Y, Imanishi M, Kimura Y, Matsui S, Asakawa H "Selective oxidation of

B800 bacteriochlorophyll a in photosynthetic light-harvesting protein LH2", Sci. Rep. 9 (2019) 3636 (IF=4.011)

57) Sou K, Chan LY, Arai S, Lee C-LK "Highly cooperative fluorescence switching of self-assembled squaraine dye at tunable threshold temperatures using thermosensitive nanovesicles for optical sensing and imaging", Sci. Rep. 9 (2019) 17991 (IF=4.011)
58) Ryoki A, Kimura Y, Kitamura S, Maeda K, Terao K "Does local chain conformation affect the chiral recognition ability of an amylose derivative? Comparison between linear and cyclic amylose tris(3,5-dimethylphenylcarbamate)", J. Chromatogr. A 1599 (2019) 144-151 (IF=3.858)
59) Kikuchi K, Nakamura J, Nagata Y, Tsuchida H, Kakuta T, Ogoshi T, Morisaki Y "Control of Circularly Polarized Luminescence by Orientation of Stacked π-Electron Systems", Chem. Asian J. 14 (2019) 1681-1685 (IF=3.698)
60) Noel JK, Noé F, Daumke O, Mikhailov AS "Polymer-like Model to Study the Dynamics of Dynamin Filaments on Deformable Membrane Tubes", Biophys. J. 117 (2019) 1870-1891 (IF=3.665)
61) Nakano M, Fukami T, Nakajima M "Adenosine deaminases acting on RNA downregulate the expression of constitutive androstane receptor in the human liver-derived cells by attenuating splicing", J. Pharmacol. Exp. Ther. 370 (2019) 408-415 (IF=3.615)
62) Nozaki K, Nakano M, Iwakami C, Fukami T, Nakajima M "RNA editing enzymes modulate the expression of hepatic CYP2B6, CYP2C8, and other cytochrome P450 isoforms", Drug Metab. Dispos. 47 (2019) 639-647 (IF=3.354)
63) Kutsukake T, Furukawa Y, Ondo K, Gotoh S, Fukami T, Nakajima M "Quantitative analysis of UDP-glucuronosyltransferase UGT1A and UGT2B mRNA expression in the rat liver and small intestine: Sex and strain differences", Drug Metab. Dispos. 47 (2019) 38-44 (IF=3.354)
64) Mizuno K, Takeuchi K, Umehara K, Nakajima M "Identification of novel metabolites of vildagliptin in rats: Thiazoline-containing thiol adducts formed via cysteine or glutathione conjugation", Drug Metab. Dispos. 47 (2019) 809-817 (IF=3.354)
65) Sumikama T, Oiki S "Queueing arrival and release mechanism for K+ permeation through a potassium channel", J. Physiol. Sci. 69 (2019) 919-930 (IF=3.341)
66) Sone E, Noshiro D, Ikebuchi Y, Nakagawa M, Khan M, Tamura Y, Ikeda M, Oki M, Murali R, Fujimori T, Yoda T, Honma M, Suzuki H, Ando T, Aoki K "The induction of RANKL molecule clustering could stimulate early osteoblast differentiation", Biochem. Biophys. Res. Commun. 509 (2019) 435-440 (IF=2.705)
67) Ando M, Ishidate R, Ikai T, Maeda K, Yashima E "Helicity Induction and Its Static Memory of Poly(biphenylylacetylene)s Bearing Pyridine N-Oxide Groups and Their Use as Asymmetric Organocatalysts", J Polym Sci Part A 57 (2019) 2481-2490 (IF=2.591)
68) Kobayashi M, Muramatsu K, Haruyama T, Uesugi H, Kikuchi A, Konno H, Noguchi N, Saito Y "Polymerization of Oxidized DJ-1 via Noncovalent and Covalent Binding: Significance of Disulfide Bond Formation", ACS Omega 4 (2019) 9603-9614 (IF=2.584)
69) Sakata Y, Furukawa Y, Akine S "Functionalized metallonanobelt derivatives having quinoxaline scaffold prepared from a common precursor", Tetrahedron Lett. 60 (2019) 2049-2053 (IF=2.259)
70) Koyano Y, Kitahata H, Mikhailov AS "Diffusion in crowded colloids of particles cyclically changing

their shapes", EPL 128 (2019) 40003 (IF=1.886)

71) Gotoh-Saito S, Abe T, Furukawa Y, Oda S, Yokoi T, Finel M, Hatakeyama M, Fukami T, Nakajima M "Characterization of human UGT2A3 expression using a prepared specific antibody against UGT2A3", Drug Metab. Pharmacokinet. 34 (2019) 280-286 (IF=1.874)

72) Watanabe S, Kitazawa S, Sun L, Kodera N, Ando T "Development of high-speed ion conductance microscopy", Rev. Sci. Instrum. 90 (2019) 123704 (IF=1.587)

73) Bahrini I, Hanayama R "Development of a method that delivers drugs to enveloped viruses", Biol. Pharm. Bull. 42 (2019) 977-981 (IF=1.54)

74) Takahashi Y "Bioimaging by a scanning probe microscope using microelectrodes and nanopipettes", Bunseki Kagaku 68 (2019) 33-41 (IF=0.382)

75) Suzuki K, Sentani K, Tanaka H, Yano T, Suzuki K, Oshima M, Yasui W, Tamura A, Tsukita S "Deficiency of Stomach-Type Claudin-18 in Mice Induces Gastric Tumor Formation Independent of H pylori Infection", Cell. Mol. Gastroenterol. Hepatol. 8 (2019) 119-142 (IF= N/A)

76) Takahashi Y, Zhou Y, Fukuma T "In situ chemical sensing by using scanning probe microscope", Folia Pharmacol. Jpn. 153 (2019) 267-272 (IF= N/A)

77) Nakano M, Nakajima M "Most recent findings on microRNA-dependent regulation of drug metabolism", Folia Pharmacol. Jpn. 154 (2019) 28-34 (IF= N/A)

78) Zhang X, Furutachi H, Ohyama Y, Fujinami S, Akine S, Suzuki M "Crystal structure of bis(μ-hydroxo)diiron(III) complex with tripodal ligands having a terminal carboxylate group", X-ray Struct. Anal.Online 35 (2019) 17-19 (IF= N/A)

79) Sekino M, Furutachi H, Tasaki K, Ishikawa T, Fujinami S, Akine S, Sakata Y, Suzuki M, Nomura T, Ogura T, Kitagawa T "Crystal structure of bis(μ-hydroxo)diiron(II) complex with a dinucleating ligand having a butyl linker", X-ray Struct. Anal.Online 35 (2019) 5-7 (IF= N/A)

80) Zhou Y, Saito M, Fukuma T, Takahashi Y "Unlabeled imaging of primary cilia by scanning ion conductance microscopy", Folia Pharmacol. Jpn. 154 (2019) 192-196 (IF= N/A)

81) Yaguchi R, Furutachi H, Shirotsuki S, Zhang X, Ishikawa T, Akine S, Tosha T, Fujinami S, Suzuki M, Kitagawa T "Synthesis and crystal structure of the bis(μ-hydroxo)diiron(II) complex with tridentate ligands having a sterically bulky imidazolyl group", X-ray Struct. Anal.Online 35 (2019) 27-29 (IF= N/A)

82) Yasuda Y, Furutachi H, Hayashi Y, Ishizaki K, Fujinami S, Akine S, Suzuki M, Nagatomo S, Kitagawa T "Crystal structure of μ-Phenoxo-μ-benzoate-bridged dinuclear fe(II) complex with a dinucleating ligand having a sterically bulky imidazolyl group", X-ray Struct. Anal.Online 35 (2019) 11-13 (IF= N/A)

2. Review articles

83) Himanen L, Geurts A, Foster AS, Rinke P "Data-Driven Materials Science: Status, Challenges, and Perspectives", Adv. Sci. 6 (2019) 1900808 (IF=15.804)

84) Ogoshi T, Kakuta T, Yamagishi T-A "Applications of Pillar[n]arene-Based Supramolecular Assemblies", Angew. Chem. Int. Ed. 58 (2019) 2197-2206 (IF=12.257)

85) Ando T "High-speed atomic force microscopy", Curr. Opin. Chem. Biol. 51 (2019) 105-112

(IF=8.544)

86) Nakayama M, Oshima M "Mutant p53 in colon cancer", J.Mol. Cell Biol. 11 (2019) 267-276 (IF=4.671)

87) Flechsig H, Mikhailov AS "Simple mechanics of protein machines", J. R. Soc. Interface 16 (2019) 20190244 (IF=3.224)

88) Fa S, Kakuta T, Yamagishi T-A, Ogoshi T "Conformation and Planar Chirality of Pillar[n]arenes", Chem. Lett. 48 (2019) 1278-1287 (IF=1.485)

3. Proceedings

89) Kolmogorov, V; Alova, A; Yudina, A; Garanina, A; Erofeev, A; Gorelkin, P; Klyachko, N; Kireev, I; Majouga, A; Edwards, C; Korchev, Y; Novak, P "Drug-induced alterations in cancer cell compartments studied by local stiffness measurement via Scanning Ion-Conductance Microscopy", FEBS Open Bio 9 (2019) 168-169 (IF=1.959)

90) Vaneev, A; Lopatuhina, E; Alova, A; Erofeev, A; Gorelkin, P; Krasnovskaya, O; Kolmogorov, V; Korchev, Y; Majouga, A; Edwards, C; Novak, P "Novel rapid method for evaluating of anticancer drugs effect on tumor cells", FEBS Open Bio 9 (2019) 169-170 (IF=1.959)

91) Akasov, R; Vaneev, A; Alova, A; Garanina, A; Erofeev, A; Gorelkin, P; Korchev, Y; Markvicheva, E; Majouga, A "Electrochemical nanoprobe for label-free and real-time analyses of 3D tumor spheroids", FEBS Open Bio 9 (2019) 387-387 (IF=1.959)

4. Other English articles

None

B. WPI-related papers

1. Original articles

92) Gopal S., Chiappini C., Penders J., Leonardo V., Seong H., Rothery S., Korchev Y., Shevchuk A., Stevens M.M. "Porous Silicon Nanoneedles Modulate Endocytosis to Deliver Biological Payloads", Adv Mater 31 (2019) 1806788 (IF=21.95)

93) Ikai T., Yoshida T., Shinohara K.-I., Taniguchi T., Wada Y., Swager T.M. "Triptycene-Based Ladder Polymers with One-Handed Helical Geometry", J. Am. Chem. Soc. 141 (2019) 4696-4703 (IF=14.357)

94) Dai Y., Kumar V.P., Zhu C., Wang H., Smith K.J., Wolf M.O., MacLachlan M.J. "Bowtie-Shaped NiCo2O4 Catalysts for Low-Temperature Methane Combustion", Adv. Funct. Mater. 29 (2019) 1807519 (IF=13.325)

95) Kumatani A., Miura C., Kuramochi H., Ohto T., Wakisaka M., Nagata Y., Ida H., Takahashi Y., Hu K., Jeong S., Fujita J.-I., Matsue T., Ito Y. "Chemical Dopants on Edge of Holey Graphene Accelerate Electrochemical Hydrogen Evolution Reaction", Adv. Sci. 6 (2019) 1900119 (IF=12.441)

96) Kose O., Tran A., Lewis L., Hamad W.Y., MacLachlan M.J. "Unwinding a spiral of cellulose nanocrystals for stimuli-responsive stretchable optics", Nat. Commun. 10 (2019) 510 (IF=12.353)

97) Peng S., Wang R., Zhang X., Ma Y., Zhong L., Li K., Nishiyama A., Arai S., Yano S., Wang W. "EGFR-

TKI resistance promotes immune escape in lung cancer via increased PD-L1 expression", Mol. Cancer 18 (2019) 165 (IF=10.679)

98) Hirose D., Kusuma S.B.W., Ina D., Wada N., Takahashi K. "Direct one-step synthesis of a formally fully bio-based polymer from cellulose and cinnamon flavor", Green Chem. 21 (2019) 4927-4931 (IF=9.405)

99) Fukuda K., Takeuchi S., Arai S., Katayama R., Nanjo S., Tanimoto A., Nishiyama A., Nakagawa T., Taniguchi H., Suzuki T., Yamada T., Nishihara H., Ninomiya H., Ishikawa Y., Baba S., Takeuchi K., Horiike A., Yanagitani N., Nishio M., Yano S. "Epithelial-to-mesenchymal transition is a mechanism of ALK inhibitor resistance in lung cancer independent of ALK mutation status", Cancer Res. 79 (2019) 1658-1670 (IF=9.13)

100) Sahoo B.R., Genjo T., Nakayama T.W., Stoddard A.K., Ando T., Yasuhara K., Fierke C.A., Ramamoorthy A. "A cationic polymethacrylate-copolymer acts as an agonist for β-amyloid and an antagonist for amylin fibrillation", Chem. Sci. 10 (2019) 3976-3986 (IF=9.063)

101) Ikai T., Takayama K., Wada Y., Minami S., Apiboon C., Shinohara K.-I. "Synthesis of a one-handed helical polythiophene: A new approach using an axially chiral bithiophene with a fixed: Syn - conformation", Chem. Sci. 10 (2019) 4890-4895 (IF=9.063)

102) O'Keeffe O., Wang P.-X., Hamad W.Y., Maclachlan M.J. "Boundary Geometry Effects on the Coalescence of Liquid Crystalline Tactoids and Formation of Topological Defects", J. Phys. Chem. Lett. 10 (2019) 278-282 (IF=8.709)

103) Nakakubo K., Hasegawa H., Ito M., Yamazaki K., Miyaguchi M., Biswas F.B., Ikai T., Maeda K. "Dithiocarbamate-modified cellulose resins: A novel adsorbent for selective removal of arsenite from aqueous media", J. Hazard. Mater. 380 (2019) 120816 (IF=7.65)

104) Nguyen T.-D., MacLachlan M.J. "Double Twisted Photonic Honeycomb Frameworks with Mesoporous Structures", Adv. Opt. Mater. 7 (2019) 1801275 (IF=7.43)

105) Nishimura T., Nakata A., Chen X., Nishi K., Meguro-Horike M., Sasaki S., Kita K., Horike S.-I., Saitoh K., Kato K., Igarashi K., Murayama T., Kohno S., Takahashi C., Mukaida N., Yano S., Soga T., Tojo A., Gotoh N. "Cancer stem-like properties and gefitinib resistance are dependent on purine synthetic metabolism mediated by the mitochondrial enzyme MTHFD2", Oncogene 38 (2019) 2464-2481 (IF=6.854)

106) Ono T., Tsukiyama Y., Hatanaka S., Sakatsume Y., Ogoshi T., Hisaeda Y. "Inclusion crystals as vapochromic chemosensors: Fabrication of a mini-sensor array for discrimination of small aromatic molecules based on side-chain engineering of naphthalenediimide derivatives", J. Mater. Chem. C 7 (2019) 9726-9734 (IF=6.641)

107) Carta V., Soto M.A., Maclachlan M.J. "Ligand-modulated ring-expansion", Chem. Commun. 55 (2019) 1245-1248 (IF=6.29)

108) Trush O., Liu C., Han X., Nakai Y., Takayama R., Murakawa H., Carrillo J.A., Takechi H., Burk K., Hakeda-Suzuki S., Sato M., Suzuki T. "N-Cadherin Orchestrates Self-Organization of Neurons within a Columnar Unit in the Drosophila Medulla", J. Neurosci. 39 (2019) 5861-5880 (IF=6.074)

109) Chang C.Y., Jeon S.-B., Yoon H.J., Choi B.-K., Kim S.S., Oshima M., Park E.J. "Glial TLR2-driven innate immune responses and CD8 + T cell activation against brain tumor", GLIA 67 (2019) 1179-

1195 (IF=5.846)

110) Watanabe Y., Nagai Y., Honda H., Okamoto N., Yanagibashi T., Ogasawara M., Yamamoto S., Imamura R., Takasaki I., Hara H., Sasahara M., Arita M., Hida S., Taniguchi S., Suda T., Takatsu K. "Bidirectional crosstalk between neutrophils and adipocytes promotes adipose tissue inflammation", FASEB J. 33 (2019) 11821-11835 (IF=5.391)

111) Ali T., Bednarska J., Vassilopoulos S., Tran M., Diakonov I.A., Ziyadeh-Isleem A., Guicheney P., Gorelik J., Korchev Y.E., Reilly M.M., Bitoun M., Shevchuk A. "Correlative SICM-FCM reveals changes in morphology and kinetics of endocytic pits induced by disease-associated mutations in dynamin", FASEB J. 33 (2019) 8504-8518 (IF=5.391)

112) Wang R., Yamada T., Arai S., Fukuda K., Taniguchi H., Tanimoto A., Nishiyama A., Takeuchi S., Yamashita K., Ohtsubo K., Matsui J., Onoda N., Hirata E., Taira S., Yano S. "Distribution and Activity of Lenvatinib in Brain Tumor Models of Human Anaplastic Thyroid Cancer Cells in Severe Combined Immune Deficient Mice", Mol. Cancer Ther. 18 (2019) 947-956 (IF=5.365)

113) Inada M., Kinoshita M., Sumino A., Oiki S., Matsumori N. "A concise method for quantitative analysis of interactions between lipids and membrane proteins", Anal. Chim. Acta 1059 (2019) 103-112 (IF=5.123)

114) Cao D., Wu Y., Jia Z., Zhao D., Zhang Y., Zhou T., Wu M., Zhang H., Tsukamoto T., Oshima M., Jiang J., Cao X. "18β-glycyrrhetinic acid inhibited mitochondrial energy metabolism and gastric carcinogenesis through methylation-regulated TLR2 signaling pathway", Carcinogenesis 40 (2019) 234-245 (IF=5.072)

115) Fleming D.G., Macfarlane W.A., Xiao J., Arseneau D.J., Dehn M.H., Kiefl R.F., Zamarion V.M., Wang P.-X., Cao Y., Maclachlan M.J., Bridges M.D. "Studies of Muonium Reactivity with Uncapped Gold Nanoparticles and with Surface-Adsorbed Benzene on These NPs in Porous Silica Hosts", J. Phys. Chem. C 123 (2019) 27628-27642 (IF=4.309)

116) Boer S.A., Wang P.-X., Maclachlan M.J., White N.G. "Open Pentiptycene Networks Assembled through Charge-Assisted Hydrogen Bonds", Cryst. Growth Des. 19 (2019) 4829-4835 (IF=4.153)

117) Okada H., Nakanishi C., Yoshida S., Shimojima M., Yokawa J., Mori M., Tada H., Yoshimuta T., Hayashi K., Yamano T., Hanayama R., Yamagishi M., Kawashiri M.-A. "Function and Immunogenicity of Gene-corrected iPSC-derived Hepatocyte-Like Cells in Restoring Low Density Lipoprotein Uptake in Homozygous Familial Hypercholesterolemia", Sci. Rep. 9 (2019) 4695 (IF=4.122)

118) Kitabayashi T., Dong Y., Furuta T., Sabit H., Jiapaer S., Zhang J., Zhang G., Hayashi Y., Kobayashi M., Domoto T., Minamoto T., Hirao A., Nakada M. "Identification of GSK3β inhibitor kenpaullone as a temozolomide enhancer against glioblastoma", Sci. Rep. 9 (2019) 10049 (IF=4.011)

119) Shimagaki T., Yoshio S., Kawai H., Sakamoto Y., Doi H., Matsuda M., Mori T., Osawa Y., Fukai M., Yoshida T., Ma Y., Akita T., Tanaka J., Taketomi A., Hanayama R., Yoshizumi T., Mori M., Kanto T. "Serum milk fat globule-EGF factor 8 (MFG-E8) as a diagnostic and prognostic biomarker in patients with hepatocellular carcinoma", Sci. Rep. 9 (2019) 15788 (IF=4.011)

120) Dodo K., Kuboki E., Shimizu T., Imamura R., Magarisawa M., Takahashi M., Tokuhiro T., Yotsumoto S., Asano K., Nakao S., Terayama N., Suda T., Tanaka M., Sodeoka M. "Development of a Water-Soluble Indolylmaleimide Derivative IM-93 Showing Dual Inhibition of Ferroptosis and NETosis", ACA

Med. Chem. Lett. 10 (2019) 1272-1278 (IF=3.737)

121) Murakami M., Kohara S., Kitamura N., Akola J., Inoue H., Hirata A., Hiraoka Y., Onodera Y., Obayashi I., Kalikka J., Hirao N., Musso T., Foster A.S., Idemoto Y., Sakata O., Ohishi Y. "Ultrahigh-pressure form of Si O2 glass with dense pyrite-type crystalline homology", Phys. Rev. B 99 (2019) 45153 (IF=3.736)

122) Söngen H., Morais Jaques Y., Zivanovic L., Seibert S., Bechstein R., Spijker P., Onishi H., Foster A.S., Kühnle A. "Hydration layers at the graphite-water interface: Attraction or confinement", Phys. Rev. B 100 (2019) 205410 (IF=3.736)

123) Buzzelli J.N., O'Connor L., Scurr M., Chung Nien Chin S., Catubig A., Ng G.Z., Oshima M., Oshima H., Giraud A.S., Sutton P., Judd L.M., Menheniott T.R. "Overexpression of IL-11 promotes premalignant gastric epithelial hyperplasia in isolation from germline gp130-JAK-STAT driver mutations", Am. J. Physiol.-Gastr. L. 316 (2019) G251-G262 (IF=3.293)

124) Hansen P.E., Kamounah F.S., Saeed B.A., MacLachlan M.J., Spanget-Larsen J. "Intramolecular hydrogen bonds in normal and sterically compressed o-hydroxy aromatic aldehydes. Isotope effects on chemical shifts and hydrogen bond strength", Molecules 24 (2019) 4533 (IF=3.06)

125) Ruscher C., Rottler J., Boott C.E., Maclachlan M.J., Mukherji D. "Elasticity and thermal transport of commodity plastics", Phys. Rev. Mater. 3 (2019) 125604 (IF=2.926)

126) Anand U., Korchev Y., Anand P. "The role of urea in neuronal degeneration and sensitization: An in vitro model of uremic neuropathy", Mol. pain 15 (2019) 1744806919881038 (IF=2.746)

127) Ohashi R., Michal C.A., Hamad W.Y., Nguyen T.-D., Mizuno M., MacLachlan M.J. "Solid-state 23Na NMR spectroscopy studies of ordered and disordered cellulose nanocrystal films", Solid State Nucl. Mag. 97 (2019) 31-39 (IF=2.674)

128) Kimura T., Kawaguchi T., Chiba Y., Yoshioka H., Watanabe K., Kijima T., Kogure Y., Oguri T., Yoshimura N., Niwa T., Kasai T., Hayashi H., Ono A., Asai K., Tanaka H., Yano S., Yamamoto N., Nakanishi Y., Nakagawa K. "Phase I/II study of intermitted erlotinib in combination with docetaxel in patients with recurrent non-small cell lung cancer (WJOG4708L)", Jpn. J. Clin. Oncol. 49 (2019) 947-955 (IF=2.183)

129) Ohtsubo K., Miyake K., Arai S., Fukuda K., Yanagimura N., Suzuki C., Otani S., Adachi Y., Tanimoto A., Nishiyama A., Yamashita K., Takeuchi S., Notohara K., Yoshimura K., Yano S. "Aberrant methylation of tumor suppressive miRNAs in bile from patients with pancreaticobiliary diseases", Anticancer Res. 39 (2019) 5449-5459 (IF=1.935)

130) Staub Y., Nishiyama A., Suga Y., Fujita M., Matsushita R., Yano S. "Clinical Characteristics Associated with Lenvatinib-induced Fistula and Tumor-related Bleeding in Patients with Thyroid Cancer", Anticancer Res. 39 (2019) 3871-3878 (IF=1.935)

131) Ohta A., Hossain F., Asakawa H., Asakawa T. "Study of the Antioxidative Properties of Several Amino Acid-Type Surfactants and their Synergistic Effect in Mixed Micelle", J. Surfactants Deterg. 23 (2019) 99-108 (IF=1.672)

132) Kusuma S.B.W., Hirose D., Takahashi K. "Transesterification reaction of cellulose with inactive esters in ionic liquids acting as both catalysts and solvents", Chem. Lett. 48 (2019) 1122-1125 (IF=1.485)

133) Sakamoto H., Koto A., Takamura E.-I., Asakawa H., Fukuma T., Satomura T., Suye S.-I. "Development of Biofuel Cell Using a Complex of Highly Oriented Immobilized His-Tagged Enzyme and Carbon Nanotube Surface Through a Pyrene Derivative", J Nanosci. Nanotechno. 19 (2019) 3551-3557 (IF=1.354)

134) Kumatani A., Takahashi Y., Miura C., Ida H., Inomata H., Shiku H., Munakata H., Kanamura K., Matsue T. "Scanning electrochemical cell microscopy for visualization and local electrochemical activities of lithium-ion (de) intercalation process in lithium-ion batteries electrodes", Surf. Interface Anal. 51 (2019) 27-30 (IF=1.263)

135) Asakawa T., Fujii A., Yoneda N., Ohta A., Asakawa H. "Enhanced Aggregation of Stimuli Responsive Surfactants by Esterolytic Reactions", J. Oleo Sci. 68 (2019) 573-580 (IF=1.208)

136) Yamamoto S., Ohta A., Hossain F., Anjani G., Asakawa H., Asakawa T. "Solubilization of genistein in phospholipid vesicles and their atioxidant capacity", Journal of Oleo Science 68 (2019) 61-66 (IF=1.182)

137) Theansungnoen T., Jangpromma N., Anwised P., Daduang S., Fukumori Y., Taoka A., Klaynongsruang S. "Membranolytic Effects of KT2 on Gram-Negative Escherichia coli Evaluated by Atomic Force Microscopy", Appl. Biochem Micro. 55 (2019) 495-505 (IF=0.727)

2. Review articles

None

3. Proceedings

None

4. Other English articles

138) Adachi Y., Yano S. "Caput Medusae-like Venous Dilatation in Lung Cancer", Internal Med. 58 (2019) 3341-3342 (IF=0.956)

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

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

Date(s)	Lecturer/Presenter's name	Presentation title	Conference name
Dec. 14, 2019	Masanobu Oshima	Multistep tumorigenesis and polyclonal metastasis of colon cancer	24th Annual Meeting of the Korean Society of Cancer Prevention
Dec. 12, 2019	Seiji Yano	Drug-tolerant persister cells and AXL	The 24th JFCR-ISCC
Dec. 2, 2019	Alexander S. Mikhailov	Simple mechanics of protein machines	21st RIES-Hokudai International Symposium
Nov. 13, 2019	Masanobu Oshima	Biological mechanism of polyclonal metastasis of colorectal cancer	50th International Symposium of the Princess Takamatsu Cancer Research Fund
Oct. 26, 2019	Shigehisa Akine	Novel metallo-molecular host molecules with open/close functions	12th China-Japan Joint Symposium on Metal Cluster Compounds
Sep. 4, 2019	Toshio Ando	High-speed AFM in Bio-Med: Its current state and future prospects	AFM BioMed Conference 2019 (Münster, Germany)
Aug. 13, 2019	Takeshi Fukuma	Visualizing Nanoscale Distribution of Corrosion Reaction Sites in Copper Fine Wires by Open-loop Electric Potential Microscopy	The 23rd International Symposium on Chemical-Mechanical Planarization
Jul. 11, 2019	Mark J. MacLachlan	New Materials from the Chiral Nematic Liquid Crystalline Phase of Cellulose Nanocrystals	Gordon Research Conference on Liquid Crystals
June 13, 2019	Tomoki Ogoshi	Assembly of Pillar[n]arenes for Molecular Scale Porous Materials	15th International Conference on Calixarenes (Calix 2019)
Apr. 8, 2019	Toshio Ando	High-speed AFM	The 23rd International Symposium on Chemical-Mechanical Planarization

3. Major Awards

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

Date	Recipient's name	Name of award
Mar., 2020	Tomoyoshi Yamano	The 48th Annual Meeting of the Japanese Society for Immunology, Best Presentation Award
Jan., 2020	Yasufumi Takahashi	Nakatani Award（Incentive Prize）
Nov. 8, 2019	Ayumi Sumino	Nanoprobe Technology Committee (JSPS No. 167 Committee) Nanoprobe Technology Incentive Award
Nov., 2019	Takeshi Fukuma	Nanoprobe Technology Committee (JSPS No. 167 Committee) Nanoprobe Technology Award
Sep., 2019	Ayumi Sumino	Incentive Award of the 66th Toxin Symposium
Sep., 2019	AKINE Shigehisa	JSCC Award for Creative Work
July, 2019	Yuko Tadokoro	The 15th Meeting of Young Investigators in Hematology (KIRIN-JUKU) Kirinji-Award
June, 2019	Masaharu Hazawa	The 57th Academic Conference of Biological Committee of Japanese Society for Radiation Oncology, Biological Committee Incentive Award
May 24, 2019	Tomoki Ogoshi	Kao Science Award 2019
Apr., 2019	Hitoshi Asakawa	Young Scientists' Prize from MEXT

Appendix 2 FY 2019 List of Principal Investigators

NOTE:

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

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

<Results at the end of FY2019> **Principal Investigators Total: 16**

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 Takeshi Fukuma	43	Nano Life Science Institute, Institute for Frontier Science Initiative	Doctor of Engineering, Electrical engineering, Nanometrology	90	October, 2017	usually stays at the institute	
Adam Stuart Foster	44	Department of Applied Physics, Aalto University	PhD in Theoretical Solid State Physics	30	October, 2017	Stays at the institute 30 days or more/per fiscal year	-Promotes understanding of the real image from the observation image while working toward the development of new nanoprobe technology -In charge of NanoLSI Educational Program at the Graduate School - In charge of Selection Committee of Jr.PI
Yuri Korchev	59	Department of Medicine, Imperial College London	Ph.D. in Biophysics and Cytology, Biophysics	30	October, 2017	Stays at the institute 30 days or more/per fiscal year	-Engaged in measuring the distribution of substances inside and outside the cell while working toward the development of new nanoprobe technology -In charge of the 2nd NanoLSI International Symposium in London held on November 19, 2018
Mark MacLachlan	46	Department of Chemistry, University of British Columbia	PhD in Chemistry	30	October, 2017	Stays at the institute 30 days or more/per fiscal year	-Engaged in development of supramolecular nanoprobes while working toward the development of new nanoprobe technology - In charge of the 3rd NanoLSI International Symposium held on August 8, 2019 at UBC

Alexander S. Mikhailov	69	Department of Physical Chemistry, Fritz Haber Institute of the Max Planck Society	Doctor of Science, Theoretical Physics, Chemical Physics, Biophysics	40	October, 2017	Stays at the institute 90 days or more/per fiscal year	-Promotes understanding of the real image from the observation image while working toward the development of new nanoprobe technology -In charge of NanoLSI Educational Program at the Graduate School -In charge of Selection Committee of Jr.PI
Richard W. Wong	45	Nano Life Science Institute, Institute for Frontier Science Initiative	Doctor of Medicine, Molecular cell biology	90	October, 2017	usually stays at the institute	
Toshio Ando	69	Nano Life Science Institute, Institute for Frontier Science Initiative	Doctor of Science, Biophysics and Nano-Bioscience	90	October, 2017	usually stays at the institute	
Rikinari Hanayama	45	Nano Life Science Institute, Institute for Frontier Science Initiative	MD, PhD, Immunology, Cell Biology	90	October, 2017	usually stays at the institute	
Shigehisa Akine	47	Nano Life Science Institute, Institute for Frontier Science Initiative	Doctor of Science, Supramolecular chemistry, Coordination chemistry	90	October, 2017	usually stays at the institute	

Tomoki Ogoshi	43	Graduate School of Engineering, Kyoto University / Nano Life Science Institute, Kanazawa Univeristy	Doctor of Engineering, Supramolecular Chemistry, Structural Organic Chemistry	20	October, 2017	Stays at the institute 20% of the total working days / per year based on the cross-appointment agreement between Kyoto univ. and Kanazawa univ.	Engaged in establishment of Nanoprobe Life Science based on supramolecular chemistry
Katsuhiro Maeda	49	Nano Life Science Institute, Institute for Frontier Science Initiative	Doctor of Engineering, Polymer chemistry	90	October, 2017	usually stays at the institute	
Masanobu Oshima	58	Nano Life Science Institute, Institute for Frontier Science Initiative	D.V.M., Ph.D., Cancer research, Genetics for Cancer modeling	90	October, 2017	usually stays at the institute	
Miki Nakajima	50	Nano Life Science Institute, Institute for Frontier Science Initiative	Doctor of Pharmaceutical Sciences, Drug Metabolism and Toxicology, Clinical Pharmacology	90	October, 2017	usually stays at the institute	
Atsushi Hirao	56	Cancer Research Institute	Doctor of Medicine, Stem Cell Biology	50	October, 2017	usually stays at the institute	
Seiji Yano	54	Cancer Research Institute	MD, PhD, Medical Oncology, Circumvention of targeted drug resistance	50	October, 2017	usually stays at the institute	
Kunio Matsumoto	61	Nano Life Science Institute, Institute for Frontier Science Initiative	Doctor of Philosophy, Biological Chemistry, Tumor Biology	90	October, 2017	usually stays at the institute	

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

Principal investigators unable to participate in project in FY 2019

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

Appendix 3-1 FY 2019 Records of Center Activities

1. Researchers and center staff, satellites, partner institutions

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

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

Special mention

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

Name	Position	employed since	previous institute
Clemens Franz	Jr. PI, TT Associate prof.	September 19 2018	Karlsruhe Institute of Technology, Germany
Satoru Okuda	Jr. PI, TT Associate prof.	April 1 2019	Japan Science and Technology Agency
Satoshi Arai	Jr. PI, TT Associate prof.	July 1 2019	WASEDA Bioscience Research Institute in Singapore (Research Institute for Science and Engineering, Waseda University)
Satoshi Toda	Jr. PI, TT Assistant prof.	October 1 2019	Department of Cellular and Molecular Pharmacology, University of California San Francisco
Yusuke Miyanari	Jr. PI, TT Associate prof.	April 1 2020	Exploratory Research Center on Life and Living Systems, National Institutes of Natural Sciences

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
Imperial College London	Yuri Korchev	Established the Agreement in January 2019 (The effective date is January 15 2019).
University of British Columbia	Mark MacLachlan	Established the Agreement in October 2018 (The effective date is April 2019).

< Partner institutions>

Institution name	Principal Investigator(s), if any	Notes
RIKEN Center for Biosystems Dynamics Research		Established the collaborative research agreement in May 2018
Nikon Instech Co., Ltd.		Established the collaborative research agreement in May 2019
MicroBiology Research Center for Sustinability, Tsukuba University		Established the collaborative research agreement in June 2019

2. Holding international research meetings

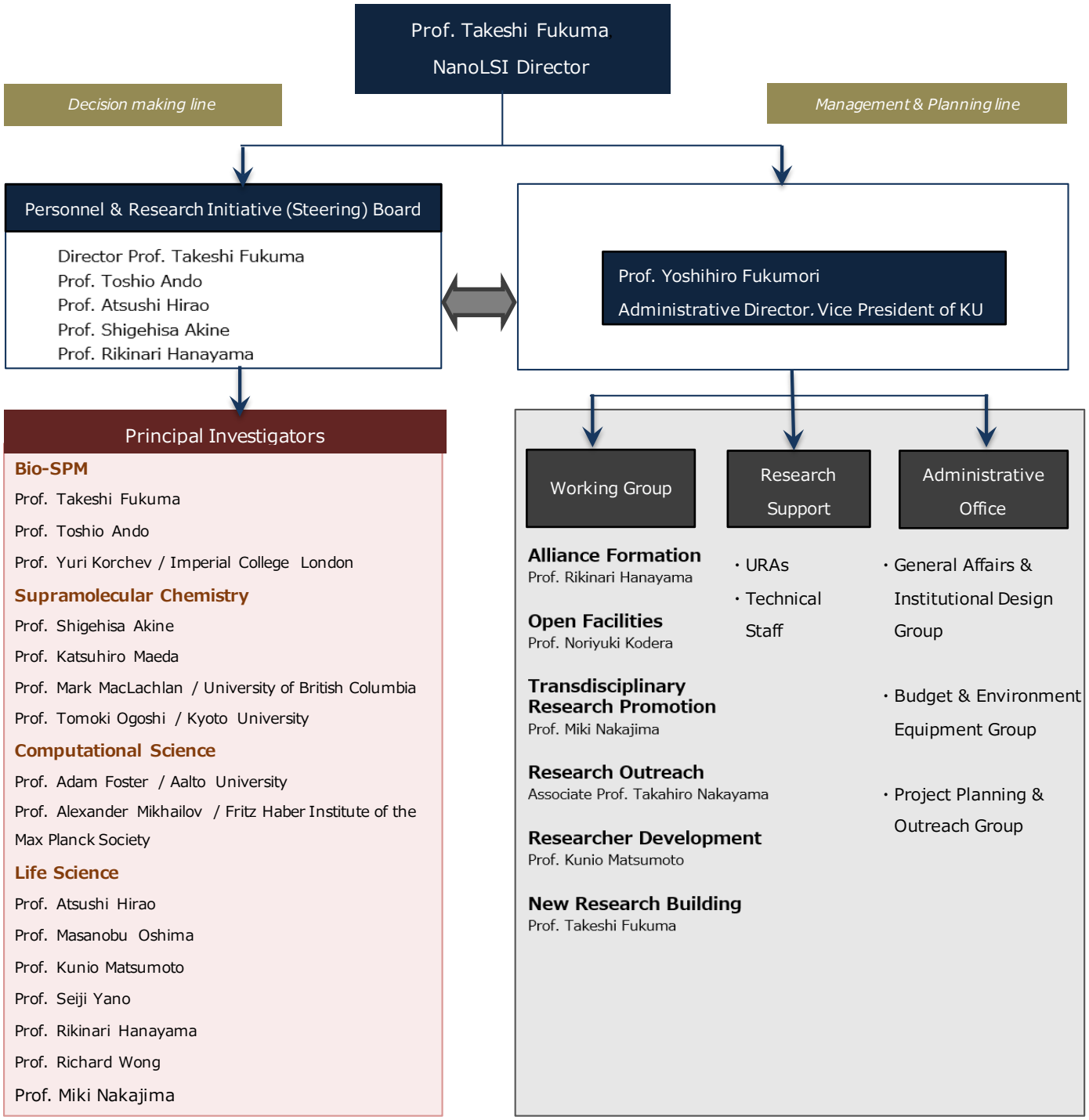
- Indicate the number of international research conferences or symposiums held in FY2019 and give up to three examples of the most representative ones using the table below.

FY 2019: 9 meetings

Major examples (meeting titles and places held)	Number of participants
The 3rd NanoLSI International Symposium – Supramolecular Chemistry and Nanoprobes in Life Sciences – The University of British Columbia, Vancouver 2019.8.8	From domestic institutions: 17 From overseas institutions: 55
International Symposium on Tumor Biology in Kanazawa 2019 Kanazawa University, Kanazawa 2019.10.29	From domestic institutions: 111 From overseas institutions: 4
MLM2020 “The 1st International Conference on Big Data and Machine Learning in Microscopy” Kanazawa University Satellite Plaza, Kanazawa 2020.1.15-17	From domestic institutions: 15 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).

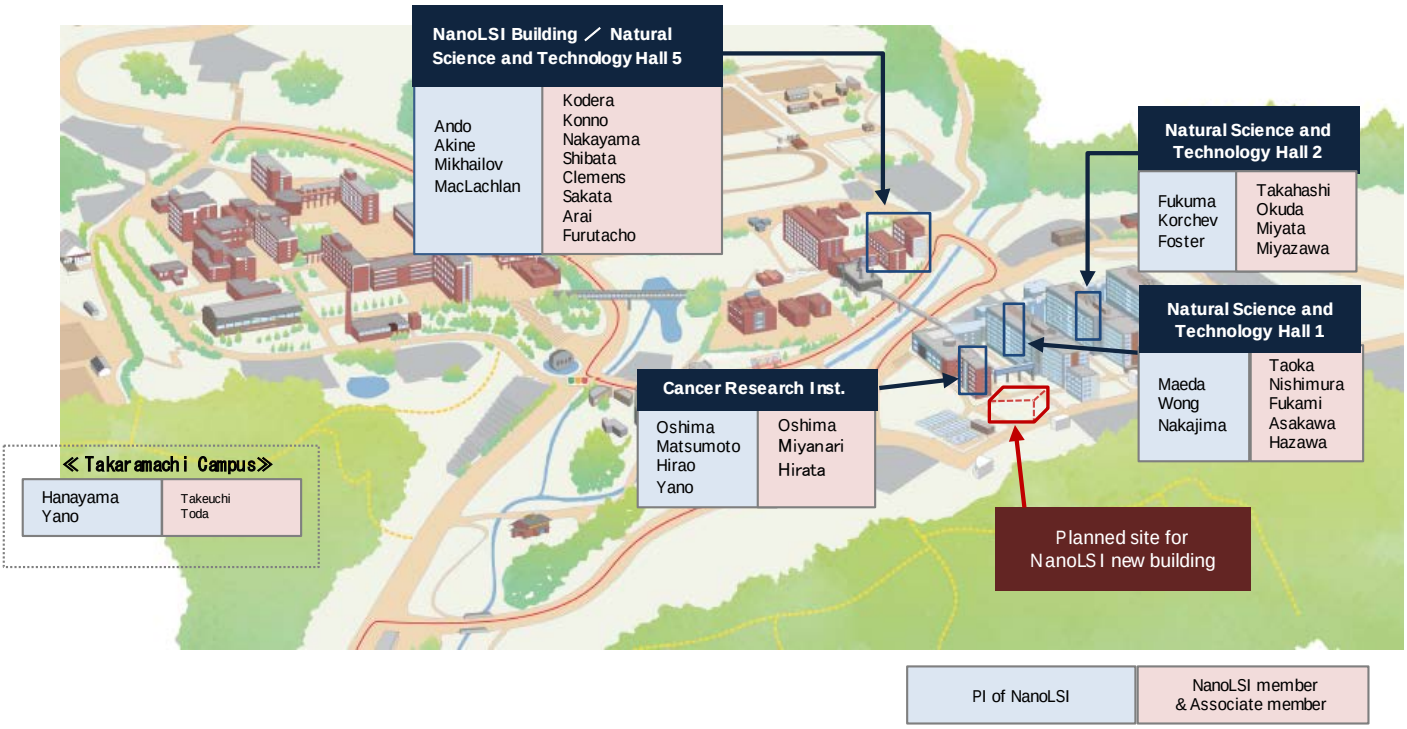


4. Campus Map

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

5. Campus Map

- Please draw a simple map of the campus showing where the main office and principle investigator(s) are located.



5. Securing external research funding*

External research funding secured in FY2019

Total: ¥1,044,068,024

- 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.)

Grant-in-Aid for Scientific Research (S): ¥30,550,000
Grant-in-Aid for Scientific Research (A): ¥25,350,000
JST-CREST: ¥55,640,000
JST-Development of Advanced Measurement and Analysis Systems: ¥34,710,000
AMED Practical Research for Innovative Cancer Control: ¥49,325,000
AMED Practical Research for Innovative Cancer Control: ¥33,580,000

Appendix 3-1a FY 2019 Records of Center Activities

Researchers and other center staff

Number of researchers and other center staff

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

a) Principal Investigators

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

(number of persons)

	At the beginning of project	At the end of FY 2019	Final goal (Date: month, year)
Researchers from within the host institution	12	12	12
Researchers invited from overseas	4	4	4
Researchers invited from other Japanese institutions	0	0	0
Total principal investigators	16	16	16

b) Total members

	At the beginning of project		At the end of FY2019		Final goal (Date: March, 2021)	
	Number of persons	%	Number of persons	%	Number of persons	%
Researchers	63		74		76	
Overseas researchers	22	35%	23	31%	23	30%
Female researchers	8	13%	8	11%	16	21%
Principal investigators	16		16		16	
Overseas PIs	5	31%	5	31%	5	31%
Female PIs	1	6%	1	6%	1	6%
Other researchers	48		56		60	
Overseas researchers	16	33%	17	30%	18	30%
Female researchers	7	15%	7	13%	15	25%
Postdocs	2		2		0	
Overseas postdocs	1	50%	1	50%	0	0%
Female postdocs	0	0%	0	0%	0	0%
Research support staffs	29		29		20	
Administrative staffs	23		24		25	
Total number of people who form the "core" of the research center	115		127		121	

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 and administrative director	23.0	9.2
	Principal investigators (no. of persons):11	157.7	50.1
	Junior Principal investigators (no. of persons):5	42.9	35.0
	Other researchers (no. of persons):54	233.0	139.1
	Research support staff (no. of persons):12	56.5	53.3
	Administrative staff (no. of persons):24	115.5	55.8
	Remuneration for RA(Research Assistant)	11.6	11.6
	Subtotal	640.2	354.1
Project activities	Gratuities and honoraria paid to invited principal investigators (no. of persons):3	8.6	8.6
	Research startup cost (no. of persons):11	41.8	41.8
	Cost of satellite organizations (no. of satellite organizations):2	18.5	18.5
	Cost of international symposiums (no. of symposiums):3	2.3	2.3
	Facility expenses	26.0	6.1
	Cost of consumables	62.1	62.1
	Cost of utilities	13.2	13.2
	Other costs	38.8	38.8
	Subtotal	211.3	191.4
Travel	Domestic travel costs	7.0	7.0
	Overseas travel costs	12.5	12.5
	Travel and accommodations cost for invited scientists (no. of domestic scientists):12 (no. of overseas scientists):12	10.9	10.9
	Travel cost for scientists on transfer (no. of domestic scientists):2 (no. of overseas scientists):5	2.2	2.2
	Subtotal	32.6	32.6
Equipment	Depreciation of buildings	0.1	0.1
	Depreciation of equipment	2.9	2.9
	Subtotal	3.0	3.0
Research projects (Detail items must be fixed)	Project supported by other government subsidies, etc. *1	116.4	0.0
	KAKENHI	188.8	0.0
	Commissioned research projects, etc.	233.9	0.0
	Joint research projects	31.5	0.0
	Ohers (donations, etc.)	2.1	0.0
	Subtotal	572.7	0.0
Total		1,459.8	581.1

Costs (Million yens)

WPI grant in FY 2019	670.0
Costs of establishing and maintaining facilities	2.2
Establishing new facilities	0.0
Repairing facilities	0.6
Others	1.6
Costs of equipment procured	89.7
Super resolution microscopy	15.0
STED FES module	15.0
Others	59.7

*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

2) Costs of satellites

(Million yens)

Cost items	Details	Total costs	Amount covered by WPI funding
Personnel	Principal investigators (no. of persons):1		
	Other researchers (no. of persons):4		
	Subtotal	14.1	14.1
Project activities	Subtotal	1.9	1.9
Travel	Subtotal		
Equipment	Subtotal		
Research projects	Subtotal		
Total		16.0	16.0

Appendix 4 FY 2019 Status of Collaboration with Overseas Satellites

1. Coauthored Papers

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

Overseas Satellite 1: **Imperial College London** (Total: 3 papers)

1) Takahashi Y., Kobayashi Y., Wang Z., Ito Y., Ota M., Ida H., Kumatani A., Miyazawa K., Fujita T., Shiku H., *Korchev Y.E.*, Miyata Y., Fukuma T., Chen M., Matsue T. "High-Resolution Electrochemical Mapping of the Hydrogen Evolution Reaction on Transition-Metal Dichalcogenide Nanosheets", Angewandte Chemie - International Edition 59 (2020) 3601-3608 (IF=12.257)

2) (Appendix 1 #20) Zhang Y., Takahashi Y., Hong S.P., Liu F., Bednarska J., Goff P.S., Novak P., Shevchuk A., Gopal S., Barozzi I., Magnani L., Sakai H., Suguru Y., Fujii T., Erofeev A., Gorelkin P., Majouga A., Weiss D.J., Edwards C., Ivanov A.P., Klenerman D., Sviderskaya E.V., Edel J.B., *Korchev Y.* "High-resolution label-free 3D mapping of extracellular pH of single living cells", Nature Communications 10 (2019) 5610 (IF=11.878)

3) Takahashi Y., Zhou Y., Miyamoto T., Higashi H., Nakamichi N., Takeda Y., Kato Y., *Korchev Y.*, Fukuma T. "High-Speed SICM for the Visualization of Nanoscale Dynamic Structural Changes in Hippocampal Neurons", Analytical Chemistry 92 (2020) 2159-2167 (IF=6.35)

Overseas Satellite 2: **University of British Columbia** (Total: 0 papers)

1)
2)
3)
4)

2. Status of Researcher Exchanges

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

Overseas Satellite 1: Imperial College London

<To satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2019					0
					0

<From satellite>

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

Overseas Satellite 2: University of British Columbia

<To satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2019	4*				4
	9*				9

* Incl. participants in The 3rd NanoLSI Symposium at UBC

<From satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2019	1	2			3
					0

Appendix 5　FY 2019 Visit Records of Researchers from Abroad

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

Total: 46

	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	Mingbo Qu	36	School of Bioengineering, Dalian University of Technology,	China	Ph.D. in Biochemical Engineering	The National Natural Science Foundation of China (2015-2017), No. 31402015, ￥240,000	2019/4/1-10/22	Joint research
2	Martin Bastmeyer	60	Professor, Zoological Institute, Cell and Neurobiology, Faculty of Chemistry and Biosciences Karlsruhe Institute of Technology (KIT)	Germany	PhD on meiotic spindle formation at the MaxPlanck Institute for Biology	A Heisenberg Stipend from the DFG (1998), spokesperson for Biomedical Photonics of the Karlsruhe School of Optics and Photonics (KSOP) and for Nano-Biology of the DFG Center for Functional Nanostructures (CFN)(2004-2011), Dean of the Faculty for Chemistry and Biosciences (2011)	2019/4/4	Lecture at NanoLSI Open Seminar
3	Xinhua Wan	-	Professor, College of Chemistry & Molecular Engineering, Peking University	China	Ph.D., Department of Chemical Fiber Engineering, China Textile University	State Council Special Allowance (1998), National Outstanding Youth Fund(2003), "Design and Synthesis of Liquid Crystal Polymers and Their Block Copolymers and Regulation of Condensed Structures", Second Prize of Natural Science of the Ministry of Education in 2018	2019/5/16	Lecture at NanoLSI Open Seminar
4	Ricardo Riguera	-	Professor, Universidad de Santiago, Santiago de Compostela	Spain	PhD in Chemistry	The Félix Serratosa Medal by the Real Sociedad Española de Química (2013)	2019/6/13	Lecture at NanoLSI Open Seminar
5	Russ Algar	37	Professor, Luminescent Materials, Bio/Chemical Sensing, The University of British Columbia	Canada	PhD in Chemistry	Governor General's Academic Gold Medal (2011), Canada Research Chair (Tier 2) in Biochemical Sensing (2012-Present), Michael Smith Foundation for Health Research Scholar (2014-Present)	2019/8/8	Invited lecture at 3rd NanoLSI Symposium at UBC in Vancouver
6	Sarah Burke	39	Professor, Nanoscale electronic and optoelectronic materials & Scanning Probe Microscopy, The University of British Columbia	Canada	Doctoral Degree in Physics	2009-2010 NSERC Postdoctoral fellowship, 2010-2020 CRC Tier 2 in Nanoscience (renewed 2015), 2011-2012 Peter Wall Institute for Advanced Studies Early Career Scholar	2019/8/8	Invited lecture at 3rd NanoLSI Symposium at UBC in Vancouver
7	David Perrin	52	Professor, The University of British Columbia	Canada	PhD in Chemistry	A Michael Smith Senior Scholar Award and the 2015 TEVA Award for Biological Chemistry (CSC)	2019/8/8	Invited lecture at 3rd NanoLSI Symposium at UBC in Vancouver
8	Amy Szuchmacher Blum	47	Professor, Design of biotemplates and nanostructured materials, McGill University	Canada	PhD in Physical Chemistry	2007 NRL Alan Berman Research Publication Award, 2008 NRL NRC/ASEE Research Publication Award for ACS Nano, 2, 1289 (2008), 2009 Canada Foundation for Innovation Leadership Opportunities Fund Award	2019/8/8	Invited lecture at 3rd NanoLSI Symposium at UBC in Vancouver
9	Ratmir Derda	39	Professor, Chemical Biology, University of Alberta	Canada	B.Sci. in Physics and Ph.D. in Chemistry	Canadian Rising Star in Global Health award from Grand Challenges Canada (2011), Young Investigator Award from Boulder Peptide Society (2014), University of Alberta Award for Outstanding Mentorship in Undergraduate Research & Creative Activities (2014)	2019/8/8	Invited lecture at 3rd NanoLSI Symposium at UBC in Vancouver
10	Ramesh Jasti	44	Professor, Curved aromatics (cycloparaphenylene), Biological imaging, University of Oregon	USA	PhD in Chemistry	NSF CAREER Award (2013-2018), Boston University Materials Science and Engineering Innovation Award (2013), Boston University Ignition Award (2013), American Chemical Society Young Academic Investigator Award (2013), Camille Dreyfus Teacher-Scholar Award (2014-2019)	2019/8/8	Invited lecture at 3rd NanoLSI Symposium at UBC in Vancouver
11	Wendell Lim	54	Professor, Probing & Programming Cell Signaling Circuits, UCSF	USA	PhD in Biochem & Biophysics	2006 Rogers Family Foundation Award (2010), Hans Neurath Award, Protein Society (2012), Wired Smart List: 50 people who will change the world	2019/8/8	Invited lecture at 3rd NanoLSI Symposium at UBC in Vancouver
12	Satoshi Toda	32	Postdoctoral Fellow, UCSF	USA	PhD in Medical Science	The Japan Society of Mechanical Engineers Hatakeyama award (2009), Kyoto University Faculty of Medicine Young Investigator Award (2012), The Japanese Biochemical Society Koichi Suzuki Memorial Award (2013)	2019/8/8, 2019/10/1-present	Lecture at 3rd NanoLSI Symposium at UBC in Vancouver, Assosiate professor at NanoLSI(2019/10/1-)
13	Luca Costa	35	CNRS Scientist, Center for Structural Biochemistry (CBS), Montpellier, France – Pierre-Emmanuel Milhiet Lab	France	PhD	Best Poster at SPMonSPM(2018),Best Talk at Labex EpiGenMed PhD Students and Postdocs Day(2016),Young Scientists Bursary to European XFEL Users' Meeting (2015)	2019/8/19-8/24	Participation in 8th Bio-AFM Summer School
14	Yusuke Sakai	32	Scientific Assistant (Postdoc researcher), Malopolska Centre of Biotechnology, Jagiellonian University	Poland	PhD in Chemistry & Biotechnology	FEBS Letter Daily Poster Awards(2019), Marie Sklodowska-Curie Actions Seal of Excellence(2017), NAR Breakthrough Article(2015)	2019/8/19-8/24, 2020/2/3-3/31	Participation in 8th Bio-AFM Summer School, joint research
15	Alberto Moreno-Cencerrado	36	Microscopy Specialist, BioOptics - IMP, Research Institute of Molecular Pathology	Austria	Dr. MSc.	Final degree project (graded with honors) on Scanning Probe Microscopy, Award(2012), Assistant Lecturer at the Advanced Materials Laboratory,Scholarship(2011)	2019/8/19-8/24	Participation in 8th Bio-AFM Summer School

16	Wan-Yu Tsai	34	Postdoc, Center for Nanophase Materials Science, Oak Ridge National Laboratory	USA	PhD in Materials Science, Paul Sabatier University, France	Second Prize of "Thesis Award" Société Chmique de France (French Chemical Society) - Région Midi-Pyrénées(2015), Young Investigator Award “Novel Insight to Electrochemical Capacitors” Symposium, International Society of Electrochemistry (ISE) Taipei, Taiwan(2015), Erasmus Mundus Full Grant (European scholarship)European Union(2009-2011)	2019/8/19-8/24	Participation in 8th Bio-AFM Summer School
17	Kenry	35	Postdoctoral Research Fellow, Pharmaceutical Sciences The University of British Columbia	Canada	PhD		2019/8/19-8/24	Participation in 8th Bio-AFM Summer School
18	Suling Liu	-	Professor, Cancer Institute, Fudan University Shanghai Cancer Center; and Institutes of Biomedical Sciences Fudan University	China	PhD	Susan G Komen postdoctoral fellowship (2005-2008), AACR Merck Scholar-in-training award (2006), AACR Susan G Komen Scholar-in-training award (2010), The NSFC award for Outstanding Young Investigator Award (2013), USCACA-NFCR Scholarship Award (2014)	2019/9/3	Lecture at Joint Symposium on Tumor Biology 2019
19	Yingjun Zhao	-	Assoc. Professor, Dept. of Oncology, Fudan University Shanghai Cancer Center; and Institutes of Biomedical Sciences, Fudan University	China	Ph.D. from State key Laboratory of Oncogenes and Related Genes	Demonstrating the function and mechanism of hepatic cancer associated genes and miRNAs.	2019/9/3	Lecture at Joint Symposium on Tumor Biology 2019
20	Zhenyu Cai	-	Professor, Cancer Institute, Fudan University Shanghai Cancer, Naval Medical University	China	Ph.D in biomedical sciences	Two of his articles published in Nat Cell Biol and Proc Natl Acad Sci U S A were selected as a high-cited paper in Web of Science Database.	2019/9/3	Lecture at Joint Symposium on Tumor Biology 2019
21	Arin Marchesi	36	Postdoctoral Fellow, UCSF, Adhesion & Inflammation Lab, Aix-Marseille Université	France	PhD in Neurobiology	Publications: Structural titration of receptor ion channel GLIC gating by HS-AFM	2019/9/13	Lecture at NanoLSI Open Seminar
22	Chih-Wen Yang		Research Specialist, Institute of Physics, Academia Sinica	China	Ph.D in Physics		2019/9/24-10/21	Joint research
23	Oleg Matusovsky		Research Associate, McGill University	Canada	PhD in Biochemistry		2019/9/27-10/23	Joint research
24	Mihail Barboiu	51	Professor, Adaptive Supramolecular Nanosystems Group, Institut Européen des Membranes –UMR CNRS	France	PhD in Science of Materials	“Costin D. Nenitescu” Medal and Honour Award of Romanian Chemical Society, 2007, Royal Society of Chemistry, RSC Surfaces and Interfaces Award 2015, 1000 Talent Program Award SAFEA China.	2019/10/8	Lecture at NanoLSI Open Seminar
25	Patrick Tan	-	Professor, Duke-NUS Medical School	Singapore	MD PhD	The Charles Yanofsky prize for Most Outstanding Graduate Thesis in Physics, Biology or Chemistry,The President’s Scholarship, Loke Cheng Kim scholarship, Young Scientist Award (A-STAR), Singapore Youth Award (twice), SingHealth Investigator Excellence Award, Chen New Investigator Award (Human Genome Organization), President’s Science Award, The Japanese Cancer Association International Award	2019/10/29	Lecture at International Symposium on Tumor Biology in Kanazawa 2019
26	David Virshup	-	Professor, Duke-NUS Medical School	Singapore	M.D. in Pediatrics	The Singapore Translational Research (STaR) Investigator Award	2019/10/29	Lecture at International Symposium on Tumor Biology in Kanazawa 2019
27	S. Tiong Ong	-	Associate Professor, Duke-NUS Medical School	Singapore	M.D.	The NMRC CSA-SI award	2019/10/29	Lecture at International Symposium on Tumor Biology in Kanazawa 2019
28	Carsten Beta	46	Professor, Department of Physics, Potsudam University	Germany	Ph.D. in Physics	Committee member of International Symposium "From Pattern Formation to Turbulence" (2019)	2019/11/19-21	Lecture at Joint UBI - NanoLSI Workshop “Trends in Molecular Biophysics of Living Cells”
29	Nguyen Bao Quoc	43	Lecturer, Research Institute for Biotechnology and Environment, Nong Lam University	Vietnam	PhD in biological and environmental sciences	JSPS postdoctoral fellow and research associate in Kobe University, Borlaug Research Fellow in Tuskegee University	2019/11/20-11/30	Joint research
30	Tak W. Mak	74	Director of the Cambell Family Institute for Cancer Research, Professor of the University of Toronto, Ontario Cancer Institute, Princess Margaret Cancer Center University Health Network Toronto	Canada	PhD in biochemistry	Gairdner Foundation International Award (Canada), Foreign Associate of the National Academy of Sciences (USA), Fellow of the Royal Society (UK), King Faisal Prize for Medicine (Saudi Arabia), Sloan Prize of the GM Cancer Foundation (USA), Paul Ehrlich and Ludwig Darmstaedter Prize (Germany)	2019/12/2	Lecture at NanoLSI Open Seminar
31	Kazunori Yamamoto	31	JSPS Postdoctoral Fellow, Guillaume Charras Lab. London Centre for Nanotechnology, University College London	England	PhD	Morishima Award (2017)	2019/12/23	Lecture at NanoLSI Open Seminar
32	Daniel Pelt	33	Researcher, Computational Imaging Group, CWI Amsterdam	The Netherlands	Ph.D. in mathematics	Grant of Learning alhorithms for large 3D images 82018)	2020/1/15-17	Tutorial, invited lecture at The 1st International Conference on Big Data and Machine Learning in Microscopy (MLM20)
33	David Gao	34	Associate Professor, Department of Physics and Astronomy, University College London	UK	PhD in Condensed Matter and Materials Physics	Director and Founder for Nanolayers Research Computing	2020/1/15-17	Tutorial, invited lecture at The 1st International Conference on Big Data and Machine Learning in Microscopy (MLM20)
34	David Glowacki	38	Royal Society Senior Research Fellow, Intangible Realities Laboratory, School of Chemistry, University of Bristol	UK	PhD in Computational Science	The Royal Society of Chemistry's Harrison-Meldola Award (2014), A Philip Leverhulme award (2016), The Molecular Graphics & Modelling Society's 'Silver Jubilee' Award (2017)	2020/1/15-17	Invited lecture at The 1st International Conference on Big Data and Machine Learning in Microscopy (MLM20)
35	Jakob Schiotz	53	Professor, DTU Physics, Technical University of Denmark	Denmark	Ph.D. in physics	P. Gorm-Petersens memorial award (1997)	2020/1/15-17	Invited lecture at The 1st International Conference on Big Data and Machine Learning in Microscopy (MLM20)
36	Philip Moriarty	51	Professor, School of Phusics & Astronomy, University of Nottingham	UK	Ph.D. in Physical Sciences	The Kelvin Medal and Prize by the Institute of Physics (2016)	2020/1/15-17	Invited lecture at The 1st International Conference on Big Data and Machine Learning in Microscopy (MLM20)
37	Ingmar Swart	39	Associate Professor, Debye Institute for Nanomaterials Science, Utrecht University	The Netherlands	Ph.D. in physical chemistry	2013 ECHO-STIP grant, (260 k€). Awarded by the Netherlands Organisation for Scientific Research (NWO), 2016 FOM-Projectruimte grant (550 k€, together with Prof. C. de Morais Smith), Awarded by NOW, 2018 FOM-Projectruimte grant (600 k€, together with Prof. Vanmaekelbergh), Awarded by the Netherlands Organisation for Scientific Research (NWO)	2020/1/15-17	Tutorial, invited lecture at The 1st International Conference on Big Data and Machine Learning in Microscopy (MLM20)

38	Yangjun Zhang	50	Senior Research Associate, Division of Medicine, Imperial College London, London, UK	England	PhD Faculty of Medicine, Imperial College London, UK	National Natural Science Foundation of China (No. 31870990)(2019/2022),Tianjin Science and Technology Support Program of China (No.14ZCZDSY00020)(2014-2017), Tianjin Natural Science Foundation of China (No.13JCYBJC21900)(2013/2016),National Natural Science Foundation of China (No. 30971184)(2010-2012)	2020/1/23-2/1	Participation in 1st WPI NanoLSI-iCeMS Joint Symposium, discussion for joint research
39	Joshua B. Edel	40	Professor, Department of Chemistry, Imperial College London	England	PhD on the development of single molecule detection	Research fellowship in single molecule biophysics at the Rowland Institute at Harvard University (2005); a prestigious ERC Starting Grant on “Nanoporous Membranes for High Throughput Rare Event Bioanalysis” (2011); an ERC Consolidator Grant related to the development of selective single molecule biosensors (2016)	2020/1/27	Lecture at NanoLSI Open Seminar
40	Batirtze Prats Mateu	-	Postdoctoral Fello, Institute of Science and Technology Austria	Austria	PhD	Performance grant from Universität für Bodenkultur(2015), FEM TECH Pratikum(Grant for 6 Months) (2013), Performance grant from Universität Wien(2013)	2020/1/30-3/5	Joint research
41	Lorena Redondo Morata	36	Researcher, Institut National de la Santé et la Recherche Mé dicale (Inserm)	France	PhD in Physical Chemistry	The AntalGenics SBE33 prize (2016)	2020/2/9-28	Lecture at NanoLSI Open Seminar, short term stay for joint research
42	Mingbo Qu	36	School of Bioengineering, Dalian University of Technology,	China	Ph.D. in Biochemical Engineering	The National Natural Science Foundation of China (2015-2017), No. 31402015, ￥240,000	2019/4/1-10/22	Joint research
43	Alexander S. Mikhailov	70	NanoLSI PI / Professor, Fritz Haber Institute of the Max Planck Society	Germany	Doctor of Science/ Theoretical Physics, Chemical Physics, Biophysics	International Solvay Chair in Chemistry (2009)	2019/5/9-5/24 2019/7/1-7/12 2019/9/9-9/26 2019/11/5-12/17 2020/1/27-3/5	Participation as principal investigator, host the Joint UBI - NanoLSI Workshop “Trends in Molecular Biophysics of Living Cells”
44	Yuri Korchev	60	NanoLSI PI / Professor, Imperial College London	UK	PhD in Biophysics and Cytology, Biophysics	Editorial Board Member, Pflugers Archiv - European Journal of Physiology	2019/6/17-6/30 2019/10/18-10/26 2020/1/23-2/1	Participation as principal investigator
45	Mark John Macachlan	46	NanoLSI PI / Professor, University of British Columbia	Canada	PhD in Chemistry	Fellow of the Royal Society of Chemistry (UK)(2016); Award for Research Excellence in Materials Chemistry (Canadian Society for Chemistry)(2016); Tier 1 Canada Research Chair in Supramolecular Materials (2015-2022); Steacie Prize for Natural Sciences (E.W.R. Steacie Memorial Fund)(2014); Rutherford Memorial Medal (Royal Society of Canada)(2013); Killam Award for Excellence in Graduate Student Mentorship (UBC)(2013); Strem Award for Pure or Applied Inorganic Chemistry (Canadian Society for Chemistry)(2013); Killam Research Prize (UBC)(2011)	2019/6/11-6/28 2019/7/22-7/26 2020/2/10-2/21	Participation as principal investigator
46	Adam Foster	45	NanoLSI PI / Professor, Aalto University	Finland	PhD in Theoretical Solid State Physics	Awarded Väisälä prize by Suomalainen Tiedeakatemia (2009)	2019/10/1-10/10 2020/1/9-1/17	Participation as principal investigator, host the 1st International Conference on Big Data and Machine Learning in Microscopy (MLM20)

Appendix 6 FY2019 State of Outreach Activities

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

Activities	FY2019 (number of activities, times held)
PR brochure, pamphlet	*Open Facility Programs Flyer (1) (EN) *WPI Pamphlet (2) (EN/JP) *Recruiting Flyer for the Graduate School Course of NanoLSI (2) (EN/JP) (Total: 5)
Lectures, seminars for general public	*Kanazawa University Open Lecture in 2019 (Lecture mainly for High school students) (1 by Kodera, 1 by Hanayama, 1 by Matsumoto) *Kanazawa University Satellite Plaza Mini Open Lecture (Lecture mainly for High school students) (1 by Matsumoto) *Open Lecture of "Hokushin Gan Pro" (Fostering Health Professionals for Changing Needs of Cancer/one of the MEXT's project) (Lectures for general public) (1 by Matsumoto, 1 by Takeuchi) *LINK-J Networking Night (Lecture mainly for entrepreneurs) (1 by Fukuma) *The Laboratory for Intellectual Innovation in Silicon Valley, California (Lectures mainly for entrepreneurs) (1 by Hanayama, 1 by Shibata) (Total: 9)
Teaching, experiments, training for elementary, secondary and high school students	*Hakui High School (1 by Akine) (Total: 1)
Science café	-
Open houses	*"Rigaku no Hiroba" (Hands-on Science Seminar for High School Students) (1 by Shibata, 1 by Sumino, 1 by Watanabe, 1 by Wong, 1 by Hazawa) *Open house for Organelle–Collegium(1 by Kodera, 1 by takahashi, 1by watanabe, 1 by Imai, 1 by Wei) (Total: 10)
Participating, exhibiting in events	*An exhibition booth at SSH meeting *An exhibition joint booth with other 12 WPI centers and JSPS at WPI Science symposium *An exhibition booth at the Study Abroad Fair in Thailand (Hosted by Kanazawa University) *Meeting with Nano Ontario Executives at Embassy of Canada to Japan (Total: 4)
Press releases	Takahashi (1), Oshima, Matsumoto, Wong (1), Yang, Flechsig, Sumino/Sumikama, Sakata/Akine, Takahashi (2), Takahashi (3), Wong (2), Watanabe/Ando, Yano, Ando, Wong (3), Konno/Nakayama (Total: 16)
Publications of the popular science books	-
Others (TV program, Video, Article)	*TV program on Kanazawa University Key Researches "KOKOKARA" (1 by Wong, 1 by Hanayama, 1 by Hirao) *Video of "Researcher's voice" (1 by Kodera, 1 by Matsumoto) *Videos on YouTube (1 by Fukuma, 1 by Oshima, 1 by Maeda, 1 by Nakajiam, 1 by Yano, 1 by Matsumoto, 1 by Wong, 1 by Hanayama, 1 By Hirao) *Article by Kodansha Bluebacks Outreach (1 by Matsumoto and Shibata) (J) (Total: 15)

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

Outreach Activities and Their Results

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

-In order to engage in active promotion of the 3rd NanoLSI Symposium, we started using Facebook in addition to the Institute's website. Compared to the 2nd Symposium in London, excluding NanoLSI members, the number of participants increased from 28 to 41 people this year. The success of the 3rd symposium led to vibrant exchanges between the NanoLSI researchers and the participants, and to the

expansion of the NanoLSI research network.
The details are as shown below:

・A postdoctoral fellow of UBC stays at NanoLSI as a JSPS Postdoctoral Fellow for Research in Japan Standard Program for two years from 2020.

・Professor Leonenko (Univ. Of Waterloo), President of the Biophysical Society of Canada, has been accepted by the NanoLSI Fellows Program. (Her visit to Japan is on hold due to the COVID-19.)

・Director Fukuma received an invitation from Professor Burke (UBC), one of the invited speakers, to the International Conference on Network Technology (ICNT), a large-scale international conference to be held in July 2020.

-Created a recruitment flyer for the Division of Nano Life Science in the Graduate School for Frontier Science Initiative to be established in April 2020, and participated in and recruited students at a study abroad fair organized by Kanazawa University in Bangkok.
As a result, we received some inquiries from students after the fair. In addition to the above, we conducted effective public relations activities such as posting advertisements on the “Nature jobs” website and receiving inquiries from overseas.

Appendix 7 FY 2019 List of Project's Media Coverage

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

	Date	Types of Media (e.g., newspaper, magazine, television)	Description
1	2019.4.5-5.29	Newspaper (1), Website (7)	Research result on mathematically-designed graphene improving electrocatalytic activity by Assoc. Prof. Yasufumi Takahashi (Hokkoku Shimbun, Phys.org, Azonano)
2	2019.4.17	Website (2)	Research result on how inflammation causing gasric cancer by Assoc. Prof. Hiroko Oshima and Prof. Masanobu Oshima (ecancer, Medical Xpress)
3	2019.5.16-5.22	Website (4)	Research result on virulence factor of the influenza A virus mapped in real-time by Assist. Profs. Kee Siang Lim and Masaharu Hazawa, Dr. Akiko Kobayashi, Profs. Noriyuki Kodera, Toshio Ando, and Richard W. Wong (Phys.org, Drug Target Review)
4	2019.5.18-6.6	Newspaper (7), Website (19), Magazine (1)	Research result on HGF-inhibitory macrocyclic peptide by Assist. Prof. Katsuya Sakai, Assoc. Prof. Mikihiro Shibata and Prof. Kunio Matsumoto (Mainichi Shimbun, Hokuriku Chunichi Shimbun, Nikkei Sangyo Shimbun, Nikkan Kogyo Shimbun, Kagaku Shimbun, Shizuoka Shimbun, Hokkoku Shimbun, Nikkei Biotech ONLINE, Yahoo News, JIJI.COM, Science Portal, Sankei Biz, Phys.org, ecancer, Nikkei Biotech Magazine)
5	2019.6.3-4	Newspaper (2), Television (1)	Safety prayer festival for NanoLSI new building (Kensetsu Kogyo Shimbun, Hokkoku Shimbun, NHK)
6	2019.6.12-6.14	Website (13)	Research result on opposite piezoresistant effects of rhenium disulfide in two principle directions by Assit. Prof. Lei Yang (Nanotechnology Now, Phys.org)
7	2019.6.25	Website (3)	Review on the power of simple physical models for complex protein machines by Assist. Prof. Holger Flechsig and Prof. Alexander Mikhailov (Phys.org)
8	2019.7.3	Website (1)	Research result on mechanism of scorpion toxin inhibition of K^+ channel elucidated using high-speed AFM by Assist. Prof. Ayumi Sumino and Dr. Takashi Sumikama (Phys.org)
9	2019.7.31	Website (2)	Research result on Multi-state switchable stationary phase in chiral separation by Assist. Prof. Daisuke Hirose and Prof. Katsuhiro Maeda (Phys.org)
10	2019.8.28-30	Newspaper (2)	WISE Program for Nano-Precision Medicine, Science, and Technology adopted (Hokkoku Shimbun)
11	2019.9.13	Web magazine (1)	Interview of Assoc. Prof. Satoru Okuda (ThermoFisher Scientific)
12	2019.10.17-10.18	Website (13)	Research result on controlling ion recognition in reactive host-guest systems by Assoc. Prof. Yoko Sakata, Prof. Shigehisa Akine (Phys.org, BioTech Gate, USA Life Sciences Database)
13	2019.11.29	Newspaper (1)	Research result on origin of resistance to lung-cancer drug by Prof. Seiji Yano et al. was selected as one of "top 10 news in 2019 in Ishikawa" (Yomiuri Shimbun)
14	2019.12.3-12.25	Newspaper (1), Website (17)	Research result on high resolution electrochemical mapping of hydrogen evolution reaction on transition metal dichalcogenide nanosheets by Assoc. Prof. Yasufumi Takahashi (Nikkei Sangyo Shimbun, Azonano, Phys.org)
15	2019.12.3-12.29	Newspaper (1), Website (30)	Research result on high-resolution label-free 3D mapping of extracellular pH of single living cells by Assoc. Prof. Yasufumi Takahashi and Prof. Yuri Korchev (Hokkoku Shimbun, OPTRONICS ONLINE, Phys.org, The Medical News)
16	2019.12.11	Newspaper (1)	Prof. Miki Nakajima and Assist. Prof. Ayumi Sumino received "Haazami Female Researcher Award" by Kanazawa University (Hokkoku Shimbun)
17	2019.12.17	Website (18)	Research result on possible strategy for cancer treatment found in nuclear transport proteins by Assist. Profs. Masaharu Hazawa, Kee Siang Lim, Prof. Richard W. Wong (The Medical News)
18	2019.12.27-2020.1.10	Website (25)	Research result on complete filling of batches of nanopipettes by Dr. Linhao Sun, Dr. Kazuki Shigyou, Prof. Toshio Ando, Assist. Prof. Shinji Watanabe (Phys.org, Chem Europe)
19	2020.1.23-2.10	Newspaper (3), Website (13)	Research result on combined drug treatment for lung cancer and secondary tumors by Assoc. Prof. Shinji Takeuchi, Assist. Prof. Koji Fukuda, Prof. Seiji Yano (Yomiuri Shimbun, Hokuriku Chunichi Shimbun, Hokkoku Shimbun, Ecancer Medicalscience, News-Medical.Net, Medical Xpress)
20	2020.2.6-2.14	Newspaper (1), Website (1)	Research result on phase separation organizing the site of autophagosome formation by Prof. Toshio Ando (Hokkoku Shimbun, Phys.org)
21	2020.2.9	Newspaper (1)	Kick-off symposium on WISE Program for Nano-Precision Medicine, Science, and Technology (Hokkoku Shimbun)
23	2020.3.25-3.26	Website (12)	Research result on Nucleoporin TPR upregulation altering MTOR-HSF1 trails and suppressing autophagy induction in ependymoma by Assist. Prof Masaharu Hazawa and Prof. Richard W. Wong (Medical Xpress)