The Nano Life Science Institute (NanoLSI) Visiting Fellows Program

Nano Life Science Institute, Kanazawa University, Japan was chosen on October 6, 2017 to become another center in MEXT's World Premier International Research Center Initiatives (WPI Centers). http://www.jsps.go.jp/english/e-toplevel/

Head of the Institute, Prof. Takeshi Fukuma, developed the world's first liquid-environment frequency modulation atomic force microscope (FM-AFM) with true atomic resolution, making it possible to observe the surface structures of biomolecules, and three-dimensional distributions of hydration and flexible surface structures with subnanometer resolution at solid-liquid interfaces. One of the PIs of our WPI project, Prof. Toshio Ando developed high-speed atomic force microscopy (HS- AFM). His team has been carrying out biophysical studies of proteins by observing molecules in action with HS-AFM.

Based on these advanced technologies, NanoLSI plans to develop "nanoendoscopic techniques". We will combine the world's most advanced bio-scanning probe microscopy (SPM) and supramolecular chemistry. This combination will allow for not only the imaging of surfaces and interior of live cells but also the analysis of metabolites and nucleic acids and the manipulation of cell activities. By introducing multi-scale simulations to these studies, we aim to construct models for the mechanisms underlying molecular and cellular functions. We also aim to understand cancer-specific abnormalities of cells by comparing normal and cancer cells. Through these studies, NanoLSI aims to achieve nano-level understandings of various life phenomena and thereby establish a new research filed termed "nanoprobe life science".

Within this framework of NanoLSI's missions, we activate international collaborations. To this end and for the purpose of disseminating our SPM techniques, we have founded NanoLSI Visiting Fellows Program. Under this program, we will invite researchers (PIs) of molecular, cellular, or structural biologists including sabbatical researchers. For a month or a few months, invited researchers will carry out research, participate in collaborations and other academic activities at NanoLSI, and thereby, catalyze international scientific cooperation between their institutions and NanoLSI.

Invited researchers can learn how to operate the FM-AFM and HS-AFM systems from experts and then perform imaging experiments by themselves on the proteins and cells that they are willing to study.

The NanoLSI Visiting Fellows Program covers:

1. Travel expenses between applicants' country and Japan
2. Accommodation expenses and daily allowance based on the KU regulations

In addition to that,

3. Applicants might be accompanied by researchers, postdoc, etc. in his/her own lab. NanoLSI will also cover *maximum 2 researchers'* travel expenses.
4. Faculty members and technicians fully support applicants' research activities at NanoLSI.

5. While staying at NanoLSI, applicants will be able to use whole laboratory, including instruments, supplies (for up to 300K JPY) etc., and the university guest house if there is a vacancy.

Applicants will be able to use the following instruments.

- **High-speed Atomic Force Microscope (HS-AFM)**

  HS-AFM can visualize moving objects in solution. Its temporal resolution is typically 100 ms, while the spatial resolution is 2-3 nm in the lateral direction and 0.15 nm in the vertical direction. When it is applied to protein molecules in action, the acquired HS-AFM images can provide a significant insight into how the molecules function. For more details, see the following review articles:

  1. T. Ando, T. Uchihashi, and S. Scheuring, "Filming biomolecular processes by high-speed atomic force microscopy", Chem. Rev. 114(6):3120-3188 (2014). DOI:10.1021/cr4003837
  2. T. Ando, T. Uchihashi, and N. Kodera, "High-speed AFM and applications to biomolecular systems", Annu. Rev. Biophys. 42: 393-414(2013). DOI: 10.1146/annurev-biophys-083012-130324
  3. T. Uchihashi, N. Kodera, and T. Ando, "Guide to video recording of structure dynamics and dynamic processes of proteins by high-speed atomic force microscopy", Nature Protocols 7(6): 1193-1206 (2012). DOI: 10.1038/nprot.2012.047

- **Frequency-modulation AFM (FM-AFM) & Three-dimensional AFM (3D-AFM)**

  FM-AFM can visualize subnanometer-scale surface structures of biomolecules in solution. Combined with 3D scanning technique, it can also visualize 3D distribution of hydration and flexible surface structures at solid-liquid interfaces. The imaging rate of FM-AFM and 3D-AFM is typically 1 min/frame. The optimal spatial resolution of the instrument is 0.3 nm in the lateral direction and 0.01 nm in the vertical direction. In the case of biomolecular imaging, the practical resolution is mostly determined by the fluctuation of the surface structures rather than the instruments. For more details, see the following articles:

  1. H. Asakawa, S. Yoshioka, K. Nishimura, T. Fukuma, “Spatial Distribution of Lipid Headgroups and Water Molecules at Membrane/Water Interfaces Visualized by Three-Dimensional Scanning Force Microscopy”, ACS Nano 6 (2012) 9013-9020.
  2. H. Asakawa, K. Ikegami, M. Setou, N. Watanabe, M. Tsukada, T. Fukuma, “Submolecular-Scale Imaging of α-Helices and C-Terminal Domains of Tubulins by Frequency Modulation Atomic Force Microscopy in Liquid”, Biophys. J. 101 (2011) 1270-1276.
  3. T. Fukuma, “Water distribution at solid/liquid interfaces visualized by frequency modulation atomic force microscopy”, Sci. Technol. Adv. Mater. 11 (2010) 033003 (18 pages).

- **Scanning ion conductance microscopy (SICM)**

  SICM has a unique measurement principle and provides an unprecedented opportunity that enables submicroscale functional imaging of single live cells by a combination of nanoscale local stimulation and noncontact topography imaging. The imaging rate of SICM is 30-300 s/frame. Spatial resolution of the instrument is 10 nm in the lateral direction and 5 nm in the vertical direction. For more details, see the following articles:

  1. P. Novak, C. Li, A. I. Shevchuk, R. Stepanyan, M. Caldwell, S. Hughes, T. G. Smart, J. Gorelik, V. P. Ostanin, M. J. Lab, G. W. J. Moss, G. I. Frolenkov, D. Klenerman, and Y. E. Korchev, "Nanoscale live-cell imaging using hopping probe ion conductance microscopy", Nat. Methods **6** (2009), 279-281.
  2. V. O. Nikolaev, A. Moshkov, A. R. Lyon, M. Miragoli, P. Novak, H. Paur, M. J. Lohse, Y. E. Korchev, S. E. Harding, and J. Gorelik, "beta(2)-Adrenergic Receptor Redistribution in Heart Failure Changes cAMP Compartmentation", Science **327** (2010), 1653-1657.
  3. Y. Zhou, M. Saito, T. Miyamoto, P. Novak, A. Shevchuk, Y. Korchev, T. Fukuma, Y. Takahashi, "Nanoscale Imaging of Primary Cilia with Scanning Ion Conductance Microscopy," Anal. Chem. 90 (2018) 2891-2895.

【Application Eligibility】

Applicants must be independent researchers who lead an independent group or run their own lab.

【Application Procedure】

Applicants should submit:

(1) Application form
(2) CV
(3) Research Proposal

Please send all documents by email to: ikemoto@staff.kanazawa-u.ac.jp

【Application Deadline】

September 30, 2019 Japan time

【Selection and Result】

Based on the submitted documents above, the Selection Committee will select and nominate candidates to the Head of the Institute. The notification will be sent to the applicants in October, 2019.

For further information, please contact:

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