Biophysical research in Hokkaido University, Japan

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The point of this commentary is to inform the reader about biophysical research occurring at Hokkaido University so that interested domestic and foreign researchers may come to Hokkaido to either work and study with us or alternatively to reach out to us if they detect an area of potential collaboration. Hokkaido University is one of the former Imperial Universities, originally launched in 1876 as the Sapporo Agricultural College. One of the basic philosophies of education and research, *frontier spirit*, originates from Dr. W. S. Clark (the third president of the Massachusetts Agricultural College) who spent 8 months in Sapporo and gave a phrase “Boys, be ambitious! (if he lived nowadays, he would surely replace “Boys” to “Boys and Girls”)” that has become our motto in education and research.

There exist a number of relevant departments and institutes in Hokkaido University in the area of biophysics and related research fields: among these, research laboratories appearing in the list of web pages of the Biophysical Society of Japan are chosen and are introduced in this commentary article.

Molecule and Life Nonlinear Sciences Laboratory, Research Institute for Electronic Science (<http://mlns.es.hokudai.ac.jp/?lang=en>)

Prof. Tamiki Komatsuzaki and his staffs have been leading the construction of data-driven theory. They have developed theories by carving out states, state transition networks, energy landscapes, and important features to infer the state (such as cancer/noncancer) of the system from the experimental data (Helal et al. 2019). They have been closely working with experimental researchers. This kind of collaborative has benefitted from the award of international grants such as the Human Frontiers Science Program (HFSP) Award (H. Mootz, T. Komatsuzaki, H. Yang, Grant award 2010; A. Boudaoud, A. Roeder, R.S. Smith, C.B. Li Grant award 2013). Recently, they developed intelligent single-cell Raman measurement algorithm to accelerate its measurement speed at the algorithm processing stage (Tabata et al. 2019). They also studied the origin of stochasticity and predictability in reactions on which one can predict the fate of reactions even in a sea of chaos.

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Structural Chemistry Laboratory, Department of Chemistry, Faculty of Science (<http://wwwchem.sci.hokudai.ac.jp/~stchem/en/>)

The principal members of this laboratory are Profs. Koichi Ishimori, Takeshi Uchida, and Tomohide Saio. They work to functionally and structurally characterize key proteins essential for biological systems including electron transfer, metal homeostasis, protein folding, and various kinds of chemical processes in cells (Uchida et al. 2018; Konno et al. 2019). They have also been developing new spectroscopic methodologies to unveil the dynamic structural and functional properties of proteins using NMR, resonance Raman, CD, and time-resolved techniques (Saio and Ishimori 2019). As one of the “Planned Research” groups (part of a university strategic initiative), this research collective joins a new research project, “Integrated Bio-metal Science: Research to Explore Dynamics of Metals in Cellular System” (<https://ibms.mixh.jp/>), which is one of the targeted Scientific Research on Innovative Areas supported by MEXT.

Laboratory of Nanobiotechnology, Research Faculty of Engineering (<http://labs.eng.hokudai.ac.jp/labo/NanoBio/english/>)

Prof. Kazutoshi Gohara and his staffs have been studying unsolved biological problems in terms of applied physics toward elucidating the nature of life and developing the state-of-the-art technology. They have focused on three research topics: imaging, neurons, and water. Relevant works have been published in papers (Suzuki et al. 2013, Maehara et al. 2019, etc.) Recently, nano-structure 3D atomic resolved imaging has been done as a part of JSPS Program of Scientific Research on Innovative Areas “3D Active-Site Science” (2014–2019).

Laboratory of Biomolecular Science, and Center for Research and Education on Drug Discovery, Faculty of Pharmaceutical Science (<http://convallaria.pharm.hokudai.ac.jp/bunshi> and <https://japanese-apricot.pharm.hokudai.ac.jp>)

Prof. Katsumi Maenaka and his staff work in the structural biology field focusing on the determination of the structure of immune cell surface receptors and viral glycoproteins by X-ray crystallography, NMR, high-speed AFM, and cryo electron microscopy (Hashiguchi et al. 2011; Kuroki et al. 2014; Kajikawa et al. 2018). Prof.

Maenaka is also a director of the center for research and education on drug discovery, which was designated by the University to be a major center of academic discovery. The center is now screening unique chemical libraries including original and FDA-approved compounds. These studies have been supported by government-directed Life Science Research finding initiatives (Basis for Supporting Innovative Drug Discovery and Life Science Research (BINDS)) to Japan Agency for Medical Research and Development (AMED), 2013 and Hokkaido University Bioconjugate and Biosurface projects (2013). In addition, the international collaboration network with University of Oxford was supported by the JSPS Strategic Young Researcher Overseas Visits Program for Accelerating Brain Circulation (2015–2017).

Laboratory of Cell Dynamics, Faculty of Advanced Life Science: Laboratory of Cell Dynamics, Faculty of Advanced Life Science (<https://life.sci.hokudai.ac.jp/en/fa/lab/cell-dynamics>)

Prof. Hisashi Haga and his staffs have been studying the collective behaviors of cells. 3D morphogenesis of animal and plant organs is one of the final mysteries in biology because the blueprints for forming 3D structures are not entirely written within DNA. Their focus is on investigating the mechanisms that determine the 3D shape of a biological body from the viewpoint of the physical properties of the extracellular environment (Imai et al. 2015). In addition, they investigate the mechanisms of malignant alteration induced by the failure of the relationship between normal cells and the extracellular environment (Nukuda et al. 2015).

Laboratory of X-ray Structural Biology, Faculty of Advanced Life Science (<http://altair.sci.hokudai.ac.jp/g6/index-e.html>)

Prof. Min Yao and staffs have been focusing on the structure-function relationship of proteins to elucidate their reaction mechanisms and intermolecular networks in organisms, by using various physical, physicochemical, and biochemical methods, such as crystallography, electron microscopy, calorimetry, and activity measurement (Chen et al. 2017; Tanzawa et al. 2018). They also investigate the use of available structural information for drug design and industrial production. In addition, they have developed novel methods and programs for X-ray structural analysis, and recently designed an extraction-freezing robot AFERO to use solutionless crystal mounting for native SAD.

Laboratory of Biological Information Analysis Science, Faculty of Advanced Life Science (<http://altair.sci.hokudai.ac.jp/infana/new/english/english.html>)

Profs. Makoto Demura, Takashi Kikukawa, and Takashi Tsukamoto have been studying the molecular mechanism of membrane proteins by focusing on causal relationships in elementary reactions, which are encoded by the protein structures. This approach is possible because the elementary reactions progress sequentially once the proteins are activated. They study these causal relationships for photoreceptive proteins belonging to the microbial rhodopsin family mainly by use of time-resolved detections of flash-induced spectral and electrochemical changes. They are also interested in functional differentiation mechanisms of proteins and the adaption strategies that they evolve for different environments. They are also studying functional mechanisms of various microbial rhodopsins which act as H^+ pumps, Cl^- pumps, Na^+ pumps, ion channels, and light sensors (Iizuka et al. 2019; Tsukamoto et al. 2018).

Laboratory of Protein Science, Faculty of Advanced Life Science (<http://altair.sci.hokudai.ac.jp/5/>)

This laboratory was established by the late professor, Shintaro Sugai. He was appointed to a professorship in 1965 and had contributed to biological macromolecular sciences over many years. One of his representative studies was the protein folding problem an area in which he published many breakthrough and pioneering papers. He also served on important positions in The Biophysical Society of Japan and was elected as an honorary member in 2010. In the present time, professor Tomoyasu Aizawa and his students are carrying on this research theme by studying proteins using NMR methodologies and protein engineering. They especially have focused on the analysis of interactions between cytokines and their receptors (Umetsu et al. 2009). Peptide research is another major topic of their research work (Ishida et al. 2016; Sénéchal et al. 2018). They have been studying the interaction of antimicrobial peptides with their target membrane using NMR. Very recently, they are also studying metabolomics as one of the interesting applications of NMR.

Laboratory of Molecular Cell Dynamics, Faculty of Advanced Life Science (http://altair.sci.hokudai.ac.jp/infmcd/English/top_eng.html)

Professor Kinjo and his staff's research focus is on quantitative characterization of the kinetics of molecular interactions

in live cells. Activities of living organisms are based on molecular function and interactions. Their interest is to understand how different reaction kinetics are affected by protein complex formation across the levels of dimerization (Oasa et al. 2018), aggregation (Kitamura et al. 2006; Akira Kitamura and Kinjo 2018), and liquid-liquid phase separation in the live cell. To this aim, they have developed and used advanced fluorescence microscopy, fluorescence correlation spectroscopy (FCS) (Yamamoto and Kinjo 2019; Yamamoto et al. 2018), and transient state monitoring (TRAST) microscopy with high spatio-temporal resolution and single-molecule sensitivity.

These are just only some examples of research laboratories in biophysics in Hokkaido University, and along *frontier spirits* of this University, lots of interdisciplinary, unique biophysical research have been carried out. The web addresses of each of the individual laboratories have been purposefully included so that the interested reader might reach out and make contact. We at the Hokkaido University biophysics collective are willing to “be ambitious” together with you.

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