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Conference Report

4th Switzerland-Japan Biomolecular Chemistry Symposium SJBCS2024

A Bridge of Biomolecular Chemistry

Chan Cao[a]*, Miki Imanishi[b]*, Eiji Nakata[c]*, and Michelle S. Frei[d]*

*Correspondence: Prof. C. Cao: Chan.Cao@unige.ch; Prof. M. Imanishi: imiki@scl.kyoto-u.ac.jp; Prof. E. Nakata: nakata@iae.kyoto-u.ac.jp; Prof. M. S. Frei: michelle.frei@org.chem.ethz.ch

[a]Department of Inorganic and Analytical Chemistry, School of Chemistry and Biochemistry, University of Geneva, CH-1211 Geneva, Switzerland; [b]Institute for Chemical Research, Kyoto University, Uji, Kyoto 611-0011, Japan; [c]Institute of Advanced Energy, Kyoto University, Uji-shi, Kyoto 611-0011, Japan; [d]Department of Chemistry and Applied Biosciences, ETH Zürich, Vladimir-Prelog-Weg 3, CH-8093 Zürich, Switzerland

The 4th Switzerland-Japan meeting on Biomolecular Chemistry was held in November, 2024, at the Uji campus of Kyoto University, marking a much-anticipated revival of this event. Frist organized by Kai Johnsson and Itaru Hamachi in 2007 (EPFL), it was hosted a second time by Hiroaki Suga in 2009 (University of Tokyo) and a third time by Jean-Louis Reymond in 2014 (University of Bern). After a prolonged pause, partly due to COVID-19, this year's event reunited the vibrant Chemical Biology communities of Japan and Switzerland celebrating long-standing collaborations and fostering new connections.

The symposium began with a fascinating presentation by ***Kaori Sugihara*** (University of Tokyo), who highlighted the methods developed in her lab to study biological membranes. By combing friction force microscopy with fluorescence microscopy, her team studied lateral force–fluorescence correlation of polydiacetylene at the nanoscale.[1] ***Chan Cao*** (University of Geneva) introduced nanopore single-molecule sensing and sequencing, detailing α-synuclein c-terminal peptide PTM detection and decoding digital polymers using engineered aerolysin nanopores. She also demonstrated nanopore applications for single-molecule force measurements addressing biophysical challenges.[2] ***Paola Laurino*** (OIST) continued with an exciting talk unveiling the properties of all high-affinity solute-binding proteins in SAR11 bacteria critical to oligotrophic adaptation. Additionally, she highlighted how a remote loop in GH19 chitinase directly interacts with fungal cell walls, offering new insights into enzyme function design.[3]

After the coffee break, ***Sascha Hoogendoorn*** (University of Geneva) provided fascinating insights into the hedgehog signaling pathway. She repurposed PROTAC technology for target identification and uncovered BET bromodomains as the target of Hedgehog pathway inhibitor-1, a selective inhibitor with important anti-cancer properties.[4] ***Donald Hilvert*** (ETH Zurich) emphasized the critical role of directed evolution and computational design for the generation of artificial enzymes. Advances in *de novo* protein design allows the generation of biocatalysts more rapidly and will likely help to address various societal challenges.[5] ***Hiroaki Suga*** (University of Tokyo) guided the audience through his lab's work on the Radom non-standard Peptides Integrated Discovery (RaPID) system, which facilitates the discovery and optimization of bioactive macrocyclic peptides. He highlighted its application as a robust platform for peptide-based drug development and gene delivery.[6]

The first plenary lecture was given by ***Shiroh Futaki*** (Kyoto University) focusing on peptide-mediated protein delivery. He discussed the importance of lipid packing effects for membrane translocation of peptides. He also showed dynamic cytosolic translocation of IgG from coacervates.[7] ***Hiroshi Abe*** (Nagoya University) discussed the PureCap method developed in his lab and how it overcame issues of low purity of current mRNA vaccines. He also talked about the effects of RNA modification, GMP manufacturing, and effective injection methods of mRNA vaccines.[8]

After the coffee break, ***Nicolas Winssinger*** (University of Geneva) talked about molecular assembly to program responsive systems based on proximity enhanced reactions, such as nucleic acid-templated azide reduction to detect specific miRNA and controllable inhibition of thrombin using cooperative binding of drugs with hybridizable oligo pairs.[9] ***Rikiya Watanabe*** (RIKEN) introduced 'SATORI', an accurate, rapid, and robust detection method for viral genes based on digital bioanalysis by combining CRISPR-Cas12a/13a and single-molecule analysis.[10] The final speaker of the first day was ***Alexandria Deliz Liang*** (University of Zürich), who talked about engineering of metalloproteins by incorporating non-canonical amino acids *via* genetic code expansion. She showed how engineered enzymes exhibit improved catalytic efficiency.[11]

All the participants of the SJBCS 2024, photo credit Keiko Takimoto.

The second day of the symposium was opened by ***Yuichiro Hori*** (Kyushu University), who discussed the development of fluorogenic probes for the photoactive yellow protein (PYP) labeling system. A series of multicolor probes with distinct cell membrane permeability allowed them to image the translocation and recycling of glucose transporter 4 (GLUT4).[12] Next was ***Pablo Rivera-Fuentes*** (University of Zurich) who took us on an intriguing journey on how to generate fluorogenic near-infrared polymethine dyes by implementing an 5-*exo*-trig cyclization. Tuning of the intramolecular nucleophile allowed them to generate fluorophores that are suited for no-wash applications.[13] ***Shinya Tsukiji*** (Nagoya Institute of Technology) introduced us to the self-localizing ligand-induced protein translocation (SLIPT) system and showcased how two orthogonal SLIPT systems allowed them to simultaneously control the Ras/ERK and PI3K/Akt signaling pathways in individual cells.[14]

After the coffee break, ***Michelle Frei*** (ETH Zurich) described her work on endowing the HaloTag system with novel properties. In particular, she introduced HaloTag as a platform for the generation of far-red fluorescent biosensors for kinase activity.[15] Moving beyond fluorescence microscopy, ***Mako Kamiya*** (Institute of Science Tokyo) detailed her group's work on the generation of Raman probes to measure enzyme activity. Using isotope editing they were able to measure three enzyme activities simultaneously.[16] The session was concluded by the presentation of ***Beat Fierz*** (EPFL) who discussed his group's work on post-translational modifications on chromatin and the cytoskeleton. He highlighted how the use of mechanism-based inhibitors allowed them to investigate the interaction between the cancer relevant histone deacylase SIRT7 and the nucleosome by cryoEM.[17]

The second plenary lecture was given by ***Stefan Matile*** (University of Geneva), who outlined his long-standing efforts in supramolecular chemistry designing molecules with diverse functions. He then delved into their recent work on thiol-mediated cell uptake, an efficient strategy for delivering substrates of interest into the cytosol, offering significant potential for advancements in drug delivery.[18] ***Kazushi Kinbara*** (Institute of Science Tokyo) continued and presented on synthetic membrane transporters, including self-assembling amphiphilic molecules for lipid membranes and engineered PEG polymers with fluorescent probes for versatile applications.[19] ***Angela Steinauer*** (EPFL) presented her work on the evolution of protein cages for RNA delivery. Using directed evolution and structure-based protein engineering they optimized cargo and carrier providing novel nonviral carriers for therapeutic uses.[20]

The last session of the symposium was started by ***Kazunori Matsuura*** (Tottori University), who talked about the design of artificial viral capsids using β-annulus peptide assembly as well as targeting strategies *via* antigen/adjuvant display.[21] ***Thomas R. Ward*** (University of Basel) discussed his group's longstanding efforts in the field of artificial metalloenzymes. Among other topics he presented how an artificial metathase based on human carbonic anhydrase II can be implemented in a cell based system to generate cycloalkanes from glucose.[22] The final talk of the symposium was given by ***Nobutaka Fujieda*** (Osaka Metropolitan University) who detailed his endeavors in engineering cupin proteins for *cis*-selective cyclopropanation. He showed how engineering of the first and second coordination sphere of the bound copper allowed them to get access to a biocatalyst with high diastereo- and enantioselectivity.[23]

Held in the inspiring setting of Kyoto, the symposium successfully brought together experts from Switzerland and Japan across diverse areas of Chemical Biology. 23 high-quality oral and 57 poster presentations fostered engaging discussions and sparked new ideas, highlighting the event's success. We would like to thank Forum on Biomolecular Chemistry (FBC) and all co-sponsors for supporting this event.[24]


Plenary speakers Shiroh Futaki (left) and Stefan Matile, photo credit Eiji Nakata.

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