Fri. Mar 19, 2021

Webiner 3

Symposium | Co-Innovation Program (CIP) | T2C. R&D of batteries for e-mobility and energy storage for realizing society with energy storage

[S03-1am] T2C. R&D of batteries for e-mobility and energy storage for realizing society with energy storage

Chair, Symposium organizer:Masashi Okubo, Eiji Hosono, Keigo Hoshina
10:30 AM - 11:40 AM Webiner 3 (Online Meeting)

[S03-1am-01] Numerical simulation technology for evaluation of actual heterogeneous electrode layer and design of porous structure
○Gen Inoue[1] (1. Kyushu University)
10:40 AM - 11:10 AM

[S03-1am-02] Machine learning approaches for degradation prediction of Li-ion battery
○Yoichi Takagishi[1], Takumi Yamanaka[1], Tatsuya Yamaue[1] (1. Kobelco Research Institute Inc.)
11:10 AM - 11:40 AM

Symposium | Co-Innovation Program (CIP) | T2C. R&D of batteries for e-mobility and energy storage for realizing society with energy storage

[S03-1pm] T2C. R&D of batteries for e-mobility and energy storage for realizing society with energy storage

Chair, Symposium organizer:Masashi Okubo, Eiji Hosono, Keigo Hoshina
1:30 PM - 4:40 PM Webiner 3 (Online Meeting)

[S03-1pm-01] How do we understand electrode/electrolyte interface in all-solid-sate batteries? ~Theoretical/experimental approaches from the viewpoint of solid state ionics~
○Koji Amezawa[1] (1. Tohoku Unviersity)
1:30 PM - 2:20 PM

[S03-1pm-02] Recent Advances in Scanning Electrochemical Cell Microscopic Analysis on Lithium-ion Batteries
○Akichika Kumatani[1,2], Yasufumi Takahashi[3], Tomokazu Matsue[1] (1. Tohoku University, 2. NIMS, 3. Kanazawa University)
2:20 PM - 2:50 PM

[S03-1pm-03] Visualization of electrochemical reactions in all-solid-state Li-ion batteries using *operando* transmission electron microscopy
○Yuki Nomura[1], Kazuo Yamamoto[2], Tsukasa Hirayama[2], Emiko Igaki[1], Koh Saitoh[3] (1. Panasonic Corporation, 2. Japana Fine Ceramics Center, 3. Nagoya University)
3:00 PM - 3:30 PM

[S03-1pm-04] All solid state Lithium ion battery employing robust nanohybrid electrolyte materials
○Itaru HONMA[1] (1. Tohoku University)
3:30 PM - 4:00 PM

[S03-1pm-05] Fast Li-ion transport at the interface between an inorganic solid electrolyte and a liquid electrolyte
○Keigo Hoshina[1], Yasuhiro Harada[1], Norio Takami[1] (1. Toshiba Corporation)
4:00 PM - 4:30 PM

Webiner 4

Symposium | Co-Innovation Program (CIP) | T3A. Smartmaterials for future medical devices and lifescience

[S04-1am] T3A. Smartmaterials for future medical devices and lifescience

Chair, Symposium organizer:Masaru Tanaka, Wataru Wakui
9:30 AM - 11:35 AM Webiner 4 (Online Meeting)

[S04-1am-01] Scaffold-free 3D cell products created with bio 3D printer technology and their medical applications
○Toshihiko Maekawa[1] (1. Cyfuse Biomedical)
9:35 AM - 10:05 AM

[S04-1am-02] Functional polymer materials for biocompatibility
○Atsushi Sugasaki[1] (1. FUJIFILM Corporation)
10:05 AM - 10:35 AM

[S04-1am-03] Transdermal vaccine as a future medical treatment and ionic liquids as drug development materials
○Masahiro Goto[1] (1. Kyushu University)
10:45 AM - 11:35 AM

Symposium | Co-Innovation Program (CIP) | T3A. Smartmaterials for future medical devices and lifescience

[S04-1pm] T3A. Smartmaterials for future medical devices and lifescience

Chair, Symposium organizer:Masaru Tanaka, Hidekazu Ohashi, Takeshi Nagasaki
12:35 PM - 5:00 PM Webiner 4 (Online Meeting)

[S04-1pm-01] Polysaccharide/DNA Complexes to Deliver Therapeutic Oligonucleotides

○kazuo sakurai[1] （1. University of Kitakyushu）

12:35 PM - 1:25 PM

[S04-1pm-02] Adhesive materials developed based on biomimetic technology

○Syuji Fujii[1] （1. Osaka Institute of Technology）

1:25 PM - 1:55 PM

[S04-1pm-03] Nanosheet Wrapping Technology ~Application to Bioimaging tool~

○Yosuke Okamura[1] （1. Tokai Univ.）

1:55 PM - 2:25 PM

[S04-1pm-04] Development of hematopoietic stem cells expansion technology and future.

○Satoshi Yamazaki[1] （1. University of Tsukuba）

2:25 PM - 2:55 PM

[S04-1pm-05] Emergence of Biomaterials inspired by the Living Body -Relation with Supramolecular Structure-

○Nobuhiko Yui[1] （1. Tokyo Medical and Dental University）

3:05 PM - 3:55 PM

[S04-1pm-06] AJICAP®: Chemical site-specific conjugation technology for next-generation ADC

○Tatsuya Okuzumi[1], Yutaka Matsuda[1], Takuya Seki[1], Kei Yamada[1], Tomohiro Fujii[1], Noriko Hatada[1], Yusuke Iwai[1], Natsuki Shikida[1], Kazutaka Shimbo[1], Brian A. Mendelsohn[2] （1. Ajinomoto Co., Inc., 2. Ajinomoto Bio-Pharma Services）

3:55 PM - 4:25 PM

[S04-1pm-07] New developments in biocompatible polymers

○Yoshitomo Nakata Nakata[1] （1. NIPPON SHOKUBAI CO.,LTD）

4:25 PM - 4:55 PM

Webiner 5

Symposium | Co-Innovation Program (CIP) | T4. The dawn of co-innovation – academia-industry collaboration toward seeds co-creation -

[S05-1am] T4. The dawn of co-innovation – academia-industry collaboration toward seeds co-creation -

Chair, Symposium organizer:Ryotaro Tsuji, Ryu Abe
9:50 AM - 12:00 PM Webiner 5 (Online Meeting)

[S05-1am-01] Open Innovation Activities in Pharmaceutical Industries

○Michio Fujisawa[1], Atsushi Endo[1], Yoshito Kanazawa[1] （1. Daiichi Sankyo Co., Ltd.）

10:00 AM - 10:30 AM

[S05-1am-02] From basic research to innovation: de novo peptide drug discovery innovation

○Hiroaki Suga[1] （1. The University of Tokyo）

10:30 AM - 11:00 AM

[S05-1am-03] A Dialogue Model for Open Innovation

○Tomoko Kawakami[1] （1. Waseda University）

11:00 AM - 11:30 AM

[1S0501-03-5add] Discussion

11:30 AM - 12:00 PM

Webiner 7

Symposium | Medium and Long-Term Program | state-of-the-art of super dimensional chemistry

[S07-1pm] state-of-the-art of super dimensional chemistry

Chair, Symposium organizer:Hochol Chang, Hitoshi Miyasaka, Shinya Hayami
1:00 PM - 3:40 PM Webiner 7 (Online Meeting)

[S07-1pm-01] Transdimensional materials created by 2D oxides

○Minoru Osada[1,2] （1. IMaSS, Nagoya Univ., 2. WPI-MANA, NIMS）

1:05 PM - 1:35 PM

[S07-1pm-02] Precision Synthesis of Low-Dimensional Nanocarbon Materials

○Akimitsu Narita[1,2] （1. Okinawa Institute of Science and Technology Graduate University, 2. Max Planck Institute for Polymer Research）

1:35 PM - 2:05 PM

[S07-1pm-03] Two-dimensional heterostructures: heterostakings and heterojunctions

○Ryo Kitaura[1] （1. Nagoya Univ.）

2:05 PM - 2:35 PM

[S07-1pm-04] Creation of molecular nanosheet crystals utilizing air-water interfaces: Controlling morphology and functionality

○Rie Makiura[1] （1. Osaka Prefecture University）

2:35 PM - 3:05 PM

[S07-1pm-05] A niche between chemistry and physics opened by mathematics: topological materials science

○Takao Sasagawa[1] （1. Tokyo Institute of Tech.）

3:05 PM - 3:35 PM

Webiner 6

Symposium | Medium and Long-Term Program | Chemical communications in living system

[S06-1am] Chemical communications in living system

Chair, Symposium organizer:Hirokazu Arimoto, Masaki Kita

9:00 AM - 11:40 AM Webiner 6 (Online Meeting)

[S06-1am-01] Chemical Communication on Insectivorous Mammals

○Masaki Kita[1], Yusuke Yano[1], Mayuko Suzuki[1], Maho Morita[1], Satoshi D Ohdachi[2] （1. Nagoya University, 2. Hokkaido University）

9:05 AM - 9:35 AM

[S06-1am-02] AUTAC: an antibacterial autophagy-inspired degrader

○Daiki Takahashi[1], Hirokazu Arimoto[1] （1. Graduate School of Life Sciences, Tohoku University）

9:35 AM - 10:05 AM

[S06-1am-03] Functional coupling between gut microbiota and enteroendocrine cells

○Takashi TSUBOI[1] （1. Graduate School of Arts and Sciences, The University of Tokyo）

10:05 AM - 10:35 AM

[S06-1am-04] Molecular/neural basis underlying mate choice mediated by individual recognition in medaka fish

○Hideaki Takeuchi[1,2] （1. Tohoku Uni, 2. Okayama Uni.）

10:35 AM - 11:05 AM

[S06-1am-05] Are Fairy Chemicals a new family of plant hormones?

○Hirokazu Kawagishi[1] （1. Shizuoka University）

11:05 AM - 11:35 AM

Symposium | Medium and Long-Term Program | Strategy for improving solar energy conversion efficiency toward the realization of artificial photosynthesis

[S06-1pm] Strategy for improving solar energy conversion efficiency toward the realization of artificial photosynthesis

Chair, Symposium organizer:Ryu Abe, Akihiko Kudo, Hiroaki Misawa

1:00 PM - 3:40 PM Webiner 6 (Online Meeting)

[S06-1pm-01] Development of a large scale solar hydrogen production system based on particulate photocatalysts

○Kazunari Domen[1] （1. The University of Tokyo/Shinshu University）

1:05 PM - 1:35 PM

[S06-1pm-02] High-efficiency artificial photosynthesis using quantum coherence under modal strong coupling conditions

○Hiroaki Misawa[1] （1. Hokkaido University）

1:35 PM - 2:00 PM

[S06-1pm-03] Application of Near-Infrared Plasmonics to Hydrogen Evolution Catalysis

○Toshiharu Teranishi[1] （1. Kyoto University）

2:00 PM - 2:25 PM

[S06-1pm-04] Enhancement of water splitting and CO2 reduction by a synthetic method and making a solid solution of photocatalysts

○Akihiko Kudo[1] （1. Tokyo University of Science）

2:25 PM - 2:50 PM

[S06-1pm-05] Water splitting by visible ligh through one-photon induced two-electron conversion to get through the photon-flux density problem of sun light

○Haruo Inoue[1] （1. Tokyo Metropolitan University）

2:50 PM - 3:15 PM

[S06-1pm-06] Improvement in efficiency of dye-sensitized molecular photocathodes in photoelectrochemical cells for photocatalytic CO_2 reduction with water as a reductant

○Osamu Ishitani[1] （1. Tokyo Institute of Technology）

3:15 PM - 3:40 PM

Webiner 7

Symposium | Medium and Long-Term Program | New paradigm of molecular systems chemistry – Concerted Molecular Functions

[S07-1am] New paradigm of molecular systems chemistry – Concerted Molecular Functions

Chair, Symposium organizer:Satoshi Takahashi, Shigehiko Hayashi, Akio Kitao

9:00 AM - 11:40 AM Webiner 7 (Online Meeting)

[S07-1am-01] Rational design of protein molecular functions
○Munehito Arai[1,2] (1. Grad. Sch. of Arts and Sci., The Univ. of Tokyo, 2. Grad. Sch. of Sci., The Univ. of Tokyo)
9:05 AM - 9:24 AM

[S07-1am-02] Micro hydration effect upon ion selectivity studied by cold ion spectroscopy
○Shun-ichi Ishiuchi[1] (1. Tokyo Institute of Technology)
9:24 AM - 9:43 AM

[S07-1am-03] Functional Polyaromatic Nanospaces: How to Recognize Biomolecules
Ryuki Sumida[1], ○Michito Yoshizawa[1] (1. Tokyo Institute of Technology)
9:43 AM - 10:01 AM

[S07-1am-04] Synthesis and Applications of Functional Molecular Systems using Proteins
○Teruyuki Komatsu[1] (1. Chuo Univ.)
10:01 AM - 10:20 AM

[S07-1am-05] Reconstituting cell membrane functions with a model membrane and nanometric space
○Kenichi Morigaki[1] (1. Kobe University)
10:20 AM - 10:39 AM

[S07-1am-06] Intracellular molecular assemblies driven by liquid-liquid phase separation
○Shunsuke F. Shimobayashi[1] (1. Princeton University)
10:39 AM - 10:58 AM

[S07-1am-07] 4D genome architecture: A ondensed polymer system in the cell nucleous
○Masaki Sasai[1] (1. Nagoya University)
10:58 AM - 11:17 AM

[S07-1am-08] *In vitro* reconstitution of cell motility and division machineries from minimum molecular components
○Makito Miyazaki[1,2,3] (1. Kyoto Univ., 2. Inst. Curie, 3. PRESTO)
11:17 AM - 11:36 AM

Webiner 9

Symposium | Asian International Symposium | Asian International Symposium - Photochemistry -

[S09-1pm] Asian International Symposium - Photochemistry -

Chair, Symposium organizer:Osamu Ishitani, Mamoru Tobisu, Kei Ohkubo, Yasuharu Yoshimi, Tadashi Mori
1:00 PM - 3:40 PM Webiner 9 (Online Meeting)

[S09-1pm-01] [6π] Photocyclization to *cis*-Hexahydrocarbazol-4-ones: Substrate Modification, Mechanism and Scope
○Sachinkumar G Modha[1,2], Alexander Pothig[2], Andreas Dreuw[3], Thorsten Bach[2] (1. Uka Tarsadia University, 2. Technical University of Munich, 3. Ruprecht-Karls University)
1:10 PM - 1:40 PM

[S09-1pm-02] Surface functionalization of polyolefin by C-H oxygenation with chlorine dioxide
○Haruyasu Asahara[1] (1. Osaka University, Pharmaceutical Sciences)
1:40 PM - 2:00 PM

[S09-1pm-03] Flow Photochemical Synthesis of Thiophene-fused Organic Semiconductors
○Yasunori Matsui[1] (1. Osaka Pref. Univ.)
2:30 PM - 2:50 PM

[S09-1pm-04] Highly efficient and selective photoreaction progress under microflow conditions
○Yasuhiro Nishiyama[1] (1. Industrial Technology Center of Wakayama Prefecture (WINTEC))
2:50 PM - 3:10 PM

[S09-1pm-05] Continuous-Flow in Photocatalysis and Automated API Synthesis
○Jie Wu[1,2] (1. National University of Singapore, 2. National University of Singapore (Suzhou) Research Institute)
3:10 PM - 3:40 PM

Symposium | Asian International Symposium | Asian International Symposium - Photochemistry -

[S09-1vn] Asian International Symposium - Photochemistry -

Chair, Symposium organizer:Osamu Ishitani, Mamoru Tobisu, Kei Ohkubo, Yasuharu Yoshimi, Tadashi Mori
4:10 PM - 5:30 PM Webiner 9 (Online Meeting)

[S09-1vn-01] carbazole-based photocatalysts bearing high reducing ability
○Ryosuke Matsubara[1] (1. Kobe University)
4:10 PM - 4:30 PM

[S09-1vn-02] Photoinduced electron transfer-promoted decarboxylative radical addition to

dehydroamino acid

○Mugen Yamawaki[1], Akiko Asano[2], Taisei Kawabata[1], Kosei Yamamoto[1], Yasuharu Yoshimi[2] (1. National Institute of Technology, Fukui College, 2. University of Fukui)

4:30 PM - 4:50 PM

[S09-1vn-03] The Selective Functionalizations of C– H bond via LMCT Catalysis

○Zhiwei Zuo[1] (1. Shanghai Institute of Organic Chemistry, CAS)

4:50 PM - 5:20 PM

Symposium | Asian International Symposium | Asian International Symposium - Electrochemistry -

[S09-1am] Asian International Symposium - Electrochemistry -

Chair, Symposium organizer:Toru Amaya, Koichi Mitsudo, Toshiki Nokami, Seiji Suga

9:00 AM - 11:40 AM Webiner 9 (Online Meeting)

[S09-1am-01] New vistas in C-H functionalization

○Yu Kawamata[1] (1. Scripps Research)

9:05 AM - 9:25 AM

[S09-1am-02] Organotransition Metal-Catalyzed Electrochemistry

○Tiansheng Mei[1] (1. Shanghai Institute of Organic Chemistry, CAS, China)

9:25 AM - 9:45 AM

[S09-1am-03] Amping Up Organic Synthesis with Electricity: An Electrocatalytic Approach to Reaction Discovery

○Song Lin[1] (1. Cornell University)

9:45 AM - 10:15 AM

[S09-1am-04] Porous Organic Polymer and its Composites for Electrocatalysis

○Kathiresan Murugavel[1] (1. CSIR-Central Electrochemical Research Institute)

10:25 AM - 10:45 AM

[S09-1am-05] Bipolar Electrochemistry for Material Synthesis in Synergy with Electrophoresis

○Shinsuke Inagi[1,2] (1. Tokyo Institute of Technology, 2. JST PRESTO)

10:45 AM - 11:05 AM

[S09-1am-06] Enantioselective Synthesis and Separation with Chiral-Encoded Metal Surfaces

○Chularat Wattanakit[1], Sunpet Assavapanumat[1], Sopon Butcha[1], Veronique Lapeyre[2], Bhavana Gupta[2], Adeline Perro[2], Neso Sojic[2], Alexander Kuhn[2] (1. Vidyasirimedhi Institute of Science and Technology, 2. Univ. de Bordeaux)

11:05 AM - 11:35 AM

Webiner 8

Symposium | Special Program | Frontiers of Molecular Science Explored by Molecular Electron Microscopy

[S08-1pm] Frontiers of Molecular Science Explored by Molecular Electron Microscopy

Chair, Symposium organizer:Koji Harano, Takayuki Nakamuro

1:00 PM - 3:40 PM Webiner 8 (Online Meeting)

[S08-1pm-01] MicroED: Conception, practice and future opportunities

○Tamir Gonen[1] (1. UCLA/HHMI)

1:05 PM - 1:35 PM

[S08-1pm-02] Dynamic molecular electron microscopy: An emerging tool for chemists

○Eiichi Nakamura[1] (1. The University of Tokyo)

1:35 PM - 2:05 PM

[S08-1pm-03] Pushing the performance limits of cryo-EM for membrane receptors

○Radostin Danev[1], Matthew Belousoff[2], Yi-Lynn Liang[2], Xin Zhang[2], Denise Wootten[2], Patrick M. Sexton[2] (1. The University of Tokyo, 2. Monash Institute of Pharmaceutical Sciences, Monash University)

2:05 PM - 2:35 PM

[S08-1pm-04] Understanding the Chemistry of electron beam-induced transformations on the molecular level

○Dominik Lungerich[1] (1. Institute for Basic Science (IBS), Center for Nanomedicine, Yonsei University)

2:35 PM - 3:05 PM

[S08-1pm-05] Atomic-resolution Imaging of Sensitive Materials Using Ultralow-dose Transmission Electron Microscopy

○Yu Han[1] (1. King Abdullah University of Science and Technology)

3:05 PM - 3:35 PM

Symposium | Special Program | Lesson from Nature – Koji Nakanishi Memorial Symposium-

[S08-1am] Lesson from Nature – Koji Nakanishi Memorial Symposium-

Chair, Symposium organizer:Kenji Monde, Jun Koshoubu,

Nobuyuki Harada, Katsuhiro Konno, Keiko Shimamoto
9:00 AM - 11:40 AM Webiner 8 (Online Meeting)

[S08-1am-01] Shapes of acting biomolecules; Natural product chemistry visualizing functional structure
○Michio MURATA Murata[1] (1. Osaka University)
9:10 AM - 9:35 AM

[S08-1am-02] Chirality of Biomolecules -CD &VCD Exciton Chirality Method-
○Kenji Monde[1] (1. Hokkaido University)
9:35 AM - 10:00 AM

[S08-1am-03] Phytochemical natural products chemistry
○Minoru Ueda[1] (1. Tohoku University)
10:00 AM - 10:25 AM

[S08-1am-04] Sexual reproduction of a plant pathogen - exploring its molecular basis -
○Makoto Ojika[1] (1. Nagoya Univ.)
10:25 AM - 10:50 AM

[S08-1am-05] Chemistry of Receptor-Lipid Ligands for Understanding of Immune System
○Yukari Fujimoto[1] (1. Keio University)
10:50 AM - 11:15 AM

[S08-1am-06] Therapeutic In Vivo Synthetic Chemistry
○Katsunori Tanaka[1,2,3] (1. Tokyo Tech., 2. RIKEN, 3. Kazan Federal U.)
11:15 AM - 11:40 AM

Webiner 10

Symposium | Special Program | Toward the new chemistry through the fusion with informatics

[S10-1am] Toward the new chemistry through the fusion with informatics

Chair, Symposium organizer:Tadafumi Adschiri, Shinji Hasebe, Kazuhiko Sato, Midori Kamimura
9:00 AM - 11:40 AM Webiner 10 (Online Meeting)

[S10-1am-01] Strategy for Generating and Collecting Chemical Data Applicable to Chemical Research with Artificial Intelligence
○Kazuhiko Sato[1] (1. Interdisciplinary Research Center for Catalytic Chemistry, National Institute of Advanced Industrial Science and Technology (AIST))
9:10 AM - 9:40 AM

[S10-1am-02] Education on information in chemistry: For utilizing AI
○Noriko Akutsu[1] (1. Osaka Electro-Communication University)
9:40 AM - 10:10 AM

[S10-1am-03] Towards Digital Transformation of Chemical Plant
○Yoshiyuki Yamashita[1] (1. TUAT)
10:10 AM - 10:40 AM

[S10-1am-04] Digitization of Organic Synthesis
○Seijiro Matsubara[1] (1. Graduate School of Engineering, Kyoto University)
10:40 AM - 11:10 AM

[1S1001-04-6add] Panel Disccusion
11:10 AM - 11:40 AM

Symposium | Co-Innovation Program (CIP) | T2C. R&D of batteries for e-mobility and energy storage for realizing society with energy storage

[S03-1am] T2C. R&D of batteries for e-mobility and energy storage for realizing society with energy storage

Chair, Symposium organizer:Masashi Okubo, Eiji Hosono, Keigo Hoshina
Fri. Mar 19, 2021 10:30 AM - 11:40 AM Webiner 3 (Online Meeting)

[S03-1am-01] Numerical simulation technology for evaluation of actual heterogeneous electrode layer and design of porous structure

○Gen Inoue[1] (1. Kyushu University)

10:40 AM - 11:10 AM

[S03-1am-02] Machine learning approaches for degradation prediction of Li-ion battery

○Yoichi Takagishi[1], Takumi Yamanaka[1], Tatsuya Yamaue[1] (1. Kobelco Research Institute Inc.)

11:10 AM - 11:40 AM

実電極層内特性評価と構造設計のための計算技術開発

（九大院工[1]）○井上 元[1]
Numerical simulation technology for evaluation of actual heterogeneous electrode layer and design of porous structure ([1]*Faculty of Engineering, Kyushu University*)○Gen Inoue[1]

In heterogeneous porous electrode layers of actual secondary batteries and fuel cells, both electrochemical reaction and mass transport have to be optimized well. We present here various simulation technologies for evaluation of cell performance and structure design in actual electrode layer, such as (1) Reaction and mass transport simulation in porous electrode, (2) Optimum structure design, (3) Dynamic structure change by volume expansion, (4) Effect of fabrication process on porous structure, and (5) Reconstruction of material structure. These technologies contribute to increase cell performance with new innovative materials.
Keywords : Numerical Simulation, Porous Electrode; Structure Design; Volume Expansion, Fabrication Process

二次電池や燃料電池において、イオン、電子、その他反応化学種を円滑にかつ均一に電極表面に供給する必要がある。ここで輸送抵抗の損失が過電圧として現れ、出力密度や充放電効率の低下を招く。また局所的に反応集中が生じた場合は電極の溶出や、短絡に繋がる金属析出が生じる可能性がある。したがって電池内部での物質輸送性能の向上は、電池の高出力化・高充放電効率化のみならず、低コスト化や耐久性向上にも寄与できると考えられる。実用電池では各反応種の輸送経路が異なるため、多孔質構造が用いられるのが一般的であるが、その構造は物質輸送特性、有効反応界面積、実効容量を踏まえ複合的に考える必要があり、その上で実際の電極内部の反応輸送現象を理解することが重要である。そしてこれらの知見が構造設計の最適化に繋がり電池性能の向上にも繋がる。そのためには数値計算技術が極めて有効であり、本講演では、実電極層内特性評価と構造設計のための各種計算技術開発について述べる。

（１）多孔質電極内の反応輸送計算

電池全体の計算として多孔質電極理論を基にしたモデルが主流であるが、均質多孔質体の１次元解析が多く、μm オーダーの粒子径分布、空間構造に反映することが困難である。そこで近年複雑３次元構造を直接解く試みも行われ、我々も PEFC 触媒層内の触媒凝集構造を考慮した数値計算を行っている（Fig.1 (a)）[1)]。なお現状材料物性や反応特性も定数的に取り扱われるものが多く、局所電位や濃度に依存した特性が再現されていない。この点はナノスケール計算の知見との連成が必要とされている。

（２）最適構造設計計算

電極内現象の数理モデルの構築は内部現象解明のみならず、構造設計にも活用できる。ここで高容量高出力を満たす LiB 電極構造の自動最適化を進める際、濃度分布や電位分布など微分方程式から成るモデルであるため、不連続問題を対象にした遺伝的アルゴリズムや機械学習の適用をしなくても、非線形計画問題の解法が適用できる。これまで complex 法を用いた材料物性同定と構造自動設計を行っている[2)]。

（３）動的構造変形を伴う計算

LiB の充放電に伴う体積変化は電極層厚さと界面積の変化を生じ、反応場がより複雑になる。特に全固体電池では固体界面の接触状態は電極層の力場に依存する。そこで活物質の体積変化を考慮した個別要素法により動的変形を再現し[3]（Fig.1 (b)）、また電解質の弾塑性変形モデルを考案し、不可逆的構造変形の影響を検討している。

（４）電極層作製プロセスに関する計算

実用電池の電極層は主に湿式法により作製されている。粒子混合スラリーを混錬、塗布、そして乾燥し成型するが、各工程の操作方法や条件によりその内部構造は大きく異なる。そこで DLVO 理論を基にスラリー中の凝集形状を再現し、形成される触媒層構造と物質輸送性能の相関評価を行っている[4]（Fig.1 (c)）。

（５）材料構造再現

カーボンブラックの比表面積、粒子径分布等の実測値を用いて三次元構造を再現し、電解質被覆率の推定を行っている[5]。またこれを用い触媒層構造の設計を行っている。

以上の技術より、材料特性やプロセスの影響を反映した電極層内計算が可能となり、新規材料の特性を最大限発揮できる電極層の設計に貢献することができる。

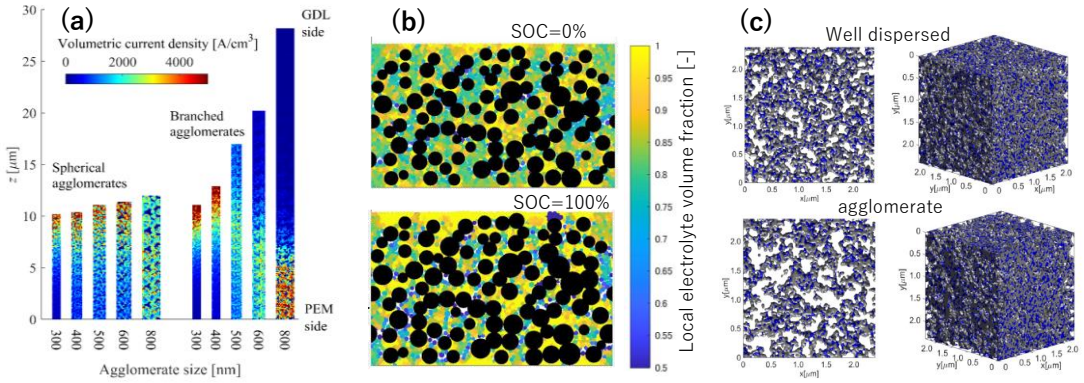


Fig.1 Numerical simulation results for evaluation of actual heterogeneous electrode layer and design of porous structure: (a) Reaction distribution in PEFC[1], (b) Structure change during charging cycle in all solid state battery[3], (c) Simulated PEFC catalyst layer with agglomerate[4].

1) M. So, K. Park, Y. Tsuge and G. Inoue, A particle based ionomer attachment model for a fuel cell catalyst layer, *J. Electrochem. Soc*., **2020**, 167, 013544.
2) G. Inoue, H. Mashioka, N. Kimura, Y. Tsuge, Identifying parameters from discharging and relaxation curves of Lithium-ion Batteries using porous electrode theory, J. Chem. Eng. Jpn. **2021**, accepted.
3) M. So, R. Hirate, K. Nunoshita, S. Ishikawa, G. Inoue and Y. Tsuge, Modelling intercalation induced stresses in all solid state batteries using discrete element method, *Proc. of PRiME 2020*, **2020**, A05-0998.
4) G. Inoue, M. Kawase, Understanding formation mechanism of heterogeneous porous structure of catalyst layer in polymer electrolyte fuel cell, *Int. J. of Hydrogen Energy*, **2016**, 41, 21352.
5) G. Inoue, T. Ohnishi, M. So, K. Park, M. Ono, Y. Tsuge, Simulation of carbon black aggregate and evaluation of ionomer structure on carbon in catalyst layer of polymer electrolyte fuel cell, J. of Power Sources, **2019**, 439, 227060.

機械学習を用いたリチウムイオン電池の劣化挙動予測

（コベルコ科研[1]）○高岸 洋一[1]・山中 拓己[1]・山上 達也[1]
Machine Learning Approaches for Prediction of Li-ion Battery Degradation ([1]*Computational Science Center, Kobelco Research Institute, Inc.*) ○Yoichi Takagishi[1], Takumi Yamanaka[1], Tatsuya Yamaue[1]

Prediction techniques of Li-ion battery (LIB) degradation have been receiving increasing attention since they have been extensively used in various fields. So far, lots of prediction models have been proposed, including the simple empirical models and physics-based models, can be classified as “Hypothesis-driven approach. Recently, “data-driven approach” with machine learning have been proposed in black box model. In this study, we propose data-driven and white box approach for battery degradation using the actual measurement data including FIB-SEM images and Deep Neural Network.
Keywords : Li-ion battery, degradation, data-driven approach, Machine Learning

リチウムイオン電池（Lithium Ion Battery, LIB）は、さまざまな機器への搭載が進んでおり、その劣化予測技術が極めて重要となっている。これまで、単純な経験則（√t 則）や仮説を立て微分方程式を解く「物理モデル」に加え、最近では機械学習を用いた「データ駆動型モデル」が盛んに研究されてきた。経験則は簡便な関数であるものの妥当性の議論が必要となる。一方、物理モデルでは、現象を想定している点では厳密であるが、現象が複雑である場合や不明な場合において適用が難しい。最近では、データ駆動型のアプローチが注目されているが、多くは回帰・予測は優れるものの、劣化要因の推定が困難であるため設計や運用へのフィードバックが難しい側面を持つ。最近我々は、データ駆動型アプローチをとりつつ、劣化現象を想定したホワイトボックス手法を提案している。このモデルでは劣化状態の特徴量が自動で抽出・選択されるため、客観的な劣化要因の推定を行いつつ、精度の高い予測が可能であるところが大きな利点となる。本講演では、高容量負極材料の一つである SiOx 電極の劣化を対象とし、各劣化状態の断面 SEM 像から深層学習による特徴量抽出を行った上で、それらの時間発展を機械学習で回帰した事例を報告する。また、従来型の物理モデルと比較し、それぞれの精度や適用範囲、他モデルとの比較を含めて解説する。

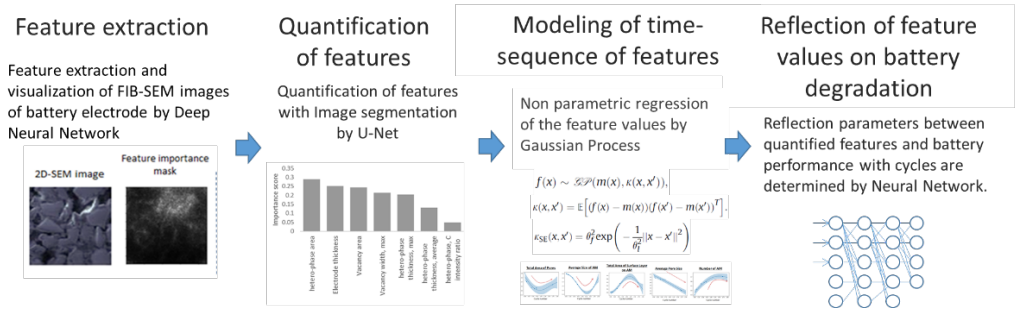


図 1　リチウムイオン電池の劣化予測モデルのスキーム.

Symposium | Co-Innovation Program (CIP) | T2C. R&D of batteries for e-mobility and energy storage for realizing society with energy storage

[S03-1pm] T2C. R&D of batteries for e-mobility and energy storage for realizing society with energy storage

Chair, Symposium organizer:Masashi Okubo, Eiji Hosono, Keigo Hoshina
Fri. Mar 19, 2021 1:30 PM - 4:40 PM Webiner 3 (Online Meeting)

[S03-1pm-01] How do we understand electrode/electrolyte interface in all-solid-sate batteries? ~Theoretical/experimental approaches from the viewpoint of solid state ionics~

○Koji Amezawa[1] (1. Tohoku Unviersity)

1:30 PM - 2:20 PM

[S03-1pm-02] Recent Advances in Scanning Electrochemical Cell Microscopic Analysis on Lithium-ion Batteries

○Akichika Kumatani[1,2], Yasufumi Takahashi[3], Tomokazu Matsue[1] (1. Tohoku University, 2. NIMS, 3. Kanazawa University)

2:20 PM - 2:50 PM

[S03-1pm-03] Visualization of electrochemical reactions in all-solid-state Li-ion batteries using *operando* transmission electron microscopy

○Yuki Nomura[1], Kazuo Yamamoto[2], Tsukasa Hirayama[2], Emiko Igaki[1], Koh Saitoh[3] (1. Panasonic Corporation, 2. Japana Fine Ceramics Center, 3. Nagoya University)

3:00 PM - 3:30 PM

[S03-1pm-04] All solid state Lithium ion battery employing robust nanohybrid electrolyte materials

○Itaru HONMA[1] (1. Tohoku University)

3:30 PM - 4:00 PM

[S03-1pm-05] Fast Li-ion transport at the interface between an inorganic solid electrolyte and a liquid electrolyte

○Keigo Hoshina[1], Yasuhiro Harada[1], Norio Takami[1] (1. Toshiba Corporation)

4:00 PM - 4:30 PM

全固体電池の電極／電解質界面をどう考えるか？～固体イオニクスの観点からの理論的・実験的アプローチ～

（東北大学　多元物質科学研究所）○雨澤　浩史

How do we understand the electrode/electrolyte interface in all-solid-state batteries? ~Theoretical/experimental approaches from the viewpoint of solid state ionics~

(Institute of Multidisciplinary Research for Advanced Materials, *Tohoku University*) ○Koji Amezawa

All-solid-state batteries (ASSBs) are expected as next-generation batteries having high energy/output power density and great safety. The performance of ASSB is often determined by peculiar ion transport properties at the solid-state interface between the electrode and the electrolyte, which are different from those in each bulk solid. Therefore, careful material selection and device design, considering ion transport properties not only in the bulk but also at the interface, are required. Although it is considered that ion transport properties at the interface are affected by variation of physical/chemical states (ion concentration/valence, chemical/electric potential, structural distortion, *etc*.) at the interface, their relationships have not been well-understood so far. In this presentation, we examine the physical/chemical states at the solid-state interface in ASSBs through theoretical and experimental approaches from the viewpoint of solid state ionics, and discuss how ion transport properties at the interface can be interpreted.

Keywords : All solid state batteries, Interface, Solid state ionics

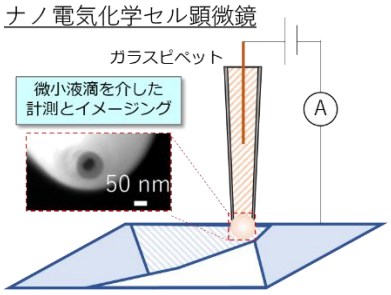
全固体電池は、高エネルギー・高入出力密度、高い安全性を兼ね備えた次世代蓄電池として、その実用化が期待されている。全固体電池の反応場である電極／電解質固固界面では、それぞれのバルク固体とは異なる特異なイオン輸送特性が発現し、これがしばしば電池の性能を左右する。したがって全固体電池の実現には、単なる材料のバルク特性だけなく、これら界面特性をも考慮した戦略的な材料選択、デバイス設計が必要とされる。電極／電解質固固界面におけるイオン輸送は、界面に局所的に生じる物理化学状態（イオン濃度・価数、化学ポテンシャル、電位、構造、歪など）の変調・分布に起因すると推測されるが、これらの影響は体系的に理解されているとは言い難い。例えば、電極／電解質固固界面の安定性や抵抗要因となる界面反応層の形成を考える場合、高温で作動する固体酸化物形燃料電池では、両極性拡散と局所平衡に基づく化学ポテンシャル分布により議論することが広く受け入れられているが、比較的低温で作動する全固体電池では、固体電解質からなる類似の固体イオニクスデバイスであるにも関わらず、このような考え方は一般的ではない。本発表では、固体イオニクスの観点からの理論的・実験的アプローチを通し、改めて全固体電池の電極／電解質固固界面について考察し、これにより全固体電池で見られる界面現象がどのように解釈されるか、また、この考え方がどこまで適用できるかについて議論する。

ナノ電気化学セル顕微鏡を用いたリチウムイオン電池研究への取り組み

（東北大 AIMR[1]・物財機構 MANA[2]・金沢大 NanoLSI[3]・JSTーさきがけ[4]・東北大[5]）
○熊谷 明哉[1,2]・高橋 康史[3,4]・末永 智一[5]
Recent Advances in Scanning Electrochemical Cell Microscopic Analysis on Lithium-ion Batteries ([1]*AIMR, Tohoku University*, [2]*MANA, NIMS*, [3]*NanoLSI, Kanazawa University*, [4]*JST-PRESTO*, [5]*Tohoku University*) ○Akichika Kumatani,[1,2] Yasufumi Takahashi,[3,4] Tomokazu Matsue[5]

Recent advances in lithium-ion batteries (LIBs) are remarkable. In particular, a size control with nanometer/atomic scale of those materials in LIBs is important to introduce their electrochemical functionalities. Whereas, a conventional electrochemical evaluation is performed in bulk. In other words, there is still open questions about their electrochemical properties in microscopic scale. In recent, we have developed and applied scanning electrochemical cell microscopy (SECCM) with a single barrel nanopipette filled with electrolyte and a reference electrode. The SECCM can analyze and visualize the local electrochemical activities on the electrodes of lithium-ion batteries. In this talk, we will present our recent advances in SECCM analysis on the battery studies.
Keywords : Scanning Probe Microscopy; Electrochemistry; Lithium-ion Batteries;

リチウムイオン電池の発展、特に新規電池材料の合成・電極活物質の微細化・被膜技術の向上などによる電池全体の高機能化により、電池性能は日々向上している。一方で、マイクロスコピックに起こるイオンの可逆的なやり取りはより複雑化し、通常のバルク体を用いた電気化学計測では、例えば電池特性に影響する粒界や被膜界面の反応分布の測定は困難となる。我々は、マイクロ・ナノスケールで起こる電気化学反応を直接検出・可視化する分析技術：走査型電気化学顕微鏡の開発に取り組んでいる。近年、電解液と参照極を充填した開口径が 50 nm 程度のガラスピペットを探針とするナノ電気化学セル顕微鏡を開発し、リチウムイオン電池研究へと応用している。本顕微鏡を用いることで、電極表面の反応性分布や構造による反応性の変化を局所的に計測・可視化し、電池特性の反応分布の検証が可能となったのでこれらを報告する。



1) Recent advances in scanning electrochemical microscopic analysis and visualization on lithium-ion battery electrodes. A. Kumatani, T. Matsue, *Curr. Opin. Electrochem.* **2020**, *22*, 228.

オペランド透過電子顕微鏡技術を用いた全固体 Li イオン電池内部の電気化学反応の可視化

(パナソニック株式会社 [1]・一般財団法人ファインセラミックスセンター[2]・名古屋大学 [3]) ○野村 優貴 [1]・山本 和生 [2]・平山 司 [2,3]・井垣 恵美子 [1]・齋藤 晃 [3]

Visualization of electrochemical reactions in all-solid-state Li-ion batteries using *operando* transmission electron microscopy ([1]*Panasonic Corporation*, [2]*Japan Fine Ceramics Center,* [3]*Nagoya University*) ○Yuki Nomura,[1] Kazuo Yamamoto,[2] Tsukasa Hirayama,[2] Emiko Igaki,[1] Koh Saitoh[3]

Research and development of all-solid-state Li-ion batteries (ASSLIB) have been widely conducted because they have the potential to improve the energy density and safety compared to conventional LIBs with liquid electrolytes. To achieve fast charging of ASSLIBs, Li ions must move smoothly through cathode, solid electrolytes, anodes, and their interfaces. Therefore, nano-scale *operando* monitoring of Li ions in ASSLIBs is seriously important.

In this study, we developed a method of *operando* transmission electron microscopy for ASSLIBs and succeeded in observing the movement of Li ions in $LiNi_{0.8}Co_{0.15}Al_{0.05}O_2$ (NCA) cathodes using electron energy-loss spectroscopy (EELS)[1,2].

Figure 1 shows an annular dark-field scanning transmission electron microscopy (ADF-STEM) image and Li-ion concentration maps acquired during the charge reaction. Dashed lines in the Li-ion concentration maps show the interfaces between primary NCA crystals. Non-uniform Li-ion distribution during charging was clearly visualized (first right panel). Additionally, the Li concentration in each primary crystal was almost uniform and changed significantly at some interfaces between crystals. This shows that there was high Li transfer resistance at the interfaces.

Keywords :all-solid-state Li-ion battery; operando; transmission electron microscopy; electron energy-loss spectroscopy; lithium

全固体リチウムイオン電池(全固体 LIB)は、電解液を用いる現行 LIB より高いエネルギー密度と高い安全性を実現する可能性があり、次世代二次電池の候補として活発に研究開発が進められている。全固体 LIB の高速な充放電には、電池材料内部や界面で Li イオンをスムーズに移動させる必要があり、そのためには、動作中の電池内部の Li イオン動きをナノメートルスケールで動的に可視化することが重要である。そこで本研究では、全固体 LIB 用のオペランド透過電子顕微鏡計測システムを開発し、電子エネルギー損失分光法(EELS)を用いて動作中の $LiNi_{0.8}Co_{0.15}Al_{0.05}O_2$ (NCA)正極内の Li イオンの動きを観察することに成功した [1,2]。

図 1 は環状暗視野走査透過電子顕微鏡(ADF-STEM)像と EELS によって取得した充電中の Li 濃度分布を示す。Li 分布内の破線は NCA 正極内の 1 次粒子界面を表している。充電にともなって生じる NCA 正極内部の不均一な Li 濃度分布が明確に捉えられている(右端図)。また、破線で示す粒界において大きな Li 濃度勾配が発生しており、粒子界面が大きな Li 移動抵抗を有していることが分かる。講演では、充電レー

トの違いが Li 濃度分布に及ぼす影響についても議論する。

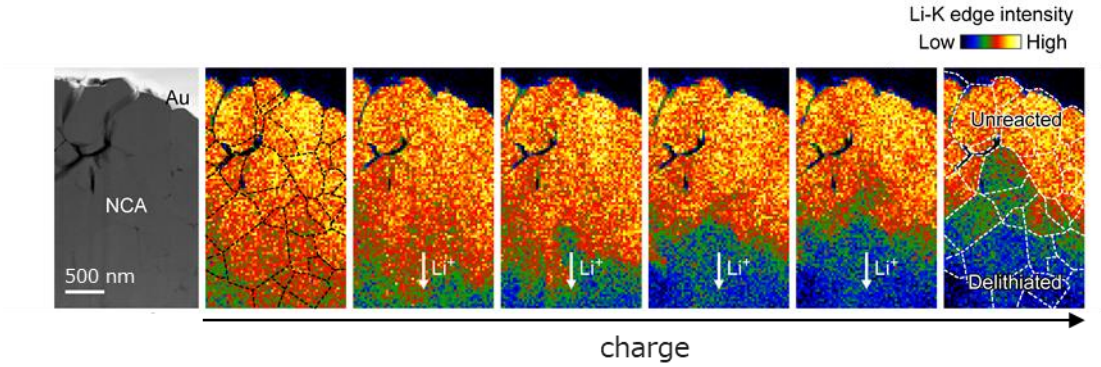


Fig. 1 An ADF-STEM image and Li concentration maps observed during the charge reaction using *operando* STEM-EELS.

1) Y. Nomura *et al.*, *Nat. Commun.* **11**, 2824 (2020).
2) Y. Nomura *et al.*, *ACS Energy Lett.* **5**, 2098–2105 (2020).

ハイブリッド材料を用いた安価・高安全性の全固体電池開発

（東北大学多元研）本間　格

All solid state Lithium ion battery employing robust nanohybrid electrolyte materials

(*IMRAM, Tohoku University*)　Itaru HONMA

we developed a new type quasi-solid-state electrolyte (QSE) employing nanohybrid materials consisting of Li ion conducting ionic liquid (LiFSI/EMI-FSI) and 7 nm silica nanoparticles. The interactions of liquid molecules at the nanoscale interfaces allow solidification on oxide surfaces, while a liquid-like mobility prevails even under macro scale solid state matrix. Although made from nanomaterials, the electrolytes are stable, flexible, processable to large size membrane and possess high ionic conductivity of 10.2 mS/cm at room temperature. All solid-state Li ion battery employing QSE demonstrated favorable charge/discharge cycle performances up to 200 cycles as well as high-rate capability over 5C, showing promise for high capacity and high power density LIB devices.
Keywords : All solid state Lithium ion battery; Solid state electrolyte; Hybrid material; Nanoparticle; Ionic liquid

１．緒言

脱炭素社会のキーテクノロジーとして電気自動車の開発が加速している状況で、車載用リチウムイオン電池 (LIB) の高容量化・安価大型化・高安全性が求められている。本講演ではこの課題解決にナノ材料を応用した例としてイオン液体とナノ粒子のハイブリッド材料を用いた全固体電池開発について報告する。現行の大型高容量 LIB システムでは安全機構や冷却部材がエネルギー密度低下の要因となっているため、高安全性の全固体電池を開発すれば蓄電エネルギー密度を高めることが出来る。我々は可燃性有機電解液と比較して安全性に優れる難燃性イオン液体に着目し、酸化物粒子のナノ界面での疑似固体化現象を利用した新奇電解質開発を行ってきた [1)]。ナノスケールではイオン液体分子は酸化物表面との相互作用によりヘテロ界面で疑似的に固体化したゲル状態となるが、その液体的イオン伝導特性がマクロスケールでも発現するバルク固体電解質材料を作製した [2-6)]（図 1)。ナノ粒子とイオン液体のレンガ構造連続体である固体電解質膜は柔軟性であり、電極活物質粒子との良好な界面接合が得られる。

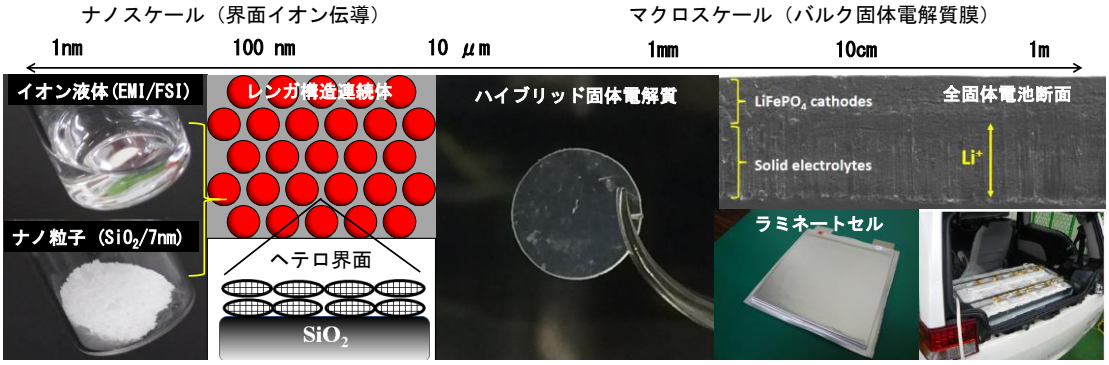


図１　ナノ界面イオン伝導型のハイブリッド電解質材料を用いた全固体電池開発

２．実験方法

リチウムビス(フルオロスルホニル)イミド(LiFSI)を[EMI][FSI]に濃度 1 M で溶解したイオン液体とシリカナノ粒子(粒径 7nm)をメタノール中で撹拌混合し、60℃、2 時間の乾燥処理によって固体粉末（イオン液体含有率 75～85 vol.%)）を作製した。この固体粉末と結着剤ポリテトラフルオロエチレン(PTFE)を 95:5 の重量比で混錬して厚さ 200 μm の疑似固体電解質シートを作製した。正極に $LiFePO_4$ (2wt%カーボン担持)と固体電解質の混合体、負極にリチウム金属を用いて全固体電池の試作・評価を行った。

３．結果と考察

高伝導性のイオン液体 1-エチル-3-メチルイミダゾリウムビス（フルオロスルホニル）イミド（EMI/FSI）を体積比率 85 vol.%で含有した擬似固体電解質のイオン伝導度は 10.2 mS/cm (25°C)であった（図２）。この電解質から作製した全固体電池の 35℃、0.1C 充電後の放電特性を図３(a)に示す。放電レート 0.1C において理論容量（$LiFePO_4$:170mA/g）近くの 160mAh/g が得られ、また 0.1C～1C においても容量利用率 90%以上と高い値を示した。放電レート 2C で 130mAh/g、5C でも 65mAh/g の容量が得られ、全固体電池の高出力特性を確認できた。図３(b)に 35℃、1C (0.6mA/cm^2)での充放電サイクル特性を示したが 200 回後でも容量劣化は見られず安定な電池特性が得られた。安価・高安全性のナノ材料から作製したハイブリッド固体電解質材料を用いて高出力特性の全固体電池を開発した。

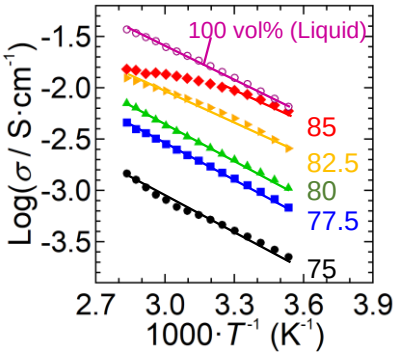


図２　疑似固体電解質のイオン伝導特性（図中数字はイオン液体体積含有率）

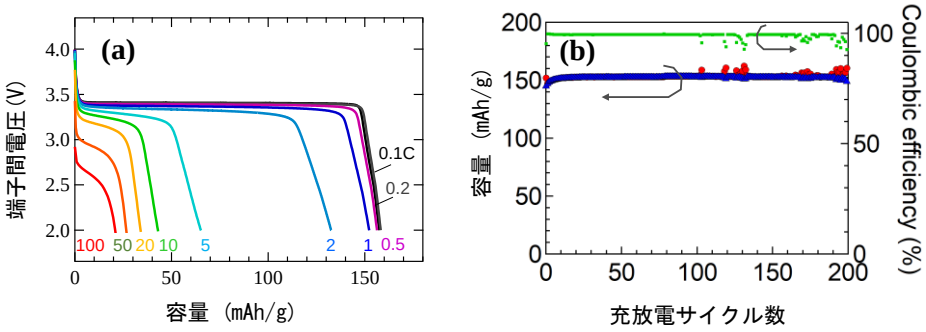


図３ (a) 全固体電池の放電レート特性（充電 0.1C ／放電 0.1C -100C, 35℃)と (b) 全固体電池の充放電サイクル特性 (1C, 35℃)

1) S. Shimano et al., *Chemistry of Materials*. **2007**, *19*, 5216.
2) M.Mezger et al., *Science*, **2008**, *322*, 424
3) K.Ueno et al., *Phys. Chem. Chem. Phys*., **2010**, *12*, 4066
4) S.Ito et al., *J. Power Sources*, **2012**, *208*, 271
5) A. Unemoto et al., *Electrochemistry*, **2019**, *87*, 100
6) K. Nishio et al., *J. Electrochemical Society*, **2020**, *167*, 040511

無機固体電解質/電解液からなるハイブリッド電解質の高速リチウムイオン伝導メカニズム

（株式会社東芝研究開発センター）○保科圭吾・原田康宏・高見則雄

Fast Li-ion transport at the interface between an inorganic solid electrolyte and a liquid electrolyte

(*Corporate Research & Development Center Toshiba Corporation*)
○Keigo Hoshina, Yasuhiro Harada, Norio Takami

Considering the demand for rechargeable batteries offering high energy, high safety, and long life, all-solid-state lithium-ion batteries have been intensively studied as the next-generation lithium-ion batteries. In addition to solid electrolytes for all-solid-state lithium-ion batteries, hybrid electrolytes containing solid electrolytes and liquid electrolytes have attracted much attention recently. We report that lithium-ion conductive ceramic enhanced lithium-ion transport in the hybrid electrolytes. PF_6^- and polar solvents are interacted with $Li_{1.2}Zr_{1.9}Ca_{0.1}(PO_4)_3$ solid electrolyte in hybrid electrolyte. Therefore, the polarized layer is formed at the surface of $Li_{1.2}Zr_{1.9}Ca_{0.1}(PO_4)_3$ particles and enables lithium ion to move smoothly in the hybrid electrolyte.

Keywords : Lithium-ion battery; Hybrid electrolyte; Lithium-ion transport;

硫化物や酸化物の無機固体電解質を用いた全固体二次電池は、次世代二次電池として実用化が期待されている。近年、固体電解質だけでなく、無機固体電解質と電解液を混合したハイブリッド電解質が注目されている[1)]。これまでに電解質をハイブリッド化することによりイオン導電率が高くなることを報告しているが[2)]、その高速リチウムイオン伝導メカニズムは明らかになっていない。本研究では無機固体電解質/電解液界面での高速リチウムイオン伝導メカニズムの解明を行った。無機固体電解質には電位窓が広く、化学的安定性の高い $Li_{1.2}Zr_{1.9}Ca_{0.1}(PO_4)_3$(LZCP)を用いた。ハイブリッド電解質のラマン分光測定から、LZCP とハイブリッド電解質中に含まれる極性溶媒であるプロピレンカーボネート(PC)やエチレンカーボネート(EC)との相互作用が示唆された。また、パルス磁場勾配核磁気共鳴法(PFG-NMR)により、ハイブリッド電解質中の PF_6^-の自己拡散が制限される傾向が見られた。これにより LZCP とハイブリッド電解質中の PF_6^-アニオンとの相互作用も示唆された。以上の結果から、電解液中の極性溶媒や PF_6^-アニオンは LZCP 粒子内の Li^+と相互作用し、LZCP/電解液界面に分極を形成すると考えられ、この分極層と電解液中のリチウムが反発することで、LZCP/電解液界面では局所的にリチウム輸送が高速化すると推察される。

1) M. Keller, A. Varzi and S. Passerini, *J. Power Sources*, **392**, 206-225 (2018)
2) K. Yoshima, Y. Harada and N. Takami, *J. Power Sources*, **302**, 283-290 (2016)

Symposium | Co-Innovation Program (CIP) | T3A. Smartmaterials for future medical devices and lifescience

[S04-1am] T3A. Smartmaterials for future medical devices and lifescience

Chair, Symposium organizer:Masaru Tanaka, Wataru Wakui

Fri. Mar 19, 2021 9:30 AM - 11:35 AM Webiner 4 (Online Meeting)

[S04-1am-01] Scaffold-free 3D cell products created with bio 3D printer technology and their medical applications

○Toshihiko Maekawa[1] (1. Cyfuse Biomedical)

9:35 AM - 10:05 AM

[S04-1am-02] Functional polymer materials for biocompatibility

○Atsushi Sugasaki[1] (1. FUJIFILM Corporation)

10:05 AM - 10:35 AM

[S04-1am-03] Transdermal vaccine as a future medical treatment and ionic liquids as drug development materials

○Masahiro Goto[1] (1. Kyushu University)

10:45 AM - 11:35 AM

日本化学会 第101春季年会 (2021)

バイオ 3D プリンタ技術で創るスキャフォールドフリー立体細胞製品とその医療応用

（株式会社サイフューズ）○前川敏彦
Scaffold-free 3D cell products created with bio 3D printer technology and their medical applications. (Cyfuse Biomedical) ○Toshihiko Maekawa

Abstract
In recent years, three-dimensional tissue construction technology has been attracting attention in many fields such as regenerative medicine, drug discovery and alternatives to animal experiments, and development at each research institution is accelerating. Together with Professor Koichi Nakayama of the Department of Regenerative Medicine and Biomedical Engineering, Faculty of Medicine, Saga University, we have developed a three-dimensional stacking technology and a bio 3D printer that can create three-dimensional tissues and organs using only cells without using any other artificial scaffolds. We are developing cell products that can be applied to the field of regenerative medicine and drug discovery. This bio 3D printer uses a cell aggregate (spheroid) that utilizes the phenomenon of cell aggregation, and its characteristics make it possible to apply it to various tissue constructions. In this talk, I will introduce some of the 3D tissue construction technologies and medical application using our bio 3D printer.
Keywords:Bio 3D printer, Scaffold-free, Cell aggregation, Regenerative medicine, Cellular product

概要
近年、再生医療分野をはじめ創薬及び動物実験代替法分野等、多くの分野で三次元組織構築技術が注目されており、各研究機関での開発が加速している。我々は佐賀大学医学部臓器再生医工学講座の中山功一教授と共にスキャフォールドを用いずに、細胞のみで立体的な組織・臓器を作製できる三次元積層技術並びにバイオ 3D プリンタを開発し、再生医療及び創薬分野に応用可能な細胞製品の開発を行っている。本バイオ 3D プリンタは、細胞の凝集現象を利用した細胞塊（スフェロイド）を用いるもので、その特性から様々な組織構築への応用が可能である。本講演では、バイオ 3D プリンタを用いた三次元組織構築技術及び医療応用事例の一部について紹介する。

1. スキャフォールドフリー三次元組織作製法

我々が開発してきたバイオ 3D プリンタ「商品名：レジェノバ®」は、複数の針を剣山様に整列配置させた冶具に対し、あらかじめデザインした位置にスフェロイドを積層することで所望の形状の細胞構造体前駆体を作製する。剣山様冶具に積層された前駆体を専用培地を満たした培養容器に入れ数日間培養を行うことで、精度高く配列されたスフェロイドが互いに融合しあい最終的に立体的な細胞構造体が完成する。このようにスフェロイド作製工程と積層工程の 2 段階の工程を経ることで細胞が死滅することなく大きな三次元構造体を作製することが可能となった。

2．再生医療への応用

現在、国内外の様々な研究機関において、本バイオ 3D プリンタ「レジェノバ®」が使用されている。当社でもこの「レジェノバ®」及び独自の基盤技術を用いて、骨軟骨再生、血管再生、神経神経再生をはじめとする様々な再生医療パイプラインの臨床開発を進めている。

現在、腎不全等により血液透析を必要とされる患者様の多くは、自己血管内シャントや人工血管を使用したバスキュラーアクセス法による治療を受けているが、自己血管を用いた治療では血管の採取に限界があり、人工血管では感染症や狭窄が生じるなどの課題がある。我々は、AMED の支援を受け、「バイオ 3D プリンタで造形した小口径 Scaffold free 細胞人工血管の臨床開発」において、佐賀大学医学部附属病院と共同で患者様の細胞のみで細胞製の血管構造体を作製し、人工透析用のシャントとして置換する新たな治療法の開発を進めている。このスキャフォールドを使用せずに作製した細胞製血管は、非臨床試験において体内の血管と同等の強度及び長期生存を確認しており、2020 年より臨床研究をスタートしてヒトでの安全性と有効性の試験を実施中である。

3．創薬への応用

新薬開発において、投与された薬物もしくは肝臓で代謝された反応生成物が肝細胞にダメージを与える肝毒性は、新薬開発中止の原因になる場合も多く、ヒトに投与する前に毒性を評価できるシステム開発が望まれている。我々は、NEDO の支援の元、バイオ 3D プリンティング技術を活用してヒト肝細胞を原料として肝小葉の大きさに近い肝臓構造体の開発を進めた。得られた球状の構造体中の肝細胞は 1 ヶ月近く生存すると共に代謝関連の遺伝子発現や酵素活性を維持しており、長期間肝臓の代謝機能を in vitro で持続する組織体の開発に成功した。この肝臓構造体の培養培地に薬物を添加して数日培養を継続すると、培地上清中には複数の薬物代謝生成物が蓄積した。その構造解析からヒト体内での反応と同等の代謝反応が進行しており、ヒト肝臓の代謝機能を再現する in vitro 評価モデルとなりうることがわかった。

この肝臓構造体を、ヒトでの肝毒性が報告されている薬物の肝毒性評価に応用した結果、従来の in vitro 評価法では検出が難しかった肝毒性を高い検出率で評価することに成功した。

4．今後の展望

紹介例の他にも国内外の共同研究先と共に、脊髄損傷や心筋、肝臓、泌尿器、皮膚など様々な組織の構築、組織再生への応用に取り組んでいる。いずれも治療法がない、もしくは既存治療法では治癒に至らず困っている患者様に新しい再生医療製品を早期に届けることを目標にしている。

生体親和性を目指した機能性重合材料

（富士フイルム（株）有機合成化学研究所[1]）　○菅﨑敦司[1]
Development of functional polymer materials for biocompatibility
([1]*FUJIFILM Corporation*)　○Atsushi Sugasaki[1]

Fujifilm has developed a variety of functional polymeric materials such as photopolymers mainly for internal use. Recently, we started to explore new possibilities of these materials while offering them as the products in the community. In this presentation, I will introduce functional polymeric materials which we have newly developed, particularly focusing on their (1) fundamental properties and (2) intriguing potentials as new biocompatible materials.
Keywords : Biomaterials; Biocompatibility; Functional Polymeric Materials; Cancer; CTC(Circular Tumor Cell)

富士フイルムはこれまでにフォトポリマーに代表される数多くの機能性重合材料を主に自社製品用に開発してきた。近年、これらの機能性重合材料を化成品（開発品）として世の中に提案しつつ、新たな価値創出の可能性を模索している。
本講演では、富士フイルムが新規開発した機能性重合材料について、(1) 基本物性、および、(2) 生体親和性を指向した新たなバイオマテリアルとしての興味深いポテンシャル特性、の 2 点について紹介する。

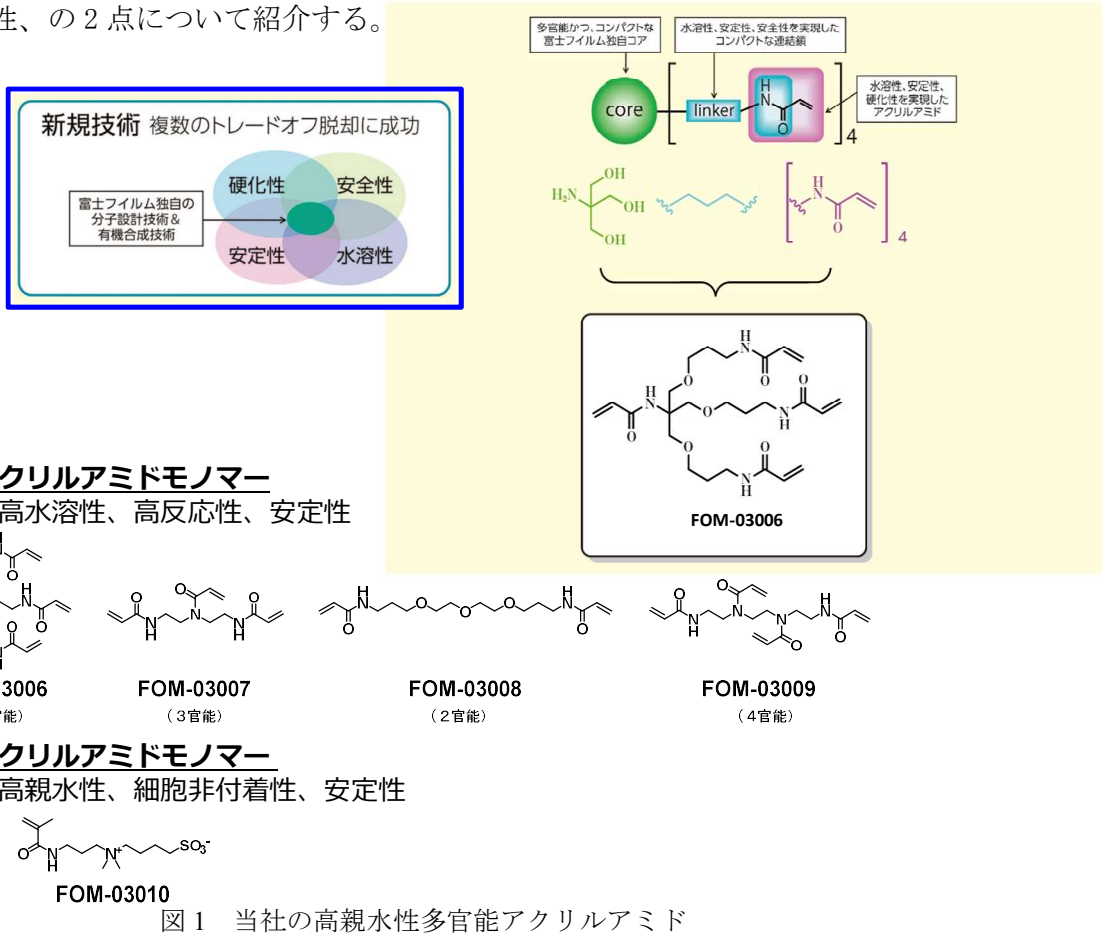


図 1　当社の高親水性多官能アクリルアミド

未来医療としての経皮ワクチンと創薬材料としてのイオン液体

（九大院工 [1,2]）○後藤　雅宏 [1,2]

Transdermal vaccine as a future medical treatment and ionic liquids as drug development materials ([1]*Graduate School of Engineering,* [2]*Center for Advanced Transdermal Drug Delivery Systems, Kyushu University*) ○Masahiro Goto,[1,2]

Transdermal vaccine[1,2)]; In the last two decades, different drug delivery methods have emerged with various targeted delivery routes; for instance, transdermal, topical, oral, injection and nasal. Among the different routes, a transdermal drug delivery (TDD) method is considered as a safe and a non-invasive technique for drug administration. TDD has attracted attention for several advantages over conventional oral or injection route. In contrast to conventional immunization by injection, transcutaneous immunization requires only topical application of antigens to the skin and is a simple, non-invasive method that does not require medical personnel. However, the major problem is that the stratum corneum (SC) serves as a strong barrier at the skin surface. In this lecture, we applied novel nanodispersion technique to the induction of cancer immunity. Cancer immunotherapy by activation of immune system against cancer has recently received attention. The key step for inducing the cancer immunity is the delivery of cancer-specific antigens to dendritic cells (DCs), followed by the antigen-presenting by the DCs. Our investigation revealed the ability of this approach to induce antigen-specific cellular immune responses against cancer by evaluating the growth of OVA-bearing tumors and the production of cytokines from splenocytes. Inhibition of tumor growth was achieved, demonstrating the applicability of S/O carriers to the induction of cancer immunity. We will show you some examples to create a novel vaccine by utilizing nanotechnology.

Pharmaceutical application of ionic liquids (ILs)[3,4)]; which are commonly defined as salt compounds composed of ionic species and melt below 100 °C, is an attractive research field in a drug delivery system (DDS). The solubilization ability for insoluble drug molecules is a promising property of ILs. In 2010, it was reported that acyclovir, a sparingly soluble drug, was dissolved in imidazolium-based ILs, and the IL-in-oil microemulsions enhanced the transdermal delivery of acyclovir. The transdermal delivery is the most studied DDS field using ILs and some hydrophobic ILs were confirmed as skin penetration enhancers due to its higher interaction with the hydrophobic skin surface barrier. Utilization of active pharmaceutical ingredients (API) as the ions of ILs is known as an alternative strategy of IL-based DDSs because the API-IL enables to tune their physical or chemical properties of ILs. To improve the transdermal delivery, drugs were robed with hydrophobic counter ions. Recently, biocompatibility has been regarded as one of the most important properties of ILs for the DDS application. Several biomolecule-derived ions such as choline and amino acids were reported to form ILs and the biocompatible ILs were used as a solvent for solubilizing poorly soluble drugs and skin penetration enhancers. These researches suggest that ILs would be a promising solvent for developing a novel DDS.

Keywords : Transdermal Vaccine; Nano Drug Carrier; Transdermal Delivery; Ionic Liquid

経皮投与は注射投与と比較して安全かつ簡便であり、経口投与と比較しても消化管や肝臓の通過がないことから、理想的な薬の投与方法と考えられている。ただし皮膚は高いバリア機能をもっていることから、現実的には経皮投与を多くの薬へ適用するのは困難である。本講演では、特に完全非侵襲性の次世代経皮技術とイオン液体の薬物利用に的を絞り、最新の技術を紹介する。

生体高分子の経皮吸収促進法としての S/O 技術:S/O 製剤とは薬を水中に封入した W/O エマルションから水を除いた状態であり、このとき薬と界面活性剤はナノ粒子(solid)の状態で油中に分散していると考えられる。現在主流となっているのがエマルションを凍結乾燥する S/O 調製方法である。この手法では、W/O エマルションを凍結することによって薬、水、界面活性剤、油(揮発性)という分子的な配置を保ち、減圧乾燥によって溶媒である水と油を同時に昇華させている。そのようにして得られた薬と界面活性剤からなるナノ粒子に、自分の使用したい油を添加することによって再分散させ、S/O 製剤を得るという方法である。この方法によってほぼ 100%のタンパク質製剤を油相に溶解することが可能である。実際には薬と界面活性剤の組合せによって分散性は大きく異なり、現在ではペプチドやタンパク質からなる薬剤とショ糖脂肪酸エステルとの組合せが最も再現性と安定性の面から適していると考えられている。バイオ医薬品の経皮デリバリーをはじめとして経皮ワクチンの構築において大きな成果を上げている[1,2]。

イオン液体による経皮吸収促進:イオン液体(IL)は、イオンからのみ成る常温・常圧下で液体の塩である。IL は、カチオン種とアニオン種の組み合わせにより物理化学的パラメータを調節可能である。例えば imidazolium をカチオンとして持つ IL は、アルキル鎖長に応じて疎水性が変化し、疎水性の高い IL は疎水性薬物を、親水性の高い IL は親水性薬物をよく溶解する。また、多くの薬物が弱酸あるいは弱塩基性の性質を持つことから、薬物自体をイオン液体の構成成分 (カチオンあるいはアニオン)として用いた Active Pharmaceutical Ingredient-Ionic Liquid (API-IL) も盛んに研究されている。経皮吸収における最大のバリアである角層への浸透性を高めるためには、溶解性改善により製剤中の薬物濃度を高めること、適度な親油性を付与することが有効である。先に述べたように、IL はその優れたデザイン性により、難溶性薬物と水素結合や van der Waals 相互作用等を持たせることで、溶解性を向上することができる。IL を薬物の溶媒として用いることで、あるいは API-IL 化により親油性を付与することで、疎水性膜である角層への薬物の分配や角層中における拡散の向上が期待される[3]。さらに、C_8 以上の長鎖アルキル基を有する imidazolium カチオンから成る IL は、界面活性剤としての性質を示すことが知られ、この性質により角層中の細胞間脂質に直接作用することで、薬物の経皮吸収を促進すると報告されている[4]。

1) M. Kitaoka, R. Wakabayashi, M. Goto, *Biotechnology Journal*., **2016,** 11, 1375.
2) R. Wakabayashi, M. Sakuragi, Y. Tahara, N. Kamiya, M. Goto, *Mol. Pharm.*, **2018**, 15, 955.
3) M. Goto, *Green Chemistry*, **2020**, 22, 8116.
4) Y. Tahara, N. Kamiya, M. Goto, *Mol. Pharm.*, **2020**, 17, 3845.

Symposium | Co-Innovation Program (CIP) | T3A. Smartmaterials for future medical devices and lifescience

[S04-1pm] T3A. Smartmaterials for future medical devices and lifescience

Chair, Symposium organizer:Masaru Tanaka, Hidekazu Ohashi, Takeshi Nagasaki
Fri. Mar 19, 2021 12:35 PM - 5:00 PM Webiner 4 (Online Meeting)

[S04-1pm-01] Polysaccharide/DNA Complexes to Deliver Therapeutic Oligonucleotides

○kazuo sakurai[1] (1. University of Kitakyushu)
12:35 PM - 1:25 PM

[S04-1pm-02] Adhesive materials developed based on biomimetic technology

○Syuji Fujii[1] (1. Osaka Institute of Technology)
1:25 PM - 1:55 PM

[S04-1pm-03] Nanosheet Wrapping Technology ~Application to Bioimaging tool~

○Yosuke Okamura[1] (1. Tokai Univ.)
1:55 PM - 2:25 PM

[S04-1pm-04] Development of hematopoietic stem cells expansion technology and future.

○Satoshi Yamazaki[1] (1. University of Tsukuba)
2:25 PM - 2:55 PM

[S04-1pm-05] Emergence of Biomaterials inspired by the Living Body -Relation with Supramolecular Structure-

○Nobuhiko Yui[1] (1. Tokyo Medical and Dental University)
3:05 PM - 3:55 PM

[S04-1pm-06] AJICAP®: Chemical site-specific conjugation technology for next-generation ADC

○Tatsuya Okuzumi[1], Yutaka Matsuda[1], Takuya Seki[1], Kei Yamada[1], Tomohiro Fujii[1], Noriko Hatada[1], Yusuke Iwai[1], Natsuki Shikida[1], Kazutaka Shimbo[1], Brian A. Mendelsohn[2] (1. Ajinomoto Co., Inc., 2. Ajinomoto Bio-Pharma Services)
3:55 PM - 4:25 PM

[S04-1pm-07] New developments in biocompatible polymers

○Yoshitomo Nakata Nakata[1] (1. NIPPON SHOKUBAI CO.,LTD)
4:25 PM - 4:55 PM

多糖核酸複合体を用いた核酸医薬の DDS

（北九州市立大学　国際環境工学部）櫻井和朗
Polysaccharide/DNA Complexes to Deliver Therapeutic Oligonucleotides
(*Department of Chemistry and Biochemistry, University of Kitakyushu*) Kazuo Sakurai

Therapeutic oligonucleotides have to be delivered inside of the target cells. Schizophyllan (SPG) is a natural glucan existing as a triple helix in water and as a single chain in alkaline solutions. When homo-polynucleotides such as poly(dA) are added to SPG alkaline solution and subsequently pH is adjusted to be neutral, the single chain of SPG forms a stoichiometric complex with the polynucleotide. We have demonstrated that Dectin-1 recognizes SPG/ODN complexes, and the complex is eventually ingested by APCs.
Keywords：Therapeutic oligonucleotides; β–(1→3)-D-glucan, Drug delivery system

多糖シゾフィラン（SPG）は菌類が産出する中性の β-1,3-グルカである。1 本の核酸と２本の SPG からなる多糖-核酸複合体を形成することを我々は見出した。また、マクロファージや樹状細胞といった免疫細胞上には SPG の受容体である dectin-1 発現している。このことから SPG が dectin-1 は発現している免疫細胞への特異的な核酸キャリアになりうる。本講演ではこの多糖核酸複合体の基礎的な特性を紹介する。

文献

1. Sakurai, K.; Shinkai, S., Molecular Recognition of Adenine, Cytosine, and Uracil in a Single-Stranded RNA by a Natural Polysaccharide: Schizophyllan. *J. Am. Chem. Soc.* **2000,** 122, (18), 4520-4521.
2. Sakurai, K.; Uezu, K.; Numata, M.; Hasegawa, T.; Li, C.; Kaneko, K.; Shinkai, S., Beta-1,3-glucan polysaccharides as novel one-dimensional hosts for DNA/RNA, conjugated polymers and nanoparticles. *Chem Commun (Camb)* **2005**, (35), 4383-98.
3. Sakurai, K.; Mizu, M.; Shinkai, S., Polysaccharide--polynucleotide complexes. 2. Complementary polynucleotide mimic behavior of the natural polysaccharide schizophyllan in the macromolecular complex with single-stranded RNA and DNA. *Biomacromolecules* **2001,** 2, (3), 641-50.
4. Brown GD, Gordon S. : Immune recognition. A new receptor for beta-glucans. *Nature* 413: 36-37, **2001.**
5. Binding assay between murine Dectin-1 and β-glucan/DNA complex with quartz-crystal microbalance. Mochizuki, S.; Morishita, H.; Adachi, Y.; Yamaguchi, Y.; Sakurai, K., *Carbohydrate research* 2014, 391, 1-8.
6. Koyama S., et al. : Plasmacytoid dendritic cells delineate immunogenicity of influenza vaccine subtypes. *Sci Transl Med* 2: 25ra4, **2010**.
7. Kobiyama et al., Nonagonistic Dectin-1 ligand transforms CpG into a multitask nanoparticulate TLR9 agonist. *PNAS* **2014,** *111*, 3086-3091.
8. Permanent acceptance of mouse cardiac allografts with CD40 siRNA to induce regulatory myeloid cells by use of a novel polysaccharide siRNA delivery system. Zhang, Q.; Ichimaru, N.; Higuchi, S.; Cai, S.; Hou, J.; Fujino, M.; Nonomura, N.; Kobayashi, M.; Ando, H.; Uno, A., *Gene therapy* 2015

生物模倣技術に基づく粘接着材料の開発

（阪工大工[1]・阪工大ナノ材研[2]）○藤井 秀司[1,2]
Adhesive materials developed based on biomimetic technology ([1]*Faculty of Engineering, Osaka Institute of Technology*, [2] *Nanomaterials Microdevices Research Center, Osaka Institute of Technology*) ○Syuji Fujii,[1,2]

Here, we introduce a new concept for fabrication of powdered adhesives (pressure-sensitive adhesives and two-part epoxy adhesives) based on liquid marble technology. Liquid marbles are liquid droplets stabilized by hydrophobic solid particles attached to the gas-liquid interface, and it is possible to treat the liquid as a non-sticky powder. Powdered pressure-sensitive adhesive consists of particles with a soft adhesive polymer core and a hard nanoparticle shell morphology, and shows no adhesion in its original form and flows like a powder. Only after application of shear stress, it then shows its adhesive nature. Adhesion is induced by rupture of the nanoparticle coating of the powder and outflow of the inner soft polymer. Powdered two-part epoxy adhesives were fabricated using epoxy monomer and curing agent as liquid phases and hydrophobic silica particles as a particulate stabilizer by homogenization with a blender. The mixture of these two liquid marble powders behaved as a free-flowing powder and no adhesion occurred to solid substrates. Interestingly, the liquid marbles showed adhesive character after application of shear stress, because of release of epoxy monomer and curing agent, followed by polymerization induced by their mixing. The powdered adhesives developed in our laboratory should be particularly useful in bonding in confined and intricate spaces, where highly viscous materials are difficult to apply.
Keywords : Liquid Marble; Dry Liquid; Adhesive; Particle; Biomimetic Technology

アブラムシの中に、肛門から排出する蜜（甘露：高粘度液体）の表面を、自身の体表から分泌する固体ワックス粒子で覆うことで、ぬれ広がらない液滴（リキッドマーブル）を作製するものがいる[1)]。この昆虫が持つ技術を工学的に応用することで、高粘度液体の粉体化、ハンドリング性の向上が実現可能になると期待できる。近年、物理化学分野でリキッドマーブルの形成性、構造、機能に注目が集まり、最近では、リキッドマーブルを基材とする材料化学研究が始まっている[2,3)]。

ものとものとを接合する接着・粘着剤は、我々の日常生活のみならず、多岐にわたる工業分野において必要不可欠な材料である。接着剤は、ものとものと貼り合わせるときは流動性のある液体であり、化学反応や溶媒の揮発により固体に変化し、界面で強固に結びつき剥離に抵抗する力を発揮する。一方、粘着剤は高粘度の液体であり、そのままの状態で被着体に接触し、その後も態の変化を起こさずに剥離に抵抗する。

本講演では、高粘度液体である蜜を内部液にしてリキッドマーブルを作製するアブラムシの技術に倣い、粘稠な液体でありハンドリング性が低く利用範囲に制限がかかっている接着・粘着剤の粉体化を行った研究を紹介する[4)]。粉体状の接着・粘着剤は、微細な空間への導入、複雑な形状を有する被着体の接着が可能であり、接着・粘着の適用範囲拡大が期待できる。

粉体状粘着剤

疎水的表面を有する炭酸カルシウム（$CaCO_3$）ナノ粒子乾燥粉体上で poly(*n*-butyl acrylate) （PBA）粒子水分散体を転がすことで、液滴表面が $CaCO_3$ ナノ粒子で覆われたリキッドマーブルを作製し、次いで水を乾燥除去することにより $CaCO_3$ ナノ粒子で覆われた PBA 粒子を得た。$CaCO_3$ ナノ粒子で覆われた PBA 粒子の集合体は、粘着性を示さない粉（粉体状粘着剤）として振る舞い、良好に漏斗を流下した(Figure 1)。粉体状粘着剤に圧縮応力、せん断応力を加えると、$CaCO_3$ 粒子殻が崩壊し、内部から PBA が漏出することで粘着性が発現した。また、タック試験を行った結果、応力を加える前はほとんどタックが測定されないが、加えた後、タックが発現し、粘着させる際に加える圧力の増加とともにタックおよび粘着エネルギーが増加することが明らかになった。

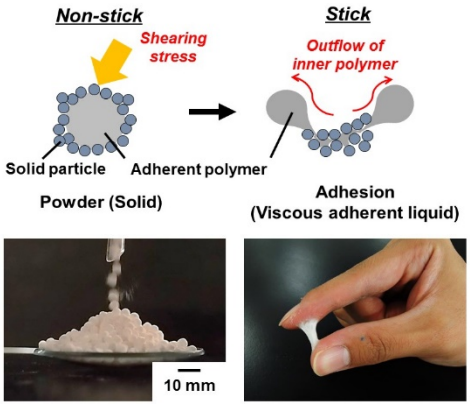


Figure 1 Schematic representation of pressure-sensitive adhesive powder consisting of particles with soft sticky polymer core and hard nanoparticle shell morphology. After application of shearing stress, adhesion property appeared because of outflow of inner soft polymer from the hard particles shell.

粉体状接着剤

エポキシモノマー（ethylene glycol diglycidyl ether）と硬化剤（polyethyleneimine）を内部液とする微小リキッドマーブルを混合することで、流動性に富むパウダー形態での 2 液混合型接着剤を創出した（Figure 2）。作製した粉体状接着剤をスライドガラス間に挟んで応力を加え、24 時間静置し硬化反応を行った後に、重りを吊り下げることで接着力を評価した結果、4.2 kNm^{-2} 以上の接着力が測定された。また、応力印加後の 2 成分の反応を pulse NMR で評価したところ、内部液の分子運動性が低下したことから、重合反応の進行を確認した。

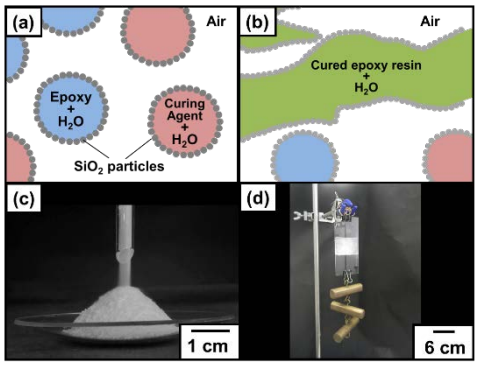


Figure 2 (a,b) Schematic representation and (c,d) optical photographs illustrating two-powder mixing type adhesive (a,c) before and (b,d) after application of shear stress.

1) M. Kasahara, S. Akimoto, T. Hariyama, Y. Takaku, S. Yusa, S. Okada, K. Nakajima, T. Hirai, H. Mayama, S. Okada, S. Deguchi, Y. Nakamura, S. Fujii, *Langmuir* 35, 6169 (2019)
2) S. Fujii, S. Yusa, Y. Nakamura, *Adv. Funct. Mater.* 26, 7206 (2016)
3) S. Fujii, *Polym. J.* 51, 1081 (2019)
4) S. Fujii, S. Sawada, S. Nakayama, M. Kappl, K. Ueno, K. Shitajima, H.-J. Butt, Y. Nakamura, *Mater. Horiz.* 3, 47 (2016)

高分子ナノ薄膜ラッピング技術　～バイオイメージング用アクセサリへの応用展開～

（東海大工[1]・東海大マイクロ・ナノ研[2]）○岡村 陽介[1,2]

Nanosheet Wrapping Technology ~Application to Bioimaging tool~ ([1]*School of Engineering, Tokai University,* [2]*Micro/Nano Technology Center, Tokai University*) ○Yosuke Okamura[1,2]

In the field of biological microscopy technology, it is still a practical challenge to obtain high quality images of tissues and suspension cells, due to the sample desiccation and undesirable cell movement that occurs during observations. We have proposed freestanding biofriendly nanosheets with a thickness of *ca.* 100 nm for biomedical applications[1,2]. These nanosheets represent unique properties such as good adhesiveness, amazingly flexibility, and a high degree of transparency. In this paper, we propose an innovative technique “polymer nanosheet wrapping” to avoid desiccation and movement of tissues and suspension cells, that is applied to a novel imaging tool for taking high quality images including *in vivo* imaging [3-5]. Furthermore, we also demonstrate coverslip-free tissue imaging using the nanosheet with a thickness of less than one-thousandth that of a coverslip in order to achieve a deep tissue imaging[6].

Keywords: polymer nanosheet; wrapping; tissues; suspension cells; imaging tool

顕微鏡を用いたライブイメージング技術は時々刻々と発展しており、生命現象をライブで可視化しありのままの情報を得る必要不可欠な観察技術である。顕微鏡本体や観察精度などのハードウェア面の開発は目を見張るものがあるものの、ソフト面「観察試料の作成法」は未だ研究者のノウハウに頼っている。例えば、生体組織をイメージングする場合、ガラス基板に緩衝液を滴下した状態で観察するのが常套手段であるが、緩衝液の蒸発に伴う組織の乾燥やステージを移動するときのぶれが課題となる。また、血球を代表とする浮遊細胞では、ブラウン運動して焦点が定まらない他、液性刺激因子を滴下した瞬間に拡散してしまう。

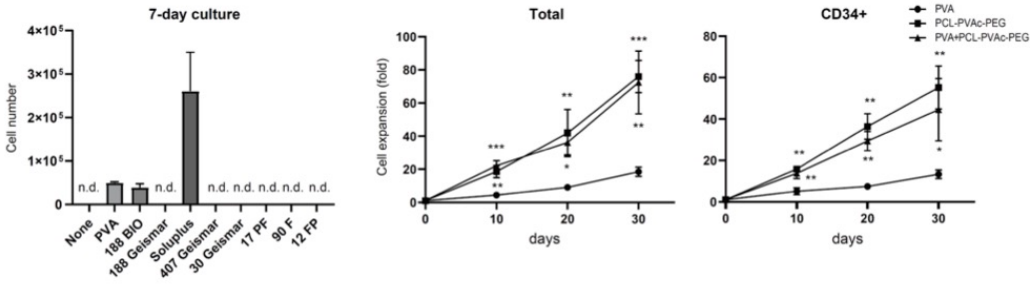
これまで著者らは、厚みをナノ寸法(膜厚 100 nm 以下)に制御した高分子超薄膜を開発してきた[1,2]。得られた超薄膜は、ナノ厚特有の柔軟性と高い接着性が発現し、反応性官能基や接着剤を使用せず物理吸着のみで生体組織等に貼付できるユニークな性質を示す。本研究では、ナノ薄膜による生体組織や浮遊細胞のラッピング技術[3-6]を提案すると共に、ぶれずに美しい像を取得するためのイメージングアクセサリへの応用例を紹介する。

【謝辞】本研究の一部は、文部科学省科学研究費補助金新学術領域研究「ナノメディシン分子科学」(No. 2306)、「共鳴誘導で革新するバイオイメージング」(18H04744)、日本医療研究開発機構「革新的技術による脳機能ネットワークの全容解明プロジェクト」(JP20dm0207087)、2020 年度生理学研究所一般共同研究(No. 20-121)の助成により行われた。

【参考文献】[1] Okamura, Y. *et al. Adv. Mater.* **21**, 4388 (2009). [2] Okamura, Y. *et al. Adv. Mater.* **25**, 545 (2013). [3] Zhang, H. *et al. Adv. Mater.* **29**, 1703139 (2017). [4] Zhang, H. *et al. J. Mater. Chem. B* **6**, 6622-28 (2018). [5] Takahashi, T. *et al. iScience* **20**, 101579 (2020). [6] Zhang, H. *et al. PLoS One* **15**, e0227650 (2020).

Hematopoietic stem cells (HSCs) are a rare cell type that reconstitute the entire blood and immune systems following transplantation. This represents a curative cell therapy for a variety of hematological diseases. However, the low number of HSCs makes both biological analyses and clinical application difficult, and the limited ability to expand human HSCs ex vivo remains a substantial barrier to the wider and safer therapeutic use of HSC transplantation. While various reagents have been tested in attempts to stimulate human HSC expansion, cytokines have long been thought to be essential for supporting HSCs ex vivo. Here we report the establishment of a novel culture system that supports the long-term ex vivo expansion of human HSCs, achieved through the complete replacement of cytokines and albumin with chemical agonists and a caprolactam-based polymer. We discovered that a phosphoinositide 3-kinase activator in combination with a thrombopoietin receptor agonist and the pyrimidoindole derivative UM171 were sufficient to stimulate expansion of umbilical cord blood (CB) HSCs. The optimized conditions expanded engraftable hematopoietic stem and progenitor cells by ~1500-fold during a 30-day ex vivo culture and also supported clonal expansion. We envision that this chemically-defined expansion culture system will help to advance clinical HSC therapies.

"Soluplus" based medium can expansion of human HSCs ex vivo



50 fold expansion was possible using Soluplus!

生体に啓発されたバイオマテリアルの創発
－超分子構造とのかかわり－

由井　伸彦　（東京医科歯科大学）

現実の研究は、想定外の嵐の中で船を操舵しているようなところがあります。大海原で如何なる状況下でも頼りになるのが羅針盤であるように、日々の研究においても冷静かつ客観的な観察と理性的な判断が大切で、その拠り所となるのは研究のビジョンです。アカデミアにとって大切なのは「新しい研究によって概念を提唱する」ことであり、その上で「学理を構築する」と云う明確なビジョンを絶えず意識することでしょう。この「新しい」と云うことが、わかっているようでなかなか難しいように思います。

バイオマテリアルに限りませんが、古くから多くの高分子が「構造-機能相関の解明」を目的の拠り所として研究されてきた背景があります。ですからラフな見方をすれば、従来と同じ構造を用いている限りは新しい機能創発の境地には辿り着けないのではないでしょうか。それでは、高分子って何でしょうか？定義としては、「繰り返し単位となる分子が共有結合で連結された巨大分子量体」と云うことでしょう。であれば、この定義の中で研究をしている限りは、上述の構造-機能相関の呪縛からは逃れられませんから、新たな境地には到達し得ないのではないでしょうか。でもその一方では、この定義を踏み外したら高分子ではないので、その恩恵も特徴も活かせないのではと不安になったりもします。それに、この定義の枠内からはみ出してまでも実施する価値が期待できるものが、そう簡単に見つかる筈もありません。

そうした時に漠然と抱いていたのは、生体の構造体にあって人工材料にはない特徴が、①非共有結合（分子間力）の緩やかな連結による機動的な機能発現と②代謝による生まれ変わりと云うことでした。①については実現可能性のある具体的な構造を、②については代謝に伴う機能発現を長く自問自答しました。

大袈裟に云うと、こうした果てに 1993 年に始めたのが現在の研究の源流になります。機械的連結様式のポリロタキサンをベースとして生体との相互作用の新たな機能創発を目指しているもとには、こうした背景があります。従来からの共有結合様式の高分子で明らかにされてきた分子の形（構造）や動き（物性）の関わりが機械的連結様式の高分子にはあてはまらないからです。だから、共有結合様式ではなく機械的連結様式の特徴を最大限に活かすことで、従来からは全く期待も想像もできないバイオマテリアルとしての機能を創発できると考えてきたからです。これが、筆者が 30 年来こだわってきた「バイオマテリアル創発」のベースとなる信念です。本講演では、そうした背景のもとで歩んだ 30 年間を振り返って明らかにしてきた成果と、今なお混沌としている未解決課題への取組について解説したいと思います。

研究には大きな遠回りが必要です。Slow and steady wins the race と云いますね。ビジョンを明確に見据えたならば、あとは着実に時間をかけて遠回りして研究に邁進するのが大事だと思います。研究成果の一つ一つが、その中での大切な里程の石となっているのです。そう云う信念で歩んできた筆者も定年退職まで残り 2 年ですが、その考えや判断に誤りはなかったと確信して今も研究に取り組んでいます。

AJICAP®: 位置選択的 ADC の次世代化学合成法の開発

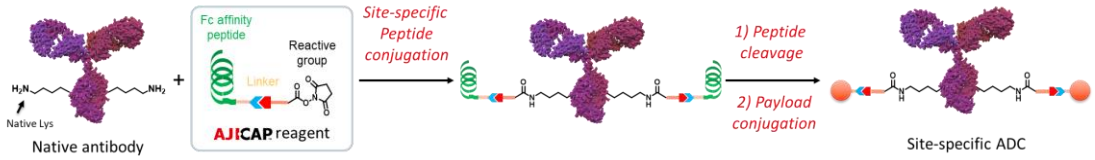
(味の素株式会社[1]・アジノモトバイオ・ファーマサービス[2]) ○奥住 竜哉[1]、松田 豊[1]、關 拓也[1]、山田 慧[1]、藤井 友博[1]、畑田 紀子[1]、岩井 佑介[1]、敷田 奈都紀[1]、新保 和高[1]、Brian Mendelsohn[2]
AJICAP®: Chemical site-specific conjugation technology for next-generation ADC
([1]*Ajinomoto Co., Inc.*, [2]*Ajinomoto Bio-Pharma Services*) ○ Tatsuya Okuzumi[1], Yutaka Matsuda[1], Takuya Seki[1], Kei Yamada[1], Tomohiro Fujii[1], Noriko Hatada[1], Yusuke Iwai[1], Natsuki Shikida[1], Kazutaka Shimbo[1], Brian A. Mendelsohn[2]

The development of conjugation technologies for biomolecules such as proteins and nucleic acids has made remarkable progress in recent years. Especially, a method for the conjugation of a specific amino acid residue in a protein has been researched over many years. These conjugation technologies are important in the field of chemical biology and the development of complex biologics. Antibody-Drug Conjugate (ADC) is a targeting drug in which a highly potent small molecule drug is conjugated to an antibody, and its development is accelerated recently. Compared to conventional chemotherapy, the advantage of ADC is the wideness between Minimum Effective Dose (MED) and Maximum Tolerated Dose (MTD), the so-called Therapeutic Index. Recent studies have reported that site-specific ADCs have a further expand Therapeutic Index, leading to safer ADCs compared with random ADCs.

Recently, we have developed a method called AJICAP® for site-specific functionalization without genetic engineering of antibodies in order to accelerate the development of next-generation site-specific ADCs.[1)] The AJICAP® technology is a chemical method that uses a peptide having an ability to bind to the Fc region of an antibody, and the peptide enable site-specific conjugation on a proximal lysine residue to peptide binding moiety. Compared with the technologies using genetic engineering or an enzyme, the manufacturing process of AJICAP® site-specific conjugation is simple and straightforward. We have succeeded in synthesizing a variety of site-specific ADCs by using AJICAP®. In the presentation, we will report the synthesis of various ADCs using AJICAP® and the expansion of Therapeutic Index comparing with random ADCs.
Keywords : Antibody Drug Conjugate; ADC; Site-specific; Conjugation

タンパク質や核酸などの生体高分子を修飾する技術の開発は近年目覚ましい発展を遂げている。その中でも、タンパク質のある特定のアミノ酸残基を位置特異的に修飾する方法は古くから研究が行われてきた。これらの修飾技術はケミカルバイオロジー分野の研究や、複雑化するバイオ医薬品の開発に重要である。抗体薬物複合体（Antibody-Drug Conjugate, ADC）は抗体に高活性な低分子薬剤をコンジュゲートした分子標的薬であり、開発研究が加速している。従来の化学療法と比較して、Minimum Effective Dose (MED)と Maximum Tolerated Dose (MTD)の差、いわゆる Therapeutic Index が広がることが最大の特徴である。最近の研究で、位置特異的に薬剤をコンジュゲートしたADCは、ランダムに薬剤をコンジュゲートしたADCよりも、さらにTherapeutic Index が拡張し、より安全性の高い ADC が作成できることが報告されている。

今回、我々は次世代型の位置特異的に薬剤がコンジュゲートされた ADC の開発を加速するため、非遺伝子改変抗体に対して、位置特異的に官能基化する手法（AJICAP™法）を開発した [1]。AJICAP™法は抗体の Fc 親和性ペプチドを利用して、ペプチドがバインドした際に近傍のリジン残基を位置特異的に官能基化する化学的手法であり、従来の抗体の遺伝子改変、あるいは、酵素を用いる手法に比較し、簡便に抗体上の位置特異的修飾が可能である。我々はこれまでに本手法を利用して、種々の位置特異的 ADC の合成に成功している。今回の講演では AJICAP™を用いた種々の ADC の合成結果、および、ランダムに薬剤をコンジュゲートした ADC と比較した場合の Therapeutic Index の拡張について報告する。



1) AJICAP: Affinity Peptide Mediated Regiodivergent Functionalization of Native Antibodies. K. Yamada, N. Shikida, K. Shimbo, Y. Ito, Z. Khedri, Y. Matsuda, B. A. Mendelsohn, *Angew. Chem., Int. Ed.* 2019, 58 (17), 5592−5597.

生体適合性ポリマーの新展開

（日本触媒） 中田善知

New developments in biocompatible polymers (*Nippon shokubai CO.,LTD.*) ○Yoshitomo Nakata

We will introduce the development of biocompatible polymers based on the intermediate water concept. We investigated the characteristics of methylene glutaric acid (MGA) polymers, which can spatially arrange functional groups at high density by conventional radical polymerization, and allyloxymethyl acrylate (AOMA) polymers, which show excellent mechanical properties in cyclopolymerization. These polymers showed a decrease in intermediate water and increase in nonfreezing water due to the rigid main chain structure. On the other hand, the side chain functional group, glycerol monoacrylate (GLMA) possessed a large amount of intermediate water and a small amount of nonfreezing water. The blood compatibility of these polymers correlated well with the amount of intermediate water and nonfreezing water, suggesting that the effect of nonfreezing water increased in region where the amount of intermediate water was small. Moreover, we examined the influence of the comonomers in the GLMA copolymer on the blood compatibility, and found that the mobility of the main chain was dominant.

In the presentation , we will introduce the excellent properties of GLMA-based polymers, application examples, and functionalization by combining with crosslinking technology.

Keywords：*biocompatible: glycerol monoacrylate*

中間水コンセプト[1)]に基づく生体適合性ポリマーの開発について紹介する。通常のラジカル重合により、官能基を空間的に高密度に配置できるメチレングルタル酸（ＭＧＡ）ポリマーや、環化重合で優れた機械物性を発現するアリルオキシメチルアクリレート（ＡＯＭＡ®）ポリマーを検討したが、硬い主鎖構造の影響で、中間水が減少し、不凍水が増加した。また、側鎖官能基についてはグリセロールモノアクリレート（ＧＬＭＡ）の中間水が多く、不凍水が少ないという特徴があった。

これらのポリマーの血液適合性評価は中間水、不凍水の量とよく相関しており、特に中間水量が少ない領域において不凍水の影響が大きくなることが示唆された。

また、ＧＬＭＡ共重合体におけるコモノマーの影響について検討し、特に主鎖の硬さ（Ｔｇ）の影響が顕著であることが分かった。[2)]

当日はＧＬＭＡ系ポリマーの優れた特性と、用途例の紹介、さらに架橋技術との組み合わせによる機能化についても紹介する。

【参考文献】

1) 田中賢　高分子論文集,vol.60,No.8,pp.415-427(2003)

2) 特開 2018-33846(日本触媒)

Symposium | Co-Innovation Program (CIP) | T4. The dawn of co-innovation – academia-industry collaboration toward seeds co-creation -

[S05-1am] T4. The dawn of co-innovation – academia-industry collaboration toward seeds co-creation -

Chair, Symposium organizer:Ryotaro Tsuji, Ryu Abe
Fri. Mar 19, 2021 9:50 AM - 12:00 PM Webiner 5 (Online Meeting)

[S05-1am-01] Open Innovation Activities in Pharmaceutical Industries
○Michio Fujisawa[1], Atsushi Endo[1], Yoshito Kanazawa[1] (1. Daiichi Sankyo Co., Ltd.)
10:00 AM - 10:30 AM

[S05-1am-02] From basic research to innovation: de novo peptide drug discovery innovation
○Hiroaki Suga[1] (1. The University of Tokyo)
10:30 AM - 11:00 AM

[S05-1am-03] A Dialogue Model for Open Innovation
○Tomoko Kawakami[1] (1. Waseda University)
11:00 AM - 11:30 AM

[1S0501-03-5add] Discussion
11:30 AM - 12:00 PM

製薬企業のオープンイノベーションの取り組み

（第一三共株式会社・研究開発本部 研究統括部[1], バイオロジクス本部 モダリティー研究所[2]）○藤澤 道雄[1]・金澤 佳人[2]・遠藤 淳[2]

Open Innovation Activities in Pharmaceutical Industries

([1]*Reserch Function, R&D Division, Daiichi Sankyo Co., Ltd.,* [2]*Biologics Function, Biologics Division, Daiichi Sankyo Co., Ltd.*) ○ Michio Fujisawa,[1] Yoshito Kanazawa,[2] Atsushi Endo[2]

Open innovation play an enormous role in research and development strategies in pharmaceutical industries by introducing the latest science and technologies from outside the company. TaNeDS, a domestic open innovation program of Daiichi Sankyo has been carried out every year since FY2011 and the purposes of the program are scouting promising research themes and constructing a network with academic researchers based on Daiichi Sankyo's needs. As the results, lots of collaborative research have been initiated with researchers not only in biology/medical fields but also in drug discovery technology fields. Similar competition programs have been carried out by several pharmaceutical companies and they have contributed the promotion of industry-academia partnership so far. It is considered necessary to deepen such programs in order to further accelerate the partnership for generation of innovative drugs.

Keywords：Open Innovation; Industry-academia partnership; TaNeDS;

製薬企業においてオープンイノベーションの活動は、社外から最新の科学や技術を導入し、自社の強みを強化し弱みを補うための戦略として非常に大きな役割を担っている。製薬各社は様々な活動に取り組んでおり、その目的は多様である。例えば、近年注目されている医薬品のモダリティーに関して、かつての生活習慣病を適応とした低分子医薬品から、中分子医薬品、またはバイオロジクス医薬品の研究開発へのドラスティックな変化に対応するには、社外からの技術導入・提携が必須である。

本講演では創薬の初期研究ステージにおけるオープンイノベーション活動として、第一三共株式会社が実施している国内ライフサイエンス系研究者を対象とした研究公募プログラム：TaNeDS（タネデス）について紹介する。TaNeDS は 2011 年度から毎年実施され、創薬標的の同定や検証、あるいは創薬プラットホーム技術の構築などを目的として、数多くのコラボレーションが生まれている。TaNeDS の特徴の一つに、募集する研究領域が多様であることが挙げられる。医学系研究者との疾患に関する研究のみならず、創薬に関係する技術研究を対象として、研究ニーズを開示しマッチする研究を求めている。その結果、これまで様々な分野の研究者とコラボレーションをもとにしたネットワークが構築され、そこから更に副次的に新たなコラボレーションも生まれている。同様のプログラムは幾つもの製薬企業において実施されており、産学連携の推進に大きな役割を果たしているが、今後さらに、産学双方にとってより有用なプログラムとなるよう深化させていく必要がある。

この講演では、長年にわたる基礎研究成果から創出された RaPID（Radom nonstandard Peptides Integrated Discovery）システムが創薬プラットフォーム技術としてどのように発展してきたか、それがもたらした創薬の常識を覆す成果と変革、さらにはベンチャー企業の創業によって進めてきた社会実走の挑戦と理念を発表する。

This lecture will present the development of RaPID (Radom nonstandard Peptides Integrated Discovery) system, as a platform technology, generated from the outcomes of basic research, it has brought about the revolution of drug discovery processes, and the challenges and concepts of the entrepreneurship by starting a venture company.

オープン・イノベーションと対話モデル

（早稲田大学大学院　経営管理研究科）川上智子
Kawakami, Tomoko, Waseda Business School, Waseda University

We can take an open innovation strategy at any stage of discovery, development, and commercialization. However, we often observe that, even if taken at the discovery stage, it fails to reach the development and commercialization stages due to the lack of organizational adaptability. The reasons include uncertainty avoidance, lack of leadership and driving forces, and inappropriate resource allocation, and so forth. As a solution to these challenges, this research proposes a dialogue type model, so called MAIN (Marketing-Innovation) model in which marketing and R&D is effectively integrated to reduce the uncertainty for decision making and accelerate development speed. We also introduce practical cases in which we applied the MAIN model.
Keywords : Open Innovation, Co-creation, Dialogue model

オープン・イノベーションは、発見・開発・市場化のどの段階でも実行可能である。しかし、発見段階でオープン化しても、組織内に受け皿がなく、開発や市場化まで到達しないケースが多い。おもな理由は、意思決定上の不確実性回避、リーダーシップと推進力の欠如、不適切な資源配分などである。それらの解決策として、本報告では、マーケティングと R&D を統合し、不確実性を回避して開発スピードを加速化させる対話型 MAIN モデル(Marketing Innovation Model)を提案し、その実践事例を紹介する。

11:30 AM - 12:00 PM (Fri. Mar 19, 2021 9:50 AM - 12:00 PM Webiner 5)

[1S0501-03-5add] Discussion

Symposium | Medium and Long-Term Program | state-of-the-art of super dimensional chemistry

[S07-1pm] state-of-the-art of super dimensional chemistry

Chair, Symposium organizer:Hochol Chang, Hitoshi Miyasaka, Shinya Hayami

Fri. Mar 19, 2021 1:00 PM - 3:40 PM Webiner 7 (Online Meeting)

[S07-1pm-01] Transdimensional materials created by 2D oxides

○Minoru Osada[1,2] (1. IMaSS, Nagoya Univ., 2. WPI-MANA, NIMS)

1:05 PM - 1:35 PM

[S07-1pm-02] Precision Synthesis of Low-Dimensional Nanocarbon Materials

○Akimitsu Narita[1,2] (1. Okinawa Institute of Science and Technology Graduate University, 2. Max Planck Institute for Polymer Research)

1:35 PM - 2:05 PM

[S07-1pm-03] Two-dimensional heterostructures: heterostakings and heterojunctions

○Ryo Kitaura[1] (1. Nagoya Univ.)

2:05 PM - 2:35 PM

[S07-1pm-04] Creation of molecular nanosheet crystals utilizing air-water interfaces: Controlling morphology and functionality

○Rie Makiura[1] (1. Osaka Prefecture University)

2:35 PM - 3:05 PM

[S07-1pm-05] A niche between chemistry and physics opened by mathematics: topological materials science

○Takao Sasagawa[1] (1. Tokyo Institute of Tech.)

3:05 PM - 3:35 PM

Trans-Dimensional Materials Created by 2D Oxides

([1]*IMaSS, Nagoya University*, [2]*WPI-MANA, NIMS*) ○Minoru Osada[1,2]
Keywords: 2D Oxides; Trans-Dimensional Materials; Self-assembly; Nanoarchitectures

Hierarchical self-assembly is a ubiquitous process in nature where it underlies the formation of complex biological structures. Over the past decades, scientists have aspired to exploit modular approaches to create new artificial materials with hierarchical structures and tailored properties. However, *de-novo* design of such hierarchical structured materials is still a major challenge. In this talk, we present new design principles for tans-dimensional materials using hierarchically structured assembly of 2D oxide nanosheets.
As a new direction for the hierarchical self-assembly, dimension-reduced approaches such as layering 2D nanostructures become an important target. Among various 2D nanosheets, 2D oxide nanosheets are important, fascinating research targets to be pursued because of the virtually infinite varieties of layered oxide materials with interesting functional properties[1,2]. Oxide nanosheets have distinct differences and advantages compared with graphene and other 2D nanosheets because of their potential to be used as insulators, semiconductors, and even conductors, depending on their chemical composition and the structures of the parent layered compounds. Oxide nanosheets also have remarkable potential as building blocks for tailoring tans-dimensional materials combined with a wide range of foreign materials such as organic molecules, gels, polymers, and inorganic nanoparticles. In practice, colloidal nanosheets can be organized into various nanostructures or combined with a range of foreign materials at the nanometer scale by applying solution-based self-assembly[3,4]. Such soft-chemical protocols relying on 2D building blocks open up pathways to create new artificial materials with kinetically controlled, hierarchical nanoarchitectures and tailored properties. We present a perspective on the advantages offered by nanosheet architectures for various applications in optoelectronics[5-7], spinelectronics[8], energy and environment technologies[8,9].

1) M. Osada and T. Sasaki, *Adv. Mater*. **2012**, *24*, 209. 2) M. Osada and T. Sasaki, *Dalton Trans*., **2018**, *47*, 2841. 3) K. Matsuba *et al*., *Sci. Adv*. **2017**, *3*, e1700414. 4) Y. Shi *et al*., *ACS Nano* **2020**, *14*, 15216. 5) S. Li *et al*., *Nat. Mater*. **2018**, *17*, 535. 6) B.-W. Li *et al*., *J. Am. Chem. Soc*. **2017**, *139*, 10868. 7) T. Taniguchi *et al*., *ACS Nano*, **2019**, *13*, 11214. 8) B.-W. Li *et al*., *J. Am. Chem. Soc*. **2016**, *138*, 7621. 9) T-P. Chen *et al*., *Adv. Energy Mater*. **2018**, *8*, 1701722. 10) T. Taniguchi *et al*., *ACS Nano*, **2020**, *14*, 6663.

低次元ナノカーボン材料の精密合成

（沖縄科技大[1]・マックス･プランク高分子研[2]）○成田 明光[1,2]
Precision Synthesis of Low-Dimensional Nanocarbon Materials ([1]*Okinawa Institute of Science and Technology Graduate University*, [2]*Max Planck Institute for Polymer Research*) ○ Akimitsu Narita,[1,2]

Whereas graphene demonstrates exceptional electronic and mechanical properties, its lack of bandgap prohibits its applications as an active semiconductor material.[1] In contrast, nanostructures of graphene, such as quasi-zero-dimensional (0D) graphene quantum dots (GQDs) and quasi-one-dimensional (1D) graphene nanoribbons, have non-zero bandgaps as well as unique electronic, optical, and magnetic properties that are distinct from those of 2D graphene and dependent on their chemical structures. Although GQDs and GNRs cannot be obtained with precise chemical structures by predominant top-down fabrication methods, as represented by the lithographic patterning of graphene, bottom-up chemical synthesis can achieve such low-dimensional nanocarbons with atomically precise structures.[1–3] For example, we have achieved π-extension of $N = 7$ armchair GNR (7-AGNR) with partial zigzag edges, which demonstrated unique topological electronic states at junctions with pristine 7-AGNR segments (Figure 1a,b),[4] highlighting further potential of bottom-up-synthesized GNRs as topological materials. We have also synthesized dibenzo[*hi*,*st*]ovalene as an atomically precise GQD with a combination of armchair and zigzag edge structures, and demonstrated its strong red fluorescence and unique photophysical properties that render DBOV interesting for optical applications such as lasering and imaging with the super-resolution microscope techniques (Figure 2c,d).[5,6]

Keywords : Nanocarbon; Bottom-up synthesis; Graphene nanoribbon; Nanographene; Polycyclic Aromatic Hydrocarbon

グラフェンのナノ構造であるナノグラフェンは、その化学構造に依存したエネルギーギャップや特異な電気的、光学的、磁気的性質を示し、次世代ナノカーボン材料として近年盛んに研究されている[1)]。特に、０次元状のグラフェン量子ドット（GQD）や１次元短冊状のグラフェンナノリボン（GNR）が注目を集めており、発光材料としての応用やナノエレクトロニクスや量子情報技術への展開も期待されている。物理学やナノテクノロジーの分野においては、グラフェンからのリソグラフィーによる切り出しに代表されるトップダウン法による研究が進められているが、このような手法では正確な構造や特定の物性を得るのが困難である。そこで我々は、有機化学や高分子化学の手法を用いたボトムアップ法により、原子レベルで正確な構造をもった GNR の合成研究を進めている[1–3)]。また、GQD とみなせる大型の多環芳香族炭化水素（PAH）の合成や物性評価を通して、構造物性相関の確立や材料応用を見据えた研究も行なっている。

GNR のボトムアップ合成は、前駆体となる有機化合物を適切な構造を持ったポリマーへと重合し、さらに脱水素環化反応により「平面化」することにより行われる[1–

[3]。前駆体の設計と合成が鍵となり、様々な構造や物性を持った GNR を合成することが可能となる。例えば、我々は Roman Fasel 教授（EMPA）との共同研究により、炭素原子 7 個分の幅を持つアームチェア型 GNR（7-AGNR）をジグザクエッジにより π 拡張することに成功し（図 1 a,b）、7-AGNR とのヘテロ接合を形成することにより、接合部位において特異なトポロジカル電子状態が発現することを示した [4]。

また、アームチェア型とジグザグ型のエッジ構造を併せ持つジベンゾ[*hi*,*st*]オバレン（DBOV）を合成し、強い赤色蛍光や誘導放出を示すことを報告した（図 1 c,d）[5]。レーザーや光ファイバー増幅器、超解像蛍光顕微鏡法への応用可能性を示唆する結果も得られている [6]。DBOV の位置選択的なブロモ化を経て、サーカムピレン（circumpyrene）の合成にも成功した [7]。

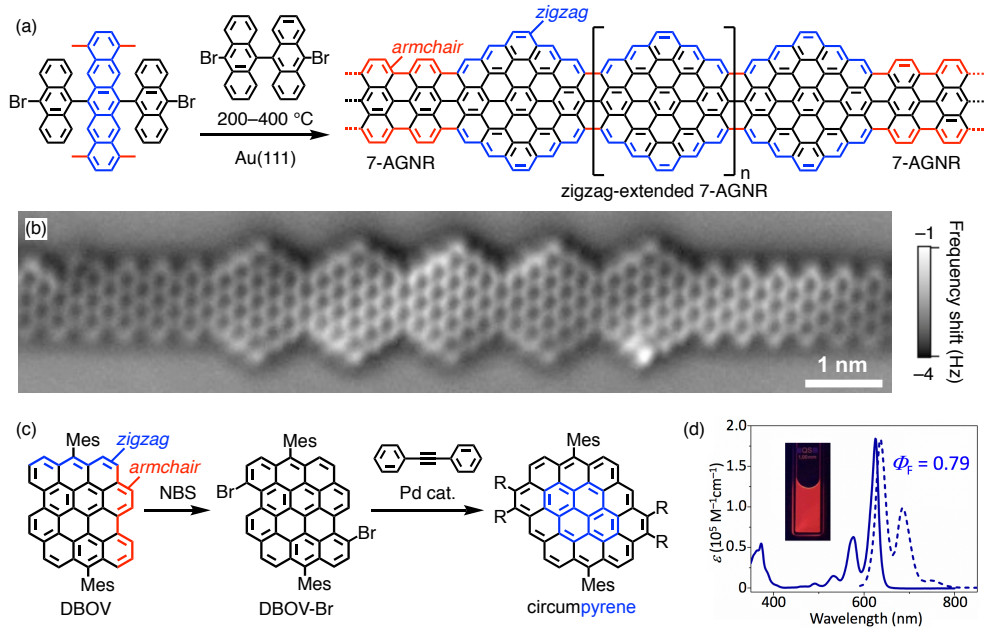


図 1 (a) ジグザグエッジ拡張した 7-AGNR と 7-AGNR のヘテロ接合の Au(111)表面上での合成. (b) 得られた GNR ヘテロ接合の AFM 像.[4] (c) DBOV のブロモ化を経た Circumpyrene の合成と(d) DBOV の光学スペクトル.[5]

1) X.-Y. Wang, A. Narita and K. Müllen, *Nat. Rev. Chem.* **2017**, *2*, 0100.
2) X. Xu, K. Müllen, A. Narita, *Bull. Chem. Soc. Jpn.* **2020**, *93*, 490.
3) Z. Chen, A. Narita, K. Müllen, *Adv. Mater.* **2020**, *32*, 2001893.
4) O. Gröning, S. Wang, X. Yao, C. A. Pignedoli, G. Borin Barin, C. Daniels, A. Cupo, V. Meunier, X. Feng, A. Narita, K. Müllen, P. Ruffieux, R. Fasel, *Nature* **2018**, *560*, 209.
5) G. M. Paternò, Q. Chen, X.-Y. Wang, J. Liu, S. G. Motti, A. Petrozza, X. Feng, G. Lanzani, K. Müllen, A. Narita, F. Scotognella, *Angew. Chem. Int. Ed.* **2017**, *56*, 6753.
6) X. Liu, S.-Y. Chen, Q. Chen, X. Yao, M. Gelléri, S. Ritz, S. Kumar, C. Cremer, K. Landfester, K. Müllen, S. H. Parekh, A. Narita, M. Bonn, *Angew. Chem. Int. Ed.* **2020**, *59*, 496.
7) Q. Chen, D. Schollmeyer, K. Müllen, A. Narita, *J Am Chem Soc* **2019**, *141*, 19994.

超構造化による二次元系の電子物性制御

（名大院理）北浦 良
Fabrication and properties of two-dimensional heterostructures ([1]*Department of Chemistyr, Nagoya University*) Kitaura, Ryo

Two-dimensional (2D) materials, including graphene, boron nitrides, and transition metal dichalcogenides (TMDs, Fig. 1), have provided a platform to explore novel physics and chemistry at the 2D limit. In addition to the fascinating properties of 2D materials themselves, 2D materials allow exploring novel 2D-based superstructures, such as heterojunctions, heterostacks, and superlattices, which give even broader possibilities. We are working on the fabrication of 2D superstructures through (1) crystal growth with metal-organic chemical vapor deposition (MOCVD) and molecular beam epitaxy (MBE), and (2) stacking 2D components with the full-dry-transfer-based manipulation technique[1)-4)]. This presentation will focus on two 2D superstructures, 2D lateral superlattices and TMD/CNT heterostacks. For example, MoS_2/WS_2 2D lateral superlattices with a periodicity of around 10 nm can be grown by MOCVD with an automatic valve control system. More details on the fabrication and optical properties of these superstructures will be addressed in this talk.
Keywords : 2D materials, heterostructures, dichalcogenides, optical properties, crystal growth

二次元物質を中心とする低次元物質の科学が大きく発展している。グラフェンの研究に端を発する二次元物質への興味は、六方晶窒化ホウ素、遷移金属ダイカルコゲナイド(TMD, 図 1)など多種多様な二次元物質の発見につながるとともに、それらを中心とした物性探索およびデバイス応用研究が現在進行系でどんどん進展している。近年では、個々の二次元物質に加えて、異なる二次元物質の接合および積層によって生まれる二次元超構造を用いて機能を引き出そうとする研究が活発に行われている。本講演では、分子線エピタキシー法や有機金属化学気相成長法などの先端薄膜成長法を利用した高結晶性二次元物質およびそのヘテロ構造の創出と、顕微分光/イメージングを用いた光学応答の観測を中心とした物性探索について、最近の結果を紹介したい。また、時間が許せば、最近取り組んでいる二次元物質とカーボンナノチューブの積層構造を用いた励起子の一次元閉じ込めについても紹介する。

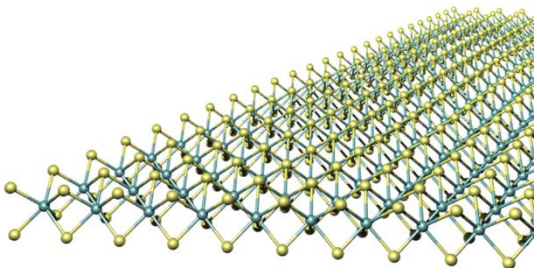


図 1. 代表的な二次元物質である単層 TMD の構造

1) T. Hotta, et. al., *ACS Nano*, **2021**, 51, 1, 1370-1377
2) T. Hotta, et. al., *Phys. Rev. B*, **2020**, 102, 115424
3) Y. Uchiyama et. al., *npj 2D Materials and Applications*, **2019**, *3*, 26
4) M. Okada, et. al., *ACS Nano*, **2018**, *12*, 2498-2505

気水界面における分子ナノシート結晶の創製：モルフォロジー制御と機能創出

（阪府大院工）○牧浦理恵

Creation of molecular nanosheet crystals utilizing air-water interfaces: Controlling morphology and functionality

(*Graduate School of Engineering, Osaka Prefecture University*) ○Rie Makiura

Development of rational methods for creating ordered two-dimensional (2D) structures with nanometer scale precision is one of the central issues in the nanoscience and nanotechnology fields because of their intrinsic physical-chemical properties which are seen in those of their equivalent bulk state. Inclusion of highly regulated nanopores into the nanosheet structure will further open the possible applications such as nanosieves, molecular/ion storage and sensor devices as well as introducing guest molecules into the nanopores tune variedly the sheet properties (electric conduction, nanoheterojunction). Utilizing molecular building units are suitable for creating such porous nanosheets because of rich variety of design and facile modification of size and shape. Furthermore, various chemical interactions such as covalent bond, coordination and hydrogen bond are applied for assembling molecular-based nanosheets.

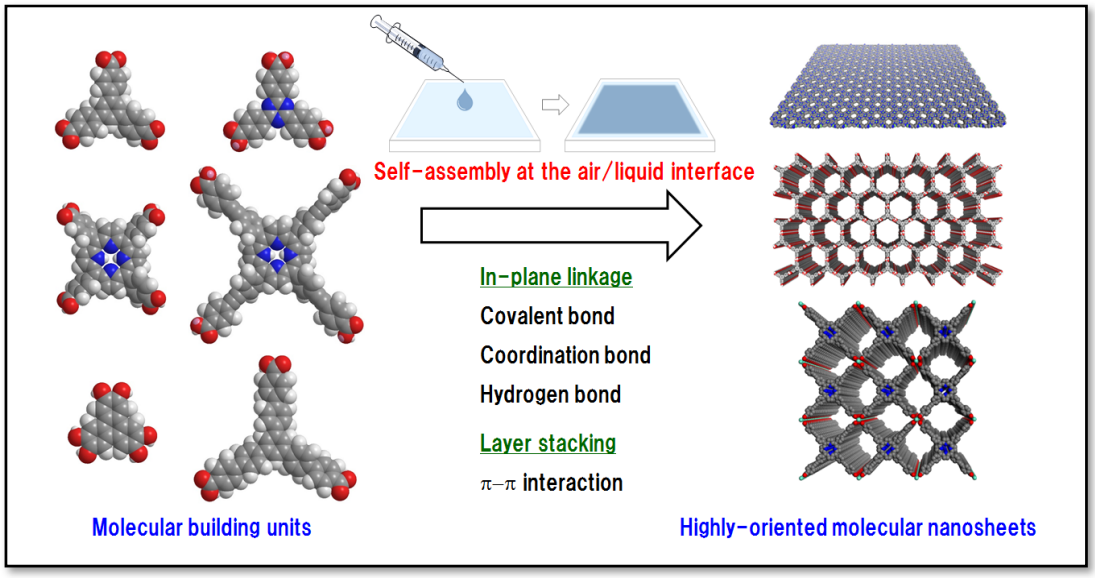
Here, I present a facile bottom-up synthesis of molecular nanosheets with both positional and size regulated nanopores utilizing air/liquid interfaces. By applying liquid interfaces, growth direction of the object can be well controlled with utilizing self-assembly feature of the molecules under mild conditions. We have succeeded to tune finely the nanosheet structures by rational modification of molecular building units [1-5]. In addition, new methodology we developed based on the liquid interface technique resulted in enlarging the nanosheet size. The highly crystalline structure remains after transferring a solid substrate from the liquid surface as well as without any supports. Notably, such highly oriented porous crystalline structure is obtained specifically by applying bottom up synthesis at air/liquid interfaces, not by other techniques such as drop cast.

***Keywords**: Nanosheet, Air/liquid interface, Metal-organic framework (MOF), Bottom-up synthesis, Oriented film,*

ナノメートルスケールの厚みを有する２次元物質（ナノシート）は、その次元性に由来した特異な化学的・物理的性質を示すことから物性研究が盛んに行われているのみならず、エレクトロニクスへの応用利用が期待される。ナノシートが多孔質である場合は、効率の良い分離・透過膜として利用できることに加え、細孔に異種分子やイ

オンを導入することで特性を変化させ多機能化を図ることができる。分子を構成要素として得られる分子ナノシートは設計の多様性に富み、分子の大きさや形状により骨格構造を変化させることができるため、多孔性ナノシートの創製に適している。また、狙いとする機能に応じたナノシートの創製に向け、分子間の連結には共有結合のみならず、金属イオンとの配位結合や水素結合を利用することも可能である（下図）。

これまでの研究において、有機配位子と金属イオンからなる多孔性の配位高分子ナノシートが得られている [1]。これは完全配向した多孔性配位高分子ナノシートの初めての例であり、気体と液体が接する２次元界面（気液界面）においてナノシートが形成されている点が特徴である。気液界面においては、均一で穏やかに反応が進行する溶液反応の特徴を活かしながら、生成物の成長方向を２次元に制御することが可能である。本発表においては、この気液界面を用いた手法を適用し、構成分子の形状・サイズを変化させることにより得られた様々な細孔サイズを有する多孔性ナノシート [2]や気液界面における錯形成反応の制御により得られたサブミクロンスケールで構造が均一な配位高分子ナノシート [3-4] に加え、水素結合により分子が連結して形成される多孔性分子ナノシート [5]に関して報告する。



1) Makiura, R., Motoyama, S., Umemura, Y., Yamanaka, H., Sakata, O., et al. *Nature Mater*. **9**, 565 (2010). 2) Makiura, R., Usui, R., Sakai, Y., Nomoto, A., Ogawa, A., et al. *ChemPlusChem*. **79**, 1352 (2014). 3) Makiura, R., Konovalov, O. *Sci. Rep*. **3**, 2506 (2013). 4) Makiura, R., Konovalov, O. *Dalton Trans*. **42**, 15931 (2013). 5) Makiura, R. Tsuchiyama, K., Pohl, E., Prassides, K., Sakata, O., et al. *ACS Nano*, **11**, 10875–10882 (2017).

数学が拓いた化学と物理の新しい狭間:トポロジカル物質材料科学

（東工大）○笹川 崇男
A Niche between Chemistry and Physics Opened by Mathematics: Topological Materials Science (*Laboratory for Materials and Structures, Tokyo Institute of Technology*)
○Takao Sasagawa

Topological materials science is a new science and technology of this century, born across chemistry and physics by applying the mathematical concept of topology (soft geometry) to electronic states. The progress of the field, from insulators to semimetals to superconductors, will be reviewed along with our contributions[1-12]. Then, the great potential and future prospects of topological quantum materials and properties will be discussed from the perspective of "trans-dimensional chemistry".
Keywords : Topological Materials Science; Topological Insulator; Topological Semimetal; Topological Superconductor

トポロジカル物質材料科学は、やわらかい幾何学という数学の概念を電子状態に適用することで化学と物理にまたがって生まれた、今世紀の新しい学問・科学技術である。絶縁体から始まり、半金属、そして超伝導体へとすそ野を拡げてきた分野の進展を講演者の研究を交えながら紹介する[1-12]。そして、トポロジカル量子物質・物性がもつ大きな可能性について、超次元化学の観点も鑑みながら話題提供し、今後の展望を議論する。

1) Evidence for a Higher-order Topological Insulator in a Three-dimensional Material Built from van der Waals Stacking of Bismuth-halide Chains. R. Noguchi, T. Sasagawa, T. Kondo *et al*., *Nature Materials* (2021), published online. DOI: 10.1038/s41563-020-00871-7.
2) Zero-energy Vortex Bound State in the Superconducting Topological Surface State of Fe(Se,Te). T. Machida, T. Hanaguri, T. Sasagawa *et al*., *Nature Materials* **18**, 811 (2019).
3) A Weak Topological Insulator State in Quasi-one-dimensional Bismuth Iodide. R. Noguchi, T. Sasagawa, T. Kondo *et al*., *Nature* **566**, 518 (2019).
4) Ubiquitous Formation of Bulk Dirac Cones and Topological Surface States from a Single Orbital Manifold in Transition-metal Dichalcogenides. M.S. Bahramy, T. Sasagawa, P.D.C. King *et al*., *Nature Materials* **17**, 21 (2018).
5)トポロジカル電子物質の開拓. 笹川 崇男, *応用物理* **86**, 381 (2017).
6) Full-gap Superconductivity in Spin-polarised Surface States of Topological Semimetal β-$PdBi_2$. K. Iwaya, T. Hanaguri, T. Sasagawa *et al*., *Nature Commun*. **8**, 976 (2017).
7) Observation of Zeeman Effect in Topological Surface State with Distinct Material Dependence. Y.-S. Fu, T. Hanaguri, T. Sasagawa *et al*., *Nature Commun.* **7**, 10829 (2016).
8) Negative Electronic Compressibility and Tunable Spin Splitting in WSe_2. J. M. Riley, T. Sasagawa, P.D.C. King *et al*., *Nature Nanotech.* **10**, 1043 (2015).
9) Topologically Protected Surface States in a Centrosymmetric Superconductor β-$PdBi_2$. M. Sakano, T. Sasagawa, K. Ishizaka *et al*., *Nature Commun.* **6**, 8595 (2015).
10) Imaging the Two-component Nature of Dirac-Landau Levels in the Topological Surface State of Bi_2Se_3. Y.-S. Fu, T. Hanaguri, T. Sasagawa *et al*., *Nature Physics* **10**, 815 (2014).
11) Discovery of a Single Topological Dirac Fermion in a Strong Inversion Asymmetric Compound BiTeCl. Y. L. Chen, Z.-X. Shen, T. Sasagawa *et al*., *Nature Physics* **9**, 704 (2013).
12) Massive Dirac Fermion on the Surface of Magnetically Doped Topological Insulator. Y. L. Chen, T. Sasagawa, Z.-X. Shen *et al*., *Science* **329**, 659 (2010).

Symposium | Medium and Long-Term Program | Chemical communications in living system

[S06-1am] Chemical communications in living system

Chair, Symposium organizer:Hirokazu Arimoto, Masaki Kita

Fri. Mar 19, 2021 9:00 AM - 11:40 AM Webiner 6 (Online Meeting)

[S06-1am-01] Chemical Communication on Insectivorous Mammals

○Masaki Kita[1], Yusuke Yano[1], Mayuko Suzuki[1], Maho Morita[1], Satoshi D Ohdachi[2] （1. Nagoya University, 2. Hokkaido University）

9:05 AM - 9:35 AM

[S06-1am-02] AUTAC: an antibacterial autophagy-inspired degrader

○Daiki Takahashi[1], Hirokazu Arimoto[1] （1. Graduate School of Life Sciences, Tohoku University）

9:35 AM - 10:05 AM

[S06-1am-03] Functional coupling between gut microbiota and enteroendocrine cells

○Takashi TSUBOI[1] （1. Graduate School of Arts and Sciences, The University of Tokyo）

10:05 AM - 10:35 AM

[S06-1am-04] Molecular/neural basis underlying mate choice mediated by individual recognition in medaka fish

○Hideaki Takeuchi[1,2] （1. Tohoku Uni, 2. Okayama Uni.）

10:35 AM - 11:05 AM

[S06-1am-05] Are Fairy Chemicals a new family of plant hormones?

○Hirokazu Kawagishi[1] （1. Shizuoka University）

11:05 AM - 11:35 AM

食虫性哺乳類における化学コミュニケーション

(名大院生命農[1]・北大低温研[2]) ○北 将樹[1]・矢野 佑介[1]・鈴木 麻佑子[1]・森田 真布[1]・大舘 智志[2]
Chemical Communication on Insectivorous Mammals ([1]*Graduate School of Bioagricultural Sciences, Nagoya University*, [2]*Institute of Low Temperature Science, Hokkaido University*)
○Masaki Kita,[1] Yusuke Yano,[1] Mayuko Suzuki,[1] Maho Morita,[1] Satoshi D. Ohdachi[2]

Eulipotyphlans are small insectivorous mammals that mainly feed on insects and earthworms. Among them, shrews are vulnerable to starvation and have a habit of paralyzing their prey using saliva venom. It has also been suggested that the muscle tissue of shrews contains insect repellents and the odor glands contain odorants that repel large mammals. In this symposium, we would like to introduce bioactive substances (chemical communication substances) related to predator-prey system derived from shrews, including their relationship with adaptive evolution.
Keywords : Insectivorous Mammals, Shrew, Saliva Venom, Repellents, Chemical Communication Substances

真無盲腸類は昆虫やミミズなどを主な餌とする食虫性の小型哺乳類である。中でもトガリネズミは飢餓に弱く、唾液の毒を用いて獲物を麻痺させて捕獲する習性がある。演者らはこれまでに、北米に棲息するブラリナトガリネズミの顎下腺より致死性プロテアーゼ毒ブラリナトキシンを発見し、その構造や薬理活性を解明した[1,2]。また、キューバ共和国にてフィールド調査を実施し、絶滅危惧種のキューバソレノドンを捕獲し、その進化系統を明らかにしている[3,4]。

一方、フィールド科学者による長年の生態観察により、トガリネズミの筋肉組織には昆虫や小動物を忌避させる物質が、また臭腺には大型哺乳類を忌避させる匂い物質が含まれることが示唆されている。例えば、キツネなど野生の哺乳類は地面を走り回るトガリネズミをその習性によって捕まえて殺してしまうが、食べずに道端に捨ててしまう。トガリネズミの臭腺は、特に雄の成体では非常に発達しており、独特の匂いを放つ。これまでに、トガリネズミ科の仲間で強い麝香臭を持つジャコウネズミの臭腺成分として dihydrocivetone (cycloheptadecanone) など３種類の環状ケトンが同定されているが、その生理学、生態学的な機能は不明である[5]。このような生物間相互作用に関わる化学物質に特に注目してプロファイリングを行うことで、それらの意外な機能や、保有する生物にとっての存在意義を解明できると期待される。本講演では、演者らが取り組んできたトガリネズミ由来の被食・補食に関わる生物活性物質（化学コミュニケーション物質）について、適応進化との関わりも含めて紹介したい。

1) M. Kita et al., *PNAS* 101, 7542 (2004); 2) D. Uemura et al., *Pure Appl. Chem.* 81, 1093 (2009); 3) J. J. Sato et al., *Sci. Rep.* 6, 31173 (2016); 4) J. J. Sato et al., *Mol. Phylogent. Evol.* 141, 106605 (2019); 5) 大舘, *Aroma Research* 18, 164 (2017).

抗菌オートファジーに着想を得た創薬技術ＡＵＴＡＣ

（東北大院生命）○高橋大輝・有本博一

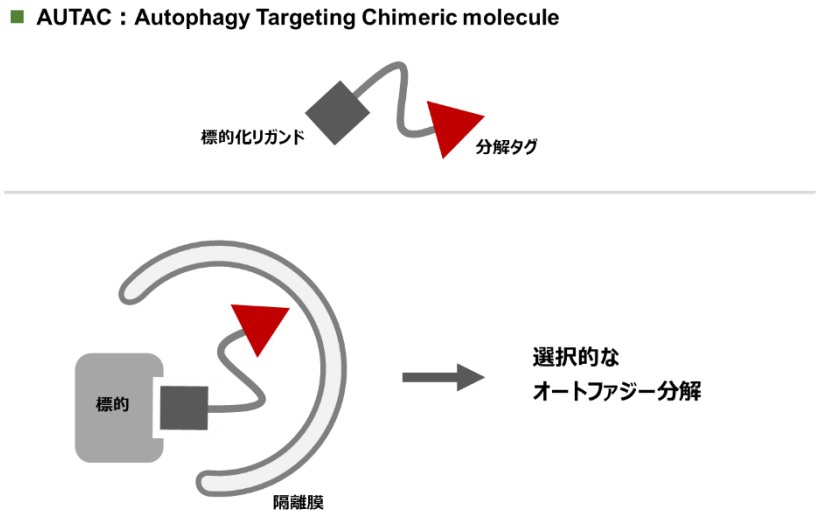
AUTAC: an antibacterial autophagy-inspired degrader

(*Graduate School of Life Sciences, Tohoku University*) Daiki Takahashi and Hirokazu Arimoto

Selective autophagy is a promising target for drug discovery because it suppresses various diseases by the removal of intracellular harmful materials. However, current degrader technologies are largely proteasome dependent. In this talk, we would like to share with you how we developed the first autophagy-based degrader technology, AUTAC (AUtophagy-TArgeting Chimera), based on our previous finding of *S*-guanylation as a selection marker for antibacterial autophagy. The potential advantages of AUTAC over current degrader technologies including PROTACs and ATTEC are also discussed.

Keywords : Autophagy; S-guanylation; Degraders; AUTACs; Mitochondria

オートファジーは，細胞内分子の除去により様々な疾患を抑制することから，創薬における活用が期待されている。私たちは，細菌のオートファジー排除において「S-グアニル化」が選択性を制御することを発見した。本講演では，細菌に限らず広範な基質を分解可能なデグレーダー技術「AUTAC[1]」の開発について述べる。PROTAC, ATTEC を含むデグレーダー技術を俯瞰して AUTAC の位置づけを紹介したい。



1. Takahashi, D. *et al.* AUTACs: Cargo-Specific Degraders Using Selective Autophagy. *Molecular Cell* **76**, 797-810.e10 (2019).

腸内細菌叢と消化管内分泌細胞との機能連関

（東大院総合文化）○坪井 貴司
Functional coupling between gut microbiota and enteroendocrine cells
(*Department of Life Sciences, Graduate School of Arts and Sciences, The University of Tokyo*)
○Takashi Tsuboi

Glucagon-like peptide-1 (GLP-1) is secreted from enteroendocrine L cells. GLP-1 secretion is regulated by various luminal nutrients, bacterial metabolites, and hormones, and secreted GLP-1 maintains homeostasis. Although various bacterial metabolites are known to cause metabolic syndromes and neuropsyhcological disorders, whether these effects are mediated by GLP-1 secretion remains unclear. In the present talk, I will present the relationship between bacterial metabolites and GLP-1 secretion from enteroendocrine cells.
Keywords : gut hormone, gut microbiota, secretory physiology, endocrinology

哺乳類宿主とその腸内細菌叢との共生関係が、宿主のエネルギー摂取や認知機能などに関与する。例えば、糖尿病や認知症、自閉症などは、腸内細菌叢の機能異常によって発症する例が報告されている。また、肥満マウスと正常マウスとを比較すると腸内細菌叢の組成や代謝産物が異なっており、肥満マウスでは特定の腸内細菌と代謝産物が増加している。しかし、腸内細菌代謝産物が、どのようなメカニズムで各種疾患発症に関与しているのかは不明である。

消化管上皮には、多種多様な消化管内分泌細胞が分布する。この消化管内分泌細胞は、管腔内の栄養素や腸内細菌代謝物、血中の生理活性物質、自律神経由来の神経伝達物質などを受容して、消化管ホルモンを分泌し、生体内の恒常性維持に寄与する。今回は、腸内細菌代謝物がどのようか機構で消化管内分泌細胞からの消化管ホルモン分泌を調節するのかについて紹介する[1-3]。

1) Glutamine-induced signaling pathways via amino acid receptors in enteroendocrine L cell line. T. Nakamura et al., *J Mol Endocrinol* **2020**, 64, 133.
2) Green fluorescent protein-based glucose indicators report glucose dynamics in living cells. M. Mita et al., *Analytical Chemistry* **2019**, 91, 4821.
3) Green fluorescent protein-based lactate and pyruvate indicators suitable for biochemical assays and live cell imaging. K. Harada et al, *Scientific Reports* **2020**, 10, 19562.

メダカの個体認知を介した配偶者選択に関わる脳の分子神経基盤

（東北大院生命科学[1]・岡大院自然[2]）○竹内 秀明[1,2]

Molecular/neural basis underlying mate choice mediated by individual recognition in medaka fish ([1]*Graduate School of Life Sciences, Tohoku University*, [2] *Graduate School of Natural Science and Technology, Okayama University Tohoku University*) ○ Hideaki Takeuchi[1,2]

Some fish species have the ability of individual recognition and individuals appropriately tailor attitudes and responses to other group members according to the social context. The neural substrate that works between sensory input and behavioral output underlying social cognition and decision-making processes, however, is vast and mysterious. To address this issue, we have focused on medaka fish, a model animal used mainly in the field of molecular genetics. Previously, we demonstrated that medaka females recognize familiar males following prior visual exposure, and social familiarity influences female mating receptivity. Medaka females exhibit a positive response (high receptivity) to familiar males, and a negative response (low receptivity) to unfamiliar males. In this talk, I would like to introduce how we determined the neural substrate which could modulate behavioral-choice processes using molecular genetics.
Keywords : neuropeptide, oxytocin, GnRH, CRISPR/Cas9

いくつかの魚類は他者を見分ける能力（個体認知能力）を持ち、他者との関係性に基づいて適切な社会行動を選択する。しかしながら、魚類の社会認知及び行動選択に関わる脳の物質的基盤は不明であり、ヒトと共通した分子機構が存在するかについては不明であった。この問題にアプローチをする目的で、分子遺伝学的手法が利用できるメダカを材料に行動実験を行なった。その結果、メダカにも個体認知能力があり、社会関係に基づいた行動選択をすることを発見した。例えば、メスは長時間そばにいたオスを視覚記憶して、「見知ったオス」を配偶相手として選択し、「見知らぬオス」を拒絶する（*Science 2014, PNAS, 2020*）。さらにメスは「顔」でオスを見分けており、ヒトの心理学実験で有名な「倒立顔効果」がメダカでも生じることを見出した（*elife, 2017*）。本学会ではどのように分子遺伝学を用いてメダカの行動選択にバイアスを与えるような脳内物質を同定したかについて紹介したい。

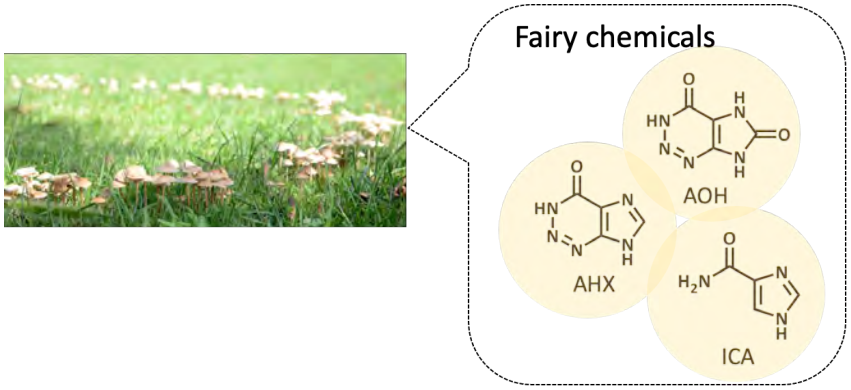
1) A neural mechanism underlying mating preferences for familiar individuals in medaka fish T. Okuyama, S. Yokoi, H. Abe, Y. Suehiro, H. Imada, M. Tanaka, T. Kawasaki, S. Yuba , Y. Taniguchi, Y. Kamei, K. Okubo, A. Shimada, K. Naruse, H. Takeda, Y. Oka, T. Kubo, and H. Takeuchi, ***Science*** **343**, 91-94 (2014).
2) Individual recognition and the 'face inversion effect' in medaka fish (*Oryzias latipes*). M.Y. Wang and H. Takeuchi, ***eLife,*** **6**, 24728 (2017).
3) Sexually dimorphic role of oxytocin in medaka mate choice. S. Yokoi, K. Naruse, Y. Kamei, S. Ansai, M. Kinoshita, M. Mito, S. Iwasaki, S. Inoue, T. Okuyama, S. Nakagawa, LJ. Young, and H. Takeuchi, ***Proc. Natl. Acad. Sci.*** **117**, 201921446 (2020).

フェアリー化合物は新しい植物ホルモンか？

（静大グリーン研）河岸 洋和
Are Fairy Chemicals a new family of plant hormones? (*Research Institute of Green Science and Technology, Shizuoka University*) Hirokazu Kawagishi

2-Azahypoxanthine (AHX) and imidazole-4-carboxamide (ICA) were isolated from a fairy-ring-forming fungus *Lepista sordida*. AHX was converted into a metabolite, 2-aza-8-oxo-hypoxanthine (AOH) in plants. It was found out that these three compounds, named as fairy chemicals (FCs), endogenously exist in plants and are biosynthesized via a new purine metabolic pathway. FCs provided tolerance to plants against various stresses and regulated the growth of all the plants tested. In addition, FCs increased the yields of rice, wheat, and other crops in the greenhouse and/or field experiments.
Keywords: plant hormone; fairy chemicals; 2-Azahypoxanthine; imidazole-4-carboxamide; 2-aza-8-oxo-hypoxanthine

芝が輪状に周囲より色濃く繁茂あるいは枯死し、後にキノコが発生する現象はフェアリーリング（fairy rings）と呼ばれ、西洋の伝説では妖精（fairy）が輪を作りその中で踊ると伝えられている。しかし、その妖精の正体（芝を繁茂させる原因）は謎のままであった。我々は、フェアリーリングを引き起こすコムラサキシメジ（*Lepista sordida*）から 2-アザヒポキサンチン（AHX）とイミダゾール-4-カルボキサミド（ICA）を発見した。AHX は植物中で代謝され 2-アザ-8-オキソヒポキサンチン（AOH）に変換された。その後、これらの 3 つの化合物（フェアリー化合物，fairy chemicals と命名，FCs と略称）はあらゆる植物中に内生し、新しいプリン代謝経路を介して生合成されることが証明された。FCs は植物に対して様々な生物的・非生物的ストレスに対する耐性を与え、試した全ての植物の成長を制御した。さらに、FCs は温室あるいは圃場試験で米、小麦、その他の作物の収量を増加させることが判明した [1-3]。



1) 河岸洋和，フェアリー化合物は植物ホルモンか？，*植物の生長調節*，**2017**, 52, 78.
2) H. Kawagishi, Fairy chemicals – a candidate for a new family of plant hormones and possibility of practical use in agriculture –, *Biosci. Biotechnol. Biochem*., **2018**, 82, 752.
3) H. Kawagishi, Are fairy chemicals a new family of plant hormones?, *Proc. Jpn. Acad., Ser. B*, **2019**, 95, 29.

Symposium | Medium and Long-Term Program | Strategy for improving solar energy conversion efficiency toward the realization of artificial photosynthesis

[S06-1pm] Strategy for improving solar energy conversion efficiency toward the realization of artificial photosynthesis

Chair, Symposium organizer:Ryu Abe, Akihiko Kudo, Hiroaki Misawa
Fri. Mar 19, 2021 1:00 PM - 3:40 PM Webiner 6 (Online Meeting)

[S06-1pm-01] Development of a large scale solar hydrogen production system based on particulate photocatalysts

○Kazunari Domen[1] (1. The University of Tokyo/Shinshu University)

1:05 PM - 1:35 PM

[S06-1pm-02] High-efficiency artificial photosynthesis using quantum coherence under modal strong coupling conditions

○Hiroaki Misawa[1] (1. Hokkaido University)

1:35 PM - 2:00 PM

[S06-1pm-03] Application of Near-Infrared Plasmonics to Hydrogen Evolution Catalysis

○Toshiharu Teranishi[1] (1. Kyoto University)

2:00 PM - 2:25 PM

[S06-1pm-04] Enhancement of water splitting and CO2 reduction by a synthetic method and making a solid solution of photocatalysts

○Akihiko Kudo[1] (1. Tokyo University of Science)

2:25 PM - 2:50 PM

[S06-1pm-05] Water splitting by visible ligh through one-photon induced two-electron conversion to get through the photon-flux density problem of sun light

○Haruo Inoue[1] (1. Tokyo Metropolitan University)

2:50 PM - 3:15 PM

[S06-1pm-06] Improvement in efficiency of dye-sensitized molecular photocathodes in photoelectrochemical cells for photocatalytic CO_2 reduction with water as a reductant

○Osamu Ishitani[1] (1. Tokyo Institute of Technology)

3:15 PM - 3:40 PM

光触媒による大規模ソーラー水素製造システム開発の現状と展望

（信大先鋭材料研[1]・東大特別教授室[2]）○堂免　一成[1,2]
Development of a large scale solar hydrogen production system based on particulate photocatalysts ([1]*Research Initiative for Supra-Materials, Shinshu University*, [2]*Office of University Professors, The University of Tokyo*)○Kazunari Domen,[1,2]

The water splitting reaction driven by sunlight is studied as a technology for producing renewable hydrogen on a large scale. To put this technology to practical use, the reaction system must not only split water efficiently but also be scalable to a large area. Systems consisting of particulate photocatalysts can be spread over large areas by relatively simple processes. Therefore, the development of highly active photocatalysts holds the key toward large-scale hydrogen production. In my talk, the latest progress in the development of particulate photocatalysts and the prospects for system development for large-scale hydrogen production is presented.
Keywords : Particulate photocatalyst; Water splitting reaction; Panel reactor

太陽光水分解反応は再生可能な水素を大規模に製造する技術として研究されている[1)]。この技術を実用化するには、反応系が効率よく水を分解するだけではなく大規模展開可能でなければならない。粉末光触媒からなる系は比較的簡便な工程で大面積展開できる可能性を秘めているため、太陽光水分解反応に高活性な光触媒を開発できれば大規模水素製造に向けて大きく前進するはずである。本講演では粉末光触媒の開発状況と大規模水素製造に向けたシステム開発の展望を述べる。

演者はこれまでに様々な半導体粉末材料を水分解用光触媒として研究してきた[2)]。近年では、$SrTiO_3$ 光触媒の調製法や助触媒の担持法を改良することで、水の完全分解反応のみかけの量子収率を近紫外光域で95%にまで向上させることに成功した（図1）[3)]。この結果は、構造が比較的単純な粉末光触媒を用いても天然光合成における光・物質変換過程と同等の高い量子効率で水分解反応を駆動できることを示しており、粉末光触媒の開発を継続する上で極めて重要な意味を持つ。

太陽エネルギーを高効率に水素に変換するには可視光応答型光触媒の開発が不可欠である。（酸）窒化物、（酸）カルコゲナイド半導体材料は価電子帯上端が O 2p 軌道よりもエネルギー準位の高い N 2p 軌道、S 3p 軌道等から構成されるため、可視光照射下での水分解反応に適したバンド構造を有するものが多い。演者はこれまでに Ta_3N_5 や $Y_2Ti_2O_5S_2$ を用いて可視光水分解反応を駆動させることに成功している[4,5)]。また、水素生成光触媒と酸素生成

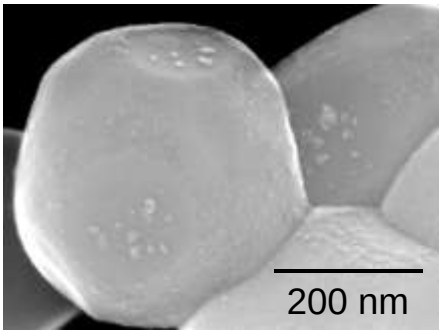


図 1　助触媒が面選択的に共担持された Al ドープ $SrTiO_3$ 光触媒の電子顕微鏡像

光触媒が導電材とともに固定化された Z スキーム型光触媒シートを用いることで、可視光照射下で二段階の光励起を利用して水を水素と酸素に分解できることを示している [6]。特に、La および Rh を共ドープした $SrTiO_3$ と Mo をドープした $BiVO_4$ からなる光触媒シートは 1.0%を超える太陽エネルギー変換効率でソーラー水素を生成する [7]。

演者は光触媒シートの大規模展開を視野にパネルリアクターの開発を進めている [8]。Al ドープ $SrTiO_3$ をベースにした光触媒シートを格納したパネルリアクターは、紫外光の照射強度を大きくすると、太陽エネルギー変換効率 10%相当の速さで水を分解して水素と酸素の気泡を放出できる。また、1 m^2 サイズの光触媒パネル反応器（図 2）は Al ドープ $SrTiO_3$ 本来の活性を損なうことなく太陽光の下で水を分解する。最近、より大面積（100 m^2）のパネルリアクターを建設し、リアクターや付帯設備の動作を長期的に試験中である。パネルリアクターは光触媒懸濁液を用いるリアクターに比べて大面積展開や光触媒の交換が容易であり、大規模ソーラー水素製造の実現に有力な形式であると考えられる。

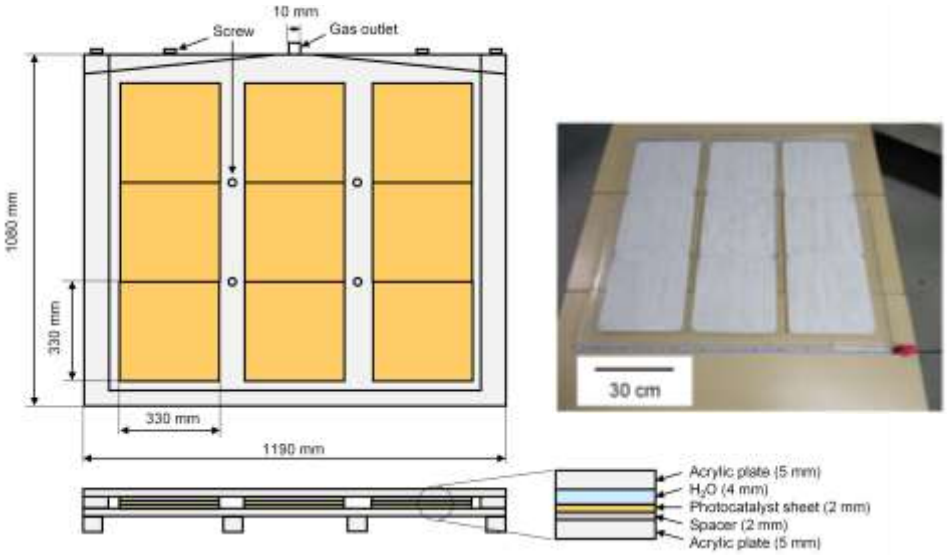


図 2　1 m^2 スケールの光触媒パネルの模式図と外観。許可を得て文献 8 より引用。© 2017 Elsevier Inc

1) Hisatomi *et al.*, *Nat. Catal.* **2019**, 2, 387.
2) Chen *et al.*, *Nat. Rev. Mater.* **2017**, 2, 17050.
3) Takata *et al. Nature* **2020**, *581*, 411.
4) Wang *et al. Nat. Catal.* **2018**, 1, 756.
5) Wang *et al. Nat. Mater.* **2019**, 18, 827.
6) Wang *et al. Nat. Mater.* **2016**, 15, 611.
7) Wang *et al. J. Am. Chem. Soc.* **2017**, 139, 1675.
8) Goto *et al. Joule* **2018**, 2, 509.

モード強結合によって生じる量子コヒーレンスを用いた高効率人工光合成

(北大電子研[1]・台湾国立交通大[2]) ○三澤 弘明[1,2]
High-efficiency artificial photosynthesis using quantum coherence under modal strong coupling conditions ([1] *Research Institute for Electronic Science, Hokkaido University,* [2] *Center for Emergent Functional Matter Science, National Chiao Tung University, Taiwan*)○Hiroaki Misawa[1,2]

In the Au nanoparticles/TiO_2 thin film/Au film (ATA) electrode, the TiO_2/Au film serves as an optical nanocavity. When the resonance wavelength of the nanocavity and the localized surface plasmon resonance of the Au nanoparticles are overlapped, the absorption intensity is enhanced and the absorption wavelength range is expanded, and a modal strong coupling capable of absorbing 85% of visible light is generated. We have revealed that the mode strong coupling generates quantum coherence between the plasmon and the cavity, resulting in highly efficient electron transfer from Au nanoparticles to TiO_2.
Keywords : localized surface plasmon resonance, optical nanocavity, modal strong coupling, quantum coherence, hot carrier

金や銀などのナノ粒子は可視域の光と共鳴し、「局在表面プラズモン共鳴」(Localized Surface Plasmon Resonance: LSPR) を示す。これまでに我々は、LSPR を用いて太陽光に豊富に含まれる可視光を有効に利用できる光エネルギー変換システムの構築を進めてきた。典型的なシステムとしては、酸化チタン基板上に金ナノ構造を搭載した光アノードであり、可視光照射によって水を電子源とする光電流の発生に初めて成功し、また水の酸化生成物として酸素、および過酸化水素が生じることを明らかにした[1)]。最近では、水の酸化助触媒として CoO_x を金ナノ粒子近傍に選択的に担持した光アノードを用いると、水を電子源とする光電流の発生が著しく増強されることも見出した[2)]。さらに、LSPR を用いて水を分解し、酸素と水素がほぼ化学量論的に発生することも明らかにした[3)]。また、還元側の助触媒としてルテニウム、さらにジルコニウムにすることにより、アンモニアの選択的な合成にも成功し、反応中間体にヒドラジンが存在することも明らかにした[4)]。

他方、金ナノ粒子を単一層担持した酸化チタンやチタン酸ストロンチウムの基板による光吸収効率はそれほど高くなく、入射光の 60%以上が透過してしまうため、水素発生やアンモニア合成に関する太陽光エネルギー変換効率は低く、それらの量子収率についても向上させる必要があった。これらの問題点をブレークスルーするためには、LSPR を用いるだけでは困難であり、新しいコンセプトの導入が必要であった。最近、我々は金ナノ粒子を酸化チタン薄膜に単一層担持したのみで、LSPR に比べて幅広い波長の可視光を高い効率で吸収することを可能にするモード強結合電極の開発に成功した。モード強結合電極の構造は、シリカ基板上に膜厚 100 nm 程度の金フィルムを成膜した後、その上に原子層堆積装置を用いて酸化チタン薄膜を成膜し、さらにその上に金ナノ粒子を担持した積層構造となる。この構造では、金フィルムと酸化チタン薄膜によってファブリ・ペロー(FP)ナノ共振器が構成される。この FP ナノ共振器の共振波長が金ナノ粒子の LSPR の共鳴波長と重なるとモード強結合が誘起され、そ

れらが混成した二つのハイブリッドモードが形成される。ハイブリッドモードの一つは元の LSPR よりエネルギーが高く（上肢）、もう一つはエネルギーが低い（下肢）ため、LSPR に比べより幅広い波長の光吸収が可能になる。これら二つのモード間のエネルギー差を分裂エネルギーと呼ぶ。本モード強結合電極を光アノードとして可視光照射により水を電子源とする光電流発生の量子収率の計測を行ったところ、金ナノ粒子/酸化チタンの通常の LSPR 電極に比べ 1.5 倍増強されることが明らかとなった[5]。

さて、同様の強結合は、共振器に分子を導入した系においてもその共振波長と分子の励起エネルギーが同等になると観測されるが、それらはアンサンブル強結合と呼ばれ、分裂エネルギーの大きさは共振器に導入した分子数の平方根に比例することが知られている。我々は、モード強結合電極による量子収率増大のメカニズムを解明するために、半導体微細加工技術を用いて直径 80 nm、厚さ 30 nm の金ナノディスクを酸化チタン薄膜上に精緻に配置した強結合電極を作製し、金ナノディスクの数密度を変化させ、分裂エネルギーの大きさとの関係を検討したところ、数密度の低い領域では金ナノディスクの数の平方根に比例して分裂エネルギーが増大することを明らかにした。また、この関係から、単一金ナノディスクと PF ナノ共振器との強結合における分裂エネルギー、およびその有効面積を求めることができ、有効面積は金ナノディスクのエクスティンクション断面積に比べ数倍大きい値となることが示された。さらに、金ナノディスクの数密度を増大させてもある密度以上では吸収強度や、近接場強度が増大せず飽和してしまうことも明らかとなった。これらの結果は金ナノディスクの LSPR と FP ナノ共振器とが量子コヒーレントカップリングをしていることを示唆しており、単一金ナノディスクと FP ナノ共振器とが量子コヒーレントカップリングを示す面積、すなわちコヒーレンスエリアは実験値から直径 400 nm、電磁場シミュレーションから 600 nm と見積もられた。

さらに、コヒーレントカップリングが金ナノディスクから酸化チタンへの電子注入にどのような影響を与えるかを過渡吸収計測によって検討した。その結果、過渡吸収減衰曲線の時間ゼロにおける最大過渡吸収強度をエクスティンクションによって規格化した値は、モード強結合電極の場合、金ナノディスクの数密度の増加に伴って増大するのに対し、通常の LSPR 電極の場合には金ナノディスクの数密度には依存しないことが明らかとなり、量子コヒーレントカップリングが金ナノディスクから酸化チタンへの電子注入を加速していることが示された。

1) Y. Nishijima et al., *J. Phys. Chem. Lett.*, **2010**, 1, 2031; X. Shi eta al., *J. Phys. Chem. C*, **2013**, 117, 2494; Y. Nishijima eta al., J. *Phys. Chem. Lett.*, **2012**, 3, 1248.
2) M. Okazaki, T. Oshikiri, H. Misawa, K. Maeda et al., *ACS Appl. Energy Mater.*, **2020**, 3, 5675.
3) Y. Zhong et al., *Angew. Chem. Int. Ed.*, **2014**, 53, 10350.
4) T. Oshikiri et al., *Angew. Chem. Int. Ed.*, **2014**, **53**, 9802; T. Oshikiri et al., *Angew. Chem. Int. Ed.*, **2016**, 55, 3942; T. Oshikiri et al., *Green Chem.*, **2019**, 21, 4443.
5) X. Shi et al., *Nat. Nanotechnol.*, **2018**, 13, 953.

近赤外プラズモニクスの開拓と水素生成触媒への展開

（京大化研）寺西 利治
Application of Near-Infrared Plasmonics to Hydrogen Evolution Catalysis
(*Institute for Chemical Research, Kyoto University*) Toshiharu Teranishi

Localized surface plasmons excited by the collective oscillation of free carriers in the nanostructures not only induce strong photoelectric fields near the nanostructure surface, but also enable carrier transfer to nearby substances. In this talk, the design and synthesis of inorganic nanoparticles that exhibit localized surface plasmon resonance in the near-infrared region will be presented as well as hydrogen evolution catalysis using near-infrared localized surface plasmon resonance.
Keywords : Localized Surface Plasmon Resonance; Nanoparticle; Carrier Transfer; Near-Infrared; Hydrogen Evolution

持続可能な社会の実現には、全消費エネルギーにおける再生可能エネルギーの割合を拡大する必要があり、中でも太陽光エネルギーへの期待が大きい。太陽光のうちエネルギー源として主に利用されているのは紫外・可視光であり、放射エネルギーの約44%を占める近赤外光はほとんど使われておらず、省・創エネルギーの観点からその有効利用が喫緊の課題である。

ナノ粒子中の自由キャリア（自由電子・ホール）は、ある特定波長の電磁波との共鳴により集団振動し、局在表面プラズモンが励起される（図1a）。その結果、ナノ粒子表面近傍に非常に強い光電場が誘起され、近接物質の光化学過程の増強や光学禁制遷移の許容化、分子の捕捉、近接物質へのキャリア移動などが可能となる。ナノ粒子の形状・キャリア密度を制御することにより、応用上重要となる可視から近赤外にわたる広範囲な領域で局在表面プラズモン共鳴（LSPR）波長を制御することができる。ヘビードープ半導体ナノ粒子は、金属ほど自由キャリア密度は高くないものの、ドープ元素のドープ量を変化させることにより、容易に自由キャリア密度を制御することができるため（10^{18}–10^{22}/cm^3 程度）、LSPR 波長を近赤外～中赤外領域の範囲で広く制御できる（図 1b）[1-3]。ヘビードープ半導体ナノ粒子に、価電子帯上端・伝導体下端を考慮したアクセプ

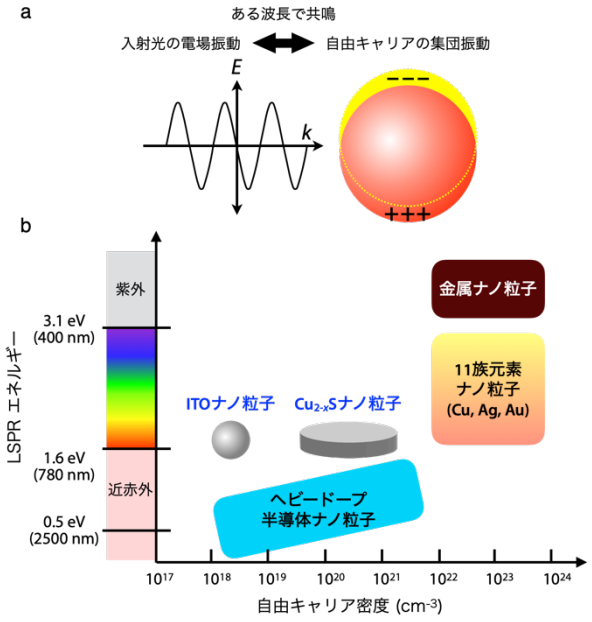


図 1. (a) LSPR の原理、(b) 自由キャリア密度と LSPR エネルギーの関係

ター半導体相を接合したヘテロ構造を構築すると、近赤外光吸収で起きる LSPR により自由キャリアが半導体相に移動し、長寿命電荷分離を実現できるとともに、光電変換や酸化・還元反応に応用展開することができる。

実際に、これらヘビードープ半導体ナノ粒子のフェルミ準位から近赤外光エネルギーでキャリア移動可能な価電子帯上端あるいは伝導体下端をもつアクセプター半導体相を、ヘビードープ半導体ナノ粒子に接合すると、近赤外光吸収による局在表面プラズモン励起・キャリア移動で長寿命電荷分離を実現できるとともに、可視光を吸収しない近赤外光のみでの光電変換や酸化・還元反応に応用展開することができる [4-6]。特に、p 型 Cu_7S_4 ディスク状半導体ナノ粒子の陽イオン交換により得られたプラズモニック p–n 接合をもつディスク状 Cu_7S_4/CdS ナノ粒子 [6,7]への近赤外光照射により、Cu_7S_4 相から CdS 伝導帯への高効率熱電子移動と長寿命電荷分離（273 μs）が達成され、世界最高外部量子収率（3.8%@1100 nm）かつ全近赤外領域での水からの水素生成に成功した（図 2）。

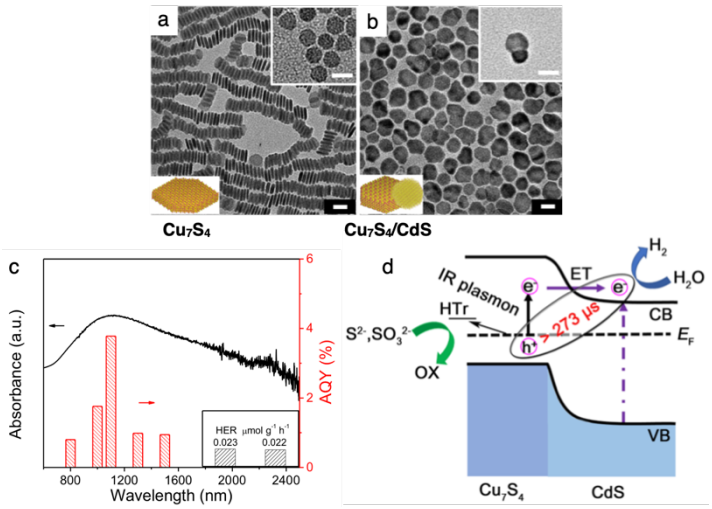


図 2. (a) ディスク状 p 型 Cu_7S_4 ナノ粒子、および、(b) Cu_7S_4/CdS ナノ粒子の TEM 像、(c) Cu_7S_4/CdS ナノ粒子の可視近赤外吸収スペクトルと外部量子収率、(d) Cu_7S_4/CdS ナノ粒子の近赤外光誘起電子移動の模式図

1) Indium tin oxide nanoparticles with compositionally tunable surface plasmon resonance frequencies in the near IR region. M. Kanehara, H. Koike, T. Yoshinaga, T. Teranishi, *J. Am. Chem. Soc.* **2009**, *131*, 17736.
2) Large-scale synthesis of high-quality metal sulfide semiconductor quantum dots with tunable surface-plasmon resonance frequencies. M. Kanehara, H. Arakawa, T. Honda, M. Saruyama, T. Teranishi, *Chem. Eur. J.* **2012**, *18*, 9230. (Frontispiece)
3) Formation of pseudomorphic nanocages from Cu2O nanocrystals through anion exchange reactions. H.-L. Wu *et al.*, *Science* **2016**, *351*, 1306.
4) Near infrared light induced plasmonic hot hole transfer at a nano-heterointerface. Z. Lian *et al.*, *Nat. Commun.* **2018**, *9*, 2314.
5) Clear and transparent nanocrystals for infrared-responsive carrier transfer. M. Sakamoto *et al.*, *Nat. Commun.* **2019**, *10*, 406.
6) Plasmonic p-n junction for infrared light to chemical energy conversion. Z. Lian *et al.*, *J. Am. Chem. Soc.* **2019**, *141*, 2446. (Cover picture)
7) Transformations of ionic nanocrystals via full and partial ion exchange reactions. M. Saruyama, R. Sato, T. Teranishi, *Acc. Chem. Res.*, under revision.

半導体光触媒を用いた水分解と二酸化炭素還元

（東理大理）工藤昭彦

Water Splitting and CO_2 Reduction using Semiconductor Photocatalysts

（Faculty of Science, Tokyo University of Science）Akihiko Kudo

Water splitting and carbon dioxide reduction of artificial photosynthesis is expected to solve energy, environment, and resources issues. Heterogeneous photocatalytic systems for the artificial photosynthesis are introduced.

Keywords:
Photocatalyst; Artificial Photosynthesis; Water splitting; H_2 production; CO_2 reduction

1. Introduction

Photocatalytic water splitting is a challenging reaction because it is an ultimate chemical reaction to solve resources, energy, and environment issues. Photocatalytic CO_2 fixation has also attracted attention. These can be regarded as artificial photosynthesis, because light energy is converted to chemical energy. In the present paper, I introduce various metal oxide and sulfide photocatalysts for the artificial photosynthesis [1].

2. Water splitting using visible-light responsive photocatalysts

Rh and Sb-codoped $SrTiO_3$ photocatalyst loaded with IrO_2 was active for water splitting into H_2 and O_2 under visible light and simulated sunlight irradiations as a single particle type photocatalyst. This photocatalyst responds to 500 nm [2]. $SrTiO_3$:Rh of a H_2-evolving photocatalyst and $BiVO_4$ of an O_2-evolving photocatalyst constructed various type of Z-schematic photocatalyst systems with Fe^{3+}/Fe^{2+}, $[Co(bpy)_3]^{3+/2+}$, $[Co(phen)_3]^{3+/2+}$, and a conductive reduced graphene oxide (RGO) as an electron mediator and even without an electron mediator. Metal sulfide photocatalysts that are normally unstable for water splitting into H_2 and O_2 in the absence of an electron donor was able to be employed for Z-schematic photocatalyst systems for water splitting. Z-schematic photocatalyst systems combining metal sulfide photocatalysts as a H_2-evolving photocatalyst with TiO_2 (RGO/TiO_2) [3] and $BiVO_4$+Co complex (an electron mediator) showed activity for water splitting into H_2 and O_2 [4]. However, Z-scheme system employing $SrTiO_3$:Rh of a H_2-evolving photocatalyst and $BiVO_4$ of an O_2-evolving photocatalyst can utilize visible light to only 540 nm. Therefore, it is a key issue to employ photocatalysts with visible light response to longer wavelength. From this viewpoint, various types of Z-scheme systems for water splitting under visible light irradiation were successfully developed by employing Rh- and Ir-doped metal oxides powdered materials with relatively narrow energy gaps (EG), $BaTa_2O_6$:Ir,La (EG: 1.9-2.0 eV), $NaTaO_3$:Ir,La (EG: 2.1-2.3 eV), $SrTiO_3$:Ir (EG: 1.6-1.8 eV), and TiO_2:Rh,Sb (EG: 2.1 eV), with conventional $SrTiO_3$:Rh of an H_2-evolving photocatalyst or $BiVO_4$ of an O_2-evolving photocatalyst, and suitable electron mediators [5]. The Z-scheme systems were classified into three groups depending on the combination of the H_2- and O_2-evolving photocatalysts and an electron mediator. Z-scheme systems combining $BaTa_2O_6$:Ir,La with $BiVO_4$, and $NaTaO_3$:Ir,La with $BiVO_4$ were active when not an $Fe^{3+/2+}$ but a $[Co(bpy)_3]^{3+/2+}$ redox couple

was used. The combination of $SrTiO_3$:Ir with $SrTiO_3$:Rh gave an activity, when $[Co(bpy)_3]^{3+/2+}$ and $Fe^{3+/2+}$ redox couples of ionic mediators were used. Z-scheme systems combining TiO_2:Rh,Sb with $SrTiO_3$:Rh showed activities by using of $[Co(bpy)_3]^{3+/2+}$ and $Fe^{3+/2+}$ redox couples and also via interparticle electron transfer by just contact with/without reduced graphene oxide (RGO). These suitable combinations can be explained based on the impurity levels consisting of doped Rh^{3+} and Ir^{3+} toward the redox potentials of ionic mediators for the Z-scheme systems employing ionic mediators, and p-/n-type and onset potentials of photocurrent in photoelectrochemical properties of those photocatalyst materials for the Z-scheme systems working vis interparticle electron transfer.

3. CO_2 reduction using water as an electron donor over powdered photocatalysts

Ag cocatalyst-loaded $ALa_4Ti_4O_{15}$ (A = Ca, Sr, and Ba) [6] and tantalates photocatalysts [7-10] such as $NaTaO_3$:Ba with 3.79–4.1 eV of band gaps showed activities for CO_2 reduction to form CO and HCOOH in an aqueous medium without any sacrificial reagents. CO is the main reduction product rather than H_2 even in an aqueous medium. Especially, the Ag/$NaTaO_3$:Ba photocatalyst gave ca. 90% of the selectivity for the CO_2 reduction. The carbon source of produced CO was confirmed to be dissolved CO_2 molecules using $^{13}CO_2$. Thus, an uphill reaction of CO_2 reduction accompanied with water oxidation was achieved using the Ag-loaded metal oxide photocatalysts. However, these metal oxide photocatalysts respond to only UV because of their wide band gaps. So, it is challenging to develop photocatalysts with visible light response for CO_2 reduction. We constructed a Z-scheme system consisting of $CuGaS_2$ photocatalyst of a CO_2-reducing photocatalyst with $BiVO_4$ of an O_2-evolving photocatalyst and RGO of an electron mediator for CO_2 reduction using water as an electron donor in the absence of any sacrificial electron donors. The Z-scheme system gave H_2, O_2, and CO simultaneously under visible light irradiation [11]. A molecular catalyst can be utilized as a CO_2 reduction site for the Z-scheme photocatalyst system [12].

References

1. A. Kudo, and Y. Miseki, *Chem. Soc. Rev.* 38, 253 (2009).
2. R. Asai, H. Nemoto, Q. Jia, K. Saito, A. Iwase and A. Kudo, *Chem. Commun.* 50, 2543 (2014).
3. K. Iwashina, A. Iwase, Y. Hau Ng, R. Amal, and A. Kudo, *J. Am. Chem. Soc.* 137, 604 (2015).
4. T. Kato, Y. Hakari, S. Ikeda, Q. Jia, A.Iwase, and A. Kudo, *J. Phys. Chem. Lett.* 6, 1042 (2015).
5. A. Kudo, S. Yoshino,T. Tsuchiya, Y. Udagawa, Y. Takahashi, M. Yamaguchi, I. Ogasawara, H. Matsumoto, and A. Iwase, *Faraday Discussions*, 215, 313 (2019).
6. K. Iizuka, T. Wato, Y. Miseki, K. Saito, and A. Kudo, *J. Am. Chem. Soc.* 133, 20863 (2011).
7. H. Nakanishi, K. Iizuka, T. Takayama, A. Iwase, and A. Kudo, *ChemSusChem* 10, 112 (2017).
8. T. Takayama, K. Tanabe, K. Saito, A. Iwase, and A. Kudo, *Phys. Chem. Chem. Phys.* 16, 24417 (2014).
9. T. Takayama, A. Iwase, and A. Kudo, *Bull. Chem. Soc. Jpn.* 88, 538 (2015).
10. T. Takayama, H. Nakanishi, M. Matsui, A. Iwase, and A. Kudo, *J. Photochem. Photobiol. A:Chem.* 358, 416 (2018).
11. A. Iwase, S. Yoshino, T. Takayama, Y. H. Ng, R. Amal, and A. Kudo, *J. Am. Chem. Soc.* 138, 10260 (2016).
12. T. M. Suzuki, S. Yoshino, T. Takayama, A. Iwase, A. Kudo, and T. Morikawa, *Chem. Commun.* 54, 10199 (2018).

太陽光の光子束密度問題を解決する 1 光子 2 電子変換による可視光水分解

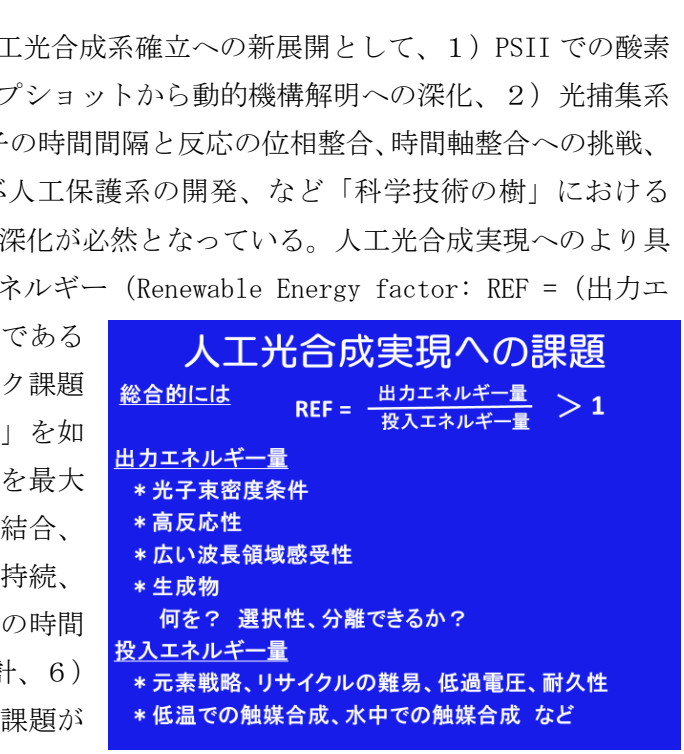
Water splitting by visible light through one-photon induced two-electron conversion to get through the photon-flux density problem of sun light

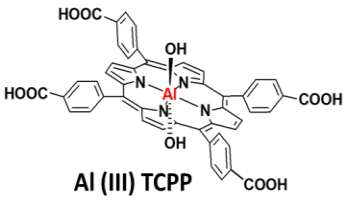
（東京都立大学大学院・都市環境）井上晴夫
Tokyo Metropolitan University, Haruo Inoue

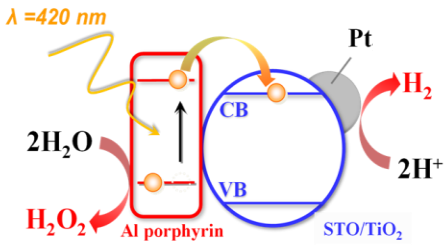
As an alternative methodology for visible light induced water splitting by molecular catalyst, one-photon induced two-electron conversion of water into hydrogen and hydrogen peroxide catalyzed by metalloporphyrin was developed to get through the bottle neck subject, photon-flux density problem of the rarefied sun light radiation.

Key words: Artificial photosynthesis, water splitting, hydrogen, hydrogen peroxide, metallopophyrin

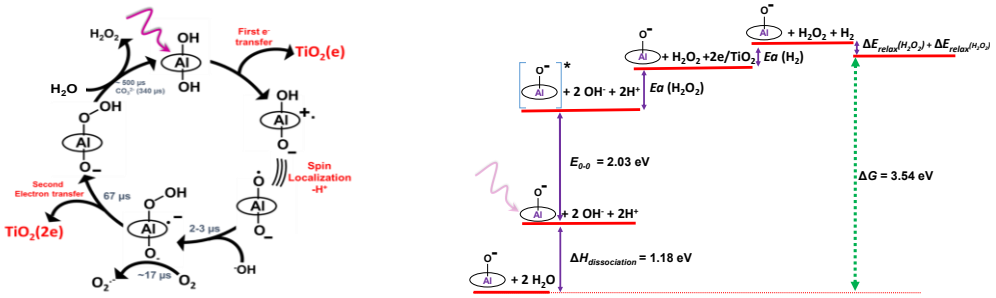
天然の光合成に学び、超えようとする人工光合成系確立への新展開として、１）PSII での酸素発生機構の解明を基礎に従来の静的スナップショットから動的機構解明への深化、２）光捕集系と反応中心の有効な結合を学び、光子―光子の時間間隔と反応の位相整合、時間軸整合への挑戦、３）タンパク質の反応中心保護効果に学ぶ人工保護系の開発、など「科学技術の樹」における Creation 軸から Innovation 軸への視点の深化が必然となっている。人工光合成実現へのより具体的な課題として、総合的には再生可能エネルギー（Renewable Energy factor: REF =（出力エネルギー）/(入力エネルギー））が１以上であることを前提として、１）最大のボトルネック課題としての「太陽光の希薄な光子束密度問題」を如何にして克服解決するか、[1] ２）可視光域を最大限吸収し得る光捕集系と反応中心の有効な結合、３）水分子光分解の高反応性の実現とその持続、４）反応システム全体として各素反応過程の時間軸整合、５）元素戦略の視点からの触媒設計、６）それらを実現し得る反応場の構築、などの課題がある。演者等は、上記課題の多くを解決し得る分子系光触媒として、従来の水分子の 4 電子酸化/酸素発生ではなく、2 電子酸化/過酸化水素の発







生に焦点を絞り、これまでに、Ge,[2a] Al,[2b,c] Si,[2d] Sn,[2e] Zn-ポルフィリン類[2f]について水分子の過酸化水素生成を報告してきた。アルミニウムポルフィリン類などによる可視光 1 光子による水分子の 2 電子酸化還元、水素/過酸化水素の同時生成系の構築にも成功している。[3] 1 光子による入力エネルギーで水分子の 2 電子酸化・還元（水素/過酸化水素の同時発生）が熱力学的に可能であることも実証した。[4]



さらに進んで、新たに Ti(IV)-ポルフィリン類の反応例を見出した。DFT 計算から Ti-TMPyP の 1 電子酸化状態のスピン分布は軸配位酸素原子が Ti-O・(oxyl radical)であることが予測され（図 1）、水分子の 2 電子酸化に活性であることが期待される。基底状態における水分子の軸配位とそのプロトン解離平衡は、他の金属ポルフィリンとは大きく異なり、5 種類の解離平衡は存在するものの、各状態間の変換速度が極端に遅いことが分かった。Ti(IV)のイオン半径とポルフィリン中心空孔の Size mismatch により対称軸配位子種と非対称種間の相互変換に比較的大きい活性化エネルギーが必要と考えられる（図 2）。酸化領域の CV は触媒電流を示し定電位電解では初期活性を有するも約 30 分後には電解活性を失うと共に、ダイアモンド電極上に着色種の沈殿が観察

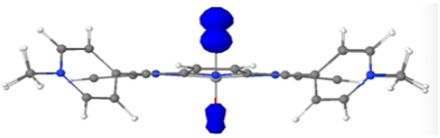


図 1　TiTMPyP(O)(O)・

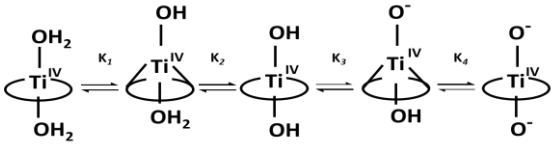


図 2　5 種間の軸配位子平衡

された。Oxyl radical（Ti-O・）と OH^- の反応と競争的に液中の軸配位子解離体基底状態が反応し 2 量体を生成すると考えられる。一方、FTO 上の SnO_2 粒子膜に軸配位させた TiTPyP への可視光照射では、数分以内での光電流の降下が認められるが、その後は安定な光カソード電流が観測され遊離過酸化水素が生成した（図 3 FY:51%）。

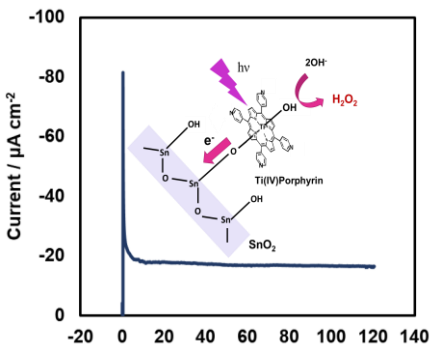


図 3　TiTPyP/SnO_2/FTO 光電流

【参考文献】

1) a) *ChemSusChem.*, **2011**, 4, 173-179., b) *Coordination Chem. Rev.*, **2018**, 377, 64-72.
2) a) *J. Photochem. Photobiol. A, Chem.* **2015**, 313, 131-136., b) *ChemSusChem.*, **2017**, 10、1909-1915., c) *ChemPhotoChem.*, **2018**, 2, 240-248, d) *Sustainable Energy & Fuels*, **2018**, 2, 1966-1973., e) *J. Photochem. Photobiol. A, Chem.*, **2020**, 401, 112732., f) *J. Photochem. Photobiol. A, Chem.*, **2020**, 400, 112619.
3) *ACS Appl. Energy Mater.*, **2019**, 2, 8045-8051.
4) a) *ChemSusChem.*, **2019**, 12, 1939-1948., b) *Sustainable Energy & Fuels*, **2020**, 4, 1945-1953.等

水による CO_2 還元を駆動する光電気化学系に用いる色素増感型分子光カソードの高効率化

（東工大 理）石谷　治

Improvement in efficiency of dye-sensitized molecular photocathodes in photoelectrochemical cells for photocatalytic CO_2 reduction with water as a reductant

(*School of Science, Tokyo Institute of Technology*) ○Osamu Ishitani

Photocatalytic CO_2 reduction by using water as a reductant is one of the main targets for constructing artificial photosynthesis. We recently reported a first dye-sensitized molecular photocathode for photocatalytic CO_2 reduction, which can be applied for constructing a Z-scheme type photoelectrochemical cell with a semiconductor photoanode for water oxidation. In this presentation, I report our recent results about drastic improvement of efficiency of the dye-sensitized molecular photocathode for CO_2 reduction.

Keywords : Dye-Sensitized Molecular Photocathode, Photocatalytic CO_2 Reduction, Artificial Z-Scheme

太陽光をエネルギー源、水を還元剤として CO_2 をエネルギー及び炭素資源化するシステム開発は、人工光合成の「本丸」とも言える研究対象であろう。CO_2 の還元と水の酸化という高エネルギーが要求される２つの反応を、可視光だけをエネルギー源として駆動するためには、比較的低エネルギーの２光子を順次的に利用することで、各反応を駆動する 2 種の触媒間に効率の良い電子移動を進行させるシステムが必要である。これに適合した光触媒システムの一つとして、光カソードと光アノードを組み合わせたＺスキーム型電気化学セルがある。我々は、CO_2 の２電子還元に必要なレドックス光増感剤と触媒を化学結合により連結した超分子光触媒を用いた色素増感型分子光カソードを世界に先駆けて開発した。これと、水の酸化を光触媒的に駆動する n 型半導体光アノード (CoO_x 担持 TaON や $BiVO_4$)を組み合わせた光電気化学セルを開発し、可視光をエネルギー、水を還元剤とした CO_2 の光触媒還元に成功している（Fig. 1）。

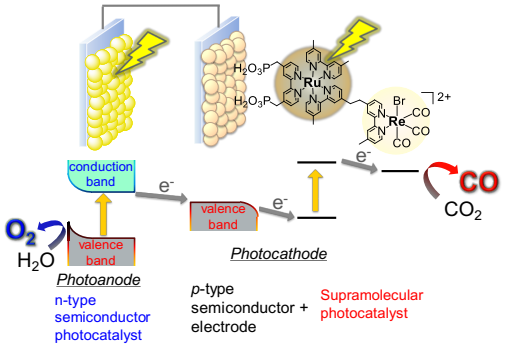


Fig. 1 水による CO_2 還元を光触媒的に駆動する光電気化学セル

本講演では、このＺスキーム型電気化学セル、特に色素増感型分子光カソードの設計指針および高機能化に関して以下の順に報告する。

1) 固体表面上に固定されても効率よく CO_2 還元を駆動する分子光触媒の設計と合成：超分子光触媒の開発とその優位性

光電子移動反応は、1 光子励起で 1 電子移動しか駆動しないが、CO_2 を還元し安定な化合物を得るためには多電子還元を行う必要がある。この「矛盾」を解決するため

に、1 電子移動を駆動するレドックス光増感剤と、それから複数の電子を受け取り CO_2 の多電子還元を駆動する（多くは 2 電子還元して CO もしくはギ酸を与える）触媒を組み合わせた光触媒系が数多く報告されている。しかし、これら 2 種の分子をバラバラに電極などの固体表面に固定化した場合、レドックス光増感剤と触媒間の分子間電子移動を効率よく進行させることが難しく、効率的に光触媒反応は進行しない。この問題を解決するために、これら 2 種の分子を化学結合で連結した超分子光触媒を開発した [1]（Fig. 1 の右側に書かれている Ru(II)錯体光増感剤と Re(I)触媒がエチレン基で結合しているものが一例）。超分子光触媒の光増感部を光電子移動により還元すると高速で触媒部に分子内電子移動が進行することを時間分解 IR によって確認しており [2]、そのため超分子光触媒は、固体表面に固定しても効率よく CO_2 還元を駆動する [3]。

2）p 型半導体電極上へ超分子光触媒を、機能を維持したまま固定化する手法の開発：色素増感型分子光カソードの高機能化

超分子光触媒の光増感部にホスフォン酸基を導入することで p 型半導体電極上に固定化することが可能である [4]。しかし、水溶液中で光触媒反応をおこなうと数時間で脱離が進行してしまう。より安定に機能する色素増感型分子光カソードを開発するため、超分子光触媒にビニル基もしくはピロール基を導入し、それらを p 型半導体上で還元もしくは酸化重合させ疎水性膜として固定化する方法を開発した [5]。これらの光カソードは、一定の外部バイアスを負荷した状態で超分子光触媒の光増感部を光励起すると CO_2 を効率的に還元し、その光触媒機能は数日間維持される [6]。

3）色素増感型分子光カソードの性能と n 型半導体光アノードと組み合わせた水による CO_2 光触媒還元反応

開発した色素増感型分子光カソードと、助触媒である CoO_x 等を担持した n 型半導体電極（TaON、$BiVO_4$）を組み合わせることにより、可視光だけをエネルギー、水を還元剤として用いた CO_2 還元を光触媒的に長時間駆動することに成功した [7]。

1) Y. Tamaki, O. Ishitani, *ACS Catalysis* **2017**, *7*, 3394-3409.
2) (a) Y. Yamazaki, K. Ohkubo, D. Saito, T. Yatsu, Y. Tamaki, S. Tanaka, K. Koike, K. Onda, O. Ishitani, *Inorg. Chem.* **2019**, *58*, 11480-11492; (b) K. Koike, D. C. Grills, Y. Tamaki, E. Fujita, K. Okubo, Y. Yamazaki, M. Saigo, T. Mukuta, K. Onda, O. Ishitani, *Chem Sci* **2018**, *9*, 2961-2974.
3) D. Saito, Y. Yamazaki, Y. Tamaki, O. Ishitani, *J. Am. Chem. Soc.* **2020**, *142*, 19249-19258.
4) (a) G. Sahara, R. Abe, M. Higashi, T. Morikawa, K. Maeda, Y. Ueda, O. Ishitani, *Chem. Commun.* **2015**, *51*, 10722-10725; (b) G. Sahara, H. Kumagai, K. Maeda, N. Kaeffer, V. Artero, M. Higashi, R. Abe, O. Ishitani, *J. Am. Chem. Soc.* **2016**, *138*, 14152-14158.
5) R. Kamata, H. Kumagai, Y. Yamazaki, G. Sahara, O. Ishitani, *ACS Appl. Mater. Interfaces* **2019**, *11*, 5632-5641.
6) (a) Kamata, H. Kumagai, Y. Yamazaki, M. Higashi, R. Abe, O. Ishitani, *J. Mater. Chem. A* **2021**; (b) H. Kumagai, G. Sahara, K. Maeda, M. Higashi, R. Abe, O. Ishitani, *Chem. Sci.* **2017**, *8*, 4242-4249.

Symposium | Medium and Long-Term Program | New paradigm of molecular systems chemistry – Concerted Molecular Functions

[S07-1am] New paradigm of molecular systems chemistry – Concerted Molecular Functions

Chair, Symposium organizer:Satoshi Takahashi, Shigehiko Hayashi, Akio Kitao
Fri. Mar 19, 2021 9:00 AM - 11:40 AM Webiner 7 (Online Meeting)

[S07-1am-01] Rational design of protein molecular functions

○Munehito Arai[1,2] (1. Grad. Sch. of Arts and Sci., The Univ. of Tokyo, 2. Grad. Sch. of Sci., The Univ. of Tokyo)

9:05 AM - 9:24 AM

[S07-1am-02] Micro hydration effect upon ion selectivity studied by cold ion spectroscopy

○Shun-ichi Ishiuchi[1] (1. Tokyo Institute of Technology)

9:24 AM - 9:43 AM

[S07-1am-03] Functional Polyaromatic Nanospaces: How to Recognize Biomolecules

Ryuki Sumida[1], ○Michito Yoshizawa[1] (1. Tokyo Institute of Technology)

9:43 AM - 10:01 AM

[S07-1am-04] Synthesis and Applications of Functional Molecular Systems using Proteins

○Teruyuki Komatsu[1] (1. Chuo Univ.)

10:01 AM - 10:20 AM

[S07-1am-05] Reconstituting cell membrane functions with a model membrane and nanometric space

○Kenichi Morigaki[1] (1. Kobe University)

10:20 AM - 10:39 AM

[S07-1am-06] Intracellular molecular assemblies driven by liquid-liquid phase separation

○Shunsuke F. Shimobayashi[1] (1. Princeton University)

10:39 AM - 10:58 AM

[S07-1am-07] 4D genome architecture: A ondensed polymer system in the cell nucleous

○Masaki Sasai[1] (1. Nagoya University)

10:58 AM - 11:17 AM

[S07-1am-08] *In vitro* reconstitution of cell motility and division machineries from minimum molecular components

○Makito Miyazaki[1,2,3] (1. Kyoto Univ., 2. Inst. Curie, 3. PRESTO)

11:17 AM - 11:36 AM

タンパク質分子機能の合理的設計

（東大院総合文化[1]・東大院理[2]）○新井 宗仁[1,2]
Rational design of protein molecular functions ([1]*Graduate School of Arts and Sciences, The University of Tokyo*, [2]*Graduate School of Science, The University of Tokyo*)○Munehito Arai[1,2]

Protein molecules are essential for life phenomena and have diverse functions including binding and catalysis. Rational design of such protein functions has been a great challenge. In this talk, I will present our efforts of theoretical protein design to strengthen protein-protein interactions and to accelerate an enzyme reaction. I will also show an example of sophisticating protein function by rational connection and multimerization of proteins.

Many proteins exert their functions through protein-protein interaction (PPI) with other proteins *in vivo*. Since PPI is also involved in various diseases, designing proteins for PPI inhibition is directly related to drug discovery. We focused on the interactions of the KIX domain of the transcriptional coactivator CBP with various transcriptional activators. These PPIs are involved in leukemia, cancer, and viral infections. Using fragments of the KIX-binding transcriptional activators MLL and c-Myb as templates, we attempted to theoretically design peptides that bind KIX more tightly than the wild type. We were able to create such peptides by rational design using the Rosetta software and secondary structure prediction.

We are also working on the development of the methods to rationally improve enzymatic activity. We searched for the mutants that could accelerate the rate-limiting step in the catalytic cycle of dihydrofolate reductase (DHFR) by theoretical comprehensive mutation analysis. Many of the designed mutants showed high activity as predicted. Moreover, we succeeded in increasing the DHFR activity by 4-fold with a single amino-acid substitution.

In addition, we rationally designed a protein that changes its binding partner in a pH-dependent manner. Specifically, by connecting an antibody-binding protein, Protein A, with a protein that dimerizes at low pH, we created a chimera that binds to antibody at neutral pH and dissociates it by dimerization at low pH. This chimera is expected to be used for purification of antibodies. Rational design of such "mutually exclusive binding" will be useful in regulating protein functions.

Keywords : Protein, Rational Design, Binding, Enzyme

タンパク質は生命現象を駆動する物質であり、結合や触媒などの多様な機能を有する。このようなタンパク質機能の合理的設計は大きな挑戦である。本講演では、我々が取り組んでいるタンパク質の理論的設計、特に、タンパク質間結合の強化や、酵素反応の高速化の例を紹介する。また、タンパク質の連結や多量体形成を合理的に行い、タンパク質機能を高度化させる例も紹介する。

多くのタンパク質は、生体内で他のタンパク質との相互作用（protein-protein interaction, PPI）を介して機能を発揮する。PPI は様々な疾患にも関与しているため、PPI 阻害タンパク質の設計は創薬と直結しうる。我々は転写コアクチベーターCBP の KIX ドメインと転写アクチベーターとの相互作用に着目した。KIX にはさまざまな転写アクチベーターが結合し、白血病やがん、ウイルス感染などに関与する。そこで、

KIX に結合する転写アクチベーターMLL や c-Myb の断片を鋳型とし、これらよりも強く KIX と結合するペプチドを理論的に設計することを試みた。タンパク質設計用ソフトウェア Rosetta や二次構造予測などを用いた合理的設計により、実際にそのようなペプチドを創出することができた。

我々はまた、酵素活性を合理的に向上させる方法の開発にも取り組んでいる。ジヒドロ葉酸還元酵素（DHFR）の酵素反応サイクルには複数の反応ステップがあるが、その律速段階を加速しうる変異体を、理論的な網羅的変異解析によって探索した。設計された変異体を実際に作製して検証した結果、多くの変異体で予測通りの高活性化がみられた。また、1 アミノ酸置換のみで DHFR の活性を 4 倍向上させることにも成功した。

さらに我々は、pH 依存的に結合相手を変えるタンパク質を合理的に設計した。具体的には、低 pH で二量体になるタンパク質と、抗体結合タンパク質（Protein A）を連結させることで、中性 pH では抗体に結合し、低 pH では二量体化して抗体を解離するキメラを作製した。このキメラは抗体医薬品などの精製に使用可能と期待される。このような「互いに排他的な結合（mutually exclusive binding）」の合理的設計は、タンパク質機能を制御するうえで有用であろう。

冷却イオン分光で見るイオン選択性に対する微視的水和効果

（東工大）石内 俊一
Micro hydration effect on ion selectivity studied by cold ion trap spectroscopy (*Department of Chemistry, School of Science, Tokyo Institute of Technology*)○Shun-ichi Ishiuchi

Valinomycin is a macrocyclic ionophore that transports K^+ across hydrophobic membranes. The mechanism of its ion selectivity depends on the hydration effect. In this work, to elucidate the hydration effect on the ion selectivity, electrospray / cold ion trap technique was applied to valinomycin / Na^+ and K^+ complexes and their hydration clusters. Based on their infrared spectra, structural difference caused by the micro hydration is discussed.

Keywords : Laser Spectroscopy; Ion Selectivity; Hydrated Cluster; Cold Ion; Ionophore

生命維持において種々のイオンの濃度を適正に維持することは極めて重要で，イオンポンプやイオンチャネルなどの特定のイオンを選択的に輸送する分子がそれを担っている。また，ある種の微生物は敵対する生物の細胞内イオンバランスを破壊するために，特定のイオンを選択的に細胞外に輸送するイオノフォアと呼ばれる分子を生成する。これはいわゆる抗生物質であり，医薬品としての応用も期待できる。人工のイオン選択性分子としてはクラウンエーテルが有名であり，環の大きさに応じて特定の金属イオンを包接することが知られている。

イオン選択性分子は，一般に，周りに水（溶媒）分子の存在しない真空中ではイオン選択性を示さない。従って，イオン選択性には水分子の存在が不可欠である。このメカニズムは，イオンが水和している方が安定か，それともイオン選択性分子に結合している方が安定かという，２状態間のエネルギー差で説明される。しかし，イオンの透過や包接・放出といった非平衡の過程はこの様な単純な描像では説明できず，水分子がイオン選択性にどの様に関わっているかを分子レベルで追跡する必要がある。本研究では，１分子ずつ水分子を付加することで微視的水和効果を分子レベルで研究できる冷却イオン分光を用いて，代表的な天然イオノフォアであるバリノマイシンのイオン選択性に対する微視的水和効果を検討した。

バリノマイシンは生体膜内で K^+を特異的に包接するイオノフォアであり，６残基のアミノ酸と６残基のヒドロキシ酸から構成された環状のデプシペプチドである（図１a）。バリノマイシンの K^+選択性は Na^+に比べて４桁以上も高い [1]。バリノマイシンは脂質膜内で K^+を包接し，膜界面では K^+を放出するので，イオン選択性の鍵は膜界面でのイオンの水和とバリノマイシンによる包接との競合にあると考えられる。これまで，NMR とＸ線結

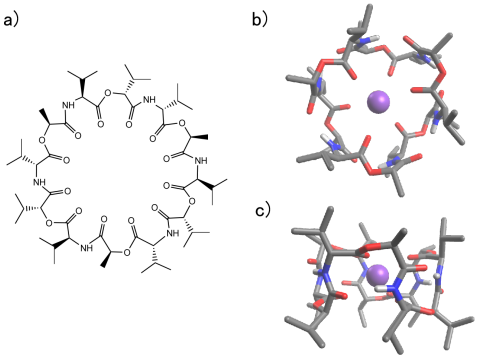


図１ バリノマイシンの a) 化学構造式，b) 結晶構造上面および c) 側面図

晶構造解析によりバリノマイシン–K^+錯体が C_3 対称に近い構造をとることが分かっている（図 1 bc）[2,3]。また，最近では，清浄表面に吸着したバリノマイシンと水の相互作用を STM で観察するという研究が報告され，水が付着するとバリノマイシンの構造が変化する様子が明らかになった [4]。しかし，我々が見たいのは，さらに金属イオンが共存したときにどうなるかである。本研究では，エレクトロスプレー法によりバリノマイシン・アルカリ金属イオン錯体を気相中に取り出し，真空中で水分子を 1 個ずつ付加しながら，その構造がどの様に変化するかを赤外分光で追跡した。

図 2 に実験装置を示す [5]。エレクトロスプレー法によりバリノマイシン–アルカリ金属錯体を気相中に取り出し，クラスター生成トラップで水和クラスターを生成した。四重極質量分析器で目的のイオンのみを選別し，極低温に冷却された四重極イオントラップ内にイオンを保持した。ここで水素を付着させ，赤外レーザーを導入し，生成したフラグメントイオンを飛行時間型質量分析器で検出した。赤外レーザーを波長掃引することで，赤外吸収スペクトルに相当する赤外光解離（IRPD）スペクトルを得た。

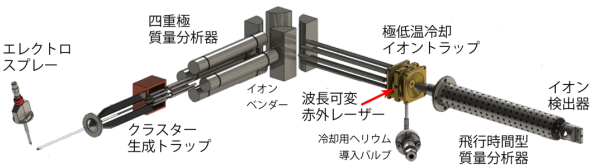


図 2　実験装置図

図 3 にバリノマイシン・Na^+錯体とその 1:1 水和クラスターおよび K^+錯体とその水和クラスターの IRPD スペクトルを示す。水なしの場合，いずれの錯体でも NH 伸縮振動が 1 本のみ観測されている。バリノマイシンは 6 個の NH 基をもつので，この結果は，対称性の高い構造をとっていることを示している。C=O 伸縮振動も測定することで，いずれの錯体も図 1 b,c に示す金属イオンを中心に包接した構造をとることが分かった。しかし，水分子を 1 個付加すると，両者のスペクトルは大きく異なる。K^+錯体では水なしの場合とほとんど同じスペクトルであり，水分子 1 個が付加しても高い対称性を保持していることが分かる。一方，Na^+錯体では NH 伸縮振動は複数のバンドに分裂しており，バリノマイシンの対称性が崩れていることが分かる。また，水分子の OH 伸縮振動も強く観測されており，水分子が電荷をもった Na^+に直接配位していることが予想される。講演では，これらの詳細な構造帰属に加え，他のアルカリ金属イオン錯体の結果も紹介し，水分子がバリノマイシンのイオン選択性や機能にどの様な役割を演じているのかを議論する。

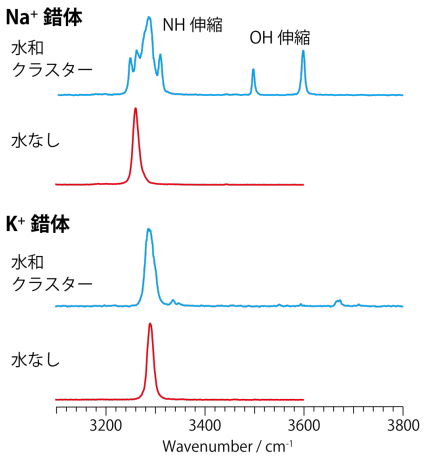


図 3　バリノマイシン・Na^+および K^+錯体とそれらの水和クラスターの IRPD スペクトル

1) M.C. Rose, R.W. Henkens, *Biochim. Biophys. Acta* **1974**, *372*, 426., 2) M. Ohnishi, D.W. Urry, *Science* **1970**, *168*, 1091., 3) K. Neupert-Laves, M. Dobler, *Helvetica* **1975**, *58*, 432., 4) Y. Chen, K. Deng, X. Qiu, C. Wang, *Sci. Rep.* **2013**, *3*, 2461., 5) S. Ishiuchi, H. Wako, D. Kato, M. Fujii, *J. Mol. Spectrosc.* **2017**, *332*, 45.

芳香環ナノ空間の機能：生体分子の見分け方

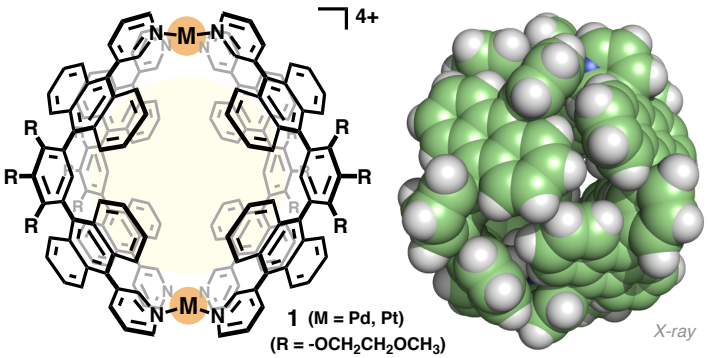
（東工大 化生研）角田瑠輝・○吉沢道人
Functional Polyaromatic Nanospaces: How to Recognize Biomolecules
(Lab. for Chem. & Life Sci., Tokyo Inst. of Tech.) Ryuki Sumida・○Michito Yoshizawa

Abstract : Here we report the recent progress in the research of our molecular capsules with well-defined polyaromatic nanospaces. For example, a representative male hormone (i.e., testosterone) is almost exclusively encapsulated by the capsule from a complex mixture with female hormones in water. In addition, long oligounsaturated fatty acids (e.g., α-linolenic acid) and volatile cyclic monoterpenes are selectively bound by the capsule in water and/or in the solid state, through effective hydrophobic effects, CH-π/π-π interactions, and hydrogen bonds. On the basis of the recent studies, we would like to propose a new strategy for the selective recognition of biomolecules by molecular receptors.
Keywords : Capsule; Recognition; Host-guest interactions; Biomolecules; Water

私達の体の中には、大小様々な有機分子が存在する。それぞれに役割があり、どれ１つとして不要な分子はない。そして、それらを識別するレセプターも存在し、識別により分子情報を正確に読み取ることで、生命活動が維持されている。このような優れた生体レセプターを模倣して、高性能なセンサーを目指した研究がこれまで盛んに行われてきた。しかしながら、水中かつ温和な条件で、高い識別能を有する人工レセプターの設計指針は示されていない。本発表では、著者らの研究グループが合成した「芳香環ナノ空間」を持つ分子カプセルが、構造や性質の異なる生体分子に対して、水中で前例のない識別能を発現したので紹介する。

芳香環ナノ空間を持つ分子カプセル

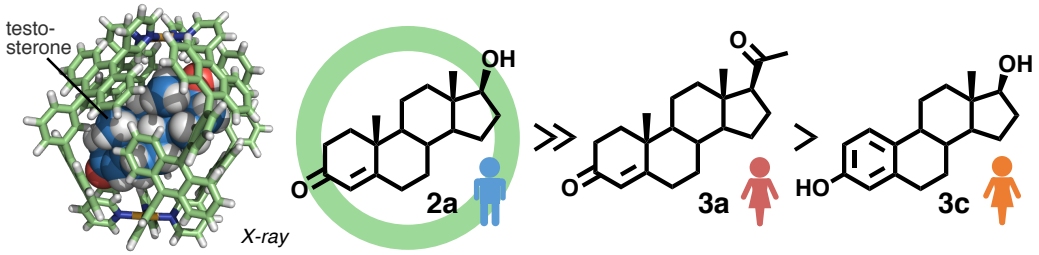
１０年前に貴志らは、M_2L_4組成の分子カプセル **1** を報告した（下図）[1]。このカプセルは、比較的大きな芳香環のアントラセンを含む湾曲型配位子と金属イオンを混合することで、定量的に組み上がる。水中・大気下で安定な化合物で、芳香環に囲まれた約１nm の球状空間を有する。この「芳香環ナノ空間」は疎水効果などを駆動力に、種々の合成化合物を効率良く内包した[2]。注目すべき点は、タンパク質からなる生体空間と構成成分も性質も全く異なるが、水中で、種々の生体分子に対して高い捕捉能と識別能を示したことである。



男性ホルモンの見分け方

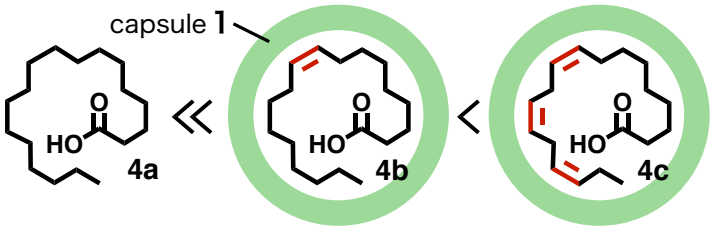
2019 年に山科らは、カプセル **1** による男性ホルモンの識別に成功した[3]。水中で、**1** と代表的な男性ホルモンのテストステロン(**2a**)と女性ホルモンのプロゲステロン

(**3a**)および β-エストラジオール(**3c**)を撹拌すると、内包体 **1**･**2a** が 98%以上の選択性で得られた（下図）。驚くべきことに、**2a** に対して **3a** と **3c** を 100 当量ずつ混合した場合も、同様の選択性で **1** は **2a** を捕捉した。結晶構造から、多点の CH-π 相互作用が識別に働くことが示された（下図左）。さらに、2020 年に土橋らはカプセル骨格への窒素導入により、女性ホルモン **3a** の選択的捕捉を達成した[4]。



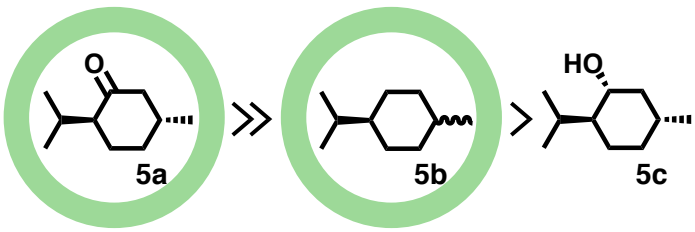
不飽和脂肪酸の見分け方

2020 年に二木らは、カプセル **1** の球状空間が長鎖脂肪酸の不飽和部位を識別できることを明らかにした[5]。**1** とステアリン酸(**4a**)を水中で混ぜると、内包体 **1**･**4a** が定量的に得られた。一方、**4a** とモノ不飽和のオレイン酸(**4b**)を混合した際、**1** は 100%の選択性で **4b** を捕捉した（下図）。計算構造から、**1** 内で **4b** はコイル構造を取り、芳香環骨格と効果的な π-π/CH-π 相互作用が働くことが示唆された。さらに、多価不飽和の脂肪酸 **4c** が優先的に **1** に捕捉された。



環状モノテルペンの見分け方

著者らはごく最近、高揮発性のテルペンがカプセル **1** に選択的に捕捉されることを見出した[6]。特に、メントン(**5a**)が他の環状モノテルペン（例えば、メンタン(**5b**)やメントール(**5c**)、カンファー）の混合物中から 90%の選択性で捕捉された（右図）。さらに、固体状態の **1** を用いた気相条件で、**5a** の優先的な捕捉が確認された。



参考文献 [1] N. Kishi, Z. Li, K. Yoza, M. Akita, M. Yoshizawa, *J. Am. Chem. Soc.* **2011**, *133*, 11438–11441. [2] M. Yoshizawa, L. Catti, *Acc. Chem. Res.* **2019**, *52*, 2392–2404. [3] M Yamashina, T. Tsutsui, Y. Sei, M. Akita, M. Yoshizawa, *Sci. Adv.* **2019**, *5*, eaav3179. [4] H. Dobashi, L. Catti, Y. Tanaka, M. Akita, M. Yoshizawa, *Angew. Chem. Int. Ed.* **2020**, *59*, 11881–11885. [5] K. Niki, T. Tsutsui, M. Yamashina, M. Akita, M. Yoshizawa, *Angew. Chem. Int. Ed.* **2020**, *59*, 10489–10492. [6] R. Sumida, M. Yoshizawa, *et al.*, in preparation.

蛋白質を用いた機能分子システムの創製と応用

（中央大理工）小松 晃之
Synthesis and Applications of Functional Molecular Systems using Proteins (*Faculty of Science and Engineering, Chuo University*) ○Teruyuki Komatsu

Proteins are ultimate biosupramolecules. The strategy to use proteins as the unit of functional materials is one of the rational molecular designs and is the frontier of bio-nanotechnology. We synthesize various protein assemblies using covalent bond, coordination bond, and electrostatic interaction hierarchically, and are striving to create concerted functions and functional molecular systems. This lecture will give an overview of our functional molecular systems and their various applications, such as artificial blood, virus trap, and swimming microtube motor. A hemoglobin (Hb) wrapped covalently with three human serum albumins (HSAs), Hb-HSA_3 cluster, becomes an artificial O_2 carrier as a red blood cell substitute. The structure, O_2 binding ability, and *in vivo* safety and efficacy have been elucidated. Protein microtubes and nanotubes have been fabricated by layer-by-layer assembly technique using porous polycarbonate membrane. The nanotubes can capture viruses efficiently. The microtubes having Pt nanoparticles or catalase on the interior surface are self-propelled in aqueous H_2O_2 solution by jetting O_2 microbubbles from the open end. More recently, water-soluble linear coordination polymers of HSA and Hb, which are connected via bis(terpyridyl)–Fe^{2+} complex, have been synthesized.
Keywords : Protein; Enzyme; Artificial Blood; Virus; Microtube Motor

生命現象の根幹を支える蛋白質は進化の過程を経て最適化されてきた究極のバイオ超分子である。その蛋白質を機能材料創製の基本ユニットとして用いる戦略は合理的な分子設計の一つであり、バイオナノテクノロジーのフロンティアといえる。我々は蛋白質を機能階層的に繋いだり、並べたり、重ねたりする方法により様々な組織体を合成し、その分子配置を利用した“協奏的機能の発現”、さらにはそれらを用いた“機能分子システムの創製”に取り組んでいる。本講演では、蛋白質を共有結合、配位結合、静電的相互作用で連結した各種機能分子システムについて 最近の成果を概説する。人工血液、ウイルストラップ、マイクロチューブモーターなど、様々な応用展開について紹介したい。

複数個の蛋白質を有機的に結合した構造明確な複合体では、個々の蛋白質では見ることのできない高次機能が発現する。ヘモグロビン（Hb）を核として、その分子表面にヒト血清アルブミン（HSA）を 3 分子結合したコア−シェル型の（ヘモグロビン−アルブミン）クラスター（Hb-HSA_3）を合成し、それが生体投与可能な人工酸素運搬体（赤血球代替物）となることを見出した（**Fig. 1A**）[1,2]。Hb-HSA_3 の AFM 像には明確な三角形構造が見てとれ、cryo-TEM 像の三次元再構成からクラスターの立体構造を解明した [3]。Hb-HSA_3 の酸素親和性（P_{50}）は原料 Hb の四次構造を固定することにより 9~56 Torr の範囲で調節可能である [4]。Hb-HSA_3 の 20wt%溶液を出血ショック状態のラットに投与すると全例が生存し、平均動脈血圧は投与前値まで回復した。また、本溶液が虚血性

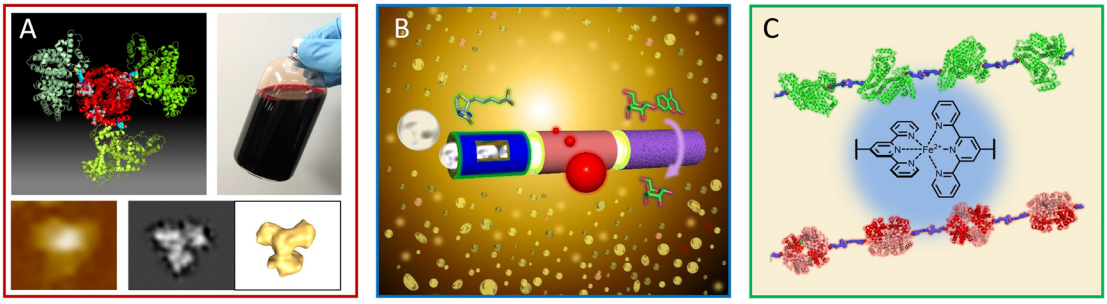


Fig. 1 (A) Hb-HSA$_3$ cluster, (B) protein microtube motor, (C) supramolecular protein nanofibers.

脳血管障害の治療薬として有効であることも実証した [5]。HSA を組換えイヌ血清アルブミン、組換えネコ血清アルブミンに変換すると、犬猫用の人工酸素運搬体となる [6,7]。組換え Hb（rHb）と組換えアルブミン（rHSA）の組み合わせで、原料血液を一切必要としない完全合成型の rHb-rHSA$_3$ も開発した [8]。

中空シリンダー構造は、内孔・管壁・外表面にそれぞれ異なる機能を付与できる点が魅力である。我々は多孔性ポリカーボネート膜を用いた独自の鋳型内交互積層法により、蛋白質からなる一群のマイクロチューブやナノチューブの合成法を確立した [9,10]。複数の蛋白質を任意の順序で階層的に積層することで、望みの機能を組み込める。得られたチューブの一次元内孔空間に、ウイルスが効率よく捕捉されることを明らかにした [11]。また、内孔壁に白金ナノ粒子やカタラーゼを配置した蛋白質マイクロチューブ（外径：1.2μm、長さ：24μm）は、H_2O_2水溶液中で末端から酸素バブルを噴出しながら自走する（**Fig. 1B**）[12–14]。このマイクロチューブモーターが大腸菌を効率よく捕集できることを見出した。さらに外表面をα-グルコシダーゼ（加水分解酵素）で被覆すると、自己攪拌型の触媒になることもわかった。マイクロリットルスケールの容器内で反応を促進するのに有効であると考えられる。

ごく最近、金属配位結合で連結した蛋白質ナノファイバーの合成に成功した（**Fig. 1C**）[15]。2 つのターピリジル基を有する HSA の水溶液に鉄イオンを添加すると、ビスターピリジン鉄錯体で連結した一次元 HSA ナノファイバーが得られた。長さは 1 μm 以上に及ぶが、沈殿凝集はなく、きわめて安定な超分子ポリマーとなった。全く同様な方法により Hb ナノファイバーを調製することも可能で、その酸素親和性は原料 Hb と同等であった。

T. Komatsu, et al.,
1) *Biomacromolecules* **2013**, *14*, 1816. 2) *ACS Omega* **2019**, *4*, 3228. 3) *J. Phys. Chem. Lett.* **2017**, *8*, 819. 4) *J. Phys. Chem. B* **2018**, *122*, 12031. 5) *Stroke* **2018**, *49*, 1960. 6) *Sci. Rep.* **2016**, *6*, 36782. 7) *J. Mater. Chem. B* **2018**, *6*, 2417. 8) *J. Mater. Chem. B* **2020**, *8*, 1139. 9) *ACS Nano* **2010**, *4*, 563. 10) *Chem. Lett.* **2020**, *49*, 1245. 11) *J. Am. Chem. Soc.* **2012**, *75*, 7644. 12) *Chem. Eur. J.* **2017**, *23*, 5044. 13) *ACS Appl. Nano Mater.* **2018**, *1*, 3080. 14) *ACS Appl. Nano Mater.* **2019**, *2*, 4891. 15) *Chem. Commun.* **2020**, *56*, 15585.

Reconstituting cell membrane functions with a model membrane and nanometric space

([1]*Biosignal Research Center, Kobe University*, [2]*Graduate School of Agrobioscience, Kobe University*) ○Kenichi Morigaki,[1,2]

Keywords: Biological membrane; Model membrane; Supported lipid bilayer; Nanofluidics

Biological membranes composed of lipid bilayer and associated proteins work as a platform for diverse cellular functions including signal transduction and energy conversion. We developed a model biological membrane on the solid substrate by combining a patterned lipid bilayer with a nanometric gap structure. A patterned polymeric bilayer was lithographically generated from polymerizable diacetylene phospholipid by UV irradiation.[1] Natural lipid bilayers having lateral fluidity were incorporated into the polymer-free regions by spontaneous spreading of vesicles (vesicle fusion). The polymeric lipid bilayer acted as a stable framework and the embedded fluid lipid bilayers mimicked the biological membrane with lateral mobility, two-dimensional organization, and membrane functions.

A nanometric gap structure (nanogap-junction) was created between the fluid bilayer and a polydimethylsiloxane (PDMS) sheet by attaching the surface of polymeric bilayer and PDMS using an adhesion layer with a defined thickness (e.g. silica nanoparticles).[2] The nanogap-junction having a thickness smaller than 100 nm acted as a selective and sensitive biosensing platform. From a mixture of proteins (cholera toxin and albumin), the target protein (cholera toxin) was selectively transported into the gap by the specific binding to a glycolipid (G_{M1}) in the fluid bilayer and lateral diffusion. This platform enabled to detect target molecules (e.g. biomarkers) with an elevated signal-to-noise-ratio due to the reduced background noise. Furthermore, single molecules of membrane proteins could be detected by using an adhesion layer with biocompatible polymer materials.

Patterned model membrane in combination with a nanometric gap structure can be applied to a wide variety of membrane systems and proteins. We recently succeeded to reconstitute the light harvesting machinery of the plant thylakoid membrane.[3] Furthermore, dopamine D2 receptor (D2R), a G-protein coupled receptor (GPCR) that plays critical roles in the neural functions and represents the target for a wide variety of drugs, could be reconstituted in the nanometric cleft between substrate and PDMS. These finding points to a new possibility to use a nanometric space as a platform for reconstituting and studying membrane proteins under the quasi-physiological conditions, which is difficult to be created by other methods.

1) K. Morigaki, T. Baumgart, A. Offenhäusser, W. Knoll, *Angew. Chem., Int. Ed.* **2001**, *40*, 172. 2) a) K. Ando, M. Tanabe, K. Morigaki, *Langmuir* **2016**, *32*, 7958. b) M. Tanabe, K. Ando, R. Komatsu, K. Morigaki, *Small* **2018**, *14*, 1802804. 3) T. Yoneda, Y. Tanimoto, D. Takagi, K. Morigaki, *Langmuir* **2020**, *36*, 5863.

液液相分離が誘起する細胞内分子集合体のフロンティア

（プリンストン大学化学生物工学科）○下林俊典
Intracellulr molecular assemblies driven by liquid-liquid phase separation (*Department of Chemical and Biological Engineering, Princeton University*) ○Shunsuke F. Shimobayashi

Intracellular molecules self-assemble into membrane-bound or membrane-less organelles to achieve their biological functions. There is emerging evidence on membrane-less organelles composed of proteins/RNA that liquid-liquid phase separation (LLPS) is a physical principal to potentially unify the assembly process. This talk will discuss synthetic approaches to understanding the physical principal through optogenetic tools to light-trigger liquid protein assemblies. The particular focus will be on how the formation rate depends on supersaturation, in which we demonstrate that the key features can be quantitatively understood through classical nucleation theory (CNT). The link to biological functions will be also discussed.
Keywords : Intracellular phase separation, membrane-less organelles, optogenetics

生物学的相分離、LLPS（liquid-liquid phase separation, 液液相分離）といった単語を頻繁に耳にするようになってきた。液液相分離とは、均一に混合されている混合系が温度や分子間相互作用等の変化に伴い、一相液体状態から二相の区別できる液体に変化することをいう。相分離は、サラダドレッシングの油滴にみられるように我々の日常にありふれた現象であり、その物理は長く研究の対象とされてきた。それがここ 10 年程で、RNA とタンパク質からなる膜を持たない（非膜型の）細胞内小器官（オルガネラ）や分子集合体が多数報告され、液液相分離はその形成過程を統一的に記述しうる物理原理として注目されている[1)]。しかしながら、分子集合を駆動する分子間相互作用やその多価性などその基礎的な物理原理はよくわかっていない。

本講演では、光で人工的に分子集合体を誘起する技術を用いることで見えてきた非膜型分子集合体の形成メカニズムについて議論する。特に、分子集合体の形成速度が系の分子の過飽和度にどのように定量的に依存するかに焦点をあて、古典的な核生成理論との整合性について言及する。さらに、分子集合体の形成と生物学的な機能との繋がりについても議論する。

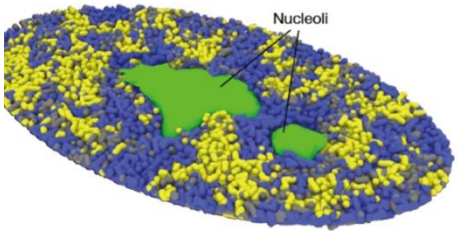
1) Y. Shin, C. P. Brangwynne, *Science* **357**, eaaf4382 (2017). DOI: 10.1126/science.aaf4382

4D ゲノムアーキテクチュア：細胞核のなかのポリマー凝縮系

（名大院工）藤城 新・○笹井 理生
4D Genome Architecture: A Condensed Polymer System in Cell Nucleus
(*Graduate School of Engineering, Nagoya University*) Shin Fujishiro ○Masaki Sasai

Human genome DNA amounts to about 2 meters in its total length, but this long DNA chain is confined in a cell nucleus in diameter of about 10 micrometers. However, this tight compaction needs to be compatible with the rapid and flexible read/write of DNA information. The recent advancement of the measurement technology has revealed that the time-dependent three-dimensional structure of genome DNA, i.e., the 4D genome architecture, plays a key role in this DNA functioning, and now, there is a strong demand for developing a computational method for a unified view to explain various experimental data. We developed a polymer model of the genome DNA to examine the self-organized phase separation of chromatin. We show that the phase separation induced by the heterogeneous interactions among densely dispersed chromatin in the nucleus is crucial for determining the 4D genome architecture.
Keywords : phase separation; chromatin; chromosome; compartment; dynamics

ヒト DNA は全長約 2 m に達するが、直径 10 μm ほどの細胞核に収納されている。この高度な圧縮にもかかわらず、DNA 情報の迅速・柔軟な読み書きを可能にする仕組みは何か？この問題は生命科学における重要な問題として、最近の注目を集めている。この問題を解くためには、ゲノム規模の DNA の構造とダイナミクス、すなわち 4D ゲノムアーキテクチャの解明が必要であるが、最近のハイスループット生化学手法、および顕微鏡技術の進歩により、4D ゲノムアーキテクチャの知識は急速に蓄積しつつある。さらに解析を進めるためには、これらの多様な測定データを統一的に理解し、ゲノムアーキテクチャの予測と制御を行うための計算モデルを開発することが強く望まれている。我々は、染色体をポリマー鎖として表す動力学計算モデルを開発し、クロマチンの局所物性に応じた相互作用を仮定することにより、この計算モデルが多くの測定データを定量的に説明することを示した。とりわけ重要なのは、核内に高密度で存在するクロマチン間の不均一な相互作用による相分離であり、この相分離によって染色体の構造と核内分布が動的に生成されることが示された。



ヒト線維芽細胞のゲノム DNA の動力学計算スナップショット。クロマチン（青と黄）及び核小体（緑）の相分離がゲノム構造を決める。

最小構成分子システムによる細胞運動・分裂機能の再構成

(京大白眉[1]・京大院理[2]・キュリー研[3]・JST さきがけ[4]) ○宮﨑 牧人[1,2,3,4]
Reconstitution of the cell motility and division machineries from minimum molecular components ([1]*The Hakubi Center for Advanced Research, Kyoto University*, [2]*Graduate School of Science, Kyoto University,* [3]*Institut Curie,* [4]*JST PRESTO*) ○Makito Miyazaki[1,2,3,4]

In the cell, hundreds or thousands of proteins work together to regulate various cellular functions. To understand how nanometer-sized proteins sense the micrometer-sized huge cellular boundary and how proteins collectively regulate cellular functions is not only a challenging frontier in the field of cell biology, but also indispensable for creating the next generation smart materials mimicking living systems.

One of the key elements of a cell is the actin cytoskeleton. The actin cytoskeleton is an essential intracellular structure mainly composed of actin filaments and myosin molecular motors. It has been known that the actin cytoskeleton regulates key cellular functions including cell motility and division, yet the regulatory mechanism remains unresolved. To uncover the mechanism, we have adopted an *in vitro* reconstitution approach. We purify actomyosin molecules from living cells, encapsulate them into artificial cells, then explore physical conditions at which functions reminiscent of cell motility and division are reproduced. Our findings will give general insights into how the actomyosin molecules self-organized into cytoskeletal networks and drive various cellular functions.
Keywords :Molecular Motor; Actomyosin; Cytoskeleton; Artificial Cell; Self-organization

細胞機能は数百、数千種類ものタンパク質によって制御されている。如何にして、ナノメートルサイズの小さなタンパク質が、マイクロメーターサイズの広大な細胞内空間を認識し、細胞機能を統制しているのだろうか？その仕組みを理解することは、細胞生物学における中心的かつ挑戦的課題であるだけでなく、生物に学んだ次世代の新規物質機能の開発に繋がると期待されている。

細胞を構成する重要な要素の一つに「アクチン細胞骨格」と呼ばれる構造がある。アクチン線維やミオシン分子モーターが自己組織的に集合し、収縮能を持ったマイクロメートルスケールのネットワーク構造を形成する。そして、ネットワークの変形や再構築が、細胞運動や細胞分裂などの生命活動に本質的な様々な機能を制御していると考えられているが、その仕組みの詳細は未解明である。そこで我々は、細胞から単離・精製したアクトミオシンを人工細胞に封入し、細胞機能が再構成される条件を探ることによって、物理的な観点から制御機構の解明に挑んでいる。本講演では最新の研究成果を紹介し、細胞機能の制御機構について議論を行う。

1) Cell-sized spherical confinement induces the spontaneous formation of contractile actomyosin rings *in vitro*. M. Miyazaki, M. Chiba, H. Eguchi, T. Ohki, S. Ishiwata, S. *Nat. Cell Biol.* **2015** *17*, 480.
2) Tug-of-war between actomyosin-driven antagonistic forces determines the positioning symmetry in cell-sized confinement. R. Sakamoto, M. Tanabe, T. Hiraiwa, K. Suzuki, S. Ishiwata, Y. T. Maeda, M. Miyazaki, *Nat. Commun.* **2020** *11*, 3063.

Symposium | Asian International Symposium | Asian International Symposium - Photochemistry -

[S09-1pm] Asian International Symposium - Photochemistry -

Chair, Symposium organizer:Osamu Ishitani, Mamoru Tobisu, Kei Ohkubo, Yasuharu Yoshimi, Tadashi Mori
Fri. Mar 19, 2021 1:00 PM - 3:40 PM Webiner 9 (Online Meeting)

[S09-1pm-01] [6π] Photocyclization to *cis*-Hexahydrocarbazol-4-ones: Substrate Modification, Mechanism and Scope

○Sachinkumar G Modha[1,2], Alexander Pothig[2], Andreas Dreuw[3], Thorsten Bach[2] (1. Uka Tarsadia University, 2. Technical University of Munich, 3. Ruprecht-Karls University)

1:10 PM - 1:40 PM

[S09-1pm-02] Surface functionalization of polyolefin by C-H oxygenation with chlorine dioxide

○Haruyasu Asahara[1] (1. Osaka University, Pharmaceutical Sciences)

1:40 PM - 2:00 PM

[S09-1pm-03] Flow Photochemical Synthesis of Thiophene-fused Organic Semiconductors

○Yasunori Matsui[1] (1. Osaka Pref. Univ.)

2:30 PM - 2:50 PM

[S09-1pm-04] Highly efficient and selective photoreaction progress under microflow conditions

○Yasuhiro Nishiyama[1] (1. Industrial Technology Center of Wakayama Prefecture (WINTEC))

2:50 PM - 3:10 PM

[S09-1pm-05] Continuous-Flow in Photocatalysis and Automated API Synthesis

○Jie Wu[1,2] (1. National University of Singapore, 2. National University of Singapore (Suzhou) Research Institute)

3:10 PM - 3:40 PM

[6π] Photocyclization to *cis*-Hexahydrocarbazol-4-ones: Substrate Modification, Mechanism and Scope‡

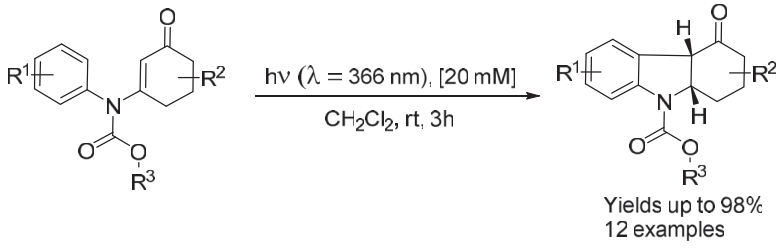
([1]*Department of Chemistry and Catalysis Research Center (CRC) Technical University of Munich*, Lichtenbergstr. 4, 85747, Garching Campus, Munich, Germany, [2]*Department of Chemistry, Maliba Campus, Tarsadi 394350, Uka Tarsadia University, Bardoli, India,* [3]*Interdisciplinary Center for Scientific Computing, Ruprecht-Karls University, Im Neuenheimer Feld 205A, 69120 Heidelberg, Germany*) ○ Sachin G. Modha,[1,2] Alexander Pöthig,[1] Andreas Dreuw,[3] Thorsten Bach[1]

Keywords: [6π] Photocyclization; hexahydrocarbazolones; enones; enaminones.

Photochemical organic transformations provide easy access to molecular structures that are difficult, if not impossible, to obtain via conventional reactions. Numerous approaches toward natural product synthesis have been reported where a photochemical transformation represents a key step.[1] Indoline derivatives are a very important class of heterocyclic compounds due to their presence as core structures in many naturally occurring alkaloids and pharmaceutical compounds. In pioneering work, Chapman and co-workers[2] demonstrated that *N*-alkyl-*N*-aryl-enamines produce upon irradiation mainly trans-fused hexahydrocarbazoles, while Schultz et al.[3] reported the formation of cis-fused dihydrobenzofurans from *β*-aryloxyenones via photochemical conrotatory ring closure followed by epimerization. These and other reports proved the efficiency of a [6π] photocyclization reaction in the generation of complex carbo- and heterocycles from simple starting materials.

In 1988, Gramain, Husson and co-workers reported a synthesis of *cis*-hexahydrocarbazolones via [6π] photocyclization of tertiary aryl enaminones.[4] Only three examples were reported and the photoproducts were found to be unstable at room temperature. There is neither a mechanistic study carried out nor NMR spectra with clear coupling constants reported so far. Thus, we were interested in revisiting this classical photoreaction and studied it in detail.[5]

During our initial attempts, we found out that the reported photoproducts were not stable on silica and the substitution on nitrogen plays an important role in stability of the photoproducts. For this modification UV-Vis absorption was used as a tool to determine the substitution change on nitrogen. The new substrate gives only *trans*-hexahydrocarbazol-4-one upon irradiation at 366 nm in dichloromethane solvent, but it converts to thermodynamically stable *cis*-hexahydrocarbazol-4-one on silica. Deuterium labeling experiments revealed that only 1,4-hydrogen shift taking place after conrotatory ring closure while triplet quenching experiments suggested a triplet pathway. It is first time that we have NMR spectra of these *trans*- and *cis*-compounds with clear coupling constants and single crystal XRD analysis of the *cis*-compound.



The energy of excited states and intermediates as well as final products were calculated with the help of computational calculations which provide insight into the mechanistic pathway of this interesting

reaction. Furthermore the *cis*-hexahydrocarbazol-4-ones could be converted to few interesting products like α-hydroxy hexahydrocarbazol-4-one, α-methyl hexahydrocarbazol-4-one, Grignard addition product and hydroxy hexahydrocarbazole via carbonyl reduction. It is worth noting that all these transformations were diastereoselective and only one diastereoisomer was obtained in all cases.

‡ S. G. Modha, A. Pöthig, A. Dreuw, T. Bach, *J. Org. Chem.* **2019**, *84*, 1139.

[1] (a) T. Bach, J. P. Hehn, *Angew. Chem., Int. Ed.* **2011**, *50*, 1000; (b) N. Hoffmann, *Chem. Rev.* **2008**, *108*, 1052.

[2] (a) O. L. Chapman, G. L. Eian, *J. Am. Chem. Soc.* **1968**, *90*, 5329; (b) O. L. Chapman, G. L. Eian, A. Bloom, J. Clardy, *J. Am. Chem. Soc.* **1971**, *93*, 2918.

[3] (a) A. G. Schultz, R. D. Lucci, *J. Org. Chem.* **1975**, *40*, 1371; (b) A. G. Schultz, R. D. Lucci, W. Y. Fu, M. H. Berger, J. Erhardt, W. K. Hagmann, *J. Am. Chem. Soc.* **1978**, *100*, 2150.

[4] a) J.-C. Gramain, Y. Troin, H.-P. Husson, *J. Het. Chem.* **1988**, *25*, 201; b) J.-C. Gramain, H.-P. Husson, Y. Troin, *J. Org. Chem.* **1985**, *50*, 5517.

[5] a) T. Bach, B. Grosch, T. Strassner, E. Herdtweck, *J. Org. Chem.* **2003**, *68*, 1107; b) V. Edtmuller, A. Pöthig, T. Bach, *Tetrahedron*, **2017**, *73*, 5038.

Surface functionalization of polyolefin by C-H oxygenation with chlorine dioxide

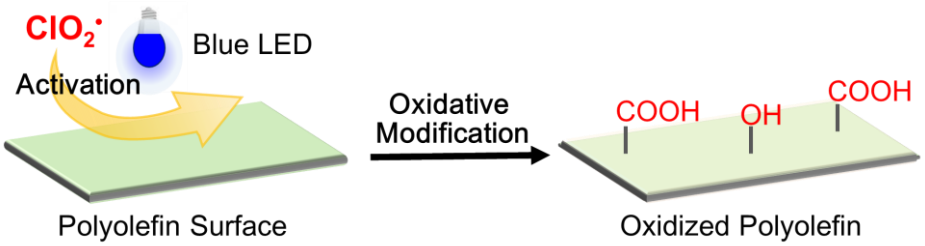
(*Graduate School of Pharmaceutical Sciences, Osaka University*) ○Haruyasu Asahara
Keywords: Chlorine dioxide, Photoreaction, Polyolefin, Surface functionalization

Polyolefins are widely used in various forms for packaging, protective coating and medical appliances owing to its superior properties such as heat resistance, better corrosion resistance, high mechanical strength to weight ratio, and easy recycling. However, the use of non-polar plastics has been limited due to its inherent hydrophobicity and poor adhesive property with dissimilar materials. Therefore, it is necessary to modify plastic surfaces to increase the surface energy and hydrophilicity without change in their bulk properties.

C–H oxygenation of saturated aliphatic long-chain hydrocarbons such as polypropylene (PP) and polyethylene (PE) is an important target reaction in polymer chemistry for functionalization of inert polymer surfaces. Generally, plasma and corona discharge treatments have been used for PP surface modification. However, the reactive species, such as ozone, and the electron beam result in C–C bond cleavage, resulting in significant decreases in mechanical strength. Additionally, the lifetime of the oxygenated state is not sufficient because ozonic –OO insertion occurs on the PP surface.

Previously, it was reported that photo-activated chlorine dioxide radical ($ClO_2^{\bullet}$) was proven to be used as an oxidizing agent to achieve the oxygenation of methane to methanol and formic acid in perfluorohexane (C_6F_{14}).[1] Chlorine radical ($Cl^{\bullet}$) generated from $ClO_2^{\bullet}$ gas upon photo-activation cleaves the C-H bond of CH_4 to form a methyl radical ($CH_3^{\bullet}$), and the subsequent addition of singlet oxygen would give oxygenated products.

In this study, we performed polyolefin surface C-H oxygenation using this photo-activated $ClO_2^{\bullet}$ (Figure). The oxygenated polymer surface allows further modification with various organic compounds via reaction with the carboxylic acid groups on the surface, which may have significant implications in synthetic polymer chemistry.[2,3]



1) K. Ohkubo, K. Hirose, *Angew. Chem. Int. Ed.* **2017**, *57*, 2126. 2) K. Ohkubo, H. Asahara, T. Inoue, *Chem. Commun*. **2019**, *55*, 4723. 3) Y. Jia, J. Chen, H. Asahara, T. Aso, H. Uyama, *ACS Appl. Polym. Mat.* **2019**, *1*, 3452.

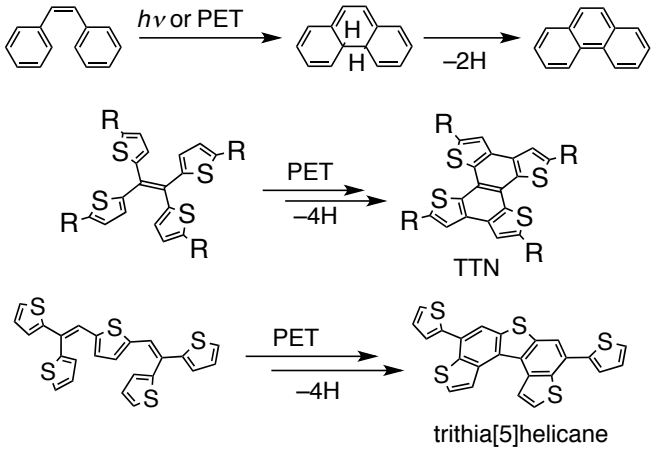
日本化学会 第101春季年会 (2021)

Flow Photochemical Synthesis of Thiophene-fused Organic Semiconductors

(*Osaka Prefecture University*)
Yasunori Matsui

Keywords: Flow Chemistry; Photoinduced Electron Transfer; Organic Field Effect Transistor; Mallory Reaction

In the past decades, many polycyclic heteroaromatic compounds have been developed as semiconductors for organic field effect transistors (OFETs). To construct polycyclic aromatic skeletons, photoinduced electron transfer (PET)-assisted tandem cyclization–dehydrogenation reaction is a typical strategy (Scheme 1). Actually, more efficient synthesis of these compounds can be achieved by utilizing photochemical flow reactors. In this work, we synthesized alkyl-substituted tetrathienonaphthalenes (TTN) and trithia[5]helicene derivatives (Scheme 1)[1,2] and fabricated OFET utilizing solution process. Also, we carried out theoretical prediction of hole mobility of C_n-TTN was based on amorphous solid simulation–statistics (ASSiST) method.[3]



Scheme 1. Tandem 6π-cyclization–dehydrogenetion reactions to provide polycyclic aromatic compounds.

Theoretical Simulation. Amorphous solid structure of 480 molecules of C_n-TTN was obtained by annealing (1000 K, 2 ns)–cooling (300 K, 1 ns) process in molecular dynamics simulation under periodic boundary condition (Fig. 1). Hole transfer rate constant (W) was obtained by using transfer integral (t) of a given focused molecules and the neighboring molecules and Marcus equation (eq. 1), where h is Planck constant, λ_{RE} is reorganization energy, k_B is the Boltzmann constant, and T

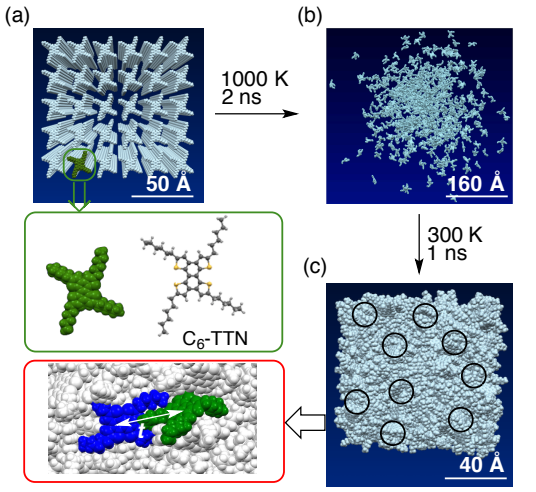


Fig. 1. Method for preparation of the amophous solid structure of C_6-TTN: (a) initial ordered configuration, (b) random configuration, and (c) created structure.

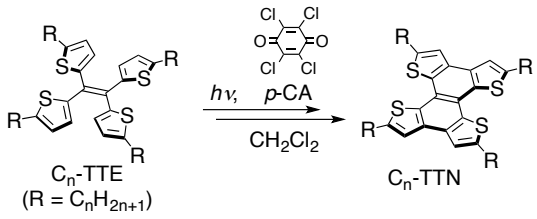
$$W = \frac{2\pi t^2}{h}\left(\frac{\pi}{\lambda_{RE} k_B T}\right)^{1/2} \exp\left[-\frac{\lambda_{RE}}{4k_B T}\right] \quad (1) \qquad \mu_{am} = \prod_N \left(\frac{1}{6}\frac{e}{k_B T}\frac{\Sigma_i r_i^2 W_i^2}{\Sigma_j W_j}\right)^{1/N} \quad (2)$$

is the temperature. Furthermore, hole mobility of the amorphous structure (μ_{am}) is estimated as a geometric mean using the modified Stokes–Einstein equation (eq. 2),[3] where N is the number of "molecular flocks", e is the elementary charge, and r is the distance between molecular centroids. Using this approach, we found that μ_{am} values are calculated to be 2.1 × 10^{-2}, 9.3 × 10^{-3}, and 1.8 × 10^{-3} cm^2 V^{-1} s^{-1} for C_6-, C_8-, and C_{10}-TTNs, respectively (Table 2). These values indicate that too long alkyl chains decrease μ_{am} in the amorphous solid and/or crystal boundary, due to reduction of t.

Photochemical Synthesis. Photoirradiation [λ_{EX} = 350 nm, 3–6 h] of a CH_2Cl_2 solution containing C_n-TTE and *p*-chloranil (*p*-CA, 2 eq) in a batch reactor led to a formation of C_n-TTN in 24–58% yield (Table 1). Use of a microflow reactor (1 × 0.5 × 915 mm) improved these reaction yields, up to 73% in an extremely short residence time. These results were explained by homogenous photoirradiation and prevention of overreaction by discharge from the reactor, originated from the effects of flow reactor.

OFET Characteristics. Thin polycrystalline films (~100 nm) of C_n-TTN were obtained by using spin-coating of the toluene solution (1 wt%) on glass substrate. The films were conducted to fabrication of top-gate bottom-contact OFET with moderate p-type characteristics with μ_{OFET} ~ 10^{-2} cm^2 $V^{-1}s^{-1}$ (Table 2). In the presentation, we also discuss interesting relationship between alkyl chain length and μ_{OFET}, and understanding of relationship between μ_{am} and μ_{OFET}.

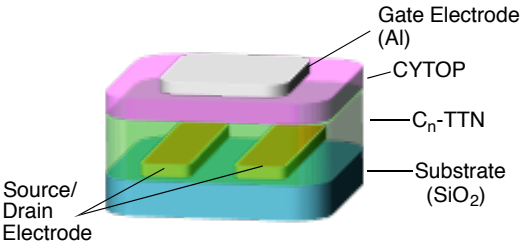
Table 1. Photoreactions of C_n-TTE Affording C_n-TTN



Sub	System	time / min	Product	yield / %
C_6-TTE	batch	360	C_6-TTN	40
	flow	1[a]		60
C_8-TTE	batch	180	C_8-TTN	58
	flow	1[a]		73
C_{10}-TTE	batch	180	C_{10}-TTN	24
	flow	1[a]		36

[a]Residence time

Table 2. Theoretical (μ_{am}) and Experimental Hole Mobility (μ_{OFET}) of C_n-TTN



Materials	μ_{am} / $cm^2V^{-1}s^{-1}$	μ_{OFET} / $cm^2V^{-1}s^{-1}$	I_{on}/I_{off}
C_6-TTN	2.1 × 10^{-2}	3.7 × 10^{-2}	10^6
C_8-TTN	9.3 × 10^{-3}	1.0 × 10^{-2}	10^5
C_{10}-TTN	1.8 × 10^{-4}	2.4 × 10^{-3}	10^4
C_{12}-TTN	NA	4.5 × 10^{-4}	10^4

1. Yamamoto, A.; Matsui, Y.; Asada, T.; Naito, H.; Ikeda, H. *et al. J. Org. Chem.* **2016**, *81*, 3168–3176.

2. Yamamoto, A.; Matsui, Y.; Ikeda, H. *et al. J. Photochem. Photobiol. A Chem.* **2016**, *331*, 48–55.

3. Asada, T.; Koseki, S. *Org. Electron.* **2018**, *53*, 141–150.

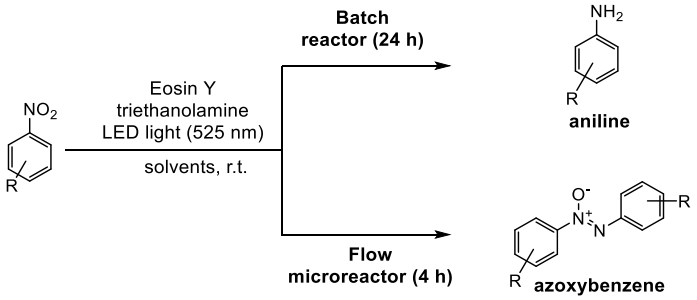
Highly efficient and selective photoreaction progress under microflow conditions

(*Department of Chemical Engineering, Industrial Technology Center of Wakayama Prefecture(WINTEC)*) ○Yasuhiro Nishiyama

Keywords: microflow condition, photoreduction, nitrobenzene, azoxybenzene, slug flow

The hydrogenation (reduction) of nitrobenzenes is an important reaction to provide various important products (aniline, azobenzene, etc.) in industry. However, nitrobenzenes which have reducible groups show the poor product selectivity in this reaction due to the difference of the reductive property of each functional group containing nitro group. Recently, it was reported that simple photocatalytic reduction of nitrobenzenes to anilines in batch with green LED light irradiation (525 nm).[1] This reaction affords aniline derivatives dominantly irrespective of the existence of other functional groups; however, it needs very long photoirradiation time (24 h) to the full conversion.[1] Microreactors which have very narrow channels, have many advantages for proceeding organic reactions efficiently. Especially, because of the very short path length, organic photoreactions in flow microreactors can proceed very smoothly compared to those in batch reactor.[2] In this work, we performed the above photoreductions in a flow microreactor in order to improve the reaction efficiency.

Consequently, nitrobenzenes were smoothly converted for 4 h photoirradiation, but different product selectivity was observed (azoxybenzenes were obtained as main products instead of anilines). In addition, even in flow microreactor, the flow rate significantly affected the chemical yield of azoxybenzene. Especially, the high flow rate afford azoxybenzene in very high yield. These results showed that the condensation reaction of nitrosobenzenes and *N*-phenylhydroxylamines, which are the intermediates in the hydrogenation of nitrobenzenes, was proceeded very smoothly in the microreactor. This reactor-dependent results were successfully applied to some kinds of substrates.[3] In this symposium, we will show further microreactor-dependent reaction results for the synthesis of various kinds of azoxybenzenes.



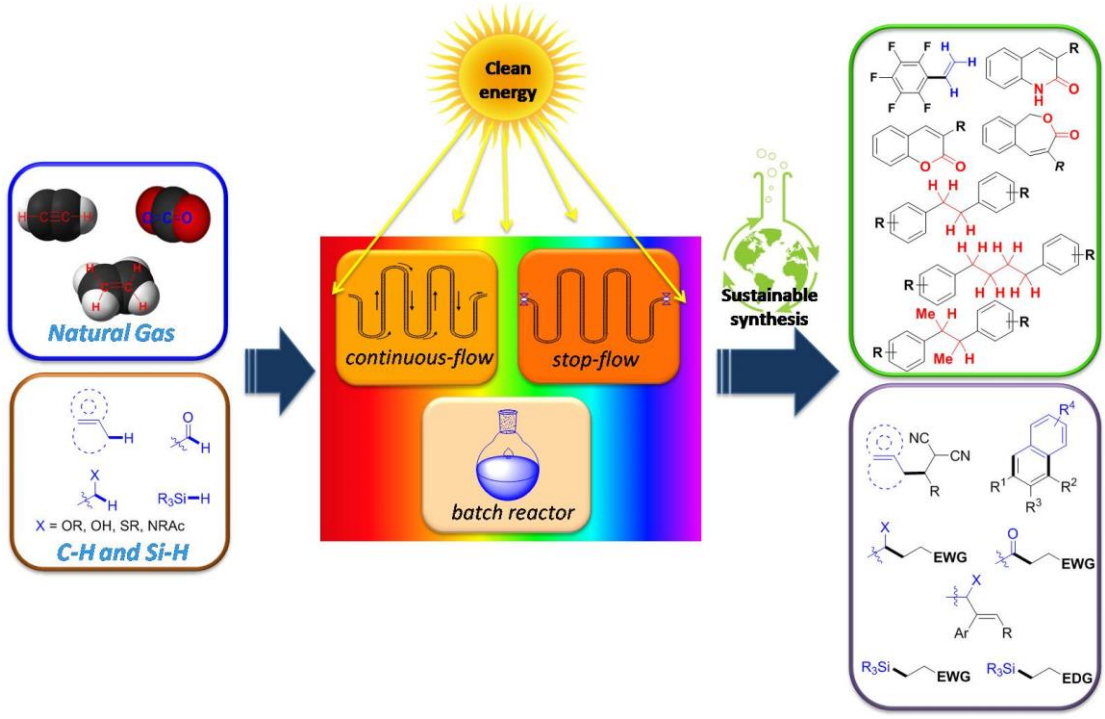
1) B. Chen, et al. *Green Chem.* **2014**, *16*, 1082. 2) ex.) K. Mizuno, et al. *J. Photochem. Photobiol. C* **2016**, *29*, 107. 3) Y. Nishiyama, et al. *React. Chem. Eng.* **2019**, *4*, 2055.

Continuous-Flow in Photocatalysis and Automated API Synthesis

([1]*Department of Chemistry, National University of Singapore*, [2]*National University of Singapore Suzhou Research Institution*) ○Jie Wu,[1,2] Hongping Deng,[1,2] Xuanzi Fan,[1] Cao Hui,[1,2] Chenguang Liu[1]

Keywords: Continuous-Flow Synthesis; Photochemistry; Stop-Flow Micro-Tubing Reactor; Automated Synthesis; Active Pharmaceutical Ingredients

Our research group focus on synthesis of fine chemicals using inexpensive natural gases and hydrocarbons as feedstocks under visible-light irradiation. Our research group at NUS has recently invented a “stop-flow” micro-tubing (SFMT) reactor platform, which represents an ideal laboratory bench model for the real world flow reactor in reaction discover applications.[1] In this context, we envision that the SFMT system provides an effective tool for developing visible-light promoted gas/liquid reactions and would be more suitable than continuous-flow technique for screening as visible-light promoted photoredox transformations are slow in many cases. In this talk, I will briefly introduce our recent progress on photochemical transformations using cheap feedstocks assisted by continuous-flow and stop-flow reactors.[2]



Compared to stepwise batch synthesis, multistep continuous flow synthesis enables the combination of multiple synthetic steps into a single and uninterrupted reactor network, thereby circumventing the need to isolate intermediates, and enabling automated synthesis.

However, despite many advantages and much progress in end-to-end API continuous-flow synthesis, several hurdles still need to be overcome. For instance, solvent and reagent incompatibility between individual steps, build-up pressure of reactors, substrate dispersion, and requirement of regeneration of reagent and scavenger columns. I this talk, I will present our recent progresses in this research field, which enables a novel automated API synthesis platform.

Reference:

1) F. Xue, H. Deng, C. Xue, D. K. B. Mohamed, K. Y. Tang, J. Wu, *Chem. Sci.* **2017**, *8*, 3623. 2) a) J. Hou, A. Ee, W. Feng, J. Xu, Y. Zhao, J. Wu, *J. Am. Chem. Soc.* **2018**, *140*, 5257-5263. b) X. Fan, J. Rong, H. Wu, Q. Zhou, H. Deng, J. D. Tan, C. Xue, L. Wu, H. Tao, J. Wu, *Angew. Chem. Int. Ed.* **2018**, *57*, 8514-8518. c) H. Deng, Q. Zhou, J. Wu, *Angew. Chem. Int. Ed.* **2018**, *57*, 12661. d) J. Hou, A. Ee, H. Cao, H. Ong, J. Xu, J. Wu, *Angew. Chem. Int. Ed*. **2018**, *57*, 17220. e) J. Li, Y. Luo, H. Cheo, Y. Lan, J. Wu, *Chem* **2019**, *5*, 192. f) X. Fan, P. Xiao, Z. Jiao, T. Yang, X. Dai, W. Xu, J. D. Tan, G. Cui, H. Su, W. Fang, J. Wu, *Angew. Chem. Int. Ed.* **2019**, *58*, 12580. g) C. Liu, J. Xie, W. Wu, M. Wang, W. Chen, S. B. Idres, J. Rong, L.-W. Deng, S. A. Khan, J. Wu, *Nat. Chem.* **2021**, accepted.

Symposium | Asian International Symposium | Asian International Symposium - Photochemistry -

[S09-1vn] Asian International Symposium - Photochemistry -

Chair, Symposium organizer:Osamu Ishitani, Mamoru Tobisu, Kei Ohkubo, Yasuharu Yoshimi, Tadashi Mori
Fri. Mar 19, 2021 4:10 PM - 5:30 PM Webiner 9 (Online Meeting)

[S09-1vn-01] carbazole-based photocatalysts bearing high reducing ability

○Ryosuke Matsubara[1] （1. Kobe University）

4:10 PM - 4:30 PM

[S09-1vn-02] Photoinduced electron transfer-promoted decarboxylative radical addition to dehydroamino acid

○Mugen Yamawaki[1], Akiko Asano[2], Taisei Kawabata[1], Kosei Yamamoto[1], Yasuharu Yoshimi[2]
（1. National Institute of Technology, Fukui College, 2. University of Fukui）

4:30 PM - 4:50 PM

[S09-1vn-03] The Selective Functionalizations of C– H bond via LMCT Catalysis

○Zhiwei Zuo[1] （1. Shanghai Institute of Organic Chemistry, CAS）

4:50 PM - 5:20 PM

Development of photochemical reactions using carbazole architecture

(*Graduate School of Science, Kobe University*) ○Ryosuke Matsubara
Keywords: Carbazole; Photoreaction; Photocatalyst; Radical; Carbon dioxide

Carbazole is a nitrogen-containing aromatic. While a parent carbazole absorbs UVA region of light, the absorption of modified carbazoles can reach longer wavelength; so carbazole is an important molecular fragment utilized widely in the optoelectronic material fields such as organic EL and OLED. In organic synthesis the carbazole architecture has also been used as a central motif in organic photocatalyst. Compared to the general transition metal-based photocatalysts, organic photocatalysts have some merits: e.g. they are less expensive and their molecular modification is relatively easy; thus, the development of capable organic photocatalysts is sought for.

Recently our group has been focusing on reductive photoreactions with carbazole-based photocatalysts by exploiting carbazole's high electron-donating ability at the excited state.[1-5] In this talk are reported the recent results in our laboratory.

1) Photochemical generation of carbon radicals via the scission of strong C–X bonds

1-1. Photocatalyzed reduction of C-I and C-Br bonds[2]

Carbon radicals are short-lived reactive species that can participate in the formation and cleavage of various bonds. Therefore, their formation and utilization in a controlled manner have been an important research topic in organic chemistry. C–X (X = Cl, Br, I) bonds are homolytically cleaved upon photoirradiation to afford the carbon radicals, but for this event short wavelength light is required. On the other hand, the carbon radical generation from the C–X bonds via photoinduced single electron transfer is also viable based on the high electron accepting capability of the C–X functionality. In this chemistry photocatalysts, represented by transition metal-centered polypyridyl complexes and π-extended organic molecules, play an important role. The literature survey found very few examples of photocatalytic radical generation from unactivated C–Br bonds, let alone C–Cl and C–F bonds, in contrast to several successful examples for the scission of C–I and activated C–Br bonds adjacent to the electron withdrawing groups.

We have developed carbazole derivative **2** as a photocatalyst. This molecule catalyzed selective reduction of iodoalkanes and unactivated bromoalkanes (Figure 1). The rational mechanisms for this catalytic activity will be discussed.

1-2. Photocatalyzed reduction of C-Cl and C-F bonds[3]

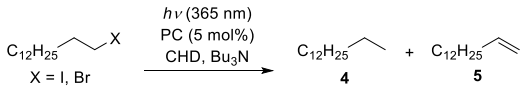
Even with carbazole **2** the electron transfer-based photochemical reduction of unactivated C–Cl and C–F bonds could not be achieved. Further studies revealed that carbazole **6** bearing more electron donating substituents is capable to reduce those unactivated C–X bonds (Figure

2). Moreover, carbazole **6** showed extended absorption bands; so the carbon radical generation has been made possible with visible light and sunlight.

2) CO_2 reduction using carbazole photocatalyst

The increasing atmospheric carbon dioxide (CO_2) concentration and fossil fuel depletion are urgent issues that humans must solve to continue living on this planet. Therefore, a technology that converts CO_2 into useful organic compounds (carbon fixation) with renewable energy is strongly desired. CO_2 is the most oxidized state of carbon; hence reduction process is necessary to enable the use of it as a carbon source. However, CO_2 is a chemical species that is extremely difficult to be reduced as it is in an extreme oxidation state of carbon, and this is the major factor that hinders the recycling of CO_2. Our recent endeavor to tackle this issue using a non-metal photocatalyst will be presented in this talk (Figure 3).

Figure 1



	X = I			X = Br
PC	yield of **4** (%)	yield of **5** (%)	selectivity	yield of **4** (%)
1	55	37	1.5	0
2	96	4	**24.0**	**52**
3	75	16	4.5	2

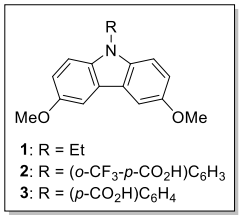


Figure 2

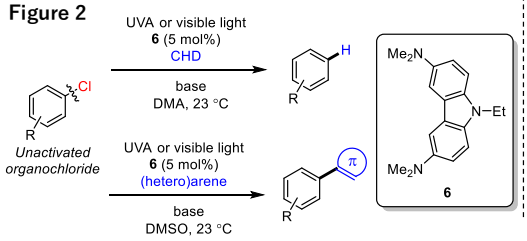
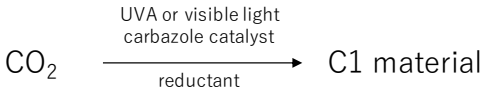


Figure 3



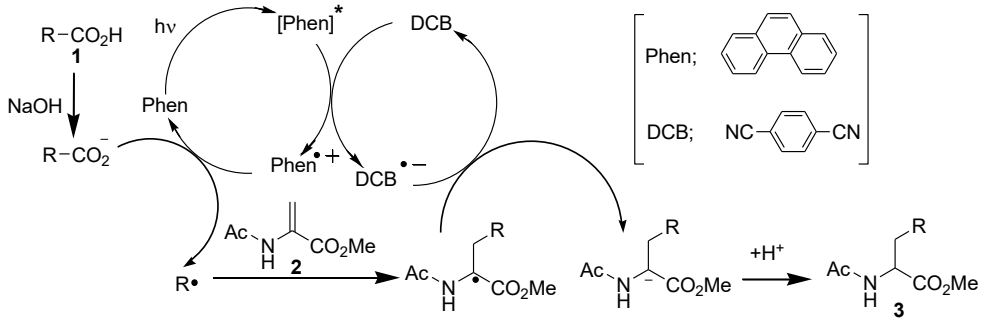
1) R. Matsubara, Y-S. Shin, T. Shimada, M. Hayashi, *Asian J. Org. Chem.* **2014**, *3*, 1054. 2) R. Matsubara, T. Shimada, Y. Kobori, T. Yabuta, T. Osakai, M. Hayashi, *Chem. Asian J.* **2016**, *11*, 2006. 3) R. Matsubara, T. Yabuta, U. Md Idros, M. Hayashi, F. Ema, Y. Kobori, K. Sakata, *J. Org. Chem.* **2018**, *83*, 9381. 4) R. Matsubara, U. Md Idros, T. Yabuta, H. Ma, M. Hayashi, K. Eda *ChemPhotoChem* **2018**, *2*, 1012. 5) T. Yabuta, M. Hayashi, R. Matsubara, *J. Org. Chem.* Accepted.

Photoinduced electron transfer-promoted decarboxylative radical addition to dehydroamino acid

(*National Institute of Technology, Fukui College*[1]*, University of Fukui*[2]) ○ Mugen Yamawaki[1], Akiko Asano[2], Taisei Kawabata[1], Kosei Yamamoto[1], Yasuharu Yoshimi[2]

Keywords: Photoinduced Electron Transfer; Organic Photocatalyst; Unnatural Amino Acid; Photoinduced Decarboxylation; Photoinduced Deboronation

Preparation of unnatural α-amino acids is one of the most important methods in organic synthesis. However, this method requires high reactive and expensive metals, high temperature, and strong acids and bases. Thus, the preparation of unique amino acids having sensitive functional groups under mild conditions is still desirable. Recently, we reported that generation of alkyl radicals via photoinduced decardoxylation of carboxylic acids **1** using organic photoredox catalysts such as phenanthrene (Phen) and 1,4-dicyanobenzene (DCB) (Scheme 1).[1] Photoinduced electron transfer (PET) between Phen and DCB generates a radical cation of Phen. The radical cation of Phen can oxidize carboxylate ions to form alkyl radicals via decarboxylation. Addition of the resulting radicals to electron-deficient alkenes proceeds efficiently to provide adducts in high yields. In this presentation, I will report the radical addition to dehydroamino acids **2** as the electron-deficient alkene via photoinduced decarboxylation of carboxylic acids **1** under mild conditions (Scheme 1). In addition to this, radical addition to **2** via photoinduced deboronation of arylboronic acids **3** will be described.



Scheme 1

Irradiation of aqueous acetonitrile solution (acetonitrile : water = 9 : 1) containing carboxylic acid **1**, dehydroamino acid **2**, Phen, DCB, and NaOH by a high-pressure mercury lamp under argon atmosphere afforded unnatural amino acid **3** as a racemic mixture (Table 1). A variety of carboxylic acids **1a-e** can be employed in this photoreaction to furnish adducts **3a-e,** and the yield of **3** is dependent on the used carboxylic acid **1**. Particularly, the use of primary carboxylic acids **1e** decreased the yield of **3e** due to the low rate of radical addition of the corresponding primary radical to **2**.

Next, synthesis of phenylalanine derivatives by photoinduced deboronation of arylboronic acid **4** with **2** was examined. As previously reported, the radical addition of aryl radicals via

deboronation of **4** to electron-deficient alkenes such as acrylonitrile led to the moderate yield of adducts.[2] Even in low yields, photoreactions of boronic acids **4** and **2** afforded phenylalanine derivatives **3f-k** (Table 1). Use of electron-rich arylboronic acids **4f-k** furnished phenylalanine derivatives **3f-k**. Thus, the photoinduced decarboxylation and deboronation of **1** and **4** with **2** was proven to be useful to prepare unique α-amino acids under mild conditions.

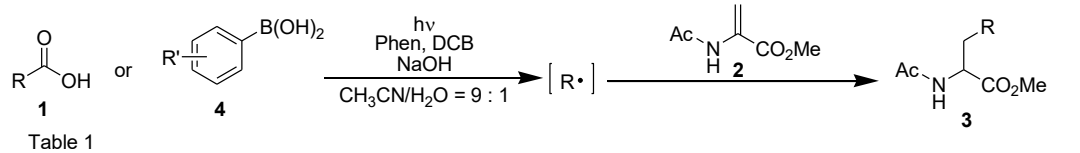
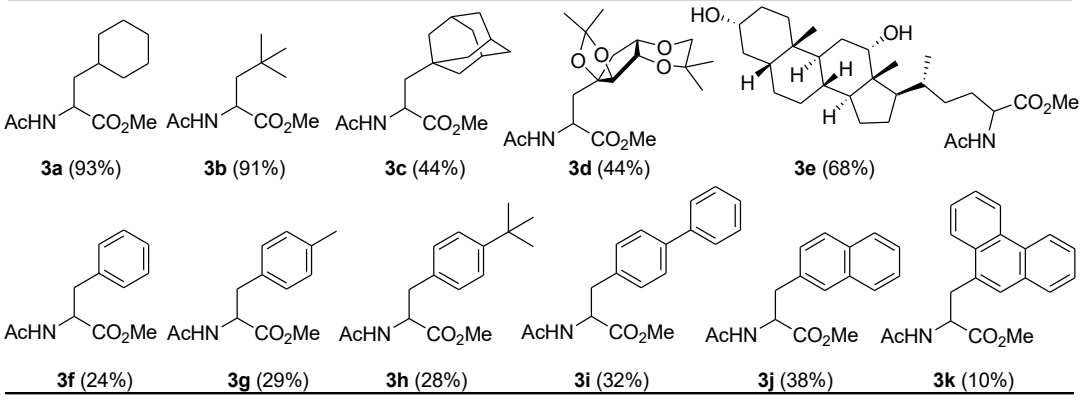
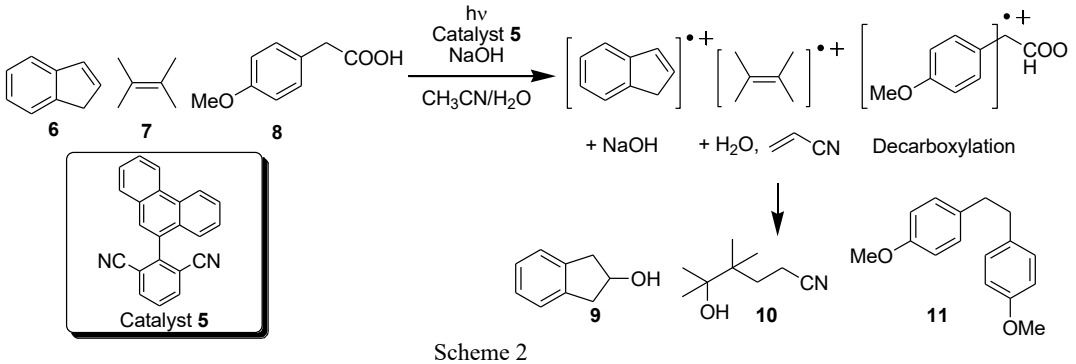


Table 1



Photoreaction of **1** and **4** using Phen-DCB direct linking catalyst **5** was examined for the preparation of **3**, but decarboxylation of **1** such as cyclohexanecarboxylic acid **1a** was unsuccessful and the starting carboxylic acid was almost recovered. On the other hand, photoreactions using of indene **6**, 2,3-dimetyl-2-butene **7**, and (4-methoxyphenyl)acetic acid **8** in the presence of **5** proceeded to provide **9**,**10** and **11** via PET, respectively (Scheme 2). [3]



Scheme 2

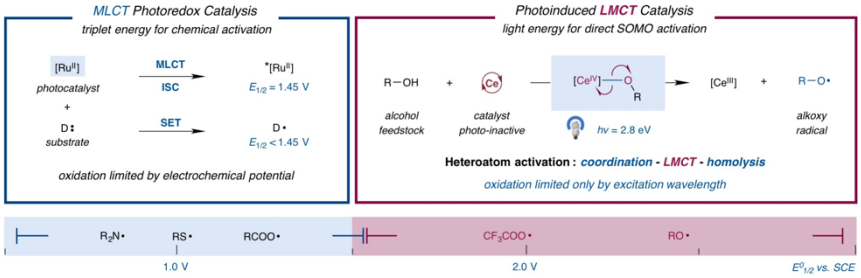
1) Y. Yoshimi, *J. Photochem. Photobio. A.* **2017**, *342*, 116–130.
2) Y. Iwata, Y. Tanaka, S. Kubosaki, T. Morita, Y. Yoshimi, *Chem. Commun*., **2018**, *54,* 1257.
3) M. Yamawaki, A. Asano, T. Furutani, Y Izumi, Y. Tanaka, K. Osaka, T. Morita, Y. Yoshimi, *Molecules*, **2020**, *24*, 4453.

The Selective Functionalizations of C–H bond via LMCT Catalysis

Zhiwei Zuo [a,*]

[a] *Shanghai Institute of Organic Chemistry, CAS*
**zuozhw@sioc.ac.cn*

Over the past decade, photoredox catalysis has emerged as a powerful tool for the construction of molecular complexity, most prominently with the generation of high-energy radicals as an enabling platform. In contrast to the commonly used metal-to-ligand charge-transfer (MLCT) which converts light energy to triplet energy for subsequent single electron transfer activation processes, ligand-to-metal charge transfer (LMCT) results in the direct single-electron oxidation of the transiently coordinated functionalities upon irradiation, producing an organic radical species in a straightforward and selective fashion.[1] Through a sequential coordination-LMCT excitation-homolysis mode, we have demonstrated that this LMCT protocol could enable the straightforward and efficient generation of alkoxy radicals from alcohols.[2-3] Taking advantage of this operationally-simple platform, we recently accomplished the selective C(sp3)–H functionalizations of alcohol feedstocks and gaseous alkanes under mild reaction conditions.[3-4]



References

1. Balzani, V.; Ceroni, P.; Juris, A., *Photochemistry and photophysics: concepts, research, applications*. John Wiley & Sons: 2014.
2. Guo, J. J.; Hu, A.; Chen, Y; Sun, J.; Tang, H.; Zuo, Z., Photocatalytic C-C Bond Cleavage and Amination of Cycloalkanols by Cerium(III) Chloride Complex. *Angew. Chem. Int. Ed.* **2016,** *55*, 15319.
3. Hu, A.; Guo, J. J.; Pan, H.; Tang, H.; Gao, Z.; Zuo, Z., delta-Selective Functionalization of Alkanols Enabled by Visible-Light-Induced Ligand-to-Metal Charge Transfer. *J. Am. Chem. Soc.* **2018,** *140*, 1612.
4. Hu, A.; Guo, J. J.; Pan, H.; Zuo, Z., Selective functionalization of methane, ethane, and higher alkanes by cerium photocatalysis. *Science* **2018,** *361*, 668.

Symposium | Asian International Symposium | Asian International Symposium - Electrochemistry -

[S09-1am] Asian International Symposium - Electrochemistry -

Chair, Symposium organizer:Toru Amaya, Koichi Mitsudo, Toshiki Nokami, Seiji Suga
Fri. Mar 19, 2021 9:00 AM - 11:40 AM Webiner 9 (Online Meeting)

[S09-1am-01] New vistas in C-H functionalization

○Yu Kawamata[1] (1. Scripps Research)

9:05 AM - 9:25 AM

[S09-1am-02] Organotransition Metal-Catalyzed Electrochemistry

○Tiansheng Mei[1] (1. Shanghai Institute of Organic Chemistry, CAS, China)

9:25 AM - 9:45 AM

[S09-1am-03] Amping Up Organic Synthesis with Electricity: An Electrocatalytic Approach to Reaction Discovery

○Song Lin[1] (1. Cornell University)

9:45 AM - 10:15 AM

[S09-1am-04] Porous Organic Polymer and its Composites for Electrocatalysis

○Kathiresan Murugavel[1] (1. CSIR-Central Electrochemical Research Institute)

10:25 AM - 10:45 AM

[S09-1am-05] Bipolar Electrochemistry for Material Synthesis in Synergy with Electrophoresis

○Shinsuke Inagi[1,2] (1. Tokyo Institute of Technology, 2. JST PRESTO)

10:45 AM - 11:05 AM

[S09-1am-06] Enantioselective Synthesis and Separation with Chiral-Encoded Metal Surfaces

○Chularat Wattanakit[1], Sunpet Assavapanumat[1], Sopon Butcha[1], Veronique Lapeyre[2], Bhavana Gupta[2], Adeline Perro[2], Neso Sojic[2], Alexander Kuhn[2] (1. Vidyasirimedhi Institute of Science and Technology, 2. Univ. de Bordeaux)

11:05 AM - 11:35 AM

The site-specific oxidation of strong C(sp^3)-H bonds is of uncontested utility in organic synthesis. In both academic and industrial circles there is a growing demand for such a transformation since it allows simplifying access to metabolites, late-stage diversification of lead compounds and truncating retrosynthetic plans. One main drawback of chemical reagents used in current C(sp^3)-H oxidations is the lack of diversity with regards to structure and reactivity that prevent a combinatorial approach for rapid screening to be employed. In that regard, directed evolution still holds the greatest promise for achieving complex C–H oxidations in a variety of complex settings. Herein we present a rationally designed platform that provides a step towards this challenge using *N*-ammonium ylides as electrochemically driven oxidants for site-specific, chemoselective C(sp^3)–H oxidation. By taking a first-principles approach guided by computation, these new mediators were identified and rapidly expanded into a library using ubiquitous building blocks and trivial synthesis techniques. The ylide-based approach to C–H oxidation exhibits tunable selectivity that is often exclusive to this class of oxidants and can be applied to real world problems in the agricultural and pharmaceutical sectors.

Organotransition Metal-Catalyzed Electrochemistry

Tian-Sheng Mei*

State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Road, Shanghai 200032

Abstract: Since transition metals have or are easy to form partly full electron-filled d orbitals, they provide unique chemical bond activation capabilities and many elementary reactions such as oxidative addition and reductive elimination. Generally, the low valence state of metals (e.g. Pd^0, Ni^0) is good for oxidation addition, the middle valence state is good for C–H activation (e.g. Pd^{II}), while the high valence state (e.g. Pd^{IV}, Ni^{III}) is good for reductive elimination. Therefore, metal-catalyzed reactions usually require chemical oxidation and reduction reagents to realize the valence control of metal species. However, chemical redox reagents generally have the following shortcomings: 1) fixed redox strength; 2) easy to interfere with the reaction; 3) easy to produce reagent by-products; 4) reagent purity, stability, solubility, and other issues. Electrochemistry has the characteristics of adjustable and controllable current and potential, so it is easy to control the different valence states of metals. It can also overcome other shortcomings of the above chemical redox reagents. In the past few years, our research group has carried out a series of work around electrochemically regulated metal-catalyzed reactions, including anodic oxidation to obtain high valence metal to promote reductive elimination or middle valence metal to achieve C–H activation and cathode reduction to obtain low valence metal to promote oxidative addition. This talk mainly focuses on metal-catalyzed C-H functionalization via anodic oxidation and reductive couplings via cathodic reduction.

Amping Up Organic Synthesis with Electrochemistry

Song Lin, Cornell University

Owing to its many distinct characteristics, electrochemistry represents an attractive approach to discovering new reactions and meeting the prevailing trends in organic synthesis. In particular, electrocatalysis—a process that integrates electrochemistry and small-molecule catalysis—has the potential to substantially improve the scope of synthetic electrochemistry and provide a wide range of useful transformations. Despite its attractive attributes and extensive applications in energy-related fields, electrocatalysis has been used only sparingly in synthetic organic chemistry. Thus, there exists a clear impetus for inventing new catalytic strategies to improve the scope of synthetic electrochemistry and provide new platforms for reaction discovery and synthetic innovations. Toward this end, we developed a new catalytic approach that combines electrochemistry and redox-metal catalysis for the functionalization of alkenes to access a diverse array of vicinally functionalized structures. This talk details our design principle underpinning the development of electrocatalytic alkene difunctionalization and hydrofunctionalization with a particular emphasis on enantioselective electrocatalysis. In addition, we harnessed the power of electrochemistry to discover a suite of radical silylation and alkylation reactions under strongly reducing potentials via the activation of chlorosilanes and alkyl halides. Finally, our recent forays into electrophotocatalysis will be discussed, in which we harness the power of both electricity and light to access catalytic species with exceptionally high oxidizing or reducing potentials.

Porous Organic Polymer and its Composites for Electrocatalysis

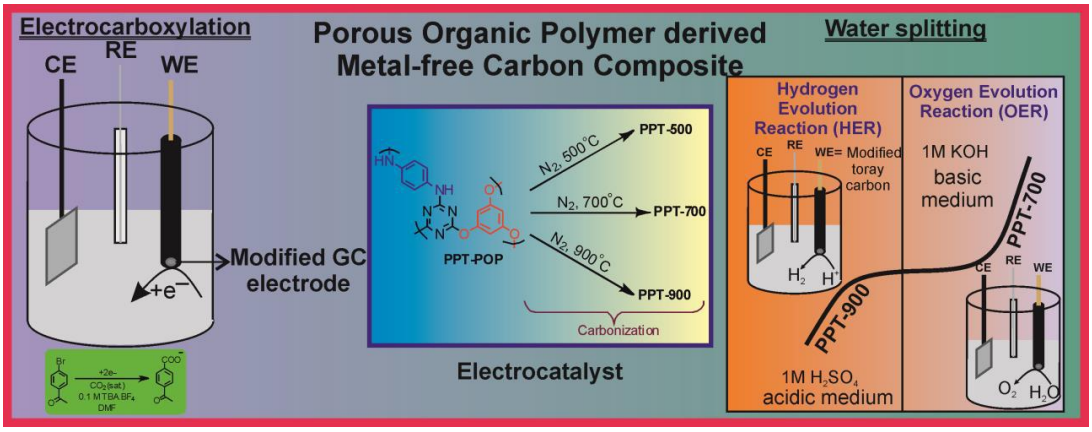
(*Electro Organic and Materials Electrochemistry Division, CSIR-Central Electrochemical Research Institute, India*) ○Kathiresan Murugavel

Keywords: Porous Organic Polymers; Electrocatalysis; Water Splitting; Covalent Triazine Frameworks; Electrochemistry

Porous organic polymers (POPs) can be conveniently engineered and produced at the molecular level, known for their high surface area and ample porosity. The POPs have confined molecular spaces for photons, excitons, electrons and holes to interact, thereby providing great catalysis ability. Porous organic polymers can be further classified based on the monomeric repeating units such as triazine based POPs, etc. Among various types, triazine based porous organic polymers exhibit excellent chemical and thermal stability due to which they find numerous applications in chemical catalysis and electrocatalysis. Electrocatalysis highly relies on the ionic/electrical conductivity of a material and in this regard, bare POP sometimes lacks such essential characteristics. There are numerous strategies followed to improve the conductivity of POPs and they include composite formation, metal doping, carbonization, etc. Although these methods are very convenient, carbonization is usually adopted over composite formation. Latest studies have further shown that carbonization of doped porous organic polymers (POPs) with heteroatoms is an effective strategy to develop highly efficient 'N' and other heteroatom doped electrocatalysts. Simple carbonization of triazine/amine porous organic polymers yield N-doped amorphous carbon, which shows excellent electrocatalytic properties towards electrocarboxylation, hydrogen and oxygen evolution reactions. In addition, metal ions can be anchored onto the triazine/amine based POP via co-ordination or metal nanoparticles can also be anchored over the POP substrate. Carbonization of such derivatives typically yields metal oxide decorated N-doped porous carbon, and in most cases these materials [combining the best activity of both (metal oxide and porous carbon)] show better catalytic effect than their parent material.

Electrocatalytic activities of polymeric material towards water-splitting reactions, and electrocarboxylation is important as they form basis for fuel-cell applications and CO_2 utilisation respectively. Especially the organic-inorganic hybrid (metal anchored POP) with excellent long-term stability (acidic as well as basic conditions) and on par performance with that of benchmark noble metal water-splitting catalysts grasps industrial importance when it comes to large scale fuel cell applications. On the other hand, conversion of CO_2 to useful products is an efficient way to mitigate greenhouse gas (global warming). In this regard, indirect electrochemical reduction of CO_2 to useful organic products offers excellent route for the synthesis of fine chemicals and pharmaceutically important intermediates. In the case of indirect electrochemical reduction, the first one electron reduction is carried out over an organic substrate such as alkyl/aryl halides, aldehydes or ketones, alkenes.

Reduction of these substrates generates a radical species which is then coupled to CO_2 and subsequent one electron reduction yields corresponding carboxylate anion. Acidic work-up of this then yields the desired product. In this talk, we will focus on the various methods of preparation of POP based electrocatalysts, and further focus will be on their application towards water-splitting applications and CO_2 utilization. Although POP based catalysts exhibit excellent catalytic activities towards conversion of CO_2 to value added products, there are certain bottlenecks that hamper their efficiency such as moisture content, use of sacrificial anodes, etc. The talk will also focus on such bottlenecks.



Bipolar Electrochemistry for Material Synthesis in Synergy with Electrophoresis

([1]*School of Materials and Chemical Technology, Tokyo Institute of Technology,* [2]*JST PRESTO*) ○Shinsuke Inagi[1,2]

Keywords: Bipolar Electrochemistry; Electropolymerization; Electrophoresis; Templated Electrolysis; Conducting Polymer

Bipolar electrochemistry, which refers to an electrochemical system at a wireless electrode (bipolar electrode, BPE) driven under an applied electric field, has been recognized as not only a simple subset of conventional electrosynthetic systems but a reaction system with a highly unique nature.[1–3] One notable feature is the presence of the electrophoretic effect due to the low electrolyte concentration. The electrophoresis enhances the mass transfer of ionic species in a specific direction, thus enabling the efficient construction of anisotropic materials.[4] For example, in the AC-bipolar electropolymerization of 3,4-ethylenedioxythiophene monomer, the corresponding conducting polymer microfibers were obtained at the terminals of BPEs, where the generated cationic oligomers/polymers migrated in the direction of the electric field, as demonstrated in our previous studies.[5–7] In this presentation, highly efficient templated electropolymerization of ionic monomers to give one-dimensional (1D) nanostructures is described.

We recently reported that electrophoresis is a promising tool for effective migration of ionic monomers into a porous template fixed on an electrode in the bipolar electrochemical setup.[8] Low concentration of supporting electrolytes is a key condition to generate an electric field, that drives BPEs and induces electrophoretic effect as well. In the electrochemical setup shown in Figure 1a,b, an anodic aluminum oxide (AAO) membrane-modified ITO was used as a BPE anode and a bare ITO was used as a BPE cathode, both of which are connected through an ammeter. This split-BPE was immersed into an electrolytic solution composed of boron trifluoride diethyl ether complex (BF_3-OEt) and potassium 3-thiophenetrifluoroborate as a monomer. Application of a certain voltage between feeder electrodes generated an electric field in the solution to drive the split-BPE for electropolymerization of the thiophene monomer on the AAO-modified BPE anode. At the same time, the negatively charged monomer migrated efficiently into the pores of the AAO by the electrophoretic effect. Consequently, highly dense and robust nanowires of the polythiophene derivative was obtained (Figure 1c) compared to those prepared by the conventional electrode system. In a similar way, we also conducted the cathodic electropolymerization of a ruthenium complex bearing vinyl groups as a positively charged monomer in the electrochemical setup with the opposite polarity (Figure 1d). Efficient electroplating of cobalt and platinum was demonstrated in the similar electrochemical cell to fabricate the corresponding robust metal nanorods.[9]

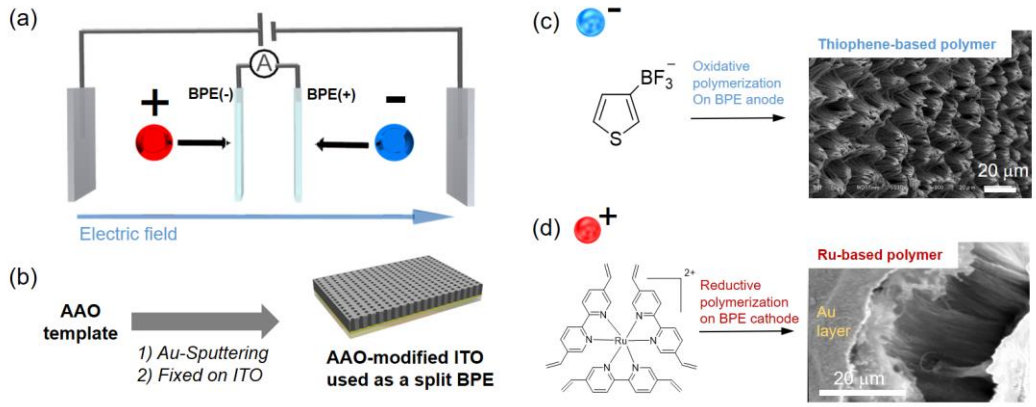


Figure 1. Electrophoresis-assisted formation of 1D materials by DC-bipolar electrolysis using AAO templates: (a) conceptual illustration; (b) preparation of an AAO-modified ITO electrode, which was used as a BPE in the split-BPE configuration; (c) oxidative polymerization of a thiophene monomer; (d) reductive polymerization of a Ru-containing vinyl monomer.

1) S. E. Fosdick, K. N. Knust, K. Scida, R. M. Crooks, *Angew. Chem. Int. Ed.* **2013**, *52*, 10438.
2) G. Loget, D. Zigah, L. Bouffier, N. Sojic, A. Kuhn, *Acc. Chem. Res.* **2013**, *46*, 2513.
3) N. Shida, Y. Zhou and S. Inagi, *Acc. Chem. Res.* **2019**, *52*, 2598.
4) N. Shida, S. Inagi, *Chem. Commun.* **2020**, *56*, 14327.
5) Y. Koizumi, N. Shida, M. Ohira, H. Nishiyama, I. Tomita, S. Inagi, *Nat. Commun.* **2016**, *7*, 10404.
6) T. Watanabe, M. Ohira, Y. Koizumi, H. Nishiyama, I. Tomita, S. Inagi, *ACS Macro Lett.* **2018**, *7*, 551.
7) Y. Zhou, N. Shida, Y. Koizumi, T. Watanabe, H. Nishiyama, I. Tomita, S. Inagi, *J. Mater. Chem. C* **2019**, *7*, 14745.
8) Y. Zhou, N. Shida, Y. Koizumi, K. Endo, I. Tomita, S. Inagi, *Macromolecules* **2020**, *53*, 8123.
9) Y. Koizumi, H. Nishiyama, I. Tomita, S. Inagi, *Chem. Commun.* **2018**, *54*, 10475.

Enantioselective Synthesis and Separation with Chiral-Encoded Metal Surfaces

([1]*Vidyasirimedhi Institute of Science and Technology, Rayong 21210, Thailand,* [2]*Univ. de Bordeaux, CNRS, ISM, UMR 5255, Pessac, France.*)
Chularat Wattanakit,[1] Sunpet Assavapanumat,[1,2] Sopon Butcha,[1] Veronique Lapeyre,[2] Bhavana Gupta,[2], Adeline Perro[2], Neso Sojic,[2] Alexander Kuhn[2]

Keywords: *Asymmetric synthesis*; *Chiral-Encoded Metals; Chiral separation; Mesoporous metals; Chiral platinum, Chiral nickel*

Enantioselective synthesis and separation of chiral compounds are of crucial importance for many potential applications ranging from sensing to catalysis. Recently, we have successfully elaborated chiral imprinted mesoporous platinum by electrochemical reduction of platinum salts in the simultaneous presence of a liquid crystal phase of nonionic surfactants and various chiral template molecules, such as enantiomers of 3,4-dihydroxyphenylalanine (DOPA), mandelic acid and phenylethanol. The chiral encoded mesoporous platinum perfectly retains the chiral information even after removal of the template and such a nanostructured platinum is able to break the symmetry during the electrosynthesis of chiral molecules such as mandelic acid and phenylethanol. By optimizing the electrochemical synthesis parameters, it is possible to achieve very high enantiomeric excess (>90 %) for the asymmetric synthesis of chiral compounds. In addition to imprinted platinum, we demonstrated also the synthesis of mesoporous chiral imprinted nickel as an alternative cheap and earth-abundant metal. Interestingly, it can also lead to very high enantiomeric excess (>80 %) during chiral electrosynthesis of phenylethanol. Apart from asymmetric synthesis, chiral separation can be achieved using also such imprinted mesoporous metals as a stationary phase in a microfluidic channel. By fine-tuning the electrostatic interactions between the encoded surfaces and the corresponding chiral molecules via applying an electric field, it is possible to achieve complete separation of chiral compounds. Therefore, these designer surfaces open new promising horizons in various fields of electrochemistry, ranging from electroseparation to electrosynthesis.

References

1) C. Wattanakit, T. Yutthalekha, S. Assavapanumat, V. Lapeyre, A. Kuhn, *Nat. Comm.* **2017**, 8: 2087.
2) S. Assavapanumat, T. Yutthalekha, P. Garrigue, B. Goudeau, V. Lapeyre, A. Perro, N. Sojic, C. Wattanakit, A. Kuhn, *Angew. Chem. Int. Ed.* **2019**, *58*, 3471–3475.
3) S. Assavapanumat, B. Gupta, G. Salinas, B. Goudeau, C. Wattanakit, A. Kuhn, *Chem. Commun*. **2019**, *55*, 10956-10959.
4) S. Assavapanumat, M. Ketkaew, A. Kuhn, C. Wattanakit, *J. Am. Chem. Soc.* **2019**, *141*, 47, 18870-18876.
5) C. Wattanakit, A. Kuhn, *Chem. Eur. J.* **2019**, DOI:10.1002/chem.201904835.

Symposium | Special Program | Frontiers of Molecular Science Explored by Molecular Electron Microscopy

[S08-1pm] Frontiers of Molecular Science Explored by Molecular Electron Microscopy

Chair, Symposium organizer:Koji Harano, Takayuki Nakamuro
Fri. Mar 19, 2021 1:00 PM - 3:40 PM Webiner 8 (Online Meeting)

[S08-1pm-01] MicroED: Conception, practice and future opportunities

○Tamir Gonen[1] （1. UCLA/HHMI）

1:05 PM - 1:35 PM

[S08-1pm-02] Dynamic molecular electron microscopy: An emerging tool for chemists

○Eiichi Nakamura[1] （1. The University of Tokyo）

1:35 PM - 2:05 PM

[S08-1pm-03] Pushing the performance limits of cryo-EM for membrane receptors

○Radostin Danev[1], Matthew Belousoff[2], Yi-Lynn Liang[2], Xin Zhang[2], Denise Wootten[2], Patrick M. Sexton[2] （1. The University of Tokyo, 2. Monash Institute of Pharmaceutical Sciences, Monash University）

2:05 PM - 2:35 PM

[S08-1pm-04] Understanding the Chemistry of electron beam-induced transformations on the molecular level

○Dominik Lungerich[1] （1. Institute for Basic Science (IBS), Center for Nanomedicine, Yonsei University）

2:35 PM - 3:05 PM

[S08-1pm-05] Atomic-resolution Imaging of Sensitive Materials Using Ultralow-dose Transmission Electron Microscopy

○Yu Han[1] （1. King Abdullah University of Science and Technology）

3:05 PM - 3:35 PM

MicroED: conception, practice and future opportunities

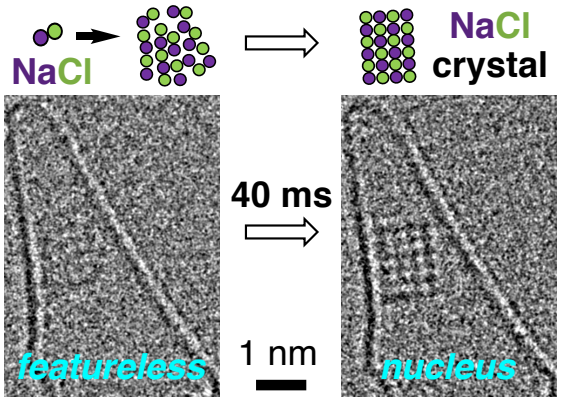
([1]*Howard Hughes Medical Institute, Departments of Biological Chemistry and Physiology, University of California, Los Angeles, Los Angeles CA USA 90095)* ○Tamir Gonen,[1]
Keywords: CryoEM, MicroED, crystallography, membrane protein

My laboratory studies the structures of membrane proteins that are important in maintaining homeostasis in the brain. Understanding structure (and hence function) requires scientists to build an atomic resolution map of every atom in the protein of interest, that is, an atomic structural model of the protein of interest captured in various functional states. In 2013 we unveiled the method Microcrystal Electron Diffraction (MicroED) and demonstrated that it is feasible to determine high-resolution protein structures by electron crystallography of three-dimensional crystals in an electron cryo-microscope (CryoEM). The CryoEM is used in diffraction mode for structural analysis of proteins of interest using vanishingly small crystals. The crystals are often a billion times smaller in volume than what is normally used for other structural biology methods like x-ray crystallography. In this seminar I will describe the basics of this method, from concept to data collection, analysis and structure determination, and illustrate how samples that were previously unattainable can now be studied by MicroED. I will conclude by highlighting how this new method is helping us understand major brain diseases like Parkinson's disease; helping us discover and design new drugs; shedding new light on chemical synthesis and small molecule chemistry; and showing us unprecedented level of details with important membrane proteins such as ion channels and G-protein coupled receptors (GPCRs).

Dynamic molecular electron microscopy: An emerging tool for chemists

(*Department of Chemistry, The University of Tokyo*) ○Eiichi Nakamura
Keywords: Molecular Electron Microscopy; SMART-EM; Single Molecule Imaging, Molecular Dynamics; Chemical Reactions

Recent technological innovations in electron microscopy, such as aberration correctors, high-speed imaging cameras, and continuous sample rotation, have ushered in an era in which the behavior of individual molecules can be analyzed. In addition to the visual impact of the images obtained, electron microscopy has become a tool for clarifying the correlation between molecular structure and function, as well as dynamics and function in materials science and biological science. In this lecture, I will report on the new paradigms of molecular electron microscopy opened up by single-molecule atomic-resolution real-time electron microscopy. Examples will include single-molecule thermodynamics and kinetics based on ultra-fast imaging of individual molecules and reaction events, in situ structural and statistical analysis of crystal growth, and the mechanism of organic crystal degradation in electron diffraction that has long confused people. We would like to reach a chemical understanding by answering academic questions that have been obscured so far, such as what we actually see and the essential meaning of what we see in electron microscopy.



Selected References

(1) M. Koshino, T. Tanaka, N. Solin, K. Suenaga, H. Isobe, and E. Nakamura, *Science*, **316**, 853 (2007).
(2) E. Nakamura, *Acc. Chem. Res.*, **50**, 1281–1292 (2017).
(3) S. Okada, S. Kowashi, L. Schweighauser, K. Yamanouchi, K. Harano, E. Nakamura, *J. Am. Chem. Soc.*, **139**, 18281-18287 (2017).
(4) E. Nakamura, K. Harano, *Proc. Jpn Acad., Ser. B,* **94,** 428–440 (2018).
(5) J. Xing, L. Schweighauser, S. Okada, K. Harano, E. Nakamura, *Nat. Commun.*, **10**, 3608 (2019).

(6) H. Hamada, T. Nakamuro, K. Yamashita, H. Yanagisawa, O. Nureki, M. Kikkawa, K. Harano, R. Shang, E. Nakamura, *Bull. Chem. Soc. Jpn.*, **93**, 776–782 (2020).
(7) T. Shimizu, D. Lungerich, J. Stuckner, M. Murayama, K. Harano, E. Nakamura, *Bull. Chem. Soc. Jpn.*,**93**, 1079-1085 (2020).
(8) H. Lu, T. Nakamuro, K. Yamashita, H. Yanagisawa, O. Nureki, M. Kikkawa, H. Gao, J. Tian, R. Shang, E. Nakamura, *J. Am. Chem. Soc.*, **142**, 18990–18996 (2020).
(9) T. Nakamuro, M. Sakakibara, H. Nada, K. Harano, E. Nakamura, *J. Am. Chem. Soc*. doi: 10.1021/jacs.0c12100.

Pushing the performance limits of cryo-EM for membrane receptors

([1]*Graduate School of Medicine, University of Tokyo*, [2]*Drug Discovery Biology, Monash Institute of Pharmaceutical Sciences, Monash University,* [3]*currently at Confo Therapeutics*)
○Radostin Danev,[1] Matthew Belousoff,[2] Yi-Lynn Liang,[2,3] Xin Zhang,[2] Denise Wootten,[2] Patrick M. Sexton,[2]
Keywords: GPCR; cryo-EM; high resolution; membrane protein

Electron cryo-microscopy (cryo-EM) saw great advances in recent years. It became a method of choice for many researchers working on high-resolution structural studies of proteins and complexes. There are a few remaining challenges,[1] such as sample preparation, but overall cryo-EM has already entered the mainstream and is generating a constant flow of outstanding results.

In our projects, we use cryo-EM to investigate the structure-function relationships of G-protein-coupled receptors (GPCRs). Their relatively small size and lack of symmetry make them a challenging target for cryo-EM. To overcome the potential performance limitations, in our earlier work we used phase plates that greatly increase the contrast of images. Our recent results, however, show that phase plates are not necessary for obtaining high-resolution structures and only complicate the experiment. For the last two years, we have been collecting data exclusively without phase plates and were able to obtain multiple GPCR structures at better than 2.5 Å resolution (Figure 1). Furthermore, we observe protein dynamics that exemplify thermal motions as the main performance-limiting factor in present cryo-EM studies of GPCRs.

There is still room for improvement of the technique and many parameters can be optimized further. Recently, we quantified the effects of energy filtering, phase plates, objective lens aperture and defocus. Overall, the Volta phase plate does not provide practical benefits and noticeably reduces the achievable resolution. Zero-loss energy filtering and lower defocus have a positive effect on the performance, while the aperture does not seem to make a difference (Figure 2).[2]

In my talk, I will present several recent GPCR structures and discuss the practical aspects of present-day cryo-EM of membrane proteins. We currently use a multi-shot beam-image shift automated data acquisition approach that allows collection of more than 7000 cryo-EM moves per day. This allows the determination of the 3D structure of a properly optimized sample with just one day of data collection. The current bottleneck in terms of project time is data processing. It usually takes one to several weeks to process the data for each sample. Further developments in image processing methods based on deep learning and floating-point calculations code optimization would hopefully alleviate this issue.

1) R. Danev, H. Yanagisawa, M. Kikkawa, *Trends Biochem Sci.* **2019**, *44*, 837. 2) R. Danev, M. Belousoff, Y.-L. Liang, X. Zhang, D. Wootten, P.-M. Sexton, *bioRxiv* **2020**, 2020.08.21.260851.

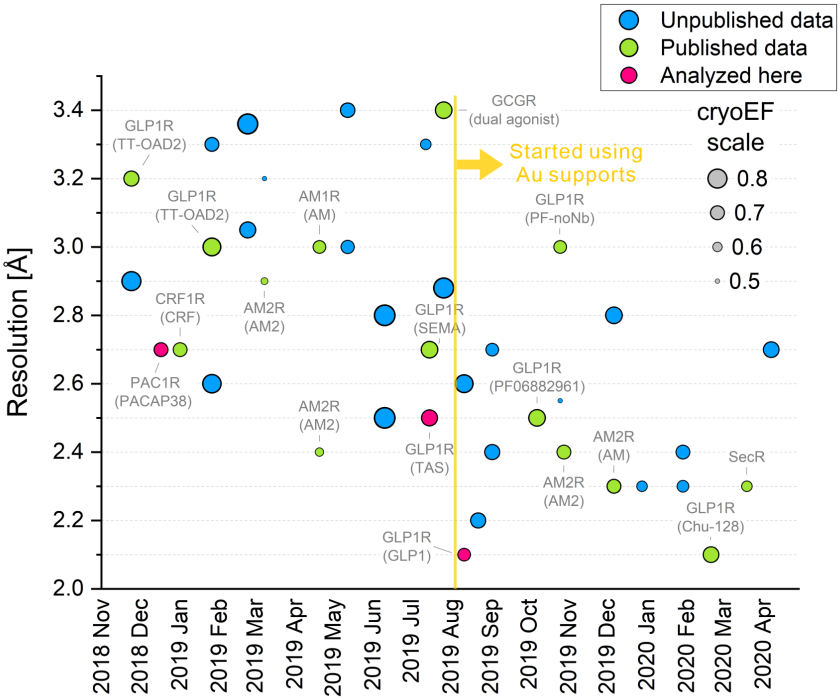


Figure 1. History of our cryo-EM GPCR reconstructions.
Over the year and a half period shown in the plot, there is a general trend towards better resolution with a significant improvement in August 2019, when the sample supports were switched from holey carbon films to gold foil grids.

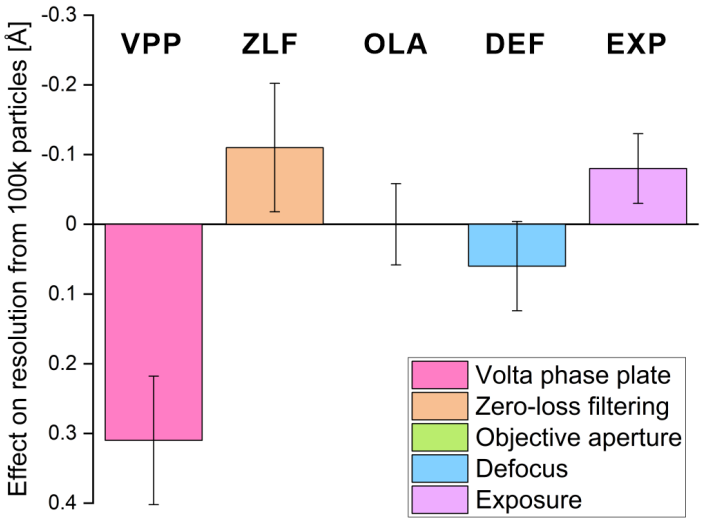


Figure 2. Effect of each experimental parameter on the cryo-EM performance for GPCRs.
VPP: Volta phase plate; ZLF: Zero-loss energy filtering; OLA: Objective lens aperture; DEF: defocus magnitude; EXP: Total electron exposure.

Understanding the Chemistry of electron beam-induced transformations on the molecular level

Dominik Lungerich[1*]

1) Center for Nanomedicine, Institute for Basic Science (IBS), IBS Hall, 50 Yonsei-ro, Seodaemun-gu, 03722, Seoul, South Korea.

Dynamical processes at the nanoscale are difficult to investigate by state-of-the-art spectroscopic techniques, because they often rely on averaged datasets, or repeatable events. With aberration-corrected transmission electron microscopy, the resolution beyond the limit of light scattering was reached, which allows nowadays to study dynamic events microscopically at the nanoscale inn real-time. Herein described as single-molecule atomic-resolution real-time electron microscopy (SMART-EM), we aim to understand quantum chemical processes of single molecules and atoms. By means of statistical analysis of multiple events, or single-object statistical analysis, SMART-EM allows for the study of otherwise unnoted processes on the atomic/molecular level. However, with the utilization of high-energy electron irradiation, it becomes important to fully understand what effects are to be expected at the molecular level, in order to interpret the dynamic processes correctly. This is not only important on the single-molecule level, which are studied in vacuo, but also for the in-situ study of nanomaterials investigated in liquid media.

C000128

Atomic-resolution Imaging of Sensitive Materials Using Ultralow-dose Transmission Electron Microscopy

Yu Han

King Abdullah University of Science and Technology (KAUST), Saudi Arabia
yu.han@kaust.edu.sa

High-resolution imaging of electron beam-sensitive crystalline materials, such as zeolites and metal-organic frameworks, is one of the most difficult applications of transmission electron microscopy (TEM). The challenges are manifold, including the acquisition of images with an extremely low beam dose, the time-constrained search for crystal zone axes, the precise alignment of successive images, and the accurate determination of the defocus value.

We reported that using a direct-detection electron-counting camera, it is possible to acquire useful high-resolution TEM images with electron dose as low as a few electrons per square angstrom to ensure that the intact structure was captured before damage occurred [1]. Later, we reported a suite of new methods that we recently developed to address the rest challenges mentioned above [2]. Our methods advance the HRTEM of extremely beam-sensitive materials from “occasionally possible” to “routine”. We demonstrate the effectiveness of our methodology by capturing atomic-resolution TEM images of several metal organic frameworks (MOFs) that are generally recognized as highly sensitive to electron beams. In the case of MOF UiO-66, individual metal atomic columns, various types of surface termination, and benzene rings in the organic linkers, are clearly identified. We also successfully apply our methods to other electron beam-sensitive materials, and achieve atomic-resolution TEM imaging of the organic-inorganic hybrid perovskite $CH_3NH_3PbBr_3$ for the first time [2]. More recently, we applied this new technology to prove the successful encapsulation of single molecule magnets in MOF NU-1000 [3], and to investigate the evolution and transformation of various defects in MOF UiO-66 [4], and to probe the subtle differences in the surface structure between various MOF MIL-101 samples [5].

In this presentation, I will also discuss iDPC-STEM as a powerful tool to probe guest molecules in sensitive porous material matrix, taking atomically dispersed Mo in zeolite ZSM-5 as an example [6]. Finally, I will introduce a new TEM specimen preparation technique, cryo-FIB, which is particularly useful for beam-sensitive materials [7].

[1] Y. Zhu, M. Pan, Y. Han et al., *Nature Materials*, 2017, 16, 532-536
[2] D. Zhang, Y. Han et al., *Science*, 2018, 359, 675-679
[3] M. Wriedt, Y. Han et al., *J. Am. Chem. Soc.*, 2019, 141, 2997-3005
[4] L, Liu, D. Zhang, Y. Han et al., *Nature Chemistry*, 2019, 11, 622-628
[5] X. Li, D. Zhang, Y. Han et al., *J. Am. Chem. Soc.*, 2019, 141, 12021-12028
[6] L, Liu, Y. Han et al, *Angew. Chem. Int. Ed.*, 2020, 132, 829-835
[7] N, Wei, D. Zhang, Y. Han et al., unpublished

Symposium | Special Program | Lesson from Nature – Koji Nakanishi Memorial Symposium-

[S08-1am] Lesson from Nature – Koji Nakanishi Memorial Symposium-

Chair, Symposium organizer:Kenji Monde, Jun Koshoubu, Nobuyuki Harada, Katsuhiro Konno, Keiko Shimamoto

Fri. Mar 19, 2021 9:00 AM - 11:40 AM Webiner 8 (Online Meeting)

[S08-1am-01] Shapes of acting biomolecules; Natural product chemistry visualizing functional structure

○Michio MURATA Murata[1] （1. Osaka University）

9:10 AM - 9:35 AM

[S08-1am-02] Chirality of Biomolecules -CD &VCD Exciton Chirality Method-

○Kenji Monde[1] （1. Hokkaido University）

9:35 AM - 10:00 AM

[S08-1am-03] Phytochemical natural products chemistry

○Minoru Ueda[1] （1. Tohoku University）

10:00 AM - 10:25 AM

[S08-1am-04] Sexual reproduction of a plant pathogen - exploring its molecular basis -

○Makoto Ojika[1] （1. Nagoya Univ.）

10:25 AM - 10:50 AM

[S08-1am-05] Chemistry of Receptor-Lipid Ligands for Understanding of Immune System

○Yukari Fujimoto[1] （1. Keio University）

10:50 AM - 11:15 AM

[S08-1am-06] Therapeutic In Vivo Synthetic Chemistry

○Katsunori Tanaka[1,2,3] （1. Tokyo Tech., 2. RIKEN, 3. Kazan Federal U.）

11:15 AM - 11:40 AM

1 SA-02
特別企画講演

生命分子の形と働き―構造決定後の天然物化学―

（阪大院理）○村田　道雄
Structures and functions of natural product-type biomolecules (*Graduate School of Science, Osaka University*) ○Michio Murata

The technology for determining the structure of low-molecular-weight organic compounds, including natural products, has advanced significantly, and many years have passed since it lost its importance as an academic research theme. Prof. Nakanishi's work on circular dichroism, nuclear Overhauser effect in NMR and infrared spectroscopy has introduced revolutionary structure determination methods in related research areas. On this opportunity, I aim to discuss the current status and future directions of the structure determination of biomolecules by highlighting the remaining issues in this field of research.

天然物を始めとする低分子有機化合物の構造決定が格段に高速化し、ルーティン化したことによって、アカデミアにおける研究テーマとしての輝きを失って久しい。中西香爾先生の赤外分光やNMRにおける核Overhauser効果、円二色性の研究は、その時代において画期的な構造決定法を提案・紹介したものであり、我が国の関連研究分野に多大なる影響を与えてきた。この機会に、中西先生が遺された教えを踏まえて、生体分子の構造決定における残された課題を、研究分野現状紹介を交えて議論する機会になれば幸いである。

Chirality of Biomolecules - CD & VCD Exciton Chirality Method -

([1]*Faculty of Advanced Life Science, Hokkaido University*)
○Kenji Monde[1]
Keywords: Circular dichroism; Chirality; Vibrational circular dichroism; Exciton Chirality method; Absolute configuration

One of the remarkable achievements of Professor Koji Nakanishi is research on chirality. Focusing on the circular dichroism spectrum, he and Prof. Harada of Tohoku University established the CD Exciton Chirality method. This stereochemical analysis method is easy to interpret, therefore is still frequently used. In this lecture, I will outline the CD Exciton Chirality method and describe the extensibility of this method toward the vibrational circular dichroism that the authors have recently developed.

The use of VCD (Vibrational Circular Dichroism) technique based on ab initio theoretical calculation has been reliable method to extract stereochemical information. However, it is hampered by the low sensitivity of vibrational absorption and by the computational demand. In 2012, we reported a new approach that required only the observation of a strong VCD couplet originating from the interaction of two IR chromophores.[1,2] The interaction yields a strong VCD couplet whose sign reflects the absolute configuration of the molecule. This new method named as VCD exaction chirality method using the bisignate VCD signals have a great advantage toward determination of absolute configuration of relatively small molecules without theoretical calculations. This can analyze various molecules (e.g. β-lactams, steroids, fravanonols, taxol derivatives, spiro-compounds, and polymers), whose absolute configuration is difficult to determine by other spectroscopic methods. Furthermore, it can significantly enhance VCD signals, sometimes by a factor of ~100.

Also, this method could have a potential for VCD application toward medium- and large molecules which are considered difficult due to theoretical calculation's limitation. In this paper, applications of this VCD exaction chirality method toward relatively complex small molecules, flexible molecular such as lipids,[3] medium-sized molecules, and macromolecules such as Poly-L-Lactic Acid showing helical structure in solution are also described.[4]

1) T. Taniguchi, K. Monde, *Yuki Gosei Kagaku Kyokaishi* **2017**, *75*, 522. 2) T. Taniguchi, K. Monde, *J. Am. Chem. Soc.* **2012**, *134*, 3695. 3) T. Taniguchi, D. Manai, M. Shibata, Y. Itabashi, K. Monde, *J. Am. Chem. Soc.* **2015**, *137*, 12191. 4) T. Hongen, T. Taniguchi, S. Nomura, J. Kadokawa, K. Monde, *Macromolecules*, **2014**, *47*, 5313.

Phytochemical natural products chemistry

([1]*Graduate School of Science, Tohoku University*, [2] *Graduate School of Life Science, Tohoku University*) ○UEDA, Minoru[1, 2]

Keywords: *Phytochemical; Natural Product; Jasmonates; Coronatine; Biosynthesis*

The interest of modern natural product research is focused on metabolites produced by microbes and plant metabolites. This is because genomic studies enables the use of abundant genetic resources for them.

Plants are skilled chemists. They use chemistry very well to produce a plethora of specialized metabolites.[1] Phytochemical natural products have provided us important chemicals for better human life and opportunities of finding new chemical concepts.

We can find some examples in the studies by late professor Koji Nakanishi; structural studies on ginkgolides from *Ginkgo biloba* leads to the use of NOE in structure determination of organic compounds. Finding of ponasterone from *Podocarpus nakaii* enables the enough supply of moulting hormone to develop the studies of insect physiology. In addition, Koji discovered a plant metabolite, trigonelline,[2] affecting the cell cycle which was re-discovered by us as a chemical factor controlling the circadian rhythmic plant leaf-movement.[3] The diversity of plant specialized metabolites has contributed to the development of natural products chemistry, bioscience including plant science. Since Koji's contributions, the significance of phytochemical natural products grows drastically in recent years. Thus, controlling the production of specialized metabolites in plant is a mojor topic of current natural product chemistry.

Jasmonates including JA-Ile are known as plant hormones regulating the biosynthesis of plant specialized metabolites, including terpenoids, alkaloids etc. The development of chemical tools for the regulation of plant hormone signaling is a promising field of research, and there have been significant advances over the past two decades. We recently developed some JA-Ile receptor agonists to dissect the complex signaling network of jasmonate hormone.[4] We recently succeeded in the development of some JA-Ile receptor agonists to dissect the complex signaling network of jasmonate hormone.[4] In this presentation, I would like to talk about our recent progress in the development of jasmonate receptor agonists, especially their effect on the production of specialized metabolites.

1 E. T. Wurtzel, T. M. Kutchan, *Science* **2016**, *353*, 1232-1236 10.1126/science.aad2062.

2 L. S. Evans, M. S. Almeida, D. G. Lynn, K. Nakanishi, *Science* **1979**, *203*, 1122-1123 10.1126/science.203.4385.1122.

3 M. Ueda, M. Niwa, S. Yamamura, *Phytochemistry* **1995**, *39*, 817-819 10.1016/0031-9422(95)00064-e.

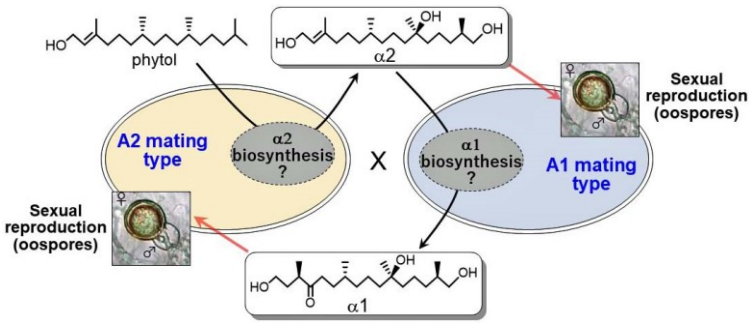
4 Y. Takaoka, M. Iwahashi, A. Chini, H. Saito, Y. Ishimaru, S. Egoshi, N. Kato, M. Tanaka, K. Bashir, M. Seki, R. Solano, M. Ueda, *Nat Commun* **2018**, *9*, 3654 10.1038/s41467-018-06135-y.

Sexual reproduction of a plant pathogen - exploring its molecular basis -

(*Graduate School of Bioagricultural Sciences, Nagoya University*) Makoto Ojika
Keywords: *Phytophthora*; sexual reproduction; mating hormone

Phytophthora is a genus of oomycetes and one of the best-known agricultural pests.[1] The most notorious species of this genus is *Phytophthora infestans*, which causes the destructive potato blight disease responsible for the "Great Irish Famine" in the mid 1840s. Sexual reproduction of the heterothallic members require two strains designated as A1 and A2 mating types, which secrete unique mating hormones α1 and α2, respectively, and regulate sexual reproduction of the counter mating type.[2] The chemical characterization of α hormones had been a long-term issue, until we isolated α1 in 2005[3] and α2 in 2011[4] from *P. nicotianae* A1 and A2 mating types, respectively.

Due to low content of the hormones, we spent a decade for α1 and an additional 6 years for α2 to identify them and huge amounts of cultures of *Phytophthora*, e. g., 1.2 mg of α1 isolated from 1,830 L cultures of A1 mating type. The interspecies universality of both hormones in *Phytophthora* was then demonstrated by hormone response experiments and hormone production analysis with 45 heterothallic strains.[5] Both the hormones are linear diterpenes, and were found to be biosynthesized from phytol by incorporation experiments using stable isotope-labelled phytol. Namely, α2 is biosynthesized from phytol by A2 mating type strains and metabolized to α1 by A1. Since each hormone promotes sexual reproduction (oospore formation) of the counter mating type, this biological event is achieved only by coexistence of the both mating types. Recently, we are making an effort to identify the hormone biosynthetic enzymes, which are possibly cytochrome P450 (CYP) because their production was suppressed by CYP inhibiters (Figure).



1) H. S. Judelson, F. A. Blanco, *Nat. Rev. Microbiol.* **2005**, 3, 47. 2) W.-H. Ko, *J. Gen. Microbiol.* **1978**, 107, 15. 3) J. Qi, et al. *Science*, **2005**, 309, 1828. 4) M. Ojika, et al. *Nat. Chem. Biol.* **2011**, 7, 591. 5) T. Tomura, et al. *Sci. Rep.* **2017**, 7, 1.

Chemistry of Receptor-Lipid Ligands for Understanding of Immune System

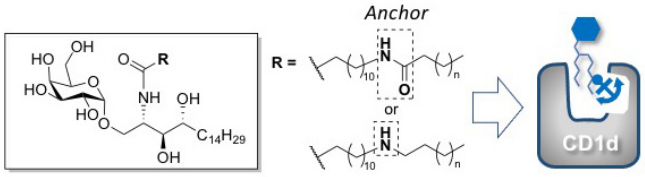
(*Faculty of Science and Technology, Keio University*) ○Yukari Fujimoto

Keywords: Glycolipid; Bioorganic Chemistry; Antigen presentation; Immunomodulation

One of the prominent research achievements of Professor Koji Nakanishi (1925 –2019) should be the investigation of molecular basis of rhodopsin, one of GPCRs responsible for vision, at the field of chemistry and biology interface. The elucidation of the mechanism and function of the photoreceptor molecule was performed with utilizing the synthesized ligand analogues and the analysis of their circular dichroism (CD). It was a pioneering work at the frontiers of bioorganic chemistry.

According to the ligand recognition of innate immune system, especially complex lipid ligands by the innate immune receptors, the detailed mechanism of the ligand binding and activation have not been fully understood, after a few decades since the first discovery of the innate immune receptors in 1998. On antigen presenting cells (eg. Dendric cells) present several innate immune receptors (eg. TLRs and CLRs) and lipid-antigen presenting molecules (eg. CD1), and some of these molecules recognize endogenous or exogenous lipid ligands to activate the immune system. Our group have synthesized various complex lipid ligands/analogues to build their compound library for elucidating their detailed immunomodulatory functions.

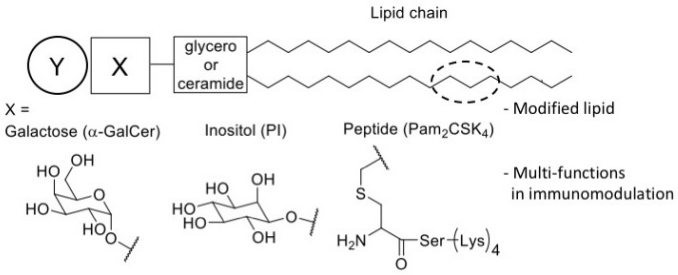
CD1d is a non-polymorphic MHC class I-like molecule, and its ligands include glycolipids such as α-GalCer (KRN7000). Complexes of glycolipid ligands and CD1d are recognized by T cell receptors (TCR) on NKT cells and induce the secretion of various cytokines, including helper-T (Th)1 and Th2 cytokines. Although Th2-biasing CD1d ligands are attractive potential candidates for adjuvants and therapeutic drugs for autoimmune diseases, the number of potent ligands is limited, and their biasing mechanism remain unclear. We have identified a series of novel Th2-biasing CD1d glycolipid ligands based on modification of their lipid part of α-GalCer structure.[1] These have shown high binding affinities and efficient Th2 cytokine production, and even truncated acyl chain-containing variants still retain their binding affinities and agonistic activities, which can be associated with an “anchoring effect.” i.e. formation of a buried hydrogen bond between a polar group (eg. amide) on the acyl chain and the CD1d lipid-binding pocket. Our analysis also indicated that the appearance rates of ligand-CD1d complexes on the cell surface were



involved in Th2-biasing responses. We demonstrated that the ligands, having the “anchor” in the shorter lipid part, would be one of the most potent Th2-biasing ligands with keeping the total cytokine induction levels, among the known ligands.[1b]

The modification of lipid moiety in lipid conjugates was also applied for an innate immune receptor, TLR2, ligands (eg. lipopeptide).[2] Although the modified ligands showed weaker activities than the original lipopeptide, the position of the lipid modification linked to the strength of binding affinity, presumably because of the hydrogen bond formation at the position with polar amino acids in the hydrophobic binding pocket.

We here demonstrated the importance of lipid binding affinity to the receptor proteins, in the lipid antigen presentation and also in the innate immune receptor recognition. The results will also be applicable to the drug development that links to the modulation of the immune system.



1) a) Inuki, S.; Aiba, T.; Hirata, N.; Ichihara, O.; Yoshidome, D.; Kita, S.; Maenaka, K.; Fukase, K.; Fujimoto, Y. *ACS Chem. Biol.* **2016**, *11*, 3132. b) Inuki, S.; Kashiwabara, E.; Hirata, N.; Kishi, J.; Nabika, E.; Fujimoto, Y. *Angew. Chem. Int. Ed.* **2018**, *57,* 9655. c) Kishi, J.; Inuki, S.; Kashiwabara, E.; Suzuki, T.; Dohmae, N.; Fujimoto, Y. *ACS Chem. Biol.* **2020**, *15*, 353.
2) Arai, Y.; Inuki, S.; Fujimoto, Y. *Bioorg. Med. Chem. Lett.* **2018**, *28*, 1638.

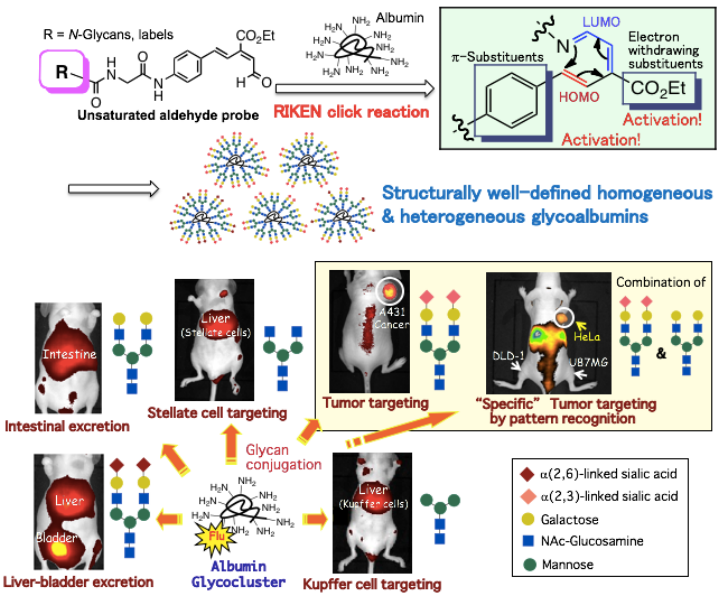
Therapeutic In Vivo Synthetic Chemistry

(*[1]Department of Chemical Science and Engineering, Tokyo Institute of Technology, [2]RIKEN Cluster for Pioneering Research, [3]Biofunctional Chemistry Laboratory, Kazan Federal University*) ○Katsunori Tanaka[1,2,3]

Keywords: Therapeutic In Vivo Synthetic Chemistry; Bioactive Natural Products; Metal Catalyzed Reaction; Drug

Although many efficient bond-forming reactions have been developed in the field of synthetic organic chemistry, their utility typically fails to translate in complex mixtures present in cellular or living biosystems. As such, only a handful of effective labeling or conjugation methods in biosystems are readily available. To address this issue, we are especially exploring the unique reactivity of conjugated imines for their potential in novel chemical reactions. Besides developing the labeling or conjugation methods, through a concept we refer to as “Therapeutic In Vivo Synthetic Chemistry”, we aim to develop an adaptable system where a cascade of organic transformations can be directly executed at target regions within the body during predefined times to generate a bioactive molecule that elicits a localized biological effect. Towards this goal, we are analyzing, with the use of molecular imaging, the complex “pattern recognition” mechanisms of natural glycans in vivo and applying the glycan-based interactions to direct various linked biomolecules to desired organs and tissues.

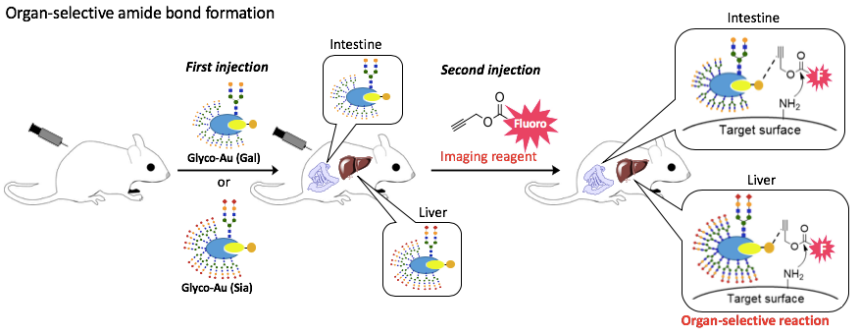
Noninvasive imaging and RI missile therapy based on RIKEN click reaction:[1-4] Previous studies of marine natural products and their enzyme inhibitory mechanisms lead us to the discovery and development of an efficient labeling method selective for amino groups present on biomolecules and the surface of live cells. This method, which is dependent on a rapid 6π-azaelectrocyclization of conjugated imines, has shown a wide range of utility such as its use with noninvasive PET or NIR (fluorescence) imaging. We improved upon the labeling method though incorporation of positron emitter metal/ligand



complexes, which are readily applicable to a variety of biomolecules, as well as to whole live-cell based PET imaging. This improved method, which is named as “RIKEN Click Reaction”, has now been applied even to MR imaging and RI missile therapy of biomacromolecules; an innovative theranostics strategy could be established and potentially be used for future diagnosis and protein- or cell-based drug discovery.

Diagnostic glycoconjugates through “glycan pattern recognition”:[5-8] One of the hurdles that prevent protein therapeutics from greater clinical usage is the lack of a general organ-selective biotargeting system, as well as greater control over excretion profiles. One approach to address this issue is to utilize glycans to direct protein accumulation in specific organs. Our research has introduced various glycan structures onto specific cells or artificial dendrons, through the RIKEN click reaction described above, as a means to investigate heterogeneous glycocluster dependence on in vivo dynamics. Through the use of molecular imaging, results have shown that glycan composition on proteins, cell or dendron templates can directly control accumulation towards specific organ and tumor, as well as affect their excretion profiles through “glycan pattern recognition” mechanisms.

Synthesis of bioactive compounds in live animals: Therapeutic in vivo synthetic chemistry:[9-12] Through the amalgamation of all research areas actively pursued above, we achieved a model system where bioactive compounds can be synthesized within living animals, which we refer to as “Therapeutic In Vivo Synthetic Chemistry”. By using the glycocusters as “in vivo metal carrier”, we succeeded for the first time in performing the metal-catalyzed reaction in target cancer cells and organs in live mice. The main benefit of this approach is that organic transformations can be directly executed at target regions within the body during predefined times to generate a bioactive molecule that elicits a localized biological effect. This method could entirely circumvent the off-target and peptide instability problems associated with the currently applied drugs.



1) *J. Am. Chem. Soc.* **2002**, *124*, 9660; 2) *Angew. Chem. Int. Ed*. **2008**, *47*, 102; 3) *Angew. Chem. Int. Ed*. **2010**, *49*, 8195; 4) *Chem. Sci.* **2019**, *10*, 1936; 5) *Adv. Sci*. **2016**, 1600394; 6) *Adv. Sci*. **2017**, 1700147; 7) *Chem. Commun.* **2018**, *54*, 8693; 8) *Small* **2020**, *16*, 2004831; 9) *Angew. Chem. Int. Ed.* **2017**, *56*, 3579; 10) *Nature Catal.* **2019**, *2*, 780; 11) *Nature Commun*. **2019**, *10*, 5746; 12) *Chem. Sci.* **2020**, *11,* 10933.

Symposium | Special Program | Toward the new chemistry through the fusion with informatics

[S10-1am] Toward the new chemistry through the fusion with informatics

Chair, Symposium organizer:Tadafumi Adschiri, Shinji Hasebe, Kazuhiko Sato, Midori Kamimura

Fri. Mar 19, 2021 9:00 AM - 11:40 AM Webiner 10 (Online Meeting)

[S10-1am-01] Strategy for Generating and Collecting Chemical Data Applicable to Chemical Research with Artificial Intelligence

○Kazuhiko Sato[1] (1. Interdisciplinary Research Center for Catalytic Chemistry, National Institute of Advanced Industrial Science and Technology (AIST))

9:10 AM - 9:40 AM

[S10-1am-02] Education on information in chemistry: For utilizing AI

○Noriko Akutsu[1] (1. Osaka Electro-Communication University)

9:40 AM - 10:10 AM

[S10-1am-03] Towards Digital Transformation of Chemical Plant

○Yoshiyuki Yamashita[1] (1. TUAT)

10:10 AM - 10:40 AM

[S10-1am-04] Digitization of Organic Synthesis

○Seijiro Matsubara[1] (1. Graduate School of Engineering, Kyoto University)

10:40 AM - 11:10 AM

[1S1001-04-6add] Panel Disccusion

11:10 AM - 11:40 AM

AI 利用を意識した化学データの戦略的収集と戦略的創出

（産総研触媒化学融合研究セ）○佐藤 一彦
Strategy for Generating and Collecting Chemical Data Applicable to Chemical research with Artificial Intelligence (*Interdisciplinary Research Center for Catalytic Chemistry, National Institute of Advanced Industrial Science and Technology (AIST)*) ○Kazuhiko Sato

Chemical information and data are valuable resources for chemical innovation. As a national strategy, it is important to collect chemical data generated in the universities and the research institutes, and construct a high-quality database that includes reproducible data which do not depend on the researchers. In this presentation, importance of the strategically generation and collection of high-quality data, the construction, the management and the utilization of the reliable database, which are directed toward the chemical innovation by artificial intelligence, will be discussed.
Keywords : database; chemical innovation; artificial intelligence

化学情報・データは、これからの化学技術革新を生み出す貴重な資源である。国として、研究・教育機関に散在する化学データをデータベースとして集約し、広くより機能的に活用するための施策が重要である。そのためには、教育・研究機関における統一的な電子実験ノートの導入、得られるデータベースの構造化を早急に行い、その情報の有効活用を推進すべきである。また、誰が行っても再現性よく同じ結果が得られるデータの蓄積が質の高いデータベース構築の大前提であり、そのためには実験・分析の自動化が望ましい。新たな物質・材料の物性や機能と構造、構造と合成法、さらに合成法と生産プロセス間の関係について、ネガティブデータを含めた新規データベースとして戦略的に収集・創出し、それを重要な資源として管理、有効活用していく仕組みを構築することが重要である。そのためには、高分子、製薬、機能性材料等の分野で化学に特化したデータベースの構築法や活用法の開発や、高度な分析機器と自動合成機能を融合させ質の良いデータを提供できる高機能物質合成システムの開発などを通して、情報化時代の化学に携わる広い分野の研究者の研究力強化を支援する組織（新化学創成センター）を設置すべきである [1)]。

1) 日本学術会議 提言「化学・情報科学の融合による新化学創成に向けて」(令和 2 年 7 月 7 日), 化学委員会化学企画分科会, P12.

「化学と AI」時代の情報教育ー学ぶ AI から使う AI へー

（大阪電通大院工 [1]）○阿久津 典子 [1]
Education of information in chemistry: For utilizing AI ([1]*Graduate School of Engineering, Osaka Electo-Communication University*) ○Noriko Akutsu[1]

Based on the government's AI strategy, the Ministry of Education, Culture, Sports, Science and Technology is promoting educational reforms so that "everyone can acquire a background in AI and mathematical data science." In chemistry as well, it is required to produce human resources who can utilize the knowledge of AI and mathematical data science. In this presentation, we will explain the educational reform required by the Ministry of Education, Culture, Sports, Science and Technology. We will also clarify the content of AI specialized education and AI literacy education in chemistry.
Keywords : Education; Machine-learning; Deep-learning

研究対象としての AI 技術ではなく、活用技術としての AI 応用は最近驚くべき速さで進んでいる。ここで言う AI 技術とは機械学習・深層学習のことである。このような背景の中で、AI 技術を万能と思い過ぎず、恐れ過ぎず、正しく認識する教育は、AI 技術を活用した社会（産業競争力の維持、AI と共存する組織への適応など）の健全な発展に貢献するだろう。政府の AI 戦略に基づき文部科学省は「国民誰もが AI・数理データサイエンスの素養を習得」できるように教育改革を推進している。化学においてもダブルメジャー制度などを活用し、AI・数理データサイエンスの知見も活用できる人材を輩出することが求められている。まず、AI リテラシー教育を行い、その上により専門的な AI・数理データサイエンス教育を行うという 2 段構えになる。すでに文部科学省から「AI 時代に求められる人材育成プログラム」の募集、採択など、「人材育成プログラム」が動き始めている。

振り返ってみれば、インターネットが誕生した頃、現代のようなスマートフォンを介したネットワーク社会・SNS 社会への変革が起きるとは考えられなかった。同じように、今後、機械学習と深層学習活用によりどの様な社会変革が生じるのか、今の時点では判らない。未来に繁栄する技術・産業の芽をいち早く見抜き、価値観を共有できる人材を幅広く育成していくことが重要である。このような状況下では、将来応用が利く、機械学習や深層学習のコアとなる考え方を AI リテラシー教育で多数の学生に教えておくことが大切である。では、AI リテラシー教育は誰が担うのか。それは化学においては、新しいことに関心を持つ化学研究者達であろう。

化学における、より専門的な AI・数理データサイエンス教育は、ケモメトリクス、あるいは化学合成ロボットなど実際に化学の分野で AI 技術を研究・開発している研究者が現場で人材育成を行うことが現実的と思われる。

機械学習や深層学習の目的は「データから知識を得る」ことである。その意味で化学と大変相性が良い。文部科学省の施策と熱意を持った化学研究者によって化学における AI 活用教育は上手くいくと考えている。

情報科学活用による化学プラントの変革に向けて

（農工大院工[1]）山下 善之[1]

Towards the Transformation of Chemical Plants through Information Technologies

([1]*Graduate School of Engineering, Tokyo University of Agriculture and Technology*) Yoshiyuki Yamashita[1]

The demand for the introduction of AI technology is growing for chemical plants in Japan, to cope with the increasing maintenance load caused by aging degradation of plants and the enhancement of product quality and added value. So far, application systems, such as the estimation of unmeasured variables and detection of abnormal situations, have been developed and used. Those systems have resulted improvements in quality and operation, reduction of cost, and avoidance of risk. However, the implementation of AI technology to chemical plants are still limited because of the shortage of meaningful data, the lack of ability to ensure the reliability of the result, and the shortage of human resource to explorer the digitalization.

To solve these problems and construct an operation support system based on AI technology will not only contribute to productivity improvement and asset maintenance in the chemical industry, but also complement the decrease of skilled engineers and lead to reform of working styles. Although several efforts have been made to resolve these issues, further development is expected in near future.

Keywords : Smart Manufacturing; Plant Operation; Industrial Safety, Machine Learning; Artificial Intelligence

日本の化学プラントにおいては、プラントの経年劣化によるメンテナンス負荷の増大や製品の高品質化・高付加価値化への対応策として、AI 技術導入の要求が高まっている。現状においても、直接測定していない変数の値を推定するソフトセンサーや、プラントの異常を検知するシステムなどが開発され、使われるようになってきており、品質・操業改善やコスト削減、リスク回避などの効果が得られている[1)]。しかし、AI 技術の適用にあたっては、必要なデータ数の不足、結果の説明性や信頼性の確保、導入を推進する人材の不足などが課題となっており、まだ十分には進められていないのが現状である。

これらの課題を解決し、AI 技術をベースとした運転支援システムを構築することは、化学産業における生産性向上や設備保全に大きく貢献するだけでなく、熟練技術者の減少を補い、働き方改革にもつながるものである。現在までにも、これらの課題のいくつかについては解決に向けた取り組みが行われてきているが、今後、さらなる積極的な取り組みが期待される[2)]。

1) 経済産業省他，「プラントにおける先進的 AI 事例集」**2020.**
2) 日本学術会議 化学委員会，提言「化学・情報科学の融合による新化学創生に向けて」**2020.**

有機合成のデジタル化

(京大院工) 松原　誠二郎

Digitization of Organic Synthesis
(*Graduate School of Engineering, Kyoto University*) Seijiro Matsubara

The core technologies of fully automated organic synthesis include the management of large amounts of accumulated reaction examples, machine learning based on these experimental results, and subsequent development of synthesis devices. Digitization of organic synthesis is key in progressing towards full automation. Various attempts at digitization are already enabling the development of a framework, in which the input of a molecular structure is converted into actual molecular synthesis.
Keywords: Computer-assisted organic synthesis, machine learning, automated synthesis

有機合成は，小さなフラスコの中に「自然ではありえない組み合わせ」を瞬時に実現できるので，どうしても考える前に手を動かすことになりがちである。それに加え，合成化学の経験者ならわかるのだが，同じ合成手順でも，うまくできる人と，全くダメな人がいる。有機合成が「できる」というのはどういうことだろう。それは「何でも知っていて」,「実験がうまくて」，そして「実験結果から合理的に解を導く」ことであるが，それは，「有機合成の過去の膨大な反応例に関する深い知識」と「その知識に基づく論理的展開力」が優れ，「根性と腕」も持ち，これらの三項目を統合的に用いることができるからに違いない。ここで，上記の三項目を「ビッグデータ」,「機械学習」，そして「ロボティクス」と言い換えれば恐ろしいことに気づかないだろうか。有機合成の AI 化すなわちデジタル化は意外と近い未来かもしれないのである。

有機合成のターゲット分子をビッグデータから作り上げる「ケモインフォマティクス」は既に手法としては確立している。しかし，ここから先の実際の合成作業が対応しておらず，一種の停滞が起きている。この停滞を解消するには，有機合成の自動化が望ましい。そのためには，1) 自動合成経路設定，2) 自動反応条件設定, 3) 自動合成装置の 3 段階が必要で，既に米国では MIT を中心に「DARPA Make-it」が，英国では Imperial College の ROAR (Rapid Online Analysis of Reaction)がめざましい発展を遂げている。これらの進展は必然的に有機合成の勢力図を大きく変化させる可能性がある。このような現況と，今からできることについて述べる。

1) 松原誠二郎, *日本化学会情報化学部会誌* **2020**,*38*,8–11.
2) S. Matsubara, *Chem. Lett.* **2021**, *50*, *in press*.

11:10 AM - 11:40 AM (Fri. Mar 19, 2021 9:00 AM - 11:40 AM Webiner 10)

[1S1001-04-6add] Panel Disccusion