

イノベーションから 応用へ

学際シンポジウム
イノベーションから応用へ

2024
16 / 18
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From Innovations to Applications

COLLOQUE

INTERDISCIPLINAIRE



20° ANNIVERSAIRE DES RELATIONS OSAKA-UNISTRA
大阪大学-ストラスブール大学 交流20周年記念

The symposium «From Innovations to Applications» is organized to celebrate the 20th anniversary and strengthen exchanges and collaborations between Osaka and Strasbourg universities.

It will focus on the relationship between innovation and cutting-edge technologies, and how they are translated into industrial applications.

The aim of the symposium is to organize a multi-disciplinary meeting bringing together researchers from different fields.

ORGANIZING INSTITUTIONS

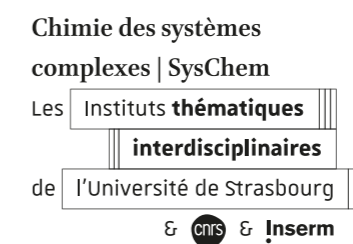
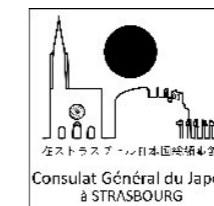
- Osaka University
- University of Strasbourg

WITH THE SUPPORT OF

- Maison Universitaire France-Japon
- Consulate General of Japan in Strasbourg
- IdEx
- JSPS Strasbourg Office
- Institute of Chemistry – UMR7177
- ITI SysChem

SCIENTIFIC COORDINATORS

- Pierre Braunstein
- Toshie Kai (Symposium)
- Takashi Kubo (Cadet)





*From
Innovation to
Applications*

8h30-8h55 Opening remarks

- ✦ MICHEL DENEKEN, PRESIDENT OF THE UNIVERSITY OF STRASBOURG
- ✦ TOSHIE KAI, SENIOR ADVISOR TO THE PRESIDENT OF OSAKA UNIVERSITY
- ✦ HIROYUKI UCHIDA, GENERAL CONSUL, CONSULATE OF JAPAN IN STRASBOURG
- ✦ TOSHIYUKI TAKAGI, DIRECTOR, JSPS STRASBOURG OFFICE
- ✦ MICHÈLE FORTÉ, DIRECTOR, MUFJ

8h55-9h00 Presentation of the Interdisciplinary Symposium: Background and Motivations

- ✦ PIERRE BRAUNSTEIN

_session 1: Innovation in Medicine and Genomics

CHAIRS: TOSHIE KAI AND FRÉDÉRIC LEROUX

9h00-9h30 Strategies for cancer therapy by controlling the intracellular dynamics of antibody drugs

- ✦ KAZUYA KABAYAMA, OSAKA UNIVERSITY

9h30-10h00 Intellectual disability: a frequent condition, 1500 rare genetic disorders and counting: from genomics to participatory research

- ✦ JEAN-LOUIS MANDEL, UNIVERSITY OF STRASBOURG

10h00-10h15 Discussion

10h15-10h45 Coffee Break and group photo

_session 2: Immunity and Medical Robotics

CHAIRS: YOICHI NAKATANI AND YUJI SATO

10h45-11h15 Sensing self- and non-self metabolites via immune systems

- ✦ SHO YAMASAKI, OSAKA UNIVERSITY

11h15-11h45 From innovation to applications in medical robotics: case studies

- ✦ MICHEL DE MATHÉLIN, UNIVERSITY OF STRASBOURG

11h45-12h00 Discussion

Afternoon Visits –Members only–

_session 3: Material Sciences

CHAIRS: PAOLO SAMORI AND AI SHINOBU

8h30-9h00 Additive Manufacturing for Metal with Blue Laser

- ✦ YUJI SATO, OSAKA UNIVERSITY

9h00-9h30 Photo(redox)active and photo(electro)switchable materials based on polyoxometalates and (iso)porphyrins

- ✦ LAURENT RUHLMANN, UNIVERSITY OF STRASBOURG

9h30-9h45 Discussion

9h45-10h15 Coffee break

_session 4: Science, Innovation and Management

CHAIRS: MICHELE FORTE AND KEI OHKUBO

10h15-10h45 Design and Functions of Polymeric Materials Based on Supramolecular Science

- ✦ YOSHINORI TAKASHIMA, OSAKA UNIVERSITY

10h45-11h15 Create long-term relations with stakeholders to favor sustainable open innovation : The case of Japan.

- ✦ MARION NEUKAM AND RENÉ CARRAZ, UNIVERSITY OF STRASBOURG

11h15-11h30 Discussion

_session 5: Chemistry and Applications

CHAIRS: JEAN WEISS AND YOSHINORI TAKASHIMA

13h15-13h45 Photodriven C-H Oxygenation of Hydrocarbons with Chlorine Dioxide

- ✦ KEI OHKUBO, OSAKA UNIVERSITY

13h45-14h15 Strategies towards fluoroalkylated building-blocks for Industrial Application

- ✦ FRÉDÉRIC LEROUX, ECPM, UNIVERSITY OF STRASBOURG

14h15-14h30 Discussion

14h30-15h00 Coffee break

_session 6: Life Sciences

CHAIRS: MARIE-CLAIRE LETT AND SHO YAMASAKI

15h00-15h30 Processing of Small RNAs Safeguarding the Germline Genome in the Non-Membrane Structure, Nuage

- ✦ TOSHIE KAI, OSAKA UNIVERSITY

15h30-16h00 From innovation to Application in advanced Liver diseases

- ✦ CATHERINE SCHUSTER, UNIVERSITY OF STRASBOURG, INSERM

16h00-16h30 Deciphering the molecular origin of cellular processes using advanced molecular dynamics simulations

- ✦ AI SHINOBU, OSAKA UNIVERSITY

16h30-16h45 Discussion

_session 7: Ethics and Perspective

CHAIRS: CATHERINE SCHUSTER AND KAZUYA KABAYAMA

16h45-17h15 Ethics in Science: The Example of Advances in Human Genetics

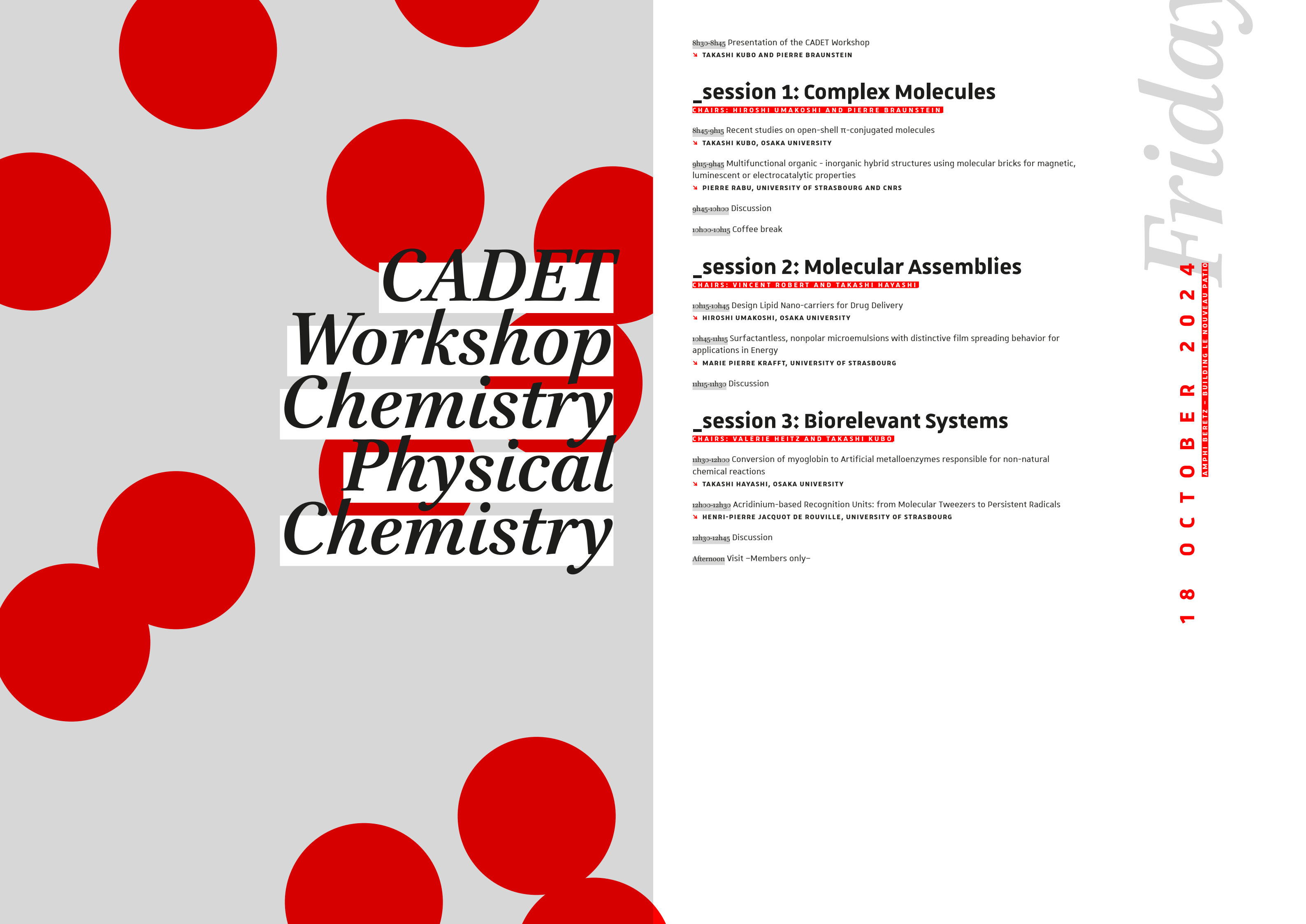
- ✦ YVES ALEMBIK, STRASBOURG

17h15-17h30 Discussion

17h30-17h45 Concluding Remarks of the Symposium

- ✦ RÉMI BARILLON, VICE-PRESIDENT OF THE UNIVERSITY OF STRASBOURG FOR RESEARCH, DOCTORAL STUDIES AND OPEN SCIENCE.

- ✦ TOSHIE KAI, SENIOR ADVISOR TO THE PRESIDENT OF OSAKA UNIVERSITY



CADET Workshop Chemistry Physical Chemistry

8h30-8h45 Presentation of the CADET Workshop

✦ TAKASHI KUBO AND PIERRE BRAUNSTEIN

_session 1: Complex Molecules

CHAIRS: HIROSHI UMAKOSHI AND PIERRE BRAUNSTEIN

8h45-9h15 Recent studies on open-shell π -conjugated molecules

✦ TAKASHI KUBO, OSAKA UNIVERSITY

9h15-9h45 Multifunctional organic - inorganic hybrid structures using molecular bricks for magnetic, luminescent or electrocatalytic properties

✦ PIERRE RABU, UNIVERSITY OF STRASBOURG AND CNRS

9h45-10h00 Discussion

10h00-10h15 Coffee break

_session 2: Molecular Assemblies

CHAIRS: VINCENT ROBERT AND TAKASHI HAYASHI

10h15-10h45 Design Lipid Nano-carriers for Drug Delivery

✦ HIROSHI UMAKOSHI, OSAKA UNIVERSITY

10h45-11h15 Surfactantless, nonpolar microemulsions with distinctive film spreading behavior for applications in Energy

✦ MARIE PIERRE KRAFFT, UNIVERSITY OF STRASBOURG

11h15-11h30 Discussion

_session 3: Biorelevant Systems

CHAIRS: VALERIE HEITZ AND TAKASHI KUBO

11h30-12h00 Conversion of myoglobin to Artificial metalloenzymes responsible for non-natural chemical reactions

✦ TAKASHI HAYASHI, OSAKA UNIVERSITY

12h00-12h30 Acridinium-based Recognition Units: from Molecular Tweezers to Persistent Radicals

✦ HENRI-PIERRE JACQUOT DE ROUVILLE, UNIVERSITY OF STRASBOURG

12h30-12h45 Discussion

Afternoon Visit -Members only-

Friday

18 OCTOBER 2024

AMPHI BERETZ - BUILDING LE NOUVEAU PATIO



Yves ALEMBIK

PEDIATRICIAN AND RETIRED GENETICIST
IN THE DEPARTMENT OF HUMAN GENETICS STRASBOURG

EDUCATION

- ✦ Doctor in Medicine, 1982
- ✦ DEA (state diploma in human genetics), 1986
- ✦ Direct research habilitation, 1995

SCIENTIFIC INTEREST

- ✦ Hospital MD in clinical until 2020
- ✦ Liberal practice in pediatrics
- ✦ Research projects in epidemiology and different subjects in clinical genetics among them:
 - Trisomy 21 in adults and exome sequencing in foeto-pathology.
- ✦ In the field of ethics
 - Chairman of the EREGE Steering Committees (Regional ethical committee in Alsace)
 - Member of the CPDPN until 2020 (regional prenatal pluridisciplinary diagnostic center)
 - Lectures at the Strasbourg Bioethics FORUM (ethical annual forum) in the genetic and pediatric fields
 - Member of THEMIS, children rights organization until 2015

LATEST PUBLICATIONS

- ✦ Widening of the genetic and clinical spectrum of Lamb-Shaffer syndrome, a neurodevelopmental disorder due to SOX5 haploinsufficiency. Zawerton A. and others. Genet Med 22, 524–537 (2020).
- ✦ A New SLC10A7 Homozygous Missense Mutation Responsible for a Milder Phenotype of Skeletal Dysplasia With Amelogenesis Imperfecta. Laugel-Haushalter V. and others. Front Genet. 2019 May 28.
- ✦ Infection risk among adults with down syndrome: a two group series of 101 patients in a tertiary center. Guffroy A. and others. Orphanet J Rare Dis. 2019 Jan.
- ✦ HCN1 mutation spectrum: from neonatal epileptic encephalopathy to benign generalized epilepsy and beyond. Marini C. and others. Brain, Volume 141, Issue 11, November 2018.
- ✦ Wiedemann-Steiner syndrome as a major cause of syndromic intellectual disability: A study of 33 French cases. Baer S. and others. Clin Genet. 2018 Jul.

Ethics in Science: The Example of Advances in Human Genetics

YVES ALEMBIK

YVES.ALEMBIK@GMAIL.COM

Scientific advances have always presented significant ethical challenges. In the field of genetics, several controversial topics warrant focus. First is eugenics, with its concepts of liberal and authoritarian eugenics, which discuss the distinction between eugenics based on individual choice—often linked to reproductive freedom—and eugenics imposed by state authorities, along with their ethical and social implications and historical background.

Next are the ethical issues surrounding cloning. Reproductive cloning raises substantial concerns, particularly regarding the identity and rights of clones, as well as the potential for misuse in creating genetically identical individuals. It leads to questions about the societal implications of cloning, including moral questions about the nature of individuality, the ethical treatment of cloned beings, and the possible consequences for human diversity.

Following this is the emerging technique of genome editing, particularly using CRISPR-Cas9 and other technologies such as ZFN. This powerful tool, often referred to as «genetic scissors,» allows for precise modification of DNA, offering the potential to correct genetic diseases. However, it also presents significant ethical challenges, including the risk of unintended consequences, the debate over where to draw the line in genetic intervention, and the societal implications of

enhancing or altering human traits. CRISPR-Cas9 could also be misused in ways that could lead to new forms of inequality or discrimination. Genetic testing raises issues of informed consent and confidentiality, as well as discrimination. Prenatal diagnosis emphasizes many issues in human medicine, such as the potential severity of an impending disease, including the legal possibility and decision to medical abortion and new possibilities for in utero treatment. Gene therapy poses difficult ethical questions, including the possibility of modifying the germline (sperm and eggs), which can be passed on to future generations. Considering somatic therapy, issues of safety, efficacy, and equitable access to genetic treatments arise.

It is interesting to compare genetic ethics between the West and Japan, analyzing both shared and divergent perspectives. While cultural differences exist, with the West emphasizing individual rights and Japan prioritizing social harmony and collective responsibility, there is a global consensus on certain ethical principles. These include the necessity for strict regulation of genetic practices, the protection of human dignity, and the prevention of discrimination based on genetic traits. National ethics committees around the world play a crucial role in upholding these standards, ensuring that scientific advances in genetics align with universally accepted ethical guidelines.



René CARRAZ

GLOBAL INNOVATION STUDY / TOYO UNIVERSITY
BETA, STRASBOURG UNIVERSITY / RESEARCH FELLOW

EDUCATION

- ✦ Doctor of Philosophy (PhD), Economics / Innovation (2010, University of Strasbourg / BETA-CNRS – France)
- ✦ Certified in Management de la Créativité (Institut Européen Entreprise et Propriété Intellectuelle - France & HEC Montreal 2019)
- ✦ Master in Economics, major in “Business science”. (2006, Kyoto University – Japan)
- ✦ Master in Economics, major in “Economics and Management of Innovation and Knowledge.” (2005, University of Strasbourg / BETA-CNRS – France)

SCIENTIFIC INTEREST

René Carraz holds the position of Associate Professor at Toyo University’s Department of Global Innovation Studies, Japan. His expertise lies in the realm of economics-driven exploration of science, technology, and innovation. Recently, he has been engaged in the development of a matching algorithm for academic patent-paper pairs. This innovative algorithm is designed to connect patents with their corresponding academic papers, facilitating a more comprehensive understanding of the relationship between scientific research and intellectual property (<https://kaken.nii.ac.jp/en/grant/KAKENHI-PROJECT-24K05092/>). Beyond this, his research spans science and technology policy, academic entrepreneurship in Japan, and the intricate interplay between urban environments and creativity.

LATEST PUBLICATIONS

- ✦ Van Thien, N. & Carraz, R. (2023). Innovative Matching Algorithm for Academic Patent-Paper Pairs: The case of Japan. Working Papers of BETA 2023-29, Bureau d’Economie Théorique et Appliquée, UDS, Strasbourg. <https://ideas.repec.org/p/ulp/sbbeta/2023-29.html>
- ✦ Oo, N., & Carraz, R. (2023) How Healthy is Japan’s Entrepreneurial Ecosystem? From the Perspective of Leading Universities in Japan. Journal of Regional Development Studies. (26) 91-116 (2023-03) <http://id.nii.ac.jp/1060/00013983/>
- ✦ Renou, T., Carraz, R., & Burger-Helmchen, T. (2023). Japan’s Corporate Governance Transformation: Convergence or Reconfiguration?. Administrative Sciences, 13(6), 14. <https://doi.org/10.3390/admsci13060141>
- ✦ Harayama, Y. and R. Carraz (2022). A digital society for an aging population. The Japanese experience. In Handbook of Smart Technologies: An Economic and Social Perspective, Edited by Heinz D. Kurz, Marlies Schütz, Rita Strohmaier and Stella Zilian., Chapter 31, Routledge, London.
- ✦ Carraz, R. and Y. Harayama (2019). Japan’s Innovation Systems at the Crossroads: Society 5.0, Panorama: Insights into Asian and European Affairs, 33-45.

*From
Innovation to
Applications*

Create long-term relations with stakeholders to favor sustainable open innovation: the case of Japan

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Michel de MATHELIN

ICUBE LABORATORY / TELECOM PHYSICS STRASBOURG /

UNIVERSITY OF STRASBOURG

CURRICULUM

- ✦ Since March 2021: First Vice-President of the University of Strasbourg
- ✦ Since January 2017: Vice-President for Innovation and relationship with the socio-economic world
- ✦ 2013-2022: Director of the ICube Laboratory with more than 750 people in the field of engineering and computer science with a strong emphasis on biomedical and environmental applications (UMR 7357 CNRS-Unistra)
- ✦ 2006-2014: Scientific advisor for automatic control and robotics at the CNRS national institute for engineering and computer science
- ✦ Since September 1999: Full Professor at Telecom Physics Strasbourg engineering school in the University of Strasbourg
- ✦ 1993-1999: Associate Professor in automation and control at the University of Strasbourg
- ✦ January 1993: PhD at the Electrical and Computer Engineering Department at Carnegie Mellon University, Pittsburgh, PA, USA
- ✦ June 1989: M.S. at the Electrical and Computer Engineering Department at Carnegie Mellon University, Pittsburgh, PA, USA
- ✦ June 1987: Electrical Engineering Diploma Magna Cum Laude from the University of Louvain, Louvain-la-Neuve, Belgium
- ✦ Belgian American Educational Foundation Fellow

SCIENTIFIC AND INNOVATION INTERESTS

- ✦ Research topics: medical robotics, medical imaging, AI
- ✦ Head of the University Innovation Campus of Alsace since November 2021
- ✦ Coordinator of the National network of robotics platforms, Equipex ROBOTEX (National Infrastructure) from 2011 to 2021
- ✦ Founder of the startups Axilum Robotics and Innen Robotics, holder of 8 patents in medical robotics
- ✦ Publications: more than 250 articles from referee journals and international conferences
- ✦ H-index: 47 – 8209 citations (Google Scholar)

LATEST PUBLICATIONS

- ✦ O. Caravaca Mora, P. Zanne, G. Liao, N. Zulina, L. Heroin, L. Zorn, M. de Mathelin, B. Rosa, F. Nageotte, M. Gora. Automatic intraluminal scanning with a steerable endoscopic optical coherence tomography catheter for Gastroenterology applications, *Journal of Optical Microsystems*, SPIE, Vol. 3(1), January 2023.
- ✦ J. Kim, M. de Mathelin, K. Ikuta, D-S. Kwon. Advancement of flexible robot technologies for endoluminal surgeries, *Proceedings of the IEEE, Institute of Electrical and Electronics Engineers (IEEE)*, Vol. 110(7):909-931, 2022.
- ✦ C-H. Mallereau, S. Baloglu, S. Chibbaro, V. Noblet, J. Todeschi, G. Noel, A. Gangi, M. de Mathelin, F. Proust, H. Cebula. Does interventional MRI-guided brain cryotherapy cause a blood-brain barrier disruption? Radiological analysis and perspectives, *Neurosurgical Review*, Springer Verlag, Vol. 45(2), October 2022.
- ✦ L. Zorn, F. Nageotte, P. Zanne, A. Legner, B. Dallemagne, J. Marescaux, M. de Mathelin. A Novel Telemanipulated Robotic Assistant for Surgical Endoscopy: Preclinical Application to ESD, *IEEE Transactions on Biomedical Engineering*, Institute of Electrical and Electronics Engineers (IEEE), Vol. 65(4):797-808, April 2018.

From
Innovation to
Applications

From innovation to applications in medical robotics: case studies

MICHEL DE MATHELIN

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The path from academic research to patient care can be very long, especially in medical robotics. From the start, it requires a very close relationship between robotics researcher with various expertise in mechatronics, vision, real-time software, control, and medical doctors and surgeons. The joint work between experts from the medical field and experts in robotics is critical to the innovation process from the early doctoral research project, to the development of the first prototypes, the in-vivo testing on animal models, and the first interdisciplinary research, another critical factor is the integration of certification constrains early on in the development process as well as implementing the right intellectual property strategy. In this presentation, several medical robotics projects at ICube will be presented with their innovation process starting from a doctoral thesis and leading to the creation of a startup. A focus will be put on the development of a robotics device for transcranial magnetic stimulation in the domain of neuro-psychiatry and a robotized interventional endoscope in the minimally invasive surgical domain.



Robotized interventional endoscope (ICube-IRCAD)



Kazuya KABAYAMA

INSTITUTE FOR RADIATION SCIENCES, DEPARTMENT OF CHEMISTRY / FOREFRONT RESEARCH CENTER / GRADUATE SCHOOL OF SCIENCE/ TRANSDIMENSIONAL LIFE IMAGING DIVISION, OTRI /OSAKA UNIVERSITY

BIOGRAPHY

In 1997, Graduated at Keio university, Faculty of science and technology (Prof. Seiichiro Ogawa). 1997-1999, Master course of graduate school of science and technology, Keio university (Prof. Seiichiro Ogawa). 1999-2002, Doctor course of graduate school of pharmaceutical sciences, Hokkaido university (Prof. Yasuyuki Igarashi). 2002-2003, Postdoctoral fellow, Graduate school of pharmaceutical sciences, Hokkaido university. 2004-2006, Research fellow, Core Research for Evolution Science and Technology (CREST) program. 2006-2008, Assistant professor, Institute of molecular biomembranes and glycobiology, Tohoku pharmaceutical University (Prof. Jin-ichi Inokuchi). 2009-2014.05, Associate professor (principal investigator), Institute of glycoscience, Tokai university. 2014.06-2024.01, Associate professor, Graduate school of science, Osaka university (Prof. Koichi Fukase). 2024.02-, Professor, Institute for Radiation Sciences, Osaka University.

SCIENTIFIC INTEREST

Innate Immunity, Antibody Drugs, Astatine, Alpha-targeted therapy, Glycoptoteins Glycolipids, Microdomains, Gangliosides, Fluorescence Microscopy, Live Cell Imaging, Cancer, Diabetes

LATEST PUBLICATIONS

- ✦ Miura A., Manabe Y.*, Kabayama K.*, Fukase K.* et al. "De novo glycan display on cell surfaces using HaloTag: Visualizing the effect of the galectin lattice on the lateral diffusion and extracellular vesicle loading of glycosylated membrane proteins." *J. Am. Chem. Soc.* in press
- ✦ Manabe Y.*, Kabayama K.*, Fukase K.* et al. "Improvement of antibody activity by controlling its dynamics using the glycan-lectin interaction." *Angew. Chem. Int. Ed.* e202304779 (2023)
- ✦ Watabe T.*#, Kabayama K.#, Fukase K. et al. "Immuno-PET and targeted alpha therapy using anti-glypican-1 antibody labeled with 89Zr/211At: A novel theranostics approach for pancreatic ductal adenocarcinoma." *J. Nucl. Med.* 64, 1949-1955 (2023) #co-first authors

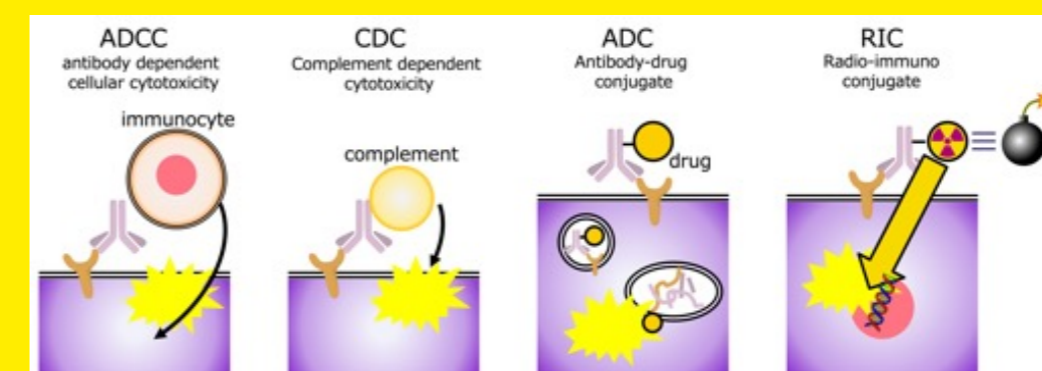
Strategies for cancer therapy by controlling the intracellular dynamics of antibody drugs

KAZUYA KABAYAMA

KABA@IRS.OSAKA-U.AC.JP

The development of antibody therapeutics has made remarkable progress, surpassing small-molecule drugs since the 2010s due to their immune-inducing activity and high target specificity. Key mechanisms include antibody dependent cellular cytotoxicity (ADCC) and complement dependent cytotoxicity (CDC). In our research, we aim to enhance these activities while also leveraging the specificity of antibodies to deliver anticancer drugs and radioactive substances to cancer cells. This approach corresponds to antibody-drug conjugates (ADCs) and radio-immuno conjugates (RICs). (Fig.1) Our recent research has enhanced CDC activity by introducing galactose-containing sugars into anti-HER2 antibodies, utilizing galectin-3 interactions to inhibit internalization¹. Additionally, studies on nuclear medicine therapy using

astatine (211At) have shown promise for targeted cancer treatment. PET imaging with zirconium (89Zr) followed by 211At labeling has demonstrated suppression of pancreatic cancer². Furthermore, improvements in antibody linkers, such as the inclusion of cleavage sites and nuclear translocation signal peptides, have increased cytotoxicity³. These studies aim to improve the functionality of antibody therapeutics by controlling their dynamics through chemical biology approaches. We are committed to continuing this research with creativity, adhering to our motto of «considering research and development until the First in Human trials,» with the ultimate goal of developing antibody therapeutics that can be marketed as drugs in the future.



References:

- 1) Manabe, Kabayama, Fukase et al., *Angew. Chem. Int. Ed. Engl.* e202304779 (2023)
- 2) Watabe, Kabayama, Fukase et al., *J. Nucl. Med.* 64, 1949-1955 (2003)
- 3) Iizuka, Manabe, Kabayama, Fukase et al., *Int. J. Mol. Sci.* 24, 9593 (2023)



Toshie KAI
GERMLINE BIOLOGY / GRADUATE SCHOOL OF FRONTIER BIOSCIENCES
DEPARTMENT OF FRONTIER BIOSCIENCES / OSAKA UNIVERSITY

EDUCATION

Apr, 1993 - Mar, 1998: Graduate School of Science, Osaka University

EMPLOYMENT

- Apr, 2021 – Present: Director of Student Mobility Unit, Center for Global Initiatives, Osaka University
- Oct, 2015 – Present: Professor, Osaka University Graduate School of Frontier Biosciences
- Jan, 2011 – Sep, 2015: Adjunct Associate Professor, Department of Biological Science, The National University of Singapore
- Oct, 2010 – Sep, 2015: Senior Principal Investigator, Temasek Lifesciences Laboratory
- Feb, 2007 – Dec, 2010: Adjunct Assistant Professor, Department of Biological Science, The National University of Singapore
- Jun, 2005 – Sep, 2010: Principal Investigator, Temasek Lifesciences Laboratory
- Jan, 2001 – Jun, 2005: Research Associate, Department of Embryology, Carnegie Institution of Washington/Howard Hughes Medical Institute
- Jan, 2000 – Dec, 2001: Long-term overseas researcher, Department of Embryology, Science and Technology Agency/Carnegie Institution of Washington
- Oct, 1999 – Dec, 1999: Research Associate, Department of Embryology, Carnegie Institution of Washington/Howard Hughes Medical Institute

SCIENTIFIC INTEREST

While individual animals perish, species are perpetuated through sexual reproduction, leading to the next generation. Individuals can be seen as vehicles, carrying genetic information in germline cells, which are the true drivers and the essential component of life. Thus, germline cells are paramount for species continuity. *Drosophila melanogaster* serves as an exemplary model organism for investigating gametogenesis. Our key questions include: How are germline stem cells maintained within the microenvironment, the niche? What are the molecular mechanisms regulating the differentiation of germline cells into oocytes and sperms? How are germline genomes safeguarded by non-coding RNAs known as piRNAs against transposon-induced damage? Our research group is focused on elucidating these molecular pathways to advance our understanding of gametogenesis.

LATEST PUBLICATIONS

- Xu F, Suyama R, Inada T, Kawaguchi K, Kai T. HemK2 functions for sufficient protein synthesis and RNA stability through eRF1 methylation during *Drosophila* oogenesis. *Development* (in press)
- Suyama R, Cetraro N, Yew J Y, Kai T. (2023) Microbes control *Drosophila* germline stem cell increase and egg maturation through hormonal pathways. *Commun. Biol.*, 6: 1287 doi: 10.1038/s42003-023-05660-x
- Lin Y, Suyama R, Kawaguchi S, Iki T, Kai T. (2023) Tejas functions as a core component in nuage assembly and precursor processing in *Drosophila* piRNA biogenesis. *J. Cell Biol.*, 222(10):e202303125 doi: 10.1083/jcb.202303125
- Iki T, Kawaguchi S, Kai T. (2023) miRNA/siRNA-directed pathway to produce noncoding piRNAs from endogenous protein-coding regions ensures *Drosophila* spermatogenesis. *Science Advances*, 9(29 doi: 10.1126/sciadv.adh0397

Processing of Small RNAs Safeguarding the Germline Genome in the Non-Membrane Structure, Nuage

TOSHIE KAI

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Transposons, or mobile genetic elements, pose significant threats to genomic integrity through their active translocation within the genome. In animals, PIWI-interacting RNAs (piRNAs) play a crucial role in defending the genome against transposon attacks. These piRNAs are produced and amplified in germline-specific, membrane-less granules known as nuage. In *Drosophila*, PIWI family proteins, Tudor-domain-containing (Tdrd) proteins, and RNA helicases assemble to form nuage, facilitating piRNA production. However, the specific molecular functions of several Tdrd proteins in piRNA biogenesis are not fully understood.

In this talk, I will introduce a recent study on one of the Tdrd proteins, Tejas (Tej). We conducted a detailed analysis of the subcellular localization of fluorescently-tagged nuage proteins and behavior of piRNA precursors. Our results demonstrated that Tej functions as a core component that recruits Vasa (Vas) and Spindle-E (Spn-E) into nuage granules through distinct motifs, thereby assembling nuage and engaging precursors for further processing. Our study also revealed that the low-complexity region of Tej regulates the mobility of Vas. Based on these results, we propose that Tej plays a pivotal role in piRNA precursor processing by assembling Vas and Spn-E into nuage and modulating mobility of nuage components.



Frederic LEROUX

UMR7042-LIMA / UNIVERSITY OF STRASBOURG

CNRS

EDUCATION

- ✦ 2023: Scientific Delegate to the CNRS Corporate Relations Division (DRE)
- ✦ 2018: Department Head (UMR7042-LIMA).
- ✦ 2016 – 2018: Vice-chair Department of Molecular Chemistry (UMR CNRS 7509).
- ✦ 2016: Director of the French Fluorine Network GIS CNRS Fluor.
- ✦ 2014 – 2024: Director joint Bayer-CNRS laboratory LabCom C2OF.
- ✦ 2009: CNRS Research Director.
- ✦ 2003 – 2009: CNRS Associate Scientist.
- ✦ 2005: Habilitation, University Louis Pasteur, Strasbourg, France.
- ✦ 2001 – 2003: Assistant Professor, ETH Lausanne, Switzerland.
- ✦ 1998 – 2001: Assistant Professor, University de Lausanne, Switzerland.
- ✦ 1998: Postdoctoral Fellow, University of Lausanne, Switzerland.
- ✦ 1997: Ph.D. in chemistry (Dr. rer. nat.), University of Konstanz, Germany.
- ✦ 1994 – 1997: Research Assistant, University of Konstanz, Germany.
- ✦ 1993: Diplom-Chemiker (M.Sc.), University of Konstanz, Germany.

SCIENTIFIC INTEREST

- ✦ Organic chemistry of heteroelements, especially fluorine; asymmetric synthesis; chemistry of polar organometals.

LATEST PUBLICATIONS

- ✦ F. Audet, M. Donnard, A. Panossian, P. Holstein, D. Bernier, S. Pazenok, F. Leroux, *Adv. Synth. Catal.* 2024, 10.1002/adsc.202400401
- ✦ L. Santos, F. Audet, M. Donnard, A. Panossian, J. P. Vors, D. Bernier, S. Pazenok, F. R. Leroux, *Chem. Eur. J.* 2023, 29, e202300792. 10.1002/chem.202300792
- ✦ C. Placais, S. J. Kaldas, M. Donnard, A. Panossian, D. Bernier, S. Pazenok, F. R. Leroux, *Chem. Eur. J.* 2023, 29, e202301420. 10.1002/chem.202301420
- ✦ A. Messara, A. Panossian, K. Mikami, G. Hanquet, F. R. Leroux, *Angew. Chem. Int. Ed.* 2023, 62, e202215899. 10.1002/anie.202215899

Strategies towards fluoroalkylated building-blocks for Industrial Application

FREDERIC LEROUX

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Fluorinated groups are ubiquitous in bioactive compounds because they can significantly improve their physicochemical properties. For example, the lipophilicity of a molecule can be adjusted by introducing appropriate fluorinated chains. The metabolic stability and potency of active ingredients can also be significantly impacted by the introduction of fluorinated groups.[1] For many years, our research has focused on the synthesis of functionalized heteroarenes bearing emerging fluorinated substituents. One of our approaches was based on the use of fluoroalkylated amine reagents (FARs) as

efficient and versatile tools for the regioselective introduction of fluorinated substituents.[2] More recently, we have developed strategies towards SO₂F₂-mediated fluoroalkylation based on the activation of fluorinated alcohols,[3] allowing the N-, and O-polyfluoroalkylation to access valuable building blocks in the life sciences. On the other hand, we have recently developed the direct deprotonative functionalization of the difluoromethyl group to access valuable difluoromethylene-containing compounds.[4] Here we will present our recent results in these areas.

References

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- ✦ a) E. Schmitt, A. Panossian, J. P. Vors, C. Funke, N. Lui, S. Pazenok, F. R. Leroux, *Chem. Eur. J.* 2016, 22, 11239-11244; b) E. Schmitt, B. Commare, A. Panossian, J. P. Vors, S. Pazenok, F. R. Leroux, *Chem. Eur. J.* 2018, 24, 1311-1316.
- ✦ a) L. Santos, M. Donnard, A. Panossian, J. P. Vors, P. Jeschke, D. Bernier, S. Pazenok, F. R. Leroux, *J. Org. Chem.* 2022, 87, 2012-2021; b) L. Santos, F. Audet, M. Donnard, A. Panossian, J. P. Vors, D. Bernier, S. Pazenok, F. R. Leroux, *Chem. Eur. J.* 2023, 29, e202300792.
- ✦ a) L. Santos, A. Panossian, M. Donnard, J. P. Vors, S. Pazenok, D. Bernier, F. R. Leroux, *Org. Lett.* 2020, 22, 8741-8745; b) A. Messara, N. Vanthuynne, P. Diter, M. Elhabiri, A. Panossian, G. Hanquet, E. Magnier, F. R. Leroux, *Eur. J. Org. Chem.* 2021, 2021, 5019-5026; c) A. Messara, A. Panossian, K. Mikami, G. Hanquet, F. R. Leroux, *Angew. Chem. Int. Ed.* 2023, 62, e202215899.



Jean Louis MANDEL

IGBMC / DEPARTMENT OF TRANSLATIONAL MEDICINE AND NEUROGENETICS / UNIVERSITY OF STRASBOURG
USIAS: UNIVERSITY OF STRASBOURG INSTITUTE FOR ADVANCED STUDY

EDUCATION

- 1973–1975: Postdoc, Dept of Medical Genetics, U. of Toronto, Canada
- 1975–1983: Reader then Assistant Professor, Biochemistry and Molecular Biology, Faculty of Medicine, Strasbourg
- 1984–2003: Associate Professor, then Professor of Medical Genetics, Faculty of Medicine and CHU Strasbourg, head of Human Molecular Genetics Research group
- 1985–2015: Founder and Head of DNA diagnostic laboratory, Strasbourg University Hospital
- 2002–2009: Director (2002–2007) or adjunct director (2007–2009) of IGBMC in Strasbourg
- 2003–2016: Professor at Collège de France, chair of Human Genetics
- Since 2012 Chair in Human genetics at USIAS, University of Strasbourg
- Since 2017 President of Fondation Maladies Rares
- Since September 2016 Life-long Emeritus Professor at the University of Strasbourg
- 2022 Kavli Prize in Neurosciences (Oslo)

SCIENTIFIC INTEREST

- JL Mandel participated, in P. Chambon's group in Strasbourg, to the discovery of multiplicity of mammalian RNA polymerases (1970), of exon-intron structure of vertebrate genes (1977–78) and published the first study showing a correlation between DNA methylation and gene expression (Mandel and Chambon, 1979).
- In 1982, he initiated a human genetic project, starting with mapping of disease loci on the X chromosome. This led to the discovery, in 1991, of the unstable triplet repeat expansion and abnormal DNA methylation in fragile X syndrome. His team then discovered similar mutations in dominant and recessive ataxias (SCA2, SCA7, Friedreich ataxia), analyzed repeat instability in families and populations and the pathomechanisms of fragile X and polyglutamine expansion disorders. In the pre-NGSeq era, his team identified singly or as major collaborator several other monogenic disease genes (adrenoleukodystrophy, Coffin-Lowry syndrome, myotubular myopathy, ataxia with vitamin E deficiency, BBS10 and 12 in Bardet Biedl syndrome...), and for some of these diseases pursued studies on cognate genes function and diseases mechanisms.
- In parallel, he developed diagnostic and genetic counseling applications based on mutation detection and created and directed a molecular diagnostic lab at Strasbourg University hospital
- His current research interests focus on intellectual disability (ID) and overlapping neurodevelopmental disorders: this includes a) GenIDA, a web-based international participatory study of comorbidities and natural history in genetic forms of ID and ASD, b) developing, with A. Piton NGS molecular diagnosis for ID-related neurodevelopmental disorders, and identifying novel ID genes and functional effect of candidate mutations.

LATEST PUBLICATIONS

- Colin F, Burger P... Koolen DA, Mandel JL; GenIDA, a participatory patient registry for genetic forms of intellectual disability provides detailed caregiver-reported information on 237 individuals with Koolen-de Vries syndrome. *Genetics in Medicine Open Volume 1*, 2023, 100817
- Burger P. Colin F... Kleefstra, T, Parrend, P, Piton, A, Koolen, DA, Mandel JL ; GenIDA: an international participatory database to gain knowledge on health issues related to genetic forms of neurodevelopmental disorders *J Neural Transmission* 2023, 130/3 459–471
- Depienne, C; Mandel, JL; 30 years of repeat expansion disorders: What have we learned and what are the remaining challenges? *Am J Hum Genet* 2021 108 764–785
- Hagerman, RJ; Berry-Kravis, E; Hazlett, HC; Bailey, DB; Moine, H; Kooy, RF; Tassone, F; Gantois, I; Sonenberg, N; Mandel, JL; Hagerman, PJ Fragile X syndrome *Nature Reviews Disease Primers* 2017 3:1–19
- Redin C, Gérard B, Lauer J,... Olivier-Faivre L, Mandel JL, Piton A. Efficient strategy for the molecular diagnosis of intellectual disability using targeted high-throughput sequencing. *J Med Genet.* 2014 Nov;51(11):724–36. doi: 10.1136/jmedgenet-2014-102554.

Intellectual disability: a frequent condition, 1500 rare genetic disorders and counting: from genomics to participatory research

JEAN LOUIS MANDEL

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Intellectual disability (ID) defined by an IQ <70 and deficit in learning and in adaptive functioning, acquired before 18y, affects about 2% of children or young adults, and is the most common indication for medical genetics consultations. It is a considerable burden for affected patients and their families, and for the health, educational and social system. It is often associated to other neurodevelopmental disorders, notably autism or childhood onset epilepsy. Thanks to the considerable progress in sequencing technology in the past 15 years from exome sequencing and now whole genome sequencing, up to 1500 genes implicated in monogenic forms of ID have been identified and new genes are being identified each month.

I will briefly present current work in our laboratory (Dr Hervé Moine and coll.) on the mechanisms of the fragile X mental retardation syndrome (FXS), the most common familial form of ID, due to the deficiency in the mRNA binding protein FMR1 and to a mutation mechanism that we and others discovered in 1991 that associates unstable expansion of a CGG repeat in the 5'UTR of FMR1 and abnormal DNA methylation in the 5' regulatory region of the gene. Unstable repeat expansions have since been found to cause 40 distinct neurological or neuromuscular disorders

(review in Depienne and Mandel, 2021). While work on FraX mouse models had identified a metabotropic glutamate receptor (mGluR5) as a promising therapeutic target (2002–2010), three clinical trials by Novartis and Roche failed to demonstrate improvement using behavioural measures as primary end-points (2014). We found that diacylglycerol kinase kappa (DGKk) is a main mRNA target of FMRP in cortical neurons and is downregulated in the absence of FMRP in the brain of Fmr1 KO mouse model (Tabet et al. 2016). We recently showed that AAV delivery of a FMRP independent form of DGKk corrects abnormal cerebral diacylglycerol homeostasis and FXS relevant behavioral phenotypes in the Fmr1 KO mouse, suggesting that DGKk is a therapeutic target in FXS (Habbas et al. 2022).

In the past 10 years I focused on a) the GenIDA project, a web-based international participatory study of comorbidities and natural history in genetic forms of ID and autism (Burger et al. 2023, Colin et al. 2023) and b) developing, with Dr Amélie Piton, molecular diagnosis for neurodevelopmental disorders, identifying novel ID genes and their genotype-phenotype correlations, with in some cases (NARS1, NOVA2 genes) unexpected mutations mechanism (Manole et al. 2020, Mattioli et al. 2020).



Marion NEUKAM

BETA LABORATORY UMR7522 / FSEG STRASBOURG

EDUCATION

- 2018: Qualification for the Function as Associate Professor
 - CNU, section 06 (Management)
- 2017: PhD "International Innovation Management"
 - University of Strasbourg, BETA (UMR 7522), Bürkert SAS (Defended on September 26th, 2017)
 - Title: The continuous generation of discontinuous innovations in international organizations
- 2013: MASTER OF SCIENCE "German-French Innovation Management"
 - University of Augsburg (G), University of Rennes 1 (F)
- 2011: BACHELOR OF ARTS "German-French Studies"
 - University of Regensburg (G), University of Clermont-Ferrand (F)

SCIENTIFIC INTERESTS

- International Innovation Management
- Knowledge Management
- Creativity Management
- Values-based innovation management
- Sustainability and CSR practices

LATEST PUBLICATIONS

- Bollinger, B., Neukam, M., (forthcoming). Réussir la transition durable face aux défis mondiaux: mobiliser les capacités dynamiques dans les organisations européennes. Management International (MI), forthcoming.
- Bollinger, B., Neukam, M., Guittard, C., 2023. Vers une RSE stratégique: une contrainte stimulant l'innovation. Innovations, Vol. 72 No. 3, pp. 65-102.
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- Neukam, M., Guittard, C., 2018. Reach for the stars: knowledge sharing in international organizations. Journal of Innovation Economics Management 27, 9-35.

Create long-term relations with stakeholders to favor sustainable open innovation : The case of Japan.

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Even though it is well known that long-term relationships with international stakeholders are crucial for sustainable open innovation (OI), there is still a gap about how firms can actually create and maintain them. This study addresses this gap by investigating Japanese public and private actors to analyze how they manage such long-term relationships with their international stakeholders. Japanese actors are known for their unique capacity to develop long-term oriented strategies that include successful long-term relationships with their internationally distributed partners. Therefore, a qualitative multiple case study design was employed, involving 12 semi-structured interviews with actors from diverse sectors in Japan. Data analysis through vertical and horizontal coding revealed that technology leadership is a fundamental driver for sustainable OI in international business. By applying stakeholder theory, we found that Japanese firms use their technological advantages to (1) select appropriate international partners, to (2) align internal processes with varying external demands regarding sustainability per country, and to (3) maintain those relationships successfully over time. However, challenges such as rigid decision-making processes, limited digitalization, and varying international regulations were identified as barriers to optimizing sustainable OI. The study highlights therefore the necessity of sufficient human capital to succeed the societal shift towards

sustainability in addition to technology leadership.

This research contributes to the literature on sustainable OI by explaining how firms can achieve long-term relationships with their international stakeholders and provide practical recommendations for firms and policymakers. KEY WORDS: sustainable open innovation; Japan; international business; stakeholder theory, long-term orientation.

Our recent research has enhanced CDC activity by introducing galactose-containing sugars into anti-HER2 antibodies, utilizing galectin-3 interactions to inhibit internalization.¹⁾ Additionally, studies on nuclear medicine therapy using astatine (²¹¹At) have shown promise for targeted cancer treatment. PET imaging with zirconium (⁸⁹Zr) followed by ²¹¹At labeling has demonstrated suppression of pancreatic cancer.²⁾ Furthermore, improvements in antibody linkers, such as the inclusion of cleavage sites and nuclear translocation signal peptides, have increased cytotoxicity.³⁾

These studies aim to improve the functionality of antibody therapeutics by controlling their dynamics through chemical biology approaches. We are committed to continuing this research with creativity, adhering to our motto of «considering research and development until the First in Human trials,» with the ultimate goal of developing antibody therapeutics that can be marketed as drugs in the future.



SHORT CV

Dr. Kei Ohkubo, Chemistry Doctor (Ph.D. Engineering), now is a Professor of Chemistry of Institute for Advanced Co-Creation Studies and Institute for Open and Transdisciplinary Research Initiatives, Osaka University, Japan. He earned his Ph.D. degree from Graduate School of Engineering, Osaka University in 2001. He was working as a JSPS fellow and a JST research fellow at Osaka University (2001–2005), a designated associate professor in Osaka University (2005–2014) and a specially appointed professor at Osaka University (2014–2017). He has been a full professor at Osaka University since 2017.

SCIENTIFIC INTEREST

Photocatalyst; C-H oxygenation; C1 chemistry, Photodynamics, Reactive oxygen species

LATEST PUBLICATIONS

- 9-(4-Halo-2,6-xylyl)-10-methylacridinium Ion as an Effective Photoredox Catalyst for Oxygenation and Trifluoromethylation of Toluene Derivatives, Ohkubo, K.; Matsumoto, S.; Asahara, H.; Fukuzumi, S. ACS Catal. 2024, 14, 2671–2684.
- Supramolecular Nanosheet Formation Induced Photosensitisation Mechanism Change of Rose Bengal Dye in Aqueous Media, Bunno, A.; Shigemitsu, H.; Yoshikawa, A.; Osakada, Y.; Fujitsuka, M.; Ishiwari, F.; Nishikubo, R.; Saeki, A.; Ohkubo, K.; Mori, T.; Kida, T. Chem. Commun. 2024, 60, 889–892.
- One-step Antibacterial Modification of Polypropylene Nonwoven Fabrics via Oxidation Using Photo-activated Chlorine Dioxide Radical, Yamamoto, K.; Asahara, H.; Harada, K.; Itabashi, Y.; Ohkubo, K.; Inoue, T., J. Mater. Chem. B 2023, 11, 5101–5107.
- Chlorine-radical-mediated C–H Oxygenation Reaction Under Light Irradiation, Itabashi, Y.; Asahara, H.; Ohkubo, K. Chem. Commun. 2023, 59, 7506–7517.

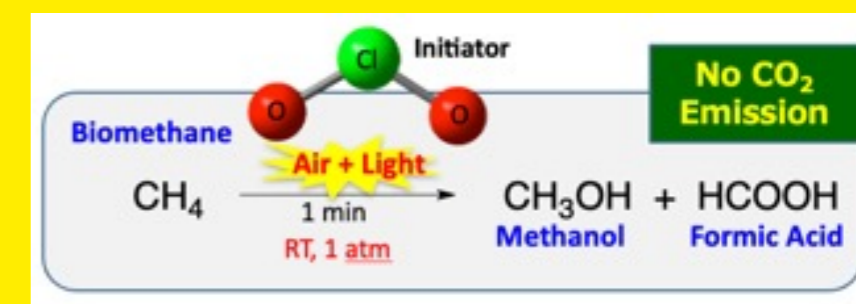
Photodriven C-H Oxygenation of Hydrocarbons with Chlorine Dioxide

KEI OHKUBO

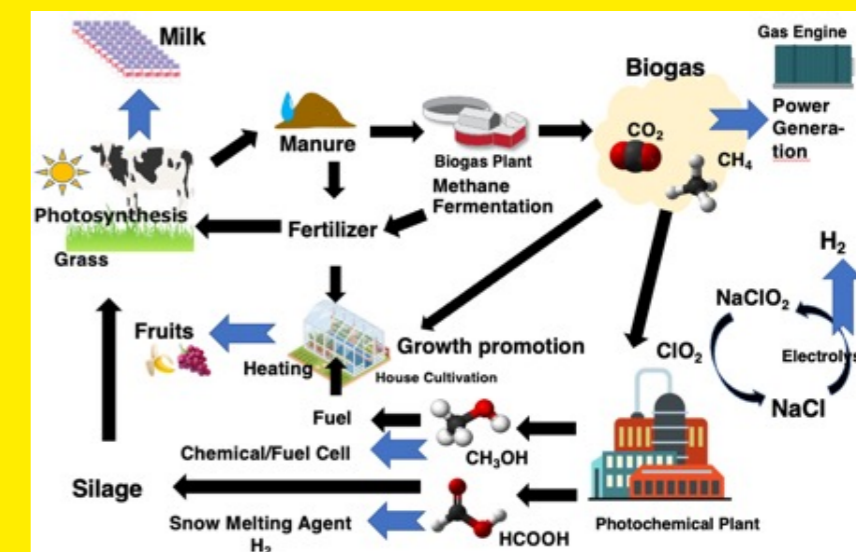
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Selective aerobic oxygenation of CH₄ into liquid products without the concomitant formation of CO₂ and CO has served as an elusive target reaction. Chlorine dioxide radical (ClO₂•) acts as an efficient oxidizing agent in the selective oxygenation of methane under photoirradiation. Here we report that oxygenation of methane in gas phase photochemically examined in the presence of ClO₂• using batch- and flow-type reactors. Photoirradiation (365 nm LED) of mixed gas containing methane and chlorine dioxide resulted in formation of methanol and formic acid in a 3,500 mL batch-type glass reactor. The conversion of methane after 40 min photoirradiation was 31% to yield methanol and formic acid. The yields of methanol and formic acid were 62% and 4%, respectively, based on the initial concentration of ClO₂• determined by ¹H NMR spectroscopic measurements. On the other hand, photochemical reaction also occurred in a flow photoreactor as shown in Fig. 1. The ratio of formation of methanol and formic acid was 20:80. The rate of formation of methanol and formic acid depends on LED light intensity, O₂ concentration and ClO₂• concentration, indicating that methane oxygenation occurred via radical chain processes. Mechanistic studies for formation methanol and formic acid revealed that the C-H bond of methane was activated with chlorine radical (Cl•) generated by photoinduced decomposition of ClO₂•. Thus, the present study provides an environmentally benign approach towards the photooxidation of organic compounds. The

1) Ohkubo, K; Hirose, K. *Angew. Chem. Int. Ed.* 2018, 57, 2126.



photochemical oxygenation of methane containing biogas using ClO₂• reported herein could be generalized to provide novel application for usage of biogas instead of gas electric power generation in biogas plant. We would like to establish the carbon neutral circular-type dairy type system as shown in Figure.





Laurent RUHLMANN

LABORATORY OF ELECTROCHEMISTRY OF THE PHYSICAL CHEMISTRY OF THE SOLID STATE / FACULTY OF CHEMISTRY / UNIVERSITY OF STRASBOURG
INSTITUTE OF CHEMISTRY / UMR N° 7177 (CNRS)

EDUCATION

Prof. Dr. Laurent Ruhlmann received his MS from University Louis Pasteur at Strasbourg, France. He had completed his PhD at the University Louis Pasteur at Strasbourg in 1997. After one post-doctorate at the Freie Universität Berlin in Germany in 1998, he became associate professor at the University Paris-Sud 11 now named Saclay University (France). He is now full professor in chemistry since 2011 in the University of Strasbourg where he is the team leader of the Laboratory of Electrochemistry and of Chemical Physics (Institute of Chemistry, UMR 7177). France. 6 June 1997.

SCIENTIFIC INTEREST

- Topics of the research: "Electrosynthesis of oligo(iso)porphyrins", "Synthesis of polyoxometalates and study of their electrocatalytic properties", "Synthesis and study of new polyoxometalate – porphyrin(s) hybrid systems including photovoltaic properties", "Studies of various electro(photo)switchable systems"; "Electrocatalysis (CO₂RR, HER, ORR, NO₃RR, OER, etc.)", "Fabrication and study of (photo)electrochromic materials and supercapacitors", "DEMS for (photo)electrocatalysis (DEMS = Differential Electrochemical Mass Spectroscopy)".
- Keywords: Electrochemistry, Electrocatalysis, Photoelectrocatalysis, Spectroelectrochemistry, Porphyrin, Polyoxometalate, Switchable systems, NO₃RR, HER.

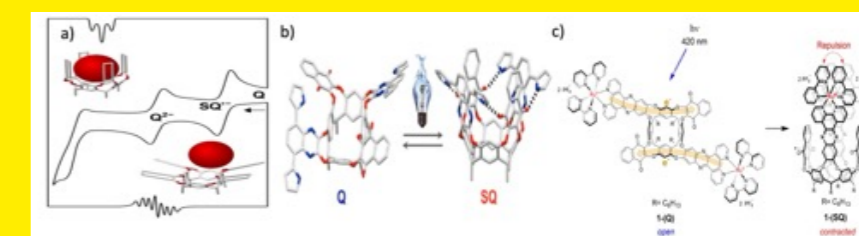
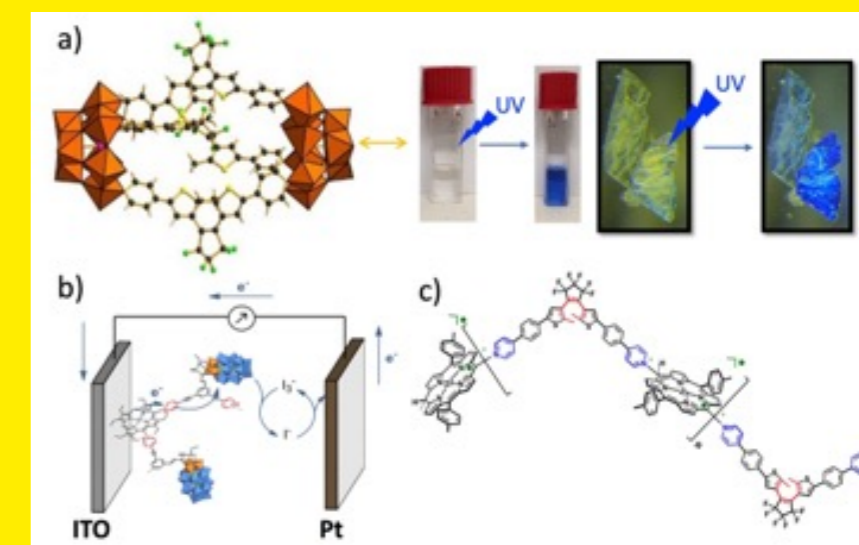
LATEST PUBLICATIONS

- J. V. Milić T. Schneeberger, M. Zalibera, F. Diederich C. Boudon, L. Ruhlmann* "Spectro-Electrochemical Toolbox for Controlling and Monitoring Photoredox-Driven Molecular Gripping", *Electrochimica Acta*, 2019, 313, 544-560.
- Y. Lv, X. Yang, W. Du, P. Ma, H. Wang, A. Bonnefont, D. Wright, C. Zhang, L. Ruhlmann,* "An Efficient Electrochromic Supercapacitor Based on Solution-Processable Nanoporous Poly[tris[4-(3,4-ethylenedioxythiophene)phenyl]amine]", *ChemSusChem*, 2020, 13, 3844-3854.
- Y. Gu, Q. Li, Y. Huang, Y. Zhu, Y. Wei,* L. Ruhlmann,* "Polyoxovanadate-IodoBodipy Supramolecular Assemblies: New Agents for High Efficiency Cancer Photochemotherapy", *Chem. Comm.* 2020, 56(19), 2869-2872.
- Y. Liang, M. N. Sokolov, M. A. Mikhaylov, H. Ibrahim, M. Goldmann, S. Choua, N. Le Breton, C. Boudon, V. Badets, A. Bonnefont, L. Ruhlmann,* "A 3D electropolymerized thin film based on an isoporphyrin and on pyridine end-decorated molybdenum(II) halide cluster: photoelectrochemical and impedance properties", *Electrochimica Acta*, 2021, 388, 138493.
- Z. Huo, Y. Liang, Y. Lv, F. Melin, P. Hellwig, H. Ibrahim, M. Goldmann, C. Boudon, V. Badets, A. Bonnefont, L. Ruhlmann,* "Enhancement of photocurrent by incorporation of Preyssler type polyoxometalate protected nanoparticles in polyporphyrin films", *Chem. Comm.* 2021, 57, 1482-1485.
- Z. Song, L. Miao, L. Ruhlmann, Y. Lv, L. Li, L. Gan, M. Liu "Proton-Conductive Supramolecular Hydrogen-Bonded Organic Superstructures for High-Performance Zinc-Organic Batteries", *Angew. Chem.*, 2023, 62, 13, e202219136.
- Y. Zhou, A. Bonnefont, C. Boudon, L. Ruhlmann, V. Badets,* "Nitrite reduction catalysed by Keggin polyoxometalates: a DEMS study of the volatile products.", *J. of Catalysis*. 2022, 405, 212-223.
- M. Choudhari, J. Xu, A. I. McKay, C. Guerrin, C. Forsyth, H. Z. Ma, L. Goerigk, R. A. J. O'Hair, A. Bonnefont, L. Ruhlmann,* S. Aloise, C. Ritchie* "A photo-switchable molecular capsule: sequential photoinduced processes", *Chemical Science*, 2022, 13, 13732-13740.

Photo(redox)active and photo(electro)switchable materials based on polyoxometalates and (iso)porphyrins

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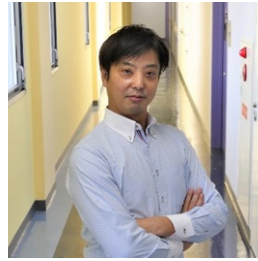
The presentation will be divided into two parts. The first part will be on the development of hybrid systems incorporating polyoxometalates (POMs) which is a promising approach to elaborate new redox active materials. To expand the practical applications, their association to a visible-light photosensitizer is needed and has been explored (Fig. 1). In this context, we have also developed a method of electropolymerization of POMs based on nucleophilic attack onto the electrogenerated porphyrin radical cation or dications. The formation of hybrid POM-porphyrin copolymeric films (Fig. 1b) can be obtained by the electro-oxidation of porphyrin in the presence of the hybrid POM bearing two pyridyl groups (Py-POM-Py).[1-2] Using the same methodology, the synthesis of a diarylethene-(iso)porphyrin photoswitchable copolymer has been developed (Fig. 1c). The incorporated diarylethene maintains its reversible photochromism upon the UV-Vis radiation with multiple cycles of ring-opening and closing.[3] A photo-switchable molecular capsule based on Keggin-type POM and diarylethene has been also formed and studied (Fig. 1a). [4] In the second part, the photoredox-switchable molecular grippers based on resorcin[4]arene cavitated platforms equipped with alternating quinone (Q) and quinoxaline walls carrying hydrogen bond donating groups will be presented. The semiquinones (SQ) state can be generated electrochemically and photochemically.[5] It



was shown that these systems adopt an open conformation in the oxidized Q state until redox interconversion to the paramagnetic SQ radical anion provides the stabilization of the closed form through hydrogen bonding.

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- Z. Huo, S. Yang, D. Zang, R. Farha, M. Goldmann, H. Xu, B. Antoine, G. Izzet, A. Proust, L. Ruhlmann *Electrochimica Acta*, 2021, 368, 137635.
- Y. Liang, M. N. Sokolov, M. A. Mikhaylov, H. Ibrahim, M. Goldmann, S. Choua, N. Le Breton, C. Boudon, V. Badets, A. Bonnefont, L. Ruhlmann, 2021, *Electrochimica Acta*, 2021, 388, 138493.
- Z. Huo, V. Badets, H. Ibrahim, M. Goldmann, H. Xu, T. Yi, C. Boudon, L. Ruhlmann, *Eur. J. Org. Chem.* 2021, 6636.
- M. Choudhari, J. Xu, A. I. McKay, C. Guerrin, C. Forsyth, H. Z. Ma, L. Goerigk, R. A. J. O'Hair, A. Bonnefont, L. Ruhlmann, S. Aloise, C. Ritchie, *Chemical Science*, 2022, 13, 13732-13740.
- J. V. Milić T. Schneeberger, M. Zalibera, F. Diederich C. Boudon, L. Ruhlmann, *Electrochimica Acta*, 2019, 313, 544-560. in biogas plant. We would like to establish the carbon neutral circular-type dairy type system as shown in Figure.



Yuji SATO

DEPT. OF LASER MATERIALS PROCESSING

JOINING AND WELDING RESEARCH INSTITUTE/ OSAKA UNIVERSITY

EDUCATION

- ▶ April 2001 – March 1997: Tokai University, Bachelor of Engineering (Dept. of Electrical Engineering)
- ▶ April 2001 – March 2005: Graduate School of Engineering, Tokai University, Dr of Engineering

SCIENTIFIC INTEREST

My areas of research interest are laser-material interactions including laser welding, laser additive manufacturing for metal, pulse laser processing and so on. Fundamental research for laser thermal processing is also under research by using high energy synchrotron radiation monochromatic X-rays and a high-speed camera. Laser welding for metals such as Iron, Aluminum, Copper and Titanium is also in my research interest.

LATEST PUBLICATIONS

- ▶ Shumpei Fujio, Yuji Sato, Mao Sudo, Keisuke Takenaka, Koji Tojo, Timotius Pasang & Masahiro Tsukamoto, Spatter reduction in deep penetration welding of pure copper using blue-IR hybrid laser, *Welding in the World* (2024)
- ▶ Keisuke Takenaka, Yuji Sato, Shumpei Fujio, Masahiro Tsukamoto, Comparison of melting efficiency between blue, green, and IR lasers in pure copper welding, *Journal of Laser Applications* 35, 042012 (2023)
- ▶ Kyohei Maeda, Yuji Sato, Reiichi Suzuki, Tetsuo Suga, Masahiro Tsukamoto, Influences of cold-sprayed steel interlayer on mechanical properties of laser welded steel/Al lap joints, *Journal of Materials Processing Technology* 118103 (2023)
- ▶ Yuji Sato, Naoki Shinohara, Tomoki Arita, Masami Mizutani, Tomomasa Ohkubo, Hitoshi Nakano and Masahiro Tsukamoto, "In situ x-ray observation of keyhole dynamics for laser beam welding of stainless steel with 16kW disk laser" *Journal of Laser Applications* 33, 042043 (2021)
- ▶ Yuji Sato, Yuta Mizuguchi, Keisuke Takenaka, Norio Yoshida, Sasitorn, Srisawadi, Dhriti Tanprayoon, Tomomasa Ohkubo, Tetsuo Suga, Masahiro, Tsukamoto, "Pure Titanium Fabrication with Spatter-less Selective Laser Melting in Vacuum" *Results in Optics* (2021),

Additive Manufacturing for Metal with Blue Laser

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Pure copper has been industrial applied for various industrial products such as heat exchangers and automobile motors because of having excellent thermal conductivity and electrical conductivity. Next generation heat exchangers and automotive motors etc. are required to have more complicated shapes for improvement of these properties. Laser metal deposition (LMD) method is one of additive manufacturing technologies, which is suitable for making metal objects with complex shape rapidly. Herein it is important point to consider the light absorption rate of pure copper. The light absorption rate of Cu is greatly depended on the wavelength of the light. A fiber laser and a disk laser were generally employed in the conventional LMD method at a wavelength of 900-1100 nm. In this wavelength range, the light absorption rate of the copper has only 10%, which results in inefficient to melt the pure copper. On the other hand, the light absorption rate of the copper increases drastically as the wavelength of light become shorter and reaches about 60% in blue region at the wavelength of 450 nm, about 6 times higher than the conventional laser at near infrared region.

Thus, we have developed a multi beam LMD system with blue diode lasers instead of NIR laser to try to form a three-dimensional object of pure copper rod. Fig.1 shows the experimental setup for the 3D rod formation. In order to clarify the mechanism of the rod formation, the melting and solidification process during a rod formation was captured with a high-speed video camera. A cross-sectional area of pure copper was observed and evaluated the pore generation to clarify the forming mechanism. In addition, electric resistivity of the pure copper rod was measured an electric resistivity and conducted elemental analysis with electron probe micro analyser.

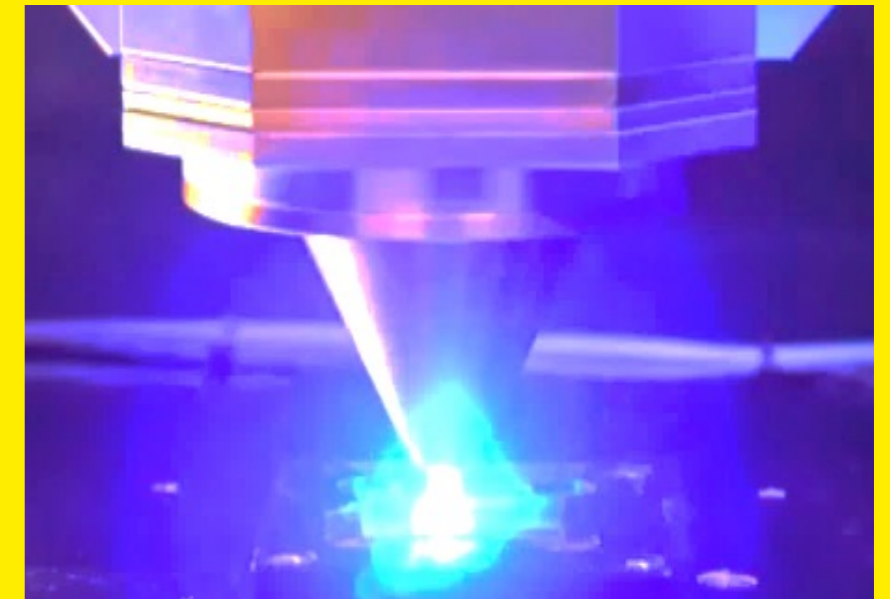


Fig.1 Experimental set up for 3D rod formation

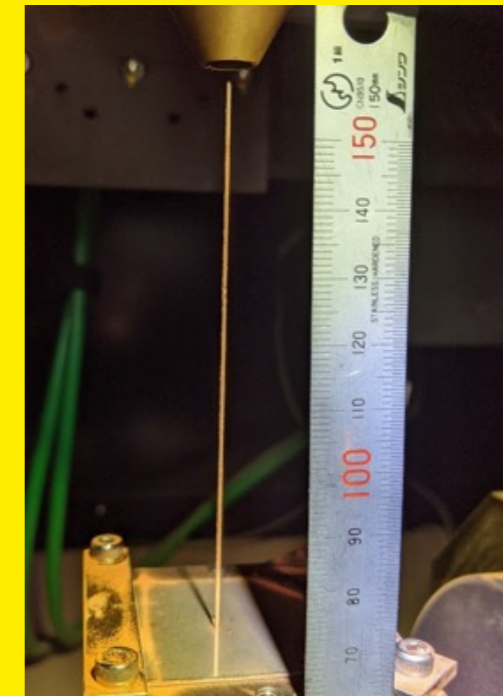


Fig.2 Additive manufactured pure copper rod



Catherine SCHUSTER

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UNIVERSITY OF STRASBOURG AND NATIONAL INSTITUTE FOR HEALTH AND MEDICAL RESEARCH (INSERM)

AFFILIATION

National Institute for Health and Medical Research – Inserm
University of Strasbourg

EDUCATION

Dr Catherine Schuster obtained her PhD, in Molecular and Cellular Biology, at IBMC at the University of Strasbourg, on the regulation of human viruses gene expression. During her post-doctoral training her scientific interests were focused on RNA Pol III transcription and the identification and characterization of specific transcription factors. She obtained a tenured position in 1995 at the National Institute for Health and Medical Research (Inserm). In 2000, she joined Dr Marie-Paule Kieny's team at the Institute of Virology, Strasbourg and started as young group leader on hepatitis C virus molecular biology. In the frame of this project, she obtained the Young Investigator Prize of the BNP Paribas - FRM foundation that supported her research during several years.

Since 2011, Dr Catherine Schuster is Director of Research at Inserm and is the Deputy Head of the Institute for Translational Medicine and Liver Disease at Strasbourg, France, including the laboratory of Excellence HepSYS (Director Pr Thomas Baumert).

SCIENTIFIC INTERESTS

- Current research, includes the molecular characterization of hepatic virus-host interactions, the role of lipid metabolism during hepatic life cycle and more recently the identification of new therapeutic avenues for chronic liver diseases and liver cancer.
- From 2018 to 2023, Dr Catherine Schuster was the Director of the Doctoral School for Life Sciences and Health from the University of Strasbourg. From 2018 to 2020, she was the nationwide coordinator for the evaluation of research in Life Science Environment and Health, for the High Council for Research and Higher Education. Since 2019, she is the Inserm scientific referent for the Regio Grand-Est, deeply involved in the implementation of Inserm national research strategies at Strasbourg University of Excellence and Lorraine University of Excellence. In 2023, she was awarded by the Ministry of Research as Chevalier de l'Ordre National du Mérite.
- Advanced liver diseases, ex vivo models for liver therapy, pre-clinical proof of concept studies

LATEST PUBLICATIONS (SELECTION)

- Roehlen N, Muller M, Nehme Z, Crouchet E, Jühling F, Del Zompo F, Cherradi S, Duong FHT, Almeida N, Saviano A, Fernández-Vaquero M, Riedl T, El Saghire H, Durand SC, Ponsolles C, Oudot MA, Martin R, Brignon N, Felli E, Pessaux P, Lallement A, Davidson I, Bandiera S, Thumann C, Marchand P, Moll S, Nicolay B, Bardeesy N, Hoshida Y, Heikenwälder M, Iacone R, Toso A, Meyer M, Elson G, Schweighoffer T, Teixeira G, Zeisel MB, Laquerriere P, Lupberger J, Schuster C, Maily L, Baumert TF. Treatment of HCC with claudin-1-specific antibodies suppresses carcinogenic signaling and reprograms the tumor microenvironment. *J Hepatol.* 2023 78:343-355. doi: 10.1016/j.jhep.2022.10.011. PMID: 36309131
- Roehlen N#, Saviano A#, El Saghire H, Crouchet E, Nehme Z, Del Zompo F, Jühling F, Oudot MA, Durand SC, Duong FHT, Cherradi S, Gonzalez Motos V, Almeida N, Ponsolles C, Heydmann L, Ostyn T, Lallement A, Pessaux P, Felli E, Cavalli A, Sgrignani J, Thumann C, Koutsopoulos O, Fuchs BC, Hoshida Y, Hofmann M, Vyberg M, Viuff BM, Galsgaard ED, Elson G, Toso A, Meyer M, Iacone R, Schweighoffer T, Teixeira G, Moll S, De Vito C, Roskams T, Davidson I, Heide D, Heikenwälder M, Zeisel MB, Lupberger J, Maily L, Schuster C, Baumert TF. A monoclonal antibody targeting nonjunctional claudin-1 inhibits fibrosis in patient-derived models by modulating cell plasticity. *Sci Transl Med.* 2022 14 :eabj4221. doi: 10.1126/scitranslmed.abj4221.PMID: 36542691 # co-first
- Crouchet E, Li S, Sojoodi M, Bandiera S, Fujiwara N, El Saghire H, Zhu S, Qian T, Rasha FA, Del Zompo F, Barrett SC, Schaeffer E, Oudot MA, Ponsolles C, Durand SC, Ghoshal S, Arora G, Giannone F, Chung RT, Slovic N, Van Renne N, Felli E, Pessaux P, Lupberger J, Pochet N, Schuster C, Tanabe KK, Hoshida Y, Fuchs BC, Baumert TF. Hepatocellular carcinoma chemoprevention by targeting the angiotensin-converting enzyme and EGFR transactivation. *JCI Insight.* 2022 Jul 8;7(13):e159254. doi: 10.1172/jci.insight.159254.

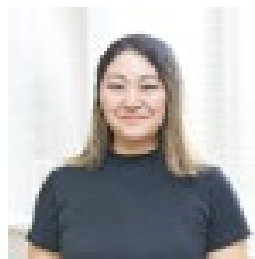
From innovation to Application in advanced Liver diseases

CATHERINE SCHUSTER

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In developed countries, organ fibrosis accounts for up to 45% of death and is a major risk factor for tumor development across organs. In the liver, the major causes of liver fibrosis are chronic hepatitis B, B/D and C, alcoholic liver disease (ALD) and non-alcoholic steatohepatitis (NASH). Liver cancer develops mainly from fibrotic liver. The aging population combined with lifestyle changes, obesity, and diabetes result in a rapidly increasing number of patients with advanced liver diseases and hepatobiliary cancer world-wide. Novel therapeutic approaches for advanced liver diseases and cancer are needed to break the plateau of approved therapies. When fibrosis progresses to

cancer, only a minority of patients are eligible for curative approaches. A major roadblock for the development of efficient anti-fibrotic therapies is the lack of model systems predicting treatment efficacy in patients. Since many compounds in clinical development target specifically human biology (such as monoclonal antibodies), patient-derived models expressing the human target are needed for fast-track development. Using an in silico screening method combined with advanced bioinformatic analysis, and state-of-the-art human derived cell models, we identified potential candidates for advanced liver disease innovative therapies.



Ai SHINOBU

LABORATORY FOR MOLECULAR SIMULATION / WPI PREMIUM RESEARCH

INSTITUTE FOR HUMAN METAVERSE MEDICINE / OSAKA UNIVERSITY

EDUCATION

- 2016: PhD from the Hebrew University of Jerusalem, Israel.
- 2017-2018: Post doctoral researcher in the University of Tokyo and Tokyo Institute of Technology.
- 2018-2023: Post doctoral researcher in RIKEN.
- 2023-current: Specially appointed associate professor, Osaka University.

SCIENTIFIC INTEREST

- In my research, I am interested in studying the relationship between the structure, dynamics, and function of biomolecules at the molecular level to elucidate the causes of disease and develop novel therapeutic strategies. The technique that I use is molecular dynamics simulations (MD). MD is a computational method in which the model of a system is propagated in time according to the laws of physics. From such simulations, we can learn about the mechanisms of biological processes at atomic resolution. Understanding the mechanism of a process, such as a disease, involves identifying which interactions are important or how the active structure differs from the inactive one. This knowledge allows us to suggest intervention methods, such as drugs or vaccines.
- Main keywords: molecular dynamics simulations, computational biophysics, structure-dynamics-function relation, protein structure, precision medicine

LATEST PUBLICATIONS

- Chyży, P., Kulik, M., Shinobu, A., Re, S., Sugita, Y., & Trylska, J. (2024). Molecular dynamics in multidimensional space explains how mutations affect the association path of neomycin to a riboswitch. *Proceedings of the National Academy of Sciences*, 121(15), e2317197121.
- Shinobu, A., Re, S., and Sugita, Y., The impact of inhibitor size and flexibility on the binding pathways to c-Src kinase. *bioRxiv* (2022).
- Shinobu, A., Re, S., & Sugita, Y. (2022). Practical Protocols for efficient sampling of kinase-inhibitor binding pathways using two-dimensional replica-exchange molecular dynamics. *Frontiers in molecular biosciences*, 9.
- Shinobu, A., Kobayashi, C., Matsunaga, Y., & Sugita, Y. (2021). Coarse-grained modeling of multiple pathways in conformational transitions of multi-domain proteins. *Journal of Chemical Information and Modeling*, 61(5), 2427-2443.
- Terayama, K.^{*}, Shinobu, A.^{*}, Tsuda, K., Takemura, K., & Kitao, A. (2019). evERdock BAI: Machine-learning-guided selection of protein-protein complex structure. *The Journal of Chemical Physics*, 151(21), 215104. (^{*}equal contribution)
- Shinobu, A., Kobayashi, C., Matsunaga, Y., & Sugita, Y. (2019). Building a macro-mixing dual basin Gō model using the Multistate Bennett Acceptance Ratio. *Biophysics and physcobiology*, 16, 310-321. DOI: 10.2142/biophysico.16.0_310
- Shinobu, A., Takemura, K., Matubayasi, N., & Kitao, A. (2018). Refining evERdock: Improved selection of good protein-protein complex models achieved by MD optimization and use of multiple conformations. *The Journal of Chemical Physics*, 149(19), 195101.

Deciphering the molecular origin of cellular processes using advanced molecular dynamics simulations

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Every disease has a molecular origin, necessitating a molecular-level understanding to develop effective solutions and therapeutics. While experimental methods have significantly advanced our understanding of molecular mechanisms, they come with inherent limitations, most critically in obtaining a molecular description, especially for intermediate or metastable states. Molecular Dynamics (MD) simulations offer a powerful approach, providing a bottom-up methodology that allows for the control of all components and conditions with atomic resolution. This precision enables the detailed observation of molecular interactions and behaviors that are often inaccessible through experimental means alone. Despite their advantages, MD simulations face challenges such as the difficulty in achieving comprehensive sampling. Addressing these challenges effectively requires the utilization of advanced methods and substantial computational resources. In this talk, I will present several projects that address key biological questions and advance medical research through the application of MD simulations.

In the first study we investigate the pathological mechanisms behind the Ala711-Glu714 deletion mutation in the ectodomain of the insulin-like growth factor 1 receptor (IGF1R). This mutation is linked to clinical symptoms, including developmental deformities and insulin resistance. It is suggested that the mutant IGF1R may interact

differently with the insulin receptor (INSR), possibly forming hybrid receptors that impair insulin sensitivity. Using MD simulations, we examine the effect of this mutation on conformational changes and interaction patterns. Understanding the molecular details of the diseased IGF1R-INSR interaction is the first step in designing new therapeutic strategies.

In the second study we explore the complete binding pathway of inhibitors to protein kinases. By conducting massive MD simulations, we gain valuable insights into the binding of these inhibitors, ranging from small molecules to peptides. We examine the intermediate steps of the binding mechanism and the role that inhibitor flexibility plays. Understanding these aspects is essential for designing effective inhibitors in cancer therapy.

In the last project, we take a novel approach to designing a vaccine against the SARS-CoV-2 virus, targeting the spike protein which plays a major role in the virus's entry into human cells. The continuous emergence of new variants makes it challenging to design long-lasting vaccines. Despite changes in the amino acid sequence, one consistent feature of the spike protein is its glycan shield, which plays a critical role in evading immune recognition. In this work, we employ MD simulations to relocate glycan sites with the aim of uncovering new epitopes and making the protein more vulnerable to immune responses.



EDUCATION

- He received his Ph.D. degree in 2003 from Osaka University, under the guidance of Prof. Akira Harada, focusing on the polymerization catalyst using group 4 transition metal catalyst. He was selected as a Research Fellow of the Japan Society for the Promotion of Science (JSPS) in 1999–2002.
- In 2004, he served as an assistant professor for Professor Akira Harada, dealing with supramolecular polymer based on cyclodextrin derivatives. In 2016, he joined the Graduate School of Science at Osaka Univ. as a lecturer. In 2018, he joined the Graduate School of Science at Osaka Univ. as a professor.
- During the winter of 2003, as a visiting fellow, he worked at Prof. Jeffrey M. Stryker's lab, Department of Chemistry, the Univ. of Alberta. In 2011, he worked at Prof. Philip A. Gale's lab, Department of Chemistry, the Univ. of Southampton as a visiting researcher. In 2018, he visited to Prof. Nicolas Guiseppone of the Institute Charles Sadron, the Univ. of Strasbourg as a visiting professor.

SCIENTIFIC INTEREST

- Supramolecular Materials (Self-Healing Materials, Stimuli-Responsive Materials)
- Composite Materials with Cellulose and Carbon Materials.
- Polymerization and Degradation with Enzymatic Catalyst (Lipase etc.)

LATEST PUBLICATIONS

- ACS Appl. Mater. Interfaces 2024, 16, 39777–39785. (DOI:10.1021/acscami.3c04395)
- ACS Polymers Au 2023, 3, 394–405. (DOI:10.1021/acspolymersau.3c00010)
- ACS Appl. Mater. Interfaces 2023, 15, 39777–39785. (DOI:10.1021/acscami.3c04395)
- NPG Asia Mater. 2022, 14, 32.
- Adv. Mater. 2020, 32, 2002008.

Design and Functions of Polymeric Materials Based on Supramolecular Science

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Supramolecular materials have received much attention, owing to their effects on adhesion, switches, mechanical properties based on molecular recognitions. Functional supramolecular polymers are relevant not only for switching properties but also for a range of other applications. Our research group has employed cyclodextrins (CDs) as host molecules. Herein, I would like to introduce our studies to realize self-healing and tough properties based on reversible and movable crosslinks (Fig. 1)¹.

Self-healing materials: Adhesion between the host hydrogel with CD and the guest hydrogel with an adamantyl (Ad) group was investigated. The CD hydrogel selectively adheres to the Ad guest hydrogel without mismatching (Fig. 2). Next, we prepared self-healing materials based on CD and Ad units. The adhered materials showed almost complete recovery of the initial material strength².

Movable crosslinked materials: We prepared elastomers with movable cross-links by copolymerization between CD monomers and main chain monomers (single movable cross-network (SC) elastomers) (Fig. 3). SC and KP elastomers show a higher toughness and Young's modulus than covalently cross-linked elastomers.

References:

- Ikura, R.; Takashima, Y. et al. *NPG Asia Mater.* 2022, 14, 10.
- Park, R.; Takashima, Y. et al. *Adv. Mater.* 2020, 32, 2002008.
- Ikura, R.; Takashima, Y. et al. *Mol. Syst. Des. Eng.* 2022, 7, 733.

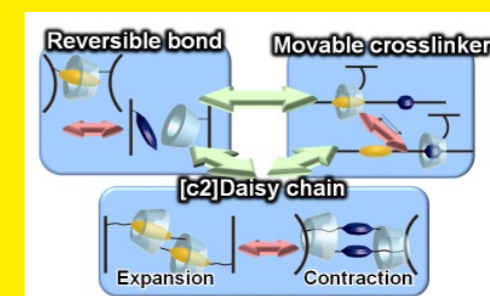


Figure 1. Network design of supramolecular materials based on reversible interaction and movable crosslinker.

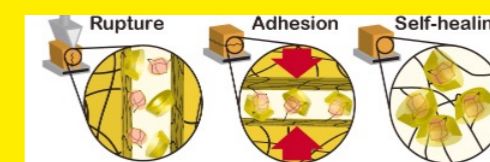


Figure 2. Self-healing materials based on host-guest interactions.

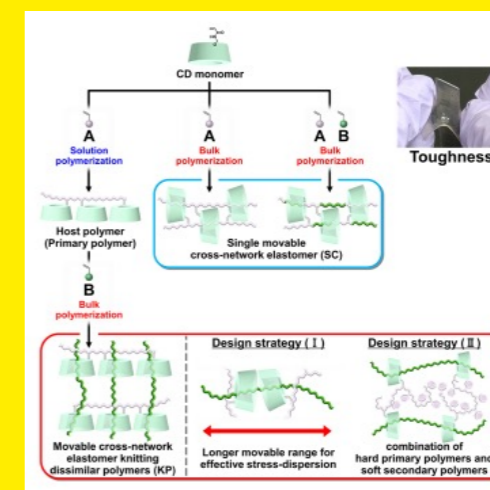


Figure 3. Bulk polymerization of liquid main chain monomers in the presence of a linear polymer bearing acetylated-cyclodextrin (TAC CD) results in movable cross-network elastomer knitting dissimilar polymers (KP elastomer). The KP elastomers successfully improve the mechanical properties based on two design strategies.



Sho YAMASAKI

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DEPUTY DIRECTOR, PROFESSOR, LABORATORY OF MOLECULAR IMMUNOLOGY / IFREC
DIRECTOR, CENTER FOR INFECTIOUS DISEASE EDUCATION AND RESEARCH / CIDER
OSAKA UNIVERSITY

EDUCATION

- 1991: B.S. Kyoto University, Agriculture
- 1993: M.S. Kyoto University, Agriculture
- 1999: Ph.D. Kyoto University, Graduate School of Agriculture

SCIENTIFIC INTEREST

- C-type lectin receptors
- Unconventional T cell receptors
- Clonotypic analysis of T cell receptors and antigens

LATEST PUBLICATIONS

- Reis E Sousa C*, Yamasaki S*, Brown GD*. Myeloid C-type lectin receptors in innate immune recognition. *Immunity* 2024
- Ito E, et al. Sulfated bile acid is a host-derived ligand for MAIT cells. *Sci. Immunol.* 2024
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- Shimizu, et al. Direct activation of microglia by α -glucosylceramide causes phagocytosis of neurons that exacerbates Gaucher disease. *Immunity* 2023
- Lu, et al. Identification of conserved SARS-CoV-2 spike epitopes that expand public cTfh clonotypes in mild COVID-19 patients. *J. Exp. Med.* 2021
- Nagata, et al. Helicobacter pylori metabolites exacerbate gastritis through C-type lectin receptors. *J. Exp. Med.* 2021

Sensing self- and non-self metabolites via immune systems

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IMMUNOLOGY FRONTIER RESEARCH CENTER (IFREC)
OSAKA UNIVERSITY
YAMASAKI@BIKEN.OSAKA-U.AC.JP

Our bodies are continuously exposed to injurious insults by infection and tissue damage, most of which are primarily sensed by immune receptors to maintain tissue homeostasis. Although immune recognition of proteins or nucleic acids has been well characterized, the molecular mechanisms by which immune receptors discriminate "lipids" to elicit suitable immune responses remains elusive. Recent studies have demonstrated that C-type lectin (CLR) family and particular T cell receptor (TCR) function as immune sensors for adjuvant derived from pathogens and damaged-self, thereby promoting innate/acquired immunity. In this symposium, we will discuss how these receptors coordinately recognize lipid components to achieve appropriate immune responses against injurious stimuli.



Takashi HAYASHI

PROFESSOR, DEPARTMENT OF APPLIED CHEMISTRY
GRADUATE SCHOOL OF ENGINEERING, OSAKA UNIVERSITY

EDUCATION

- Ph.D., Graduate School of Engineering, Kyoto University, Japan (1990)
- M. Sc., Graduate School of Engineering, Kyoto University, Japan (1987)

SCIENTIFIC INTEREST

- Takashi Hayashi received his Doctor degree from Kyoto University in 1991 under the supervision of Professor Y. Itoh. He joined Kyoto University as an Assistant Professor in 1990. In addition, he worked as a Visiting Scientist with Prof. C.-H. Wong in the Scripps Research Institute at La Jolla, California in 1995-1996. Then, he moved to Kyushu University, as an Associate Professor in 1997. He was promoted to be a Full Professor at Department of Applied Chemistry, Osaka University in 2005. He received Progress Award in Synthetic Organic Chemistry, Japan, and 1st JPP Young Investigator Award in Porphyrin Chemistry in 2000. Furthermore, he received the Chemical Society of Japan Award for Creative Work in 2009, and Humboldt Research Award from Die Alexander von Humboldt-Stiftung in 2022. His current research interests lie in the area of bioinorganic chemistry, emphasizing directions to the modification of hemoproteins to obtain functionalized proteins and biomaterials. He has published ca. 220 original papers.

LATEST PUBLICATIONS

- Redox Engineering of Myoglobin by Cofactor Substitution to Enhance Cyclopropanation Reactivity, Kagawa, Y.; Oohora, K.; Himiyama, T.; Suzuki, A.; Hayashi, T. *Angew. Chem. Int. Ed.* in press.
- Chitin- and Streptavidin-Mediated Affinity Purification Systems: A Screening Platform for Enzyme Discovery, Kato, S.; Takeuchi, K.; Iwaki, M.; Miyazaki, K.; Honda, K.; Hayashi, T. *Angew. Chem. Int. Ed.* 2023, 62, e20230376.
- Evolutionary Engineering of Cp^{*}Rh(III) Complex-Linked Artificial Metalloenzyme with a Chimeric α -Barrel Protein Scaffold, Kato, S.; Onoda, A.; Schwaneberg, U.; Hayashi, T. *J. Am. Chem. Soc.* 2023, 145, 8285–8290.
- Focusing on a nickel hydrocorphinoid in a protein matrix: methane generation by methyl-coenzyme M reductase with F430 cofactor and its models, Miyazaki, Y.; Oohora, K.; Hayashi, T. *Chem. Soc. Rev.* 2022, 51, 1629–1639.
- Hemoproteins Reconstituted with Artificial Metal Complexes as Biohybrid Catalysts, Oohora, K.; Onoda, A.; Hayashi, T. *Acc. Chem. Res.* 2019, 52, 945–954.

Conversion of myoglobin to Artificial metalloenzymes responsible for non-natural chemical reactions

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Myoglobin is a dioxygen storage protein with protoheme IX (heme b) as a metallocofactor. The heme cofactor is bound into the heme pocket via non-covalent and coordination interactions. It is known that the heme cofactor can be released from the heme pocket and then the apoprotein is available under acidic conditions. Therefore, our group has focused on inserting artificial metallocofactor into apomyoglobin to generate new metalloenzymes. Furthermore, compared to conventional catalysts, there are some advantages to using a protein scaffold: Proteins can act as an attractive second coordination sphere, and it is easy to modify the structure of the coordination sphere to optimize substrate binding and reaction proceeding events by mutagenetic approach. Here, I present the following reactions catalyzed by myoglobin reconstituted with artificial metallocofactors (Figure 1).

- Hydroxylation of inert alkane species: Although cytochrome P450 and myoglobin have the same heme b cofactor, myoglobin shows no activity for alkane hydroxylation. Recently, our group prepared myoglobin reconstituted with manganese porphycene which can convert ethylbenzene to 1-phenylethanol with high enantioselectivity.
- Nitrile synthesis: The conversion of aldoximes to nitriles is an important industrial process. Myoglobin reconstituted with iron porphycene is found to catalyze the dehydration of aldoximes as seen in aldoxime dehydratase.
- Cyclopropanation of styrene with ethyl benzoacetate (EDA): Myoglobin reconstituted with iron porphycene is found to accelerate the formation of iron-carbenoid species affording 1-phenylcyclopropane derivative.

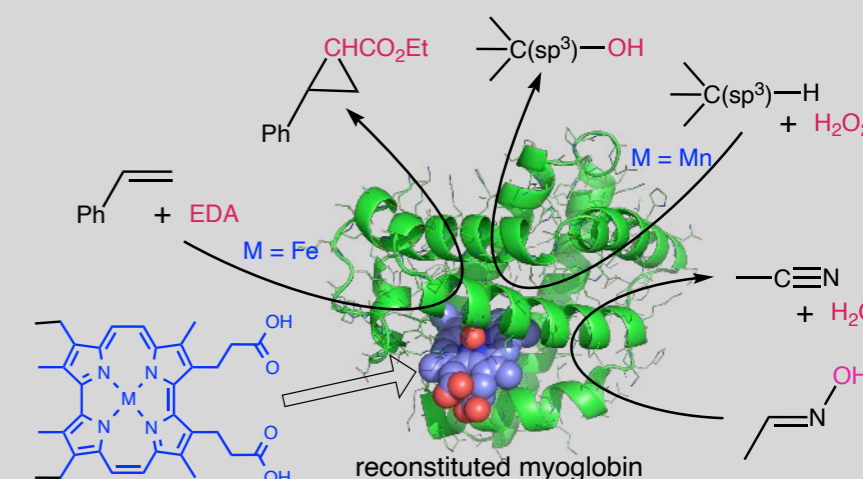


Figure 1. Catalytic reactions by myoglobin reconstituted metalloporphycenes.



EDUCATION

Henri-Pierre Jacquot de Rouville graduated from the University Paul Sabatier of Toulouse. In 2007, he joined C. Joachim's Group and obtained a PhD degree for his synthesis of technomimetic molecules for nanomechanical applications under the supervision of Professor G. Rapenne (CEMES-CNRS, Toulouse). From 2010 to 2012, he joined Professor J. F. Stoddart's Group as a postdoctoral fellow where he investigated the chemistry of mechanically interlocked molecules. Then, he moved back to France where he worked as a postdoctoral fellow with N. McClenaghan (ISM, Bordeaux). In 2013, he was appointed as Chargé de Recherche (Full Time Researcher at the CNRS) at the laboratory ITODYS, Paris. In November 2017, he moved at the Institut de Chimie of Strasbourg where he joined the LSAMM research group.

SCIENTIFIC INTEREST

Molecular Mechanics | Molecular Machines and Switches | Organic Synthesis | Supramolecular Chemistry | Electro- and Photo-Active Molecules.

LATEST PUBLICATIONS

- ▶ Johnny Hu, Jean-Pierre Launay, Alain Chaumont, Valérie Heitz,* Henri-Pierre Jacquot de Rouville* Chem. Eur. J., 2024, e202401866.
- ▶ A. Edo-Osagie, D. Serillon, F. Ruani, X. Barril, C. Gourlaouen, N. Armaroli,* B. Ventura,* H.-P. Jacquot de Rouville,* V. Heitz* J. Am. Chem. Soc., 2023, 145, 10691–10699.
- ▶ J. Hu, S. Adrouche, E. S. Gauthier, N. Le Breton, M. Cecchini, C. Gourlaouen, S. Choua, V. Heitz,* H.-P. Jacquot de Rouville* Chem. Eur. J., 2022, 28, e202202840.
- ▶ H.-P. Jacquot de Rouville,* J. Hu, V. Heitz,* ChemPlusChem, 2021, 86, 110–129
- ▶ J. Hu, J. S. Ward, A. Chaumont, K. Rissanen, J.-M. Vincent,* V. Heitz,* H.-P. Jacquot de Rouville,* Angew. Chem. Int. Ed., 2020, 59, 23206–23212.

Acridinium-based Recognition Units: from Molecular Tweezers to Persistent Radicals

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We recently reported bis-acridinium supramolecular receptors able to bind guest molecules (Figure 1)¹. Surprisingly, acridinium-based receptors are scarcely exploited in supramolecular chemistry despite their multi-responsive properties. Indeed, they respond to chemical and redox signals by reversibly modifying their shape, their chemical and optical properties². This class of receptors exhibits i) self-complementary behaviors leading to the formation of entwined dimers, 1a ii) narcissistic self-sorting, 1b iii) -donor/ -acceptor host-guest behaviors and were also studied as selective phase transfer agents in perfluorocarbons³. In addition, the multi-switching properties of these receptors were investigated to alter their recognition events with guests. An increasing complexity has been achieved by the introduction of acridinium units in mechanically interlocked molecules⁴. The dual-readout of the mechanical response of a [2]rotaxane structure was thus probed. The combination of the acridinium unit to another multi-responsive unit, namely porphyrin core, led to complex supramolecular systems exhibiting more than eight different states⁵. Finally, when the acridinium core is derivatized properly at its 9-position, a new photochemistry was observed leading to a stable radical able to dimerize in perfluorocarbons and H₂O.

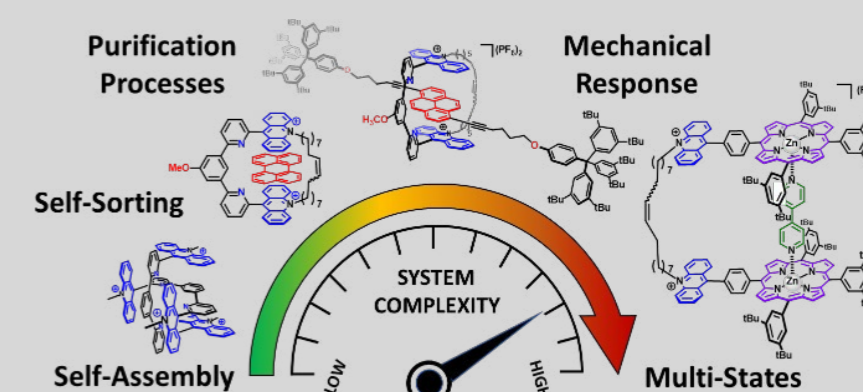


Figure 1. Increasing Complexity in Multi-Responsive Acridinium Supramolecular Systems.

[1] a) H.-P. Jacquot de Rouville, N. Zorn, E. Leize-Wagner, V. Heitz, Chem. Commun., 2018, 54, 10966–10969; b) H.-P. Jacquot de Rouville, C. Gourlaouen, V. Heitz, Dalton Trans., 2019, 48, 8725–8730.

[2] H.-P. Jacquot de Rouville, J. Hu, V. Heitz, ChemPlusChem, 2021, 86, 110–129.

[3] J. Hu, J. S. Ward, A. Chaumont, K. Rissanen, J.-M. Vincent, V. Heitz, H.-P. Jacquot de Rouville, Angew. Chem. Int. Ed., 2020, 59, 23206–23212.

[4] J. Hu, S. Adrouche, E. S. Gauthier, N. Le Breton, M. Cecchini, C. Gourlaouen, S. Choua, V. Heitz, H.-P. Jacquot de Rouville, Chem. Eur. J., 2022, 28, e202202840.

[5] A. Edo-Osagie, D. Serillon, F. Ruani, X. Barril, C. Gourlaouen, N. Armaroli, B. Ventura, H.-P. Jacquot de Rouville, V. Heitz, J. Am. Chem. Soc., 2023, 145, 10691–10699.



Marie Pierre Krafft

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EDUCATION

Marie Pierre Krafft is Research Director at the Institut Charles Sadron (ICS, CNRS), University of Strasbourg (France). After her Ph.D. Thesis with Prof. Jean G. Riess at the University of Nice, she did post-doctoral work as a JSPS Fellow with Prof. Toyoko Imae (University of Nagoya), and in the US in San Francisco (Prof. Joel Cohen) and in the R&D department of Alliance Pharmaceutical (San Diego). Marie Pierre started an independent scientific career at the ICS in 1997 as Chargée de Recherches. She was an Invited Scientist by Goho Life Science Foundation in Kyoto (Doshisha University, 2013).

SCIENTIFIC INTERESTS

Marie Pierre's research focusses on the design, engineering and investigation of fluorocarbon-promoted molecular self-assemblies, colloids and interfaces, including nanoemulsions, microbubbles, micelles and vesicles, life-mimicking active droplets, fluorocarbon-based therapeutics. More recently, she is also concerned with PFAS-related environmental remediation issues, including remediation of heavily polluted sites. She published over 200 papers, holds 12 patents, delivered over 100 invited lectures in International Meetings. She received Awards from the French Académie des Sciences, Chemical Society of Japan, Fluorous Technology Committee, is a Member of the European Academy of Sciences and Chevalier de la Légion d'honneur. She is Co-Editor-in-Chief of Current Opinion in Colloid and Interface Science and sits on the Editorial Board of Scientific Reports and of Frontiers in Soft Matter. She led several projects with potential benefits for the society in the medical field and in material science that were supported by the European Commission, National Agency for Research, CNRS-Innovation and by Industry (Areva, Superbranche, TotalEnergies).

Keywords: Fluorocarbons, Perfluoroalkylated amphiphiles, Supramolecular assemblies, Fluid interfaces, Nanoemulsions, Microbubbles, Soft Matter, PFAS pollution remediation.

LATEST PUBLICATIONS

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Surfactantless, nonpolar microemulsions with distinctive film spreading behavior for applications in Energy

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Thermodynamically stable oil-in-water (or water-in-oil) microemulsions are transparent, macroscopically homogenous solutions that have applications in cleaning, cosmetics, food, pharmaceuticals, and other industries. A surfactant is required to form the interfacial film between the oil and aqueous phases. Surfactantless microemulsions were achieved by adding to water a second polar solvent, a so-called hydrotrope that is water-soluble yet capable of solubilizing the oil. However, the surfactantless microemulsions reported so far all contain water or a polar solvent and rely on a balance between hydration forces and entropy. Such aqueous microemulsions have no application potential in organic media. We report waterless, surfactantless, nonpolar

microemulsions that comprise a hydrocarbon, a semi-fluorinated alkane and a fluorocarbon, and form spontaneously. They have a droplet size of a few nanometers and are thermodynamically stable, as assessed by dynamic light scattering and small-angle X-ray scattering. The nanodrops readily adsorb to a hydrocarbon/air interface, as assessed by bubble profile analysis tensiometry, thereby covering it with a thin, nonflammable fluorocarbon film. When protected by this spontaneously adsorbed film, a cooling fluid used in Li-ion battery thermal management did not exhibit a measurable flash point. These fire-proofing nonpolar microemulsions could be the next-generation cooling fluids for electric vehicle batteries.



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EDUCATION

- Ph.D. Graduate School of Science, Osaka University, Japan (1996)
- M. Sc., Graduate School of Science, Osaka University, Japan (1993)

SCIENTIFIC INTEREST

- Takashi Kubo graduated from Osaka University in 1991, received M.Sc. in 1993 under the guidance of Professor Ichiro Murata, and received Ph.D. in 1996 under the guidance of Professor Kazuhiro Nakasuji. After working at Mitsubishi Chemical Co., he joined Professor Nakasuji's group at Department of Chemistry, Graduate School of Science, Osaka University in 2000 as Assistant Professor. In 2006 he served as Associate Professor. Since 2006 he is Professor of Graduate School of Science, Osaka University. His research interests are structural and physical organic chemistry, mainly the syntheses and properties of polycyclic aromatic compounds with open-shell character, and the development of cooperative proton and electron transfer systems based on transition metal complexes.

LATEST PUBLICATIONS

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Recent studies on open-shell π -conjugated molecules

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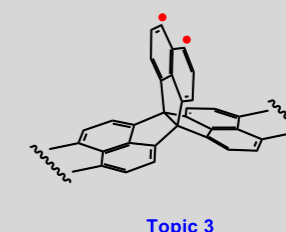
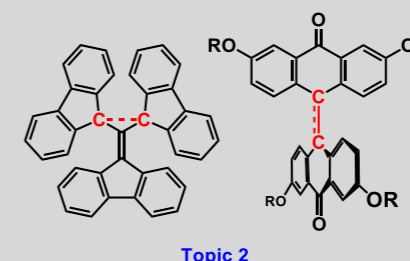
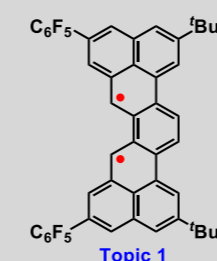
Research on organic radical species has become a pivotal domain within chemistry, fostering innovative advancements in the field. Since Gomberg's discovery of the triphenylmethyl radical in 1900, the chemistry of organic radicals has seen continuous progress. These radical species, characterized by unpaired electrons, typically defy the octet rule on their spin-center atoms, making them highly reactive. This inherent reactivity has been leveraged to use radical species as essential intermediates in constructing complex molecular frameworks.

The unique electronic structures of radicals, absent in many closed-shell compounds, have attracted the interest of physical chemists. Various measurement techniques have been developed to elucidate the properties of these radical species. Furthermore, their magnetic moments, derived from electron spins, and the easily

exchangeable electron characteristics of singly occupied molecular orbitals (SOMOs), have enabled applications in materials with functionalities such as magnetism and electroconductivity. It is evident that deepening our understanding of radical species has relied heavily on the creation of novel radical compounds, which has played a critical role in advancing this research area.

My talk focuses on the following three topics:

- Elucidation of the electronic structure of singlet diradical molecule and exploration of its characteristic properties
- Bonded or not? Investigation of weakly coupled C-C covalent bonds
- Tip-induced rearrangement of 1,8-naphthalenediyl fixed on PAH nanoribbons. Studies of these diradicaloid compounds provide new insights into the interactions between unpaired electrons.





Pierre RABU

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EDUCATION

➤ Pierre Rabu, born in 1964 in Nantes, France, obtained his PhD in solid state chemistry from the University of Nantes, France, in 1990. He was then recruited by CNRS as researcher at IPCMS, Strasbourg, France to work on low-dimensional magnetic materials. He was short term JSPS fellow at Institute for Fundamental Organic Chemistry, Kyushu University, Fukuoka, Japan, in 1996 and visiting fellow of Advanced Materials Research Institute, University of New Orleans, USA, in 2001. He awarded the 1998 prize of the Solid State Chemistry division of the French Chemical Society and is Distinguished Fellow of the French Chemical Society (since 2021). In 1999, he received his Habilitation from the University Louis Pasteur, Strasbourg, France, on the theme «Low-dimensional magnetism: from molecules to hybrid materials». In 2005-2008, Pierre Rabu was director of the CNRS national group of research on Multifunctional Hybrid Materials. He was Head of the Department of Chemistry of Inorganic Materials of IPCMS (2014-2017). He is since 2018 the director of IPCMS, Strasbourg, France. Pierre Rabu authored more than 170 publications in peer reviewed journals or as books chapters.

SCIENTIFIC INTEREST

- General: Pierre Rabu focuses his activities on the design of molecular, inorganic or hybrid organic-inorganic solids, with a special emphasis on synthesis, structure-properties relationships, modelling and analysis of the magnetic behavior of Low-Dimensional systems. His current activities concern especially layered organic-inorganic magnetic and multifunctional materials, multifunctional hybrid materials and magnetic, photo active, chiral nanostructures, and metal coordination networks, with special emphasis on multiferroic systems.
- Main keywords: Materials chemistry, Inorganic structures, organic-inorganic hybrids, multifunctional structures, magnetism, photoluminescence, structure-property relationships.

LATEST PUBLICATIONS

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Multifunctional organic - inorganic hybrid structures using molecular bricks for magnetic, luminescent or electrocatalytic properties

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The development of hybrid systems to obtain multifunctional materials is finding applications in many fields of research¹. Among these materials, layered hydroxides or oxides are excellent candidates, as the possibility of functionalizing them with organic molecules has been widely demonstrated^{2,3}. Ion-exchangeable hydroxides or perovskites exhibit especially interesting physical properties such as magnetism, ferroelectricity or optical properties, for instance. These materials can be functionalized via insertion reactions. This key-feature allows to finely tune the interlayer spacing size and content, and hopefully the properties of the final hybrid compounds. Furthermore, these layered nanostructures can be exfoliated into nanosheets⁴, which can be considered as building blocks in the field of nanoarchitectonics⁵. In previous works, we have been particularly

interested in the functionalization of transition metal hydroxides with luminescent, magnetic or electro-catalytic molecules. More recently, we have been able to functionalize or post-functionalize an Aurivillius phase of formula Bi₂SrTa₂O₉ (BST), known for its ferroelectric properties. Hence, using microwave activation, we functionalized BST with a variety of molecules, including chiral or aromatic amines and poly-amines, (poly)alcohols, phosphonic acids, or luminescent molecules^{6,7,8}. Our investigation in inserting organic or inorganic molecular species in layered structures with different compositions using soft chemistry approaches will be presented. I will describe the methods and mechanisms used to functionalize these phases of increasing complexity in order to endow the obtained hybrids with new properties (chirality, luminescence, magnetic properties...).

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EDUCATION

- Ph.D. Graduate School of Engineering Science, Osaka University, Japan (1997)
- M. Sc., Graduate School of Engineering Science, Osaka University, Japan (1994)

SCIENTIFIC INTEREST

- Hiroshi Umakoshi is currently a Professor / Vice Dean in the Graduate School of Engineering Science at Osaka University in Japan. He obtained his PhD in Chemical Engineering at Osaka Univ., Japan in 1997. He worked as a post-doctoral fellow (JSPS) at Department of Biochemistry, School of Science, Lund University, Sweden, 1997 to 1998. Currently, he is conducting research on "Bio-Inspired Chemical Engineering", focusing on the utilization of "Self-Organizing System" as core materials. He is pioneering the systematic method to characterize the surface properties of the self-assembly systems. He is also working as a director of Society of Chemical Engineers, Japan (SCEJ), vice president of Society of Separation Process and Engineering, Japan (SSPEJ), and a councillor of Society of Membrane, Japan (SMJ). He is also a member of ACS and AIChE.

LATEST PUBLICATIONS

- Ni'matul Izza, Nozomi Watanabe*, Y. Okamoto, K. Suga, Y. Wibisono, N. Kajimura, K. Mitsuoka, Hiroshi Umakoshi*: Dependence of the Core-Shell Structure on the Lipid Composition of Nanostructured Lipid Carriers: Implications for Drug Carrier Design, *ACS Applied Nano Materials*, 2022, 5(7), 9958-9969
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Design Lipid Nano-carriers for Drug Delivery

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A "Biomembrane" is a highly-organized self-assembly of biomolecules (i.e. lipid, protein etc.) and a key interface for the survival of biological cell. The "Membranome" can be defined as the properties of vesicle (or liposome), which arise from the bilayer molecular assembly of amphiphiles, focusing on "emergent properties" which are not present in the individual components, and is gradually recognized as an important research methodology to investigate the potential functions of vesicles (or liposome) and to apply them for the bioprocess design. "Self-Organizing System", such as liposome or vesicle, possesses several benefits in the recognition of (bio) molecules, where it can recognize them with (i) electrostatic, (ii) hydrophobic interaction, and (iii) stabilization effect of hydrogen bonds at its surface. A key of next chemical engineering is the use of "Self-Organizing System", where "enthalpy-driven" nature of chemical process would be converted to "entropy-driven" one. We call this strategy as "Bio-Inspired Chemical Engineering".

As for potent application to design and development of nano medicine, nanostructured lipid carriers (NLCs) are a new generation of lipid vectors for drug delivery systems (DDSs), which are composed of solid and liquid lipids dispersed throughout the inner lipid matrix. In this presentation, a systematic method to characterize the "interface" of various NLCs will be introduced by selecting some case studies, such as (i) standard vesicles, (ii) model biomembranes, (iii) cubosomes, (iv) cataniosomes, and (v) covid19-carrier (DSPC/cholesterol/cationic lipid (SM102)). The method includes the (1) conventional physical characterization methods (i.e. DLS, SANS, etc) and (2) (our original) physicochemical ones (i.e. multi-probes fluorescence spectroscopy, time-resolved / decay-associated fluorescence spectroscopy, (surface enhanced) Raman spectroscopy etc). These systematic results can be used to clarify the design space of the NLC composition to show the drug delivery.

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