Title of Project : Molecular design of innovative drugs based on molecular assembly

NAGASAKI Yukio
(University of Tsukuba, Faculty of Pure and Applied Sciences, Professor)

Research Project Number : 19H05458 Researcher Number : 90198309
Keyword : Molecular assembling drug, Antioxidant, Parkinson disease, Oligo-nucleic acid, Cancer

【Purpose and Background of the Research】

Administration of conventional antioxidants such as vitamins and N-acetyl cysteine distribute nonspecifically and a serious disadvantage of destroying redox reactions in normal cells because of small molecules. We found that covalent attachment of antioxidants to macromolecules with self-assembling property suppresses uptake into normal cells and accumulates at inflammatory sites to effectively eliminate reactive oxygen species (ROS). This result indicates the possibility that the self-assembly of small molecules can realize pharmacological functions and therapeutic effects that cannot be obtained by small molecules alone. In this research, we develop a new drug discovery principle that exerts drug effects by self-molecular organization as a third drug modality, next to a conventional low molecular weight drugs and protein drugs. The results of this research are expected to be the foundation of innovative pharmaceutical industry and lead to the creation of patient-friendly medical technology.

【Research Methods】

This project is aimed at establishment of the concept for the molecular-assembling-drugs. Although amino acids and peptides show various physiological activities, and thus they are useful, they are water-soluble and rapid to metabolize and are difficult to carry and use to the target site. We have recently designed polypeptide based nano-assembles, which are stable under physiological conditions. After accumulation of the polypeptide in target site, it is metabolized to original amino acid by endogenic enzymes and functions as peptide drug. In addition to our original antioxidant self-assembling drugs, we will investigate versatile self-assembling drugs such as amino acids, fatty acids. Other types of molecular-assembling drugs such as the smart oligonucleotides incorporating a non-reactive molecule into the oligonucleotide, which can be activated by forming the hybridized complex with the target DNA or RNA. Self-assembling peptide derivatives that cause gelation at an extremely low concentration in a cancer cell, lead to selective cancer cell death. These new concepts will also be constructed.

【Expected Research Achievements and Scientific Significance】

Numerous numbers of synthetic drugs have been synthesized by organic synthesis for over 100 years. With the development of biotechnology in recent years, drug discovery is shifting from organic synthesis to biopharmaceutical synthesis. Based on such a paradigm shift, drug discovery technology has dramatically advanced and an extremely large market is anticipated, but due to protein engineering the cost of drug development is abnormally rising.

Unlike organic synthesis and biopharmaceuticals, the development of molecular assembling drugs is expected as a new drug discovery field (Fig.). As Japan is pioneering in the materials nanotechnology field, it is extremely important for us to develop a future academic field and create a new drug discovery field that does not follow the other countries. To discover new drugs and develop new medicine fields, it is important to take our own methods and way.

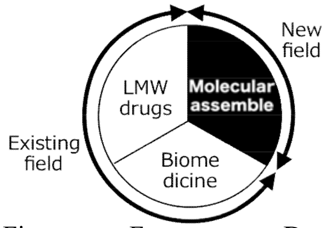

Fig. Future Drug Developments Area

【Publications Relevant to the Project】

- Yukio Nagasaki, Design and Application of Redox Polymers for Nanomedicine, ***Polymer Journal, (Review),*** Volume 50, No. 9, 821-836(2018). (10.1038/s41428-018-0054-6)
- Long Binh Vong, Shinya Kimura, Yukio Nagasaki, Newly designed silica-containing redox nanoparticles for oral delivery of novel TOP2 catalytic inhibitor for treating colon cancer, ***Advanced Healthcare Materials,*** Vol.6,1700428(2017) (0.1002/adhm.201700428)

【Term of Project】 FY2019-2023

【Budget Allocation】 481,700 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.ims.tsukuba.ac.jp/~nagasaki_lab/index.htm
happyhusband@nagalabo.jp

Title of Project : Molecular electron microscopy for dynamic studies on molecules and their assemblies

NAKAMURA Eiichi
(The University of Tokyo, Graduate School of Science, Project Professor)

Research Project Number : 19H05459 Researcher Number : 00134809
Keyword : Structural analysis, Electron microscopy, Microanalysis, Organic chemistry

【Purpose and Background of the Research】

Video imaging of the dynamic behavior of a single organic molecule captured by high-resolution electron microscopy was reported first in 2007 (Single Molecule Atomic-resolution Real-Time Electron Microscopy, SMART-EM), linking organic chemistry to EM that had then focused largely on analysis of periodic structures and solid samples in biological and materials research. With a recently acquired state-of-the-art EM equipped with an ultrafast camera, we will capture high-speed two-dimensional videos at millisecond, and also acquire nano level three-dimensional information. Our purpose is to establish a new experimental method to be called "molecular electron microscopy" for studying the dynamic behavior of molecules and molecular assemblies.

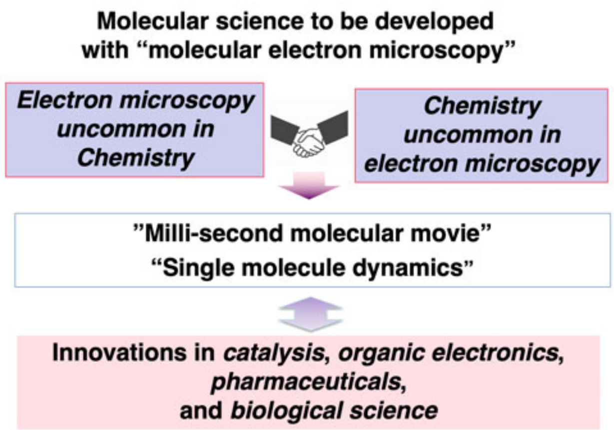

Figure. Research overview

【Research Methods】

SMART-EM is an imaging method fundamentally different from "cryo-EM" and "micro electron diffraction (ED)" in that it provides real time images of the dynamic behavior of a single molecule, enabling video imaging of single molecules and linking them to the understanding of macroscopic physicochemical properties and reactivities. The method will open up an experimental approach previously considered impossible, such as isolation and structure determination of a single molecule in a reaction mixture, and in situ observation of the time course of chemical reaction events.

It has been a chemists' dream to see in situ and at atomic resolution a molecule that changes its shape and reacts. The most advanced camera can capture 1,600 electron microscopic images per second. Through software development such as denoising and automatic video analysis, high-speed imaging of molecular motions and reactions will be achieved, providing hitherto unavailable basic knowledges in molecular science.

【Expected Research Achievements and Scientific Significance】

This research aims for the development of a variety of electron microscopic techniques centering on the SMART-EM method and solving problems in catalysis, organic electronics, pharmaceuticals, and life sciences. Elucidation of the dynamic behavior of molecular species, which cannot be studied by previously known methods, will be made possible by capturing and identifying a molecular amount of reaction intermediates and analyzing amorphous organic aggregates.

This study will realize a dream of people since Dalton's atomic theory in the 19th century, that is, seeing in situ the motions and reactions of the single molecules as they happen. By sharing such experience with young people, we will be able to make the world of atoms and molecules more familiar to people at large.

【Publications Relevant to the Project】

・M. Koshino, T. Tanaka, N. Solin, K. Suenaga, H. Isobe, E. Nakamura, Imaging of Single Organic Molecules in Motion, *Science*, **316**, 853, (2007).
・E. Nakamura, K. Harano, Chemical Kinetics Study through Observation of Individual Reaction Events with Atomic-Resolution Electron Microscopy, *Proc. Jpn. Acad., Ser. B*, **94**, 428-440, (2018).

【Term of Project】 FY2019-2023

【Budget Allocation】 475,200 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.chem.s.u-tokyo.ac.jp/~common/NakamuraLab.html
nakamura@chem.s.u-tokyo.ac.jp

Science and Engineering

Title of Project：Creation of two-dimensional conjugated polymer, coordination nanosheet, and manifestation of higher-order functions using high quality and hetero-structured nanosheets

NISHIHARA Hiroshi
(The University of Tokyo, Graduate School of Science, Professor)

Research Project Number：19H05460　Researcher Number：70156090
Keyword：two-dimensional material, metal complex, crystal, hetero-structure, energy storage

【Purpose and Background of the Research】

The coordination nanosheet (CONASH) refers to ultra-thin film of a two-dimensional (2D) conjugated polymers composed of metal ions and planar bridging organic π-ligands. We reported the nickelladithiolene (NiDT) CONASH, the first example to show metallic properties, in 2013. Contrarily to inorganic nanosheets such as graphene, CONASH can be synthesized at the liquid-liquid and gas-liquid interface. There are numerous combinations of metals and ligands, such that various chemical structures can be obtained. Also, most coordination reactions proceed under ambient conditions, such that easy and cheap bottom-up synthetic method can be employed. The purpose of this project is to open up new areas of CONASH research in fundamental science and engineering leading to further applications that will contribute to the advancement of our society.

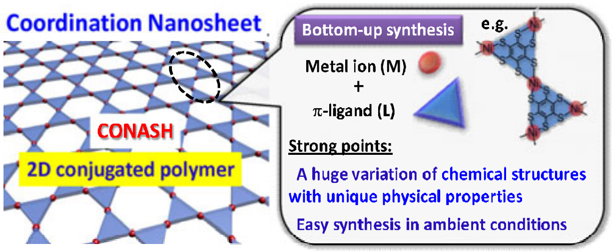

Fig. 1. Concept of CONASH.

【Research Methods】

In this research, the following four issues will be tackled; 1) to create new functional CONASHs by combining with a theoretical calculation, 2) to synthesize single crystalline CONASHs of high purity and large area (100 μm^2) for understanding the essential structure-property correlations, 3) to uncover ultimate physical and chemical functions based on the features of both metal complexes and 2D conjugated structures, and 4) to fabricate hetero-structures (van der Waals-layers and lateral hetero-junction) of CONASHs and discover their unique properties and functions. These issues will be investigated using our past research method and our collaborative research network with physicists and electronic engineers, but a giant leap is necessary in order to synthesize high quality CONASHs. We will achieve this leap by introducing our original new techniques and methods, and will find unprecedented functions and phenomena of CONASH. In particular, we will study on the electrochemical energy storage/conversion functions of CONASH in collaboration with Dr. Ken Sakaushi (NIMS).

【Expected Research Achievements and Scientific Significance】

It has been demonstrated that CONASH is a promising material group utilizable for various applications by the extensive researches since our report of the electronically conducting NiDT CONASH. However, there is still challenge for CONASH to install it in practical applications, *i.e.* a general synthetic approach to prepare high quality nanosheet samples in large scale. One of the aims of this project is to develop a method to obtain the high-quality sample of CONASHs, which directly leads to revealing intrinsic parameters of their physical and chemical properties important for basic science and manifesting high performance important for applications.
Other aims of this project are to design new functional CONASH to investigate ultimate physical and chemical functions, and to fabricate hetero-structures of CONASHs. The progresses of researches on these issues using high quality CONASHs will expand the field of basic and applied research on materials science, chemistry, physics, and electronic engineering etc.

【Publications Relevant to the Project】

- π-Conjugated Nickel Bisdithiolene Complex Nanosheet. T. Kambe, R. Sakamoto, K. Hoshiko, K. Takada, M. Miyachi, J. Ryu, S. Sasaki, J. Kim, K. Nakazato, M. Takata, H. Nishihara, *J. Am. Chem. Soc.* **2013**, *135*, 2462-2465.
- Coordination nanosheets (CONASHs): strategies, structures and functions. R. Sakamoto, K. Takada, T. Pal, H. Maeda, T. Kambe, H. Nishihara, *Chem. Commun.* (Feature article) **2017**, *53*, 5781-5801.

【Term of Project】 FY2019-2023

【Budget Allocation】 418,700 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.chem.s.u-tokyo.ac.jp/~inorg/
nisihara@chem.s.u-tokyo.ac.jp

Title of Project : Protein Encapsulation by Synthetic Cages for Functional Control and Structure Determination

FUJITA Makoto
(The University of Tokyo, Graduate School of Engineering, University Distinguished Professor)

Research Project Number : 19H05461 Researcher Number : 90209065

Keyword : Protein encapsulation, NMR structure analysis, X-ray structure analysis, self-assembly, cage compounds

【Purpose and Background of the Research】

The principal investigator (PI) has pioneered a variety of self-assembled hollowed complexes and created a number of new scientific concepts related to the functions of their inner nanocavities since 1990. In this project, we aim to explore the potential of proteins encapsulated within precisely designed molecular capsules. More accurately, we will develop our technology based on the following perspectives: 1) control the property of protein (e.g., stability, ligand affinity or selectivity), 2) control enzymatic reactivity (e.g., activity or new function) and furthermore 3) develop new analytical methodology (coupled with NMR, X-ray, MS or cryoEM etc.). We envision to contribute to the field of life science by providing them the preceding fundamental technologies.

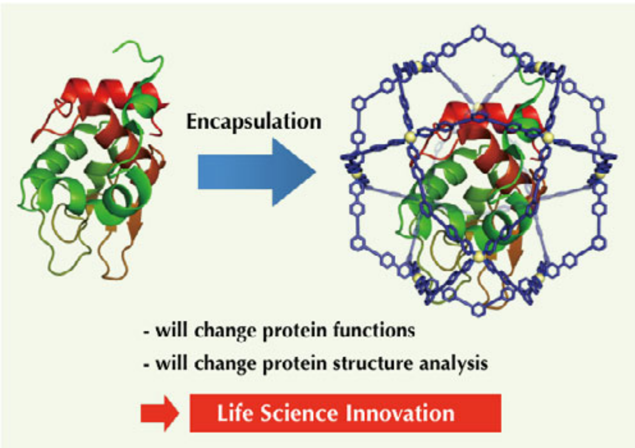

Figure 1. The basic concept of the project

【Research Methods】

We have already developed a mathematical design theory for the self-assembly of gigantic cage without critical upper size limits. Based on this theory, we further scale the size of synthetic molecular capsules. Basic methods for protein encapsulation in the cages have been also established. We are particularly interested in applications of the protein encapsulation that aids protein structural analysis. There still be many limitations in conventional protein structural analysis. Protein encapsulation in this study has the potential to solve some of the problems. As specific research projects, we will work on a) NMR data acquisition under non-biological conditions, b) Structural analysis of agglutinative proteins/peptides stabilized by encapsulation, c) Dynamic structural change analysis of proteins as typified by the folding process and d) New methodologies for facile X-ray or CryoEM structural analysis.

【Expected Research Achievements and Scientific Significance】

Taking the privilege to be the first one to explore this area of protein spatial modification, we are confident to unveil many fruitful results benefit multiple fields that handle protein molecules either in academic or industry. The true importance and necessity should accompany the following points: 1) the research stands on applicant's original science, 2) the research is not on the simple extension of the past, 3) no other groups has the similar research direction and 4) massive academic impact to be expected when it gets materialized.

【Publications Relevant to the Project】

・Self-Assembly of Tetravalent Goldberg Polyhedra from 144 Small Components, D. Fujita, Y. Ueda, S. Sato, N. Mizuno, T. Kumasaka, M. Fujit, Nature 2016, 540, 563-566.
・Protein encapsulation within synthetic molecular hosts, D. Fujita, K. Suzuki, S. Sato, M. Yagi-Utsumi, Y. Yamaguchi, N. Mizuno, T. Kumasaka, M. Takata, M. Noda, S. Uchiyama, K. Kato, and M. Fujita, Nature Commun. 2012, 3, 1093.

【Term of Project】 FY2019-2023

【Budget Allocation】 480,000 Thousand Yen

【Homepage Address and Other Contact Information】

http://fujitalab.t.u-tokyo.ac.jp
mfujita@appchem.t.u-tokyo.ac.jp

【Grant-in-Aid for Specially Promoted Research】

Science and Engineering

Title of Project : Development of "super-bio-functions" by plasma-activated biological substances

HORI Masaru
(Nagoya University, Center for Low-temperature Plasma Sciences, Professor)

Research Project Number : 19H05462 Researcher Number : 80242824
Keyword : plasma, Low-temperature Atmospheric Pressure Plasma, Plasma Medicine, Plasma Agriculture

【Purpose and Background of the Research】

We found that biological liquids irradiated with plasma (aggregate of active particles [radicals, ions, electrons, light]) exhibit highly selective anti-tumor effects against various cancers. We also found that plasma propagates central nerve cells that could not be conventionally reproduced and surprisingly promotes plant growth. We have also systematically analyzed effects of plasma-activated liquids on biological systems (gene expression, metabolism, immunity, and signal transduction) by developing plasma science within the fields of medical science and molecular biology. In this project, we plan to investigate the molecular structures and physical properties of plasma-activated biological substances and to integrally understand interactions among the substances and biological system to elucidate the expression of “super bio-functions” by plasma as a universal molecular mechanism in eukaryotes for processes such as cell death, proliferation, and differentiation. Based on the findings, we expect to provide an academic foundation for “Plasma Life Science” as a compass for pioneering new industries such as plasma medicine and agriculture, and will produce innovations to resolve problems with intractable and food shortages.

【Research Methods】

The primary objective is to focus on elucidating the molecular structure and physical properties of bioactive substances resulting from the interactions between plasma and biological fluids.

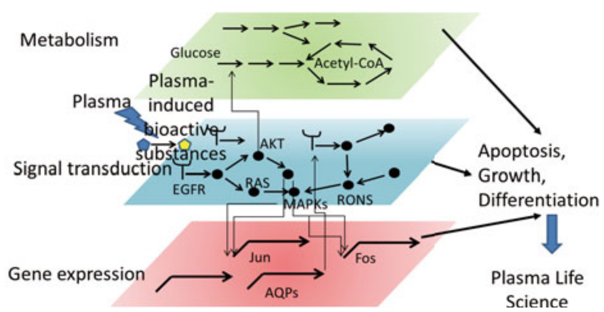

Figure 1 M olecular reactions between plasm -induced bioactive substances and living bodies.

Next, we will systematically investigate molecular reactions (signal transduction, gene expression, metabolism, immunity, hormones) between plasma-induced bioactive substance and the living body at the cellular level with respect to selective death and regeneration/proliferation phenomena caused by interactions between each substance and animal and plant cells (Figure 1). The second objective is to clarify the mechanisms of death, regeneration and growth from the transcriptome (exhaustive gene expression) and metabolomic analysis in animal models (mouse, rat) and plant models (model plants, strawberry, rice). Finally, the third objective is to open up studies of plasma as a life science by clarifying the essence of the phenomenon.

【Expected Research Achievements and Scientific Significance】

Our researches focusing on cell death and regeneration among phenomena caused by combined exposure to bioactive substances result in a comprehensive understanding of these phenomena and opening up the field (plasma life science) to clarify the "essence of living body" responses to plasma. These results will be a compass to approach to the Plasma Life Science producing the incredible academic impact.

【Publications Relevant to the Project】

・F. Utsumi, H. Kajiyama, K. Nakamura, H. Tanaka, M. Mizuno, K. Ishikawa, H. Kondo, H. Kano, M. Hori, F. Kikkawa, Effect of Indirect Nonequilibrium Atmospheric Pressure Plasma on Anti-Proliferative Activity against Chronic Chemo-Resistant Ovarian Cancer Cells In Vitro and In Vivo, Plos One, 8 (2013) e81576/1-10.
・H. Tanaka, K. Nakamura, M. Mizuno, K. Ishikawa, K. Takeda, H. Kajiyama, F. Utsumi, F. Kikkawa, M. Hori, Non-thermal atmospheric pressure plasma activates lactate in Ringer's solution for anti-tumor effects, Sci Rep, 6 (2016) 36282/1-11.

【Term of Project】 FY2019-2023

【Budget Allocation】 464,100 Thousand Yen

【Homepage Address and Other Contact Information】

http://horilab.nuee.nagoya-u.ac.jp/
hori@nuee.nagoya-u.ac.jp

Title of Project : Creation of unexplored molecular nanocarbons

ITAMI Kenichiro
(Nagoya University, Institute of Transformative Bio-Molecules (ITbM), Professor and Director)

Research Project Number : 19H05463 Researcher Number : 80311728
Keyword : π-extended compounds, organic materials, selective synthesis, supramolecular chemistry, chemical biology

【Purpose and Background of the Research】

Nanocarbons, nanometer-sized carbon materials, conduct electricity, absorb and emit light, and exhibit interesting magnetic properties. In addition to well-known nanocarbons such as spherical fullerenes, cylindrical carbon nanotubes, and sheet-shaped graphenes, theoretical simulations have predicted a number of exotic three-dimensional nanocarbon structures that have yet to be synthesized. At present, however, synthetic routes to nanocarbons almost invariably lead to mixtures of compounds displaying a range of different structures and properties; these mixtures cannot be easily separated into pure forms. The "*mixture problem*" that arises during the synthesis of nanocarbons represents one of the most significant challenges in the science and technology of nanocarbons.

The objectives of this project are (1) to design and synthesize novel nanocarbons as single structures, individually distinguishable and identifiable, and (2) to create highly advanced functional materials based on these single-molecule materials. We combine chemical and physical methods for the controlled synthesis of single-molecule nanocarbons, and conduct interdisciplinary research that encompasses the control of molecular arrangement and orientation, structural and functional analysis, and applications in devices and biology. Through this project bringing molecular science and materials science together, we aim to establish the new field of *molecular nanocarbon science*.

【Research Methods】

1. Carbon nanotubes

Carbon nanobelt is the molecule that represents the fully fused cylindrical aromatic hydrocarbon (e.g. *Science* 2017). In this project, we establish the synthetic methods of carbon nanobelts having various lengths, diameters, and structures. As a further challenge, we perform the CNT growth using carbon nanobelt as a seed to provide CNTs with uniform physical properties.

2. Graphene nanoribbons

We have synthesized graphene nanoribbons (GNRs) with various widths, edge structures, lengths, and periodic defects by using APEX reactions (e.g. *Science* 2018) developed by our group. Here we challenge to create APEX polymerization reactions to control the length of GNR precisely. Sequential oxidative annulation reaction can proceed to the formation of adjacent carbon-carbon bonds to form planar GNRs. By utilizing this technique, we synthesize various GNRs (fjord-type GNRs and armchair-type GNRs) having different width and edge structures by using precisely designed silole monomers.

3. Three-dimensional nanocarbon network

In this subject, we work on the creation of three-dimensional carbon networks that enables condensed conjugation with only carbon atoms. Three-dimensional carbon networks consisting solely of sp^2 carbon atoms are substance groups of dreams considering the theoretical prediction of outstanding physical properties. In this research, we apply molecular nanocarbon synthesis technology such as APEX reaction of aromatic compounds.

【Expected Research Achievements and Scientific Significance】

The concept of "molecularity and molecular materials" will lend new values and creativity to nanocarbon science, which is already starting to create a social ripple effect, and the creation of innovative molecular nanocarbon materials will have a huge impact on industry. Furthermore, many new methodologies and techniques for molecular synthesis and structural analysis will be developed throughout this project. Synthesis and analysis techniques are not particular to a single type of molecule or substance. Therefore, these methodologies will bring breakthroughs to many chemical, physical, or biological fields as molecular sciences.

【Publications Relevant to the Project】

・Segawa, Y.; Itami, K. *et al.,* Synthesis of a carbon nanobelt, *Science* **2017**, *356*, 172–175.
・Murakami, K.; Itami, K. *et al.,* Synthesis of partially and fully fused polyaromatics by annulative chlorophenylene dimerization, *Science* **2018**, *359*, 435–439.

【Term of Project】 FY2019-2023

【Budget Allocation】 491,500 Thousand Yen

【Homepage Address and Other Contact Information】
http://synth.chem.nagoya-u.ac.jp

Title of Project : Study on Self-compression Type Detonation Propulsion: Evolutionary Space-Flight Demonstration Study Using Sounding Rockets

KASAHARA Jiro
(Nagoya University, Institute of Materials and Systems for Sustainability, Professor)

Research Project Number : 19H05464 Researcher Number : 60312435
Keyword : Propulsion, Thermo-fluid dynamics, Detonation, Aerospace Engineering, Sounding Rocket

【Purpose and Background of the Research】

The detonation (hypersonic combustion) propulsion mechanism is now causing a revolution in the field of aerospace engineering. In the present research, we study a revolutionary self-compression-process disc-shaped rotating detonation engine with porous injectors and a detonation combustion actuator in the effort to realize an integrated propulsion device with an airplane body. We investigate the principles of advanced high performance and light weight for an aerospace system.

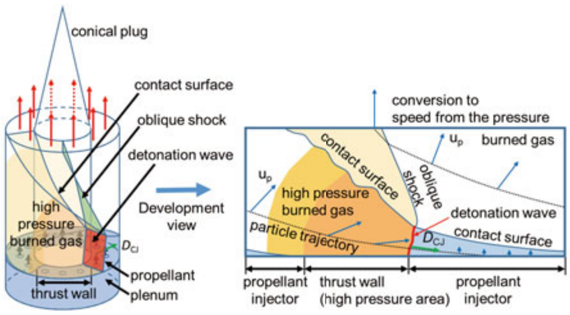

Figure 1 Detonation Engine

【Research Methods】

In the present research, we perform experimental and numerical studies in which we vary the inner diameter of the disc-shaped rotating detonation engine, in addition to the injection condition and mixture condition. We also clarify the most fundamental combustion phenomena in this engine, and the mechanism of pressure gain. We verify the limitation of the pressure gain using a multi-staged disc-shaped rotating detonation engine. We fabricated a porous cooling wall injector-type rotating detonation engine. On the fuel-oxidizer injector wall of this engine, detonation wave propagation was maintained stably. We experimentally and numerically clarify the detonation structure and heat flux into the wall, and the heat transfer coefficient from the gas flow to the wall.

We fabricate the small detonation actuator using the state-of-the-art nanometer-order machining technique, and clarify the high-speed-flow thrust characteristics of the actuator and performance of the ejector effect. We also clarify the thrust and aerodynamic characteristics (lift and drag force and rolling torque coefficients) when the engine and body are integrated by these small actuators.

【Expected Research Achievements and Scientific Significance】

We will also demonstrate the principles investigated to achieve objectives with a rocket system in a low-earth-orbit flight test using the third stage of the sounding rocket system in 2025. The present research will allow us to realize innovative propulsion performance and body structure, and will create a completely new area in the aerospace engineering field.

【Publications Relevant to the Project】

・ K. Goto, J. Nishimura, A. Kawasaki, K. Matsuoka, J. Kasahara, A. Matsuo, I. Funaki, D. Nakata, M. Uchiumi, K. Higashino, Experimental Propulsive Performance and Heating Environment of Rotating Detonation Engine with Various Throat Geometries, Journal of Propulsion and Power, Vol. 35, No. 1, 2019, pp.213-223.
・ Kawasaki, T. Inakawa, J. Kasahara, K. Goto, K. Matsuoka, A. Matsuo, I. Funaki, Critical Condition of Inner Cylinder Radius for Sustaining Rotating Detonation Waves in Rotating Detonation Engine Thruster, Proceedings of the Combustion Institute, Vol. 37, No. 3, 2019, pp. 3461-3469.

【Term of Project】 FY2019-2023

【Budget Allocation】 480,900 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.prop.nuae.nagoya-u.ac.jp/
kasahara@nuae.nagoya-u.ac.jp

Title of Project：Fusing nanomaterials and strong electric field nonlinear optics for new advances in photonics

KANEMITSU Yoshihiko
(Kyoto University, Institute for Chemical Research, Professor)

Research Project Number：19H05465 Researcher Number：30185954
Keyword：Optical properties of materials, nanomaterials, strong electric field nonlinear optics, high harmonic generation, terahertz spectroscopy

【Purpose and Background of the Research】

Sophisticated high-power laser techniques are becoming a fundamental part of new photonics research, with recent advances in high intensity and ultrashort pulse laser technology opening up new avenues of optical science. Irradiating solids with strong laser pulses can introduce new nonlinear optical phenomena, such as high harmonic generation, which produces multiple frequencies of the incident laser's frequency. Ultrashort (attosecond) pulsed light sources covering a wide range of wavelengths from the infrared to X-ray have many potential technological applications. Strong optical pulses dramatically change the electronic states of solids, inducing phenomena such as Zener tunneling. In this research, we study the nonlinear optical properties of solids with novel electronic states and nanoscale structures by means of advanced laser techniques. We promote the development of new high-field photonics and foster future applications into material phase control, optical switching, and spectroscopic analysis.

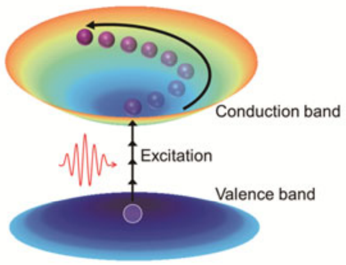

Fig. 1 Strong field-induced optical phenomena caused by accelerated carriers in the band.

【Research Methods】

Our investigations into the optical response of new solid materials draw on our strong research background in nanomaterials science. Using ultrafast coherent spectroscopy, we aim to discover new optical phenomena of nanomaterials generated under high fields. Electronic motions and states in solids and nanomaterials are altered using high electric field optical and terahertz pulses. Modern high-field science and photonics are furthered through the precise control of the phase and polarization of these pulses.

【Expected Research Achievements and Scientific Significance】

Advanced laser technologies are expected to revolutionize current research and open up new disciplines of study. While initially developed for atomic and molecular systems, we will extend the study of strong-field nonlinear phenomena to include nanomaterials. Examining the fundamental physics of nanomaterials is expected to lead to new spectroscopic technologies, new material control technologies, light processing technologies, and light energy conversion technologies, etc., which will dramatically advance optical science research and impact on a wide range of research fields.

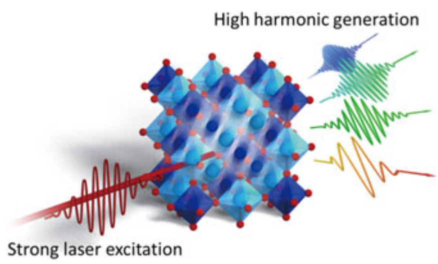

Fig. 2 Schematic of high harmonic generation from electrons driven by strong laser excitation.

【Publications Relevant to the Project】

・H. Tahara, Y. Kanemitsu *et al.*, "Harmonic quantum coherence of multiple excitons in PbS/CdS core-shell nanocrystals", *Phys. Rev. Lett.* **119**, 247401 (2017).
・Y. Sanari, Y. Kanemitsu, H. Hirori *et al.*, "Zener tunneling breakdown in phase-change materials revealed by intense terahertz pulses", *Phys. Rev. Lett.* **121**, 165702 (2018).

【Term of Project】 FY2019-2023

【Budget Allocation】 429,300 Thousand Yen

【Homepage Address and Other Contact Information】

https://www.scl.kyoto-u.ac.jp/~opt-nano/index-e.html