Title of Project : Chemical Biology using bioactive natural products as specific ligands: identification of molecular targets and regulation of bioactivity

Minoru Ueda
(Tohoku University, Graduate School of Science, Professor)

【Purpose of the Research Project】

A naturally occurring ligand is a bioactive molecule isolated from the creature. This is the molecule is committed as a key which controls a biofunction of living body. Though research on naturally occurring ligands was traditionally popular in our country, interest concerning an organic chemistry of their complex structure has been placed in center for a long time. This new scientific research on innovative area will emphasize the charm of the bioactivity of the naturally occurring ligands and aim at the establishment of "chemical biology of naturally occurring ligand" which involves chemical biology, biochemistry, molecule biology and bioinformatics unite in the good structure organic chemical base.

【Content of the Research Project】

It is widely known that naturally occurring ligands combines with the target protein in the living body to develop a bioactivity. This relationship is compared to the relations between "the key and the keyhole". But, as for naturally occurring ligands, it is recently found that it works as "a bunch of keys" to combine with plural target protein more than "a key" to combine with one target protein. The bioactivity which naturally occurring ligands shows is the total peace of the bioactivity which more than one "key" brings, and we have been discussing the "most conspicuous" one. This complexity of the bioactivity has been one of the great obstacles for the foundation research which naturally occurring ligands are used for as well as its application. Recently, it was revealed that disassembly of "the bunch of keys" into individual key or modification of the structure of "the master key" can enable the dramatic change of molecular target and bioactivity of a naturally occurring ligand.

This innovative area research aims at the establishment of novel theory of science that target identification and the analysis of ligand-target complex structure brings rational identification of the "key" structure which can be used as a scaffold of the molecular tool for the rational control of biofunction. The disassembly of "the bunch of keys" realizes the simplification of structure of the naturally occurring ligands. Additionally, modification of "the key" structure by organic synthesis will create a new functional tools for the control of biofunction.

【Expected Research Achievements and Scientific Significance】

During this innovative area research, we will establish a protocol of the target identification which can be applied to any naturally occurring ligand as well. The analysis of ligand-target complex structure leads to the logical molecule design of "the key structure analog " of desired bioactivity.

This innovative area research goes through from naturally occurring ligands (chemistry), via target identification (biology), reaches the development of the key structure analog (chemistry). This spiral structure of research organization should be called chem-bio-chemistry. It will also bring an innovation in a philosophy of natural products chemistry “from structure to the bioactivity”.

【Key Words】

Naturally occurring ligand: bioactive molecule isolated from the creature (natural product).
Molecular target: Target of the naturally occurring ligand in a living system.

【Term of Project】 FY2011-2015

【Budget Allocation】 1,030,500Thousand Yen

【Homepage Address and Other Contact Information】

http:// www.chembiochem.jp

Title of Project : New Frontiers of Extrasolar Planets: Exploring Terrestrial Planets

Masahiko Hayashi
(Tokyo University , Graduate School of Science, Professor)

【Purpose of the Research Project】

Since the discovery of extrasolar planets (or exoplanets) in 1995 orbiting around stars other than the sun, they have been drastically changing our vision of the universe. With more than 500 discovered so far, exoplanets exhibit an astonishing diversity we have never imagined before when we knew only eight planets of our own solar system. Some exoplanets are rocky like the earth. Some may hold liquid water (like oceans) on their surfaces and be capable of sustaining life.
For decades, we have been leading planetary formation theories in the world with renditions such as the Kyoto model of our solar system formation. Radio observations of protoplanetary disks began as early as their presence was recognized. Subaru telescope discovered disks with peculiar morphology and successfully imaged an exoplanet recently.
The purpose of this project is to expand these research activities in Japan. With new instruments to be developed, we would like to make a survey for rocky planets possibly holding liquid water. We will take direct images of exoplanets, get their spectra, and analyze their atmospheric characteristics. We also observe the formation process of planets using the newly completed radio interferometer called ALMA. We will also develop theories of planet formation and planetary atmosphere. Comparison of the observations with theories will allow us to comprehensively understand the origin, formation and evolution of planets. Raising young generations of researchers and students to lead this exciting field in the future is also one of the purposes of this project.

【Content of the Research Project】

This research project consists of the following four subprojects.
A01: Direct Imaging and Spectroscopy of Gas Giants and Detection of Earth-like Planets — including indirect detection of earth-like planets, and direct detection and spectroscopy of gas giants.
A02: Numerical Modeling of Exoplanetary Atmosphere and Characterization — to develop comprehensive models of planetary atmosphere and interpret spectroscopic data of exoplanets.
B01: From Disks to Planets — to carry out observations of protoplanetary disks with ALMA and Subaru.
B02: Theory of the Formation of Habitable Earth-like Planets — to develop comprehensive models of the formation of planets including those that can sustain life.

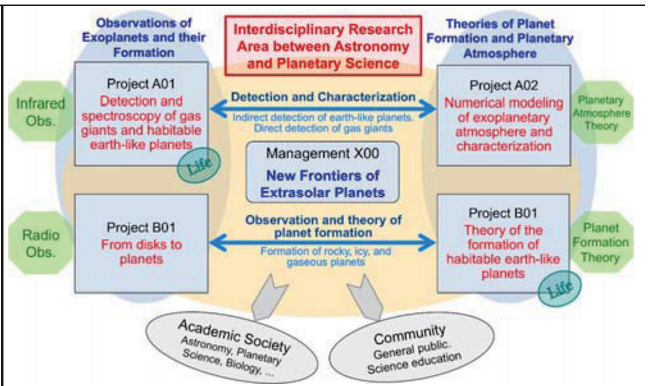


Fig. 1 — Overview of the project

【Expected Research Achievements and Scientific Significance】

Implication of exoplanet research is profound in the sense that human beings, after thousands of years of wondering, have attained the possibility of finding the first real answers to one of the most meaningful questions such as "how we and our world came to be?" It will surely be one of the most important research fields in the 21st century. We hope that, with our project, we will consolidate the foundations of exoplanetary research in Japan so that we will continuously make significant contributions to this field. We would thus like to raise younger generations in addition to achieve expected results such as the detection of habitable rocky planets, etc.

【Key Words】

Exoplanets: Planets orbiting around stars other than the sun.
Protoplanetary disks: Disks around young stars and the site of planet formation.

【Term of Project】 FY2011-2015

【Budget Allocation】 946,800 Thousand Yen

【Homepage Address and Other Contact Information】

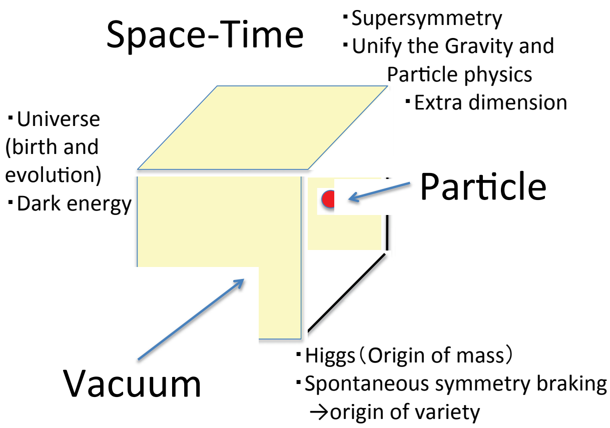
http://exoplanets.astron.s.u-tokyo.ac.jp/

Title of Project : Particles Physics opening up the Tera-scale horizon using LHC

Shoji Asai
(Tokyo University, Graduate school of Science, Associate Professor)

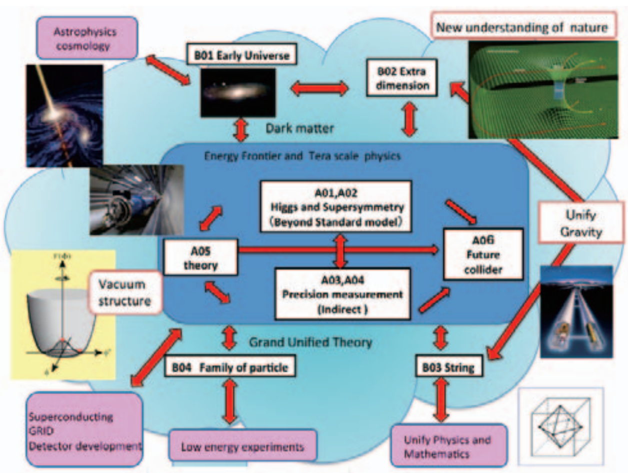
【Purpose of the Research Project】

LHC (Large Hadron Collider) is the energy frontier collider operated at CERN, and it is the first time to research “Tera-scale physics” directly in the history of the human race. We will discover Higgs boson and Supersymmetric particles (or another phenomena beyond the Standard Model) using the LHC. Based on these experimental results, we explore researches of the structure of vacuum, the origin of mass, the relation of particle and scape-time. These researches make paradigm-shift including “particle”, “vacuum” and “space-time”.



【Content of the Research Project】

Structures of this Project are as follows:
(1) 6 groups including one theoretical group



focus on the research using the ATLAS detector at LHC. Purposes of these groups are to discover the Higgs boson, the Supersymmetric particles and new phenomena beyond the Standard Model. New technologies of the detector and accelerator are also developed for the future experiment.

(2) 4 groups expand the results obtained at Tera-scale to the various researches of the cosmology, early Universe, the vacuum structure, the origin of mass, structure of space-time, family of the fermion, the supergravity, and the super-string theory.

【Expected Research Achievements and Scientific Significance】

(1) Discovery of Higgs boson: Higgs boson is the proof that the symmetry of our vacuum is spontaneously broken, and it becomes origin of mass. The broken symmetries play important role of inflation, and the evolution of our Universe.
(2) Discovery of new Phenomena beyond the Standard Model (BSM): Supersymmetry(SUSY) is the most promising candidate of BSM. SUSY is the fundamental symmetry to exchange Boson and Fermion. The lightest Supersymmetric particle is a good candidate of the dark matter in the Universe. Furthermore SUSY is the necessary symmetry to unify the general relativity and the quantum theory.
(3) Development of the advanced technologies for the detector and accelerator. These will be used in The High Luminosity LHC project (Start from 2020) and also in the future experiments.

【Key Words】

Higgs boson, SUSY, LHC

【Term of Project】 FY2011-2015

【Budget Allocation】 1,083,800 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.icepp.s.u-tokyo.ac.jp/terascale/

Title of Project : Advanced Molecular Transformations by Organocatalysts

Masahiro Terada
(Tohoku University, Graduate School of Science, Professor)

【Purpose of the Research Project】

Synthetic organic chemistry, which is a fundamental and important research field, has been significantly contributing to the foundation of advanced manufacturing in various fields. Although synthetic methods for numerous useful substances have been realized, it is important for the future of Japan, a country with limited natural resources, not to be satisfied with the current level of science and technology. Japan must develop cutting-edge manufacturing science and technology in accordance with the most critical challenges in the 21st century: to avoid using rare and depleted resources, to create a sustainable recycling-oriented society. To these ends, we have organized research groups that focus on a common theme, organocatalysis. We strive to develop methodologies with a superior total efficiency to synthesize useful substances by sharing and integrating valuable intellectual foundations. We intend to create the future vision of manufacturing based on innovative scientific and technological approaches.

【Content of the Research Project】

To advance the science of sustainable manufacturing and to develop effective and innovative catalytic systems, we promote three research topics as shown in Figure 1.

<u>A01 Group: Design of Controlling Systems in Organocatalysis</u>: To realize the guiding principles in catalyst design, the development of organocatalysis is a major research topic, including development of new functions, elucidation of catalytic phenomena, and scientifically understanding the mechanisms.

<u>A02 Group: Development of Molecular Trans-formations by Organocatalysts</u>: To achieve intelligent construction of catalytic systems, various molecular transformations are pursued by developing new reactions using organocatalysts and molecular transformations via innovative methodologies.

<u>A03 Group: Practical Synthesis of Useful Substances Using Organocatalysts</u>: By applying organocatalysts to develop practical synthetic methods for useful substances, biologically active compounds and functional materials, will be synthesized utilizing organocatalysts and the catalytic systems.

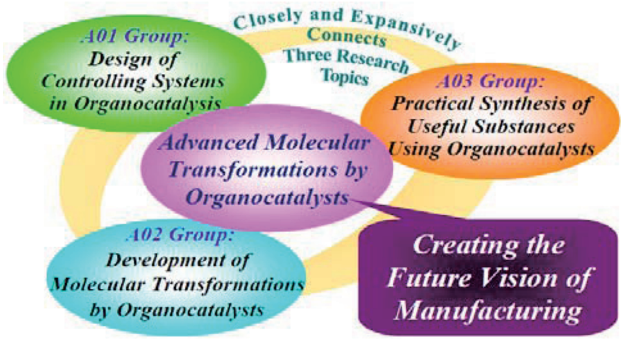


Figure 1　Three research topics and purpose

【Expected Research Achievements and Scientific Significance】

Through conducting intensive research in this area, it is anticipated that development of organocatalysts with superior characteristics, including enhanced catalytic activities, handling ease, and stereochemical controllability. Moreover, to elucidate the underlying mechanisms of substrate/catalyst interactions, it can be also expected cultivation of molecular transformation systems that cannot be achieved by metal catalysts and novel molecular transformations based on new methodologies. Development of practical synthetic processes based on truly advanced molecular transformations using organocatalysis leads to not only establishing a new academic research field, advanced molecular transformations by organocatalysts, but also significantly contributing to the science of manufacturing.

【Key Words】

Organocatalysts:　It is a small organic molecule that has the catalytic function and has come to steal the limelight suddenly on the boundary of 2000 as a clean reactive catalyst of the next generation by academia and industry because of excluding metallic element.

【Term of Project】　FY2011-2015

【Budget Allocation】　1,180,200 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.organocatalysis.jp/
mterada@m.tohoku.ac.jp

Title of Project : Hyper Bio Assembler for 3D Cellular Innovation

Tatsuo Arai
(Osaka University, Graduate School of Engineering Science, Professor)

【Purpose of the Research Project】

The main purpose of this research project is to establish a new and innovative methodology: Bio Assembler. This methodology is intended for creating 3D cellular systems such as functional tissue in vitro environments, in which active cells selected from a living organism are used to create the 3D cellular system. This new methodology will bring innovation to the next generation of tissue engineering and will become the world's first creation of 3D cellular systems in vitro environments. This innovation will be achieved by developing a methodology of hyper micro-nano measurement and control. The outcome of this innovation will bring great technological advancements to engineering science and biological science in Japan.

The research consists of three areas: (1) Hyper measurement and separation of useful active cells, (2) Hyper assembling of 3D cellular system from selected active cells, and (3) Analysis and evaluation of 3D cellular systems. The technical development and understanding in these fields will bring progress and systematization to micro-nano engineering science and biological science.

【Research Project Content】

Three research groups corresponding to three research areas are organized to participate in the development of the Bio Assembler research project. Collaborative research will be promoted among these three groups to achieve the creation of the 3D cellular system.

(1) Measurement and Control of Cell Characteristics Group (A01): establishing and systematizing a methodology for measurement of cell characteristics and separation of useful active cells by applying hyper micro-nano robotics.

(2) Assembling of 3D Cellular System Group (A02): establishing and systematizing a methodology for assembling 3D cellular systems from selected active cells by applying hyper micro-nano robotics.

(3) Analysis and Evaluation of 3D Cellular Systems Group (A03): analyzing and evaluating functions of developed 3D cellular systems.

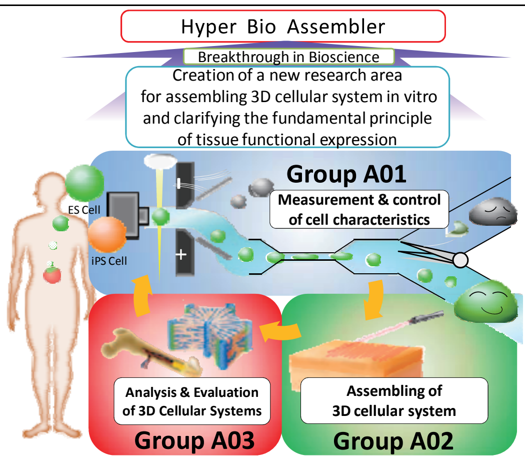


Figure 1 Scheme of the project and its expected achievements

Collaboration of these three research groups with public applied researches will be promoted to enhance diversity of methodologies and research targets.

【Expected Research Achievements and Scientific Significance】

The methodologies for measurement of cell characteristics and separation of useful active cells, and assembling 3D cellular systems from selected active cells will be established and systematized. The fundamental principle of functional expression of 3D cellular systems will be clarified. This research project will bring great technological advancements to engineering science and biological science in the world as well as in Japan.

【Key Words】

Bio Assembler : Methodology and systems to create functional 3D cellular systems

3D Cellular System : 3D structure fabricated by using selected active cells in vitro

【Term of Project】 FY2011-2015

【Budget Allocation】 1, 198, 600 Thousand Yen

【Homepage Address and Other Contact Information】

http://bio-asm.jp

Title of Project: Nanomedicine Molecular Science

Kazuhiko Ishihara
(Tokyo University , Graduate School of Engineering, Professor)

【Purpose of the Research Project】

Nanomedicine Molecular Science focuses on molecular reactions in the cells, which constitute the living organism and control its biological activities. The cellular environment, however, differs from the chemical reaction environment. The goal of this project is to develop molecular reaction parameters to quantify and examine such reactions. The studies, therefore, are part of a scientific initiative focusing on cells and have the following main objectives: establishing the theoretical basis of molecular reactions in the cell, and understanding the cellular environment and intracellular chemical reaction mechanisms. The achievement of these objectives will enhance the understanding of and facilitate multidisciplinary discussion about the system that coordinates molecular reactions in individual cells and living organisms.

【Content of the Research Project】

Theme A01 “Molecular Science of Nanomedicine”: This initiative aims to examine, establish, and review the principles for measuring parameters describing the intracellular reaction environment. Theme A02 “Molecular Science for Nanomedicine”: This initiative aims to directly observe the intracellular reactions and develop and examine the parameters. Theme A03 “Molecular Science with Nanomedicine”: This initiative aims to understand pathological conditions by using the parameters describing molecular reactions in the cellular environment and to design molecular structures for nanotherapy. The emphasis will be on molecular reactions for innovative therapeutic approaches or equipment.
We will undertake sponsored research programs and promote interdisciplinary research to promote the synthesis of knowledge and establish molecular nanomedicine. Furthermore, we will provide technological insights to the knowledge base of molecular science and develop novel research strategies for medical technology and industry.
On the basis of the research findings, we aim to develop approaches for treating the root cause of diseases and equipment using molecules regulating cell cycles and reactions.
Sponsored research projects will include topics related to the origin of cellular functions, which will provide knowledge indispensable for molecular nanomedicine; topics required for establishing molecular nanomedicine; topics that may help integrate the research projects and promote constructive interactions among researchers; and topics that encourage original ideas to solve difficulties in the field.

【Expected Research Achievements and Scientific Significance】

This project will provide new insights into intracellular molecular reactions and develop accurate parameters for those reactions. Moreover, they will help develop innovative chemotherapies and efficient computer-assisted drug designs, promote innovative medical-equipment development and reliable production of cells, including iPS cells. They may positively influence research on molecular dynamics in the cellular environment, development of less-invasive diagnostic and therapeutic approaches for improving the quality of life, establishment of novel technology driving medical innovations, growth of medical and pharmaceutical industries, restoration of international competitiveness, and development of potential leaders among scientists.

【Key Words】

Cellular environment: Includes the cell membrane and intracellular substances and provides a molecular reaction field.
Molecular reaction parameters: Constants for molecular reactions, including reaction rate, activation energy, diffusion, binding, and intermolecular interaction.

【Term of Project】 FY2011-2015

【Budget Allocation】 901,400 thousand Yen

【Homepage Address and Other Contact Information】

http://www.tmd.ac.jp/nanomedicine
nanomedicine.ibb@tmd.ac.jp

Title of Project : Frontier of Materials, Life and Particle Science Explored by Ultra Slow Muon Microscope

Eiko Torikai
(Yamanashi University Interdisciplinary Graduate School of Medicine and Engineering, Professor)

【Purpose of the Research Project】

For the function of materials and living substances, the boundary conditions such as interfaces take an important role. The interface does also provide the place for advancing superconductivity and exotic properties. In the present research area, by establishing a new real-space imaging method of the Ultra-Slow Muon Microscope, the fundamental mechanism of various phenomena in physics, chemistry and biology will be investigated in order to promote new academic field for the material design.

The positive muons which are produced by accelerator, have a nature of the polarization, namely, oriented spin directions which can be used to probe with a high sensitivity the behavior of the surrounding atoms and molecules at the stopping sites in the materials. The Ultra-Slow Muon Microscope is the first-in the-world experimental instrumentation with the following two excellent capabilities which are essentially important for the materials and life science experimental research; "Utra-Slow muon" with nm depth resolution and "high-density Micro-Beam" with μm spatial resolution.

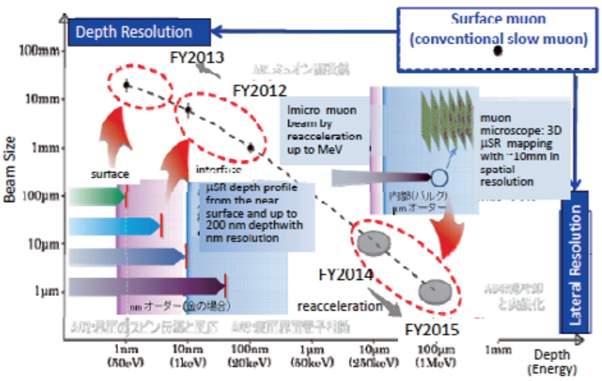


Fig. 1 Depth and beam size of the ultra-slow muon microscope with scenario of development

【Content of the Research Project】

The research area consists of four core research groups and individually applied researchers;
(A01) Establishment of the Ultra Slow Muon Microscope and micro-scale μSR:
(A02) Spin transport and catalytic reactions in the boundary regions:
(A03) Heterogeneous electron correlation in the surface-bulk boundary:
(A04) Extreme cooling and sharpening of the beam towards the "new physics" frontier beyond the standard model:

【Expected Research Achievements and Scientific Significance】

It is highly expected that the local and overall understanding of electronic states associated with surface, interface and thin film phenomena will bring us a revolutionary progress in both fundamental and application research. Fortunately, this remarkable project will be only realized in Japan based upon both the world-strongest pulsed muon beam available in a year at J-PARC and the world-strongest pulsed lasers developed at RIKEN. In the present project, in order to complete the best Ultra-Slow Muon Microscope, all the experience and expertise are assembled from the fields of condensed matter, chemistry, life science, particle and nuclear physics, accelerator and laser science. The project will contribute to establish the center for interface science at J-PARC. At the same time, with the help of related institutions, the Trial Use beam time will be arranged to encourage the use of muons by fresh muon users, researchers of the outer fields and industrial societies.

【Key Words】

Positive muon: an elementary particle with positive elementary charge, spin 1/2, and 1/9 of proton mass, decays by life time of 2.2 μs emitting positron to direction of the spin.

【Term of Project】 FY2011-2015

【Budget Allocation】 1,152, 500 Thousand Yen

【Homepage Address and Other Contact Information】

http://slowmuon.kek.

Title of Project : Materials Science on Synchronized LPSO Structure − Innovative Development to Next-generation Lightweight-structural Materials −

Yoshihito Kawamura
(Kumamoto University, Graduate School of Science and Engineering, Professor)

【Purpose of the Research Project】

New ultra-high-strength magnesium-base alloys have been developed in Japan and are now the focus of wide attention in many parts of the world. The new alloys are strengthened by a unique phase having a novel structure called "Synchronized Long-Period Stacking Ordered (LPSO) Structure", which features synchronization with respect to chemical and stacking modulations (Fig. 1). The synchronized LPSO structure has great potential to exhibit many advantageous material properties including high strength. However, much remains to be learned concerning the fundamentals of this structure.

To establish a new innovative research area of synchronized LPSO structure, (1) determination of its unique crystallography, (2) elucidation of the principles of its formation, and (3) clarification of its strengthening mechanisms will be focal points of our investigations. Furthermore, our efforts will be further devoted to the innovative development of not only ultra-high-strength LPSO-type Mg alloys created in Japan, but also other new lightweight structural materials.

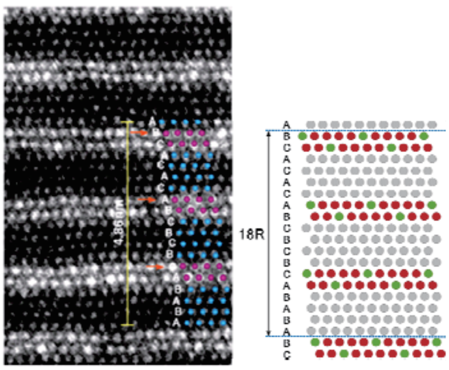


Figure 1 Synchronized LPSO structure (18R) observed in the $Mg_{97}Zn_1Y_2$ alloy

【Content of the Research Project】

The following three research themes will be pursued through nine planned tasks and also ones invited publicly from the 2012 fiscal year.

A01: Elucidation of LPSO structural science by determination of the atomic arrangement
A02: Design of chemical and stacking modulations in LPSO structure through clarification of its formation mechanisms
A03: Study of strengthening mechanisms and deformation dynamics in LPSO structure based on microanalyses and computational mechanics

【Expected Research Achievements and Scientific Significance】

(1) The development of ultra-high strength LPSO-type Mg alloy created in Japan can be put to practical use, which will make great contributions toward solutions to environmental and energy problems.
(2) The elucidation of the formation mechanisms will not only lead to innovative developments of other new lightweight structural materials such as titanium alloys strengthened by the synchronized LPSO structure, but will also help establish new fields of materials science concerning long period structures.
(3) Gaining and understanding of the strengthening mechanisms can give rise to a new concept of materials strengthening, namely, "kink band strengthening." The kink deformation mechanism may be applied to not only the development of high strength alloys but also to the development of highly ductile ceramic materials.

【Key Words】

Long-period stacking ordered structure; staking fault; structural modulation; chemical modulation; kink deformation; kink band strengthening; disclination

【Term of Project】 FY2011-2015
【Budget Allocation】 1,152,300,000 JPY

【Homepage Address and Other Contact Information】

http://www.msre.kumamoto-u.ac.jp/~LPSO/
rivervil@gpo.kumamoto-u.ac.jp