Title of Project：Conquering Cancer through Neo-dimensional Systems Understanding

Satoru Miyano
(The University of Tokyo, The Institute of Medical Science, Professor)

Research Project Number：15H05907　Researcher Number：50128104

【Purpose of the Research Project】

We will deepen our integrative systems understanding of cancer by investigating genesis, evolution and heterogeneity of cancer, genetic diversity in an individual due to mosaicism of embryonic/somatic cells, unknown functions of non-coding RNAs, and malignancy in regard to cellular context. "Systems Cancer Research" utilized methodologies such as mathematical modeling, large-scale data analysis, and statistical genetics enhanced with supercomputers as the driving force. By newly integrating an innovative information technology "Cognitive Computing" into cancer research, "Systems Cancer in Neo-dimension" will achieve a new paradigm for shuttling skillfully between the targets of interest in individual cancer and the entire pictures of cancer unraveled with the systems cancer research methodologies. Simultaneously, we establish the cancer ELSI that will ensure consistency with not-yet encountered issues springing out from big data, and bolster, sometimes face off against, currently inconceivable future cancer genome research and medicine.

【Content of the Research Project】

We develop methodologies for acquiring large-scale precise global views of systems disorders in cancer and then pinpointing target parts of interest (genes, pathways, etc.) by cognitive computing utilizing cancer big data.

[A01] New challenges of integrative systems understanding of cancer

The first issue is "global view on whole-genomes of human populations" in disease-wise or population-wise way based on large-scale omics data and phenome data. The second issue is "local view on genomes" for understanding the functions of cancer genomes. We deepen our understanding of systems disorders in caner by integrating these two issues with the innovation in genome analysis and supercomputer ability. We investigate cancer systems spatiotemporally and/or topologically from the viewpoints of cellular context, evolution and heterogeneity, and non-coding RNA, that shall lead to innovations for prevention, early-diagnosis, therapeutics, and escape from resistance of therapy.

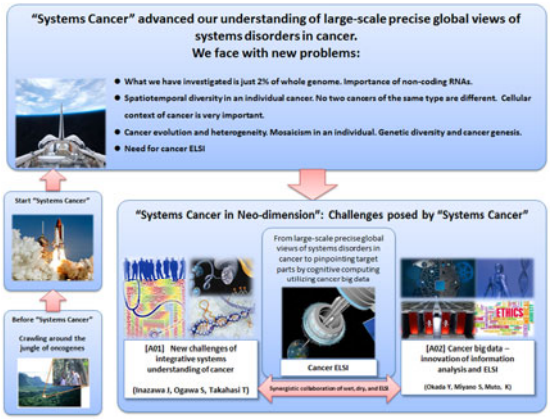


Fig. 1 Overview of Research

[A02] Cancer big data – innovation of information analysis and ELSI

We develop a framework for mathematical methods (mathematical modelling, data analysis, statistical genetics, etc.) to encounter with cancer big data. Innovative information technologies such as "Cognitive Computing" will be exploited to advance integrative systems understanding of cancer. [A1] will produce personal whole genomes and will unravel mosaicism in cells and how mutations in hematopoietic stem cell are accumulated by aging. To cope with the emergency of cancer big data society, we establish a new cancer ELSI.

【Expected Research Achievements and Scientific Significance】

We can advance systems understanding of heterogeneity and complexity of cancer in terms of genomes, non-coding RNAs, and cellular context of cancer together with innovative analytics. Applications of cognitive computing to cancer analytics will lead to an innovation, and the establishment of cancer ELSI will have an increasing impact over the aging society.

【Key Words】

Systems Cancer Research: An interdisciplinary field to understand cancer as system disease by combining mathematical modeling/simulation, large-scale data analysis and experimental systems analysis.

【Term of Project】 FY2015-2019

【Budget Allocation】 1,101,600 Thousand Yen

【Homepage Address and Other Contact Information】 http://neosystemscancer.hgc.jp/en/

Title of Project：Ocean Mixing Processes：Impact on Biogeochemistry, Climate and Ecosystem

Ichiro Yasuda
(The University of Tokyo, Atmosphere and Ocean Research Institute, Professor)

Research Project Number：15H05817　Researcher Number：80270792

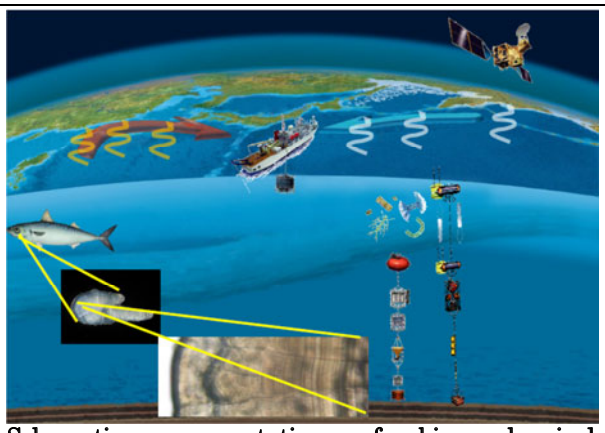
【Purpose of the Research Project】

Ocean diapycnal mixing is a fundamental physical process that regulates ocean vertical circulations of water, nutrients, carbon and heat; however, its distribution and generation mechanisms have not been known because of the difficulties of observations. This research project will develop efficient observing system of ocean diapycnal mixing and next-generation numerical models, those of which are able to quantify the maintenance mechanism of deep and bio-geochemical circulations and to reproduce observed bi-decadal ocean and climate variability. This new interdisciplinary study on ocean mixing opens the integrated sciences from physical, chemical, biological oceanography to climate and fisheries sciences.

【Content of the Research Project】

Based on extensive and/or intensive in-situ observations, turbulent vertical mixing and physical, chemical and biological oceanic processes in the western North Pacific, especially in the Oyashio and Kuroshio regions and their upstream regions including East-Asian marginal Seas, will quantify the transport of water and nutrients. Implementation of the observed data and new findings on physical and biogeochemical processes into a data-synthesis system and prognostic models makes possible to further quantify those without observations. With diapycnal diffusivity and its 18.6-year variability, high-resolution newly developing next-generation models with atmosphere and biogeochemical components will enable us to pursue the effects of local vertical mixing such as Kuril Straits mixing on global ocean and climate and their bi-decadal and its related variabilities.

Changes in biomass and species of major phytoplankton will be analyzed by19-years time series settling particle samples. Biogeochemical responses to the environmental change will also be monitored by sensors equipped with up-down winch system (see figure). Stable isotope analysis technics of fish otoliths will be developed to elucidate influences of ocean mixing variability on fluctuations of the fish stocks (see figure).



Schematic representation of bio-geochemical observations and our hypothesis: strong tide-induced diapycnal mixing in the upstream Oyashio and Kuroshio supplies nutrients and maintains abundant ecosystem including fish species.

【Expected Research Achievements and Scientific Significance】

Integrated observations of diapycnal diffusivity and physical, bio-geochemical and fish-recruitment processes in the western North Pacific are implemented to next generation (data-assimilation and prognostic) models which reproduce ocean biogeochemical circulation and observed long-term ocean and climate variability. Those observations and models elucidate our hypotheses that diapycnal upwelling of nutrients in the upstream Oyashio and Kuroshio makes the ocean around Japan productive and that 18.6-year period tidal mixing leads to ocean, climate and marine ecosystem bi-decadal variability, which enhance long-term predictive skills of climate and marine ecosystems including fish stocks.

【Key Words】

Ocean diapycnal mixing: vertical mixing of seawater and dissolved substances due to turbulent eddies. In deep water, these eddies are caused by breaking internal waves generated by currents as tides over rough bottom topography, inducing ocean vertical water, heat and material circulations.

【Term of Project】 FY2015-2019

【Budget Allocation】 1,112,600 Thousand Yen

【Homepage Address and Other Contact Information】 http://omix.aori.u-tokyo.ac.jp
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Title of Project：Non-linear Neuro-oscillology: Towards Integrative Understanding of Human Nature

Atsushi Nambu
(National Institute for Physiological Sciences, Division of System Neurophysiology, Professor)

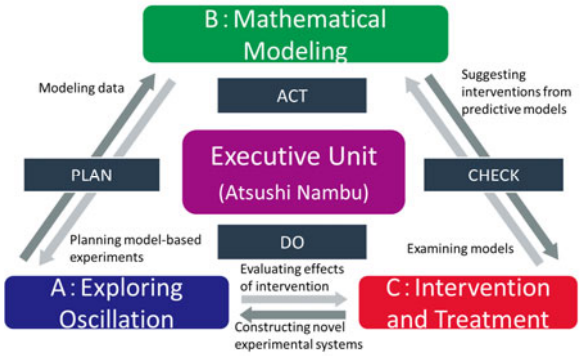
Research Project Number：15H05871　Researcher Number：80180553

【Purpose of the Research Project】

In this program, we intend to create a new academic field of neuro-oscillology, which enables us to understand human nature. “Oscillology” is a pragmatic knowledge that approaches "human brain" combining findings from state-of-the-art experimental research and ideas from a non-reductionism perspective that regard complex human being as indivisible unitary system. We share a working hypothesis that the spontaneous oscillation and synchronization in the neuronal systems yield its functional differentiation and self-organization, and also share a database of a body of relevant experimental research. We unify the team to create a new academic field “oscillology” which harmonizes neuroscience, mathematics, and clinical medicine to achieve mathematical and systematic neuroscientific comprehension of human nature.

【Contents of the Research Project】

The research team for this project is composed of three groups of research units that associatively proceed research activities: exploring oscillation, mathematical modeling, and the intervention and treatment.



Group A will explore the novel multi-dimensional and multi-layered oscillatory phenomena, working on intracellular events, primate/rodent models, direct recordings of human brain activity, and advanced measurements of human brain systems. Group B will develop mathematical models of functional differentiation and self-organization of the multi-dimensional and multi-layered oscillatory neuronal network. Group C will investigate genetic engineering and optogenetic intervention into oscillatory phenomena in animal models, control of dynamics in human neural network by non-invasive brain stimulation methods, and induction of reorganization of nervous system and clinical intervention for network diseases in human, including neurological and psychiatric disorders.

Establishing oscillology requires close association between experimental and theoretical studies. As shown in the schema, group B draws up model-based experimental plans and then groups A and C cooperatively perform examinations on the suggested models. Also, group B will model novel oscillatory phenomena observed by groups A and C and develop ways to manipulate them. In addition, group A will analyze the effect of intervention methods developed by group C and examine validity of the models provided from group B.

【Expected Research Achievements and Scientific Significance】

Based on an oscillological perspective, we can regard various neurological and psychiatric disorders, such as dementia, epilepsy, Parkinson’s disease, and schizophrenia, as “network diseases”, that is, dysfunction in dynamism of spontaneous networks in human brain.

With the progress of this field, we expect the advent of “clinical mathematical scientists” who can treat and control neurological and psychiatric disorders based on mathematical models of the phenomena of non-linear collective oscillation.

We also expect that our field contributes to psychological and sociological comprehension of human nature with oscillological perspective. Human being do not always make complete rational judgments, but sometimes make irrationalistic decisions, which evoke fluctuation in social and economic activities. Oscillology will clarify associations between human irrationality and a wide range of neuro-oscillation and provide scaffolding to understanding such complex behaviors by the non-linear nature of the human nervous system.

【Key Words】 Brain and Nervous System, Soft-Computing, Mathematics for Complex Systems, Neurological and Psychiatric Disorders, Physiology

【Term of Project】 FY2015-2019

【Budget Allocation】 1,149,700 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.nips.ac.jp/oscillology/
oscillology@nips.ac.jp

Title of Project : "LIVING IN SPACE" - Integral Understanding of life-regulation mechanism from "SPACE"

Satoshi Furukawa
(Japan Aerospace Exploration Agency, Head of Space Biomedical Research Group, Astronaut)

Research Project Number : 15H05935　Researcher Number : 20726260

【Purpose of the Research Project】

We investigate plasticity and collapse of life from extreme environment in space perspective. Plasticity is homeostasis by adaptation, restoration, resistance and resilience. Collapse is irreversible damage that destroys the homeostasis. It is a risk when staying in space for a long time. We investigate mainly three risks of extreme environment in space: zero-gravity, isolation, space radiation and microorganism. The purpose of our study is to integratedly understand the life controlling system from molecular-cell to high-levels, to comprehend the interrelation and combined effects and to challenge an unknown territory. Furthermore, we would like to apply the knowledge that we get to overcome challenges in super-aging and high-stress society.

【Content of the Research Project】

Our team consists of mainly eight universities and two research institutions including JAXA. We have three major research items.

In A01, molecular-cell bases of responses to gravity is investigated at cell, tissue and organ levels. The three research topics here are cell mechanosensing, nerve/muscle/metabolism and maintenance of skeletal muscles and stem cells.

In A02, effect of long duration stay in space on high-level homeostasis is handled. The five research topics here are circulatory control system, plasticity of vestibular system, autonomic nervous system, sleep-awakening, zero gravity and isolation environment.

In A03, space radiation and microorganism risk is chosen. The three research topics here are acute and late effects of space radiation, change of microorganisms.

Keeping these three pillars, our team members cooperate each other in a coordinated fashion.

We actively promote joint researches with researchers overseas, i.e., inviting advanced researchers and holding symposiums, sending young researchers abroad, and creating a global base that contributes to activation of international exchange.

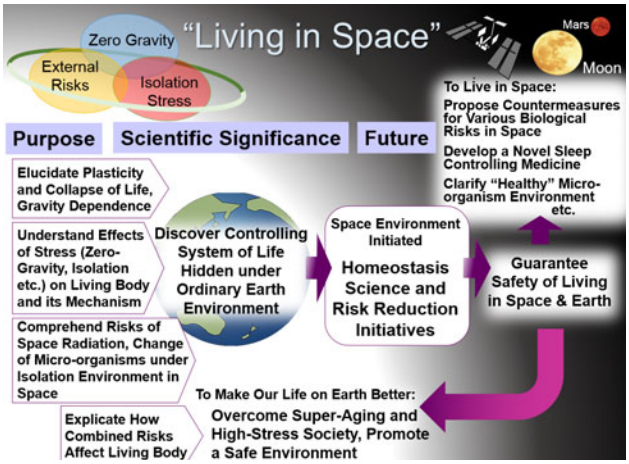


Fig. 1. Purpose, Scientific Significance and Future

【Expected Research Achievements and Scientific Significance】

Integrated understanding of the new controlling system of life from space point of view will enable us not only to overcome risks during long stay in space, but also to contribute to solving challenges in super-aging and high-stress society and to make our life on Earth better (Fig. 1).

Our achievements would affect philosophical view of life as well as science and medicine. Moreover, they stimulate the young's interest in space and science.

【Key Words】

Extreme environment in space: Zero gravity induces muscle atrophy, bone mass decrease and irregularity in the circulatory system. Psychological stress in long time isolation in space causes imbalance in autonomic nervous and endocrine systems as well as dysregulation of the immune system. "Healthy" microorganism environment and protection from space radiation are needed.

【Term of Project】 FY2015-2019

【Budget Allocation】 1,172,900 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.living-in-space.jp

Title of Project : Understanding human recognition of material properties for innovation in SHITSUKAN science and technology

Shin'ya Nishida (Human Information Science Lab, NTT Communication Science Laboratories, Nippon Telegraph and Telephone Corp, Senior Distinguished Scientist)

Research Project Number : 15H05914　Researcher Number : 20396162

【Purpose of the Research Project】

Recognition of SHITSUKAN (see Keywords) is a marvelous ability of human's brain to read out the nature of objects. We obtain indispensable information for our living from SHITSUKAN sensed through multiple modalities. SHITSUKAN plays important roles not only in perception, but also in value-based behavior selection and body motor control. How our brain reads out SHITSUKAN from complex high-dimensional source information embedded in sensory signals is a hard but critical research question for scientific understanding of human sensory processing and advancement of information technologies. Our previous research project, "Brain and Information Science on SHITSUKAN (FY2010-2014)", has been successfully developing an interdisciplinary SHITSUKAN research in Japan. To continue and expand this world-leading activity, our new project is aiming at revealing the computational principle and neural mechanisms of human recognition of a wide range of SHITSUKAN in the real world, and at developing innovative technologies and applicable engineering scheme, through tight cooperation among information engineering, psychophysics and neuroscience.

【Content of the Research Project】

We will adopt two approaches for scientific understanding of SHITSUKAN recognition. Research groups in A01 will mainly adopt hypothesis-driven approaches to understand computational principles and neural mechanisms of recognition of a variety of SHITSUKAN, including surface properties given by complex optical processes, acoustic atmosphere, and emotion-evoking stimuli. Research groups in B01, on the other hand, will mainly adopt data-driven approaches. Integrating machine learning techniques (e.g., deep learning) and advanced cortical information decoding, we will develop a novel high-throughput scheme of SHITSUKAN research. Finally, research groups in C01 will develop cutting-edge SHITSUKAN technologies in haptics, computer graphics, digital fabrication and appearance control.

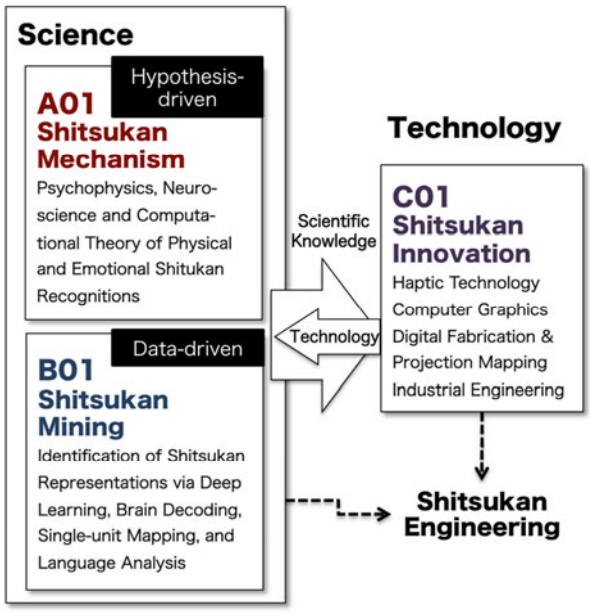


Figure 1 Area Organization

【Expected Research Achievements and Scientific Significance】

We will scientifically reveal computational principles and hierarchical cortical processing of recognition of a variety of SHITSUKAN. We will develop technologies for recognition, reproduction, edition, and control of a variety of SHITSUKAN, and eventually establish a field of SHITSUKAN engineering that can support industrial manufacturing and art.

【Key Words】

SHITSUKAN: A Japanese word that literarily means "the sense of quality." In this project, we use this term to refer to the senses of physical property (gloss, translucent), physical state (wet, dusty), material category (metal, ceramic), and subjective value (beautiful, yummy).

【Term of Project】 FY2015-2019

【Budget Allocation】 1,086,200 Thousand Yen

【Homepage Address and Other Contact Information】

http:// shitsukan.jp/ISST