Research area in Strategic Objective *"Integrated understanding of human multi-sensing networks and elucidation of their control mechanisms"*

Multisensory Integration in Biological Systems

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Overview

This research area aims for an integrated understanding of "multi-sensing systems," which encompass biological sensory systems and the peripheral nervous network, and the development of ways to visualize and control these. To achieve this, the Japan Science and Technology Agency (JST) and the Japan Agency for Medical Research and Development (AMED) have simultaneously established four programs (CREST, PRESTO, AMED-CREST, and PRIME), which will promote research while collaborating with each other. Therefore, this research area has Program Supervisor (PS) for collaborate with four programs in addition to Research Supervisor (RS). Also, JST may share with proposal with AMED during the selection process. Please be understanding in advance that JST's sharing this proposal with AMED.

Policy of Program Supervisor

Sensory functions and the autonomic nervous system play an important role as feedback systems that make sure the body is always fulfilling its functions. On the other hand, the decline and failure of sensory functions due to internal and external stresses such as increasing age, as well as impairment to the peripheral nervous system are major risk factors for health problems and the onset of chronic illness. Thus, by gaining an integrated understanding of the physiological mechanisms of "multi-sensing," which encompasses biological sensory systems and the peripheral nervous network, we expect that it will become possible to develop new treatment methods that can target illnesses related to the organs across the body, to improve quality of life (QOL), and thus to extend healthy life expectancy. Moreover, the social implementation of innovative technologies via multi-sensing systems, such as sensory substitution and sensory sharing, could contribute to the realization of a richer, happier society.

JST aims to expand sensing functions and to acquire new functions, based on the clarification of basic principles and the development of foundational and applied technologies. Meanwhile, AMED's

objective is the restoration and preservation of lost functions, i.e. the restoration, preservation, and prevention of sensing and regulatory functions, based on medical applications from basic research with a view to channeling these into health and medical care.

More specifically, we aim to clarify the operating mechanisms of multi-sensing systems, to explain pathological conditions, to develop technology that visualizes and quantifies states of activity, and, based on these, to develop treatment and prevention methods with few side effects and to create medicines, medical equipment, and minimally invasive devices that are suitable for individuals. At the same time, JST and AMED will work together to encourage this, on the understanding that the expansion of the multi-sensing functions of living organisms and the application of advanced sensing mechanisms will create seeds of innovation.

In this research area, researchers from the four programs will create a network-based research institute, and in so doing will advance mutual collaboration between young researchers and encourage further development of research. Moreover, Goal #2 of the Moonshot Research and Development Program (from the 2019 academic year to the 2029 academic year) is “Realization of ultra-early disease prediction and intervention by 2050,” and we will act on this with our sights set on collaboration with AMED’s Strategic Research Program for Brain Sciences/Brain Mapping by Integrated Neuro-technologies for Disease Studies/Strategic International Brain Science Research Promotion Program (from the 2014 academic year to the 2023 academic year).

Policy of Research Supervisor

Within living organisms, external/internal input stimuli are encoded as sensory information (such as special sensations, visceral sensations, and somatic sensations) by various sensory receptors, and turned into electrical signals. After this, these signals are transmitted to the central nerves via the peripheral nerves. This research area aims to comprehensively clarify biological multisensory systems that integrate these biological senses with the peripheral nervous network.

Research on the senses of living organisms developed in a way that notably put analysis of sight and hearing before that of other senses. In recent years, we have also gradually started to gain new information on other senses: for example, single-cell omics analysis technology and the development of the functional and structural analysis of proteins has led to the identification of new receptors related to taste and smell, and their operating principles are becoming clear. On the other hand, existing research on the senses has advanced by specializing in each sense, and we have not sufficiently analyzed sensory systems from the perspective of their integrated mechanisms, such as coordination between the different senses. Moreover, recently, as areas such as information science and engineering devices develop, we are also clarifying new biological sensing functions by applying these devices to living organisms. ICT technologies, represented by virtual reality and augmented reality, are making rapid progress, and so, in addition to the clarification of this kind of biological multisensory system,

we are combining the knowledge that we have gained through research on biological senses to date with these ICT technologies. Technologies that will contribute to the extension of human sensing functions and improved sensitivity are also becoming more important in terms of academia and industry

In light of the above, this research area will promote the clarification of the functions of biological multisensory systems in vital activity, and the development of technology that applies these functions and their operational principles.

Research Supervisor's Policy for Application, Selection, and Management of the Research Area

1. Background and Overview

Sensing refers to the phenomenon of awareness caused by the sensory receptors distributed around the body receiving internal or external stimuli, and this reaching the central nervous system in the brain via peripheral nerves. Notably, in the past, research relating to sight and sound has preceded research on other senses. For example, research on sight identified rhodopsin, a photoreceptor protein, in the 19th century, and around 100 years later progressed to explicating molecular movements and functions, including clarifying its amino acid sequences, crystal structures, and even action principles. Today, this knowledge is being applied to tools for life science, such as the development of optogenetics using the properties of rhodopsin.

Senses such as taste and smell involve receptors that receive chemical substances; ligands, which serve as stimuli, were identified a long time ago, but there are many unclear points about receptors, and we still do not understand their detailed molecular mechanisms. In recent years, several of these sensory receptors have been identified thanks to the evolution of large-scale single-cell omics analysis; following this, their operating principles are being made clear using structural analysis of proteins.

On the other hand, we know a lot about sensing via the so-called five senses—a combination of the special senses of sight, hearing, taste, and smell, and the somatic sense of touch, but that's not all there is. For example, the special senses also include the sense of balance, and somatic senses include senses for deep sensations and visceral sensations; the sensory receptors that deal with these senses are expressed in internal organs and places in which the body receives sensory stimuli. However, in recent years it has become clear that these receptors are expressed all over the body, not just in the specific sensory organs thought to take in sensory stimuli. The possibility that the role of these sensory receptors themselves involves multiple functions has also been pointed out. Furthermore, recent research has led us to understand that synergistic effects are created by the coordinated actions of the different sensory receptors and the peripheral nerves that respond to them. Meanwhile, it has also become clear that animals and microorganisms have sensory functions (super sensing) that exceed the sensory levels of humans.

Moreover, the development of virtual reality (VR) and augmented reality (AR) is making dramatic progress thanks to the evolution of information science, and today we want this virtual space and/or human sensitivity enhancement to reflect the knowledge we have gained from research on biological senses.

2. Expected targets to be achieved and specific examples of research and development projects

This research area aims to clarify sensory systems within living organisms and the cooperative relationships between sensory organs to gain a comprehensive understanding of biological multisensory systems that integrate various biological senses and the peripheral nervous network. We will also develop new technologies that make practical use of the functions and operating principles of biological multisensory systems. When researchers are carrying out research on biological multisensory systems, we expect it to be difficult to obtain innovative results just using conventional analysis techniques, so this research area is also developing foundational technologies based on new concepts and analysis techniques for large amounts of data so we can come closer to understanding functions.

We offer examples of more specific research and development projects below. These are only examples, and we anticipate proactive proposals outside of these.

(1) Clarifying the receiving, processing, and operating mechanisms of biological multisensory systems

- Clarifying the mechanisms for information reception and processing in sensory receptors–peripheral nerves–central nerves using structural analysis techniques, imaging technologies, etc.
- Clarifying the operating mechanisms of biological sensory systems on molecular and cellular levels (including clarification of biological sensory systems that have not conventionally been subject to research)
- Clarifying the mechanisms of biological sensory systems that can be applied to devices such as artificial sensory organs, etc.
- Clarifying the mechanisms of biological sensory systems that affect cognition, emotion, and behavior

(2) Developing foundational technologies that measure and control biological multisensory systems

- Developing foundational technologies that measure and quantify the mechanisms of action of biological multisensory systems with high space-time resolution, on a large scale or at high speed

・Developing analysis technologies that process large amounts of data obtained by measuring biological multisensory systems

(3) Clarifying sensory network mechanisms

・Clarifying the cooperative relationship between the sensory organs and the peripheral nervous network

・Clarifying the functions of the cooperative relationship between the sensory organs

・Clarifying the cooperative relationship between physicality and artistry

(4) Developing applied technologies that contribute to humanity using biological multisensory systems

・Clarifying the super sensing functions of animals and microorganisms, etc., and developing foundational technologies that put these to practical use.

・Developing technologies that make use of the operating mechanisms of biological multisensory systems to strengthen and/or expand human sensing functions

・Developing technologies to be applied to the fields of art, design, design engineering, and barrier-free in operating mechanisms of biological multisensory systems

Last year, we received many research proposals to study for clarifying "the receiving, processing, and operating mechanisms of biological multisensory systems", and "sensory network mechanisms," while few proposals related to development of "foundational technologies that measure and control biological multisensory systems" and of "applied technologies that contribute to humanity using biological multisensory system". Therefore, in this year proposals, we strongly expect proposals that aim to develop foundational technologies that measure and control biological multisensory systems and to develop applied technologies that contribute to humanity using biological multisensory system. We also expect proposals for the clarification of relationship between art/artistry and multisensory systems, barrier-free research/ disability studies, and XR research (VR, MR, AR, SR) for creation of new technologies to expand sensory function.

3. Management policies for this research area

We emphasize a sense of creativity, challenge, and the integration of different fields in applications for this research area.

This includes original technology and ingenuity of perspective. In your application, please clearly state the originality and creativity of your proposal content via an accurate comparison with other research. From the perspective of training human resources, the focus of the selection in this research area will also be your ability to collaborate with other researchers in a way that transcends the boundaries between fields. Current scientific research demands joint research outcomes via the integration of

different fields that cannot be achieved through individual research, rather than just individual researchers' efforts to promote their research. Thus, we will question your ability to come up with new technology and ideas through collaboration with other researchers. Please state proponents' thoughts and achievements from this perspective.

We expect research proposals related to art/artistry. Research area management advisors, Kaoru Kondo (Concertmaster of the Tokyo Philharmonic Orchestra), and Yutaka Hasegawa (President & CEO of Sony Design Consulting Inc.) will provide advice on artwork. We will also introduce and propose artists and designers who collaborate as joint researchers. Within this research area, research on physicality and artistry, such as research on the cooperative relationship between physical activity (breathing patterns, brain wave patterns, etc.) and artistic expression, and research on the gap of the sensory perception and emotion between artists and audiences, is ongoing with the research area management advisors. We expect proposals from researchers that wish to collaborate with artists in research on developing foundational technologies that measure and control biological multisensory systems, on clarifying the receiving, processing and operating mechanisms of biological multisensory systems, and on clarifying sensory network mechanisms.

We also expect research proposals related to barrier-free research and disability studies, and the research by user-researchers. Research area advisor, Shin-ichiro Kumagaya (Associate Professor, The Research Center for Advanced Science and Technology, The University of Tokyo), will provide advice on barrier-free/disability studies. We will also introduce user-researchers and members of the community of people with disabilities as joint researchers. Within this research area, we plan to establish a study group for joint research between disability studies and other multi-sensory systems research fields. Based on the idea of co-production of research, we strongly expect proposals from researchers who collaborate, or wish to collaborate with the community of people with disabilities in all processes from research proposal to publication of research results.

We anticipate that maximizing the use of forums for collaboration with researchers inside and outside of this research area, including the CREST research area "[Multi-sensing] Investigating biological multi-sensing systems and creating applied technologies" and the AMED-CREST/PRIME research R&D project "Integrated understanding of multi-sensing networks and elucidation of their control mechanisms leading to the innovation of medical technologies" which were set up based on the same strategic objectives and research and development targets, will mean that this PRESTO research will serve as an important step in the progress of the future research of the researchers themselves.

In view of the importance of innovation in recent science and technology policies, this research area will support participating researchers in acquiring intellectual property rights.

4. Collaboration and cooperation with other research areas

When managing this research area, we aim to promote collaboration with research areas such as

CREST's "[Multi-sensing] Investigating biological multi-sensing systems and creating applied technologies," PRESTO's "Multisensory Integration in Biological Systems," and AMED-CREST/PRIME's "Integrated understanding of multi-sensing networks and elucidation of their control mechanisms leading to the innovation of medical technologies" We will jointly hold research area meetings and workshops, etc., as necessary. Furthermore, we are considering holding joint symposiums and research meetings to encourage collaboration with research institutions, other research areas and relevant academic conferences.

In accordance with the policy described in "Chapter 9: Limitation on Duplicate Applications within the Strategic Research Promotion Projects" of the Call for Proposals, the Strategic Research Promotion Projects have a limitation on duplicate applications, which means that a researcher may apply for only one research proposal from among all the research areas or research and development areas of CREST, PRESTO, ACT-X, AMED-CREST, and PRIME that will be publicly advertised in FY2021.

Regarding PRESTO "Multisensory Integration in Biological Systems" research area, as an exceptional measure, it is possible to submit duplicate application with AMED's PRIME "Integrated understanding of multi-sensing networks and elucidation of their control mechanisms leading to the innovation of medical technologies" R&D project, which is established under the same Strategic Objective. Please note that each application shall be done with using the format specified by JST (PRESTO) and AMED (PRIME) for the proposal. If the proposal form error happens, it will not be accepted. Also, it will not be selected in two areas at the same time.

5. Research period and research costs

The research period is three years and six months or less; budgets have an upper limit of a total of 40 million yen (not including indirect costs).