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

Research on multi-sensing biosystems and development of adaptive technologies

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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.

Conception of the 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 Neurotechnologies for Disease Studies/Strategic International Brain Science Research Promotion Program (from the 2014 academic year to the 2023 academic year).

Conception of the Research Supervisor

This program will create a novel research area of biological multisensing systems synthesized across the sensory organs of multiple modalities and the peripheral nerves innervating them by crossing the boundaries of conventional life sciences (*e.g.*, sensory physiology, molecular and cellular biology, and neuroscience) to interact with a broader spectrum of disciplines, including electronic and mechanical engineering, information and mathematical sciences, and cognitive psychology, resulting in the development of fundamental and applied technologies to be implemented in daily social environments.

Currently, advancing measurement technologies have opened avenues to discover novel sensing functions and mechanisms and have revealed that sensory systems interact with the immune, metabolic, and endocrine systems to maintain homeostasis and at unconscious levels affect various perceptions or emotions that contribute to shaping our view of humanity and the world. Additionally, the application of advanced Information and Communication Technologies (ICTs; *e.g.*, XRs, wearable devices) would allow the expansion of human internal and external sensing functions.

This research area encourages research synthesizing a wide spectrum of sensory information, from internal and external environments to the biological functions of the body as a whole; however, reductionist approaches within conventional boundaries are discouraged. The development of technologies that realize biological sensor fusion by applying the principles of these multisensing mechanisms is also encouraged, including, for example, the visualization, manipulation, transmission, and representation of multiple sensory modalities. Furthermore, super-sensing mechanisms (by nonhuman animals or by engineering beyond ordinary human abilities) also fall within the scope of this research area in terms of incorporating them into human sensing systems through the development of their governing principles and the associated detection devices.

Research Supervisor Policy for the Call for Research and Selection and Management of the Research Area

1. Background and Overview

This program will create a novel research area of biological multisensing systems synthesized across the sensory organs of multiple modalities and the peripheral nerves innervating them by crossing the boundaries of conventional life sciences (*e.g.*, sensory physiology, molecular and cellular biology, and neuroscience) to interact with a broader spectrum of disciplines, including electronic and mechanical engineering, information and mathematical sciences, and cognitive psychology, resulting in the development of fundamental and applied technologies to be implemented in daily social environments. This research area does not promote projects as straightforward extensions of existing paradigms limited by the boundaries of sensory organs and the peripheral nervous system but aims to make a leap through distributed and local interactions with other biological systems, such as the immune, metabolic,

and endocrine systems. These breakthroughs will be expected to create novel rich and healthy human sensory environments (*Umwelt*), which will allow us to take the next step forward to extend the human society of the near future and engender innovation to realize such an advance.

Japan has a long tradition of sensory research with significant previous achievements in a variety of species at multiple levels of biological hierarchies. This tradition comprises a great strength associated with an extensive body of knowledge and a diverse spectrum of technologies that have been accumulated to date. Additionally, recently advanced measurement technologies have started to open avenues to discover novel sensing functions and mechanisms or uncover sensory systems that interact with the immune, metabolic, and endocrine systems to maintain homeostasis and at unconscious levels affect various perceptions or emotions that contribute to shaping our view of humanity and the world. Additionally, the application of advanced ICTs (*e.g.*, XRs—VR, AR, SR, MR, wearable devices) would allow the expansion of human internal and external sensing functions.

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As such, this research area will serve as a hub to liaise a wide range of research fields in Japan that have independently accomplished significant achievements to date and create a systematic platform for a synergistic effect among life sciences, electronic/mechanical engineering, information and mathematical sciences, and cognitive psychology, which have rarely interacted in the past. Through these incubation mechanisms, a novel biological multisensing research area that has originated in Japan will be promoted to impact global research communities. Furthermore, to establish the next generation's novel academic field, training and support of the human resources of young leaders will be provided, and a novel value axis for research evaluation will be created. Through these activities, this research area will collectively pursue principles of multisensing and development of technologies for the social implementation of multisensing systems, which will lead to the creation of a new concept of humanity that should eventually contribute to the development and enrichment of the human society of the near future.

2. Project Goals and Selection Policies

This research area promotes integrated studies that interact across different research fields, and beyond the boundaries of conventional ones, to achieve the "priority strategies of science and technology" through, but not limited to, themes such as (1) to (4) below. Last year, we received many proposals to study mechanisms of "reception, processing, and operation of multiple sensations" and of "integration across multi-sensory systems and with other biological systems and organs", while few related to development of technologies for "measuring and controlling multiple sensory modalities", "expanding sensing abilities utilizing nonhuman organisms and engineering devices" or "creating new theories to synthesize multiple senses". In this year's call for proposals, we strongly expect proposals that aim to create a new sensory world by expanding existing senses, and research proposals based on theory-driven approaches such as mathematical science. We also expect research proposals to link

with other biological systems such as immunity, metabolism, and endocrinology, psychology, and the creation of new technologies using XRs (VR, MR, AR, SR) to extend our senses, which were expected in last year's call but the number of applications was limited. The selection criteria for the proposals include i) the conceptual structure of the series of previous achievements, ii) the state of past achievements within the conventional framework, and iii) readiness for the next synthesizing stage of the proposed project. Although future plans will be central to the evaluation process, the association of the proposed project with past results will at least be considered.

(1) Signal transduction, processing, and operating mechanisms of multiple sensory modalities

Studies should extend previous fundamental concepts (reduced to single molecules, receptors, and circuits) to the complexity of their dynamic states, *e.g.*, intracellular multimolecular states and interactions across a wide range of different biological hierarchies, from the electronic states of atoms comprising functional molecules through conditions of environments (internal and external) in which information is acquired via mechanisms other than signal transduction at receptor cells. Such proposals, for example, might want to aim at the following:

- Mechanisms for detecting information at various sensors (including receptor cells) to feed, via peripheral nerve networks, the central nervous system for processing through structural and functional analyses using state-of-the-art imaging technologies.
- Operating mechanisms of biological sensory systems across atomic, molecular, and cellular levels.
- Mechanisms of sensing functions by organs other than conventional sensory receptors and interactions among them.
- Effects of the functions of sensing systems on the perceptions, emotions, and behaviors of individuals and social groups.

(2) Integration across multiple sensory systems and with other biological systems and organs

Studies should consider intermodal relationships and their integration principles across distant sensations (vision, audition), proximal sensations (taste, olfaction, haptics, pain, itch, etc.), and interoceptive, visceral, vestibular sensations and their distributed and local interactions with other biological systems, such as the immune, metabolic and endocrine systems, which would result in further interactions with hierarchical information processing in the central nervous system. Such proposals, for example, might want to aim at the following:

- Mechanisms of complementary interactions (*i.e.*, biological sensor fusion) among sensory organs of different modalities.
- Structures and functions of circular networks across multiple internal organs, including the brain.
- Distributed local information processing at the level of sensory organs and/or innervating peripheral nerves and their interactions with other biological systems.

(3) Technologies for measuring and controlling multisensing systems

Devices should be developed to measure and visualize the real-time spatiotemporal dynamics of (both known and unknown) sensory receptor system functions distributed throughout the whole body. Additionally, technologies (including XRs; VR, AR, SR, MR) should be developed to acquire, transmit, and represent proximal and interoceptive sensations that remain rather undeveloped compared with distant sensations (vision, audition), and the influences of such

devices on social activities and mental functions should be theoretically assessed once they have been socially implemented. Such proposals, for example, might want to aim at the following:

- Wearable devices and basic technologies for high-speed and large-scale measurement and quantification of structures and functions of biological multisensing systems.
- Technologies to analyze and process large-scale data from biological multisensing systems.
- Exploration of previously unknown senses and principles to integrate them into existing human sensory systems to contribute to the extension and enhancement of human societies of the immediate future.
- Technologies to control, represent, and extend human sensing systems by integrating the biological mechanisms of sensory organs and ICT technology and/or engineering.

(4) Technologies to utilize the sensing abilities of nonhuman organisms and engineering devices

Technologies should be developed to utilize information from existing sensory modalities but beyond the human-detectable dynamic range, those from sensory systems of nonhuman organisms undetectable by humans, and from those detectable only via nonbiological devices, for contribution to the extension and enhancement of human societies of the immediate future. Additionally, the influences of those technologies on social activities and mental functions should be theoretically assessed once socially implemented. Such proposals, for example, might want to aim at the following:

- "Supersensing" functions of nonhuman organisms (including animals, microorganisms, plants) and engineering approaches and technologies for their application.
- Principles and conceptual framework for a novel human sensory environment (*Umwelt*) as a result of sensor fusion across multi- and supersensing mechanisms and novel technologies for their social implementations.
- Technologies to complement biological multisensing systems to substitute for and extend human sensing functions.

3. Project Duration and Funding Scale

The research period for each project should be no longer than five years and six months. The initial research budget should not exceed a total of 300 million yen (direct costs) per project. Substitutional support to accelerate research may be considered during the research period. In some cases, the research costs may be adjusted based on careful evaluation by the supervisor.

4. Management Policies

(1) Research and development

This research area promotes projects to integrate otherwise unencountered research fields, but rather than being a straightforward extension of existing paradigms, it makes a leap to groundbreaking outcomes that could never be achieved through studies in single disciplines. To encourage risk-taking and challenging approaches to achieve this goal, judicious effort-based but not immediate results-based evaluation of research achievements will be respected. Specifically, when there is an early-stage lack of success, processes and details of the failure will be examined, and an internal advisory system will support the project to maximize the values of experiences accumulated through such failures for the benefit of making the next leap forward. Simultaneously, novel evaluation criteria and procedures will be sought to develop, establish this research field of novel concepts, independent of conventional frameworks, to eventually make them international standards. For this purpose, we will raise the

international appeal of this field through contribution of newly joined international advisors. Additionally, an internal program will be organized to study the development and of this research area itself over the project duration. As such, project budgets will be reviewed on a yearly basis and thus may be adjusted according to the research progress. Additionally, the composition of the research team and budget may require reconsideration upon interim evaluation of the research progress and outcomes, including merging with other research projects or inviting additional external researchers to join in addition to mere reorganization within the project. For effective management as a network-based research institute, the research supervisors' discretionary budget will be fully utilized to provide supplementary budgets for projects making outstanding progress and/or those making significant contributions to the research area. It will also be used, as depicted below, for internal programs for training young project participants to become leaders of the next generation who will drive this new research area and to promote internal and external collaboration.

(2) Human resources (training and support)

Training and support will be provided for young researchers to foster and create career paths for them to become leaders of the future interdisciplinary multisensing research field. When aiming at integration with previously unrelated fields, initial understanding and mutual respect of each field's fundamental aspects is mandatory, including the basic terminology, ways of thinking, types of outcomes, and prioritized values. Conflicts in these areas may be unconscious but thus are critical barriers that need to be explicitly and intentionally overcome at the beginning. To accomplish such training, interdisciplinary lecture series (by volunteering project PIs and advisors) for young members across research projects will be organized using occasions of regular biannual research area meetings.

In addition, by utilizing ICTs, including social media, young researchers will be supported in creating an accessible environment for bold and ambitious discussions across different fields. The research supervisors' discretionary budget may be allocated to young researchers' internal minicollaboration projects, upon a proposal-evaluation basis, that emerge from such discussions. Through these activities, an atmosphere will develop that allows junior colleagues to discuss their projects with the PIs of other projects in different disciplines, thus triggering ideas for the next generation's important project to be proposed by them. Moreover, with the support of PIs in different disciplines, opportunities will be provided for young researchers to attend academic conferences and meetings in other fields, and environment will be constructed that lowers the psychological hurdles related to crossing disciplinary borders towards their future development.

(3) Internal and external collaborations

CREST projects are collectively regarded as a network-based research institute and are managed collaboratively and comprehensively. Further links with PRESTO and with AMED-CREST and PRIME will be promoted under the leadership of the PS responsible for all four JST-AMED programs.

Within CREST, proactive and open-minded interactions among members from different disciplines will be fostered through the establishment of a forum structure that will support joint and collaborative research. Corresponding to the core facilities of the physical research institute, our network institute will create a database platform in which member researchers can share a variety of data and resources to pursue the effectiveness, standardization and integrity of their research outcomes.

Throughout the four JST/AMED programs, a platform for regular exchanges of ideas will be established to seek potential constructive and innovative joint enterprises. External to the four programs, under the PS's leadership, joint proposals will be sought for symposiums/workshops in

domestic and international academic conferences, conventions and meetings. To globalize these Japan-originated new research areas, special issues under the themes of this research area will be organized in international journals, and international collaborations under such themes with overseas institutions and organizations will be supported.

5. Addendum

This research area emphasizes the research and development of biological multisensing systems comprising the sensory organs and the peripheral neural network of humans and model organisms. Proposals utilizing atypical species for the research and development of their evolutionarily acquired supersensing functions are also accepted.

Original and challenging research proposals from midcareer researchers and female researchers are particularly encouraged.