Unique & Exciting Campus

2016 Annual Report

The University of Electro-Communications

Brain Science Inspired Life Support Research Center

http://blsc-uec.net/en/

Preface

There are concerns that the decline of physical strength and sensory functions due to diseases and ageing leads to the lowering of QOL (quality of life) of individuals in the mental as well as physical aspects. These declined activities result in not only individual handicaps but also a lot of disadvantages for societies surrounding them. This indicates that one of the most important issues is the efficient prevention and treatment of decline of physical abilities and sensory functions, and moreover how we live together symbiotically with people of lowered QOL.

Since Brain Science Inspired Life Support Research Center (BLSC) was launched in 2013, researchers from a wide spectrum of sciences such as neuroscience, information science, robotics, ergonomics, bioengineering and optical science have cooperated and collaborated to carry out investigation and development aiming at medical prevention and care, improvement of quality of medicine, sophistication of medicine for post-treatment recovery. In 2016, we reorganized BLSC that was originally composed of 3 research groups by adding a theoretical group. Now BLSC has 4 research groups: Basic technology development of optical measurements group; Measurement and monitoring of *in vivo* brain functions group; Technology development for motor function recovery for medical welfare group; and Theoretical and computational neuroscience group. Under this reorganized group structure, we became to identify clearly the missions of respective groups and easily recognize similarities and differences among studies conducted by individual BLSC members. This in turn revitalizes individuals' research by working together more closely within a group and cooperating with other groups to produce innovative technologies for life support. Also we devote ourselves to fostering young scientists and engineers who will further promote such innovative research and development.

The present annual report is to summarize all our activities in 2016 to restart our activities towards the future. We reaffirm our determination to perform research more cooperatively and more collaboratively making the best use of the current results reported here. If we could have your understanding and support successively, we would be very happy.

August 25, 2017
Brain Science Inspired Life Support Research Center
Director Takuji Koike

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Theoretical and Computational Neuroscience Group

Mission

BLSC aims to study science and engineering necessary for people to live peacefully. In more detail, BLSC's objective is to construct science and technology for alleviating inconvenience in the elderly and handicapped so as to live like a human being, based on medicine engineering cooperation. Another objective is to foster human resources to be able to pursue such research.

There are many people who feel decline in the ability of perception, cognition, communication and body action due to ageing, and hence have daily anxiety and inconvenience. Therefore BLSC is charged with a primary mission that it provides such people with advanced technology for the fulfillment of their potentials by assisting and strengthening their weakened functions. To complete the mission, UEC researchers from different research fields got together to organize BLSC. This fact made BLSC to have highly diversified and heterogeneous research areas.

In today's medicine, people are judged to be either patients or healthy people according to certain indices to identify the pathology, and the latter, if they do not feel well, is difficult to receive medical treatment because of "not disease". From the standpoint of preventive medicine, however, health promotion technology is demanded for those people. Similar cases are the elderly with weakened functions of perception, cognition and movement. Thus, research and education on the development of assist technology, rehabilitation and practical training programs for the elderly without disease are the issues that BLSC needs to address.

Group Structure

BLSC promotes project-based programs in research and education aiming at fostering innovative human resources who are responsible for meeting technological needs in the onsite medical welfare treatment. For this purpose, BLSC set the following 3 research groups that support the programs. Students develop expertise and practical skills necessary for innovative research, solving problems under the project-based programs.

Basic technology development of optical measurements group

This group focuses on research and education for the development of new optical probes, optical imaging technology and multidimensional image analysis to evaluate the capabilities of plasticity, self-recovery, and regeneration of organic functions. (Members: Yamada, Niwa & Maki)

Measurement and monitoring of *in vivo* brain functions group

This group focuses on research and education on the measurement of individual cells' activities in response to external stimuli, the brain imaging of activities associated with motor functions, and the monitoring and control of brain activities using BMI technology. (Members: Masamoto, Miyawaki, Shouno & Matsuda)

Technology development for motor function recovery for medical welfare group

This group focuses on research and education on the technology development for motor control and rehabilitation based on measurements of brain activities associated with motor functions. (Members: Koike, Yokoi, Kano, Okada, Koizumi, Jiang & Sun)

Theoretical and computational neuroscience group

This group devotes itself to research and education on mathematical modeling of the nervous system at the levels of cells and/or networks to understand the mechanisms of the brain structure, function and plasticity for the development of a next-generation artificial intelligence and engineering application to neurorehabilitation. (Members: Kashimori, Tanaka & Yamazaki)

Personnel Organization （as of 31 March, 2017 ）

Name	Web site	Position
KOIKE Takuji	http://www.bio.mce.uec.ac.jp/index.html	Director (2016-)
KANO Yutaka	http://www.ecc.es.uec.ac.jp/	Vice Director (2016-)
YOKOI Hiroshi	http://www.hi.mce.uec.ac.jp/yklab/	Professor
OKADA Hidetaka	http://www.hb.mce.uec.ac.jp/	Professor
KASHIMORI Yoshiki	http://granule.pc.uec.ac.jp/wiki/wiki.cgi	Professor
SHOUNO Hayaru	http://daemon.inf.uec.ac.jp/ja/	Professor
MASAMOTO Kazuto	http://kjk.office.uec.ac.jp/Profiles/55/0005461/	Professor
	profile.html	Professor
MIYAWAKI Yoichi	http://www.nvu.mi.uec.ac.jp	Professor
TANAKA Shigeru	http://tanaka-lab.net/jp/	SA Professor
NIWA Haruki	http://www.firefly.pc.uec.ac.jp/	SA Professor
YAMADA Yukio	http://www.nvu.mi.uec.ac.jp/old_html/index.html	SA Professor
MATSUDA Shinji	http://www.matsuda-lab.es.uec.ac.jp/	Associate Professor
KOIZUMI Norihiro	http://www.medigit.mi.uec.ac.jp/	Associate Professor
YAMAZAKI Tadashi	http://numericalbrain.org/	Associate Professor
JIANG Yinlai	http://www.hi.mce.uec.ac.jp/yklab/	Associate Professor
MAKI Shojiro	http://www.firefly.pc.uec.ac.jp/	Assistant Professor
SUN Guanghao	http://cargocollective.com/guanghao_sun	Assistant Professor
		*SA: Specially Appointed

Visiting Scientists

Name	Affiliation	Position
ARAMAKI Yu	Chukyo University School of Health and Sport Sciences, Professor	Visiting Professor
KATO Ryu	Faculty of Engineering Division of Systems Research, Associate Professor	Visiting Associate Professor
KANSAKU Kenji	Systems Neuroscience Section, Research Institute of National Rehabilitation Center for Persons with Disabilities・Chief	Visiting Professor
TAKAGI Takehiko	Department of Orthopaedic Surgery, Tokai University Assistant Professor	Visiting Professor
TAKAYAMA Shinichiro	Department of Surgical Specialities, National Center for Child Health and Development Director	Visiting Professor
TAKITA Masatoshi	Brain Function Measurement Group, Human Informatics Research Institute, National Institute of Advanced Industrial Science and Technology (AIST) Senior Researcher	Visiting Professor
NAKAMURA Tadashi	UEC Professor Emeritus http://kaeru.pc.uec.ac.jp/	Visiting Professor
HOSHI Yoko	Department of Biomedical Optics, Institute for Medical Photonics Research, Preeminent Medical Photonics Education & Research Center, Hamamatsu University School of Medicine Professor	Visiting Professor
YAMAMURA Osamu	University of Fukui School of Medicine Associate Professor	Visiting Professor
YU Wenwei	Department of Medical System Engineering, Graduate School of Engineering, Chiba University Professor	Visiting Professor
LU Baoliang	Department of Automation, School of Electronic, Information and Electrical Engineering, Shanghai Jiao Tong University, China Professor	Visiting Professor
CAO Qixin	Director, Engineering Training Center, Shanghai Jiao Tong University, China Professor	Visiting Professor

Achievements in 2016

1． Research

A. Refereed papers： 47
（including 7 papers published in IF>4 journals）

B. Presentations at international conferences：22

C. Master patent applications：6

D. Productization：1

2． Education

A. Student guidance：64（Bachelor：43, Master：19, Doctor：2）

B. Awards：12 （Faculty members：4, Students：8）

3． Public relations & Outreach activities

A. Media release：20

B. High school visit：9

Research Funding in 2016

Total budget：182,416,000 yen

（Breakdown）

○**Project expense**:

"New human resource development program to support the super-aged society by brain science inspired life support innovation"

FY 2016 Special expense: 4,488,000 yen； UEC burden: 4,488,000 yen

○**Grants-in-aid for Scientific Research (Kakenhi)**:

（Scientific Research (A): 1, Scientific Research (B): 6, Scientific Research (C): 11, Challenging Exploratory Research: 4, Innovative Areas: 4, Young Scientist: 1）

Total expense: 55,190,000 yen

○**Research funding from governmental resources other than Kakenhi:**

Total expense: 109,621,000 yen (9 applications)

○**Private foundations:**

Total expense: 3,997,000 yen (2 applications)

○**Expense for collaboration and donation from private companies:**

Total expense: 4,632,000 yen (5 applications)

Seminars and Events

For general audience interested in neurosciences and technological research for life support in aged societies, we have held “BLSC Seminar Series” continually about once a month since BLSC was established. We also held “BLSC Spring School for High School Students” for FY2016. Summaries of these events and educational activities are described below (in more detail, see the BLSC website: http://blsc-uec.net/). (Note: English translations from Japanese are not authorized by the speakers, and technical terms may not be correct.)

1. BLSC Seminar Series

BLSC Seminars were held twelve times from 37th to 48th in FY2016. The member of BLSC who proposed a subject and speaker was supposed to organize the seminar in turn.

37th seminar

Date and time: Apr. 15 (Fri.), 2016, 13：30 - 14：30

Place: Meeting Room #306, Building E-3, UEC

Speaker: Dr. Mamoru Fukuchi (Assistant Professor, Laboratory of Molecular Neurobiology, Graduate School of Medicine and Pharmaceutical, University of Toyama)

Chair: Assis. Prof. Shojiro Maki

Title: Study of the expression control mechanism of brain-derived neurotrophic factor (BDNF) gene; Toward understanding of the expressions of higher order functions of the brain-nerve system and creations of new drugs

38th seminar

Date and time: May 18 (Wed.), 2016, 13：30 - 14：30

Place: Meeting Room #306, Building E-3, UEC

Speaker: Dr. Kazunori Hase (Professor, Mechanical Engineering, Graduate School of Science and Engineering, Tokyo Metropolitan University)

Chair: Prof. Hidetaka Okada

Title: Simulation of human walking with a nerve-musculoskeletal model and its applications

39th seminar

Date and time: Jun. 21 (Tue.), 2016, 16：15 - 17:45

Place: Room #802, Building E-4, UEC

Speaker: Dr. Yu Aramaki (Professor, School of Health and Sport Sciences, Chukyo University)

Chair: Assoc. Prof. Yoichi Miyawaki

Title: Sports and voxel-based morphometry (VBM)

40th seminar

Date and time: Jul. 27 (Wed.), 2016, 13：00 - 14:30

Place: Meeting Room #306, Building E-3, UEC

Speaker: Dr. Satoko Koganemaru (Researcher, Human Brain Research Center, Graduate School of Medicine Kyoto University)

Chair: Assis. Prof. Tadashi Yamazaki

Title: Changes in brain activity and modification of human walking by transcranial oscillatory stimulations of brain

41st seminar

Date and time: Sep. 9 (Fri.), 2016, 13：00 - 14:30

Place: Meeting Room #306, Building E-3, UEC

Speaker: Dr. Michisuke Yuzaki (Professor, Department of Physiology, School of Medicine, Keio Univeristy)

Chair: Assoc. Prof. Shinya Matsuda

Title: Bridge over Troubled Synapses

42nd seminar

Date and time: Oct. 26 (Wed.), 2016, 13：00 - 14:30

Place: Meeting Room #301, Building E-3, UEC

Speaker: Dr. Hidenori Sakanashi (Senior Researcher, The Artificial Intelligence Research Center, National Institute of Industrial Science and Engineering (AIST))

Chair: Prof. Hayaru Shouno

Title: Support for medical diagnostics with image recognition technology

43rd seminar

Date and time: Nov. 29 (Tue.), 2016, 13：00 - 14:30

Place: Meeting Room #306, Building E-3, UEC

Speaker: Dr. Kiyohiko Nakamura (Professor, Interdisciplinary Graduate School of Science and Engineering, Tokyo Institute of Technology)

Chair: Prof. Yoshiki Kashimori

Title: Neuro-mechanism which demands information

44th seminar

Date and time: Dec. 21 (Wed.), 2016, 13：00 - 14:30

Place: Meeting Room #306, Building E-3, UEC

Speaker: Dr. Norihiro Koizumi (Associate Professor, Department of Mechanical Engineering and Intelligent Systems, University of Electro-Communications)

Chair: Prof. Yukio Yamada

Title: Development of robots for ultrasonic diagnosis and therapy with ultra-high accuracy through Me-Dic IT

45th seminar

Date and time: Jan. 27 (Fri.), 2016, 13：00 - 14:30

Place: Meeting Room #306, Building E-3, UEC

Speaker: Dr. Zhu Xiaoxiao (Specially Appointed Associate Professor, Global Alliance Laboratory, University of Electro-Communications, and Researcher, Institute of Robotics, Shanghai Jiaotong University, China)

Chair: Prof. Hiroshi Yokoi

Title: ROS based Control of a 7-DoF Robot Arm for BMI

46th seminar

Date and time: Feb. 23 (Thu.), 2016, 13：00 - 14:30

Place: Meeting Room #306, Building E-3, UEC

Speaker: Dr. Sun Guanghao (Assistant Professor, Department of Mechanical Engineering and Intelligent Systems, University of Electro-Communications)

Chair: Assoc. Prof. Norihiro Koizumi

Title: Development of practical medical devices for non-contact measurement of vital signs by bio-sensors using microwave radar etc.

47th seminar

Date and time: Mar. 9 (Thu.), 2016, 13：00 - 14:30

Place: Meeting Room #306, Building E-3, UEC

Speaker: Dr. Gentaro Taga (Professor, Developmental Brain Science Laboratory, Department of Physical and Health Education, Graduate School of Education, The University of Tokyo)

Chair: Prof. Yukio Yamada

Title: Study of brain development using hPod (hemoglobin Phase of oxygenation and deoxygenation) in fNIRS (functional near-infrared spectroscopy)

48th seminar (In cooperation with Industry-UCB-UEC Workshop 2017 (IUUWS 2017))

Date and time: Apr. 27 (Mon.), 2017, 14:30 - 15:30

Place: Meeting Room #301, Building E-3, UEC

Speakers: Dr. Gerard Marriott (University of California, Berkeley, Professor)

Dr. Shojiro Maki (Department of Engineering Science, UEC, Assist. Prof.)

Titles: [Dr. Gerard Marriott] Engineering platelets and optical probes for applications in translational medicine

[Dr. Shojiro Maki] Chemistry of firefly bioluminescence

The statistics of the attendees to the seminar series in FY2016 are listed in the table below. In averages, the number of the total attendees per seminar was 27.7, and the numbers of the faculties of UEC, the students of UEC and the others were 13.0, 13.0 and 1.7, respectively.

Number	Faculties of UEC	Students of UEC	Others	Total
37th	13	14	6	33
38th	15	13	3	31
39th	16	9	5	30
40th	13	23	1	37
41st	11	17	0	28
42nd	10	7	1	18
43rd	17	16	1	34

44th	10	21	0	31
45th	13	8	1	22
46th	12	2	1	15
47th	13	13	0	26

2. BLSC Spring School for High School Students

BLSC modified part of the hands-on training course for graduate students and designed contents of the spring school easy for high school students to learn. In 2017, 2nd “Brain Science Life Support Research Center Spring School” was held for 4 days Mon. Mar. 27 to Thu. Mar. 30, 2017. Seventeen high school students attended from Tokyo, Ibaraki and Chiba prefectures. The time of the school per day was four and half hours, and one topic spent two days for each of the first and second periods. Two topics were selected from the hands-on training course for graduate students, and a manual for high school students was made by modifying the text of the hands-on training course. The titles of the lectures and experiments, schedules, and numbers of participants are as follows. Details of the Spring School are listed on the center's homepage (http://blsc-uec.net/wpblsc/wp-content/uploads/ReportBLSC-SpringSchool2017.pdf).

The participants learned the following two topics:

1st topic: See the hearing

Place: Labs. #730 and #507, Building E-4, UEC

Instructor: Prof. T. Koike

Teaching Assistants: N. Li, M. Sato, R. Kuroda, Y. Yoshimura

Contents:

1st day: Measurement of auditory brainstem response.

After normal hearing tests, weak electroencephalograms from brainstem induced by sound stimulus were measured.

2nd day: Measurement of distortion components of otoacoustic emissions.

The distortion product otoacoustic emission generated in the ear by sound stimulus were measured and the hearing ability was estimated.

2nd topic: Let’s make lightning of firefly

Place: Lab. #837, Building E-6, and lab. #408, SVBL Building, UEC

Instructor: Assis. Prof. S. Maki

Teaching Assistants: A. Kitada, R. Morimitsu, Y. Hachiro

Contents:

1st day: Organic synthesis of firefly D-luciferin was performed.

2nd day: Structure confirmation of the synthesized D-luciferin with instrument analyses (nuclear magnetic resonance, mass, and infrared spectra).

Firefly bioluminescence was observed by using the synthesized D-luciferin.

The participants were grouped into the following two.

1st group:

Date and time: Mon. Mar. 27, 2017, 13:00-17:30 and Tue. Mar. 28, 2017, 13:00-17:30

Number of participants: Five for the 1st topic, and four for the 2nd topic

2nd group:

Date and time: Wed. Mar. 29, 2017, 13:00-17:30 and Thu. Mar. 30, 2017, 13:00-17:30

Number of participants: Three for the 1st topic, and five for the 2nd topic

Yukio YAMADA Laboratory

1. Outline of Research and Education

1. 1 Basic Policy in Research and Education

The major research topics are medical and biological measurements using near infrared light, such as (1) diffuse optical tomography (DOT) for imaging blood oxygenation and blood volume based on near infrared spectroscopy (NIRS), (2) optical mapping (or optical topography) for imaging brain function based on NIRS, (3) fluorescence tomography for imaging the distribution of fluorophore concentration inside bodies, (4) noninvasive and continuous measurement of blood glucose contents (BGC) using NIRS and (5) detection of aspiration by the use of fluorescence in the near infrared wavelength range. In addition, as an industrial application of NIRS (6) noncontact measurement of temperature and concentration distributions of aqueous solutions in a microchannel is being examined. Summaries of the above research topics are described below.

(1) **Diffuse Optical Tomography (DOT)**

The near infrared wavelength range from about 700 nm to 1200 nm is called as the biological optical window because light in the wavelength range is weakly absorbed by biological tissue, and it is possible to detect the light scattered and absorbed by tissue with the thickness of about 10 cm. Utilizing this characteristics of weak absorption of the near infrared light by tissue, DOT has been developed to obtain tomographic images of tissue or organs of the size larger than a few centimeters. DOT reconstructs the image of the absorption properties of the tissue for the near infrared light, and the reconstructed absorption images are converted to tomographic images of physiological information of the changes in blood statuses such as the concentrations of oxy- and deoxy-hemoglobins and blood volume. In contrast to X-ray computed tomography (X-ray CT) where X-ray propagates straight in bodies, near infrared light does not propagate straight but is strongly scattered by tissue. Therefore, the algorithm of image reconstruction for X-ray CT cannot be applied to DOT, and other algorithms are needed to be developed, which are in the category of the inverse problem based on the equation of light propagation in biological tissue. For solving the forward problem in the inverse problem, in this research, we study the methods to solve the radiative transfer equation and the photon diffusion equation describing light propagation in tissue as well as Monte Carlo methods statistically reproducing light propagation. Figure 1 shows a photo of DOT measurement for investigation of the muscle activity in the forearm during hand gripping (top), and the DOT image which reveals the increase in the deoxy-hemoglobin concentration by 100 μM due to the muscle activity (bottom). Prof. Yamada collaborated

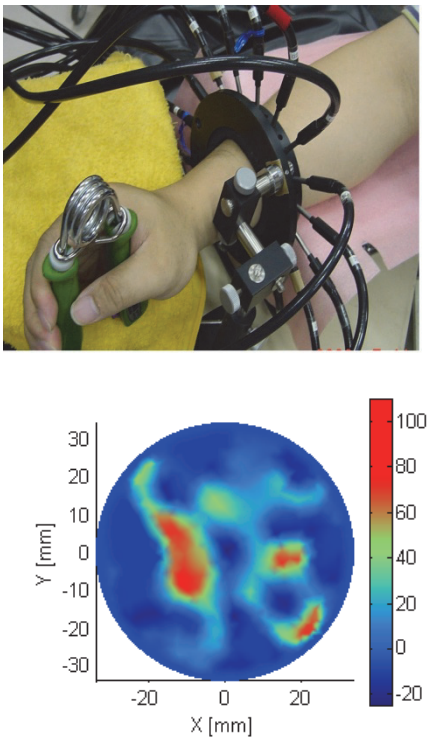


Fig. 1 (Top) Photo of DOT measurement at a forearm, and (Bottom) DOT image showing the increase in the deoxy-hemoglobin concentration due to the muscle activity in the forearm.

with Prof. Y. Hoshi, University of Hamamatsu School of Medicine, who was the leader of a project for DOT sponsored by Japan Agency for Medical Research and Development (AMED), and with Prof. Y. Iso, Kyoto University, who is the leader of a project of "Mathematical analyses of light propagation in biological tissue toward medical applications" sponsored by Japan Society for Promotion of Science (JSPS).

(2) **Optical mapping (Optical topography)**

Optical mapping images the changes in the blood status in the brain using NIRS as DOT does, but cannot obtain tomographic images. Optical mapping simply maps the 2D distribution of the light intensities which are detected at multiple positions on the head surface after the source light is irradiated on the head surface, propagates through the brain surface, and is reemitted from the head surface. Although the mapping images reflect the changes in the blood status caused by the brain activity, interpretation of the images needs careful understanding of the phenomena occurring inside the head because the images are affected by various factors such as the spatial variation of the skull thickness, and the change in the blood volume (or blood flow) in the skin. Prof. Y. Yamada worked in cooperation with Japan Optical Brain Functional Imaging Society in this research topic.

(3) **Fluorescence tomography**

As an application of DOT, fluorescence tomography is developed to image the distribution of fluorophore concentration inside a body. When a body contains fluorophore which emits fluorescence in the near infrared wavelength range, it is possible to obtain a tomographic images of the fluorophore concentration by measuring the fluorescence light emitted from the body surface. This technology is expected to be used mainly for small animals in the development of new drugs for early diagnosis of breast cancers, and so on. Prof. Y. Yamada collaborated with Prof. G. Nishimura, Hokkaido University, who was the leader of a project for fluorescence tomography sponsored by AMED,

(4) **Noninvasive measurement of blood glucose contents (BGC) by NIRS**

If the conventional method of BGC measurement using blood sampling with painful finger pricking is replaced by a noninvasive measurement method, pains experienced by diabetes patients will be greatly alleviated. However, the development of noninvasive measurement of BGC is very difficult and still unsuccessful even after a few tens of years so far. The purpose of this research is to develop a noninvasive measurement method of BGC using NIRS. The most frequently used method in the past utilized multivariate analyses to build calibration functions from simultaneously measured BGC and spectra of light reflected from the skin by pre-experiments. However, the performance of this method using multivariate analyses was found to be limited. So we have been developing two new approaches: one approach builds calibration functions in multivariate analyses from numerically simulated measurement data without the necessity of pre-experiments, and the other approach modifies the classical least squares (CLS) method to introduce imaginary components for canceling out the change in the scattering properties of the skin during the measurement.

(5) **Aspiration detection using fluorescence**

At the occasion of the symposium co-sponsored by the University of Electro-Communications UEC) and Japan Commons for Collaborating Medicine and Engineering, which was held on Nov. 15, 2015, Dr. Y. Michiwaki of Musashino Red Cross Hospital (MRCH) gave a presentation titled as “Development of medical devises assisting the reduction of suffocation accidents and serious pneumonia caused by dysphagia of elderly patients.” After his presentation, UEC started a research project in collaboration with MRCH to develop a new method for aspiration detection by the use of fluorescence, which is useful to examine whether food is trapped at the branch between the trachea and esophagus. Hokkaido University joined the collaboration by providing a high performance fluorescence measurement instrument.

(6) **Noninvasive measurement of temperature of aqueous solution and solute concentration**

The optical absorption spectrum of water in the near infrared wavelength range slightly changes with temperature. Using the characteristics of the spectrum, a new method to noninvasively measure and image the change in the temperature of aqueous solutions has been developed in this research. Additionally using the dependency of the absorption strength on the solute concentration in the aqueous solution, it is possible to simultaneously measure and image the changes in the temperature and solute concentration in the aqueous solution. This method will be applied to measure and image the temperature, solute concentration, reaction rate, etc. in microscale channels in biochips and chemical chips.

1.2 Achievements and State of Progress (April, 2016 - March, 2017)

(1) **Diffuse optical tomography**

As for the results and present status of the research topic of DOT, we have developed a new method for solving the radiative transfer equation which is considered as the most accurate equation describing the phenomena of light propagation in biological tissue, and have found the effect of void regions like the trachea on the light propagation. Also we wrote a review article about DOT. These results were published in international journals (Refs. 1 to 4 of Item 2.1).

(2) **Optical mapping**

Japan Optical Functional Brain Imaging Society (JOFBIS) started a committee for publishing a guidebook for beginners working with optical mapping. This guidebook gives notes and advices in measurements of optical mapping and functional brain imaging using NIRS in general. Yukio Yamada was assigned for the chair of the committee and the first edition was published and expected to contribute to sound development of this technology (Ref. 1 of Item 2.2)

(3) **Fluorescence tomography**

As for the fluorescence tomography, Yukio Yamada worked as a collaborating researcher to a project of Japan Agency for Medical research and Development (AMED) for developing a new algorithm of image reconstruction and for improving the image quality.

(4) **Noninvasive measurement of blood glucose contents (BGC) by NIRS**

By cooperating with a company which has been collaborating with our group for a few years in the past, a new method of noninvasive NIRS measurement of BGC has been developed and the second paper is in preparation to be submitted to an academic journal. Also Yukio Yamada was invited by Samsung, Korea, to give a talk and to discuss about this topic. Our research of this topic is progressing steadily despite its difficulty.

(5) **Aspiration detection using fluorescence**

This research started in December 2015, and we made preliminary experiments after some discussions about the fluorophores, phantom experiments, etc. But, we failed to detect fluorescence in the preliminary experiments using an existing measuring instrument in UEC. Then, another measuring instrument developed by Hokkaido University in the project of the item (3) above was used for detecting fluorescence with a higher sensitivity. We succeeded in detecting fluorescence emitted from the fluorophore embedded in beef. We prepared documents for application to the approval of human experiments. Also we prepared documents for patent application.

(6) **Noninvasive measurement of temperature of aqueous solution and solute concentration**

This topic has been developed to simultaneous measurement and imaging of both temperature and solute concentration, and a paper describing the results was published in an international journal (Ref. 5 of Item 2.1). The paper was highly evaluated and selected one of the highlights in 2016 of the journal indicating that our research activities are progressing soundly and steadily.

1. 3 Future Plan

For the research topics of (1) diffuse optical tomography and (3) fluorescence tomography, the projects sponsored by Japan Agency for Medical Research and Development (AMED) were terminated at the end of the fiscal year of 2016. But the principal investigator will continue to collaborate with the researchers involved in the projects. For the topic of (2) optical mapping, the principal investigator will take part in translation of the pamphlet in Japanese into English under the collaboration with Japan Optical Functional Brain Imaging Society (JOFBIS). Also he will cooperate with researchers who are preparing for an international conference to be held at the University of Tokyo in September 2018.

For the topic of (4) noninvasive measurement of blood glucose contents (BGC) by NIRS, the principal investigator will continue collaboration with the related company, and will submit a paper to an international journal. For the topic of (5) aspiration detection using fluorescence, the group including the principal investigator will continue to accumulate data by preliminary experiments and proceed to *in vivo* experiments using human in 2017. For the topic of (6) noncontact measurement of temperature and solute concentration in aqueous solution, the principal investigator will continue to work in collaboration with the associate professor of Tokyo Metropolitan University.

2. Research Achievements

2. 1 Reviewed papers [○: Impact factor greater than 4]

For the topic of (1) Diffuse optical tomography

(1) Hiroyuki Fujii, Shinpei Okawa, Ken Nadamoto, Eiji Okada, Yukio Yamada, Yoko Hoshi, and Masao Watanabe Numerical Modeling of Photon Migration in Human Neck Based on the Radiative Transport Equation. *Journal of Applied Nonlinear Dynamics* 5, 117–125 (2016).

(2) Yoko Hoshi and Yukio Yamada Overview of diffuse optical tomography and its clinical applications. *Journal of Biomedical Optics* 21 (9) 091312 (2016). doi: 10.1117/1. JBO.21.9.091312. (Invited Review Paper)

(3) Hiroyuki Fujii, Shinpei Okawa, Yukio Yamada, Yoko Hoshi, Masao Watanabe Renormalization of the highly forward-peaked phase function using the double exponential formula for radiative transfer. *Journal of Mathematical Chemistry* published on line: 21 July 2016. DOI: 10.1007/s10910-016-0670-3.

(4) H. Fujii, Y. Yamada, K. Kobayashi, M. Watanabe and Y. Hoshi Modeling of light propagation in the human neck for diagnoses of thyroid cancers by diffuse optical tomography. *International Journal for Numerical Methods in Biomedical Engineering* Version of Record online : 27 Oct. 2016, DOI: 10.1002/cnm.2826.

For the topic of (6) Noninvasive measurement of temperature of aqueous solution and solute concentration

(5) Naoto Kakuta, Hiroki Yamashita, Daisuke Kawashima, Katsuya Kondo, Hidenobu Arimoto and Yukio Yamada Simultaneous imaging of temperature and concentration of ethanol–water mixtures in microchannel using near-infrared dual-wavelength absorption technique. *Measurement Science and Technology* 27 (2016) 115401 (12 pages). doi:10.1088/0957-0233/27/11/115401. (Selected as one of the 2016 Highlights of Measurement Science and Technology)

2.2 Book, non-refereed articles and translation

For the topic of (2) Optical mapping

(1) Y. Yamada et al. Ed., For better measurement of fNIRS (functional near-infrared spectroscopy). 1st. Ed., Japan Optical Functional Brain Imaging Society (JOFBIS). Mar. 2017.

2.3 Invited lectures

(1) (Invited Talk) Yukio Yamada, “Non-invasive near-infrared blood glucose measurement: two new approaches,” Current Challenges on Noninvasive Glucose Sensing and Its Future Directions, Samsung Future Tech Forum, Suwan, Korea, Oct. 25, 2016.

2.4 Award

(1) For the topic of (6) Noninvasive measurement of temperature of aqueous solution and solute concentration, The paper published in the journal of *Measurement Science and Technology* titled as Simultaneous imaging of temperature and concentration of ethanol–water mixtures in microchannel using near-infrared dual-wavelength absorption technique. 27 (2016) 115401, was selected as one of

the Highlights in 2016.

3. Research funding

None

4. Collaboration

4.1 Inside BLSC

(1) For the topic of (5) Aspiration detection using fluorescence, collaboration with Profs. Shojiro Maki, Haruki Niwa, and Takuji Koike.

4.2 Outside UEC

(1) For the topic of (1) Diffuse optical tomography, collaboration with Prof. S. Hoshi, Department of Biomedical Optics, Institute for Medical Photonics Research, Preeminent Medical Photonics Education & Research Center, Hamamatsu University School of Medicine, and with Assoc. Prof. H. Fujii, Faculty of Engineering, Hokkaido University.

(2) For the topic of (3) Fluorescence tomography, collaboration with Assis. Prof. G. Nishimura, Research Institute for Electronic Science, Hokkaido University.

(3) For the topic of (4) Noninvasive measurement of blood glucose contents (BGC) by NIRS, collaboration with Dr. K. Maruo, Panasonic Healthcare co. Ltd.

(4) For the topic of (5) Aspiration detection using fluorescence, collaboration with Dr. Y. Michiwaki of Musashino Red Cross Hospital (MRCH) and Assis. Prof. G. Nishimura, Research Institute for Electronic Science, Hokkaido University.

(5) For the topic of (6) noncontact measurement of temperature and concentration distributions of aqueous solution, collaboration with Prof. N. Kakuta of Tokyo Metropolitan University.

5. Outreach activities

5.1 Paper review of academic journals

(1) Optical Review

(2) Biomedical Optics Express

(3) Journal of Biomedical Optics

(4) Physics in Medicine and Biology

5.2 Other outreach activities

(1) Visiting Professor, Faculty of Engineering, Nihon University

(2) Visiting Researcher, Health Research Institute, National Institute of Advanced Industrial and Scientific Technology (AIST)

1. Outline of Research and Education

1.1 Basic Policy in Research and Education

(1) Development of bioluminescent substrates emitting near-infrared "biological optical window" light.

Bioimaging that utilizes the firefly bioluminescence system (Fig. 1) is widely applied as the standard imaging technology in bioscience for visualizing various phenomena. Light in the near-infrared (NIR) region from about 650 nm to 1200 nm is known as the "biological optical window"; light in this region is highly tissue-permeable and thus optimal for visualizing deep site phenomena. However, the bioluminescence wavelength (λ_{max}) using natural D-luciferin (**1**) and synthetic D-luciferin analogs such as CycLuc1 (**3**) is shorter than 610 nm, and there are no practical substrates emitting in the NIR biological optical window that is suitable for visualizing deep site phenomena. Efforts to elongate the bioluminescence emission wavelength are being actively pursued all over the world. There are two approaches for controlling the emission wavelength, one approach targets the luciferase enzyme and the other targets the substrate luciferin. We aim to develop a practical firefly bioluminescent material that emits light in the NIR biological optical window region by changing the chemical structure of the substrate.

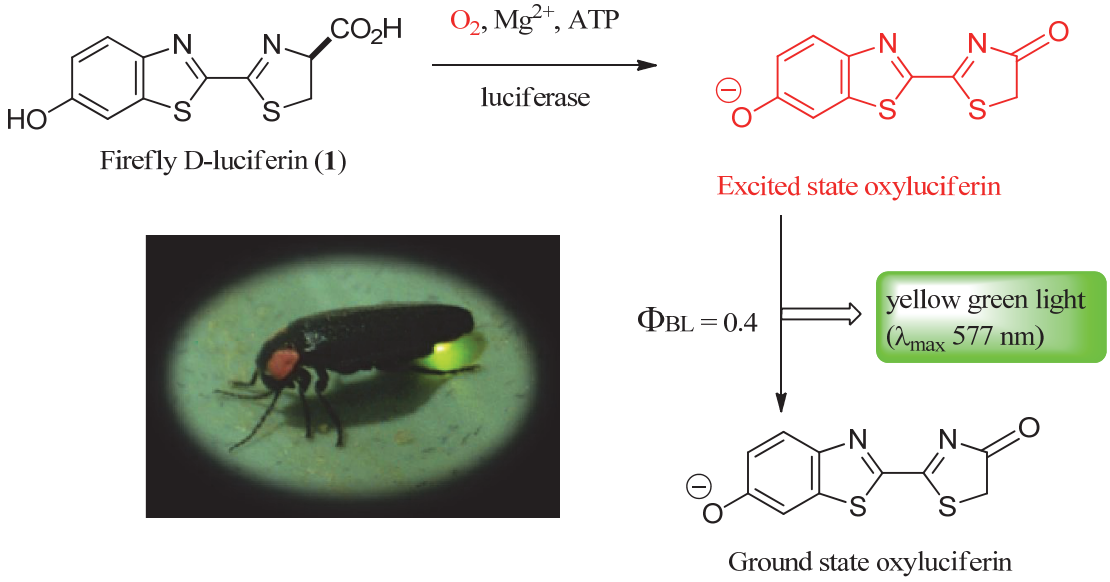


Figure 1. Bioluminescence reaction of firefly.

(2) Development of a non-invasive pulmonary aspiration risk detection system that utilizes NIR biological optical window light.

One of the main causes of death among elderly people is pneumonia. More than 90% of pneumonia in elderly people is caused by pulmonary aspiration (mis-swallowing). As a cause of pulmonary aspiration, it is reported that ingested food unconsciously remains in the junction of the esophagus and the trachea (piriform sinus located in the laryngeal cavity) and flows into the trachea. Therefore, if the remnant food residue in the piriform sinus can be detected at an early stage, the risk of pulmonary aspiration can be detected, leading to the prevention of pulmonary aspiration. However, there is no simple practical device

and method for non-invasive detection of the remnant food residue in the piriform sinus leading to aspiration from outside the body. Therefore, we aim to develop a noninvasive and simple system for detecting food remains in the piriform sinus using fluorescence in the NIR biological optical window with high tissue permeability.

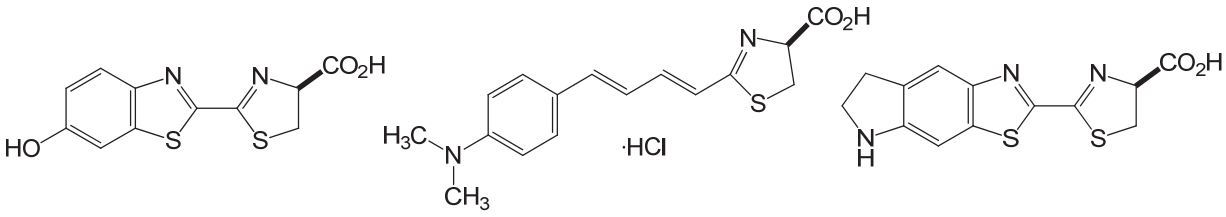
(3) Brain Science Inspired Life Support Research Center (BLSC) Spring School for high school students.

As part of the outreach activities of BLSC, we operate the Spring School every year, so that high school students can gain experience at the forefront of brain science research.

1.2 Achievements and State of Progress (April 2016–March 2017)

(1) Development of bioluminescent substrates emitting near-infrared "biological optical window" light.

The previously developed firefly bioluminescent substrate "AkaLumine" that emits light in the NIR "biological optical window" has an emission wavelength (λ_{max} 677 nm) applicable for deep site bioimaging (Ref. 1). However, AkaLumine was found to possess poor water solubility (<2 mM), which is inconvenient for practical use *in vivo*. We, therefore, developed AkaLumine hydrochloride [AkaLumine-HCl (**2**); solubility: <40 mM] and evaluated its bioluminescence performance using cancer-cell bearing mice inoculated with firefly luciferase-expressing lung cancer cells. When AkaLumine-HCl (**2**) was used as the bioluminescent substrate, more light was detected on the mouse body surfaces in comparison with D-luciferin (1) (λ_{max} 577 nm) or a synthetic luciferin analog CycLuc1 (**3**) (λ_{max} 603), indicating that AkaLumine-HCl (**2**) is more effective for deep site bioimaging than D-luciferin (**1**) and CycLuc1 (**3**) (Ref.2).



1 (D-luciferin) **2** (AkaLumine hydrochloride) **3** (CycLuc1)

(2) Development of a non-invasive pulmonary aspiration risk detection system that utilizes NIR biological optical window light.

Simulation experiments for the detection of remnant food residue in the piriform sinus by utilizing high tissue-permeable NIR region (biological window) light were carried out in a joint study. NIR fluorescence from samples containing a fluorescent dye could be detected through a biological tissue model of more than 2 cm thickness.

(3) BLSC Spring School for high school students.

In March 2017, the second “Brain Science Life Support Research Center Spring School” was held over 4 days. The lecture and experiment for each subject took 4.5 h (3 school h) per day for 2 days. In the Spring School, the students tackled two subjects at the forefront of brain science research, supported by the

instructors and teaching assistants. The titles of the lectures and experiments, schedules, and participants are as follows. Details of the Spring School are listed on the center's homepage (http://blsc-uec.net/wpblsc/wp-content/uploads/ReportBLSC-SpringSchool2017.pdf).

1.3 Future Plans

(1) Development of bioluminescent substrates emitting NIR "biological optical window" light.

We will continue the development of new bioluminescent substrates with the enhanced brightness and improved water solubility when compared with AkaLumine-HCl (**2**).

Furthermore, we eager to develop new bioluminescent substrates emitting NIR light in "the second biological optical window (>1000 nm)"; the light in this region is more tissue-permeable than the first biological optical window (650–700 nm) light and should be optimal for visualizing deep site phenomena.

(2) Development of a non-invasive pulmonary aspiration risk detection system that utilizes NIR biological optical window light.

We will continue the collaborative study on the construction of a noninvasive aspiration risk detection system.

(3) BLSC Spring School for high school students.

We will continue to implement the Spring School with new titles.

2. Research Achievements

2. 1 Reviewed papers [○: Impact factor greater than 4]

(1) Masahiro Kiyama, Ryohei Saito, Satoshi Iwano, Rika Obata, Haruki Niwa, Shojiro A. Maki Multicolor Bioluminescence Obtained Using Firefly Luciferin. *Current Topics in Medicinal Chemistry* 16 (24) 2648-2655, 2016.

(2) Takahiro Kuchimaru, Satoshi Iwano, Masahiro Kiyama, Shun Mitsumata, Tetsuya Kadonosono, Haruki Niwa, Shojiro Maki, and Shinae Kizaka-Kondoh A luciferin analog achieves highly sensitive deep-tissue imaging using near-infrared bioluminescence. *Nature Communications* 7, 11856-, 2016.

3. Research funding

None

4. Collaboration

4.1 Inside BLSC

(1) Shojiro Maki: Development of a non-invasive pulmonary aspiration risk detection system that utilizes NIR biological optical window light (2015~).

4.2 Outside UEC

(1) Dr. Yukihiro Michiwaki (Japanese Red Cross Musashino Hospital):
Development of a non-invasive pulmonary aspiration risk detection system that utilizes NIR bi ological optical window light (2015~).

(2) Assistant Professor Goro Nishimura (Hokkaido University):
Development of a non-invasive pulmonary aspiration risk detection system that utilizes NIR bi ological optical window light (2016~).

5. Outreach activities

5.1 Other outreach activities

(1) Part-time lecturer of Department of chemistry, Graduate school of Science, Toho University.

Shojiro MAKI Laboratory

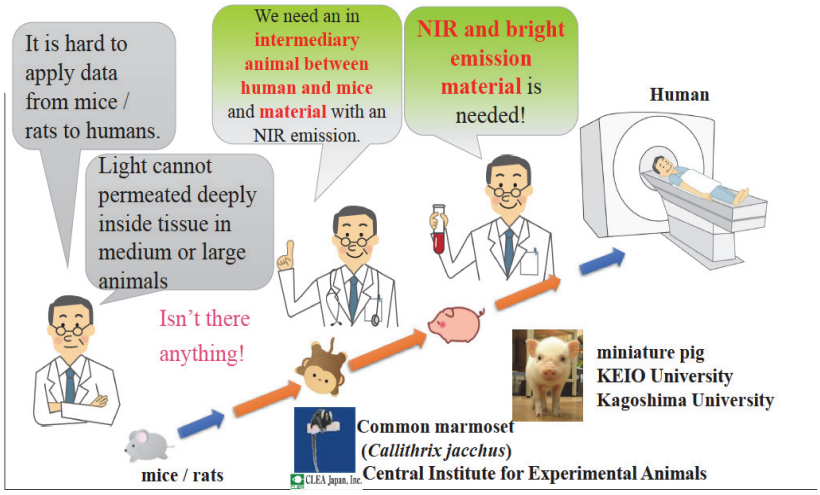
1. Outline of Research and Education

1. 1 Basic Policy in Research and Education

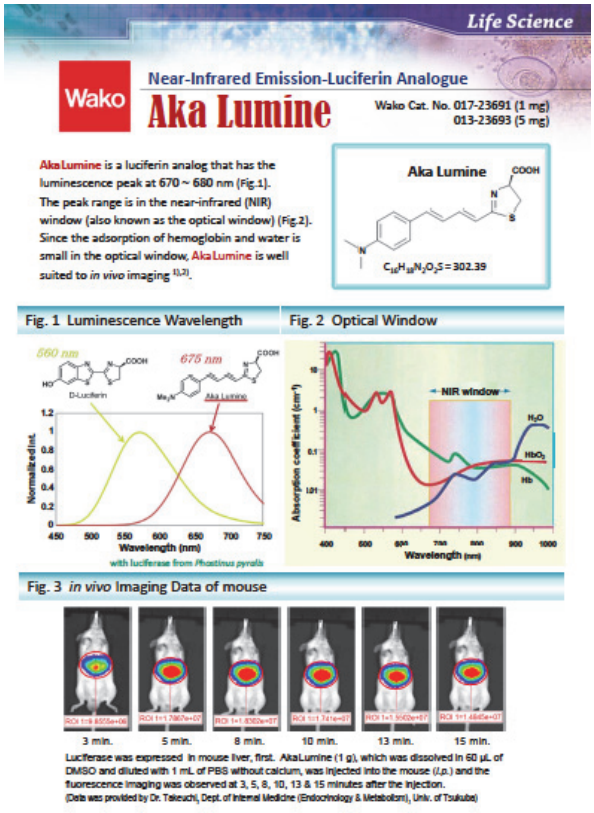
Our principle is “innovation of optical *in vivo* imaging by artificial luciferins” for future life science technology. Our principles also include “Orphan Drug” development which is high risk and may be avoided by researchers.

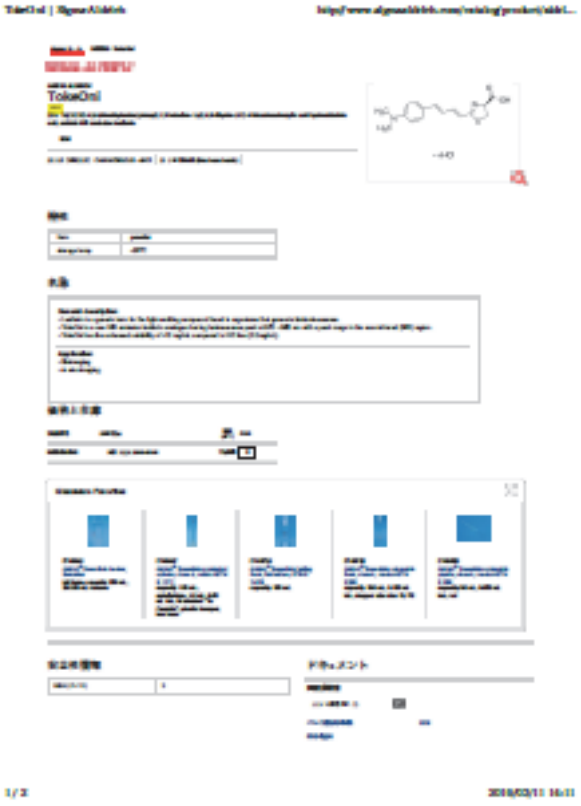
“Cancer Eradication (anti-cancer)” and “Practical Applications of Regenerative Medicine” are the most important goals in life science research. It’s no exaggeration to say that these are universal targets. Deep tissues are challenging for optical imaging technology. MRI, CT, and X-ray are good for *in vivo* imaging, however they do not have as high a resolution as optical imaging. Many top scientists think that R&D is hindered by today’s resolution limits. Whereas optical imaging has high resolution, it is hardly suitable for deep tissues because the wave number (ca. 560-630 nm) is too short for deep tissue imaging using traditional methods.

So, our challenge is to innovate an NIR (near infrared) probe and practical applications. It is more suitable for bioluminescent probes than fluorescent probes because bioluminescence does not require irradiation. Researchers need NIR bioluminescent probes for imaging cancer cells and/or graft cells in regenerative medicine research. In traditional technology, the natural firefly (ca. 560 nm) and the sea firefly (ca. 480 nm) are employed as bio-luminescent probes and are ill-suited for imaging deep tissues. Top scientists long for a modified NIR emission using a man-made probe based on the firefly bioluminescence system.



Recently, top scientists wish to observe medium or large animals for practical application of regenerative medicine. To promote research, a bio-optical (650-900 nm) light with high permeability of body tissue is needed. The technology race is very hot in the world for optical *in vivo* imaging. In our lab, we have marketed two NIR luciferins (“AkaLumine”: Wako Pure Chemical Industries, Ltd. and “Tokeoni”: Sigma-Aldrich Co. LLC.). These are the only two luciferins sold as NIR luciferins in the world.





1.2 Achievements and State of Progress (April, 2016 - March, 2017)

We have innovated a new luciferin analogue “SeMpai” and solved the low solubility of “Aka Lumine” (Wako Pure Chemical Industries, Ltd.) and the low pH problems of “TokeOni” (Sigma-Aldrich Co. LLC.). Industrial production of “SeMpai” is in progress by KUROGANE KASEI Co., Ltd. We have successfully performed *in vivo* optical imaging of a miniature swine using “TokeOni” as a probe.

1. 3 Future Plan

We will develop technology for *in vivo* optical imaging of miniature swine by optimization of probe, animal, and instrument. We strive to innovate a system for high-performance *in vivo* optical imaging.

2. Research Achievements

2. 1 Reviewed papers [○: Impact factor greater than 4]

(1) Shuji Ioka, Tsuyoshi Saitoh, Satoshi Iwano, Koji Suzuki, Shojiro Maki, Haruki Niwa, Atsushi Miyawaki, Masaya Imoto, Shigeru Nishiyama Synthesis and evaluation of the luminescent properties of firefly luciferin analogues. *Chemistry, A European Journal* **22**, 1-9 (2016).

(2) Takahiro Kuchimaru, Satoshi Iwano, Masahiro Kiyama, Shun Mitsumata, Tetsuya Kadonosono, Haruki Niwa, Shojiro Maki, and Shinae Kizaka-Kondoh, A luciferin analog generating near-infrared bioluminescence achieves highly sensitive deep-tissue imaging. *Nature Communications* **7**, 11856 (2016).

(3) Yoshihisa Suzuki, Minoru Yamaji, Shojiro Maki, Takashi Hirano Enhanced brightness of 2,6-diphenylthiazolo[4,5-b]pyrazines by introducing double electron donating groups. *Journal of Photochemistry and Photobiology A: Chemistry* 314, 93-95 (2016).

(4) Masahiro Kiyama, Ryohei Saito, Satoshi Iwano, Rika Obata, Haruki Niwa, Shojiro Maki Multicolor bioluminescence obtained using firefly luciferin. *Current Topics in Medicinal Chemistry* 16 (24)**,** 2648-2655 (2016).

(5) Sojiro Hachiya, Daisuke Hashizume, Hiroshi Ikeda, Minoru Yamaji, Shojiro Maki, Haruki Niwa, Takashi Hirano, Spectroscopic properties of BF_2 complexes of N-(5-phenyl-2-pyrazinyl) pivalamides exhibiting fluorescence in solution and solid state. *Photochemistry and Photobiology A: Chemistry* 311, 206-214 (2016)

(6) Shuji Ioka, Tsuyoshi Saitoh, Satoshi Iwano, Koji Suzuki, *Shojiro A. Maki,* Atsushi Miyawaki, Masaya Imoto and Shigeru Nishiyama Synthesis of firefly luciferin analogues and evaluation of the luminescent properties. *Chemistry A European Journal* 22 (27), 9330–9337 (2016).

2.2 Book, non-refereed articles and translation

(1) Hidenori Kato and Shojiro Maki Development of NIR luciferin. *Bio industry*, 33 (10), 22-27 (2016).

(2) Shojiro Maki Firefly Bioluminescence toward to in vivo imaging. *The Journal of Japan Society for LASER surgery and medicine* 37 (4), 448-453 (2017).

2.3 Invited lectures

(1) Shojiro Maki, “Innovation of firefly bioluminescence for NIR in vivo imaging probe” The 12th International Symposium on Organic Reactions and the 6th German-Japanese Symposium on Electro-synthesis, Kyoto, Japan, April 22-24 (2016).

(2) Shojiro Maki, “Chemistry of firefly bioluminescence”, Industry-UCB-UEC-Workshop 2017 (IUUWS2017), Tokyo, Japan, March 27-28 (2017).

(3) Shojiro Maki, “Realities of the research of practical application for top of the word technology”, 40th Symposium on Electro-Organic Chemistry, Meeting for Young Scientists, Nigata, June 24 (2016).

(4) Shojiro Maki, “Discovery of imaging technology by firefly bioluminescence”, 50th Symposium of kougaku5-kansai.org, Osaka, December 11 (2016).

(5) Shojiro Maki, “Discovery of imaging technology by firefly bioluminescence”, 3rd IPU Minato Mirai Symposium, Yokohama, February 20 (2017).

2.4 Media release

(1) Press Release ”First Development of NIR Luciferin for *in vivo* imaging” June 14 (2016).

(2) “Development of NIR Luciferin”, The Chemical Daily, June 15 (2016).

(3) “Development of Luciferin having 40 folds up brightness”, *The NIKKAN KOGYO SHIMBUN, LTD.*, June 24 (2016).

(4) ”First Development of NIR Luciferin for *in vivo* imaging”, UEC Social media, July 25 (2016).

(5) “Luciferase gets deep and sensitive”, Nature Methods, 13, 615 (2016).

(6) “Cancer cell is emitted. Live Swine Imaging succeeded”, *The NIKKAN KOGYO SHIMBUN, LTD.*, February 20 (2017).

2.5 Patent

(1) P2017-063253 “A new coelenterazine analogue”
Inventor：Masahiro Kiyama, Shojiro MAKI, Takashi Hirano, Satoshi Iwano, Atsushi Miyawaki.
Applicant: RIKEN, Institute of Physical and Chemical Research, The University of Electro-Communications
Date of application: March 28, 2017

2.6 Productization

(1) “TokeOni” Kurogane Kasei Co. Ltd., Sigma-Aldrich Co. LLC. (2016~)

2.7 Award

(1) Nobuo Kitada, JSPS Fellowships for Japanese Junior Scientist April 2016.
(2) Nobuo Kitada, poster award (Society of Bioluminescence & Chemiluminescence) February 2017.
(3) Nobuo Kitada, Best Student Award (The University of Electro-Communications) March 2017

2.8 Student guidance

(1) Yoshifumi Hachiro, 2016, Bachelor (engineering)
(2) Narumi, Higashi, 2016, Bachelor (engineering)

2.9 Study abroad programs for students

(1) Ryohei Saito, University of California Berkeley (Cell engineering, G. Marriott lab.) 2016. 10- 2017.3

3. Research funding

3.1 Grant-in-aid for scientific research

(1) Shojiro Maki (allot) ”resonance Bio-imaging”, 3704, 2015-2019, total 20,000: yen (Grant-in-Aid for Scientific Research on Innovative Areas)

3.2. Competitive external research funding

(1) Shojiro Maki (allot) “Practical application of *in vivo* imaging material for deep inside body (AS 2614119N)” A-step (Ministry of Education, Culture, Sports, Science and Technology, Japan) 2014-2016, total: 34,460,000 yen
(2) Shojiro Maki (representative) “Practical application of imaging material”, Kurogane Kasei Co., Ltd. 2012-current, 500,000 yen annually.

4. Collaboration

4.1 Inside BLSC

(1) Prof. Atsushi Nakamura “Innovation of *in vivo* optical imaging technology without transgenic”

4.2 Outside UEC

(1) Prof. Tsuyoshi Saito, Prof. Masaya Imoto, Prof. Koji Suzuki, Prof. Rika Obata, Prof. Shigeru Nishiyama, Tsukuba University and Keio University “Study of imaging material” 2014 July – current

(2) Mr. Hidenori Kato, Kurogane Kasei Co., Ltd., “Innovtion & Practical Application of NIR firefly luciferin” 2012 April – current

(3) Prof. Shotaro Yamano, The Cancer Institute Of JFCR, “Development of in vivo imaging material”, 2014 October - current

(4) Prof. Yoshihiro Miwa, Tsukuba University,”Study of imaging technology by new firefly luciferin”, 2014 April – current

(5) Prof. Shinae Kondo and Prof. Takahiro Kuchimaru, Tokyo Institute of Technology “Development of in vivo imaging technology”, 2014 April – current

(6) Prof. Kazuhiro Chiba, “Study of bio-imaging material”, 2015 Augst – current

(7) Prof. Kenji Hirayama, Nagasaki University, “Dynamics study of in vivo imaging material in live body”, 2015 November – current

(8) Prof. Rika Numano, Toyohashi University of Technology, “Study of firefly imaging material”, 2015 November – 2017 November

(9) Dr. Yoshiyuki Ito, JEOL Ltd. “New aspect for instrumental analysis”, 2016 December – current

NDA (Non-disclosure agreement)

(1) Prof. Ken Annoura, National Institute of Infectious Diseases, Japan, “About NIR imaging material”, 2014 January – current

(2) Dr. Hiroyuki Sato, Perkin Elmer Japan, Co., Ltd. “Study of imaging material”, 2017 March – current

MTA (Material transfer agreement)

(1) Prof. Rika Numano, Toyohashi University of Technology, “Study of firefly imaging material” 2012 December - unlimited

5. Outreach activities

5.1 Extension lectures

(1) Extension lecture for children (experimental class, Shibuya-ku, Tokyo), 11 June 2016

(2) Extension lecture for children (experimental class, The University of Electro-Communications), 25 July, and 2 August 2016

(3) School visit. Kakegawa Nishi Shizuoka Prefectural High School, Shizuoka, 7, September 2016

(4) School visit. Tachikawa International High School, Tokyo, 6, October 2016

(5) Extension lecture for children (experimental class, Shibuya-ku, Tokyo), January 2017

(6) Spring School for High School Students, (The University of Electro-Communications), 27-30 March, 2017

5.2 Other outreach activities

(1) Research and education at other universities Expert Network Investigator Science and Technology Foresight Center of National Institute of Science & Technology Policy (NISTEP)

(2) Scientific Support Programs for Cancer Research, Grant-in-Aid for Scientific Research on Innovative Areas, Ministry of Education, Culture, Sports, Science and Technology

(3) Executive Board Member (Society of Electro Transfer Chemistry)（2008- current）

Kazuto MASAMOTO Laboratory

1. Outline of Research and Education

1. 1 Basic Policy in Research and Education

The goal of our research is to elucidate the cellular mechanism of neurovascular communications in maintaining appropriate balances of energy supply-demand in the brain. To achieve this goal, we are working to develop new imaging and analytical methods to capture and quantify the long-term changes in cellular networks in the neurovascular unit. By using live imaging techniques with two-photon laser scanning fluorescence microscopy, we are trying to understand the structural and functional plasticity of the neurovascular unit in both healthy and disease condition. This is critically important to prevent and manage neurodegenerative disorders, such as Alzheimer's disease and age-dependent cognitive declines.

In our laboratory, an experimental animal model with chronic hypoxia exposure has been used to develop new imaging and analysis techniques and to test their feasibility for understanding a large volume of the cellular structures and functions in *in vivo* mouse brains. Chronic hypoxia is the condition under which the animals were exposed to low oxygen environment, such as 8-9% oxygen in nitrogen balanced, up to 2-3 weeks continuously. This is the minimum condition of oxygen availability that the animal can survive by adjusting their physiological states. It was well-characterized that the hypoxia-induced adaptation of brain vasculature completes within 3 weeks of hypoxia induction. Hypoxia is one of the strongest stimulant to provoke morphological and metabolic changes in the brain and is involved in pathogenesis of many brain diseases, such as cerebral ischemia and hypoperfusion.

The experiments have been carried out by using several transgenic mice that express fluorescent proteins in neurons, glia, and vascular cells, while the imaging was performed using two-photon microscopy through a closed cranial window (3-4 mm in diameter) according to a Tomita-Seylaz method, made on the cortex. The animals were housed in a hypoxic chamber to expose hypoxia (8-9% oxygen), and follow-up imaging was repeatedly performed at the same cortical location. The image was typically captured over 0.5 mm by 0.5 mm areas and depths up to 0.8 mm from the cortical surface. The blood plasma and astrocyte/oligodendrocyte were labeled with intraperitoneal injection of sulforhodamine 101 (10 mM in saline, 8 mL/kg body weight). The images captured were three-dimensionally reconstructed and quantitatively analyzed using custom-written Matlab software.

1.2 Achievements and State of Progress (April, 2016 - March, 2017)

First of all, we showed that microglia, one of glia in the brain, participate in growth and connection of new capillaries formed under chronic hypoxia. This finding is novel, while microglia in the rodent cortex is well-defined as an active player to monitor and modulate neural synaptic connections. Our results first time showed that the microglia is also an active player that reconstruct the cortical vascular networks in the adult brains.

Secondly, we successfully characterized that the cerebral blood flow (CBF) response to neural and astrocyte stimulation has different signaling pathways, depending on the neural circuits evoked. This work was a collaborative work with Professors Norihiro Suzuki and Kenji F Tanaka in Keio university school of

medicine, Japan. We used transgenic mice that express photosensitive cation channel (i.e., channelrhodopsin-2; ChR2) in either cortical neurons under muscarinic acetylcholine receptor (mAChR) M4 and astrocytes, and compared the CBF responses to photostimulation to them using laser speckle flowgraphy. Also, we topically applied several drugs over the stimulated cortex to identify signaling pathways involved in this process of the CBF responses. The response of CBF to the ChR2-neuron stimulation was shown to be localized over the irradiated spot, whereas the CBF response to the ChR2-astrocyte stimulation showed a rather widespread increase. This observation is partly supported by the result of pharmacological manipulation on the CBF response to photostimulation.

Thirdly, we newly established hemodynamic measurement tools for human brain microcirculation under neurosurgery and the capillary-level hematocrit changes using green fluorescence protein (GFP)-labeled red blood cells (RBCs) in the transgenic rats. These results were presented at Japanese microcirculation conference held in Toyama at the end of March, 2017.

1. 3 Future Plan

For *in vivo* microscopic imaging, we will introduce a series of new transgenic animals that allow for real time *in vivo* imaging of cellular activities with a high sensitivity. For acquired images of the brain cells and microvessels, we will work to develop an image-based quantitative method for 3d reconstruction images of the cellular and vascular morphology. In addition to these technical improvements, new animal models to assess behavior and cognitive functions of the animals as well as to explore these plastic changes in neurovascular unit during physical or optogenetic activation of cerebral blood flow.

2. Research Achievements

2. 1 Reviewed papers [○: Impact factor greater than 4]

(1) Kanno I, Seki C, Takuwa H, Jin ZH, Boturyn D, Dumy P, Furukawa T, Saga T, Ito H, Masamoto K. Positron emission tomography of cerebral angiogenesis and TSPO expression in a mouse model of chronic hypoxia. Journal of Cerebral Blood Flow and Metabolism. 2017 Jan 1 (in press)

(2) Ito H, Takuwa H, Tajima Y, Kawaguchi H, Urushihata T, Taniguchi J, Ikoma Y, Seki C, Ibaraki M, Masamoto K, Kanno I. Changes in effective diffusivity for oxygen during neural activation and deactivation estimated from capillary diameter measured by two-photon laser microscope. The Journal of Physiological Sciences 67(2):325-330. (2017)

(3) Hoshikawa R, Kawaguchi H, Takuwa H, Ikoma Y, Tomita Y, Unekawa M, Suzuki N, Kanno I, Masamoto K. Dynamic Flow Velocity Mapping from Fluorescent Dye Transit Times in the Brain Surface Microcirculation of Anesthetized Rats and Mice. Microcirculation. 23(6):416-425. (2016)

(4) Masamoto K, Hoshikawa R, Kawaguchi H. Fluorescence Imaging of Blood Flow Velocity in the Rodent Brain. Current Topics in Medicinal Chemistry 16(24):2677-2684. (2016) Review

(5) Unekawa M, Tomita Y, Masamoto K, Toriumi H, Osada T, Kanno I, Suzuki N. Dynamic diameter

response of intraparenchymal penetrating arteries during cortical spreading depression and elimination of vasoreactivity to hypercapnia in anesthetized mice. Journal of Cerebral Blood Flow and Metabolism 37(2):657-670. (2017)

(6) Nishino A, Tajima Y, Takuwa H, Masamoto K, Taniguchi J, Wakizaka H, Kokuryo D, Urushihata T, Aoki I, Kanno I, Tomita Y, Suzuki N, Ikoma Y, Ito H. Long-term effects of cerebral hypoperfusion on neural density and function using animal model of misery perfusion. Scientific Reports 6, 25072 (2016)

(7) Sudo H, Tsuji AB, Sugyo A, Takuwa H, Masamoto K, Tomita Y, Suzuki N, Imamura T, Koizumi M, Saga T. Establishment and evaluation of a new highly metastatic tumor cell line 5a-D-Luc-ZsGreen expressing both luciferase and green fluorescent protein. International Journal of Oncology 48(2):525-532 (2016)

2.2 Book, non-refereed articles and translation

(1) Nishijima Y, Akamatsu Y, Masamoto K, Liu J. Chapter 19 - Vascular remodeling after cerebral ischemia. (Caplan LR, Biller J, Leary MC, Lo EH, Thomas AJ, Yenari M, and Zhang JH, eds. Primer on Cerebrovascular Diseases, Second Edition. San Diego: Academic Press). (2017/03/18).

(2) Masamoto K, Hirase H, Yamada K. Preface. Progress in Brain Research 225:xv. (2016)

(3) Kanno I, Masamoto K. Bridging macroscopic and microscopic methods for the measurements of cerebral blood flow: Toward finding the determinants in maintaining the CBF homeostasis. Progress in Brain Research 225:77-97 (2016)

(4) Masamoto K, Hirase H, Yamada K, Kanno I. Neurovascular coupling-What next? Progress in Brain Research 225:269-272 (2016)

2.3 Invited lectures

(1) Masamoto K: Optogenetic investigation of blood flow regulation in the brain: toward understanding the role of neurogenic and gliogenic control of cerebral microcirculation. The 10th Asia-Pacific Laser Symposium (APLS 2016) May 11-14, Jesu island, Korea

(2) Masamoto K, Kanno I, Tomita Y, Suzuki N: Cerebral microvascular restructuring and microglial adaptation to chronic hypoxia in the animal models. The 41th Annual Meeting of Japanese Society for Microcirculation (2016.09.23) Kokuyo hall, Tokyo

(3) Masamoto K: Astrocytic regulation of cerebral blood flow. Optogenetics 2016 (2016.09.29) Keio University, Tokyo

(4) Masamoto K: Four-dimensional imaging of neurovascular unit by in vivo two-photon microscopy. Oxygen Dynamics seminar (2016.1014) Nihon University, Fukushima

(5) Masamoto K: Chronic microscopic imaging of neurovascular units. The 23th Tohoku Cerebral Blood Flow conferences (2016.11.19) Koyo Grand hotel, Miyagi

(6) Masamoto K: Optogenetic perturbation of glio-vascular coupling in the mouse cerebral cortex. The 39th

Annual Meeting of the Molecular Biology Society of Japan (2016.12.2) Pacific Yokohama, Kanagawa

2.4 Award

(1) The Best Presentation Award: Sugashi T, Yoshihara K, Hachiya R, Takuwa H, Kanno I, Tomita Y, Suzuki N, Masamoto K: Morphological analysis of 3D in vivo images by correcting inhomogeneity of optical resolutions. Symposium on Fuzzy, Artificial Intelligence, Neural Networks and Computational Intelligence in Osaka (FAN 2016), (2016.10.27), Osaka University, Osaka

2.5 Student guidance

(1) Masahiro Nitta, M.Eng 2016
(2) Hiroya Yuki, M.Eng 2016
(3) Satoshi Sasaki, B.Eng 2016
(4) Nao Hatakeyama, B.Eng 2016
(5) Ryota Hachiya, B.Eng. 2016

3. Research funding

3.1 Grant-in-aid for scientific research

(1) Kiban C (H28-30) Understanding the role of cerebral angiogenesis and blood flow enhancer against the cognitive decline. (PI: Masamoto K)

4. Collaboration

4.1 Inside BLSC

(1) Miyawaki's laboratory
(2) Kano's laboratory

4.2 Outside UEC

(1) National Institute of Radiological Sciences, Department of Functional Brain Imaging Research
(2) Keio University, School of Medicine
(3) Hirosaki University, Graduate School of Medicine and School of Medicine
(4) Osaka University, Graduate School of Engineering Science
(5) Tokyo Metropolitan Geriatric Hospital
(6) Edogawa Hospital
(7) Korean Brain Research Institute

5. Outreach activities

5.1 Editor of academic journals

(1) Editorial Board: Journal of Cerebral Blood Flow and Metabolism
(2) Editorial Board: Japanese Society of Cerebral Blood Flow and Metabolism

5.2 Paper review of academic journals

(1) Journal of Cerebral Blood Flow and Metabolism

(2) Cerebral Blood Flow and Metabolism

(3) NeuroImage

(4) Brain Research

(5) Medial Physics

(6) International Journal of Numerical Methods in Biomedical Engineering

(7) Journals of the Japan Society of Mechanical Engineers

Yoichi MIYAWAKI Laboratory

1. Outline of Research and Education

1. 1 Basic Policy in Research and Education

Representation of sensory and perceptual information in the human brain

We receive sensory information by seeing, hearing, and touching the physical world. Sensory information propagates to the brain and yields our perception. Although we perform these sensory/perceptual information processing naturally and smoothly in the daily life, such tasks are very hard for machines to perform even with the state-of-art technologies.

Figure 1: Experiments using fMRI system (ATR-Promotions BAIC).

Our laboratory aims to elucidate how the human brain processes and represents sensory and perceptual information so naturally and smoothly by performing psychophysical experiments and human brain imaging.

Our psychophysical experiments uses systematically-controlled sensory stimuli (mainly in visual, auditory, and tactile domains) and quantifies perceptual contents of human observes of the stimuli. Stimuli and behavioral responses are analyzed with techniques such as statistics, information theory, and system identification.

Figure 2: Experiments using MEG system (ATR-Promotions BAIC).

Human brain imaging is also a major part of research activity in our laboratory as well as psychophysical experiments. Particular sensory and perceptual experience corresponds to particular activity pattern of the human brain. Thus, objective measurement and analysis of brain activity patterns is promising approach to unveil subjective sensory and perceptual experience. We mainly use functional magnetic imaging (fMRI) and magnetoencephalography (MEG) to measure human brain activity noninvasively. fMRI measures signals related to blood flow changes associated with neural activity in the brain with high-spatial resolution, whereas MEG measures magnetic field signals generated by neural current in the brain with high-temporal resolution. We choose either of these methods or combine both depending on the purpose of experiments.

Computational analysis of brain activity patterns

Human brain activity is a large-scale high-dimensional data. Standard measurement of fMRI and MEG signals consists of 10^{4-5} –dimension data points per every second. Conventional analysis focused on only limited aspects of such data set and information contained in the rest were simply discarded or ignored. For example, a typical method of fMRI data is to perform statistical tests on intensity changes in fMRI signals for each single brain location independently. The method does not consider correlational information between multiple brain locations, although fMRI signals at 10^5 different brain locations are obtained simultaneously.

Our laboratory uses novel methods that exploit as much as information contained in the large-scale high-dimensional brain activity data. Machine learning is one of such examples.

One example is analysis of brain activity patterns using machine learning techniques. In this method, brain activity are converted into multidimensional patterns and computer programs are trained to learn statistical relationship between the brain activity patterns and the corresponding experimental conditions. Close investigations on learning processes and acquired parameters of the computer programs provide important clues for understanding of information representation in the brain activity patterns while taking correlational information between multiple brain locations into account.

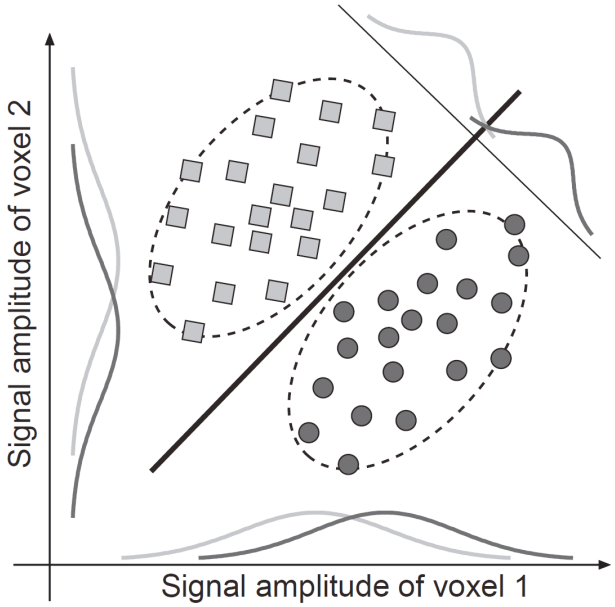


Figure 3: Classification analysis using multivariate signal patterns.

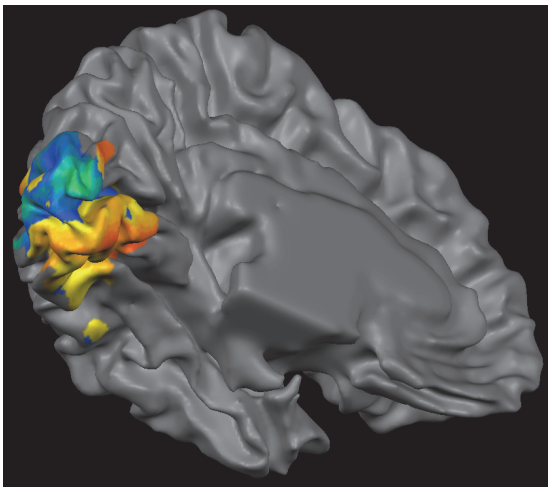


Figure 4: Retinotopy map identified in lower visual cortex.

Application to medical engineering

The trained computer programs can be also used to predict experimental conditions corresponding to given brain activity patterns. This feature is also useful in designing brain-machine interface that translates human thoughts into machine commands. By developing computer programs with high performance in prediction, we will realize prosthetic limbs that can be controlled by human motor intention and monitor systems that visualize what we are imagining in mind.

1.2 Achievements and State of Progress (April, 2016 - March, 2017)

Dynamics of neural representation of visual object categories

We can visually recognize objects quickly and accurately. Object recognition of human vision is superior in its speed and accuracy to machine vision. It has been considered as one of the most difficult function to realize by artificial systems. To elucidate how the human brain performs object recognition so quickly and accurately, we have conducted experiments that combine MEG and fMRI to achieve high resolution in temporal and spatial domains.

In this year, we proceeded with experiment based on the results obtained in the last year and succeeded with analyses of information of object category represented in the brain activity patterns of the specified brain areas at the specified time. In particular, we found the temporal relationship between the level of category abstraction and the representation time of the object category. In addition, we started to measure eye movement while a subject observes images and reveled its temporal characteristics.

Neural representation of tactile information

We can obtain spatial information of the external environment by touch as well as vision. We perform fMRI experiments to measure brain activity patterns evoked by simple tactile stimuli given to the fingertips to explore where and how tactile information is represented in the human brain.

In this year, we applied the searchlight method that enables us to examine information representation over the whole brain as well as analyses based on the region of interests, to achieve hypothesis-free analysis and evaluation.

Development of analysis tools and simulation methods

To analyze brain activity patterns effectively, it is also important to develop analysis tools and simulation methods. In the previous year, we developed a method based on deep convolutional neural network to extract higher-order features contained in object images. In this year, we proceeded with this method to apply other data sets than object images used in our experiments.

In addition, we developed a statistical model that learns relationship between brain activity patterns and experimental conditions while selecting only important brain areas as input features to the model. The model is based on L0-norm optimization and succeeded in outperforming the previous models.

It is also important to identify source location corresponding to the measured MEG signals for the analysis of MEG data. We developed a novel method to evaluate accuracy of MEG source localization and found a new problematic phenomenon when MEG source localization and pattern classification analysis are combined.

1. 3 Future Plan

Dynamics of neural representation of visual object categories

In addition to the analysis of relationship between the level of category abstraction and the representation time of object categories, we proceed with analysis of specificity of the representation time of each object category. We also proceed with experiments and analyses to

examine relationship between eye movement and object recognition.

Neural representation of tactile information

We proceed with analyses to reveal where and how tactile information is represented in the brain activity patterns. We are planning to use various types of tactile stimuli in addition to those used previously.

Development of analysis tools and simulation methods

We proceed with image feature extraction using DCNN and other methods to analyze relationship between extracted image features and brain activity patterns. In addition, we apply L0-norm-optimized classification model and the evaluation method of MEG source localization to real data and examine their methodological validity.

2. Research Achievements

2. 1 Reviewed papers [○: Impact factor greater than 4]

(1) Yoichi Miyawaki, "Analysis of human brain activity using sparse modeling," system/control/information, vol.61, no.4, pp.138 - 145 (2017).

(2) Yoichi Miyawaki, "Multivariate analysis of magnetic resonance imaging signals of the human brain," Current Topics in Medicinal Chemistry, vol.16, pp.2685 - 2693 (2016).

2.2 Book, non-refereed articles and translation

(1) Yoichi Miyawaki, "What are you seeing? Inside of your brain can be seen – neural information decoding: techniques to visualize mind from brain activity," in Science of mind and brain from perspectives of usual and unusual situations, eds. Makoto Miyazaki, Masaki Abe, Yuki Yamada, Corona publishing (in press).

2.3 Invited lectures

(1) Yoichi Miyawaki, "Study of visual image representation in human brain using neural decoding," The fifth MEET Young Cardiologists, Niigata University (Chuo-ku, Niigata) (October 10, 2017, scheduled).

(2) Yoichi Miyawaki, Noriki Ito, Masashi Sato, Yoshiyuki Kabashima, "Inferring informative brain areas by sparse feature selection," The 40th Japan Neurosceience Society, Makuhari Messe（Mihama-ku, Chiba）(July 20 – 23, 2017, scheduled).

(3) Yoichi Miyawaki, "Analysis of brain activity using machine learning and mechanisms of human sensation and perception," Plenary of engineers' meeting of the University of Electro-Communications, The University of Electro-Communications（Chofu, Tokyo）(July 16, 2017, scheduled).

(4) Yoichi Miyawaki, Masashi Sato, "Neural representation of perceptual experience revealed by multivariate pattern analysis of human brain activity," Industry-UCB-UEC Workshop 2017, The University of Electro-Communications (Chofu, Tokyo), March 27 – 28, 2017.

(5) Yoichi Miyawaki, “Analyzing mechanism of brain and mid using information science,” Public lectures of the University of Electro-Communications and the Yomiuri Shimbun, “Expanding future by advanced technology of the 21st century: message from comprehensive communications sciences，The University of Electro-Communications（Chofu, Tokyo），October 8, 2016.

(6) Yoichi Miyawaki, “Deciphering visual information represented by human brain activity patterns,” Invited visit and talk at LIRMM/CNRS, Montpellier, France, June 27, 2016.

2.4 Media release

(1) “電気通信大学・読売講座 詳報 － 脳活動から視覚解く”，読売新聞 2016 年 10 月 15 日多摩版 27 面

(2) “電気通信大学・読売講座 － 人の夢 脳活動で判別”，読売新聞 2016 年 10 月 9 日多摩版 22 面

(3) “電気通信大学・読売講座 － 脳とこころ情報科学で解明”，読売新聞 2016 年 10 月 7 日多摩版

2.5 Student guidance

(1) Shota Eto，2016，Bachelor（Engineering）

(2) Kazuaki Akamatsu，2016，Master（Engineering）

(3) Noriki Ito，2016，Master（Engineering）

(4) Megumi Nozaki，2016，Master（Engineering）

2.6 Visit of oversea researchers and students

(1) Yu Aramaki，Brain Science Inspired Life Support Research Center, Visiting Professor/Chukyo University, Professor, Research theme: Analysis of neural information of athletes，2016/4－2017/3.

(2) Masashi Sato，Research fellowship for young scientists (DC2), Japan Society for the Promotion of Science/Ph.D. students, Department of Mechanical Engineering and Intelligent Systems, Graduate School of Informatics and Engineering，Research theme: Study of temporal structure of object category representation in the human visual cortex，2016/4－2019/3.

2.7 Study abroad programs for students

(1) Shotaro Fuchibe，LIRMM/CNRS, Montpellier University（André Crosnier’s lab.），2016/8－2016/10（International internship）.

3. Research funding

3.1 Grant-in-aid for scientific research

(1) Yoichi Miyawaki（P.I.）, Analysis of human brain activity at high spatio-temporal resolution and identification of informative brain areas using sparse modeling, KAKENHI Innovative Areas “sparse modeling”, FY2016- FY2017.

(2) Yoichi Miyawaki（Co-P.I.）, Controlling artificial limbs as own limb: natural learning of artificial limbs using human brain activity, KAKENHI challenging Exploratory Research, FY2015- FY2016.

(3) Yoichi Miyawaki（P.I.）, Study of tactile information representation in the visual cortex using neural decoding technique, KAKENHI (C), FY2014-FY2016.

3.2. Competitive external research funding

(1) Yoichi Miyawaki（P.I.）, Research and development of fast object recognition algorithm based on neural information representation, SCOPE, FY2014 – FY2016.

(2) Yoichi Miyawaki（P.I.）, Study of fast extraction of object recognition information from human brain activity, Yazaki Memorial Foundation for Science and Technology, Specific Research Grant, FY2015 – FY2017.

(3) Yoichi Miyawaki（P.I.）, Development and application of high spatio-temporal resolution analysis of human neural activity, The Naito Foundation, Research Grant, FY2015 – FY2016.

4. Collaboration

4.1 Inside BLSC

(1) Kazuto Masamoto, Image analysis of structural features of astrocytes, FY2015-

(2) Hiroshi Yokoi, Soichiro Morishita, Substitution of motor and communication functions using BMI（development of intelligent electric assistance devices for BMI control）, FY2013-

4.2 Outside UEC

(1) Gowrishankar Ganesh, CNRS-AIST Joint Robotics Laboratory, CNRS - Institut des sciences de l'ingénierie et des systèmes (INSIS)（university/national institute）, Controlling artificial limbs as own limb: natural learning of artificial limbs using human brain activity, FY2015-

(2) Norihiro Sadato, Ryo Kitada, NIPS／SOKENDAI（national institute/university）, Study of tactile information representation in the visual cortex using neural decoding technique, FY2014-

(3) Yukiyasu Kamitani , Kyoto University ／ ATR computational neuroscience laboratories（university/private company）, Study of tactile information representation in the visual cortex using neural decoding technique, FY2014-

(4) Yoshiyuki Kabashima, Tokyo Institute of Technology（university）, Development of L0-norm optimization algorithm, FY2015-

(5) Okito Yamashita, Masa-aki Sato, ATR computational neuroscience laboratories（private company）, Study of MEG source localization, FY2015-

5. Outreach activities

5.1 Paper review of academic journals

(1) Reviewer of Scientific reports

(2) The 31st International Congress of Psychology (ICP2016) Program Committee

(3) Review committee of the best presentation award of Vision Society of Japan 2016 winter meeting

(4) Recommendation and selection committee of Japanese Neural Network Society

5.2 Other outreach activities

(1) Board member of Japanese Neural Network Society

(2) Board member of SIGTX of Virtual Reality Society of Japan

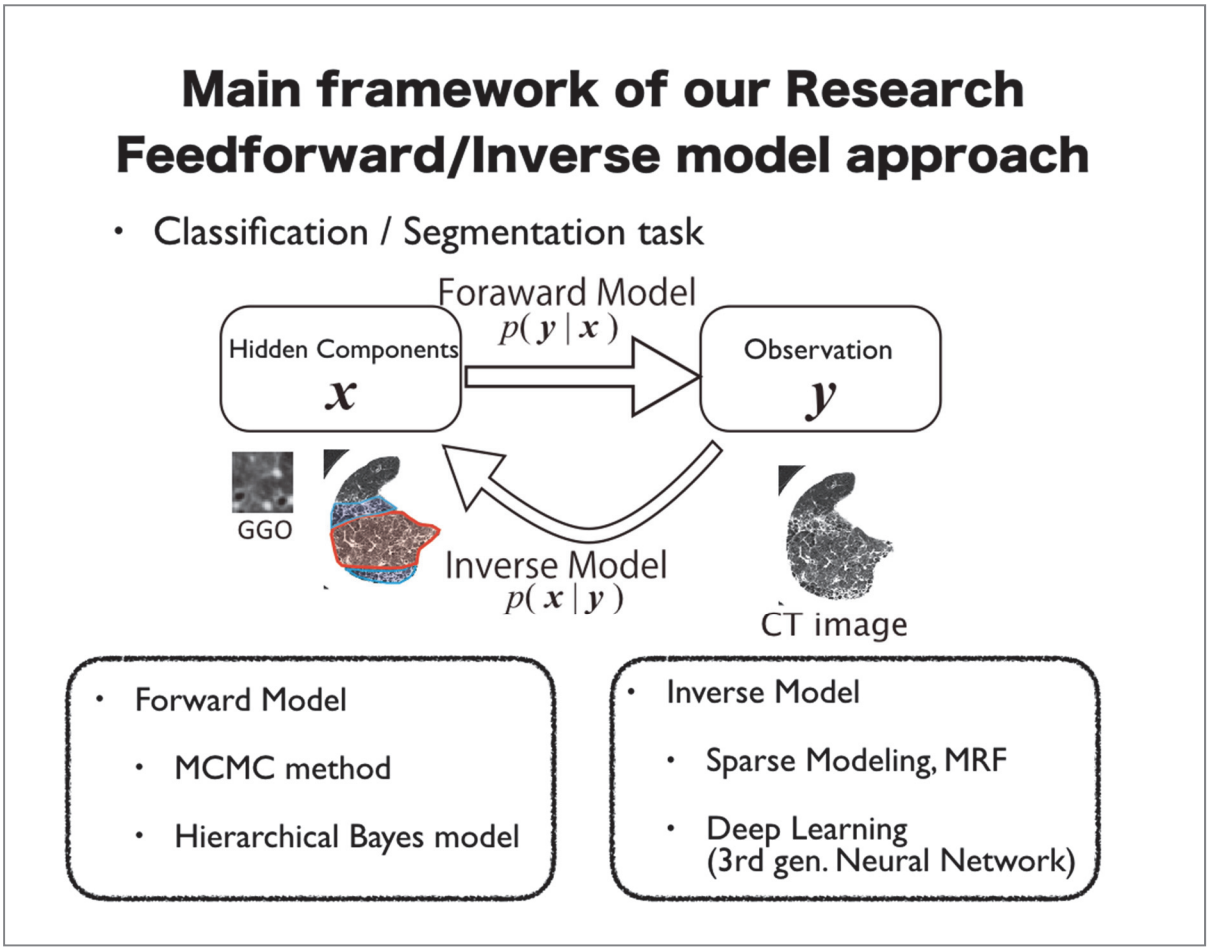
(3) Lecture in Tochigi high school

(4) Public lecture of the University of Electro-Communications and the Yomiuri Shimbun

1. Outline of Research and Education

1.1 Basic Policy in Research and Education

Our main research field is in medical application using the technique in the artificial intelligence, such like deep learning, sparse modeling, Bayesian inference and so on. In these years, our main research field is in a lot of ways of medical image application, lung thesis detection, classification, noise reducing in medical image, PET or CT image reconstruction and so on. We solve these problems in one simple principle forward and inverse model. The following figure shows a concept schematic diagram of the model. In the model, we assume the observation data $\boldsymbol{y}$ comes from some hidden components $\boldsymbol{x}$ through the model described by the conditional probability $p(\boldsymbol{y} \mid \boldsymbol{x})$. So when we infer the hidden components $\boldsymbol{x}$ from the observed data $\boldsymbol{y}$, we should consider the inverse model $p(\boldsymbol{x} \mid \boldsymbol{y})$. In each forward and inverse model, we apply some machine learning techniques. For example, considering the classification task of lung disease, we should extract several effective components from the image data and evaluate the efficacy of each component.



1.2. Achievements and State of Progress (April, 2013 - March, 2016)

(1) Classification of Diffuse Lung Disease with Deep Convolution Neural Network

Deep convolutional neural networks (DCNNs) are inspired from the vision system. The DCNN shows good performance for the classification task in the field of computer vision and machine learning. In our

study, we train the DCNN using the transfer-style learning, which introduce some other domain's knowledge into the learning machine. In 2015, we propose reusing method of the feature extractor part in the DCNN that is trained with massive natural images. The feature extractor for the natural image shows improving the classification performances. In 2016, we extend the transfer style method in multiple stage. At the first we train the DCNN with massive natural image. After that, we also train the DCNN with texture dataset. And at last, we train the DCNN with the target CT image of diffuse lung disease. Now we obtain the 97.2% accuracy for the small dataset of the CT image.

(2) The relationship analysis for the DCNN with Network-in-Network (NIN).

In the DCNN architecture, the basic operations, which are called convolution and pooling operations, repeat for obtaining a good feature representations. This mechanism was identical to the Fukushima's Neocognitron. On the other hand, the importance on the interaction of feature extraction was ignored in the network architecture. In these years, in order to embed the feature relationship, the Network-In-Network (NIN) structure has been proposed. We can consider the NIN as a embedding of translational symmetric Perceptron into the feature extraction layer. The NIN is only proposed for improving classification performance. We focused on the weight coupling of the Perceptron and interpreted what NIN means when we define the neighborhood relation of cells to be extracted by this weight. As a result, in the lower level of feature extraction layer, NIN plays a role of emphasizing the similar orientation feature and depress the orthogonal feature. In the higher order layer, the NIN also emphasize similar curvature and suppress the opposite side curvature. Moreover, the face like features are suppressed.

In the early visual area, such like V1 area in the monkey, the orientation continuity of the column is observed. The cells which are responding to the similar orientations are assigned in the near position, and the cell prefers opposite orientation are assigned in the further. This structure coincides to the NIN structure. So that, the orientation continuity might have a meaning from the viewpoint of the classification.

(3) Feature selection using Monte Carlo method

In the field of machine learning such like classification and regression task, the feature selection is a useful method not only improving the performance but also the estimating the statistical structure. Especially, in the texture classification problem, estimating the efficient feature combinations is an important problem. In order to estimate the statistical structure, we apply a Monte Carlo based method. The Monte Carlo based method is an enumerated method, so it requires a lot of computational cost, however, we can obtain the better feature combination rather than that of the other optimization method such like sparse modeling based method.

1. 3. Future Plan

In our future plan, we integrate the component techniques into a system. In the next step we analyze the feature in the DCNN, and design the effective feature. Currently, it is hard understanding what is happened in the DCNN, so that interpretation of the representation in the DCNN is important task for understand the hidden components.

Moreover, our application for small database system might be applicable for another field application. Thus, we are going to try to analyze some other field.

We also apply image restoration task for real application. Now we are going to apply the noise reduction method into a positron emission tomography (PET) image reconstruction. The PET image is noisy and clear image is desired for diagnosis.

2. Research Achievements

2.1 Non-refereed articles or translation

(1) (invited) H. Shouno, A. Suzuki, S. Suzuki, and S. Kido, Deep Convolution Neural Network with 2-stage transfer learning for medical image classification. The Brain & Neural Networks, Vol.24(2017) No.1 pp 3-12, (in Japanese), http://doi.org/10.3902/jnns.24.3

(2) (invited) H. Shouno, S. Suzuki, An application of deep learing for medical image analysis, Vol.33(2016), pp75-80, (in Japanese)

(3) (invited) H. Shouno, Basic Technology for Sparse Modeling with Some Historical View, Vol.99(5), pp.376-380, (in Japanese)

2.2 Student guidance

4 undergraduate and 3 master course students

3. Research funding

3.1. Grant-in-aid for scientific research

(1) Grant-in-aid for scientific research on Innovative Areas, MEXT, Japan, 16H01542 “Establishment of sparse texture image analysis using deep learning”

(2) Grant-in-aid for scientific research on Innovative Areas, MEXT, Japan, 26108002, "Multidisciplinary Computational Anatomy and Its Application to Highly Intelligent Diagnosis and Therapy”

(3) Grant-in-aid for scientific research (C), MEXT, Japan, 16K00328, “Development of algorithm for reconstruction of tomographic image using sparse basis”

4. Collaborators

None

5. Outreach activities

None

Shinji MATSUDA Laboratory

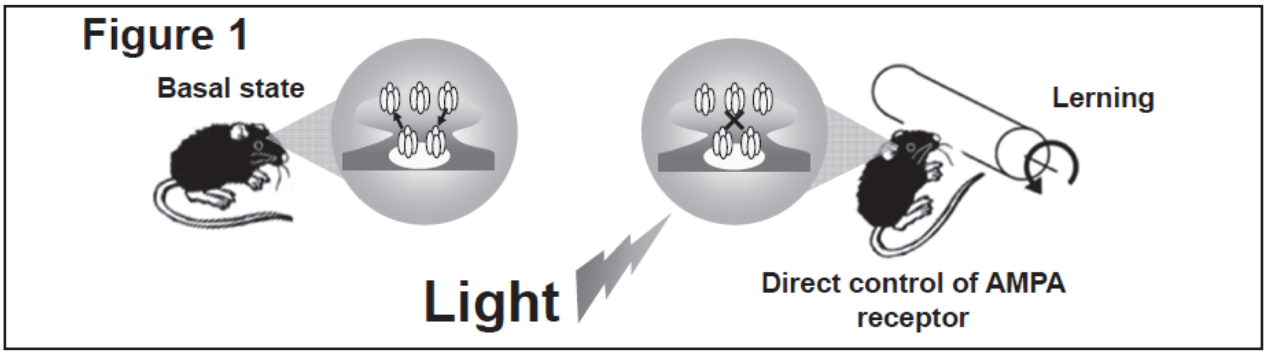
1. Outline of Research and Education

1. 1 Basic Policy in Research and Education

Research

Brains are composed from numerous number of neurons and Glial cells. The function of brains, including higher brain functions, are mediated by the signal transduction between neurons. The signal transduction between neurons are called synaptic transmission, and the efficiency of synaptic transmission can be regulated by neural activities. This phenomena is called synaptic plasticity, which is thought to be the cellular basis for memory and learning. The molecular mechanisms for synaptic plasticity have been actively studied all over the world.

I have been studied the molecular basis for the long-term depression (LTD) which is the one form of the synaptic plasticity: the efficiency of synaptic transmission is reduced for a long term. Recently, I also tried to develop the new technique to control LTD by light stimulation, and to directly examine the relationship between LTD and learning by using this technique. When the cerebellar LTD was blocked by light by using this technique, motor learning was impaired. These results indicated that the cerebellar LTD directly control the motor learning. Moreover, I also study the molecular mechanism of long term potentiation (LTP) another form of synaptic plasticity, in which the efficiency of synaptic transmission is enhanced for a long term. I would like to also develop the controlling method for LTP.



Educations

I would like to bring up the students who can contribute to the progress of the science. For the students in “Bioscience and Technology Program”, I am going to give lectures not only on neuroscience but also on the basic biology. Moreover, I will discuss with the students about how the basic knowledge of biology can be obtained and how life should be studied in the future.

For the students out of the “Bioscience and Technology Program”, I am going to start with be fundamentals on biology and move to the current knowledge. Recently, the fusion research between biology and other fields are actively carried out. Therefore, students need to prepare for these studies even though they will not be specialists for the biology.

For the students in my own laboratory, I would like to carry out the forefront research in the neuroscience field together with them. I also would like to bring up the top scientists who can contribute the

neuroscience. For this purpose, I will let them think research plan by themselves and let them carry out their plans by themselves.

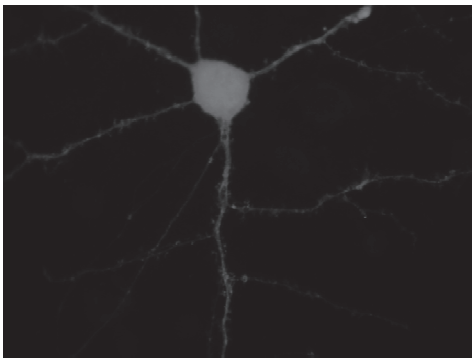
1.2 Achievements and State of Progress (April, 2016 - March, 2017)

Although it is well established that the LTD is induced by the clathrin mediated endocytosis of AMPA receptors, it was unknown how clathrin can be recruited to the postsynaptica site by neuronal activities. Until 2017, we have develop the new technique to control the induction of LTD by light stimulation in order to directly examine the relationship between synaptic plasticity and learning. We have also generated knock in mouse, whose cerebellar LTD can be blocked by light stimulation. By using this mouse, we have examined whether the motor learning such as OKR could be affected by the light stimulation to the cerebellum. The results indicated that the light stimulation significantly reduced the motor learning efficiency of the knock in mouse, although these mice can normally learn the OKR in the absence of light stimulations. These results indicated that the cerebellar LTD plays critical roles for certain kinds of motor learning. I also contributed to generate the chemical labeling method for AMPA receptors.

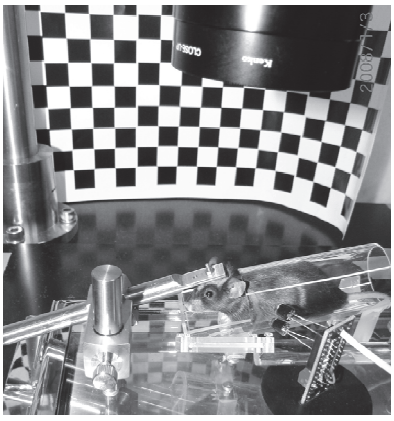
1. 3 Future Plan

For the future direction, we are going to express Light-driven proton pump in various brain regions and try to examine the relationship between LTD and learning process. We are going to express our proton pump in cerebellum and block the cerebellar LTD at various timing, and we would like to examine the relationship between the timing of LTD induction and motor learning (Figure 2).

Figure 2



Cultured neuron



Memory test of mouse

We would like to directly examine the relationship between cellular level phenomena, such as synaptic plasticity and behavior of living animals such as memory and learning. By these approach, we would like to contribute to the progress of neuroscience.

2. Research Achievements

2. 1 Reviewed papers [○: Impact factor greater than 4]

(1) Wakayama S, Kiyonaka S, Arai I, Kakegawa W, Matsuda S, Ibata K, Nemoto YL, Kusumi A, Yuzaki M, Hamachi I. Chemical labelling for visualizing native AMPA receptors in live neurons. *Nature Commun*. 2017 Apr 7; 8: 14850. doi: 10.1038/ncomms14850.

2.2 Book, non-refereed articles and translation

(1) Matsuda S, Yuzaki M. AP-4. *Encyclopedia of Signaling Molecules* 2nd Edition, Springer (2016).

2.3 Student guidance

(1) Hiroki Yamazaki: M1

(2) Rikako Ito, Shunichi Koga, Ryusuke Suzuki: B4

3. Research funding

3.1 Grant-in-aid for scientific research

(1) JSPS KAKENHI Grant Number 17K07048

4. Collaboration

4.1 Outside UEC

Michisuke Yuzaki, Keio University、Molecular mechanisms and controlling of synaptic plasticity, 2013~

5. Outreach activities

5.1 Paper review of academic journals

(1) PLOS ONE reviewer

Takuji KOIKE Laboratory

1. Outline of Research and Education

1. 1 Basic Policy in Research and Education

In modern society, the importance of various information has increased each day, and the reduced ability related to information exchange through hearing has impaired not only physical wellness but also mental-health status. The impairment of ability brings disadvantage to both of individuals and the society surrounding them. Thus, prevention of hearing loss, effective treatments, and construction of an inclusive society are the most important issues in the modern society.

The auditory system consists of the external ear, the middle ear, and the inner ear (cochlea). The cochlea is filled with lymph fluid, and the sensory cells exist on the basilar membrane which divides the cochlear duct. Sounds travelling through the atmosphere are converted into the vibration of the lymph fluid and perceived by the sensory cells. The middle ear serves as an impedance matching device between the air and the lymph fluid and effectively transmits the sound energy to the cochlea. The ossicles are supported in the tympanic cavity by ligaments and tendons to make it easier to vibrate. However, if these ligaments and tendons are pathologically ossified, the ossicular vibration is restricted, and conductive hearing loss occurs. If the cochlear functions and the auditory nerve functions are impaired, the sensorineural hearing loss occurs. In addition, mixed hearing loss in which both kinds of hearing loss are mixed may occur.

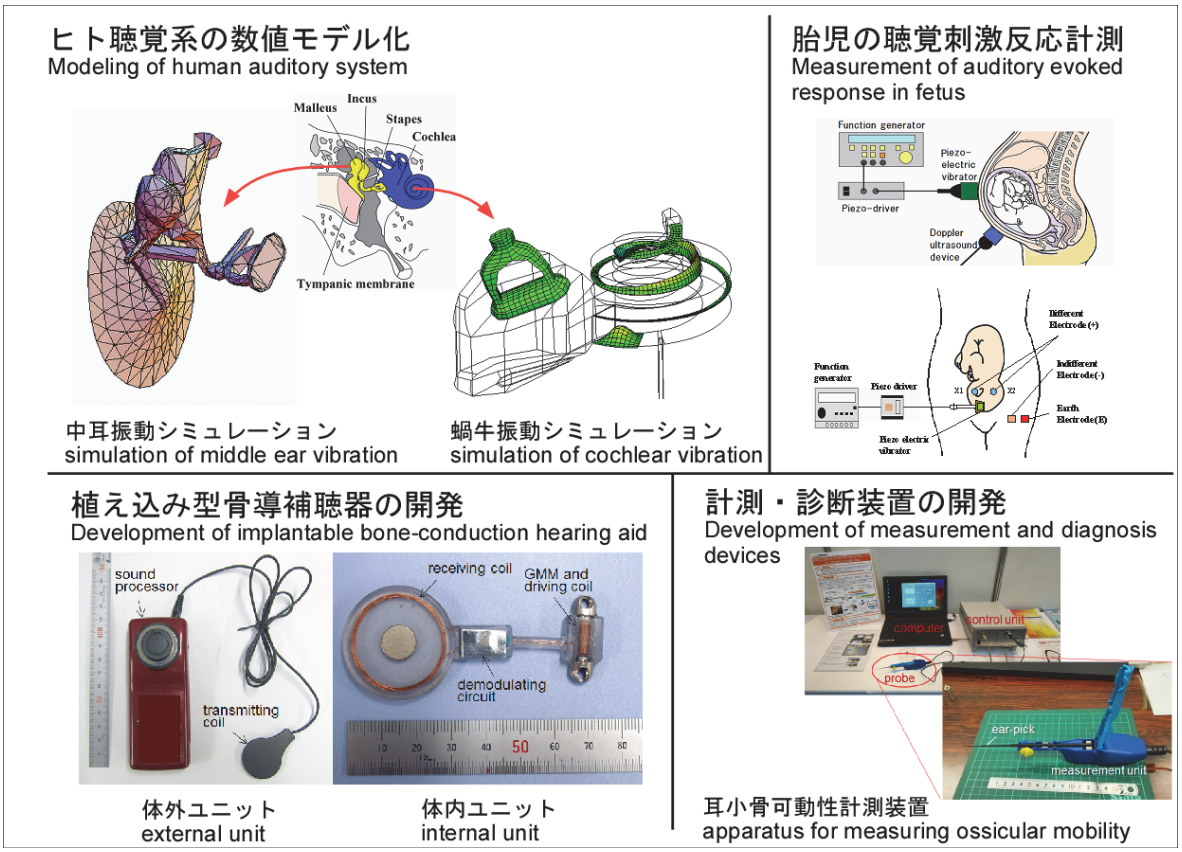


Figure 1 Researches in audiology

The relationships between the changes in the vibrations in the auditory system and healing loss have not been fully clarified, because the auditory system exists intracranially and its vibration is in nanometer order. Hence, we have investigated the mechanisms of auditory disorders and the methods for treatments collaborating with the neighboring medical departments and hospitals. The topics are as follows:

- Modelling of the auditory systems; Clarification of the vibration of the auditory periphery and its pathological changes, and development of the effective methods for treatment.
- Measurement of auditory evoked response in fetus; Development of new hearing screening methods for fetuses by measuring hart rate changes induced by the stimulus vibrations which are applied on the surface of the abdomen of a mother.
- Development of implantable bone conduction hearing aid; Hi-Fi and minimally invasive devices for better QOL.
- Development of surgery assisting apparatus; Measurements of ossicular mobility during surgery.

1.2 Achievements and State of Progress (April, 2016 - March, 2017)

(1) Modelling of the auditory systems

This research intends to clarify the mechanisms of hearing disorders and to develop better methods of treatments, which are difficult to identify through clinical researches and specimens. Numerical cochlear models in which the active motilities of the outer hair cells are considered have been constructed. Simulations were performed using the models, and the vibrations of the lymph liquid and basilar membrane in the cochlea were analyzed. Through the simulations, the transmission mechanisms in the peripheral auditory systems have been clarified. As clinical applications, the mechanisms of hearing losses caused by otosclerosis and endolymphatic hydrops were investigated. The Outstanding Presentation Award was given to the research from the Society for Bioacoustics.

(2) Measurement of auditory evoked response in fetus

Measurements of heart rate variability and brain waves induced by vibratory stimulation applied to maternal abdominal wall were performed. Positive reactions were obtained from approximately 90% of the fetuses with normal hearing which is confirmed after the birth.

(3) Development of implantable bone conduction hearing aid

A prototype of the bone-conduction hearing aid in which Giant Magnetostrictive Material is used as the vibrator was created. By improving the design of the vibrator and the method of transdermal signal transmission, the device showed higher efficiency comparing to the existing bone-conduction hearing aid. We got a European Patent for the basic specifications and operating function of the hearing aid and are working with a company toward practical use of the new hearing aid.

(3) Development of surgery assisting apparatus

An apparatus for measuring ossicular mobility has been developed, and the ossicular mobility in patients has been measured during tympanoplasty. This work was supported by Saitama Leading Edge

Project (Medical Innovation) in this year, and some prototypes were constructed and tested with the help of medical equipment makers and medical institutions.

1. 3 Future Plan

With regard to the modeling of the auditory system, we have tried to construct more detailed models in which the ionic flux at the hair cells, the organ of Corti, gap junctions, the spiral ligaments, and the stria vascularis are considered. Then, the mechanoelectrical transduction in the cochlea will be investigated using the models. We will also advance the developments of the implantable hearing aid and the apparatus for measuring ossicular mobility toward commercialization.

2. Research Achievements

2. 1 Invited lectures

(1) TAKANASHI Takuma, SAKAMOTO Hironori, SKALS Niels, FUKUI Shuji, MATSUI Yasuhiro, KOIKE Takuji, NISHINO Hiroshi, Vibration sensitivity in longicorn beetles and biomimetic potential for insect pest control, International Symposium on Engineering Neo-Biomimeteics VII, February 17 (2017)(invited)

2.2 Patent

(1) 2017-016331, System for evaluation of mobility and mobility evaluation method, Takuji Koike, Kai Takakuwa, Yuka Irie, Sho Kanzaki, Chee Sze Keat, Takenobu Higo, Masaaki Hayashi, Univ. Electro Communications, Keio Univ., Mechano Transformer Corp., Leadence Corp., Daiichi Medical Co.

(2) EP 2329802, Embedded audiphone, Takuji Koike, Naohito Hato, Kensei Yamamoto, Univ. Electro Communications, Univ. Ehime.

2.3 Award

(1) Sinyoung Lee, Outstanding Presentation Award, The Society for Bioacoustics, December 11, 2016

(2) Takuji Koike, JSME fellow 9141811.

2.4 Student guidance

(1) Ryo Ebine, 2016 year, Bachelor

(2) Takahiro Suzuki, 2016 year, Bachelor

(3) Kenta Mito, 2016 year, Bachelor

(4) Yohei Wagai, 2016 year, Bachelor

(5) Nobutaka Hayashi, 2016 year, Bachelor

(6) Sinyoung Lee, 2016 year, Master

(7) Kai Takakuwa, 2016 year, Master

2.5 Study abroad programs for students

(1) Miho Sato, National Higher School of Mechanics and Microtechnology, Besanzon, France, Aug 22, 2016 – Sep 26, 2016.

3. Research funding

3.1 Grant-in-aid for scientific research

(1) Takuji Koike, Grant-in-Aid for Scientific Research (C), 2015-2017

3.2. Competitive external research funding

(1) Takuji Koike, Cross-ministerial Strategic Innovation Promotion Program, 2014-2017

(2) Takuji Koike, Saitama Leading Edge Project (Medical Innovation), 2016

4. Collaboration

4.1 Outside UEC

(1) Katsuhisa Ikeda, Department of Otorhinolaryngology, Jyuntendo University

(2) Naohito Hato, Department of Otorhinolaryngology, Ehime University

(3) Sho Kanzaki, Department of Otorhinolaryngology, Keio University

5. Outreach activities

5.1 Editor of academic journals

(1) Journal of Biomechanical Science and Engineering, 2 years

5.2 Paper review of academic journals

(1) Hearing Research

(2) The Journal of the Acoustical Society of America

(3) The Journal of the Association for Research in Otolaryngology

(4) Acoustical Science & Technology

5.3 Other outreach activities

(1) Scientific Committee, International Union of Theoretical and Applied Mechanics, Stuttgart, Germany, 2016

Yutaka KANO Laboratory

1. Outline of Research and Education

1. 1 Basic Policy in Research and Education

The loss of the muscle mass associated with non-active state such aging, bedridden or metabolic disease (ex. diabetes) is a risk factor to be connected directly with Quality of Life (QOL) or health life expectancy. However, adequate understanding is not obtained about the mechanism of the myocytes adaptation to maintain muscle mass. This laboratory performs physiological analysis about biological response for various bio-stimulation (stress) in the locomotorium (skeletal muscle). The results of research in our laboratory were demonstrated by *in vivo* bioimaging that we originally developed in rodent (rat, mouse) model. This research model attracts attention as the research model which is evaluable in intracellular molecules dynamics in real time by a living individual. The exercise acts on whole body as combined vital stress. This stress is classified roughly into endogenous (including the growth hormone) and exogenous (mechanical, hypoxia, heat) factors. Our research elucidates that these vital stress factors change cytoplasmic ion balance and oxygen dynamics. The change of intracellular various ions and oxygen is important to elucidate an adaptation phenomenon of the skeletal muscle fiber. Therefore, these basic research contributes to development of effective prophylaxis for the muscle atrophy by bedridden/aging and development of the training method to maintain muscle mass.

1.2 Achievements and State of Progress (April, 2016 - March, 2017)

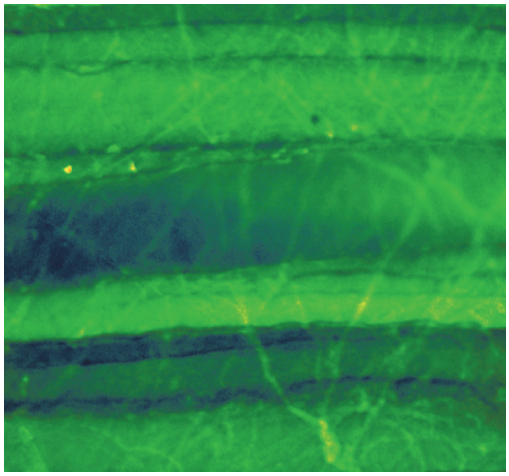
Our laboratory performed research subject about the homeostasis of the intracellular hydrogen ion (H^+) in this year. Most physiological processes are pH-sensitive, and pH within individual cells in skeletal muscles (pH_i) must be carefully regulated to maintain normal cellular functioning. During intensive exercise, and also in certain diseases, levels of a cationic form of hydrogen (H^+) rise rapidly within cells, causing pH_i levels to plummet and become more acidic. There are three membrane transporters known to be involved in regulating pH_i, but their precise individual roles are unclear.

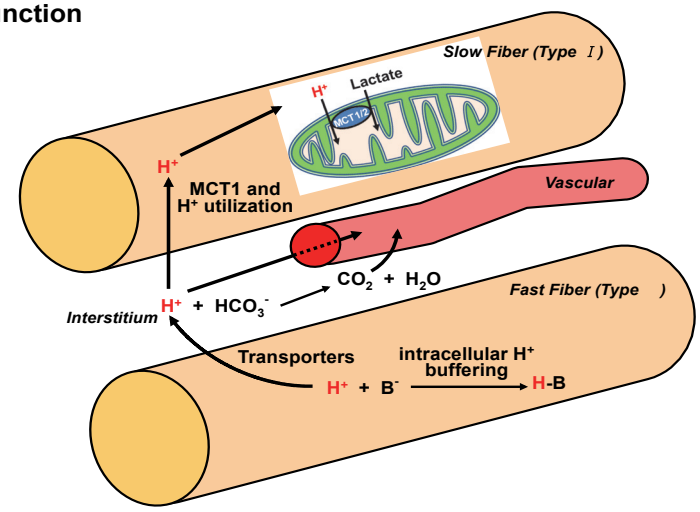
Our research group conducted experiments using *in vivo* bioimaging models to verify the roles of these transporters in pH_i regulation. The team tested the effects of an injection of H^+ into single muscle fibers in rats. They blocked each transporter involved in pH_i regulation – namely, lactate/H^+ cotransporter (MCT), Na^+/ H^+ exchange transporter (NHE) and Na^+ / HCO_3 cotransporter (NBC) – one at a time and then all together. They compared their results with a control group with normal transporter functioning.

Their results showed that two stages exist in pH_i recovery; an initial rapid stage followed by a second, more gradual recovery stage. We discovered that the three transporters were not involved in the rapid stage. While individual transporter inhibition did not impact on pH_i recovery, blocking all three transporters prevented the second stage (gradual recovery) from occurring.

The study also revealed that the pH of surrounding fibers changed following H^+ injection, suggesting that they take up excess H^+ to alleviate stress in affected cells.

in vivo bio-imaging and muscle fiber function





1. 3 Future Plan

Currently, two research projects progress, 1: the new development of the Ca^{2+} evaluation procedure, 2: the evaluation of post-exercise Ca^{2+} dynamics. The new bioimaging method combined laser microscope (2 photon and photothermal) with the in vivo model (*Sonobe et al. 2008,2010, Eshima et al. 2013, 2015*), and it is the highest system in the biology field (top efficiency of temporal, spatial resolution). As a result, in addition to Ca^{2+} dynamics in cytoplasm, this method can evaluate Ca^{2+} dynamics with the endoplasmic reticulum - mitochondria simultaneously under *in vivo* environment. This is the first *in vivo* animal experiment model highlighting regulatory mechanism of the Ca^{2+} at an organelle level in myocytes.

2. Research Achievements

2. 1 Reviewed papers [○: Impact factor greater than 4]

(1) Sudo M, Ando S, Kano Y. Repeated blood flow restriction induces muscle fiber hypertrophy. Muscle Nerve. 2017 Feb;55(2):274-276. doi: 10.1002/mus.25415. Epub 2016 Oct 20. PubMed PMID: 27668404. IF 2.713

(2) Nakajima T, Yasuda T, Koide S, Yamasoba T, Obi S, Toyoda S, Sato Y, Inoue T, Kano Y. Repetitive restriction of muscle blood flow enhances mTOR signaling pathways in a rat model. Heart Vessels. 2016 Oct;31(10):1685-95. doi: 10.1007/s00380-016-0801-6. Epub 2016 Feb 1. PubMed PMID: 26833042. IF 2.293

(3) Tanaka Y, Inagaki T, Poole DC, Kano Y. pH buffering of single rat skeletal muscle fibers in the in vivo environment. Am J Physiol Regul Integr Comp Physiol. 2016 May 15;310(10):R926-33. doi: 10.1152/ajpregu.00501.2015. Epub 2016 Mar 16. PubMed PMID: 26984893. IF 3.529

(4) Tanaka Y, Poole DC, Kano Y. pH Homeostasis in Contracting and Recovering Skeletal Muscle: Integrated Function of the Microcirculation with the Interstitium and Intramyocyte Milieu. Curr Top Med Chem. 2016;16(24):2656-63. Review. PubMed PMID: 27072709. IF 2.95

2.2 Student guidance

(1) Naoki Nakada, Hiroshi Horikawa, Mutsumi Murase 2016 Bachelor (engineering)

(2) Takuro Mashio. 2016, Master (engineering)

(2) Yoshinori Tanaka. 2016 Doctor (science)

2.3 Visit of oversea researchers and students

(1) Leslie Carina Orozco Landa, Instituto Politecnico Nacional

3. Research funding

3.1 Grant-in-aid for scientific research

(1) Yutaka Kano (representative), Change of the muscle fiber type as the multinucleate cell, Grant-in-Aid for challenging Exploratory Research, 2015-2016, 3,770,000 yen

(2) Yutaka Kano (representative), Importance of postexercise calcium ion dynamics to determine the adaptation of myocytes Grant-in-Aid for Scientific Research (B), 2016-2019, 17,030,000 yen

3.2. Competitive external research funding

(1) The vehicle racing commemorative foundation, 2016, 1,500,000 yen

4. Collaboration

4.1 Inside BLSC

(1) Hidetaka Okada, Evaluation musculotendinous composition by the high speed camera, 2013-present

(2) Takayoshi Kobayashi, Development of the bioimaging method with the high-powered laser, 2015-present

4.2 Outside BLSC in UEC

(1) Hideki Shirakawa, Calcium ion and cell functions,

4.3 Outside UEC

(1) Shinji Miura, University of Shizuoka, Myofunctional evaluation using the PGC1 model mouse, 2013-present

(2) Toshiaki Nakajima, Dokkyo medical college Hospital heart center, Development of the pressurization load method to maintain skeletal muscle mass, 2013-present

(3) Mikiyasu Shirai, Hirotsugu Tsuchimochi, Tadakatsu Inagaki, Department of Cardiac Physiology, National Cerebral and Cardiovascular Center Research Institute, Evaluation of cardiovascular dynamics under the hyperbaric hyperoxia environment, 2013-present

(4) Kazuyoshi Yagishita, Clinical Center for Sports Medicine and Sports Dentistry, Hyperbaric Medical Center/Sports Medicine Clinical Center, Medical Hospital of Tokyo Medical and Dental University, Evaluation of cardiovascular dynamics under the hyperbaric hyperoxia environment, 2013-present

(5) David C. Poole, Kansas state university College of veterinary medicine, Microcirculation and skeletal muscle function, 2003-present

5. Outreach activities

5.1 Paper review of academic journals

(1) American Journal of Pathology, 2016

(2) Journal of Applied Physiology, 2016

(3) Neurochemical Research, 2016

(4) Physiological Reports, 2016

(5) Research in Veterinary Science, 2016

(6) Training Science, 2016

Hiroshi YOKOI/Yinlai JIANG Laboratory

1. Outline of Research and Education

1. 1 Basic Policy in Research and Education

The main aims of the Yokoi/Jiang lab are the redevelopment of the theoretical framework and peripheral technologies for human-based engineering, starting with the scientific study of humans and other organisms from an engineering perspective, and research into the natural interfaces between humans and machines, society and machines and technologies integrating the two.

The lab engages in theoretical and technological developments in measurement and control in the field of robotics, as well as their applications, with a focus on the development of systems integrating humans and machines. The theoretical backbone consists of artificial intelligence, bioelectrical measurements and analysis, as well as design and development of coupled tendon-driven mechanisms, based on information processing, learning, evolutionary computation and combinatorial optimization. The main areas of application are the development of myoelectric prostheses, power assist devices, neural rehabilitation for the recovery of motor function with the goal of utilizing machines in the areas of welfare and medical care through medicine-engineering collaboration.

1. 2 Achievements and State of Progress (April, 2016 - March, 2017)

(1) Development of myoelectric prosthetic hand and application for registration of parts for completion

Myoelectric prosthetic hands are used to restore upper limb function. They therefore must resemble human hands in fit, have the functionality to carry out necessary daily movements, be light enough to minimize the burden on the body, and be usable by anyone. In FY 2016, the lab mainly developed a myoelectric prosthetic hand equipped with a force magnification mechanism, a pressure-sensitive cosmetic glove and a conductive silicon myoelectric sensor. An application was also made to the Ministry of Health, Labor and Welfare for their registration as parts for completion.

a. Development of prosthetic hand with force magnification mechanism

The left image in Figure 1 shows the ball-chain driven force magnification device developed to increase the grip function. In order to improve the mechanical adaptability when gripping, we introduced an artificial tendon sheath mimicking a human hand. Furthermore, in order to increase the range of motion of the MP joint on the 4 fingers, we set the actuator to unlimited rotation and fitted a limit switch to the rotation axis of the MP joint. In order to compare the grip of each device, we selected 23 objects frequently used in daily life and carried out a pick-and-place experiment. The radar chart on the right in Figure 1 shows the results of the experiment. The 4 types of myoelectric prosthesis are shown in different colors. The axis of the radar chart shows the number of successes. The larger the area surrounded by the line, the more successfully the prosthetic hand performed. As shown by the red line, the prosthesis with unlimited rotation force magnification mechanism with artificial tendon sheath had the greatest number of successes with almost every object, demonstrating the improved grip function.

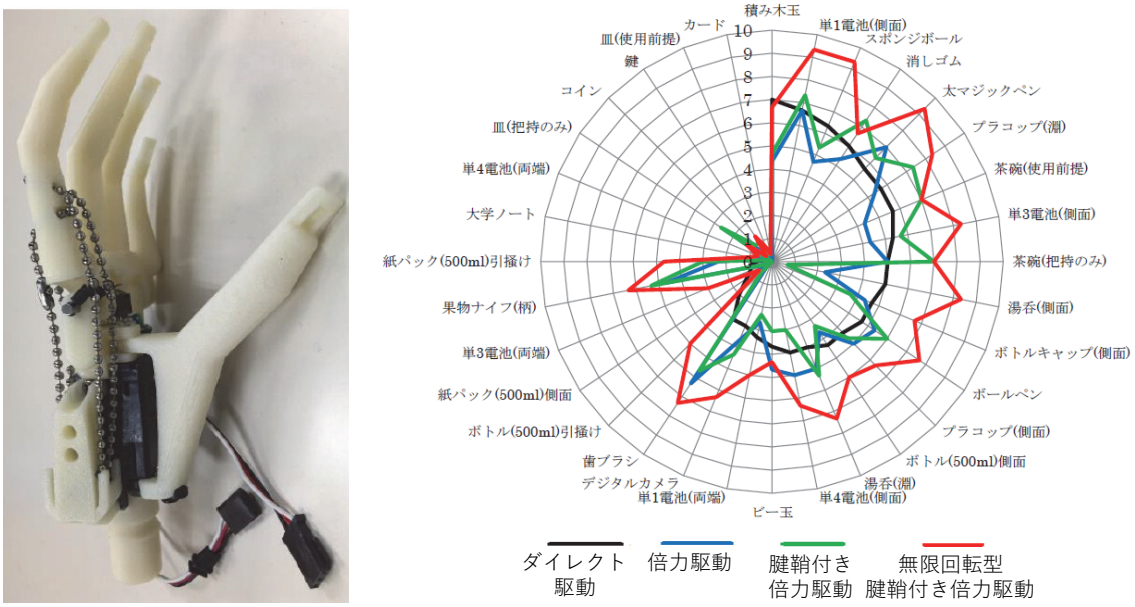


Figure 1: prosthetic hand with ball-chain driven force magnification mechanism and evaluation results

b. Development of pressure-sensitive glove for prosthetic hand

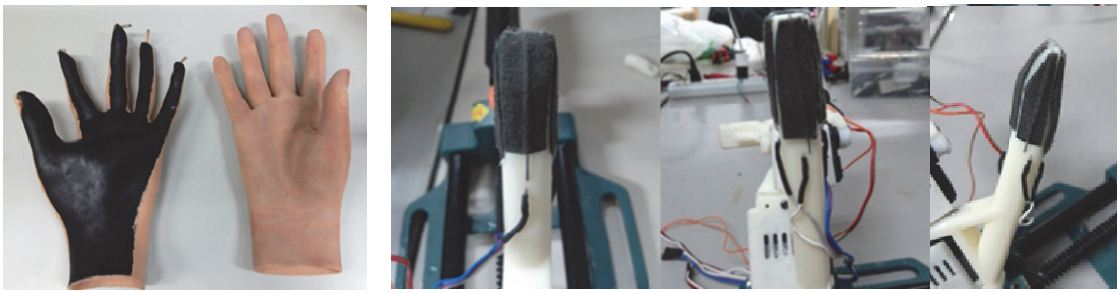


Figure 2: Glove fitted with conductive silicon (l) and pressure sensor fitted to prosthesis finger (r)

Gloves for prostheses must reproduce the sensory functions of a human hand, as well as imitating its outer appearance, touch and texture. In order to produce tactile sensation, the lab has developed a thin, light and flexible pressure sensor by attaching conductive silicon to the inside surface of the prosthesis glove (Figure 2). The material for the electrodes attached to the robotic prosthesis is conductive non-woven fabric. In order to investigate the omni-directionality, force was applied from 4 directions to a prosthetic hand fitted with sensors. Omni-directionality was confirmed by the characteristics of the sensors. Furthermore, the fact that the sensors produced different outputs depending on the direction of force allowed us to determine the pressed face. In addition, by attaching pressure sensors to the front and right side of the thumb and index fingers, we can detect the type of grip being undertaken by the prosthetic hand.

c. Development of a myoelectric sensor using conductive silicon

For the smooth operation of myoelectric prosthetic hand, electrodes for sEMG (surface myoelectrogram) measurement must be resistant to sweat, pressure, and other causes of noise in users' daily lives. In FY 2016, we developed a conductive silicon-based myoelectric sensor (Figure 3). Test

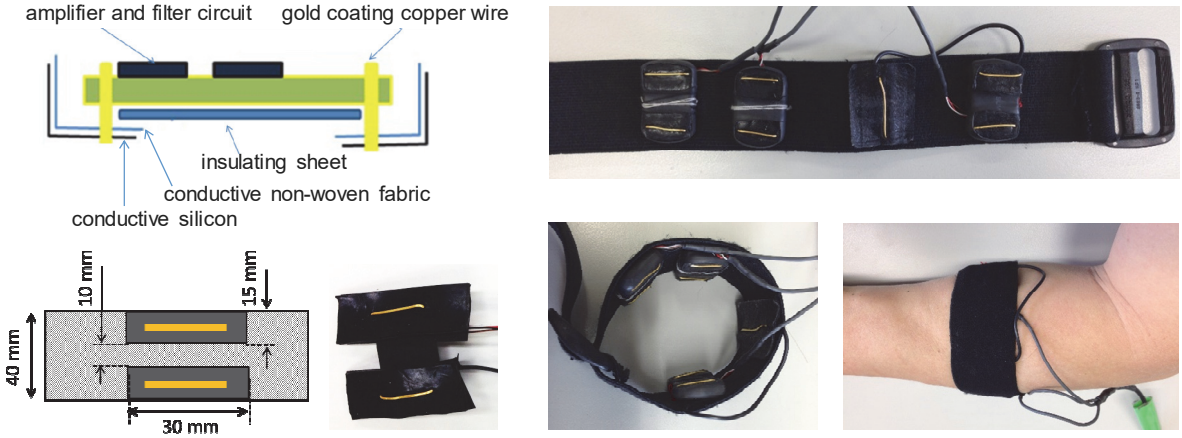
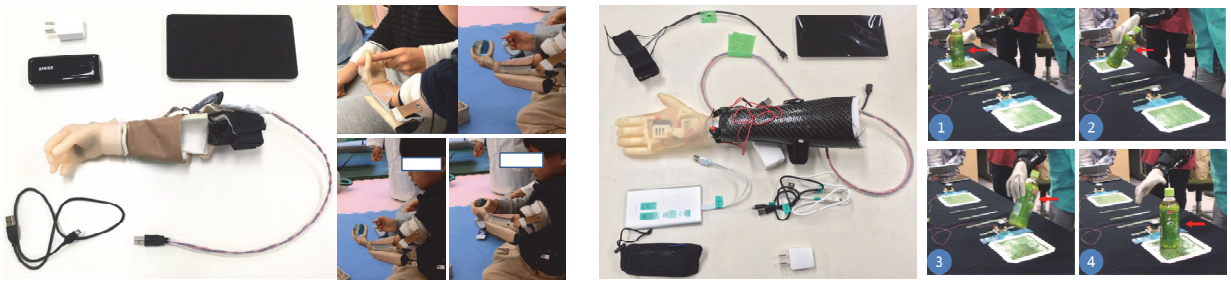


Figure 3: Structure of myoelectric sensor using conductive silicon (left) and sensor band (right)

results showed that compared to electrodes made of conductive silicon alone and the conductive polymer electrodes developed the previous year, electrodes made with gold plated wires and conductive silicon adhered more stably to the skin and reduced the effect of sweat. Furthermore, tests were carried out to investigate how the external force exerted on the electrodes influenced the myoelectric signal. This was done by measuring the sEMG signal while periodically applying external force. This revealed that when pressure is stable fluctuation in the sEMG signal is low, but when pressure is variable, fluctuation is high, particularly at low frequencies (20~50Hz).

d. Application for registration as parts for completion



（a） 1 DoF myoelectric prosthetic hand for children (b) 2 DoF myoelectric prosthetic hand for adults

Figure 4: Prosthetic hand for registration as parts for completion and clinical trials

For the development of products acceptable from the perspective of design and functionality, we carried out clinical trials using the myoelectric prostheses and received feedback to make improvements. Clinical trials began in November 2015, after we had undergone an ethics examination with the cooperation of the National Center for Child Health and Development and Tokai University Hospital. In FY 2016, we selected subjects suitable to take part in trials, based on the judgements of medical institutions. We carried out clinical tests on 20 subjects, based on evaluations of ADL (Activities of Daily Living) while using a prosthesis and upper body function tests. Adult subjects took part in the trials at Tokai University Hospital and pediatric subjects took part at the National Center for Child Health and Development. Both groups were supervised by doctors during the trials (Figure 4). The ADL test evaluated how freely subjects could grip and move objects around them. Even children with congenital defects were able to grip plates and throw building blocks and

balls, and succeeded in many ADLs. Based on feedback from subjects about the manipulation of the prosthesis and the priority of finger movements, we carried out improvements in the myoelectric controller (movement prediction method), myoelectric sensor, and the user interface. In FY 2016, we made improvements to the prototype for a low-cost, high-safety myoelectric prosthetic hand. We also applied for registration of parts for completion for mainstream distribution.

In addition to a~d mentioned above, we also conducted research and development of myoelectric prosthetic hand for hand amputation and prosthetic arm for shoulder disarticulation, as well as support systems for the guardians of pediatric amputees.

(2) Improvement of tendon-driven robot arm and construction of control system

We lightened and strengthened the tendon-driven arm designed in FY 2015. We achieved a balance between low weight and high power: at the maximum reach of 0.8m, the arm can lift 1.5kg, despite weighing under 2.5kg overall (excluding power supply). In addition, the maximum tangential speed of the fingertip is 2m/s, almost reproducing the speed of humans' everyday movements. We developed an intelligent prosthesis that automatically identifies the gripping object and determines the grip orientation, based on ROS (Figure 5). In order to make the automatic gripping and moving of objects smoother, we implemented a route planning algorithm for the selection of grip orientation and grip movement, by using an RGBD sensor to automatically identify the target object and running a high speed simulation. We introduced a ROS simulator for intelligent control at Osaka University, in preparation for the introduction of a BMI system for clinical research.

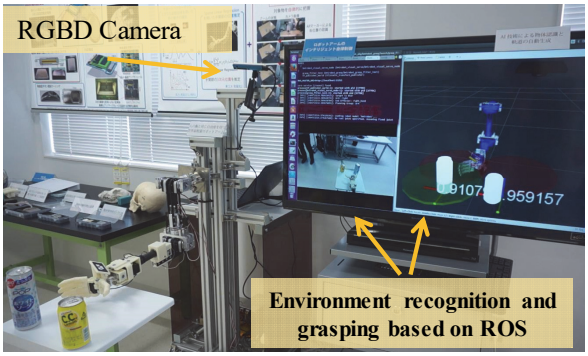


Figure 5: Gripping of objects by robot arm using ROS

In collaboration with Osaka University and Tokyo Institute of Technology, we proposed the strategies for switching between autonomous control and BMI control depending on the distance from the object in an autonomous-BMI hybrid control system for the robot arm. We used an SSVEP system for the BMI control (Figure 6). Subjects control the arm to approach the object using SSVEP. When the object has been identified through data from the RGBD sensor and the hand has entered the autonomous control area of the object (within a radius of 15cm from the object), the robot arm switches to autonomous control, generates the grip posture and trajectory and automatically grips and moves the object. Each test took 90 seconds, and we were able to confirm that the task could be completed repeatedly.

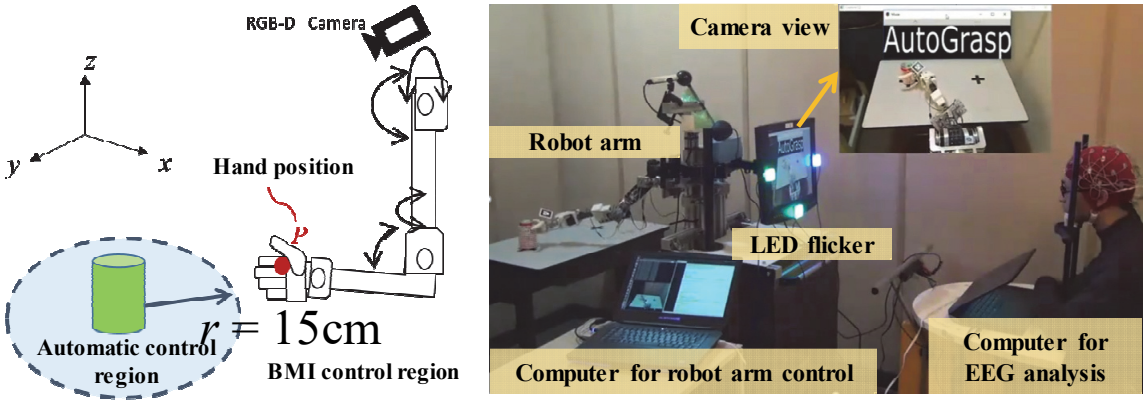


Figure 6: Switch between BMI control and autonomous control based on distance from object

(3) Motor point tracking functional electric stimulation using multiple surface electrodes

Functional electrical stimulation is effective as a form of rehabilitation for patients who have suffered strokes or spinal cord injuries, but there is the issue of it contributing to muscle fatigue that weakens muscle contraction induced by the same signal. Stimulation of the motor point between nerve and muscle can induce muscle contraction more effectively, so the laboratory developed a method of stimulation by following the movement of the motor point through non-isometric muscle contraction (Figure 7). Stimulation electrodes are applied to the motor points of the biceps in the upper arm during extension and flexion of the elbow. Two methods were proposed: motor point tracking based on the angle of the scapula (JASS), and motor point tracking based on the stimulation time (TSS). The experimental results with eight subjects revealed no significant difference between JASS and TSS. Both were shown to enable more stable maintenance of muscle contraction than conventional simultaneous stimulation.

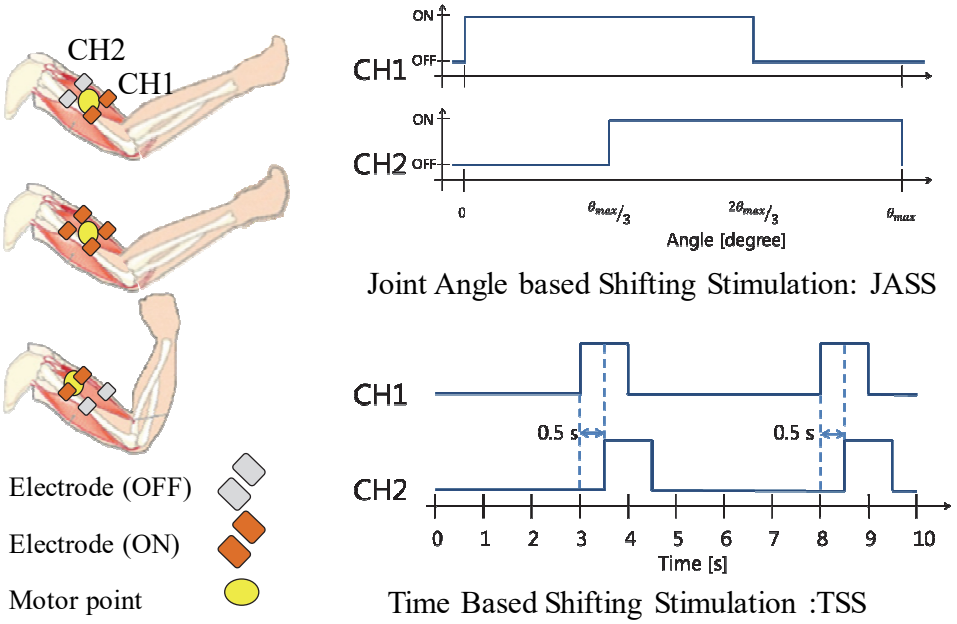


Figure 7: Following motor point electrical stimulation based on joint angle (JASS) and time (TSS)

(4) Measurement of gait with proximity sensor during use of walking support machine

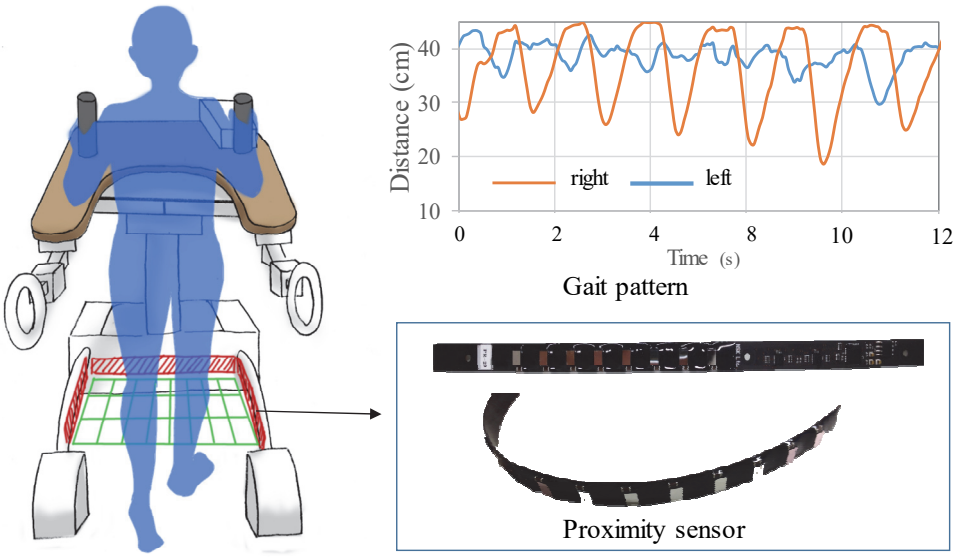


Figure 8: Gait measurement using proximity sensor

When controlling walking machines to support the rehabilitation and movement in daily life of individuals with gait disorders, it is necessary to detect the gait of the user and adjust the speed and/or direction accordingly. Measurements from conventional environmental cameras have different accuracy depending on the position of the subject, and measurements cannot be made when the subject is occluded due to movement or obstacles. Moreover, measurements with motion sensors needs to attach and calibrate sensors on each occasion, which causes great inconvenience. The laboratory proposed a new method of detecting gait, by attaching proximity sensors to the inside of the walking machine and measuring the movement of the lower limbs in a 2D plane. In FY 2016 we developed a gait measuring system by attaching array proximity sensors (NSK Ltd.) to the area surrounding the feet in a walking support machine and measuring the distance between the feet and the machine. Using this measurement system, we confirmed that the difference in gait between the left and right leg increased in pseudo walking difficulty (through binding the knee joint).

1.3 Future Plan

We will engage with the following issues regarding research into myoelectric prostheses, robot arms, functional electrical stimulation, and walking support.

(1) Increasing the functionality and practicality of myoelectric prostheses

In order to increase the freedom of prostheses, we will develop a wire-driven module that can be fitted inside the structure of the prosthesis. Furthermore, in order to realize a greater number of grip postures without increasing the number of motors, we will add finger joints that move passively and optimize the angle of the finger joints. In order to realize a myoelectric hand that possesses tactile function as well as replicating the motor function of the fingers, we will develop omni-directional pressure sensors that fit to the fingers and sensory feedback equipment using functional electrical stimulation and oscillations. These will be adapted for use by shoulder, upper arm, lower arm and hand amputees. In order to evaluate the

effectiveness of myoelectric prostheses, we will, in addition to performance tests, use fNIRS and fMRI to take brain measurements of the brain activity of users and evaluate the degree to which the prosthesis feels like it belongs to the body, as well as observing the changes in patterns of brain activity through long term use.

(2) Optimization of robot arm and motor control

We will improve the mechanism and autonomous system of the wire-driven robot arm, combine this with the BMI controller developed at Osaka University and carry out clinical trials. On the hardware side, grip power, control precision and maintainability will be improved by reducing the weight of the mechanism and modularizing it. The safety of movements will be improved by introducing motors capable of speed and torque control. On the software side, we will design an interface for the combination with BMI control and equip a system for switching between BMI control and autonomous control.

(3) Investigation of electrical stimulation signals and patterns

We will investigate stimulation signals that effectively induce sensation and muscle contraction respectively. In order to construct an algorithm that can efficiently investigate the stimulation patterns of functional electrical stimulation utilizing multi-point surface electrodes, we will develop a high speed method of exploring stimulation patterns and a clustering method for finger posture.

(4) Motion control for a gait-adjusted walking support machine

We will attempt to realize versatile methods of measuring and analyzing gait, which will serve as the underlying technologies increasing the intelligence and safety of the walking machine. We will extract *the characteristics of lower limb movement from data measured by proximity sensors and develop a* method of distinguishing gait patterns. The proximity sensors utilize the reflection intensity of infrared light, so in order for them not to be affected by light in the environment, we will develop a data processing algorithm using active sensing. In addition, we will develop a method of inferring the shape and posture of the target using distance information from multiple sensor arrays.

2. Research Achievements

2. 1 Reviewed papers [○: Impact factor greater than 4]

Journal articles

(1) Yinlai Jiang, Takeru Togane, Baoliang Lu, Hiroshi Yokoi sEMG Sensor Using Polypyrrole-coated nonwoven fabric sheet for practical control of prosthetic hand. *Frontiers in Neuroscience* 11/ 33, 2017/02/06, 10.3389/fnins.2017.00033 .

(2) Tatsuhisa Takahashi, Yinlai Jiang, Shuoyu Wang, Masanaga Ikegami, Akihito Yoshimura, Shinichi Watanabe, Takashi Matsuo, Hirotaka Yanagida Identification of fragmented letters through minimum-distance interpolation. *Therapeutic Research* 37/ 8, 795-802, 2016.

(3) Rintaro Kamihira, Misato Kasuya, Yinlai Jiang, Shunta Togo, Masao Sugi, Hiroshi Yokoi Maintenance of muscle contraction improves during dynamic exercise by multi-channel functional electrical stimulation with time shifting stimulation. *International Journal of Bioscience, Biochemistry and Bioinformatics (IJBBB)* 7 (1) 30-40, 2017.

(4) Takufumi Yanagisawa, Ryohei Fukuma, Ben Seymour, Koichi Hosomi, Haruhiko Kishima, Takeshi Shimizu, Hiroshi Yokoi, Masayuki Hirata, Toshiki Yoshimine, Yukiyasu Kamitani, Youichi Saitoh Induced sensorimotor brain plasticity controls pain in phantom limb patients. *Nature Communications* 7 Article number: 13209 (2016) doi:10.1038/ncomms13209.

(5) Xiaoxiao Zhu, Qixin Cao, Hiroshi Yokoi, Yinlai Jiang Large scale indoor 3D mapping using RGB-D sensor. *Intelligent Robotics and Applications* 313-321, 2016.

(6) Yoshiko Yabuki, Kazumasa Tanahashi, Masahaku Ishihara, Suguru Hoshikawa, Tatsuhiro Nakamura, Yinlai Jiang, Ryu Kato, Hiroshi Yokoi Development of new cosmetic gloves for a myoelectric prosthetic hand by using elastomer, *Bulletin of the Japanese Society of Prosthetic and Orthotic Education, Research and Development* 32, 177-185, 2016 (in Japanese).

International conference journals

(1) Hesong Ye, Xiang Feng, Yoshiko Yabuki, Shunta Togo, Yinlai Jiang and Hiroshi Yokoi, "Force-magnification mechanism with artificial tendon sheath for myoelectric prosthetic hand for children", IEEE International Conference on robotics and biomimetics (ROBIO2016), SuC04.1, Qingdao China, 2016.

(2) Rintaro Kamihira, Misato Kasuya, Yinlai Jiang, Shunta Togo, Masao Sugi and Hiroshi Yokoi, "Maintenance of Muscle Contraction Improves during Dynamic Exercise by Multi-channel Functional Electrical Stimulation with Time Shifting Stimulation", International Conference on Biomedical Signal and Bioinformatics (ICBSB), AUT University, New Zealand, 2016.

(3) Yoshiko Yabuki, Kazumasa Tanahashi, Yuta Suzuki, Tatsuhiro Nakamura, Ryu Kato, Yinkai Jiang and Hiroshi Yokoi, "Development of Artificial Skin for the Myoelectric Prosthetic Hand by using Hyper Elastic Materials with tactile sensor", The International Workshop on modern Science and Technology 2016(IWMST2016), pp.26-32, Taichung, Taiwan, 2016.

(4) Hesong Ye, Shintaro Sakoda, Yinlai Jiang, Soichiro Morishita and Hiroshi Yokoi, "Prosthetic Hand with Wire-Driven Force-Magnification Mechanism for Children", The International Workshop on modern Science and Technology 2016(IWMST2016), pp.40-45, Taichung, Taiwan, 2016.

(5) Mai Nozakura, Soichiro Morishita, Misato Ohdaira, Yinlai Jiang and Hiroshi Yokoi, "A method for evaluation of dependency between diseased side and opposite side of hemiplegia patient during FES-Cycling by using transfer entropy", XXI International Society of Electrophysiology and Kinesiology (ISEK) Congress, Chicago, USA, 2016.

(6) Yoshiko Yabuki, Kazumasa Tanahashi, Suguru Hoshikawa, Tatsuhiro Nakamura, Ryu Kato, Yinkai Jiang and Hiroshi Yokoi, "Development of new Cosmetic Gloves for Myoelectric Prosthetic Hand by using Thermoplastic Styrene Elastomer", The 14th International Conference on Intelligent Autonomous Systems (IAS-14), Shanghai,China, 2016.

(7) Yuta Murai, Suguru Hoshikawa, Shintaro Sakoda, Yoshiko Yabuki, Masahiro Ishihara, Tatsuhiro Nakamura, Takehiko Takagi, Shinichiro Takayama, Yinlai Jiang and Hiroshi Yokoi, "Development of a Myoelectric Hand Incorporating a Residual Thumb for Transmetacarpal Amputees", The 14th International Conference on Intelligent Autonomous Systems (IAS-14), Shanghai, China, 2016.

2. 3 Invited lectures

(1) Hiroshi Yokoi Human-machine fusion systems and their applications, Robot engineering seminar, 2016/10/31

2. 4 Media releases

(1) Super J Channel Information News Show, Toretate, Akita Asahi Broadcasting, 2017/3/22

(2) Myoelectric Prosthetic Hand, Grasp the future～ Low cost domestic newest technology to be in practical use～, The Asahi Shimbun, 2016/11/24

(3) Read and Understand the Electrical Signals of Brain and Muscle, Yomiuri Lecture at the University of Electro-Communications, Yomiuri Shimbun, 2016/06/10, 2016/06/12

2. 5 Patent

(1) Hiroshi Yokoi, Yinlai Jiang, Shunta Togo, Yoshiko Yabuki, Yuta Murai, Signal measurement device, and signal measurement method, The University of Electro-Communications, Patent application No.2017-029981, 2017/2/21.

(2) Hiroshi Yokoi, Yinlai Jiang, Manipulator, The University of Electro-Communications, Patent application No.2016-109120, 2016/5/31.

2. 6 Awards

(1) Excellent Paper Award: Rintaro Kamihira, Misato Kasuya, Yinlai Jiang, Shunta Togo, Masao Sugi and Hiroshi Yokoi 2016 International Conference on Biomedical Signal and Bioinformatics (ICBSB 2016) 2016/11/22

(2) Best Conference Paper Award Finalist: Yoshiko Yabuki, Kazumasa Tanahashi, Suguru Hoshikawa, Tatsuhiro Nakamura, Ryu Kato, Yinlai Jiang and Hiroshi Yokoi The 14th International Conference on Intelligent Autonomous Systems 2016/07/06

2. 7 Student guidance

(1) Daiki Ikuzawa, 2016, Bachalor（engineering）

(2) Taihei Kuwahara, 2016, Bachalor（engineering）

(3) Yuki Kojoma, 2016, Bachalor（engineering）

(4) Akane Fujimoto, 2016, Bachalor（engineering）

(5) Kentaro Maeda, 2016, Bachalor（engineering）

(6) Yasuhiro Mouri, 2016, Bachalor（engineering）

(7) Rintaro Kamihira, 2016, Master（engineering）

(8) Mai Nozakura, 2016, Master（engineering）

(9) Yuya Sakai, 2016, Master（engineering）

(10)Hesong Ye, 2016, Master（engineering）

2.8 Visit of oversea researchers and students

(1) Xiaoxiao Zhu, Postdoctoral researcher, Shanghai Jiaotong University, 2016.7.1～2017.1.31.

(2) Baiqing Sun, Associate professor, Shenyang University of Technology, 2016.6.28～2016.7.15

(3) Dianchun Bai, Lecturer, Shenyang University of Technology, 2016.6.26～2016.7.3

3.Research funding

3.1 Grant-in-aid for scientific research

(1) Hiroshi Yokoi (PI) Artificial hand with conductive silicon skin, Challenging Exploratory Research, 2016/4/1～2019/3/31.

(2) Yinlai Jiang (PI) Bio-adaptive sEMG measurement method for control of welfare machines , Scientific Research (C) 2016/4/1～2019/3/31.

(3) Hiroshi Yokoi (CI) Understanding brain plasticity on body representations to promote their adaptive functions (Posture/walking rehabilitation using sensory intervention), Scientific Research on Innovative Areas, 2014/4/1～2019/3/31.

(4) Hiroshi Yokoi（CI）Research on control technology of welfare robots that induce body-fusion in the brain, Scientific Research (A) 2014/4/1～2017/3/31.

(5) Hiroshi Yokoi（CI）Development of BMI devices for rebuilding body function that can enhance senses of agency and ownership. Scientific Research (B) 2015/4/1～2018/3/31.

(6) Hiroshi Yokoi (CI) Information gain assistive technologies for the deafblindness using tactile fingerspelling robot. Scientific Research (C) 2014/4/1～2017/3/31.

3.2 Competitive external research funding

(1) Hiroshi Yokoi (PI) Integrated research and development of BMI utilizing Japanese strengths (development of technology for input and output type devices and examination of cranial nerve ethics for the purposes of BMI). Japan Agency for Medical Research and Development 2012-2017.

(2) Hiroshi Yokoi (PI) Development and commercial distribution of 5 digit myoelectric prosthesis for children and infants. Japan Science and Technology Agency（A-STEP) 2012-2016.

(3) Hiroshi Yokoi (PI) Development of adaptive myoelectric prosthetic hand for children. Takahashi Industrial and Economic Research Foundation 2014～2016.

4. Collaboration

4.1 Inside BLSC

(1) Analysis method of fNIRS data（with Tanaka Lab）

4.2 Outside BLSC in UEC

(1) Control method of robot arm（with Kurihara Lab）

4.3 Outside UEC

(1) Development of multi-channel electrical stimulation device for neural rehabilitation, with System Instruments Co. Ltd, private enterprise. 2014/11/1-2017/3/31.

(2) Development of myoelectric prosthesis, with Meltin MMI, private enterprise. 2015/3/1-2017/2/28.

(3) sEMG sensor using stretchable wiring technology, Panasonic Corporation, 2016/11/1～2017/9/30.

5. Outreach activities

5.1 Editor of academic journals

(1)Yinlai Jiang，Journal of Advanced Computational Intelligence and Intelligent Informatics,editorial member, 2016.3～

(2) Yinlai Jiang，Journal of Japan Society for Fuzzy Theory and Intelligent Informatics，2015.9～

5.2 Peer review of academic journals

(1) PLOS ONE, Sensors, Industrial Robot, Mechatronics, Mobile Information Systems, Control Engineering Practice, Neural Networks, Journal of Advanced Computational Intelligence and Intelligent Informatics

5.3 Other outreach activities

(1) Host of the 29th symposium on autonomous distributed system，2017/ 1/30～31

1. Outline of Research and Education

1. 1 Basic Policy in Research and Education

The organs of our body such as locomotive system, cardiorespiratory system and so on consequently produce physical movement as results of their functional activities. In our laboratory, we are studying basic human movement in order to send new findings that can be useful for maintenance of the activities of daily living (ADL) or the coaching of athletes.

We are mainly analyzing human movement mechanically. Specifically we are describing the kinematics of each body segment during physical movement and calculating internal forces such as joint torques by using inverse dynamics method (Figure 1).

Applying the results from these biomechanical analyses, it is possible to develop a new training method for obtaining superior motor skills and to evaluate the degree of aging of basic human movement.
In the education, I hope to bring up a talented person contributing to the society and the affluent life of the individuals based on scientific knowledge and technique. I want students to acquire basic knowledge of engineering and to cultivate practical ability to conduct the researches of biomechanical area. However, I think that it is more important to learn the problem solving procedures acquired through the process of

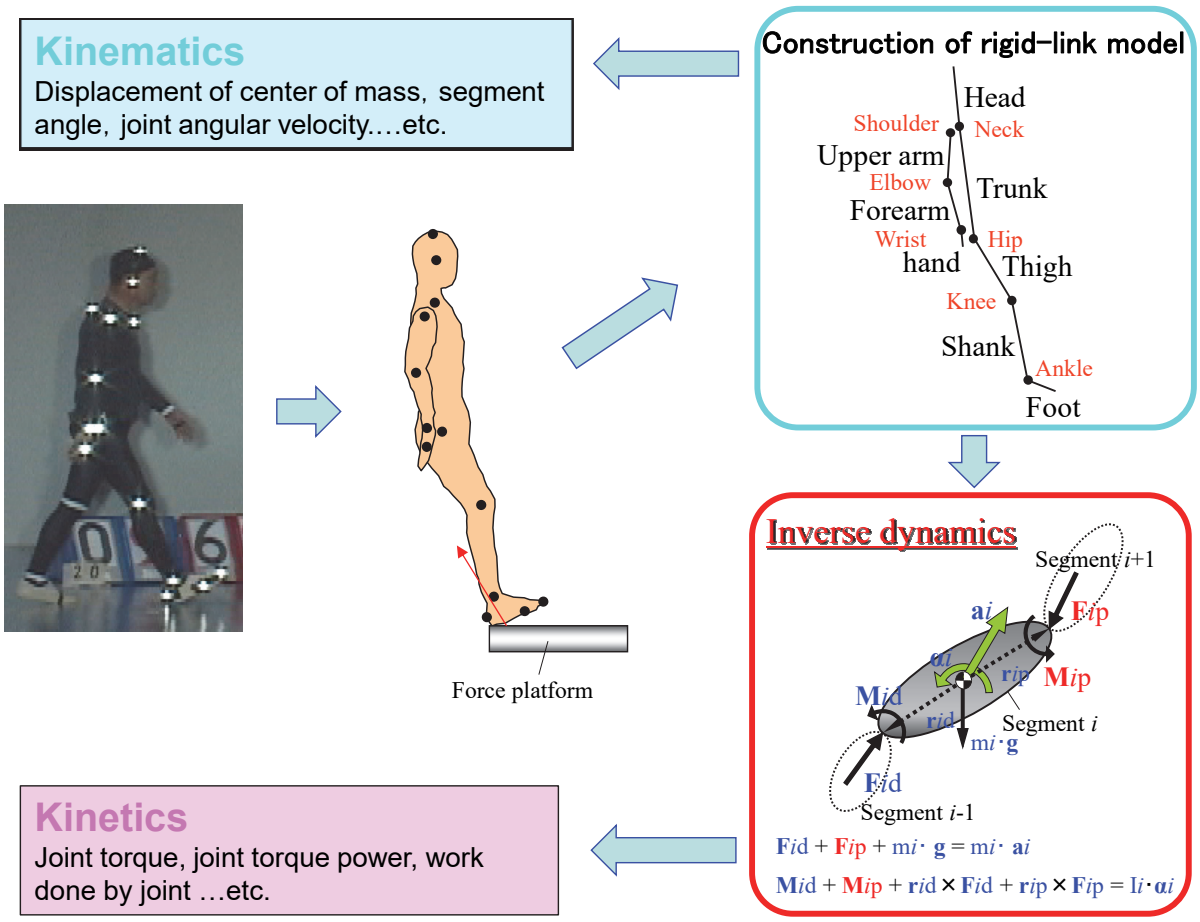


Figure 1 Outline of motion analysis

pursuit of studies, the surge of the thought provided from repetition of deep consideration, and teamwork by the collaboration with the colleagues. Acquiring these would be certainly demanded in the various studies or the various areas other than study.

1.2 Achievements and State of Progress (April, 2016 - March, 2017)

We conducted the research focusing on the analysis of gait motion. The outline and results are as follows.

(1) Effect of physical fitness factors change with aging on the variability of walking motion

In Japan, the declining birthrate and aging population is progressing, and it is an important task to support the elderly so that they can live their lives without needing care. In order to send a healthy old age, it is indispensable that ADL (Activities of Daily Living) can be carried out without trouble. Among the ADLs, walking, which is the basis of various behaviors, plays a crucial role. Previous studies have compared the elderly and young people to know the characteristics of walking motion of the elderly, but in comparison with the study of walking motion itself, a study reporting the variability (stability) of walking motion is small. It is thought that observing the variability of walking motion is effective in evaluating the ease of tripping, the presence of a disorder, bilateral coordination of limbs, and the like. In addition, since it is known that the physical functions supporting ADLs are known to decrease with age, it is thought that a measure for the maintenance and improvement of independent walking can be indicated by clarifying the relationship between the physical fitness factors and the variability of walking motion.

In this study, walking motion, muscle strength, physical fitness, balance ability, and range of joint movement were measured for adult females of a wide range of age from young people to the elderly. The purposes of this study were 1) to clarify the effect of aging on the variability of walking motion and 2) to examine the relationship between the variability of walking motion and the various physical fitness factors. The subjects were 35 healthy females from 19 to 82 years old, divided into three groups according to age. MEXT's new physical fitness test, muscle strength measurement, and ROM measurement were conducted. In addition, walking motion was measured using a motion capture system, and the stride characteristics and three-dimensional kinematics during walking were calculated.

As a result of investigating the relationship between the variability of walking motion and physical functions, significant negative correlation with the dynamic balance ability was observed in the variability of the step length and the step frequency, and the variability of the phase time had a significant negative correlation with the static balance ability. As the static balance ability tended to decrease with age, the variability of the phase time among the stride characteristics seems to be strongly influenced by aging. The variabilities of the joint angles at the heel contact and the toe-off had significant negative correlation with static balance function, ankle plantar flexor strength, and hip flexion ROM. As described above, it is suggested that the deterioration of physical functions due to aging may affect the variabilities of phase time and the lower limb joint angles at the heel contact and the toe-off.

(2) Effect of difference of marker-set on the results of lower limb motion analysis

Motion analysis is performed in various research fields, and roughly divided into two methods,

two-dimensional motion analysis and three-dimensional motion analysis. There are various marker sets in three-dimensional analysis and also there is a method for analyzing in three-dimensional as a simplified. Since there are several methods for marker set and analysis method, differences are occurred in each study. We do not know how much these differences will affect our research results. Nevertheless, comparison of different research results is frequently done. The influence of the differences of such methods on the results is an important factor underlying the validity of the study, so it will be necessary to quantify and evaluate. Moreover, by clarifying the influence due to the difference of the method, it is thought that it is possible to propose a simpler analysis method and experiment method even for the same content measurement. In this study, we analyzed the walking motion of adult males using different methods. The purposes of this study were 1) to quantify the influence of difference of marker set and difference of analysis method on the motion analysis results, 2) to recommend a suitable marker set and analysis method for aim and accuracy desired in a study.

Ten healthy males in their twenties participated as subjects. Sixty-four retroreflective markers were attached to the body of the subjects. Two typical marker sets, plug-in-gait (PiG) marker set and IOR marker set were used for the motion analysis. Subjects were asked to walk at two speeds (normal walk(NW) and fast walk(FW)) on a walkway of about 8 m. Three-dimensional coordinates of markers were measured at 200 Hz by a motion capture system comprising eleven infrared cameras. Local coordinate system for each lower limb segment was defined from each of PiG marker set (3DP) and IOR marker set (3DI). From these local coordinate systems, lower limb joint angles (ankle, knee, and hip) about three axes (extension-flexion, abduction-adduction, and external rotation-internal rotation) were calculated. In addition, similar analysis was carried out using the method of Yuki (1996) using only the marker coordinates of the joint point (3DY). In addition, two-dimensional coordinates in the sagittal plane were extracted from the three-dimensional coordinates of the joint point marker and a two-dimensional motion analysis (2D) was performed. From the comparison of the results by each method, the following conclusions were obtained.

1) Pattern similarity of the joint angle of y axis (anterior-posterior axis) and z axis (longitudinal axis) is low amongst the methods, so it is necessary to pay attention to the measuring method for the joint angles about these axes.
2) The hip joint angle about the x axis (medial-lateral axis) was different in the 2D method from other methods, but the difference amongst the 3D methods was small. Therefore, it can be said that there is no problem in analyzing with the 3DY method (simplified 3D method) in a restricted measuring environment.
3) The knee joint angle about the x axis is different between (3DP, 3DI) and (3DY, 2D). Therefore, measurement by 3DP method and 3DI method, which can be said to be generally high accuracy, is recommended.
4) It can be said that there is no big difference in the ankle joint angle about the x axis amongst any methods.

(3) Effect of components of ground reaction force on the ankle joint torque during walking

In normal walking motion analysis, the lower limb joint torque is calculated using motion capture system (or video image) and force platform measurements. However, there are limitations on the

measurement place and the number of steps in the measurement using these, so a foot pressure sensor may be used as a substitute for the force platform. However, the foot pressure sensor has the convenience of not choosing the measurement location, but since it can measure only the vertical ground reaction force, it has not been used conventionally for inverse dynamics. Therefore, if it is possible to estimate the ankle joint torque component due to the horizontal ground reaction force, it can be considered that it is possible to use the foot pressure sensor for the inverse dynamics analysis. In this study, we aimed to clarify the effect of each component of the ground reaction force on the ankle joint torque during walking and to examine the estimation method of the ankle joint torque component due to the horizontal ground reaction force.

Subjects were 266 healthy adults from 21 to 86 years old. Subjects were asked to walk at four walking speeds (Normal Walk (NW), Slow Walk (SW), Fast Walk (FW), and Maximum-speed Walk (MW)) on a walkway of about 8 m. Retroreflective markers were attached to 7 body landmarks of the right lower limb (toe, head of the 5th metatarsal, heel, ankle joint, knee joint, hip joint, suprasternal), and walking motion was videotaped at 60fps from the right side of subjects. The ground reaction force acting on the right foot of the subject was measured at 200 Hz using a force platform embedded in the walkway.

Based on the two-dimensional inverse dynamics method, the ankle joint torque and the breakdowns in the sagittal plane (term obtained by the horizontal ground reaction force, term obtained by the vertical ground reaction force, terms obtained by the acceleration of the center of mass of the foot, and term obtained by the angular acceleration of the foot) were calculated. In addition, among the breakdowns, a method for estimating the term due to horizontal ground reaction force was examined. As a result, it was shown that using either of the walking speed, ankle joint torque component due to the vertical ground reaction force, step length, and step frequency, the ankle joint torque component due to the horizontal ground reaction force was estimated with an RMS error of about 4%.

1. 3 Future Plan

Based on the accumulated walking motion data, we plan to establish the standard gait motion (standard value) of each age of Japanese adult males and females and to examine the aging degree evaluation method of gait motion based on the standard motion change by aging. We are also developing a system for feeding back the gait motion in real time with the aim of promoting learning of gait motion.

2. Research Achievements

2. 1 Reviewed papers [○: Impact factor greater than 4]

(1) Yokozawa T, Tsujimura R, Kubo Y, Takahashi H, Okada H. (2016) Body segment inertial parameters for Japanese elite athletes in various competitive events. *Japanese Journal of Elite Sports Support* 8: 11-27. (in Japanese)

2.2 Student guidance

(1) Niitsu, T., 2017, Bachelor of Engineering

(2) Matsumoto, T., 2017, Bachelor of Engineering

(3) Sugimoto, T., 2017, Master of Engineering

3. Research funding

3.1 Competitive external research funding

(1) Joint research (with Univ. of Tsukuba), Study on development of a special strength training appliance specialized in Judo, ¥2,727,273

4. Collaboration

4.1 Outside UEC

(1) Okada, H., University of Tsukuba, Study on development of a special strength training appliance specialized in Judo, Fiscal Year 2010-2015

5. Outreach activities

5.1 Paper review of academic journals

(1) Journal of the Society of Biomechanisms

(2) The Japan Journal of Coaching Studies

5.3 Other outreach activities

(1) Participation in administrative agencies as an academic expert

・Chofu Sports Promotion Council, vice-chairperson

(2) Diffuse awareness raising activity at local governments and schools

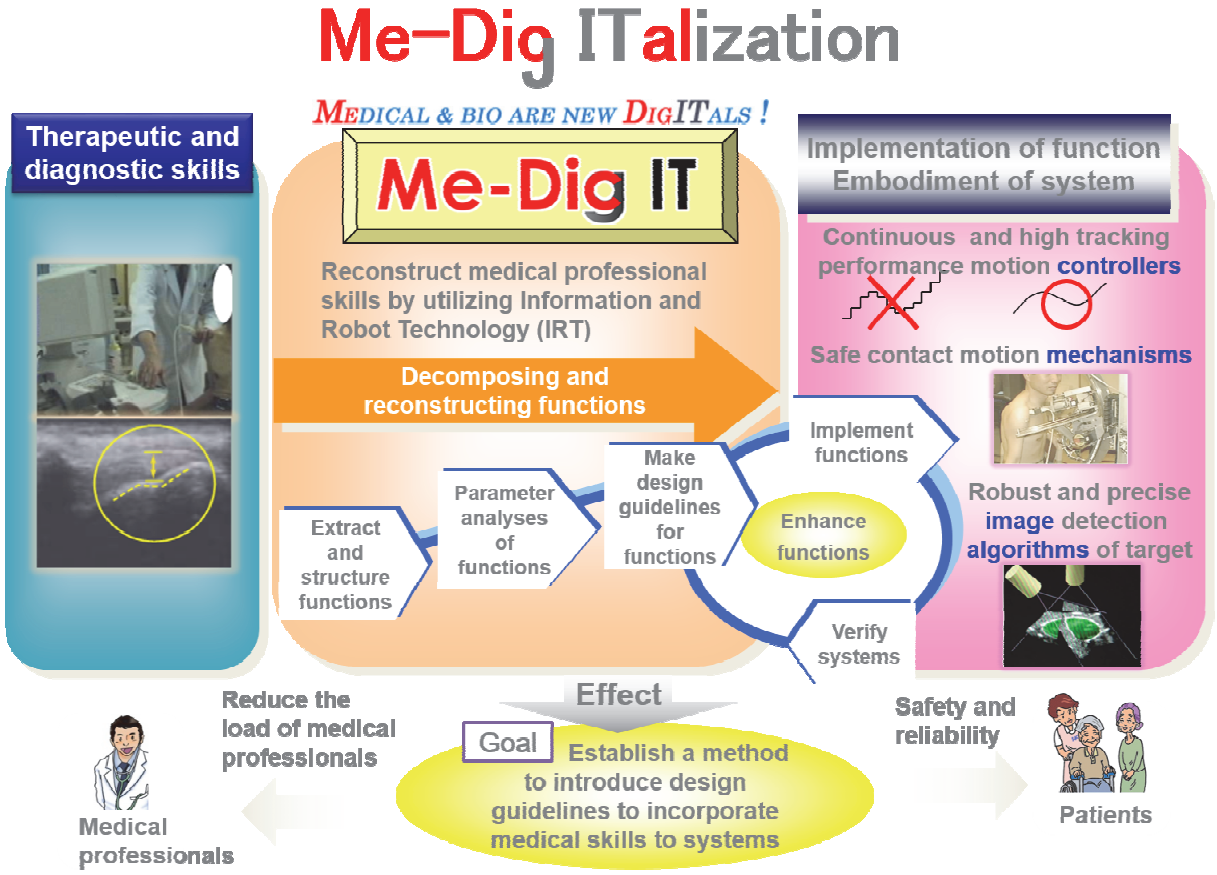
・Japan Association of Athletic Federations Spread Nurturing Committee, member

・Chofu city kids running classroom (4 times. Total 105 kids)

1. Outline of Research and Education

1. 1 Basic Policy in Research and Education

Promote the digitization of medicine (medical diagnosis) by deploying robot technology to medical care. Medical knowledge, expertise and skills closed among some experts are commonly shared by reproducing the doctor's view of the world and medical skills using digital (especially robot) technology and by copying it, Leading to new innovation in medical care. In this laboratory, we will promote the use of ultrasound diagnostic and therapeutic skills as medical targets for medical diagnosis. We collaborate with medical institutions and medical device manufacturers to develop high quality medical devices and train medical students and fusion personnel capable of developing them.



Concept of Medical DigITalization (Me-DigIT)

1.2 Achievements and State of Progress (April, 2016 - March, 2017)

Papers were published / accepted in the first class journals: International topic journal International Journal of Endocrinology (IJE, IF = 2.4), International Journal of Medical Robotics and Computer Assisted Surgery (IJMRCAS, IF = 1.5), Advances in Experimental Medicine and Biology (IF = 2.0). We exhibited at JST Innovation Japan 2016, exhibited 2017 degrees and presented lectures at the new technology briefing (12 out of 400). A paper on the development project of visceral fat area measurement techniques using

ultrasonic waves carried out jointly with Hitachi, Ltd. was published in MEDIX magazine (issued by Hitachi, Ltd.).

1. 3 Future Plan

Promote Medical DigITalization (Me-DigIT) using ultrasound diagnosis / treatment skills as the main target. We collaborate with medical institutions and medical device manufacturers to develop high quality medical devices and train medical students and fusion personnel capable of developing them.

2. Research Achievements

2. 1 Reviewed papers [○: Impact factor greater than 4]

(1) Takeharu asano, Naoto Kubota, Norihiro Koizumi, Kazunori Itani, Tsuyoshi Mitake, Kazuhito Yuhashi, Hongen Liao, Mamoru Mitsuishi, Shigemi Takeishi, Toshiaki Takahashi, Shin Ohnishi, Shiro Sasaki, Ichiro Sakuma and Takashi Kadowaki , "Novel and simple ultrasonographic methods for estimating the abdominal visceral fat area," *International Journal of Endocrinology (IJE)*, Accepted, IF=2.4 Preprint

(2) Tatsuya Fujii, Norihiro Koizumi, Atsushi Kayasuga, Dongjun Lee, Hiroyuki Tsukihara, Hiroyuki Fukuda, Kiyoshi Yoshinaka, Takashi Azuma,Hideyo Miyazaki, Naohiko Sugita, Kazushi Numata, Yukio Honma, Yoichiro Matsumoto, Mamoru Mitsuishi, "Servoing performance enhancement by respiratory organ motion prediction model for non-invasive ultrasound theragnostic system," *Journal of Robotics and Mechatronics (JRM)*, Vol.29, No.2, pp.434-446, DOI: 10.20965/jrm.2017.p0434, 2017.

(3) Joonho Seo, Norihiro Koizumi, Mamoru Mitsuishi, and Naohiko Sugita, "Ultrasound image based visual servoing for moving target ablation by high intensity focused ultrasound," *International Journal of Medical Robotics and Computer Assisted Surgery (IJMRCAS)*, e1793, DOI: 10.1002/rcs.1793, 2016. IF=1.5

(4) Teiichiro Ikeda, Shin Yoshizawa, Norihiro Koizumi, Mamoru Mitsuishi, and Yoichiro Matsumoto," Focused ultrasound and Lithotripsy," *Advances in Experimental Medicine and Biology (ADV EXP MED BIOL)*, Vol.880, pp.113-129, 2016 (DOI: 10.1007/978-3-319-22536-4). IF=2.0

2.2 Book, non-refereed articles and translation

(1) Hirofumi Namba, Motohiro Kawasaki, Tomonari Kato, Toshikazu Tani, Takahiro Ushida, and Norihiro Koizumi Evaluation of the pain and local tenderness in bone metastasis treated with magnetic resonance-guided focused ultrasound surgery (MRgFUS). AIP Conference Proceedings 1821, 160007 (2017); doi: http://dx.doi.org/10.1063/1.4977660.

(2) Dongjun Lee, Norihiro Koizumi, Hiroyuki Tsukihara, Akira Nomiya, Kiyoshi Yoshinaka, Naohiko Sugita, Yukio Homma, Yoichiro Matsumoto, and Mamoru Mitsuishi Construction of kidney phantom model with acoustic shadow by rib bones and respiratory organ motion. AIP Conference Proceedings 1821, 150007 (2017); http://doi.org/10.1063/1.4977651.

2.3 Invited lectures

4 Japanese lectures.

2.4 Media release

(1) Rad Fan Online "The 41st Ultrasonic Doppler and New Technical Studies Conference", 2017.03.31.

2.5 Patent

Japanese Patent Application No. 2017-040348, 2017.3.3

2.6 Award

2 Japanese awards (For students)

2.7 Student guidance

Fumio Eura, FY2016, Bachelor (Eng.)

Tatsuya Genda, FY2016, Bachelor (Eng.)

Ryosuke Kondo, FY2016, Bachelor (Eng.)

Kyouhei Tomita, FY2016, Bachelor (Eng.)

Izumu Hosoi, FY2016, Bachelor (Eng.)

3. Research funding

3.1 Grant-in-aid for scientific research

(1) FY2017 - FY2020 Grant-in-Aid for Scientific Research (17H03200) Grant-in-Aid for Scientific Research (B).

(2) FY2014 - 2016 Grant-in-Aid for Scientific Research of the Ministry of Education, Culture, Sports, Science and Technology (26289061) Basic Research (B).

(3) Grant-in-Aid for Scientific Research, Ministry of Education, Culture, Sports, Science and Technology, FY2015 - FY2016 Grant-in-Aid for Scientific Research (15K15557) Challenging sprouts research.

3.2. Competitive external research funding

(1) Ministry of Education, Culture, Sports, Science and Technology JST Research Outcomes Development Project Matching Planner Program

(2) Saitama prefecture new technology and Product development subsidy

4. Collaboration

None

5. Outreach activities

(1) Norihiro Koizumi, Medical robotics: Technological and digital transfer of medical skills. Gunma-prefectural Kiryu High School, Gunma, Dec. 7, 2016.

1. Outline of Research and Education

1. 1 Basic Policy in Research and Education

Due to the most competitive advantage in allowing users fully unconstrained, noncontact bio-measurement technology will play a vital role in future clinical practice. Guanghao SUN Laboratory focus on developing novel medical devices based on noncontact bio-measurement technology, such as, infection screening system, home healthcare monitoring system, and etc.

1.2 Achievements and State of Progress (April, 2016 - March, 2017)

To promote the widespread use of infection screening system, we have been working on systems with minimum hardware requirements to achieve a system that is more suitable for real world settings. The most reliable solution is to enhance the functionality of the conventional infrared thermography systems that are already installed at international airports. By incorporating the latest advances in image processing techniques, these infrared thermography systems can acquire thermal and visible images together by integrating visible and thermal cameras. In this study, we used high image and temperature resolution infrared thermography that combines visible and thermal images to acquire multiple vital sign measurements from facial images using remote sensing. The benefit of this approach is that it only requires a CMOS camera that is equipped with IRT rather than a large-scale system. As shown in Figure 1, we simultaneously measured peoples' respiration rates by monitoring temperature changes around the nasal areas, and facial skin temperatures from thermal images. Facial blood circulation causes tiny color changes in visible facial images that enable the determination of heart rates. A logistic regression discriminant function predicted the likelihood of infection within 10 s, based on the measured vital signs.

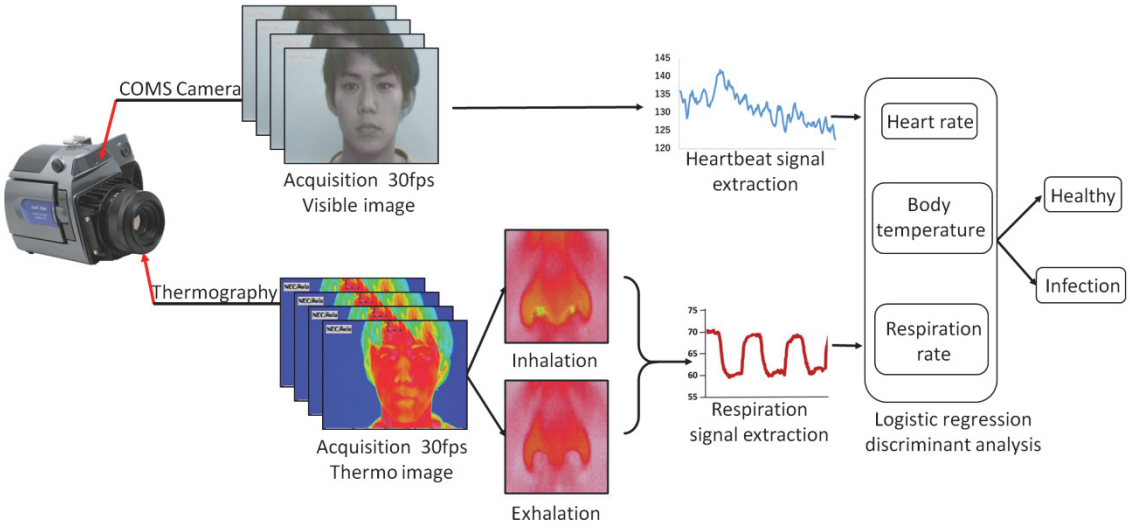


Figure 1. Schematic representation of the visible and thermal image processing method that remotely senses multiple vital signs and the multiple logistic regression function that predicts the possibility of infection.

2. Research Achievements

2. 1 Reviewed papers [○: Impact factor greater than 4]

(1) Guanghao Sun, Yosuke Nakayama, Sumiyakhand Dagdanpurev, Shigeto Abe, Hidekazu Nishimura, Tetsuo Kirimoto, Takemi Matsui Remote sensing of multiple vital signs using a CMOS camera-equipped infrared thermography system and its clinical application in rapidly screening patients with suspected infectious diseases. *International Journal of Infectious Diseases*, 55, 113-117, 2017.

(2) Guanghao Sun, Toshikazu Shinba, Tetsuo Kirimoto, and Takemi Matsui An Objective Screening Method for Major Depressive Disorder Using Logistic Regression Analysis of Heart Rate Variability Data Obtained in a Mental Task Paradigm. *Frontiers in Psychiatry*, 2016.

(3) Enrique Dorronzoro Zubiete, Keigo Nakahata, Nevrez Imamoglu, Masashi Sekine, Guanghao Sun, Isabel María Gómez and Wenwei Yu Evaluation of a home bio-monitoring autonomous mobile robot. *Computational Intelligence and Neuroscience*, 2016.

(4) Guanghao Sun, Masahiko Akanuma, Takemi Matsui Clinical Evaluation of the Newly Developed Infectious Disease/Fever Screening Radar System Using the Neural Network and Fuzzy Grouping Method for Travellers with Suspected Infectious Diseases at Narita International Airport Clinic. *Journal of Infection*, 72(1), 121-123, 2016.

(5) Yu Yao, Guanghao Sun, Takemi Matsui, Yukiya Hakozaki, Stefan van Waasen, Michael Schiek Multiple Vital-sign Based Infection Screening Outperforms Thermography Independent of the Classification Algorithm. *IEEE Transactions on Biomedical Engineering*, 63(5), 1025-1033, 2016.

Conference proceedings paper

(1) Xiaofeng Yang, Guanghao Sun, Koichiro Ishibashi Non-Contact Acquisition of Respiration and Heart Rates Using Doppler Radar with Time Domain Peak-Detection Algorithm. *The 39th Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, 2017, Jeju Island, Korea.

(2) Mai Kobayashi, Guanghao Sun, Toshikazu Shinba, Takemi Matsui, Tetsuo Kirimoto Simple and Objective Screening of Major Depressive Disorder by Heart Rate Variability Analysis During Paced Respiration and Mental Task Conditions. *The 39th Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, 2017, Jeju Island, Korea.

(3) Guanghao Sun, Wenwei Yu Development of an EMG-based Human-Machine Interface on Open-source Linux Platform for Evaluating the Motor Skill Acquisition Process. *The 16th International Conference on Biomedical Engineering*, 2016, Singapore.

(4) Guanghao Sun, Yu Yao, Sumiyakhand Dagdanpurev, Satoshi Suzuki, Takemi Matsui, Tetsuo Kirimoto A Comparative Study between Piezoelectric Pressure Sensor and Doppler Radar for Noncontact Monitoring of Respiration Rate. *The 16th International Conference on Biomedical*

Engineering, 2016, Singapore.

(5) Takemi Matsui, Guanghao Sun, Bazarragchaa Ts., Sumiyakhand D., Yukiya Hakozaki, Lodoiravsal Ch., Buyanjargal Ya., Odmaa E., Myagmarjav Z., Suvdmaa N., Batsukh B. The rapid screening of patients with suspected infection in Mongolia using infection screening system with a compact radar, a thermopile array and a pulse photo-sensor. *International Scientific Conference on Tackling Infectious Diseases: Information for Action*, 2016, Ulaanbaatar, Mongolia.

2.2 Book, non-refereed articles and translation

(1) 小型マイクロ波レーダーによる心拍、呼吸の計測技術 第2章第2節 : 生体情報センシングとヘルスケアへの最新応用 ～ウェアラブル、非侵襲・非接触計測、連続モニタリング～, 2017.

(2) Guanghao Sun, Takemi Matsui, Tetsuo Kirimoto, Yu Yao, Shigeto Abe Applications of Infrared Thermography for Noncontact and Noninvasive Mass Screening of Febrile International Travelers at Airport Quarantine Stations. Chapter: Application of Infrared to Biomedical Sciences, 347-358, Springer, 2017.

2.3 Media release

新聞　日刊工業新聞　感染症、AIで即時特定　2017/02/23

2.4 Student guidance

(1) Mai Kobayashi (Bachelor)

3. Research funding

3.1 Grant-in-aid for scientific research

(1). 若手研究(B) :大規模な生体情報データ計測に基づくリアルタイム感染症サーベイランスシステムの開発

(2). 基盤研究(B)一般:マイクロ波を用いた非接触による血圧変動推定方法の開発

(3). 基盤研究(C)一般:ニューラルネットワークを用いた完全非接触-感染症・熱中症スクリーニングシステム

4. Collaboration

None

5. Outreach activities

5.1 Editor of academic journals

(1) Journal of Sensors

5.2 Paper review of academic journals

(1) Measurement

(2) Frontiers in Bioengineering and Biotechnology

(3) Journal of the Royal Society Interface

(4) Informatics in Medicine Unlocked

(5) Computers in Biology and Medicine

Yoshiki KASHIMORI Laboratory

1. Outline of Research and Education

1. 1 Basic Policy in Research and Education

Research

We study the neural mechanisms of information processing in sensory systems such as visual, auditory, gustatory, and electrosensory systems. Our approach is based on modeling and simulation studies. In our study, we adopt two viewpoints of the brain systems, as shown in Fig. 1. One is a viewpoint of a system, providing the idea that the brain is a complex system consisting of feedforward and feedback flows of information. Another is a viewpoint of dynamic system, providing the intriguing idea that dynamic properties of neuronal ensembles have crucial roles in sensory coding and memory formation. With the two viewpoints, we are working on modeling studies on the neural mechanisms of sensory perception and recognition.

Education

Under my mentorship, 2 graduate students took master's degrees in 2016. I would like to continue to guide graduate school students who can play an active part in the research field of computational neuroscience.

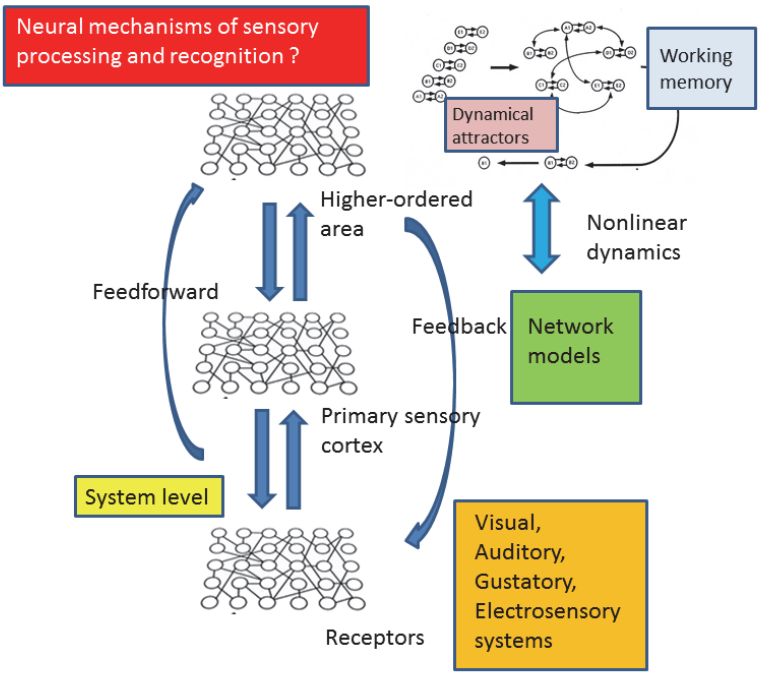


Fig.1 Two viewpoints in our work

1.2 Achievements and State of Progress (April, 2016 - March, 2017)

We studied the neural mechanisms of four types of sensory systems. A first research is on the best frequency (BF) shifts in bat's auditory system. Experimental studies have demonstrated that in the mustached bat, auditory neurons have a BF shifting away from a stimulated frequency, or centrifugal BF shift. To explore address the neural mechanism of the centrifugal BF shift, we developed a neural model of the bat's auditory system. Using our model, we showed the centrifugal BF shifts (Fig. 2) and found the receptive field properties of feedback signals from the auditory cortex to the inferior colliculus, necessary for the centrifugal BF shift. Second is the research on taste perception. Taste perception is significantly affected by other sensory modalities such as vision, smell, and somatosensation. Such taste sensation elicited by integrating gustatory and other sensory information is referred to as flavor. We developed network models of primary gustatory cortex (GC) and orbitofrontal cortex (OFC), and presented the neural mechanism of how flavor emerges from the interaction between GC and OFC (Fig. 3). Third is the research on top-down influence on V1 responses in perceptual learning. Experimental studies have shown that V1 responses are modulated depending on task contexts. This suggests that early visual areas such as V1 could be involved in visual recognition, via top-down signals from higher visual areas. To elucidate the neural mechanism underlying the modulations of V1 responses, we developed a neural model that consists of V1 network and a higher area, and explored the neural mechanism of the top-down influence. Forth is the research on GPGPU calculation of large sizes of neural systems. This research is a preliminary work for studying the neural mechanism of electrosensory processing of a weakly electric fish. We developed a GPGPU-calculation system, and evaluated the computation time and accuracy for simulations of neuronal populations constructed with various neuron models. We found that CUDA calculation was an effective method for calculating large systems, compared with Open-MP method.

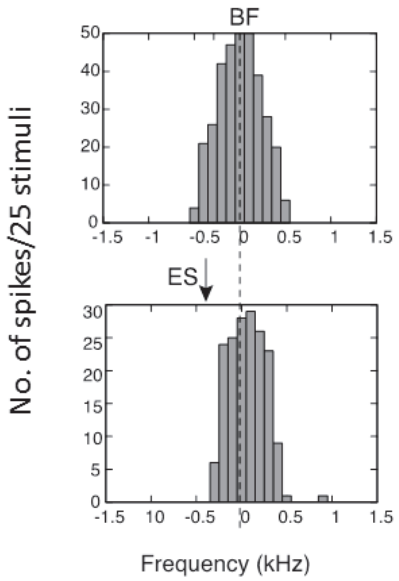


Fig.2 Centrifugal BF shift in the tuning curves of IC neurons.

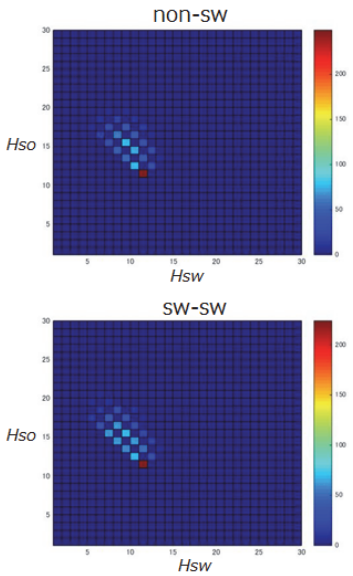


Fig. 3 Dynamic states of GC network in the space of Hamming distance.

1. 3 Future Plan

Brain rhythms have crucial roles in gating of sensory information and enhancement of neuronal responses to stimulus features relevant to behaviors. Interareal interactions, mediated by slower oscillations such as alpha and beta rhythms, have a pivotal role in gating of sensory information relevant to behaviors. In contrast, intracortical interactions, mediated by faster oscillations such as gamma rhythms, are involved in representation of sensory information. However, how the brain rhythms contribute to sensory processing and recognition is poorly understood. To address this issue, we study top-down influence on V1 responses in perceptual learning. The top-down influence may be mediated by the brain rhythms. We will explore the neural mechanism by which task-relevant information is gated by top-down signals and multiple brain oscillations. We also focus on taste perception in taste preference and avoidance behaviors. orbitofrontal cortex (OFC) is known to contribute to value evaluation and decision making, and is closely involved in behavior evoked by taste perception. Moreover, amygdala plays a pivotal role in associative learning of multisensory information. As a next step towards understanding the neural mechanism of taste recognition, we will study how taste preference and avoidance behaviors emerge from the interaction between gustatory, olfactory cortices, OFC, and amygdala. Furthermore, we have a project on the study in electrosensory systems (Grant-in-aid for scientific research). Electrosensory systems have simpler circuit structures compared with those in visual and auditory systems, and the sensory coding of electrosensory systems is well-defined. Therefore, they provide an ideal system for studying sensory processing mechanism by means of a large-scale parallel computing method such as GPGPU computing. We developed a GPGPU-calculation system and showed the usefulness of GPGPU method for the calculation in neural populations constructed with various neuron models. As a next step, we will study the geometry of electric field around a fish and sensory processing mechanism of central nervous systems.

2. Research Achievements

2. 1 Reviewed papers [○: Impact factor greater than 4]

(1) K. Kamiyama, K. Fujita, Y. Kashimori (2016). A neural mechanism of dynamic gating of task-relevant information by top-down influence in primary visual cortex. BioSystems, 150:138-148.

(2) Takahiro Shimemura, Kazuhisa Fujita, Yoshiki Kashimori (2016). A neural mechanism of taste perception modulated by odor information. Chemical Senses. 41:579-589

(3) Kazuhisa Fujita and Yoshiki Kashimori (2016). Neural mechanism of corticofugal modulation of tuning property in frequency domain of bat's auditory system. Neural Processing Letters, 43:537-551

(4) Kazuhisa Fujita and Yoshiki Kashimori (2016). GPU-accelerated simulation of an electric stimulus and neural activities in electrolocation. Lecture Notes in Computer Science, 9950, 213-220

(5) Yuki Abe, Kazuhisa Fujita, Yoshiki Kashimori (2016). A neural model for retaining object information required in a categorization task. Lecture Notes in Computer Science, 9948, 391-398

2.2 Student guidance

(1) Bachelors

Reira Antake
Eiki Hayashi
Miyuki Asanuma

(2) Master's degree:
Yuuki Abe
Koya Onodera

3. Research funding

3.1 Grant-in-aid for scientific research

(1) Yoshiki Kashimori (Principal investigator). A theoretical study aimed at the system-level understanding of information processing mechanism of electrosensory systems. Scientific research (C), 2015-2017, 4,420,000 yen

4. Collaboration

4.1 Outside UEC

(1) Kazuhisa Fujita, Tsuyama National College of Technology (see subsection 3.1)

5. Outreach activities

5.1 Editor of academic journals

(1) Cognitive Neurodynamics 2006~

5.2 Paper review of academic journals

(1) Cognitive Neurodynamics, May. 2016
(2) Cognitive Neurodynamics, June. 2016

1. Outline of Research and Education

1. 1 Basic Policy in Research and Education

The basic policy of this laboratory is to provide students with opportunity to learn how to solve problems in the contemporary society through the education of theoretical research in neurosciences. For research, towards the understanding of information representation and processing in the visual and auditory cortices, brain mechanisms underlying working memory, attention and consciousness, we are carrying out theoretical research on (1) the self-organization of visual cortical maps during development, (2) neural dynamics in auditory continuity illusion, (3) zero-lag remote synchronization, (4) tripartite synapses under neuron-glia interaction and (5) the establishment of functional near infrared spectroscopy measurement and analysis methods for future research on human working memory. Figure 1 illustrates major targets of our theoretical studies.

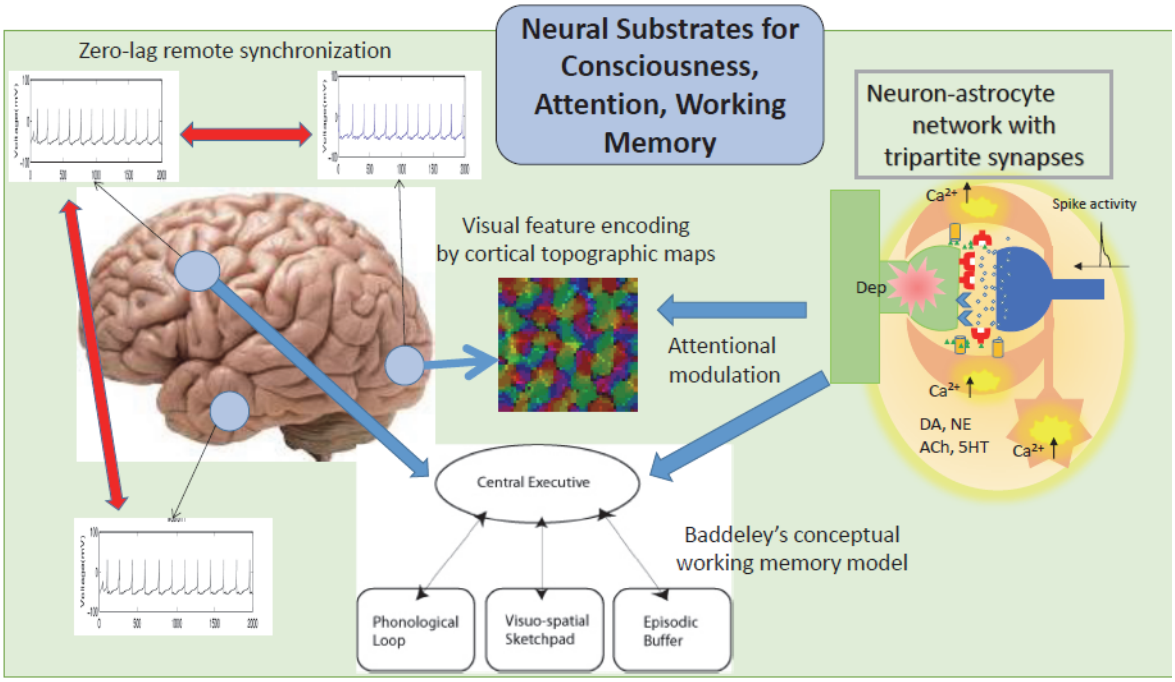


Figure 1 Overview of our laboratory's research

1.2 Achievements and State of Progress (April, 2016 - March, 2017)

(1) Elaboration of our model for the self-organization of visual cortical maps

Based on the elaboration of our model for the activity-dependent self-organization of geniculo-cortical afferent inputs, we derived the free energy Fokker-Planck equation that describes receptive field formation of orientation and direction selective simple cells in the primary visual cortex. This provides a solid basis of mathematical explanation of not only simple cell receptive fields but also visual cortical feature representations formed during development. We also elaborated a spin-glass theory that can describe the transition between the orderly map representation and salt-and-pepper-like random representation of preferred orientations. Using this theory, we can explain the reason why the number of

orientation-unselective neurons increased markedly in addition to the emergence of salt-and-pepper-like random orientation representation in the rodent visual cortex.

(2) Neural dynamics in auditory continuity illusion

The auditory continuity illusion is a well-known phenomenon: When a continuous melody is partially replaced with periodic silent periods (gaps), we feel the melody to be unpleasantly fragmented. However, when the periodic gaps are further replaced with noise, we hear the continuous melody as a background of the periodic noise. That is, the insertion of noise recovers the sensation of continuity in the original melody although it is still fragmented. To elucidate the neural mechanisms underlying this illusion theoretically, we examined dynamic activities of a neural network in the primary auditory cortex (AI) composed of spiking neuron models. Each neuron in the model received self-organized inputs from the MGB and excitatory and inhibitory lateral inputs from other AI neurons. The following three types of stimuli were presented: (a) continuous 800-Hz pure tone, (b) 800-Hz pure tone periodically fragmented with gaps, and (c) 800-Hz pure tone with a periodic insertion of the band-pass noise into the gaps in (b). For stimulus (b), the spike responses of 800-Hz pure tone selective neurons were observed only during the presentation of the pure tone but not generated in the gaps. On the other hand, the same neurons elicited spikes continually in response to stimulus (c), and temporal patterns of firing were similar to those for stimulus (a). Furthermore, we carried out dynamic simulations without lateral interactions in the model AI in response to the three types of stimuli. Firing rate of model AI neurons in the noise periods was six-fold higher than that in the melody periods for stimulus (c), whereas the level of activation was almost the same for the other two types of stimuli irrespective of the presence or absence of the lateral interactions. These results indicate that the lateral interactions are involved in the gain control of neuronal responses in AI. Next, we examined the similarity of temporal firing patterns of model neurons in response to stimulus (c) between those to stimulus (a), changing the noise intensity. The dependence of the similarity on the noise intensity showed an excellent agreement with a human psychometric function representing the dependence of the sensation of continuity on the noise intensity. Taken together, it is suggested that the topographic map and lateral interactions in AI contribute to the generation of auditory continuity illusion.

(3) Elucidation of the mechanisms underlying zero-lag remote synchronization

Synchronous firing of neurons has received much attention in relation to the generation of brain wave rhythms, and information processing at various aspects in the neuronal systems, such as feature binding, cognition, memory processes, odor perception, etc. Synchronization with zero phase lag has been observed between remote areas in human brains despite that time from

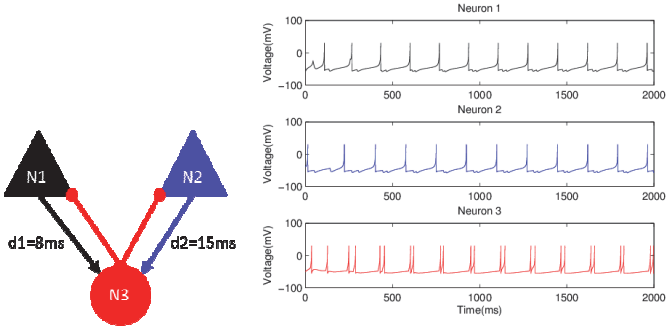


Figure 2 Zero-lag synchronization among three neurons

spike generation at a presynaptic neuron to the change of membrane potential at a postsynaptic neuron after spike conduction along the axon can amount to several tens of milliseconds. We started a theoretical study to elucidate mechanisms of how neurons between remote regions can form neural populations that fire at the same timing despite non-negligible temporal delays. We obtained simulation results that phenomenologically reproduced such zero-lag synchronization in the two excitatory and 1 inhibitory neurons whose reciprocal connections had different conduction delays (Fig. 2).

(4) Mathematical modeling of tripartite synapses

We built a mathematical model of neuron-glia interaction, which gives a possible interpretation that tripartite synapses enhance signal-to-noise ratio in neuronal information transmission mediated by the elevation of intracellular calcium concentration in astrocytes under the secretion of neuromodulator noradrenaline. We used the Hodgkin-Huxley model as a neuron model. We added models of the exocytosis of glutamate containing vesicles from the presynaptic neuron and of ATP and D-serine containing vesicles from astrocytes surrounding the synaptic junction, which are all dependent on the intracellular calcium concentration. We also took into account metabotropic glutamate receptors expressed on the cell surface of astrocytes, which generate IP3 (inositol trisphosphate) to bind to specific receptors on the endoplasmic reticulum (ER) activating the Ca^{2+}-permeable channel and thus causing the release of stored Ca^{2+} to the cytoplasm. Carrying out computer simulations based on this set of models, we observed the enhanced signal-to-noise ratio in the transmission at tripartite synapses. When we applied the same set of models to the activation of an orientation selective neuron in the primary visual cortex, orientation tuning became sharper under the volume transmission of noradrenaline, due to the stronger activation of postsynaptic NMDAR by increased release of D-serine and suppression of the exocytosis of glutamate-containing vesicles at presynaptic sites by increased release of ATP from astrocytes (Fig. 3).

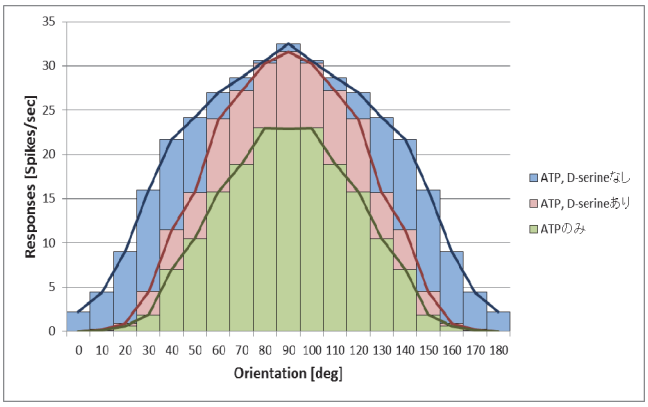


Figure 3 Sharpening of orientation tuning under the effect of noradrenaline via tripartite synapses

(5) Establishment of functional near-infrared spectroscopy for brain activity measurements

It is still likely that in the data analysis of functional near-infrared spectroscopy (fNIRS) for human brain activity measurement reliable methods have not yet been established. So we are trying to develop a suite in Matlab environment for the processing of raw data obtained from fNIRS measurement to eliminate periodic artifacts arising from oscillatory systemic processes and motion artifacts. Figure 4 shows a cross-correlogram which displays a pseudo-color map of the correlation in measured signals among different

channels. The channels identified by the numbers are reordered and grouped by how correlated they are with each other using the k-nearest neighbor algorithm.

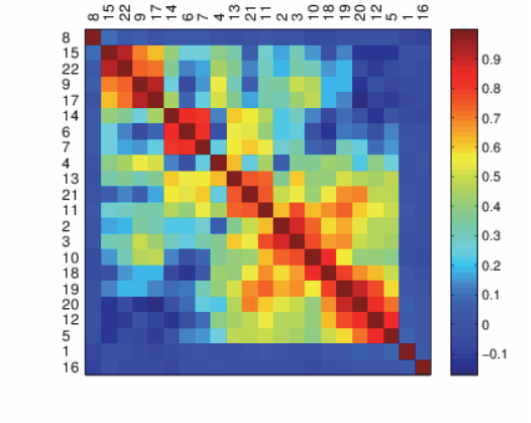


Figure 4 Cross-correlogram of NIRS signals among different channels

1. 3 Future Plan

We will continue to elaborate the mathematical theory of the activity-dependent self-organization of afferent inputs, and consequently the formation of receptive field profiles and feature maps in the visual cortex, because the theory provides a firm basis for a mathematical study of neural network dynamics. Also we will extend a mathematical model of tripartite synapses, taking into account glutamate release as one of gliotransmitters. We have a hypothesis that glutamate released from astrocytes enhances dendritic excitability mediated by extrasynaptic NMDARs. Integrating the self-organized visual cortical functional maps and neuronal information processing through tripartite synapses, we will try to figure out the mechanisms of the expansion of a neuronal responsive range of stimulus spatial frequencies in the primary visual cortex of awake animals. Furthermore, we will construct a mathematical model of neuronal networks in the visual cortex taking into account complex cells, chandelier cells and double bouquet cells as well as simple cells, and carry out computer simulations to understand neural mechanisms of dynamic sparse coding. Also, we will investigate a simple network composed of a small number of spiking neuron models to elucidate how the zero-lag synchronization is generated among remote neuronal clusters. Continuing the effort to develop the fNIRS signal analysis method, we will attempt to use fNIRS measurement to obtain a better understanding of the mechanisms of human working memory functions.

2. Research Achievements

2. 1 Book, non-refereed articles and translation

(1) Tanaka S. Topology inherent in the visual cortical information representation. *Journal of Japanese Neural Network Society* 23 (2): 60-67, 2016.

(2) Tanaka S, Miyashita M. Theory of the formation of columnar organization. *Clinical Neuroscience* 34 (August): 880-884, 2016.

(3) Ishikawa S, Miyashita M, Horikawa J, Tanaka S. Functional roles of orientation representation for visual information preservation. 39th Annual meeting of Japanese Society for Neuroscience（Yokohama） 7.21, 2016.

(4) Miyashita M, Tanaka S. Theoretical study of regularity in orientation representation and preservation of visual information. 20th Visual Science Forum（Osaka） 8.26, 2016.

(5) Endo T, Miyashita M, Horikawa J, Tanaka S. A computational study of neural dynamics in the auditory cortex for the generation of auditory continuity illusion. 3rd Annual meeting of Bioacoustic Society

（Irago）12.10-11, 2016.

(6) Tanaka S. Ten years after receiving research grant. *Public Relations Magazine of The Naito Foundation* 99（March）2017.

2.2 Student guidance

(1) Masaki Hayashi，FY2016, Bachelor degree（Engineering）

(2) Shuhei Okawa，FY2016，Bachelor student

3. Research funding

3.1 Grant-in-aid for scientific research

(1) Shigeru Tanaka （PI）fMRI study for the understanding of sound symbolism and common sense. Challenging Exploratory Research, 2014-2016, 3,770,000 yen.

(2) Shigeru Tanaka (CI) Understanding of complementary motor learning with multiple plasticity sites distributed in the cerebellum. Scientific Research (C), 2014-2016, 5,070,000 yen.

(3) Shigeru Tanaka（CI）A study of mathematical modeling of auditory cortical information representation: Auditory continuity illusion. Scientific Research (C), 2016-2018, 5,200,000 yen.

4. Collaboration

4.1 Inside BLSC

(1) Tadashi Yamazaki, Theoretical study of the cerebellum, 2013/04-

(2) Hiroshi Yokoi, Yinlai Jiang, Establishment of basic methods for fNIRS measurement and analysis, 2016/4-

(3) Vasileios Tserolas, Mathematical study of zero-lag remote synchronization, 2015/4- , Establishment of basic methods for fNIRS measurement and analysis, 2016/4-

4.2 Outside BLSC

(1) Masaki Hisano, fMRI measurement for understanding of the mechanisms of sound symbolism, 2014/4-

4.3 Outside UEC

(1) Masanobu Miyashita (Numazu National College of Technology) Neural dynamics in the auditory continuity illusion 2015/4-, Self-organization of visual cortical receptive fields and related maps, 2013/4-

(2) Tomoki Fukai (RIKEN Brain Science Institute) fMRI measurement for understanding of the mechanisms of sound symbolism, 2014/4-

5. Outreach activities

5.1 Editor of academic journals

(1) ISRN Neuroscience, 2012-present

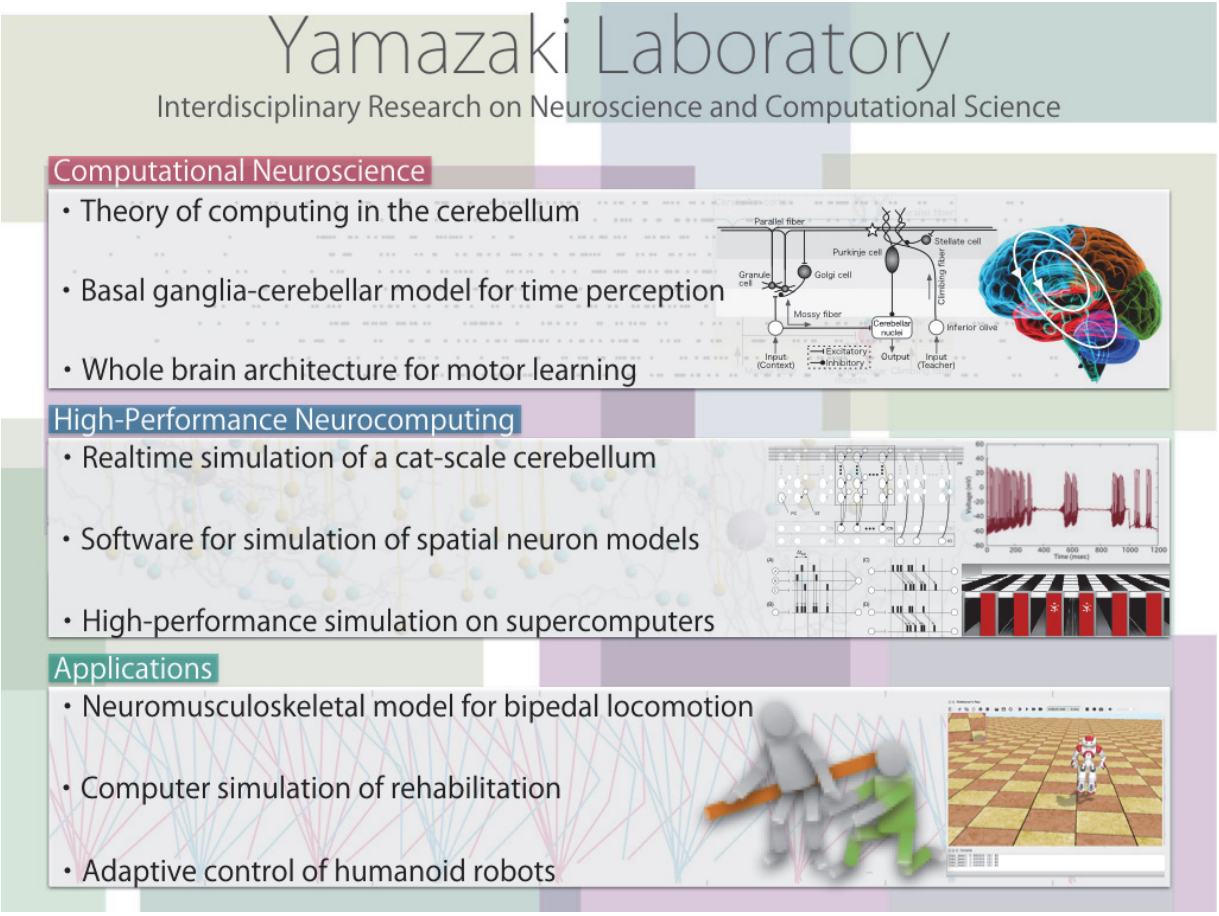
(2) Science Postprint, 2013-present

5.2 Paper review of academic journals

(1) Neuroscience 2016/8

Tadashi YAMAZAKI Laboratory

1. Outline of Research and Education



1. 1 Basic Policy in Research and Education

We are conducting research in the interdisciplinary area between neuroscience and high-performance computing. Specifically, we are engaged with theoretical modeling of neural networks of the brain and large-scale computer simulation on supercomputers. Our final goal is to understand the neural mechanisms of human-specific higher-order functions such as bipedal locomotion and language. Currently as an initiative project, we are working on the following projects: (1) building a whole-brain-scale functional model for motor learning and control, (2) development of high-performance neurocomputing methods for accelerators such as graphics processing units (GPUs), and (3) applications of an artificial brain for controlling musculoskeletal models and humanoid robots, and for rehabilitation.

Students in the lab participate to one of the above projects. In other words, they take part of a world-class advanced research project from the beginning as an on-the-job training to gain practical experience on research. We stress the importance of publishing results to students. Master course students must present their results in international conferences at least once. We also strongly encourage students to publish a research paper. To achieve these, we have generous research funds and provide the best environment and equipment for students.

We also have a research scientist and a technical staff in the lab who are leading our science

aggressively and helping management.

1.2 Achievements and State of Progress (April, 2016 - March, 2017)

We have achieved the following:

(1) In our NEDO project, we built a computational model of cerebro-basal ganglia loop for motor leaning, representation and generation. We studied the network dynamics empirically, and demonstrated the ability using a small humanoid robot. We also built a unified model of a basal ganglia model and a cerebellar model for representation of time, and studied the dynamics analytically and empirically. We submitted a paper on robust representation of time by feedback signals to an international journal. We successfully passed the stage gate of NEDO project.

(2) We achieved realtime simulation of a spiking network model of the cerebellum composed of 1 billion neurons on Shoubu, an energy-efficient supercomputer installed at RIKEN ACCC. We implemented synaptic plasticity so that the model can perform online learning. We submitted a paper to an international journal. Our project was accepted for MEXT Post-K Supercomputing Project.

(3) We built a brain-musculoskeletal model composed of a cerebellar model and a bipedal locomotion model for stable walk against proprioceptive feedback delays. Specifically, we assumed that the cerebellar model compensates the feedback delay, and replaced a feedback control with a feedforward control. We submitted a paper on the model to a Japanese journal. We also started to acquire parameters for robust locomotion of a small humanoid robot using genetic algorithms.

1. 3 Future Plan

(1) We continue our NEDO project. In particular, to obtain a large amount of human motion data, we develop a method to extract human body motion data from movies on YouTube. We also develop a spiking neuron version of our basal ganglia model that can perform reinforcement learning.

(2) We plan to build a human-scale cerebellar model composed of 100 billion neurons on the next-generation PEZY-SC chips. We also continue MEXT Post-K Supercomputing Project.

(3) We realize locomotion control of a humanoid robot using our cerebellar model. We also conduct computer simulation of abnormal walking by cerebellar patients.

2. Research Achievements

2. 1 Reviewed papers [○: Impact factor greater than 4]

(1) Tsukasa Tsuyuki, Yuki Yamamoto, Tadashi Yamazaki(2016), Efficient numerical simulation of neuron models with spatial structure on graphics processing units, A. Hirose et al. (Eds.), ICONIP 2016, Part IV, LNCS 9950(279–285), DOI: 10.1007/978-3-319-46681-1 34

(2) Ohki Katakura, Tadashi Yamazaki(2016), Computational model of the cerebellum and the basal ganglia for interval timing learning, A. Hirose et al. (Eds.), ICONIP 2016, Part IV, LNCS 9950(244–251),

DOI: 10.1007/978-3-319-46681-1 30

2.2 Book, non-refereed articles and translation

(1) Tadashi Yamazaki. Cerebellar clocks. Annual Review Shinkei 2016. Chugai Igakusha. 1-6, 2016. (Japanese article)

(2) Tadashi Yamazaki, Junichiro Makino, Toshikazu Ebisuzaki. Perceptron and cerebellum. Rinsho Shinkeigaku 34(8):889‐891, 2016 (Japanese article).

2.3 Invited lectures

(1) Tadashi Yamazaki, Toward building an artificial cerebellum, Advances in Neuroinformatics 2016, RIKEN, 2016/5/28-29

(2) Tadashi Yamazaki, A cat-scale artificial cerebellum on Shoubu (In Japanese), RIKEN Symposium "Supercomputer HOKUSAI and Shoubu, advances in computational science", RIKEN, 2016/6/8

(3) Tadashi Yamazaki, Cat-scale artificial cerebellum on an energy-efficient supercomputer Shoubu, Workshop on Brain-inspired Hardware, The Artificial Intelligence Research Center, 2017/3/30

2.4 Media release

(1) Nikkei technology online, Reproducing a cat cerebellum on a supercomputer (In Japanese), 2016/6/13
(2) My Navi News, A cat cerebellum on supercomputer Shoubu (In Japanese), 2016/6/20
(3) UEC:Report, Can a Next-generation Supercomputer Reveal How the Brain Works? , 2016/7/6

2.5 Award

(1) Toshiki Kusano, Hiroki Kurashige, and 5 more persons. Research Award, Japanese Neurol Network Society, 2016/10/19

2.6 Student guidance

(1) Ohki Katakura, 2014, Master (Engineering)
(2) Daisuke Ichimura, 2014, Master (Engineering), now in Doctor course
(3) Tsukasa Tsuyuki, 2015, Bachelor (Engineering), now in Master course
(4) Wataru Furusho, 2016, Bachelor (Engineering), now in Master course

3. Research funding

3.1 Grant-in-aid for scientific research

(1) Tadashi Yamazaki (PI), Study on Synergistic Motor Control Mechanisms of Distributed Plasticity in the Cerebellum, Grant-in-Aid for Scientific Research (C), 2014/4/1-2017/3/3

3.2. Competitive external research funding

(1) Tadashi Yamazaki (PI), R&D of Artificial Motor Cortices, NEDO Next-Generation Artificial Intelligence R&D, 2015/7/1-2018/3/31

(2) Tadashi Yamazaki (PI), MEXT Post-K Supercomputing Project, 2016/8/1-2017/3/31

4. Collaboration

4.1 Inside BLSC

(1) Shigeru Tanaka, Theoretical study on the cerebellum, 2013/04−

4.2 Outside BLSC in UEC

(1) Adjunct member, Artificial Intelligence eXploration Research Center, 2016/07-

4.3 Outside UEC

(1) Neuroinformatics Japan Center, RIKEN, Study on Neural Network Simulation, 2013-

(2) AI Research Center, AIST, R&D of Brain-style Artificial Intelligence, 2015-

(3) Junichiro Makino, Kobe University, Large-Scale Simulation of the Cerebellum on PEZY-SC, 2015

(4) Toshikazu Ebisuzaki, RIKEN, Large-Scale Simulation of the Cerebellum on PEZY-SC, 2015-

(5) Jun Igarashi, RIKEN, Computer Simulation of the Cerebellar Network Model on GPUs, 2013-

(6) Tmagawa Hospital, Computer Simulation of Rehabilitation with Neuromusculoskeletal models, 2014-

(7) Chung Tin, City Universyty of HongKong, Cerebellar circuit simulation on FPGAs, 2013-

5. Outreach activities

5.1 Editor of academic journals

(1) Review Editor, Frontiers in Computational Neuroscience, 2012/05-

(2) Action Editor, Neural Networks, 2016/01-

5.2 Paper review of academic journals

Many times from prestigious journals including PNAS and Science to technical journals including Neural Networks and Frontiers in Computational Neuroscience.