Unique & Exciting Campus

2017 Annual Report

The University of Electro-Communications

Brain Science Inspired Life Support Research Center

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

Preface

Japan is a super-aged and depopulating society unlike any other in the world and faces big challenges to maintain social activity. The social activity is the activity of individuals, and if the individual's activity is lost due to a decline in the quality of life (QOL) of individuals in terms of physical and mental aspects, the social productivity is lost. In addition, the economic burden due to the increase in the medical and social welfare budgets will make it further worse.

These indicate that the important issues are the prevention and efficient treatment of decline of physical abilities, and moreover how we live together symbiotically with people of lowered QOL.

In the Brain Science Inspired Life Support Research Center (BLSC), the 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. From this year, in order to implement more integrated medical-engineering collaborative activities and to establish a comprehensive support system for medicine, the 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 are activating our center activities and conducting new research and development to create innovation in the life support field.by cooperating with each other within the own group and among the groups.

The present annual report is to summarize all our individual and collaborative activities in 2017. 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 30, 2018
Brain Science Inspired Life Support Research Center
Director Takuji Koike

Index

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.

Research Groups

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 （as of 31 March, 2018 ）

Laboratory Heads：

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

Visiting Scientists

Yu ARAMAKI	Professor, Chukyo University School of Health and Sport Sciences
Ryu KATO	Associate professor, Faculty of Engineering Division of Systems Research
Kenji KANSAKU	Chief, Systems Neuroscience Section, Research Institute of National Rehabilitation Center for Persons with Disabilities
Takehiko TAKAGI	Assistant professor, Department of Orthopaedic Surgery, Tokai University
Shinichiro TAKAYAMA	Director, Department of Surgical Specialities, National Center for Child Health and Development
Masatoshi TAKITA	Senior researcher, Brain Function Measurement Group, Human Informatics Research Institute, National Institute of Advanced Industrial Science and Technology (AIST)
Tadashi NAKAMURA	UEC Professor Emeritus
Yoko HOSHI	Professor, Department of Biomedical Optics, Institute for Medical Photonics Research, Preeminent Medical Photonics Education & Research Center, Hamamatsu University School of Medicine
Osamu YAMAMURA	Associate professor, University of Fukui School of Medicine
Wenwei YU	Professor, Department of Medical System Engineering, Graduate School of Engineering, Chiba University
Baoliang LU	Professor, Department of Automation, School of Electronic, Information and Electrical Engineering, Shanghai Jiao Tong University, China
Qixin CAO	Professor, Director, Engineering Training Center, Shanghai Jiao Tong University, China
Weidong CHEN	Professor, Department of Automation, School of Electronic, Information and Electrical Engineering, Shanghai Jiao Tong University, China
Junyou YANG	Professor, Department of Electrical Engineering, Shenyang University of Technology, China
Baiqing SUN	Associate professor, School of Electrical Engineering, Shenyang University of Technology, China
Qiang HUANG	Professor, Director of Intelligent Robotics Institute, School of Mechatronics Engineering, Beijing Institute of Technology, China
Feng DUAN	Professor, Department of Automation, College of Computer and Control Engineering, Nankai University, China

Numerical Data of BLSC Activity 2017

1. Project expense：10,000,000 yen (FY 2017 Special expense)

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

2. Research

A. Reviewed papers：36
（including 8 papers published in IF>4 journals）

B. Books, review articles, etc.：10

C. Invited lectures：33

D. Patent applications：8

E. Productization：2

F. Collaboration inside BLSC：12

G. Collaboration outside BLSC：62

H. External funding：14

I. Grants-in-aid for scientific research：30

3. Education

J. Student guidance：80（Bachelor: 42, Master: 35, Doctor: 3）

K. Awards：6 件

4. Public relations & Outreach activities

L. Exhibition and Media release： 12

M. High school visit：14

5. Special notes

Basic technology development of optical measurements group in investigating the mechanisms of luminescence emitted from organs of mice using the near infrared luminescent substrate AkaLumine, which is an analog of the firefly luminescent substrate. This phenomenon is a new finding that shows light emission associated with chemical reaction of some materials intrinsic to mammals and the artificial substrate. This suggests that we are able to establish a technology to

selectively detect the activity of specific intrinsic enzymes without genetic manipulation. The same group also successfully developed an artificial bioluminescence system AkaBLI to observe the deep part of the brain noninvasively in collaboration with RIKEN Center for Brain Science, and published a paper in Science. This technology can be applied to primates and will lead to the application to the real time visualization of higher brain functions.

Technology development for motor function recovery for medical welfare group developed a robotic hand with in-skeleton tendon-driven mechanism, a laminated EMG sensor, and a 4-DoF shoulder disarticulation prosthesis. An application of these components was made to the Ministry of Health, Labor and Welfare for their registration as parts for completion, and approved.

Basic technology development of optical measurements group and Technology development for motor function recovery for medical welfare group developed a noninvasive and simple system to detect food remaining in the piriform sinus using fluorescence in the near-infrared window of high permeability in biological tissue, and using fluorescent food it was confirmed that the system works well to evaluate the risk of aspiration. At present, collaborating with Japanese Red Cross Musashino Hospital, the groups are applying for an ethics review to perform human demonstration experiments.

Measurement and monitoring of *in vivo* brain functions group and Technology development for motor function recovery for medical welfare group elucidated the relationship between a vascular permeability factor, the VEGF protein, and microvascular permeability, by applying an analysis method of 3D microvascular networks in the brain visualized by the two-photon laser microscopy to the analysis of skeletal muscle tissue, and submitted a paper to an international journal. Measurement and monitoring of *in vivo* brain functions group analyzed the morphology of astrocytes using machine learning. Theoretical and computational neuroscience group built a mathematical model for the possible roles of glial cells in synaptic transmission, which will be a theoretical contribution to a future collaboration with Measurement and monitoring of *in vivo* brain functions group.

In co-sponsorship with The Society for Bioacoustics, BLSC held the 4th Annual Meeting of The Society for Bioacoustics in the UEC campus on December 9-10 in 2017 as a part of internationalization activity.

Research progress was reported by graduate school students following every BLSC seminar. This activity strengthened mutual communications and understandings among the four groups.

Seminars and Events

1. BLSC Seminar Series

62nd

Date & Time: March 26 (Mon.), 2018, 13:00 – 14:30

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

Speaker: Ryo KITADA, Ph.D. (Nanyang Associate Professor, School of Social Sciences, Nanyang Technological University, Singapore)

Chair: Yoichi MIYAWAKI

Title: Brain networks underlying haptic texture perception and its illusion

61st

Date & Time: March 19 (Mon.), 2018, 13:00 – 14:30

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

Speaker: Dr. Kazuhiro SAKAMOTO (Associate Professor, Department of Neuroscience, Faculty of Medicine, Tohoku Medical and Pharmaceutical University)

Chair: Yoshiki KASHIMORI

Title: Understanding of higher brain functions as emergent phenomena in complex systems

60th

Date & Time: March 2 (Fri.), 2018, 13:00 – 14:30

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

Speaker: Dr. Motohiro KAWASAKI (Lecturer, Department of Orthopaedic Surgery, Kochi Medical School, Kochi University)

Chair: Norihiro KOIZUMI

Title: Treatment of chronic pain associated with bone and joint diseases by using focused ultrasound

59th

Date & Time: January 19 (Fri.), 2018, 13:00 – 14:30

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

Speaker: Dr. Ken TAKIYAMA (Associate Professor, Department of Electrical and Electronic Engineering, Tokyo University of Agriculture and Technology)

Chair: Hayaru SHOUNO

Title: Prospective coding in human motor learning and decision making

58th

Date & Time: December 15 (Fri.), 2017, 13：00 – 14:30

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

Speaker: Dr. Jun IGAEASHI (Senior Center Researcher, Advanced Center for Computing and

Communication, RIKEN)

Chair: Tadashi YAMAZAKI

Title: Simulation of the neural network with the size of the human cerebral cortex using an exa-flops class computer

57th

Date & Time: November 28 (Tue.), 2017, 14：00 – 15:30

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

Speaker: Dr. Kazuhisa KOHDA (Professor, Laboratory of Physiology, St. Marianna University School of Medicine)

Chair: Shinji MATSUDA

Title: How does the signaling of Cbln1-delta2glutamate receptor control the formation, maintenance and plasticity of synapses?

56th

Date & Time: November 14 (Tue.), 2017, 13：00 – 14:30

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

Speaker: Dr. Dmitri B. PAPKOVSKY (Professor, School of Biochemistry and Cell Biology, University College Cork, Cork, Ireland)

Chair: Kazuto MASAMOTO

Title: New insights into cell/tissue function and metabolism by means of phosphorescent oxygen sensing probes

55th

Date & Time: October 25 (Wed.), 2017, 13：00 – 14:30

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

Speaker: Dr. Soichi ANDO (Associate Professor, Department of Mechanical Engineering and Intelligent Systems, Graduate School of Informatics and Engineering, The University of Electro-Communications)

Chair: Hidetaka OKADA

Title: Transient excise and cognitive function

54th

Date & Time: August 4 (Fri.), 2017, 13：00 – 14:30

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

Speaker: Dr. Tomoki FUKAI (Laboratory Head, Laboratory for Neural Circuit Theory, Brain Science Institute, RIKEN)

Chair: Shigeru TANAKA

Title: Brain’s network mechanisms to model the external world

53rd

Date & Time: July 20 (Thu.), 2017, 13：00 – 14:30

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

Speaker: Prof. CAO QIXIN (Professor, School of Mechanical Engineering, Shanghai Jiaotong University, Visiting Professor of BLSC, UEC)

Chair: Yinlai JIANG

Title: Present Status and Future Prospect in Application of Robotics to Surgical Operations

52nd

Date & Time: June 13 (Tue.), 2017, 13：00 – 14:30

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

Speaker: Dr. Haruo HOSOYA (and Dr. Aapo HYVARINEN) (Senior Researcher, Department of Dynamic Brain Imaging, Brain Information Communication Research Laboratory Group, Advanced Telecommunications Research Institute International (ATR))

Chair: Yoichi MIYAWAKI

Title: A mixture of sparse coding models explaining properties of face neurons related to holistic and parts-based processing

51st

Date & Time: June 9 (Fri.), 2017, 13：00 – 14:30

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

Speaker: Dr. Hiroshi KAWAGUCHI (Senior Researcher, Brain Function Measurement Research Group, Human Informatics Research Institute, National Institute of Advanced Industrial Science and Technology (AIST))

Chair: Kazuto MASAMOTO

Title: R&D of elementary technologies of fNIRS for brain function monitoring in human life environment — toward actual implementation of neuro-rehabilitation —

50th

Date & Time: May 23 (Tue.), 2017, 15：00 – 16:30

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

Speaker: Dr. Tatsuhiko HARADA (Professor, Otorhinolaryngology, Atami Hospital, International University of Health and Welfare)

Chair: Takuji KOIKE

Title: Otoacoustic emission — From its fundamentals to clinical applications —

49th

Date & Time: Apr. 19 (Wed.), 2017, 13：00 – 14:30

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

Speaker: Dr. Takeshi NISHIJIMAN, (Associate Professor, Sport Neuroscience Laboratory, Department of Health Promotion Science, Graduate School of Human Health Science, Tokyo Metropolitan University)

Chair: Yutaka KANO

Title: Relationship between physical activities and brain functions

2. BLSC Spring School for High School Students

BLSC holds spring school activity for high school students who are interested in neuroscience and biomedical engineering by modifying part of the hands-on training courses designed for UEC graduate school students so as to adjust them to those for high school students. The third BLSC Spring School was held for 2 days, Mar. 28 (Wed.) and Mar. 29 (Thur.), 2018. Twenty one high school students attended from Tokyo, Saitama, Kanagawa, Chiba and Niigata prefectures. In the Spring School, two hands-on training courses were offered. Each was 1-day course of 4.5 h, which were held twice. The students tackled subjects at the forefront of brain science research, supported by the instructors and teaching assistants. 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 as follows:
http://blsc-uec.net/wpblsc/wp-content/uploads/H29SpringSchoolReport.pdf.

● Title 1: Let’s reproduce brain with supercomputer

Instructor: Associate Professor Tadashi Yamazaki.

Contents: After brief learning of neural network system in brain, students simulated signal transmission in neural network models by using a supercomputer.

Number of students: 9 on Mar. 28 (Wed) ; 9 on Mar. 29 (Thu) .

● Title 2: Let's manipulate robot arms.

Instructor: Associate Professor Yinlai Jiang.

Contents: After brief learning of myoelectric signals generated by muscles construction, students operated robot arms by using myoelectric signal generated from their own arms.

Number of students: 4 on Mar. 28 (Wed); 4 on Mar. 29 (Thu).

Basic technology development of optical measurements group

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) noninvasive and continuous measurement of blood glucose contents (BGC) using NIRS and (4) detection of aspiration by the use of fluorescence in the near infrared wavelength range. In addition, as an industrial application of NIRS (5) 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

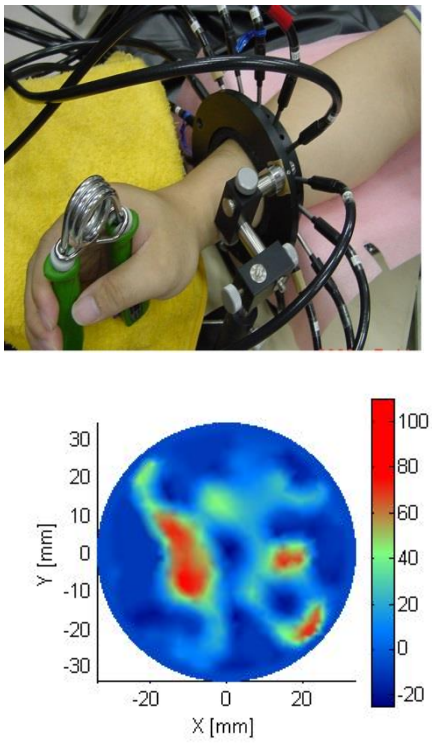


Fig. 1 (Top) Photo of DOT measurement at a forearm, and (Bottom) DOT image showing the increase in the deoxy-hemoglobin concentration due to the muscle activity in the forearm.

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 has been collaborating with Prof. Y. Hoshi, University of Hamamatsu School of Medicine, Assoc. Prof. H. Fujii, Hokkaido University, and Prof. Y. Iso, Kyoto University, who is the leader of a KAKENHI project (A) 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 has been working in cooperation with Japan Optical Brain Functional Imaging Society in this research topic.

(3) 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. Also Prof. Yamada has frequently been responding to academic consultation requests from industries interested in this technology.

(4) 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 using fluorescence, which is useful to examine whether food is trapped at the branch between the trachea and esophagus. Hokkaido University joined this project by providing a high-performance fluorescence measurement instrument. Preliminary and fundamental experiments using biological phantoms have been conducted, and preparations for experiments using humans are being made.

(5) 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 changes 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 aqueous solutions, it is possible to simultaneously measure and image the changes in the temperature and solute concentration in the aqueous solutions. This method will be applied to measure and image the temperature, solute concentration, reaction rate, etc. in microscale channels in biochips and chemical chips. This research topic is in collaboration with Assoc. Prof. Kakuta of Tokyo Metropolitan University.

1.2 State of Progress in Research and Education (April, 2017 - March, 2018)

(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. Also we have found the effect of void regions like the trachea on the light propagation, and the results were published in academic journals (Refs. 1 to 2, Subsection 2.1). Prof. Yamada gave an invited talk on this topic at Tianjin University, China (Ref. 1, Subsection 2.3).

(2) Optical mapping

Japan Optical Functional Brain Imaging Society (JOFBIS) published a guidebook for beginners working with optical mapping. The society decided to publish the guidebook in English for dissemination abroad. Yukio Yamada who was a chairperson of the committee for editing the guidebook was assigned for translation from Japanese to English, and the English version will be published in May, 2018. This guidebook is expected to contribute the healthy development of the technology.

(3) Noninvasive measurement of blood glucose contents (BGC) by NIRS

By cooperating with a company which has been collaborating with our group for many years in the past, a new method of noninvasive NIRS measurement of BGC was developed and the efforts to improve the method was continually made for submitting the second paper of the first one published in an academic journal in 2015. Prof. Yamada also worked for consulting from other several companies interested in this technology to explain the difficulties of this technology. Prof. Yamada was invited by Tianjin University, China, to give a talk and to discuss about this topic (Item 1, Subsection 2.3). Our research of this topic is

progressing steadily despite its difficulty.

(4) Aspiration detection using fluorescence

Continuing to the achievements in the last year, our preliminary experiments using biological phantoms have shown that it is feasible to detect fluorescence from fluorophores at the depths of about 25 mm inside biological tissues by changing the distance between the excitation source position and the fluorescence detector position. We have also studied the effects of non-soft tissues such as bones and trachea on light propagation in tissues. Resultantly we have found that bones have little effects on light propagation and that trachea works advantageously for detection of fluorescence from deep tissue. We presented these results of preliminary experiments in an international conference (Item 3, Subsection 2.1). A student of Koike Lab. joined our team and greatly contributed for progress of this study.

For *in vivo* human experiments, we have made documents for application to the approval by the ethical committees of UEC and MRCH. The ethical committee of UEC have approved the application under the condition of following approval by the ethical committee of MRCH. At the end of the fiscal year of 2017 (the end of March, 2018), we were waiting for the approval from the ethical committee of MRCH. We also applied for a patent to UEC, but regretfully the department for the PATENT in UEC rejected our application.

(5) Noninvasive measurement of temperature of aqueous solution and solute concentration

This technology has been developed to simultaneous measurement and imaging of both temperature and solute concentration, and papers describing the results were published in international journals (Ref. 4, 5, and 6, Subsection 2.1). This technology has been applied to imaging transient changes in temperature distributions surrounding a small metallic sphere heated by electro-magnetic induction in liquid. A paper describing the results was submitted to an academic journal and accepted for publication. These achievements indicate that our research activities are progressing soundly and steadily.

1. 3 Future Plan

For the research topic of (1) diffuse optical tomography, the project sponsored by Japan Agency for Medical Research and Development (AMED) was terminated at the end of the fiscal year of 2016. So significant progresses in this topic are not expected, but the BLSC researchers in this topic will continue to collaborate with the researchers involved in the project, particularly in fundamental studies such as numerical methods for solving light propagation in biological tissue.

For the topic of (2) optical mapping, the BLSC researcher will take part in translation of the guidebook 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 (3) noninvasive measurement of blood glucose contents (BGC) by NIRS, the BLSC researcher will continue collaboration with the related company and prepare for a paper to an international journal. There may be a possibility of collaboration with Tianjin University, China, where Prof. Yamada gave an invited talk on this topic.

For the topic of (4) aspiration detection using fluorescence, the group including the BLSC researchers will continue to accumulate data by preliminary experiments and proceed to *in vivo* experiments using human in 2018. With the approvals from the ethical committees of UEC and MRCH, in vivo experiments using aged people will be conducted at both UEC and MRCH. Applications to various funding will be made for acquiring research fund.

For the topic of (5) noncontact measurement of temperature and solute concentration in aqueous solution, the BLSC researcher will continue to work in collaboration with the associate professor of Tokyo Metropolitan University aiming submissions and publications of papers.

2. Research Achievements

2. 1 Reviewed papers

For the topic of (1) Diffuse optical tomography:

(1) Fujii H, Yamada Y, Kobayashi K, Watanabe M, Hoshi Y. 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* 33, e2826, 2017, DOI: 10.1002/cnm.2826.

For the topic of (4) aspiration detection using fluorescence:

(3) T. Suzuki, R. Saito, N. Kitada, T. Koike, S. Maki, Y. Michiwaki, G. Nishimura, H. Niwa and Y. Yamada, "Aspiration Risk Detection Using Oral Administration of Fluorescent Food --- Preliminary Experiments Using Meat Phantoms ---," 2017 IEEE International Conference on Cyborg and Bionic Systems (CBS 2017), Beijing, China, Oct. 17-19, 2017.

For the topic of (5) Noninvasive measurement of temperature of aqueous solution and solute concentration:

(2) Kakuta N, Nishijima K, Kondo K, Yamada Y. Near-infrared measurement of water temperature near a 1-mm-diameter magnetic sphere and its heat generation rate under induction heating. *Journal of Applied Physics* 122, Paper No. 044901 (2017); doi: 10.1063/1.4995284.

2.2 Invited lectures

(1) Yamada Y. Recent progresses of DOT and blood glucose measurement. Special talk, College of Precision Instrument and Optoelectronics Engineering, Tianjin University, China, May 30, 2017.

4. Collaboration

4.1 Inside BLSC

(1) For the topic of (4) Aspiration detection using fluorescence, collaboration with Shojiro Maki, Haruki Niwa, and Takuji Koike.

4.2 Outside UEC

(1) For the topic of (1) Diffuse optical tomography, collaboration with S. Hoshi, Department of Biomedical Optics, Institute for Medical Photonics Research, Preeminent Medical Photonics

Education & Research Center, Hamamatsu University School of Medicine, and with H. Fujii, Faculty of Engineering, Hokkaido University.

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

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

(4) For the topic of (5) noncontact measurement of temperature and concentration distributions of aqueous solution, collaboration with 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

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)

(3) Visiting Class: “See, Watch and Diagnose Human Bodies by Light,” Yonezawa-Kojokan Senior High School, Yamagata Prefecture, July 6, 2017.

1. Outline of Research and Education

1. 1 Basic Policy in Research and Education

(1) Development of bioluminescent substrates emitting near-infrared (NIR) light

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. Bioimaging that utilizes the firefly bioluminescence system (Fig. 1) is widely applied as the standard imaging technology in bioscience for visualizing various phenomena. However, the bioluminescence wavelength (λ_{max} ~570 nm) using natural D-luciferin (**1**) is not suitable for visualizing deep site phenomena. Thus, 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.

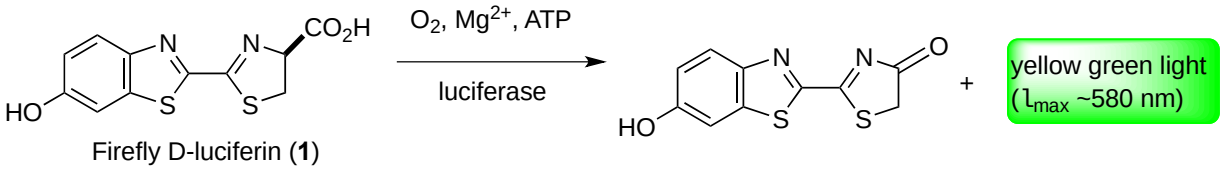


Fig. 1. Firefly bioluminescence system.

(2) Development of a non-invasive pulmonary aspiration risk detection system

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 (Fig. 2).

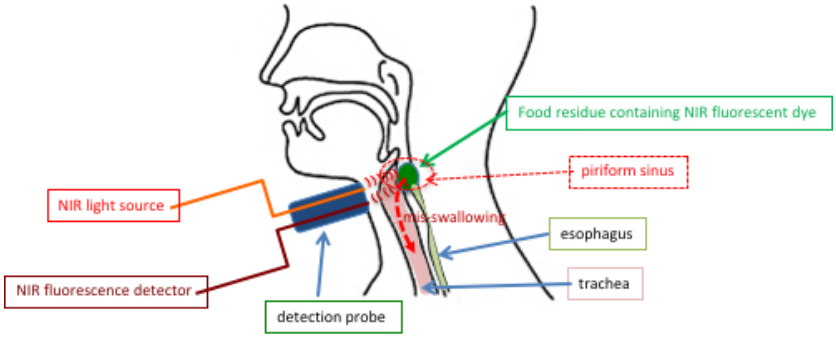


Fig. 2. Detection of fluorescent dye-containing food residue remained in piriform sinus in hypopharynx (junction of esophagus and trachea).

(3) BLSC Spring School for high school students

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

1.2 State of Progress in Research and Education (April, 2017 - March, 2018)

(1) Development of bioluminescent substrates emitting near-infrared (NIR)

Although Recently we developed a firefly bioluminescent material "Akalumine" that emits light in the NIR biological optical window region (λmax 677 nm), we continued the development of the substrate emitting the more longer wavelength. As a result, we succeeded the development of a new NIR light emitting substrate **2** whose λmax is 690 nm (Fig. 3).

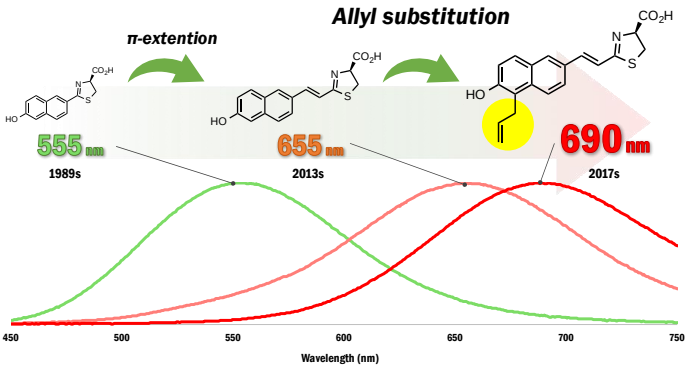


Fig. 3. Structures and light-emitting wavelengths of newly developed firefly bioluminescent substrates.

(2) Development of a non-invasive pulmonary aspiration risk detection system

Simulation experiments for the detection of remnant food residue in the piriform sinus by utilizing high tissue-permeable NIR region (biological window) light were continuously carried out in the joint study similarly as last year. NIR fluorescence from samples containing a fluorescent dye could be detected through a biological tissue model of more than 2 cm thickness. In order to proceed for measurement in human subject, we applied for the experimental protocol to the ethics review committee of the university, and that was approved recently.

(3) 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. The third BLSC Spring School was held for 2 days, Mar. 28 (Wed.) and Mar. 29 (Thur.), 2018. Twenty one high school students attended from Tokyo, Saitama, Kanagawa, Chiba and Niigata prefectures. In the Spring School, two hands-on training course were offered. Each was 1-day course of 4.5 h, which were held twice. The students tackled subjects at the forefront of brain science research, supported by the instructors and teaching assistants. 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 as follows:

http://blsc-uec.net/wpblsc/wp-content/uploads/H29SpringSchoolReport.pdf

● Title 1: Let’s reproduce brain with supercomputer

Instructor: Associate Professor Tadashi Yamazaki.

Contents: After brief learning of neural network system in brain, students simulated signal transmission in neural network models by using a supercomputer.

Number of students: Mar. 28 (Wed.) , 9; Mar. 29 (Thur.) , 9.

● Title 2: Let's manipulate robot arms.

Instructor: Associate Professor Yinlai Jiang.

Contents: After brief learning of myoelectric signals generated by muscles construction, students operated robot arms by using myoelectric signal generated from their own arms.

Number of students: Mar. 28 (Wed.) , 4; Mar. 29 (Thur.) , 4.

1.3 Future Plan

(1) Development of bioluminescent substrates emitting NIR light

We will continue the development of new bioluminescent substrates with the enhanced brightness and improved water solubility when compared with newly developed **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

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

(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

(1) Kitada N, Saitoh T, Ikeda Y, Iwano S, Obata R, Niwa H, Hirano T, Miyawaki A, Suzuki K, Nishiyama S, Maki S. Toward bioluminescence in the near-infrared region: Tuning the emission wavelength of firefly luciferin analogues by allyl substitution. *Tetrahedron Letters* 59 (12): 1087-1090, 2018.

4. Collaboration

4.1 Inside BLSC

(1) Yukio Yamada, Takuji Koike, 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) Yukihiro Michiwaki (Japanese Red Cross Musashino Hospital) Development of a non-invasive pulmonary aspiration risk detection system that utilizes NIR biological optical window light (2015~).

(2) Goro Nishimura (Hokkaido University) Development of a non-invasive pulmonary aspiration risk detection system that utilizes NIR biological 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 (November 2017)

Shojiro MAKI Laboratory

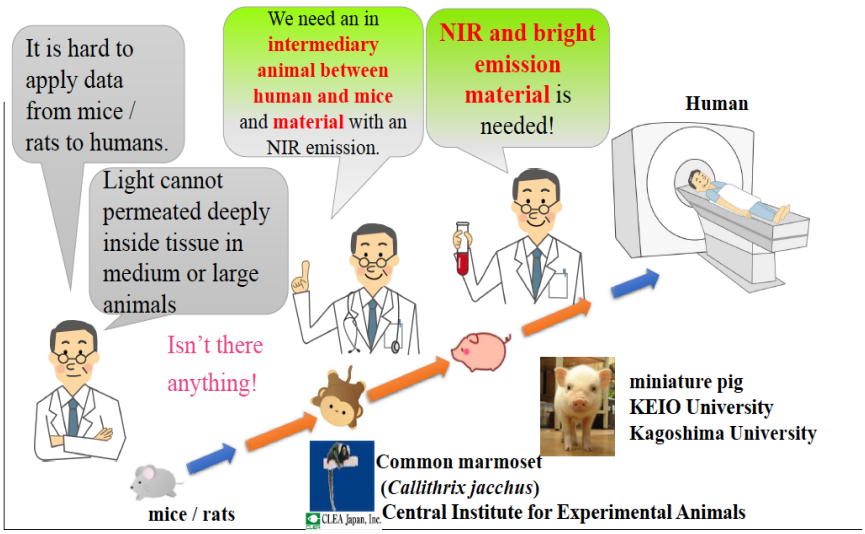
1. Outline of Research and Education

1. 1 Basic Policy in Research and Education

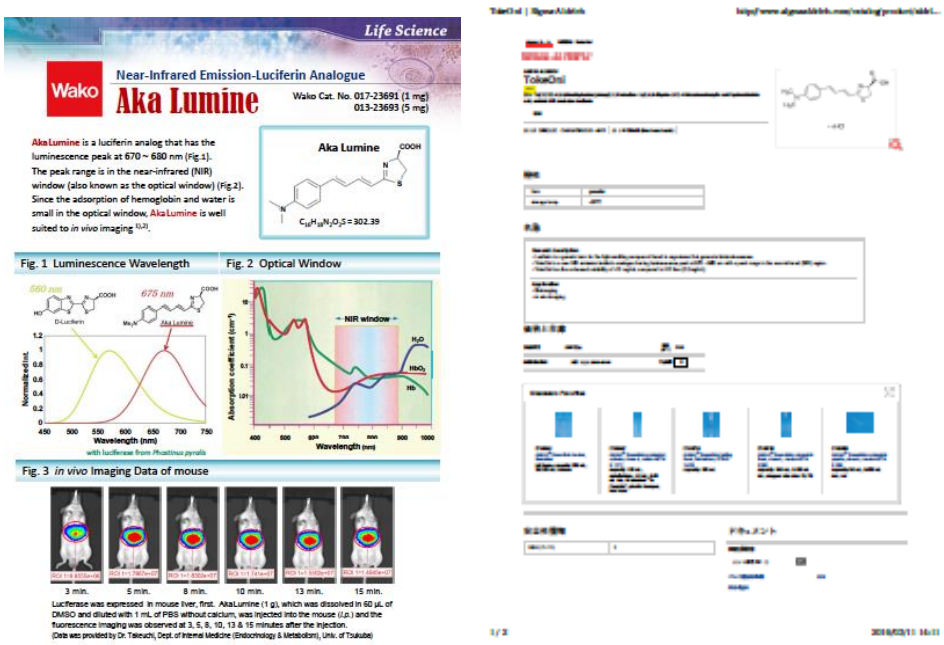
Our principle is “innovation of optical *in vivo* imaging by artificial luciferins” for future life science technology. Our principles also include “Orphan Drug” development which is high risk and may be avoided by researchers.

“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 bioluminescent 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 State of Progress in Research and Education (April, 2017 - March, 2018)

(1) Establishment of near infrared spectroscopy measurements and analysis methods (as part of a collaboration project with Yokoi lab, BLSC)

Although “TokeOni” is a good NIR probe, it has a disadvantage; the pH of blood is lowered owing to the presence of HCl salt. We have designed a novel product “SeMpai” that has water solubility (20 mg/mL) and NIR emission (ca. 675 nm) similar to “TokeOni”. The industrial production of “SeMpai” will be managed by Kurogane Kasei Co. Ltd. Currently, Kurogane Kasei Co. Ltd. is in discussion with a US-based company regarding the marketing aspect. Dr. Miyawaki and colleagues are our collaborators and have published a paper on in vivo imaging that uses “TokeOni” in *Science*; further, they conducted a press release for it (http://www.riken.jp/pr/press/2018/20180223_1/).

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) Iwano S, Sugiyama M, Hama H, Watakabe A, Hasegawa N, Kuchimaru T, Tanaka KZ, Takahashi M, Ishida Y, Hata J, Shimozono S, Namiki K, Fukano T, Kiyama M, Okano H, Kizaka-Kondoh S, McHugh TJ, Yamamori T, Hioki H, Maki S, Miyawaki A. Single-cell bioluminescence imaging of deep tissue in freely moving animals. *Science*. 2018 Feb 23; 359 (6378): 935-939. doi: 10.1126/science.aaq1067.

(2) Fukuchi M, Izumi H, Mori H, Kiyama M, Otsuka S, Maki S, Maehata Y, Tabuchi A, Tsuda M. Visualizing

changes in brain-derived neurotrophic factor (BDNF) expression using bioluminescence imaging in living mice", *Scientific Reports*, 7, 4949, 2017.

(3) Kakiuchi M, Ito S, Kiyama M, Goto F, Matsuhashi T, Yamaji M, Maki S, Hirano T. Electronic and steric effects of cyclic amino substituents of luciferin analogues on a firefly luciferin−luciferase reaction. *Chemistry Letters* 46: 1090-1092, 2017.

(4) Kakiuchi M, Ito S, Yamaji M, Viviani VR, Maki S, Hirano T. Spectroscopic properties of amine-substituted analogues of firefly luciferin and oxyluciferin. *Photochemistry and Photobiology* 93: 486–494, 2017.

2.3 Book, non-refereed articles and translation

(1) Maki S, Firefly bioluminescence toward to in vivo imaging technology. *The Journal of Japan Society for Laser Surgery and Medicine* 37: 448-453, 2017.

2.4 Media release

(1) "Cancer cells lighted up successfully in living pig (in Japanese)", *The NIKKAN KOGYO SHIMBUN, LTD.* Feb. 20 (2017).

(2) "Secret of firefly's light (in Japanese)", Fushigi Kagakukan, Yomiuri Shimbun: May. 20 (2017).

(3) KIDSASHI (Ministry of Education, Culture, Sports, Science and Technology National Institute of Science and Technology Policy) "Creating organs via regenerative medicine (in Japanese)" (https://stfc.nistep.go.jp/horizon2030/index.php/ja/weekly-weakly-signals/354): Aug. 18 (2017).

(4) Press Release (RIKEN)「seeing cells from outside the body with synthetic bioluminescence: AkaBLI」(http://www.riken.jp/pr/press/2018/20180223_1/): Feb. 23 (2018).

2.5 Patent

(1) P2018-090192 "Pharmaceutical composition for treatment of leukemia (in Japanese)"
Inventor : Takahiko Hara, Kazuya Miyashita, Takuya Yagi, Azusa Takechi, Shojiro Maki, Yoshifumi Hachiro, Chihiro Yoshida.
Applicant: Tokyo Metropolitan Institute of Medical Science, The University of Electro-Communication
Date of application: May 8, 2018.

2.6 Productization

(1) "Akalunine HCl", Wako Pure Chemical Industries, Ltd., Apr. 2017.

2.7 Award

(1) Chihiro Yohshida: Student Award (Meguro Alumni Association of The University of Electro-Communications, March 2018).

2.8 Student guidance

(1) Shota Tamaki, 2017, Bachelor (engineering)

(2) Chihiro Yoshida, 2017, Bachelor (engineering)

2.8 Visit of oversea researchers and students

(1) Winson Lu, The University of Sydney, Dept. of Medicine (B2). Dec. 2017.

2.9 Study abroad programs for students

(1) Yoshifumi Hachiro, Nanyang Technological University (Singapore), Division of Chemistry & Biological Chemistry School of Physical & Mathematical Science (Assoc. Prof Roderick Wayland Bates) Aug.16-Oct. 3, 2017.

(2) Chihiro Yohshida, Instituto Politecnico Nacional (Mexico), (Prof. José Manuel De La Rosa Vázquez) Feb. 17-Mar. 21, 2017.

3. Research funding

3.1 Grant-in-aid for scientific research

(1) Maki S. (CI) ”Resonance Bio-imaging”, 3704, 2015-2019, total ¥ 20,000 (Grant-in-Aid for Scientific Research in Innovative Areas).

3.2. Competitive external research funding

(1) Maki S. (PI) “Practical application of imaging material”, Kurogane Kasei Co., Ltd. 2012-present, ¥ 500,000 per year.

(2) Maki S. (PI) “Study on the possibility of development of new application utilizing mass spectrometer (in Japanese)”, JEOL Ltd. 2017-present, ¥ 918,000 per year.

4. Collaboration

4.1 Inside BLSC

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

4.2 Outside UEC

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

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

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

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

(5) Shinae Kondo, Takahiro Kuchimaru, Tokyo Institute of Technology “Development of in vivo imaging

technology", April 2014-present.

(6) Kazuhiro Chiba, "Study of bio-imaging material", August 2015-present.

(7) Kenji Hirayama, Nagasaki University, "Dynamics study of in vivo imaging material in live body", November 2015-present.

(8) Rika Numano, Toyohashi University of Technology, "Study of firefly imaging material", November 2015-November 2017.

(9) Yoshiyuki Ito, JEOL Ltd. "New aspect for instrumental analysis", December 2016-present.

Non-disclosure agreement (NDA)

(1) Ken Annoura, National Institute of Infectious Diseases, Japan, "About NIR imaging material", January 2014-present.

(2) Hiroyuki Sato, Perkin Elmer Japan, Co., Ltd. "Study of imaging material", March 2017-present.

Material transfer agreement (MTA)

(1) Rika Numano, Toyohashi University of Technology, "Study of firefly imaging material" December 2012 onward (no end-date for validity).

5. Outreach activities

5.1 Paper review of academic journals

(1) Non-disclosure

5.2 Other outreach activities

(1) Extension lecture for children (experimental class), June 10, 2017 (Shibuya-ku, Tokyo).

(2) Extension lecture for children (experimental class), August 1, 2017 and August 9, 2017 (The University of Electro-Communications).

(3) Extension lecture for high-school students, October 5, 2017 (Tachikawa International High School, Tokyo).

(5) Extension lecture for children (experimental class), January 20, 2018 (Shibuya-ku, Tokyo).

Measurement and monitoring of *in vivo* brain functions group

Kazuto MASAMOTO Laboratory

1. Outline of Research and Education

Our research focus is to understand the cellular communications in the brains under healthy and diseased conditions. One of the current goal is to develop a method to monitor brain states based on the hemodynamic measurements without using clinical instrument in the hospital.

1. 1 Basic Policy in Research and Education

A variety of cells cooperate in the brain to maintain normal neural activity (Fig. 1). Blood flow is the most important element that feeds brain cells. Therefore, to understand the regulation mechanism of the blood flow, our research focus on visualization and quantification of whole three-dimensional structures of living brain cells and their interaction with blood flow by using *in vivo* optical imaging techniques. Furthermore, based on the image data, substance transport from blood to cells is analyzed to clarify the neurovascular relationship. Specifically, we are currently working on the following research themes.

1. Development of new techniques for monitoring brain activity: non-invasive measurement to quantify the brain activity based on vasomotion of the brain.

2. Development of image analytical software to evaluate spatiotemporal dynamics of cerebral blood flow during neurosurgery.

3. Studies on neuromodulation based on mass transport by enhancing cerebral blood flow.

4. Development of quantification software for multidimensional images of neurovascular unit.

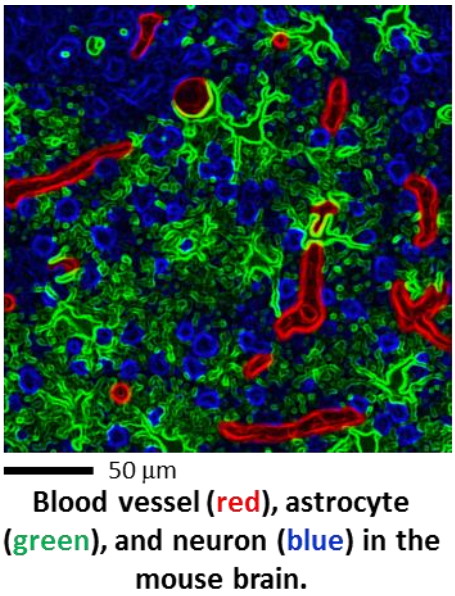


Fig. 1 Exampled picture of the brain tissue cells captured with in vivo two-photon laser scanning microscopy in the anesthetized mouse cortex

1.2 Achievements and State of Progress (April, 2017 - March, 2018)

(1) Development of a new technique for brain activity monitoring: Imaging and quantification of small amplitude of vasomotion in the brain

In this fiscal year, we investigated a method to measure the spatiotemporal fluctuation of the blood flow in the brain microvascular bed. To directly visualize the red blood cell flow in microvessels of the brain, genetically modified rats (KikGR - RBC Wistar Rat, 27 month old, N = 4) which expressed the fluorescent protein Kik-GR in the red blood cell membrane were used. A portion of the skull over the somatosensory area was removed under anesthesia. Then, sulforhodamine 101 (SR 101) was administered intraperitoneally and the plasma component was fluorescently labeled. The excitation wavelength was set to 920 nm of two-photon laser scanning fluorescence microscope (two-photon microscope), fluorescent imaging of labeled red blood cells (525/50 nm) and plasma (610/75 nm) was conducted simultaneously through a 20-fold water immersion objective lens. Fluorescent components of plasma and erythrocytes were separated into respective signal intensities using a linear discrimination method (Fig. 2).

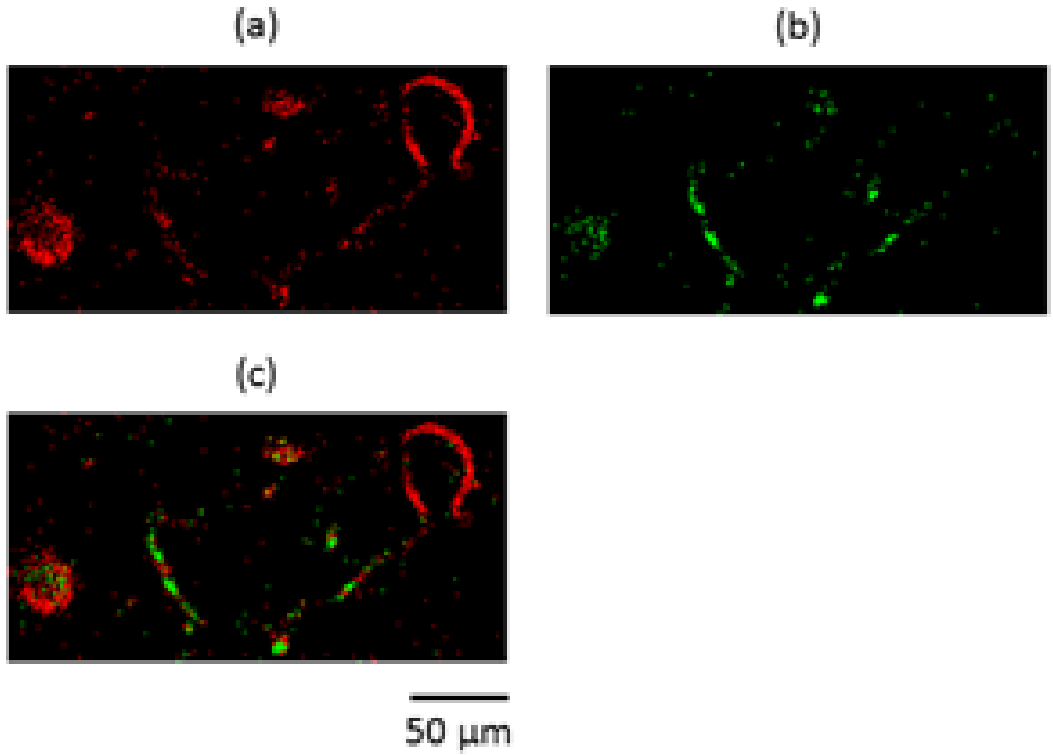


Fig 2. Single slice images of segmented plasma (a) and red blood cells (b) with a linear discrimination method (c: overlap images of a and b)

The average pixel value was projected through all frames captured and used as a reference image for the following analysis. The displacement of the position of each frame image was corrected by adjusting a region of autofluorescence on the reference image. Next, only the frames where no positional deviation from the reference image was observed were extracted, and the maximum projection image was created to determine blood vessel region to be analyzed. The sum of the number of pixels occupied by plasma, erythrocytes, and blood vessels was calculated in each frame. The area occupied by the red blood cells was

divided by the area occupied by the plasma, and the relative occupancy of the red blood cells was calculated.

Because the image of the penetrating vessel appear as a cross section of the vessel, the short diameter of the ellipse fitted to the outline of the blood vessel edge is measured as a vessel diameter in their binarized images. On the other hand, cross section of the vessel having a length of 3 pixels or more in the longitudinal direction of the vessel is extracted for analysis of capillaries. A center line of the vessel was also drawn by applying a thinning method. The minimum width was calculated in the cross section of the vessel. Next, for each 100 frames, the red blood cell and vessel images were projected as their mean value, and then the red blood cell image was divided by the vessel region image to calculate the apparent dwell time of the red blood cells (Fig. 3). From those images, apparent dwell time on the center line of the vessel was used as a representative value, and the apparent dwell time image was created (Fig. 3). Furthermore, the vessels having branch points at both ends of the vessel were divided into segments, and statistics on the apparent dwell time were calculated for each segment.

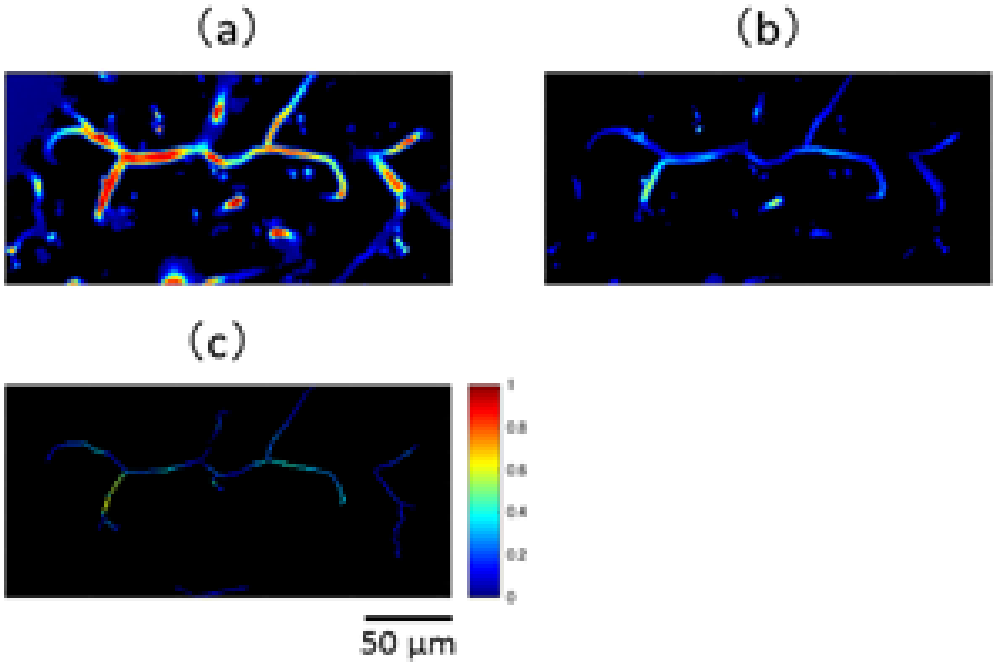


Fig 3. Measurement of apparent RBC dwell time (a: average projection image of vessel signals, b: average projection image of RBC signals, c:apparent dwell time image made by dividing (a) with (b))

The fluctuation range of the vessel diameter was 11 ± 3% of the average diameter in the artery whose vessel diameter was smaller than 15 μm, and 7 ± 5% in the artery with the vessel diameter of 20 μm or more. For the vein (15 μm or less in diameter), the fluctuation range of the vessel diameter was about 11 ± 5%, and fluctuation similar to that of the artery was observed. Next, frequency analysis was performed to determine temporal fluctuations of the vessel diameter. As a result, it was confirmed that fluctuation of high frequency erythrocyte flow originates from fluctuation of systemic circulation.

Next, in order to evaluate the relationship between the diameter and flow of capillaries, relationship between flow velocity and erythrocyte occupancy rate was analyzed. For 5 capillaries in the same imaging

region, it was found that the red blood cell occupancy decreases exponentially with increasing the flow rate. For the spatial distribution of red blood cells, the apparent residence time was observed to be short around branching location and tended to be long at the confluence point immediately after branching. This suggests that the fluctuation of the blood flow in the capillary region may be controlled near the branch point of the capillary. The future work is needed to investigate the mechanism of blood flow regulation by vascular pericyte and endothelial cells localized at the branch site and the correlation with the activity of neurons and glial cells.

Regarding temporal fluctuation of erythrocytes in the capillary bed, low frequency fluctuation (0.2 Hz or less) was mainly detected. No correlation was found between the fluctuation of these RBC flow and the changes in the nearby vessel diameters. Assuming that the size of the red blood cells is approximately 8 μm which is similar size of the capillary diameters, the flow regulation is driven by the diameter of the vessel and change in the viscosity depending on the resistance of the flow arising from the contact with the vascular endothelial surface layers. Therefore, it seems that there was no correlation with the diameter of the blood vessel and flow changes in the capillary region. In the future, we will conduct a blood flow simulation based on these actual measurement data, and consider the mechanical interaction with vascular endothelial cells and RBCs etc.

As mentioned above, in this fiscal year, we clarified that capillary flow fluctuation, in particular for the low frequency fluctuations, occur in the capillary region, and that flow velocity changes spatially occurred around the bifurcation of the capillaries.

(2) Development of image analytical software to evaluate spatiotemporal dynamics of cerebral blood flow during neurosurgery (collaborative works with Edogawa Hospital and Jikei Hospital)

We previously reported mapping method for microvascular flow velocity in the experimental animals by measuring transit time of fluorescent dye transiently administered into the blood (Hoshikawa et al., Microcirculation 2016). In this fiscal year, the objective of the present project was to extend the proposed method for clinical situations such as during brain surgical operation.

With collaboration with Edogawa hospital and jikei hospitals, the movies captured by intraoperative ICG fluorescent angiography before and after vascular anastomoses surgery were used and analyzed using numerical analysis software Matlab. First, in order to reduce motion artifacts due to respiratory heartbeat, motion correction was performed on each frame bas5s, and a vascular region was extracted based on ICG changes. Next, segmentation was made for each branch point or end point of the extracted vessels, and the length and diameter of the vessel were calculated. Then, a rise time of the ICG was determined for each pixel. Linear approximation was applied over the rising phase of the ICG luminance based on the least square methods, and the time for reaching to 50% of the peak was defined as the rise time, and a slope of the straight line approximated was defined as the rising speed of ICG infusion. The rise time was plotted on the center line of each blood vessel and the maximum blood flow velocity was calculated from the difference between distances on the center line defined by Euclidean distance method and their rise time between those two-points.

Our preliminary results showed that the estimated flow velocity was 1.3-7.3 cm/s before the

anastomotic operation in the cerebral artery, and it is possible to compare changes in the flow velocity in a single vessel before and after the operation. In this fiscal year, we confirmed that the proposed flow velocity mapping method allows for comparison of the velocity changes within a single vessel scale using intraoperative ICG fluorescence angiography images.

(3) Studies on neuromodulation based on mass transport by enhancing cerebral blood flow (a collaboration with Keio University School of Medicine)

In this fiscal year, to further understand the signaling mechanisms for cerebral adaptation to hypoxia, pharmacological studies in the experimental animals were conducted, specifically focusing on a role of microglia.

To visualize the microglia *in vivo*, genetically modified mice (CX3CR1-GFP, The Jackson Laboratory; N = 12, male 10, female 2, 17-36 g, 27-44 weeks old) in which the green fluorescent protein (GFP) was expressed in the microglial chemokine receptor were used for the experiments. To measure the microglia morphology repeatedly for a long time, a chronic closed cranial window (Tomita et al., JCBFM 2005) was installed in the area of the parietal cortex of the mice. The animals were kept in a low oxygen chamber (oxygen concentration at 7 to 9%) under normal atmospheric pressure. We observed a shape of individual microglia and vascular structure at the same location in the cerebral cortex up to 27 days from exposure to hypoxia. Two mice were simultaneously tested in the same cage, and one was administered minocycline hydrochloride, and the other was administered the same amount of physiological saline as a control group.

As a result, for the group administered with minocycline, the cell body cross-sectional area and the number of protrusions of the microglia both decreased significantly as compared with the control group. Next, mice housed under normal atmospheric conditions were fed feed mixed with PLX3397 for 2 weeks. After 2 weeks, the mice fed with PLX3397 were moved into the hypoxic chamber, and similar feed was given until the end of the experiment. There was no significant difference in the cell body shape of the PLX3397 group compared to the control group, but the cell number was significantly decreased in the PLX 3397 animals. From the vascular structure image, the maximum intensity projection image related to the newly formed microvessel was created and the length of the vessel was visually measured. Regarding the microglia situated near the newly formed vessel site, the presence or absence of protrusions of cells touching a tip of the new vessel was judged. The results confirmed that newly-formed vessel sprouts with nearby microglia presence tends to connect with other microvessels, and the newly formed vessel without nearby microglia or suppressed microglia with induction of minocycline detracts eventually.

(4) Development of quantification software for multidimensional images of neurovascular unit (collaborative works with the National Institute of Radiological Sciences)

In this fiscal year, we investigated the quantitative relationship of both neural activity and microvascular responses in the cerebral cortex using two-photon microscopy images of the mouse braisy.

A genetically engineered mouse (Cre-CaMKII/GCaMP3, N = 24) in which GCaMP3, a sensor protein of intracellular calcium ion concentration, was expressed in the cortical neurons was used for the

experiments. Before starting the experiments, a closed cranial window was placed under anesthesia immediately above the cerebral cortex corresponding to the somatosensory area (Tomita et al., JCBFM 2005). At the time of the experiment, the mouse was fixed on the stage and imaged under arousal. Immediately before observation, sulforhodamine 101 was intraperitoneally administered to fluorescently label blood plasma. During imaging, mechanical stimulation was given to whiskers, and neural activity and vascular response were compared for resting and activation conditions. In addition, kainate was intraperitoneally administered to evoked epilepsy, and similar measurements were carried out.

The obtained image was analyzed using a custom-written Matlab software. Before the image analysis, the brightness in the image was corrected by shading correction. The GCaMP3 positive cell image and SR101 labeled blood vessel image were separately binarized and three dimensional image reconstruction was performed. Next, to quantify the neural activity, the center of gravity position of the GCaMP3 positive cells was calculated (Fig. 4). The shortest distance from the vessel for each cell was defined by a Euclidean distance method.

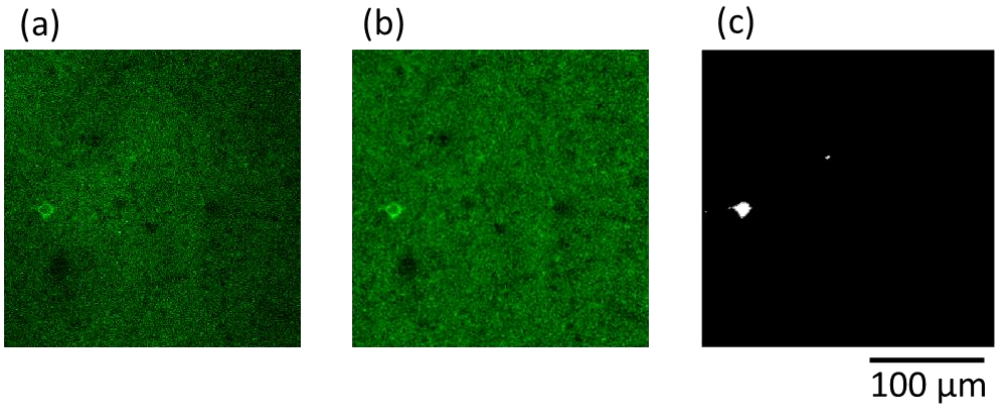


Fig 4. Representative image of GCaMP3 positive cells (a: an original slice image captured at a depth of 215 μm, b: shading correction, c: binarization)

For the vessel images, the diameter of the vessel around the center point was measured at each point (n = 4,000 to 11,000 points) of the vessel after applying shading correction and smoothing filter.

The number of GCaMP3 positive cells increased by 1.7 fold, 2.2 fold, and 2.5 fold in response to stimulation at 1, 4, and 8 Hz, respectively (N = 7). On the other hand, the average value of the capillary diameter was 5.5 ± 1.4 μm, 5.5 ± 1.4 μm, and 5.6 ± 1.4 μm for rest, 1 Hz, and 4 Hz stimuli, respectively. The stimulation-induced increases in the diameter relative to the rest condition was 1.6% ± 2.8% at 4 Hz stimulation. Next, t value was calculated (rest vs. stimulation) at each measurement point (n = 4,437), and accordingly, measurement points were grouped into 3 levels of t-value changes; $t \geqq 2$ as dilation group (n = 314), $-2 < t < 2$ as unchanged group (n = 4,437), and $t \leqq -2$ as constriction group (n = 23). The average diameter change in diameters for dilation and constriction group showed a change of 6.2% ± 2.6% and -5.3% ± 2.2%, respectively.

Next, kainate was intraperitoneally administered to induce epilepsy. As a result, the number of GCaMP positive cells gradually increased after induction, and the maximum 128 cells were detected. This

result is more than six times the maximum neural activity measured for somatosensory stimuli. For the kinate stimulation, the vessel diameter gradually expanded, and the average diameter was measured as 6.2 ± 1.6 μm when the neurons were highly activated.

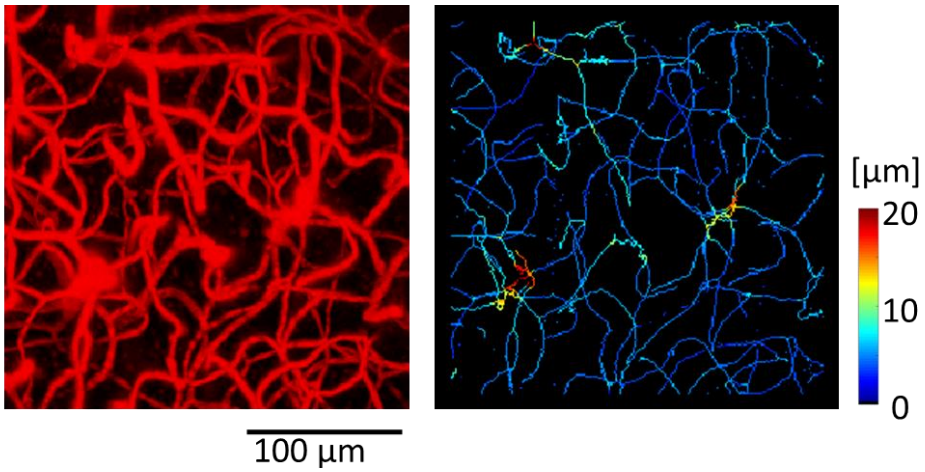


Fig. 5 Representative image for microvascular diameter measurements. (left) Original image that was made by maximum intensity projections over cortical depths of 100-300 μm from the cortical surface. (right) Measured diameters along center lines of the microvascular networks.

In this fiscal year term, we successfully developed a method for quantitative comparison between evoked neural activity and vascular response in three dimensional image space domains with two-photon microscopy.

1. 3 Future Plans

For future works, we need to determine causal-relationships between chronic hypoperfusion in the brain and development of cognitive decline. It is also important to provide a normal standard value of brain blood flow to manage a risk of dementia.

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. *J Cereb Blood Flow Metab*. 38: 687-696, 2018.

2.2 Book, non-refereed articles and translation

(1) Kanno I, Masamoto K, Yuki H, Sugashi T, Unekawa M, Tomita Y, Suzuki N. Repeated longitudinal in vivo imaging of cortical microglia under chronic hypoxia in the mice using two-photon microscopy with a closed cranial window technique. BS02-6 *Journal of Cerebral Blood Flow & Metabolism* 37(S1): 12-13, 2017.

(2) Unekawa M, Tomita Y, Toriumi H, Osada T, Masamoto K, Kanno I, Suzuki N. Effect of spreading

depolarization on cerebral blood flow and development of infarction under experimental ischemia in anesthetized mice. PS04-060 *Journal of Cerebral Blood Flow & Metabolism* 37(S1): 348, 2017.

(3) Hatakeyama N, Masamoto K, Unekawa M, Takuwa H, Kanno I, Matsui K, Tanaka KF, Tomita Y, Suzuki N. Spatiotemporal changes in cerebral blood flow induced by transcranial photostimulation to cortical neurons or astrocytes in the transgenic mice expressing channelrhodopsin-2. PS04-087 *Journal of Cerebral Blood Flow & Metabolism* 37(S1): 367-368, 2017.

(4) Takeda H, Sugashi T, Takuwa H, Ji B, Sahara N, Suhara T, Higuchi M, Kanno I, Masamoto K. Individual neural activity and capillary diameter responses measured in a three-dimensional spatial domain of awake mouse somatosensory cortex. PS04-090 *Journal of Cerebral Blood Flow & Metabolism* 37(S1): 370-371, 2017.

(5) Sugashi T, Takuwa H, Kanno I, Unekawa M, Tomita Y, Suzuki N, Masamoto K. Capillary dilation and tissue shrinkage during adaptation to chronic hypoxia in mouse cerebral cortex. ISOTT 2017 Abstract Book, Aug 21, Halle, Germany, 2017.

(6) Hatakeyama N, Masamoto K, Unekawa M, Takuwa H, Kanno I, Matsui K, Tanaka KF, Tomita Y, Suzuki N. 1677 Cerebral blood flow responses to photosimulation in the transgenic mice expressing channelrhodopsin-2 in the cortical neurons or astrocytes. XXIII World Congress of Neurology, Sep. 18, Kyoto, Japan, *Journal of the Neurological Sciences* 381 Supplement, 605-606, 2017.

(7) Yuki H, Masamoto K, Utekawa M, Sugashi T, Tomita Y, Kanno I, Suzuki N. Longitudinal two-photon imaging of microvascular remodeling and microglial response to chronic hypoxia in in vivo mouse cortex. The 42th microcirculation society conference F-12, pp.35 (2017.3.27) Toyama.

(8) Hachiya R, Takeda H, Sugashi T, Ishikawa M, Masamoto K. Flow velocity mapping of human brain microcirculation based on transit times of indocyanine green captured with fluorescent microscopy under neurosurgery. The 42th microcirculation society conference F-13, pp.36 (2017.3.27) Toyama.

(9) Kurihara U, Sugashi T, Takuwa H, Kanno I, Masamoto K. Dynamic two-photon microscopic imaging of spatiotemporal fluctuations in the volumes of blood plasma and red blood cells in the capillaries of the anesthetized rat brains. The 42th microcirculation society conference F-14, pp.36 (2017.3.27) Toyama

2.3 Invited lectures

Only for domestic

2.4 Student guidance

(1) PhD student 1, Graduate students 5, Undergraduate 4

2.5 Visit of oversea researchers and students

(1) Prof. Dmitri B Papkovsky from University College Cork, Cork, Ireland, who gives a BLSC seminar

3. Research funding

3.1 Grant-in-aid for scientific research

(1) Kakenhi

4. Collaboration

4.1 Inside BLSC

(1) Kano Lab, Miyawaki Lab, Tanaka Lab

4.2 Outside UEC

(1) Korean Brain Research Institute, University College Cork (Ireland)

5. Outreach activities

5.1 Editor of academic journals

(1) Serve as a member of Editorial Board for Journal of Cerebral Blood Flow and Metabolism, and Japanese Journal of Cerebral Blood Flow and Metabolism

5.2 Paper review of academic journals

(1) Reviewed 5 articles for Journal of Cerebral Blood Flow and Metabolism in this year term, and contributed as a referee for other journals; The Journal of Physiological Sciences, Expert Systems With Applications, Experimental Animals, Nature Protocols, NeuroImage, and Japanese Journal of Cerebral Blood Flow and Metabolism.

5.3 Other outreach activities

(1) Grant application review for an Einstein Strategic Professorship

(2) Co-chairs of Program Committee for Brain 2019 & Brain PET 2019, Director Board and Education Committee for International Society on Cerebral Blood Flow and Metabolism

(3) Domestic conferences/academic societies; N/A

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 and 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.

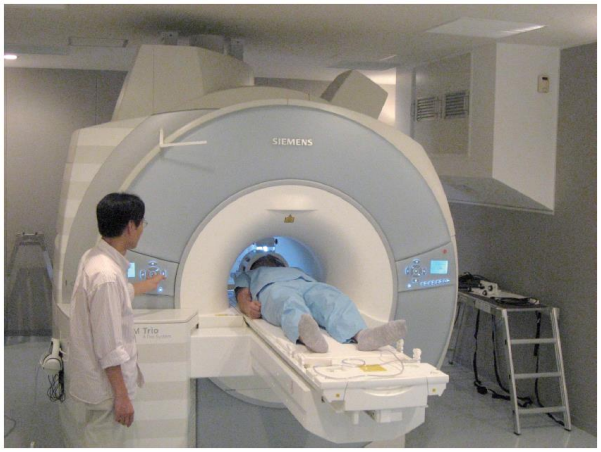


Figure 1: Experiments using fMRI system (ATR-Promotions BAIC).

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 use systematically-controlled sensory stimuli (mainly in visual, auditory, and tactile domains) and quantifies perceptual contents of human observing 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.

One example is analysis of brain activity patterns using machine learning techniques. In this method, brain activity is converted into multidimensional patterns and computer programs are trained to learn statistical relationship between brain activity patterns and 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.

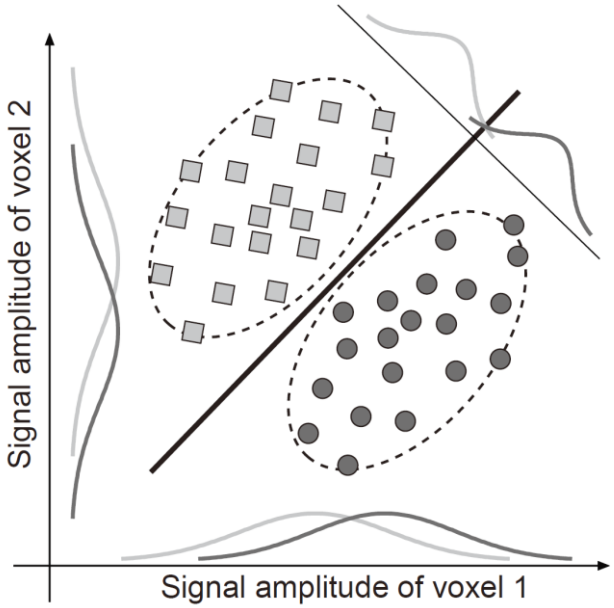


Figure 3: Classification analysis using multivariate signal patterns.

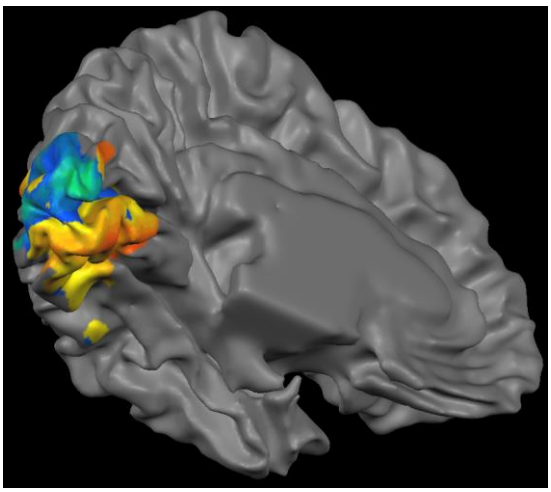


Figure 4: Retinotopy map identified in lower visual cortex.

Application for 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, 2017 - March, 2018)

Dynamics of neural representation of sensory and perceptual information

We visually recognize objects quickly and accurately. Object recognition of human vision is superior in its speed and accuracy and 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 experiments and analyses based on the results obtained in the last year and succeeded with publishing our achievement in an international journal paper, in which we analyzed information spreading that occurred when analyzing activation patterns estimated by MEG source localization. We believe that our findings of information spreading contributed to reveal the limitation of MEG source localization methods.

Furthermore, experiments of gaze direction measurement during natural scene observation have been progressed and we succeeded in finding new relationship between temporal characteristics of gaze direction and image features in natural scenes. A part of this project was accepted by JST PRESTO and have been supported by it.

In addition to visual information representation, we started to analyze information representation in human somatosensory systems. A part of this project has been supported by JST ERAO Inami JIZAI body project.

Research on neural activity analysis at high spatio-temporal resolution

We have used combination of MEG and fMRI to analyze human brain activity patterns at high spatio-temporal resolution. To complement this approach, we started to analyze human brain activity signals measured by ultra-high-field fMRI. Since this project is collaboration with National Institutes of Health (NIH) in US, international expansion of the research scope can be expected.

Development of analysis tools and simulation methods

To analyze brain activity patterns effectively, it is also important to develop analysis tools and simulation methods. Our previous project has conducted image feature extraction from object images using deep convolutional neural network (DCNN). In this year, we extensively used this method to analyze microscopic cellular images. This research project is a joint work with Masamoto laboratory in BLCS.

Furthermore, we proposed new methods to include fMRI information into MEG source localization, and proceeded with its implementation. A part of this project was accepted by JST PRESTO and have been supported by it.

1.3 Future Plan

Dynamics of neural representation of sensory and perceptual information

We proceed with experiments of gaze measurement during natural scene observation and systematically analyze critical factors to control dynamics of gaze direction, particularly focusing on image feature analysis.

Furthermore, we combine new analysis methods described below with our previous method to alleviate information spreading, and aim at achieving accurate brain activity pattern analysis. In addition to visual information representation, we apply similar methods to analyze somatosensory information representation while refining methodology to be generalized to multiple domains.

Research on neural activity analysis at high spatio-temporal resolution

While we proceed with human brain activity analysis by combination of MEG and fMRI at high spatio-temporal resolution, we particularly focus on human activity measurement and analysis using ultra-high-field fMRI. As described earlier, we plan to perform this project under international collaboration with NIH and will conduct fMRI experiments in NIH if necessary.

Development of analysis tools and simulation methods

We apply image feature extraction based on DCNN and other methods to natural scene image and compare results with that obtained from human gaze measurement experiments during natural scene observation. We also apply similar methods to analysis of cellular images, particularly targeting temporal changes in cellular morphology. We further proceed with developing sparse modeling and new MEG source localization methods aiming at suppression of information spreading, and apply them to real data to examine their methodological validity.

2. Research Achievements

2. 1 Book, non-refereed articles and translation

(1) Miyawaki Y. 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, 2017.

2.2 Invited lectures

(1) Miyawaki Y. Application of machine learning for analysis of functional neuroimages and cellular morphology. Neurovascular Unit research meeting 2018, Daiichi Sankyo Co., Ltd. (Chuo-ku, Tokyo), January 2018.

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

(3) Miyawaki Y, Ito N, Sato M, Kabashima Y. Inferring informative brain areas by sparse feature selection. The 40th Japan Neurosceience Society, Makuhari Messe (Mihama-ku, Chiba), July 2017.

(4) Miyawaki Y. 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 2017.

2.3 Student guidance

(1) Naoki Ishibashi, 2017, Bachelor（Engineering）
(2) Ryo Hidano, 2017, Bachelor（Engineering）
(3) Kenichi Inayama, 2017, Bachelor（Engineering）
(4) Sosuke Tanaka, 2017, Master（Engineering）
(5) Shotaro Fuchibe, 2017, Master（Engineering）
(6) Yuta Suzuki, 2017, Master（Engineering）
(7) Jiahao Wu, 2017, Master（Engineering）
(8) Masashi Sato, 2017, withdrawal from Ph.D. course with the completion of course requirements（to obtain Ph.D. in 2018）

2.4 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，2017/4－2018/3.
(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.

2.5 Study abroad programs for students

(1) Shota Eto，Nanyang Technological University，2017/9－2017/10（International internship）.

3. Research funding

3.1 Grant-in-aid for scientific research

(1) Miyawaki Y.（PI）Integrative research of dynamics of gaze shift and visual object recognition in natural scene. Grant-in-Aid for Scientific Research (B), FY2017- FY2020.
(2) Miyawaki Y.（PI）Visualization of cellular morphological features and their pathological changes using deep neural network. Grant-in-Aid for Scientific Research on Innovative Areas “Multidisciplinary Computational Anatomy”, FY2017- FY2018.
(3) Miyawaki Y.（PI）Analysis of human brain activity at high spatio-temporal resolution and identification of informative brain areas using sparse modeling. Grant-in-Aid for Scientific Research on Innovative Areas “Sparse modeling”, FY2016- FY2017.
(4) Miyawaki Y.（Co-PI）Controlling artificial limbs as own limb: natural learning of artificial limbs using human brain activity. Grants-in-Aid for Challenging Exploratory Research, FY2015- FY2016 (extended to FY2017).
(5) Miyawaki Y.（PI）Study of tactile information representation in the visual cortex using neural decoding technique. Grant-in-Aid for Scientific Research (C), FY2014-FY2016 (extended to FY2017).

3.2 Competitive external research funding

(1) Miyawaki Y.（PI）Research on dynamics of real world recognition under natural condition using neural information analysis at high spatio-temporal resolution. PRESTO, Japan Science and Technology Agency (JST), FY2017 – FY2020.

(2) Miyawaki Y.（PI）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) Miyawaki Y.（member）Inami JIZAI body project," ERATO, Japan Science and Technology Agency (JST), FY2017 – FY2022.

*No research expense is provided to research organization (The University of Electro-Communications) in FY2017.

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) Peter Bandettini, National Institutes of Health/National Institute of Mental Health (national institute), Measurement and analysis of human brain activity signal using ultra-high-field fMRI, FY2017 -

(2) 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-

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

(4) 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-

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

(6) 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) Reviewer of IEICEJ

(3) Cognitive Computational Neuroscience 2017 review committee

(4) Review committee of the 27th Annual Conference of Japanese Neural Network Society

(5) 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 Tokyo University of Foreign Studies

(4) Secretary of the 1st research meeting of next generation brain-like artificial intelligence (representative)

(5) Secretary of the 2nd research meeting of next generation brain-like artificial intelligence (representative)

Hayaru SHOUNO Laboratory

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.

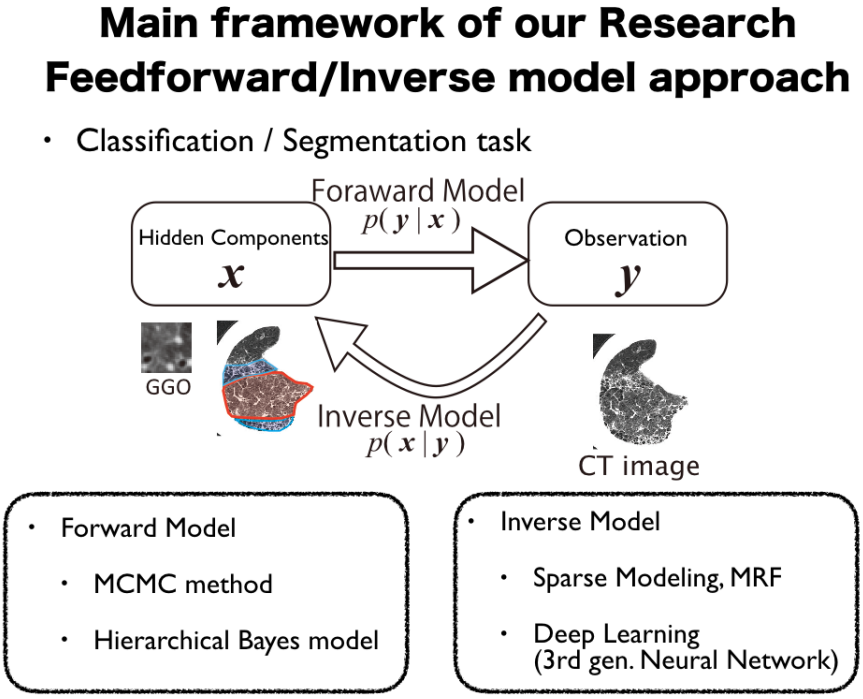


Figure1: Our laboratory applies forward/inverse model for the image restoration, classification, generation and so on. Especially, our target is in medical imaging. In order to drive each model, we use several sophisticated tools.

1.2 State of Progress in Research and Education (April, 2017 - March, 2018)

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

Deep convolutional neural networks (DCNNs) are inspired from the vision system. We train the DCNN using the transfer-style learning, which introduce some other domain's knowledge into the learning machine. Our laboratory has been tried to apply this method into diffuse lung disease (DLD) pattern

classification. From FY2015 to FY2016, we extend the transfer style method in 2 stage transfer. 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. In FY2017, we evaluate the system robustness, that is, the transfer-style learning is efficient for the less size of dataset. As the result, the 2-staged transfer shows the more robust rather than the other methods. Moreover, we investigate what the feature is obtained in higher feature detector in those DCNNs. We apply several back-projection methods called Deconvnet, Salinet, and DeSalinet, which are using for visualization of detected features. Using these visualization methods, we confirm simple lung disease dataset is not enough to train the modern DCNN.

(2) Feature selection method for DLD classification.

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.

(3) Generative Model of Textures Using Hierarchical Probabilistic Principal Component Analysis

Modeling of textures in natural images is an important task to make a microscopic model of natural images. Portilla and Simoncelli proposed a generative texture model, which is based on the mechanism of visual systems in brains, with a set of texture features and a feature matching. On the other hand, the texture features, used in Portillas' model, have redundancy between its components came from typical natural textures. We propose a contracted texture model which provides a dimension reduction for the Portillas' feature. This model is based on a hierarchical principal components analysis using known group structure of the feature. In the experiment, we reveal that effective dimensions to describe texture is fewer than the original description. Moreover, we also demonstrate how well the textures can be synthesized from the contracted texture representations

1.3 Future Plan

We try to 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 Reviewed papers

1) Sasaki H, Gutmann MU, Shouno H, Hyvärinen A. Simultaneous estimation of nongaussian components and their correlation structure. *Neural Computation* 29(11): 1-38, 2017.
2) Suzuki S, Shouno H. Support vector machine histogram: New analysis and architecture design method of deep convolutional neural network. *Neural Processing Letters* 47: 767-782, 2018, First Online: 03 July 2017.

2.2 Book, non-refereed articles and translation

1) AI 白書 2017～人工知能がもたらす技術の革新と社会の変貌～，独立行政法人情報処理推進機構 AI 白書編集委員会 (編集)，1.2.3 節 脳における視覚系のモデル，角川アスキー総合研究所, (2017)

2.3 Invited lectures

1) 庄野逸，ディープラーニングと画像処理への応用，電気通信大学 100 週年記念行事スマートテクノロジーフォーラム 2017，Sep(2017)
2) 庄野逸， Medical Texture Image Classification using Deep Convolution Neural Network with Transfer Style learning，第 27 回日本神経回路学会シンポジウム「スパースモデリングの深化と高次元データ駆動科学の創成」，Sep.(2017)
3) 庄野逸， Texture classification on Medical CT image using Deep Learning，第 55 回日本生物物理学会シンポジウム「データ駆動科学が拓く新しい生命計測データ解析」，Sep.(2017)
4) 庄野逸,医用画像識別におけるスパース特徴選択手法について，電子情報通信学会ソサエティ大会「人工知能の数理モデル」，Sep.(2017)
5) 庄野逸，ディープラーニングを用いた医用画像工学応用，第 42 回光学シンポジウムチュートリアル「機械学習と光」，Jun.(2017)
6) 庄野逸，医療診断支援技術に向けての AI とディープラーニング : 現状と将来，第 73 回日本放射線技術学会総会学術大会，Apr.(2017)

2.4 Award

(1) IEEE Computational Intelligence Society Japan Chapter Young Research Award (IEICE Neurocomputing) A Generative Model of Textures using Hierarchical Probabilistic PCA.
(2) 第117回 情報処理学会 数理モデル化と問題解決(MPS)研究会ベストプレゼンテーション賞, Feature Representation Analysis of Deep Convolutional Neural Network using 2-staged Transfer Learning -An Application for Diffuse Lung Disease Classification

2.5 Student guidance

3 undergraduate students, 4 graduate students, 2 exchange students

2.6 Visit of oversea researchers and students

1 under graduate student, 1 graduate student

3. Research funding

3.1 Grant-in-aid for scientific research

(1) Grant-in-Aid for Scientific Research on Innovative Areas (Research in a proposed research area)

26120515

(2) Grant-in-Aid for Scientific Research on Innovative Areas (Research in a proposed research area) 26108002

(3) Grant-in-Aid for Scientific Research (C), 16K00328

4. Collaboration

4.1 Outside UEC

(1) Hidenori Sakanashi AIRC, National Institute of Advanced Industrial Science and Technology (AIST)

(2) Shoji Kido, Yamaguhi University

(3) Masato Okada, University of Tokyo

(4) Kenji Nagata, AIRC, National Institute of Advanced Industrial Science and Technology (AIST)

5. Outreach activities

5.1 Editor of academic journals

1) Neural Networks

2) IPSJ trans. mathematical modeling and its application

5.2 Paper review of academic journals

(1) Neural Networks

(2) IEICE transaction D

(3) IPSJ trans. mathematical modeling and its application

(4) Journal of the Physical Society of Japan

(5) Journal of Physics: Conf. Ser

Shinji MATSUDA Laboratory

1. Outline of Research and Education

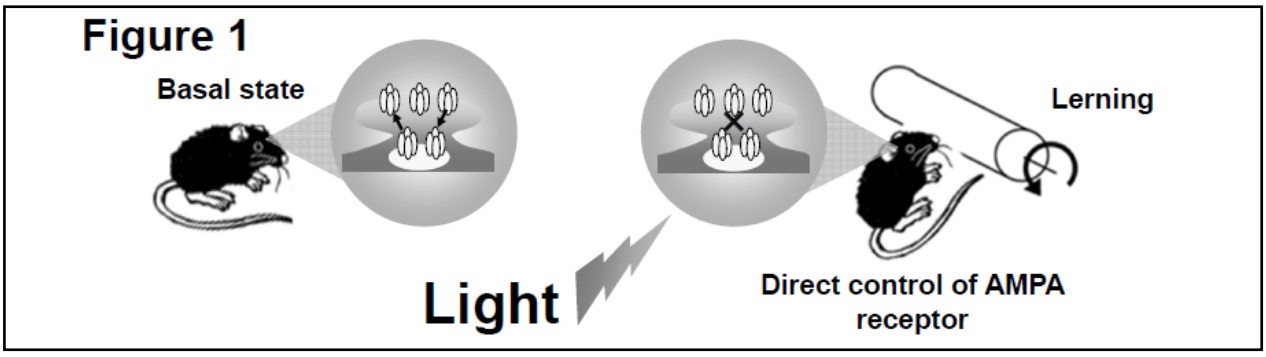
Synaptic plasticity, such as long term depression (LTD) and long term potentiation (LTP) has been proposed to the cellular basis for memory and learning. The molecular mechanism for LTD and LTP has been shown to be induced by the intracellular trafficking of AMPA-type glutamate receptor (AMPA receptor). However, it is not clear whether the AMPA receptor trafficking directly regulate the memory and learning. We tried to clarify the molecular mechanism for the intracellular trafficking of AMPA receptor and generate the technique which can control the trafficking of AMPA receptor. I would like to also bring up the students who can contribute to the progress of the science by researching neurons and synaptic plasticity.

1. 1 Basic Policy in Research and Education

Research

Brains are composed from an enormous number of neurons and Glial cells. The functions of the brain 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 also tried to develop the controlling method for LTP by controlling the function of lysosomes, which plays the essential roles for LTP induction.



Educations

I would like to bring up the students who can contribute to the progress of the science. For the

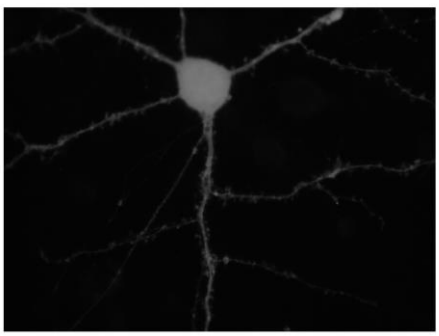
students in “Bioscience and Technology Program”, I am going to give lectures not only on neuroscience but also on the basic biology. Moreover, I will discuss with the students about how the basic knowledge of biology can be obtained and how life should be studied in the future.

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 State of Progress in Research and Education (April, 2017 - March, 2018)

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 postsynaptic site by neuronal activities. We have developed 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. We have submitted these results to Neuron. I also contributed to generate the chemical labeling method for AMPA receptors. We also generated the light driven proton pump which can targeted to lysosome which play essential roles for LTP induction.



Cultured neuron

Memory test of mouse

Figure 2

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）

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. We also try to control the LTP induction by using lysosomal targeted proton pump.

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 Communications.* 2017 Apr 7;8:14850. doi: 10.1038/ncomms14850.

2.2 Book, non-refereed articles and translation

(1) Principles of Neurobiology

2.3 Invited lectures

(1) Shinji Matsuda Optogenetical control of AMPA receptor endocytosis clarified that the cerebellar long term depression directly regulate motor learning. UK-Japan Neuroscience Symposium.

2.4 Student guidance

(1) Rikako Ito, Shunichi Koga, Ryusuke Suzuki: M1

(2) Shin-nosuke Kohara, Ichigo Saga, Takaya Mizoguchi: B4

3. Research funding

3.1 Grant-in-aid for scientific research

(1) Grant-in-Aid for Scientific Research (C)

4. Collaboration

4.1 Outside UEC

(1) Department of Physiology, Keio University School of Medicine

(2) Department of Physiology, Tokai University School of Medicine

(3) Department of Physiology, St. Marianna University School of Medicine

(4) Department of Anatomy, University of Fukui School of Medical Sciences

5. Outreach activities

5.1 Paper review of academic journals

(1) HELIYON

(2) Nature Communications

Measurement and monitoring of *in vivo* brain functions group

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.

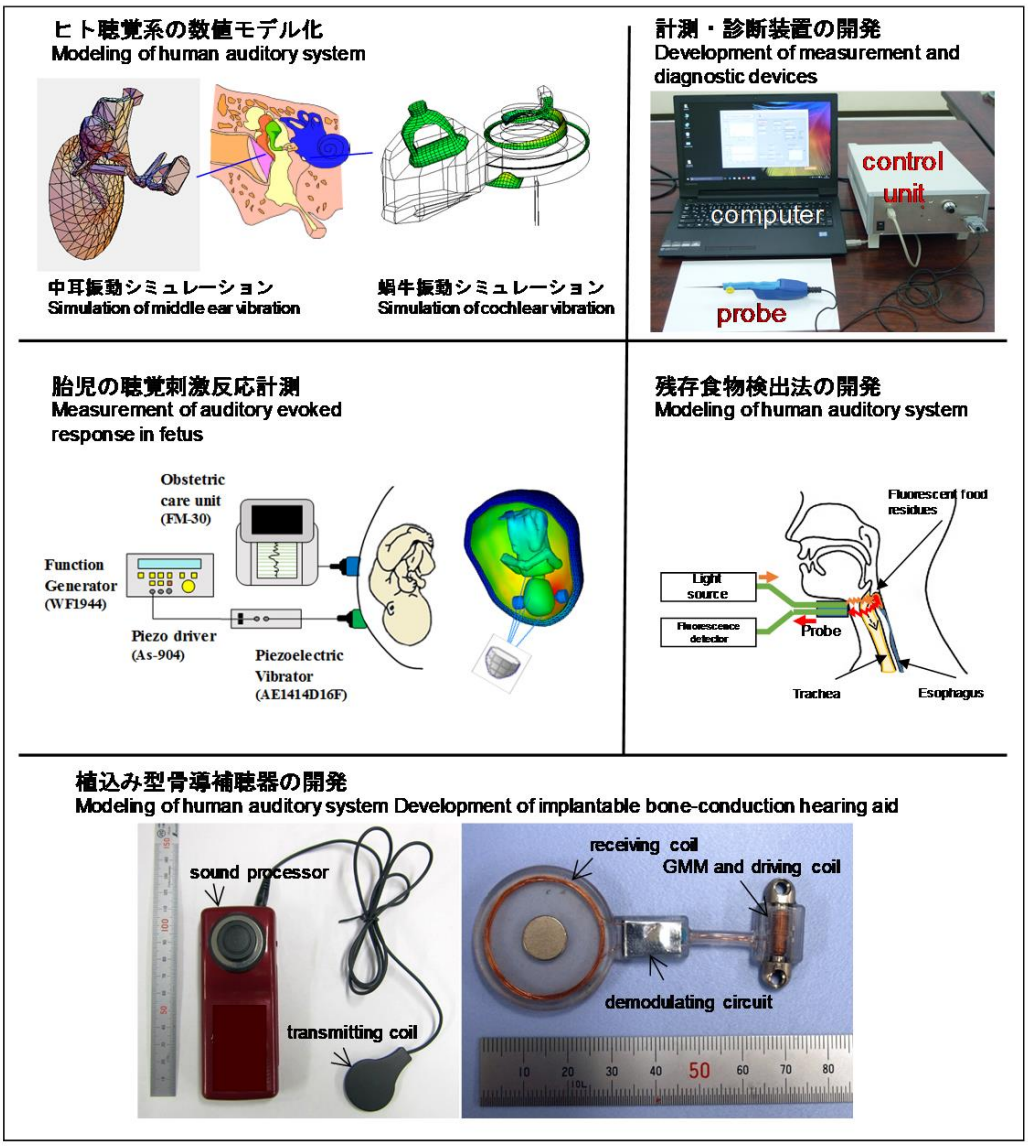


Figure 1　Researches in audiology

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.

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.

In addition, as collaborative research within the BLSC, educational research on the following research item was started.

- Aspiration risk detection using oral administration of fluorescent food; Development of a system for detecting the presence of residual food in the piriform sinus by detecting the fluorescence of the food from outside the body using near infrared light.

1.2 State of Progress in Research and Education (April, 2017 - March, 2018)

(1) Modelling of the auditory systems

Combining the finite element model of the cochlea with taking the amplification mechanism of the outer hair cells into account and the inner hair cell membrane potential model, the mechanical vibration of the basilar membrane generated by sound stimulation applied to the cochlea. We attempted to clarify how hair cells amplify the vibration of the basilar membrane and convert it to electric signals. As a result, due to the amplification mechanism of the outer hair cells, the basilar membrane shows the maximum amplitude at the site corresponding to the input frequency, and the change of the membrane potential of hair cells and the Ca^{2+} concentration show the maximum value at the site. Thus, it was suggested that the cochlea has a more sensitive frequency discrimination ability due to Ca^{2+} concentration change of inner hair cells in addition to the activity of outer hair cells. The Outstanding Presentation Award was given to the research from the

Society for Bioacoustics.

(2) Measurement of auditory evoked response in fetus

Toward the realization of audiometry in embryonic phase, we performed acoustic analysis using a finite-element model of fetus in maternal organs. In addition, measurements of brain wave fluctuation and heart rate fluctuation in fetuses when sound stimulation was given to the fetus from the outside of the maternal body were performed. As a result, the latency of the fluctuation in electroencephalogram measured from the maternal body surface was similar to the latency of the auditory evoked response, so it was considered that audiometry could be performed by measuring brain wave fluctuation. In addition, it was suggested that the target week of heart rate variability measurement should be 24 to 27 weeks.

(3) Development of implantable bone conduction hearing aid

Aiming at practical application of a bone-conduction hearing aid using Giant Magnetostrictive Material (GMM) as an implant transducer, we propose a new driving method of the transducer and made a prototype of the external unit. Magnetic field generated around the external unit was measured using a special made probe coil. The results suggest that the vibration generated by the implanted internal unit can be controlled by the current applied to the prototype external unit. In addition, the frequency characteristic was flat, and the SN ratio was also good. On the other hand, because the required electric power is larger than that of the commercially available bone-conduction hearing aid, power saving and realization of high efficiency are future tasks.

(4) Development of surgery assisting apparatus

We have developed a new type of the measurement device for ossicular mobility and measured the mobility of an artificial ossicles. In addition, the ossicular mobility and sound transmission characteristics of experimental animals were measured. The previous method for measuring ossicular mobility was modified and improved so that the measurements can be performed more stably. This research was supported by Strategic Core Technology Advancement Program 2017 (Supporting Industry Program), and was performed in collaboration with medical device manufacturers and neighboring medical institutions etc.

(5) Aspiration risk detection using oral administration of fluorescent food

Ingested food unconsciously remaining in the piriform sinus occasionally flows into the trachea leading to aspiration. If food remaining in the piriform sinus is noninvasively detected from outside the body, the risk of pulmonary aspiration can be evaluated. We developed a measurement method that can evaluate aspiration constitution non-invasively. Using a phantom, the maximum depth at which food can be detected was evaluated and factors that affect the maximum depth were investigated.

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. Regarding the aspiration prevention research, we are applying for ethical approval and will confirm whether residual foods can be detected from outside in patients who are actually at risk for aspiration.

2. Research Achievements

2. 1 Reviewed papers

(1) Matsuoka R, Lee S, Sato M, Hibiya R, Shimanuki Y, MKasai M, Kamiya K, Itakura A, Koike T, Ikeda K. Piezoelectric vibrator-stimulated potential and heart rate accelerations detected from the fetus. *International Journal of Pediatric Otorhinolaryngology* 101: 204-210, 2017.

(2) Lee S, Koike T. Simulation of the basilar membrane vibration of endolymphatic hydrops, *Procedia IUTAM*, 24: 64–71, 2017.

2.2 Invited lectures

(1) Takanashi T, Sakamoto H, Skals N, Fukui S, Matsui Y, Koike T, Nishino H. Vibration sensitivity in longicorn beetles and biomimetic potential for insect pest control, *International Symposium on Engineering Neo-Biomimeteics* VII, Feb. 17, 2017.

2.3 Patent

(1) PCT/JP2018/003162, System for evaluation of mobility and mobility evaluation method, Koike T, Takakuwa K, Irie Y, Kanzaki S, Keat CZ, Higo T, Hayashi M. Univ. Electro Communications, Keio Univ., Mechano Transformer Corp., Leadence Corp., Daiichi Medical Co., Date of application: January 31, 2018.

2.4 Award

(1) Sinyoung Lee, Outstanding Presentation Award, The Society for Bioacoustics, December 10, 2017

2.5 Student guidance

(1) Reiki Oishi, 2017 year, Bachelor
(2) Kengo Shibata, 2017 year, Bachelor
(3) Takaaki Fujishiro, 2017 year, Bachelor
(4) Daiki Fujiyama, 2017 year, Bachelor
(5) Kouta Kuroda, 2017 year, Master
(6) Miho Sato, 2017 year, Master
(7) Yuta Yoshimura, 2017 year, Master

3. Research funding

3.1 Grant-in-aid for scientific research

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

(2) Koike T. Grant-in-Aid for Scientific Research (C), 2017-2019

3.2. Competitive external research funding

(1) Koike T. Strategic Core Technology Advancement Program 2017 (Supporting Industry Program), 2017-2019

4. Collaboration

4.1 Inside BLSC

Yukio Yamada, Haruki Niwa, Takuji Koike, Shojiro Maki, Goro Nishimura (Hokkaiado Univ.), Yukihiro Michiwaki (Musashino Red Cross Hospital), Aspiration risk detection using oral administration of fluorescent food.

4.2 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

(4) Takuma Takanashi, Forestry and Forest Products Research Institute

5. Outreach activities

5.1 Editor of academic journals

(1) Journal of Biomechanical Science and Engineering

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) The 4th Annual Meeting of the Society for Bioacoustics, Chair

(2) The Society for Bioacoustics, Director

(3) Audio-Technica Scholarship Foundation, Councilor

(4) Japan Audiological Society, Terminology committee member

Hiroshi Yokoi/Yinlai Jiang/Togo Shunta Laboratory

1. Outline of Research and Education

1. 1 Basic Policy in Research and Education

The main aims of the Yokoi/Jiang/Togo 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.

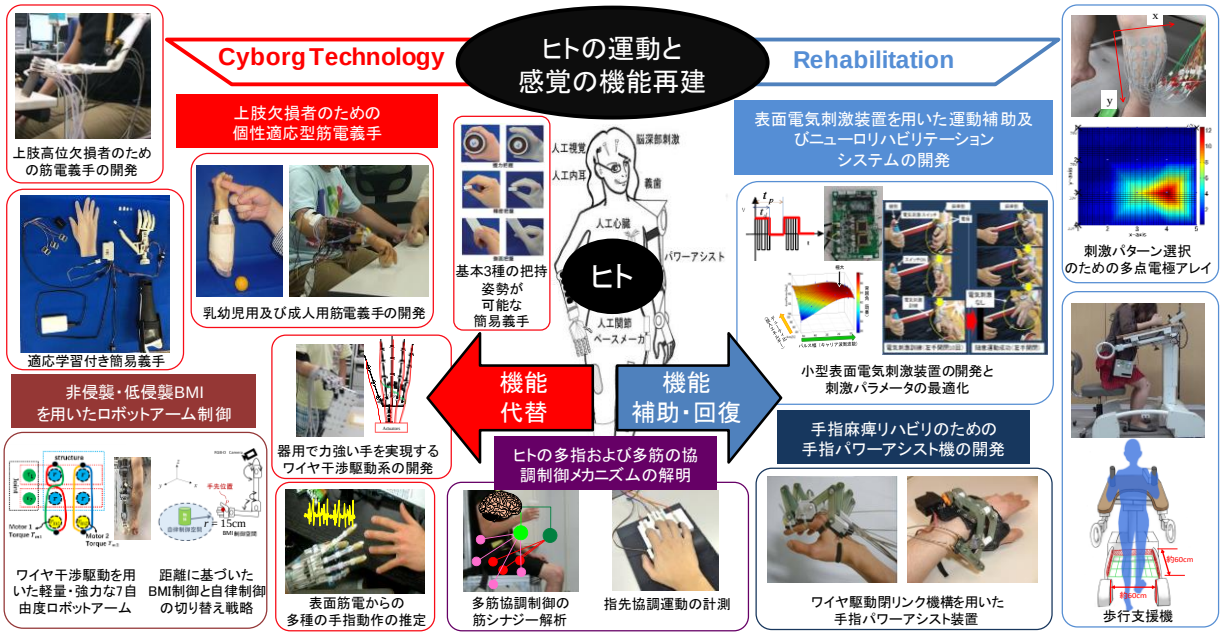


Fig.1 Research outline

1.2 State of Progress in Research and Education (April、 2017 - March、 2018)

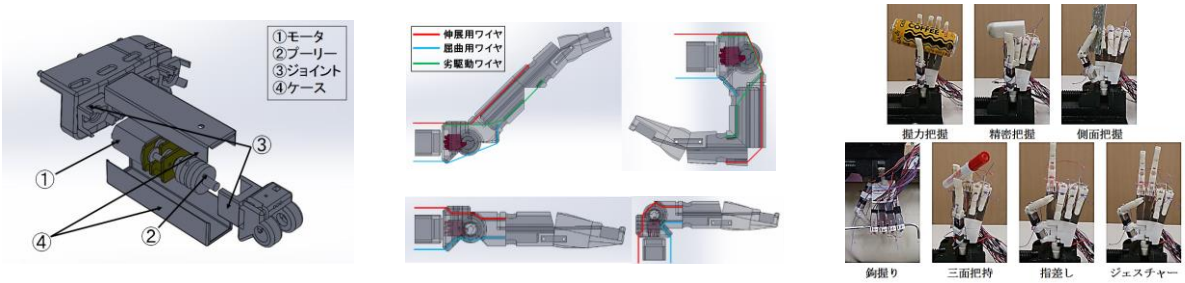
(1) Development of myoelectric prosthetic hand and application for registration of parts for completion

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 2017, we mainly developed a robotic hand with in-skeleton tendon-driven mechanism, a laminated EMG sensor, and a 4-DoF shoulder disarticulation prosthesis. An application was also made to the Ministry of Health, Labor

and Welfare for their registration as parts for completion. The application was approved.

a. Robotic hand with in-skeleton tendon-driven mechanism

Power grasp, precision grasp, lateral grasp, medium wrap grasp, tripod grasp, pointing and gesture are the most necessary hand function in daily life. It requires multiple degree of freedoms (DoFs) to realize all the 7 functions. The more joints a hand has, the more actuators are needed to drive them, thus lead to the increase of weight. We proposed an in-skeleton tendon-driven mechanism (Fig.2). The micro motor whose shaft is connected to a pulley is fixed between the MP joint and the wrist bone to embed the light weight and small tendon-driven mechanism into the palm. The under actuated PIP joint enables full finger flexion from horizontal posture. The robot hand with the proposed mechanism is 180g with 10 DoFs. It is confirmed the hand can perform all the 7 functions.



(a) in-skeleton tendon-driven mechanism (b) Tendon routing (c) 7 regular functions of hand

Fig.2. Robot hand with in-skeleton tendon-driven mechanism

b. Laminated EMG sensor using flexible conductive polymer (Tanac Co., Ltd.)

Dry electrodes are necessary to stably measure EMG signal from skin surface to control myoelectric hand. Previous studies of this lab have developed biocompatible hybrid electrodes with conductive silicon and metal wire. However, the exposure of the metal wire causes local pressures and leaves a mark on the skin after long time use. In FY 2017, we developed a laminated EMG sensor that encapsulates the metal wire(Fig.1). The lamination consists of conductive silicon layers with different percentages of carbon black. The gold-coated wire sandwiched in the layers is connected to the amplifier. The concentration of carbon black of the silicon layer attached to the metal wire was 4%. The concentration of carbon black of the silicon layer attached to the skin was investigated. The experimental results suggested that the silicon layer of 2.6% carbon black obtained the most stable EMG measurement.

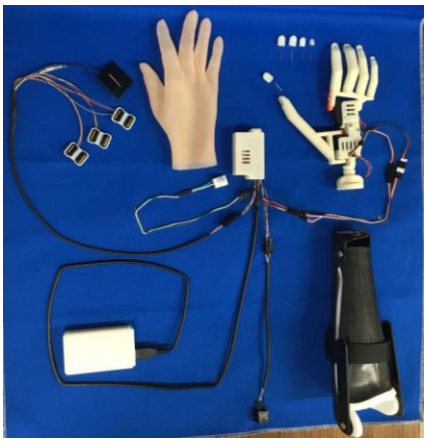
(a) Section view of the electrode (b) sEMG sensor

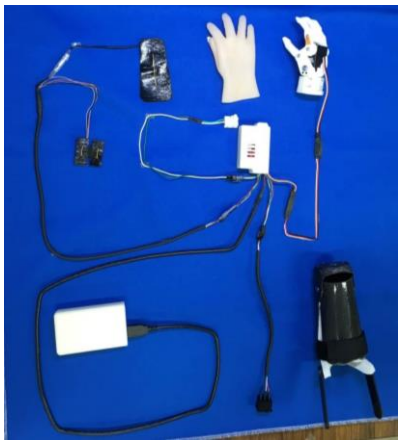
Fig.3. Laminated EMG sensor using flexible conductive polymer

c. Application for registration as parts for completion（Yokohama Nation University, Tokai University, National Center for Child Health and Development, eHand(NPO)）.

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. From FY 2016, we carried out clinical tests on subjects suitable to take part in trials, based on the judgements of medical institutions. The experiments on adult subjects were carried out at the Tokai University Hospital, and the experiments on minor subjects at National Center for Child Health and Development. In FY 2017,

according to the comments on the application of last year, we improved the prosthetic hand for adults and minors that are low cost, safe, and utility, and applied to the Ministry of Health, Labor and Welfare for their registration as parts for completion. The application of the prosthetic hand for adults was approved.



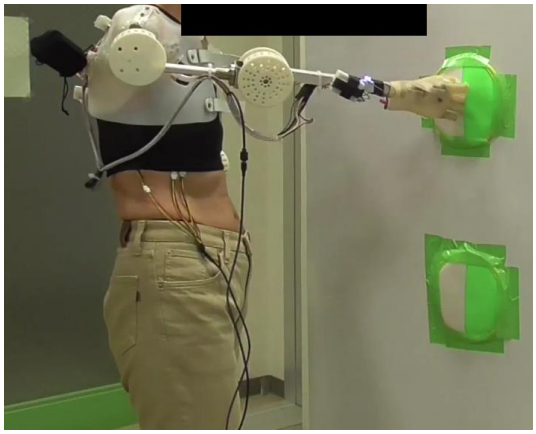


(a) 2 DoFs prosthetic hand for adults （b） 1 DoFs prosthetic hand for minors

Fig.4 Prosthetic hands for parts for completion と臨床試験の様子

d. 4-DoF shoulder disaticulation prosthesis（JR Tokyo General Hospital）

A shoulder disaticulation prosthesis controlled by the EMG of trunk were developed for an amputee with both shoulders disacticulated. By applying the design concept and control method of the prosthetic hand, the shoulder disaticulation prosthesis was developed for intuitive use without requiring longtime training (Fig.5(a). In FY 2017, we stabilized the EMG measurement with the laminated EMG sensor, and carried out evaluation experiments. The adapted the laminated EMG sensor to measure the EMG signal from the trunk by adjusting the shape and size. Furthermore, water proof and resistance to sweat were realized by covering the sensor with silicon case. The influence of ECG was reduced by signal processing. An evaluation experiment of pick-and-place a soft ball from a wall was carried out (Fig. 5(b)). The subject successfully moved the ball vertically 3 times and horizontally twice thanks to the signal stabilization.



(a)4 DoF shoulder disaticulation prosthesis (b) Scene of the experiment

Fig. 5 4 Shoulder disaticulation prosthesis

Besides the a.～d. mentioned above, a parent wireless assistive interface of myoelectric prosthetic hands for children (Fig.6) and prosthesis for partial amputation (Fig.7) were also developed in FY 2017.

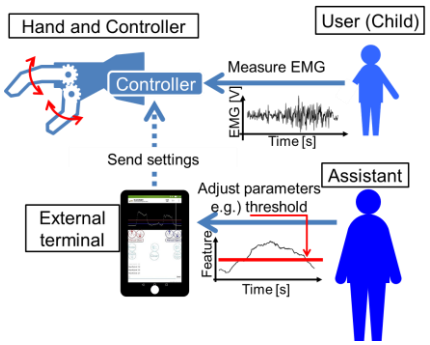


Fig. 6 Parent wireless assistive interface

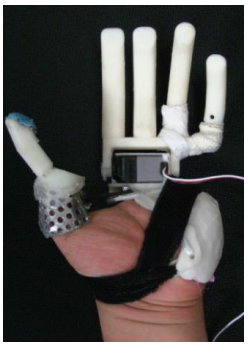
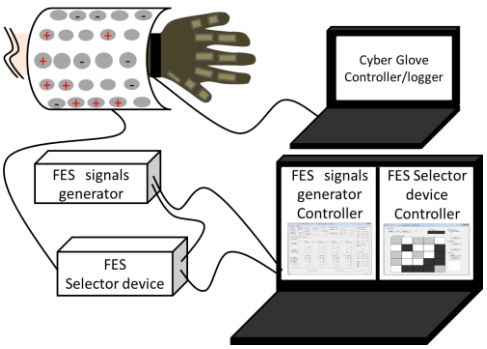
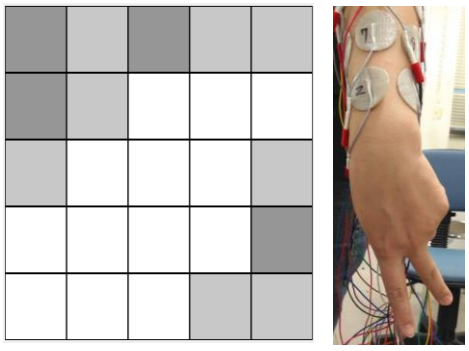


Fig.7 prosthesis for partial amputation

(2) A Search Method of Electrode Patterns for Use in Electrical Stimulation Using Multichannel Surface Electrodes（System Instruments Co.,Ltd）

The purpose of this study was to develop an arm exercise function recovery system based on surface electrical stimulation using multi-channel electrodes (Fig.8(a)) for a patient to undergo rehabilitation without assistance at home. As the training equipment, we used functional electrical stimulation (FES) with surface electrodes, which is a non-invasive method. Stimulating a specific muscle is difficult using FES with surface electrodes. Therefore, we traced an electrode pattern including many electrode points to achieve appropriate stimulation. In the case of multi-channel surface electrodes, we considered that there should be as many electrode patterns as possible. We used the electrode pattern that had the highest estimated joint precision obtained by estimating joint angles using an artificial neural network (Fig.8(b)). We identified the electrode patterns that evoked exercise, and found around 17 to 31 clusters of finger and hand positions. These findings suggest that a variety of exercises can be evoked without assistance. Based on the clustering result, we made a table of the required positions and the corresponding electrode patterns. Using this table, a patient can easily find the pattern appropriate to the desired position.





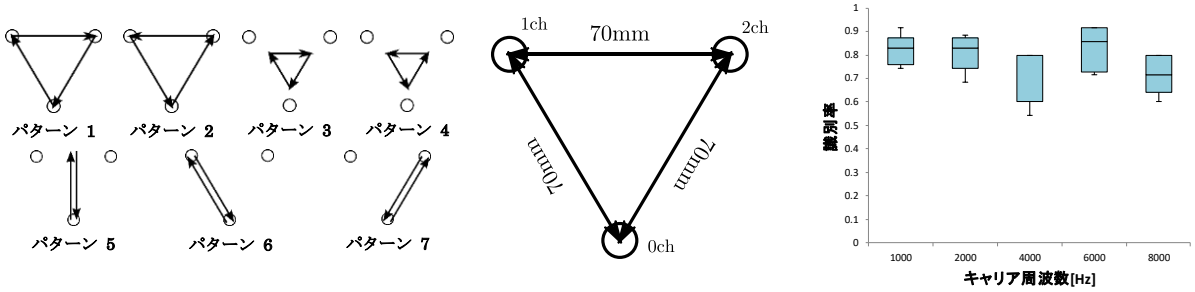
（a） Multi-channel FES　　(b) An example of pattern search

Fig.8　Automatic stimulation pattern search for multi-channel FES

(3) FES induced phantom sensation for sensory feedback.

FES induced phantom sensation is the phenomenon that only one stimulus is sensed inbetween the two stimulating points. It has been utilized as a method for sensory feedback available with a small

number of electrodes. The sensible stimulus point is adjacent to the stimulating point with stronger stimulation. 2 dimensional phantom sensation has been realized with 3 stimulating electrodes. In FY 2017, we searched the carrier frequency with high pattern recognition accuracy. The experimental results suggest that it is possible to find a carrier frequency in the high frequency domain with high pattern recognition accuracy. It is important to set the carrier frequency according to the presented pattern (Fig. 9).

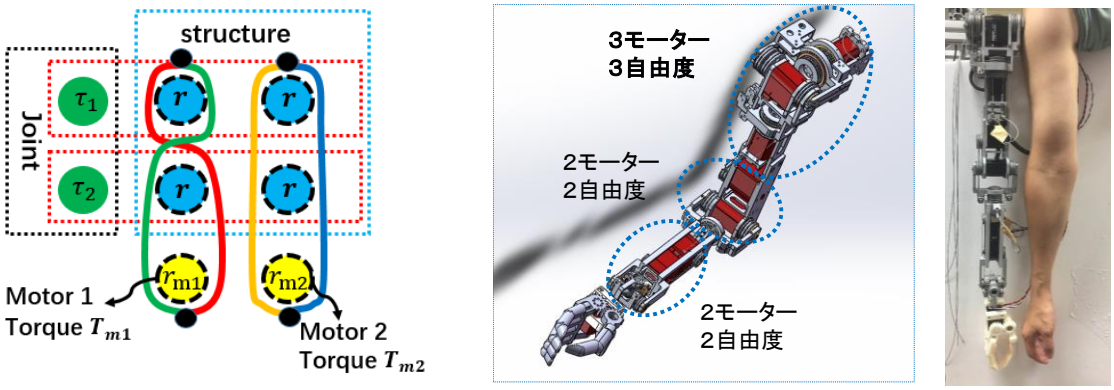


(a) 7 patterns presented in the experiment (b) Pattern recognition accuracy

Fig.9 Phantom sensation with FES

(3) Robotic arm development with tendon-driven joint modules（Shenyang University of Technology, Shanghai Jiao Tong University）

Tendon driven mechanisms have been studied as a promising option for the design of robot arms since they allow the freedom of motor position and weight allocation, and provide high safety with the flexibility of tendons. Meanwhile, challenges still exist when using coupled tendon-driven mechanisms. One is that the mechanism becomes complex when the degree of freedom (DoF) increases. Another challenge is the difficulty of maintaining the tendons. To solve these challenges, coupled tendon-driven joint modules are proposed and an anthropomorphic robot arm was developed using the proposed modules (Fig.10). There were 7 DoF in the anthropomorphic robot arm, which is the same as a human arm. The robot arm weighed 2.2 kg, including the robot hand and not including the power supply and the control system. It could pick up a 1.5 kg load with full outreach as illustrated in the supplementary video. This is the lightest 7 DoF anthropomorphic robot arm with a payload of 1.5 kg.

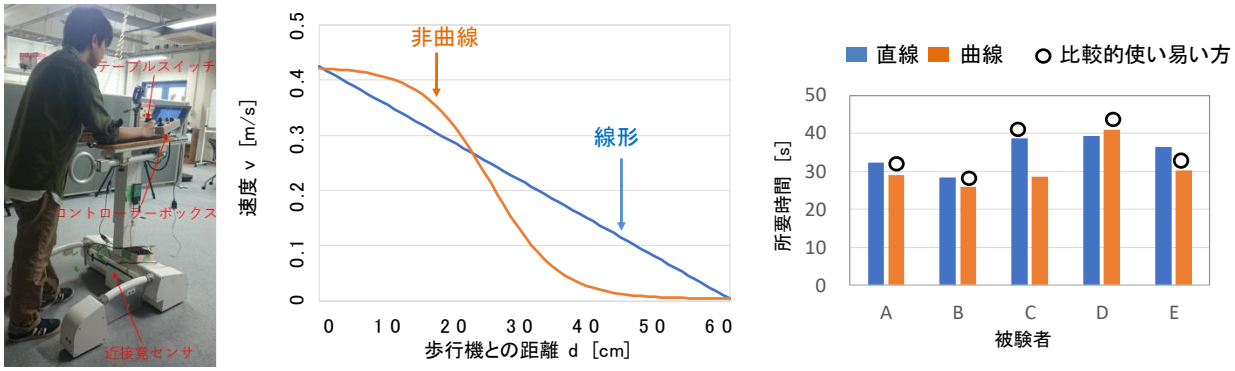


(a) 2-motor-2-DoF joint module (b) 7 DoF Anthropomorphic robot arm

Fig.10 Anthropomorphic robot arm using coupled tendon-driven modules.

(4) Gait analysis at the time of using the walking support machine（NSK Ltd.）

The lack of caregivers in an aged society with low birth rate has become a serious social problem. The independent living ability of elderly people are expected, and walking ability is necessary to live an independent life. We are developing a walking assistive robot that can be adapted to the user's walking condition. This study uses proximity sensors, which were attached to the front of the walking support robot, to measure the walking of a user gait analysis and control of the robot according to the gait. Gait analysis was performed based on the relative distance of the user's leg to the inner front of the robot. (Fig. 11(a)). In FY 2017, we compared two speed control methods: one is to control the speed linearly according to the distance between legs and the walker; the other is to control the speed considering the speed change of legs in a gait cycle (Fig.11(b)). The experimental results showed that subjects walked more smoothly by considering speed change of legs.



(a)Walking Support Machine (b) Distance based speed control (c)Experimental results

Fig.11 Speed control using proximity sensor

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

Journal articles

(1) Yamanoi Y, Morishita S, Kato R, Yokoi H. Development of myoelectric hand that determines hand posture and estimates grip force simultaneously. *Biomedical Signal Processing and Control* 38: 312-321, 2017. https://doi.org/10.1016/j.bspc.2017.06.019.

(2) Kasuya M, Morishita S, Jiang Y, Sugi M, Yokoi H. Development of a search method of electrode patterns for use in electrical stimulation using multichannel surface electrodes for upper limb motor function recovery in patients with paralysis. *Transactions of Japanese Society for Medical and Biological Engineering* 55 (5): 193-204, 2017. (in Japanese) https://doi.org/10.11239/jsmbe.55.193.

(3) Togo S, Imamizu H, "Empirical evaluation of voluntarily activatable muscle synergies", *Frontiers in Computational Neuroscience* 11 (82): 2017. | https://doi.org/10.3389/fncom.2017.00082.

International conference proceedings

(1) Jiang Y, Murai Y, Kuwahara T, Togo S, Yabuki Y, Yokoi H. Conductive silicon based sEMG sensor for myoelectric control of prosthetic hands: Structure design and evaluation", The 2017 IEEE

International Conference on Real-time Computing and Robotics (IEEE RCAR 2017), Okinawa, Japan, 2017.

(2) Mizuochi C, Yabuki Y, Mouri Y, Togo S, Morishita S, Jiang Y, Kato R, Yokoi H. Real-time cortical adaptation monitoring system for prosthetic rehabilitation based on functional near-infrared spectroscopy. 2017 IEEE International Conference on Cyborg and Bionic Systems (CBS 2017), pp130-135, Beijing, China, October 17. 2017.

(3) Murai Y, Yabuki Y, Ishihara M, Takagi T, Takayama S, Togo S, Jiang Y, Yokoi H. Designs of tailor-made myoelectric prosthetic hand for trans-metacarpal amputations with remaining fingers and joint moving functions", 2017 IEEE International Conference on Cyborg and Bionic Systems (CBS 2017), pp119-124, Beijing, China, October 17. 2017.

2.2 Book, non-refereed articles and translation

(1) 横井 浩史，矢吹 佳子，東郷 俊太，姜 銀来，加藤 龍，杉 正夫，"電気刺激による運動と感覚の再生"，オーグメンテッド・ヒューマン，(株)エヌ・ティー・エス，2017．978-4-86043-515-8

(2) 横井 浩史，矢吹佳子,"手の百科事典"，朝倉書店，2017. 978-4-254-10267-3

2.3 Invited lectures

(1) Yinlai Jiang, Challenges of translating robotic prostheses from academia into practice, International Workshop on Intelligent Robots and Systems, Beijing, China, June 16, 2017.

(2) Hiroshi Yokoi, Lecture as the Director of UEC China Research and Education Center, Opening Event of UEC China Research and Education Center, 2017/10/19.

(3) 横井浩史，サイボーグ技術と医用福祉機械の展開，聖心女子大学，2017年11月8日

(4) 横井浩史，サイボーグ技術と医用福祉機械の展開，神奈川県立柏陽高等学校，2017年11月14日

(5) Hiroshi Yokoi, Mutual Adaptable Systems for Functional Recovery, Shanghai Jiao Tong University, 2018/3/9.

2.4 Media release

(1) NHK金沢放送 かがのとイブニング　ことじろうのこれってどいね？「もっと便利に！義手開発最前線」2017/06/09

(2) NHK金沢放送 おはよう石川　リポート「”義手の可能性を広げたい”学生たちの取り組み」2017/06/13

(3) テレビ朝日 テレメンタリー２０１７　その手で未来を～筋電義手とつかむ可能性～ 2017/08/27

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, Application No.2017-029981

(2) Rintaro Kamihira, Hiroshi Yokoi, Yinlai Jiang, Shunta Togo, Masao Sugi, FES system, and FES method The University of Electro-Communications, Application No.2017-074607.

2.6 Productization

(1) UEC-eHand（Myoelectric Prosthetic Hand for adults and for children）<for research purposes>

（Distributor：eHand(NPO)）

2.7 Award

(2) Best Student Paper Award, IEEE CBS 2017,Yuta Murai, Yoshiko Yabuki, Masahiro Ishihara, Takehiko Takehiko Takagi, Shinichiro Takayama, Shunta Togo, Yinlai Jiang, Hiroshi Yokoi: 2017.

2.8 Student guidance

(1) Yutaro HIYOSHI，2017，Master
(2) Naoyuki TANI，2017，Master
(3) Susumu KIMIZUKA，2017，Master
(4) Takaki Shimura，2017 , Bachelor
(5) Tomohiro Shimizu，2017 , Bachelor
(6) Takuma Harada，2017 , Bachelor
(7) Yuki Kuroda，2017 , Bachelor
(8) Kazuaki Matsumoto，2017 , Bachelor
(9) Naoya Matsumoto，2017 , Bachelor
(10)Kyouhei WAKAMATSU，2017 , Bachelor
(11)Takeru NIWATA，2017 , Bachelor

2.9 Visit of oversea researchers and students

(1) Dianchun Bai, Lecturer, Shenyang University of Technology， Nov. 27-Dec.10, 2017, Feb.6-13, 2018.
(2) Xiaoxiao Zhu, Postdoctoral fellow， Shanghai Jiao Tong University, Nov.27- Dec. 3, 2017.
(3) Donghui Zhao， Shenyang University of Technology， Nov. 1 - Dec. 28, 2017

2.10 Study abroad programs for students

(1) Yuki Kuroda, University of Vermont， Sep. 2017 – Feb. 2018

3. Research funding

3.1 Grant-in-aid for scientific research

(1) Yokoi H. (PI) Artificial hand with conductive silicon skin, Challenging Exploratory Research, 2016/4/1～2019/3/31.
(2) Jiang Y. (PI) Bio-adaptive sEMG measurement method for control of welfare machines， Scientific Research(C), 2016/4/1～2019/3/31.
(3) Yokoi H. (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) Yokoi H. (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) Yokoi H. (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) Togo S. (PI) Grant-in-aid for young scientist (B), Modelling of human multiple muscle control system focused on intuitive independent activation and its application to shoulder disaticulation prosthesis, 2017/4/1～2019/3/31.

3.2 Competitive external research funding

(1) Yokoi H. (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) Yokoi H. (PI) JST Sakura Science Program with Shanghai Jiao Tong University, Jul. 15 - 22, 2017.

4. Collaboration

4.1 Inside BLSC

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

4.2 Outside UEC

(1) Multi-channel FES for neuro-rehabilitation, System Instrument Co., Ltd., 2014/11/1～2018/3/31

(2) Development of myoelectric prosthetic hand, Meltin MMI, 2015/3/1～2018/2/28

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

(4) Haptic sensor and sensory feedback for myoelectric prosthetic hand, Panasonic Corporation, 2017/6/1～2018/3/30.

(5) Robot control algorithm using proximity sensor, NSK Co., Ltd., 2017/4/1～2018/3/31

5. Outreach activities

5.1 Editor of academic journals

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

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

5.2 Paper review of academic journals

(1) PLOS ONE, Frontiers in Neural Robotics, IEEE Sensors Journal, International Journal of Control, Journal of Japan Society for Fuzzy Theory and Intelligent Informatics, JACIII, IJAMECHS.

5.3 Other outreach activities

(1) Togo S, Yokoi H, Jiang Y. Myoelectric controller for human-machine integration system, Innovation Japan 2018.

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.

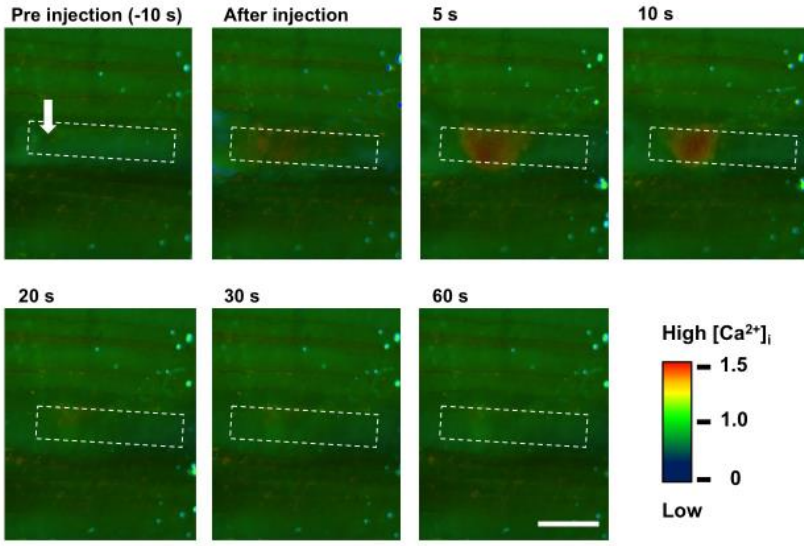
1.2 State of Progress in Research and Education (April, 2017 - March, 2018)

(1) In skeletal muscle fibers, voltage-induced Ca^{2+} release (VICR) is thought to be a major mechanism for promoting muscle contraction. On the other hand, cardiomyocytes clearly show that store-operated Ca^{2+} release (SOICR) contributes to muscle contraction. The physiological role of SOICR has not been elucidated as Ca^{2+} release system from the sarcoplasmic reticulum (SR) of skeletal muscle fibers. We observed Ca^{2+} microinjection combined with *in vivo* bioimaging technique to observe the phenomenon in which the cytoplasmic Ca^{2+} dynamics after direct Ca^{2+} injection are amplified. Furthermore, we clarified that SOICR is involved in this amplification.

(2) To elucidate the cytoplasmic Ca^{2+} buffering capacity by mitochondria, experiments were performed using genetically modified mice overexpressing PGC-1α (mitochondrial increased model). It was revealed that mitochondria has a buffering capacity to directly affect cytoplasmic Ca^{2+} dynamics in Ca^{2+} buffer after muscle contraction.

(3) The change in the pharmacological right shift of the hemoglobin oxygen dissociation curve to the peripheral oxygen supply demand balance was examined from the change in the oxygen partial pressure dynamics by the oxygen quenching method. In the rat of the claudication model (peripheral arterial disease, PAD), the increase in oxygen supply amount by the right shift and the fatigue resistance of the muscle contraction were revealed.

(4) In order to clarify factors of cellular stress causing muscle hypertrophy, we developed a blood flow restriction + muscle contraction stimulation model using rats. These models are useful as an experimental model for prevention and treatment of disuse muscle atrophy by aging and various diseases that induce muscle atrophy.



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) Watanabe A, Poole DC, Kano Y. The effects of RSR13 on microvascular PO2 kinetics and muscle contractile performance in the rat arterial ligation model of peripheral arterial disease. *J Appl Physiol* (1985). 2017 Oct 1;123(4):764-772. doi: 10.1152/japplphysiol.00257.2017.

(2) Eshima H, Miura S, Senoo N, Hatakeyama K, Poole DC, Kano Y. Improved skeletal muscle Ca2+ regulation in vivo following contractions in mice overexpressing PGC-1α. *Am J Physiol Regul Integr Comp Physiol.* 2017 Jun 1;312(6):R1017-R1028. doi: 10.1152/ajpregu.00032.2017. Epub 2017 Apr 24.

(3) Tomimatsu T, Miyazaki J, Kano Y, Kobayashi T. Photothermal imaging of skeletal muscle mitochondria. *Biomedical Optics Express* 8 (6): 2965-2975, 2017.

(4) Wakizaka M, Eshima H, Tanaka Y, Shirakawa H, Poole DC, Kano Y. In vivo Ca2+ dynamics induced by Ca2+ injection in individual rat skeletal muscle fibers. *Physiol Rep*. 2017 Mar;5(5). pii: e13180. doi: 10.14814/phy2.13180.

(5) 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.

(6) Hirai DM, Craig JC, Colburn TD, Eshima H, Kano Y, Sexton WL, Musch TI, Poole DC. Skeletal muscle microvascular and interstitial PO2 from rest to contractions. *J Physiol.* 2018 Mar 1;596(5):869-883. doi: 10.1113/JP275170. Epub 2018 Jan 30.

2.2 Student guidance

(1) Takuro Harada, Kohei Makino, Hiroki Tanaka, Ayaka Tabuchi; 2017 Bachelor (engineering)

(2) Masao Koizumi, Koji Hatakeyama, Aiko Watanabe 2017; Master (engineering)

2.3 Study abroad programs for students

(1) Aayaka Tabuchi, Kansas State University, 2017.8. - 2018.3.

3. Research funding

3.1 Grant-in-aid for scientific research

(1) Kano Y. (PI), Change of the muscle fiber type as the multinucleate cell, Grant-in-Aid for challenging Exploratory Research, 2015-2017, 3,770,000 yen.

(2) Kano Y. (PI), 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) Kano Y. (PI), Development of bioimaging technique to identify skeletal muscle fiber type in vivo, Grant-in-Aid for challenging Exploratory Research, 2017-2019, 6,240,000 yen.

3.2. Competitive external research funding

(1) The vehicle racing commemorative foundation, 2017, 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) Acta Physiologica, 2017

(2) Acta Physiologica Hungarica, 2017

(3) Diabetologia, 2017

(4) Biomaterials, 2017

(5) The Journal of Physiological Sciences、2017

(6) The Journal of Physical Fitness and Sports Medicine, 2017

(7) Microvasucular Research, 2017

(8) Journal of Running Science, 2017

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

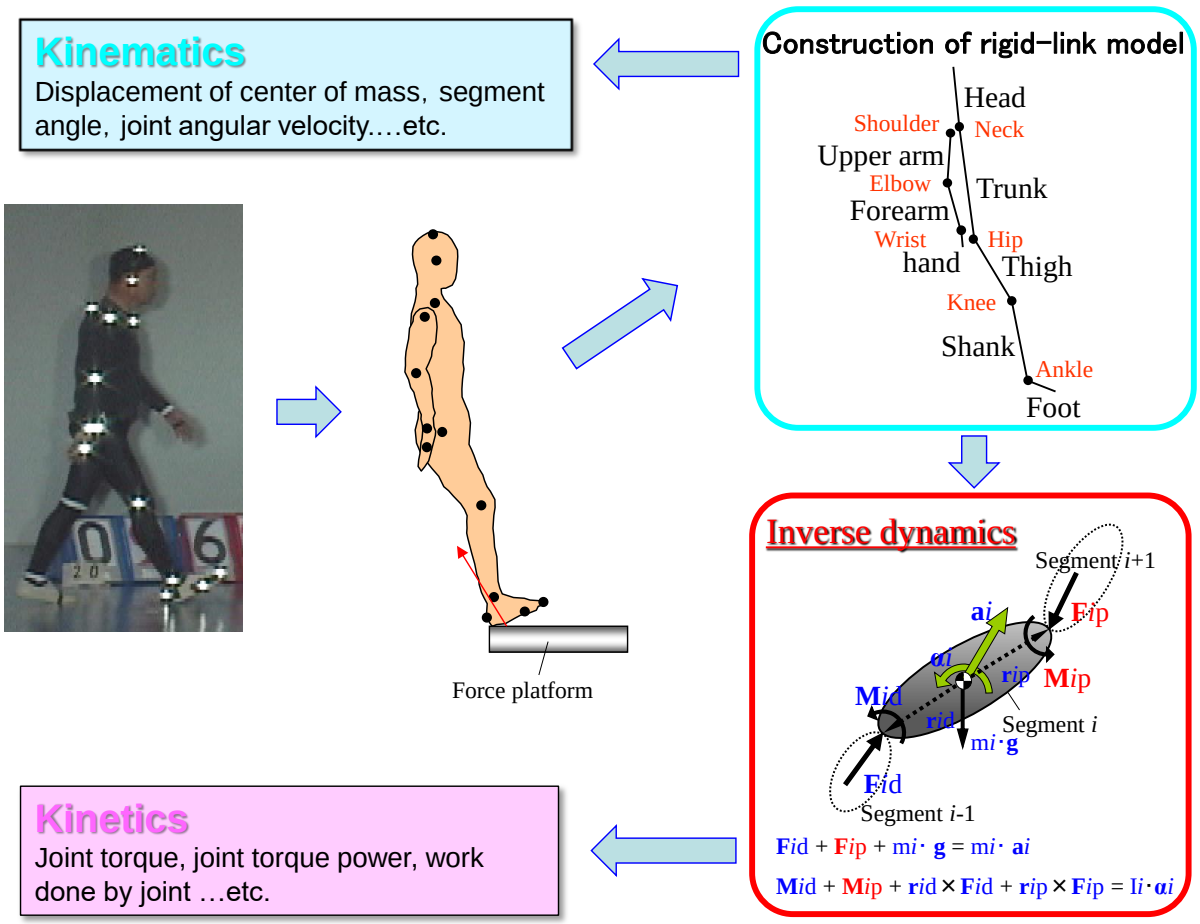


Figure 1 Outline of motion analysis

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 State of Progress in Research and Education (April, 2017 - March, 2018)

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

(1) Development of a walking motion biofeedback system using an inertial sensor

Among ADL (Activities of Daily Living), walking motion is the most important motion in daily life. Since walking motion changes with aging, maintaining walking ability by daily walking learning is thought to lead to an improvement in the quality of life. As an effective walking learning, it is considered effective to measure walking motion, quantitatively evaluate, and feedback improvement points to pedestrians. Although motion capture systems and video cameras are used to measure walking motion, it is not suitable for routine walking learning because there are restrictions on the measurement place and they are expensive. Therefore, it seems that routine walking learning becomes possible by using an inertial sensor which is inexpensive compared with a motion capture system and is portable, and is not limited to the place. In this study, we developed a walking motion learning system capable of measuring and analyzing stride characteristics and foot angle during walking in real time at a wide range of walking speed and feeding it back to the learner. We also evaluated its ability. This system consists of an inertial sensor, data transmitter, measurement control software, walking motion analysis program, and PC. In this system, the inertial sensor is attached to the heel. Stride characteristics and foot angle are estimated from the measured acceleration and angular velocity, and these can be fed back to the pedestrian in real time. As a result of testing the accuracy of the stride characteristics and foot angle estimated using this system, the stride characteristics were within the RMS error of about 5% through a wide range of walking speeds. As the walking speed decreased, the RMS error of foot angle increased, and it became the maximum near the peak value during a walking cycle. However, since high similarity of the foot angle waveform pattern between the true value and the estimated value is seen, it can be considered that estimation of the foot angle pattern is possible from this system. Regarding the feedback method of this system, both real-time auditory feedback and offline visual feedback are adopted, and it is considered that effective walking motion learning is possible by utilizing them in combination. In this research, we verified the immediate feedback effect of this system. As a result, in the case of using this system, the achievement rate of each parameter significantly increased in all evaluation parameter (walking speed, step length, step frequency) as compared with the case of verbal instruction. From this, it is considered that walking learning by immediate feedback using this system is a more effective learning method than verbal instruction.

(2) Research on margin evaluation of running motion

It is clearly different how the athletes run at Ekiden or marathon race and how the people running in parallel along the road for cheering are running. The running speed is the same for both, and even though the athletes are running overwhelmingly long distance, the general people running along the road seem to be

desperately running than the athletes. From this, it can be seen that even at the same running speed, the running motion between individuals varies greatly depending on the running ability of the individual. Therefore, it seems that we can judge how much motion margin is there (or how much motion margin is not there) by investigating the running motion. However, it is not clear what kind of motion is involved in the margin. If we can evaluate the margin of running motion objectively, it is considered that running ability can be inferred from the motion. In this research, the method of evaluating the margin of running motion was examined based on the biomechanical approach. Subjects are seven healthy men in their twenties who do not have track and field experiences. They ran 40 seconds for each nine speed set (120, 160, 200, 240, 280, 320, 360, 400, 440 m / min) using a treadmill. Using the optical motion capture system composed of 14 infrared cameras (OptiTrack S250e and OptiTrack Prime 13, Natural Point Inc.), the three-dimensional coordinates of retro-reflective markers attached to 49 body landmarks were captured at 200 Hz. For all the measured trials, the step length (SL), step frequency (SF), running ratio (SL / SF), stance time (ST), swing time (SW), percent stance time (%ST), percent swing time (%SW), the variability of joint angle and joint angular velocity (SD_θ, CVRMS_ω) during 10 cycles for each of the three lower extremity (hip (H), knee (K), ankle (A)), positive work(PW), negative work (NW), absolute work (ABW) during the swing phase for each of the lower extremity joints, joint contribution (% PW,% NW,% ABW), vertical excursion of CM (CMUD, CMUD/SL), medio-lateral excursion of CM (CMML, CMML/SL), total body work (Wwb), energy compensation (Twb), and energy compensation ratio (Twb / Wn) were calculated. From these parameters related to the running motion, a method of evaluating the margin of running motion was examined. As a result, there seemed a gap between subjective margin and objective margin. It was also suggested that the hip joint contribution in positive work during the swing phase and the stride characteristics may be important variables for evaluating the margin.

1.3 Future Plan

We will further analyze walking motion and consider the method of evaluating the degree of aging in walking motion based on the standard change in motion with age. We will also analyze the running motion and examine biomechanical factors to determine long-distance running performance and running economy.

2. Research Achievements

2. 1 Book, non-refereed articles and translation

(1) Okada H. Modeling of walking motion and its age-related change and remedial measures (Chapter 1 Section 2). In *Augmented Human*, pp. 25-31, NTS, Tokyo, 2018.

2.2 Invited lectures

(1) Okada H. Running economy and lower limb motion, lower limb muscle activity (Symposium "Running economy and performance"), The 30th conference of Society for Running, University of Tsukuba, March 31, 2018

2.3 Media release

(1) "Rational motion to dominate long-distance running", The Nikkei, March 28, 2018.

2.4 Patent

(1) Okada H. Walking motion evaluation device, walking motion evaluation method, and program, Japanese Patent Application No. 2017-215352, November 8, 2017.

2.5 Student guidance

(1) Tsuboi Y. 2017, Bachelor of Engineering

(2) Hirota K. 2017, Bachelor of Engineering

(3) Nishimura T. 2017, Master of Engineering

5. Outreach activities

5.1 Paper review of academic journals

(1) Japan Journal of Physical Education, Health and Sport Sciences

(2) Journal of Running Science

5.2 Other outreach activities

(1) Participation in administrative agencies as academic experts

· Vice Chairman of Chofu City Sports Promotion Council

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

· Running promotion subcommittee member, Promotion and development committee, Japan Association of Athletics Federations

· Chofu city kids running classroom (total 233 people)

· Fuchu city Junior Track & Field Classroom (total 160 people)

Norihiro KOIZUMI Laboratory

1. Outline of Research and Education

1. 1 Basic Policy in Research and Education

The expectation that intersections of various science and engineering technologies such as mathematics, information, control, artificial intelligence, robot technology, etc. in medicine and biology have enormous possibilities are rapidly expanding day by day. Bill Gates says, "If I were a student I would learn biology," Nicolas Negroponte said "Bio is new digitals." It is a very clear phrase to predict that biology will be reconstructed by fusion of bio and IT technology. In our laboratory, we study the medical digitization (Me-DigIT) in the field of medical ultrasound and core technologies for Me-DigIT.

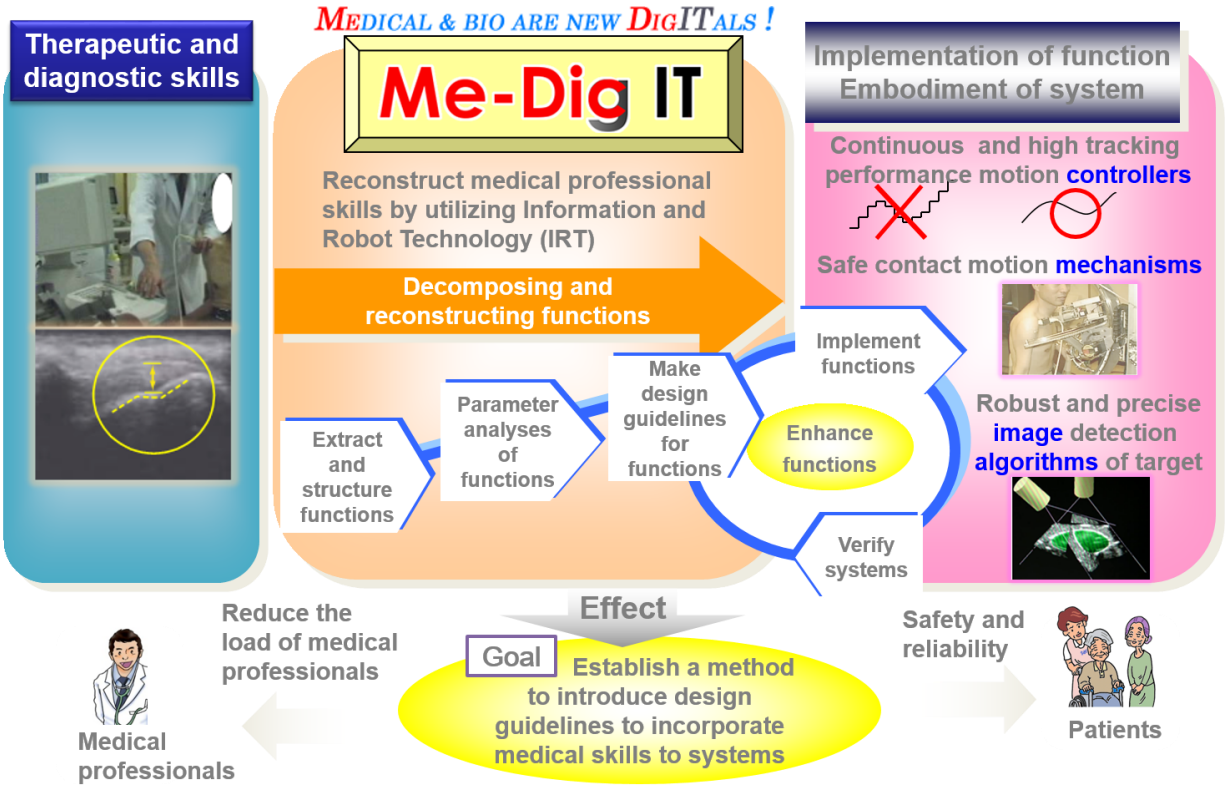


Fig.1 Concept of Medical DigITalization (Me-DigIT)

1.2 State of Progress in Research and Education (April, 2017 - March, 2018)

(1) Development of mechanism technology for Me-DigIT

We promoted the development and research of mechanism technology for Me-DigIT. As a result, we developed a compact portable ultrasound diagnostic robot for home healthcare. This robot is compact and lightweight, and even a woman can carry the robot without difficulty.

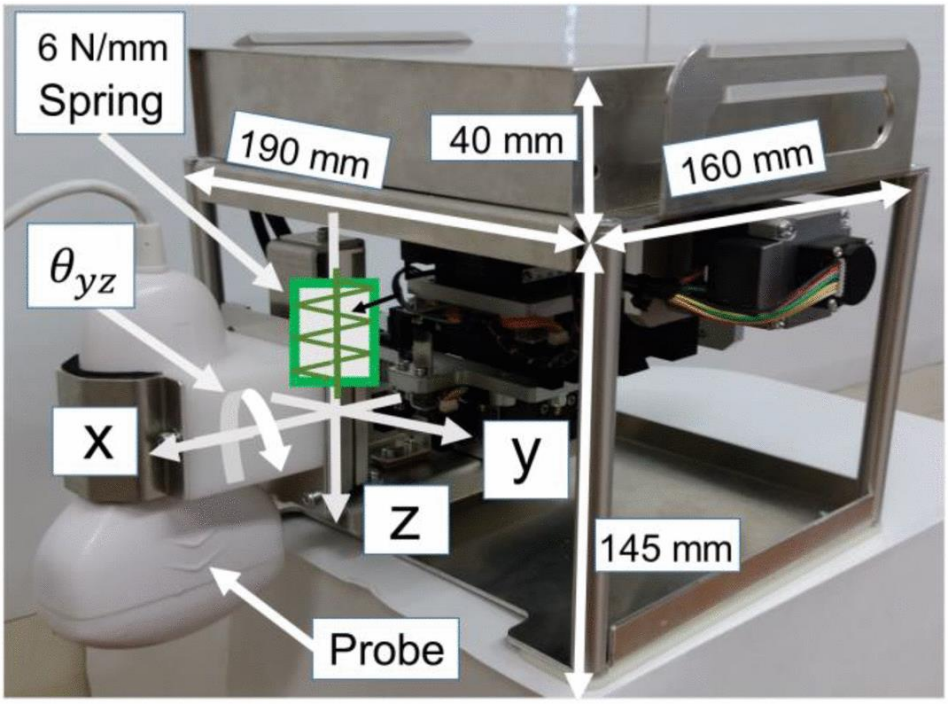


Fig.2 Compact portable ultrasound robot for home healthcare.

(2) Development of control technology for Me-DigIT

We promoted the development and research of control technology for Me-DigIT. As a result, we developed a compensation technique for respiratory body movement for c ompact portable ultrasound robot for home healthcare**.**

(3) Development of image processing algorithms technology for Me-DigIT

We promoted the development and research of image processing algorithm technology for Me-DigIT. As a result, we developed a technology that tracks the affected area with high accuracy while switching between multiple templates, and developed a technique to identify the contours of organs with high precision in real time.

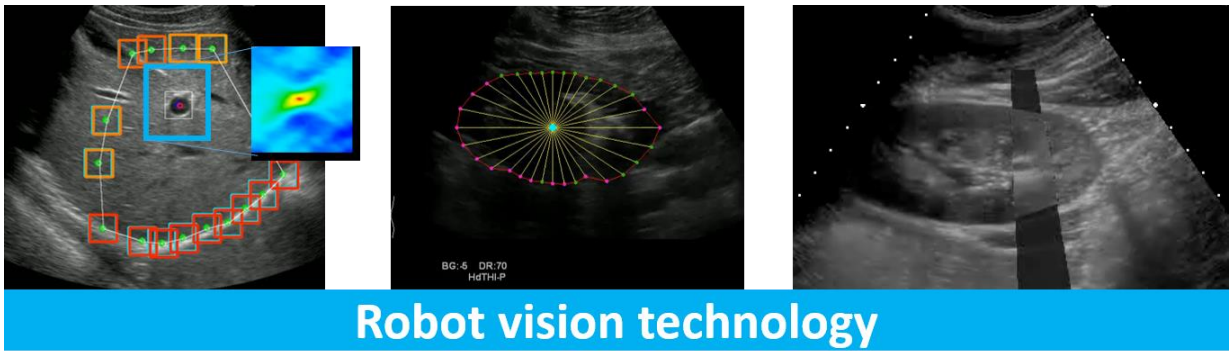


Fig.3 Robot vision technology for Me-DigIT.

1.3 Future Plan

In order to accelerate the realization of a ultra Me-DigIT society, we will promote research on mechanism, control and image processing algorithms, which is the core foundation technology for Me-DigIT. For this purpose, we will actively incorporate deep learning technology.

2. Research Achievements

2. 1 Reviewed papers

(1) Asano T, Kubota N, Koizumi N, Itani K, Mitake T, Yuhashi K, Liao H, Mitsuishi M, Takeishi S, Takahashi T, Ohnishi S, Sasaki S, Sakuma I, Kadowaki T. Novel and simple ultrasonographic methods for estimating the abdominal visceral fat area. *International Journal of Endocrinology* Volume 2017 (2017), Article ID 8796069, 12 pages, https://doi.org/10.1155/2017/8796069, 2017.

(2) Doba N, Fukuda H, Numata K, Hao Y, Hara K, Nozaki A, Kondo M, Chuma M, Tanaka K, Takebayashi S, Koizumi N, Kobayashi A, Tokuda J, Maeda S. A new device for fiducial registration of image-guided navigation system for liver RFA. *International Journal of Computer Assisted Radiology and Surgery* 2018 Jan; 13(1):115-124. doi: 10.1007/s11548-017-1647-9. Epub 2017 Jul 17.

(3) Fujii T, Koizumi N, Kayasuga A, Lee D, Tsukihara H, Fukuda H, Yoshinaka K, Azuma T, Miyazaki H, Sugita N, Numata K, Honma Y, Matsumoto Y, Mitsuishi M. Servoing performance enhancement by respiratory organ motion prediction model for non-invasive ultrasound theragnostic system. *Journal of Robotics and Mechatronics* 29 (2) 434-446, 2017.

2.2 Book, non-refereed articles and translation

(1) Kurihara S, Nagai T, Koizumi N, Utsumi A, Sakamoto M, Kuno M.Artificial intelligence and society: Future prospect of 2025, Ohmsha, Ltd., ISBN-13: 978-4274221811, 2018.2.15, in Japanese.

2.3 Invited lectures

(1) Koizumi N. Promotion of Medical DigITalization (Me-DigIT) and robotic medical ultrasound diagnostics and therapeutics, JST fair, Tokyo Big Sight 4th East hall, 2017.8.31.

2.4 Media release

(1) Medtec Online, Sharing medical world view utilizing robot and IT, 2017.06.27.

2.5 Patent

(1) US15/876233, 2018.1.22.

(2) US15/867302, 2018.1.10.

(3) JP2017-158071, 2017.8.18.

2.6 Student guidance

Master course students: 3, Bachelor students: 3

3. Research funding

3.1 Grant-in-aid for scientific research

(1) Ultrasound diagnostic and therapeutic system realized by Me-DigIT, Fundamental research (B), 2017.04.01-2021.03.31.

3.2 Competitive external research funding

(1) Development of next generation biological monitoring device using affected part following ultrasonic probe, Saitama prefecture New technology and product development subsidy, 2017.06.13-2018.02.28.

4. Collaboration

4.1 Outside UEC

(1) The Univ. of Tokyo, Yokohama City University, Nihon Univ., Tokai Univ.

Guanghao SUN Laboratory

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 State of Progress in Research and Education (April, 2017 - March, 2018)

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.

2. Research Achievements

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

(1) Matsui T, Shinba T, Sun G. The development of a novel high-precision major depressive disorder screening system using transient autonomic responses induced by dual mental tasks. *Journal of Medical Engineering of Technology* 2018 Feb;42(2):121-127. doi: 10.1080/03091902.2018.1435744. Epub 2018 Mar 23.

(2) Sun G, Matsui T, Watai Y, Kim S, Kirimoto T, Suzuki S, Hakozaki Y. Vital-SCOPE: Design and evaluation of a smart vital signs monitor for simultaneous measurement of pulse rate, respiratory rate and body temperature for patient monitoring. *Journal of Sensors* Volume 2018, Article ID 4371872, 7 pages https://doi.org/10.1155/2018/4371872.

(3) Sun G, Trung NV, Matsui T, Ishibashi K, Kirimoto T, Furukawa H, Hoi LT, Huyen NN, Nguyen Q, Abe S, Hakozaki Y, Kinh NV. Field evaluation of an infectious disease/fever screening radar system during the 2017 dengue fever outbreak in Hanoi, Vietnam: A preliminary report. *Journal of Infection* 75(6): 590-593 (2017).

(4) Yu W, Nakahata K, Huang SY, Sun G, Namiki A, Xie L, Wang J, Suwa S, Tsujimura M. Efficient active sensing with categorized further explorations for a home-behavior-monitoring robot. *Journal of Healthcare Engineering* Volume 2017, Article ID 6952695, 16 pages https://doi.org/10.1155/2017/6952695.

Conference proceedings

(1) Sun G. Vital sign acquisition in the national hospital of tropical diseases of Hanoi. *The 4th UEC Seminar in ASEAN*, 2018, Bangkok March 2, 2018.

(2) Negishi T, Sun G, Kirimoto T. An optical and thermal image fusion approach using estimated homography matrix for noncontact vital-sign measurements and its application to infectious disease screening system. *The 4th Annual Meeting of the Society for Bioacoustics*, 2017, Tokyo.

(3) Hashimoto T, Tsuji K, Yamazaki Y, Sun G. Estimation of autonomic nervous activity toward affective human-robot interaction. *The 2017 IEEE Symposium Series on Computational Intelligence*, 2017, Hawaii, USA.

(4) Yang X, Ishibashi K, Negishi T, Kirimoto T, Sun G. Short time and contactless virus infection screening system with discriminate function using doppler radar. *12th International Conference on Bio-Inspired Computing: Theories and Application*, 2017, Harbin, China.

(5) Yao Y, Sun G, Kirimoto T, Matsui T, Schiek M. Online state space filtering of biosignals using neural network-augmented Kalman filter. *The 10th Biomedical Engineering International Conference*, 2017, Hokkaido, Japan.

2.2 Book, non-refereed articles and translation

(1) Sun G「機械学習クラスタ解析を応用した感染症スクリーニングシステムの研究開発」第 5 章第 1 節：AI 導入によるバイオテクノロジーの発展, 2018.

2.3 Invited lectures

(1) 孫光鎬，松井岳巳，桐本哲郎「非接触バイタルサインセンシング技術とその医療応用」電子情報通信学会大会　2018.

2.4 Media release

[新聞] デング熱、その場で判別　電通大、精度90％超のシステム開発. 日刊工業新聞、2017.12.29.

[WEB] 非接触バイオセンシングによる感染症スクリーニング. MEDTEC Japan、2017.6.23.

2.5 Patent

(1) 孫光鎬・石橋 孝一郎・楊 小鳳「心拍・呼吸計測システム及び心拍・呼吸計測方法」特願 2017-133367，2017 年 7 月.

2.6 Student guidance

(1) Toshiaki Negishi (Bachelor)

(2) Mai Kobayashi (Master)

2.7 Visit of oversea researchers and students

(1) Dr. Yao Yu, University of Zurich and ETH Zurich, Switzerland.

(2) Dr. Liu He, Harbin University of Science and Technology, China.

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

4.1 Outside BLSC in UEC

(1) Ishibashi T.

(2) Kirimoto T.

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

(6) Frontiers in Physiology

(7) Sensors

(8) Frontiers in Neuroscience

(9) Journal of Sensors

Theoretical and computational neuroscience group

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, 4 graduate students took master's degrees in 2017. I would like to continue to guide graduate school students who can play an active part in the research field of computational neuroscience.

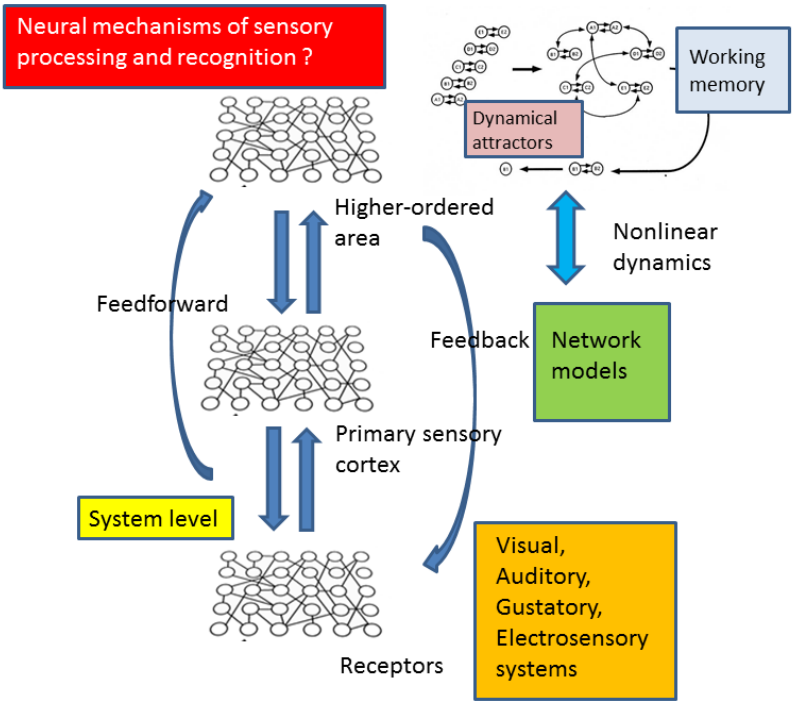


Fig.1 Two viewpoints in our work

1.2 State of Progress in Research and Education (April, 2017 - March, 2018)

(1) Evaluation of computational efficacy of a GPGPU method in calculating the dynamics of large-scale neural networks (collaborated with Komatsu University)

To investigate the neural dynamics of large-scale spiking neural networks, 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 could be an effective method for calculating large systems, compared with Open-MP method (Fig. 2). We also evaluated the accuracy of single-precision calculation for large-scale networks of various neuron models.

(2) Neural mechanism of working memory in visual categorization task

The ability to group items and events into functional categories is a fundamental function for visual recognition. Experimental studies have shown the different roles in information representations of inferior temporal (IT) and prefrontal cortices (PFC) in a categorization task. However, it remains elusive how category information is generated in PFC and maintained in a delay period, and how the interaction between IT and PFC influences category performance. We show that category information in PFC is represented by two dynamical attractors weakly linked, resulting from the difference in firing thresholds of PFC neurons. We also show that top-down signal from PFC to IT improves the ability of PFC neurons to categorize the mixed images that are located nearly at a category boundary (Fig. 3).

(3) Modeling study on the interaction between orbitofrontal cortex and amygdala in taste recognition

Taste recognition is not only information processing of chemical substances but also related with the processing of other sensory modalities such as vision and olfaction. It is also important for taste recognition to estimate the value of foods that is acquired by action of animals. Several brain areas, orbitofrontal cortex (OFC), amygdala (Amy), and sensory cortices are involved in the value estimation. However, it remains unclear what roles these areas play in the value evaluation. We focus on preferred and aversive behaviors of rats in taste recognition induced by odors, and offered the neural mechanisms by which taste evaluation and outcome expectation are performed via the interaction between OFC and Amy.

(4) Representation of object' shape by electric images in active electrolocation (collaborated with Komatsu University)

Electrosensory systems have simpler circuit structures compared with those in visual and auditory systems, and the sensory coding of electrosensory systems is well-defined. Thus the system provides an ideal system for investigating computational principles that may be common with those in visual and auditory systems. We explored how weakly electric fish perceive object's shape in active electrolocation. To this end, we developed a computational model for electric field near the fish and electric fields modulated by nearby objects. We used a finite-element-method to calculate these fields, and calculated the voltage differences across the fish skin, called electric images. We found that shape information is not represented by a single image but represented by multiple images acquired during exploratory behaviors of the fish.

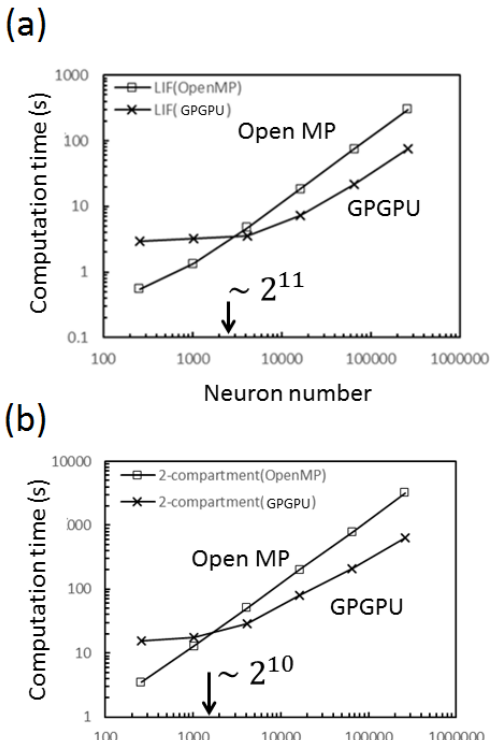


Fig.2 Comparison of computation time for two different methods. (a) Leakey integrate-and –fire neuron. (b) 2-compartment model Two methods is Open MP and GPGPU.

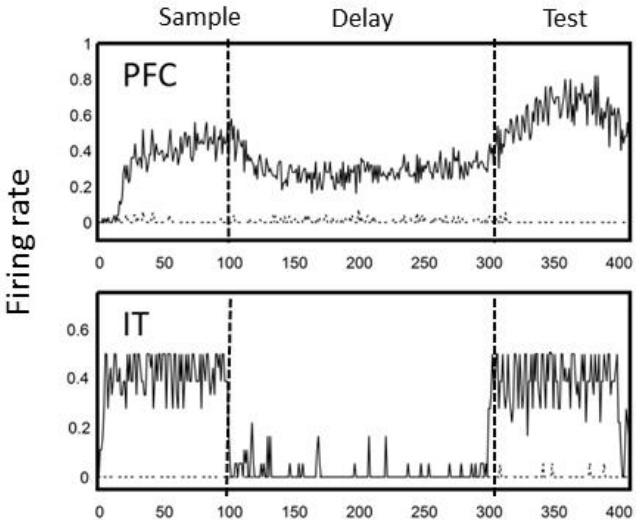


Fig.3 Temporal courses of firing rates of PFC and IT neurons during a dog/cat categorization task. The solid and dashed lines denote the activities of dog-and cat-selective PFC neurons, respectively (Top) and they denote the activities of dog- and cat-sensitive IT neurons (Bottom).

1. 3 Future Plan

(1) Roles of top-down signals in visual recognition

We can recognize rapidly and effortlessly complex visual scenes. Such amazing ability in visual recognition needs the effective processing of visual information along the multiple stages of visual pathways. Visual system has abundant feedback connections, whose number is even larger than the feedforward ones. However, it is poorly understood how top-down pathways contribute to visual recognition. We focus on the visual tasks by Li et al. (2004, Nat Neurosci). We study how top-down signals emerge in higher visual areas and how they influence on the activity of early visual areas. We also study the neuronal dynamics of early visual areas in the absence of stimulus, which is responsible for prediction of forthcoming stimulus.

(2) Functional roles of brain rhythms in visual recognition

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 (Li et al. 2004, Nat Neurosci). 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.

(3) Neural coding of information of object's shape in electrosensory system

We have studied the representation of object shape in electrosensory system in a project of Grant-in-aid for scientific research (2015-2017). 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. Using this method, we found that shape information are represented by an integration effect of the peak amplitude and half-maximum width of electric image. As the next step, we will study the neural coding of shape information in receptors and the hindbrain.

2. Research Achievements

2. 1 Reviewed papers

(1) Okuno S, Fujita K, Kashimori Y, Computational efficacy of GPGPU-accelerated simulation for various neuron models. *Lecture Notes in Computer Science* 10638: 802-809, 2017.

(2) Fujita K, Kashimori Y. Neural representation of object's shape at the electroreceptor afferents on electrolocation. *Lecture Notes in Computer Science* 10636: 877-884, 2017.

2.2 Award

(1) 2017 Research Excellent Award of the Japanese Neural Network Society (2017.09)

2.3 Student guidance

(1) Bachelors (2017)

Taihei Kosaka

Daiki Takaya

Boldbaatar Khuslent

(2) Master's degree: (2017)

Shun Okuno

Kenji Takei

Kazuya Sakurai

Ryo Tani

3. Research funding

3.1 Grant-in-aid for scientific research

(1) Kashimori Y. (PI) 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, Komatsu University, Cooperation researcher of the scientific research (see subsection 3.1).

5. Outreach activities

5.1 Editor of academic journals

(1) Cognitive Neurodynamics 2006~present.

5.2 Paper review of academic journals

(1) Cognitive Neurodynamics, 2017.06.

(2) Cognitive Neurodynamics, 2018.01.

**** Paper review of International conferences and domestic ones**

(1) The 14th International Conference on Natural Computation, Fuzzy Systems and Knowledge Discovery (ICNC-FSKD 2017).
Reviewing : 6 papers

(2) Annual meeting of the Japanese neural network society (2017).
Reviewing : 6 papers

1. Outline of Research and Education

1. 1 Basic Policy in Research and Education

A basic policy in education of this laboratory is to provide students with many opportunities to consider how they can address various types of problems in the contemporary neuroscience and to find their own solutions to the problems. For research, this laboratory aims at obtaining a better understanding of how the brain works. In 2017, we carried out theoretical research on (1) building an integrated theory of the self-organization of visual cortical orientation representations in different species such as cats and rodents, (2) elucidation of neural dynamics to generate auditory continuity illusion, (3) understanding of zero-lag synchronization in firing between remote neuron pairs and (4) understanding of functional roles of tripartite synapses under neuron-glia interaction. We also performed (5) the preparation of two-photon Ca^{2+} imaging of neurons in the primary visual cortex of mice and psychological experiments to find a possible utilization of the cocktail party effect in learning material. Figure 1 illustrates main research targets of this laboratory.

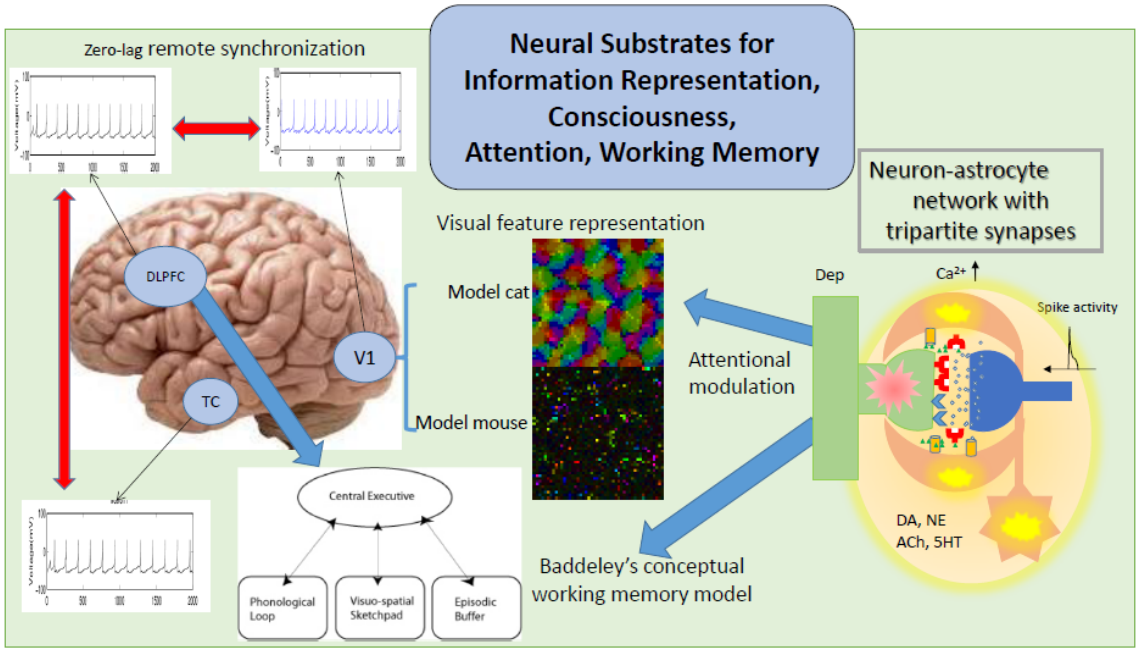


Figure 1 Overview of our laboratory's research

1.2 State of Progress in Research and Education (April, 2017 - March, 2018)

(1) Mathematical modeling of species-dependent orientation representation formation (collaborated with National Institute of Technology, Numazu College)

We have previously proposed a mathematical model of the activity-dependent self-organization of geniculo-cortical afferents, and successfully reproduced regular orientation maps as observed in the cat visual cortex and salt-and-pepper-like orientation representation in the rodent visual cortex for different randomness in the short-range excitatory connections. To understand the mechanism of the transition between regular orientation maps and salt-and-pepper-like orientation representation, we devised a simple

form of Hamiltonian composed of the mixture of XY spins and Ising spins, each of which describes orientation-selective neurons and orientation-unresponsive ones, respectively. We confirmed that the behavior of this system was similar to simulation results of the afferent input self-organization model, which indicates that the spin model extracts an essential mechanism in the formation of orientation representation in rodents as well as in cats. Using this Hamiltonian and applying the replica trick and steepest descent, we obtain a set of nonlinear equations satisfied with order parameters as mean field solutions. In 2018, we will solve the nonlinear equations numerically to draw the phase diagram of orientation representation to identify the connection probability in the cat and rodent visual cortices.

(2) Long-range zero-lag synchronization

In 2017, we mainly focused on the dynamics of a two-neuron model to examine how the zero-lag synchronization of firing occurs for different values of the conduction delay of action potential between two remote neurons. We used Izhikevich's neuron model as a spiking neuron model because it shows type I and II excitabilities according to the values of parameters although it is relatively simple.

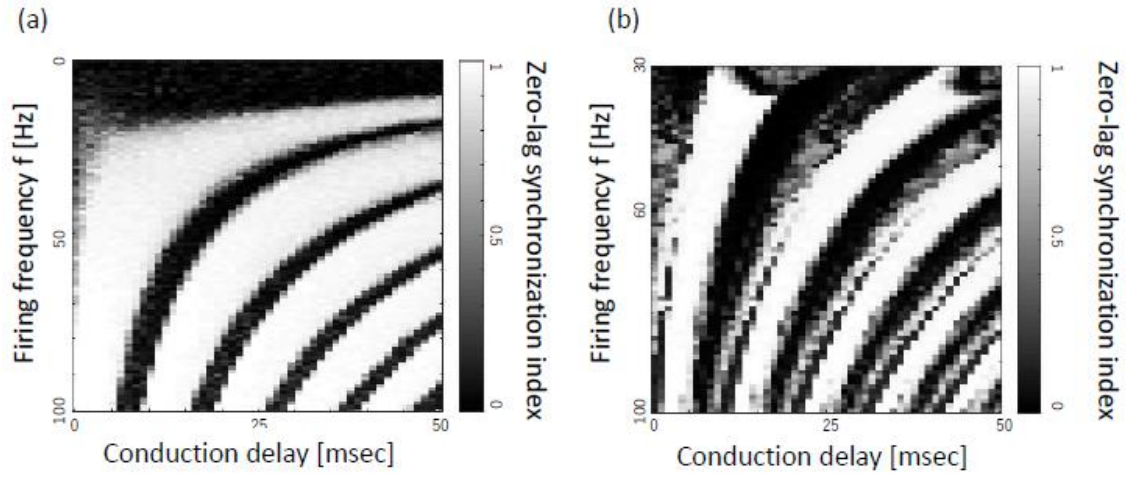


Figure 2 Zero-lag synchronization index for a Type I neuron model (a) and for a Type II neuron model (b)

A Type I neuron is a model of regular spiking (RS) neurons corresponding to cortical pyramidal cells, whereas a type II neuron is a model of fast spiking neurons corresponding to cortical interneurons. So, the synaptic connections were assumed to be excitatory for the Type I neuron pair and inhibitory for the Type II neuron pair. In Fig 2, bright regions indicate the emergence of zero-lag synchronization, whereas dark regions indicate the occurrence of anti-phase synchronization. Simulation results showed that the zero-lag synchronization of firing can take place in both types of neuron pairs for different conduction delays. Comparing Fig. 2a with Fig. 2b, we found that in the pair of type I neurons linked by excitatory synaptic connections, the zero-lag synchronization was more likely to occur for various conduction delays than in the pair of type II neurons linked by inhibitory synaptic connections.

(3) Mathematical modeling of neuron-glia interaction

In 2016, we built a mathematical model of neuron-glia interaction, and showed that the exocytosis of ATP and D-serine from astrocytes under the secretion of neuromodulator is able to enhance signal-to-noise ratio (SNR) in neuronal information transmission. This year, we attempted to elaborate our mathematical model to be able to express the release of glutamate as a gliotransmitter. Simulation results of the elaborated model showed that there can be different effects of neuromodulators such as facilitation and suppression of neuronal activity and enhancement of SNR according to the balance of efficiency among the three gliotransmitters. (Fig. 3).

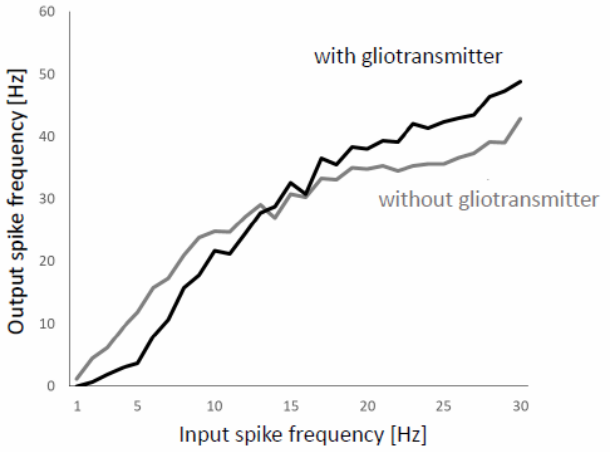


Figure 3 Gliotransmitter controls SN ratio in synaptic transmission

1.3 Future Plan

Using the cat-like and mouse-like model visual cortices that receive self-organized afferent inputs, we will carry out simulations of neuronal activities in response to temporally changing visual stimuli in order to elucidate the mechanism of dynamical representation of visual scenes in the primary visual cortex. Specifically, we will build a model of cortical circuits composed not only of spiny stellate cells and pyramidal cells but also of inhibitory interneurons such as basket cells, double bouquet cells and chandelier cells. Next, we will address to possible effects of wakefulness and attention on the visual information representation/processing by integrating the model circuit with the mathematical model of tripartite synapses. In such a detailed model, we will study the mechanisms underlying zero-lag synchronization of firing among remote neurons. Furthermore, to obtain real data of neuronal activities in the visual cortex, we plan to start two-photon Ca^{2+} imaging in the primary visual cortex (OC1) of genetically manipulated mice.

2. Research Achievements

2. 1 Conference Presentations

(1) Miyashita M, Tanaka S. A computational model for the generation of auditory continuity illusion. Annual Meeting of Japanese Society for Neuroscience, Chiba, July, 2017.

(2) Miyashita M, Endo T, Tanaka S. A theoretical study of cortical neural dynamics for the generation of auditory continuity illusion. Society for Neuroscience Meeting, Washington DC, Nov, 2017.

(3) Miyashita M, Tanaka S. Neural mechanisms of auditory continuity illusion. 4th Annual Meeting of the Society for Bioacoustics, Tokyo, Dec. 9, 2017.

2.4 Invited lectures

(1) Tanaka S, Miyashita M. Species differences in the functional architecture of primary visual cortex between cats and rodents. 4th Annual Meeting of the Society for Bioacoustics, Tokyo, Dec. 9, 2017.

2.5 Student guidance

(1) Masaki Hayashi (M1)
(2) Ryo Kanomata (B4)
(3) Shuhei Ohkawa (B4)
(4) Akihiro Ohsawa (B4)

3. Research funding

3.1 Grant-in-aid for scientific research

(1) 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.
(2) Shigeru Tanaka (PI) Functions of the primary visual cortex in the wakefulness: The mechanisms of sparse representation of dynamic visual information. Scientific Research (C), 2017-2019, 4,810,000 yen.

4. Collaboration

4.1 Inside BLSC

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

(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) Keiji Tanaka (RIKEN Center for Brain Science) fMRI measurement for understanding of the mechanisms of sound symbolism, 2017/4-

5. Outreach activities

5.1 Editor of academic journals

(1) ISRN Neuroscience, 2012-present

(2) Science Postprint, 2013-present

Tadashi YAMAZAKI Laboratory

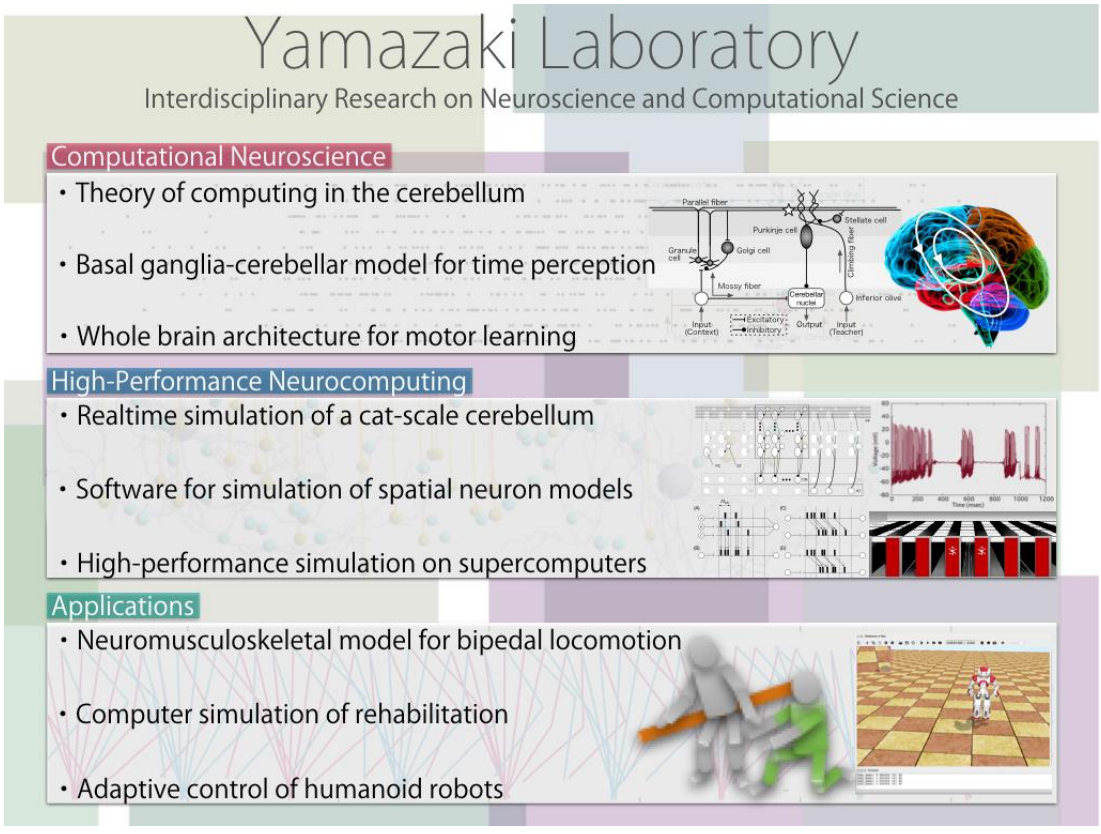
1. Outline of Research and Education (12point)

1. 1 Basic Policy in Research and Education (11point)

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, 2017 - March, 2018)

(1) Reevaluation of a theory of cerebellar cortex

We reevaluated the computational power of the cerebellum based on the recent findings on molecular layer interneurons and their synaptic plasticity. We proposed that the cerebellar cortex acts as a reinforcement learaning machine.

(2) Building a spiking network model of the basal ganglia

We built a spiking network model of the basal ganglia based on known anatomy and physiology. The model was built on a GPU and runs in realtime, so the model can perform reinforcement learning online.

(3) Simulation of cerebellar motor learning based on Ca2+ imaging data on Purkinje cells

Based on Ca2+ imaging data of cerebellar Purkinje cells in behavioral animals, we conducted computer simulation of behavior acquisition, and succeeded to reproduce the experimental results.

(4) Simulation of cerebrocerebellar communication loop

On K supercomputer, we developed an interface that connects a cerebral cortex model and our cerebellar model using MPI, and conducted computer simulation of cerebrocerebellar communication loop. We found that the cerebral cortex and the cerebellum synchronized at a theta frequency range.

(5) Bulding a monkey-scale artificial cerebellum

On supercomputer Gyoukou, we built a large-scale spiking network model of the cerebellum composed of more than 8 billion neurons.

1.3 Future Plan

We will establish a whole-brain learning architecture composed of the cerebral cortex, basal ganglia, and cerebellum.

2. Research Achievements

2. 1 Reviewed papers

(1) Tadashi Yamazaki, Jun Igarashi, Junichiro Makino, Toshikazu Ebisuzaki. Realtime simulation of a cat-scale artificial cerebellum on PEZY-SC processors. International Journal of High Performance Computing Applications, In Press.

(2) Daisuke Ichimura, Satoshi Yano, Tadashi Yamazaki. Computer simulation of a cerebellar-musculoskeletal model for bipedal locomotion with feedback compensation of foot contact. IEICE Transactions on Information and Systems (Japanese Edition) Vol.J100-D No.8 pp.808-816, 2017.

2.2 Book, non-refereed articles and translation

(1) Tadashi Yamazaki. Reservoir Computing (Japanese article). Encyclopedia of Artificial Intelligence

(JSAI ed.), pp. 528-530, Kyoritsu Shuppan, 2017.

(2) Tadashi Yamazaki, Jun Igarashi. High-performance neurocomputing for realtime simulation of neural network models (Japanese article). The Brain and Neural Networks 24(4): 172–181, 2017.

2.3 Invited lectures

(1) Tadashi Yamazaki. High-performance neurocomputing: unifying computational neuroscience and high-performance computing towards human-scale brain network simulation. Inter-disciplinary workshop, March 6, 2018, NAIST, Nara

(2) Tadashi Yamazaki. Cat-scale artificial cerebellum on an energy-efficient supercomputer Shoubu (Invited). Workshop on Brain-inspired Hardware, March 30, 2017, AIST AI Research Center.

(3) Tadashi Yamazaki. Towards human-scale neural network simulation: Case study on the cerebellum (In Japanese, Invited). Scientific Systems Symposium. Oct 26, 2017, ANA Crown Plaza Kobe.

2.4 Media release

(1) My Navi News: Simulating the cerebellum with 8 billion neurons in realtime (In Japanese). March 19, 2018.

2.5 Student guidance

(1) 1 B4, 1 M1, 1 M2, 1 D1

3. Research funding

3.1 Grant-in-aid for scientific research

(1) Grant-in-Aid for Scientific Research (C)

(2) Grant-in-Aid for Scientific Research on Innovative Areas Brainfordynamics

3.2. Competitive external research funding

(1) NEDO Next generation AI and robot core technology

(2) MEXT Post-K Exploratory Research #4

(3) MEXT Large-scale computational science on hetero-manycore processors

4. Collaboration

4.1 Outside BLSC in UEC

(1) Tetsu Narumi on Neuromorphic computing

4.2 Outside UEC

(1) Junichiro Makino (Kobe), Toshikazu Ebisuzaki (RIKEN), Jun Igarashi (RIKEN), Kenji Doya (OIST) on high-performance computing

(2) Shin Ishii (Kyoto), Kazuo Kitamura (Yamanashi) on Ca2+ imaging simulation

5. Outreach activities

5.1 Editor of academic journals

(1) Action Editor, Neural Networks

(2) Review Editor, Frontiers in Computational Neuroscience

5.2 Other outreach activities

(1) Tadashi Yamazaki. Tutorial: Introduction of high-performance computing for neuroinformatics. Advances in Neuroinformatics 2017 (AINI2017), November 20-21, Wako.

(2) Tadashi Yamazaki. Building the brain on supercomputers. BLSC Spring School, March 28–29, 2017, UEC.