Unique & Exciting Campus

2015 Annual Report

The University of Electro-Communications

Brain Science Inspired Life Support Research Center

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

Preface

Due to rapid ageing and birthrate declining, Japan has been a super-aged and population reduction society without parallel in the world, and has serious problems in maintaining a vitality of the society. However, if the elderly can continue to work with health in mind and body, medical and welfare national expenditure can be suppressed and an increase in the number of the healthy elderly will compensate a decrease in the working age population. Consequently, it is expected that the Japanese society will be revitalized.

To realize a longevity society, in which the elderly are healthy in mind and body and enjoy their lives, the following three factors are needed: (1) the progress of preventive medicine and public health, (2) the advancement of the quality of medical care and (3) the sophistication of rehabilitation therapy for medically treated patients. All these factors mainly rely on the development of biomedical sciences. On the other hand, it is important to establish a support system for the progress of medical research fields based on science and engineering. Particularly, for the above factor (3), it is advocated that the development of technologies for the functional recovery from post-operative damage or accidental amputation of part of a body requires integrative medicine engineering cooperation

In UEC, there are experts working in various research fields such as information engineering, bioengineering, ergonomics, robotics and optical science. Making the best use of such a rich human resource, UEC should conduct research and development of technologies needed in the onsite medical welfare treatment. Also, it should foster researchers with creativity and practical skills, who can cooperate and collaborate with others working in different areas of expertise. To promote such research and education, UEC established Brain Science Inspired Life Support Research Center (BLSC) in 2013.

This annual report is a report that contains achievements for 3 years from 2013 to 2015, because since BLSC was launched, we have been swamped with putting a system in order and unable to issue annual reports 2013 and 2014.

Finally, BLSC would be delighted to have your understanding and continued support.

2017 May

Brain Science Inspired Life Support Research Center

Director Hiroshi YOKOI

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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.

Project expense

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

FY 2013 Special expense 20,868,000Yen　UEC burden 3,000,000Yen
FY 2014 Special expense 14,959,000Yen　UEC burden 3,000,000Yen
FY 2015 Special expense 11,219,000Yen　UEC burden 3,000,000Yen

Group structure

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

Basic technology development of optical measurements

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.

Measurement and monitoring of *in vivo* brain functions

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.

Technology development for motor function recovery for medical welfare

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.

Personnel organization（as of 31 May, 2016 ）

Name	Web site or affiliation	Position
SHIMOJO Makoto		Director (2013-2014)
YOKOI Hiroshi	http://www.hi.mce.uec.ac.jp/yklab/	Director (2015-)
KOIKE Takuji	http://www.bio.mce.uec.ac.jp/index.html	Professor
OKADA Hidetaka	http://www.hb.mce.uec.ac.jp/	Professor
KASHIMORI Yoshiki	http://granule.pc.uec.ac.jp/wiki/wiki.cgi	Professor
KANO Yutaka	http://www.ecc.es.uec.ac.jp/	Professor
SHONO Hayaru	http://daemon.inf.uec.ac.jp/ja/	Professor
TANAKA Shigeru	http://tanaka-lab.net/jp/	SA Professor
NIWA Haruki	http://www.firefly.pc.uec.ac.jp/	SA Professor
YAMADA Yukio	http://www.nvu.mi.uec.ac.jp/old_html/index.html	SA Professor
MASAMOTO Kazuto	http://kjk.office.uec.ac.jp/Profiles/55/0005461/profile.html	Associate Professor
MIYAWAKI Yoichi	http://www.nvu.mi.uec.ac.jp	Associate Professor
MATSUDA Shinji	http://www.matsuda-lab.es.uec.ac.jp/	Associate Professor
JIANG Yinlai	http://kjk.office.uec.ac.jp/Profiles/67/0006631/profile.html	SA Associate Professor
MAKI Shojiro	http://www.firefly.pc.uec.ac.jp/	Assistant Professor
YAMAZAKI Tadashi	http://numericalbrain.org/	Assistant Professor
MORISHITA Soichiro		SA Assistant Professor

*SA: Specially Appointed

ARAMAKI Yu	Chukyo University School of Health and Sport Sciences, Professor	Visiting Professor
KATO Ryu	Faculty of Engineering Division of Systems Research, Associate Professor	Visiting Associate Professor

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

Events and Seminars in BLSC

For general audience interested in neurosciences and technological research for life support in aged societies, we have held symposia and workshops co-sponsored with outside institutes or organizations. We have also held “BLSC Seminar Series” continually about once a month, which have been organized by Yukio Yamada, since BLSC was established. At the initiative of Haruki Niwa, we have designed “Hands-on Training Course” for UEC graduate school students and examined its feasibility. To contribute to the enhancement of high school/university connections, we made an attempt to hold “BLSC Spring School for High School Students”. Summaries of these events and educational activities are described below (in more detail, see the BLSC website: http://blsc-uec.net/). (Note: English translations from Japanese are not authorized by the speakers, and technical terms may not be correct.)

1. BLSC Kick-off Meeting

Date: May 14 (Tue.), 2013

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

Program:

13:15~13:30	Opening address: M. Kajitani, President of UEC
13:30~14:30	“Biomechanics of hemodynamics in brain,” Prof. K. Tanishita, Waseda University
14:30~15:30	“Subjects toward success of collaborative research between medicine and engineering,” Prof. I. Sakuma, The University of Tokyo
15:45~16:15	“Development and application of materials emitting bioluminescence by firefly in the near infrared wavelength range,“ Prof. S. Maki
16:15~16:45	“Evaluation of muscle performances by bio-imaging and its application,” Prof. Y. Kano
16:45~17:15	“Study of working memory toward the elucidation of human thinking processes,” Prof. S. Tanaka
17:15~17:45	“R&D for recovery of motion performances using brain-machine-interface (BMI),” Prof. H. Yokoi
17:45~18:00	Closing remarks: M. Shimojo, Director of BLSC
18:00~	Reception

2. Hand-on Training Course for UEC Graduate School Students

One of BLSC missions is to nurture innovative human resources who develop new interdisciplinary technology responding to the needs in the field of medicine and welfare. For this purpose, we designed a curriculum of a hands-on training course in 2013, and then we prepared a detailed experimental manual. The feasibility study of the training course was performed with the cooperation of several monitor students in 2014. We found that the training course was well designed and feasible as one of the class subjects that BLSC provides for graduate school students in UEC.

1st hands-on training

Date and Time: May. 22 (Thu.), 2014, 13:00 – 16:10

Place: Meeting room #701b, Building E-3 and then Laboratory #737, Building E-6, UEC

Instructor: Prof. Haruki Niwa

Teaching Assistant: Kazuma Karube

Title: 1. Organic synthesis and instrumental analysis of firefly bioluminescence substrate（1st day）

2nd hands-on training

Date and Time: May. 23 (Fri.), 2014, 13:00 – 16:10

Place: Meeting room #701b, Building E-3 and then Laboratory #737, Building E-6, UEC

Instructor: Prof. Haruki Niwa

Teaching: Assistant: Kazuma Karube

Title: 1. Organic synthesis and instrumental analysis of firefly bioluminescence substrate（2nd day）

3rd hands-on training

Date and Time: May 29 (Thu.), 2014, 13:00 – 16:10

Place: Meeting room #701b, Building E-3 and then Laboratory #737, Building E-6, UEC

Instructor: Prof. Haruki Niwa

Teaching Assistant: Kazuma Karube

Title: 2. Measurement of firefly bioluminescence（1st day）

4th hands-on lecture

Date and Time: Jun. 5 (Thu.), 2014, 13:00 – 16:10

Place: Meeting room #701b, Building E-3 and then Laboratory #737, Building E-6, UEC

Instructor: Prof. Haruki Niwa

Teaching Assistant: Kazuma Karube

Title: 2. Measurement of firefly bioluminescence (2nd day)

5th hands-on training

Date and Time: Jun. 13 (Fri.), 2014, 13:00 – 16:10

Place: Exercise room, Judo Gymnasium, UEC

Instructor: Prof. Hidetaka Okada

Teaching Assistant: Shuhei Kurita

Title: 6. Measurement and analysis of human motion by means of an optical motion capture system (1st day)

6th hands-on training

Date and Time: Jun. 20 (Fri.), 2014, 13:00 – 16:10

Place: Exercise room, Judo Gymnasium, UEC

Instructor: Prof. Hidetaka Okada

Teaching Assistant: Shuhei Kurita

Title: 6. Measurement and analysis of human motion by means of an optical motion capture system (2nd day)

7th hands-on training

Date and Time：Jun. 26 (Thu.), 2014, 13:00 – 16:10

Place: Meeting room #701b, and then Laboratory #726, Building E-3, UEC

Instructors: Assis. Prof. Soichiro Morishita and Assoc. Prof. Yinlai Jian

Teaching Assistants: Misato Ohdaira and Tatsuya Seki

Title: 5. Brain activity and body movement measurement of players playing a board game such as Japanese shogi game (1st day)

8th hands-on training

Date and Time：Jul. 3 (Thu.), 2014, 13:00 – 16:10

Place：Meeting room #701b, and then Laboratory #726, Building E-3, UEC

Instructors：Assis. Prof. Soichiro Morishita and Assoc. Prof. Yinlai JianG

Teaching Assistants: Misato Ohdaira and Tatsuya Seki

Title 5. Brain activity and body movement measurement of players playing a board game such as Japanese shogi game (2nd day)

9th hands-on training

Date and Time: Jul. 10 (Thu.), 2014, 13:00 – 16:10

Place: Meeting room #701b, and then Laboratory #129, Building E-4, UEC

Instructor: Prof. Takuji Koike

Teaching Assistants: Eri Tanaka

Title: 7. Measurement of auditory brainstem response (ABR) (1st day)

10th hands-on training

Date and Time: Jul. 17 (Thu.), 2014, 13:00 – 16:10

Place: Meeting room #701b, and then Laboratory #129, Building E-4, UEC

Instructor: Prof. Takuji Koike

Teaching Assistants: Eri Tanaka

Title: 7. Measurement of auditory brainstem response (ABR) (2nd day))

11th hands-on training

Date and Time: Jul. 24 (Thu.), 2014, 13:00 – 16:10

Place: Laboratory #129, Building E-4, UEC

Instructor: Prof. Takuji Koike

Teaching Assistants: Eri Tanaka

Title: 8. Measurement of distortion otoacoustic emissions (DPOAEs) (1st day)

12th hands-on training

Date and Time: Jul. 31 (Thu.), 2014, 13:00 – 16:10

Place: Laboratory #129, Building E-4, UEC

Instructor: Prof. Takuji Koike

Teaching Assistants: Eri Tanaka

Title: 8. Measurement of distortion otoacoustic emissions (DPOAEs) (2nd day)

13th hands-on training

Date and Time: Aug. 21 (Thu.), 2014, 13:00 – 16:10

Place: Laboratory #618, Building E-3, UEC

Instructor: Assoc. Prof. Yoichi Miyawaki

Teaching Assistants: Masashi Sato

Title: 10. Functional mapping of human brain activity using functional magnetic resonance imaging (fMRI) (1st day)

14th hands-on training

Date and Time: Aug. 22 (Fri.), 2014, 14:40 – 17:45

Place: Laboratory #618, Building E-3, UEC

Instructor: Assoc. Prof. Yoichi Miyawaki

Teaching Assistants: Masashi Sato

Title: 10. Functional mapping of human brain activity using functional magnetic resonance imaging (fMRI) (2nd day)

15th hands-on training

Date and Time: Aug. 28 (Thu.), 2014, 13:00 – 16:10

Place: Meeting room #701b, Building E-3, and then Laboratory #263, Building E-4, UEC

Instructors: Prof. Hiroshi Yokoi and Assis. Prof. Soichiro Morishita

Teaching Assistants: Masahiro Kasuya

Title: 12. Control of external device by processing electromyogram (EMG) (1st day)

16th hands-on training

Date and Time: Aug. 29 (Fri.), 2014, 14:40 – 17:45

Place: Meeting room #701b Building E-3, and then Laboratory #263, Building E-4, UEC

Instructors: Prof. Hiroshi Yokoi and Assis. Prof. Soichiro Morishita

Teaching Assistants: Masahiro Kasuya

Title: 12. Control of external device by processing electromyogram (EMG) (2nd day)

17th hands-on training

Date and Time: Sep. 18 (Thu.), 2014, 13:00 – 16:10

Place: Meeting room #701b, and then Laboratory #726, Building E-3, UEC

Instructor: Prof. Hiroshi Yokoi

Teaching Assistants: Misato Ohdaira

Title: 12. Control of external device by processing electromyogram (EMG) (1st day)

18th hands-on training

Date and Time: Sep. 19 (Fri.), 2014, 14:40 – 17:45

Place: Meeting room #701b, and then Laboratory #726, Building E-3, UEC

Instructor: Prof. Hiroshi Yokoi

Teaching Assistants: Misato Ohdaira

Title: 12. Control of external device by processing electromyogram (EMG) (2nd day)

19th hands-on training

Date and Time: Sep. 25 (Thu), 2014, 13:00 – 16:10

Place: Meeting room #306, Building E-1, UEC

Instructor: Prof. Yutaka Kano

Teaching Assistants: Yoshinori Tanaka

Title: 9. Measurement of muscle fatigue and the motor unit (motor nerve, muscle fiber) function (1st day)

20th hands-on training

Date and Time: Sep. 26 (Fri), 2014, 14:40 – 17:45

Place: Meeting room #306, Building E-1, UEC

Instructor: Prof. Yutaka Kano

Teaching Assistants: Yoshinori Tanaka

Title: 9. Measurement of muscle fatigue and the motor unit (motor nerve, muscle fiber) function (2nd day)

21st hands-on training

Date and Time: Oct. 31 (Fri), 2014, 14:40 – 17:45

Place: Laboratory #618, Building E-3, UEC

Instructor: Assoc. Prof. Yoichi Miyawaki

Teaching Assistants: Masashi Sato

Title: 14. Basics of visual psychophysical experiments (1st day)

22nd Hands-on training

Date and Time: Nov. 7 (Fri), 2014, 14:40 – 17:45

Place: Laboratory #618, Building E-3, UEC

Instructor: Assoc. Prof. Yoichi Miyawaki

Teaching Assistants: Masashi Sato

Title: 14. Basics of visual psychophysical experiments (2nd day)

23rd hands-on training

Date and Time: Nov. 14 (Fri), 2014, 14:40 – 17:45

Place: Meeting room #701b, and then Laboratory #726, Building E-3, UEC

Instructors: Prof. Hiroshi Yokoi and Assoc. Prof. Soichiro Morishita

Teaching Assistant: Tatsuya Seki

Title: 13. Basics of visual psychophysical experiments (1st day)

24th hands-on training

Date and Time: Nov. 28 (Fri), 2014, 14:40 – 17:45

Place: Meeting room #701b, and then Laboratory #726, Building E-3, UEC

Instructors: Prof. Hiroshi Yokoi and Assoc. Prof. Soichiro Morishita

Teaching Assistant: Tatsuya Seki

Title: 13. Basics of visual psychophysical experiments (2nd day)

25th hands-on training

Date and Time: Dec. 4 (Thu), 2014, 14:40 – 17:45

Place: Meeting room #701b, and then Laboratory #726, Building E-3, UEC

Instructors: Prof. Yukio Yamada

Teaching Assistant: Rei Murata

Title: 3. Luminescence imaging (1st day)

26th hands-on training

Date and Time: Dec. 11 (Thu), 2014, 14:40 – 17:45

Place: Meeting room #701b, and then Laboratory #726, Building E-3, UEC

Instructors: Prof. Yukio Yamada

Teaching Assistant: Rei Murata

Title: 3. Luminescence imaging (2nd day)

27th hands-on training

Date and Time: Dec. 19 (Fri), 2014, 14:40 – 17:45

Place: Meeting room #701b, and then Laboratory #726, Building E-3, UEC

Instructors: Assis. Prof. Soichiro Morishita

Title: 4. A practice of brain-machine interfaces by analyzing electroencephalogram (EEG) (1st day)

28th hands-on training

Date and Time: Dec. 19 (Fri), 2014, 14:40 – 17:45

Place: Meeting room #701b, and then Laboratory #726, Building E-3, UEC

Instructors: Assis. Prof. Soichiro Morishita

Title: 4. A practice of brain-machine interfaces by analyzing electroencephalogram (EEG) (2nd day)

3. Symposium "Practical Implementation of Developed Medical Devices in the Field of Life Support Technology"

Co-sponsored with Japan Manufacturing Commons for Collaboration of Medicine and Engineering

Organizing committee: Prof. K. Tanishita, Prof. H. Yokoi, Mr. S. Kashino, Prof. Bao-liang Lu, Prof. Y. Yamada, Prof. H. Niwa, Prof. Y. Jiang, Assis. Prof. S. Morishita, Assoc. Prof. K. Masamoto, Ms. K. Yabuki

Date: Nov. 26 (Thu.), 2015

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

Program:

13:10 Opening address: T. Fukuda, President of UEC

13:15 "Matching of medical requirements and engineering developments through Japan Manufacturing Commons for Collaboration of Medicine and Engineering," K. Tanishita and S. Kashino, Japan Manufacturing Commons for Collaboration of Medicine and Engineering

13:45 "Medical device industry: present statuses and future prospects," H. Kubota, K and K Japan, Co. Ltd.

14:30 "Development of medical devises assisting the reduction of suffocation accidents and serious pneumonia caused by dysphagia of elderly patients," Y. Michiwaki, Musashino Red Cross Hospital (MRCH)

15:00 “Development of diagnostic and therapeutic devices in otolaryngology,” T. Koike, BLSC, UEC

15:40 “Hemiplegia therapy system applying facilitation by motion intention and development of magnetic device stimulating peripheral nervous system.” S. Ideé, Rehabilitation medical engineering, Tohoku University School of Medicine

16:10 “Activities of collaboration between medicine and engineering at BLSC, UEC,” H. Yokoi, Director of BLSC, UEC

16:50 “Emotion recognition and driving fatigue detection from EEG,” Bao-Liang Lu, Shanghai Jiaotong University

17:50 Closing remark: K. Tanishita, Japan Manufacturing Commons for Collaboration of Medicine and Engineering

18:30 Reception

4. Workshop “Brain, Mind and Life Support Technologies”

"Pre-symposium workshop: Brain, Mind, and Life Support Technology@BLSC"

Organizing committee: Prof. K. Tanishita, Prof. H. Yokoi, Mr. S. Kashino, Prof. Bao-liang Lu, Prof. Y. Yamada, Prof. H. Niwa, Prof. Y. Jiang, Prof. S. Morishita, Prof. K. Masamoto, Ms. K. Yabuki

Date: Nov. 25 (Wed.), 2015

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

Program:

13:00 Invited talk 1, “Neurological mechanism of generation and control of emotion in brain for social activities,” Prof. Y. Hoshi, Hamamatsu University School of Medicine

14:00 Invited talk 2, “Toward the society to fostering brain,” Dr. A. Maki, Hitachi Ltd.

15:15 BLSC session 1

Mr. Otsuka (Maki Lab., Department of Engineering Science, UEC)

Mr. Sato (Miyawaki Lab, Center for Frontier Science and Engineering, UEC)

Mr. Murakoshi (Hashimoto Lab., Department of Mechanical Engineering and Intelligent Systems, UEC)

17:00 BLSC session 2

Assoc. Prof. Y. Jiang (BLSC, UEC)

Assoc. Prof. K. Masamoto (Department of Mechanical Engineering and Intelligent Systems, UEC)

18:00 Reception

5. BLSC Seminar Series

BLSC Seminars were held once a month, on average. The member of BLSC who proposed a subject and speaker was supposed to organize the seminar in turn.

1st seminar

Date and time: Jul 18 (Thu.), 2013, 13:30 - 14:30

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

Speaker: Dr. Yoichi Miyawaki (Assoc. Prof., Center for Frontier Science and Engineering, UEC)

Title: Neurological expressions of sensation and perception in human brain

2nd seminar

Date and time: Aug. 29 (Thu.), 2013, 13:30 - 14:30

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

Speaker: Dr. Takuya Hashimoto (Assis. Prof., Department of Mechanical Engineering and Intelligent Systems, UEC)

Chair: Prof. Takuji Koike

Title: Robotic technology assisting lives of people

3rd seminar

Date and time: Sep. 12 (Thu.), 2013, 13：30～14：30

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

Speaker: Dr. Yoko Hoshi (Project Leader, Tokyo Metropolitan Institute of Medical Science)

Chair: Prof. Yukio Yamada

Title: Optical imaging of emotion and neurological mechanism

4th seminar

Date and time: Oct. 25 (Fri.), 2013, 13:30 - 14:30

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

Speaker: Dr. Soichiro Morishita (Assis. Prof., BLSC, UEC)

Chair: Prof. Hiroshi Yokoi

Title: Idea and design of brain-machine interface

5th seminar

Date and time: Nov. 29 (Fri.), 2013, 14:00 - 15:00

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

Speaker: Dr. Yoshiyuki Sato (Assis. Prof., Department of Human Media System, UEC)

Chair: Prof. Yutaka Sakaguchi

Title: Bayesian model of sensory motor function

6th seminar

Date and time: Dec. 7 (Sat.), 2013, 13:00 - 14:00

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

Speaker: Dr. Hideaki Masaya (Prof., University of Tsukuba)

Chair: Prof. Yutaka Sakaguchi

Title: Fitness of brain and motion (Special talk, at Kanto regional meeting of the 159th Meeting of Japanese Society of Physical Fitness and Sports Medicine)

7th seminar (closed)

Date and time: Dec. 20 (Fri.), 2013, 13:00 -

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

Speaker: Dr. Yinlai Jiang (Lecturer, Kochi University of Technology)

Chair: Prof. Hiroshi Yokoi

Title: Building health for ultra-aged society --From the point of views of cognitive and walking function--

8th seminar

Date and time: Jan. 17 (Fri.), 2014, 13:00 - 14:30

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

Speaker: Dr. Masaki Usui (Prof., Kanagawa University of Human Sevices)

Chair: Prof. Hiroshi Yokoi

Title: Goals of nursing care policy --On the problems of nursing care in Korea--

9th seminar

Date and time: Feb. 24 (Mon.), 2014, 13:00 - 14:30

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

Speaker: Dr. Kazuhiro Sohya (Researcher, Riken Brain Science Institute, Riken)

Chair: Prof. Shigeru Tanaka

Title: Action control mechanism of awakening brain by choline activated neuron through suppression neurological circuit

10th seminar

Date and time: Apr. 25 (Fri.), 2014, 13:00 - 14:30

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

Speaker: Dr. Kazuto Masamoto (Assoc. Prof., Department of Mechanical Engineering and Intellectual Systems, UEC)

Chair: Prof. Yukio Yamada

Title: Light and blood flow in brain ---From visualization to manipulation---

11th seminar

Date and time: May 30 (Fri.), 2014, 15:00 - 16:30

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

Speaker: Dr. Tadashi Nakamura (Prof., Department of Engineering Science, UEC)

Chair: Prof. Haruki Niwa

Title: Information conversion of chemical sensation and its related neurological mechanism

12th seminar

Date and time: Jun. 27 (Fri.), 2014, 13:00 - 14:30

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

Speaker: Dr. Masatoshi Takita (Senior Researcher, National Institute of Advanced Industrial Science and Technology (AIST))

Chair: Prof. Makoto Shimojo

Title: Consideration of the mechanism of higher order functions of brain ---From the view point of the biological structure of prefrontal cortex

13th seminar

Date and time: Jul. 25 (Fri.), 2014, 13:00 - 14:30

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

Speaker: Dr. Narihisa Matsumoto (Researcher, National Institute of Advanced Industrial Science and Technology (AIST))

Chair: Assoc. Prof. Yoichi Miyawaki

Title: Hierarchical category classification in inferotemporal lobe of monkeys

14th seminar

Date and time: Sep. 26 (Fri.), 2014, 13:00 - 14:30

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

Speaker: Dr. Kamiya Kazusaku (Assoc. Prof., Juntendo University School of Medicine)

Chair: Prof. Takuji Koike

Title: Genes and molecular mechanism of neurological diseases and auditory disorders

15th seminar

Date and time: Oct. 25 (Fri.), 2014, 13:00 - 14:30

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

Speaker: Dr. Takashi Ushida (Prof., The University of Tokyo School of Medicine)

Chair: Prof. Yukio Yamada

Title: Three definitive factors in regenerative medicine and additional one factor

16th seminar

Date and time: Nov. 13 (Fri.), 2014, 13:00 - 14:30

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

Speaker: Dr. Andrew Subduhi (Assoc. Prof., Department of Biology, University of Colorado, USA)

Chair: Prof. Yutaka Kano

Title: Acute mountain sickness: mechanisms and prevention

17th seminar

Date and time: Nov. 25 (Tue.), 2014, 13:00 - 14:30

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

Speaker: Dr. Wenwei Yu (Prof., Center for Frontier Medical Engineering, Chiba University)

Chair: Prof. Hiroshi Yokoi

Title: Toward development of biological function assisting devices to be used in ordinary life

18th seminar

Date and time: Dec. 19 (Fri.), 2014, 13:00 - 14:30

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

Speaker: Dr. Yoshikazu Seki (Senior Researcher, National Institute of Advanced Industrial Science and Technology (AIST))

Chair: Prof. Yutaka Sakaguchi

Title: Visually handicapped and sound

19th seminar

Date and time: Jan. 30 (Fri.), 2015, 13:00 - 14:30

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

Speaker: Dr. Shinya Matsuda (Assoc. Prof., Department of Engineering Science, UEC)

Chair: Prof. Yutaka Kano

Title: Study of molecular mechanism of plasticity of synapse and development of its control method

20th seminar

Date and time: Feb. 16 (Mon.), 2015, 16:00 - 17:00

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

Speaker: Dr. Gregory T. Clement (Assoc. Prof., Lerner College of Medicine, Case Western University, USA)

Chair: Prof. Tomoo Kamakura

Title: Sound Medicine: Some contemporary and prospective uses of acoustics in medicine

21st seminar

Date and time: Feb. 23 (Mon.), 2015, 13:00 - 14:30

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

Speaker: Dr. Kenji Kansaku (Chief, Systems Neuroscience Section, Research Institute, National Rehabilitation Center for Persons with Disabilities)

Chair: Prof. Hiroshi Yokoi

Title: Toward the medical and welfare applications of brain-machine interface (BMI)

22nd seminar

Date and time: Apr. 10 (Fri.), 2015, 13:00 - 14:30

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

Speaker: Dr. Harumi Hotta (Vice Director, Autonomic Neuroscience, Tokyo Metropolitan Institute of Gerontology)

Chair: Assoc. Prof. Kazuto Masamoto

Title: Mechanism of brain functions supported by body stimulations

23rd seminar

Date and time: Apr. 24 (Fri.), 2015, 13:00 - 14:30

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

Speaker: Dr. Yoshiki Kasimori (Prof., Department of Engineering Science, UEC)

Chair: Prof. Haruki Niwa

Title: Mechanism of hierarchical processing of sensory information

24th seminar

Date and time: Apr. 28 (Tue.), 2015, 13:00 - 14:30

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

Speaker: Dr. Katsuya Yamada (Assoc. Prof., Hirosaki University Graduate School of Medicine)

Chair: Prof. Takayoshi Kobayashi

Title: Development of cancer diagnosis using a fluorescent derivative of L-glucosamine, fLG

25th seminar

Date and time: May 28 (Thu.), 2015, 16:30 – 18:00

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

Speaker: Dr. Kaoru Sakatani (Prof., College of Engineering Worldwide Research Center for Advanced Engineering & Technology (NEWCAT), School of Medicine, Nihon University)

Chair: Prof. Yukio Yamada

Title: Clinical applications of near-infrared spectroscopy (NIRS): present statuses and future prospects

26th seminar

Date and time: Jun. 26 (Fri.), 2015, 13:00 – 14:30

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

Speaker: Dr. Motoyuki Akamatsu (Prime Senior Researcher, Automotive Human Factors Research Center, National Institute of Advanced Industrial Science and Technology (AIST))

Chair: Prof. Makoto Shimojo

Title: Expectation to neuroscience from the view point of automotive driving study

27th seminar

Date and time: Jul 17 (Fri.), 2015, 13:90 – 14:30

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

Speaker: Dr. Tatsuhiro Tajima (Postdoc. Researcher, Lab of Cognitive Computational Neuroscience, University of Geneva, Switzerland)

Chair: Assoc. Prof. Yoichi Miyawaki

Title: Untangling complex brain dynamics

28th seminar

Date and time: Jul. 24 (Fri.), 2015, 13:00 – 14:30

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

Speaker: Dr. Toru Takahata (Prof., Zhejiang University, Interdisciplinary Institute of Neuroscience and Technology (ZIINT), China)

Chair: Prof. Shigeru Tanaka

Title: Comparative anatomy of primate visual cortices using gene expression patterns

29th seminar

Date and time: Aug. 25 (Tue.), 2015, 13:00 – 14:30

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

Speaker: Dr. Gowrishankar Ganesh (Senior Researcher, Intelligent Systems Research Institute, National Institute of Advanced Industrial Science and Technology (AIST))

Chair: Assoc. Prof. Yoichi Miyawaki

Title: Human Centric Robotics: from neuroscience to robot control during human-robot interactions

30th seminar

Date and time: Sep. 11 (Fri.), 2015, 13:00 – 14:30

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

Speaker: Dr. Eriko Aeba (Assis. Prof., Department of Human Media Systems, UEC)

Chair: Prof. Takkuji Koike

Title: Musicians and their auditory senses

31st seminar

Date and time: Oct. 15 (Thu.), 2015, 13:00 – 14:30

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

Speaker: Dr. Zhiwei Luo (Prof., Organization of Advanced Science and Technology, Kobe University)

Chair: Assoc. Prof. Yinlai Jiang

Title: Development of human interactive robots for aging society

32nd seminar

Date and time: Dec. 17 (Thu.), 2015, 13:00 – 14:30

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

Speaker: Dr. Shigeru Tanaka (Prof., BLSC, UEC)

Chair: Prof. Yukio Yamada

Title: Studies of unsolved problems in the self-organization of the primary visual cortex

33rd seminar

Date and time: Jan. 21 (Thu.), 2016, 13:00 – 14:30

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

Speaker: Dr. Yoshihisa Kudo (Prof. Emer., Tokyo University of Pharmacy and Life Sciences)

Chair: Prof. Haruki Niwa

Title: Roles of glial cells in expression of brain functions

34th seminar

Date and time: Feb. 26 (Fri.), 2016, 13:00 – 14:30

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

Speaker: Dr. Dingguo Zhang (Assoc. Prof., Institute of Robotics, School of Mechanical Engineering, Shanghai Jiao Tong University, China)

Chair: Prof. Yinlai Jiang

Title: Electromyography (EMG) Applications for Rehabilitation and Prosthesis (in English)

35th seminar

Date and time: Mar. 1 (Tue.), 2016, 13:00 – 14:30

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

Speaker: Dr. Ryohei Kanzaki (Prof., Research Center for Advanced Science and Technology, The University of Tokyo)

Chair: Prof. Tadashi Nakamura

Title: Brain science investigated by collaboration of insects and robotics ---Create, understand and utilize brain---

36th seminar

Date and time: Mar. 24 (Thu.), 2016, 13:00 – 14:30

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

Speaker: Dr. Takehiko Takagi (Lect., Tokai University School of Medicine, Visiting Assoc. Prof. of BLSC, UEC)

Chair: Prof. Hiroshi Yokoi

Title: Nerve-machine interface and surgery of the hand

6. Special Invited Talks and Exchange Lectures

These talks and lectures were held in cooperation with the Technical English Course of the Department of Mechanical Engineering and Intelligent Systems.

Date and time: Jul. 2 (Thu.), 2015, 16:15～17:45

Venue: Practice room, Information Technology Center, UEC

Chair: Prof. Hiroshi Yokoi

Talk/Lecture #1

Speaker: Dr. Qixin CAO (Professor, Director, Engineering Training Center, Shanghai Jiao Tong University)

Title: Robotics and Digital Factory

Talk/Lecture #2

Speaker: Weidong CHEN (Professor, Department of Automation, School of Electronic, Information and Electrical Engineering, Shanghai Jiao Tong University)

Title: Improving Safety and Autonomy of intelligent Wheelchair in Dynamic Environments

7. Technical Meeting "Data Driven Approach for Understanding the Cerebellar Central Nerve System Which Controls Eye Movements"

Co-sponsored by Japanese Neural Network Society and BLSC, UEC

Date: Aug. 1, 2016

Venue: Multi-media Hall, 3rd Fl., Bld. E3, UEC

Chairs: Akira Katoh (Tokai Univ), Tadashi Yamazaki (UEC Tokyo)

Program:

10:00-10:05 Opening remarks

10:05-10:35 Kenichiro Miura (Kyoto Univ), Visual control of eye movements in mice: the optokinetic response

10:35-11:05 Shuntaro Miki (Chubu Univ), Cerebellar dependent predictive optokinetic response associated with oculomotor velocity storage mechanism in goldfish, carp, zebrafish, medaka, and human

11:05-11:20 Coffee break & Open discussion

11:20-11:50 Naoko Inaba (Kyoto Univ), The role of the cortical areas MT and MST in coding of visual motion during pursuit eye movements

11:50-12:20 Pablo M Blazquez (Washington Univ St. Louis), Thinking inside the box. Signal processing by cerebellar cortex interneurons in the macaque ventralparaflocculus

12:20-13:30 Lunch (and a meeting for speakers with organizers)

13:30-14:00 Tatyana Yakusheva (Washington Univ St. Louis), Role of GABAergic inhibition in the vestibular signal transformation carried out by the cerebellar nodulus and uvula

14:00-14:30 Aya Takemura (AIST), Neural activity in monkey's cortical area MST Represents Retinal Error during Motor Learning

14:30-14:45 Coffee break & Open discussion

14:45-15:15 Yoshiko Kojima (Univ Washington)., ubstantia nigra pars reticulata influences the error signals for the saccade adaptation

15:15-15:45 Shinji Matsuda (UEC Tokyo), Understanding and controlling synaptic plasticity

15:45-16:00 Coffee break & Open discussion

16:00-16:30 Seiji Ono (Tsukuba Univ), Role of visual velocity and position error signals in smooth pursuit adaptation

16:30-17:00 Yutaka Hirata (Chubu Univ), Promoted motor learning of oculomotor velocity to position neural integrator under hyper-gravity and brighter visual stimulation

17:00- Closing remarks

8. International Symposium on Object Vision in Human, Monkey, and Machine

Sponsored by The University of Electro-Communications

Co-sponsored by: RIKEN Brain Science Institute, Grant-in-Aid for Scientific Research on Innovative Areas "Initiative for high-dimensional data-driven science based on sparse modeling," and Brain Science Inspired Life Support Research Center

Date and time: November 5-6, 2015, 13:00-19:00

Venue: 80th Anniversary Memorial Hall 3F, The University of Electro-Communications

Organizers: Manabu Tanifuji (RIKEN Brain Science Institute), Yoichi Miyawaki (The University of Electro-Communications)

Program:

【Nov. 5, 2015】

13:00-13:05 Opening remarks

Session 1

13:05-13:40 Jun Kawaguchi (Nagoya University), "Implicit influence of memory on object recognition"

13:40-14:15 Isamu Motoyoshi (The University of Tokyo), "Visual perception of objects and materials"

14:15-14:50 Tsutomu Murata (Center for Information and Neural Networks), "Emergent recognition: how does the brain disambiguate objects hidden in degraded images?"

14:50-15:25 Satoshi Eifuku (Fukushima Medical University), "Symbolic representation of individual identities in the anterior inferior temporal cortex of monkeys"

15:25-16:00 Yasuko Sugase-Miyamoto (National Institute of Advanced Industrial Science and Technology), "Face inversion decreased information about facial identity and expression in macaque area TE"

16:00-16:20 Coffee break

Session 2

16:20-16:55 Kowa Koida (Toyohashi University of Technology), "Contextual effect on brightness perception and coding in macaque area TE"

16:55-17:30 Toshiyuki Hirabayashi (National Institute of Radiological Sciences (NIRS)), "Microcircuit mechanisms for representation and retrieval of associative object memory in macaque temporal cortex"

17:30-18:05 Manabu Tanifuji (RIKEN Brain Science Institute), "Searching for visual features driving face neurons in inferior temporal cortex"

18:05-18:40 Daniel L. K. Yamins (Massachusetts Institute of Technology), "Using computational models to predict neural responses in higher visual cortex"

19:00- Reception

【Nov. 6, 2015】

Session 3

9:00-9:35 Hayaru Shouno (The University of Electro-Communications), "Novel texture classification with Deep Convolution Neural Network-Evaluation with Lung CT Images-"

9:35-10:10 Ryo Karakida (The University of Tokyo), "On the capability of restricted Boltzmann machine learning to extract appropriate input features"

10:10-10:45 Ilker Yildirim (Massachusetts Institute of Technology), "Efficient analysis-by-synthesis in primate face processing"

10:45-11:05 Coffee break

Session 4

11:05-11:40 Shinji Nishimoto (Center for Information and Neural Networks), "Modeling of brain activity during natural vision: object and beyond"

11:40-12:15 Yoichi Miyawaki (The University of Electro-Communications), "Neural dynamics of object representation in the human brain"

Session 5

12:15-12:45 Panel discussion

12:45-12:50 Closing remarks (Masato Okada, The University of Tokyo)

9. Research Exchange Program through Life Support Technologies Based on Electrophysiology

Sponsored by Sakura Science Plan, JST

Invited people: Nine graduate school students and one professor, Department of Information and Control, Nankai University, China

Dates: Feb. 26 to Mar. 6, 2016

Venue: Graduate School of Informatics and Engineering, and BLSC, UEC

Summary: The research exchange program sponsored by the Sakura Science Program aims to promote collaborative research projects in the field of life support technologies. In the program, the participants were

divided into two groups for hands-on experiments, one for manufacturing bio-electric controlled prosthetic hands and the other for measuring brain activities related to functional electric stimulation, and each group experienced hands-on learning. Sixteen students worked for the program. Chinese participants enjoyed Japanese science and technology as well as nature and culture of Japan. The program was highly appreciated by all participants, and seemed to facilitate mutual understanding between China and Japan. It is expected that experience and mutual understanding obtained from this program will become a solid basis of a future development of research collaboration.

10. BLSC Spring School for High School Students

BLSC modified part of the hands-on training course for graduate students and designed contents of the spring school easy for high school students to learn. In 2016, 1 st "Brain Science Life Support Research Center Spring School" was held for 4 days until the end of March. Sixteen high school students attended from Tokyo, Shizuoka, Ibaragi, Tochigi and Akita prefectures. The participants learned the following topics:

1. Three-dimensional imaging with laser scanning fluorescence microscopy (Assoc. Prof. Kazuto Masamoto)
2. Manufacturing and manipulating cyborg prosthesis (Assoc. Prof. Yinlai Jiang and Assis. Prof. Soichiro Morishita)

1. The first group

Date and Time: 1st day: Mar. 28 (Mon.) 2016, 14:40 – 17:45
2nd day: Mar. 29 (Tue.) 2016, 14:40 – 17:45

Title 1: Three-dimensional imaging with laser scanning fluorescence microscopy
Place: Laboratory #267, Building E-4 UEC
Instructor: Assoc. Prof. Kazuto Masamoto
Teaching Assistants: Yuika Kurihara, Hiroya Yuki, Hiroshi Takeda, Masahiro Niita
High school students: 4 people

Title 2: Manufacturing and manipulating cyborg prosthesis
Place: Laboratory #203, Building E-9, and then Laboratory #263, Building E-4 UEC
Instructors: Assoc. Prof. Yinlai Jiang and Assis. Prof. Soichiro Morishita
Teaching Assistants: Masahiro Kasuya and Yutaro Hiyoshi
High school students: 5 people

2. The second group

Date and Time: 1st day: Mar. 30 (Wed.) 2016, 14:40 – 17:45
2nd day: Mar. 31(Thu.) 2016, 14:40 – 17:45

Title 1: Three-dimensional imaging with laser scanning fluorescence microscopy
Place: Laboratory #267, Building E-4 UEC
Instructor: Assoc. Prof. Kazuto Masamoto

Teaching Assistants: Yuika Kurihara, Hiroya Yuki, Hiroshi Takeda, Masahiro Niita

High school students: 4 people

Title 2: Manufacturing and manipulating cyborg prosthesis

Place: Laboratory #203, Building E-9, and Laboratory #263, Building E-4 UEC

Instructors: Assoc. Prof. Yinlai Jiang and Assis. Prof. Soichiro Morishita

Teaching Assistants: Masahiro Kasuya and Yutaro Hiyoshi

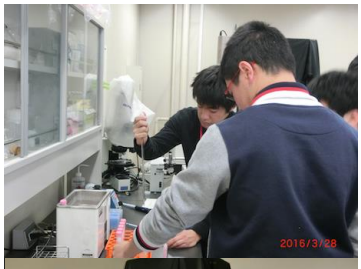
High school students: 6 people

The lecture and experiment for each subject took 4.5 hours (3 school hours) per day for 2 days. In the Spring School, the students tackled two subjects at the forefront of brain science research, supported by the instructors and teaching assistants.

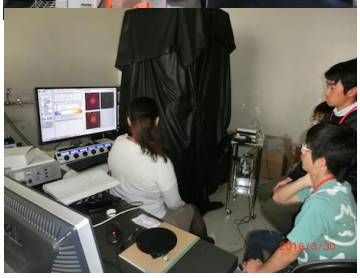
The following are daily digests from the Spring School.

1-1) 3D imaging with laser scanning fluorescence microscopy (Day 1)

• Teaching assistants lectured on the principles of laser scanning fluorescence microscopy and outlined the experiments.



• Students prepared a gelatinous phantom model (live brain tissue model) containing fluorescence and light scattering beads. The phantom model was used for imaging with laser scanning fluorescence microscopy the following day. The apparatus for research use were provided for the experiment.



• The teaching assistant displayed live transgenic mouse cerebrum tissue with a laser scanning fluorescence microscope in two-photon mode.

• The cerebrum tissue expressed green fluorescence protein (GFP). The teaching assistant used the same mouse each day for her research. Students observing this cutting-edge research were impressed.

• Chatting with teaching assistants during break time. Students discussed their research and campus life.

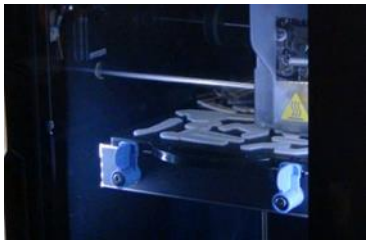
1-2) 3D imaging with laser scanning fluorescence microscopy (Day 2)

• Students observed the handmade phantom models containing fluorescence and light scattering beads (left) with a laser scanning fluorescence microscope (right).

• Students constructed 3D images of the fluorescent beads in the phantom model using MATLAB numerical analysis soft. Students determined the position of the fluorescent beads in the phantom model under the guidance of the teaching assistants.

2-1) Manufacturing and manipulating cyborg prosthesis (Day 1)

• After receiving the experiment outline, students designed a cyborg prosthesis using CAD software. Students found their first attempt operating CAD to be very interesting. They simulated the shape of the prosthesis to grasp items such as dishes, rice bowls, a PET bottle, a tennis ball and a marble, and determined a suitable shape for prosthetic fingers.



• The CAD-designed fingers of the cyborg prosthesis were shaped using a 3D printer. The production of the fingers was completed the following morning.

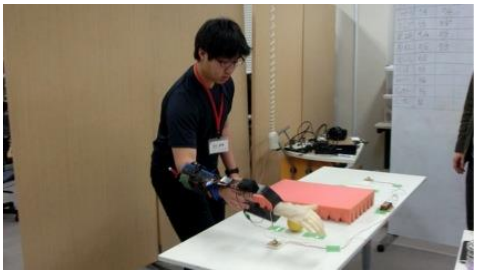
• Students assembled a servo motor to drive the cyborg prosthetic fingers. Students were keen to tackle this handwork.

• Students checked the operating conditions for the 3D printer shaping the cyborg fingers at the end of Day 1.

2-2) Manufacturing and manipulating the cyborg prosthesis (Day 2)

• Students completed the manufacture of the cyborg prosthesis by connecting the 3D printer-manufactured fingers to the driving servo motor. Students cut screw threads using threading taps for first time.

• Students learned to drive the prosthetic hand using their own forearm myoelectric signals. Teaching assistants edited the controlling program in accordance with the shape of the prosthetic hand. Students found it unexpectedly difficult to operate the prosthetic hand using their own myoelectric signals.



• The scene of pick-and-place experiments: the performance of the prosthetic hand was evaluated by grabbing and moving everyday objects. Students smiled involuntarily when they were able to grab and move objects well. Marbles were the most difficult thing to grasp in this experiment.

Participants' Typical Comments described in the Post-Questionnaire Survey

"I enjoyed the research atmosphere at the college."

"I had a great opportunity to experience valuable experiments."

"The school gave me a good opportunity to consider my future (selection of major area)."

"Please continue to provide the Spring School for high school students."

The Spring School content and style left a favorable impression on the attendees.

Hiroshi YOKOI/Yinlai JIANG/Soichiro MORISHITA Laboratory

1. Outline of Research and Education

1.1 Basic policy in educational research

The main objective of our lab is to establish novel research and education for science and engineering relevant to the mechanisms of mutual adaptation among humans and machines. We study a possible theoretical formulation of learning mechanisms that enable humans and machines to adapt flexibly to unexpected environmental changes during motor execution. Based on such scientific studies, we develop feasible and applicable engineering technologies to support people who have physical disabilities on their sensor and motor functions.

The application area is the prosthetics and orthosis of rehabilitation engineering. We are currently engaged in the development of EMG prosthetic hands for upper limb amputee and congenital defects. In order to detect intentions of motion from EMG signals, a machine learning approach based on the conditional entropy evaluation method has been developed, and we have obtained high performance recognition of fifteen patterns of intensions of motion separately, by using three channels of EMG sensors.

A sensory feedback system has been developed for detecting human characteristics of adaptation. This system is based on an electrical stimulation method by using the burst modulation of high frequency carrier signals composed of rectangular waves. An fMRI study has been conducted in a subject using an EMG prosthetic hand with a tactile sensory feedback system, and we found a typical illusion of the exchange of the left and right arms in a task with a mirror. The sensory feedback system was applied to rehabilitation trials for the functional recovery of motion, and we obtained recovery of finger open and close motion for chronic hemi-paralyzed patients by stroke.

On the other hand, an artificial prosthetic hand has been used for BMI (brain machine interface) research. The international collaboration on this research has led to the construction of a light-weight seven-DOF (degrees of freedom) robot arm and a sixteen-DOF robot hand by using the wire tendon interference driven system. This prosthetic hand is in the schedule of practical application to BMI research.

1.2 2013-2015 research results and current progress

(1) Development and practical application of myoelectric prostheses

In order to rebuild upper arms in limb amputated patients, a myoelectric prosthetic hand is required to resemble a human hand, be light enough to avoid an excess amount of strain on the body, and be easily manipulated by anyone. Thus far, we have developed a simple prosthesis (Figure 1) in order to fulfil these requirements. This system consists of the following five parts.

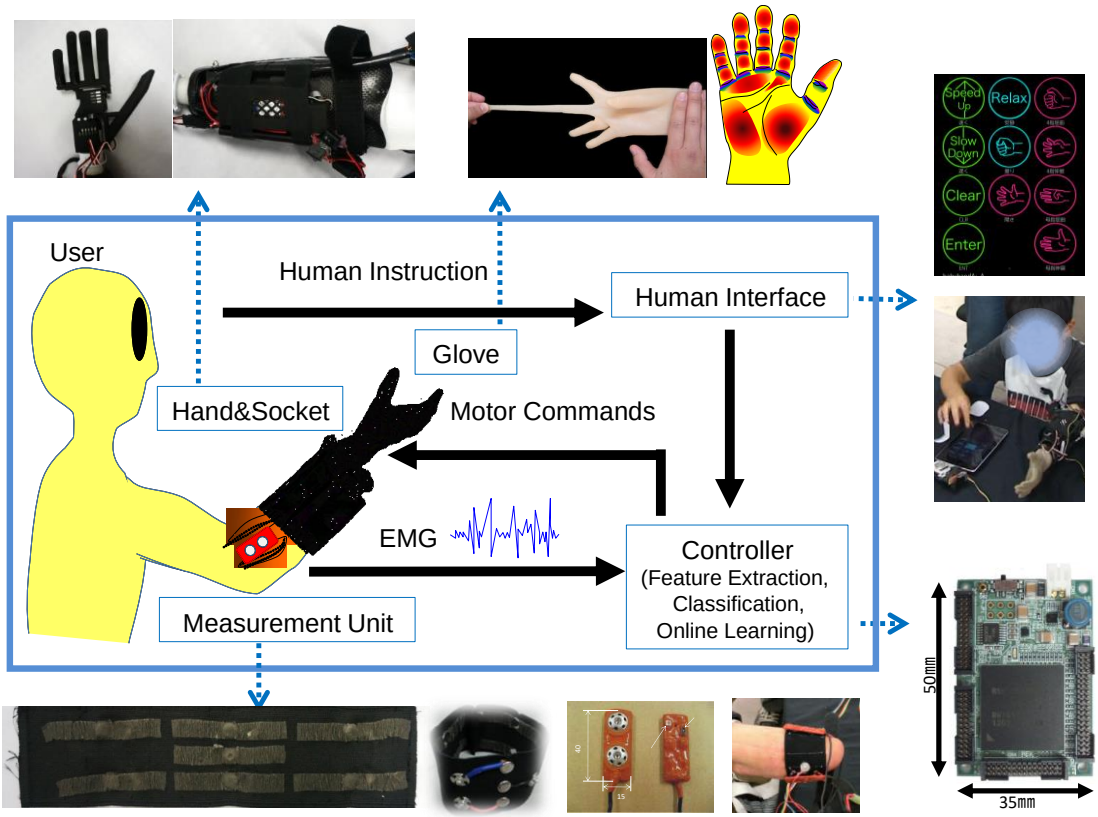


Figure 1 Simple prosthesis system and structure

(a) Light-weight robotic hand and support: Human hands contain numerous joints and are capable of forming various shapes. However, three types of grip position – power grip, precision grip and lateral grip – account for 85% of the ADL (Activities of Daily Living). Therefore, we developed a robotic hand with a combined four-finger MP joint and a thumb MP joint with two degrees of freedom, enabling these three types of grip. We lightened the support fitting the prosthesis to the stump by using carbon fiber, thus enabling an operating mechanism that can be operated with one hand.

(b) Elastomer gel cosmetic glove for myoelectric prosthesis: The cosmetic glove of prosthesis has the following five requirements: appearance, grip function, durability, texture and flexibility. These involve, respectively, having an outer appearance that mimics the physical characteristics of a human hand; having a thickness that allows familiarity with the gripped object; being durable in everyday usage; having a texture similar to the viscoelasticity of human skin; and achieving smooth movement that does not prevent the drive of the joints. We succeeded in developing an elastomer gel cosmetic glove with a 1300% expansion/contraction rate, whilst fulfilling these conditions.

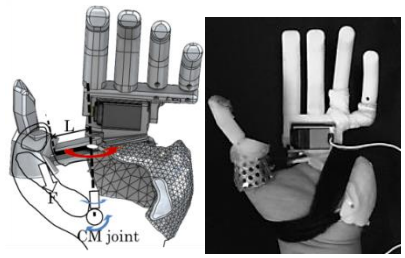
(c) A user-friendly operating interface: In order to make it possible for anybody to use the mutually adaptable myoelectric control system developed in the lab, we developed an operating interface for smartphones and tablets. In consideration of one handed operation by amputees, we designed a GUI (graphical user interface) for the wireless terminal. We had users try the system and verified

that one handed operation of the screen and calibration of the myoelectric prosthesis were possible.

(d) Prosthesis controller balancing high computational ability and low electrical consumption: in order to achieve high speed measurement and analysis of EMG signals as well as control of the robotic hand at low voltage, we developed a controller using SH72544R (manufactured by Renesas Electronics Corporation). We formulated communication standards between the controller and the wireless terminal, and built a set a programs allowing signal programming for EMG calibration. We furthermore developed and implemented a time series algorithm to distinguish between myoelectric patterns.

(e) Skin adhesion, customization, easily fittable myoelectric measuring system: We succeeded in stabilizing measurements by using flexible conductive elements (polypyrrole and conductive silicon) for the electrodes in the myoelectric sensor and increasing the adhesiveness with the skin. By implementing this between electrodes, and between electrodes and amps, we made adjustment of impedance matching possible from the EMG controller. The electrode-skin impedances of the two electrodes were matched by adjusting the impedance components with a compensation circuit.

In addition, we are furthering development and trials of prostheses for infants (Figure 2), hand prostheses (Figure 3) and coupled drive robotic arms for shoulder prostheses (Figure 4) in order to provide for amputees of various ages and with various conditions.



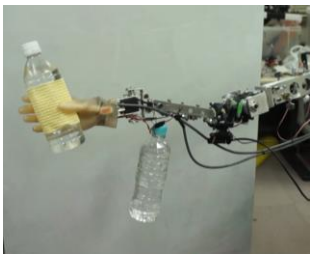


Figure 2 infant prosthesis Figure 3 hand prosthesis Figure 4 coupled drive robotic ar**m**

(2) Functional electrical stimulation using multiple surface electrodes

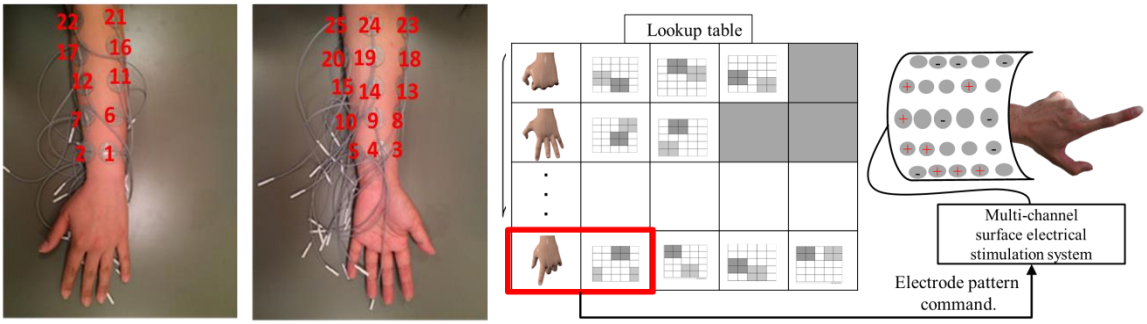


Figure 5 Multi electrode electical stimulation with automatic pattern search

The aim of this research is for patients themselves to be able to conduct rehabilitation to recover movement function without requiring the presence of a caregiver. The focus is on recovery of

movement function in the upper limbs, with the development of an upper limb movement function recovery system using multiple surface electrode electrical stimulation. Using the surface electrode method, it is difficult to target and stimulate specific muscles. In order to solve this issue, we developed the multiple surface electrodes in tandem with a FES selector device (Figure 5). Furthermore, in order to find an electrode pattern capable of expressing the target posture, we used the neural network to estimate the angle of each joint from the electrode pattern. It was possible to confirm approximately 17-31 patterns of hand and finger movement and thus the possibility of expressing a wide variety of movements without aid.

(3) Evaluation of methods of replacing or recovering movement function for the purposes of brain activity measurement/function

We have linked existing brain function and joint angle measurement devices and have begun maintaining an environment in which such data can be recorded simultaneously, and in which the electric support devices for robotic prostheses can be controlled online. Specifically, we constructed a system in which one computer can gather fNIRS measurement data online while simultaneously recording the position of electrodes and, based on this, controlling the electrical support devices (Figure 6).

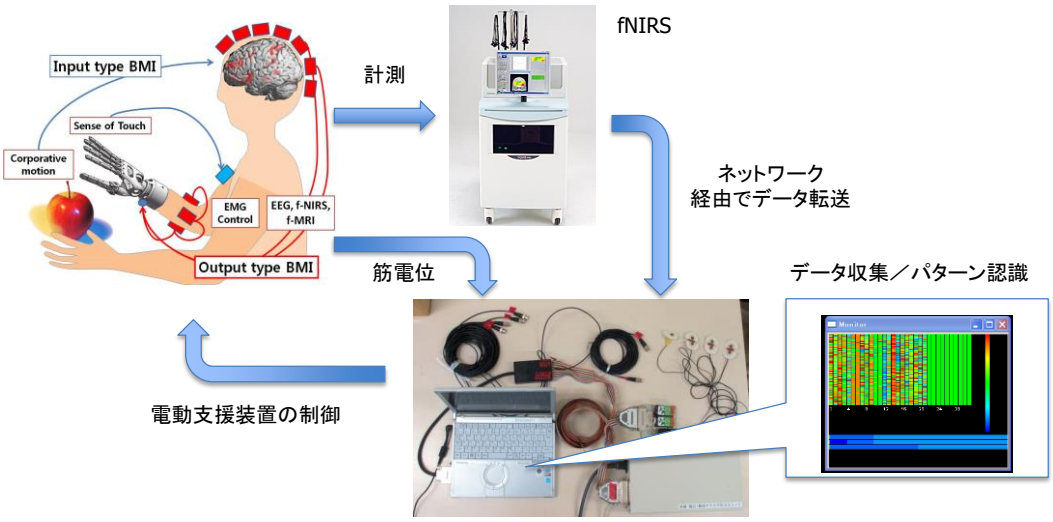


Figure 6　Overview of the system integrating brain and muscle activity with electrical support device control

The results of a brain activity evaluation conducted with the above system when a myoelectric prosthesis is in use are shown in Figure 7. The subject is a male right arm amputee wearing the simple prosthesis mentioned above. In the first 15 seconds after the start of brain activity measurements (first row of Figure 7), the subject is at rest and no change in brain activity is observed. Immediately following the start of the task, the motor area and the prefrontal area begin to activate, and this continues whilst the task is being carried out (second and third rows of Figure 7). When the task finishes and the subject returns to rest, activation of brain activity also reduces (fourth row of Figure 7).

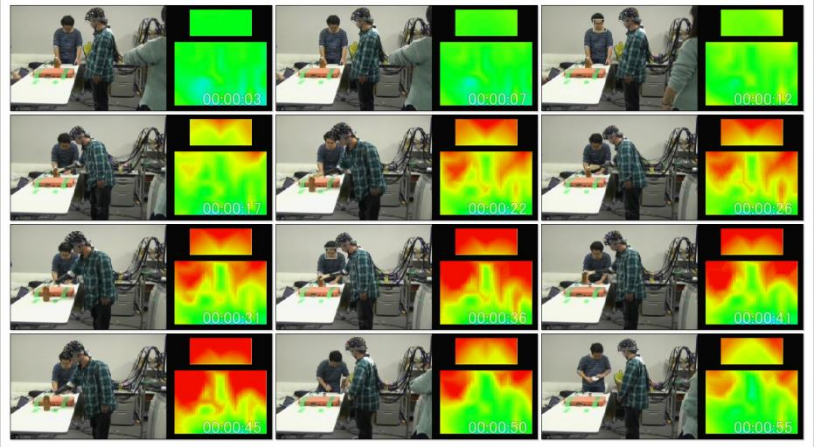
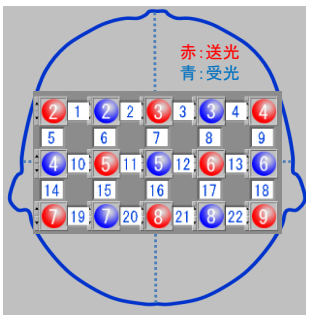


Figure 7　Changes in brain activity during a pick and place test using a myoelectric prosthesis

In the area of research into motion recovery through Functional Electric Stimulation (FES), we established a method of identifying which areas of the brain activate using fNIRS through means of regular FES-invoked muscle contraction and sensory stimulation (Figure 8). Furthermore, based on a hypothesis taking into account periods of relative lack of muscle response, we devised an optimization model for stimulus wave pattern parameters, verifying the model's validity through trials. Moreover, with the cooperation of guest associate professor Osamu Yamamura (Fukui University Hospital), we were able to confirm the effect of FES rehabilitation based on brain activity measurements from PET (Figure 9).



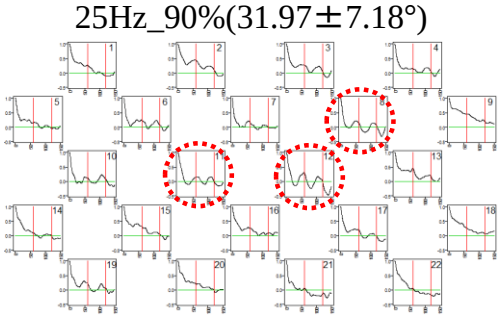


Figure 8 Detection of changes in brain activity accompanying sensory stimulation from FES

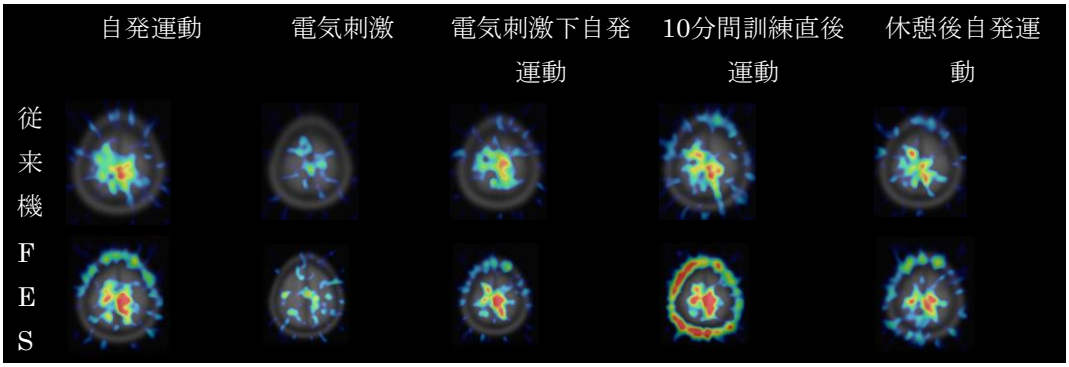


Figure 9　Comparison of brain activation during FES rehabilitation using conventional and new devices

1.3 Future plans

We will engage with the following issues, with a focus on EMG prosthetics and Functional Electrical Stimulation.

(1) Intelligent Control, adjusted to the extent of disabilities

In addition to the use of brain waves and the application of electrodes to the head and shoulder, we will employ posture detection using inertial sensors, collision avoidance using proximity sensors and environment awareness by using AR markers, all in concert with amputees' remaining limb function. Thus we will develop a method of intelligent control for prosthetic arms making greatest possible use of remaining limb function, and apply this to shoulder, upper arm, lower arm and hand amputees.

(2) Addition of sensory feedback function

In order to achieve an EMG prosthetic that provides sensory function as well as replacing movement function of the hand, we will develop an omnidirectional pressure sensor as well as sensory stimulation devices using electrical stimulation and vibrations.

(3) Establishment of automatic pattern searching

In order to construct an algorithm enabling efficient searching for stimulation patterns from multi surface electrode FES, we will develop methods of high speed searching for electrode patterns as well as clustering methods for finger posture taking into account electrode patterns.

(4) Evaluation of prosthetics and electrical stimulation through brain measurements

In order to evaluate the effectiveness of EMG prosthetics and functional electrical stimulation, we will use either fNIRS or fMRI not only when conducting performance tests but also when evaluating sense of body ownership through brain activity measurements or when observing changes in brain activity patterns associated with long term use.

2. Research Achievements

2.1 Reviewed papers [○: Impact factor greater than 4]

(1) Yoshiko Yabuki，Issou Tanahashi，Suguru Hoshikawa，Tatsuhiro Nakamura，Yinlai Jiang，Ryu Kato，Hiroshi Yokoi (2016）. Development of new Cosmetic Gloves for Myoelectric Prosthetic Hand by using Elastomer. *The Japanese Society of Prosthetics and Orthotics*, Vol. 32, No. 3. (in press)

(2) Suguru Hoshikawa，Shintaro Sakodo，Yusuke Yamanoi，Ryu Kato，Soichiro Morishita，Tatsuhiro Nakamura，Tatsuya Seki，Yinlai Jiang，Hiroshi Yokoi (2015). Development and Evaluation of a Simplified Myoelectric prosthetic Hand Realizing Basic Grasp Function in ADL. *Journal of Japan Society for Fuzzy Theory and Intelligent Informatics*, Vol. 27, No. 6, 885-897.

(3) Masahiro Kasuya，Ryu Kato，Hiroshi Yokoi (2015). Development of a Novel Post-processing

Algorithm for Myoelectric Pattren Classification. *Japanese Society for Medical and Biological Engineering*, Vol. 53 No. 4: 217-224.

(4) Ryohei Fukuma, Takufumi Yanagisawa , Shiro Yorifuji, Ryu Kato, Hiroshi Yokoi, Masayuki Hirata, Youichi Saitoh, Haruhiko Kishima, Yukiyasu Kamitani, Toshiki Yoshimine (2015). Closed-Loop Control of a Neuroprosthetic Hand by Magnetoencephalographic Signals. *PLoS ONE*, Vol. 10, No. 7.

(5) Soichiro Morishita, Keita Sato, Hidenori Watanabe, Yukio Nishimura, Tadashi Isa, Ryu Kato, Tatsuhiro Nakamura and Hiroshi Yokoi (2014). Brain-Machine Interface to Control a Prosthetic Arm with Monkey ECoGs during Periodic Movements (submitted). *Frontiers in Neuroscience*, Vol. 8, Article 417, 1-9.

(6) Tatsuya Seki, Tatsuhiro Nakamura, Ryu Kato, Soichiro Morishita, and Hiroshi Yokoi (2014). Development of Five-Finger Multi-DoF Myoelectric Hands with a Power Allocation Mechanism. J*ournal of Mechanics Engineering and Automation*, Vol. 4, 97-105.

(7) Masafumi Kubota，Osamu Yamamura，Tomoko Kamisawa，Igarashi Chiaki，Matsuo Hideaki，Hiroaki Naruse，Seichiro Shimada，Ryu Kato，Hiroshi Yokoi，Kenzo Uchida，Hisatoshi Baba (2014). Immediate Effects of Functional Electrical Stimulation on Kinematic and Kinetic Variables and Oxygenation in Medial Sensorimotor Cortices during Gait in Patients with Acute Cerebral Infarction. *Physical Therapy Research*, Vol. 41. No. 1, 13-20.

(8) Yinlai Jiang, Isao Hayashi, Shuoyu Wang (2014), Knowledge acquisition method based on singular value decomposition for human motion analysis, *IEEE Transactions on Knowledge and Data Engineering*, Vol. 26, No. 12, 3038-3050.

(9) Yinlai Jiang, Shuoyu Wang, Kenji Ishida, Yo Kobayashi, and Masakatsu G. Fujie (2014), Directional control of an omnidirectional walking support walker: Adaptation to individual differences with fuzzy learning, *Advanced Robotics*, Vol. 28, No. 7, 479-485.

Proceedings

(1) Yinlai Jiang, Shintaro Sakoda, Masami Togane, Soichiro Morishita, Hiroshi Yokoi, One-handed Wearable sEMG Sensor for Myoelectric Control of Prosthetic Hands, The International Conference on Wearable Sensor and Robot (ICWSR2015), No. 56, 2015/10/18.

(2) Yinlai Jiang, Shintaro Sakoda, Takeru Togane, Soichiro Morishita, Bao-Liang Lu, Hiroshi Yokoi , A Highly Usable and Customizable sEMG Sensor for Prosthetic Limb Control Using Polypyrrole-Coated Nonwoven Fabric Sheet, IEEE Sensors 2015: Nov. 1-4, 2015/11/03.

(3) Yusuke Yamanoi, Soichiro Morishita, Ryu Kato, Hiroshi Yokoi, Selective Linear-Regression Model for Hand Posture Discrimination and Grip Force Estimation using Surface Electromyogram Signals, 37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC15): 4812-4815, 2015/08/27.

(4) Hesong Ye, Shintaro Sakoda, Yinlai Jiang, Soichiro Morishita, Hiroshi Yokoi, Pinch-Force-Magnification Mechanism of Low Degree of Freedom EMG Prosthetic Hand for Children, The 37th Annual International Conference of theIEEE Engineering in Medicine and

Biology Society (EMBC2015): 2466-2469, 2015/08/27.

(5) Suguru Hoshikawa, Yinlai Jiang, Ryu Kato, Soichiro Morishita, Tatsuhiro Nakamura, Yoshiko Yabuki, and Hiroshi Yokoi , Structure design for a two-DoF myoelectric prosthetic hand to realize basic hand functions in ADLs (submitted), The 37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC2015): 4781-4784, 2015/08/27.

(6) Masahiro Kasuya, Ryu Kato, Hiroshi Yokoi, Analysis and Optimization of Novel Post-processing Method for Myoelectric Pattern Recognition, International Conference on Rehabilitation Robotics (ICORR): 985-990, 2015/08/14.

(7) Misato Ohdaira, Tomoko Kamisawa, Soichiro Morishita, Yinlai Jiang, Masao Sugi, Osamu Yamamura, Hiroshi Yokoi, fNIRS-based analysis of temporal changes of brain activation during long-term conditioning with functional electrical stimulation, international Convention on Rehabilitation Engineering&Assistive Technology (i-CREATe) 2015 : P4, 3-, 2015/08/11.

(8) Misato Ohdaira, Tomoko Kamisawa, Soichiro Morishita, Yinlai Jiang, Osamu Yamamura, Hiroshi Yokoi , fNIRS-based analysis of brain activation with knee extension induced by functional electrical stimulation, IUPESM 2015 World Congress on medical physics & biomedical engineering, IFMBE Proceedings: Vol. 51, 1137-1141, 2015/06.

(9) Daiki Suzuki, Yusuke Yamanoi, Hiroshi Yamada, Ko Wakita, Ryu Kato, Hiroshi Yokoi , Grasping-posture classification using myoelectric signal on hand pre-shaping for natural control of myoelectric hand, 2015 IEEE International Conference on Technologies for Practical Robot Applications (TePRA2015), 2015/05.

(10) Tatsuya Seki, Yinlai Jiang and Hiroshi Yokoi, Approximate model for interactive-tendon driven mechanism of a multiple-DoFs myoelectric prosthetic hand, Proceedings of the 2014 IEEE International Conference on Robitics and Biomimetics: 999-1004, 2014/12/14.

(11) Yinlai Jiang, Shintaro Sakoda, Suguru Hoshigawa, Hesong Ye, Yoshiko Yabuki, Tatsuhiro Nakamura, Masahiro Ishihara, Takehiko Takagi, Shinichiro Takayama, and Hiroshi Yokoi, Development and evaluation of simplified EMG prosthetic hands , Proceedings of the 2014 IEEE International Conference on Robitics and Biomimetics: 1368-1383, 2014/12/14.

(12) Yuki Shimizu, Masao Sugi, Misato Ohdaira, Soichiro Morishita, Tatsuhiro Nakamura, Ryu Kato, and Hiroshi Yokoi: Force Estimation by Surface Electromyography during Functional Electrical Stimulation, Proceedings of the 2014 IEEE International Conference on Robotics and Biomimetics (ROBIO2014), 1345-1350, 2014.

(13) Osamu Yamamura, Tomoko Kamisawa, Masahumi Kubota, Chiaki Igarashi, Yudai Watabe, Seiichiro Shimada, Tetsuya Tsujikawa, Hidehiko Okazawa, Ryu Kato, Hiroshi Yokoi, Kenzo Uchida, Hisatoshi Baba, Tadanori Hamano, Yasunari Nakamoto, Effect of burst stimulation by high frequency biphasic square-wave pulse on cortical perfusion after stroke: A pilot study, American Society of Neurorehabilitation Annual Meeting, 2014/11.

(14) Xiaobei Jing, Xu Yong, Yinlai Jiang, Hiroshi Yokoi, and Ryu Kato, A low-degree of freedom EMG prosthetic hand with nails and springs to improve grasp ability, Proceedings of the 2014 7th International Conference on BioMedical Engineering and Informatics: 466-471, 2014/10/14.

(15) Xu Yong, Xiaobei Jing, Yinlai Jiang, Hiroshi Yokoi, and Ryu Kato, Tendon drive finger mechanisms for an EMG prosthetic hand with two motors, Proceedings of the 2014 7th International Conference on BioMedical Engineering and Informatics: 472-476, 2014/10/14.

(16) Masahiro Kasuya, Masatoshi Seki, Kazuya Kawamura, Yo Kobayashi,Masakatsu G. Fujie, Hiroshi Yokoi, Robust grip force estimation under electric feedback using muscle stiffness and electromyography for powered prosthetic hand, (ICRA2013) 2013 IEEE International Conference on Robotics and Automation: 93-98, 2013/05.

(17) Tatsuya SEKI, Tatsuhiro NAKAMURA, Ryu KATO, Soichiro MORISHITA and Hiroshi YOKOI, Development of Five-Finger Multi-DoF Myoelectric Hands with a Power Allocation Mechanism, 2013 IEEE International Conference on Robotics and Automation (ICRA2013): 2046-2051, 2013/05.

2.2 Book or Book Chapter

(1) Hiroshi Yokoi，Yuki Sato，Minako Suzuki，Yoshiko Yabuki，Tatsuhro Nakamura，Takashi Mori，Soichiro Morishita，Ryu Kato，Osamu Yamamura，Masafumi Kubota，Tomoko Kamisawa，Chiaki Igarashi，Tadashi Isa，Tatsuya Umeda，Hidenori Watanabe，Yukio Nishimura，Katsunori Ikoma，and Tamaki Miyamoto , Engineering Approach for Functional Recovery Based on Body Image Adjustment by Using Biofeedback of Electrical Stimulation, Chapter 12 Clinical Systems Neuroscience: 203-247, Springer Japan, 2015 (Co-author).

(2) Soichiro Morishita，Hiroshi Yokoi, BMI for robotic rehabilitation of motor function of upper limb, Ishiyaku Publishers: 99-104, 2014/01.

(3) Hiroshi Yokoi，et al. chapter 2 Technological support for everyday life，section 2.2 Movement support，section 2.2.6 Prosthesis (artificial arm・artificial leg), 125 Years of The Institute of Electrical Engineers of Japan (1888-2013), The Institute of Electrical Engineers of Japan: 471-473. 2013/10 (Co-author).

(4) Hiroshi Yokoi，Ryu Kato，Tatsuhiro Nakamura，Soichiro Morishita, welfare technology handbook －to support healthy living, Asakura Publishing: 218-225, 2013/10/24 (Co-author).

2.3 Non-refereed articles or translation

(1) Ryu Kato, Hiroshi Yokoi, Five-finger Myoelectric Hand for realizing a Precise human-hand Function, Precision Engineering: 80/ 3, 259-264，2014/03.

(2) Hiroshi Yokoi，Yoshiko Yabuki, Tatsuya Seki, Tatsuhiro Nakamura, Soichiro Morishita，Ryu Kato，Takehiko Takagi, Shinichiro Takayama, Prosthesis of myoelectric control type, Society of Biomechanisms Japan: Vol.38/ No. 1, 39-46，2014/01.

(3) Soichiro Morishita, Hiroshi Yokoi，BMI for robotic rehabilitation of motor function of upper limb，Medical progress: Vol. 246/ No. 13, 1117-1122，2013/09/01.

(4) Tatsuhiro Nakamura, Ryu Kato, Soichiro Morishita, Hiroshi Yokoi, Producing a learning type electric hand, Interface/computer・science＆technology professional journal: 39/ 7, 62-73，2013/07/01.

2.4 Invited lectures

(1) Yinlai Jiang, “Assistance and substitution of body function by robots - walking support machine and myoelectric prosthesis”, The Society of Instrument and Control Engineering, System and Information Division Technical Committee on Human-Machine Systems， 2014/11.

(2) Hiroshi Yokoi, “Robotics rehabilitation projects based on mutual adaptation”, 16th International Graphonomics Society Conference (IGS2013)， Nara, Japan， 2013/06.

(3) Hiroshi Yokoi, Research into a mutually adaptable EMG prosthetic hand”, The Japan Society of Mechanical Engineers, 25th bioengineering lecture, 2013/01.

2.5 Media releases

(1) Imitating the function of hands and feet: pursuing the latest prosthetic limb technology, BS FUJI (TV), 2016/02/14.

(2) Myoelectric arm with learning function: reflecting the difference in individuals’ movements, The Nikkan Kogyo Shimbun “Business and Technology Daily News” (newspaper), 2015/12/09.

(3) Life commentary「How to coexist? Robots and Humans　The founding of the Robot Law Association」, NHK (TV), 2015/11/24.

(4) The Prosthetic Hand that moves just as you want it to-using electrical signals from the muscle, Yomiuri Shimbun (newspaper), 2015/11/12.

(5) Kakushin no izumu “Innovative –isms” ～the wild remarks of innovators～, BSFUJI (TV), 2015/07/03.

(6) Sakidori↗ “Forerunner”, NHK (TV), 2015/06/07.

(7) Dear Mr Galileo, FUJITV, 2015/05/31.

(8) Dream★dream Engine!　TBS radio, 2015/05/30.

(9) TV future heritage: We’re fighting these diseases 2015 Tearful and emotional 10 year commemoration. TBS TV, 2015/04/01.

(10) TV future heritage: 3.8 billion year life special – The latest mystery in neuroscience: what is it to be human!?. TBS TV, 2015/02/11.

(11) Easily produced with a 3D printer Turning muscle movement into electrical signals. The Nikkan Kogyo Shimbun “Business and Technology Daily News” (newspaper), 2014/12/02.

(12) Japan’s Robots: The forefront of cyborg technology. Amazing! Japan Science Encyclopdia. Futaba Publishers Ltd, 2014/02/06.

(13) Mitsubishi UFJ Business Square SQUET Front Runner – Knowledge Pioneers, Mitsubish UFJ Research and Consulting Ltd, 2013/08/01.

(14) Tell me! Kamen Riders: exploring the possibilities of “improved humans”, KK Bestsellers, 2013/04/01.

2.6 Participation in exhibition

(1) YumeNAVI LIVE2014, 2014/7/12, Tokyo BIGSIGHT.

(2) JST Science Agora 2014, 2014/11/7-2014/11/9, Miraikan.

(3) The 29th General Assembly of The Japan Medical Congress, 2015/4/10-2015/4/13, Graduate School of Medicine, Kyoto University.
(4) JSTFair2015, 2015/8/27 -2015/8/28, Tokyo BIGSIGHT.
(5) ICT innovation forum 2015, 2015/10/7, Makuhari Messe.

2.7 Patent

(1) Masahiro Kasuya, Hiroshi Yokoi, Ryu Kato, Myoelectric signal pattern recognition using time-series data and myoelectric prosthetic hand. The University of Electro-Communications, Meltin MMI Co., Ltd., patent application No. 2015-212840, 2015/10/29.
(2) Hiroshi Yokoi, Yousuke Fuyama, Probe holder, The University of Electro-Communications, patent application No. 2015-188245, 2015/09/25.
(3) Hiroshi Yokoi, Hesong Ye, Soichiro Morishita, Shintaro Sakoda, Motor driven hand, The University of Electro-Communications, patent application, No. 2015-165296, 2015/08/24.
(4) Hiroshi Yokoi, Yinlai Jiang, Yoshiko Yabuki, Shintaro Sakoda, Kazunari Tanahashi, Kazumasa Tanahashi, Interface parts, interface devices, and assistance device, The University of Electro-Communications, Tanac Co., Ltd. patent application No. 2015-163683, 2015/08/21.
(5) Takeshi Akiba, Hiroshi Yokoi, Electrical stimulation device, Training apparatus, and Electrical stimulation method, System Instruments, Co., Ltd, The University of Electro-Communications, PCT/JP2014/069429, 2014/07/23, WO2016/013067, 2016/01/28.
(6) Hiroshi Yokoi, Masahiro Ishihara, Pinch mechanism utilizing residual function of finger, patent application No. 2014-022903, 2014/02/08, patent publication No. 2015-146998, 2015/08/20.
(7) Hiroshi Yokoi, Masahiro Ishihara, Kenji Hirai, Pinch mechanism utilizing residual function of palm, patent application No. 2014-019858, 2014/02/04, patent publication No. 2015-146839, 2015/08/20.
(8) Yuki Sato, Minako Suzuki, Hiroshi Yokoi, Ryu Kato, Tatsuhiro Nakamura, Electrical stimulation system and measurement system, patent application No. 2013-259481, 2013/12/16, patent publication No. 2014-133123, 2014/07/24.

2.8 Awards

(1) Yinlai Jiang. Japan Society for Fuzzy Theory and Intelligent Informatics, Encouragement Award, 2013.

2.9 Student guidance

(1) Masahiro Kasuya, 2015, Doctor (Engineering).
(2) Suguru Hoshikawa, 2015, Master (Engineering).
(3) Yusuke Yamanoi, 2015, Master (Engineering).
(4) Shintaro Sakoda, 2015, Master (Engineering).
(5) Yuta Suzuki, 2015, Bachelor (Engineering).
(6) Naoyuki Tani, 2015, Bachelor (Engineering).

(7) Xiang Feng, 2015, Bachelor (Engineering).
(8) Yutaro Hiyoshi, 2015, Bachelor (Engineering).
(9) Keita Kimura, 2014, Bachelor (Engineering).
(10) Rintaro Kamihira, 2014, Bachelor (Engineering).
(11) Mai Nozakura, 2014, Bachelor (Engineering).
(12) Takeru Tohgane, 2014, Bachelor (Engineering).
(13) Yuki Sato, 2014, Master (Engineering).
(14) Daiki Suzuki, 2014, Master (Engineering).
(15) Syunsuke Takazawa, 2014, Master (Engineering).
(16) Xu yong, 2014, Master (Engineering).
(17) Taruki Takashi, 2013, Bachelor (Engineering).
(18) Chida, 2013, Bachelor (Engineering).
(19) Minako Suzuki, 2013, Master (Engineering).
(20) Keita Tanaka, 2013, Master (Engineering).

2.10 Visits by overseas researchers and students

(1) Dianchun Bai, Development of an intelligent robot arm with interactive-tendon-driven mechanism.
(2) Dingguo Zhang, Substitution and assistance of body functions with myoelectric prosthetic hand and functional electrical stimulation.
(3) Xiaoxiao Zhu, Environment measurement for autonomous running robots. 2015.11.23-2015.11.28
(4) Qixin Cao, Weidong Chen, Life support robots, 2015.6.30-2015.7.3.
(5) Baoliang lu Emotion Recognition and Driving Fatigue Detection from EEG.
(6) Xin Li, Wentao Sun, Haotian She (Students of Prof. Qiang Huang of Beijing Institute of Technology), Practical applications of simplified myoelectric prosthetic hand.2015.6.7-2015.8.28.
(7) 10 students of Prof. Feng Duan of Nankai University, Life Support Technologies based on Electrophysiology, 2016.2.26-2016.3.6.

2.11 Study abroad programs for students

(1) Rintaro Kamihira, Strathclyde University, 9.2015 -2.2016.

3. Research funding

3. 1 Grant-in-aid for scientific research

(1) Hiroshi Yokoi (representative), Development of human-machine coadaptation technology inducing brain adaption, Scientific Research (A), 2013/4/1～2016/3/31, total: 45630 Kyen.
(2) Hiroshi Yokoi (representative), The derivative of muscle fatigue with respect to electromyography and functional electrical stimulation to quicken functional recovery, 2012/4/1～2015/3/31, 2012: 1430Kyen 2013: 1430Kyen 2014: 1040 Kyen.
(3) Hiroshi Yokoi (joint leader), Holon Embedded Self-propagating Instructional System,

Challenging Exploratory Research, 2011/4/28～2014/3/31, 2011: 1820 Kyen　2012: 1300 Kyen 2013: 65 0Kyen.

(4) Hiroshi Yokoi (joint leader), Research and development of integrative tactile sense architecture, Scientific Research (A), 2010/4/1/～2014/3/31, total: 44070 Kyen.

(5) Yinlai Jiang (representative), Construction and application of the psychological neurophysiological model involved in the recognition of fragmentary words, Grant-in-Aid for Young Scientists (B), 2013/4/1～2016/3/31, total: 4,030 Kyen.

3.2 Competitive external research funding

(1) Hiroshi Yokoi (representative), Research and development of movement and sensation reproduction using input type BMI electrical stimulation, Ministry of Internal affairs and Communications (SCOPE),2012-2014, 15,918,500 yen.

(2) Hiroshi Yokoi (representative), Development and commercial distribution of 5 digit myoelectric prosthesis for children and infants, Japan Science and Technology Agency (A-step), 2012-2016, 44,230,000 yen.

(3) Hiroshi Yokoi (representative), 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), Ministry of Education, Culture, Sports, Science and Technology,2012-2017, 25,600,000 yen.

4. Collaborators

4.1 Outside UEC

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

(2) Development of myoelectric prosthesis, with Meltin MMI, private enterprise. March 1st 2015-February 28th 2017.

(3) Development of imitation organs for medical use reproducing multilayer structure and sensation of body tissue, and development of multi-layer gel used for imitation body tissue in robotic hands, with Issou Tanabashi at Tanac Ltd. (private enterprise). April 2013-March 2015.

5. Outreach activities

5.1 Editor of academic journals

(1)Yinlai Jiang, Journal of Advanced Computational Intelligence and Intelligent Informatics, editorial member, Mar., 2016 ～.

(2) Yinlai Jiang, Journal of Japan Society fuzzy Theory and Intelligent Informatics, editorial member, Sep., 2015～.

Takuji KOIKE Laboratory

1. Outline of Research and Education

1.1 Basic Policy in Research and Education

In the modern society, the importance of capability to process multimedia information has been increasing each day. Particularly, the reduced ability related to information exchange through hearing has impaired not only physical wellness but also mental health. It also brings disadvantage to disabled individuals and even the society surrounding them. Thus, prevention of hearing loss, effective treatments, and construction of an inclusive society are the most important issues in the modern society.

The auditory system consists of the external ear, the middle ear, and the inner ear (cochlea). The cochlea is filled with lymph fluid, and the sensory cells exist on the basilar membrane which divides the cochlear duct. Sounds travelling through the air 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 auditory ossicles are supported in the tympanic cavity by ligaments and tendons to make them easier to vibrate. However, if these ligaments and tendons are pathologically ossified, the ossicular vibration is restricted, and conductive hearing loss occurs. In addition, if the cochlear functions and the auditory nerve functions are impaired, the sensorineural hearing loss occurs.

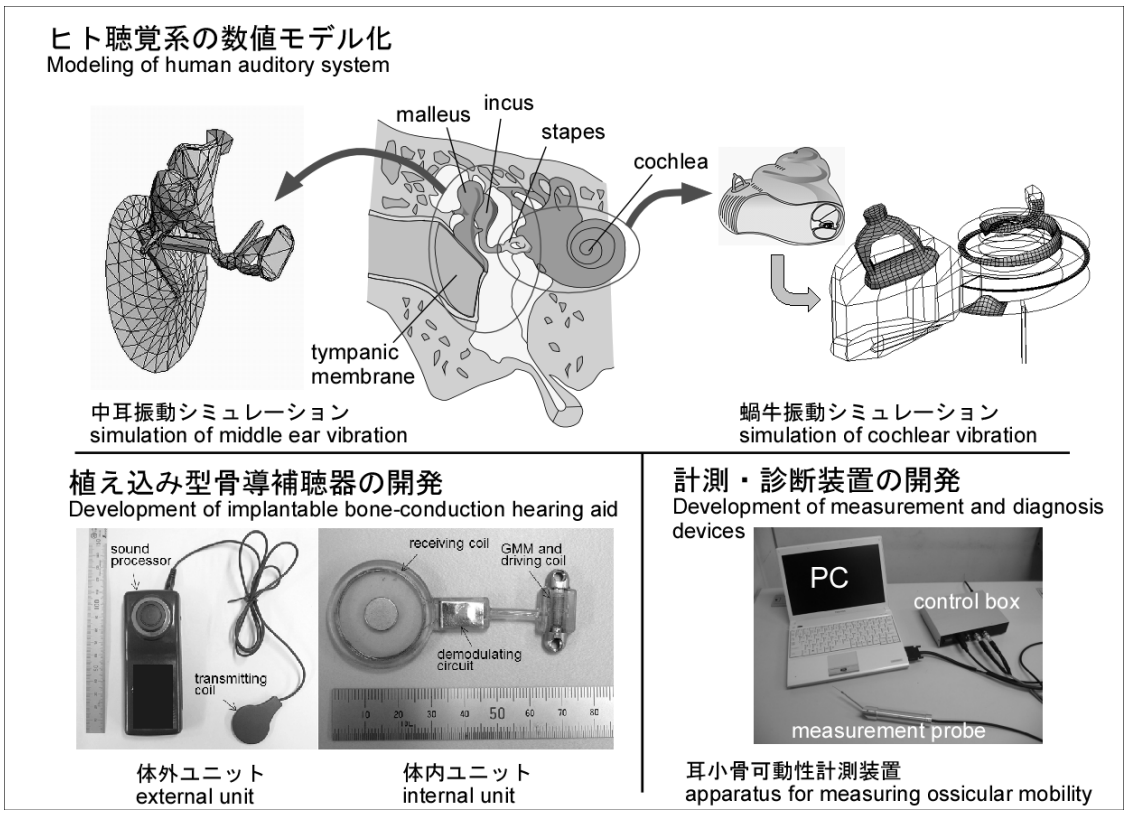


Figure 1 Researches in audiology

The relationships between changes in the ossicular vibration and healing loss have not been fully clarified, because the most of the part of the auditory system exists intracranially and the ossicular vibration is of the nanometer order. Hence, we have investigated the mechanisms of auditory disorders and the methods for treatments collaborating with neighboring medical institutes 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.
- Development of implantable bone conduction hearing aid; Hi-Fi and minimally invasive devices for better QOL.
- Development of surgery assisting apparatus; measurements of ossicular mobility during surgery.

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

(1) Modelling of the auditory systems

This research is intended to clarify the mechanisms of hearing disorders which are difficult to identify through conventional clinical research and specimens and to develop better methods of treatments. Numerical cochlear models in which the active motilities of the outer hair cells are considered have been constructed. Simulations were performed using the models, and the vibrations of the lymph liquid and basilar membrane in the cochlea were analyzed. Through the simulations, the transmission mechanisms in the peripheral auditory systems have been clarified. As clinical applications, the mechanisms of hearing losses caused by otosclerosis and endolymphatic hydrops were investigated. In addition, the optimal design of a cochlear implant was explored, and the effects of the length and insert position of the electrode of the cochlear implant on residual hearing were investigated. Two papers summarizing these results have been invited to medical congresses.

(2) Development of implantable bone conduction hearing aid

A prototype of the bone-conduction hearing aid was created. This device consists of an external unit and an internal unit, and Giant Magnetostrictive Material is used as the vibrator installed into the internal unit. By improving the design of the vibrator and the method of transdermal signal transmission, the device showed higher efficiency comparing with the existing bone-conduction hearing aid. This result provides a prospect of practical use of the new implantable bone-conduction hearing aid. We have already obtained a patent on its basic specifications and work with a company toward practical use of the new hearing aid.

(3) Development of surgery assisting apparatus

An apparatus for measuring ossicular mobility has been developed, and the ossicular mobility in patients has been measured during tympanoplasty. The compliances in patients with ossicular fixation were significantly different from those in normal subjects, and the ossicular mobility can be

quantitatively evaluated based on the compliance. These results suggest that the apparatus enables selection of the optimal method of surgery, improvement of treatment results, and reduction of reoperation ratio. We have started commercialization of the apparatus with a medical device company and neighboring hospitals.

1.3 Future Plan

With regard to the modeling of the auditory system, we have tried to construct network models of ionic flux at the hair cells, the organ of Corti, gap junctions, the spiral ligaments, and the stria vascularis. By coupling them to the cochlear model, the mechanoelectrical transduction in the cochlea will be clarified. We will also advance the development of the implantable hearing aid and the apparatus for measuring ossicular mobility toward commercialization.

2. Research Achievements

2.1 Reviewed papers [○: Impact factor greater than 4]

(1) Takuji Koike, Hideyuki Mochizuki, Tasuku Sakashita (2013), Modeling of the cochlea and its clinical applications, *The Auditory Research Meeting Sponsored by the Technical Committee of Psychological and Physiological Acoustics*, 43(3), 207-211. (in Japanese)

(2) Takuji Koike (2013), Simulation of vibration of mammalian auditory periphery, *Biological Science*, 65(2), 75-81. (in Japanese)

(3) Tsukasa Ito, Hideyuki Mochizuki, Tomoo Watanabe, Toshinori Kubota, Takatoshi Furukawa, Takuji Koike, Seiji Kakehata (2014), Safety of Ultrasonic Bone Curette in Ear Surgery by Measuring Skull Bone Vibrations, *Otology & Neurotology*, 35(4), e135-9.

2.2 Invited lectures

1. Takuji Koike: Medicine and engineering collaborative researches in ENT area, The 28th EHA, Ehime, Matsuyama, March 6 (2016).
2. Takuji Koike: Transfer functions of normal and pathologic middle ears - theoretical analysis -, International Symposium on Middle-Ear Mechanics in Research and Minimally Invasive Otology, Beijing, China, April 20-21 (2013).
3. Takuji Koike, Eri Tanaka, Naoki Hayashi, Takuya Hashimoto, Sho Kanzaki, Naohito Hato, Development of semi-implantable bone-conduction hearing aid using giant magnetostrictive material, The 4th Japan-Switzerland Workshop on Biomechanics, Sept. 1-4, Shima, Mie, Japan (2014).

2.3 Patent

Koike et al., EMBEDDED AUDIPHONE, United States Patent, Patent No. 8,520,867, Date of Patent Aug. 27,2013.

2.4 Awards

Eri Tanaka (student), JSME Fellow Prize, 2015

2.5 Student guidance

Kouta Kuroda, 2016, Bachelor.

Miho Sato, 2016, Bachelor.

Zhao Yan, 2016, Bachelor.

Yamato Murakami, 2016, Bachelor.

Yuta Yoshimura, 2016, Bachelor.

Naoki Hayashi, 2016, Master.

Atuko Murakoshi, 2016, Master.

3. Research funding

3.1 Grant-in-aid for scientific research

Takuji Koike, Grant-in-Aid for Scientific Research (C), 2013-2015.

Takuji Koike, Japan Agency for Medical Research and Development (AMED), 2013-2017.

Takuji Koike, Grant-in-Aid for Scientific Research (B), 2014.

3.2 Competitive external research funding

Takuji Koike, Cross-ministerial Strategic Innovation Promotion Program, 2014-2018.

4. Collaborators

4.1 Outside UEC

Katsuhisa Ikeda, Department of Otorhinolaryngology, Jyuntendo University.

Naohito Hato, Department of Otorhinolaryngology, Ehime University.

Sho Kanzaki, Department of Otorhinolaryngology, Keio University.

5. Outreach activities

5.1 Editor of academic journals

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

5.2 Paper review of academic journals

(1) Applied Bionics and Biomechanics、1 year.

(2) Computational and Mathematical Methods in Medicine、1 year.

(3) Computer Methods and Programs in Biomedicine、1 year.

1. Outline of Research and Education

1.1 Basic Policy in Research and Education

The organs of our body such as a locomotive system and a cardiorespiratory system produce physical movement as a consequence of their functional activities. In our laboratory, we are studying basic human movement to obtain 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 movements mechanically. Specifically we are describing the kinematics of each body segment during physical movements and calculating internal forces such as joint torques by using inverse dynamics method (Figure 1).

Based on these biomechanical analyses, it is possible to develop a new training method to achieve superior motor skills and to evaluate the degree of aging of basic human movements.

In the education, I hope to bring up a talented person contributing to the society and the affluent life of individuals based on scientific knowledge and techniques. I want students to acquire a basic knowledge of engineering and to cultivate practical ability to conduct the research in the biomechanical area. However, I think that it is more important to learn problem solving procedures acquired through a process of pursuit of studies, to feel a surge of creativity emerging from repetitive deep considerations,

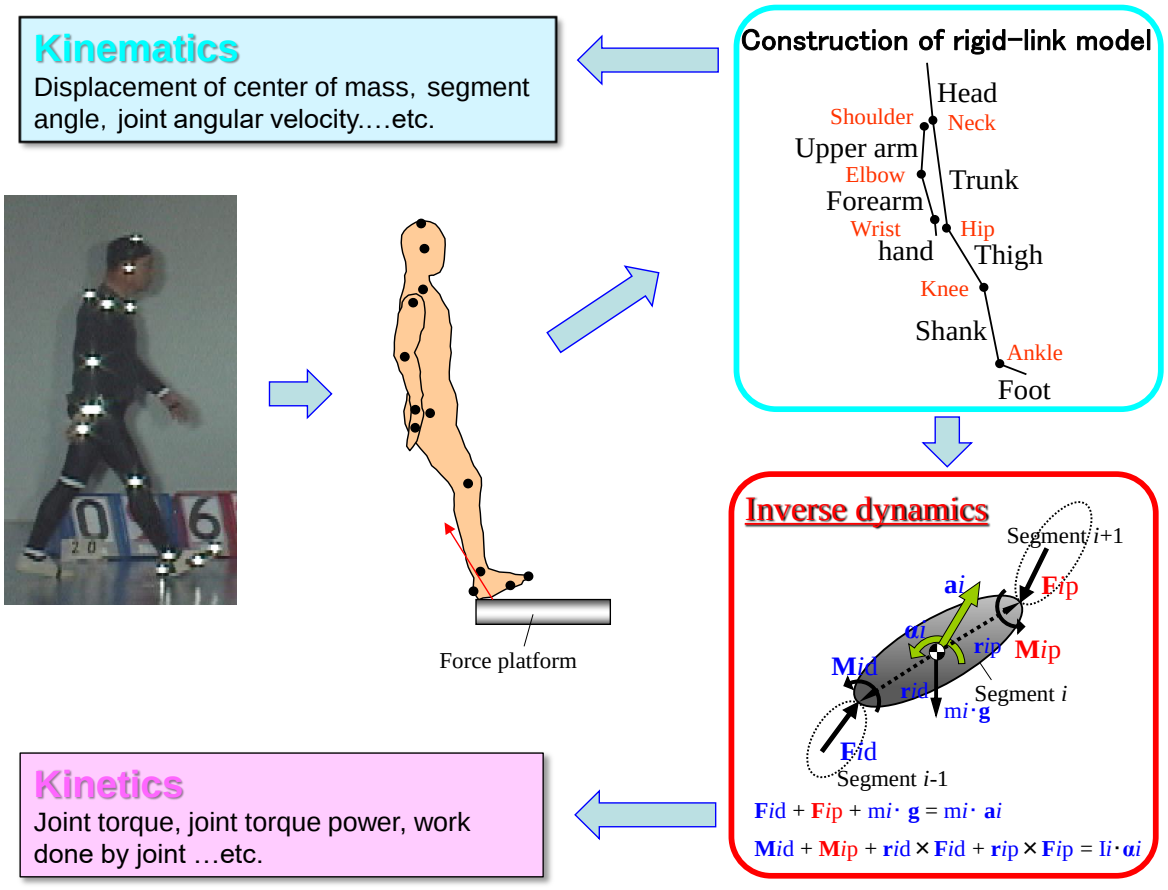


Figure 1 Outline of motion analysis

and to build a spirit of teamwork through the collaboration with colleagues, because these experiences will be certainly utilized in the future in any studies, business or daily lives.

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

I conducted three study themes. The summary is as follows:

(1) Gait motion analysis and application

Accomplishing activities of daily living (ADL) is essential to maintain the quality of life (QOL). This is particularly important in our country which reached super aged society. The locomotion can be considered as the base on carrying out various activities of the life. Walking ability and gait motion change with the aging as the result of changes in various physical functions. It is important and needs of society to clarify the changes and to consider the strategy for the maintenance or improvement of the walking ability and the gait motion.

We analyzed the gait motion for 294 adult males and females and it was clarified that with aging step length was decreased, three lower limb joints showed more flexed position during one gait cycle, work done by the lower limb joints and the contributions changed, and these changes with aging showed the differences between the sexes.

(2) Investigation into the motor skills of athletes

We conducted the kinematic analysis for the baseball pitching and the basic motion of Aikido and the clarified the characteristics of skilled athletes.

In the study of baseball pitching, we analyzed the kinematics of the trunk for the professional pitchers. From the results of the analysis it was suggested that the particularly superior pitcher raised the twist of the trunk by shorten the step length and used the rotatory interlocking of the waist and the shoulders.

In the study of Aikido, we analyzed the “Tenkan” movement that is one of the basic motions in Aikido and clarified the differences of motion by the level of skill. It was suggested that the persons with advanced skills decreased the lowering of center of gravity during the first half of the rotation in Tenkan and rotated about the narrow area of the sole by fixing the ankle joint.

(3) Body segment inertial parameters for top athletes

In the motion analysis, body segment inertial parameters (BSP) are necessary to calculate the center of gravity of whole body and kinetics such as joint torque and angular momentum. BSP is the general term of the mass, the position of center of mass, and the moment of inertia for each body segment. Knowing the BSP for top athletes seems to contribute the grasping the morphological characteristics of various athletic events. Furthermore, calculating the BSP for an athlete who is a subject of the motion analysis precisely contributes the improvement of accuracy of the motion analysis.

We calculated the BSP precisely for 683 Japanese top athletes by using 3D scanner and 3D CAD and showed the mean values for various athletic events. Using these values it became possible to analyze the center of gravity and kinetics for athletes more accurately.

1.3 Future Plan

We are going to proceed with the above three themes.

About the gait motion analysis, we want to calculate the standard value in each generation of Japanese adult men and women based on the data collected so far. In addition, based on the standard aging change, we want to examine the evaluation method of the aging degree of the gait motion.

About the study on the skill of athletes, we are planning to examine the determinants of running economy during the distance running from the view point of kinematics and kinetics.

About the study on the BSP, we attained certain results. We want to classify the morphology and to seek a method to estimate the BSP from simple anthropometric measures in future.

2. Research Achievements

2.1 Reviewed papers [○: Impact factor greater than 4]

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

(2) Saito, M., Iteya, M., Okada, H., Yanagisawa, H., Saito, S., Masuchi, C., Okada, H., and Kimura, M. (2015) Characteristics of power exertions of the pushing movement in Judo. *Bulletin of the Association for the Scientific Studies on Judo, Kodokan*, 15:83-93. (in Japanese)

(3) Kikkawa, K., Okada, H., and Oishi, R. (2014) Age-associated changes of walking parameters in Japanese adult women. *Rejuvenation Research*, 17(2): 229-234.

(4) Kikkawa, K., Okada, H., Mori, T., and Kanamaru, J. Longitudinal development of motor ability and physical fitness among high school Aikidoist. *Japanese Journal of Human Growth and Development Research*, 59:20-26. (in Japanese)

2.2 Book or Book Chapter

(1) Miyanishi, T., Okada, H., and Fujii, N. (2016) Sports Biomechanics, Kagaku-Dojin Publishing Company,INC, Kyoto. (in Japanese)

(2) Nagasawa, J., Tsurugano, S., Tanaka, K., Okada, H., Kano, Y., Ando, S., Fukasawa, K., Ohkawara, K., and Kurotani, K. (2016) Health theory for undergraduate student. Douwashoin Publishing Company, Tokyo. (in Japanese)

2.3 Non-refereed articles or translation

(1) Okada, H. (2013) How to run correctly - thinking running form-, Running World, 16:72-81. (in Japanese)

(2) Kano, Y., Enomoto, Y., Chubachi, S., and Okada, H. (2013) Thinking two-hour marathon, Journal of Running Science, 24(2): 19-42. (in Japanese)

(3) Okada, H. (2013) Skip-run RUN! Run-eco UP! Strength exercise, Runners, Sept.2013, 20. (in Japanese)

2.4 Awards

(1) Kurita, S., Okada, H. 5th Conference of the Asia Society of Sport Biomechanics Excellent Oral Paper Award, 2014.

2.5 Student guidance

(1) Kurita, S., 2016, Master of Engineering
(2) Etoh, K., 2015, Master of Engineering
(3) Ueda, S., 2016, Bachelor of Engineering
(4) Shiihara, A., 2016, Bachelor of Engineering
(5) Kuratomi, H., 2016, Bachelor of Engineering
(6) Yamagishi, D., 2016, Bachelor of Engineering
(7) Wakiyama, K., 2016, Bachelor of Engineering
(8) Arai, S., 2015, Bachelor of Engineering
(9) Hannya, R., 2015, Bachelor of Engineering
(10) Yabiku, S., 2015, Bachelor of Engineering
(11) Uemura, H., 2014, Bachelor of Engineering
(12) Otabe, K., 2014, Bachelor of Engineering
(13) Kurita, S., 2014, Bachelor of Engineering

3. Research funding

3.1 Grant-in-aid for scientific research

(1) Okada, H.（Principal Investigator）, Comprehensive study on the lower extremity motions and muscle activities during distance running, Grant-in-Aid for Scientific Research (C), Fiscal Year 2012-2014, ¥ 5,330,000.
(2) Okada, H.（Co-Investigator）, Study on changes in coherence of the technical factors with the mastering of the aikido skill (Principal Investigator: Kikkawa, K.）, Grant-in-Aid for Scientific Research (C), Fiscal Year 2013-2015, ¥ 150,000.
(3) Okada, H.（Co-Investigator）, Development of the next-generation strength/power training assessment (Principal Investigator: Zushi, K.), Grant-in-Aid for Scientific Research (B), Fiscal Year 2013-2015, ¥ 200,000.

3.2 Competitive external research funding

(1) Okada, H.（Principal Investigator）, Body segment inertial properties of elite athletes in various competitive events, The Japan Science Society Overseas Presentation Promotion Aid, Fiscal Year 2013, ¥ 293,000.

4. Collaborators

4.1 Outside UEC

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

5. Outreach activities

5.1 Paper review of academic journals

(1) The Japan Journal of Coaching Studies, 2013-2014.

(2) Human Factors, 2013.

(3) Japanese Journal of Biomechanics in Sports and Exercise, 2015.

(4) Journal of Running Science, 2013, 2015.

(5) Japan Journal of Physical Education, Health and Sport Sciences, 2014-2015.

5.2 Other outreach activities

(1) Chofu Sports Promotion Council, vice-chairperson (2013-).

(2) Japan Association of Athletic Federations Spread Nurturing Committee, member (2013-).

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 the 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, 5 graduate students took master's degrees in 2013~2015. I would like to continue to guide graduate school students who can play an active part in the research field of computational neuroscience.

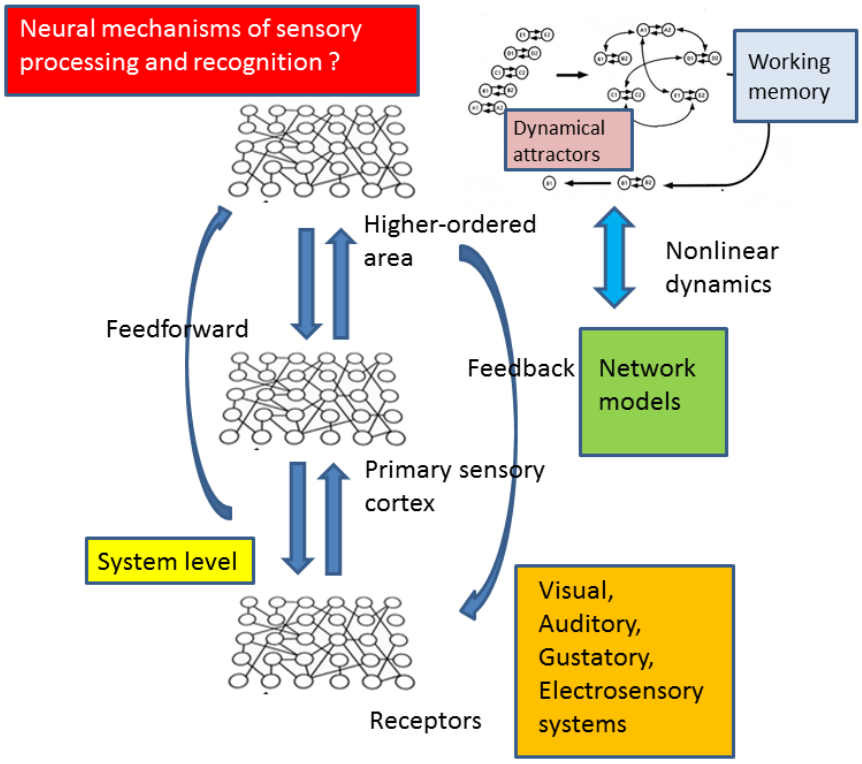


Fig.1 The strategy of our work

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

We have so far obtained four results about three sensory systems. A first one is on the visual system. An experimental study of neural activity in the primate inferior temporal (IT) cortex has reported that stimuli of face objects elicited neural activities that were more strongly correlated than stimuli of non-face objects. To investigate the neural mechanism of the strong correlations, we developed a neural model of the visual system that contains inferior temporal cortex and V4 (Fig. 2). Using the model, we explored the neural mechanism underlying the correlated responses of IT neurons to face objects, and showed the mechanism of how IT neurons create semantic information of objects. Second is on the auditory systems. Sound stimuli evoke spatiotemporal activities of neurons in the primary auditory cortex (A1). However, it remains unclear what kind of information is represented in the spatiotemporal activities. To address this issue, we developed a 3-layered network model that consists of A1 and 2 higher areas (Fig. 3). Using an attractor model, we showed the neural mechanism of how spatiotemporal activities of A1 are transformed to semantic phonemes and words. Furthermore, in our study of bat's auditory systems, we proposed the neural mechanism by which inferior colliculus neurons are phase-locked to sinusoidal-amplitude modulations of sounds. Third is on taste perception. Taste perception is significantly affected by other sensory modalities such as vision, smell, and somatosensation. Such taste sensation elicited by integrating gustatory and other sensory information is referred to as flavor. We developed network models of the primary gustatory cortex (GC) and orbitofrontal cortex (OFC), and presented the neural mechanism of how flavor emerges from the interaction between GC and OFC.

These results demonstrated in our studies of the visual, auditory, and gustatory systems indicate the importance of the viewpoints of system-level dynamical modeling to obtain better understandings of sensory processing in the brain.

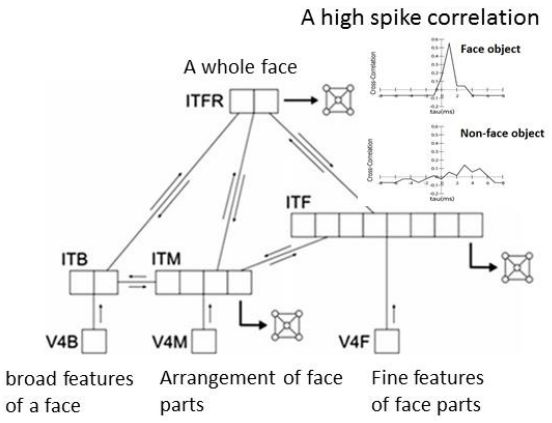


Fig. 2 The model of IT network

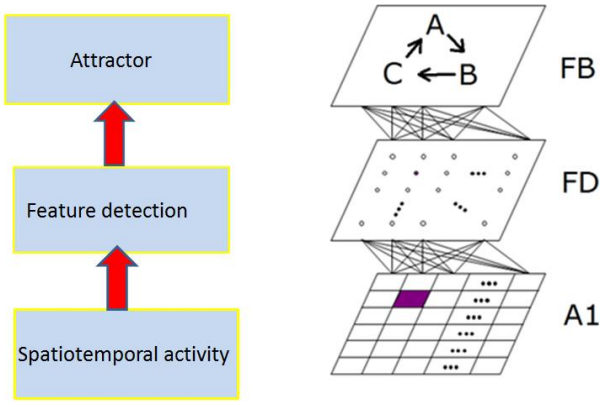


Fig.3 The model of auditory system

1.3 Future Plan

Brain rhythms have crucial roles in the 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 sensory information relevant to behaviors. In contrast, intracortical interactions, mediated by faster oscillations such as gamma rhythm, are involved in representation of sensory information. However, how the brain rhythms contribute to sensory processing and recognition is poorly understood. To address this issue, we study top-down influence on V1 responses in perceptual learning. The top-down influence may be mediated by the brain rhythms. We will explore the neural mechanism by which task-relevant information is gated by top-down signals and multiple brain oscillations. We will also explore the functional roles of rhythmic oscillations in auditory and taste perception. Furthermore, we have a project on the study in electrosensory systems (Grant-in-aid for scientific research). Electrosensory systems have simpler circuit structures compared with those in visual and auditory systems, and the sensory coding of electrosensory systems is well-defined. Therefore, they provide an ideal system for studying sensory processing mechanism by means of a large-scale parallel computing method such as GPGPU computing. Using GPGPU, we will study the geometry of electric field around a fish and sensory processing mechanism of central nervous systems.

2. Research Achievements

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

(1) Takahiro Shimemura, Kazuhisa Fujita, Yoshiki Kashimori (2016). A neural mechanism of taste perception modulated by odor information. Chemical Senses. doi:10.1093/chemse/bjw062

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

(3) Takayuki Kato, Kazuhisa Fujita, and Yoshiki Kashimori (2015). A neural mechanism of phase-locked responses to sinusoidally amplitude-modulated signals in the inferior colliculus. BioSystems, 134, 24-36

(4) Kazuhisa Fujita, Yusuke Hara, Yoichi Suzukawa, Yoshiki Kashimori (2014). Decoding word information from spatiotemporal activity of sensory neurons. Cognitive Computation, 6:145-157

(5) Yuichiro Yamada,Yoshiki Kashimori (2013) Neural mechanism of dynamic responses of neurons in inferior temporal cortex in face perception. Cognitive Neurodynamics, 7:23-38

2.2 Book or Book Chapter

Yoshiki Kashimori, Chap.4-29, In: Researchers teach you animal experimentation Vol. 2. - Neurons and muscles -. Kyoritsu-Syuppan (2015)

2.3 Invited lectures

Yoshiki Kashimori, Dynamic coding of sensory processing and memory. The 39th Annual meeting of the Japan Neuroscience Society, Symposium:Theoretical and experimental approach for the brain function (Kobe, July 2015)

2.4 Student guidance

(2013-2015)

(1) bachelors

Shun Okuno, 2015

Kenji Takei, 2015

Kohei Yoshino, 2015

Ryo Tani, 2015

Hatsuho Aoshima, 2014

Takashi Iida, 2014

Yuki Abe, 2014

Koya Onodera, 2014

Koh Yonekura, 2013

Akira Takazawa, 2013

Takahiro Shimemura, 2013

Yuto Fukada, 2013

(2) Master's degree:

Noboru Aita, 2013

Shunsuke Matsuoka, 2013

Takayuki Kato, 2013

Akikazu Kamiyama, 2014

Takahiro Shimemura, 2015

3. Research funding

3.1 Grant-in-aid for scientific research

Yoshiki Kashimori (Research leader). 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. Collaborators

4.1 Outside UEC

Kazuhisa Fujita, Tsuyama National College of Technology, Cooperation researcher of scientific research (see subsection 3.1)

5. Outreach activities

5.1. Editor of academic journals

Cognitive Neurodynamics, 2006~

5.2. Paper review of academic journals

Cognitive Neurodynamics, May. 2015

Cognitive Neurodynamics, Oct. 2014

Cognitive Neurodynamics, Sep. 2013

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 the 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 a 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 for elucidating an adaptation phenomenon of the skeletal muscle fibers. Therefore, such basic research contributes to the development of effective prophylaxis for the muscle atrophy by bedridden/aging and development of the training method to maintain muscle mass.

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

Recently, we focus on calcium ion (Ca^{2+}) dynamics. In a role of the Ca^{2+} in myocytes, the best known function is regulation of the excitation-contraction coupling (muscle contraction and relaxation). This system is famous as control mechanism clarified by the Japanese researchers led by Ebashi et al. at the 1960s. In addition, the Ca^{2+} in the cytoplasm performs an important function as a signal substance to regulate various cellular adaptations. For example, *in vitro* (*ex vivo*) experiments such as culture cells show that the Ca^{2+} contributes to protein synthesis (mTOR pathway) and breakdowns (calpains pathway). In vital stress such as exercise, heat and hypoxia, we elucidated the Ca^{2+} pathway which flowed in cytoplasm from the cellular outside by *in vivo* model. The Ca^{2+} flows in intracellularly from the cellular outside through ion channel (stretch-activated channels: SAC) of the plasma membrane. We evidenced that the pharmacologic inhibition of the channel suppressed Ca^{2+} influx. Also, there are sex differences in Ca^{2+} influx, and the Ca^{2+} inflow in female is restricted than male rats. In humans, men have larger induction degree of the muscle damage than female. It may be the factor that the difference in inflow of the Ca^{2+} occurs with sex differences of the muscle damage. Also, the diabetes status induces cytoplasmic Ca^{2+} accumulation during muscle contractions. It is expected that the muscle atrophy to progress by diabetes is associated with the failure of the Ca^{2+} homeostasis.

Also, using *in vivo* model, we work on elucidating the oxygen partial pressure dynamics of myocytes by the oxygen quenching method. In particular, we focus on the balance of oxygen supply and consumption as the biological system. AMP kinase (AMPK) activated by AMP due to muscle contractions contributes to cellular energy homeostasis (i.e. activity to keep a fixed ATP as the energy

source in cells). We elucidated that AMPK takes the role as an oxygen sensor contributing to balance of oxygen supply and the consumption.

Peroxisome proliferator-activated receptor gamma coactivator 1-α (PGC-1 α) is a factor to regulate a gene promoting mitochondria and a capillary development. It was reported that muscle endurance ability drastically improves the mouse which overexpressed PGC-1 α in skeletal muscle. We elucidated improvement of the oxygen utilization with the mitochondria in this model mouse. These results show that mitochondrial oxygen utilization potential is determinant of the endurance performance.

Our laboratory applied the *in vivo* bioimaging method to skeletal muscle and built the measurement model that could evaluate intracellular substance dynamics with live individual. This research technique is major advantage in physiology research.

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) Yoshinori Tanaka, Tadakatsu Inagaki, David C. Poole and Yutaka Kano. pH buffering of single rat skeletal muscle fibers in the in vivo environment. *Am J Physiol Regul Integr Comp Physiol.* 2016 Mar in press. IF 3.529

(2) Kohei Yamakoshi, Kazuyoshi Yagishita, Hirotsugu Tsuchimochi, Tadakatsu Inagaki, Mikiyasu Shirai, David C Poole and Yutaka Kano. Microvascular oxygen partial pressure during hyperbaric oxygen in diabetic rat skeletal muscle. *Am J Physiol Regul Integr Comp Physiol.* 2015 Dec 15;309(12): R1512-20. IF 3.529

(3) Yoshinori Tanaka, David C. Poole and Yutaka Kano. pH homeostasis in contracting and recovering skeletal muscle: Integrated function of the microcirculation with the interstitium and intramyocyte milieu. *Curr Top Med Chem.* 2015, in press IF 3.402

(4) Mizuki Sudo, Soichi Ando, David C. Poole and Yutaka Kano. Blood flow restriction prevents muscle damage but not protein synthesis signaling following eccentric contractions. *Physiol Rep*. 2015 Jul;3(7). pii: e12449.

(5) Hiroaki Eshima, David C. Poole, and Yutaka Kano. In vivo Ca2+ buffering capacity and

microvascular oxygen pressures following muscle contractions in diabetic rat skeletal muscles: fiber-type specific effects. *Am J Physiol Regul Integr Comp Physiol*. 2015 Jul 15;309(2): R128-37. IF 3.529

(6) Hiroaki Eshima, David C. Poole, and Yutaka Kano. In vivo calcium regulation in diabetic skeletal muscle. *Cell Calcium*. 2014 Nov;56(5): 381-9. IF 3.513

(7) Yutaka Kano, Shinji Miura, Hiroaki Eshima, Osamu Ezaki and David C. Poole. The effects of PGC-1α on control of microvascular PO2 kinetics following onset of muscle contractions. *J Appl Physiol* (1985). 2014 Jul 15;117(2): 163-70. IF 3.434

(8) Hiroaki Eshima, Yoshinori Tanaka, Takashi Sonobe, Tadakatsu Inagaki, Toshiaki Nakajima, David C. Poole, and Yutaka Kano. In vivo imaging of intracellular Ca2+ after muscle contractions and direct Ca2+ injection in rat skeletal muscle in diabetes. *Am J Physiol Regul Integr Comp Physiol*. 2013 Sep 15;305(6): R610-8. IF 3.529

(9) Yutaka Kano and Kunihiro Sakuma. Effect of aging on the relationship between capillary supply and muscle fiber size. *Adv. Aging Res*. 2: 37-42, 2013.

(10)Tomonobu Sakurai, Osamu Kashimura, Yutaka Kano, Hideki Ohno, Li Li Ji, Tetsuya Izawa, Thomas M. Best. Role of nitric oxide in muscle regeneration following eccentric muscle contractions in rat skeletal muscle. *J Physiol Sci*. 2013 Jul;63(4): 263-70. IF 1.899

2.2 Book or Book Chapter

(1) Multi-authored textbook, Exercise physiology 20 schemes, In Japanese, Asakura Publishing Co., Ltd. 2015

(2) Multi-authored textbook, Health theory for university students, In Japanese, Douwa Publishing Co., Ltd. 2016

2.3 Non-refereed articles or translation

(1) Yutaka Kano and Yoshinori Tanaka, Adaptation of the skeletal muscle microcirculation for HIT, Journal of health, physical education and recreation, 63(9): 695－700,2013, in Japanese

2.4 Invited lectures

(1) Yutaka Kano. Muscle damage and the intracellular calcium ion caused by the eccentric contraction. Japanese Society of Physical Fitness and Sports Medicine, Tokyo (2013,3)

(2) Yutaka Kano. Microcirculation blood flow and oxygen partial pressure dynamics during exercise. Japan Society of Exercise and Sports Physiology, Saitama (2013,7)

(3) Yutaka Kano. The myofunctional evaluation by the bioimaging and the application. Medical Innovation Forum, Tokyo (2013,7)

(4) Yutaka Kano. Capillary remodeling and exercise program of the skeletal muscle. Japanese Society of Physical Fitness and Sports Medicine, Tokyo (2013,9)

2.5 Student guidance

(1) Takuya Saito, Hirotaka Kono, Mario Wakizaka. 2013 Bachelor (engineering)
(2) Saiichiro Koide. 2013, Master (engineering)
(3) Masatoshi Kanazawa, Naoki Inoue, Naoki Shintani, TakuroMashio, Shunsuke Nogami. 2014 Bachelor (engineering)
(4) Tomosada Ishiguro, Kohei Ymakoshi. 2014 Master (engineering)
(5) Hiroaki Eshima. 2014 Doctor (science)
(6) Masao Koizumi, Koji Hatakeyama, Aiko Watanabe. 2015 Bachelor (engineering)
(7) Mario Wakizaka. 2015 Master (engineering)

3. Research funding

3.1 Grant-in-aid for scientific research

(1) Yutaka Kano (representative), Visualization of the mitochondrial behavior for the oxygen environment in myocytes, Grant-in-Aid for challenging Exploratory Research, 2013-2014, 3,770,000 yen
(2) Yutaka Kano (representative), Change of the muscle fiber type as the multinucleate cell, Grant-in-Aid for challenging Exploratory Research, 2015-2016, 3,770,000 yen
(3) Yutaka Kano (representative), Importance of postexercise calcium ion dynamics to determine the adaptation of myocytes Grant-in-Aid for Scientific Research (B), 2016-2019, 17,030,000 yen

3.2 Competitive external research funding

(1) Yutaka Kano (representative), The effects of Intracellular calcium ion and exercise stress on skeletal muscle size, The Uehara Memorial Foundation, 2013, 5,000,000 yen
(2) Yutaka Kano (representative), Cytoplasm calcium ion dynamics are determined for muscle damage and the muscle hypertrophy for the strength training, The Nakatomi Foundation, 2015, 1,500,000yen

4. Collaborators

4.1 Inside BLSC

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

4.2 Outside BLSC in UEC

Takayoshi Kobayashi, Development of the bioimaging method with the high-powered laser, Advanced Ultrafast Laser Research Center, 2015-present

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) Biotechnic & Histochemistry, 2013
(2) BioMed Research International, 2014
(3) Cardiology, 2014
(4) European Journal of Applied Physiology, 2014
(5) The Japanese Journal of Physical Fitness and Sports Medicine, 2014
(6) Journal of Training Science for Exercise and Sport, 2014
(7) Age, 2015
(8) Journal of Applied Physiology, 2015
(9) PLOS ONE, 2015
(10) Journal of Running Science, 2015

5.2 External review board

(1) Japan Society for the Promotion of Science, 2013-2015

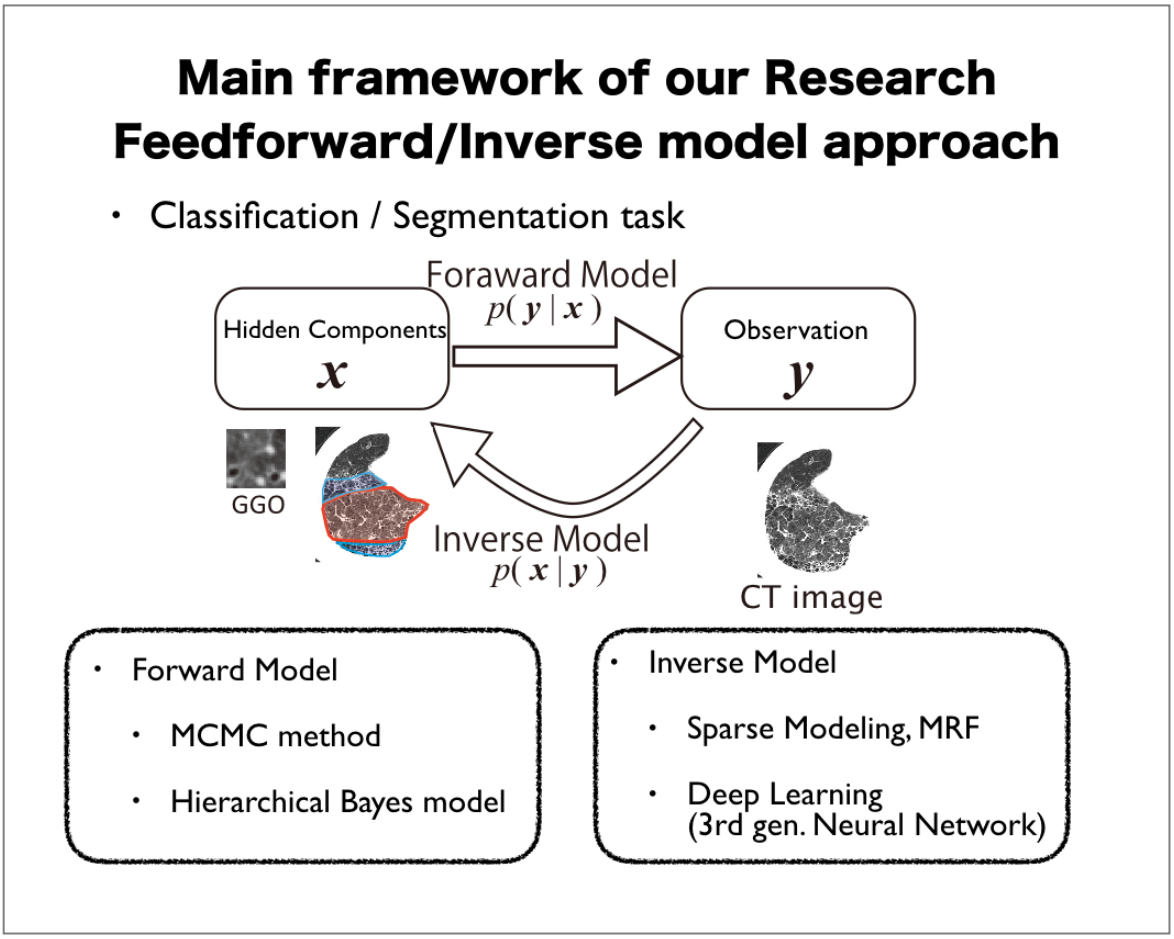
5.3 Thesis jury member in other universities

(1) Tatsuya Yamada, Kanazawa University, 2015.1.27
(2) Eri Ishizawa, Kanazawa University, 2015.1.27
(3) Ronald D. Ray Hamidie, Kanazawa University, 2015.8.3

1. Outline of Research and Education

1.1 Basic Policy in Research and Education

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



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

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

Deep convolutional neural networks (DCNNs) are inspired from the vision system. The DCNN shows good

performance for the classification task in the field of computer vision and machine learning. The DCNN is a kind of multi layer neural network that can learn feature representation from the large amount of training data. However, in the field of the medical imaging, the acquisition cost of large amount of data is high since it requires diagnosed labels. A small number of the training data for the DCNN sometimes lead to over-training. In these years, we introduced the DCNN, which is trained with large amount of natural image data, for the initial state of the novel medical image recognition task. The recognition task is to classify the diffuse lung diseases (DLD) on High-resolution computed tomography (HRCT). We compare DCNNs with training of 1) DLD HRCT images only, 2) natural images only, and 3) DLD HRCT images + natural images. In the result, we show the results of 3) performs 80.04% accuracy, which is the best classification results among those features. Moreover, the results of 2), that performs 75.78%, is just better than that of the case 1) that is 74.13%. Thus, we conclude the pre-matured initial state is important for such novel pattern classification.

(2) Image reconstruction under the low dose observation

We treat an image restoration problem with a Poisson noise channel using a Bayesian framework. In the low dose observation, the photon count variable obeys the Poisson process. Thus, the Poisson randomness might be appeared in observation of low contrast object in the field of imaging. The noise observation is often hard to treat in a theoretical analysis. In our formulation, we interpret the observation through the Poisson noise channel as likelihood, and evaluate the bound of it with a Gaussian function using a latent variable method. We then introduce a Gaussian Markov random field (GMRF) as the prior for the Bayesian approach, and derive the posterior as a Gaussian distribution. The latent parameters in the likelihood and the hyperparameter in the GMRF prior could be treated as hidden parameters, so that, we propose an algorithm to infer them in the expectation maximization (EM) framework using loopy belief propagation (LBP). We confirm the ability of our algorithm in the computer simulation, and compare it with the results of other image restoration frameworks.

1.3 Future Plan

In our future plan, we integrate the component techniques into a system. In the next step we analyze the feature in the DCNN, and design the effective feature. Currently, it is hard understand 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 [○: Impact factor greater than 4]

(1) Li, Yibing, Fu, Qiang, Ye, Fang, Hayaru Shouno, Dark channel prior based blurred image restoration method using total variation and morphology, *Journal of Systems Engineering and Electronics*, No.4, pp.177-184 (2015).

(2) Hayaru Shouno, Bayesian Restoration for Poisson Corrupted Image using a Latent Variational Method with Gaussian MRF, *IPSJ Transactions on Mathematical Modeling and Its Applications*, Vol.8 (1), pp.62-71 (2015).

(3) Yoshinori Ohno, Kenji Nagata, Hayaru Shouno, Masato Okada. Distribution estimation of hyperparameters in Markov random field models, *Journal of Physics A: Mathematical Theoretical* 47, 045001 (2014).

(4) Hiroaki Sasaki, Michael U. Gutmann, Hayaru Shouno, Aapo Hyvärinen. Correlated Topographic Analysis: Estimating an Ordering of Correlated Components. *Machine Learning*, 92: 285-317 (2013).

(5) Y. Arakaki, H.Shouno, K. Takahashi, T.Morie. A hierarchical extension of the HOG model implemented in the convolutional-net for human detection, *IPSJ Transactions on Mathematical Modeling and Its Applications*, Vol. 5(3), pp.54-62 (2013).

2.2 Invited lectures

(1) (invited talk) The 11th Asia-Pacific Conference on Vision APCV 2015, Diffuse Lung Disease Pattern Recognition with Deep Convolutional Neural Network, Jul.11, 2015, Singapore

(2) (invited talk) International Symposium on Object Vision in Human, Monkey, and Machine, Novel texture classification with Deep Convolution Neural Network-Evaluation with Lung CT Images-, Nov. 6, 2015

2.3 Student guidance

Number of undergraduate/Graduate Students

2013 6 Bachelors, 1 Master

2014 4 Bachelors, 2 Masters

2015 6 Bachelors, 1 Master

2.4 Visit of oversea researchers and students

2015 2 short-term exchange students

2014 2 short-term exchange students

3. Research funding

3.1 Grant-in-aid for scientific research

Grand-in-aid for scientific research (C) 25330285: 2013-2015

Grand-in-aid for scientific research on Innovative areas 26120515: 2014-2015

Grand-in-aid for scientific research on Innovative areas 21103008: 2009-2014

4. Collaborators

4.1 Outside UEC

Shoji Kido, Yamaguchi University

Masato Okada, University of Tokyo

Muneyuki Sakata, Tokyo Metropolitan Geriatric Hospital and Institute of Gerontology

Yuichi Kimura, Kinki University

Tomohisa Okada, Kyoto University

Kazuyuki Hara, Nihon University

Kunihiko Fukushima, Fuzzy logic system institute

Seiji Miyoshi, Kansai University

5. Outreach activities

5.1 Editor of academic journals

2012-2014, Associate Editor,IPSJ Transactions on Mathematical Modeling and Its Applications

5.2 Paper review of academic journals

IEICE Transactions on Systems and Information, Neural Networks

1. Outline of Research and Education

1.1 Basic Policy in Research and Education

In aged societies like Japan, there are inevitably many elderly people who have some deficit in the higher cognitive functions. To suppress the increase in the number of such people and in national health care expenditure, we must urgently develop low-cost technologies that support preventive medicine. However, we have little knowledge, if any, about how the brain works for higher cognitive functions, which makes it difficult to develop efficient and useful technologies to ensure the quality of life of those people. On the other hand, recently the technology of artificial intelligence (AI) has been advocated to be a key technology for data mining, pattern recognition and the internet of things (IoT). The theoretical basis of the artificial intelligence is the so-called computational intelligence based on the neural network models in which deep learning and sparse coding are implemented. To develop further the AI akin to humanity, we need to learn more about how the brain processes a huge amount of information every second to make decisions to perform adequate actions in an adequate timing in response to environmental changes. This laboratory is engaged in investigating the underlying mechanisms of how the brain works. One of my major research targets is to obtain a better understanding of developmental mechanisms of the functional architecture that represents visual information, as shown in Fig. 1.

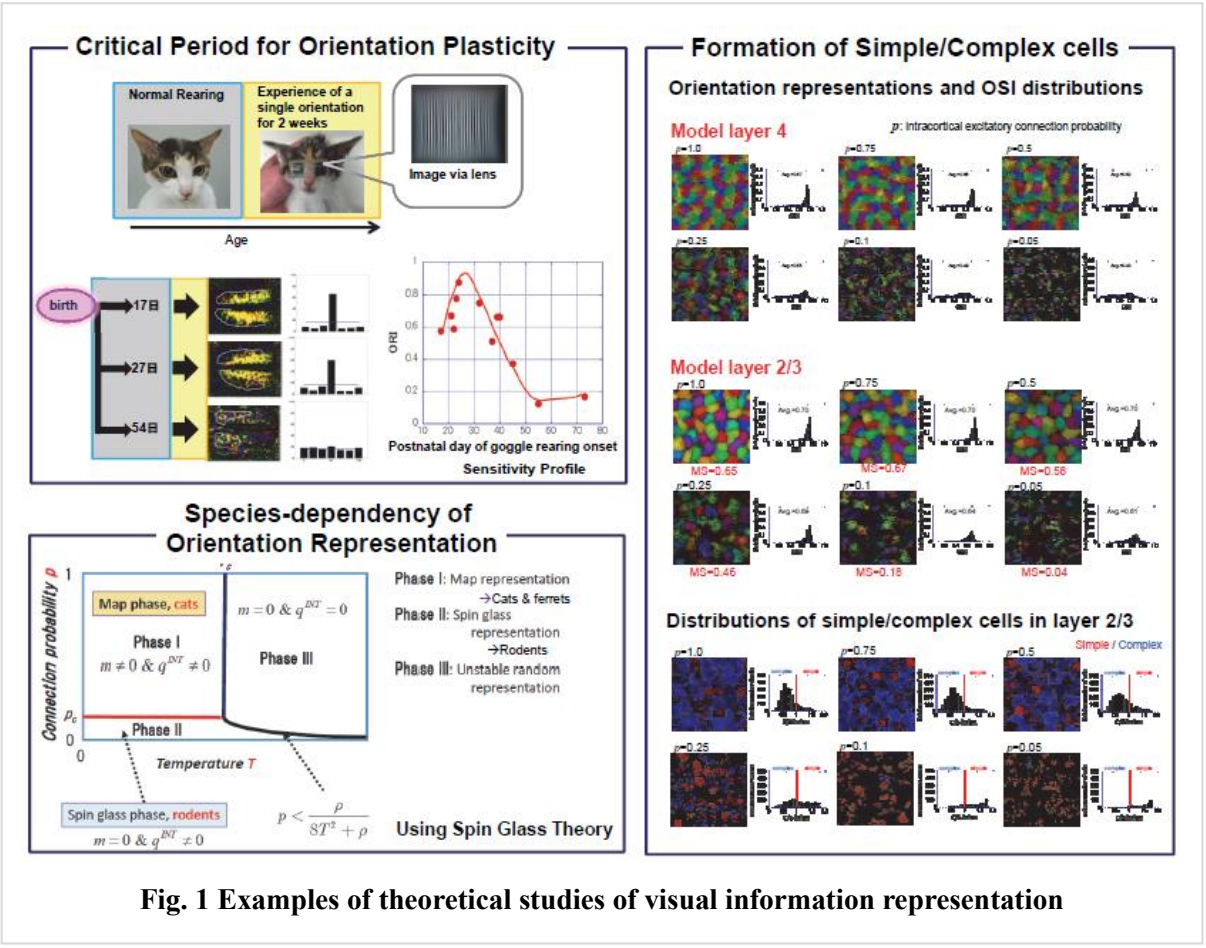


Fig. 1 Examples of theoretical studies of visual information representation

Another major research target is the modeling of working memory. The Baddeley's conceptual model of working memory is composed of phonological loop, visuo-spatial sketchpad, episodic buffer and central executive that is a supervisory system and controls the information flow. This model has been widely accepted for further neuropsychological studies of working memory. However, the central executive in the model may be regarded as the so-called homunculus that is somewhere inside the brain and governs all brain functions. The *a priori* assumption of the central executive results in an infinite regress. To avoid the infinite regress in the working memory model, I study the neural correlate of the central executive for working memory, which is exactly a core of thinking such as reasoning, reflection, planning and scheduling.

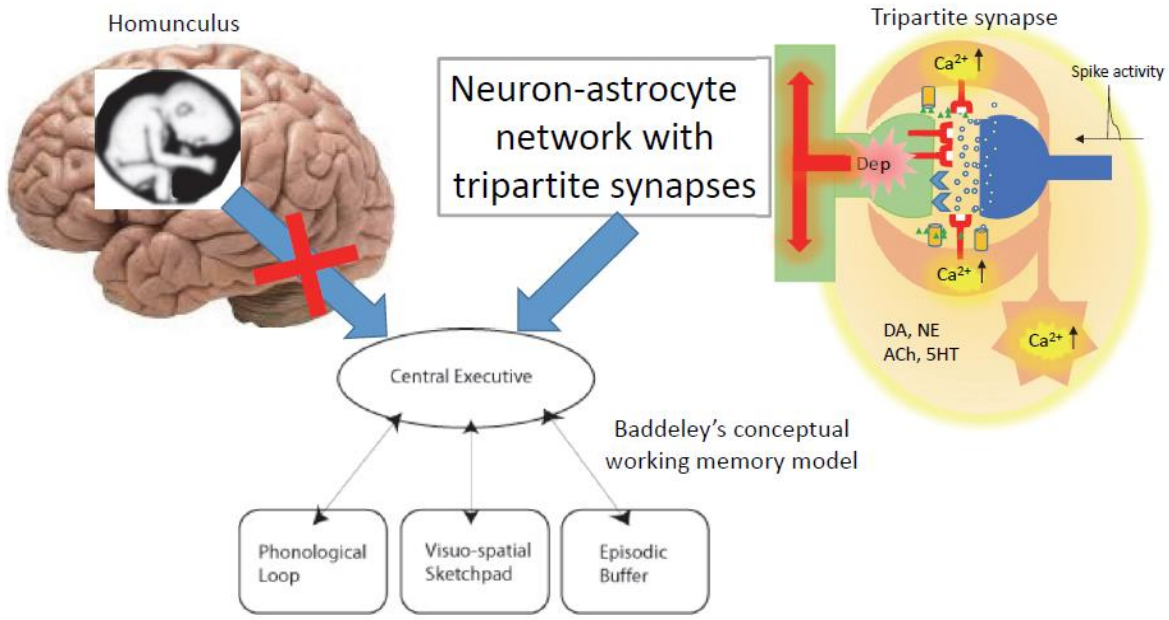


Fig. 2 Construction of working memory model with biological bases

The laboratory had no students during the pertinent period. Hereafter, I describes only the research aspects of achievements.

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

(1) Self-organization of feature representation in the visual cortex

I conducted simulations with collaborators outside of UEC based on my mathematical model of the activity-dependent self-organization of afferent inputs from the lateral geniculate body to layer 4 of the primary visual cortex and afferent inputs from layer 4 to layer 2/3. We successfully reproduced spatiotemporal receptive fields of not only simple cells in layer 4 but also complex cells in layer 2/3. We also obtained orientation, direction and retinotopic maps, which were juxtaposed between layer 4 and layer 2/3, suggesting the formation of columnar organization. Geometrical and topological structures in the simulated maps were found in cat visual cortical maps reconstructed by intrinsic signal optical imaging.

Then, assuming the probabilistic connectivity among nearby excitatory neurons in the visual cortex, we conducted simulations based on the same model. When the value of connection probability p is greater than 0.1, orientation maps with regular arrangement were obtained. In contrast, when the value of p is less

than 0.1, orientation maps were disrupted, despite individual model neurons responsive to visual stimuli exhibited orientation and direction selectivity. About 20% of neurons in the model visual cortex were unresponsive to visual stimuli. It was also found that simulated orientation representations were not juxtaposed between layer 4 and layer 2/3, suggesting the absence of orientation columns. All these properties of feature representations closely resembled those observed in the rodent visual cortex by using the two-photon microscopic calcium imaging. Taken together, simulations of our model suggest that lateral excitatory connections are sparser in the rodent visual cortex than in the cat visual cortex.

To understand how the single parameter *p* can control the qualitative properties of orientation representation as stated above, I analyzed a 2D XY spin model derived from the simplification of our original self-organization model. Applying the so-called replica trick and the mean-field approximation to the simplified model, I obtained a phase diagram of orientation representation. The phase diagram indicated that a phase transition between the orderly map phase and the random and frozen representation phase occurs at small *p* values, where the two phases correspond to the ferromagnetic phase and the spin glass phase in the XY spin system.

In my previous job, I had been exposed kittens to single orientations restrictedly through cylindrical lens-fitted head-mount goggles during critical period, and I found that the representation of the exposed orientation occupied larger cortical territory than the representation of the other orientations. To reveal mathematically how the over-representation of the exposed orientation takes place and what determines the sensitivity profile for orientation plasticity in early life, with my collaborator, I carried out simulations of the same self-organization model for the same simulation steps, for which a model animal is exposed to a single orientation, changing only the starting step of single-orientation exposure. The simulations reproduced the experience-dependent reorganization of orientation maps observed in goggle-reared kittens. The sensitivity for orientation plasticity was defined by the ratio in the area of cortical territory representing the exposed orientation to the area of territory representing the other neurons. We obtained a sensitivity profile for orientation selectivity, which was similar to that observed in intrinsic signal optical imaging in the visual cortex of the goggle-reared kittens. These simulation results suggest that the critical period for orientation plasticity can be determined by sharpness in orientation selectivity rather than the timing of the expression and/or disappearance of functional proteins regulating synaptic plasticity.

Having gained a lot of achievements, as mentioned above, the laboratory is currently in a phase of publishing papers as many as possible.

(2) Mathematical modeling of working memory

I have previously built a network model that correctly works for a working memory task, 1-2-AX task taking into account global networks between the cerebral cortex and subcortical structure such as basal ganglia and thalamus. Particularly, neuron models of medium spiny neurons in the striatum, which show bi-stability in the resting membrane potential, were incorporated in the network model. A working memory model is required to store temporally a sequence of previous actions in a task performance until the sequence is judged to be adequate for getting some reward. Unfortunately, it was found to be difficult for the model to store any sequence of actions flexibly. This flaw in the modeling led me to the skepticism

about the widely believed doctrine – Only neurons processes information, whereas glial cells simply support the survival of neurons without being involved in information processing. However, recently many reports have been accumulated on the presence of intimate neuron-glia communications and synaptic plasticity mediated by these cell-cell communications. Such new findings suggest that various brain functions emerge from not only neuronal networks but also more complicated networks among neurons and astrocytes with tripartite synapses. I postulated a hypothesis that for reinforcement learning of sequential actions, astrocytes preserve neuronal activity patterns with the elevation of intracellular calcium concentration persisting for the time of the order of several seconds. According to this hypothesis, currently I am struggling to build a mathematical model of learning rules of tripartite synapses, which I believe to become a building block indispensable for a biologically plausible working memory model.

1.3 Future Plan

First of all, based on our theoretical studies of the visual cortex, I attempt to construct a general framework for the activity-dependent self-organization of neural networks. Specifically, I will build mathematical models of the reorganization of neural circuits associated with the performance of working memory tasks, taking into account biological findings about tripartite synapses. The central executive for working memory coordinates neural activities among different brain regions, each of which is related to sensory perception, motor control, cognition、 emotion, or some other functions. Its action is thought to emerge from the dynamics of neuron-astrocyte networks under the regulation of neuromodulators such as acetylcholine, dopamine, serotonin and norepinephrine, which are secreted from the basal forebrain and midbrain nuclei depending on awareness, vigilance, reward and emotion. Towards the construction of a unified theory of sensory, motor and cognitive functions of the brain, I will be devoted to modeling of the central executive for working memory, and thereby get rid of a nuisance in the conceptual model of working memory, the homunculus. We will also explore clues for the prevention and medication for psychiatric diseases.

So far this laboratory had no UEC students, and most of research has been conducted collaborating with outside research institutes. In the near future, I will make effort to educate and collaborate with students assigned to the laboratory to obtain some research achievements.

2. Research Achievements

2.1 Reviewed papers [○: Impact factor greater than 4]

(1) Sasaki KS, Kimura R, Ninomiya T, Tabuchi Y, Tanaka H, Fukui M, Asada1 YC, Arai T, Inagaki M, Nakazono T, Baba M, Kato D, Nishimoto S, Sanada TM, Tani T, Imamura K, Tanaka S, Ohzawa I. (2015) Supranormal orientation selectivity of visual neurons in orientation-restricted animals. *Scientific Reports* 10.1038/srep16712.

(2) Yamazaki T, Nagao S, Lennon W, Tanaka S. (2015) Modeling memory consolidation during posttraining periods in cerebellovestibular learning. *Proc Natl Acad Sci USA* **112** (11): 3541–3546.

(3) Takahata T, Miyashita M, Tanaka S, Kaas JH. (2014) Identification of ocular dominance domains in New World owl monkeys by immediate-early gene expression. *Proc Natl Acad Sci USA* **111** (11): 4297-4302.

2.2 Non-refereed articles or translation

(1) Tanaka S. Activity-dependent self-organization: Mammalian mind mapping. International Innovation (Research Media) 131: 27-29, 2014.

2.3 Invited lectures

(1) Tanaka S. Essay of unsolved questions about the self-organization of the primary visual cortex. Seminar at Miyakawa laboratory, Tokyo University of Pharmacy and Life Sciences. 2016, Feb. 9.

(2) Tanaka S. Neuroscience using big data. Megurokai Smart Technology Forum, 2014, Sep. 18.

(3) Tanaka S. Orientation columns revisited: Visual experience, critical period, difference in species. Physiological research symposium "Toward understanding of visual perception – physiological, psychophysical and computational exploration. Okazaki Conference Center, Natural Science Organization, National Institute of Natural Sciences. 2013, Sep. 12-13.

3. Research funding

3.1 Grant-in-aid for scientific research

(1) Shigeru Tanaka （PI）fMRI study for the understanding of sound symbolism and common sense. Challenging Exploratory Research, 2014-2016, 3,370,000 yen.

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

(3) Shigeru Tanaka（CI）Mathematical modeling study of visual information decoding. Scientific Research (C), 2013-2015, 5,200,000 yen.

(4) Shigeru Tanaka（CI）Simulations of brain functions based on computational learning theory. Scientific Research (B), 2011-2013, 19,110,000 yen.

4. Collaborators

4.1 Inside BLSC

(1) Tadashi Yamazaki, Understanding of complementary motor learning with multiple plasticity sites distributed in the cerebellum. 2013-present.

4.2 Outside BLSC in UEC

(1) Masaki Hisano, fMRI study for the understanding of sound symbolism and common sense. 2014-present.

4.3 Outside UEC

(1) Masanobu Miyashita, National College of Technology, Self-organization of visual cortical information representation. 2006-present.

(2) Toru Takahata, Zhejiang University, Interdisciplinary Institute of Neuroscience and Technology

(ZIINT)（National university）, Comparative study of monkey visual cortex using immediate early gene expression. 2012-present.

(3) Jerome Ribot, Visual cortical map representation in cats. 2009-present.

(4) Tomoki Fukai, RIKEN Brain Science Institute, Brain representation of subjective impressions based on sound symbolism. 2014-present.

5. Outreach activities

5.1 Editor of academic journals

(1) ISRN Neuroscience, 2012-present

(2) Science Postprint, 2013-present

(3) NeuroInformatics, 2004-2014

5.2 Paper review of academic journals

(1) IEICE Transactions on Fundamentals of Electronics, Communications and Computer Sciences Aug-Sep. 2013.

(2) Journal of Eye and Brain Dec. 2013.

(3) Frontiers in Computational Neuroscience June-July, 2014.

(4) PLoS Computational Biology March-July, 2015.

(5) International Journal of Neural System Nov. 2015-March, 2016.

(6) Neuroscience Letters Dec. 2015.

5.3 Other outreach activities

(1) Lectures in high schools

Tokyo Metropolitan Showa High School, Oct. 9, 2015.

Tokyo Metropolitan Mitaka Secondary High School, June 17, 2015.

Tokyo Metropolitan Sumidagawa High School, Nov. 5, 2014.

Ono Gakuen Woman's High School, Oct. 25, 2014.

Nihonbashi Jogakkan High School, Oct. 8, 2014.

Tokyo Metropolitan ChofuKita High School, Sep. 24, 2014.

Tokyo Metropolitan Mitaka Secondary High School, Nov. 28, 2013.

Oomachi High School in Nagano Prefecture, Nov. 20, 2013.

Shukutoku High School, Oct. 24, 2013.

Tokyo Metropolitan Showa High School, July. 18, 2013.

1. Outline of Research and Education

1.1. Basic Policy in Research and Education

Research

1) Study of the molecular basis of bioluminescence systems

Bioluminescence is a phenomenon of light emission from organisms. In the bioluminescence reaction, a substrate (luciferin) is oxidized with the aid of an enzyme (luciferase). Light is emitted from the oxidized molecule (oxyluciferin) when it undergoes a transition from an excited state to the ground state (Figs. 1 and 2).

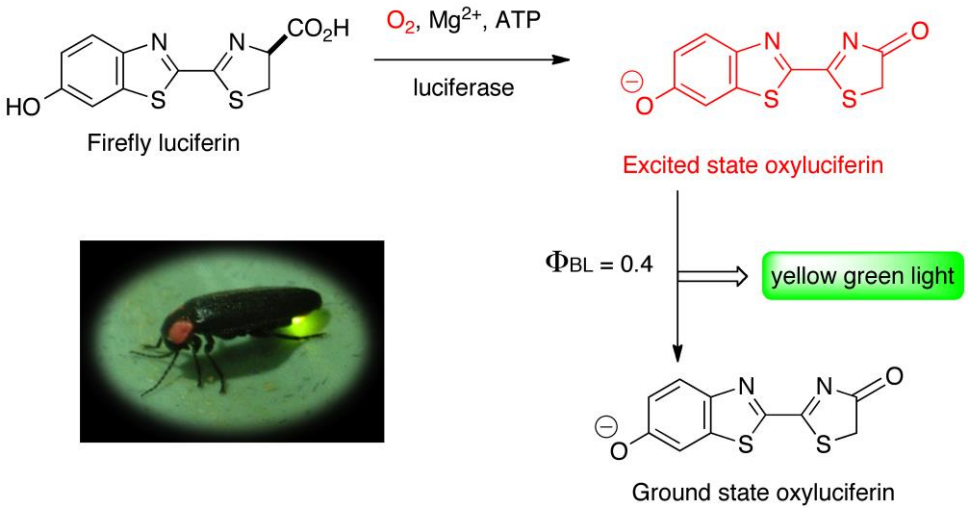


Fig. 1 Bioluminescence reaction in the firefly

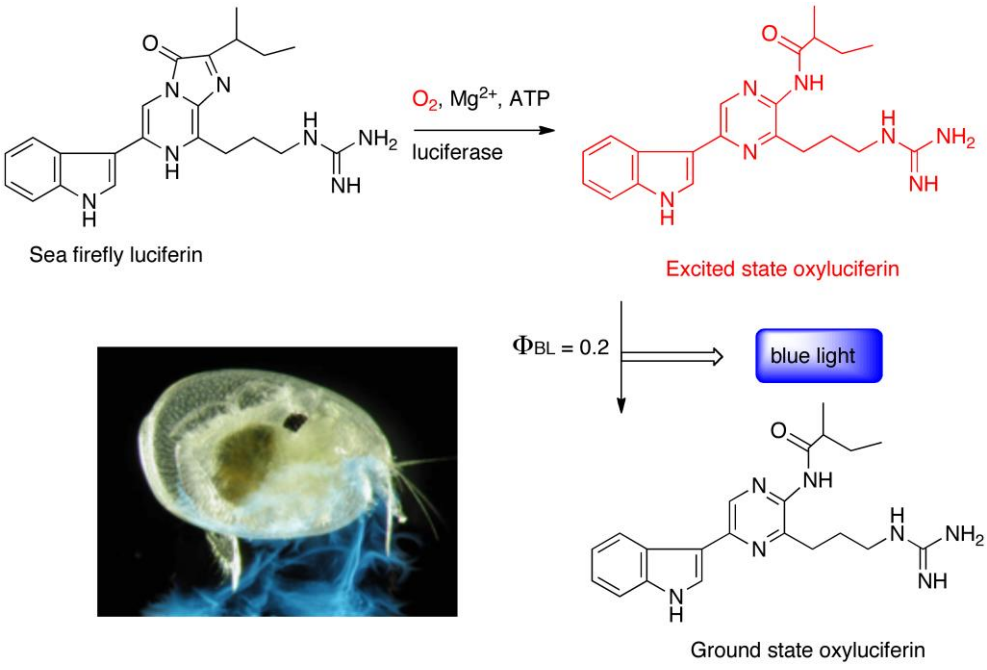


Fig. 2 Bioluminescence reaction in the sea firefly (*Umihotaru* in Japanese)

There are many luminescent organisms, although not all luciferins have been identified. Among those, we are investigating the molecular structures of luciferins of the luminous fungus *Mycena chlorophos* (*Yakoutake* in Japanese) and the sea fireworm *Odontosyllis undecimdonta* (Fig. 3).

Fig. 3 Mycena chlorophos (Yakoutake) (left) and sea fireworm Odontosyllis undecimdonta (right)

2) Development of new luminescent materials inspired by bioluminescence systems

The chemical nature and luminescence property of luciferins, and the corresponding oxyluciferins, give us valuable inspiration for developing unprecedented luminescent materials with useful electronic properties for application in various luminescence devices. Based on the structures of the sea firefly and luminescent jellyfish luciferins, and their corresponding oxyluciferins, we have developed new luminescent materials.

3) Development of firefly bioluminescent substrate for bioimaging of deep site phenomena

Bioimaging with the use of the firefly bioluminescence system is widely used as the standard imaging technology in bioscience for the visualization of various biological phenomena. The wavelength of firefly bioluminescence is around 570 nm (yellow-green). Light emission in the near-infrared (IR) region ("biological window") is highly tissue-permeable and thus optimal for the visualization of deep site phenomena. However, there is no practical substrate of such nature. Therefore, we have developed a practical firefly bioluminescence substrate that emits light in the near-IR region.

4) Development of a noninvasive pulmonary aspiration detection system utilizing highly tissue-permeable near-IR region ("biological window") light

One of the main causes of death among the elderly is pneumonia. More than 90% of pneumonia cases in the elderly are due to pulmonary aspiration. The detection of pulmonary aspiration is therefore very important in preventing aspiration pneumonia. However, there is no practical equipment for easily detecting pulmonary aspiration at home. We therefore have developed a noninvasive, simple aspiration detection system utilizing highly tissue-permeable near-IR region ("biological window") light.

Education

1) Design of a hands-on course for graduate school students

One of the aims of Brain Science Inspired Life Support Research Center (BLSC) activities is to nurture innovative human resources that engage in the development of new interdisciplinary technology and respond to the needs of the medicine and welfare fields by understanding the plasticity of the central nervous system. We have designed a curriculum for a hands-on training course in which students can take part in

graduate-level experiments in a variety of related fields.

2) Design of a hands-on training course for high school students

As part of the outreach activities of BLSC, we designed a hands-on training course for high school students to experience the forefront of research in life support and brain science.

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

Research

1) Study on molecular basis of bioluminescence systems

No significant progress has been made on the isolation and structure determination of luciferins of luminous fungus (Fig.3, left) and sea fireworm *Odontosyllis undecimdonta* (Fig. 3, right).

2) Development of new luminescent materials inspired by luciferin structures

(1) Chemiluminescent properties of 6,8-diaryl-2-methylimidazo[1,2-a]pyrazin-3(7H)-ones were investigated (Fig. 4.; reviewed paper No. 3). The chemiluminescence maxima of the compounds were in the range of 513–553 nm with a bathochromic shift that increased with the electron-withdrawing character of the substituent R.

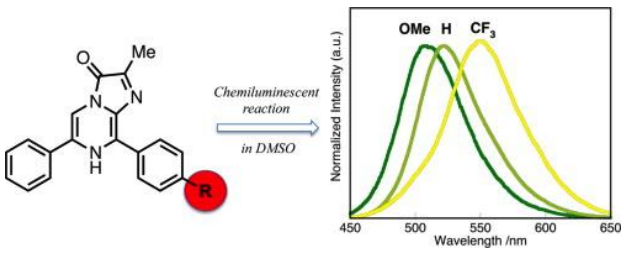


Fig. 4. Chemiluminescence spectra of 6,8-diaryl-2-methylimidazo[1,2-a]pyrazin-3(7H)-ones

(2) Substituent effects on the fluorescence properties of thiazolo[4,5-b]pyrazine derivatives (TPys) were investigated (Fig. 5.; reviewed paper No. 4). TPys were readily prepared from the corresponding amidopyrazines by reaction with Lawesson's reagent. Introduction of electron-donating groups onto the 2-phenyl moiety of the TPys derivatives increased the fluorescence yield and appearance of solvatochromic character.

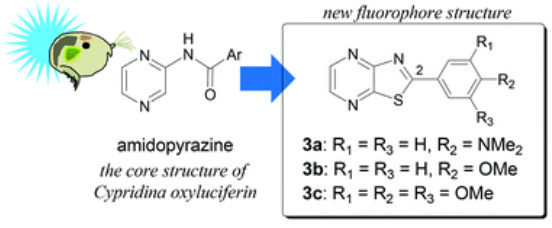


Fig. 5. New fluorophores inspired from the structure of sea firefly oxyluciferin

(3) Newly designed diphenylthiazolo[4,5-b]pyrazines based on sea firefly oxyluciferin structure were synthesized, and the fluorescence properties were investigated (Fig. 6.; reviewed paper No. 5). 2,6-diphenyl derivatives emitted fluoresce more efficiently than 2,5-diphenyl derivatives. Furthermore, a 2,6-diphenyl

derivative with an additional cyano group on the 2-phenyl ring was found to be an excellent fluorophore possessing strong solvatochromic properties with high fluorescence efficiency.

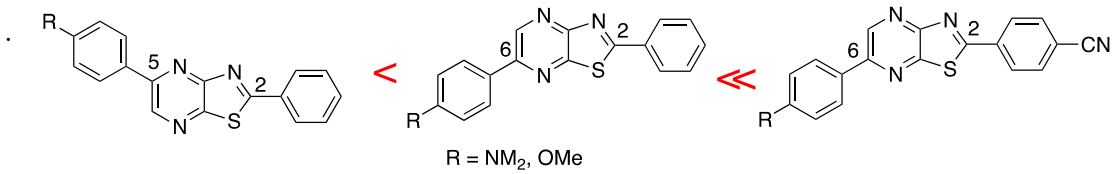


Fig. 6. Fluorescence efficiency of Diphenylthiazolo[4,5-b]pyrazine

(4) New fluorescence substances, BF_2 complexes of *N*-(5-phenyl-2-pyrazinyl)pivalamide and its derivatives based on sea firefly structure, were prepared. The prepared BF2 complexes show fluorescence in solution and in the solid state. The spectroscopic properties were studied by crystal structures and density functional theory calculations. The present work would provide guidance for designing BF2 complexes of amidopyrazines that exhibit solid-state fluorescence (Fig. 7.; reviewed paper No. 6).

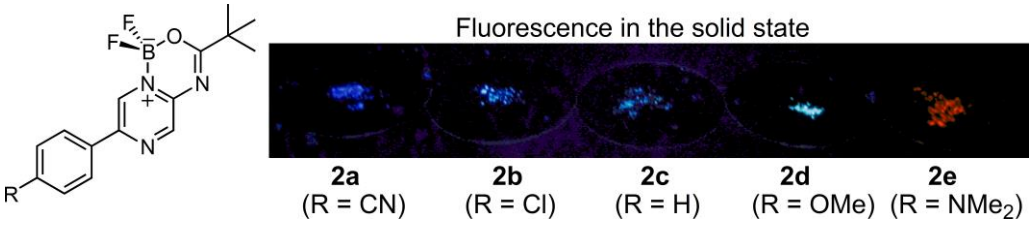


Fig. 7. Fluorescence properties of BF2 complexes of *N*-(5-phenyl-2-pyrazinyl)pivalamide and its derivatives in the solid state

3) Development of a firefly bioluminescent substrate for bioimaging of deep site phenomena

Based on a series of structure–activity relationship studies, we were able to develop a practical firefly bioluminescence substrate for the first time in the world, which emits maximally a near-IR ("biological window") light suitable for deep site visualization (Fig. 8; reviewed papers No. 1 and 2). The developed substrate was found to be more effective for deep site bioimaging than natural firefly D-luciferin (D-LH_2) (Fig. 9). The near-IR light emissive substance was marketed as AkaLumine® and will become a powerful tool for the visualization of deep site phenomena of experimental animals in regenerative medicine and cancer treatment research.

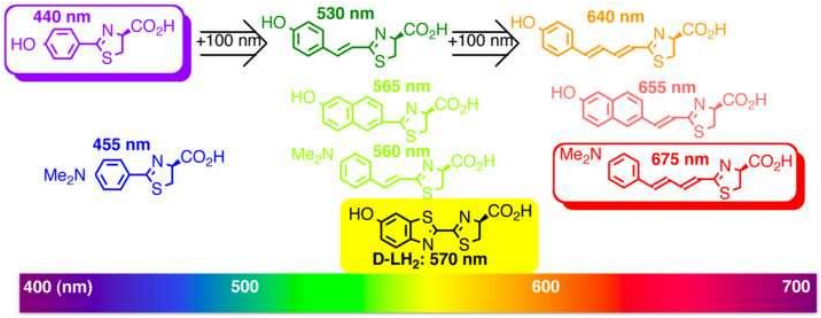


Fig. 8. Bioluminescence maxima of luciferin analogs

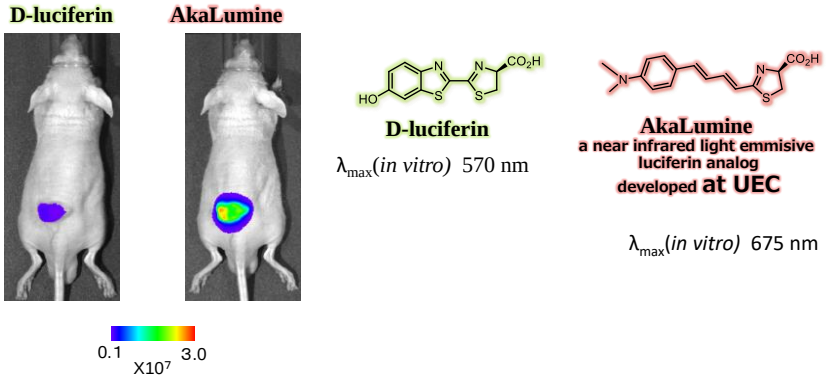


Fig. 9. Bioluminescence imaging of subcutaneous tumor expressing firefly luciferase after injection of AkaLumine or D-luciferin (0.1 mL of 0.5 mM solution). AkaLumine (right) is more effective for deep site imaging than D-luciferin (left). Photos by Takahiro Kuchimaru and Shinae Kizaka-Kondoh (Graduate School of Bioscience and Biotechnology, Tokyo Institute of Technology).

4) Development of a noninvasive pulmonary aspiration detection system utilizing highly tissue-permeable light in the near-IR region ("biological window")

Joint research into the development of a simple noninvasive pulmonary aspiration detection system utilizing highly tissue-permeable near-IR light began with collaboration between Dr. Yukihiro Michiwaki (Japanese Red Cross Musashino Hospital), Professor Yukio Yamada, Assistant Professor Shojiro Maki, and Assistant Professor Soichiro Morishita.

Education

1) Design of a hands-on training course for graduate school students

(1) Activity in 2013:

A curriculum of a hands-on training course for graduate school students was designed through collaboration with Professor Yukio Yamada and Assistant Professor Soichiro Morishita. The following 14 experiments were designed by the Center members. A detailed experiment manual was prepared by a researcher who proposed each subject (manual authors and responsible instructors shown in parentheses).

1. Organic synthesis and instrumental analysis of firefly bioluminescence substrate (Haruki Niwa)
2. Measurement of firefly bioluminescence (Haruki Niwa)
3. Luminescence imaging (Yukio Yamada)
4. Practice of brain–machine interfaces by the analysis of electroencephalogram (EEG) (Soichiro Morishita)
5. Brain activity and body movement measurements from players during a board game such as the Japanese game *shogi* (Soichiro Morishita)
6. Measurement and analysis of human motion by means of an optical motion capture system (Hidetaka Okada)
7. Measurement of auditory brainstem response (ABR) (Takuji Koike)

8. Measurement of distortion otoacoustic emissions (DPOAEs) (Takuji Koike)
9. Measurement of muscle fatigue and motor unit (motor nerves, muscle fibers) function (Yutaka Kano)
10. Functional mapping of human brain activity using functional magnetic resonance imaging (fMRI) (Yoichi Miyawaki)
11. An exercise assistance system using an electrical stimulation device (Hiroshi Yokoi, Soichiro Morishita)
12. Rapid prototyping of experimental equipment using a three-dimensional (3D) printer (Hiroshi Yokoi, Soichiro Morishita)
13. Control of external devices by electromyogram (EMG) processing (Hiroshi Yokoi, Soichiro Morishita)
14. Basics of visual psychophysical experiments (Yoichi Miyawaki)

(2) Activity in 2014:

Based on the experimental manual, the feasibility of the hands-on training course was tested under the cooperation of several student monitors. Each subject was prepared as a 2-day training course, which consisted of a lecture and experiment for 3 hours a day. After an instructor explained the subject background and experimental procedure (1–2 school hours), course students carried out laboratory work under the guidance of the instructor and a teaching assistant. Each subject of the training course was held twice for nine months.

Under the present educational system at the graduate level, students have no opportunity to experience laboratory work on some subjects unrelated to their own major. This hands-on training course is an unprecedented, unique attempt, in that graduate students are able to experience advanced research in areas outside of their own major. This is expected to be very inspiring for them, strongly stimulate their intellectual curiosity, and broaden the scientific views. Actually, according to the post-training reports of the monitor students, it was found that they were fully satisfied with the content of the hands-on training course. We are convinced that the experience of the hands-on training course will lower a hurdle to the cooperation and collaboration with people who work in different areas.

(3) Activity in 2015:

The laboratory manual of the hands-on training course was improved by the revision of descriptions of the individual contents. Also, we added a new laboratory work content “Three-dimensional imaging with laser scanning fluorescence microscopy” designed by Professor Kazuto Masamoto.

1.3. Future Plans

Research

1) Development of a firefly bioluminescent substrate for the bioimaging of deep site phenomena

Currently, the bioluminescence brightness and water solubility of the newly developed, near-IR light emissive substrate AkaLumine remain unsatisfactory. We will continue the development of the brightening and water-soluble substrates.

2) Development of a noninvasive pulmonary aspiration detection system utilizing highly tissue-permeable near-IR region (“biological window”) light

We will develop a noninvasive, pulmonary aspiration detection system utilizing highly tissue-permeable near-IR region (“biological window”) light.

Education

We will continue to develop content for a hands-on training course for UEC graduate school students. We will hold BLSC Spring School for high school students with the new topics.

2. Research Achievements

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

1. Satoshi Iwano, Rika Obata, Chihiro Miura, Masahiro Kiyama, Kazutoshi Hama, Mitsuhiro Nakamura, Yoshiharu Amano, Satoshi Kojima, Takashi Hirano, Shojiro Maki, and Haruki Niwa. Development of simple firefly luciferin analogs emitting blue, green, red, and near-infrared biological window. *Tetrahedron*, Vol. 69, No. 19, 3847-3856 (2013).
2. Chihiro Miura, Masahiro Kiyama, Satoshi Iwano, Kazuto Ito, Rika Obata, Takashi Hirano, Shojiro Maki, and Haruki Niwa. Synthesis and luminescence properties of biphenyl-type firefly luciferin analogs with a new, near-infrared light-emitting bioluminophore. *Tetrahedron*, Vol. 69, No. 46, 9726-9734 (2013).
3. Ryota Saito, Takashi Hirano, Shojiro Maki, Haruki Niwa. Synthesis and chemiluminescent properties of 6,8-diaryl-2-methylimidazo[1,2-a]pyrazin-3(7H)-ones: Systematic investigation of substituent effect at para-position of phenyl group at 8-position. *J. Photochem. Photobiol. A: Chemistry*, Vol. 293, 12-25 (2014).
4. Tatsuki Nakagawa, Minoru Yamaji, Shojiro Maki, Haruki Niwa, and Takashi Hirano. Substituent effects on fluorescence properties of thiazolo[4,5-b]pyrazine derivatives. *Photochem. Photobiol. Sci.*, Vol. 13, No. 12, 1765-1772 (2014).
5. Tatsuki Nakagawa, Minoru Yamaji, Shojiro Maki, Haruki Niwa, and Takashi Hirano. Fluorescence properties of diphenylthiazolo[4,5-b]pyrazines tuned by donor-acceptor substituent effects. *Photochem. Photobiol., Vol.* 91, No. 4, 807-813 (2015).
6. Sojiro Hachiya, Daisuke Hashizume, Hiroshi Ikeda, Minoru Yamaji, Shojiro Maki, Haruki Niwa, and Takashi Hirano. Spectroscopic properties of BF_2 complexes of N-(5-phenyl-2-pyrazinyl) pivalamides exhibiting fluorescence in solution and solid state. *J. Photochem. Photobiol. A: Chemistry*, in press. (http://dx.doi.org/10.1016/j.jphotochem.2015.10.014)

2.2 Patent

(1) Patent Number: P5464311：Luminescent substrate for firefly luciferase
Inventors：Shojiro Maki, Satoshi Kojima, Haruki Niwa
Applicant：University of Electro-Communications
Date of registration：2014. 1 .31

(2) Patent: P5550035：The wavelength-controlled luminescence substrate for firefly luciferase, and the

preparation method

Inventors：Shojiro Maki, Satoshi Kojima, Haruki Niwa

Applicant：University of Electro-Communications

Date of registration：2014/05/30

(3) Patent Application: P2013-097755：New Salts with hydrogen chloride

Inventors：Shojiro Maki, Haruki Niwa.

Applicant：University of Electro-Communications

Date of application ：2013/05/07.

Publication of the application：P2014-218456 (2014/11/20)

(4) Patent application: P2013-198998 New heterocyclic compounds, the salts of those, and the bioluminescent contents containing those.

Inventors：Shojiro Maki, Haruki Niwa.

Applicant：University of Electro-Communications

Date of application：2013/09/25.

Publication of the application：P2015-193584 (2015/11/05)

4. Collaborators

4.1 Inside BLSC

(1) Professor Yukio Yamada and Assistant Professor Soichiro Morishira:
Development of non-invasive pulmonary aspiration detection system utilizing high tissue-permeable near infrared region (biological window) light (~2015).

4.2 Outside BLSC in UEC

(1) Assistant Professor Shojiro Maki (Department of Engineering Science , Graduate School of Informatics and Engineering):
Development of non-invasive pulmonary aspiration detection system utilizing a high tissue-permeable near infrared region (biological window) light (~2015).

4.3 Outside UEC

(1) Dr. Yukihiro Michiwaki (Japanese Red Cross Musashino Hospital):
Development of non-invasive pulmonary aspiration detection system utilizing a high tissue-permeable near infrared region (biological window) light (~2015).

5. Outreach activities

5.1 Paper review of academic journals

(1) Tetrahedron

5.2 Other outreach activities

(1) Part-time lecturer of Department of Chemistry, Graduate School of Science, Toho University (in December, 2015).

Yukio YAMADA Laboratory

1. Outline of Research and Education

1.1 Basic Policy in Research and Education

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

(1) Diffuse Optical Tomography (DOT)

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

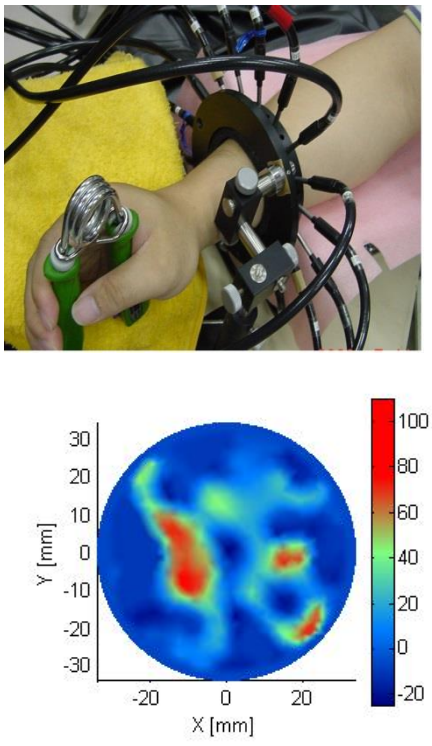


Fig. 1 (Top) Photo of DOT measurement at a forearm, and (Bottom) DOT image showing the increase in the deoxy-hemoglobin concentration due to the muscle activity in the forearm.

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). DOT imaging has also been applied to successfully show the change in the oxygenation status in the head of a premature infant.

(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. In this research, the effects of the various factors on the mapping images are quantitatively investigated by numerical simulations. Figure 2 indicates that the increase in the skull thickness from 5 mm to 10 mm significantly changes the mapping image while the brain activity remains the same.

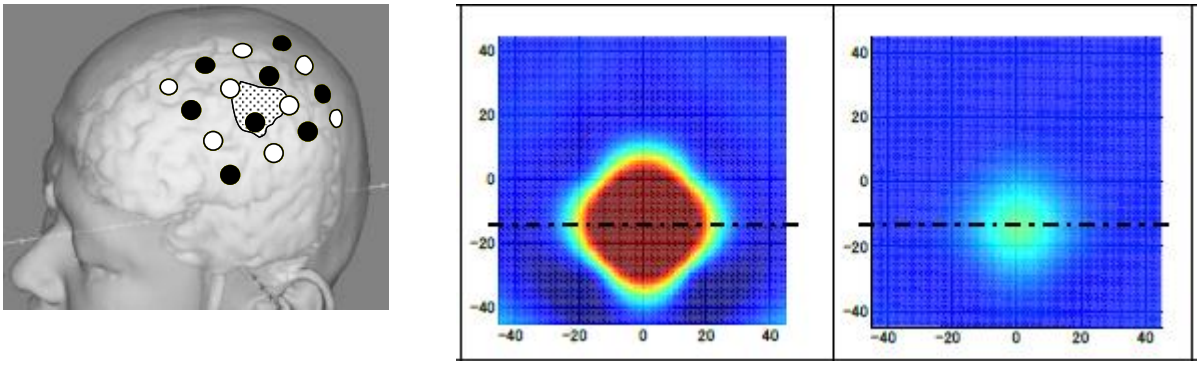


Fig. 2 Illustration of optical mapping with ● and ○ indicating the positions of the sources and detectors, respectively (left panel, courtesy of Hitachi Ltd.). Simulated optical mapping images for the skull thickness of 5 mm and 10 mm, respectively (middle and right panels).

(3) Fluorescence tomography

As an application of DOT, fluorescence tomography is developed to image the distribution of fluorophore concentration inside a body. When a body contains fluorophore which emits fluorescence in the near infrared wavelength range, it is possible to obtain a tomographic images of the fluorophore concentration by measuring the fluorescence light emitted from the body surface. This technology is expected to be used mainly for small animals in the development of new drugs for early diagnosis of breast cancers, and so on. Figure 3 shows a result of fluorescence tomography depicting the concentration distribution of the fluorophore (Indocyaninegreen, ICG) embedded under the skin of a mouse in our *in vivo* experiment.

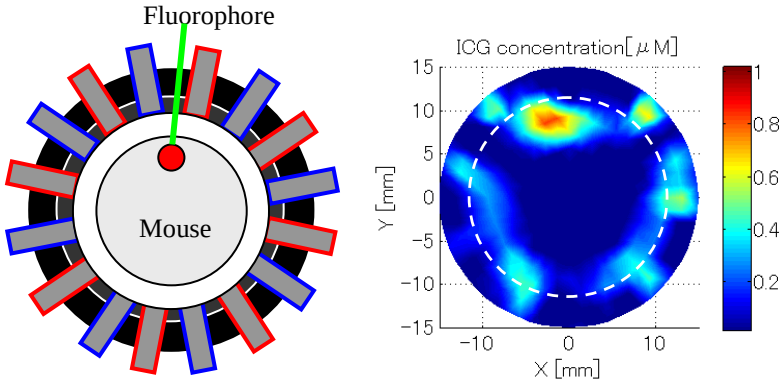


Fig. 3 Experiment of fluorescence tomography. (Left) Arrangement of the probes and a mouse with an embedded fluorophore (Indocyaninegreen, ICG) for fluorescence tomography. (Right) The obtained tomographic image of the ICG concentration.

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

If the conventional method of BGC measurement using blood sampling with painful finger pricking is replaced by a noninvasive measurement method, pains experienced by diabetes patients will be greatly alleviated. However, the development of noninvasive measurement of BGC is very difficult and still unsuccessful even after a few tens of years so far. The purpose of this research is to develop a noninvasive measurement method of BGC using NIRS. The most frequently used method in the past utilized multivariate analyses to build calibration functions from simultaneously measured BGC and spectra of reflected light at the skin by pre-experiments. However, the performance of this method using multivariate analyses was found to be limited. So we have been developing new methods: a method which builds the calibration functions from numerically simulated measurement data without the necessity of pre-experiments, a method which cancels out the changes in the factors influencing the accuracy of predicting BGC, and so on.

(5) Aspiration detection using fluorescence

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

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

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

concentration in the aqueous solution. This method will be applied to measure and image the temperature, solute concentration, reaction rate, etc. in microscale channels in biochips and chemical chips.

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

(1) Diffuse optical tomography

As to the results and present status of the research topic of DOT, we have developed a new method for solving the radiative transfer equation which is considered as the most accurate equation describing the phenomena of light propagation in biological tissue, and have found the effect of void regions like the trachea on the light propagation. These results have been presented in international conferences and also published in academic journals (Ref. 3 and 4). Furthermore, DOT images about the muscle activities in human forearms have been obtained. In this study of DOT for muscle activity, a method has been developed to determine which muscles among many muscles in the forearm are active by comparing the DOT images with the magnetic resonance (MR) images of the human forearms. These results of DOT of active muscles have been published as a dissertation of a Ph.D. candidate (note below). In addition, the Optical Society of Japan invited us to write a review article about DOT, and the article has been published in the journal of "Optical Review" (Ref. 2). The research of DOT has been progressing gradually but certainly.

(Note: Yukari Tanikawa, "*In vivo* Measurements of Muscle Activities of Human Forearm Using Diffuse Optical Tomography," Ph.D. Dissertation, The University of Electro-Communications, Dec. 2014.)

(2) Optical mapping

This study has made clear the effects of various factors on mapping images by numerical simulation quantitatively, and published as a Ph.D. dissertation of a PhD candidate (note below). Based on many studies including this study, Japan Optical Functional Brain Imaging Society (JOFBIS) has started a committee for publishing a guidebook for beginners working with optical mapping. This guidebook gives notes and advices in measurements of optical mapping and functional brain imaging using NIRS in general. Yukio Yamada was assigned for the chair of the committee and is contributing to the development of this field.

(Note: Shuping Wang, "Influences of Anatomy and Blood Flow Changes in the Head Layers on Optical Mapping," Ph.D. Dissertation, UEC, Mar. 2014.)

(3) Fluorescence tomography

As to the fluorescence tomography, a research group that Yukio Yamada participates in has developed a new algorithm for fluorescence image reconstruction to improve the image quality, and a paper has been published in an academic journal. Yukio Yamada has been working and contributing as a collaborating researcher to a project of Japan Agency for Medical research and Development (AMED) (a project of Japan Science and Technology by the fiscal year of 2014).

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

By cooperating with a company which has been collaborating with our group for a few years in the past, a new method of noninvasive NIRS measurement of BGC has been developed and the results have

been published in an academic journal. Our research of this topic is progressing steadily despite its difficulty.

(5) Aspiration detection using fluorescence

This research has started in December 2015. Within the newly organized research group we have discussed the efficiency of a fluorophore we used through the analysis of preliminary and phantom experiments. We believe that a good start has been made toward the development of a new method for aspiration detection using fluorescence at the initiative of our group.

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

Dr. Kakuta, an associate professor of Tokyo Metropolitan University, who used to be an assistant professor in the University of Electro-Communications, has been taking a leadership for conducting this research. At the beginning, only the temperature distribution was the target of noncontact measurement and imaging, but at present, we are trying to carry out simultaneous measurement and imaging of both temperature and solute concentration due to the technical development. The research group has received awards from the Heat Transfer Society of Japan and Japan Council for Near Infrared Spectroscopy. These awarding indicate that our achievements are highly evaluated and that further development is expected.

1.3 Future Plan

For the research topics of (1) diffuse optical tomography and (3) fluorescence tomography, the principal investigator continues to participate in the research activities as a collaborator of the projects titled “Establishment of fundamental technology of quantitative fluorescence molecular tomography sponsored by Japan Agency for Medical Research and Development (AMED) (the fiscal year 2016 is the final year) and “Mathematical analyses of light propagation in biological tissue toward medical applications” sponsored by Japan Society for Promotion of Science (the fiscal year 2016 is the first year). For the topic of (2) optical mapping, the principal investigator continues to take part in the activity as a committee chair of Japan Optical Functional Brain Imaging Society (JOFBIS). For the topic of (4) noninvasive measurement of blood glucose contents (BGC) by NIRS, the principal investigator continues collaboration with the related company. For the topic of (5) aspiration detection using fluorescence, the group including the principal investigator performs the preliminary and clinical tests from the fiscal year of 2016. For the topic of (6) noncontact measurement of temperature and solute concentration in aqueous solution, the principal investigator continues to work in collaboration with the associate professor of Tokyo Metropolitan University.

2. Research Achievements

2.1 Reviewed papers [○: Impact factor greater than 4]

For the topics (1) diffuse optical tomography:

(1) Eduardo Zamora-Rojas, Ana Garrido-Varo, Ben Aernouts, Dolores Pérez-Marín, Wouter Saeys, Yukio Yamada, José Emilio Guerrero-Ginel, "Understanding near infrared radiation propagation in pig skin reflectance measurements," Innovative Food Science and Emerging Technologies, Vol. 22, pp. 137–146 (2014).

(2) Yukio Yamada and Shinpei Okawa, "Diffuse Optical Tomography: Present Status and Its Future," Optical Review, Vol. 21, No. 3, pp. 185-205 (2014). (Invited Review Paper)

(3) Hiroyuki Fujii, Shinpei Okawa, Yukio Yamada, and Yoko Hoshi, "Hybrid model of light propagation in random media based on the time-dependent radiative transfer and diffusion equations," Journal of Quantitative Spectroscopy and Radiative Transfer, Vol. 147, pp. 145–154 (2014).

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

For the topic of (3) fluorescence tomography:

(5) Shinpei Okawa, Akira Yano, Kazuki Uchida, Yohei Mitsui, Masaki Yoshida, Masashi Takekoshi, Andhi Marjono, Feng Gao, Yoko Hoshi, Ikuhiro Kida, Kazuto Masamoto, and Yukio Yamada, "Phantom and mouse experiments of time-domain fluorescence tomography using total light approach," Biomedical Optics Express, Vol. 4, No. 4, pp. 635-651 (2013).

(6) Shinpei Okawa, Tatsuya Ikehara, Ichiro Oda, and Yukio Yamada, "Reconstruction of localized fluorescent target from multi-view continuous-wave surface images of small animal with lp sparsity regularization," Biomedical Optics Express, Vol. 5, Issue 6, pp. 1839-1860 (2014).

For the topic of (4) noninvasive measurement of blood glucose contents (BGC) by NIRS:

(7) Katsuhiko Maruo and Yukio Yamada, "Near-infrared noninvasive blood glucose prediction without using multivariate analyses: introduction of imaginary spectra due to scattering change in the skin," Journal of Biomedical Optics, Vol. 20, No. 4, Paper No. 047003, pp. 1-11 (April, 2015)

For the topic of (6) noncontact measurement of temperature and concentration distributions of aqueous solution:

(8) Naoto Kakuta, Katsuya Kondo, Hidenobu Arimoto, and Yukio Yamada, "Reconstruction of Cross-Sectional Temperature Distributions of Water around a Thin Heating Wire by Inverse Abel Transform of Near-Infrared Absorption Images," International Journal of Heat and Mass Transfer, Vol. 77, pp. 852–859 (2014).

2.2 Non-refereed articles or translation

(1) Naoto Kakuta, Katsuya Kondo, Hidenobu Arimoto, and Yukio Yamada, "Non-contact temperature imaging using characteristics of near-infrared absorption by water," ISCIE (the Institute of Systems,

Control and Information Engineers) Journal 'Systems, Control and Information,' Vol. 57, No. 12, pp. 493-497 (2013). (in Japanese)

2.3 Invited lectures

(1) (Seminar talk) Yukio Yamada, "Near-infrared spectroscopy and diffuse optical tomography/fluorescence tomography," Meeting of research Institute for Mathematical Science, Kyoto University, "Mathematical and numerical analyses of the inverse problems for partial differential equations," Kyoto, July 16-18, 2013. (in Japanese)

(2) (Invited talk) Yukio Yamada, "Development of biomedical photonics, collaboration between industries and academia, and their future prospects," The Sixth Conference of BioOpto Japan, Yokohama, Oct. 15, 2014. (in Japanese)

(3) (Special lecture) Yukio Yamada, "Biological Measurements in Photonics," College of Engineering, Nihon University, Kohriyama, July 7, 2014. (in Japanese)

(4) (Invited talk) Yukio Yamada, "Development of non-invasive optical measurement of blood glucose level," Seminar, Nihon University College of Engineering Worldwide Research Center for Advanced Engineering & Technology (NEWCAT), Kohriyama, Aug. 21, 2014. (in Japanese)

(5)(Invited talk) Yukio Yamada, "Fundamentals of time-resolved spectroscopy," Seminar, Nihon University, College of Engineering Worldwide Research Center for Advanced Engineering & Technology (NEWCAT), Kohriyama, Sep. 28, 2014. (in Japanese)

2.4 Awards

(1) Yukio Yamada, Honorary member, The Heat Transfer Society of Japan, May 22, 2014.

(2) Yukio Yamada, Prize for Credit, Bioengineering Division, The Japan Society of Mechanical Engineers, Jan. 9, 2015.

2.5 Student guidance

(1) Shuping Wang, "Influences of Anatomy and Blood Flow Changes in the Head Layers on Optical Mapping," Ph.D. Dissertation, The University of Electro-Communications, Mar. 2014 (Yukio Yamada, the former advisor).

(2) Yukari Tanikawa, "*In vivo* Measurements of Muscle Activities of Human Forearm Using Diffuse Optical Tomography," Ph.D. Dissertation, The University of Electro-Communications, Dec. 2014 (Yukio Yamada, the former advisor). (in Japanese)

3. Research funding

3.1 Grant-in-aid for scientific research

(1) Yukio Yamada (collaborating researcher with the principal researcher of Prof. Yusuke Iso, Kyoto University), Title: Fundamental research for realization of high resolution diffuse optical tomography by the approach of numerical analyses and applied mathematics, Category: Scientific

Research (B), Period: 2013-2015 (three years), Expenses: ¥ 200,000 (2013), ¥ 250,000 (2014), ¥ 200,000 (2015).

(2) Yukio Yamada (collaborating researcher with the principal researcher of Prof. Hiroshi Yokoi, The University of Electro-Communications), Title: Derivation of a derivative function describing the muscle fatigue as a function of the muscle potential and functional electric stimulation for prompting muscle function recovery, Category: Challenging Exploratory Research, Period: 2012-2014 (three years), Expenses: ¥ 200,000 (2012), ¥ 200,000 (2013), ¥ 200,000 (2014).

3.2 Competitive external research funding

(1) Yukio Yamada (collaborating researcher with the principal researcher of Prof. Goro Nishimura, Hokkaido University), Title: Establishment of fundamental technology of quantitative fluorescence molecular imaging enabling deep tissue imaging of humans, Sponsor: Japan Science and Technology Agency (JST) (2011-2014) and Japan Agency for Medical Research and Development (AMED) (2015-2016), Category: Collaborative Research Based on Industrial Demand, Program: Building of Innovative Biophotonics Technology toward human body imaging, Period: 2011-2016, Expenses: ¥ 769,000 (2011), ¥769,000 (2012), ¥769,000 (2013), None (2014-2016).

(2) Yukio Yamada (collaborating researcher with the principal researcher of Prof. Naoto Kakuta, Tokyo Metropolitan University), Title: Development of simultaneous imaging of temperature and water content in microscale regions using near-infrared spectroscopy, Sponsor: The Canon Foundation, Category: Creation of Industrial Bases, Period: 2012-2013, Expenses: ¥ 250,000 (2012-2013).

4. Collaborators

4.1 Inside BLSC

For the research topic of (5) aspiration detection using fluorescence, collaboration with Profs. Shojiro Maki, Haruki Niwa, and Soichiro Morishita.

4.2 Outside UEC

1. For the research topic of (1) diffuse optical tomography, collaborations with Prof. Y. Hoshi at Hamamatsu University School of Medicine, Prof. H. Fujii at Hokkaido University, Prof. S. Okawa at National Defense Medical College.
2. For the research topic of (3) fluorescence tomography, collaborations with Prof. G. Nishimura at Hokkaido University and Prof. S. Okawa at National Defense Medical College.
3. For the research topic of (4) noninvasive measurement of blood glucose contents (BGC) by NIRS, collaboration with Dr. K. Maruo at Panasonic Healthcare co. Ltd.
4. For the research topic of (5) aspiration detection using fluorescence, collaboration with Dr. Yukihiro Michiwaki of Musashino Red Cross Hospital (MRCH).
5. For the research topic of (6) noncontact measurement of temperature and concentration distributions of aqueous solution, collaboration with Prof. N. Kakuta of Tokyo Metropolitan

University.

5. Outreach activities

5.1 Paper review of academic journals

(1) Journal of Biomedical Optics.

(2) Biomedical Optics Express.

(3) Physics in Medicine and Biology.

(4) Computers in Biology and Medicine.

(5) Optical Review.

5.2 Other outreach activities

(1) Participation to governmental organization as an academic expert

· From Feb. 20, 2014 to Mar. 31, 2014, from Feb. 1, 2015 to Mar. 31, 2015, and from Sep. 1, 2015 to Mar. 31, 2016: Chair of the Working Group for Development of PDT Apparatuses in Medical Navigation, in the Guides Formulation for Developments of Medical Devices, managed by National Institute of Advanced Industrial Science and Technology (AIST).

· From Oct. 2011 to Sep. 2016, Committee member, No. 185 Committee on "Optical Imaging Technique Development," University-Industry Cooperative Research Committees, The Japan Society for the Promotion of Science (JSPS).

· From Mar. 2014 to present, Reviewer of the proposals for various projects sponsored by NEDO for development of industrial technologies, New Energy and Industrial Technology Development Organization (NEDO).

(2) Participation to committees of academic societies

· From Aug. 1, 2015 to present: Chair of the committee for publishing "Guidebook for measurements of functional near-infrared spectroscopy (fNIRS)", Japan Optical Functional Brain Imaging Society (JOFBIS).

(3) Research and education in other organizations

· From Jun. 1, 2013 to Mar. 31, 2015 and from Oct. 1, 2015 to Mar. 31, 2017: Professor of Nihon University, College of Engineering Worldwide Research Center for Advanced Engineering & Technology (NEWCAT).

· From Apr. 1, 2013 to Mar. 31, 2017: Visiting Researcher of Theranostic Device Research Group, Health Research Institute, National Institute of Advanced Industrial Science and Technology (AIST).

Kazuto MASAMOTO Laboratory

1. Outline of Research and Education

1.1 Basic Policy in Research and Education

Using two-photon laser scanning fluorescence microscopy recently introduced in Brain Science Inspired Life Support Research Center (BLSC), our lab aimed to understand the signaling mechanisms and cellular interplays in the brain neurovascular unit, specifically focusing on bio-transportation and cell-to-cell communications in a microscopic scale. The ultimate goal of our research activities is to develop and establish the diagnostic methods for early detection and prevention against the pathogenesis of neurodegenerative and cerebrovascular diseases, such as vascular dementia and mental diseases.

A. Research on functional plasticity in the neurovascular coupling by using bio-photonic imaging techniques

Normal brain functions are maintained by cellular interplays among the neurons, glial, and vascular cells. In this study, fluorescently-labeled brain cells with genetically encoded indicators were automatically assigned with respect to their locations relative to the vascular networks. Each cell's activity was characterized with massive imaging data and quantitatively compared to understand the heterogeneity of the cellular states and plasticity. To this end, a variety of bio-photonic imaging and quantitative analytical techniques have been developed (a collaborative work with National Institute of Radiological Sciences).

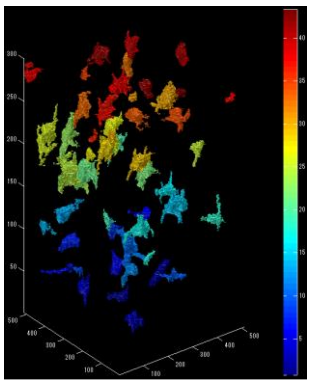


Fig. 1 A three-dimensionally reconstructed image of fluorescently- labeled cells with genetically-encoded calcium indicator in mouse brain.

B. Research on *in vivo* cellular restructuring in the neurovascular unit based on multi-dimensional imaging data

To accurately simulate realistic flow, metabolism, and bio-transportation of the factors used in and out of the brain cells, it is prerequisite for capturing the imaging data on neurovascular unit at high spatiotemporal resolution. Here, we develop a novel algorithm to accurately visualize and quantify the 3D or 4D imaging data on neurovascular structures and functions with a custom written software.

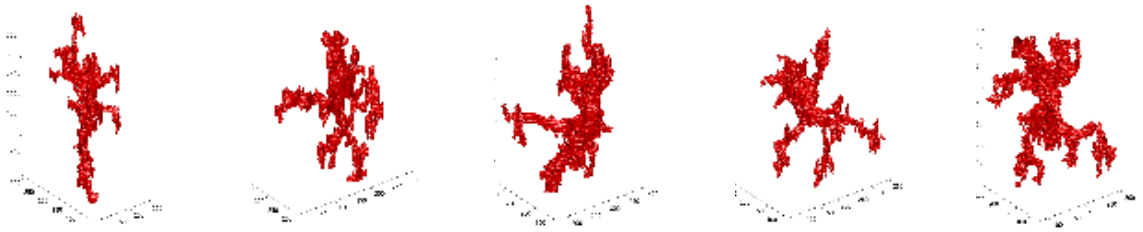


Fig. 2 Three-dimensionally reconstructed images of fluorescently-labeled astrocytes.

C. Research on Physiological Diversity of Astrocytes based on the Automatic Recognition of Astrocytic Morphology

It is well-known that astrocytes of a star-like shape (Red in Figure) are cells interacting with neurons and vascular cells to maintain homeostasis of the cellular environment. The astrocytes change their morphology upon the disturbance of the neural and/or vascular functions. We have studied the underlying mechanism of their morphological changes associated with brain diseases. It may be possible to use a pattern of the morphological changes of the astrocytes as a potential biomarker for diagnosis of brain diseases.

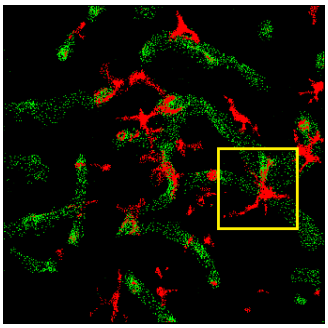


Fig. 3 A morphological image of cortical vessels (green) and astrocytes (red).

D. Research on Spatiotemporal Fluctuation in Brain Microcirculation toward the development of a Non-invasive Brain Health Monitoring System

A long lasting reduction of brain blood flow eventually causes a variety of brain diseases. To prevent and detect the early sign of the disturbance of brain circulation, we have been developing the monitoring methods for states of brain circulation using the spectra of spatiotemporal fluctuations in brain microcirculation with non-invasive near infrared optical measurement techniques.

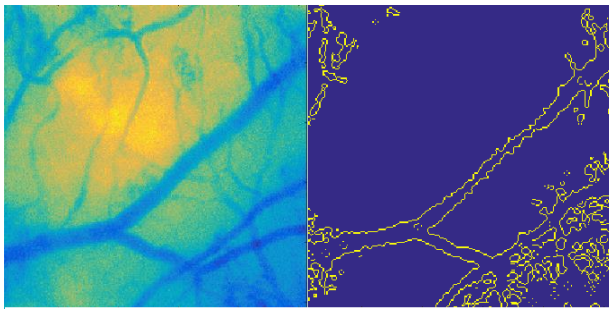


Fig. 4 A vascular structure (left) and its reconstructed image (right) of rat cortical surface captured with EM-CCD camera.

E. Research on Neurogenic and Gliogenic Mechanisms of Brain Blood Flow Regulation and Its Local Enhancement with Optogenetic Tools

Recently, we demonstrated that local brain blood flow transiently can be augmented by optogenetically activating the cortical astrocytes in *in vivo* mouse brains. In this study, to further understand the physiological role of neurogenic and gliogenic regulation of brain blood flow. To this end, we have recently established an animal model to activate a specific type of the cells non-invasively by using optogenetic tools. (a collaborative work with School of Medicine, Keio University).

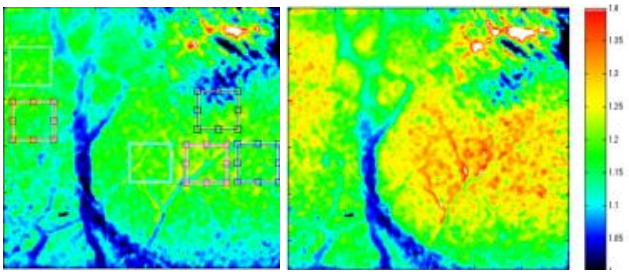


Fig. 5 An optically- evoked increase in brain blood flow captured with laser speckle flowgraphy in the mouse cortical surface (left: pre-stimulation. right: post-stimulation).

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

・Using longitudinal *in vivo* two-photon microscopy in the mouse model of chronic cerebral hypoxia, we have characterized morphological changes in cerebral microvascular networks (Yoshihata et al.,

AdvExpMedBiol 2013), the hypoxia-induced adaptation of cerebrovascular functions (Sekiguchi et al., JCBFM 2014) and neurovascular coupling flow responses to chronic hypoxia (Takuwa et al., JCBFM 2013; Tajima et al., JCBFM 2014).

- Live imaging with longitudinal *in vivo* two-photon microscopy revealed vascular plasticity (i.e., capillary angiogenesis) and its effect on glio-vascular interface where newly-formed microvessel got covered with thin processes of the neighboring astrocytes (Masamoto et al., JCBFM 2014).
- Using optogenetic tools, we have demonstrated that a cell-specific activation of cortical astrocytes leads to a robust increase in local blood flow in the *in vivo* mouse cortex (Masamoto et al., Sci Rep 2015).

1.3 Future Plan

A. Studies on Brain Cell Spacing: To identify and quantify the cellular locations and their activities based on 3D two-photon microscopic images of the brain cells and microvessels, in order to characterize changes in the spatial relationships between a specific type of the cells and the vascular networks during aging and/or in ischemic or dementia brains with comparison to normal brains. Quantifying spatial relationships between microvessels and brain cells, and morphological features of individual cells in the reconstructed 3D structure of neurons, glial cells and microvessels in the mouse brain, we will examine changes of brain tissue in aged mice and the mouse model of diseases such as cerebral hypoxia and dementia.

B. Studies on Blood-Brain Exchange: To probe the cellular interplays between the vascular and brain cells during the alteration of the brain microvascular networks and blood flow by specifically focusing on environmental changes and cellular bio-transportation. We will investigate the effects of vascular genesis and increase of blood flow on the functions of neurons and glial cells, paying attention to cellular bio-transportation and changes in cellular environment.

C. Studies on Brain Health Monitoring: To determine physiological sources of the slow oscillation of the microvascular blood flow and its link to cellular states, functions, and environments by introducing systemic changes and/or pharmacologically manipulating the local/global brain activities.

2. Research Achievements

2.1 Reviewed papers [○: Impact factor greater than 4]

(①) Masamoto K, Unekawa M, Watanabe T, Toriumi H, Takuwa H, Kawaguchi H, Kanno I, Matsui K, Tanaka KF, Tomita Y, Suzuki N. Unveiling astrocytic control of cerebral blood flow with optogenetics. *Sci Rep* 5: 11455. (2015).

(②) Unekawa M, Tomita Y, Toriumi H, Osada T, Masamoto K, Kawaguchi H, Itoh Y, Kanno I, Suzuki N. Hyperperfusion counteracted by transient rapid vasoconstriction followed by long-lasting oligemia induced by cortical spreading depression in anesthetized mice. *J Cereb Blood Flow*

Metab 35(4): 689-98 (2015).

(③) Sekiguchi Y, Takuwa H, Kawaguchi H, Kikuchi T, Okada E, Kanno I, Ito H, Tomita Y, Itoh Y, Suzuki N, Sudo R, Tanishita K, Masamoto K. Pial arteries respond earlier than penetrating arterioles to neural activation in the somatosensory cortex in awake mice exposed to chronic hypoxia: an additional mechanism to proximal integration signaling? *J Cereb Blood Flow Metab* 34(11): 1761-70. (2014).

(④) Tajima Y, Takuwa H, Kokuryo D, Kawaguchi H, Seki C, Masamoto K, Ikoma Y, Taniguchi J, Aoki I, Tomita Y, Suzuki N, Kanno I, Saeki N, Ito H. Changes in cortical microvasculature during misery perfusion measured by two-photon laser scanning microscopy. *J Cereb Blood Flow Metab* 34(8): 1363-72. (2014).

(5) Murata R, Takada Y, Takuwa H, Kawaguchi H, Ito H, Kanno I, Tottori N, Yamada Y, Tomita Y, Itoh Y, Suzuki N, Yamada K, Masamoto K. Vessel specific imaging of glucose transfer with fluorescent glucose analogue in anesthetized mouse cortex. *Adv Exp Med Biol* 812: 241-246 (2014).

(6) Sugashi T, Yoshihara K, Kawaguchi H, Takuwa H, Ito H, Kanno I, Yamada Y, Masamoto K. Automated image analysis for diameters and branching points of cerebral penetrating arteries and veins captured with two-photon microscopy. *Adv Exp Med Biol* 812: 209-215 (2014).

(7) Tajima Y, Takuwa H, Nishino A, Matsuura T, Kawaguchi H, Ikoma Y, Taniguchi J, Seki C, Masamoto K, Kanno I, Saeki N, Ito H. Cerebral hemodynamic response to acute hyperoxia in awake mice. *Brain Res* 1557: 155-163 (2014).

(8) Tajima Y, Takuwa H, Kawaguchi H, Masamoto K, Ikoma Y, Seki C, Taniguchi J, Kanno I, Saeki N, Ito H. Reproducibility of measuring cerebral blood flow by laser-Doppler flowmetry in mice. *Front Biosci (Elite Ed)* 6: 62-68 (2014).

(⑨) Masamoto K, Takuwa H, Seki C, Taniguchi J, Itoh Y, Tomita Y, Toriumi H, Unekawa M, Kawaguchi H, Ito H, Suzuki N, Kanno I. Microvascular sprouting, extension, and creation of new capillary connections with adaptation of the neighboring astrocytes in adult mouse cortex under chronic hypoxia. *J Cereb Blood Flow Metab* 34: 325-331 (2014).

(10) Masamoto K, Takuwa H, Ito H, Kanno I. Hypoxia-induced adaptation of cerebral microvasculature. *Microvascular Reviews and Communications* 6: 13-18 (2014).

(11) Takuwa H, Tajima Y, Kokuryo D, Matsuura T, Kawaguchi H, Masamoto K, Taniguchi J, Ikoma Y, Seki C, Aoki I, Tomita Y, Suzuki N, Kanno I, Ito H. Hemodynamic changes during neural deactivation in awake mice: A measurement by laser-Doppler flowmetry in crossed cerebellar diaschisis. *Brain Res* 1537: 350-355 (2013).

(⑫) Maruyama M, Shimada H, Suhara T, Shinotoh H, Ji B, Maeda J, Zhang MR, Trojanowski JQ, Lee VM, Ono M, Masamoto K, Takano H, Sahara N, Iwata N, Okamura N, Furumoto S, Kudo Y, Chang Q, Saido TC, Takashima A, Lewis J, Jang MK, Aoki I, Ito H, Higuchi M. Imaging of tau

pathology in a tauopathy mouse model and in Alzheimer patients compared to normal controls. *Neuron* 79: 1094-1108 (2013).

(13) Sekiguchi Y, Masamoto K, Takuwa H, Kawaguchi H, Kanno I, Ito H, Tomita Y, Suzuki N, Sudo R, Tanishita K. Measuring the vascular diameter of brain surface and parenchymal arteries in awake mouse. *Adv Exp Med Biol* 789: 419-425 (2013).

(14) Masamoto K, Takuwa H, Tomita Y, Toriumi H, Unekawa M, Taniguchi J, Kawaguchi H, Itoh Y, Suzuki N, Ito H, Kanno I. Hypoxia-induced cerebral angiogenesis in mouse cortex with two-photon microscopy. *Adv Exp Med Biol* 789: 15-20 (2013).

(⑮) Hotta H, Masamoto K, Uchida S, Sekiguchi Y, Takuwa H, Kawaguchi H, Shigemoto K, Sudo R, Tanishita K, Ito H, Kanno I. Layer-specific dilation of penetrating arteries induced by stimulation of the nucleus basalis of Meynert in the mouse frontal cortex. *J Cereb Blood Flow Metab* 33: 1440-1447 (2013).

(16) Okawa S, Yano A, Uchida K, Mitsui Y, Yoshida M, Takekoshi M, Marjono A, Gao F, Hoshi Y, Kida I, Masamoto K, Yamada Y. Phantom and mouse experiments of time-domain fluorescence tomography using total light approach. *Biomed Opt Express* 4: 635-651 (2013).

(⑰) Takuwa H, Masamoto K, Yamazaki K, Kawaguchi H, Ikoma Y, Tajima Y, Obata T, Tomita Y, Suzuki N, Kanno I, Ito H. Long-term adaptation of cerebral hemodynamic response to somatosensory stimulation during chronic hypoxia in awake mice. *J Cereb Blood Flow Metab* 33: 774-779 (2013).

(18) Unekawa M, Tomita Y, Toriumi H, Masamoto K, Kanno I, Suzuki N. Potassium-induced cortical spreading depression bilaterally suppresses the electroencephalogram, but only ipsilaterally affects red blood cell velocity in intraparenchymal capillaries. *J Neurosci Res* 91: 578-584 (2013).

(19) Yoshihara K, Takuwa H, Kanno I, Okawa S, Yamada Y, Masamoto K. 3D analysis of intracortical microvasculature during chronic hypoxia in mouse brains. *Adv Exp Med Biol* 765: 357-363 (2013).

(20) Masamoto K, Kawaguchi H, Ito H, Kanno I. Dynamic two-photon imaging of cerebral microcirculation using fluorescently labeled red blood cells and plasma. *Adv Exp Med Biol* 765: 163-168 (2013).

2.2 Invited lectures

(1) Masamoto K. 【Invited speaker】Optical imaging and stimulation of neurovascular coupling. KAIST Program of Brain and Cognitive Engineering Seminar, Nov. 19, 2015, Daejeon, South Korea.

(2) Masamoto K, Kanno I. 【Invited speaker】Neurogenic and astrogliogenic perturbation of local CBF. Brain & Brain PET 2015, June 27-30, 2015, Vancouver, Canada.

(3) Masamoto K, Kanno I. 【Invited speaker】Astrocytic adaptation during cerebral angiogenesis follows the new vessel formation induced through chronic hypoxia in adult mouse cortex, Proc. SPIE 8928, Optical Techniques in Neurosurgery, Neurophotonics, and Optogenetics, 89281W, Feb.

2014, San Francisco, USA.

2.3 Student guidance

(1) Takuma Sugashi, M.Eng 2013, B.Eng 2011
(2) Masashi Takekosi, M.Eng 2013, B.Eng 2011
(3) Rei Murata, MEng 2014, BEng 2012
(4) Taku Katou, MEng 2015
(5) Ryo Hoshikawa, MEng 2015, BEng 2013
(6) Tatsushi Watanabae, MEng 2015, BEng 2013
(7) Naotomo Tottori, BEng 2013
(8) Hiroaki Maeda, BEng 2013
(9) Hideaki Suzuki, BEng 2014
(10) Masahiro Nitta, BEng 2014
(11) Hiroya Yuki, BEng 2014
(12) Minoru Fukasawa, BEng 2014
(13) Takeru Shiosato, BEng 2014
(14) Satoshi Katakura, BEng 2015
(15) Yuika Kurihara, BEng 2015
(16) Hiroshi Takea, BEng 2015
(17) Tomomi Nakahara, BEng 2015

3. Research funding

3.1 Grant-in-aid for scientific research

WAKATE (B) （H25-26: 4,160,000 yen）.

4. Collaborators（including codevelopment）

4.1 Inside BLSC

Prof. Yoichi Miyawaki (H27-).
Prof. Hiroshi Yokoi (H25-H26).

4.2 Outside UEC

Dr. Iwak Kanno, Hiroshi Ito, National Institute of Radiological Sciences (H23-H26).
Dr. Harumi Hotta, (H26-).

5. Outreach activities

5.1 Editor of academic journals

Progress in Brain Research: volume 225, New Horizons in Neurovascular Coupling (2015-2016).

5.2 Paper review of academic journals

Journal of Cerebral Blood Flow and Metabolism, Editorial Board (2007-).

5.3 Other outreach activities

(1) Program Committee member, International Society for Cerebral Blood Flow and Metabolism (ISCBFM) (2013-2015).

(2) Executive Organizing Committee member, European Conference on Biomedical Optics (ECBO, SPIE) (2014-2015).

(3) Program Committee member, Neurophotonics, Progress in Biomedical Optics (2012-2013)

(4) Executive Committee member, International Society on Oxygen Transport to Tissue (ISOTT) (2011-2014).

Yoichi MIYAWAKI Laboratory

1. Outline of Research and Education

1.1 Basic Policy in Research and Education

Representation of sensory and perceptual information in the human brain

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

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

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

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

Figure 2: Experiments using the 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 a particular activity pattern of the human brain. Thus, the objective measurement and analysis of brain activity patterns is a promising approach to unveil subjective sensory and perceptual experience. We mainly use functional magnetic resonance imaging (fMRI) and magnetoencephalography (MEG) to measure human brain activity in a noninvasive manner. fMRI measures signals related to blood flow changes associated with neural activity in the brain at high spatial resolution, whereas MEG measures magnetic field signals generated by neural current in the brain at 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. The standard measurement of fMRI and MEG signals consists of 10^4-5 –dimension data points per second (or every second). Conventional analyses focus on only limited aspects of such data sets and information contained in the rest is simply discarded or ignored. For example, a typical method of fMRI data is to perform statistical tests on intensity changes in fMRI signals atsingle brain locations independently. The method does not deal with correlational information between multiple brain locations, despite fMRI provides signals at 10^5 different brain locations simultaneously.

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

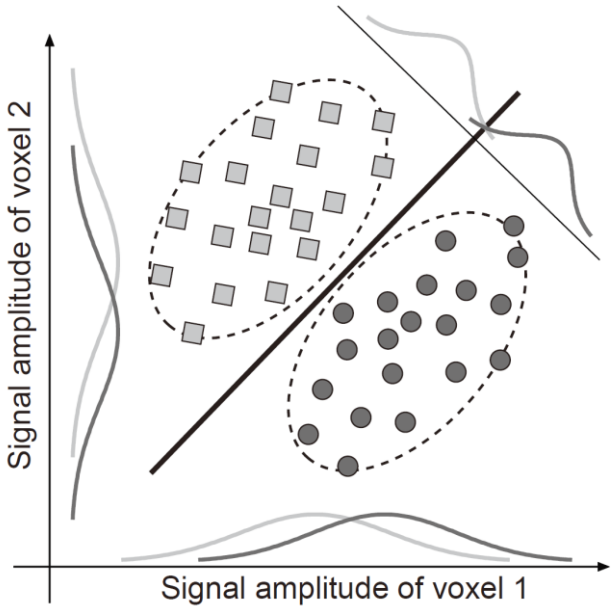


Figure 3: Classification analysis using multivariate signal patterns.

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

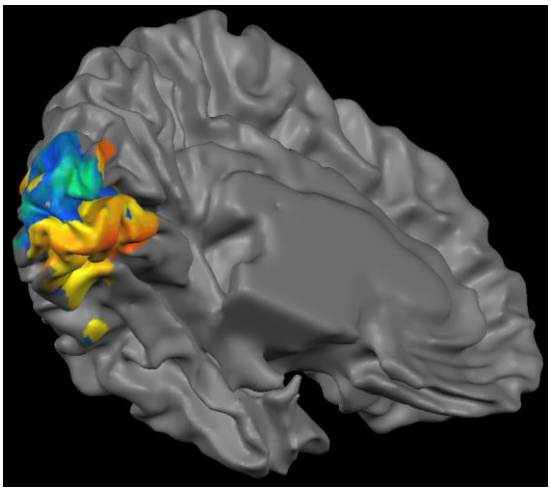


Figure 4: Retinotopic map identified in lower visual cortex the primary visual cortex?.

Application to medical engineering

The trained computer programs can be also used to predict experimental conditions corresponding to given brain activity patterns. This feature is also useful in designing a brain-machine interface that translates human thoughts into machine commands. By developing computer programs with high performance precision? 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, 2013 - March, 2016)

Dynamics of neural representation of visual object categories

We can visually recognize objects quickly and accurately. Object recognition in the human vision is superior in its speed and accuracy to that in the machine vision. It has been considered as one of brain functions most difficult to realize by artificial systems. To elucidate how the human brain performs object recognition so quickly and accurately, we have conducted experiments combining MEG and fMRI to achieve high resolution in the temporal and spatial domains. Results partially reveal the timing at which information of particular object categories is represented after the stimulus presentation (Sato and Miyawaki, 2014).

Neural representation of tactile information

We can obtain spatial information of the external environment by touch as well as vision. We perform fMRI experiments to measure brain activity patterns evoked by simple tactile stimuli given to the finger tips to explore where and how tactile information is represented in the human brain. Results suggest that the parietal cortex in addition to the somatosensory cortex play important roles for information representation of tactile stimuli consisting of moving lines (Nakatani et al., 2015).

Development of image processing techniques

To analyze brain activity patterns evoked by natural object images, it is also important to investigate what kind of image features has major effects on brain activity patterns. For this purpose, we perform image feature analysis by using deep convolutional neural network (DCNN) to extract higher-order features contained in the natural object images (Tanaka et al., 2015).

1.3 Future Plan

Dynamics of neural representation of visual object categories

We proceed with analyses of dynamics of neural representation for various object categories. In particular, we focus on how the hierarchy of object categories is represented in the brain.

Neural representation of tactile information

We proceed with analyses to reveal where and how tactile information is represented in the brain. In addition to the tactile stimuli that we currently use, we will use other types of stimuli defined by different features.

Development of image processing and brain activity data processing techniques

We proceed with image feature analyses using DCNN to reveal relationships between higher-order features and brain activity patterns. We also plan to introduce sparse modeling techniques for efficient analysis of natural images and brain activity patterns.

2. Research Achievements

2.1 Reviewed papers [○: Impact factor greater than 4]

(1) Miyawaki, Y. (in press), Multivariate analysis of magnetic resonance imaging signals of the human brain, *Current Topics in Medicinal Chemistry*.

(2) Yoichi Miyawaki (2015), Deciphering neural codes by functional magnetic resonance imaging, *System/Control/Information*, 59: 353 - 359. (In Japanese)

(3) Yamada, K., Miyawaki, Y., Kamitani, Y. (2015), Inter-subject neural code converter for visual image representation, *NeuroImag*e, 113: 289 - 297.

(4) Horikawa, T., Tamaki, T., Miyawaki, T., Kamitani, Y. (2013), Neural decoding of visual imagery during sleep, *Science*, 340: 639 - 642.

(5) Fujiwara, Y., Miyawaki, Y., Kamitani, Y. (2013), Modular encoding and decoding models derived from Bayesian canonical correlation analysis, *Neural Computation*, 25: 979-1005.

2.2 Book or Book Chapter

Yoichi Miyawaki (co-author), "Visualize information in the brain, " Unique Exciting Science II Chapter 1, pp. 7–37, Kindai kagaku sya (2013).

2.3 Non-refereed articles or translation

(1) Tomoyasu Horikawa, Yoichi Miyawaki, Yukiyasu Kamitani (2014), Visualizing mind from human brain activity, Japanese journal of optics, 43: 104 – 110.

2.4 Invited lectures

(1) Masashi Sato, Yoichi Miyawaki, Study of temporal structure of visual object representation in the human visual cortex, Pre-symposium workshop: Brain, Mind, and Life Support Technology, UEC Tokyo, November 2015.

(2) Yoichi Miyawaki, Masashi Sato, Neural dynamics of object representation in the human brain, International Symposium on Object Vision in Human, Monkey, and Machine, UEC Tokyo, November 2015.

(3) Yoichi Miyawaki, Masashi Sato, Temporal relationship between visual object category representation and categorical hierarchy, Symposium of Center for Systems Vision Science, Ritsumeikan university, New movement of visual information processing-from local circuit to recognition, Ritsumeikan university, March 2014.

(4) Yoichi Miyawaki, Approach toward understanding of mechanism of sensation and perception using neural decoding techniques, Japan Health Sciences Foundation Research Resource Committee Seminar, UEC Tokyo, September 2013.

(5) Yoichi Miyawaki, Image basis representation in the visual cortex, The Japanese Psychological

Association, Sapporo Convention Center, September 2013.

(6) Yoichi Miyawaki, Decoding of sensory and perceptual information from human brain activity, The 2nd telexistence research meeting, Keio university, July 2013.

(7) Yoichi Miyawaki, Neural representation of sensory and perceptual information in the human brain, Brain Science Inspired Life Support Research Center Seminar, UEC Tokyo, July 2013.

2.5 Media release

(1) Warashibe mad scientist, “Brain information – research on direct reading of information from the human brain”, Weekly ASCII, March 18, 2015.

(2) “Research grant for 16 awardees in this fiscal year Yazaki Memorial Foundation for Science and Technology”, THE MID JAPAN ECONOMIST, page 10, March 16, 2015

(3) “最新鋭のひみつ「これな～んだ」, ”調布電通大どおり, 2014 年 No. 39 autumn 秋号.

(4) “神は雲の中にあられる 最新の脳研究によると、私の 1 ビットがあなたの頭の中にあるかもしれません。”, 週刊アスキー, 2014 年 7 月 1 日.

(5) Tech a GO! GO!, 遠藤諭の『デジタルの、これからを聞く』, "電通大宮脇准教授に聞く、視覚に関する脳研究の最新事情－わたしたちの脳は、目にしたものをどのように認識しているのか”, ASCII.JP, 2014年6月19日.

(6) "出町中後輩に助言 宮脇電気通信大准教授", 北日本新聞 23 面, 2013 年 12 月 19 日.

(7) "宮脇准教授脳科学語る 砺波・出町中", 富山新聞 30 面, 2013 年 12 月 19 日.

(8) "人の夢が見える", 東京新聞朝刊1面, 2013年4月5日.

(9) "あなたの夢当てます", 読売新聞朝刊34面, 2013年4月5日.

(10) "夢解読できた", 朝日新聞朝刊38面, 2013年4月5日.

(11) "見ている夢解読", 毎日新聞朝刊24面, 2013年4月5日.

(12) "「夢」の解読成功 的中率7割", 産経新聞朝刊1面, 2013年4月5日.

(13) "「夢」の解読初の成功", 産経新聞朝刊2面, 2013年4月5日.

(14) "夢の内容ばれる？ ", 日本経済新聞朝刊34面, 2013年4月5日.

(15) "(余録)", 毎日新聞朝刊1面, 2013年4月6日.

(16) "(編集手帳)", 読売新聞朝刊1面, 2013年4月6日.

(17) "(春秋)", 日本経済新聞朝刊1面, 2013年4月6日.

(18) "(産経抄)", 産経新聞朝刊1面, 2013年4月6日.

2.6 Awards

For P.I.（with students)

(1) Masashi Sato, Yoichi Miyawaki, Excellent research award of Japanese Neural Network Society (2015).

(2) Tomoyasu Horikawa, Masako Tamaki, Yoichi Miyawaki, Yukiyasu Kamitani, Best paper award of Japanese Neural Network Society (2014).

For students

(1) Masashi Sato，IEEE CIS Japan Chapter Young Researcher Award (2015).
(2) Masashi Sato，Student award of UEC Tokyo (2015).
(3) Masashi Sato，Megurokai award (2013).

2.7 Student guidance

(1) Masashi Sato, 2012, Bachelor（Engineering), 2014, Master（Engineering)
(2) Ryo Obata, 2013, Bachelor（Engineering), 2015, Master（Engineering)
(3) Shun Nakatani, 2013, Bachelor（Engineering), 2015, Master（Engineering)
(4) Takashi Niijima, 2013, Bachelor（Engineering)
(5) Kazuaki Akamatsu, 2014, Bachelor（Engineering)
(6) Megumi Nozaki, 2014, Bachelor（Engineering)
(7) Sosuke Tanaka, 2015, Bachelor（Engineering)
(8) Shotaro Fuchibe, Bachelor（Engineering)

3. Research funding

3.1 Grant-in-aid for scientific research

(1) Yoichi Miyawaki（Co-P.I.), Controlling artificial limbs as own limb: natural learning of artificial limbs using human brain activity, KAKENHI challenging Exploratory Research, FY2015- FY2016, 800,000 JPY.
(2) Yoichi Miyawaki（P.I.), Study of dynamics of object image representation in the human brain using sparse modeling, KAKENHI Innovative Areas “sparse modeling”, FY2014- FY2015, 5,100,000 JPY.
(3) Yoichi Miyawaki（P.I.), Study of tactile information representation in the visual cortex using neural decoding technique, KAKENHI (C), FY2014-FY2016, 3,500,000 JPY.

3.2 Competitive external research funding

(1) Yoichi Miyawaki（P.I.), Research and development of fast object recognition algorithm based on neural information representation, SCOPE, 2015 年度, FY2014 – FY2016, 34,670,000 JPY.
(2) Yoichi Miyawaki（P.I.), Study of fast extraction of object recognition information from human brain activity, Yazaki Memorial Foundation for Science and Technology, Specific Research Grant, FY2015-FY2017, 10,000,000 JPY.
(3) Yoichi Miyawaki（P.I.), Development and application of high spatio-temporal resolution analysis of human neural activity, The Naito Foundation, Research Grant, FY2015-FY2016, 3,000,000 JPY.
(4) Yoichi Miyawaki（P.I.), Object Vision in Human, Monkey, and Machine, UEC Tokyo Research Activity Support System（research meeting support), FY2015, 869,000 JPY.
(5) Yoichi Miyawaki（P.I.), Study of object representation in the human brain, KDDI Foundation Research Grant, FY2014-FY2015, 2,750,000 JPY.

(6) Yoichi Miyawaki（P.I.), Study of temporal properties of object recognition mechanism in the human brain, Narishige Neuroscience Research Foundation, FY2014, 300,000 JPY.
(7) Yoichi Miyawaki（working member), Substitution of motor and communication functions using BMI（development of intelligent electric assistance devices for BMI control), Strategic Research Program for Brain Sciences, FY2013-FY2017, 120,000,000 JPY (for UEC Tokyo).
(8) Yoichi Miyawaki（P.I.), Study of temporal structure of neural representation of object categories, UEC Tokyo Research Activity Support System（KAKENHI acceptance support), FY2014, 1,400,000 JPY.

4. Collaborators

4.1 Inside BLSC

(1) Kazuto Masamoto, Image analysis of structural features of astrocytes, FY2015-.
(2) Hiroshi Yokoi, Soichiro Morishita, Substitution of motor and communication functions using BMI（development of intelligent electric assistance devices for BMI control), FY2013-.

4.2 Outside UEC

(1) Gowrishankar Ganesh、CNRS-AIST Joint Robotics Laboratory, CNRS - Institut des sciences de l'ingénierie et des systèmes (INSIS)（university/national institute), Controlling artificial limbs as own limb: natural learning of artificial limbs using human brain activity, FY2015-.
(2) Norihiro Sadato, Ryo Kitada, NIPS／SOKENDAI（national institute/university), Study of tactile information representation in the visual cortex using neural decoding technique, FY2014-.
(3) Yukiyasu Kamitani, Kyoto university ／ ATR computational neuroscience laboratories（university/private company), Study of tactile information representation in the visual cortex using neural decoding technique, FY2014-.

5. Outreach activities

5.1 Editor of academic journals

(1) Editorial board of IEICE ISS（FY2013 – FY2015)

5.2 Paper review of academic journals

(1) Cortex, ad hoc reviewer.
(2) Frontiers in Computational Neuroscience, ad hoc reviewer.
(3) NeuroImage, ad hoc reviewer.
(4) Human Brain Mapping, ad hoc reviewer.
(5) Journal of Neuroscience Methods, ad hoc reviewer.
(6) VISION, ad hoc reviewer
(7) PLOS ONE, ad hoc reviewer

(8) IEICE TRANSACTIONS, ad hoc reviewer

5.3 Other outreach activities

Academic society

(1) Japanese Neural Network Society board member（for strategic plan)（2015 –)
(2) Special Interest Group on Telexistence, Virtual Reality Society Japan（2014 –)
(3) The 31st International Congress of Psychology (ICP2016), Program Committee（2013 –)
(4) The 25th Annual Conference of Japanese Neural Network Society Organizing committee （2014 – 2015)
(5) Augmentend Human 2014, Senior Reviewer（2014)
(6) The 24th Annual Conference of Japanese Neural Network Society Program Committee（20 14)
(7) European Coordinated Research on Long-term Challenges in Information and Communication Sciences & Technologies ERA-Net (Chist-Era), Funding reviewer (2014)

Outside lectures

(1) Koshigayakita high school, Saitama（2013)
(2) Demachi junior high school, Toyama（2013)
(3) YumeNavi Live 2014, Tokyo（2014)
(4) Shukutoku high school, Tokyo（2014)
(5) Shonan gakuen high school, Tokyo（2014)
(6) Bunkyo high school, Tokyo（2014)

Shinji MATSUDA Laboratory

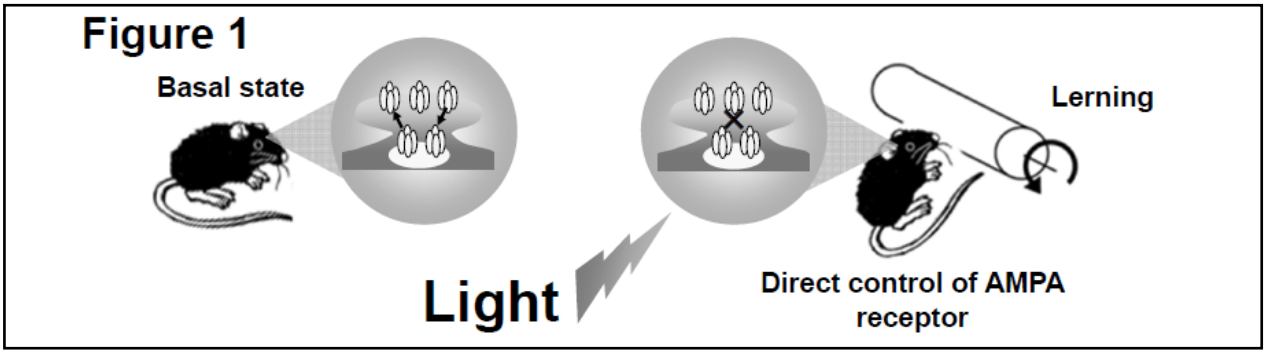
1. Outline of Research and Education

1.1 Basic Policy in Research and Education

Research

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

I have been studied the molecular basis of long-term depression (LTD) which is the one form of synaptic plasticity: the efficiency of synaptic transmission is reduced for a long term. Recently, I have 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. Moreover, I have also studied 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. To further promote the LTP research, I am planning to develop new methods for controlling LTP.



Education

I would like to bring up the students who can contribute to the progress of the science. For students in "Bioscience and Technology Program", I am going to give lectures not only on neuroscience but also on basic biology. Moreover, I will discuss with the students general issues of 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 teaching fundamentals of biology and then to step up to giving lectures of current knowledge. Recently, fusion research between biology and other fields has been actively promoted. Therefore, students need to prepare for such kinds of interdisciplinary studies even though they may not become specialists in biological sciences.

For education in my own laboratory, I would like students to carry out some forefront research in neurosciences collaborating with me, and to bring them up to top scientists contributing to

the advancement of neurosciences. For this purpose, I will let them make their own research plans and urge them to carry out research according to their plans as much as they can.

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

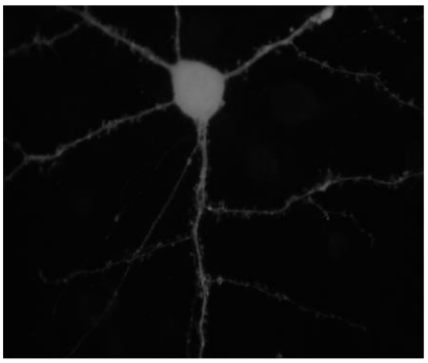
Although it is well established that the LTD is induced by the clathrin mediated endocytosis of AMPA receptors, little is known about how clathrin is recruited to the postsynaptic site by neuronal activities. Also, it is also well known that the dephosphorylation of TARP (Transmembrane AMPA receptor Regulatory Protein) is required for the induction of LTD. However, there remains to be clarified about how the dephosphorylation of TARP contributes to LTD.

Before 2013, we found the following facts: PIP5Kg was activated by LTD inducing stimuli such as NMDA treatment, and generates phosphatidyl inositol di phosphate (PIP2) at postsynaptic sites where Adaptor Protein complex (AP-2) was recruited. Then, clathrin was bound to AP-2 and accumulated at the postsynaptic site. After 2013, we successfully clarified the following facts: the AMPA-receptor-TARP complex binds to AP-2, which plays an essential role for the clathrin mediated endocytosis, and to AP-3A, which mediates the lysosomal targeting of membrane proteins, when TARPs are dephosphorylated. These results indicated that the AMPA receptors are incorporated into the clathrin coated pit via interaction between TARP and AP-2 and that AMPA receptors are transported to lysosome via TARP-AP-3 interaction and degraded. From these results, we proposed the following model for LTD: When LTD inducing stimulus was applied to neurons, TARPs are dephosphorylated and by this dephosphorylation AMPA receptor-TARP complex binds to AP-2 and internalized via clathrin mediated endocytosis. Then, via TARP-AP-3 binding, AMPA receptor-TARP complexes are transported to lysosome and the amount of cell surface AMPA receptors are reduced for a long term.

More recently, we tried to develop a new technique to control the induction of LTD by light stimulation in order to directly examine the relationship between synaptic plasticity and learning. We succeeded to control LTD by expressing light driven proton pump in the endosome of neurons.

1.3 Future Plan

We are going to express light-driven proton pump in living animals and try to control the behavior by light stimulation. Specifically, we are going to express our proton pump in cerebellum, hippocampus and amygdala in mice and examine various learning behaviors with or without light stimulation, which is expected to clarify which brain region controls the learning and memory by LTD induction.



Cultured neuron

Memory test of mouse

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 learning and memory. By these approach, we would like to contribute to the progress of neuroscience.

2. Research Achievements

2.1 Reviewed papers [○: Impact factor greater than 4]

(1) Takashi Sato, Tomohiko Iwano, Masataka Kunii, Shinji Matsuda, Rumiko Mizoguchi, Yongwook Jung, Haruo Hagiwara, Yoshihiro Yoshihara, Michisuke Yuzaki, Reiko Harada, Akihiko Harada: Rab8a and Rab8b are essential for multiple apical transport pathways but insufficient for ciliogenesis. *J Cell Sci* (2014) 127: 422-31.

(2) Shinji Matsuda, Wataru Kakegawa, Timotheus Budisantoso, Toshihiro Nomura, Kazuhisa Kohda, Michisuke Yuzaki: Stargazin regulates AMPA receptor trafficking through adaptor protein complexes during long-term depression. *Nat Commun*, 4: 2759 DOI: 10.1038/ncomms3759 (2013).

2.2 Invited lectures

Shinji Matsuda　Understanding and controlling synaptic plasticity　Japanese Neural Network Society Workshop 「Data-driven approach for understanding cerebellar mechanisms on eye movement control」University of Electro-Communications　August 11/2015.

2.3 Student guidance

Hiroki Yamazaki、2016

Marine Sakayauchi、2016

3. Research funding

3.1 Competitive external research funding

Shinji Matsuda, JST PRESTO, 2011~2016, 91100(thousand yen).

4. Collaborators

4.1 Outside UEC

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

Shojiro MAKI Laboratory

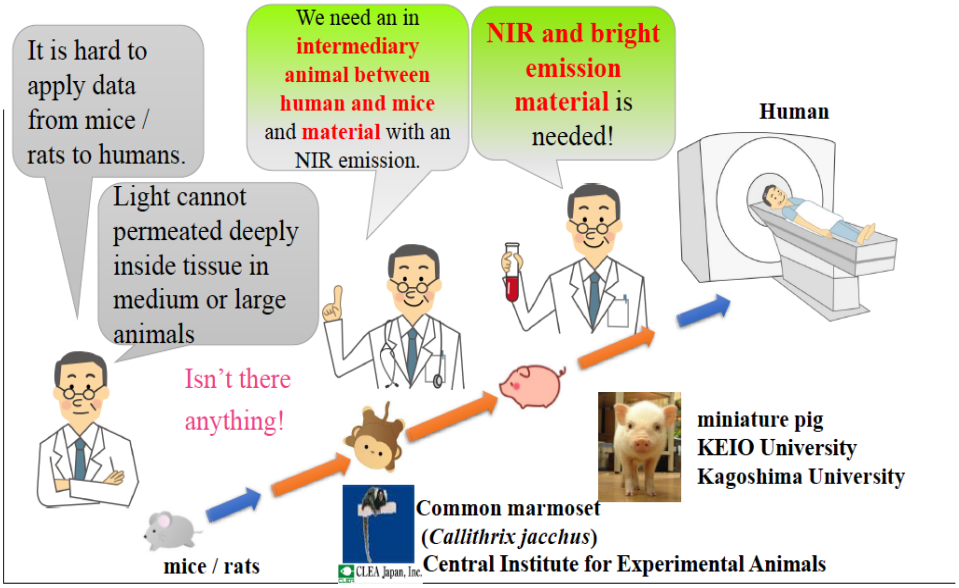
1. Outline of Research and Education

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.

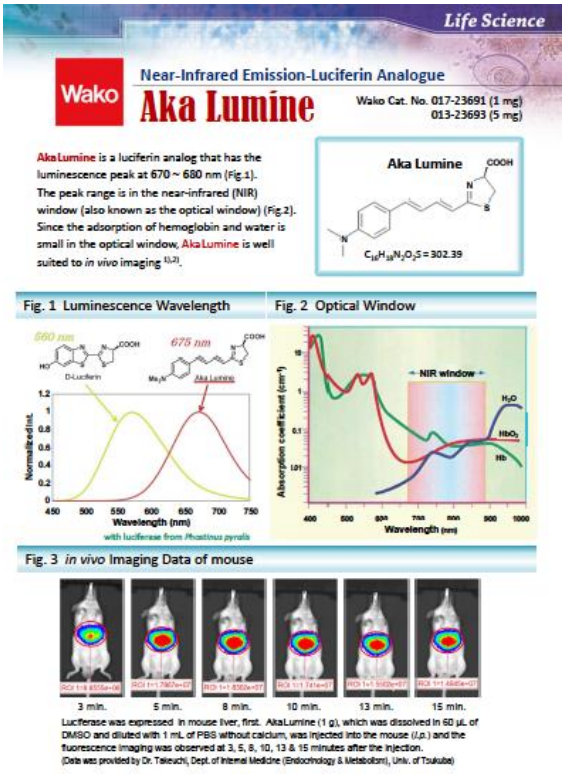
“Cancer Eradication (anti-cancer)” and “Practical Applications of Regenerative Medicine” are the most important goals in life science research. It’s no exaggeration to say that these are universal targets. Deep tissues are challenging for optical imaging technology. MRI, CT, and X-ray are good for *in 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.

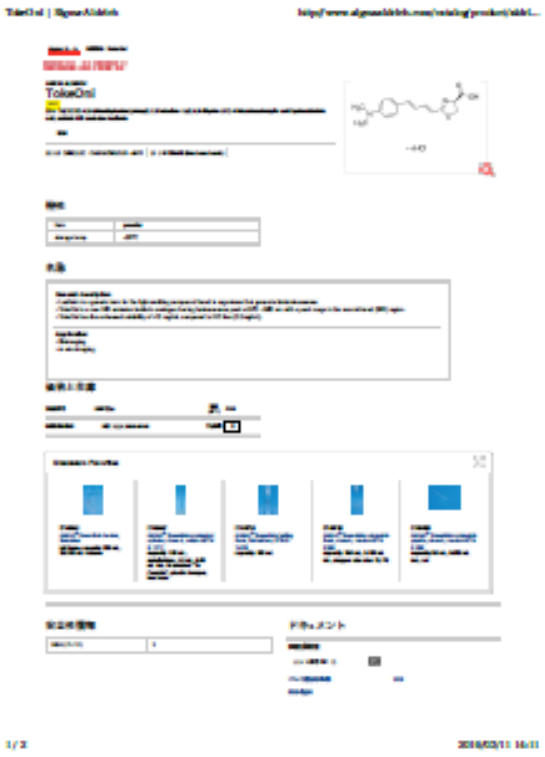
So, our challenge is to innovate an NIR (near infrared) probe and practical applications. It is more suitable for bioluminescent probes than fluorescent probes because bioluminescence does not require irradiation. Researchers need NIR bioluminescent probes for imaging cancer cells and/or graft cells 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 Achievements and State of Progress (April, 2013 - March, 2016)

1. 2011.10. "AkaLumine®" is put on market (Wako Pure Chemical Industries, Ltd.)
2. 2012.10. "AkaLumine®" is opened to the public in Report of Academic-Industrial Collaboration in 2011 (Ministry of Education, Culture, Sports, Science and Technology)
3. 2016. 3. "TokeOni" is put on market (Sigma-Aldrich Co. LLC.)

Our laboratory developed "Akalumine®" and "TokeOni" as NIR luciferins. Whereas top scientists in the life science field longed for this technology, no one successfully innovated a new NIR luciferin. In Oct. 2011, we developed and marketed the first NIR luciferin in the world.

In March 2016, "Tokeoni" with an NIR emission (λ_{max}=675 nm) for *in vivo* imaging was put on market from Sigma-Aldrich Co. LLC. In October 2011, we marketed "AkaLumine® (Wako Pure Chemical Industries, Ltd.)" with an NIR emission for use as an *in vivo* imaging probe as the first NIR luciferin in the world. "TokeOni" is a next generation luciferin with improved water solubility compared to AkaLumine®. For deep tissue imaging, top scientists long for an NIR probe. Researchers with transgenic model animals for their research want deep tissue imaging with a different (improved) luciferin. Cancer and regenerative medicine researchers need an NIR luciferin because optical imaging has high resolution compared with MRI, CT, and X-ray imaging.

"AkaLumine®" and "TokeOni" with NIR emission spectra could solve imaging technology problems in deep tissue optical *in vivo* imaging. These probes are sold worldwide for advancing high value science.

This technology must be the best technology in the world for the life science field.

Practical application research requires reasonable cost, stability, usability and so on. In other words, a practical application technology should provide a comprehensive solution. Also, we should develop a synthesis method for industrial production. Normally, life science researchers cannot synthesize material, and they want to keep their results secret so as to market new material quickly. It is quite difficult to advance life science technology merely by publishing in an academic journal, but it can be quite easy to market new compounds. Our materials not only show high performance, but they are synthesized industrially. This technology research contributes to society in a broader context and it is not just academic research.

1.3 Future Plan

1. Innovation of next generation material "TokeOni"

Although "TokeOni" has better water solubility than "Akalumine®", its acidic conditions present a practical problem in animal experiments because of the HCl salt. We should innovate the next generation material to solve this problem while maintaining performance (brightness and NIR emission, >650nm). We have a candidate compound now being tested in animal experiments. When we achieve good results in animal experiments, we will start to scale to industrial production.

2. Innovation of optical *in vivo* imaging technology for medium and/or large animals

It is hard to translate experiment data from mice and rat to human. We need imaging of medium and/or large animals for reliability and reproducibility in higher animals. In regenerative medicine (personalized medicine), optical imaging technology with high resolution is more suitable than MRI, CT, and X-ray. In this application, grafts are repeatedly monitored for activity, and higher brain function changes must be confirmed. For human graft research, the pig is a suitable animal; for higher brain function research, the common marmoset is useful. We think it is quite important technology for imagining the whole human. Collaboration with animal experiment researchers is in progress.

2. Research Achievements

2.1 Reviewed papers [○: Impact factor greater than 4]

(1) Hirano Takashi, Nakagawa Tatsuki, Kodaka Ai, Maki Shojiro, Niwa Haruki and Yamaji Minoru (2013), "5-[4-(Dimethylamino)phenyl]-2-benzamidopyrazines:fluorescent dyes based on Cypridina oxyluciferin", *Rsearch on Chemical Intermediates*, **39**, 233.

(2) Iwano Satoshi , Obata Rika , Miura Chihiro , Kiyama Masahiro , Hama Kazutoshi , Nakamura Mitsuhiro , Amano Yoshiharu , Kojima Satoshi , Hirano Takashi , Maki Shojiro , Niwa Haruki (2013), "Development of simple firefly luciferin analogs emitting blue, green, red, and near-infrared biological window light", Tetrahedron, 69, 3847-3856.

(3) Iwano Satoshi, Kojima Satoshi, Hirano Takashi, Maki Shojiro, Niwa Haruki, (2013), "Evaluation of Bioluminescence Activity of Firefly Luciferin Nucleotide Derivatives", *ECS Transactions*, **50**, 1-3.

(4) Miura Chihiro, Kiyama Masahiro, Iwano Satoshi, Ito Kazuto, Obata Rika, Hirano Takashi, Maki Shojiro, Niwa Haruki, (2013), “Synthesis and luminescence properties of biphenyl-type firefly luciferin analogs with a new, near-infrared light-emitting bioluminophore”, *Tetrahedron*, **69**, 9726-9734.

(5) Saito Ryota, Hirano Takashi, MakiShojiro, Niwa Haruki, (2014), “Synthesis and chemiluminescent properties of 6,8-diaryl -2- methylimidazo [1,2-a] pyrazin -3(7H)-ones: Systematicinvestigation of substituent effect at para-position of phenyl group at 8-position”, *Journal of Photochemistry and Photobiology A: Chemistry*, **293** 12–25.

(6) Nakagawa Tatsuki, Yamaji Minoru, Maki Shojiro, Niwa Haruki and Hirano Takashi, (2014), “Substituent effects on fluorescence properties of thiazolo[4,5-b]pyrazine derivatives”, *Photochem. Photobiol. Sciences*, **13**, 1765-1772.

(7) Nakagawa Tatsuki, Yamaji Minoru, Maki Shojiro, Niwa Haruki and Hirano Takashi, (2015), “Fluorescence Properties of Diphenylthiazolo [4,5-b]pyrazines Tuned by Donor-Acceptor Substituent Effects”, *Photochemistry and Photobiology*, **91**, 807–813.

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

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

(10) Hachiya Sojiro, Hashizume Daisuke, Ikeda Hiroshi, Yamaji Minoru, Maki Shojiro, Niwa Haruki, Hirano Takashi, (2015) “Spectroscopic properties of BF_2 complexes of N-(5-phenyl-2-pyrazinyl) pivalamides exhibiting fluorescence in solution and solid state”, *Photochemistry and Photobiology A: Chemistry*, **311**, 206-214 (2016).

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

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

2.2 Book or Book Chapter

(1) General editor: Makoto kajitani, Shigeru Tanaka, “Unique & Exciting science II” <ISBN978-4-7649-0453-8>, p. 129-158, Kindai Kagakusha (2013)

(2) General editor:Mitsuhiro Seki, “Tama no Chikara”, <ISBN978-4-87751-508-9> p. 36-39, p. 68-71, p. 72-75, p. 80-83, p. 84-87, p. 92-95, p. 108-111, p. 120-123, p. 184-187, p. 210-213, Keyaki-Shuppan (2013)

(3) Gan-Kenkyu Tokuhon 3 (Cancer Research Book 3), (e-book:

http://ganshien.umin.jp/research/epub/index.html), Chapter 3, (Ministry of Education, Culture, Sports, 2014)

2.3 Non-refereed articles or translation

(1) Shojiro MAKI, “Making Firefly Bioluminescence by Chemistry”, *KagakutoKyoiku,* The Chemical Society of Japan, Vol 61, No. 8, 392-395, (2013)

(2) Shojiro MAKI, “Innovation of Firefly Bioluminescence in vivo imaging material”, *Pharmacia*, Vol 50, No. 2, 117-120 (2014)

(3) Shojiro MAKI, “New Firefly Bioluminescence in vivo imaging material having water solubility”, *Hikari alliance*, Vol. 25, 33-35 (2014)

(4) Shojiro MAKI, “A Challenge to innovate multicolor Firefly Bioluminescence”, *Seibutsu kougakukaishi*, Vol. 92 (8), 432-436 (2014)

(5) Shojiro MAKI, “Innovation of NIR firefly luciferin analogues”, *Chemical engineering*, Vol. 60 (8), 28-33 (2015).

2.4 Invited lectures

・International

(1) Maki, Shojiro, “Chemistry on firefly bioluminescence”, The Irago Conference 2015, Irago, Japan, October 22-23, 2015.

・Domestic

(1) Maki, Shojiro, “Chemistry on firefly bioluminescence”, , Chiba, December 4, 2014.

(2) Maki, Shojiro, “Chemistry on firefly bioluminescence”, Society of Imaging of mice, Tokyo, January 20, 2015.

(3) Maki, Shojiro, “Innovation of NIR firefly bioluminescence”, Autumn meeting of The Electrochemical Society of Japan 2015, Saitama, September 12, 2015.

2.5 Media release

(1) “Cancer cell could image out of the body by NIR luciferin”, *The Nikkei*, March 26, 2013

(2) “Water solubility 2000 fold rising up: convenience for animal experiment”, *The NIKKAN KOGYO SHIMBUN,LTD*. May 17, 2013

(3) “In vivo imaging probe Practical Application of mass production”, *The NIKKAN KOGYO SHIMBUN,LTD*. march 8, 2016

2.6 Patent

(1) P2014-218456A ”NOVEL HYDROGEN HALIDE SALTS”

Inventor：Shojiro MAKI, Haruki NIWA.

Applicant: The University of Electro-Communications

Date of filing May 7, 2013 (P2013-097755)

Date of publication of application: November 20, 2014

(2) P2015-193584A “NOVEL HETEROCYCLIC COMPOUNDS AND SALTS THEREOF, AND LUMINESCENT SUBSTRATE COMPOSITIONS”
Inventor：Shojiro MAKI, Haruki NIWA.
Applicant: The University of Electro-Communications
Date of filing: Sep. 17, 2014 (P2014-189314)
Date of publication of application: Nov. 5, 2015

(3) P2014-108957A “METHOD OF PRODUCING CYCLIZED COMPOUND, AND METHOD OF CAUSING SOLUTION CONTAINING CYCLIZED COMPOUND TO EMIT LIGHT”
Inventor：Takeshi SAITO, Shigeru NISHIYAMA, Shuji IOKA, Shojiro MAKI, Haruki NIWA.
Applicant: KEIO GIJUKU and The University of Electro-Communications
Date of filing: Dec. 04, 2012 (P2014-189314)
Date of publication of application: Dec. 06.2014

2.7 Practical use

(1) “AkaLumine®”, Kurogane Kasei Co. Ltd., Wako Pure Chemical Industries, Ltd. (2011~)
(2) “TokeOni” Kurogane Kasei Co. Ltd., Sigma-Aldrich Co. LLC. (2016~)

2.8 Awards

(1) Shojiro Maki, Incentive award of electron transfer chemistry (Society of Electron transfer Chemistry) 2005
(2) Shojiro Maki, Best Teacher award (The University of Electro- Communications) 2012
(3) Kazuma Karube, Good Student award (Meguro-Kai: An alumni association of The University of Electro- Communications) 2013
(4) Kazuma Karube, poster award (Society of Bioluminescence & Chemiluminescence) 2013
(5) Ryohei Saito, Incentive research award (Scientific Support Programs for Cancer Research, Grant-in-Aid for Scientific Research on Innovative Areas, Ministry of Education, Culture, Sports, Science and Technology) 2014
(6) Nobuo Kitada, Best Student award (Meguro-Kai: An alumni association of The University of Electro- Communications) 2012
(7) Nobuo Kitada, Good Presentation award (Dept. of Engineering Science, Graduation School of The University of Electro- Communications)
(8) Nobuo Kitada, vice-poster award (Society of Bioluminescence & Chemiluminescence) 2014
(9) Nobuo Kitada, JSPS Fellowships for Japanese Junior Scientist 2016.
(10) Masahiro Kiyama, vice-poster award (Society of Bioluminescence & Chemiluminescence) 2014
(11) Satoshi Iwano, poster award (9th Joint Symposiom of TUAT & UEC) 2011
(12) Satoshi Iwano, SPI award (in vivo imaging forum) 2013
(13) Satoshi Iwano, poster award (3ed CSJ festa 2013) 2013
(14) Satoshi Iwano, Best Student award (The University of Electro- Communications) 2014

2.9 Student guidance

(1) Ryohei Saito, 2014, Bachelor (engineering)
(2) Satoshi Ohtsuka, 2015, Bachelor (engineering)
(3) Rei Morimitsu, 2016, Bachelor (engineering)
(4) Yoshinao Kobyashi, 2014, Master (engineering)
(5) Kazuma Karube, 2015, Master (engineering)
(6) Ryohei Saito, 2016, Master (engineering)
(7) Satoshi Iwano, 2014, Doctor (science)

2.10 Visit of oversea researchers and students

(1) Winson Lu, "Synthesis of new firefly luciferin" 2013, June-September (UCLA, Dept. of Chemical & Biochemistry, internship student)
(2) Winson Lu, "Synthesis of new firefly luciferin" 2015, September-2016, Janurly (JST visiting Scientist)

2.11 Study abroad programs for students

(1) Satoshi Iwano, University of California Berkeley (Cell engineering, G. Marriott lab.) 2012. 3-4
(2) Masahiro Kiyama, University of California Berkeley (Cell engineering, G. Marriott lab.) 2014. 9-10
(3) Nobuo Kitada, University of California Berkeley (Cell engineering, G. Marriott lab.) 2015. 3-8

3. Research funding

3.1 Grant-in-aid for scientific research

(1) Shojiro Maki (representative) "Confirmation of control point for Innovating NIR luciferin (24650633)" 2012-2014, total 3,000 thousand yen (challenging Exploratory Research)
(2) Shojiro Maki (allot) "resonance Bio-imaging", 3704, 2015-2019, total 20,000 thousand yen (Grant-in-Aid for Scientific Research on Innovative Areas)

3.2 Competitive external research funding

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

4. Collaborators（including codevelopment）

4.1 Inside BLSC

Prof. Atsushi Nakamura "Innovation of new in vivo optical imaging technology without transgenic animal"

2016~

4.2 Outside BLSC in UEC

1 Prof. Rei Furukawa “Development of organic waveguide sensing system for health monitoring of shield tunnelling “ (Department of Engineering Science), 2015-2017

4.3 Outside UEC

(1) Prof. Tsuyoshi Saito, Masaya Imoto, Koji Suzuki, Rika Obata, Shigeru Nishiyama, Tsukuba University and Keio University “Study of imaging material” 2014 July – 2016 June
(2) Hidenori Kato, Kurogane Kasei Co., Ltd., “Innovtion & Practical Application of NIR firefly l uciferin” 2012 April – current
(3) Prof. Taichiro Kato, Kagoshima University, “Development of new firefly bioluminescence mat erial”, 2014 October -2016 September
(4) Prof. Shotaro Yamano, Osaka prefectural university, “Development of in vivo imaging materi al”, 2014 October -2016 September
(5) Prof. Iijima Nippon Medical School, “Study of in vivo imaging on brain and neuron”, 2013 November -2015 October
(6) Prof. Yoshihiro Miwa, Tsukuba University,”Study of imaging technology by new firefly lucife rin”, 2014 April – 2016 March
(7) Prof. Shinae Kondo and Takahiro Kuchimaru, Tokyo Institute of Technology “Development o f in vivo imaging technology”, 2014 April – 2016 March
(8) Prof. Kazuhiro Chiba, “Study of bio-imaging material”, 2015 Augst – 2016 March
(9) Prof. Kenji Hirayama, Nagasaki University, “Dynamics study of in vivo imaging material in live body”, 2015 November – 2017 October
(10) Prof. Rika Numano, Toyohashi University of Technology, “Study of firefly imaging materia l”, 2015 November – 2017 November

4.4 NDA (Non-disclosure agreement)

(1) Prof. Ken Annoura, Jikei University, “About NIR imaging material”, 2014 January – 2018 December

4.5 MTA (Material transfer agreement)

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

5. Outreach activities

5.1 Research and education in other universities

(1) Experts Network Investigator Science and Technology Foresight Center of National Institute of Science & Technology Policy (NISTEP)
(2) APEC foresight center member
(Roadmapping Converging Technologies to Combat Emerging Infectious Diseases)
(3) Meeting Experts Network Investigator Science and Technology Foresight Center of National Institute of Science & Technology Policy
(4) Scientific Support Programs for Cancer Research, Grant-in-Aid for Scientific Research on Innovative Areas, Ministry of Education, Culture, Sports, Science and Technology
(5) Executive Board Member (Society of electro transfer chemistry)（2008- current）
(6) Executive Board Member (Society of Electrochemistry Japan, branch of Kanto) (2010-2012)

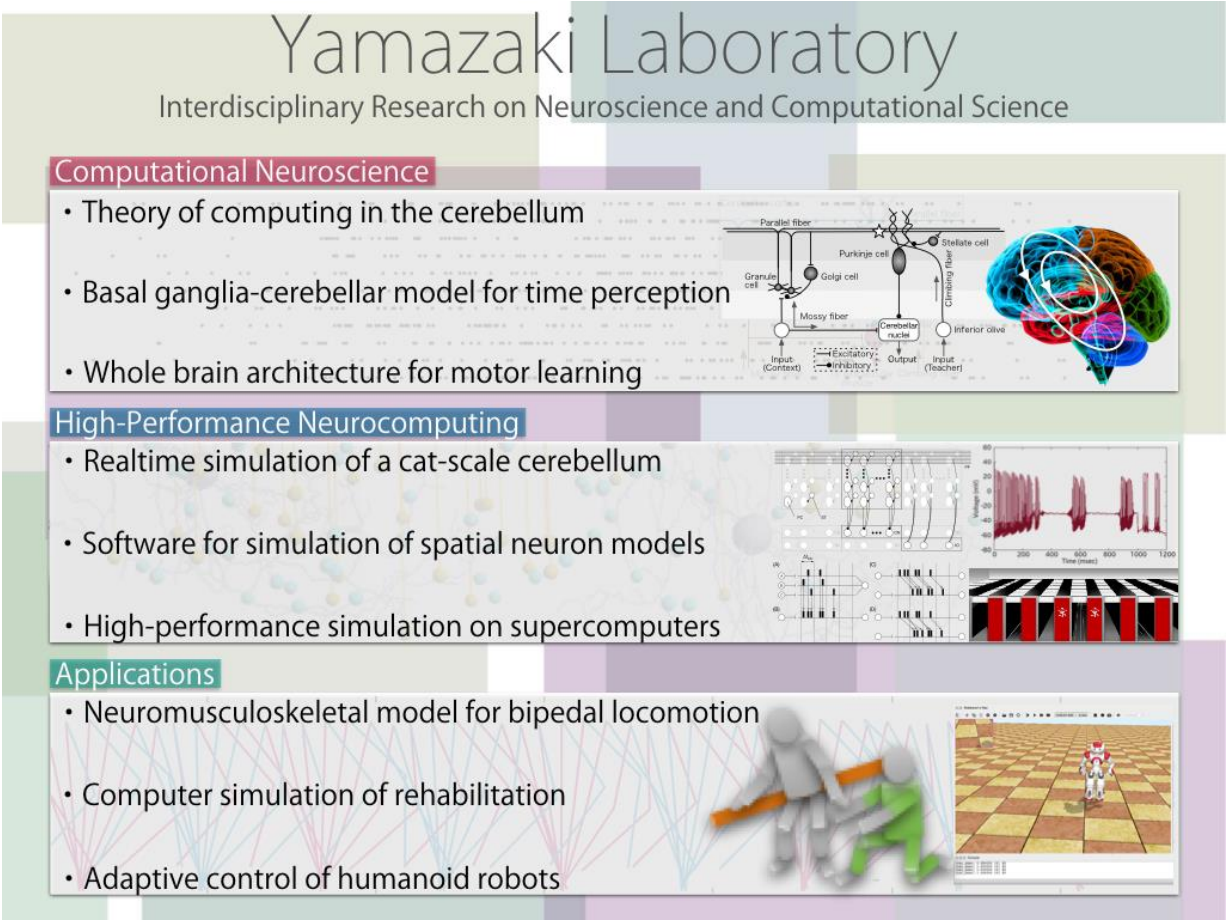
5.2 Other outreach activities

(1) Extension lecture for children (experimental class), August and December 2011 (JST program)
(2) Extension lecture for children (experimental class), August 2012 (Shibuya-ku, Tokyo)
(3) Extension lecture for children (experimental class), June 2015 (Shibuya-ku, Tokyo)
(4) Extension lecture for children (experimental class), July 2015 (The University of Electro-communications)
(5) Extension lecture for children (experimental class), August 2015 (Shibuya-ku, Tokyo)
(6) Extension lecture for children (experimental class), January 2016 (Shibuya-ku, Tokyo)

Tadashi YAMAZAKI Laboratory

1. Outline of Research and Education

1.1 Basic Policy in Research and Education



We are conducting research in the interdisciplinary area between neuroscience and high-performance computing. Specifically, we are engaged in mathematical 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 in one of the above projects. In other words, they take part in 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, 2013 - March, 2016)

1. Theory of memory consolidation in the cerebellum

The location of memory in the cerebellum has been a matter of debate over 30 years. In particular, recent experiments using genetically manipulated animals have provided paradoxical results, which makes the debate complicated. We built a simple theoretical model of the cerebellum for memory consolidation, and succeeded to interpret almost all previous experimental results including the paradoxical genetic experiments with the model. We published the paper in PNAS and made a press release. Part of this study was supported by JSPS KAKENHI. We wrote a book chapter and a review article.

2. Large-scale simulation of the cerebellar circuit

Accelerators such as GPUs allow us to carry out computer simulation of neural networks efficiently in parallel. Using 4 GPUs simultaneously, we achieved realtime simulation of a cerebellar model composed of more than 1 million neurons. We published a referred paper in an international journal. We have been collaborating with overseas researchers to built a cerebellar model on Field Programmable Gated Aray (FPGA), and published another referred paper. Furthermore, we achieved realtime simulation of a cat-scale cerebellum composed of 1 billion neurons using a supercomputer Shoubu built by PEZY Computing/Exascaler. We have submitted a paper to an international conference. We also published a review paper.

3. Unified basal ganglia-cerebellar model for time perception

Time perception is inevitable for our daily life. It has been shown that the basal ganglia is responsible for time perception longer 1 second, whereas the cerebellum for that shorter than 1 second for precise motor control. We built a unified basal ganglia-cerebellar model that represents the passage of time accurately for a long interval. This study was supported by JSPS KAKENH. We published a book chapter on this issue and are preparing a research paper.

4. Whole-brain functional model for motor learning and control

By adding a model of the motor cortex to the basal ganglia-cerebellar model, we are building a whole-brain functionl model for motor learning and control. The cerebral cortex, basal ganglia, and cerebellum play roles of representation, production and adjustment of motor sequences, respectively, and work together synergistically. We have started a collaboration with AIST AI Research Center while receiving a research fund on “Next-Generation Artificial Intelligence Technology Research and Development”, and are hiring a research scientist and a technical staff.

5. Bipedal locomotion by a neuromusculoskeleta model towards simulated rehabilitation

We built a musculoskeletal model of lower limbs which is controlled by a set of neural oscillators for bipedal locomotion. By adding a predictive control of our artificial cerebellum, the model succeed to walk. When a half hemisphere of the artificial cerebellum is stopped, the leg on the same side tended to move crudely, suggesting that crude movement of cerebellar patients would be due to the failure of predictive control by the cerebellum. We have submitted a paper to a journal.

6. Predictive control of humanoid robots by the artificial cerebellum

We make Aldebaran Robotics NAO to play table tennis. Using our realtime artificial cerebellum, NAO predicts the trajectory of a flying ball and the correct timing to swing a racket to hit the ball. This study was supported by Artificial Intelligence Research Promotion Foundation.

1.3 Future Plan

We will extend the whole-brain functional model for motor learning and control to human –specific higher-order functions such as language acquisition and production. We are in progress to conduct computer simulation of a human-scale brain on K computer and Post-K computer. We are collaborating with AIST AI Research center on brain-style artificial intelligence projects, where we are focusing on applications of our brain models. We expect that our collaboration realizes various applications such as adaptive control of factory robots for agriculture, and personalized rehabilitation by building a detailed neuromusculoskeletal model for a specific patient and carrying out computer simulation of rehabilitation to test whether a rehabilitation method is effective or not.

2. Research Achievements

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

(1) Masato Gosui, Tadashi Yamazaki (2016) Real-world-time simulation of memory consolidation in a large-scale cerebellar model. *Frontiers in Neuroanatomy*, 10(21): 1–10.

(2) Junwen Luo, Graeme Coapes, Terrence Mak, Tadashi Yamazaki, Chung Tin, Patrick Degenaar (2016) Real-Time Simulation of Passage-of-Time Encoding in Cerebellum Using a Scalable FPGA-based System. *IEEE Transactions on Biomedical Circuits and Systems*, 10(3): 742-53.

(3) Tadashi Yamazaki, Soichi Nagao, William Lennon, Shigeru Tanaka (2015) Modeling memory consolidation during post-training periods in cerebellovestibular learning. *Proceedings of the National Academy of Sciences of the United States of America*, 112(11): 3541-3546.

(4) William Lennon, Tadashi Yamazaki, Robert Hecht-Nielsen (2015) A Model of In Vitro Plasticity at the Parallel Fiber – Molecular Layer Interneuron Synapses. *Frontiers in Computational Neuroscience*, 9(150): doi: 10.3389/fncom.2015.00150.

(5) Leonard F. Koziol, Deborah Budding, Nancy Andreasen, Stefano D'Arrigo, Sara Bulgheroni, Hiroshi Imamizu, Masao Ito, Mario Manto, Cherie Marvel, Krystal Parker, Giovanni Pezzulo,

Narender Ramnani, Daria Riva, Jeremy Schmahmann, Larry Vandervert, Tadashi Yamazaki (2014) Consensus Paper: The Cerebellum's Role in Movement and Cognition. *The Cerebellum*, 13(1):151-177.

(6) William Lennon, Robert Hecht-Nielsen, Tadashi Yamazaki (2014) A spiking network model of cerebellar Purkinje cells and molecular layer interneurons exhibiting irregular firing. *Frontiers in Computational Neuroscience*, 8(157): 1-10.

(7) Tadashi Yamazaki, Jun Igarashi (2013) Realtime Cerebellum: A large-scale spiking network model of the cerebellum that runs in realtime using a graphics processing unit. *Neural Networks*, 47: 103-111.

(8) Soichi Nagao, Takeru Honda, Tadashi Yamazaki (2013) Transfer of memory trace of cerebellum-dependent motor learning in human prism adaptation: A model study. *Neural Networks*, 47: 72-80.

2.2 Book or Book Chapter

(1) Author・Annual Review Shinkei 2016 (Clock and Cerebellum), Chugai Igaku Sha, 2016.

(2) Co-author・Cerebellar Learning, Volume 210 (Long-Term Depression as a Model of Cerebellar Plasticity), Progress in Brain Research, 2014.

2.3 Non-refereed articles or translation

(1) Tadashi Yamazaki, Junichiro Makino, Toshikazu Ebisuzaki. Perceptron and Cerebellum (Japanese article), Clinical Neuroscience, in press.

(2) Tadashi Yamazaki. Computer Simulation of the Cerebellar Network (Japanese article), Bulletin of Japan Society of Arfificial Intelligence, 30(5): 639－646, 2015.

(3) Tadashi Yamazaki. Cerebellar Internal Clock and Timing Control (Japanese article), Shinkei Naika 78(6): 635－641, 2013.

2.4 Invited lectures

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

(2) Tadashi Yamaznaki. An artificial cerebellum (in Japanese), Tokai University Symposium, Tokai University, 2015/1/10.

(3) Tadashi Yamazaki, Building a 1 mm^3 cerebellar module on a computer, INCF Congress Neuroinformatics 2015, Cairns, Australia, 201/8/20-22.

(4) Tadashi Yamazaki Neural Network Models for sequence and timing control, 8th Whole-Brain-Architecture Workshop (Japanese), Gran-Toyo South Tower, 2014/11/10.

(5) Tadashi Yamazaki, Building the cerebellum on a computer (Japanese), Jichi University, 2013/2/19.

(6) Tadashi Yamazaki. Creating an artificial cerebellum on a computer, Neuro2013 Satellite Symposium "Neuroscience on the Cerebellum", Kyoto, 2013/5/22..

(7) Tadashi Yamazaki, Realtime simulation of a cerebellar spiking network model using a GPU, Open

Source Brain Kickoff Meeting , Sardina, Italy , 2013/5/13 -15.

(8) Tadashi Yamazaki, Realtime Cerebellum: GPU-accelerated numerical simulation of a cerebellar spiking network model in realtime, Computational Neuroscience (CNS) 2013 Paris, Paris, France, 2013/7/17-18.

2.5 Media release

(1) NVIDIA Blog: Better Batting with CUDA: How GPU-based Brain Research Helped Japanese Robot Swing for the Fences. Apr 26, 2013.

(2) WIRED Enterprise: Scientists Build Baseball-Playing Robot With 100,000-Neuron Fake Brain. Apr 27. 2013.

(3) insideHPC: GPU-based Brain Research Hits it Out of the Park. Apr 27, 2013.

(4) CNN: Scientists build baseball-playing robot with 100,000-neuron fake brain. Apr 29, 2013.

(5) Bio IT World: Swing Batter, Batter: GPUs and Baseball. Apr 29, 2013.

(6) WIRED Japanese Edition: GPU-Controlled Artificial Cerebellum: Baseball Robot by UEC and OIST (Japanese article). Apr 30, 2013.

(7) UEC e-Bulletin vol.4, 2014: Artificial intelligence: Brain-training for baseball robot. Dec 24, 2014.

(8) UEC: [Media Release] Practice makes perfect: a theoretical model of memory consolidation in the cerebellum. Mar 3, 2015.

(9) My Navi News: (In Japanese). Mar 4, 2015.

(10) UEC e-Bulletin vol.5, 2015: Motor memory: the long and short of it. Mar 25, 2015.

(11) MedicalXpress: Research explains the formation of long-term motor memory. Mar 26, 2015.

(12) The Japan Neuroscience Society: [Neuroscience Topics] Practice makes perfect: a theoretical model for memory consolidation in the cerebellum. Apr 24, 2015.

(13) UEC eBulletin vol.8, 2015: Neuroscience: Creating realistic computational models of the cerebellum. Dec 25, 2015.

2.6 Data release

(1) Cerebellar PF, http://cerebellum.neuroinf.jp/, 2006-.

(2) Simulation PF, http://sim.neuroinf.jp/, 2009-.

2.7 Awards

Tadashi Yamazaki, Jun Igarashi. Best Paper Award. Japanese Neural Network Society, 2014.

2.8 Student guidance

(1) Manabu Inaba, 2013, Master (Engineering).

(2) Mamoru Kubota, 2013, Master (Engineering).

(3) Shusei Yasumuro, 2014, Bachelor (Engineering).

(4) Masato Gosui, 2015, Master (Engineering).

(5) Yuki Yamamoto, Tokyo Medical and Dental University,
(Internship from 205/6/1 to 2015/11/20).

(6) Tsukasa Tsuyuki, 2015, Bachelor (Engineering), now in Master course.
(7) Ohki Katakura, 2014, Bachelor (Engineering), now in Master course.
(8) Daisuke Ichimura, 2014, Bachelor (Engineering), now in Master course.

2.9 Visit of oversea researchers and students

(1) William Lennon, Spiking neural network simulation of plasticity at stellate and basket cells in the cerebellum, 2013/6/18-8/20.

3 Research funding

3.1 Grant-in-aid for scientific research

(1) Tadashi Yamazaki (Leader), Model Study on Representation of Time, Grant-in-Aid for Scientific Research on Innovative Areas “Science of Mental Time”, 2014/4/1-2016/3/31, 2100 KYen.
(2) Tadashi Yamazaki (Leader), Study on Synergistic Motor Control Mechanisms of Distributed Plasticity in the Cerebellum, Grant-in-Aid for Scientific Research (C) , 2014/4/1-2017/3/3 3900 KYen.

3.2 Competitive external research funding

(1) Tadashi Yamazaki (Leader), Adaptive Control of Small Humanoid Robots by an Artificial Cerebellum, Artificial Intelligence Research Promotion Foundation, 2014/4/1-2016/3/31, 500 KYen.
(2) Tadashi Yamazaki (Leader), R&D of Artificial Motor Cortices, NEDO Next-Generation Artificial Intelligence R&D, 2015/7/1-2019/3/31, 20000 KYen/Year.
(3) Tadashi Yamazaki (Leader), Development of Neuroinformatics Platforms, RIKEN, 2013-, 1000 KYen/Year.

4. Collaborators

4.1 Inside BLSC

(1) Shigeru Tanaka. Theoretical study on the cerebellum. 2013/04-.

4.2 Outside UEC

(1) Neuroinformatics Japan Center, RIKEN, Study on Neural Network Simulation, 2013-.
(2) AI Research Center, AIST, R&D of Brain-style Artificial Intelligence, 2015-.
(3) Junichiro Makino, Kobe University,, Large-Scale Simulation of the Cerebellum on PEZY-SC, 2015.
(4) Toshikazu Ebisuzaki, RIKEN, Large-Scale Simulation of the Cerebellum on PEZY-SC, 2015-.
(5) Jun Igarashi, RIKEN, Computer Simulation of the Cerebellar Network Model on GPUs, 2013-

Tmagawa Hospital, Computer Simulation of Rehabilitation with Neuromusculoskeletal models. 2014-.

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

5. Outreach activities

5.1 Editor of academic journals

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

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

5.2 Paper review of academic journals

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

5.3 External review board

(1) Ministry of Internal Affairs and Communications, Information and Communications Bureau, Brain-informatics AI WG, 2015/12-.

(2) IEICE, Neurocomputing WG, 2014/04-.

5.4 Other outreach activities

(1) Lecturer, Autumn School on Computational Neuroscience, Japanese Neural Network Society, 2014/10.