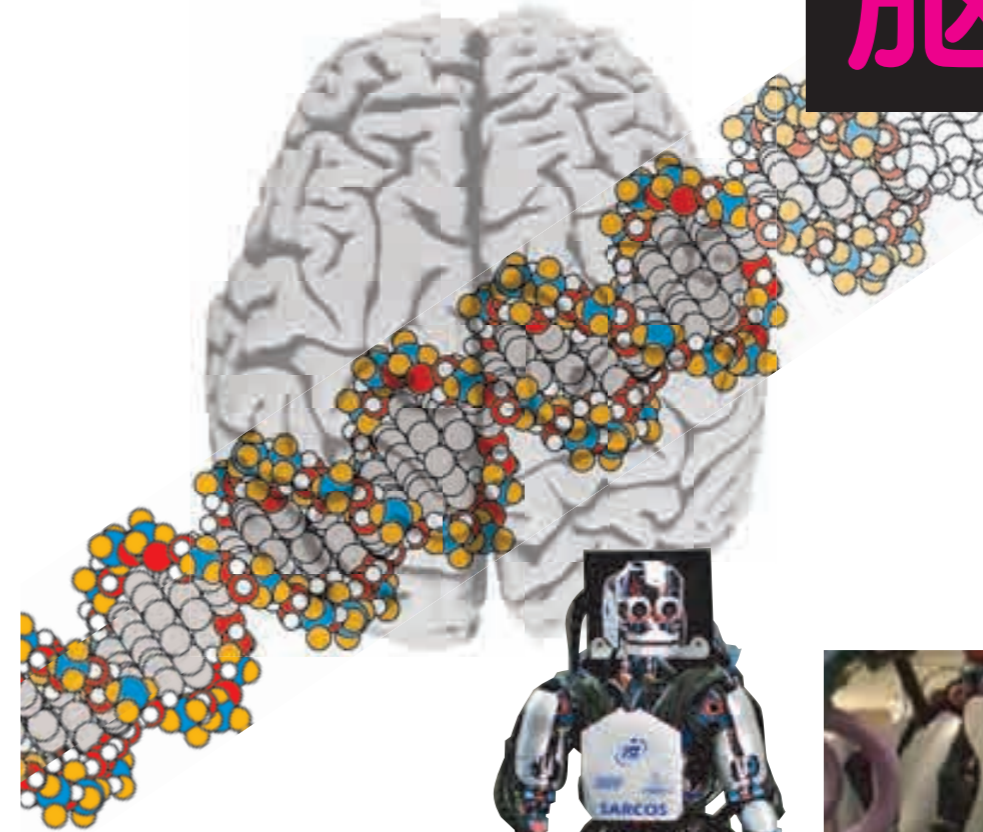


脳科学研究戦略推進プログラム第1回公開シンポジウム  
日英ブレイン・マシン・インターフェース国際ワークショップ

# 脳科学の 最先端

BMIと新しい  
モデル動物



[問い合わせ先]  
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主催ー脳科学研究戦略推進プログラム公開シンポジウム運営委員会  
共催ー文部科学省(12~13日共通)、英国大使館(12日)

[会場] **有楽町朝日ホール スクエア**

[日時] **2009年2月12日(木), 13日(金)**

**予稿集**  
Proceeding

# 2009年2月12日 木

日英ブレイン・マシン・インターフェース国際ワークショップ (課題A, B 公開シンポジウム)

9:45 ~ 10:00 **Opening Remarks**  
Ichiro Kanazawa President of the Science Council of Japan  
John Beddington UK Government Chief Scientific Adviser  
Shigetada Nakanishi Program Director / Osaka Bioscience Institute  
Colin Ingram Newcastle University

**Session 1** (Chair Mitsuo Kawato)  
10:00 ~ 10:30 **Spinal cord interneuronal network and functional electrical stimulation of the spinal cord with chronically implanted electrodes**  
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Stuart Baker Newcastle University  
Andrew Jackson Newcastle University

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16:45 ~ 17:45 **General discussion + Statement**

# 2009年2月13日 金

霊長類脳での遺伝子改変研究の展開 (課題C 公開シンポジウム)

司会：赤澤 智宏  
文部科学省脳科学研究戦略推進プログラム・プログラムオフィサー／東京医科歯科大学

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伊佐 正 文部科学省脳科学研究戦略推進プログラム課題C・拠点長／自然科学研究機構生理学研究所

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※プログラムは一部変更となる可能性があります。

# 2009年2月12日(木)

日英ブレイン・マシン・インターフェース国際ワークショップ(課題A, B 公開シンポジウム)

## Opening Remarks

Ichiro Kanazawa President of the Science Council of Japan  
John Beddington UK Government Chief Scientific Adviser  
Shigetada Nakanishi Program Director / Osaka Bioscience Institute  
Colin Ingram Newcastle University

(Chair Mitsuo Kawato)

## Session 1

### Spinal cord interneuronal network and functional electrical stimulation of the spinal cord with chronically implanted electrodes

脊髄介在ニューロンネットワークと慢性埋込電極を使った脊髄の機能的電気刺激

Tadashi Isa National Institute for Physiological Sciences

### Restoring motor function with Brain-Machine Interfaces

ブレイン・マシン・インターフェースを使った運動機能の回復

Stuart Baker Newcastle University

Andrew Jackson Newcastle University

(Chair Mitsuo Kawato)

## Session 2

### Visual prosthesis with suprachoroidal transretinal stimulation system

脈絡膜上-経網膜刺激方式による人工視覚

Takashi Fujikado Osaka University

Yasuo Tano Osaka University

### Towards a high-resolution retinal prosthesis for degenerative retinal diseases

網膜変性疾患のための高解像度人工網膜の開発に向けて

Keith Mathieson Glasgow University

### Towards totally implantable neural prostheses for inner ear rehabilitation

内耳機能回復のための完全埋込型神経装具に向けて

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## Session 3

### Robot control by human brain with subdural electrodes

硬膜下電極を用いたヒト脳によるロボット・コントロール

Toshiki Yoshimine Osaka University

### Gamma oscillations encode the structure of static visual environments: a mechanism for monitoring constancy of sensory input?

ガンマ振動が静的視覚環境構造を符号化する：感覚入力の恒常性の監視機構か？

Avgis Hadjipapas Aston University

### Leading edge of cybernetics and BMI / BCI

最先端のサイバニクスとBMI / BCI

Yoshiyuki Sankai University of Tsukuba

(Chair Colin Ingram)

## Session 4

### Experience of neuroprostheses for motor function after spinal cord injury

脊髄損傷後の運動機能のための神経装具実施経験

Nick Donaldson University College London

### New aspects of BMI

BMIの新たな展開

Mitsuo Kawato ATR Computational Neuroscience Laboratories

## Opening Remarks

### ● Ichiro Kanazawa

President of the Science Council of Japan / Medical Supervisor for the Royal Families, Imperial Household Agency / Chairman of the Brain Science Committee launched in the MEXT

Ichiro Kanazawa, M.D. was appointed as President of the Science Council of Japan on 2006, and as Chairman of the Brain Science Committee launched in the MEXT on 2007. From 1991 to 2001, he was a professor at Department of Neurology, University of Tokyo (Professor Emeritus, 2002 ~). Since 2002, he has been Medical Supervisor for the Royal Families, and from 2003 to 2007 he served as a President at National Centre for Neurology and Psychiatry (President Emeritus, 2007 ~).

His main area of research has been the internal medicine, clinical neurology, clinical neurogenetics, molecular neurobiology, and neurochemical pharmacology.

He is particularly interested in neurological disorders such as Huntington's disease, Parkinson's disease, Hereditary cerebellar degeneration, Involuntary movements and etc.

### ● John Beddington

UK Government Chief Scientific Adviser

Professor John Beddington was appointed as Government Chief Scientific Adviser (GCSA) on 1 January 2008. John's main research interests are the application of biological and economic analysis to problems of Natural Resource Management including inter alia: fisheries, pest control, wildlife management and the control of disease. He was Professor of Applied Population Biology at Imperial until his appointment as GCSA.

He has been adviser to a number of government departments, including the Foreign and Commonwealth Office (on Antarctic and South Atlantic matters), the Department for Environment, Food and Rural Affairs (where he chaired the Science Advisory Council), the Department for International Development, the Ministry of Defence and the Cabinet Office.

He has acted as a senior adviser to several government and international bodies, including the Australian, New Zealand and US Governments, the European Commission, the United Nations Environment Programme and the Food and Agriculture Organisation. In 2001 he became a Fellow of the Royal Society.

### ● Shigetada Nakanishi

Program Director / Osaka Bioscience Institute

Professor Nakanishi is a neuroscientist who obtained his PhD from Kyoto University in the field of biochemistry. After 3-year postdoctoral fellow at National Cancer Institute, NIH, he was appointed as Associate Professor of Kyoto University, Faculty of Medicine in 1974 and then as Professor of the same University in 1981. He took up the Director of Osaka Bioscience Institute in 2005. His main area of research has been in molecular neuroscience, focusing on molecular mechanisms of glutamate receptor functions and integrative synaptic mechanisms of the neural network. Professor Nakanishi is a foreign honorary member of the American Academy of Arts and Sciences and a foreign associate member of the National Academy of Sciences, USA and received the Bristol-Myers Squibb Neuroscience Award and the Gruber Neuroscience Prize.

### ● Colin Ingram

New Castle University

Professor Colin Ingram is a neurobiologist who obtained his PhD from Cambridge University in the field of neuroendocrinology. In 1986 he moved to Bristol where he held successive positions as a Medical Research Council Training Fellow and Royal Society University Research Fellow, before being appointed as Reader in Neurobiology. In 2000 he took up the Chair of Psychobiology at the University of Newcastle and in 2004 was appointed the Director of the Institute of Neuroscience at Newcastle. Professor Ingram was responsible for creating the Institute which brings together over 60 research leaders covering a wide range of basic and clinic neuroscience fields. His main area of research has been in neuropharmacology, but through the Institute he also leads major research initiatives in neuroinformatics and neurotechnology. Professor Ingram is also Honorary Secretary of the British Neuroscience Association, the UK's principle society serving the neuroscience community.

## Spinal cord interneuronal network and functional electrical stimulation of the spinal cord with chronically implanted electrodes

### 脊髄介在ニューロンネットワークと慢性埋込電極を使った脊髄の機能的電気刺激

Tadashi Isa

Department of Developmental Physiology,  
National Institute for Physiological Sciences

Functional electrical stimulation (FES) of the spinal cord is expected to work as an effective neuroprosthesis to compensate the motor function of the patients with spinal cord injury at the higher cervical level or brain stroke, with which the difficulty of FES of skeletal muscles, such as muscle fatigue, could be overcome. However, for this purpose, it is essential to understand the neuronal organization of the premotor interneuronal circuits of the spinal cord and primary effects of FES of the spinal cord circuits. In addition, development of flexible electrodes is also necessary to minimize the mechanical damage and induction of gliosis of the spinal tissue during the long term implantation.

In this presentation, I will present the data of our recent experiments on non-human primate preparations in which we tested the spatio-temporal pattern of interactions between motor sites in the cervical spinal cord and long-term stability of the stimulating electrodes.

Professor Tadashi Isa has an affiliation in the National Institute for Physiological Sciences in Okazaki since 1996. He has been intensively working on the organization of spinal cord interneuronal systems in non-human primates (NHPs) and their role in functional recovery from the spinal cord injury (SCI) by collaboration with Swedish colleagues since his postdoc time in the laboratory of Anders Lundberg in Göteborg. He is also working on the role of cortical circuitries in functional recovery from the SCI. Kazuhiko Seki joined in Isa's laboratory after he finished his postdoc in Eb Fetz lab in Seattle, USA and he introduced the technique of single neuron recordings from spinal cord in awake behaving NHPs. Seki and Isa are collaborating with Andrew Jackson and Stuart Baker in Newcastle, for developing the chronically implantable electrodes for functional electrical stimulation of the spinal cord.

## Restoring motor function with Brain-Machine Interfaces

### ブレイン・マシン・インターフェースを使った運動機能の回復

**Stuart Baker**

Institute of Neuroscience, Newcastle University

**Andrew Jackson**

Institute of Neuroscience, Newcastle University

Implanted devices that relay electrical signals directly to and from the nervous system may form the basis of future neural prostheses to restore function following spinal cord injury and other neurological conditions. However key technical and scientific challenges must be overcome before electronics can be successfully integrated with the brain. In this talk we will discuss progress in several areas. First, advanced microfabrication techniques are enabling a new generation of electrodes for chronic implantation into nervous tissue with improved long-term performance. Second, low-power autonomous electronic implants implementing continuous bidirectional interfaces with the nervous system are providing new insights into plastic reorganisation of neural circuits. Such plasticity is likely to be crucial for the successful operation of neural prostheses, and may have a beneficial role in rehabilitation following injury.

Professor Stuart Baker

After undergraduate and postgraduate study at Cambridge and London, Professor Baker established a laboratory for multiple single electrode recording from sensorimotor cortex, brainstem and spinal motor centres. His research interests include the role of oscillatory activity in motor control, the neural circuits mediating bimanual co-ordination, and the role of the reticulospinal pathway in the recovery from injury. He is a Wellcome Trust Senior Fellow and Chair of Movement Neurosciences in the Institute of Neuroscience at Newcastle University.

Dr. Andrew Jackson

After receiving his PhD in neuroscience in 2002, Dr. Andrew Jackson pursued post-doctoral research at the University of Washington where he led an interdisciplinary collaboration developing implantable electronics (Neurochips) for neural recording and stimulation in unrestrained primates. In 2006 he moved to the Institute of Neuroscience at Newcastle University where he has established a laboratory researching neural coding and plasticity in the motor system, and continues to develop new technologies for interfacing with the brain.

## Visual prosthesis with suprachoroidal transretinal stimulation system

### 脈絡膜上-経網膜刺激方式による人工視覚

**Takashi Fujikado**

Department of Visual Science, Osaka University Medical School

**Yasuo Tano**

Department of Ophthalmology, Osaka University Medical School

For the last few decades, ophthalmologists, visual scientists and medical engineers have closely been collaborating in quest of realization of clinically applicable visual prosthesis which would benefit blind patients of outer retinal disorders such as retinitis pigmentosa. We have been developing a unique visual prosthesis with suprachoroidal transretinal stimulation (STS) system since 2001 when the consortium of the Japan Artificial Vision Project was organized. Validity of the STS system has been assessed by various aspects such as studies on efficacy, safety and stability in animal eyes, evaluation of spatial resolution by the system, development of animal models of retinal degeneration, neuroprotective effect by transcorneal electrical stimulation, acute human clinical trial and so forth. We have constructed prototype of a visual prosthesis with STS system. Currently preclinical studies are being conducted in expectation to produce a commercially-available visual prosthesis with STS system in the near future.

Dr. Yasuo Tano is the Professor and Chairman of the Department of Ophthalmology at Osaka University Medical School. His research interests have been focused on patho-physiology of vitreoretinal disorders. He has been a principal investigator of Japan Artificial Vision Project since 2001. Clinically Dr. Tano was one of the first to perform pars plana vitrectomy in Japan as a trailblazer. He is internationally known as one of the leading surgeons in vitreoretinal surgery. He has invented many fine vitreoretinal instruments, which had contributed advances in vitreoretinal surgery. He also has keen interests on medical retina and has served as a principal investigator on several important clinical trials on retinal diseases. He has also dedicated his time to train aspiring surgeons thus paving the way for continuing excellence in the field of surgical and medical retina into the next generation.

## Towards a high-resolution retinal prosthesis for degenerative retinal diseases

### 網膜変性疾患のための高解像度人工網膜の開発に向けて

**Keith Mathieson**

Retinal Prosthesis Group, Glasgow University

Degenerative photoreceptor diseases, such as age-related macular degeneration and retinitis pigmentosa, are the most common forms of blindness in the developed world. There has been world-wide interest in developing a retinal prosthesis for these diseases by electrically activating the retinal output (ganglion) cells. We have developed a system to detect the visual scene and translate the image into a train of electrical pulses that stimulates retinal tissue. The imaging device is a CMOS pixel sensor with over 500 pixels fabricated in a 0.35 micron CMOS process. Each pixel contains a photodiode and on-pixel circuitry that translates the intensity of the incoming light into a certain frequency of output current pulses. The sensor includes an on-chip neural network that replicates the biological process of lateral inhibition, by suppressing areas of like contrast. The outputs of the pixels are connected to a biocompatible microelectrode array which makes contact with the retinal cells.

Dr. Keith Mathieson holds a personal research fellowship from the Royal Society of Edinburgh and leads a research group in the Department of Physics and Astronomy at the University of Glasgow aimed at developing a retinal prosthesis for the blind. He has pioneered the development of high-density microelectrode arrays to study the response of retinal tissue to electrical stimulation in collaboration with the University of California Santa Cruz and the Salk Institute for Biological Studies in San Diego. Additionally, he leads a collaboration with the Rutherford Laboratories aimed at producing a retinal stimulation sensor with an on-chip neural network to replicate aspects of retinal processing. He holds grants from the Science and Technology Facilities Council, Engineering and Physical Sciences Research Council and the Royal Society of Edinburgh.

## Towards totally implantable neural prostheses for inner ear rehabilitation

### 内耳機能回復のための完全埋込型神経装具に向けて

**Timothy Constandinou**

Institute of Biomedical Engineering, Imperial College London

With ever decreasing electrode-nerve interface proximities, typical stimulus magnitudes for neural activation are decreasing and, therefore, the bottleneck in the power budget of implant devices is now the signal processing. Commercial cochlear implant systems overcome this challenge by incorporating a two module solution encompassing an implanted stimulator and external auditory processing hardware. Recent advances in ultra low power microelectronics, however, have now presented new opportunities for implementing totally implantable solutions. Sensory artificial prostheses are ideal candidates to exploit such techniques, building on the success of cochlear implants. Two such examples of recent advances will be presented. Firstly, a 16-channel, fully-programmable, mixed-signal cochlear prosthesis, with total power consumption of 126  $\mu$ W. Secondly, a new emerging neuroprosthetic device for the restoration of balance is the vestibular prosthesis. We will present the world's first such integrated system, based on a hybrid CMOS/MEMS implementation of a 5-channel prosthesis.

Dr. Timothy Constandinou obtained a BEng in Electrical and Electronic Engineering and PhD from the Circuits and Systems Group both at Imperial College London. He is currently Research Officer in Bionics at the Institute of Biomedical Engineering at Imperial and holds a position of research Fellow at the University of Cyprus. During his research career he has contributed to several research projects including a MEMS-based vestibular prosthesis, a cochlear prosthesis demonstrator platform, neurostimulation microelectronics, biologically-inspired vision systems, various smart imagers, integrated CMOS ISFET sensors, efficient cross-correlation hardware for cardiac monitoring and a number of miniature wearable biomedical devices. His research interests are in ultra low power circuits and systems for biomedical and biologically-inspired applications, including implantable neuroprosthetic devices, body-worn instrumentation, integrated smart sensors and vision systems. Dr Constandinou is a member of the Sensory Systems and BioCAS Technical Committees of the IEEE Circuits and Systems Society.

## Robot control by human brain with subdural electrodes

### 硬膜下電極を用いたヒト脳によるロボット・コントロール

**Toshiki Yoshimine**

Department of Neurosurgery, Osaka University Medical School

High quality neural signals are acquirable with a set of electrodes implanted beneath the skull, directly on the surface of the brain (subdural electrodes). By decoding those signals, we may conjecture the content of some brain activity. We recently succeeded to discriminate several types of hand movement by decoding the signals obtained from a specific area of the brain (primary motor cortex). The instantaneous decoding enabled real-time activation of a robotic arm.

Although implantation of the electrodes is partially invasive, the quality of signals obtained is far superior to those obtained over the scalp. The clinical risk is relatively low. A multidisciplinary cooperative project is launched to develop clinically applicable system of this type of brain-machine interface (BMI) to help people suffering from severe motor disabilities.

Dr. Toshiki Yoshimine is a professor and chairman of Department of Neurosurgery, Osaka University Medical School. He is specialized in the surgical treatment of brain tumor and epilepsy. He is one of the pioneers who developed a computerized navigation system for brain surgery. For the last few decades, he studies topographic human brain function with intracranial electrodes and with magnetoencephalography (MEG).

His recent work focuses on the development of motor brain-machine interface (BMI) which controls the external devices by decoding the neural signals obtained from intracranial electrodes.

He is a president of the Asian Conference of Epilepsy Surgery, a director of Japan Neurosurgical Society and a member of Nominating Committee of the World Federation of Neurosurgical Societies (WFNS).

## Gamma oscillations encode the structure of static visual environments: a mechanism for monitoring constancy of sensory input?

### ガンマ振動が静的視覚環境構造を符号化する：感覚入力の恒常性の監視機構か？

**Avgis Hadjipapas**

The Wellcome Trust Laboratory for MEG Studies,  
The School of Life and Health Sciences, Aston University

Our recent studies show that information about the structure of the static visual world can be decoded from the spectral patterns of gamma oscillations in the human MEG. Crucially, stimulus decoding is still possible when only utilizing the sustained part of the oscillations. We introduce single-trial measures of stimulus-specificity (using SVM-methodology) and observe a parametric dependence of the degree of specificity in epochs that immediately precede stimulus-change and subsequent behavioural and evoked responses. The results are robust but somewhat counterintuitive: if the spectral pattern in the preceding epoch is typical for the subsequent stimulus class, then behavioural responses are accelerated and evoked transients facilitated; analogously, if the pattern is typical for a class of stimuli different to the subsequent stimulus, the converse occurs. These results are consistent with a mechanism embodied in the gamma network state, which monitors sensory constancy and provides a reference frame for sensory changes.

Dr. Avgis Hadjipapas has an MD from the University of Kiel, Germany, an MS in Cognitive Science/Electroencephalography from the Central and Eastern European Center in Cognitive Science, Sofia, Bulgaria, and PhD in Neuroscience from the Wellcome Trust Laboratory for MEG studies, Aston University, UK. He has held an appointment as a Research Fellow at Aston University since 2005. His research interests are in the field of functional neuroimaging in humans, mostly focused in the time series analysis of magneto- and electroencephalographic (MEG/EEG) signals, the modelling of the underlying network generators of these macroscopic brain signals and their identification from the dynamics of the measured time series both in health and disease. He has developed expertise in non-invasive characterization of local dynamics underlying basic functions in visual cortex and the assessment of functional/dysfunctional long-range signal coupling in the brain.

## Leading edge of cybernetics and BMI / BCI 最先端のサイバニクスとBMI / BCI

**Yoshiyuki Sankai**

Leader of Global COE "CYBERNETICS",  
Graduate School of Systems and Information Engineering, University of Tsukuba

Cybernetics is a new domain of interdisciplinary academic field of human-assistive technology to enhance, strengthen, and support human's cognitive and physical functions, which challenges to integrate and harmonize humans and robots (RT: robotics technology) with the basis of information technology (IT) in a functional, organic, and social manner. We aim to develop the frontier science Cybernetics, which is centered on cybernetics, mechatronics, and informatics, and it challenges to integrate neuroscience, robotics, systems engineering, information technology, "kansei" engineering, ergonomics, physiology, social science, law, ethics, management. The goal of the Program represents a Grand Challenge that makes breakthroughs in the innovative creation and fusion of forefront researches based on information science. In this talk, I will deliver the outline Cybernetics approach based on our experienced and introduce the work performed in Cybernetics. And, I may present BMI / BCI what we have done related in this fields.

Yoshiyuki Sankai received a PhD in engineering from University of Tsukuba in Japan in 1987. He was Assistant Professor, Associate Professor, Professor at the Institute of Systems & Engineering at the University of Tsukuba, and a Visiting Professor of Baylor College of Medicine in Houston, Texas in the United States. Currently, he is professor of the Graduate School of Systems & Information Engineering at the University of Tsukuba, and president and CEO of CYBERDYNE Inc. In 2007, he was appointed as leader of Global COE (Centre of Excellence) program for Cybernetics by the Japanese Ministry of Education, Culture, Sports, Science and Technology of Japan),

Among the awards he won are: World Technology Award (2005), Good Design Gold Award (2006), Japan Innovator Award (2006), Best Paper Award (International Journal of Advanced Robotics) (2006), Award from American Society for Artificial Organs, Award from International Society for Artificial Organs, Award from the Minister of Economy, Trade and Industry of Japan (2007), Award from National Institute of Science and Technology Policy (2007).

## Experience of neuroprostheses for motor function after spinal cord injury 脊髄損傷後の運動機能のための神経装具実施経験

**Nick Donaldson**

Department of Medical Physics and Bioengineering, University College London

Recently in Europe, funding of research into neuroprosthetics has been available with expectations that successful technological development will lead to new industrial products and higher quality of life for disabled people. Perhaps the rise of the cochlear implant has been the outstanding example of such development. An old idea is that people who have been disabled by spinal cord injury might have leg function restored using nerve stimulators. Yet despite considerable research effort in the last 40 years, very few patients are actually given stimulation devices during their rehabilitation. Professor Donaldson will explore some of the reasons for this poor outcome, based on his experience. Understanding these difficulties may help those who wish to develop other types of neuroprosthesis including those with Brain-Computer Interfaces.

Professor Nick Donaldson studied Engineering and Electrical Sciences at Cambridge University. From 1977 to 1992 he worked for the Medical Research Council, Neurological Prostheses Unit, under the direction of Professor G.S. Brindley. In that period, his main field of research was the technology and use of implanted device for the restoration of useful leg function to paraplegics. Since 1992, he has been Head of the Implanted Devices Group at University College London where he holds a chair position. He has been Principal Investigator for many projects related to implanted devices and functional electrical stimulation. His research interests now includes the development of implanted devices that use natural nerve signals as inputs; stimulators of nerve roots; the use of electrical stimulation for recreational exercise of paralysed legs; and methods to encourage functional neurological recovery after injury.



## New aspects of BMI

### BMIの新たな展開

#### Mitsuo Kawato

ATR Computational Neuroscience Laboratories,  
Research Supervisor of ICORP Computational Brain Project, JST

Brain-computer interfaces (BCI), brain-machine interfaces (BMI), and brain-network interfaces (BNI) are revolutionary new man-machine interfaces that directly connect brains and computers, robots and/or internets bypassing sensory and motor organs. These interfaces are expected as one of the most promising and influential application fields of the system neuroscience, and also expected to provide an entirely new experimental paradigm that guarantees cause-and-effect analyses for the system neuroscience, unlike usual experimental efforts demonstrating mere temporal correlations between hypothetical variables and neural or brain activities. For further developments of BCI, BMI and BNI, many conceptual, technical and computational problems should be resolved. Examples are neuroethics, high spatiotemporal resolution non-invasive brain measurement technology (Kawato), artificial neural circuits that are embedded in the biological nervous system (Fetz), electrocorticogram-based low-invasive BMI (Kato), BMI based neuro-rehabilitation (Isa), rigorous proof of computational theories based on BNI (Kawato). This symposium highlights recent advances in these emerging problems in BCI, BMI and BNI by lectures of 5 leading scientists in this field.

Mitsuo Kawato received a B.S. degree in physics from Tokyo University in 1976 and M.E. and Ph.D. degrees in biophysical engineering from Osaka University in 1978 and 1981, respectively. From 1981 to 1988, he was a faculty member and lecturer at Osaka University. From 1988, he was a senior researcher and then a supervisor in the ATR Auditory and Visual Perception Research Laboratories. Since 2003, he has been Director of ATR Computational Neuroscience Laboratories. In 2004, he became an ATR Fellow. From 1996 to 2001, he served as director of the Kawato Dynamic Brain Project, ERATO, JST. From 2004 to 2009, he served as research Supervisor of the Computational Brain Project, ICORP, JST. In 2008, he was jointly appointed as a Research supervisor of PRESTO, JST. He is now concurrently working as a visiting professor at Kanazawa Institute of Technology, Nara Institute of Science and Technology, Osaka University, the National Institute for Physiological Sciences, Toyama Prefectural University, Kyoto Prefectural University of Medicine, and National Institute of Informatics.

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霊長類脳での遺伝子改変研究の展開 (課題c 公開シンポジウム)

司会：赤澤 智宏

文部科学省脳科学研究戦略推進プログラム・プログラムオフィサー／東京医科歯科大学

開会の辞

伊佐 正 文部科学省脳科学研究戦略推進プログラム課題C・拠点長／自然科学研究機構生理学研究所

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霊長類の大脳皮質の特徴

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閉会の辞

中西 重忠 文部科学省脳科学研究戦略推進プログラム・プログラムディレクター／  
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### ●中西 重忠（なかにし しげただ）

文部科学省脳科学研究戦略推進プログラム プログラムディレクター  
財団法人大阪バイオサイエンス研究所 所長

1966年京都大学医学部卒業、71年京都大学大学院医科研究科修了（生理系専攻）。71～74年米国国立衛生研究所（NIH）、癌研究所（NCI）、分子生物学教室客員研究員、74年京都大学医学部医化学教室助教授（医学博士）、81年京都大学医学部免疫研究施設第二部門教授、95年京都大学大学院医学研究科教授、99年京都大学大学院生命科学研究科教授（兼務）、2000年京都大学大学院医学研究科科長・医学部長、05年京都大学名誉教授を経て、同年より現職。

専門は生化学、分子生物学、神経科学。グルタミン酸受容体の分子メカニズム、神経ネットワークのシナプス伝達機構の研究を進める。

95年プリストルマイヤーズスクイブ神経科学賞、95年米国芸術・科学アカデミー外国人名誉会員、97年恩賜賞・日本学士院賞、200年全米科学アカデミー外国人会員、06年文化功労者、07年米国グローバー賞など受賞多数。

### ●赤澤 智宏（あかざわ ちひろ）

文部科学省脳科学研究戦略推進プログラム プログラムオフィサー  
文部科学省再生医療実現化プロジェクト プログラムオフィサー  
東京医科歯科大学大学院保健衛生学研究科 准教授（分子生命情報解析学分野）

1988年東京医科歯科大学医学部卒業。1994年東京医科歯科大学大学院博士課程修了。同年ソーク生物学研究所ポストドクトラルフェロー、1996年国立精神・神経センター神経研究所室長を経て、2007年より現職。

専門は神経科学。特に損傷神経の再生メカニズム。  
現在は細胞内タンパク質制御に関心を持つ。

### ●伊佐 正（いさ ただし）

自然科学研究機構生理学研究所認知行動発達機構研究部門 教授

1985年東京大学医学部医学科卒業。1989年同大学大学院医学系研究科単位取得済み退学。医学博士。同年同大学医学部附属脳研究施設助手、1988～1990年スウェーデン王国イエテボリ大学客員研究員、1993年群馬大学医学部講師、1995年同助教授を経て、1996年より岡崎国立共同研究機構生理学研究所教授。2004年より改組にて現職。

専門は神経生理学。特に手と眼球の運動を制御する神経回路。  
現在は特に中枢神経系損傷後の機能代償機構に関心を持つ。

日本神経科学学会庶務理事。

## 霊長類の脳皮質の特徴

山森 哲雄

自然科学研究機構基礎生物学研究所

私を含め、多くの人は、自分自身を含めた「ヒト」の認知・情動行動の科学的理解や脳精神疾患の原因と治療に関心を持っていると思うが、そうした興味と関心に科学的に答える為には、モデル動物の選択がその成功の可否を決定する一つの重要な要因である。例えば、神経活動の伝導機構の研究に於いては、ヤリイカの巨大神経が、神経伝達物質の受容体に遺伝子の同定と機能解明には、アフリカツメガエルの卵母細胞が用いられて、神経活動の素過程の解明に重要な役割を果たしてきた。そこで、本講演では、高次脳機能に重要な役割を果たす霊長類大脳新皮質における遺伝子発現の最近の研究の幾つかについて紹介し、哺乳類のモデル動物の代表であり、脳科学に於いても、最も良く用いられるマウスと霊長類の遺伝子発現の異同を示したい。その上で、霊長類を用いた脳研究の重要性と可能性について論じてみたい。

### ●やまもり てつお

自然科学研究機構基礎生物学研究所神経生物学領域脳生物学研究部門 教授

1974年京都大学理学部卒業。1981年京都大学大学院博士課程修了（理学博士）。同年コロラド大学研究員、1986年カリフォルニア工科大学研究員、1991年理化学研究所フロンティア研究員を経て、1994年より現職。

専門は分子脳科学。現在は霊長類の大脳皮質領野の形成と機能に関心をもつ。  
著書に、『神経回路の機能発現のメカニズム』（共編者、共立出版、2004年）、『ヒトの進化』（シリーズ進化学5巻、共著者、岩波書店、2006年）、『神経の分化、回路形成、機能発現』（共編者、共立出版、2008年）等がある。

## ウイルスベクターを用いたサル脳への遺伝子導入： パーキンソン病の遺伝子治療研究

高田 昌彦

財団法人東京都医学研究機構東京都神経科学総合研究所

近年、ウイルスベクターを用いた遺伝子導入技術により、高次脳機能を解明しようとする研究や、神経変性疾患に対する遺伝子治療法を開発しようとする研究が注目を集めている。このような研究を展開していく上で、ヒトに近縁のサルを使用することが必要不可欠であることは言うまでもない。本講演では、私の研究グループが現在進めている、アデノウイルス、アデノ随伴ウイルス、レンチウイルス由来の組換え体ウイルスベクターを用いた遺伝子導入により、パーキンソン病に対する新たな遺伝子治療法の開発を目指した基礎的研究の成果を紹介したい。本研究で試みた遺伝子治療戦略は、パーキンソン病の責任細胞である黒質ドーパミン細胞にその変性・脱落を抑制するような機能分子であると考えられるカルビンディン（カルシウム結合蛋白）やパーキン蛋白（ユビキチンリガーゼ）の遺伝子導入を行い、パーキンソン病の発症を防御することである。

●たかだ まさひこ

財団法人東京都医学研究機構東京都神経科学総合研究所 副参事研究員

1982年広島大学歯学部歯学科卒業。同年京都大学大学院博士課程入学。1984年トロント大学医学部研究員、1989年テネシー大学医学部助教授、1991年京都大学医学部助手講師、同大学助手、同大学講師を経て、1998年4月より現職。専門はシステム神経科学。特に大脳皮質－大脳基底核連関。現在は霊長類脳への遺伝子導入に関心をもつ。1994年日本解剖学会奨励賞受賞。

## ヒト疾患モデルマーマーモセット作出に向けた 基礎研究

佐々木 えりか

財団法人実験動物中央研究所

マウスでは様々な発生工学的手法が確立し、現在までにトランスジェニック動物、標的遺伝子のノックアウト／ノックイン動物など多くの遺伝子改変動物が作出され、ヒト疾患のモデル動物として、疾患の発症メカニズムの解明、治療法の開発などに貢献している。しかしながら、マウスとヒトの間には生理的・機能的・形態的な違いが多くあり、げっ歯類を用いた動物実験だけでは、新規治療法の開発においてその治療効果・安全性を予測するには不十分であり、よりヒトに近いヒト疾患実験動物が必要である。特に精神・神経病の研究分野においては、よりヒトに近い動物種による疾患モデルの作出が望まれている。

霊長類の実験動物は数種類あるが、中でもコモンマーマーモセットは、繁殖力が高いこと、小型で扱い易いこと、性成熟が早いことなどから、遺伝子改変による疾患モデル動物作出に最も適していると考えられる。マーマーモセットを用いた遺伝子改変動物を作製するためには、その基礎となる採卵、体外受精、胚培養、遺伝子改変法などの様々な発生工学研究が重要となる。マーマーモセットでこれらの発生工学的技術を確認する場合、特に倫理的・経済的な観点から、生体より試料を採取できること、なるべく非侵襲的であることが望まれ、また小型であるため、独自の手法の工夫が必要となっている。

我々が現在までに取り組んできた遺伝子改変マーマーモセット作出に向けたマーマーモセットの発生工学研究の取り組みについて紹介する。

●ささき えりか

財団法人実験動物中央研究所マーマーモセット研究部応用発生生物研究室 室長

1989年筑波大学卒業。1995年同大学大学院博士課程修了（農学博士）。同年新技術事業団特別研究員、1996年ゲルフ大学（カナダ）博士研究員、2001年1月東京大学医科学研究所リサーチアソシエイト、2002年九州大学生体防御医学研究所リサーチアソシエイト（勤務先は東京大学医科学研究所）、2003年先端医療振興財団主任研究員、（財）実験動物中央研究所バイオメディカル研究部霊長類研究室研究員、2004年慶應義塾大学医学部助手（兼任）を経て、2007年より現職。同年5月より慶應義塾大学ヒト代謝システム生物学研究センター特別研究准教授（兼任）。専門は繁殖学および発生工学。現在は有用動物および希少動物の発生工学技術を用いた個体復元に関心をもつ。

## 脳科学のためのコモンマーモセットを用いたMR画像解析

岡野 栄之  
慶應義塾大学医学部

我々は、霊長類コモンマーモセットを用いた中枢神経系のMR画像解析を行っている。すでに我々は、マーモセットMR脳アトラスを2008年に発刊したが、今回はdiffusion tensor tractography (DTT) とq-space imaging (QSI) に注目し、マーモセットの脊髄損傷に対するこれらの撮像法の有用性を検討してきた。

DTTによりサル脊髄半切損傷における軸索の切断部の明瞭な描出、さらには圧挫損傷においても損傷部をよけて白質の辺縁を走行する軸索の描出に成功し、これら描出された神経線維数と運動機能の回復に相関があることを明らかにした。本結果より、DTTは脊髄損傷の程度や損傷を免れた軸索の変化を表しており、ヒト脊髄損傷に対してもDTTが有力な評価方法になりうる可能性が示唆された。QSI法は、水分子の拡散変異分布から制限構造のサイズを $\mu\text{m}$ 単位で推定することが可能であり、この情報を可視化したdisplacement mapは顕微鏡的MRIといえる。マーモセット脊髄損傷モデルの測定により、QSIは灰白質の破壊や空洞形成、脱髄を鋭敏に捉えていた。われわれ独自のMyelin enhanced mapは、髄鞘染色を正確に反映していた。これらの結果から、従来組織学的に評価せざるをえなかった脊髄の組織変化を非侵襲的に知ることが可能となった。

### ●おかの ひでゆき

慶應義塾大学医学部生理学教室 教授 医学博士

1983年慶應義塾大学医学部卒業。

慶應義塾大学医学部生理学教室助手、大阪大学蛋白質研究所助手、米国ジョンズホプキンス大学医学部研究員、東京大学医科学研究所助手、筑波大学基礎医学系教授、大阪大学医学部神経解剖学教授を経て、2001年より現職。2007年10月より慶應義塾大学大学院医学研究科委員長。

専門は神経発生の分子生物学的研究・神経幹細胞の基礎生物学と中枢神経系の再生医学。(最近ではコモンマーモセットの発生工学とイメージング技術に興味を持つ)

1988年三四会賞、1995年加藤淑裕賞、1998年北里賞、2001年塚原伸晃賞、2004年東京テクノフォーラム21・ゴールドメダル賞、日本医師会医学賞、イタリアCatania大学Distinguished Scientists Award、2006年「幹細胞システムに基づく中枢神経系の発生・再生研究」文部科学大臣表彰(科学技術賞)、2007年STEM CELLS Lead Reviewer Award受賞。2008年井上學術賞(井上科学振興財団)。