Final Lecture by Professor Shoogo Ueno at the Main Auditorium, Faculty of Medicine, the University of Tokyo, Tokyo, Japan, at 14:00-16:00, March 9, 2006

Studies on Magnetism for 40 Years

Wonder of Biomagnetism, and Human Brain Stimulation and Imaging

Shoogo Ueno

Professor, the University of Tokyo

- 1. My first teacher who was like Miss Sullivan
- 2. Visit to the medical campus
- 3. EEG topography
- 4. Magnetic nerve stimulation
- 5. Research in Sweden
- 6. TMS with a figure-eight coil
- 7. MEG measurements by SQUID
- 8. Combustion control by magnetic curtain
- 9. Culture shock
- 10. Parting water by magnetic fields: The Moses effect
- 11. Embryonic development under magnetic fields
- 12. The University of Tokyo: Fusion of different fields
- 13. Lectures for graduate students in Electronic Eng.
- 14. The deep forest of biomagnetics
- 15. A big grant: Specially Promoted Research
- 16. Improvement of hippocampus function by rTMS
- 17. Imaging of brain electrical properties by MRI
- 18. Pulsed magnetic fields for cancer therapy
- 19. Bone lengthening by magnetic fields
- 20. Observation of the amazing human brain
- 21. Harvest time and seeding for tomorrow
- 22. Thousand thanks

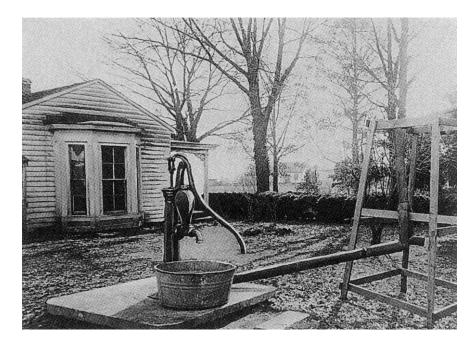
The unfolding of your words gives light : it gives understandings to the simple.

The Psalms 119 : 130









Well in Tuscumbia

Everything has its name.



Professor Koosuke Harada

Hysteresis Model of Partial Flux Reversal in Ferrite Cores

SHOOGO UENO AND KOOSUKE HARADA, SENIOR MEMBER, IEEE

Abstract-A hysteresis model of partial flux reversal in a ferrite core under voltage pulsed excitations is proposed in order to explain the relation between partial flux sets and the memory characteristics of magnetic analog memories. The model is based on the assumption that the slope of the irreversible region declines in proportion to the reversed flux level. The recurrence equations for flux levels derived from the model explain the hysteresis phenomenon in the meomory characteristics.

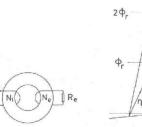
INTRODUCTION

CINCE THE introduction of the transfluxor [1], 3 square-loop ferrite cores have been studied for accurate analog memories from a standpoint of partial flux switching [2]-[8]. However, the relation between the magnetizing characteristic of the core and the memory characteristic has not been successfully explained. When the polarity of the write-in pulses is reversed at a memorized level, a hysteresis effect appears in the memory characteristics, which depends upon the history of the excitation required to achieve the reversed level.

A new hysteresis model discussed here explains this history effect. The partial flux state in the core due to a train of voltage pulses is described by recurrence equations of flux levels. These results were confirmed by experiments on a Mn-Cu ferrite core.

Hysteresis Model

The basic circuit to be discussed here is shown in Fig. 1. We consider the partial flux switching due to a train of voltage pulses. That is, the input resistance R_1 is so small that the waveform of the MMF in the core does not rise



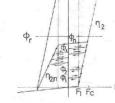


Fig. 1. Basic circuit.

Fig. 2. Hysteresis model.

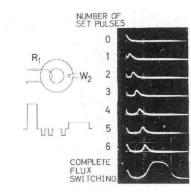
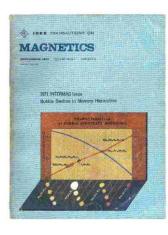


Fig. 3. Pulse responses to verify model. Core is Mn-Cu ferrite with 10-mm OD, 4-mm ID, 1-mm hole D; horizontal scale is 2 µs/div; vertical scale is 1 V/div.

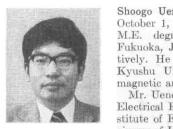
pulses with 10-V height and 1-µs width were applied through the primary winding with resistance $R_1 = 50 \ \Omega$. Finally, induced voltage was observed [11] in the winding



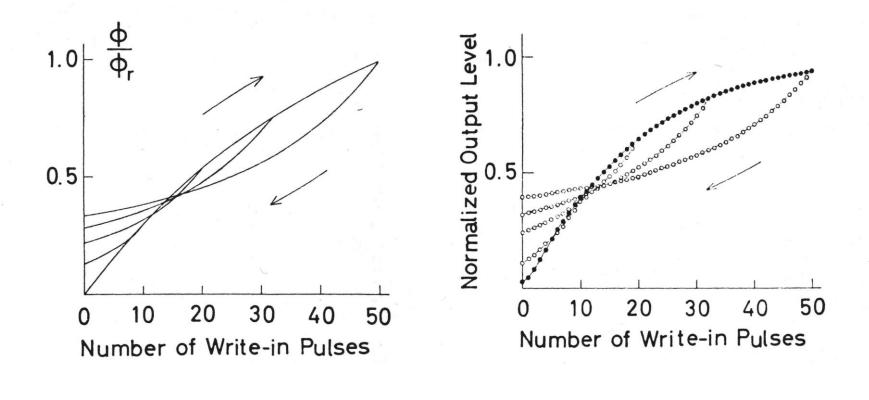




Since 1959 ment of E where he is active in the cluding mag



Mr. Uene Electrical **H** stitute of E gineers of Ja



Calculated results

Experimental results

S. Ueno and K. Harada: IEEE Trans. Magn. (1971)

Visit to the Medical Campus

S. Ueno	"I want to study brain at medical campus. Lecture by Dr. Motohiro Kato was so attractive."
Prof Harada	"Which Department Dr. Kato works at?"
S. Ueno	"Dr. Kato works at Department of Neurology"
Prof Harada	"Chairman of the Department of Neurology is Prof Yoshigoro Kuroiwa?"
	Searching the telephone number, Prof Harada calls Prof Kuroiwa.
Prof Harada	"Dr. Ueno in my lab wants to study brain research at your Department. Could you accept him?"
Prof Kuroiwa	"OK. Come to my office on 4 th January."

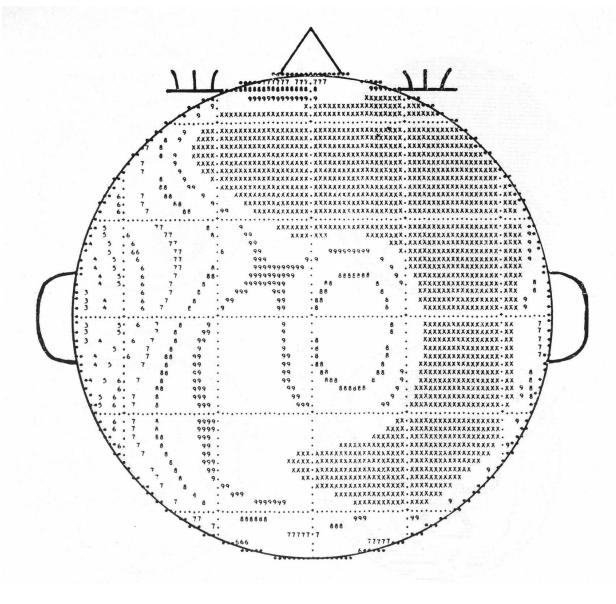
Direction of my life was decided in 3 min.



Professor Yoshigoro Kuroiwa

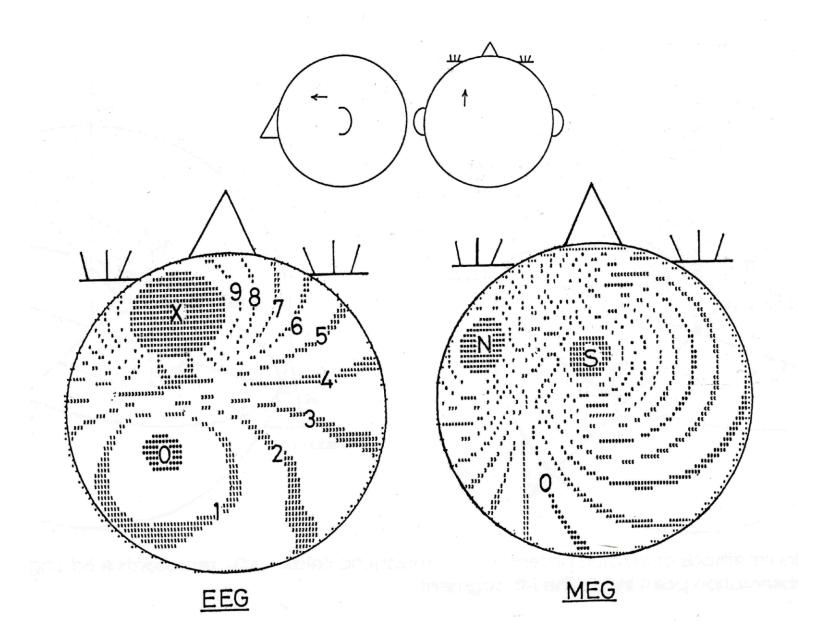


Professor Shigeaki Matsuoka



EEG topography

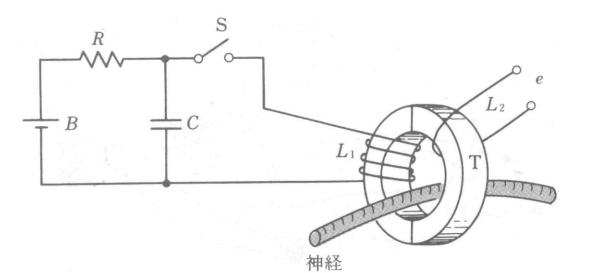
S. Ueno, S. Matsuoka, T. Mizoguchi M. Nagashima, and C. L. Cheng (1975)



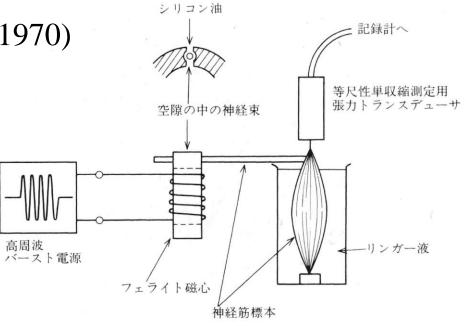
S. Ueno and Y. Fukui (1978)



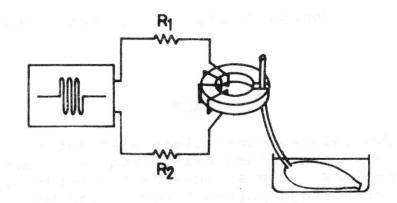
Professor Yutaka Oomura



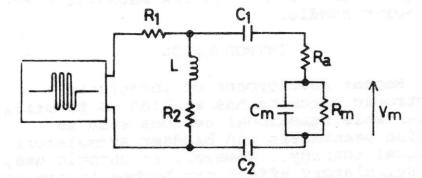
J.A. Maass and M.M. Asa (1970)

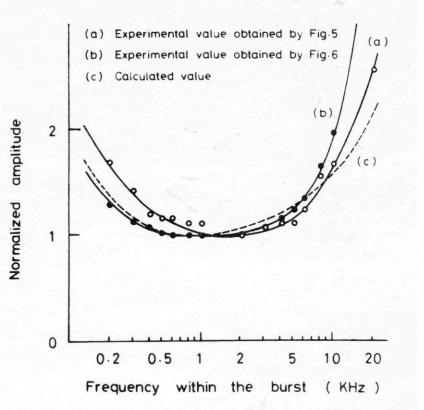


P.A. Oberg (1973)



Experimental set up





Equevalent circuit

Frequency characteristics

S. Ueno, S. Matsumoto, K. Harada, and Y. Oomura: IEEE Trans. Magn. (1978)

IFMBE Conference at Ottawa, Canada, August 1976

Discussion at the Conference

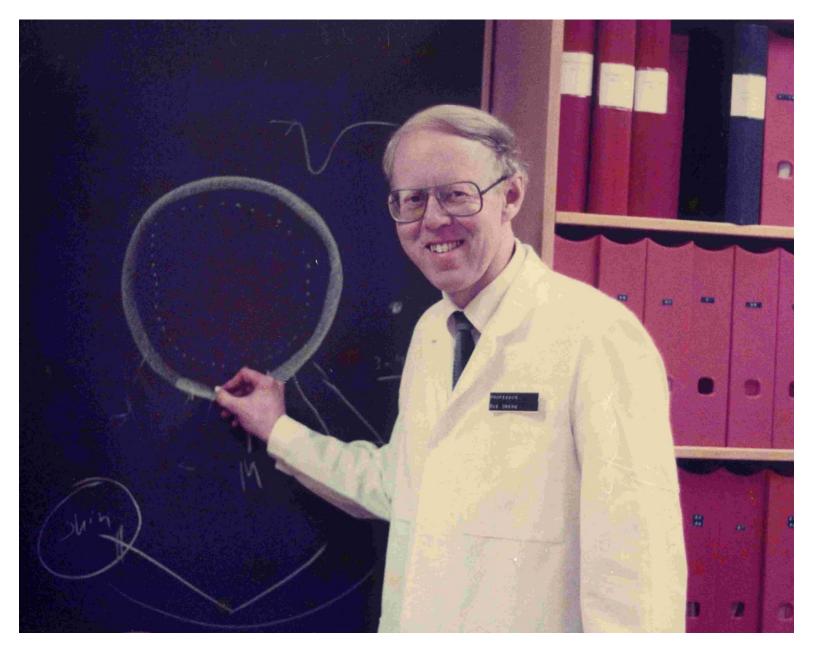
Myself: "Your method of nerve stimulation is not magnetic stimulation but instead might be capacitive stimulation, I think."

Ake Oberg: "Why don't you come to my lab to work together?" Application for Japan-Sweden Foundation Interview at Swedish Embassy in Tokyo

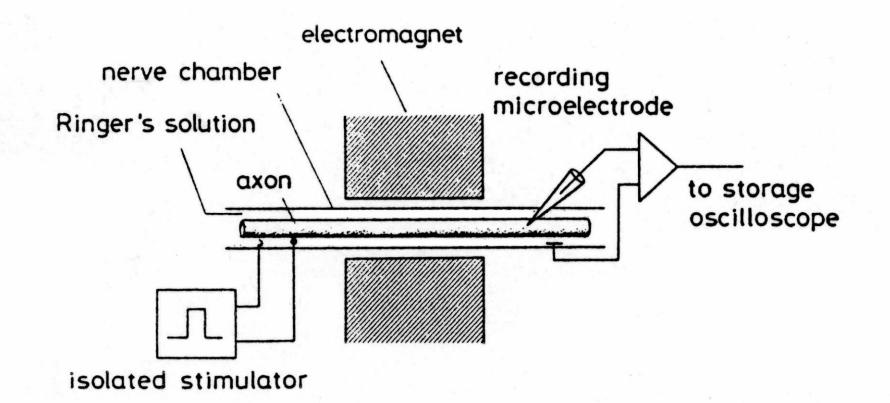
- 1 Year Not succeeded
- 2 Year Succeeded (Prof Kazuhiko Atsumi, Examiner)

I studied magnetic nerve stimulation using lobster giant axons at Linkoping University, Linkoping, Sweden, for 20 months from August 1979 to March 1981.

Former guest researchers supported by Japan-Sweden Foundation Dr. Kenji Ikeda, Dr. Nozomu Hoshimiya, and Dr. Akira Kamiya



Professor Ake Oberg



Experimental set up to measure action potentials intracellularly from lobster giant axon during magnetic field exposures

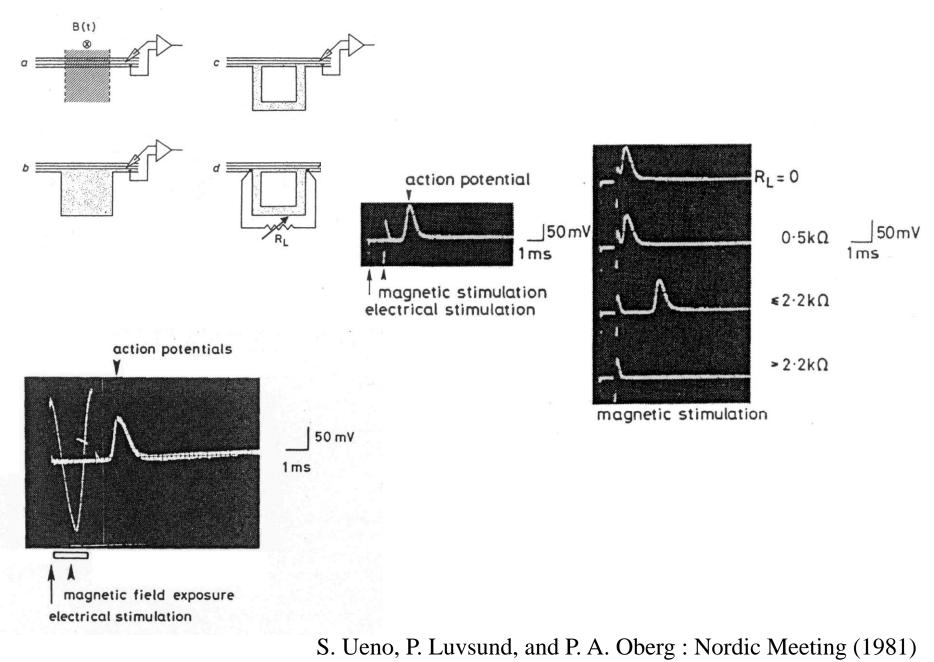




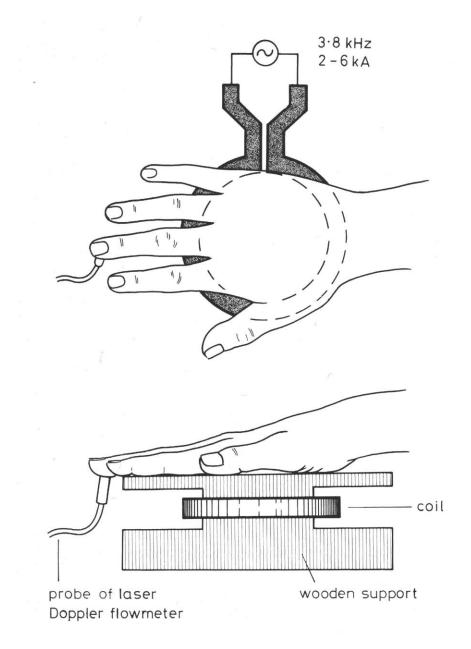




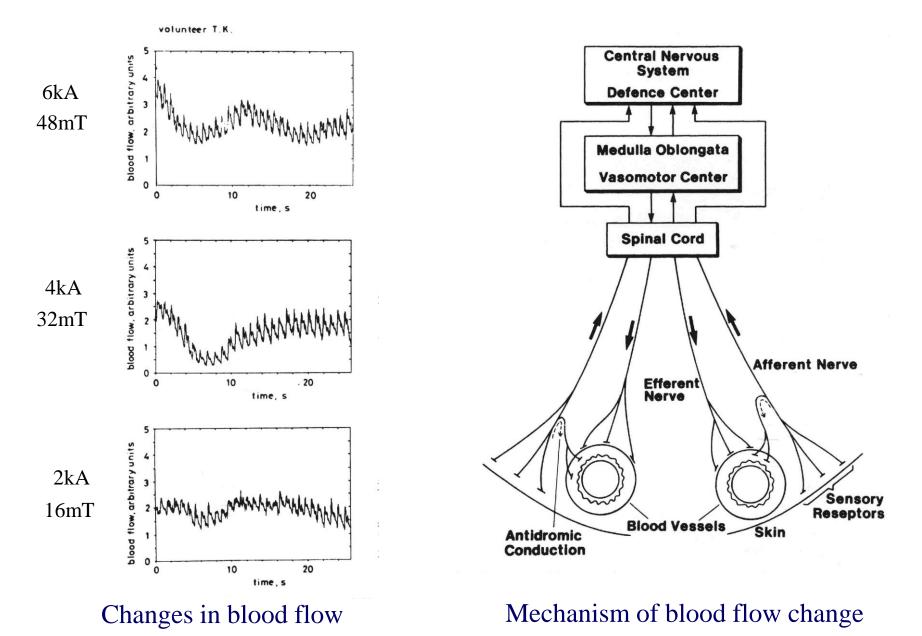
Linkoping, Sweden, January 1980



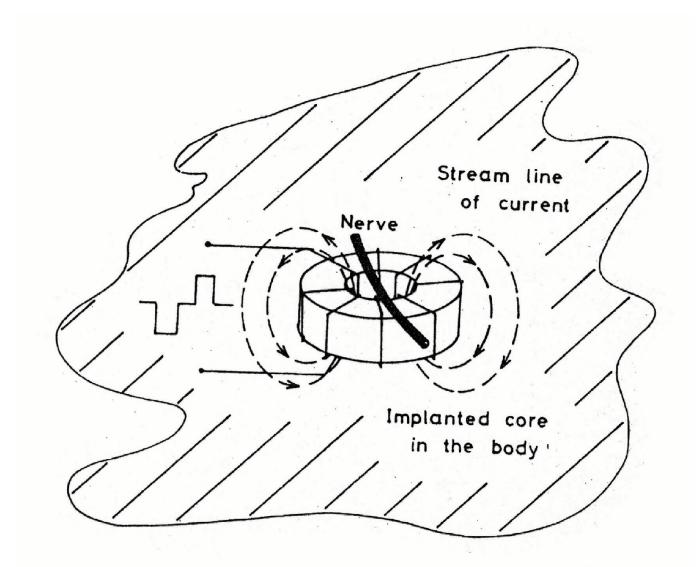
S. Ueno, P. Luvsund, and P. A. Oberg : Med. & Biol. Eng. & Comput. (1986)



Hand is positioned on an induction coil



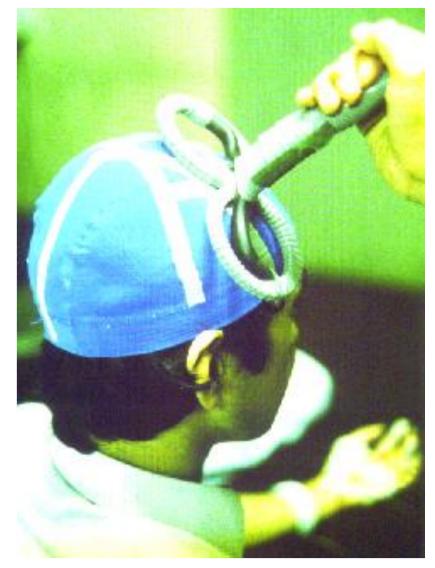
S. Ueno, P. Luvsund, and P. A. Oberg : Nordic Meeting (1981) S. Ueno, P. Luvsund, and P. A. Oberg: Med. & Biol. Eng. & Comput. (1986)

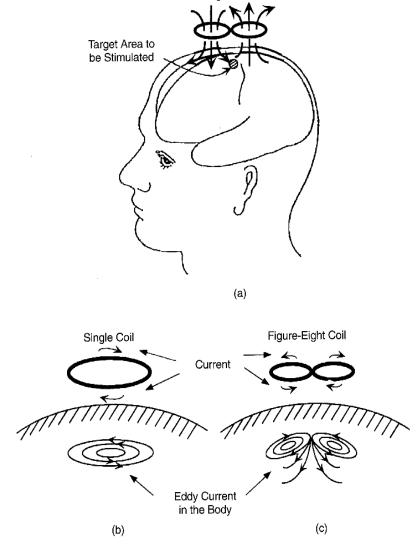


Magnetic nerve stimulation without interlikage between nerve and magnetic flux

S. Ueno, K. Harada, C. Ji, and Y. Oomura : IEEE Trans. Magn. (1984)

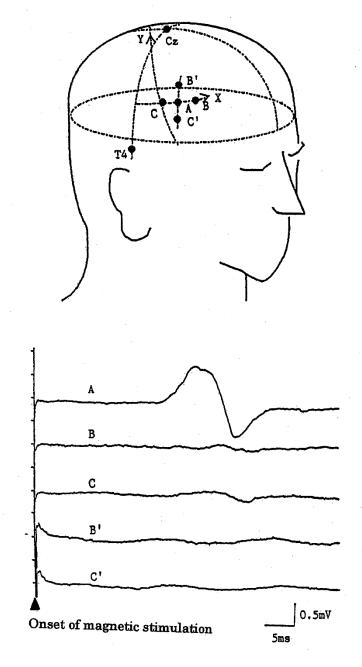
Transcranial Magnetic Stimulation (TMS) with a Figure-Eight Coil





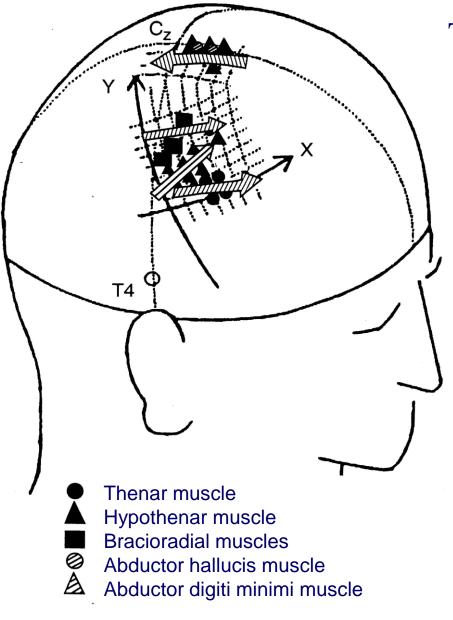
Magnetic Flux

Motor evoked potentials (MEPs) respondedS. Ueno (1987)to magnetic brain stimulation are measured.S. Ueno, T. Tashiro, and K. Harada, J. Appl. Phys. (1988)



Motor cortex is transcranially stimulated within a 5 mm resolution

S. Ueno, T. Matsuda, and M. Fujiki: Biomag. New York (1989) S. Ueno, T. Matsuda, and M. Fujiki: IEEE Trans. Magn. (1990)



TMS controls finger movements

The arrows show optimal directions of induced currents for brain stimulation.

Comment from the floor

"Play Chopin's piano !!!"

IEEE International Magnetics Conference (Washington, D.C. March 1989)

Ueno S, Matsuda T, and Fujiki M: IEEE Trans. Magn., MAG-26 (1990)

Transcranial Magnetic Stimulation (TMS): From Measurements to Treatments

- Functional brain mapping
- Creation of virtual brain lesions
- Neuronal plasticity and modulation of neuronal networks
- Modulation of neuro-transmitting processes
- Parkinson's disease
- Depression, epilepsy, Alzheimer's disease, and etc.
- Motivation and creativity
- Deep brain stimulation
- Safety aspects of TMS and repetitive TMS (rTMS)

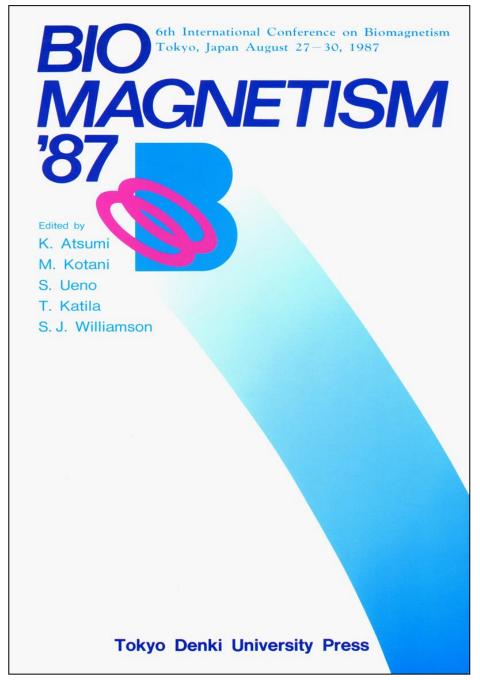
Activities for 24 hours at Ueno's laboratory

Hiroshi Esaki Keiji Iramina Tsuruo Matsuda Osamu Hiwaki Masakazu Iwasaka Hideki Yoshida RyouichiTsuda Masakuni Iwahashi Takao Suda Seiya Uchida Minoru Fujiki (Neurosurgery) Takashi Yoshiura (Radiology)

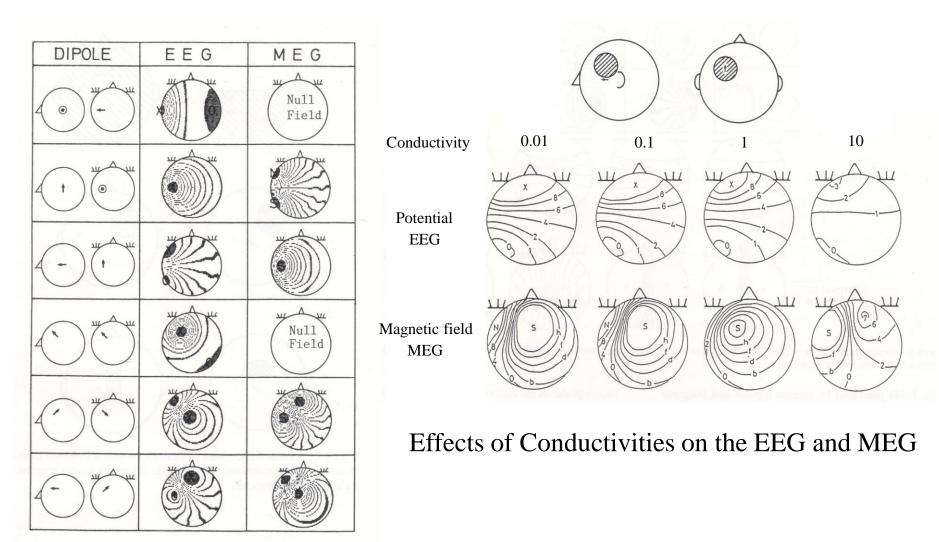
Ueno Convenient Store Ueno Zoo (Smelling of animals)

Graduate and Undergraduate Students

Thanks to Professor Yutaka Omura (Neurophysiology) Professor Yoshigoro Kuroiwa (Neurology) Professor Katsutoshi Kitamura (Neurosurgery) Professor Shigeaki Matsuoka (Neurosurgery) Professor Motohiro Kato (Clinical Neurophysiology) Professor Hitoshi Fukui (Neurosurgery) Professor Hitoshi Fukui (Neurosurgery) Professor Koji Masuda (Radiology) Professor Hitoo Nakano (Gynecology) Professor Yoshiaki Nose (Medical Informatics)



6th International Conference on Biomagnetism Tokyo, Japan August 27-30,1987



Forward Problems in EEG and MEG

S. Ueno, and Y. Fukui (1978)

S. Ueno, H. Wakisako, and S. Matsuoka (1983)

S. Ueno, K. Iramina, and K. Harada (1987)

K. Iramina, and S. Ueno (1987)

S. Ueno, K. Iramina, (1990)

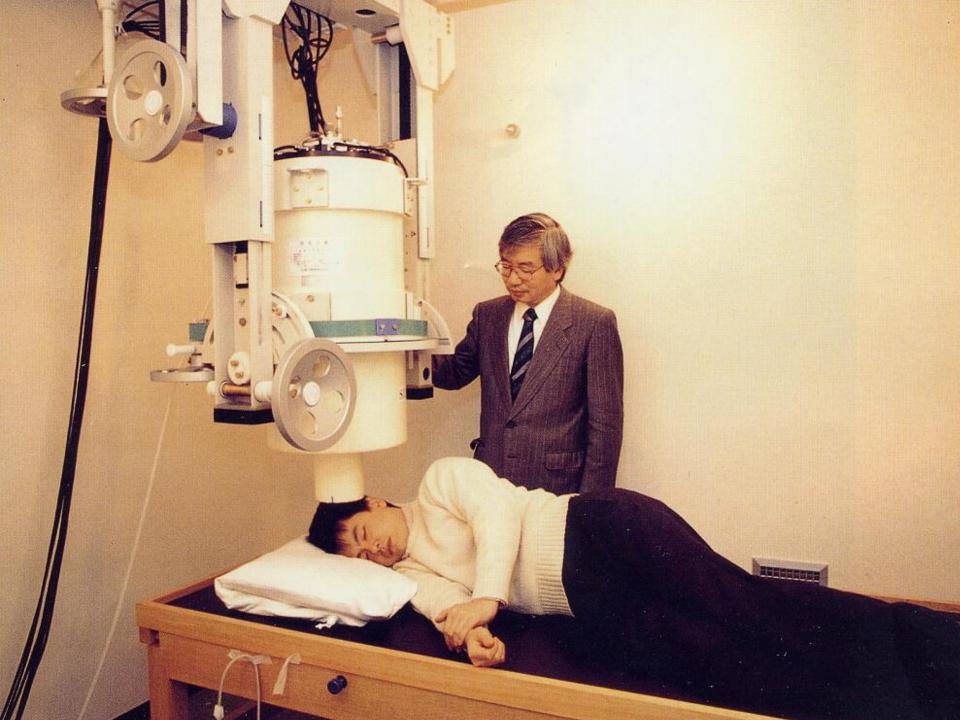
Fabrication of MEG system

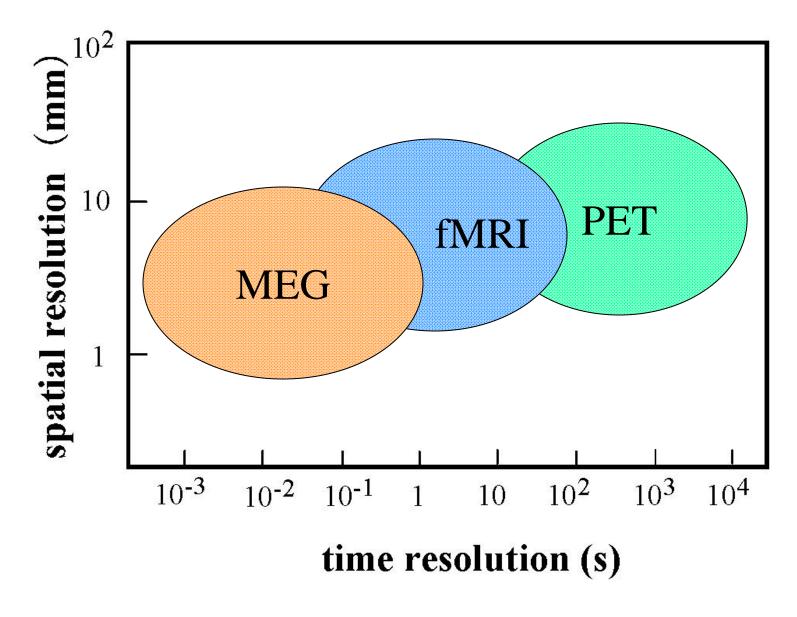
Project on Fabrication of MEG System for Functional Brain Research

Project Research (A) (1) granted by Ministry of Education, Culture, Sports, Science and Technology (MEXT), Japan 1991~1993 fiscal years Research Number: 03505002

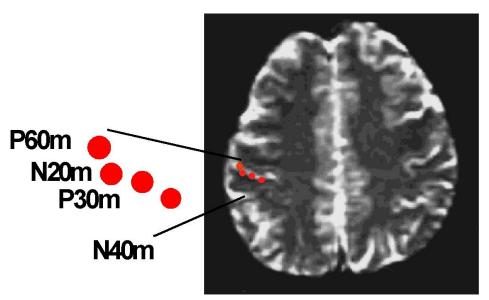
Dr. Naoko Kasai, National Institute of Advanced Industrial Science and Technology (AIST), Japan
Dr. Kazuo Chinone, Seiko Instruments Technology Ltd.
Dr. Keita Yamazaki, Takenaka Corporation Ltd.
and other coworkers contributed to the project.

We developed a useful and reliable MEG system for brain research.

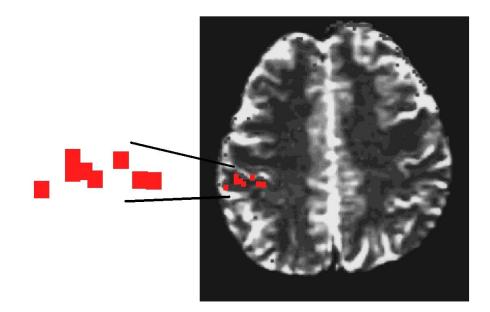




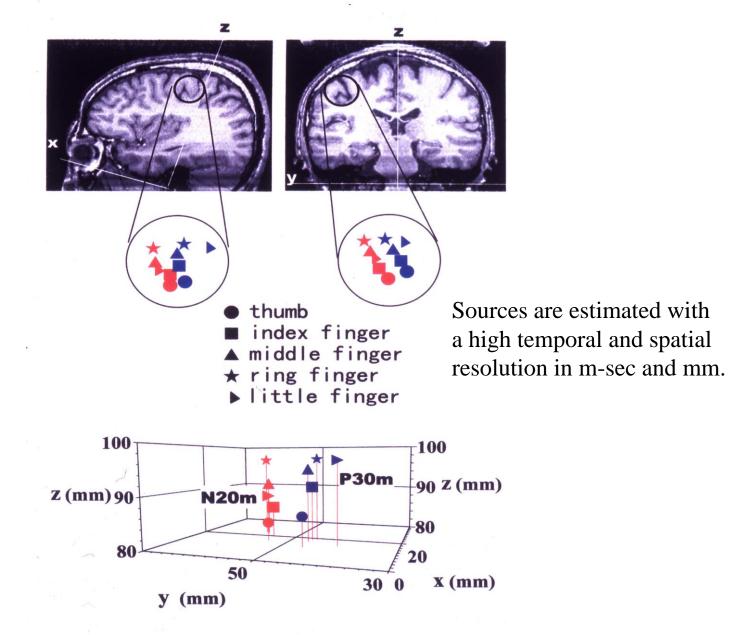
Spatial and Temporal Resolution for Brain Imaging



(a) MEG

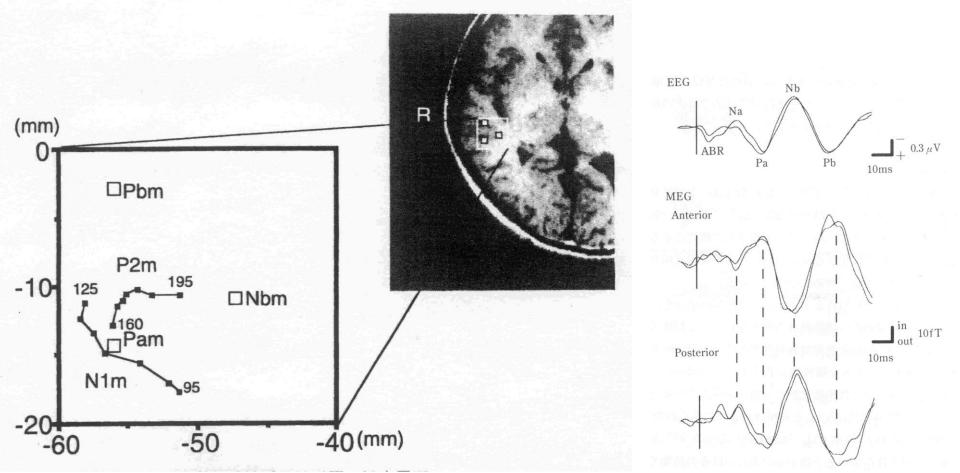


(b) fMRI



Sources of activation in the somatosensory area responded to electrical stimulation of each finger.

Auditory evoked magnetic fields and source estimation



Source estimation of long latency and middle latency auditory evoked magnetic fields. Long latency evoked fields N1m and P2m show travelling sources in ms. The middle latency evoked fields Pam, Nbm, and Pbm show sources \Box in the auditory cortex.

T. Yoshiura, S. Ueno, K. Iramina, and K. Masuda: Neuroscience Letters (1994)

Effects of Static Magnetic Fields ?

Oxygen and Combustion Dissolved Oxygen under Magnetic Fields Combustion and Magnetic Curtain Chemical Reaction and Radicals Cystotome C in Hem Proteins

Focused on paramagnetic properties

Effects of magnetic fields on combustion of alcohol catalyzed by platinum catalysis

Professor Taku Matsuo "Use well known and well specified fuel."

Slowly processing combustion of alcohol catalyzed by platinum catalysis is carried out under magnetic fields, changing the number of carbons (C1~C4).

Combustion velocity is reduced by magnetic fields.

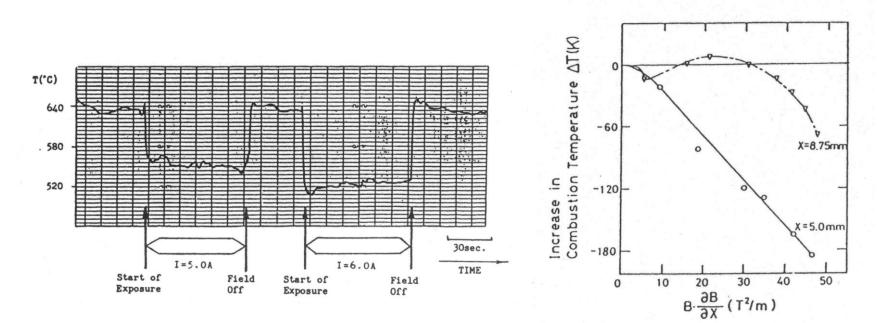
Methanol	(CH ₃ OH)	-5%	0.9T
Ethanol	(C_2H_5OH)	-3%	0.6T
Propanol	(C_3H_7OH)	-18%	0.6T
Normal-butanol	(C_4H_9OH)	-80%	0.7T
Iso-butanol	(C_4H_9OH)	-19%	0.5T

Successive experiments have been done over nights for two weeks. Hiroshi Esaki worked heard for this experiment.

S. Ueno, H. Esaki, and K. Harada; IEEE Trans. Magn. (1985)

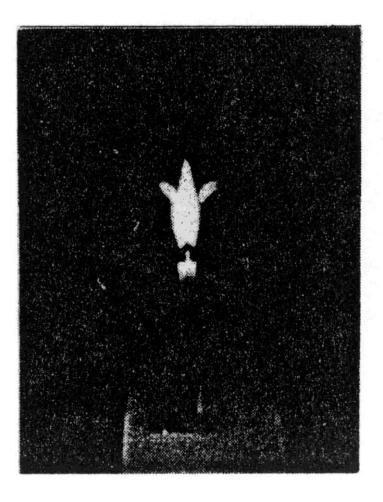
Unexpected Results

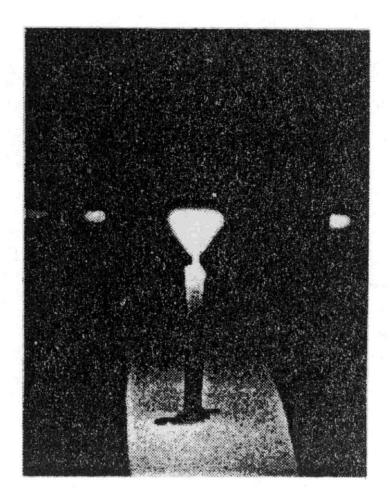
We expected that combustion temperature might increase in rich oxygen atmosphere. Adversely, combustion temperature decreased during magnetic field exposures.



Changes in combustion temperature by magnetic field exposures

Combustion temperature *vs* magnetic force.



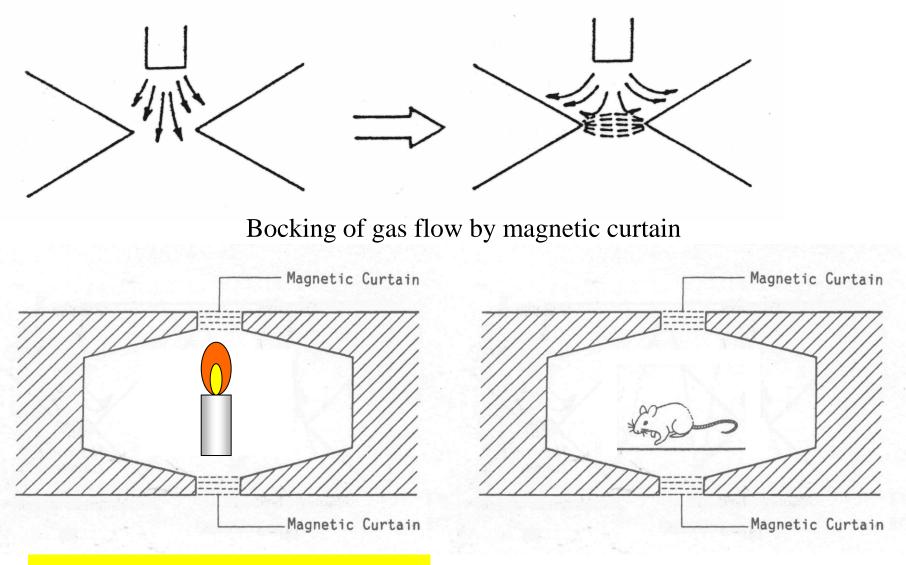


Before magnetic field exposure

During magnetic field exposure



Wonder of magnetism: Flame dance and duet with magnetic fields from Nishinippon Shinbun (Newspaper in Kyushu) issued on January 26, 1988

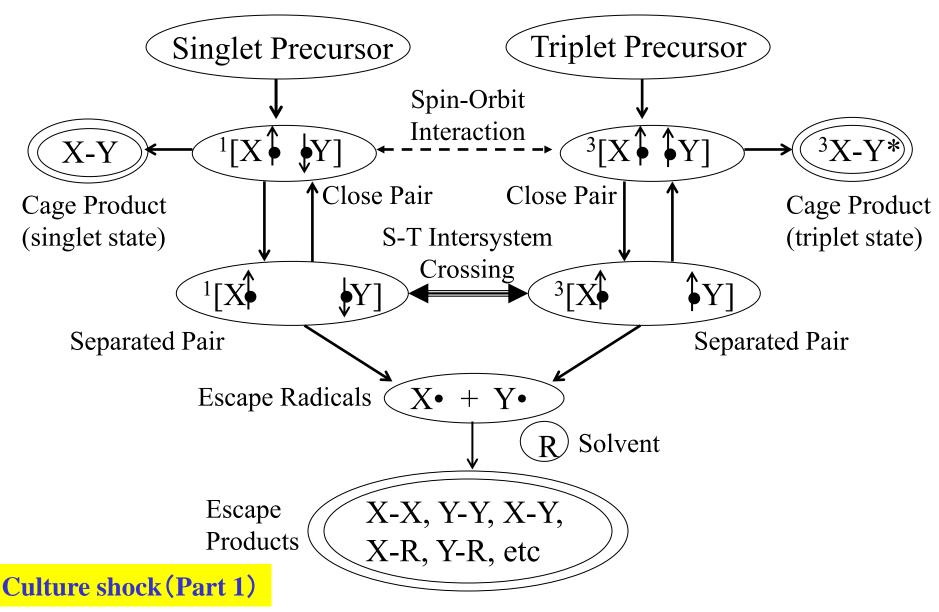


Candle flame is quenched by magnetic curtain!

S. Ueno, et al. (1986, 1987) S. Ueno: J. Appl. Phys. (1989)

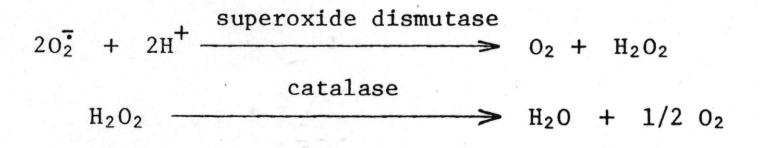


Professor Saburo Nagakura, Founder of spin chemistry



Magnetic field effects of chemical reaction via radical pairs

Reaction scheme of radical pairs generated from singlet and triplet precursors. (Modified from Hisaharu Hayashi (2004))



Possible effects of magnetic fields on biochemical reactions catalyzed by xanthine oxidase and by catalase are examined.

Dr. Michio Nakamura worked for us, teaching us biochemical experiments.

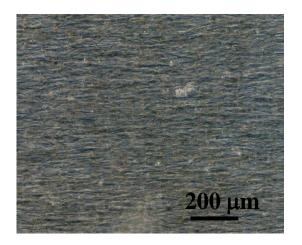
(1985 - 1986)

Important roll of Diamagnetism

• J. Torbet et al. Nature (1981) Magnetic orientation of fibrin

When polymerization process from fibrinogen to fibrin is exposed to strong magnetic fields, fibrin fibers orient in parallel to magnetic fields.

We learned blood coagulation and resolution processes by Prof Hiroko Tsuda.

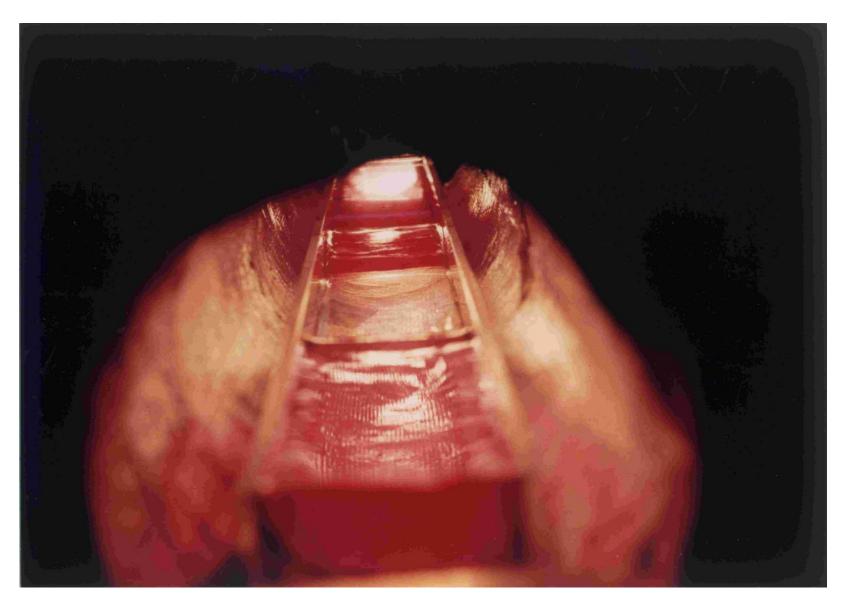






Parting of water by magnetic fields

S. Ueno and M. Iwasaka (1993, 1994)

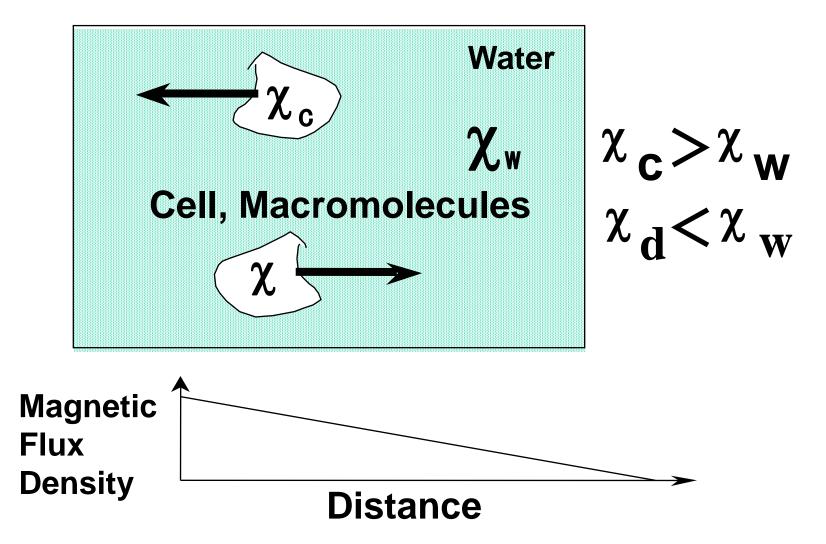


Dried bottom appeared in water chamber. Magnetic force = 0.3 N(1/3 of the earth gravity)



Moses parted the Red Sea.

Magnetic Cell Manipulation



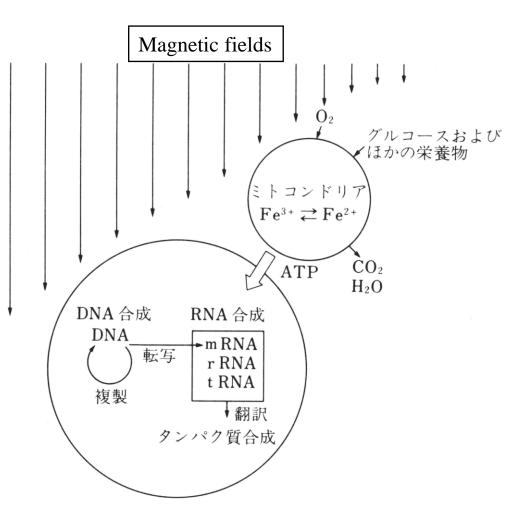


Professor Koichiro Shiokawa

- 1.2 T No effects
- 4.0 T No effects
- 6.34 T No effects
- 8.0 T No effects
- 14.0 T No effects

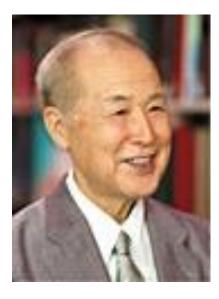
Developmental Biology and Magnetic Fields

Early development of Xenopus laevis





The University of Tokyo: Fusion of different fields Prof Shoogo Ueno started his work at the University of Tokyo on 1st April 1994.



Your Own Research: 60 % For the Nation: 40 % ?

Prof Masao Saito "This chair is not for an ordinary professor's position, but for humble professor's position to serve people and nation. You should look at not only US and Europe but also other countries, in particular, Asian countries."

Professor Masao Saito

Biological and biomedical engineering, Circuit theory, Biomaterials, etc. President, International Federation for Medical and Biological Engineering President, Japanese Society for Medical and Biological Engineering

Encounter and Fusion of Different Fields

Research activities in Graduate School of Medicine, the University of Tokyo, are leading the world.

Re-modelling of blood endothelial cells by shear stresses Artificial heart in living goat; world record in survival days Leg lengthening; extension of leg 1 mm a day. Colon cancer and surgical oncology Radiology, diagnosis and treatments, MRI, PET Auditory evoked brainstem response, cochlear implant Tolerance against cerebral ischemia, apoptosis Treatments of incontinence, prostate cancer, etc. Motor proteins and molecular cell biology **Cell informatics** Cell cycles Memory and cognition Plasticity in synapses Immunology

Supported by many people at the Faculty of Medicine

Institute of Medical Electronics Prof Akira Kamiya, Director of the Institute Prof Ko Imachi Prof Joji Ando

Coworkers and Graduate Students

Prof Takahide Kurokawa, Dean of the Faculty Prof Kozo Nakamura

Prof Tetsuichiro Muto, Director of the Hospital Prof Hirokazu Nagawa

Prof Kimitaka Kaga Prof Fumio Eto Prof Kazuki Kawabe Prof Tadaichi Kitamura Prof Kanjiro Masuda Prof Makoto Araie Prof Nobumasa Kato Dr. Shigeru Ichioka

MEG

Prof Akiyuki Ohkubo Prof Kazuhiko Nakahara Dr. Masato Yumoto Administration

Thanks to Stuffs in Administration office.

Graduate students Dr. Makoto Kobayashi

Dr. Giichiro Tsurita Dr. Hironori Yamaguchi Dr. Keisuke Hata

Dr. Takako Saotome Dr. Yutaka Maeno Dr. Hellen Ahamedo Dr. Tetsuyuki Fujishiro Dr. Keiichi Goto

Dr. Kiyoto Kasai

Lecture for Graduate Students at Department of Electronic Engineering, Graduate School of Engineering

Prof Hiroshi Harashima "Good morning. I introduce to you Prof Ueno who will give a lecture on Biological Engineering for you."



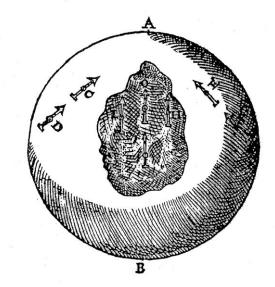
I started lecture on 11th April 1994.

Building No. 3, Faculty of Engineering

I luckily received the graduate students from Department of Electronic Engineering to work with them in the next years.



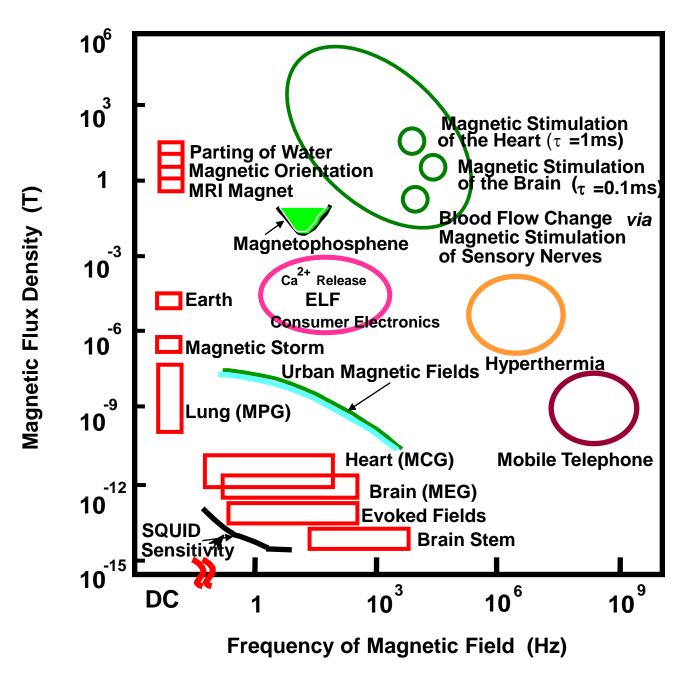
William Gilbert, Father of Magnetism "The Earth is itself a huge magnet."



De Magnete, William Gilbert (1600)

"Magnetic force is animate or imitates life; and in many things surpasses human life, while this is bound up in the organic body."

William Gilbert, 1600



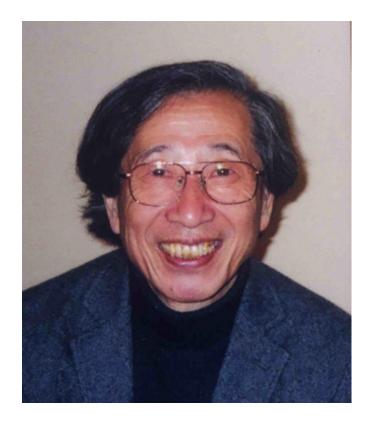
Specially Promoted Research granted by the Government

Study on Functional Brain Dynamics by Magnetic Brain Stimulation and Imaging Grant-in-Aid for Specially Promoted Research, Ministry of Education, Science,

Sports, Culture and Technology, Japan (No. 12002002)

1993 1994 1995 1996 1997 1998	Failed Failed Failed Passed at 1 step Failed at interview Passed at 1 step Failed at interview Failed
1999	Passed at 1 step Failed at interview
2000	Passed at 1 step Succeeded at interview, Promoted
2001	Promoted
2002	Promoted
2003	Promoted
2004	Promoted
2005	Promoted (until March 31, 2005)

Succeeded in getting a big grant after 7 trials !



Professor Shun-ichi Amari

Pioneer of information geometry and mathematical neuroscience Director, RIKEN Center for Brain Science Professor Emeritus, the University of Tokyo

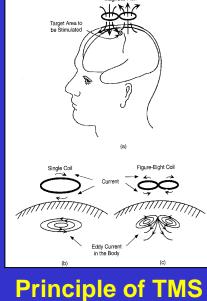
TMS and Brain Dynamics

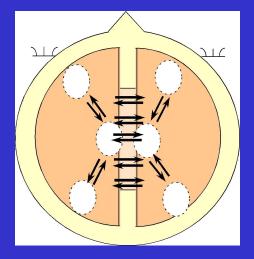


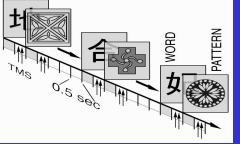


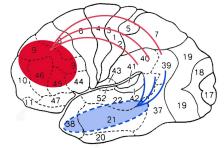
Brain Dynamics

TMS

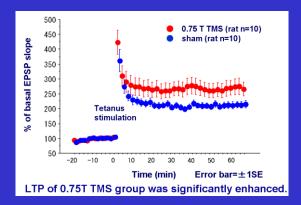








Working Memory Task

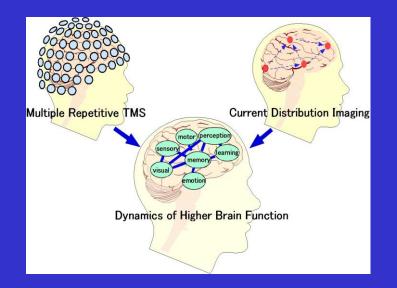


Long-Term Potentiation

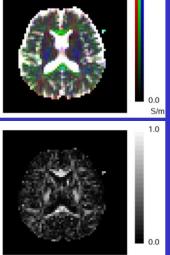
Therapeutic Application of TMS Control of Neuronal Plasticity Treatment of Depression

Neuronal Connectivity

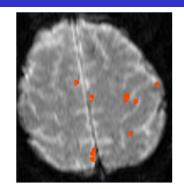
Biomagnetic Imaging and Brain Dynamics



(a) 0.14 (b) 0.7 0.00 λ_1 0.7 λ_2 0.00 λ_3 0.14 (d) 0.7 0.120.660.00 0.00 0.120.66 0.000.00 0.00 0.12 0.660.00 0.00 0.00 0.12 0.660.00 0



Study of Brain Dynamics by TMS, MRI, and EEG



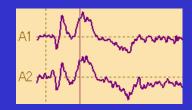
- States of the second se
- (a) fMRI

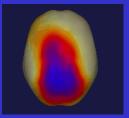
brain during middle finger and thumb tapping.

(b) current MRI

Conductivity Tensor MR Imaging







MEG and EEG

Current MR Imaging

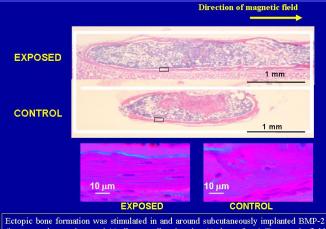
(a)fMRI and (b) current MRI mapping of the neuronal currents in the

Parting of Water and Cell Orientation by Magnetic Fields



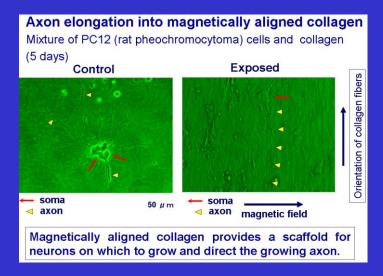
Parting of Water





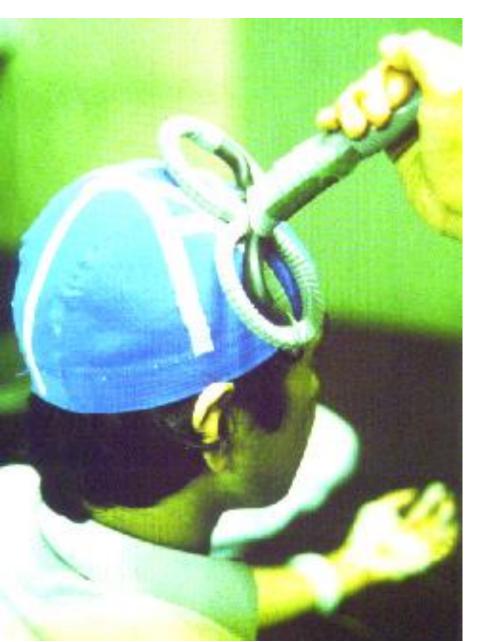
Ectopic bone formation was stimulated in and around subcutaneously implanted BMP-2 (bone morphogenetic protein)/collagen pellets in mice 21 days after 8 T magnetic field exposure for 60 h. The newly formed bone was extended parallel to the direction of the magnetic field.

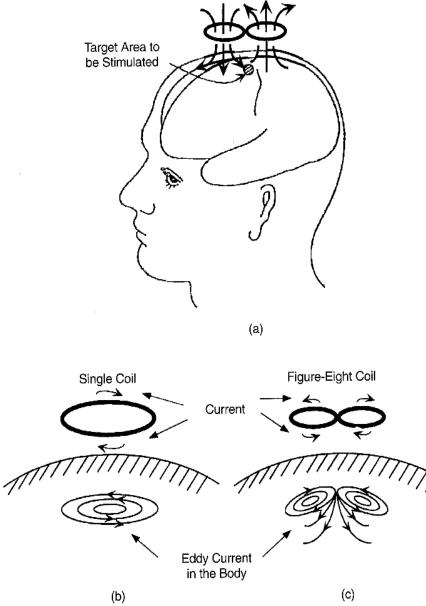
Bone Growth by Magnetic Field



Magnetic Orientation of Adherent Cells Axonal Growth by Magnetic Field

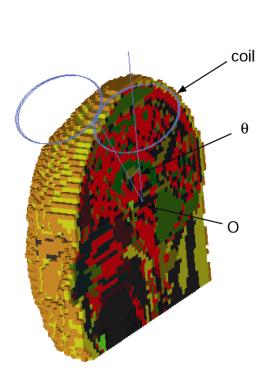
TMS(Transcranial Magnetic Stimulation)



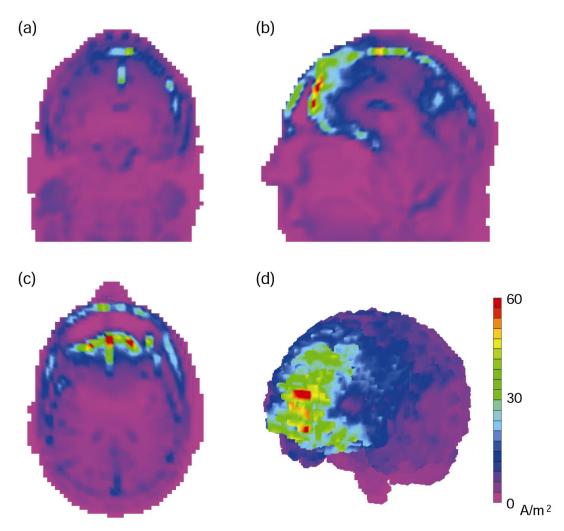


Magnetic Flux

Current Distributions in TMS



Numerical model of the human head



Current distributions in TMS represented in (a) coronal, (b) sagittal, and (c) transversal slices, and (d) the brain surface.

Medical Applications of Transcranial Magnetic Stimulation

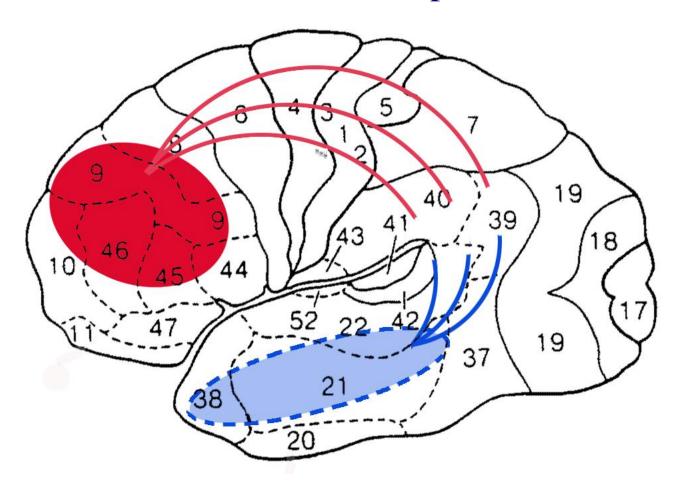
- 1. Estimation of localized brain function
- 2. Creating virtual lesions to disturb dynamic neuronal connectivities
- 3. Damage prevention and regeneration of neurons
- 4. Modulation of neuronal plasticity
- 5. Therapeutic and diagnostic applications for the treatment of CNS diseases and mental illnesses

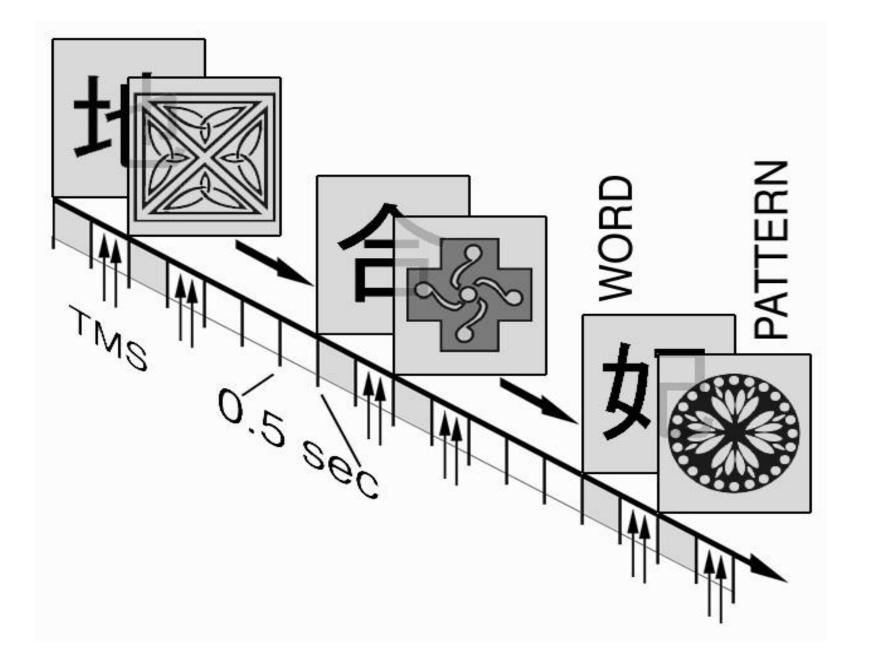
Effect of TMS on associative learning for visual patterns



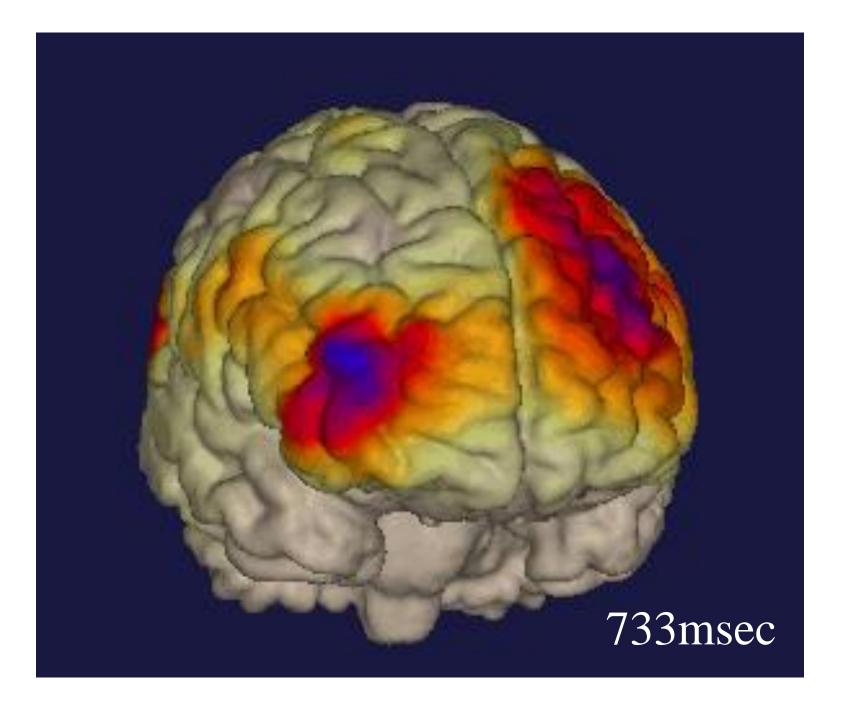
Working memory is dependent on prefrontal granular cortex.

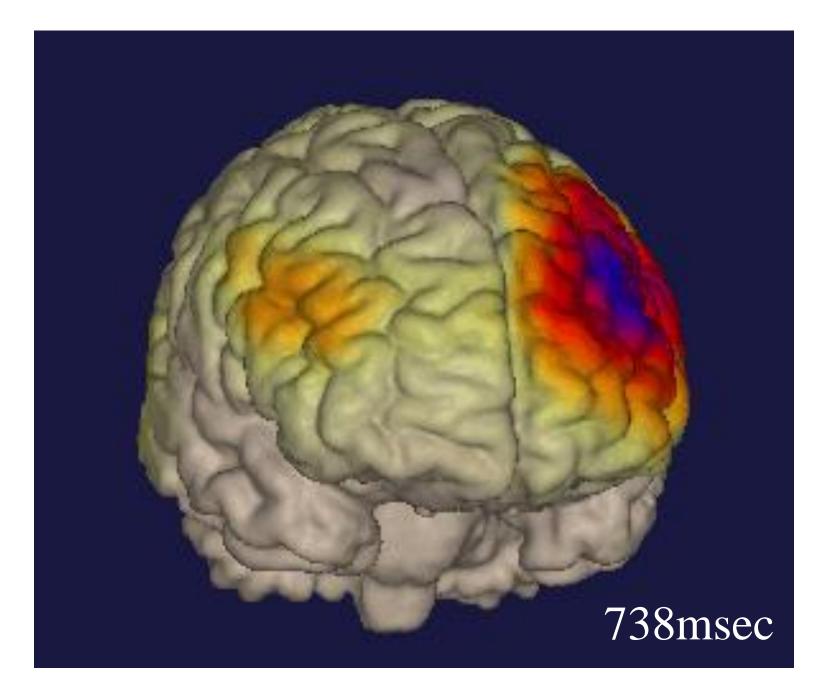
Associative memory is dependent on the hippocampus and temporal lobe.

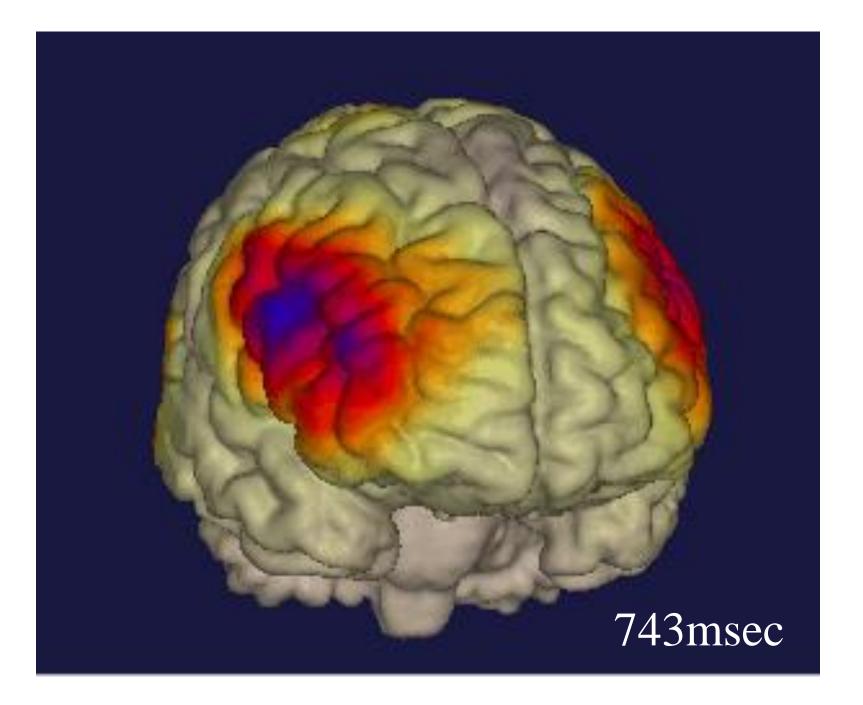


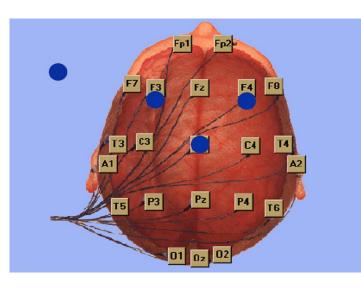


725~745msec









Brain function revealed by TMS

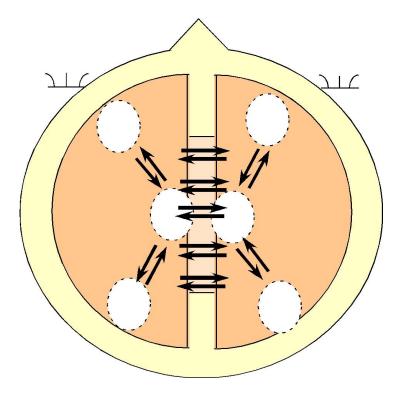
Percentage of Correct Responses by TMS Stimulation Site

70 60 50 40 30 20 10 0 Left Vertex Right Control DLF \star p < .05

Right dorsolateral prefrontal (DLF) cortex has an important roll in retrieval of information related to short-term and associative memory task.

C. M. Epstein, et al., S. Ueno: Neuroscience Letters (2002)

Intra- and Interhemispheric Connectivity

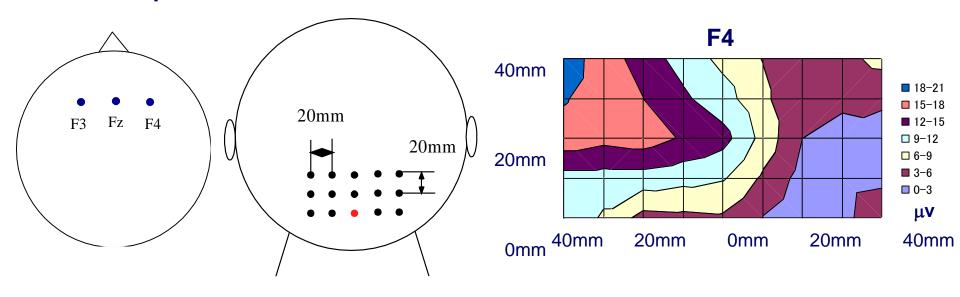


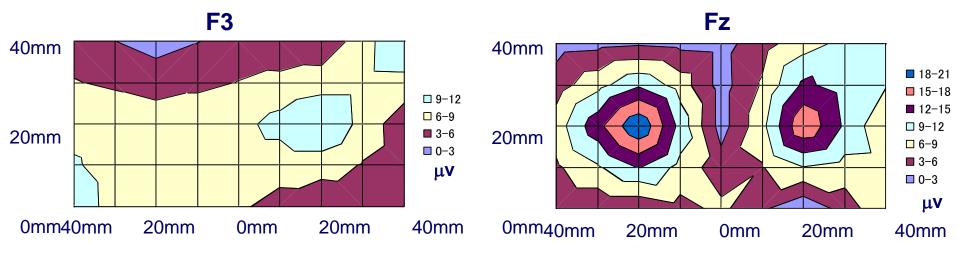
Interhemispheric connectivity

Commissural fibers

- corpus callosum
- anterior/posterior commissure
- hippocampal commissure

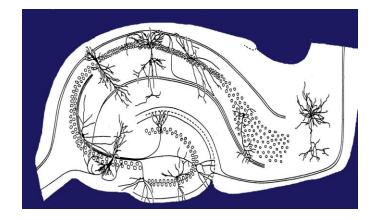
Topography of the amplitude of the 9 ms EEG component





Effect of pulsed magnetic fields on rat hippocampus

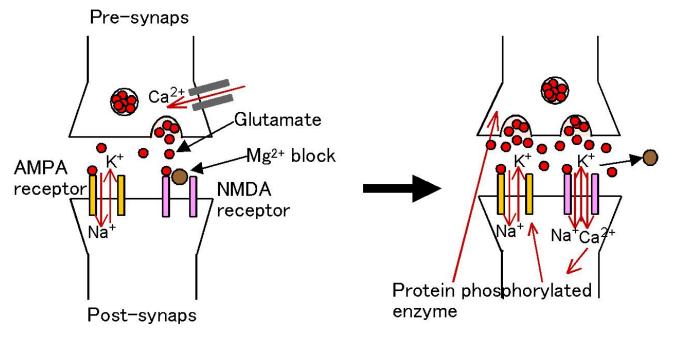




Long-term potentiation, LTP

Long-lasting increase in synaptic efficacy resulting from high-frequency stimulation of afferent fibers.

LTP in the hippocampus = typical morel of synaptic plasticity related to learning and memory.

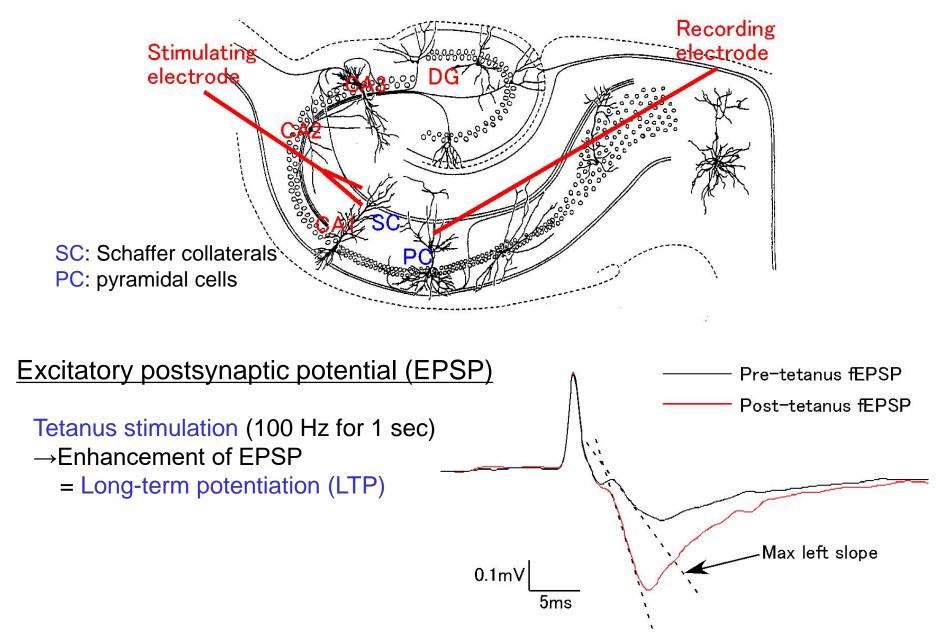


Synaptic transmission

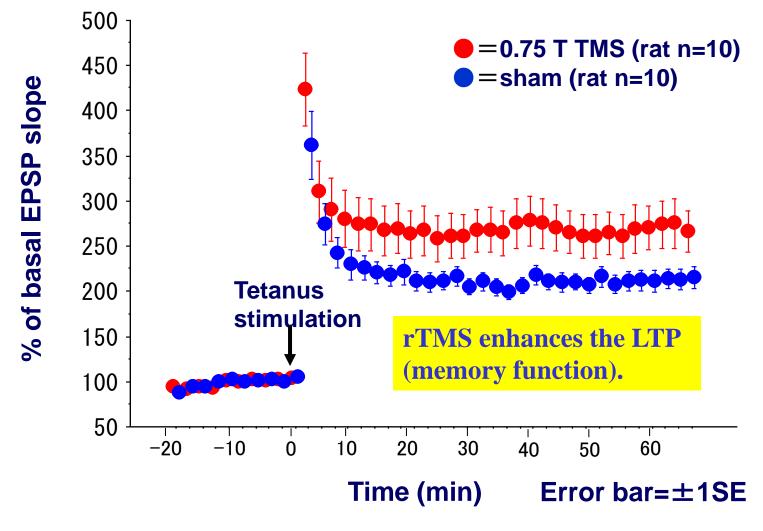
After high-frequency stimulation

- Enhancement of transmitter release
- Activation of AMPA and NMDA receptors

Measurement of fEPSP and LTP

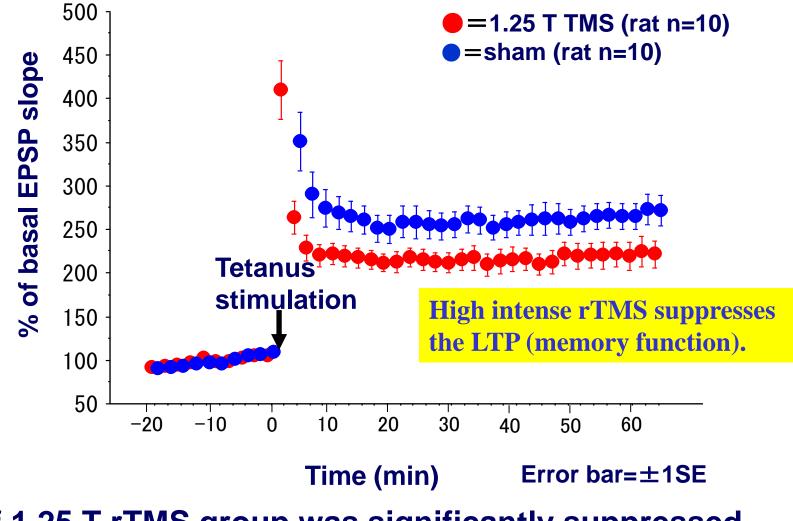


LTPs of 0.75 T rTMS



LTP of 0.75T rTMS group was significantly enhanced (p=0.0408). Ogiue-Ikeda M, Kawato S, and Ueno S: Brain Research (2003)

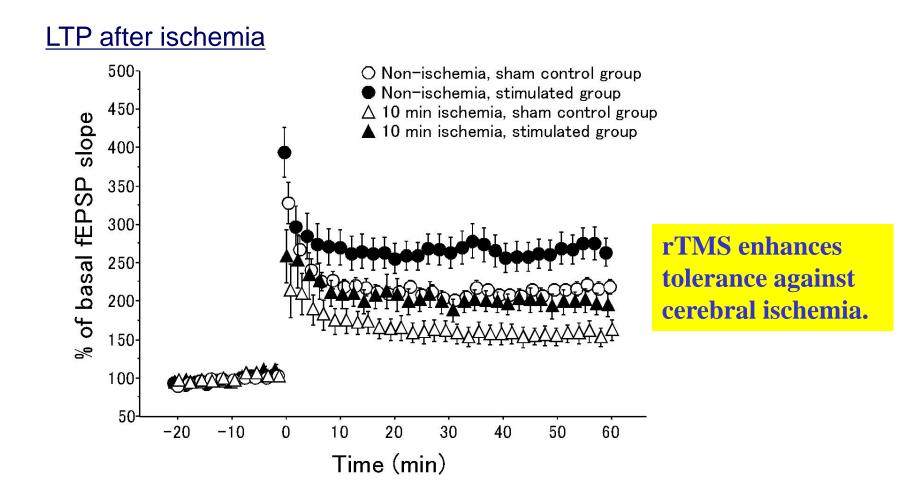
LTPs of 1.25 T rTMS



LTP of 1.25 T rTMS group was significantly suppressed (p=0.0289). Ogiue-Ikeda M, Kawato S, and Ueno S: Brain Research (2003)

Acquisition of ischemic tolerance by 0.75 T rTMS

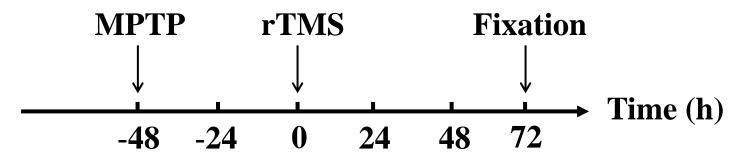
Ischemic condition: 10 min, ischemic ACSF (without glucose, oxygen).



0.75T rTMS has potential to protect hippocampal function from ischemic injury.

Ogiue-Ikeda M, Kawato S, and Ueno S: Brain Research, 1037 (2005)

Effect of rTMS on injured neurons



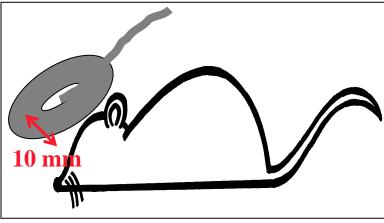
- Subjects: Wistar rats (3) 5 weeks old
- Neurotoxin: MPTP

(1-methyl-4-phenyl-1,2,3,6tetrahydropyridine) (20 mg/kg)



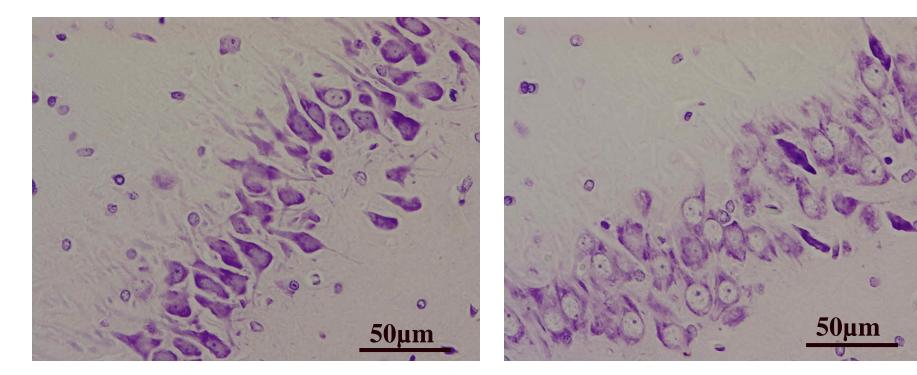
Magnetic field: 1.25 T at the center of coil 25 pulses/sec × 8 sec × 10 trains (= 2000 pulses) per day Interval between trains = 10~15 min

Funamizu H, Ogiue-Ikeda M, Mukai H, Kawato S, and Ueno S: Neuroscience Letters (2005)



Effect of rTMS on the injured neurons in the hippocampal CA3

nissl stain

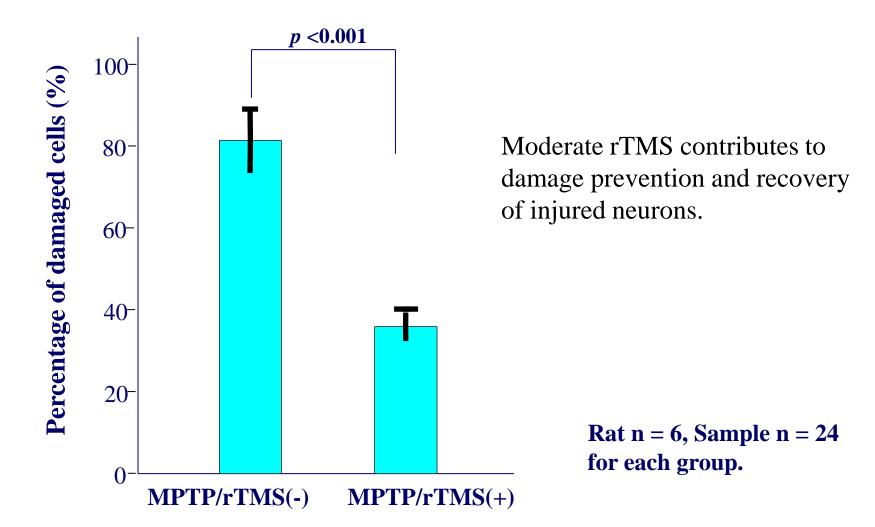


MPTP/rTMS(-)

MPTP/rTMS(+)

rTMS prevents damage to hippocampal CA3 pyramidal neurons.

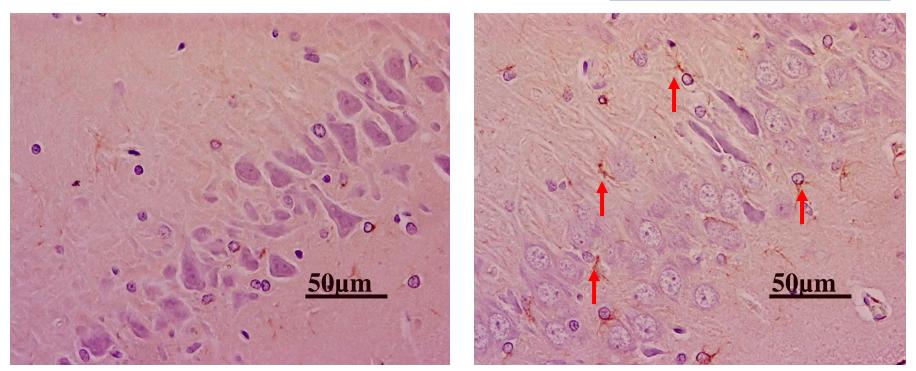
Percentage of damaged cells in hippocampal CA3



The percentage of damaged cells of the MPTP/rTMS(+) group was significantly lower than that of the MPTP/rTMS(-) group.

Activation of astrocytes in the hippocampal CA3

immunocytochemistry



MPTP/rTMS(-)

MPTP/rTMS(+)

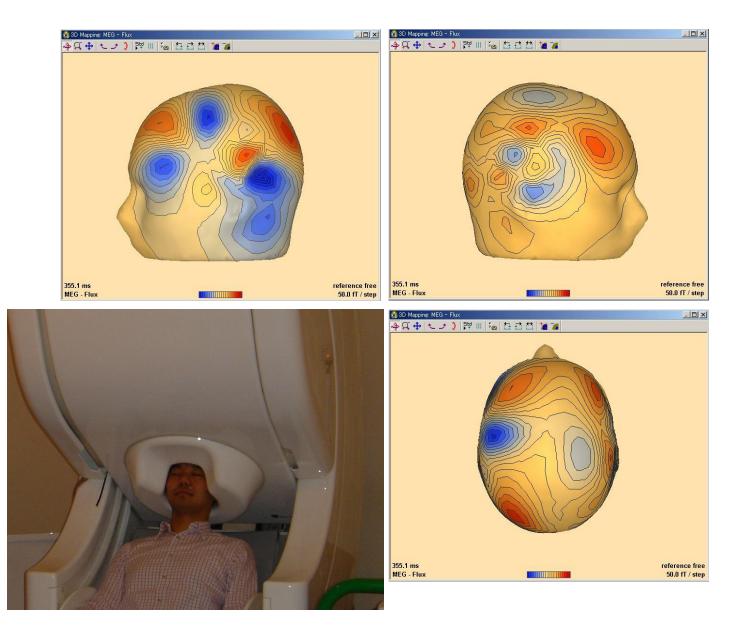
Arrows indicate GFAP (glial fibrillary acidic protein) positive astrocytes. GFAP is a cell specific marker in astrocytes.

• rTMS **increases** the **GFAP immunoreactivity** in the hippocampal CA3.

Potential Treatments by rTMS

rTMS (repetitive TMS) modulates or contributes to memory function learning and memory processes neuronal plasticity prevention of neurons against injury recovery of injured neurons acquisition of tolerance against cerebral ischemia

Whole cortex type of MEG system



Inverse Problem

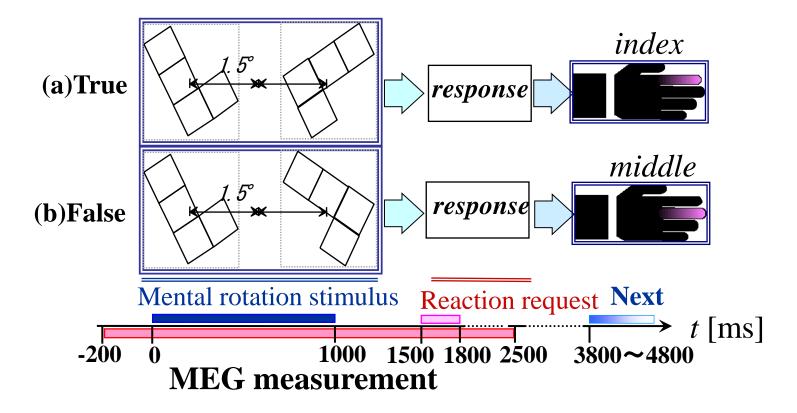
I. Estimation of Current Dipoles

- * Newton Iteration Method
- * Marquardt's Method
- * Simulated Anneling Method
- * Genetic Algorithm

II. Estimation of Current Distribution

- * Fourier's Transformation Method
- * Pattern Matching Method
- * Minimum Norm Estimation
- * MUSIC (Multiple Signal Classification) Algorithm
- * Sub-Optimal Least-Squares Subspace Scanning Method
- * Spatial Filtering Method
- * LORETA (Low Resolution Brain Electromagnetic Tomography)

Mental rotation task

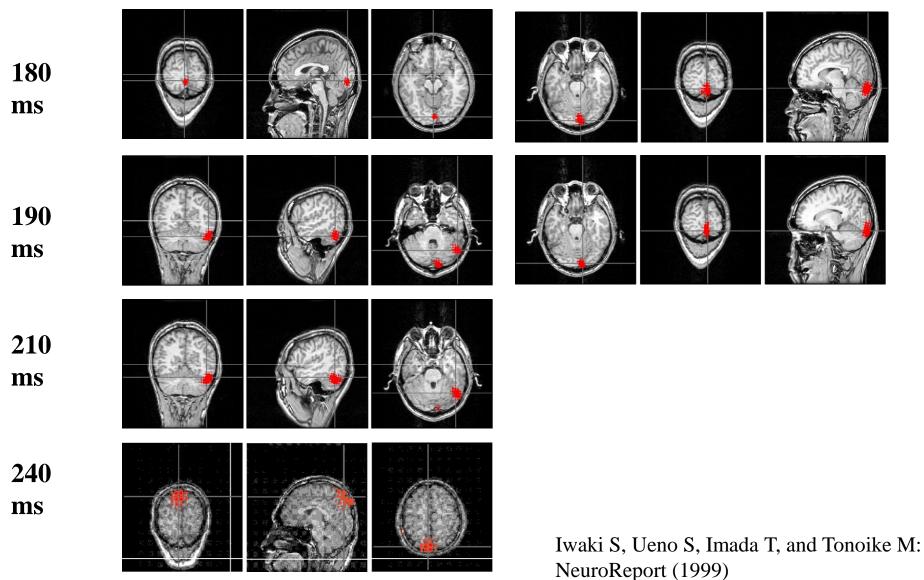


A mental rotation process requires rotation and matching of a pair of mental images.

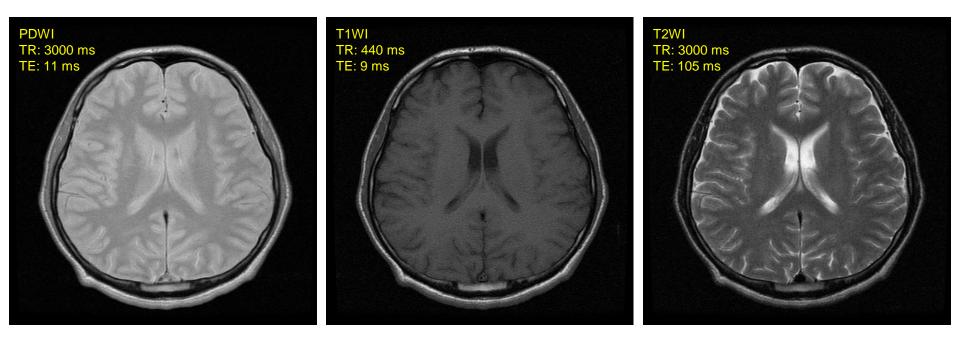
Estimated source distributions (mental rotation)

Mental rotation task

Control task



Conductivity imaging of the brain



Images were obtained using a GE 1.5 T MRI system.

Maximum magnetic field gradient: 33 mT/m, Maximum rate of rise: 150 mT/m/ms Maximum b value: 10000 s/m²

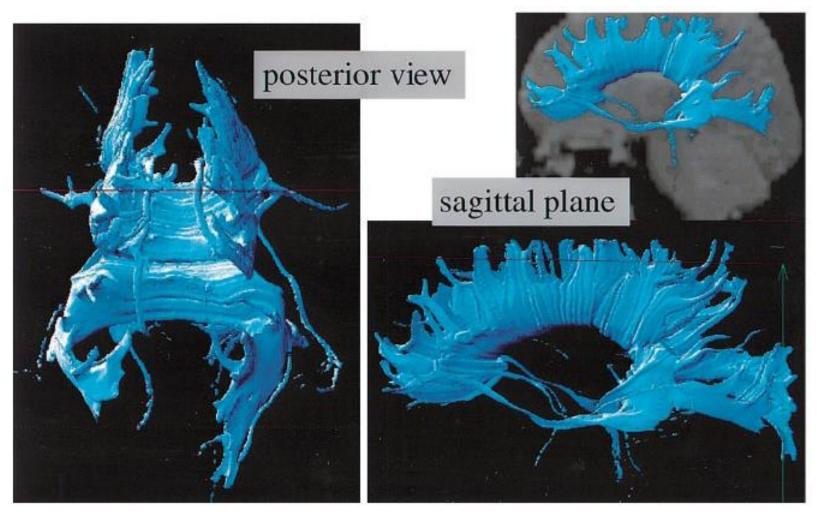


Functional MRI (fMRI) based on Blood Oxygenation Level Dependent (BOLD) effects was invented by Dr. Seiji Ogawa.

Dr. Seiji Ogawa was awarded Japan Prize in 2003, and Canada Gairdner International Award in 2003.

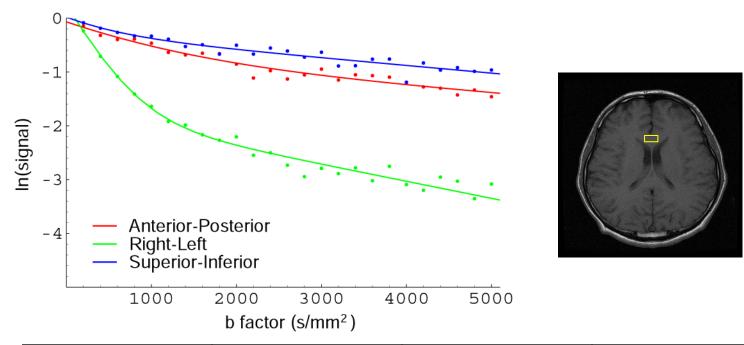
Dr. Seiji Ogawa

Fiber-Tract Trajectories of the Corpus Callosum



Basser PJ, Pajevic S, Pierpaoli C, Duda J, Aldroubi A. Magn Reson Med 2000;44:625-632.

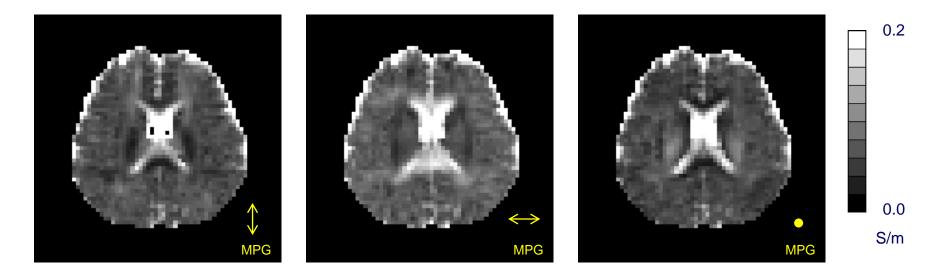
Relationships between the b-factor and the logarithm of the signal intensity in the corpus callosum

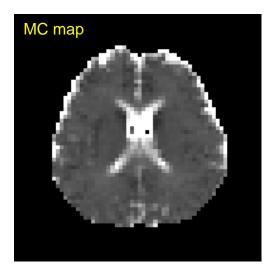


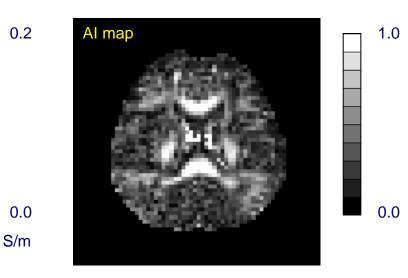
	Annerior-Posterior	Right-Left	Superior-Inferior
D _{fast} (×10 ⁻³ mm ² /s)	2.09 ± 0.45	2.46 ± 0.55	2.32 ± 0.71
f _{fast}	0.58 ± 0.04	0.54 ± 0.07	0.56 ± 0.05
D _{slow} (×10 ⁻³ mm ² /s)	0.50 ± 0.11	0.42 ± 0.07	0.44 ± 0.09
f _{slow}	0.42 ± 0.04	0.46 ± 0.07	0.44 ± 0.05

An application of the MPG in the right-left direction caused the most rapid signal attenuation.

Conductivity images

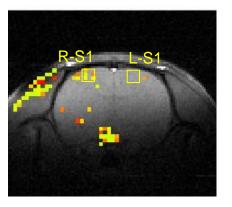




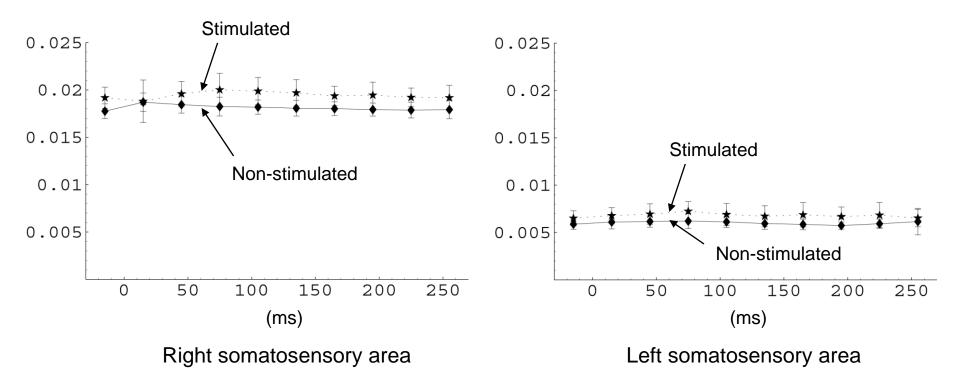


M. Sekino, Y. Inoue, and S. Ueno (2005)

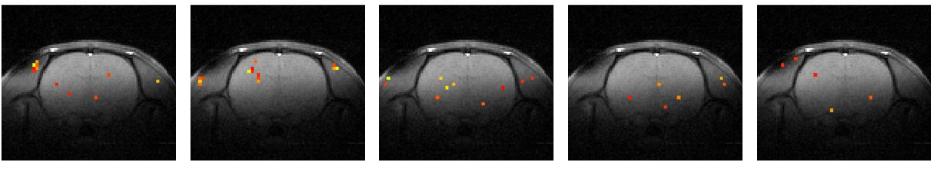
Detection of change of magnetic fields related to neuronal electrical currents by MRI



BOLD-fMRI of the somatosensory area activated by electrical stimulation of the left hindpaw of a rat.



Comparison of the signal intensity between the images obtained at adjacent time points after electric stimulation 0.05 0.00



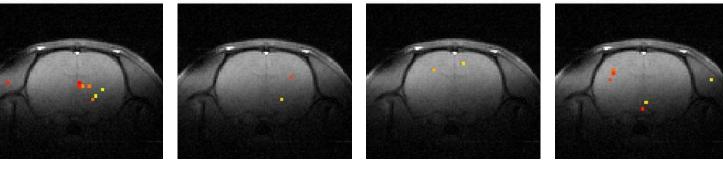
0~30 ms $30 \sim 60 \text{ ms}$

30~60 ms 60~90 ms

60~90 ms 90~120 ms

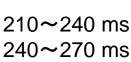
90~120 ms 120~150 ms

120~150 ms 150~180 ms



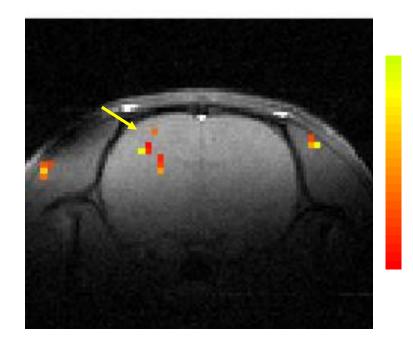
150~180 ms 180~210 ms

180~210 ms 210~240 ms



240~270 ms 270~300 ms

Current MR Imaging: Imaging of magnetic fields caused by neuronal electrical activities in the brain



0.00

Subtraction image of signals at 30 – 60 ms from signals at 60 – 90 ms.

0.05

Pulse Sequence : gradient echo Spatial Resolution : 500 μm Slice Thickness: 2 mm

Color scales show p-values.

Theoretical limit of the detection of magnetic field by MRI

Magnetic field generated by neuronal electrical current

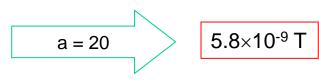
 $5 \text{ pT} = 5.0 \times 10^{-12} \text{ T}$ on the surface of the human head (30 mm away from the source)

 4.5×10^{-9} T at the vicinity of neurons 1 mm away from the neurons

Limit of sensitivity after a times averaged.

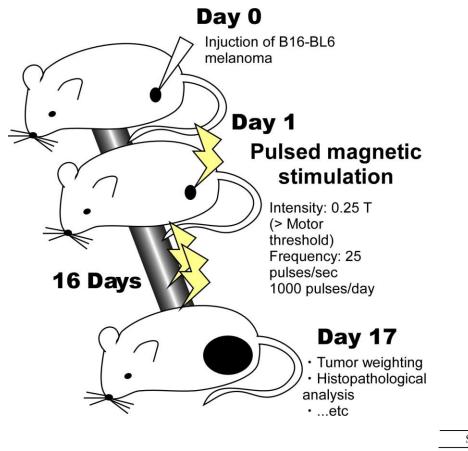
$$\sigma_B = \frac{N}{S\gamma T_E \sqrt{a}} \qquad \qquad R_s = 1.17(\Omega)$$
$$N = n\sqrt{4kT_S\Delta fR_S}$$
$$= 1.11 \times 10^{-5}(V)$$

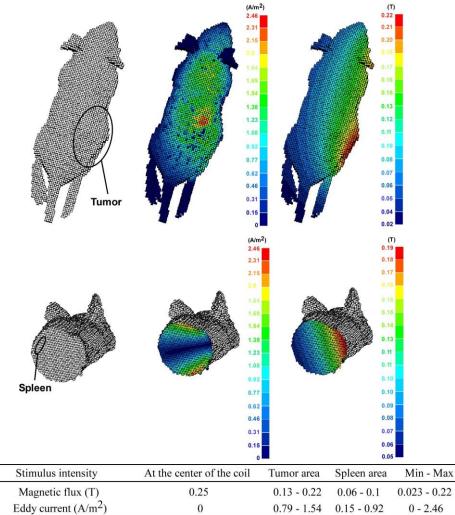
Limit of sensitivity at the gray matter $\sigma_{\rm B} = 2.61 \times 10^{-8} \, {\rm T}$



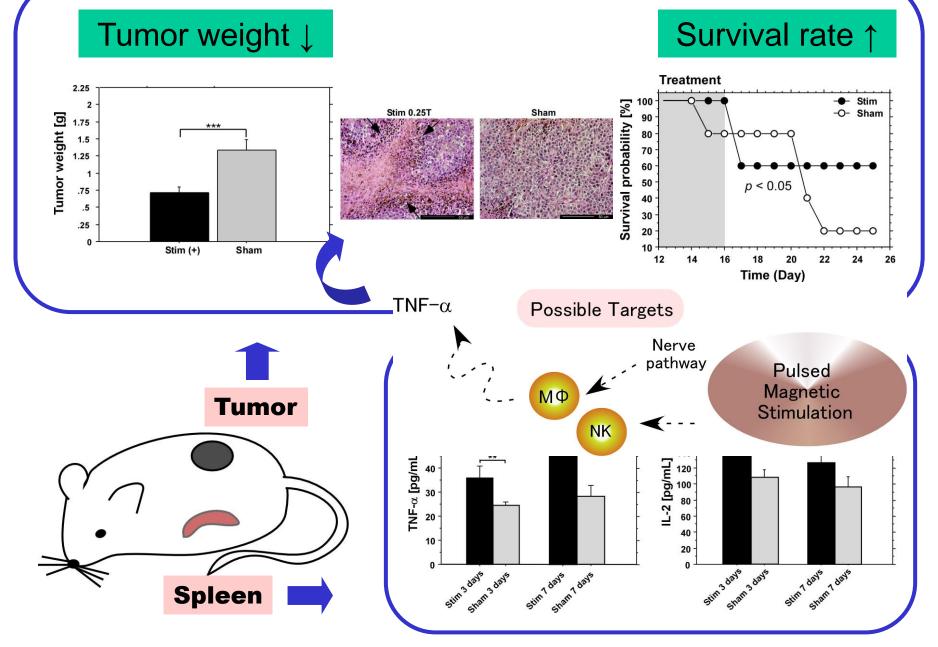
	Human	Rat
Repetition time (T _R)	400 ms	333 ms
Echo time (T _E)	5 ms	30 ms
Static field (B ₀)	1.5 T	4.7 T
RF field (B ₁)	2×10 ⁻⁶ T	3.5×10⁻⁵ T
Field of view (L)	220 mm	32 mm
Slice thickness (h)	6 mm	2 mm
Flip angle (θ)	90°	20°
Number of pixels (n)	256	64
Resistance (R)	1.17 Ω	0.08 Ω
Number of averages (a)	20	20
Limit of sensitivity (σ_B)	5.8×10 ⁻9 T	4.3×10⁻¹¹ T

Effects of Pulsed Magnetic Stimulation on the Tumor Development Processes





S. Yamaguchi, M. Ogiue-Ikeda, M. Sekino and S. Ueno, Bioelectromagnetics (2006)



S. Yamaguchi, M. Ogiue-Ikeda, M. Sekino and S. Ueno, Bioelectromagnetics (2006)

Cell Destruction by Pulsed Magnetic Force and Magnetizable Beads

Materials and Methods

Cells: TCC-S (Leukemic cells) expressing CD33 antigen

Beads: Dynabeads Pan Mouse IgG (Dynal),

diameter = $4.5 \pm 0.2 \,\mu$ m,

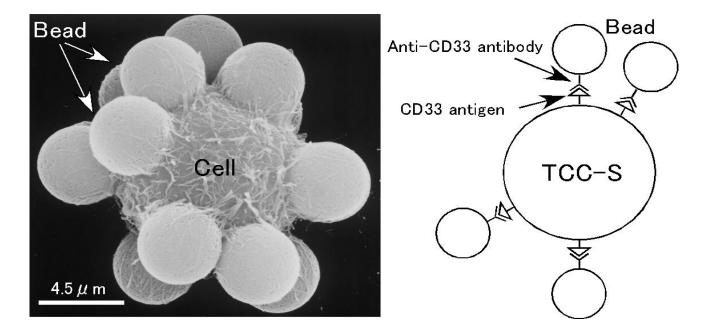
magnetic mass susceptibility

 $= (16 \pm 3) \times 10^{-5} \text{ m}^{3}/\text{kg}$

Dynabeads:

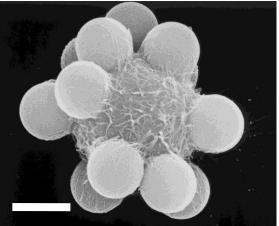
mono-sized, superparamagnetic, macroporous particles with narrow pores, in which magnetizable materials are distributed in the pores throughout the whole volume of the particles.

TCC-S cells and beads were bound together by an antigenantibody reaction \rightarrow cell/bead/antibody complex

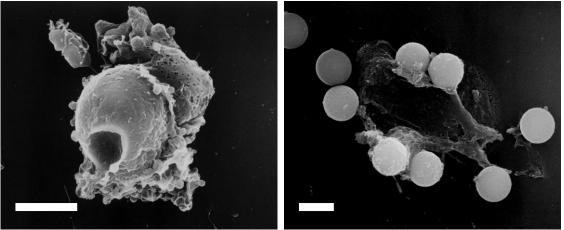


Electron scanning micrograph of the stimulates and nonstimulated cell/bead/antibody complex

Nonstimulated



Stimulated



Scale bars = $4.5 \,\mu m$

The cells were damaged by penetration of the beads or rupturing by the beads.

The instantaneous pulsed magnetic forces cause the beads to forcefully penetrate or rupture the targeted cells.

M. Ogiue-Ikeda, Y. Sato, and S. Ueno: IEEE Trans. NanoBiosci. (2003)

Electromagnetic wave: heat

Ultrasonic wave: heat, microbubbles

Magnetic forces: no heat, no microbubbles

The absence of heat and microbubbles makes this a potentially viable treatment modality for solid tumor type cancers as well as leukemia in which cells are distributed throughout the whole body.

Mechanisms of biological effects of electromagnetic fields

1) Time-varying magnetic field

eddy currents $J = -\sigma \frac{\partial B}{\partial t}$

heat SAR =
$$\sigma \frac{E^2}{\rho}$$

- 2) Static magnetic fields
 - i) homogenous magnetic field magnetic torque

$$T = -\frac{1}{2\mu_0} B^2 \Delta \chi \sin 2\theta$$

ii) inhomogeneous magnetic field magnetic force

$$\mathbf{F} = \frac{\chi}{\mu_0} \text{ (grad B) } \mathbf{B}$$

3) Multiplication of magnetic fields and other energy

photochemical reactions with radical pairs singlet-triplet intersystem crossing

nerve stimulation

thermal effects

magnetic orientation of biological cells

parting of water by magnetic fields (Moses effect)

yield effect of cage -product and escape -product

- Diamagnetic Materials
 - Water
 - Fibrin, Collagen
 - Erythrocytes
 - Oxyhemoglobin
- Paramagnetic Materials
 - Oxygen
 - Deoxyhemoglobin
- Ferro- and Ferrimagnetic Materials
 - Magnetites Fe₃O₄
 - Magnetic Particles
 - Magnetic Fluids

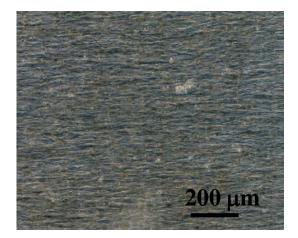


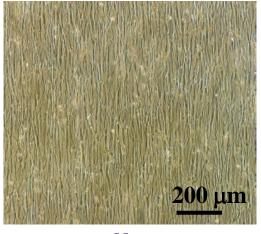
Parting water by magnetic fields: The Moses effect

S. Ueno, M. Iwasaka (2003, 2004)

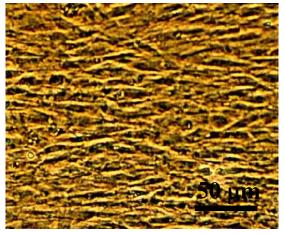
Magnetic orientation of adherent cells

Direction of magnetic field



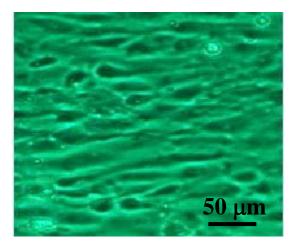


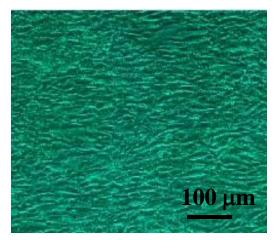
collagen

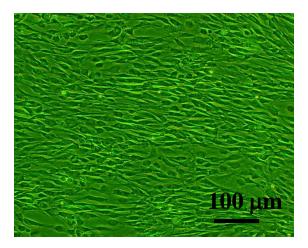


osteoblasts

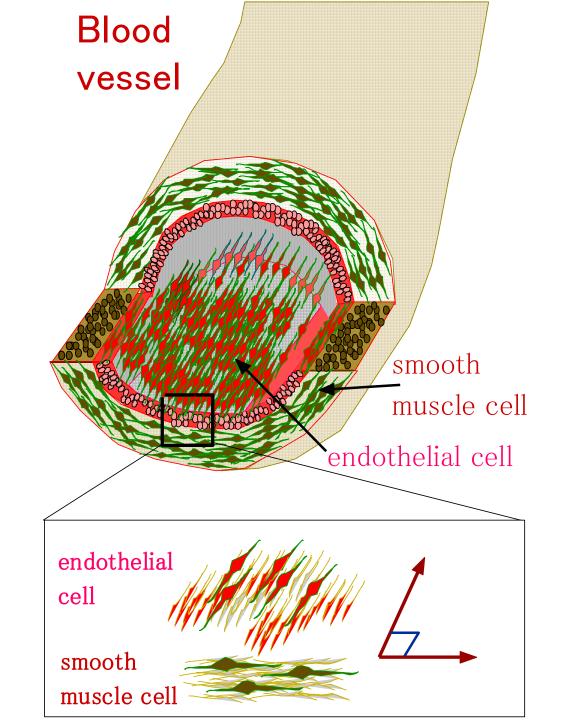
fibrin



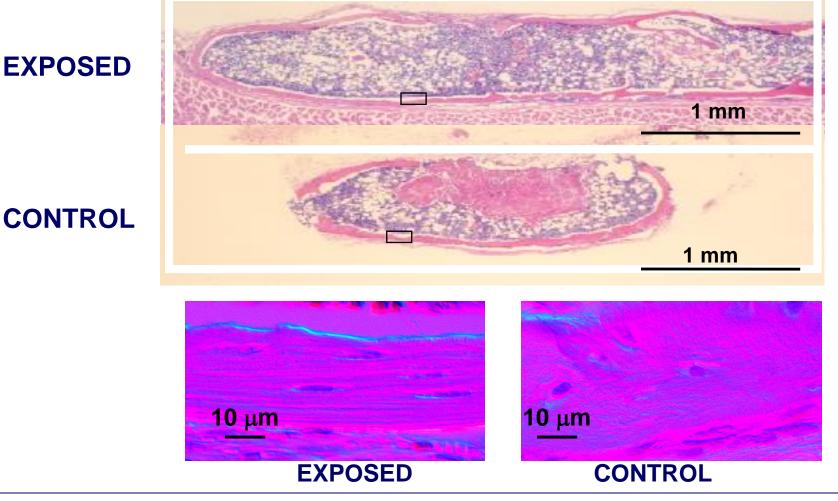




endothelial cells smooth muscle cells Schwann cells

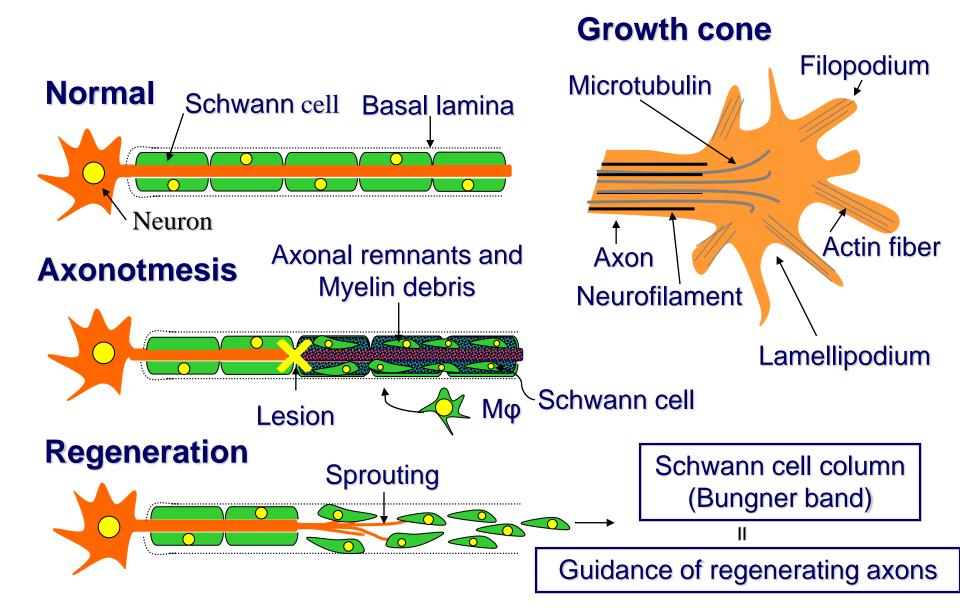


Direction of magnetic field



Ectopic bone formation was stimulated in and around subcutaneously implanted BMP-2 (bone morphogenetic protein)/collagen pellets in mice 21 days after 8 T magnetic field exposure for 60 h. The newly formed bone was extended parallel to the direction of the magnetic field. H. Kotani, S. Ueno, et al. (2002)

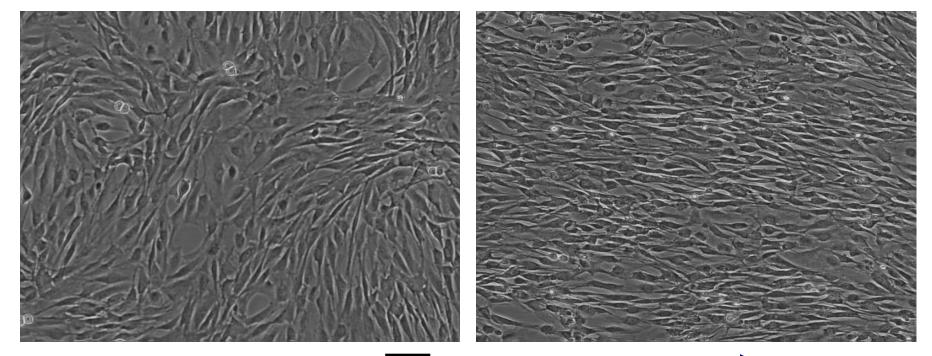
Wallerian degeneration & sprouting



Magnetic orientation of Schwann cells

Control





100 µm

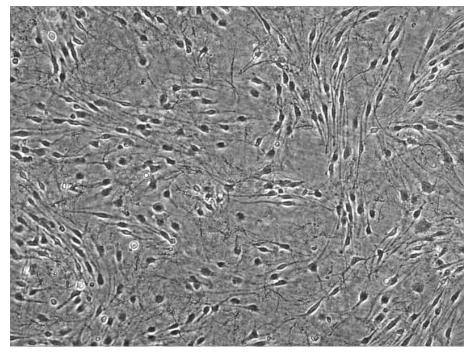
8 T magnetic field 100 μm

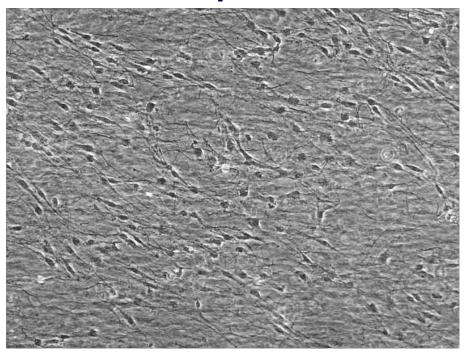
Schwann cells oriented parallel to the direction of the magnetic field after 8 T exposure for 60 h in the confluent condition.

Magnetic orientation of a mixture of Schwann cells and collagen

Control

Exposed



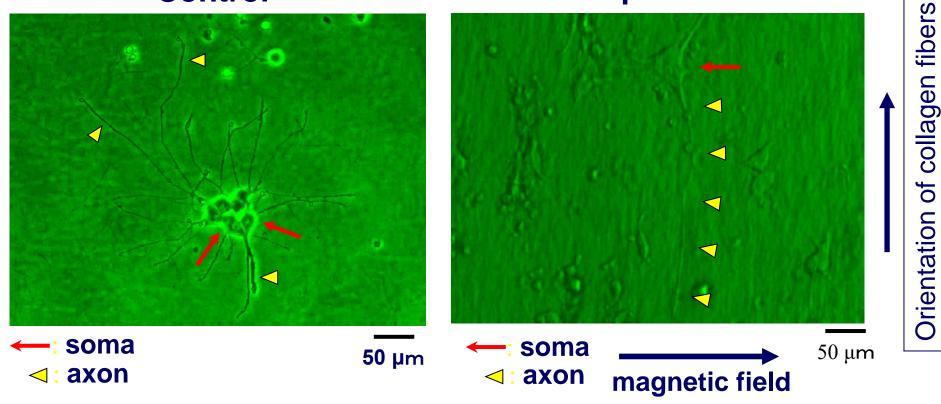


100 µm

Orientation of collagen fibers

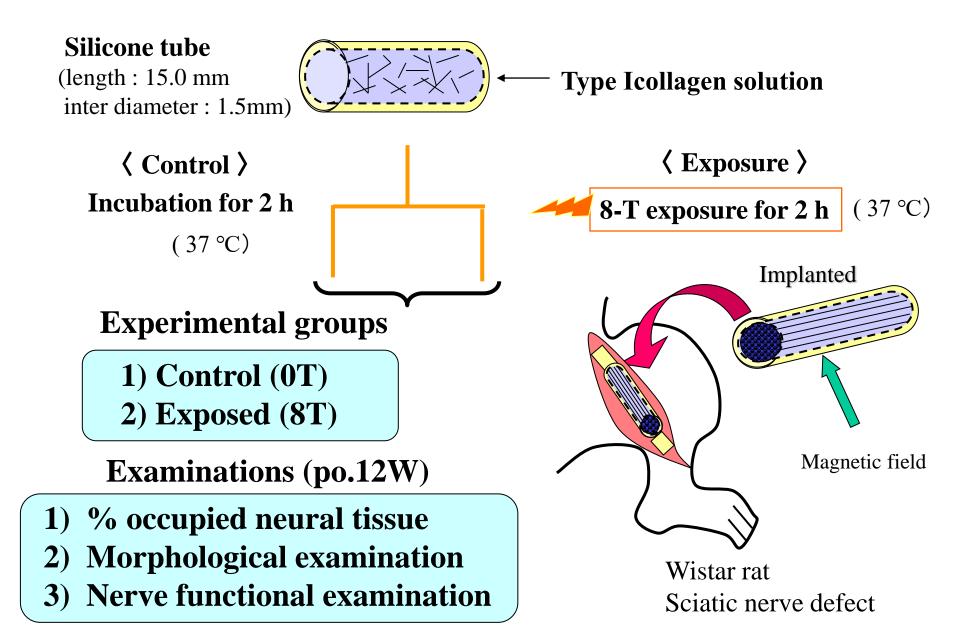
Schwann cell alignment along the magnetically oriented collagen fibers was observed on the 6th day in culture after 8 T magnetic field exposure for 2 h.

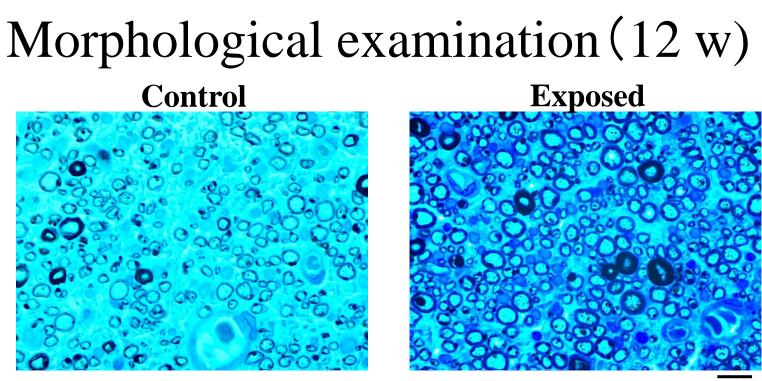
Axon elongation into magnetically aligned collagen Mixture of PC12 (rat pheochromocytoma) cells and collagen (5 days) Control Exposed



Magnetically aligned collagen provides a scaffold for neurons on which to grow and direct the growing axon.

Medical application for artificial nerve graft



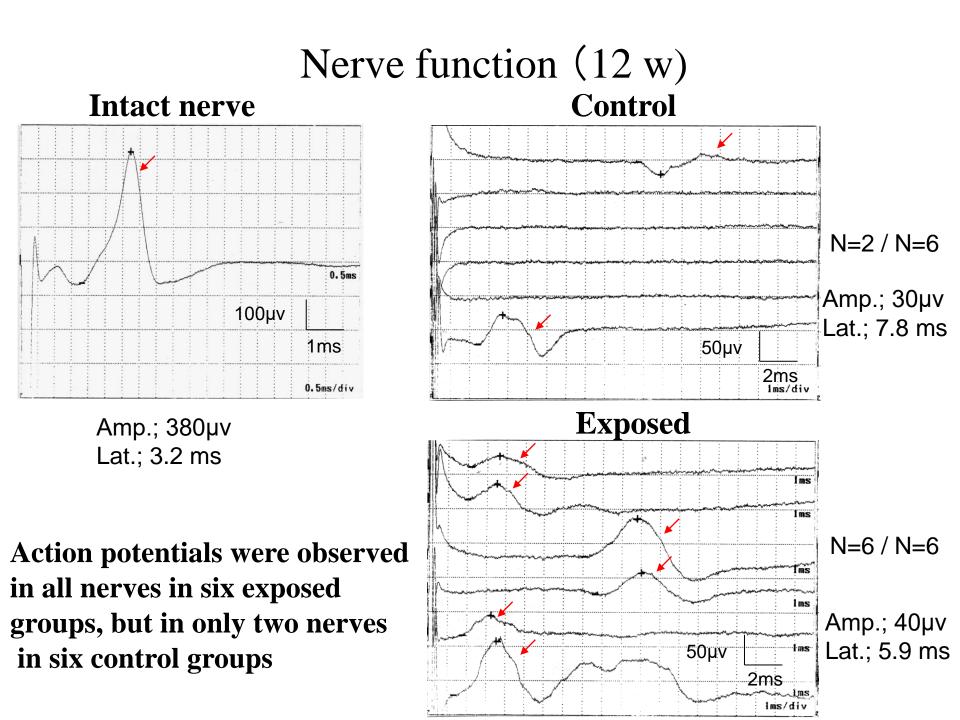


20 µm

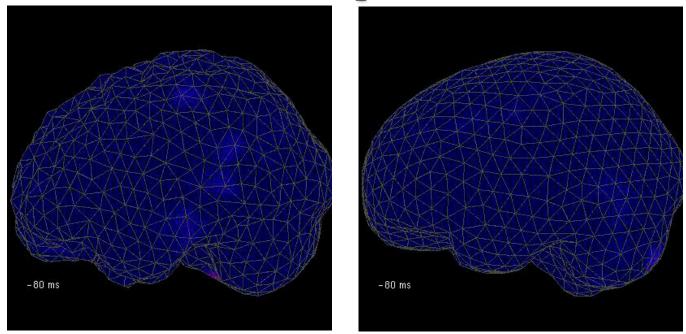
Numbers and diameters of myelinated fibers (po.12W)

	Control	Exposed
Numbers	274.0 ± 11.7	$373.4 \pm 27.6^{**}$
Diameters (µm)	5.53 ± 0.064	$5.81 \pm 0.087*$

*p<0.05, **p<0.01

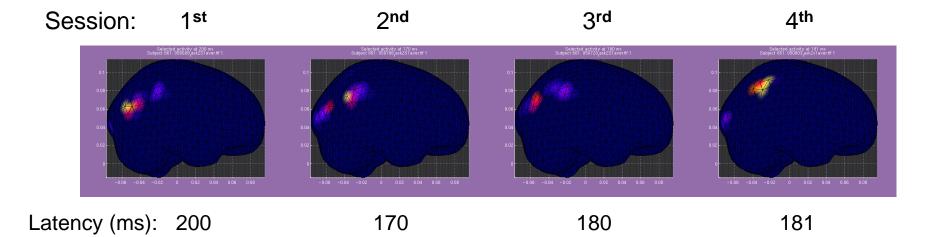


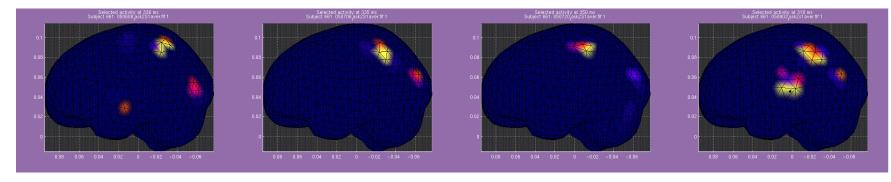
Reading of Kanji and Kana words: A comparative study between native and nonnative speakers



Kanji Reading Left (Native), Right (Non-native)

Study of the Evolution of Neuronal Plasticity during the Learning of a New Language





Latency (ms): 336

335

350



Harvest time and seeding for tomorrow: List of Doctoral Degrees

Ph.D. in Graduate School of Medicine Study on middle latency auditory evoked magnetic fields measured by MEG * Takashi Yoshiura, February 1996 Study on the relationship between direction of induced electric fields and motor evoked potentials elicited by magnetic nerve stimulation with a figure-eight coil Makoto Kobayashi, March 1998 Study on the effects of alternating magnetic fields on morphogenesis of SOD-deficient E. coli and slime molds** Miyuki Kohno, March 1999 Dynamic encoding of facial information represented by neuronal responses in the primate temporal cortex Yasuko Sugase, March 2000 Study on biological effects of repetitive pulsed magnetic stimulation and radio-frequency magnetic fields Giichiro Tsurita, March 2000 Study on the effects of magnetic fields on bone formation in mice Hiroko Kotani, March 2001 Study on vocabulary prosody (pitch accent) in understanding Japanese spoken language using MEG Ryoko Hayashi, November 2001 Study on visually evoked magnetic fields associated with geometric and phonetic discrimination task S F Huang, March 2003 Study on the effects of repetitive TMS on injured neurons in rat brain Hirofumi Funamizu, March 2003 Study on injected current distribution images using diffusion weighted MRI Kikuo Yamaguchi, March 2003 The effects of transcranial magnetic stimulation on the rat hippocampus Mari Ogiue-Ikeda, March 2004 Study on the effects of repetitive TMS on autonomic nervous system in rats Byonchoru Hong, March 2004 Study on the dominance of the left oblique view in activating the cortical network for face recognition Yasuyuki Kowatari, March 2005 Source estimation of the P300 or P300m and P2 or P2m event-related responses using EEG and MEG Takashi Maeno, March 2005 Study on evaluation of atrophic muscles after denervation using magnetic resonance imaging Takako Saotome, March 2005 Study on character cognition processes in Chinese-Japanese bilingual using MEG Hiroyuki Hara, September 2005 Study on reconstruction of nerve function under strong magnetic fields Yawara Eguchi, March 2006

Dr. Eng. (Ph.D.) in Graduate School of Engineering MEG measurements and source model in the brain* Keiji Iramina, March 1991 H-reflex and modeling of nerve excitation elicited by magnetic stimulation* Osamu Hiwaki, March 1992 Magnetic stimulation of the brain* Tsuruo Matsuda, March 1992 High sensitive magnetic sensor by magneto-resistive effect using high-Tc superconducting ceramic materials* Hideo Nojima, March 1993 Integrated DC-SQUID system for measurements of magnetic fields produced by the living body* Kazuo Chinone, October 1993 Studies on the detection sensitivity of multinuclear magnetic resonance imaging and spectroscopy of biological tissues Norio Iriguchi, December 1995 Effects of magnetic fields on blood coagulation and resolution processes Masakazu Iwasaka, March 1996 Measurements and source estimation of the functional brain activities using MEG* Hideki Yoshida, March 1996 Measurements and Inverse problem in MEG Sunao Iwaki, March 1998 Modeling and estimation of distributed sources in the brain by EEG and MEG measurements Kenichi Ueno, March 1998 Studies on transcranial magnetic stimulation (TMS): fabrication and safety aspects of TMS Masaru Yarita, June 1998 Reduction of noise in SQUID magnetometer for measurement of living system Yoichi Takada, September 1998 Source estimation of short-term memory and cognitive process in the human brain by MEG measurements Seiji Nakagawa, March 1999 Cortical activations of Japanese-English mental transration revealed by fMRI and MEG Netsiri Chaiyapoj, March 1999 Studies on behaviors of erythrocyte under strong magnetic and electric fields Takao Suda, December 1999 Measurements of brain and cardiac electric activities of rats by a SQUID system with a high spatial and temporal resolution Seiya Uchida, March 2001 Brain electrical activities associated with perception of visual apparent movement Ryoichi Tsuda, March 2001 Studies on the effects of static magnetic fields on microcirculatory hemodynamics and blood pressure in mammals Hideyuki Okano, September 2002 Magnetic resonance imaging and numerical simulations of electric phenomena in living bodies Masaki Sekino. March 2005

Data processing in the brain associated with mental rotation task Hiroaki Kawamichi, January 2006 RF inhomogeneity correction method for quantitative magnetic resonance imaging Hiroaki Mihara, March 2006 Studies on relaxation and diffusion processes of water molecules in fibral gel states by magnetic resonance imaging technique Michihiro Tekeuchi, 2006 (on going)

Master Degree in Medicine

Studies on the effects of pulsed magnetic fields on tumors Sachiko Yamaguchi, March 2004

Master Degree in Engineering

Study of short-term memory processes in the human brain by MEG Kenji Yamanami, March 1997 Study of induced electric fields and nerve excitation model in TMS Ren Liu, March 1997 Studies on rf inhomogeneity and its correction in MR imaging Hiroaki Mihara, March 1998 Effects of magnetic fields on hemoglobin oxygenation and deoxidation Masakatsu Hori, March 1998 Auditory evoked magnetic fields responded to various sonic stimuli Tomohiro Morikawa, March 1998 Effects of magnetic fields on oxygen dissolving process into water Nobuo Yagi, March 1999 Study on a method to visualize tissue conductivity by MRI Yasuhiro Yukawa, March 1999 Study on nerve excitation processes exposed to strong magnetic field exposures Naoki Ishihama, March 2000 Studies on the effects of magnetic fields on oxygen adsorption of hemoglobin and oxygen dissociation Yutaka Yoshimura. March 2000 Quantitative evaluation of alignment of adherent cells oriented by strong magnetic fields Akinori Umeno, March 2002 Electric current imaging based on magnetic resonance imaging Masaki Sekino, March 2002 Study on MR imaging using a frequency shift method Tatsuki Matsumoto, March 2003 Studies on metabolism of muscles and evaluation of tissue structures using magnetic resonance Ruwan Victor Perera, March 2004

Study on estimation of in vivo distortion by diffusion tensor magnetic resonance imaging Akihisa Kaneko, March 2004 Study on restricted diffusion of water molecules in the living body using diffusion weighted MRI Masato Sano, March 2004 Study on imaging of extremely weak magnetic fields caused by electric currents using MRI Hirohisa Hatada, March 2005 Study on visually evoked magnetic fields responded to visual stimuli associated with sense of taste Maki Tagaya, March 2006 Study of language and cognitive processes through magnetoencephalography Takai Rafael Barbosa, Marc 2006 Study on source estimation in EEG and MEG using mutual correlation coefficient Masuji Yamada, March 2006

Ph.D. candidates at Graduate School of Medicine

Study on measurement of electrical activities in nerve-muscle junctions using a high sensitive magnetic sensor Hikari Tachikawa Assessment of visual and auditory working memory processes in the human brain using noninvasive electromagnetic measurements Klevest Gjini Studies on the effects of pulsed magnetic fields on tumors Sachiko Yamaguchi

given by Kyushu University
 given by Osaka University
 given by the University of Tokyo









Prof Ueno was awarded *Doctor Honoris Causa* from Linkoping University on 6th June 1998.



President Bertil Andersson and Professor Anders Tornval visited the University of Tokyo on 16th August 2001.

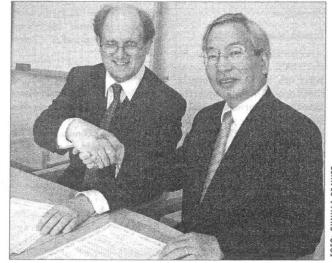
Tokyo-universitetet

dpunkten ligger på teknikmen vi räknar med att ofiska fakulteten ska kuntta av avtalet, säger Anders

fram till ett avtal har varit i första kontakten togs rem år när Anders Törnvall I:s dekanus Mille Millnert n dåvarande dekanen för fakulteten. Men det var rektor Bertil Andersson sedan träffade sin rektorsasaki som samarbetsplafaştare form. Sedan dess rån båda sidor filat på inavtalet. kelperson i kontakterna har varit professorn i medicinsk teknik Shoogo Ueno, vars mångåriga samarbete med Linköpingsprofessorn Åke Öberg ledde till att han blev hedersdoktor vid Linköpings universitet 1998. Professor Ueno är väl bekant med Linköping, inte minst efter sina två år som gästforskare här 1979-81.

Det var också professor Ueno som representerade Tokyo-universitet vid undertecknandet av avtalet.

– Rektor Sasaki hade ingen möjlighet att komma nu, men kommer hit i höst tillsammans med sin vice rektor, berättar Anders Törnvall. LENNART FALKLÖF



Ett handslag för ett gott framtida samarbete! Rektor Bertil Andersson och den japanske professorn och hedersdoktorn Shoogo Ueno.



Professor Bertil Andersson, President, Linkoping University Sweden, enjoyed the TMS.

Prof Shoogo Ueno visited President Bertil Andersson at Linkoping University, Linkoping, Sweden, on behalf of President Takeshi Sasaki, the University of Tokyo, on 3rd June 2002.



International symposium on electromagnetics in biology and medicine, April 2-4, 2001 S. Ueno, Chairman, Commission K: Electromagnetics in Biology and Medicine, URSI (The International Union of Radio Science)

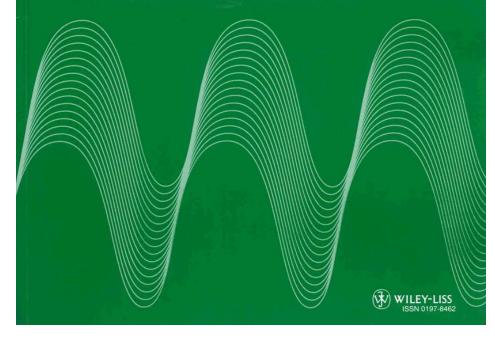


Boat cruise on the Sumida River, April 5th, 2001

Big B

THE SOCIETY FOR PHYSICAL REGULATION IN BIOLOGY AND MEDICINE

THE EUROPEAN BIOELECTROMAGNETICS ASSOCIATION







S. Ueno, President, The Bioelectromagnetics Society (BEMS), 2003-2004











日本学術会議MEフォーラム10回記念講演会 司会 上野照剛(東京大学) 南谷晴之(慶應義塾大学) 黒川 清 (日本学術会議会長) 阿部 博之 (総合科学技術会議議員) 長倉 三郎 (日本学士院長) 13:15-14:55 1. 脳磁気科学とバイオマグネティックス 2. バイオメカニクスとバイオナノテクノロジー 15:00 - 17:30司会 堀 正二(大阪大学) 梶谷文彦(川崎医科大学) 5. ライフサイエンス研究に対する取り組み 山本 光昭 (内閣府 科学技術政策担当 参事官) 杉野 剛 (文部科学省研究振興局学術研究助成課長) 7. ライフサイエンス分野の動向と文部科学省の取り組み 松尾 泰樹 (文部科学省研究振興局ライフサイエンス課長) 石野 利和 (文部科学省 高等教育医学教育課長) 9. 医療福祉における医用生体工学への期待 給木 康裕 (厚生労働省 医政局研究開発振興課長) 10. 我が国の医療機器産業の現状と方向性 堀口 光 (経済産業省 医療・福祉機器産業室長) 連絡先: 東京大学大学院医学系研究科 医用生体工学講座 生体情報学教室

ME Forum, Science Council of Japan

Sanjo Conference Hall, the University of Tokyo

- December 1994
- 2 December 1996
- 3 December 1998
- December 1999
- January 5 2001
- 2002 January 6
- 2003 7 January
- 8 January 2004
- 9 January 2005
- 2006 January 10





Discussion at ME Forum

Sanjo Conference Hall, the University of Tokyo





Annual Conference of Japanese Society for Medical and Biological Engineering at Tsukuba, Japan, 24th~ 27th April 2005.





Annual Meetings of the Magnetics Society of Japan, Koganei, Tokyo, Japan, September 2002.



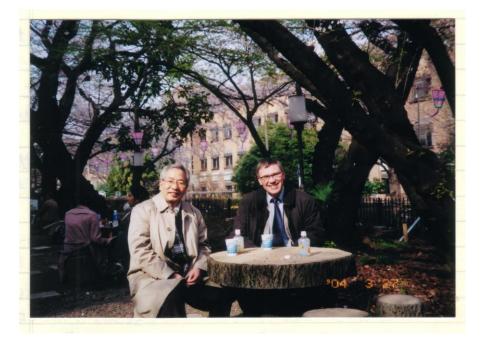
Annual Meeting of the Magnetics Society of Japan, Nagano, 19th~22nd September 2005.







































Mother Sue and Father Haruo Ueno



I thank all of you for your supports and guidance over the years.

I wish you all the best and success in the future.

I hope the University of Tokyo goes onward for further leap and development.

Thank you very much for your attention.

Thousand Thanks !!



Shoog Ueno