Imperial Prize and Japan Academy Prize to:

Seiji OGAWA
Special University Professor Emeritus,
Tohoku Fukushi University
Guest Specialist, Center for Information and
Neural Networks (CiNet)
Honorary Fellow, National Institutes for Quantum
Science and Technology (QST)
Guest Professor, Brain and Mind Research Center,
Nagoya University

for "Discovery of the Basic Principle of Functional Magnetic Resonance Imaging and its Development of the Method in Brain Science"

Outline of the work:

Dr. Seiji Ogawa discovered the principle of BOLD contrast in magnetic resonance imaging (MRI) which appears as variation of MRI signals due to changes in blood oxygenation induced by blood physiology. Based on this principle, he introduced an MRI approach for measuring functional activity of the brain (BOLD based functional MRI, fMRI).

Dr. Ogawa studied Applied Physics at the University of Tokyo for his Bachelor of Engineering and later earned his Ph.D. in Chemistry at Stanford University, after which he worked at AT&T Bell Laboratories, Murray Hill, New Jersey, as an influential research member for 33 years. He returned to Japan in 2001 to become the director of the Ogawa Brain Function Research Laboratory in Tokyo. In 2008, he became a specially appointed professor at Tohoku Fukushi University. In the same year, he was appointed a special professor at the Neuroscience Research Institute of Gachon Medical University in Korea to lead the research with the newly introduced 7 Tesla ultra-high field MRI system. Since 2011, he has been associated with CiNet (Center for Information and Neural Networks) of National Institute of Information and Communications Technology as an advisor and as a visiting technical specialist. For his contribution to the field of fMRI, he has received many prestigious honors and prizes such as a member of National Academy of Medicine (USA), Japan Prize, Asahi Prize, Gairdner International Award, Keio Medical Science Prize and Japan Medical Research and Development Grand Prize.

Dr. Ogawa's achievements have roots in the wide range of research experience and knowledge on the structure and function of hemoglobin he acquired during his tenure at Bell Laboratories. The knowledge cultivated there gave him the basics for understanding the variation of MRI signals influenced by blood oxygenation, and this understanding led him to find that MRI images depended on the variation of blood oxygenation in the brain. He succeeded in showing such MRI contrast variation in a series of creative experiments with rodent brains. In 1990, he coined the technical term 'BOLD' (Blood Oxygenation Level Dependent) to describe this contrast. He then collaborated with Dr. Kamil Uğurbil of University of Minnesota to apply the BOLD contrast method to study of the human brain, and this collaboration was successful in observing localized neuro-activation using MRI in the brain of a healthy person. More specifically, in experiments with a task of visual stimulation, they demonstrated that it was possible to map the activation in gray matter regions of visual area.

The starting point of the discovery of BOLD contrast traces back to Dr. Ogawa's research work on the biophysical matters of hemoglobin at Bell Laboratories. Twenty years prior to the first BOLD experiment, he was researching the effect of paramagnetic state of the iron on the allosteric oxygen binding of hemoglobin and on its NMR signals. In the early 1970's, he published some important papers on the topics of 'structure and function' of hemoglobin. After the period until the 1980's, he worked on a biochemical problem of *in vivo* cellular energy metabolism using phosphorus-31 NMR spectroscopy.

From these series of the foregoing research works, i.e., on the biophysics of hemoglobin and brain energy metabolism, Ogawa succeeded in conducting leading *in vivo* experiments on the rodent brain using MRI at high magnetic field and high spatial resolution. As a result, MRI signals of water in blood vessels and their surroundings were found to vary by some subtle magnetic field variation induced by the change of magnetization of hemoglobin. This research result was published in a series of papers in the 1990's and the approach of BOLD based fMRI was thereby established. Before such approach, it was generally understood that MRI could not measure functional activity in the brain. The period of the 1990's when Ogawa conducted these research works was in 'the decade of the brain', as acknowledged by the nationwide presidential slogan in the US, and the method was well accepted as a non-invasive way to study brain activity. Unlike previous MRI methods which used externally imposed contrast agents, the method of BOLD based MRI has used the character of blood as an intrinsic contrast agent. As a result, the advantage of BOLD MRI method for studying brain activities was immediately recognized. In the past 30 years, the method became the non-invasive way with high sensitivity to image human brain activity and has provided various basic knowledge of brain activity for research in cognitive neuroscience and for clinical usage of general brain imaging.

Dr. Ogawa is still active in the field of functional brain mapping after his discovery of BOLD contrast. His research has covered a wide variety of topics and applications related to BOLD contrast approach to the brain, such as the basic research on the biophysical aspect of the BOLD phenomena, on the complex mutual interaction between oxygen metabolism and blood system behavior, follow up topics arisen by encountering some unexpected phenomena in brain activity, on functional networks in the brain and on the functional plasticity of the brain. Recently he has also been involved in imaging physiological phenomena of general blood circulation which is unrelated to brain activation.

List of Main Publications

Papers

1) S. Ogawa and Y.-W. Sung. Selected topics relating to functional MRI study of the brain. Keio J. Med. **68**, 73–86 (2019).
2) U.-S. Choi, Y.-W. Sung and S. Ogawa. Steady-state and dynamic network modes for perceptual expectation. Sci. Rep. **7**, 140626 (2017).
3) Y.-W. Sung, M. Kamba and S. Ogawa. An fMRI study of the functional distinction of neuronal circuits at the sites on ventral visual stream co-activated by visual stimuli of different objects. Exp. Brain Res. **181**, 657–663 (2007).
4) S. Ogawa, T.-M. Lee, R. Stepnoski, W. Chen, X.-H. Zhu and K. Uğurbil. An approach to probe some neural systems interaction by functional MRI at neural time scale down to milliseconds. Proc. Natl. Acad. Sci. U.S.A. **97**, 11026–11031 (2000).
5) S. Ogawa, R. S. Menon, S.-G. Kim and K. Uğurbil. On the characteristics of functional magnetic resonance imaging of the brain. Annu. Rev. Biophys. Biomol. Struct. **27**, 447–474 (1998).
6) P. P. Mitra, S. Ogawa, X. Hu and K. Uğurbil. The nature of spatiotemporal changes in cerebral hemodynamics as manifested in functional magnetic resonance imaging. Magn. Reson. Med. **37**, 511–518 (1997).
7) R. S. Menon, S. Ogawa, X. Hu, J. P. Strupp, P. Anderson and K. Uğurbil. BOLD based functional MRI at 4 Tesla includes a capillary bed contribution: echo-planar imaging correlates with previous optical imaging using intrinsic signals. Magn. Reson. Med. **33**, 453–459 (1995).
8) S. Ogawa, T.-M. Lee and B. Barrere. The sensitivity of magnetic resonance image signals of a rat brain to changes in the cerebral venous blood oxygenation. Magn. Reson. Med. **29**, 205–210 (1993).
9) S. Ogawa, R. S. Menon, D. W. Tank, S.-G. Kim, H. Merkle, L. M. Ellermann and K. Uğurbil. Functional brain mapping by blood oxygenation level-dependent contrast magnetic resonance imaging. A comparison of signal characteristics with a biophysical model. Biophys. J. **64**, 803–812 (1993).
10) S. Ogawa, D. W. Tank, R. Menon, J. M. Ellermann, S.-G. Kim, H. Merkle and K. Uğurbil. Intrinsic signal changes accompanying sensory stimulation: functional brain mapping with magnetic resonance imaging. Proc. Natl. Acad. Sci. U.S.A. **89**, 5951–5955 (1992).
11) S. Ogawa and T.-M. Lee. Magnetic resonance imaging of blood vessels at high fields: in vivo and in vitro measurements and image simulation. Magn. Reson. Med. **16**, 9–18 (1990).
12) S. Ogawa, T.-M. Lee, A. R. Kay and D. W. Tank. Brain magnetic resonance imaging with contrast dependent on blood oxygenation. Proc. Natl. Acad. Sci. U.S.A. **87**, 9868–9872 (1990).

13) S. Ogawa, T.-M. Lee, A. S. Nayak and P. Glynn. Oxygenation-sensitive contrast in magnetic resonance image of rodent brain at high magnetic fields. Magn. Reson. Med. **14**, 68–78 (1990).
14) J. M. Salhany, T. Yamane, R. G. Shulman and S. Ogawa. High resolution 31P nuclear magnetic resonance studies of intact yeast cells. Proc. Natl. Acad. Sci. U.S.A. **72**, 4966–4970 (1975).

* Ogawa published 110 peer-reviewed papers in total.

Reports

1) Z. H. Cho, Y. D. Son, E. J. Choi, H. K. Kim, J. H. Kim, S. Y. Lee, S. Ogawa and Y. B. Kim. In vivo human brain molecular imaging with a brain-dedicated PET/MRI system. Magn. Reson. Mater. Phys. **26**, 71–79 (2013).
2) S.-G. Kim and S. Ogawa. Biophysical and physiological origins of blood oxygenation level-dependent fMRI signals. J. Cereb. Blood Flow Metab. **32**, 1188–1206 (2012).
3) 小川誠二「サイエンス・インタビュー　科学のいま、そして未来　脳機能の解明に大きな道を拓いた fMRI」『ミルシル』**3**(4), 3–5 (2010).
4) 小川誠二・上野照剛（監修）『非侵襲・可視化技術ハンドブック — ナノ・バイオ・医療から情報システムまで』エヌ・ティー・エス、東京 (2007).
5) 小川誠二・成烈完・神波雅之・長岡司「fMRI によって脳機能組織の相互作用のダイナミクスを追う（特集　第三八回脳のシンポジウム　高次脳機能解析法と機能局在）」『神経研究の進歩』**47**, 902–908 (2003).
6) S.-G. Kim and S. Ogawa. Insights into new techniques for high resolution functional MRI. Curr. Opin. Neurobiol. **5**, 607–615 (2002).
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8) 小川誠二「機能的 MRI と脳機能研究　特別講演」『医用電子と生体工学』**38** (Supplement), 3 (2000).
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12) 小川誠二「Functional MRI の方法とその応用」『脳卒中』**17**, 489–496 (1995).
13) 小川誠二「磁気共鳴法による脳機能のマッピング」『科学』**63**, 691–692 (1993).
14) R. G. Shulman, T. R. Brown, K. Uğurbil, S. Ogawa, S. M. Cohen and J. A. den

Holander. Cellular applications of ^{31}P and ^{13}C nuclear magnetic resonance. Science **205**, 160–166 (1979).
15) R. G. Shulman, J. J. Hopfield and S. Ogawa. Allosteric interpretation of hemoglobin properties. Q. Rev. Biophys. **8**, 325–420 (1975).
16) 小川誠二「核磁気共鳴によるヘモグロビンの研究」『生物物理』**14**, 183–199 (1974).
17) 小川誠二「生体機能の研究への磁気共鳴法の応用」『応用物理』**42**, 214–225 (1973).