

# Bold Bio

Google Slides Version for embedded videos:

<https://docs.google.com/presentation/d/1cQc-t2F1cUXF4SHo9cQVg-Zm8e-Fuo3OMy9eBYFjeMQ/edit?usp=sharing>

# **Magnetic Resonance Imaging of Blood Vessels at High Fields: *In Vivo* and *in Vitro* Measurements and Image Simulation**

SEIJI OGAWA AND TSO-MING LEE

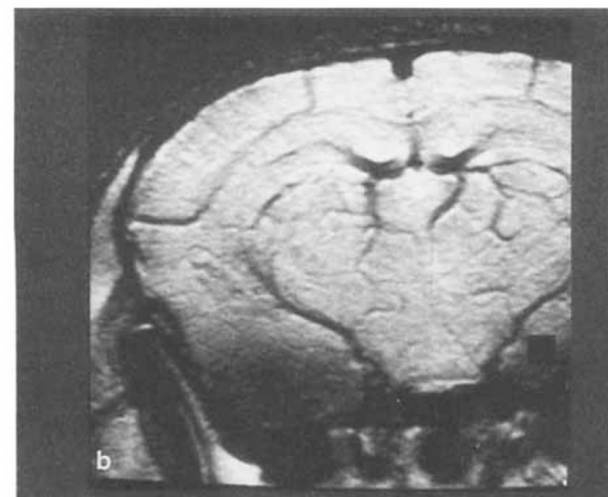
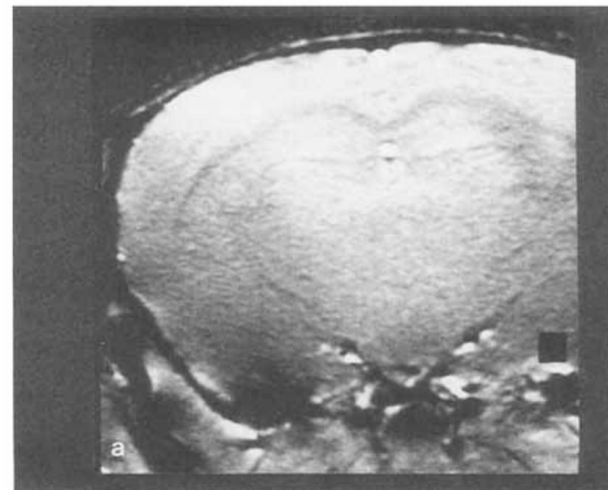
## **Oxygenation-Sensitive Contrast in Magnetic Resonance Image of Rodent Brain at High Magnetic Fields**

SEIJI OGAWA, TSO-MING LEE, ASHA S. NAYAK,\* AND PAUL GLYNN

## **Brain magnetic resonance imaging with contrast dependent on blood oxygenation**

(cerebral blood flow/brain metabolism/oxygenation)

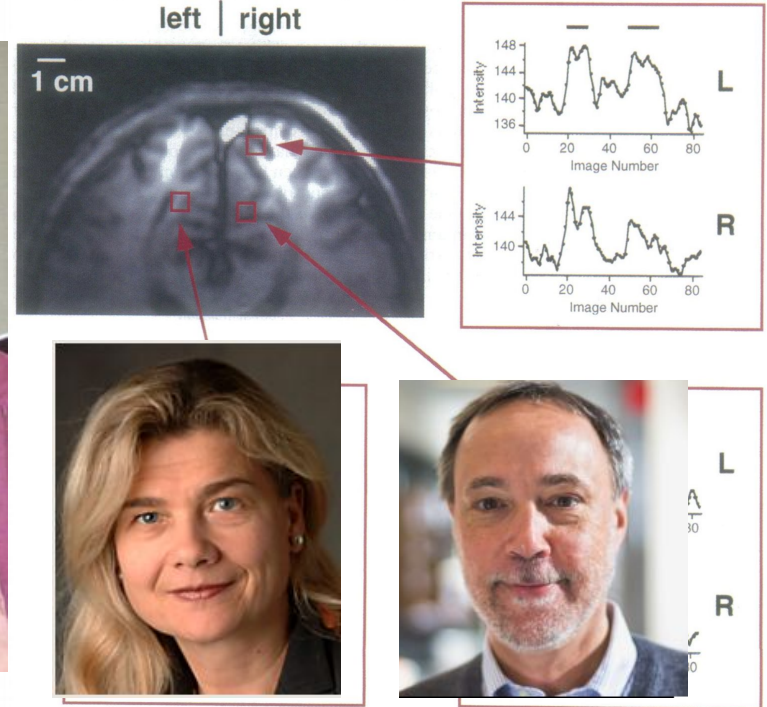
S. OGAWA, T. M. LEE, A. R. KAY, AND D. W. TANK

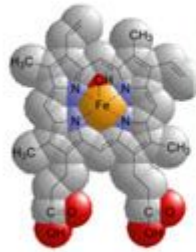


# Intrinsic signal changes accompanying sensory stimulation: Functional brain mapping with magnetic resonance imaging

(cerebral blood flow/blood oxygenation/visual cortex/positron emission tomography/magnetic susceptibility)

SEIJI OGAWA<sup>†</sup>, DAVID W. TANK<sup>†</sup>, RAVI MENON<sup>‡</sup>, JUTTA M. ELLERMANN<sup>‡</sup>, SEONG-GI KIM<sup>‡</sup>,  
HELLMUT MERKLE<sup>‡</sup>, AND KAMIL UGURBIL<sup>‡</sup>





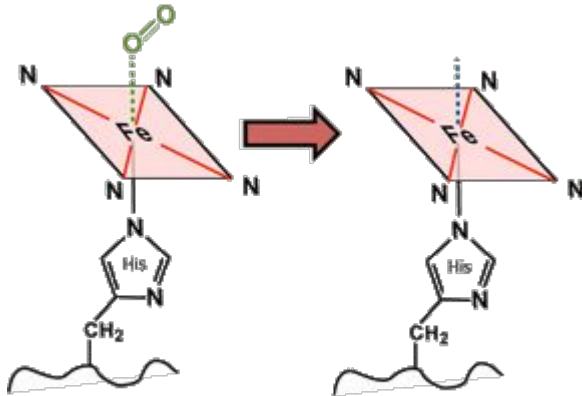
Heme



Hemoglobin

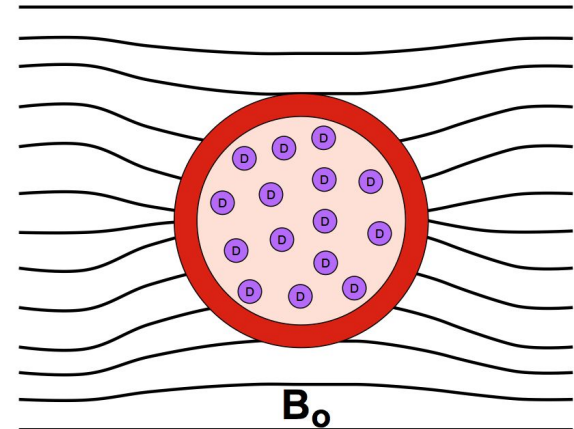


Erythrocyte

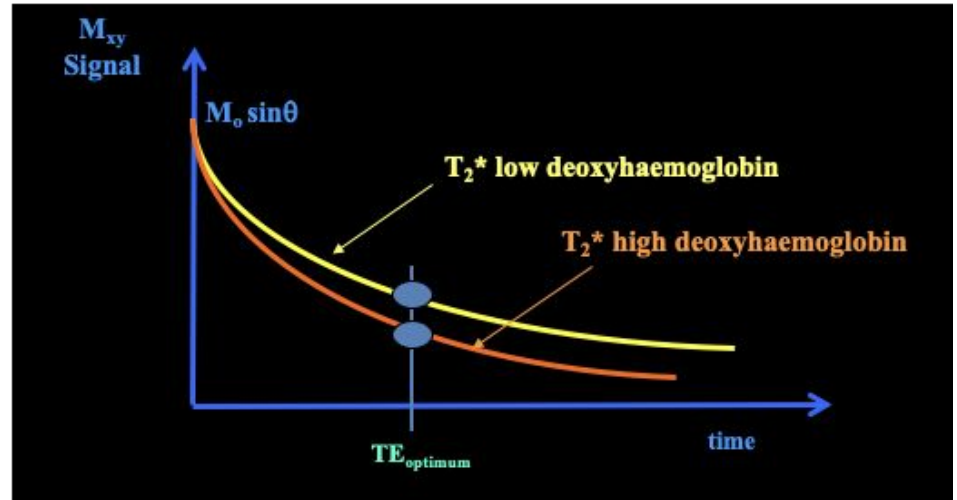
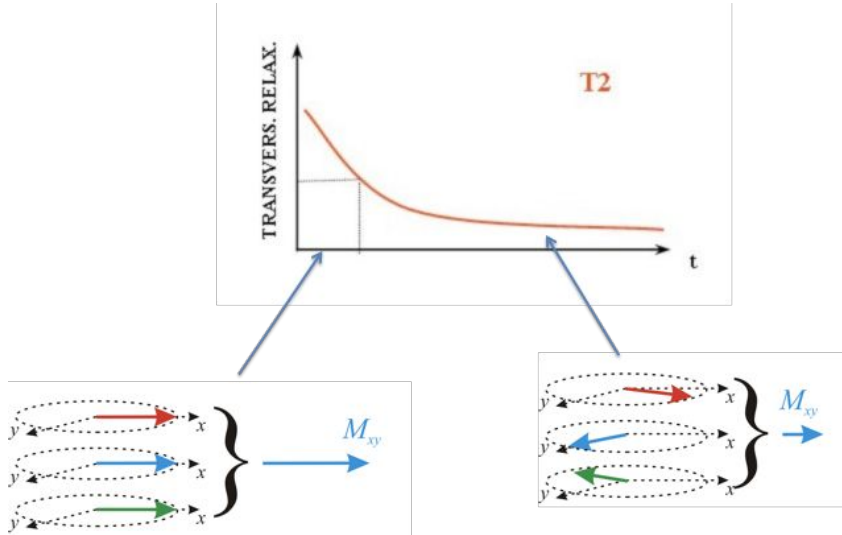


Oxyhemoglobin

Deoxyhemoglobin



# More deoxyhemoglobin, more dephasing...



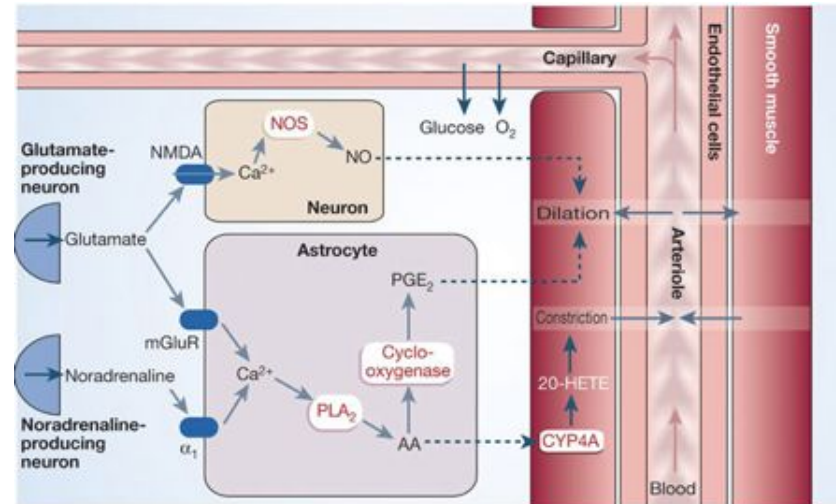
# Local Activity↑, Oxygenation↑

## Focal physiological uncoupling of cerebral blood flow and oxidative metabolism during somatosensory stimulation in human subjects

(positron emission tomography)

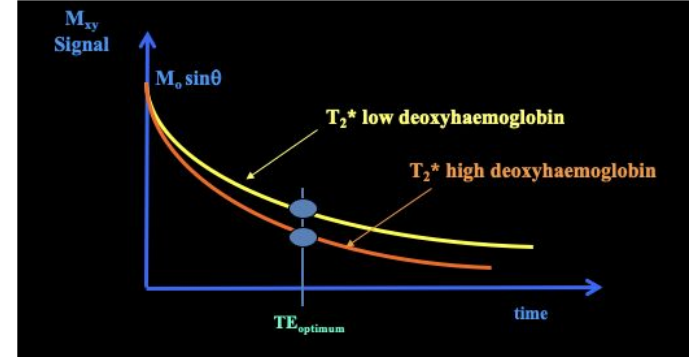
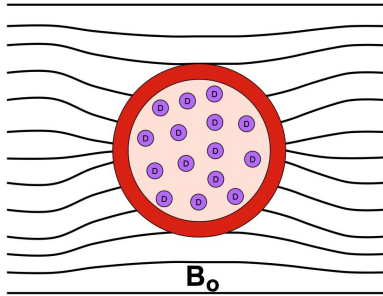
PETER T. FOX<sup>\*†‡</sup> AND MARCUS E. RAICHLE<sup>\*†</sup>

- “...augmentation of cerebral blood flow (29% mean) far exceeded the concomitant local increase in tissue metabolic rate (mean, 5%)...”



*Peppiatt & Attwell, 2004*

# A thing changes $T_2^*$ signal *in vivo*



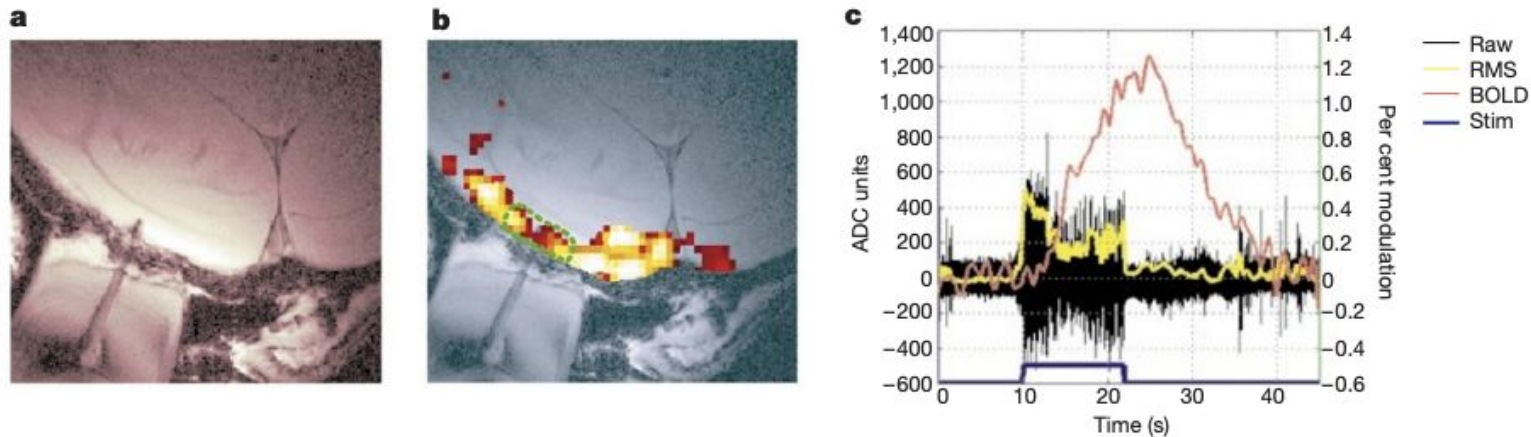
Biological Events  $\longrightarrow$  Blood Oxygenation  $\longrightarrow$  Signal



# Neurophysiological investigation of the basis of the fMRI signal

Nikos K. Logothetis, Jon Pauls, Mark Augath, Torsten Trinath & Axel Oeltermann

Max Planck Institute for Biological Cybernetics, Spemannstrasse 38, 72076 Tuebingen, Germany

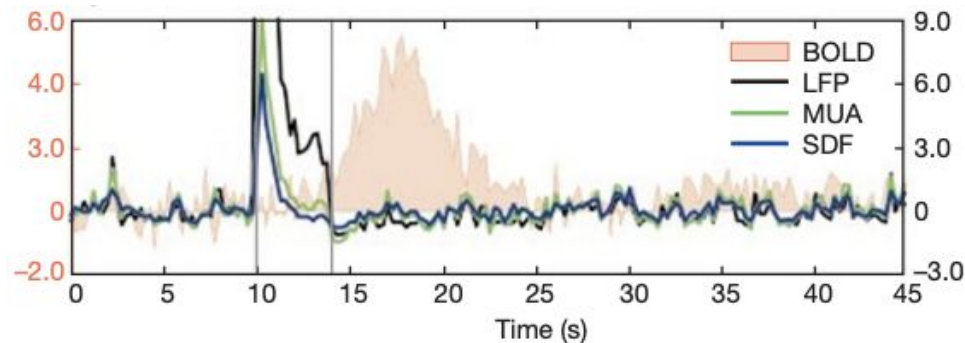




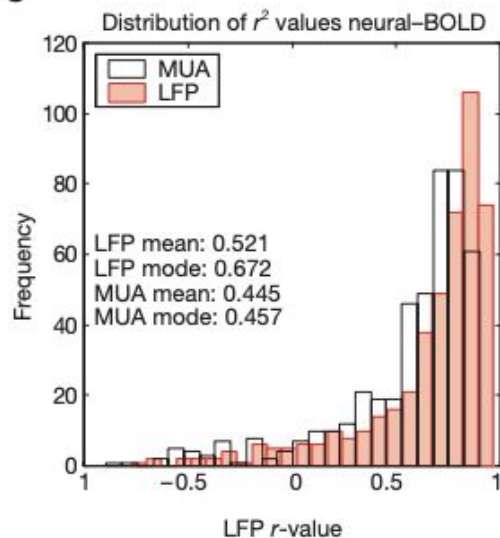
# Neurophysiological investigation of the basis of the fMRI signal

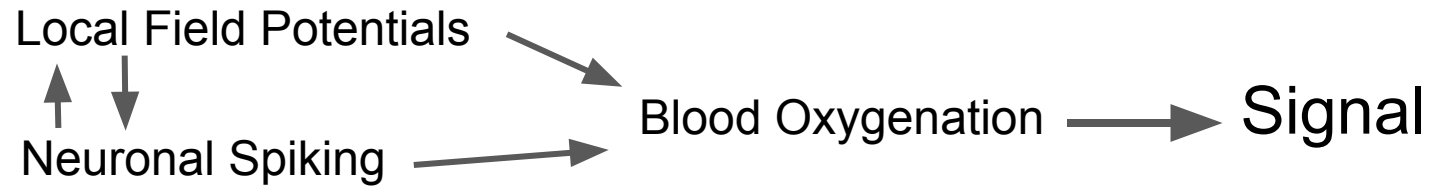
Nikos K. Logothetis, Jon Pauls, Mark Augath, Torsten Trinath & Axel Oeltermann

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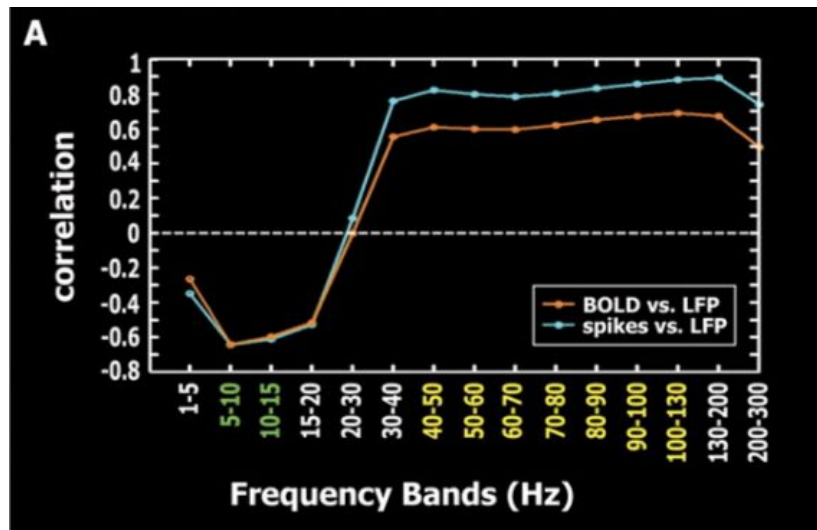


**c**

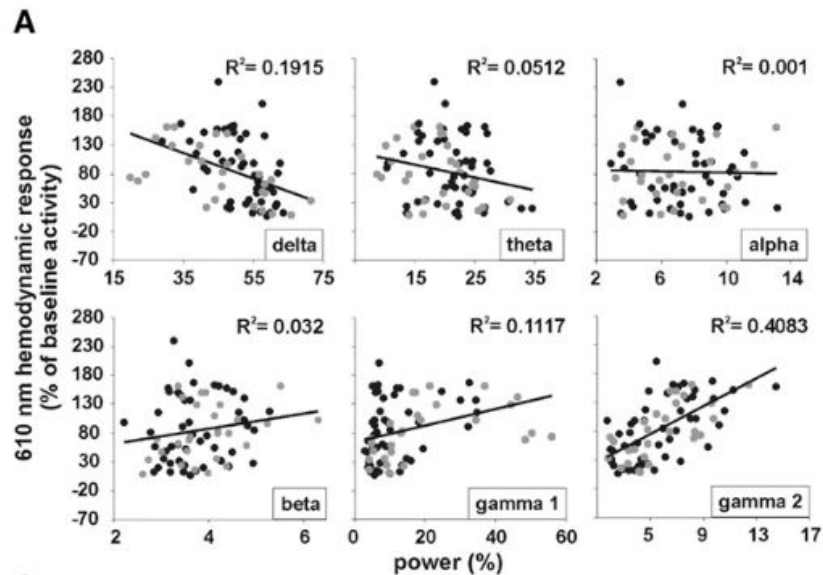




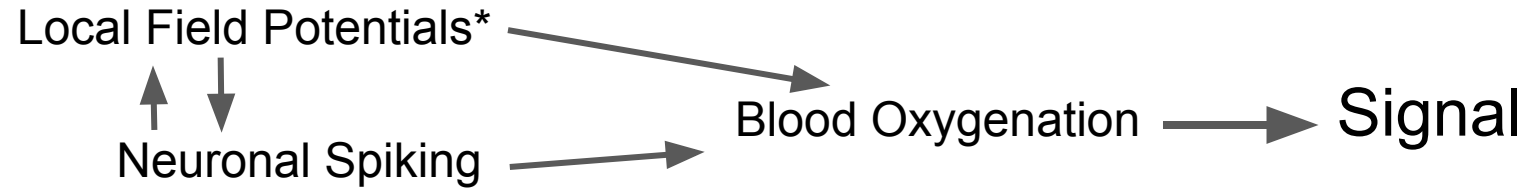
# Is there specificity?



*Mukamel et al., 2005*

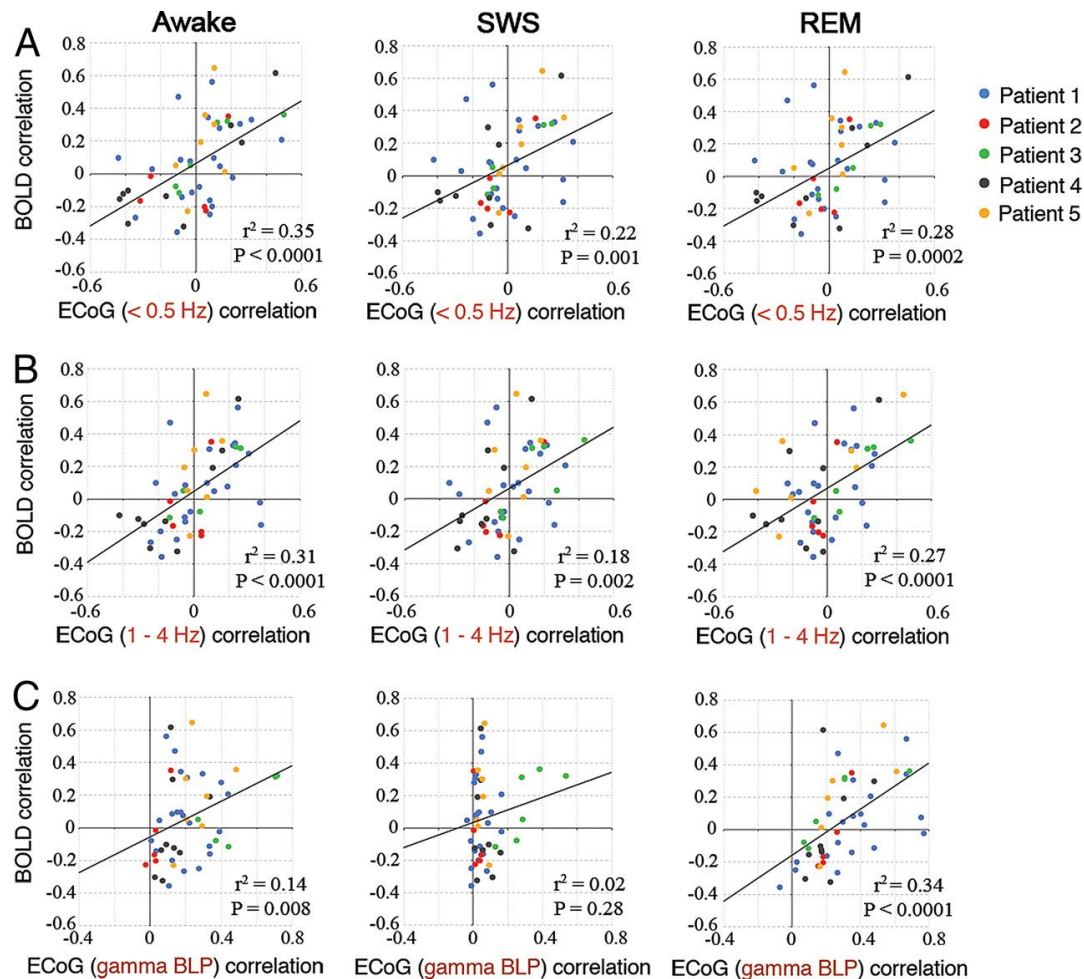


*Niessing et al., 2005*



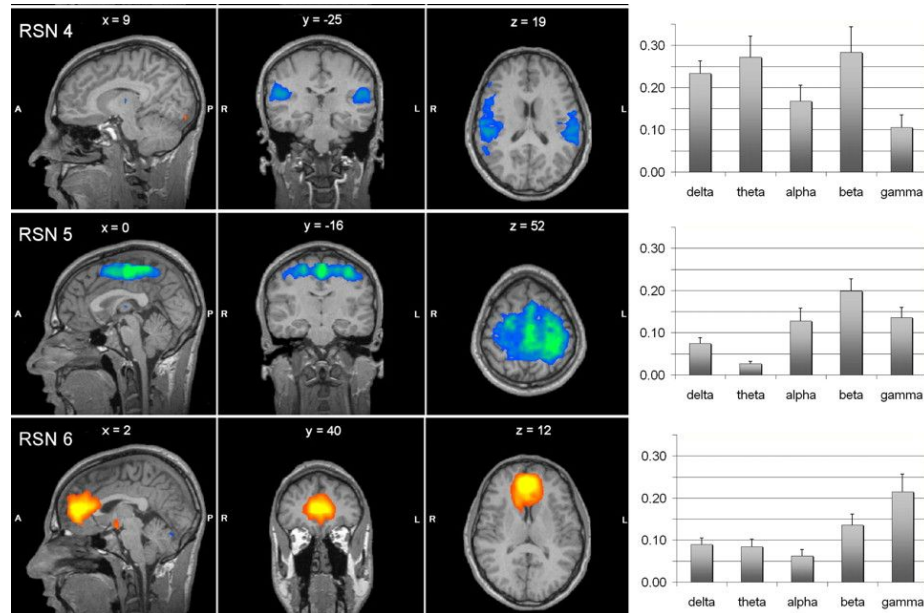
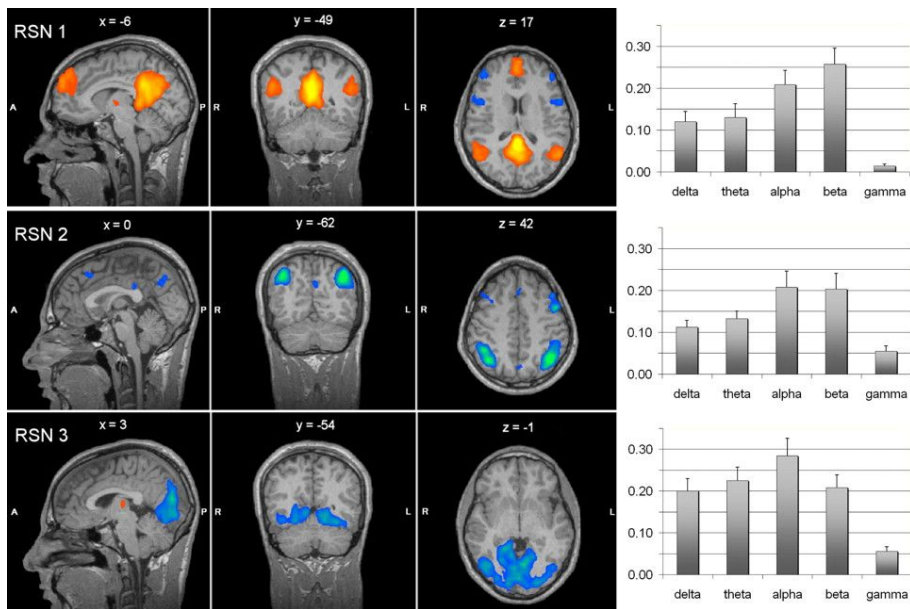
\*Frequency dependent

# Specific to state?

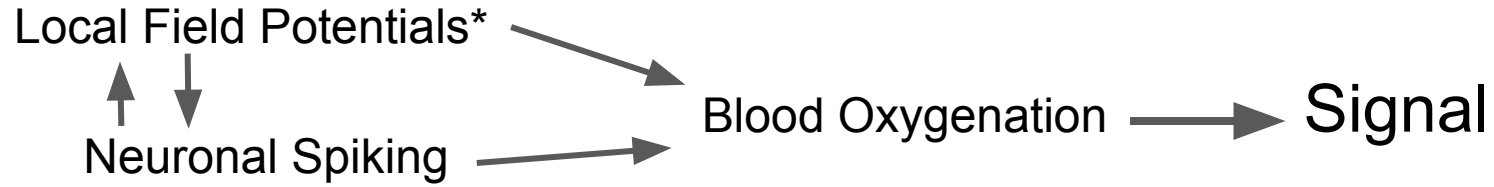


*He et al., 2008*

# Specific to Resting State Network?



*Mantini et al., 2007*

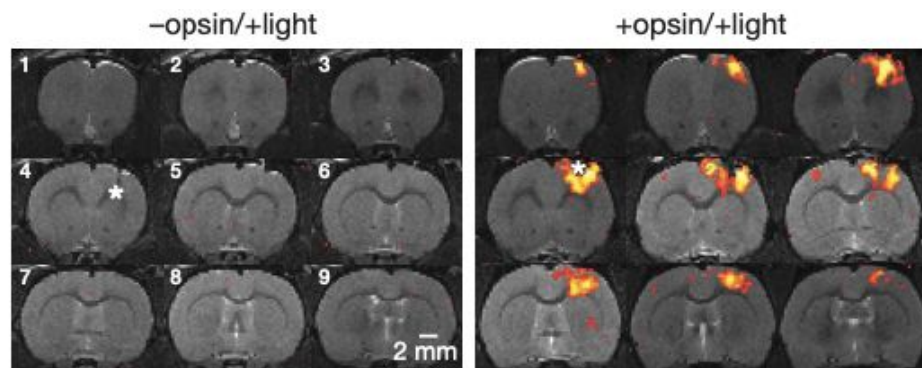


\*Frequency, Brain State, and Brain Area dependent

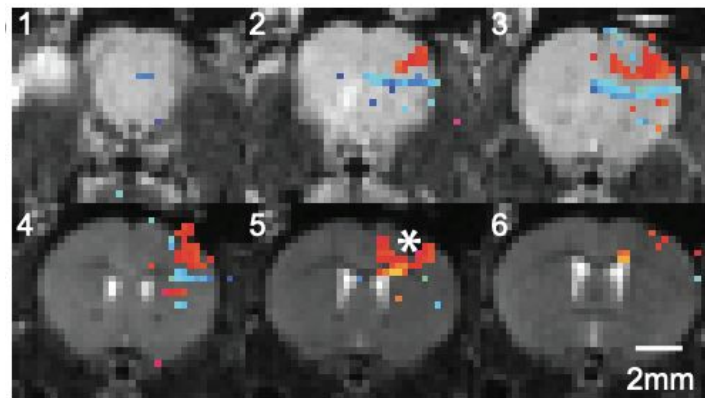


# Global and local fMRI signals driven by neurons defined optogenetically by type and wiring

Jin Hyung Lee<sup>1,2\*</sup>, Remy Durand<sup>2\*</sup>, Viviana Gradinaru<sup>2</sup>, Feng Zhang<sup>2</sup>, Inbal Goshen<sup>2</sup>, Dae-Shik Kim<sup>3,4</sup>, Lief E. Fenno<sup>2</sup>, Charu Ramakrishnan<sup>2</sup> & Karl Deisseroth<sup>2,5,6,7</sup>



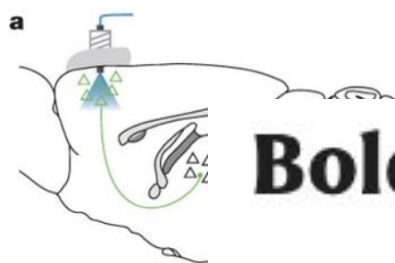
Excitatory



Inhibitory

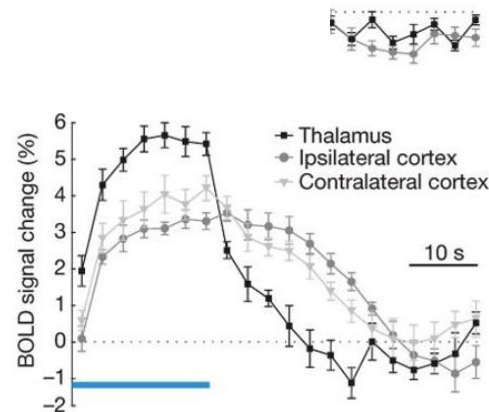
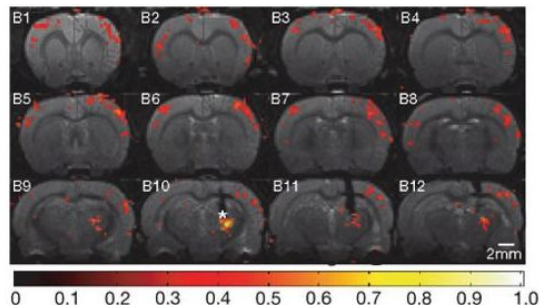
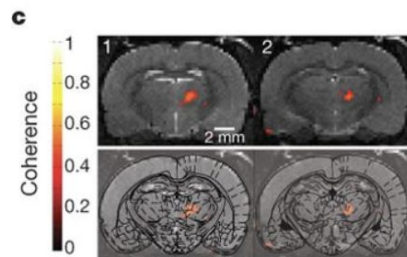
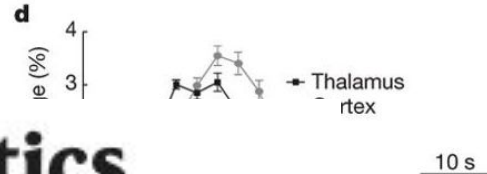
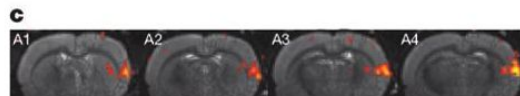
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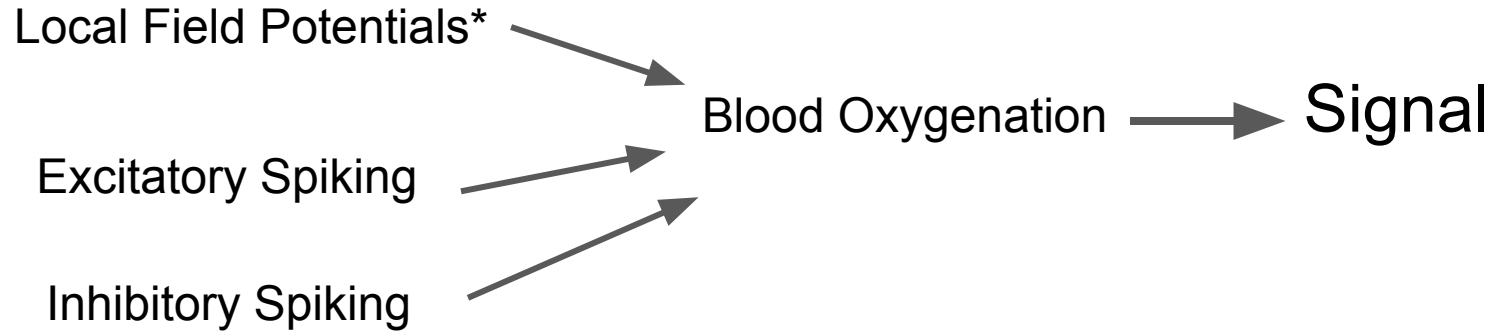
Jin Hyung Lee<sup>1,2\*</sup>, Remy Durand<sup>2\*</sup>, Viviana Gradinaru<sup>2</sup>, Feng Zhang<sup>2</sup>, Inbal Goshen<sup>2</sup>, Dae-Shik Kim<sup>3,4</sup>, Lief E. Fenno<sup>2</sup>, Charu Ramakrishnan<sup>2</sup> & Karl Deisseroth<sup>2,5,6,7</sup>



## Bold claims for optogenetics

Nikos K. Logothetis





\*Frequency, Brain State, and Brain Area dependent

# Cortex-wide BOLD fMRI activity reflects locally-recorded slow oscillation-associated calcium waves



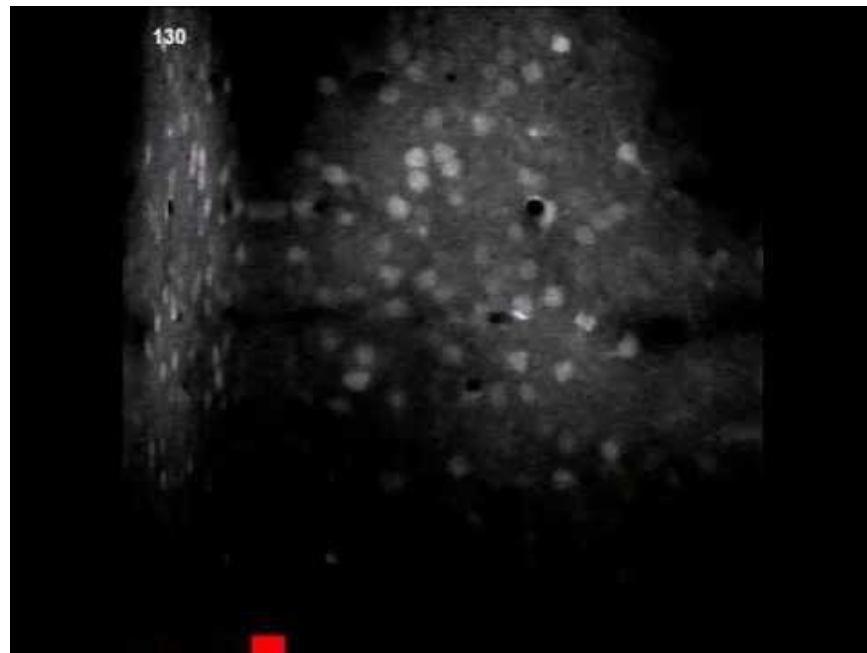
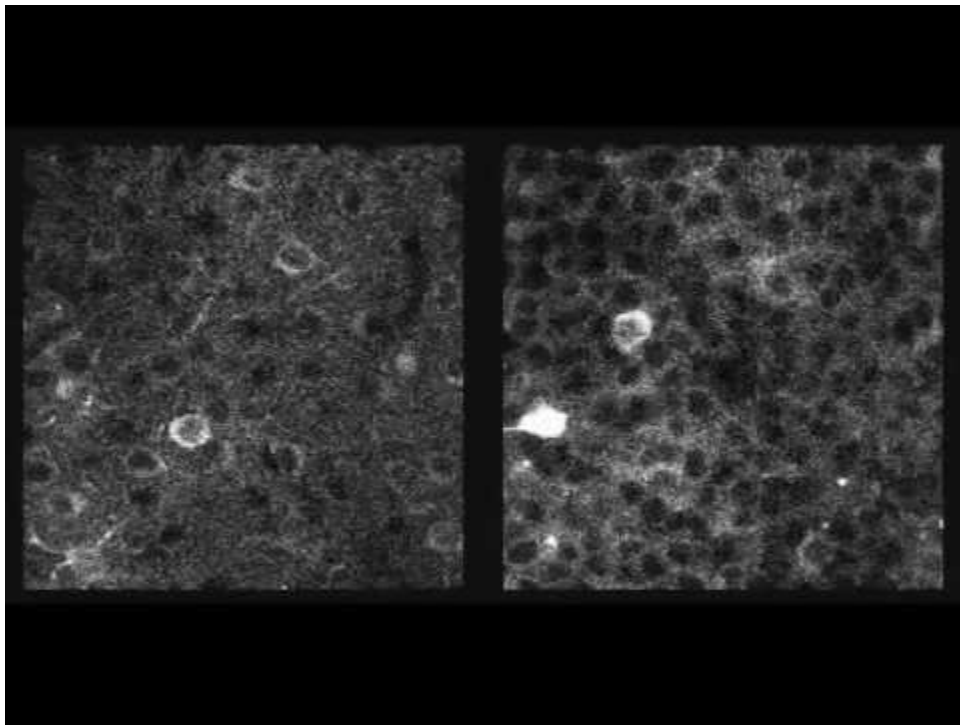
Miriam Schwalm, Florian Schmid, Lydia Wachsmuth, Hendrik Backhaus, Andrea Kronfeld, Felipe Aedo  
Jury, Pierre-Hugues Prouvot, Consuelo Fois, Franziska Albers [see all »](#)

Johannes Gutenberg-University Mainz, Germany; Goethe University Frankfurt am Main, Germany; University Hospital  
Münster, Germany

# Transient neuronal coactivations embedded in globally propagating waves underlie resting-state functional connectivity

Teppei Matsui<sup>a,b,1,2</sup>, Tomonari Murakami<sup>a,b,1</sup>, and Kenichi Ohki<sup>a,b,c,2</sup>

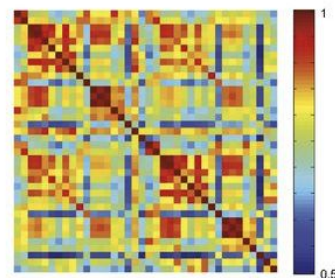
# Calcium



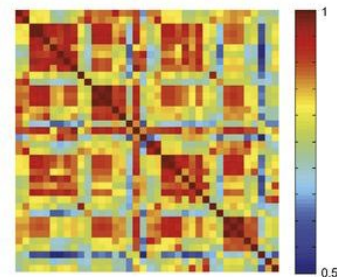
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**B** ROI-based FC matrix in CaS (zero-lag temporal correlation)

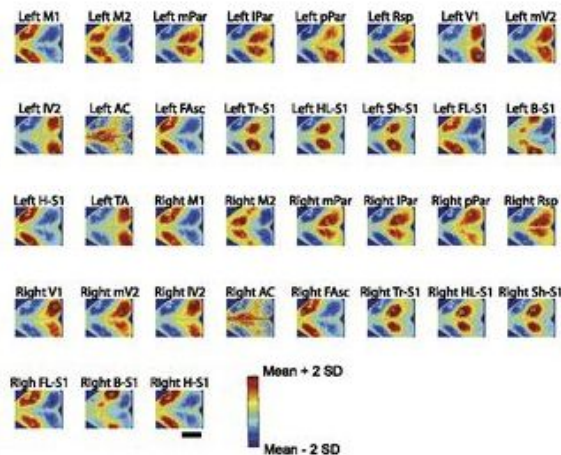


**D** ROI-based FC matrix in HemoS (zero-lag temporal correlation)



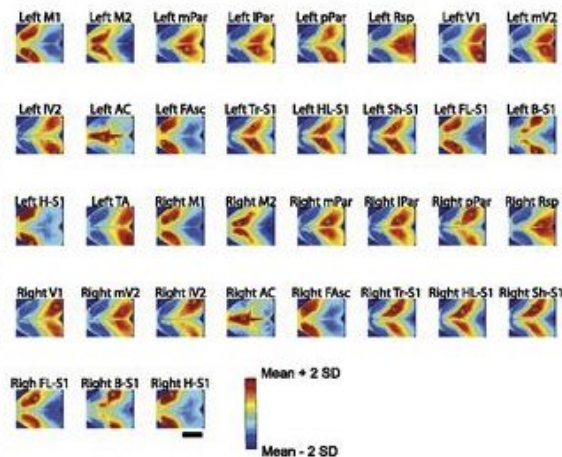
**E**

Ca-FC Maps

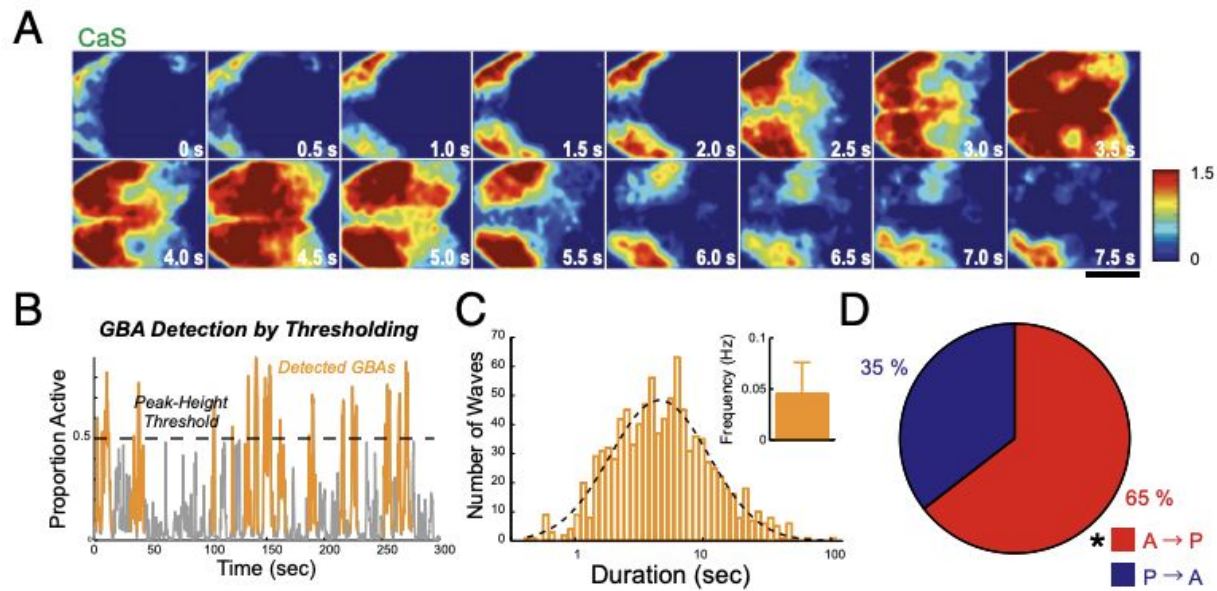


**F**

Hemo-FC Maps

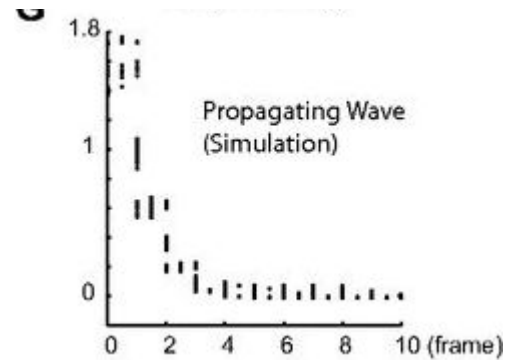
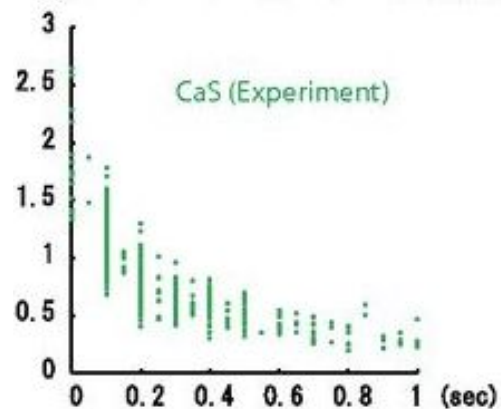
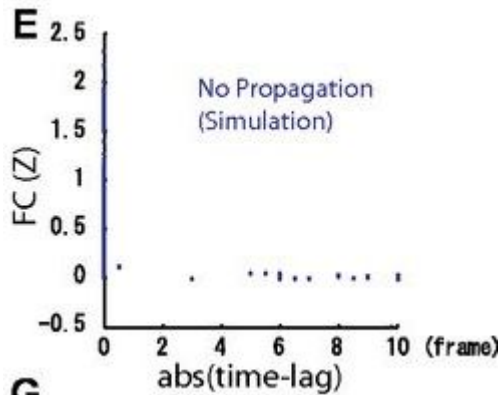








*“...FC arising from propagating activity rather than that arising from nonpropagating flash-like coactivations...”*

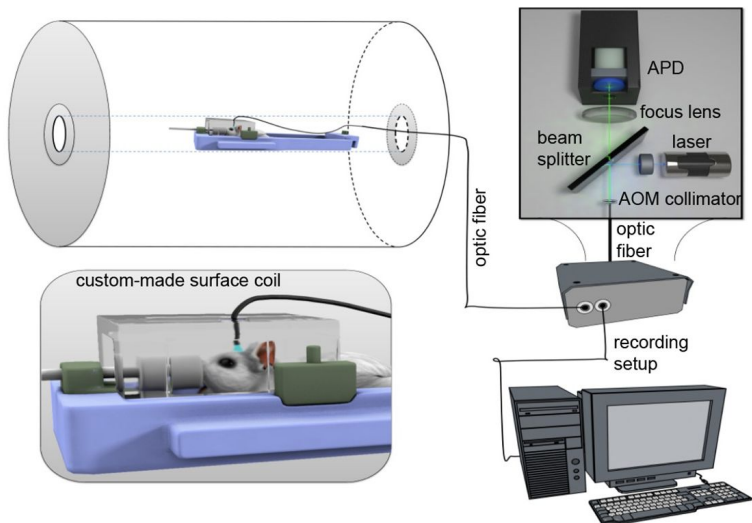


# Cortex-wide BOLD fMRI activity reflects locally-recorded slow oscillation-associated calcium waves

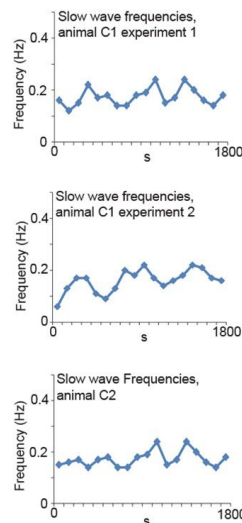


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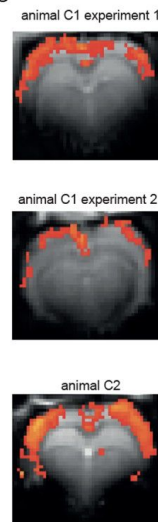
A



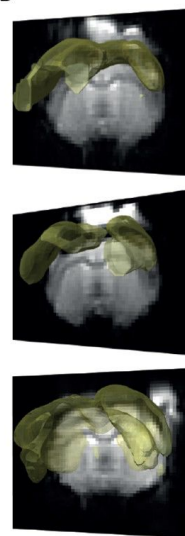
B



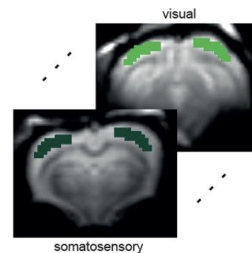
C



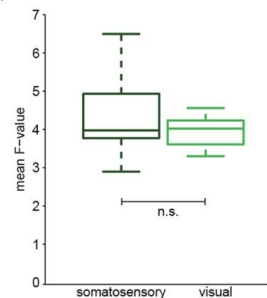
D

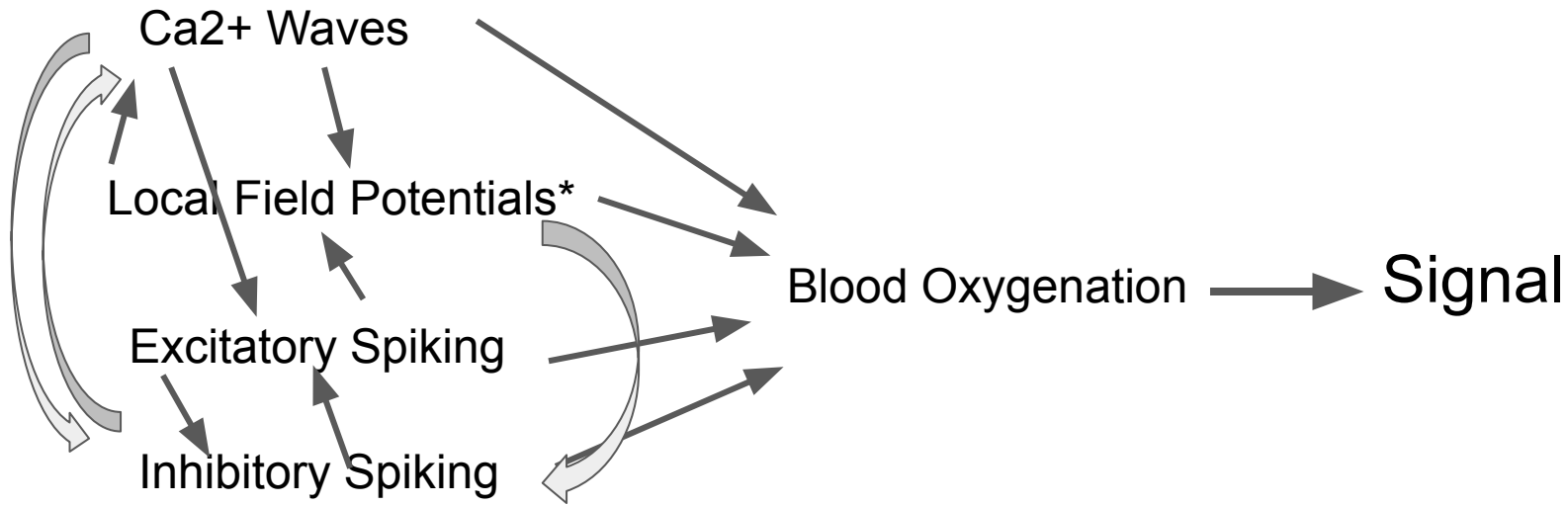


E



F

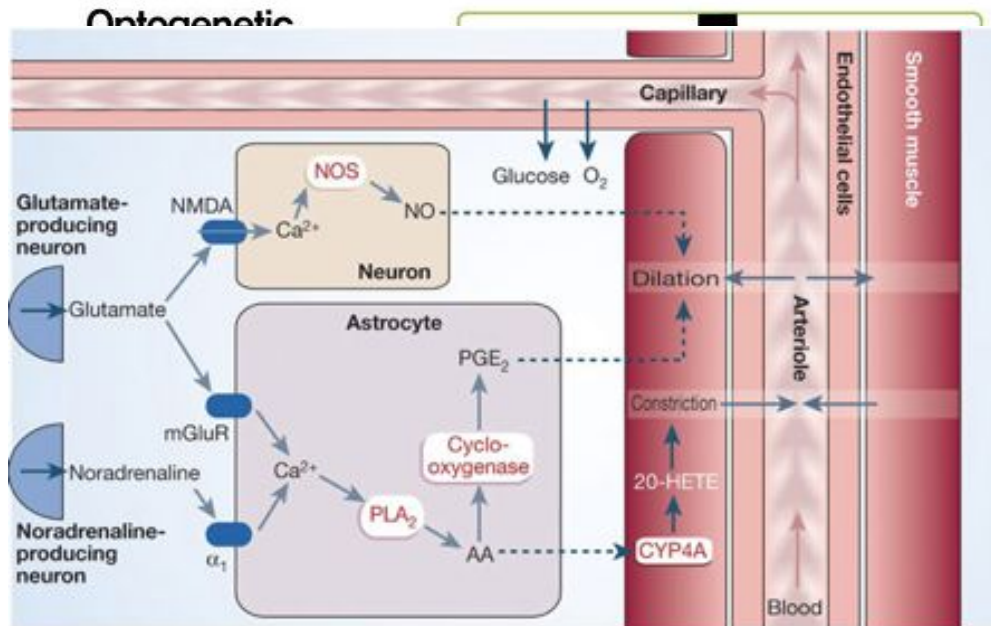




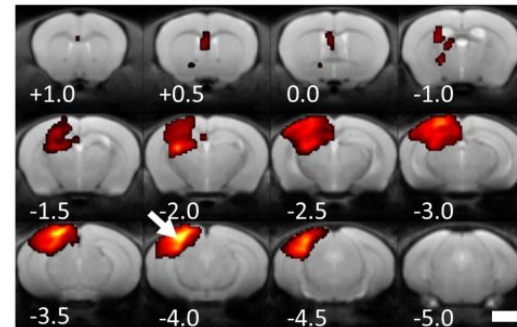
\*Frequency, Brain State, and Brain Area dependent

# Optogenetic astrocyte activation evokes BOLD fMRI response with oxygen consumption without neuronal activity modulation

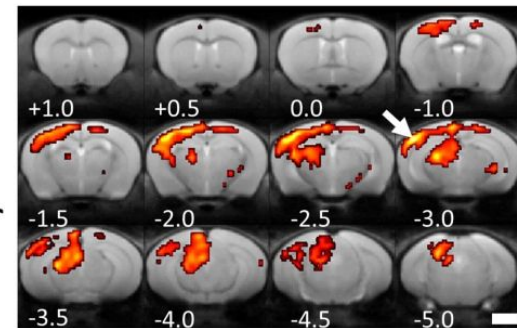
Norio Takata✉, Yuki Sugiura, Keitaro Yoshida, Miwako Koizumi, Nishida Hiroshi, Kurara Honda, Ryutaro Yano, Yuji Komaki, Ko Matsui, Makoto Suematsu, Masaru Mimura ... [See all authors](#) ✓

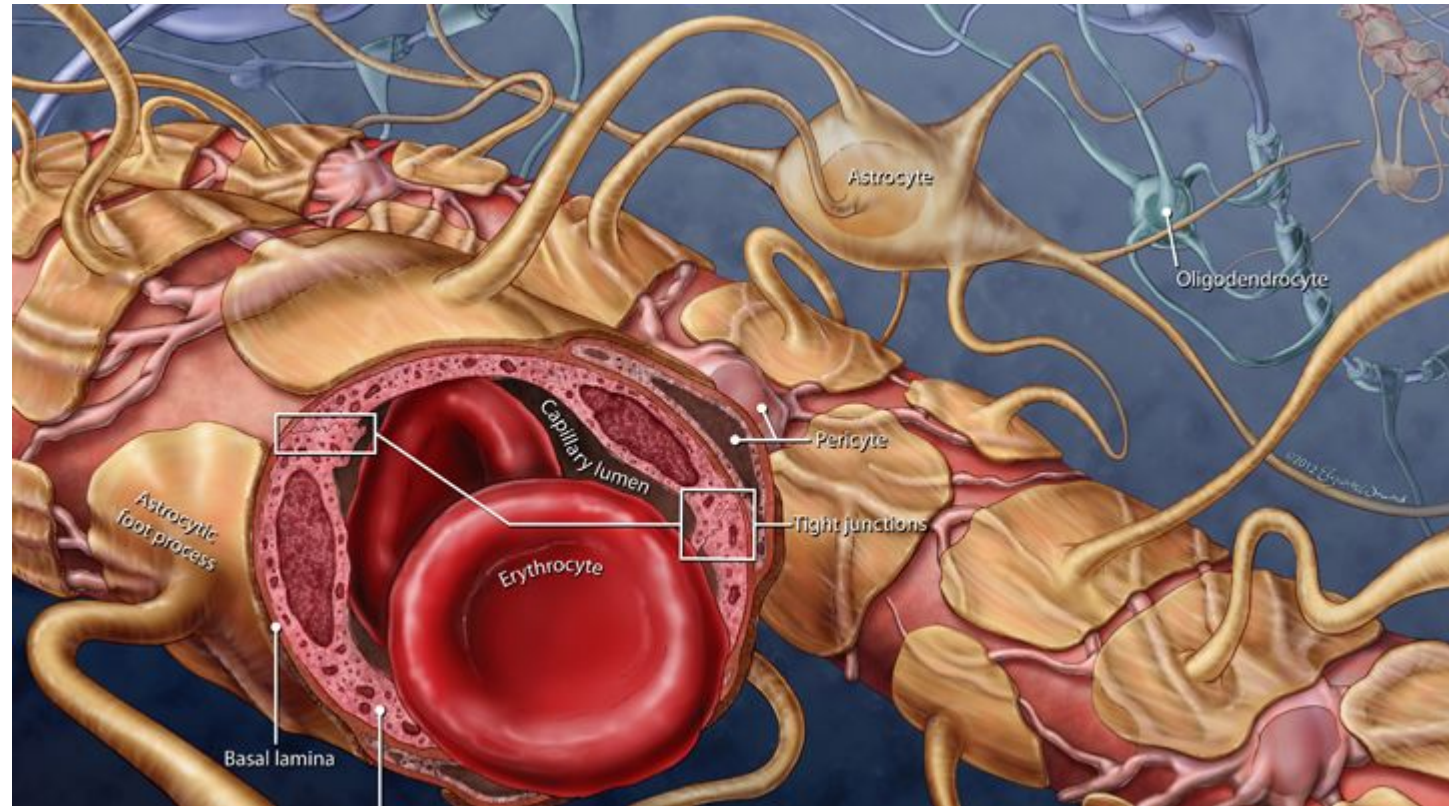


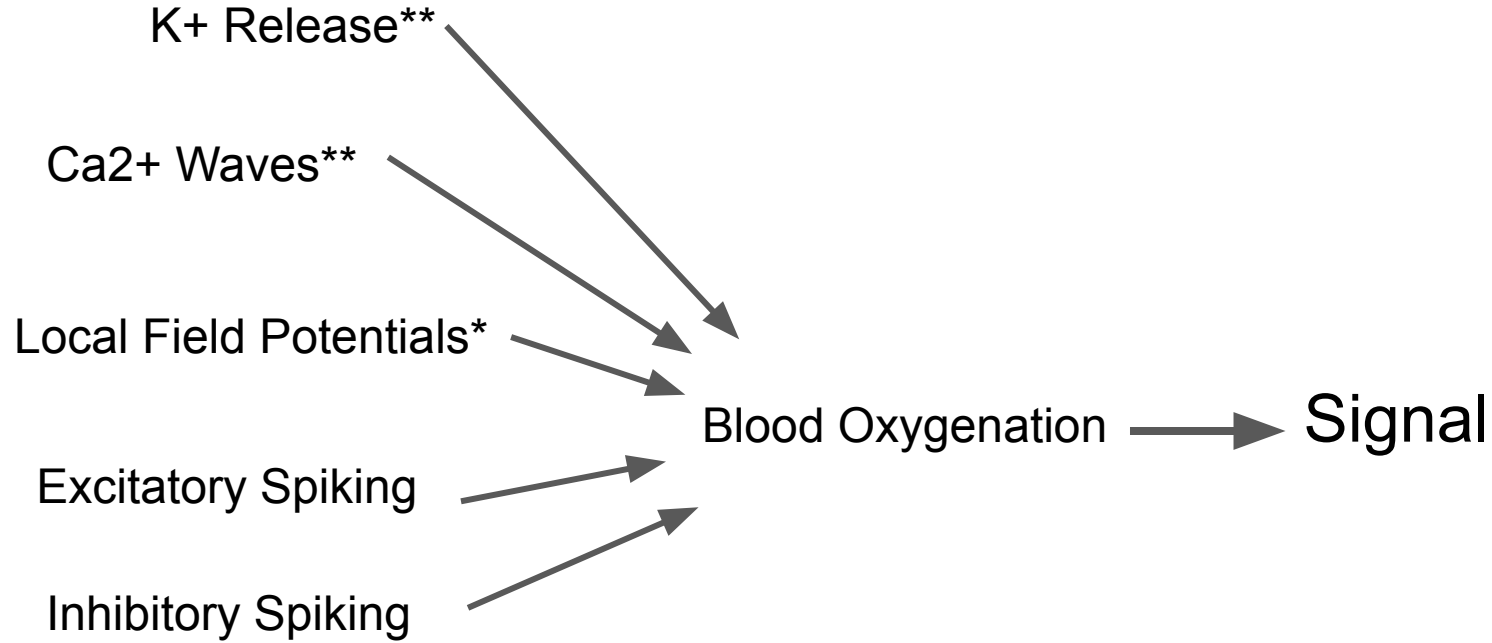
**a** Neuron-ChR2



**c** Astrocyte-ChR2







\*Frequency, Brain State, and Brain Area dependent

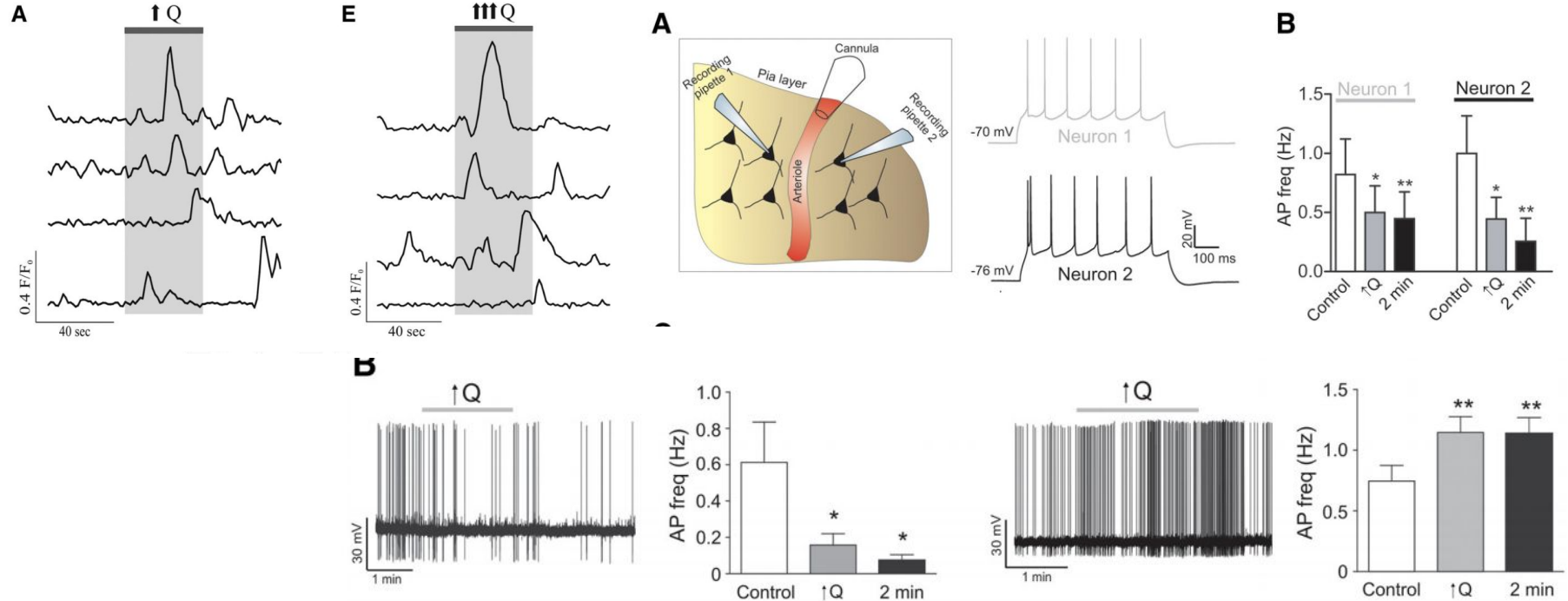
\*\*Neuronal and Astrocytic



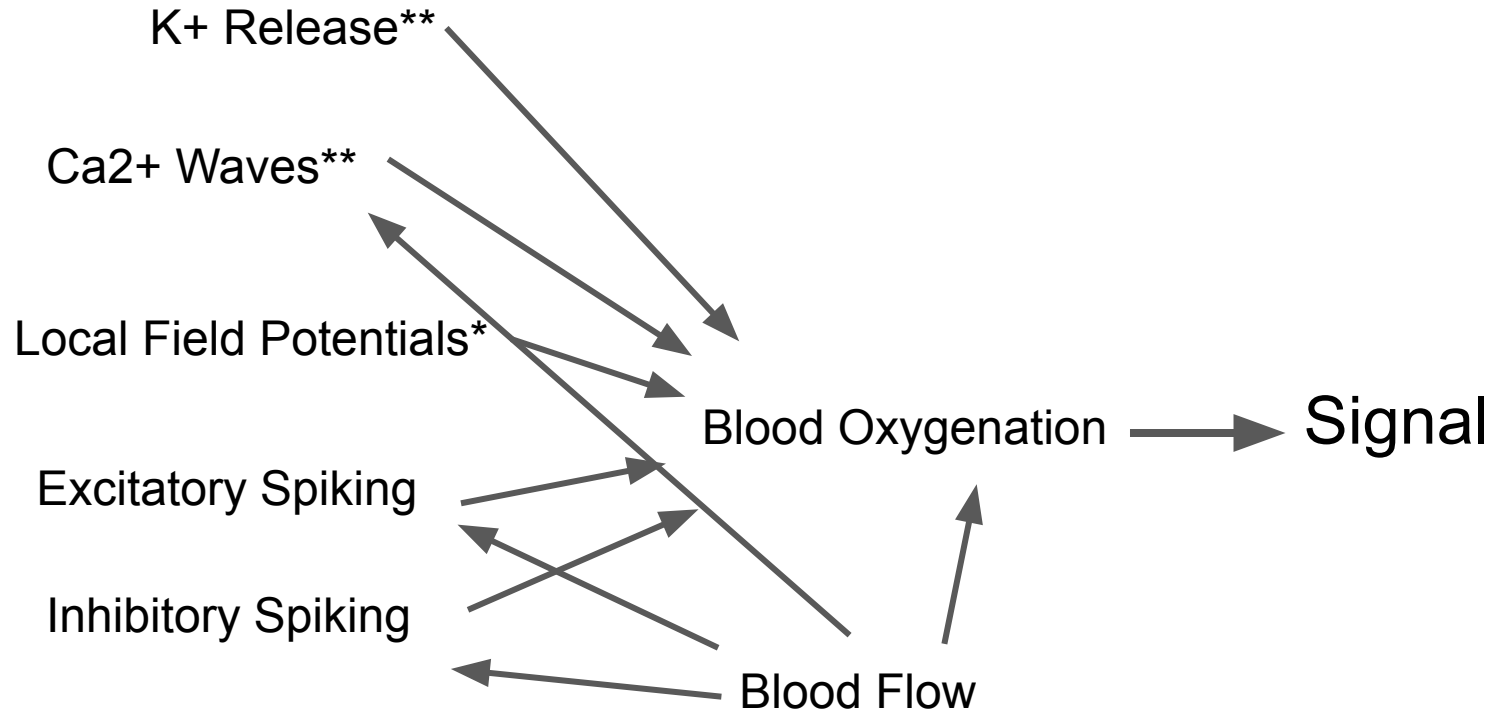
# Vasculo-Neuronal Coupling: Retrograde Vascular Communication to Brain Neurons

Ki Jung Kim, Juan Ramiro Diaz, Jennifer A. Iddings, and Jessica A. Filosa

Department of Physiology, Augusta University, Augusta, Georgia 30912







\*Frequency, Brain State, and Brain Area dependent

\*\*Neuronal and Astrocytic

# Individual Differences in Neurovascular Coupling

Trial-by-trial relationship between neural activity, oxygen consumption, and blood flow responses

Kazuto Masamoto <sup>a</sup> , Alberto Vazquez <sup>a</sup>, Ping Wang <sup>a</sup>, Seong-Gi Kim <sup>a, b</sup>

- Hypo/hypertension

Distinctions among real and apparent respiratory motions in human fMRI data

Jonathan D. Power <sup>a</sup> , Charles J. Lynch <sup>b</sup> , Benjamin M. Silver <sup>a</sup> , Marc J. Dubin <sup>c</sup> , Alex Martin <sup>d</sup> , Rebecca M. Jones <sup>a</sup> 

- Breathing (amongst others)

The physiology of developmental changes in BOLD functional imaging signals

Julia J. Harris <sup>1</sup>, Clare Reynell <sup>1</sup>, David Attwell <sup>1</sup> 

- Development

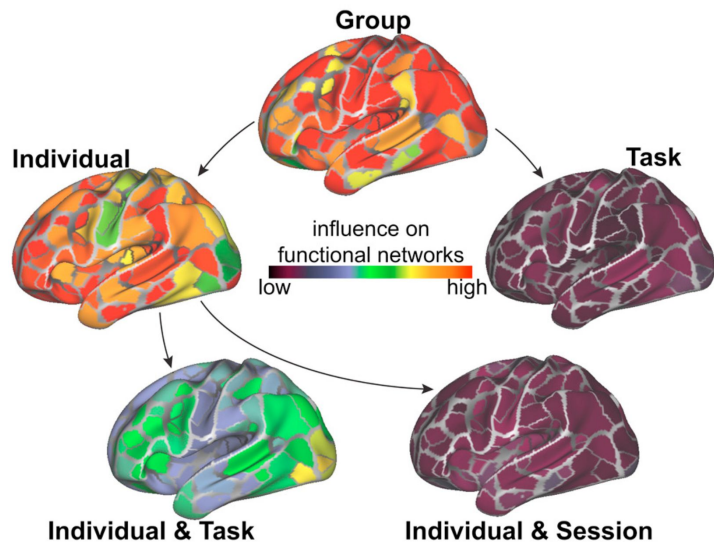
Coupling between gamma oscillation and fMRI signal in the rat somatosensory cortex: Its dependence on systemic physiological parameters

Akira Sumiyoshi <sup>a</sup> , Hideaki Suzuki <sup>b</sup>, Takeshi Ogawa <sup>a</sup>, Jorge J. Riera <sup>a</sup>, Hiroaki Shimokawa <sup>b</sup>, Ryuta Kawashima <sup>a</sup>

- Heart rate

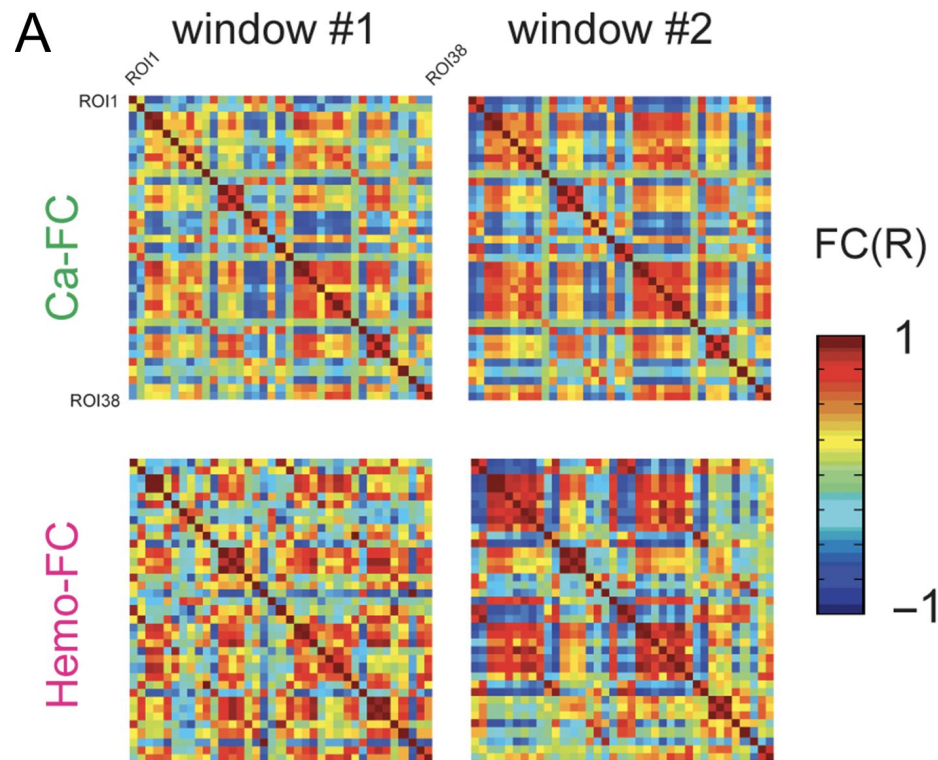
# Connectivity

Variance in human functional brain networks attributable to:



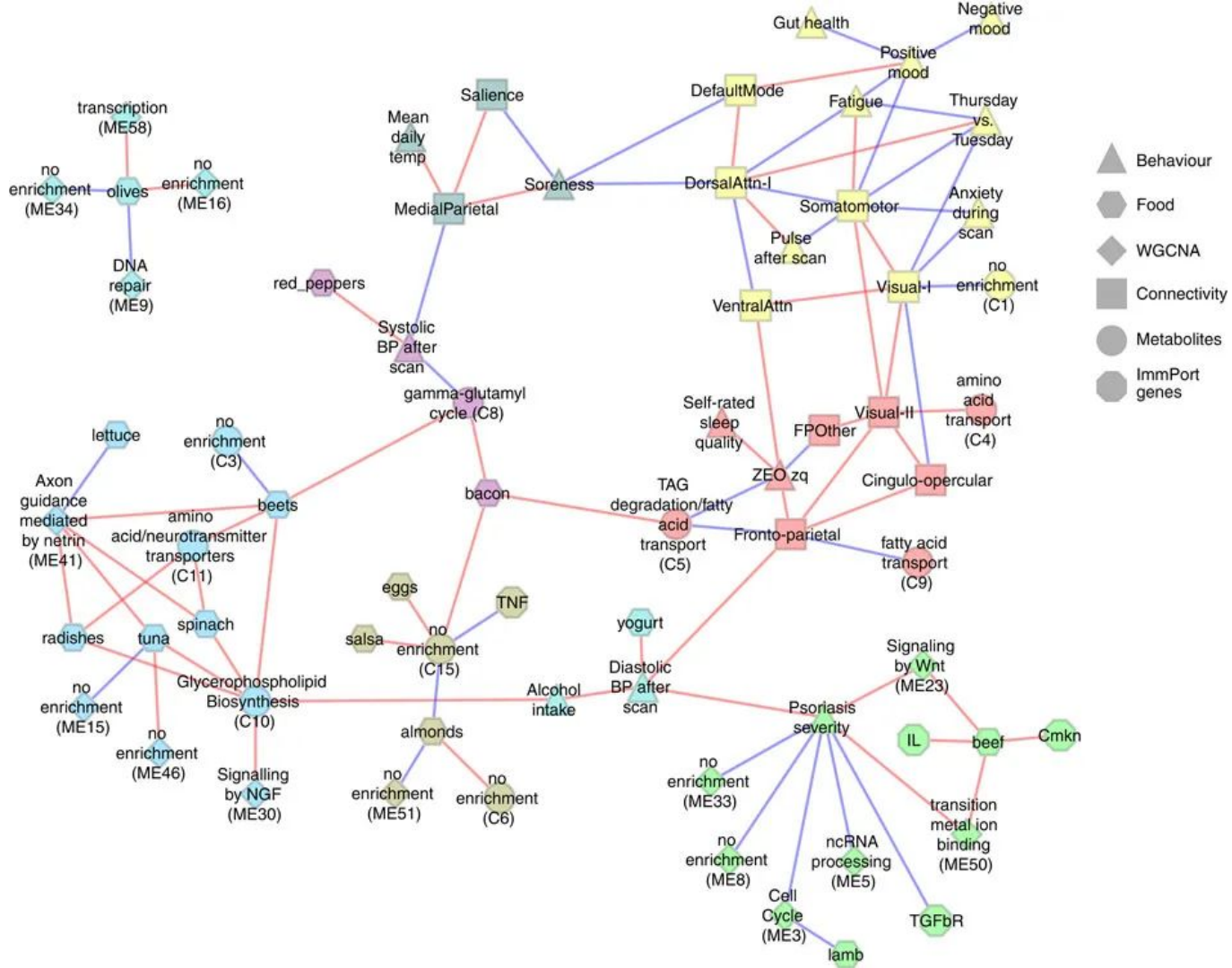
Stability and sensitivity to individual differences suggests utility in precision medicine

Gratton et al., 2018



Matsui, Murakami, & Ohki, 2019

# Connectivity



*Poldrack et al., 2015*

# Has our understanding of BOLD Matured?

- Frequency bands
- Sleep
- Between subject variability
- Between region variability

