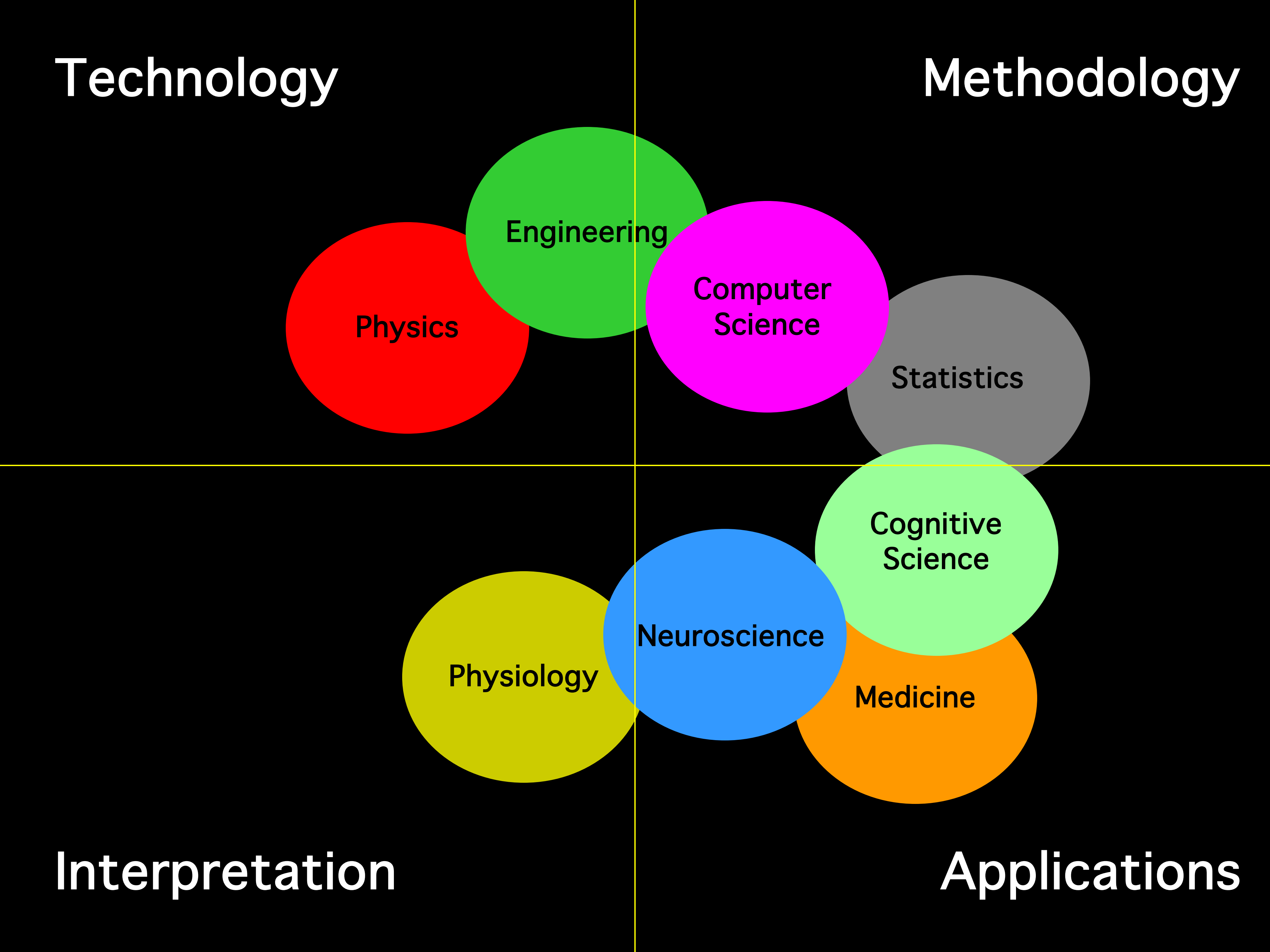
Functional MRI Mechanisms and Limits

Peter A. Bandettini, Ph.D

bandettini@nih.gov

Unit on Functional Imaging Methods
&
3T Neuroimaging Core Facility

Laboratory of Brain and Cognition
National Institute of Mental Health



Technology

Methodology

Engineering

Physics

Computer Science

Statistics

Cognitive Science

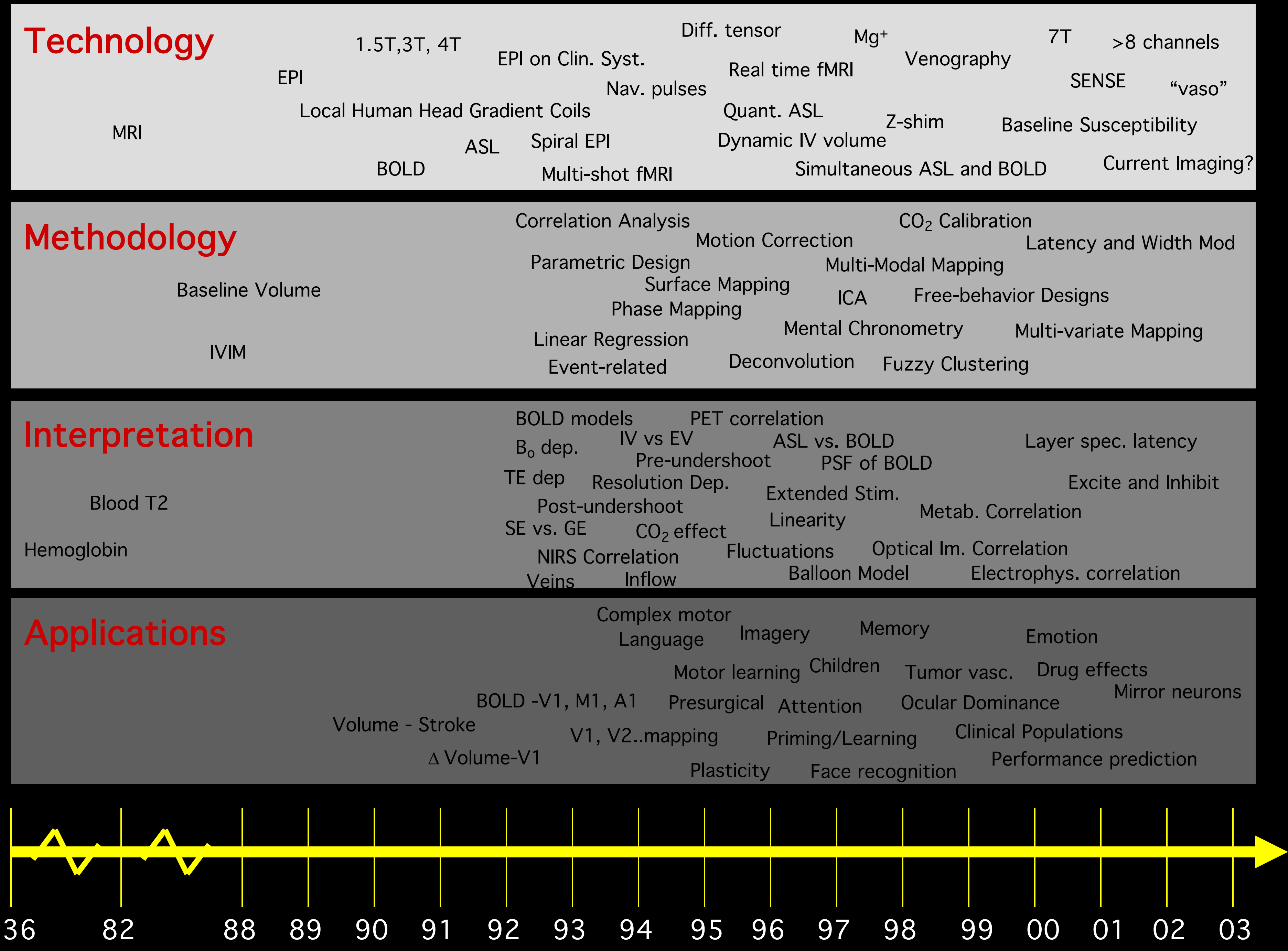
Neuroscience

Physiology

Medicine

Interpretation

Applications



Technology

MRI
EPI
1.5T,3T, 4T
Local Human Head Gradient Coils
BOLD
ASL
EPI on Clin. Syst.
Spiral EPI
Multi-shot fMRI
Nav. pulses
Diff. tensor
Real time fMRI
Quant. ASL
Dynamic IV volume
Simultaneous ASL and BOLD
Mg^+
Venography
Z-shim
7T
SENSE
Baseline Susceptibility
>8 channels
“vaso”
Current Imaging?

Methodology

Baseline Volume
IVIM
Correlation Analysis
Parametric Design
Surface Mapping
Phase Mapping
Linear Regression
Event-related
Motion Correction
Deconvolution
Multi-Modal Mapping
ICA
Mental Chronometry
Fuzzy Clustering
CO_2 Calibration
Free-behavior Designs
Latency and Width Mod
Multi-variate Mapping

Interpretation

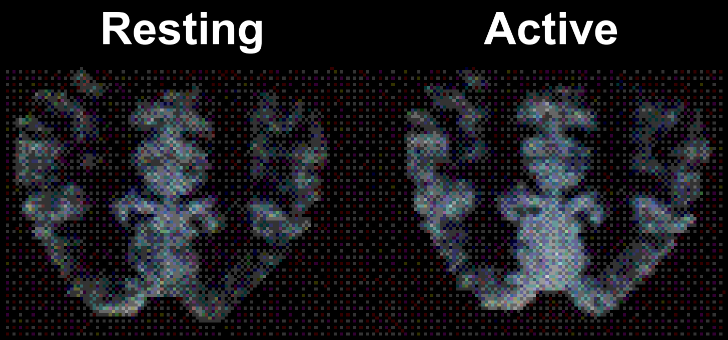
Blood T2
Hemoglobin
BOLD models
B_o dep.
TE dep
SE vs. GE
Veins
IV vs EV
Resolution Dep.
Post-undershoot
CO_2 effect
NIRS Correlation
Inflow
PET correlation
Pre-undershoot
Fluctuations
ASL vs. BOLD
Extended Stim.
Linearity
Balloon Model
PSF of BOLD
Optical Im. Correlation
Metab. Correlation
Layer spec. latency
Excite and Inhibit
Electrophys. correlation

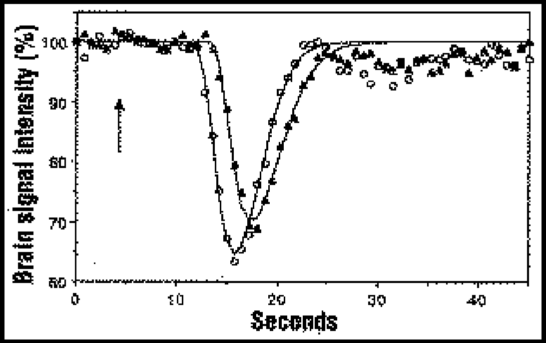
Applications

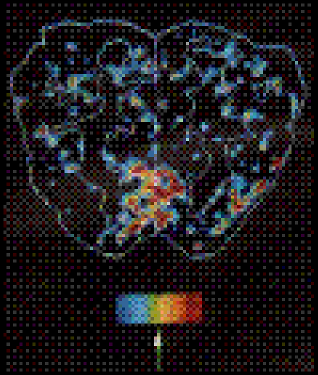
Volume - Stroke
∆ Volume-V1
BOLD -V1, M1, A1
Complex motor
Language
V1, V2..mapping
Motor learning
Presurgical
Plasticity
Imagery
Children
Attention
Priming/Learning
Memory
Face recognition
Tumor vasc.
Ocular Dominance
Clinical Populations
Emotion
Drug effects
Performance prediction
Mirror neurons

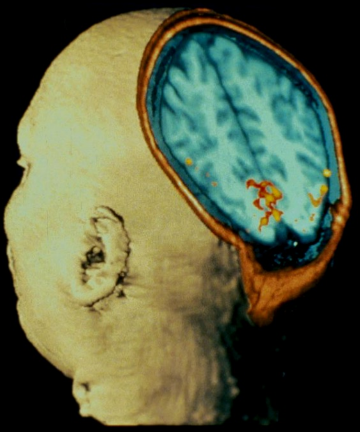
Blood Volume Imaging

Susceptibility Contrast agent bolus injection and time series collection of T2* or T2 - weighted images









Photic Stimulation

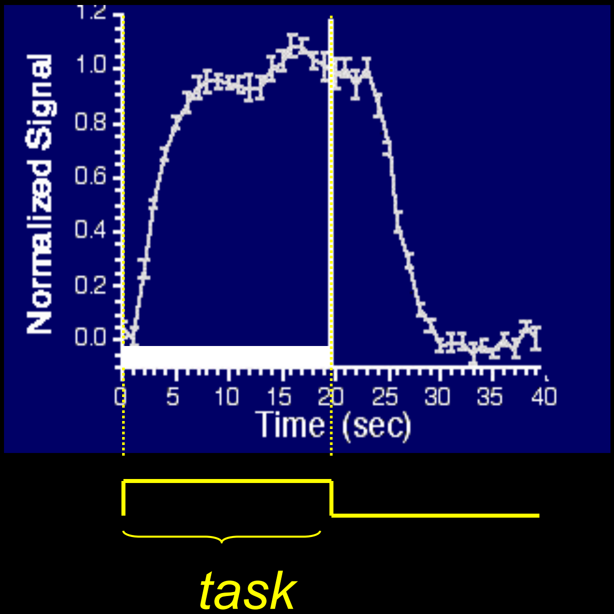
MRI Image showing activation of the Visual Cortex

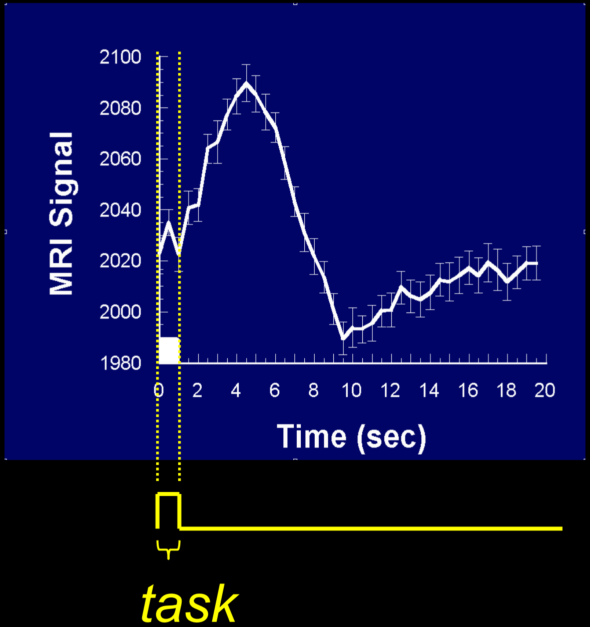
From Belliveau, et al. Science Nov 1991

MSC - perfusion

Blood Oxygenation Imaging

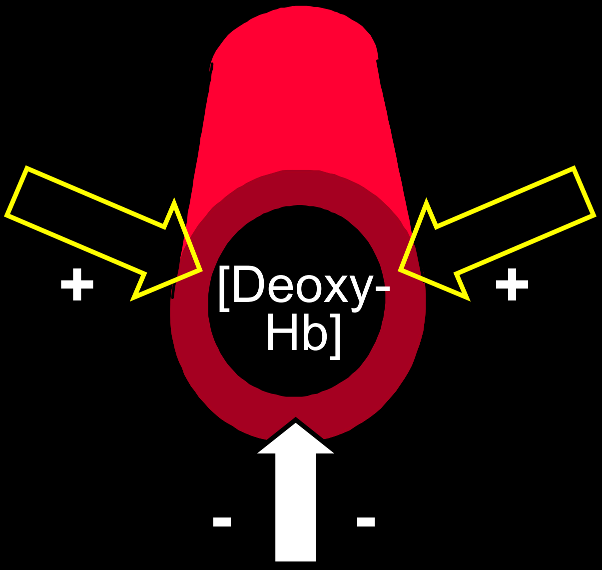
- K. K. Kwong, et al, (1992) "Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation." Proc. Natl. Acad. Sci. USA. 89, 5675-5679.
- S. Ogawa, et al., (1992) "Intrinsic signal changes accompanying sensory stimulation: functional brain mapping with magnetic resonance imaging. Proc. Natl. Acad. Sci. USA." 89, 5951-5955.
- P. A. Bandettini, et al., (1992) "Time course EPI of human brain function during task activation." Magn. Reson. Med 25, 390-397.
- Blamire, A. M., et al. (1992). "Dynamic mapping of the human visual cortex by high-speed magnetic resonance imaging." Proc. Natl. Acad. Sci. USA 89: 11069-11073.





The vascular response

Factors influencing [Deoxy-Hb] concentration



Oxygen consumption

PET

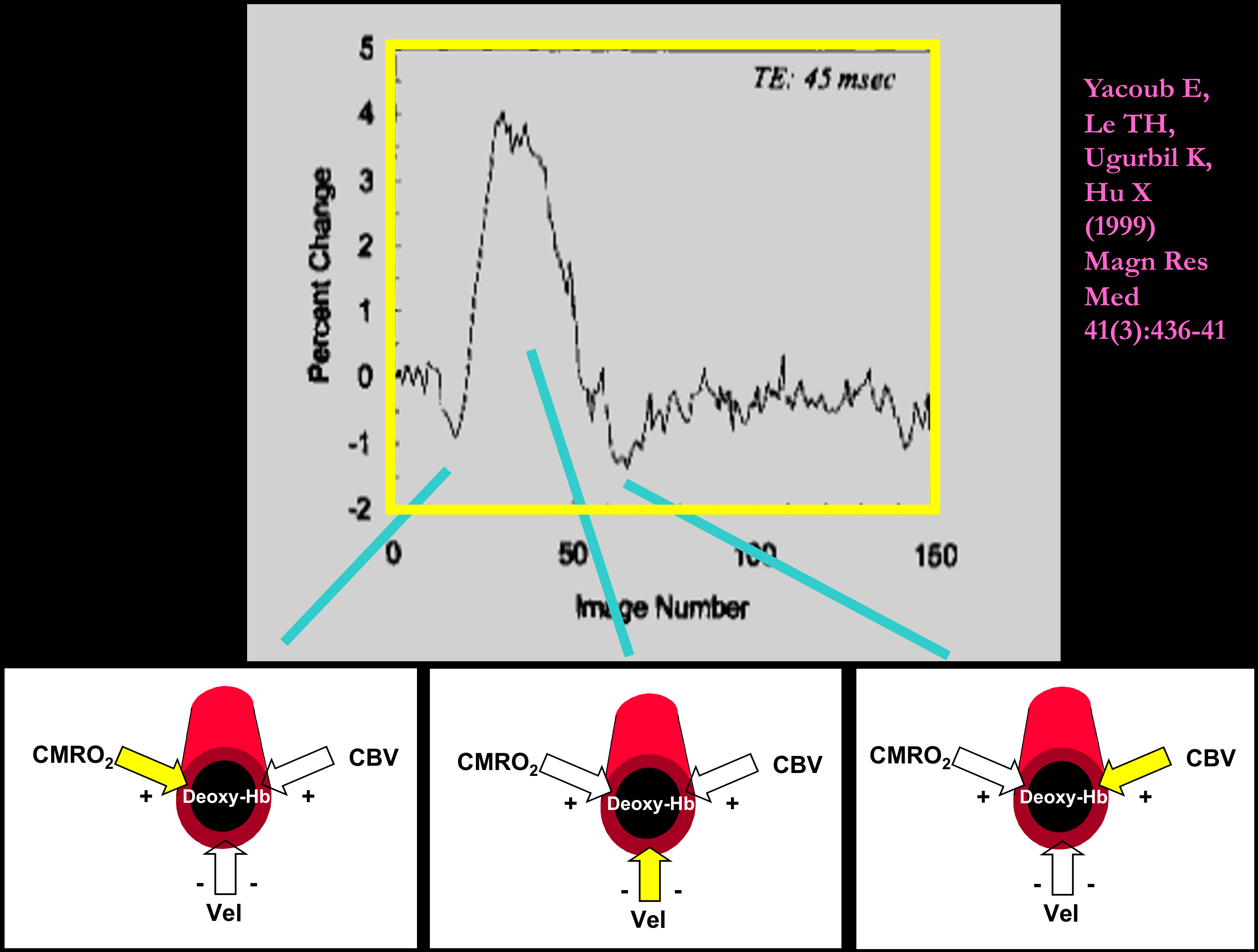
$\Delta CBF >> \Delta CMRO_2$

Blood Volume

Blood Flow Velocity

Courtesy of Arno Villringer

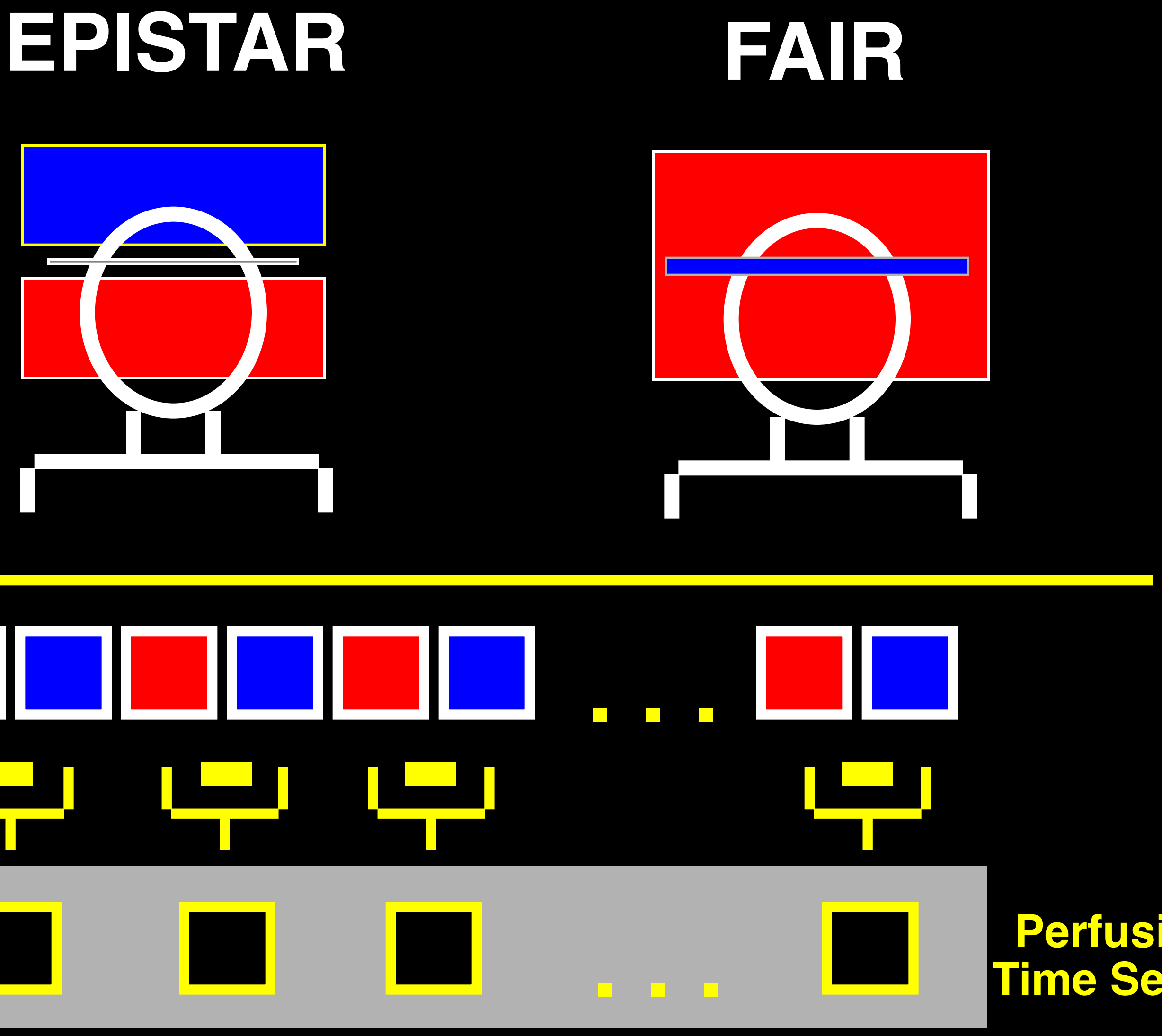
Time course of BOLD signal

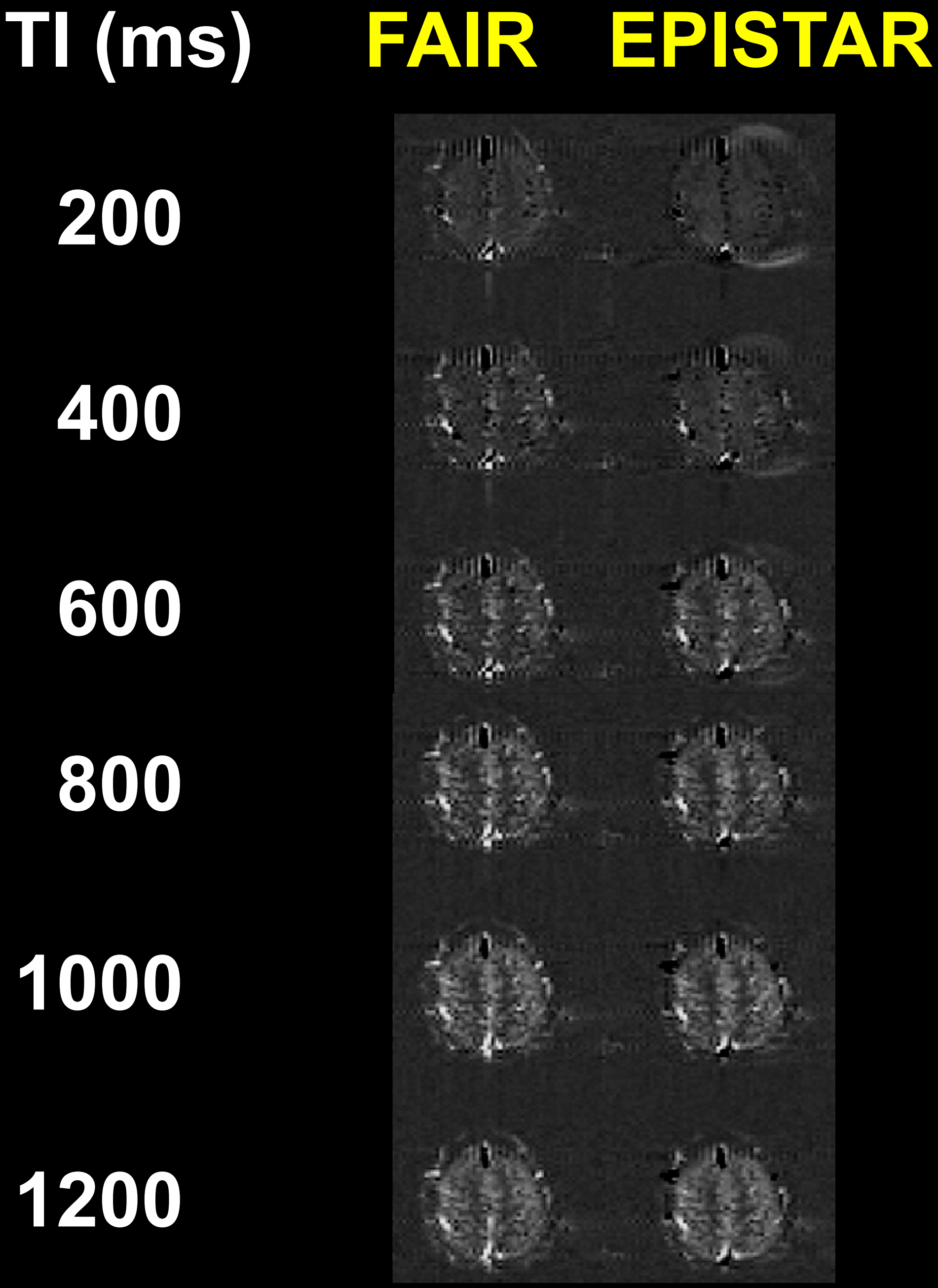


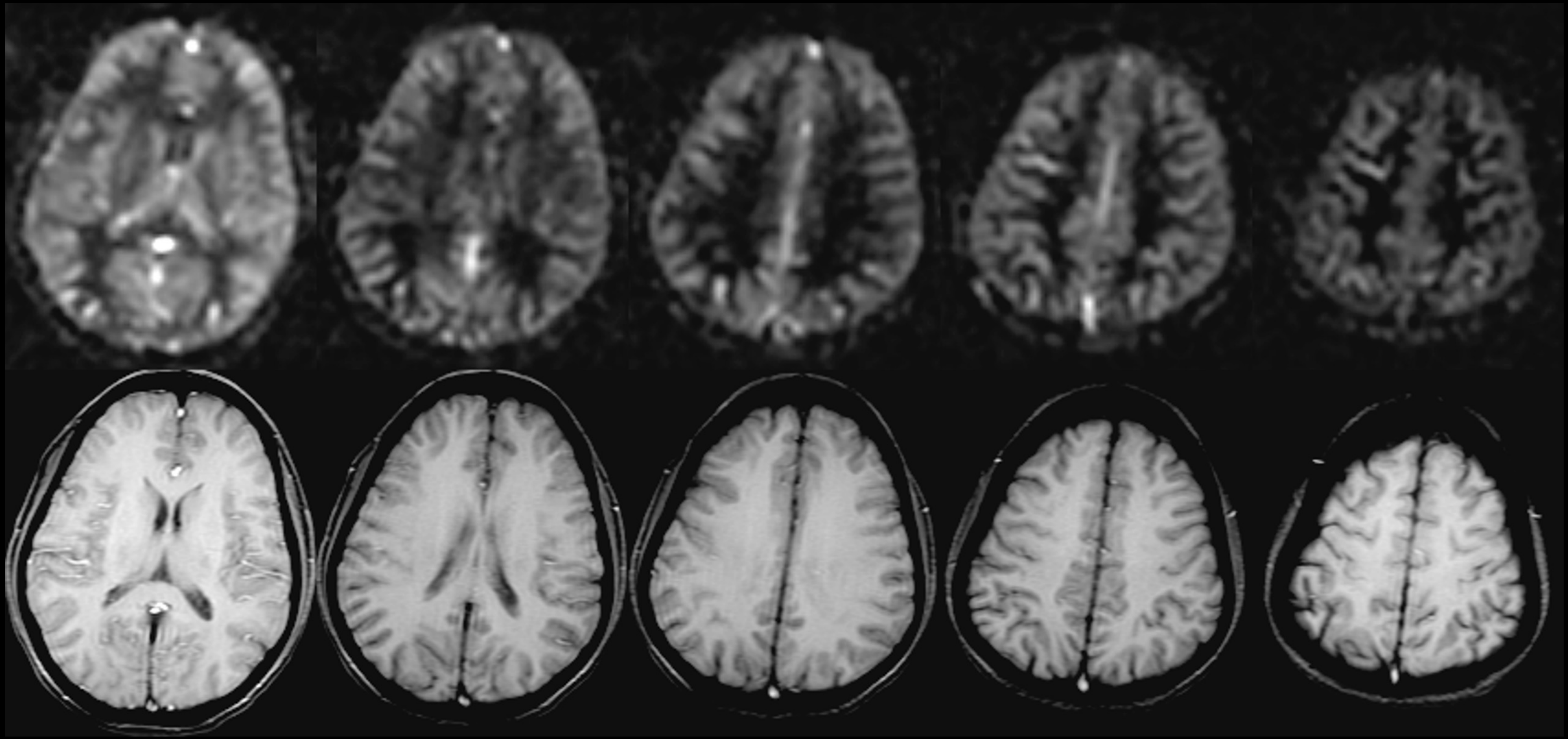
Yacoub E,
Le TH,
Ugurbil K,
Hu X
(1999)
Magn Res
Med
41(3):436-41

Courtesy of Arno Villringer

Blood Perfusion Imaging




TI (ms)
FAIR
EPISTAR
200
400
600
800
1000
1200



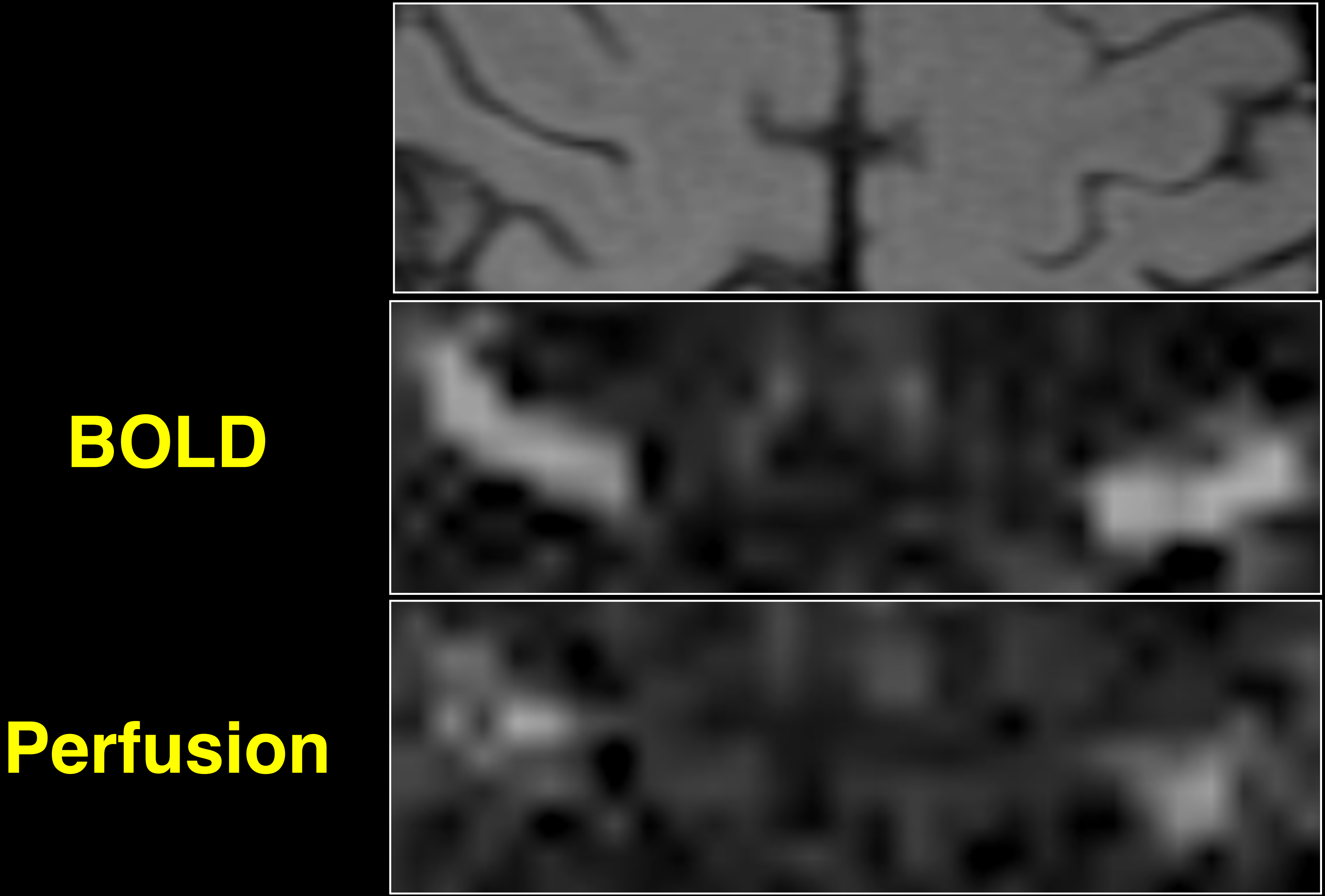
Williams, D. S., Detre, J. A., Leigh, J. S. & Koretsky, A. S. (1992) “Magnetic resonance imaging of perfusion using spin-inversion of arterial water.” Proc. Natl. Acad. Sci. USA 89, 212-216.

Edelman, R., Siewert, B. & Darby, D. (1994) “Qualitative mapping of cerebral blood flow and functional localization with echo planar MR imaging ans signal targeting with alternating radiofrequency (EPISTAR).” Radiology **192**, 1-8.

Kim, S.-G. (1995) “Quantification of relative cerebral blood flow change by flow-sensitive alternating inversion recovery (FAIR) technique: application to functional mapping.” Magn. Reson. Med. **34**, 293-301.

Kwong, K. K. et al. (1995) “MR perfusion studies with T1-weighted echo planar imaging.”Magn. Reson. Med. **34**, 878-887.

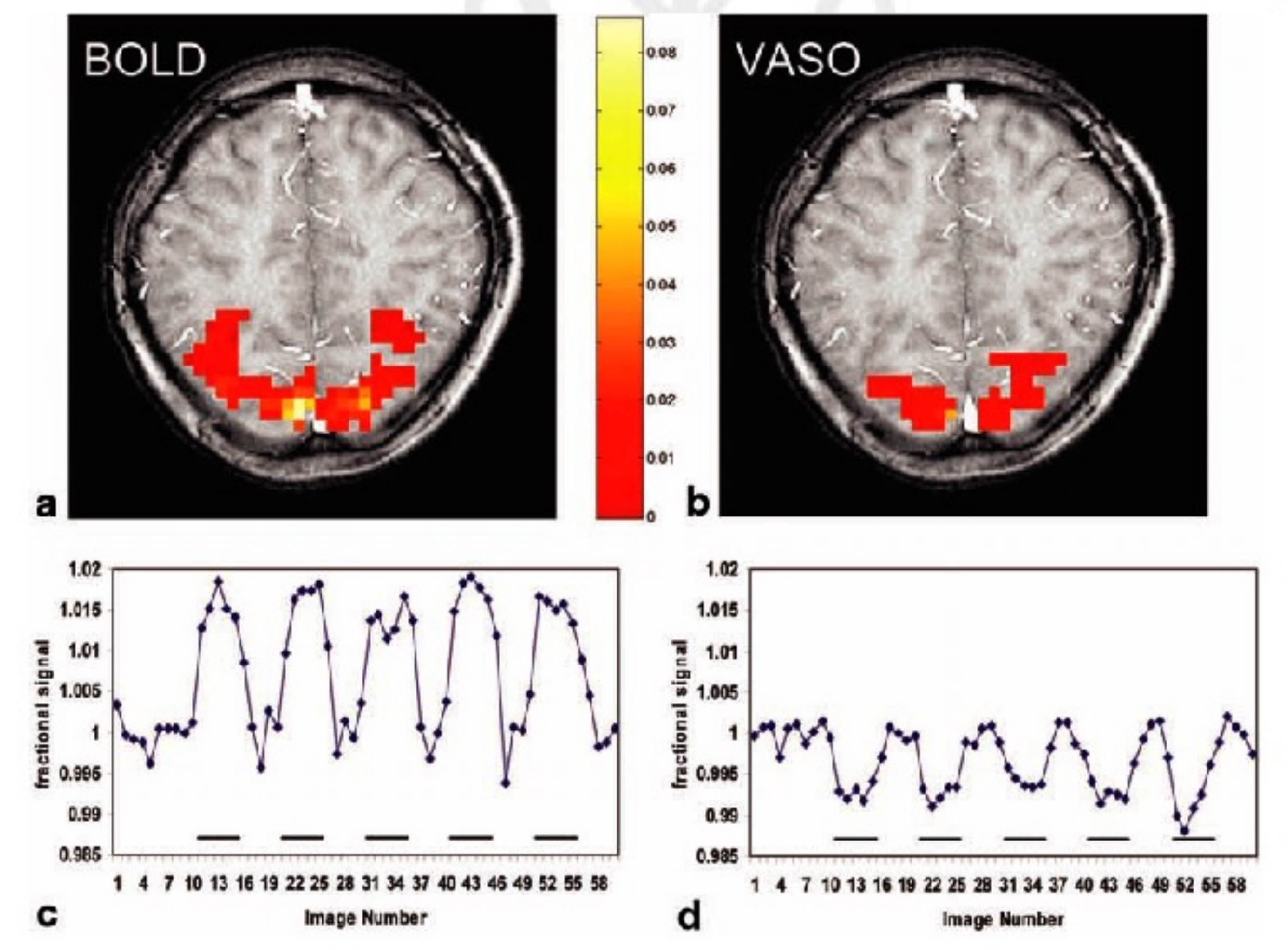
Simultaneous BOLD and Perfusion



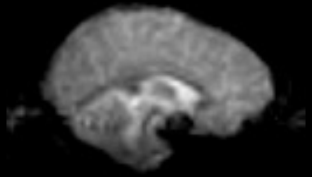
Functional Magnetic Resonance Imaging Based on Changes in Vascular Space Occupancy

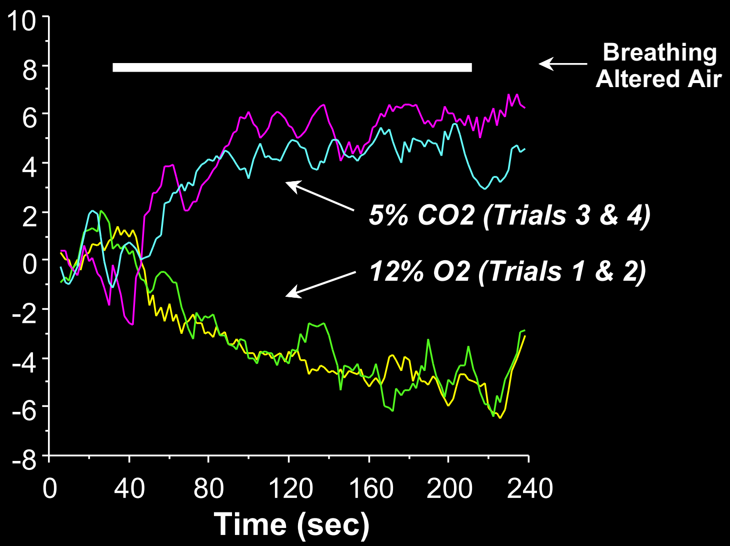
Hanzhang Lu,[1–3] Xavier Golay,[1,3] James J. Pekar,[1,3] and Peter C.M. van Zijl[1,3*]

MAGNET RESON MED 50 (2): 263-274 AUG 2003

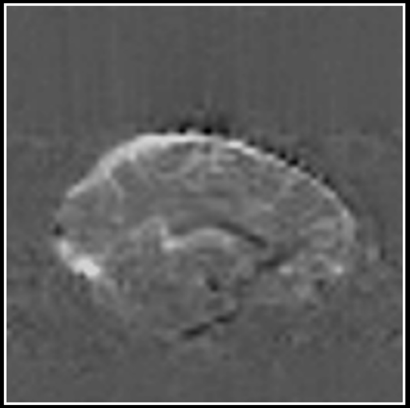


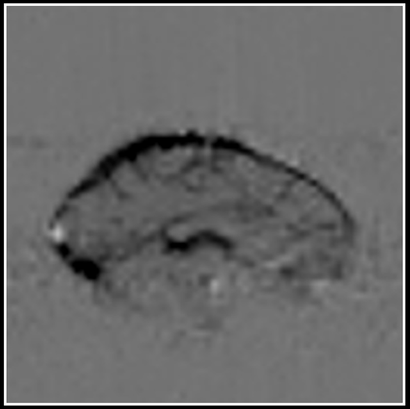
Effect of Hemodynamic Stress on BOLD Contrast





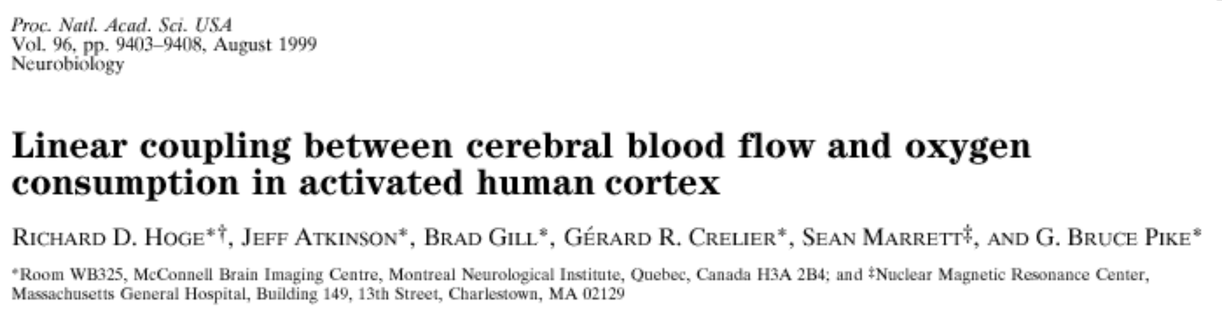
5% CO2





12% O2

P. A. Bandettini, E. C. Wong, A hypercapnia - based normalization method for improved spatial localization of human brain activation with fMRI. *NMR in Biomedicine* 10, 197-203 (1997).

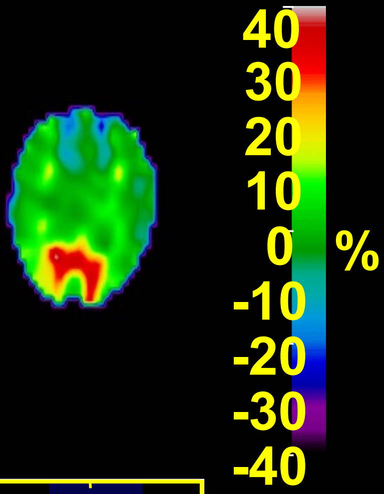


Proc. Natl. Acad. Sci. USA
Vol. 96, pp. 9403–9408, August 1999
Neurobiology

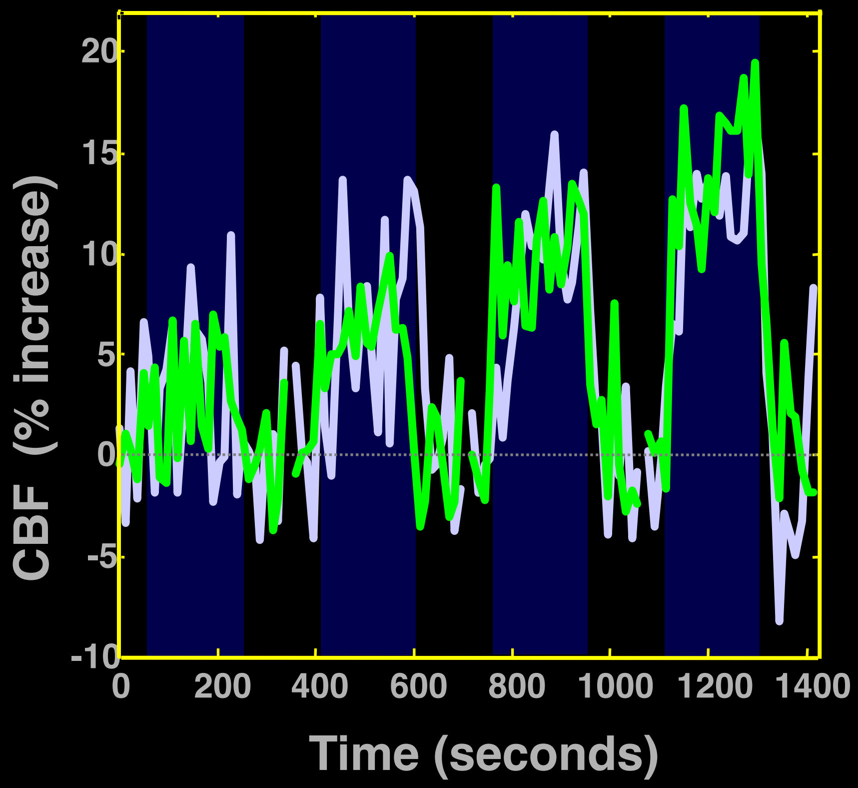
Linear coupling between cerebral blood flow and oxygen consumption in activated human cortex

RICHARD D. HOGE*†, JEFF ATKINSON*, BRAD GILL*, GÉRARD R. CRELIER*, SEAN MARRETT‡, AND G. BRUCE PIKE*

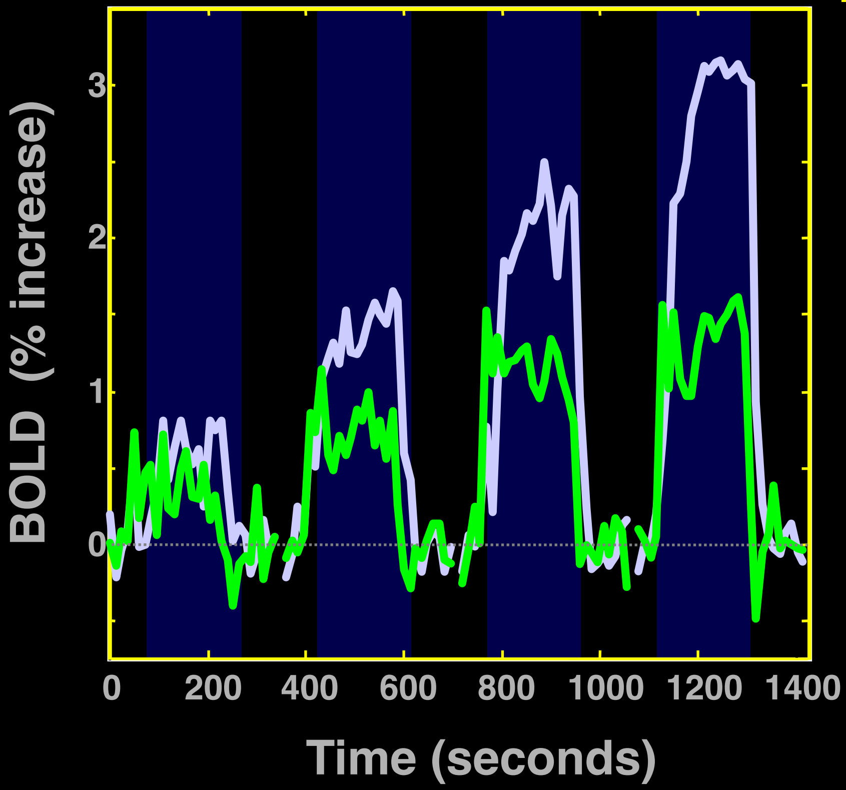
*Room WB325, McConnell Brain Imaging Centre, Montreal Neurological Institute, Quebec, Canada H3A 2B4; and ‡Nuclear Magnetic Resonance Center, Massachusetts General Hospital, Building 149, 13th Street, Charlestown, MA 02129



CBF

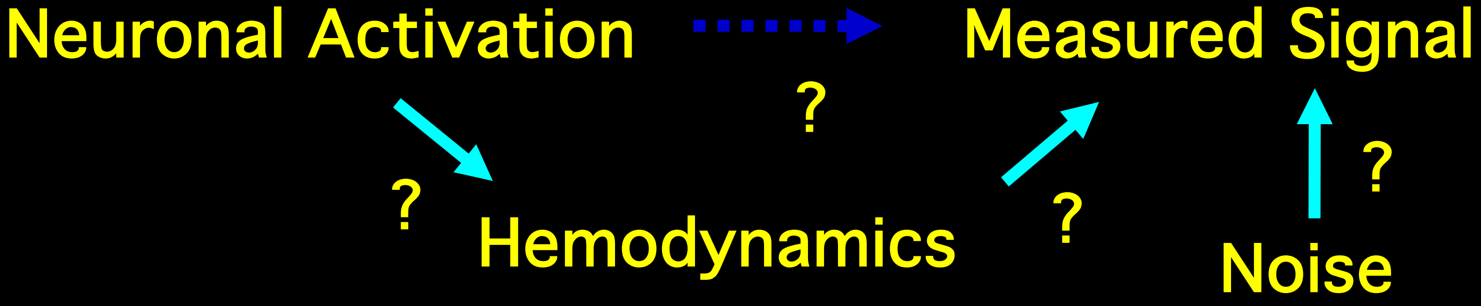


BOLD



Simultaneous Perfusion and BOLD imaging during graded visual activation and hypercapnia

The Problem



Neuronal Activation

Measured Signal

?

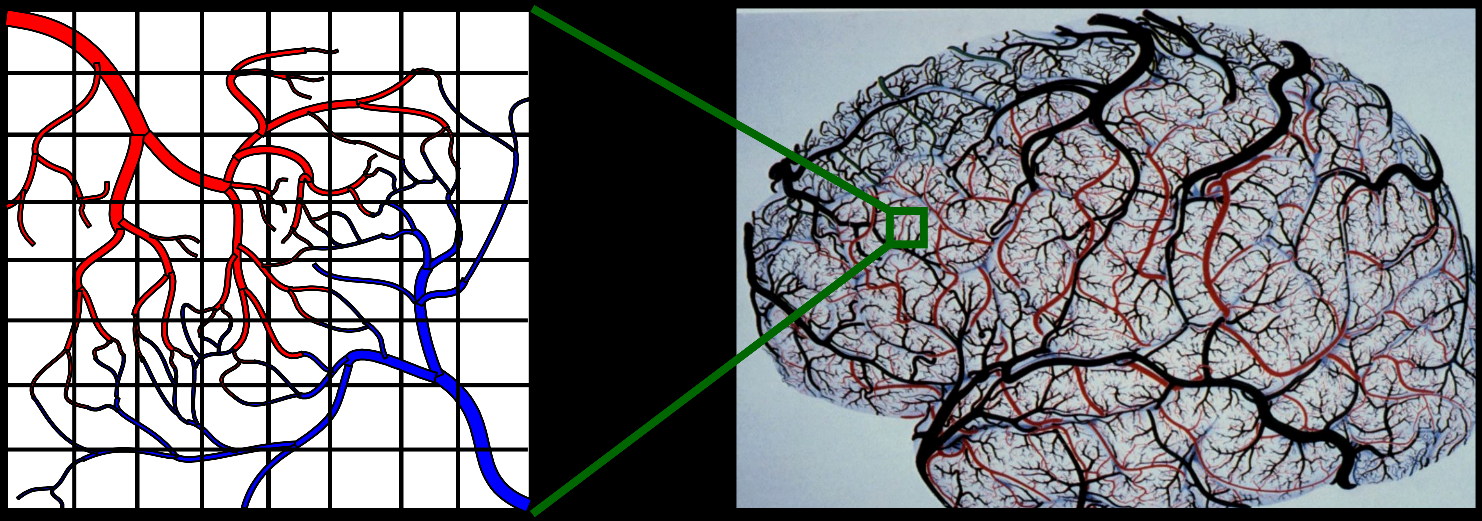
?

Hemodynamics

?

?

Noise



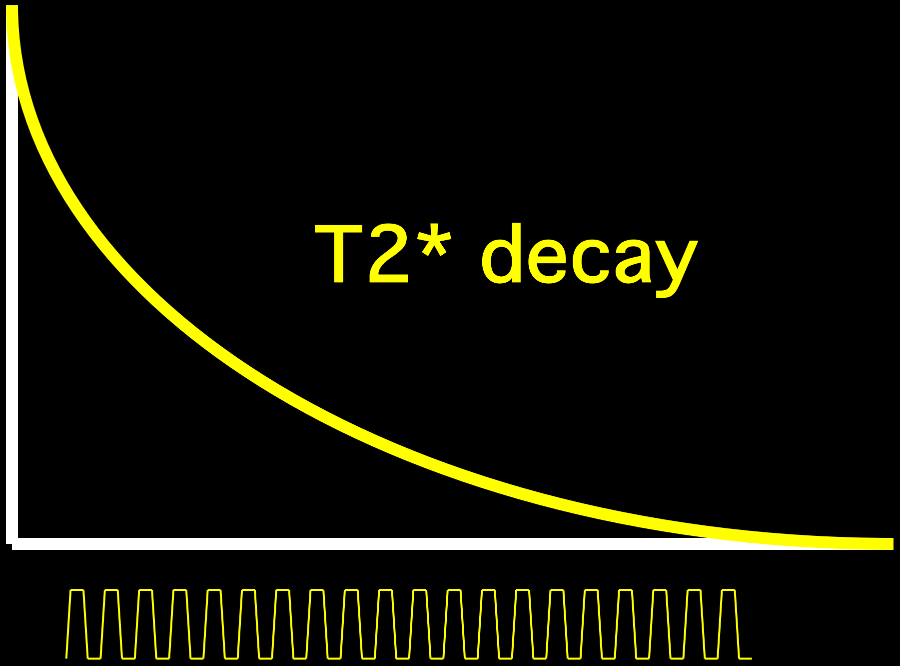
Latest Developments...

1. Temporal Resolution
2. Spatial Resolution
3. Sensitivity and Noise
4. Information Content
5. Implementation

Latest Developments...

1. Temporal Resolution
2. Spatial Resolution
3. Sensitivity and Noise
4. Information Content
5. Implementation

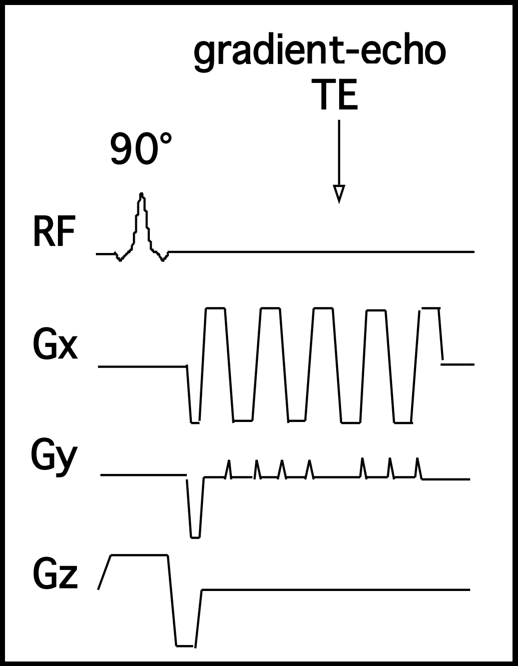
Single Shot EPI

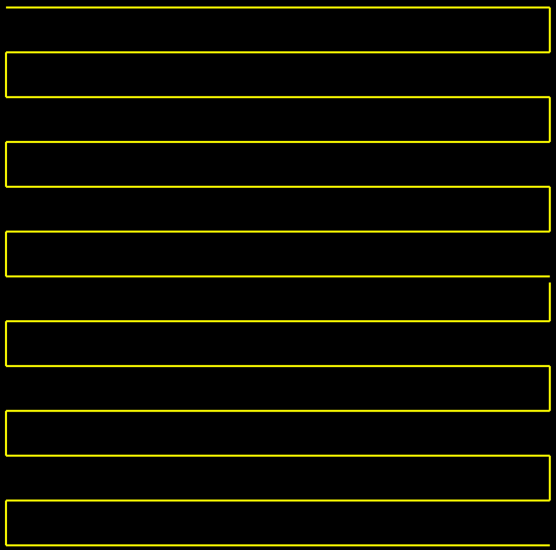


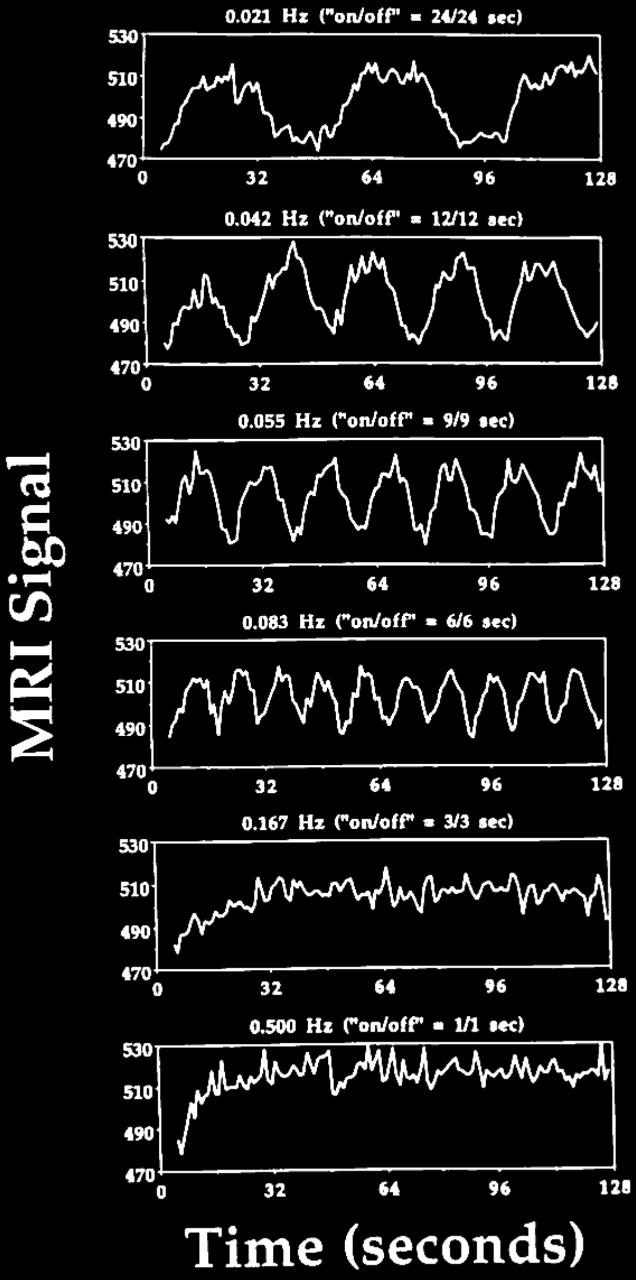
T2* decay

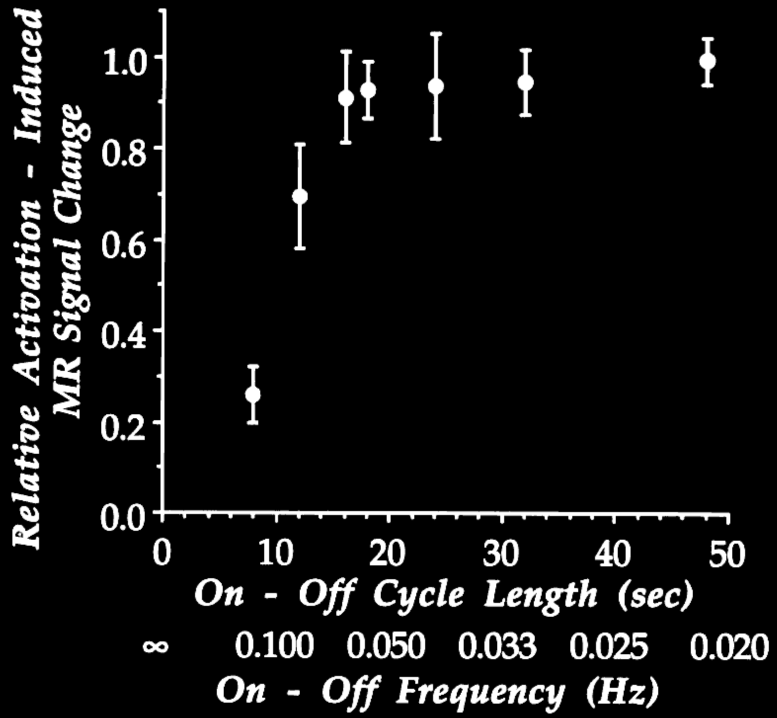
EPI Readout Window

≈ 20 to 40 ms



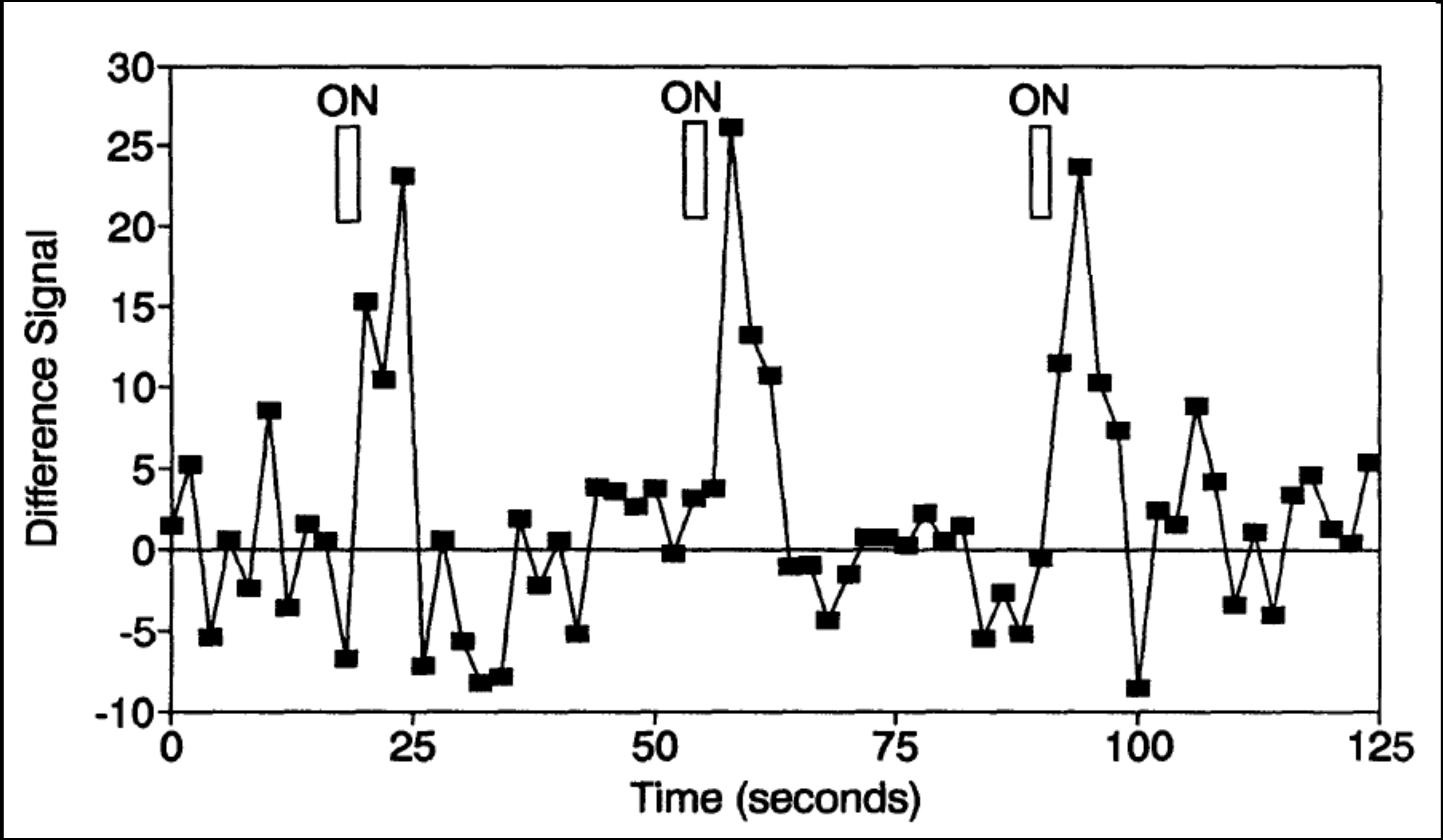




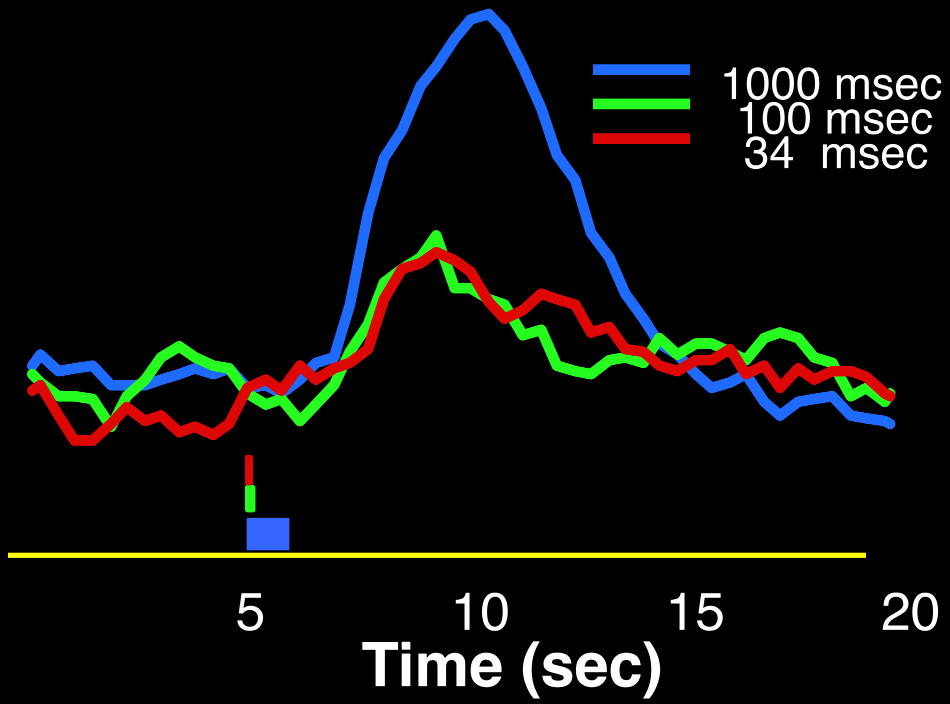


P. A. Bandettini, Functional MRI temporal resolution *in* "Functional MRI" (C. Moonen, and P. Bandettini., Eds.), p. 205-220, Springer - Verlag,. 1999.

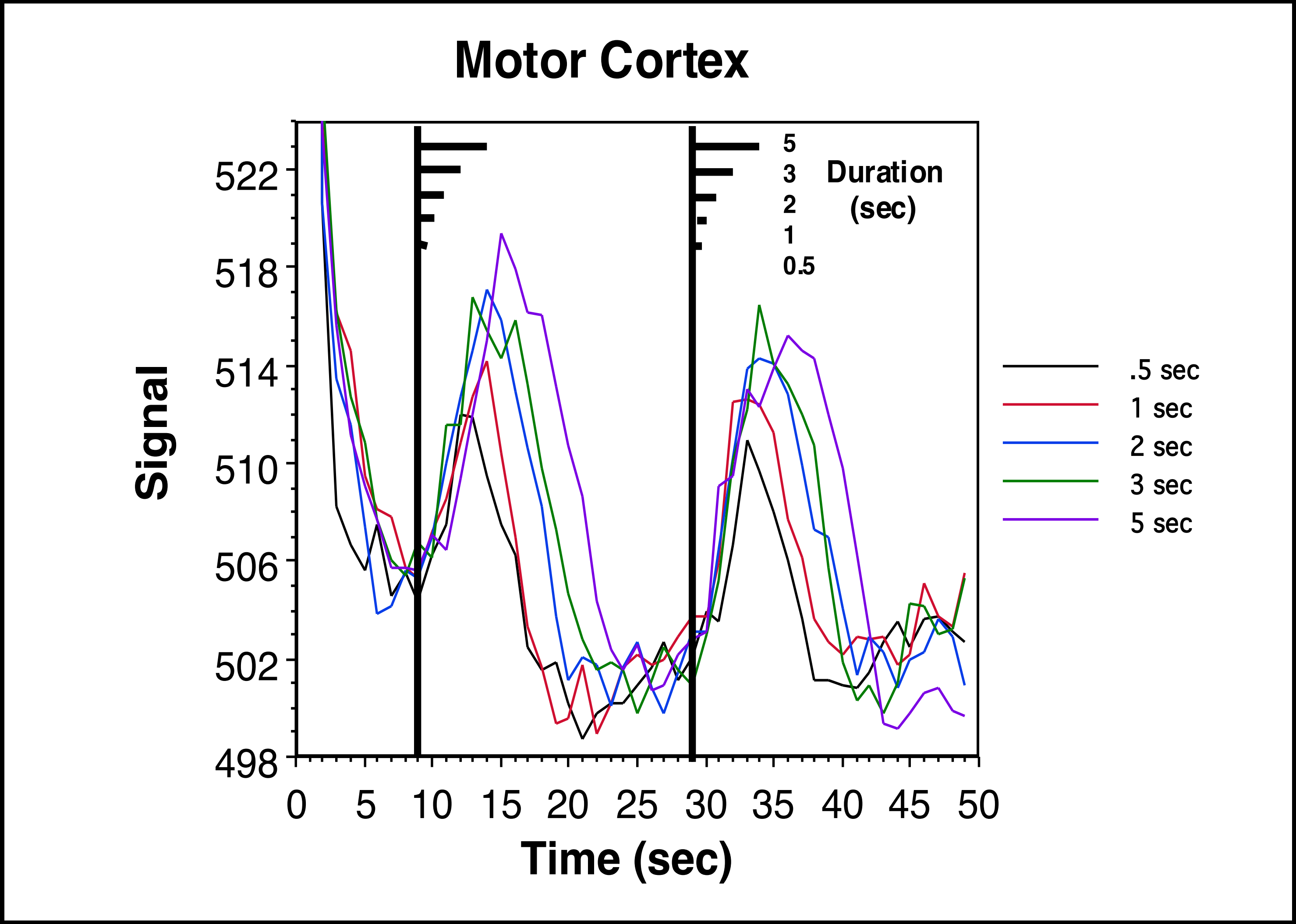
First Event-related fMRI Results



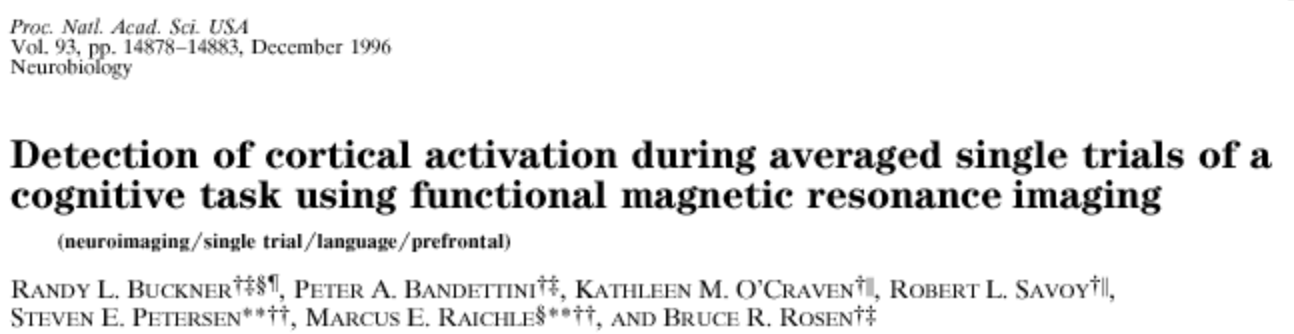
Blamire, A. M., et al. (1992). "Dynamic mapping of the human visual cortex by high-speed magnetic resonance imaging." Proc. Natl. Acad. Sci. USA 89: 11069-11073.



R. L. Savoy, et al., Pushing the temporal resolution of fMRI: studies of very brief visual stimuli, onset variability and asynchrony, and stimulus-correlated changes in noise [oral], 3'rd Proc. Soc. Magn. Reson., Nice, p. 450. (1995).



Bandettini, et al., The functional dynamics of blood oxygenation level contrast in the motor cortex, 12'th Proc. Soc. Magn. Reson. Med., New York, p. 1382. (1993).

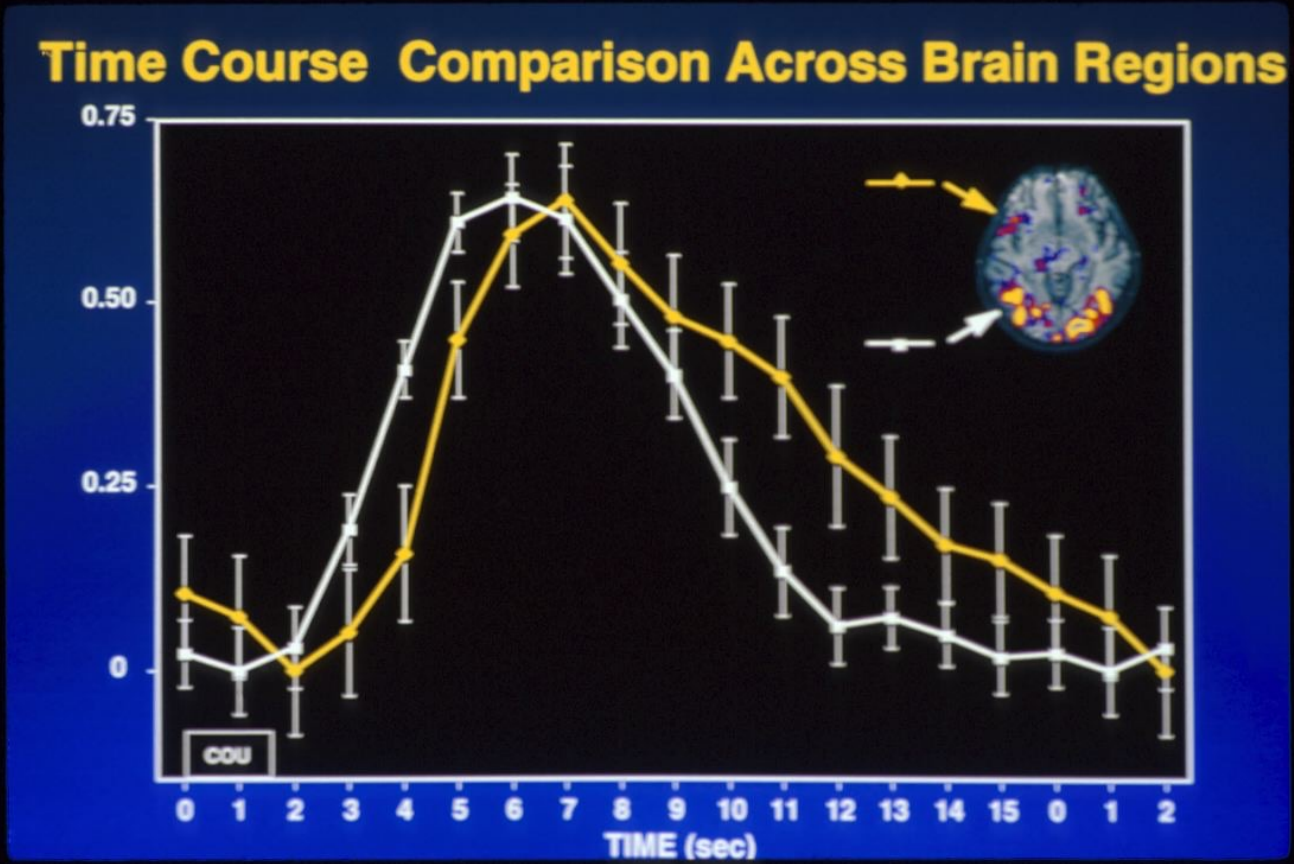


Proc. Natl. Acad. Sci. USA
Vol. 93, pp. 14878–14883, December 1996
Neurobiology

Detection of cortical activation during averaged single trials of a cognitive task using functional magnetic resonance imaging

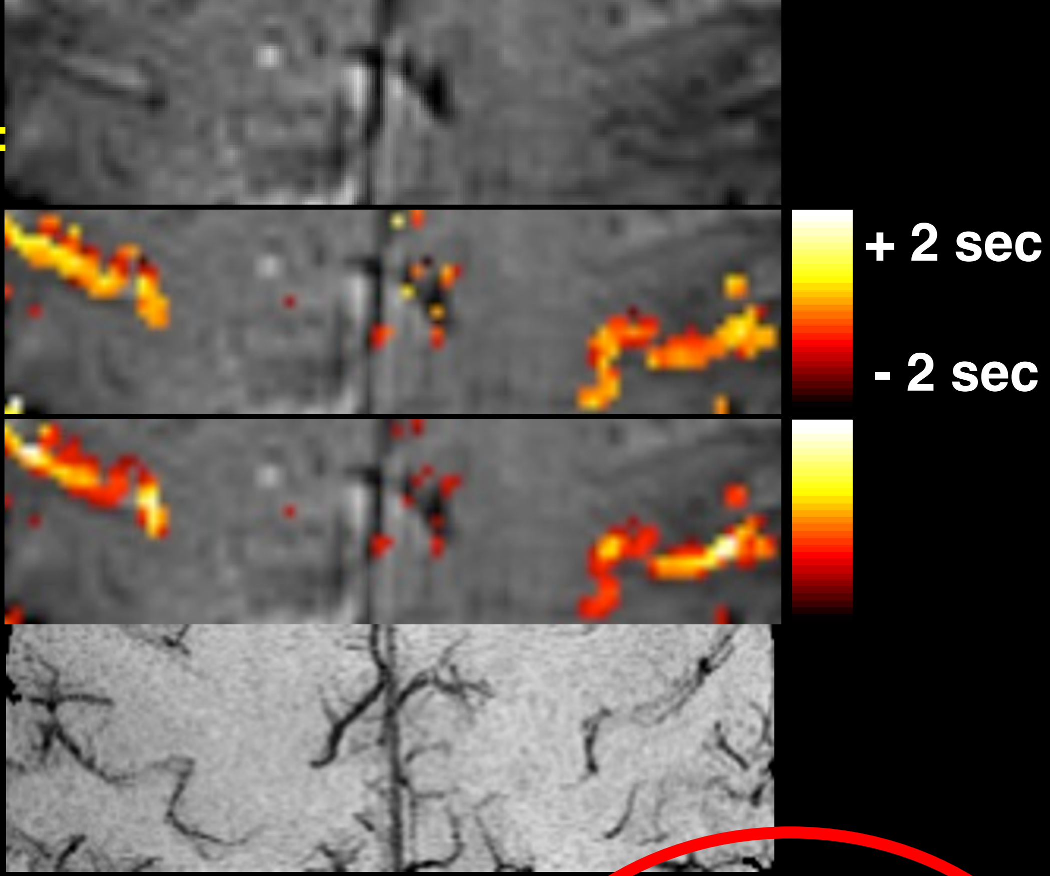
(neuroimaging/single trial/language/prefrontal)

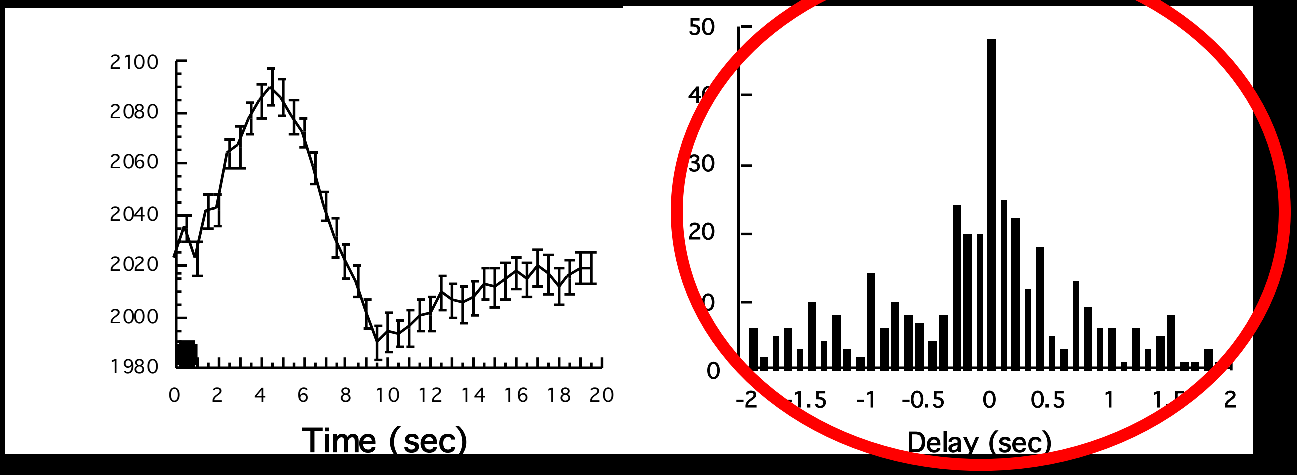
RANDY L. BUCKNER[†‡§¶], PETER A. BANDETTINI[†‡], KATHLEEN M. O'CRAVEN[†‖], ROBERT L. SAVOY[†‖],
STEVEN E. PETERSEN[**††], MARCUS E. RAICHLE[§**††], AND BRUCE R. ROSEN[†‡]



Time Course Comparison Across Brain Regions

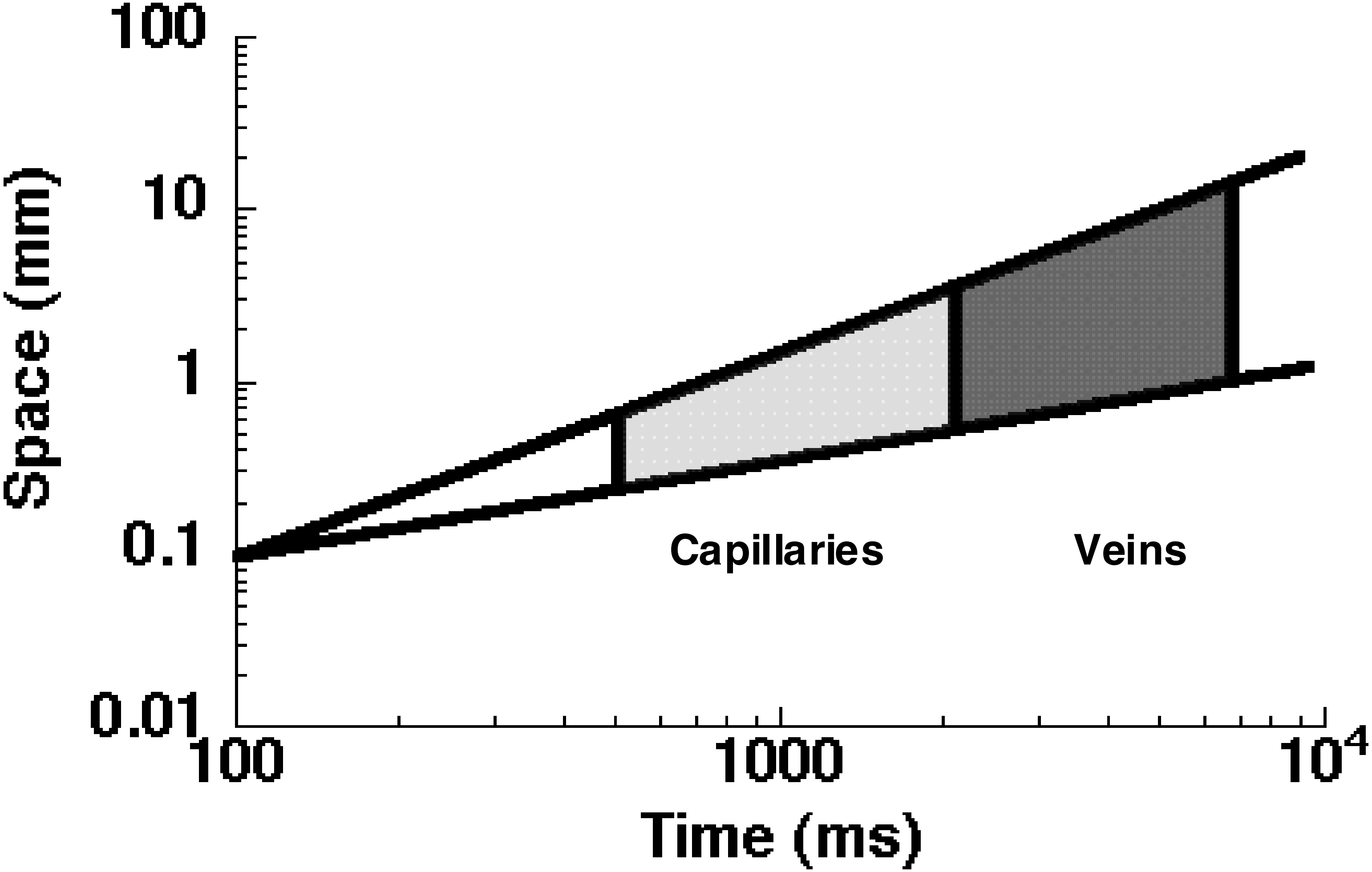
The major obstacle in BOLD contrast temporal resolution:





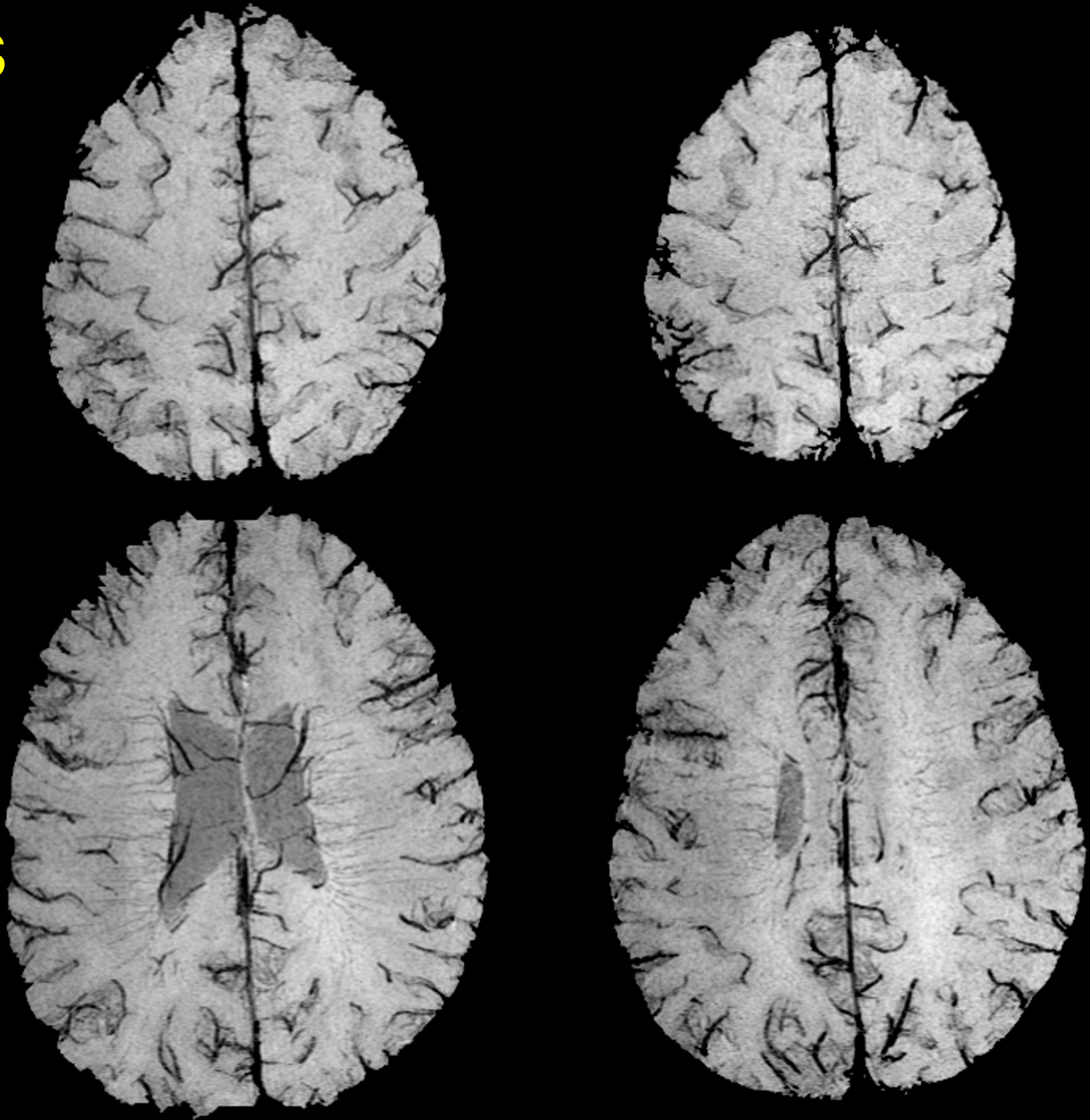
P. A. Bandettini, The temporal resolution of Functional MRI *in* "Functional MRI" (C. Moonen, and P. Bandettini., Eds.), p. 205-220, Springer - Verlag,. 1999.

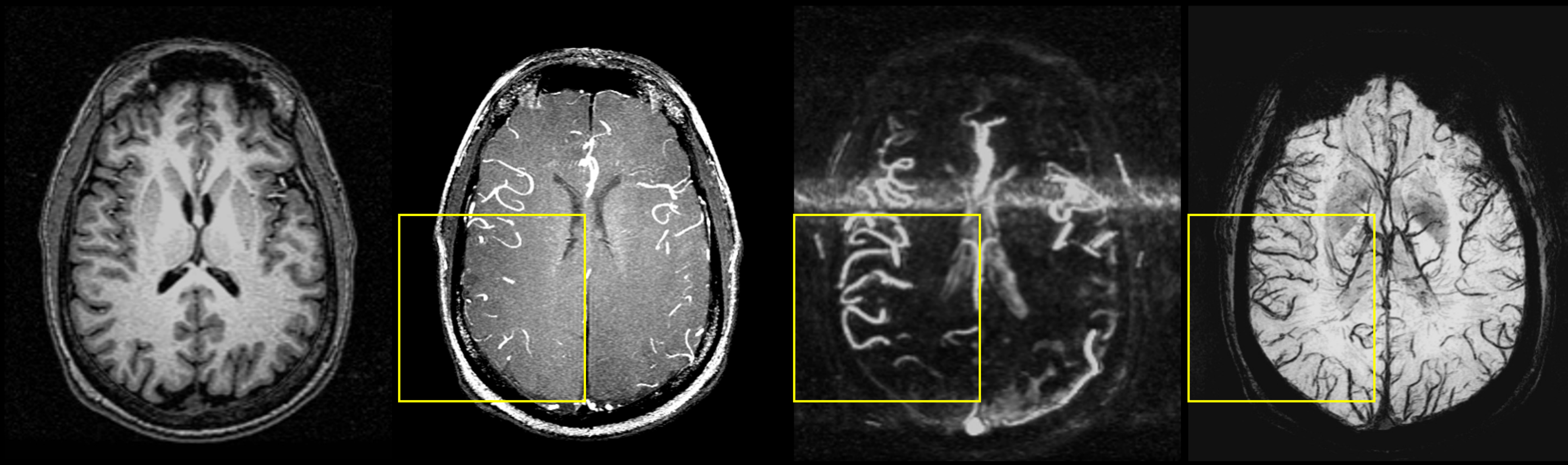
Hemodynamic Latency and Variability Following Neuronal Activation



A tangent into venograms

(3 Tesla)

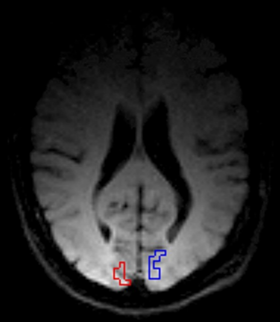




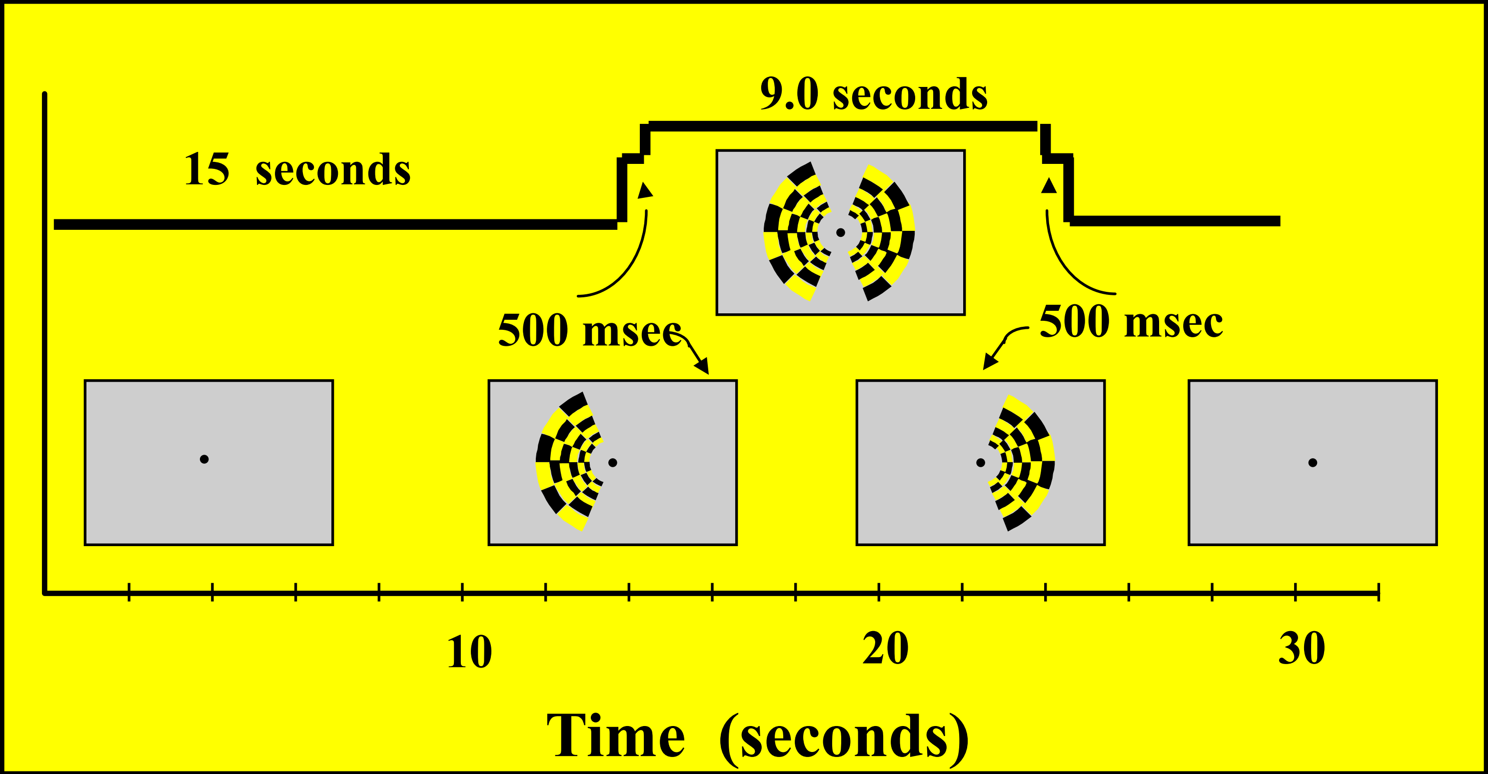
MP-RAGE **3D T-O-F MRA** **3D Venous PC** **MR Venogram**

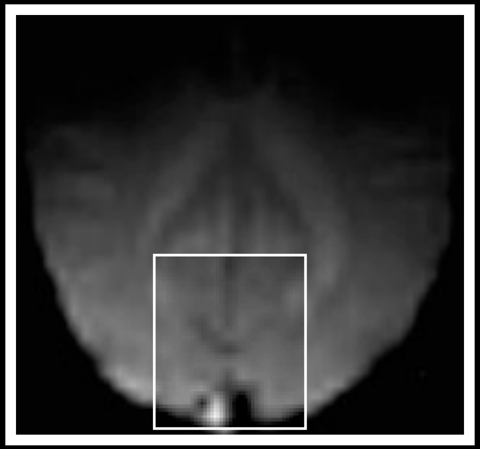
Hemi-Field Experiment

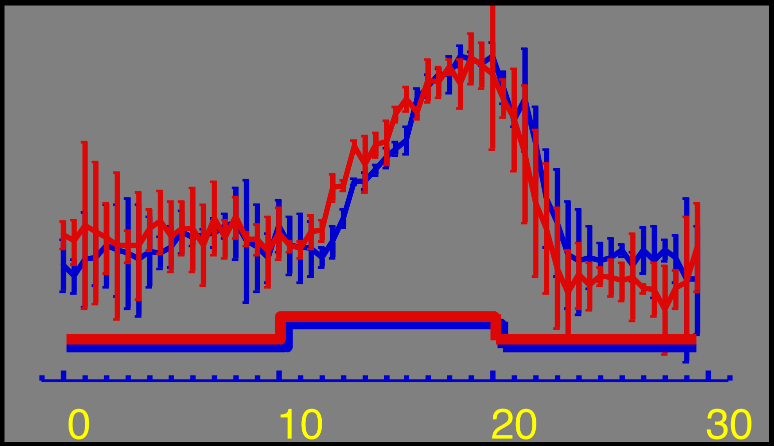
Right Hemisphere

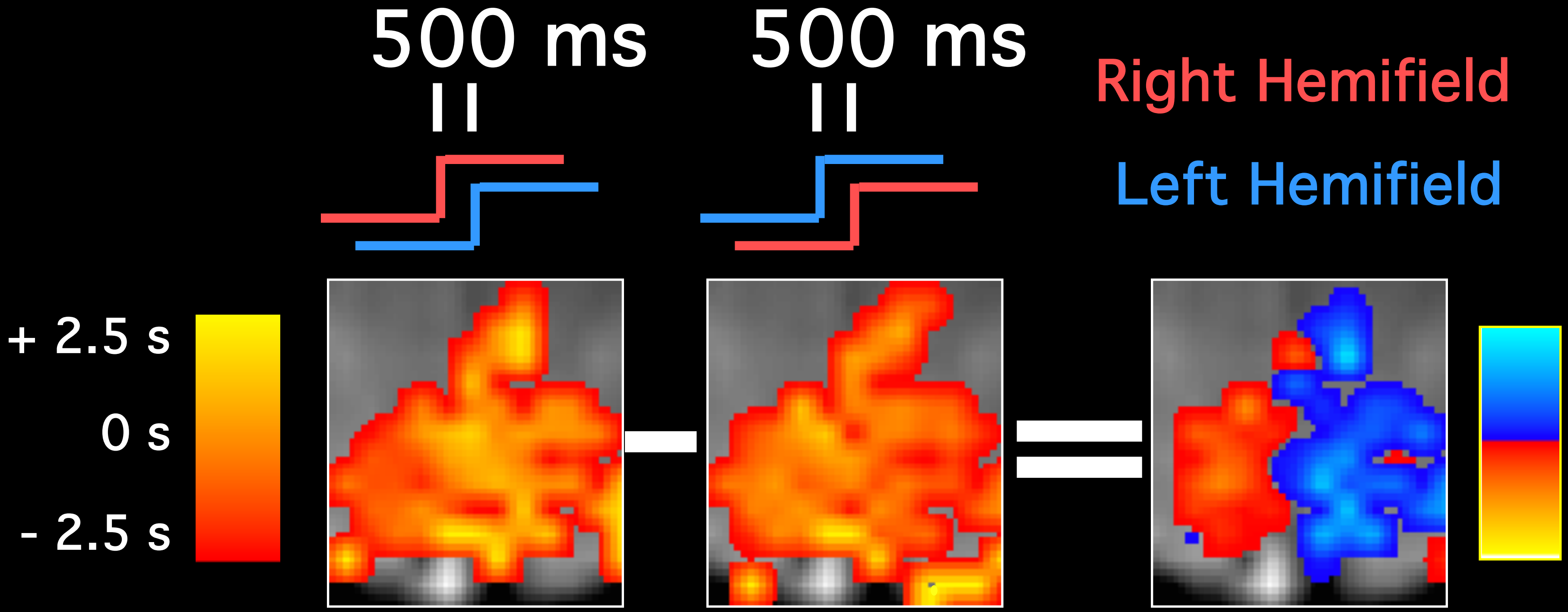


Left Hemisphere






0
10
20
30


500 ms
||
500 ms
||
Right Hemifield
Left Hemifield
+ 2.5 s
0 s
- 2.5 s
-
=

Cognitive Neuroscience Application:

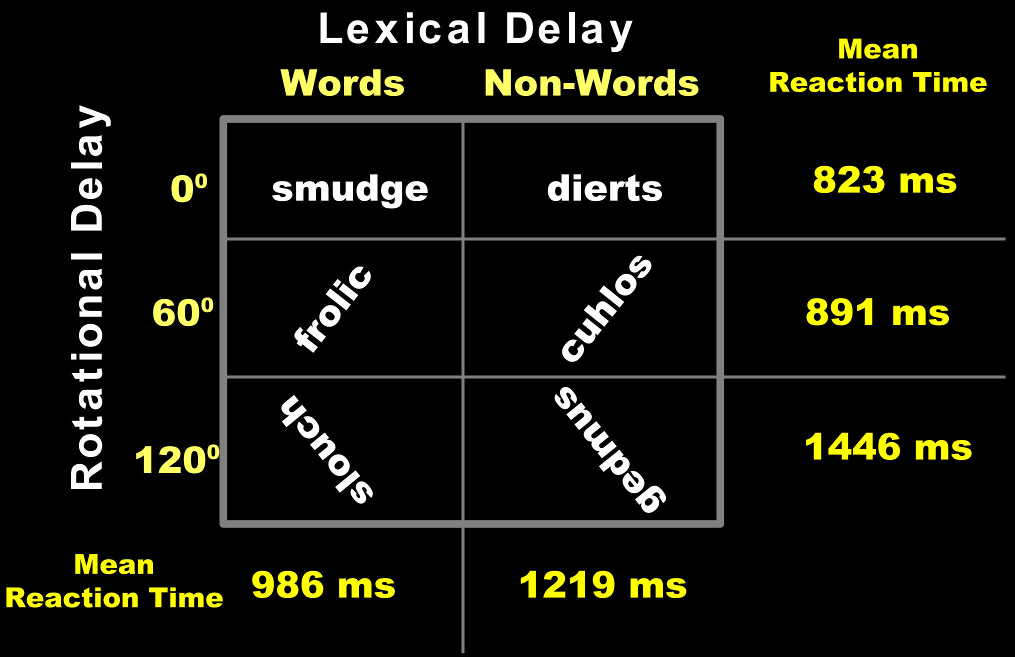
Understanding neural system dynamics through task modulation and measurement of functional MRI amplitude, latency, and width

PNAS

P. S. F. Bellgowan*[†], Z. S. Saad[‡], and P. A. Bandettini*

*Laboratory of Brain and Cognition and [‡]Scientific and Statistical Computing Core, National Institute of Mental Health, Bethesda, MD 20892

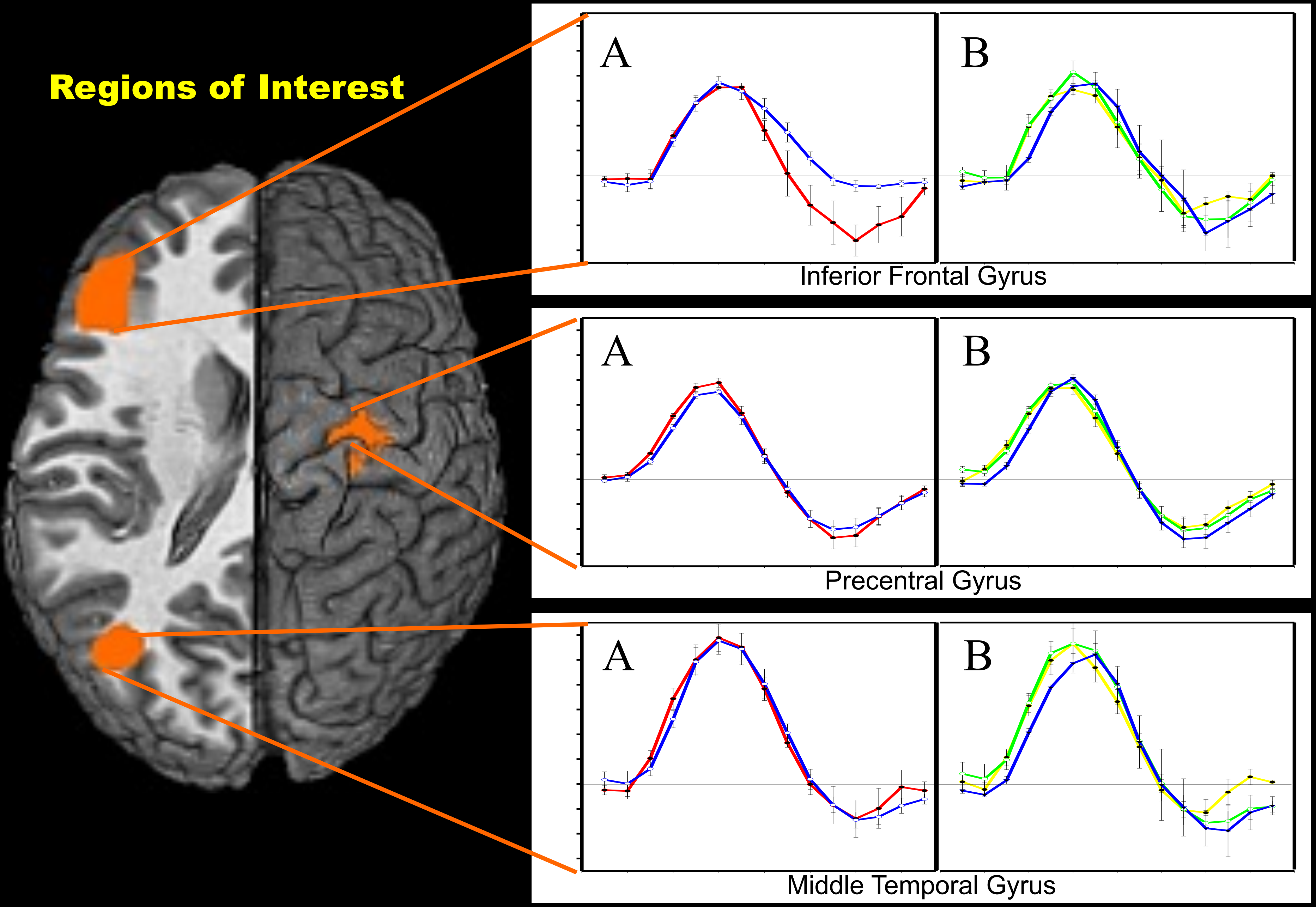
Communicated by Leslie G. Ungerleider, National Institutes of Health, Bethesda, MD, December 19, 2002 (received for review October 31, 2002)



		Lexical Delay		
		Words	Non-Words	Mean Reaction Time
Rotational Delay	0^0	smudge	dierts	823 ms
	60^0	frolic	cuhlos	891 ms
	120^0	slouch	gedmus	1446 ms
	Mean Reaction Time	986 ms	1219 ms	

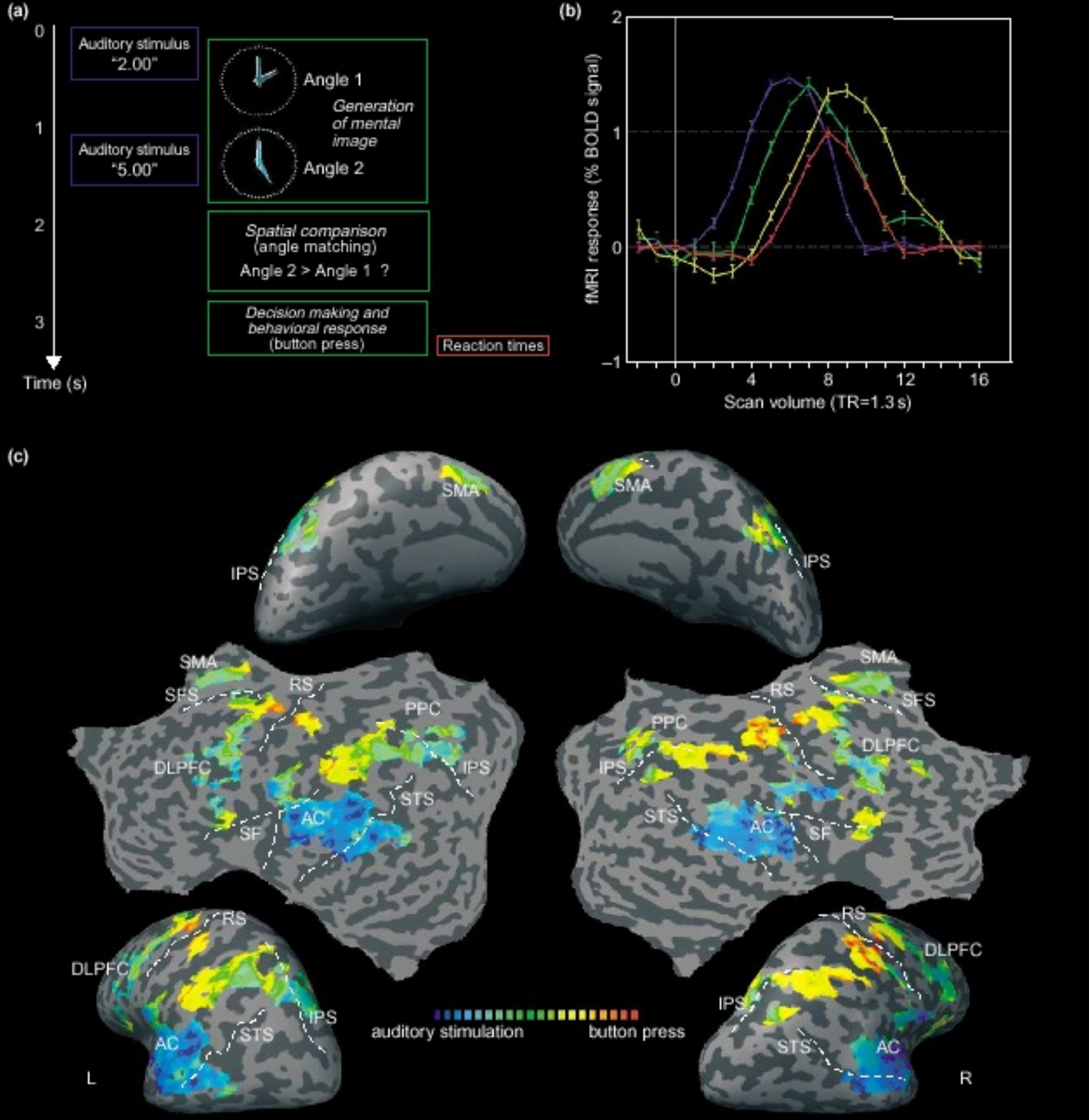
Word vs. Non-word   0°, 60°, 120° Rotation

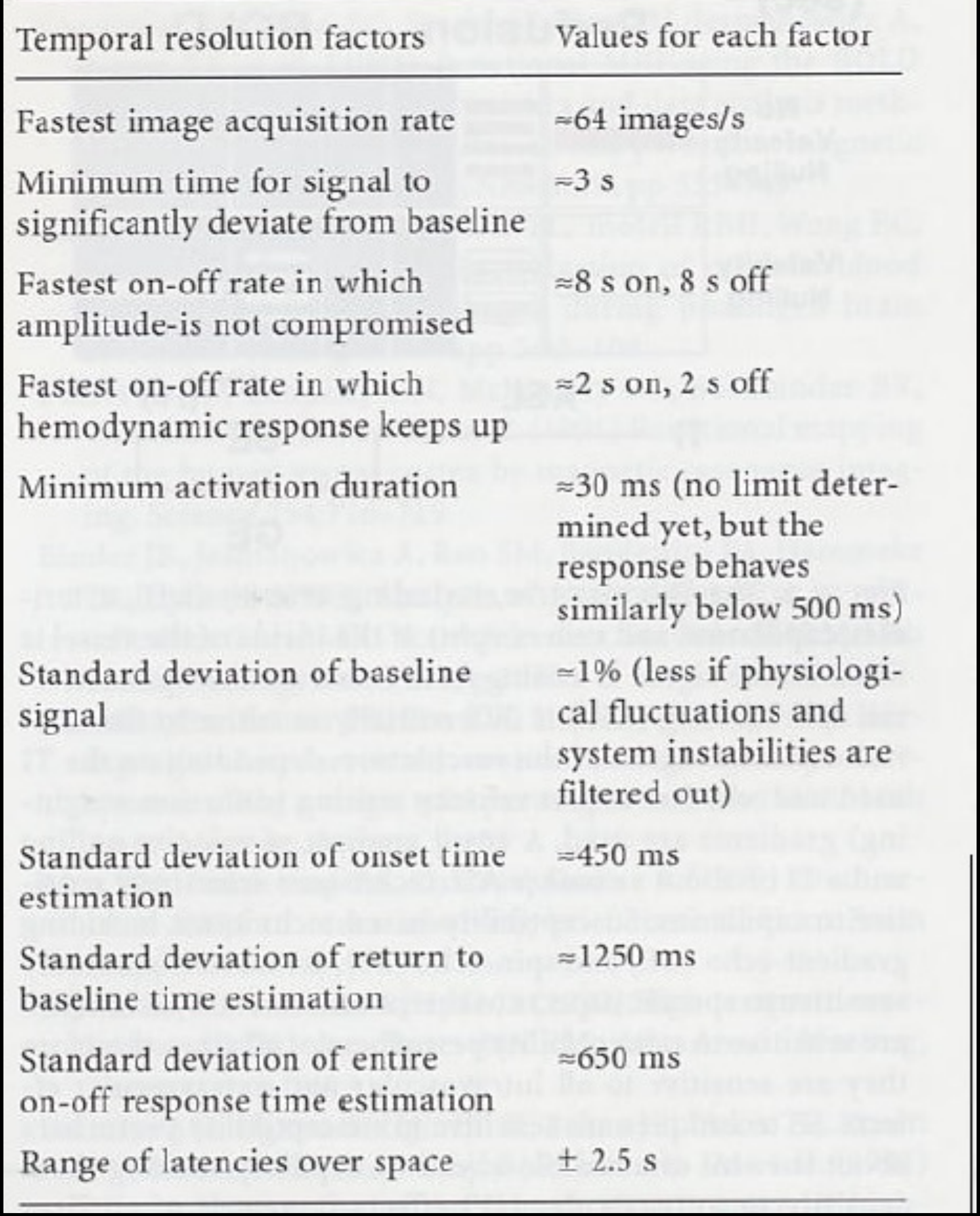
Regions of Interest



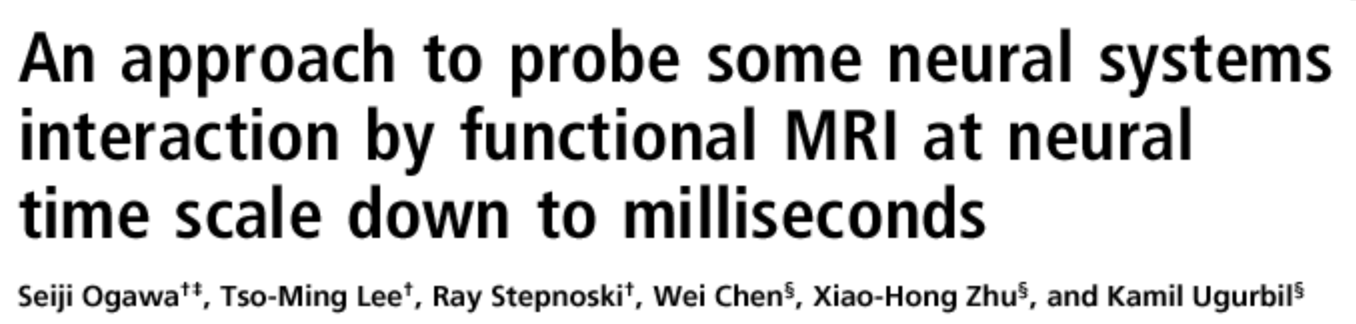
No calibration

Formisano, E. and R. Goebel, *Tracking cognitive processes with functional MRI mental chronometry.* Current Opinion in Neurobiology, 2003. **13**: p. 174-181.



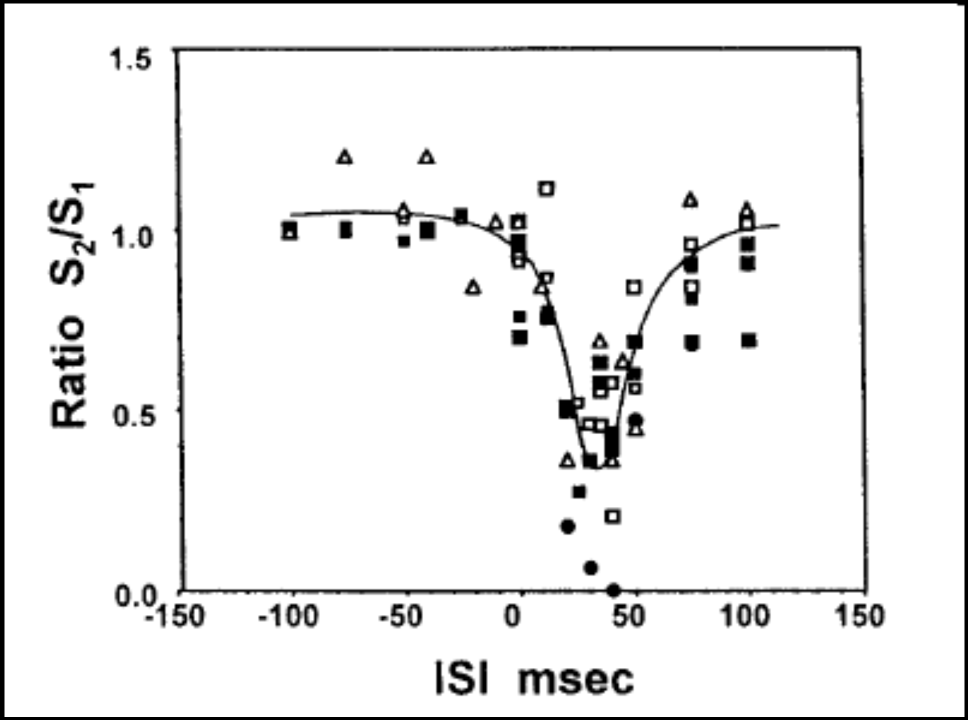


Temporal resolution factors	Values for each factor
Fastest image acquisition rate	≈64 images/s
Minimum time for signal to significantly deviate from baseline	≈3 s
Fastest on-off rate in which amplitude-is not compromised	≈8 s on, 8 s off
Fastest on-off rate in which hemodynamic response keeps up	≈2 s on, 2 s off
Minimum activation duration	≈30 ms (no limit determined yet, but the response behaves similarly below 500 ms)
Standard deviation of baseline signal	≈1% (less if physiological fluctuations and system instabilities are filtered out)
Standard deviation of onset time estimation	≈450 ms
Standard deviation of return to baseline time estimation	≈1250 ms
Standard deviation of entire on-off response time estimation	≈650 ms
Range of latencies over space	± 2.5 s



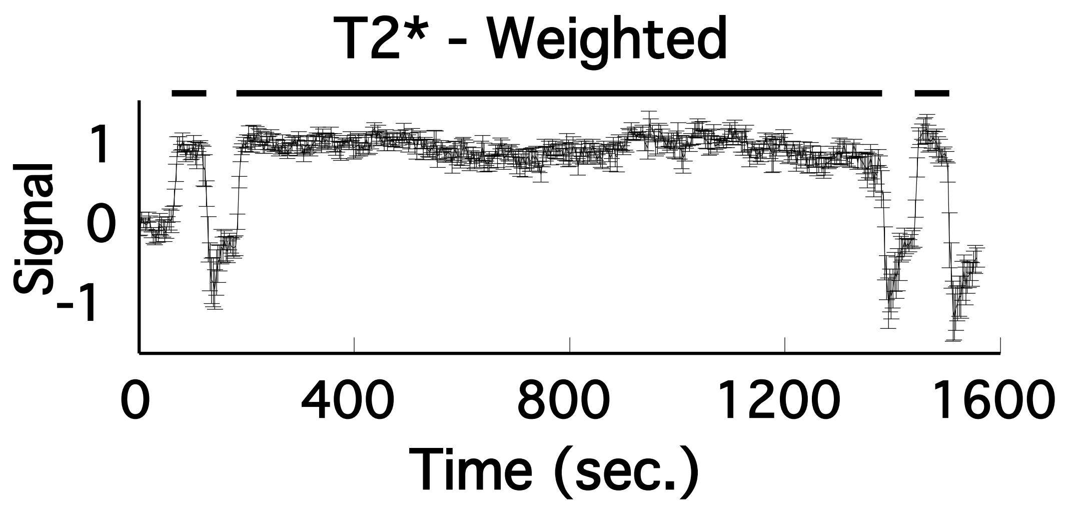
An approach to probe some neural systems interaction by functional MRI at neural time scale down to milliseconds

Seiji Ogawa[†‡], Tso-Ming Lee[†], Ray Stepnoski[†], Wei Chen[§], Xiao-Hong Zhu[§], and Kamil Ugurbil[§]

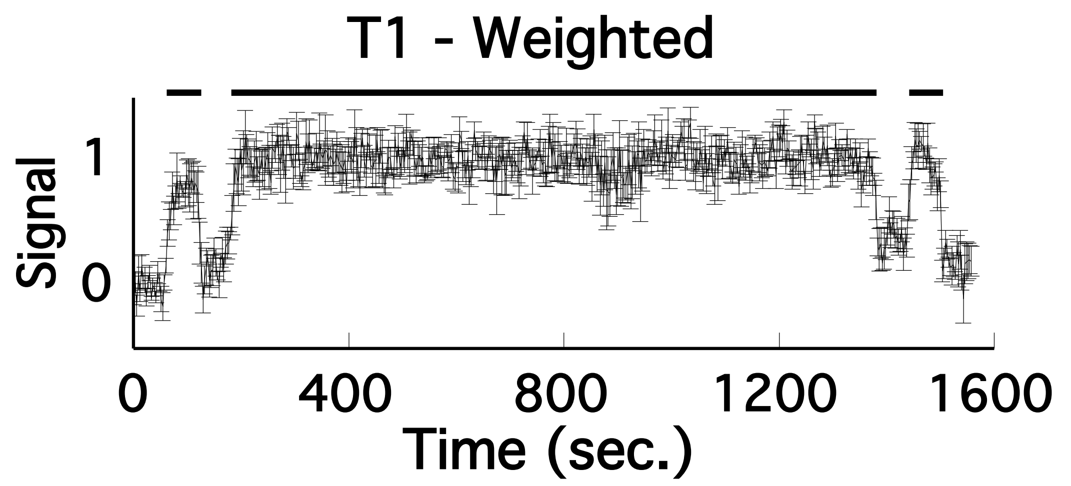


11026–11031 PNAS **September 26, 2000** vol. 97 no. 20

BOLD



Flow

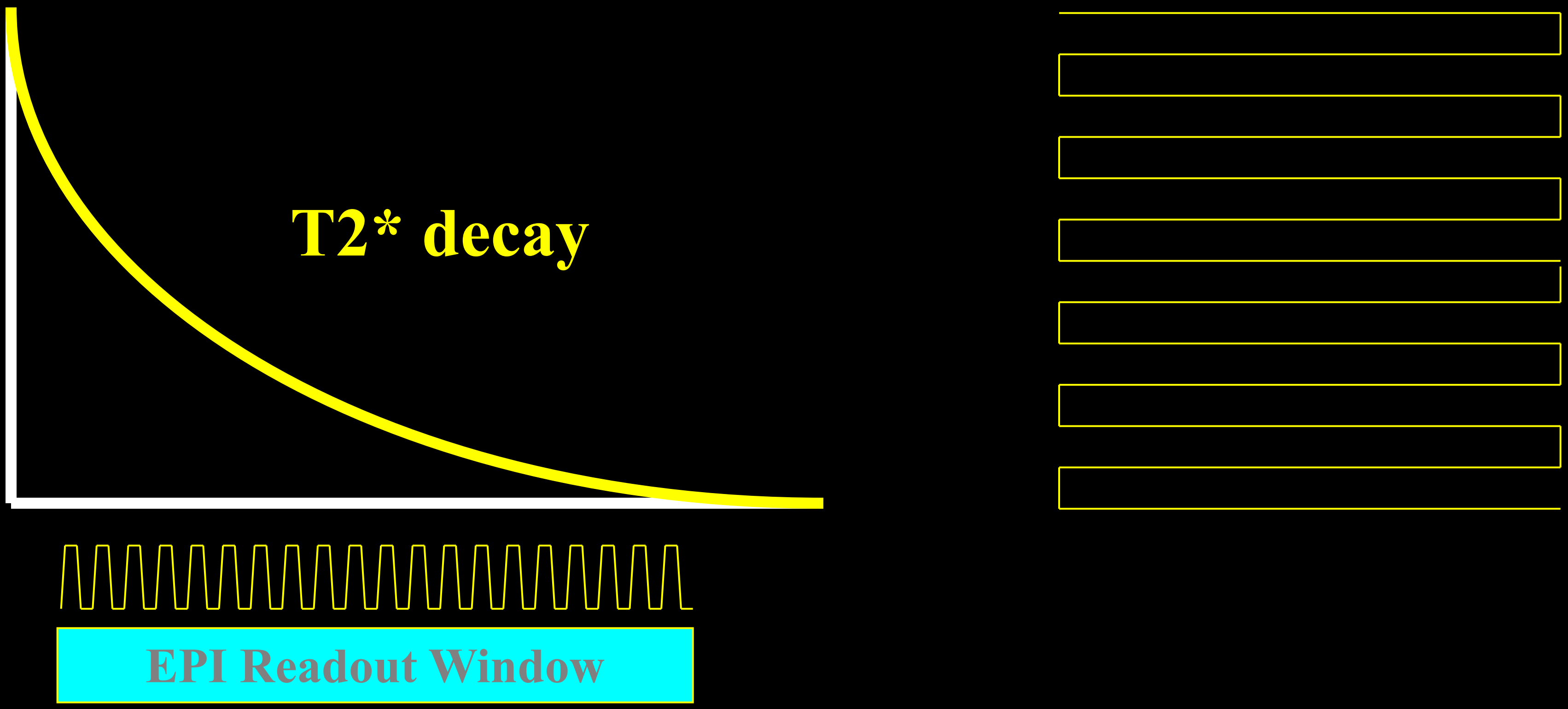


P. A. Bandettini, K. K. Kwong, T. L. Davis, R. B. H. Tootell, E. C. Wong, P. T. Fox, J. W. Belliveau, R. M. Weisskoff, B. R. Rosen, (1997). "Characterization of cerebral blood oxygenation and flow changes during prolonged brain activation." ***Human Brain Mapping*** **5, 93-109.**

Latest Developments...

1. Temporal Resolution
2. Spatial Resolution
3. Sensitivity and Noise
4. Information Content
5. Implementation

Single Shot Imaging

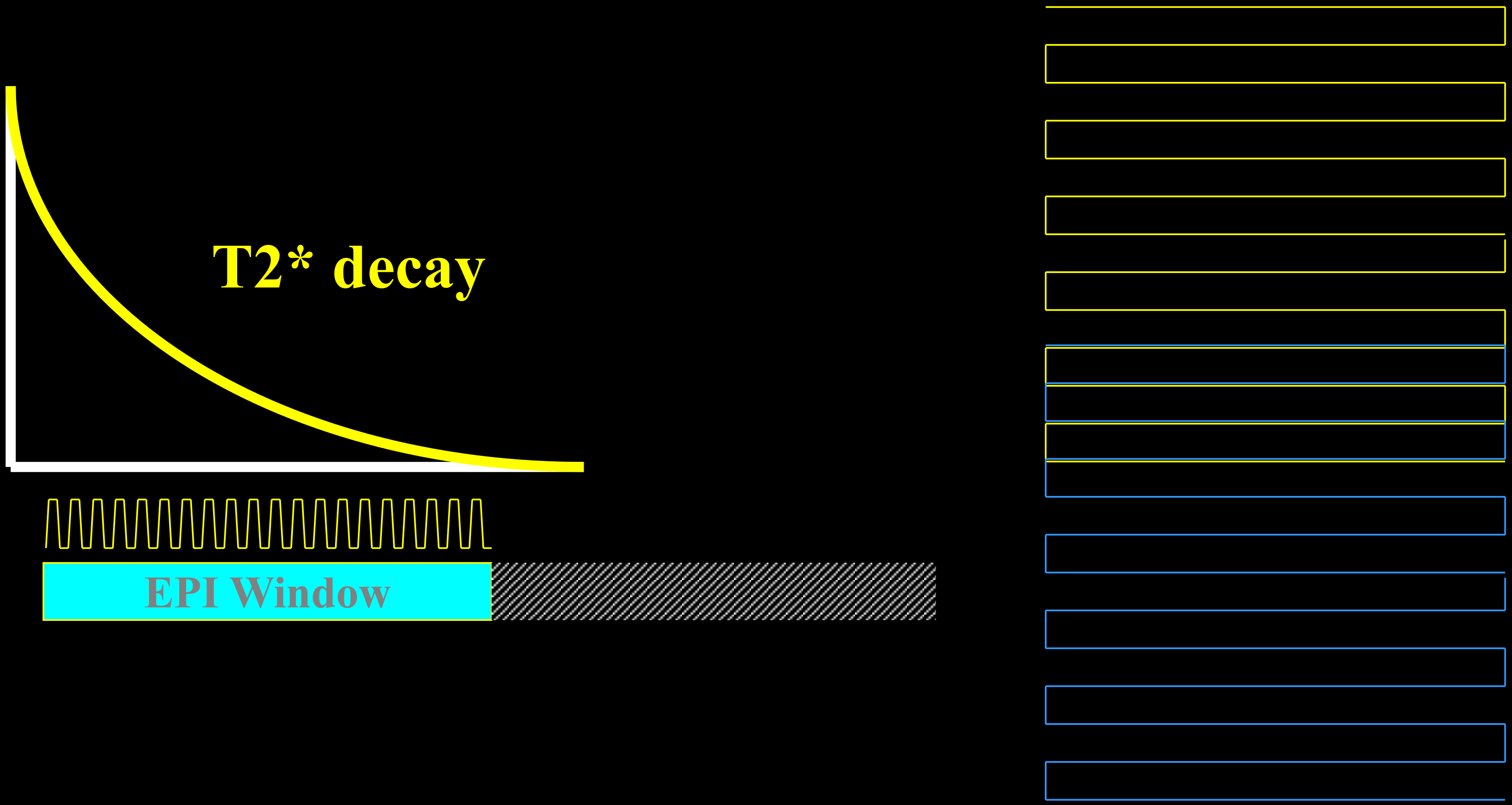


T2* decay

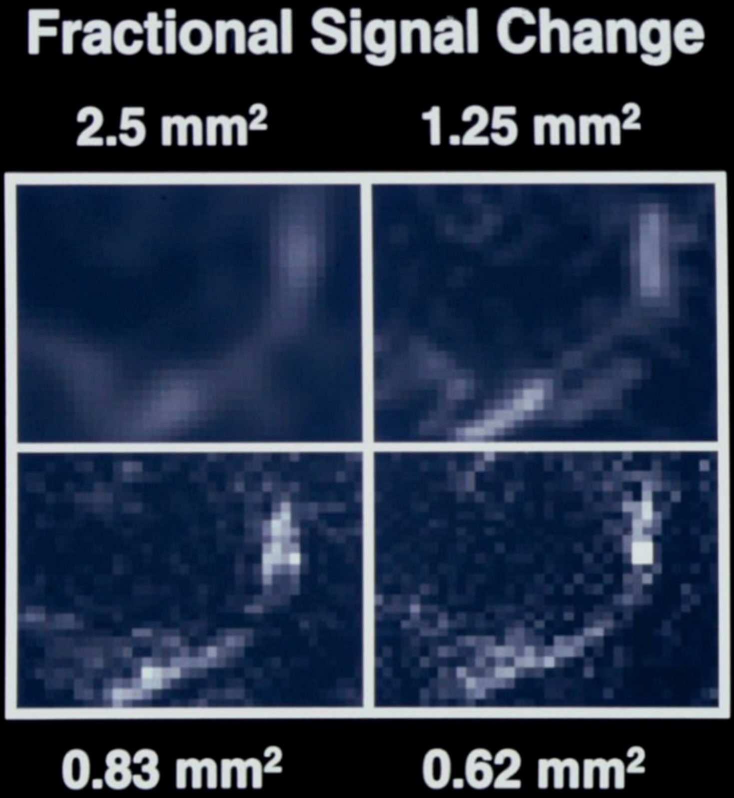
EPI Readout Window

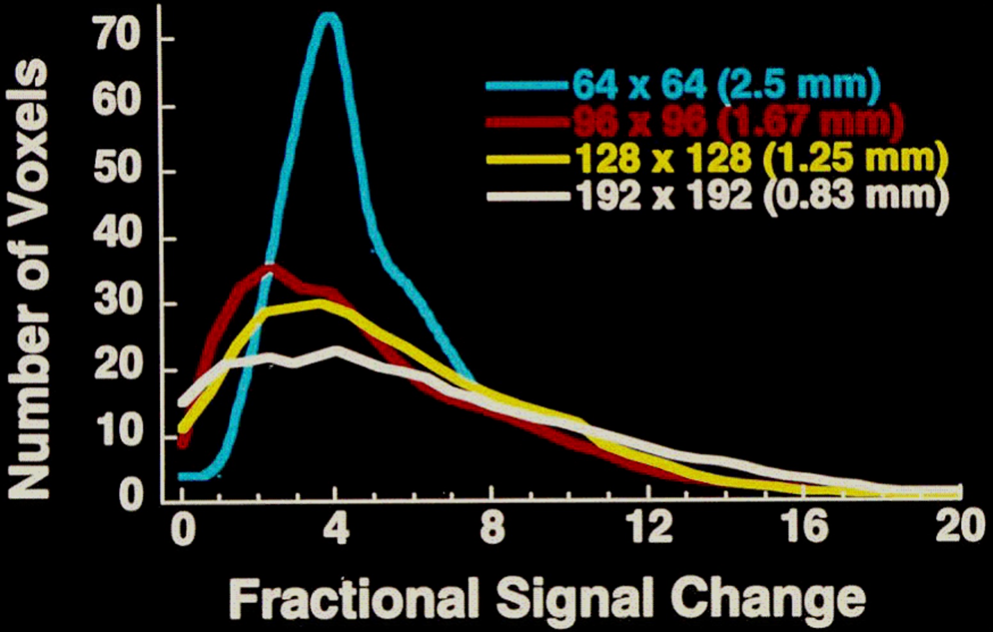
≈ 20 to 40 ms

Partial k-space imaging



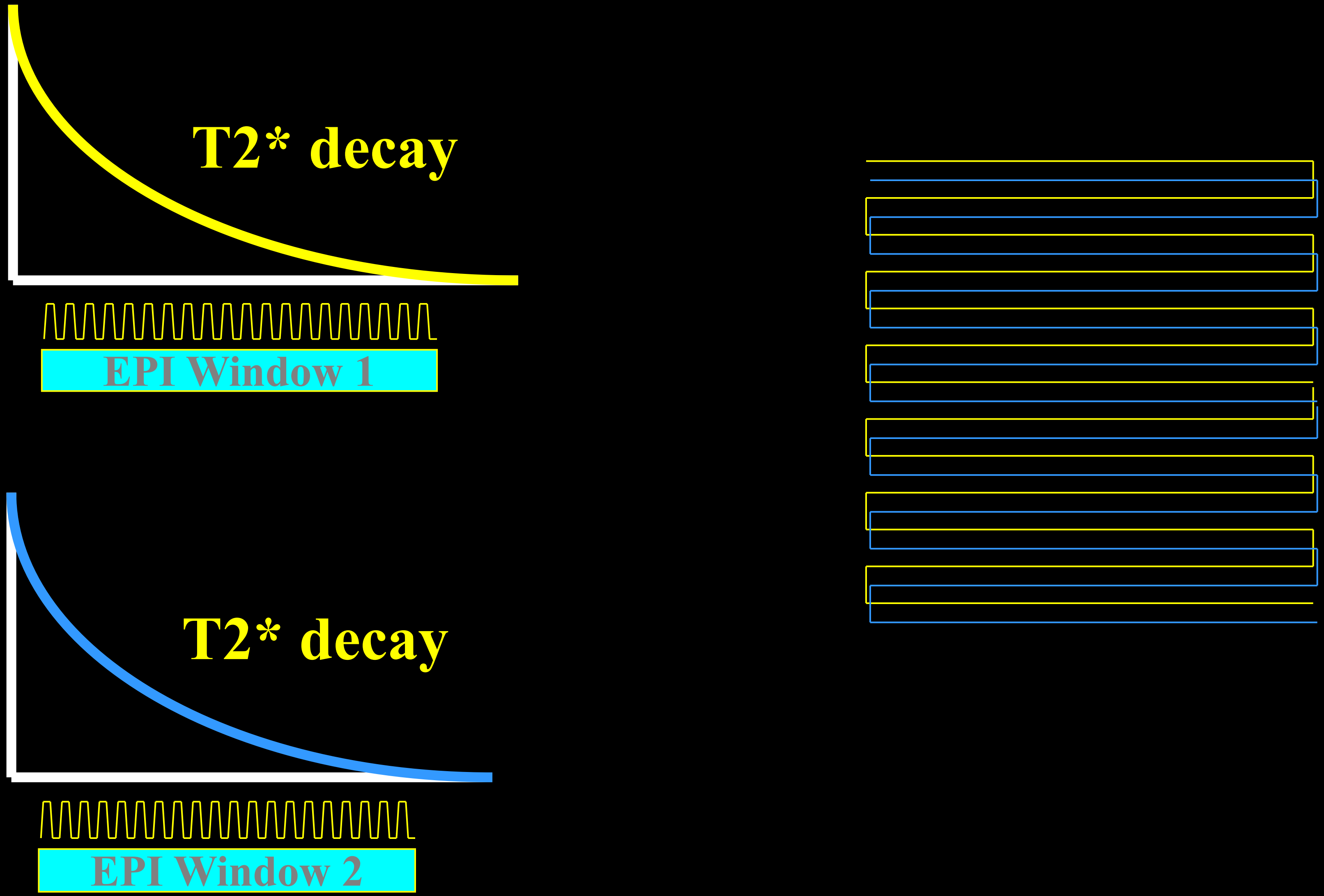
Partial k-space imaging





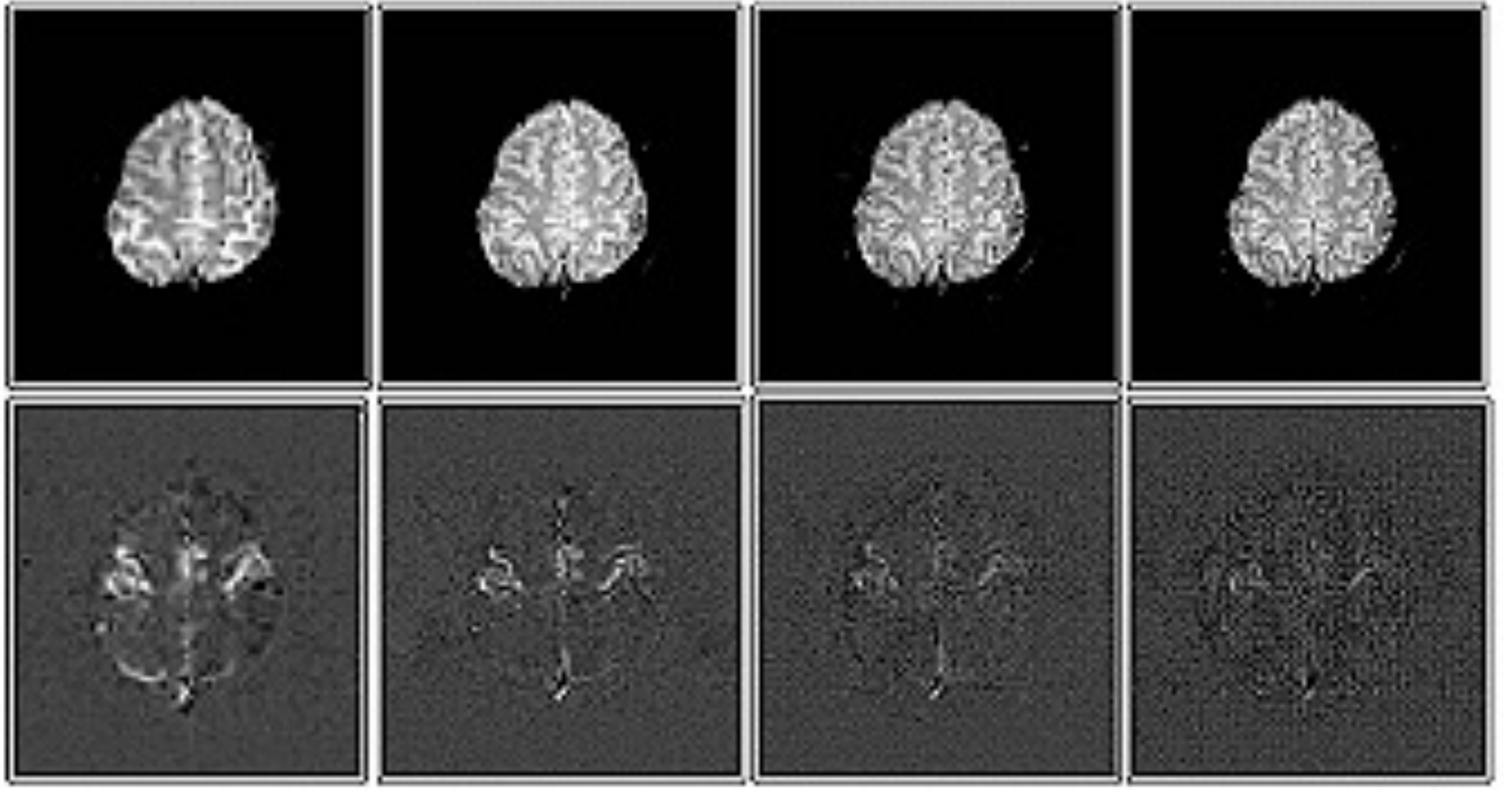
Jesmanowicz, P. A. Bandettini, J. S. Hyde, (1998) "Single shot half k-space high resolution EPI for fMRI at 3T." ***Magn. Reson. Med.*** **40, 754-762.**

Multishot Imaging

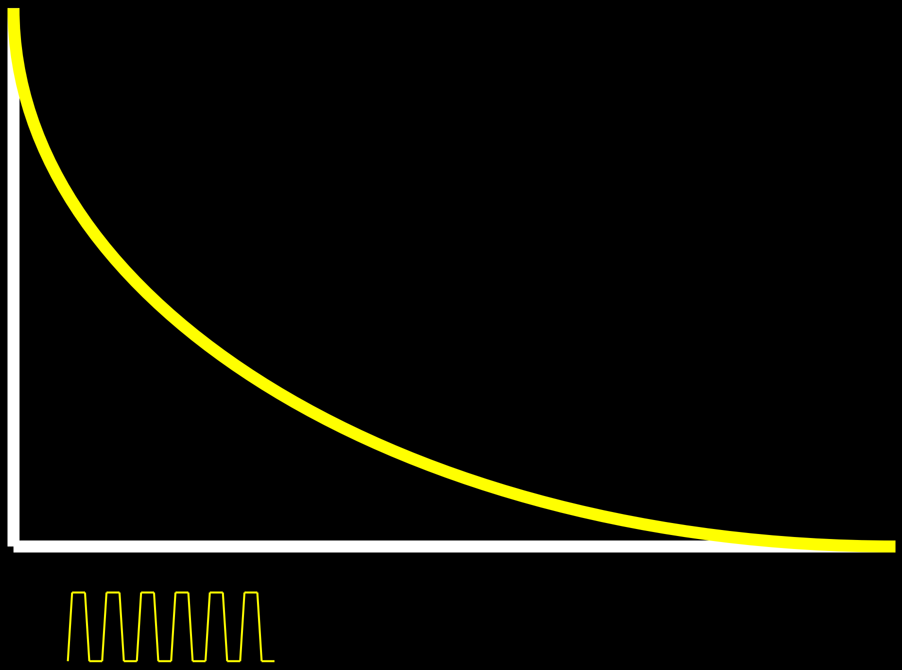


Multi Shot EPI

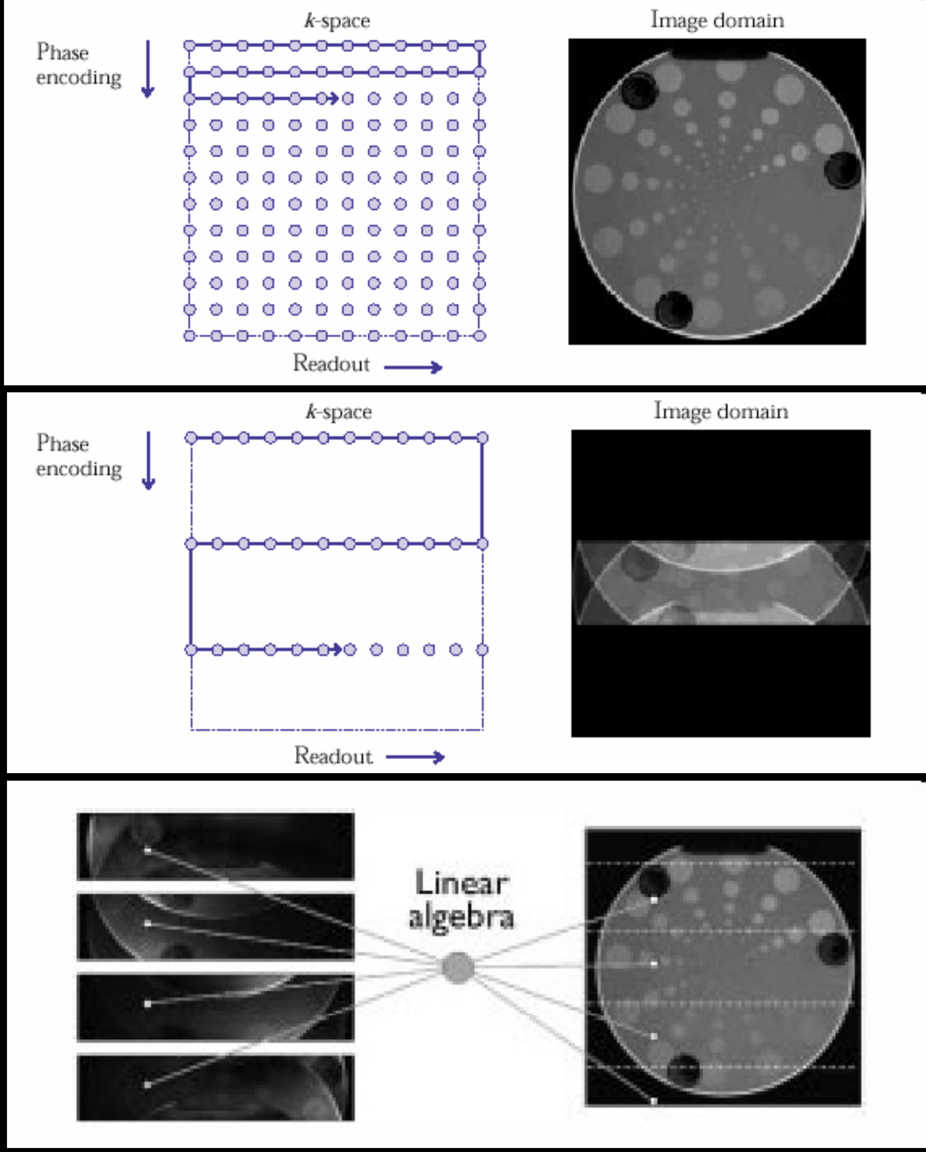
Excitations	1	2	4	8
Matrix Size	64 x 64	128 x 128	256 x 128	256 x 256



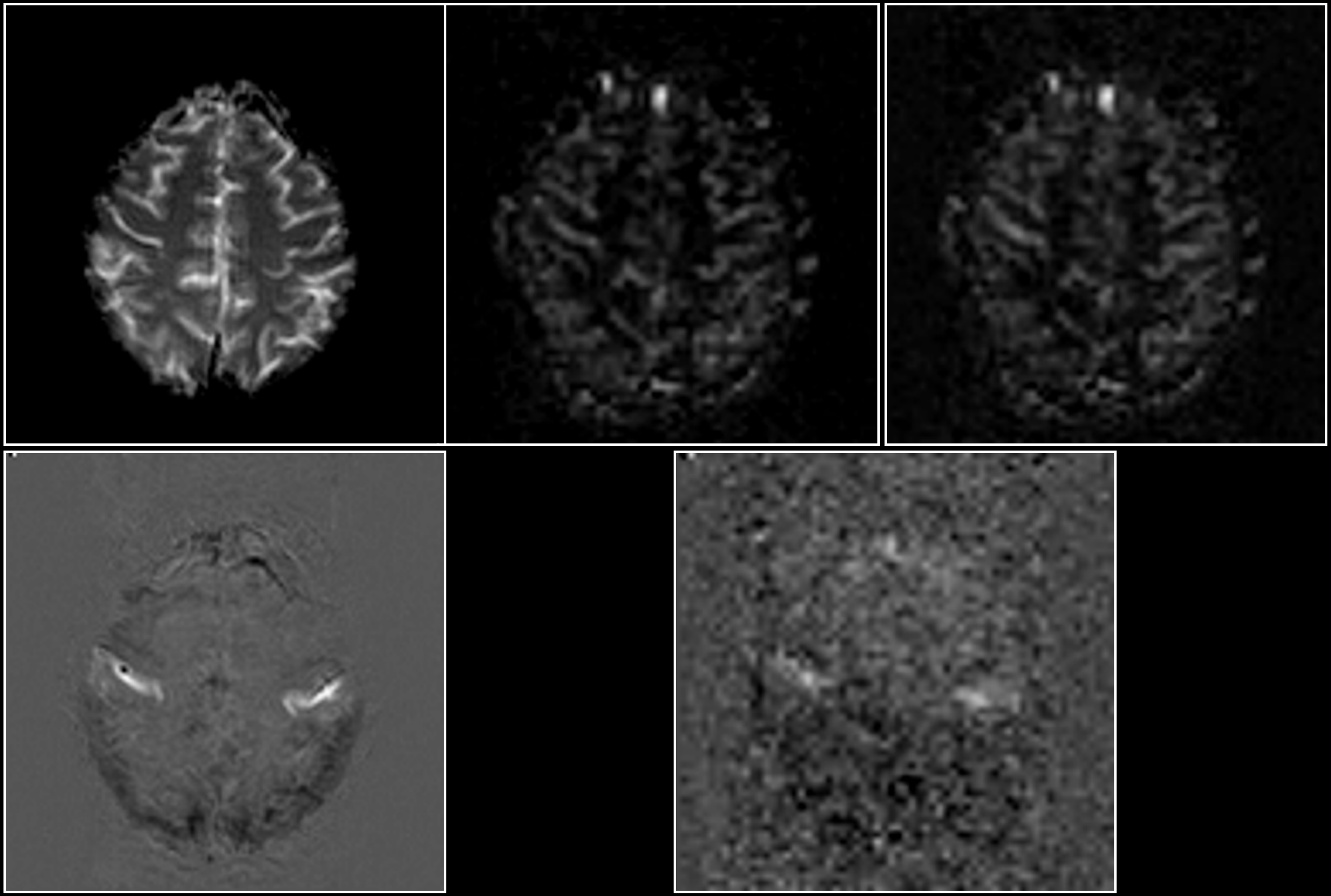
SENSE Imaging



≈ 5 to 30 ms



Pruessmann, et al.



Perfusion

BOLD

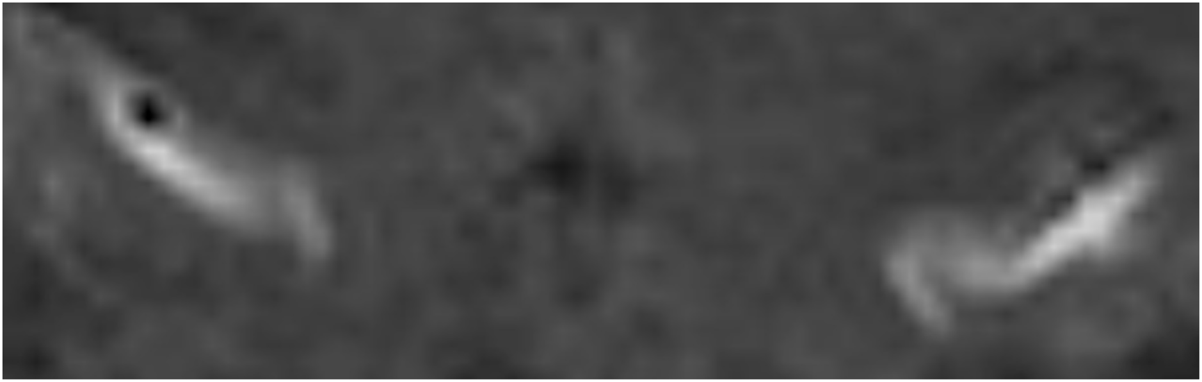
Rest

Activation

P. A. Bandettini, E. C. Wong, Magnetic resonance imaging of human brain function: principles, practicalities, and possibilities, *in* "Neurosurgery Clinics of North America: Functional Imaging" (M. Haglund, Ed.), p.345-371, W. B. Saunders Co., 1997.

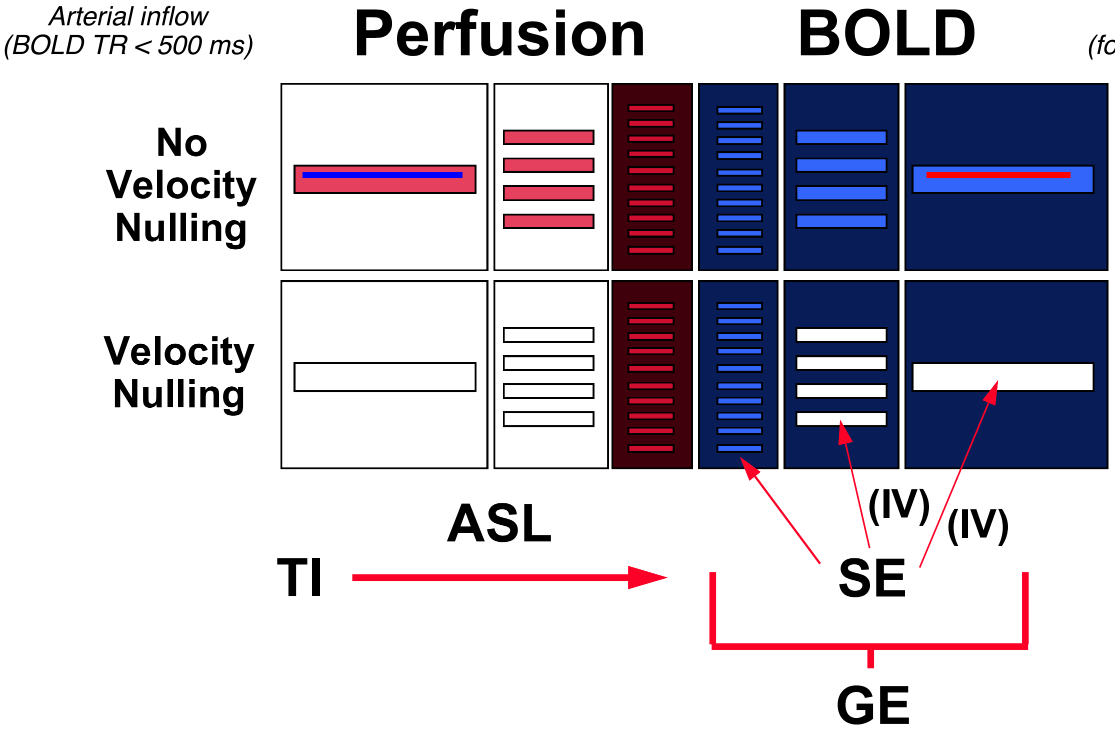
Anatomy

BOLD



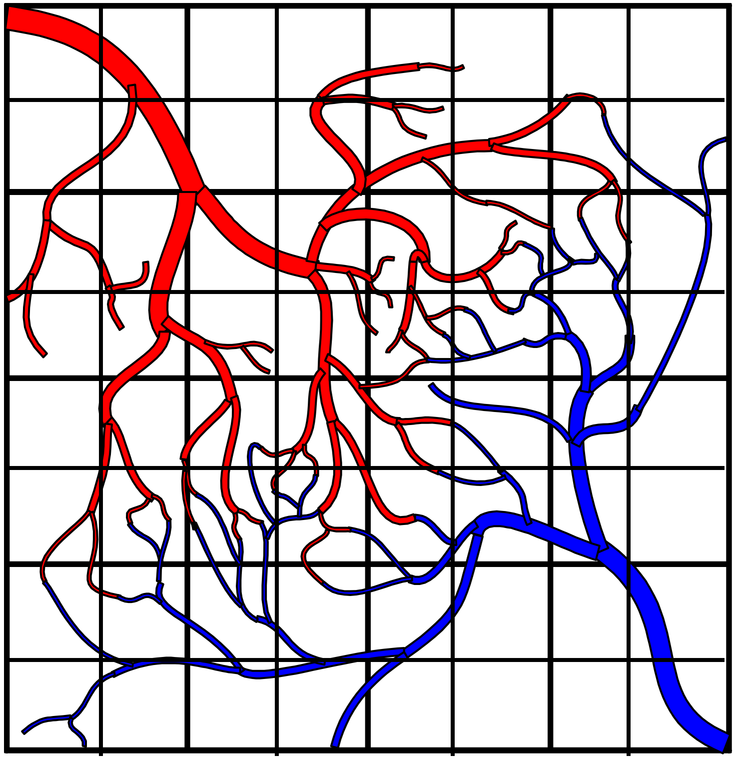
Perfusion

P. A. Bandettini, E. C. Wong, Magnetic resonance imaging of human brain function: principles, practicalities, and possibilities, *in* "Neurosurgery Clinics of North America: Functional Imaging" (M. Haglund, Ed.), p.345-371, W. B. Saunders Co., 1997.



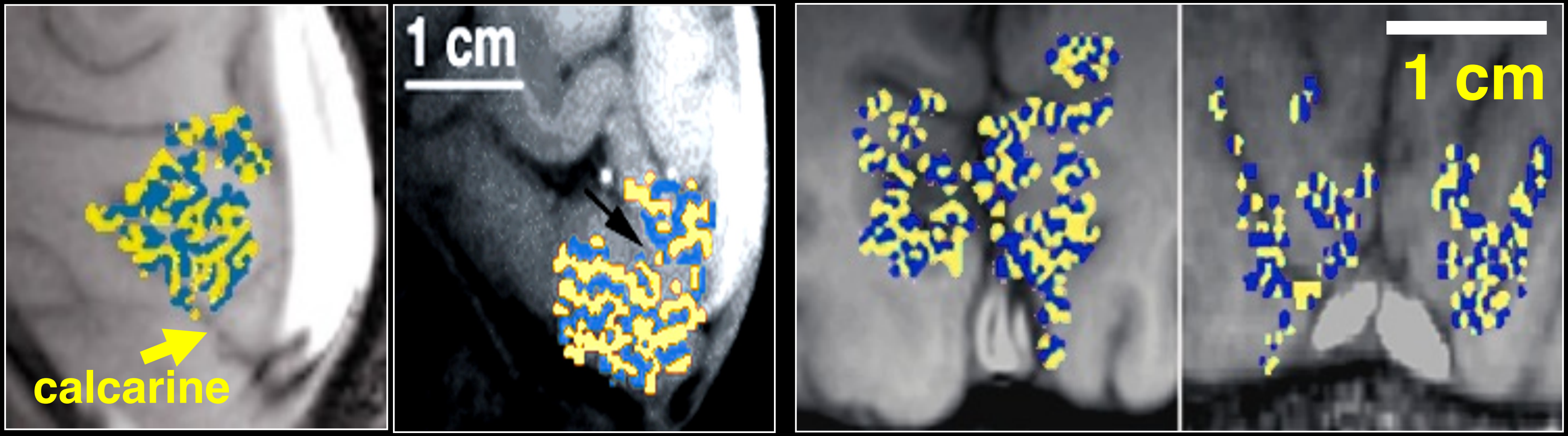
Pulse Sequence Sensitivity

Spatial Heterogeneity



Menon, et al

ODC Maps using fMRI

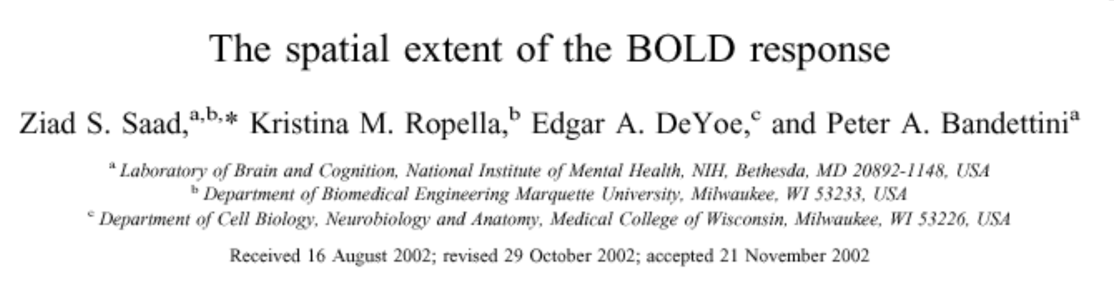


- Identical in size, orientation, and appearance to those obtained by optical imaging[1] and histology[3,4].

[1] Malonek D, Grinvald A. *Science* 272, 551-4 (1996).
[3] Horton JC, Hocking DR. *J Neurosci* 16, 7228-39 (1996).
[4] Horton JC, et al. *Arch Ophthalmol* 108, 1025-31 (1990).

Latest Developments...

1. Temporal Resolution
2. Spatial Resolution
3. Sensitivity and Noise
4. Information Content
5. Implementation



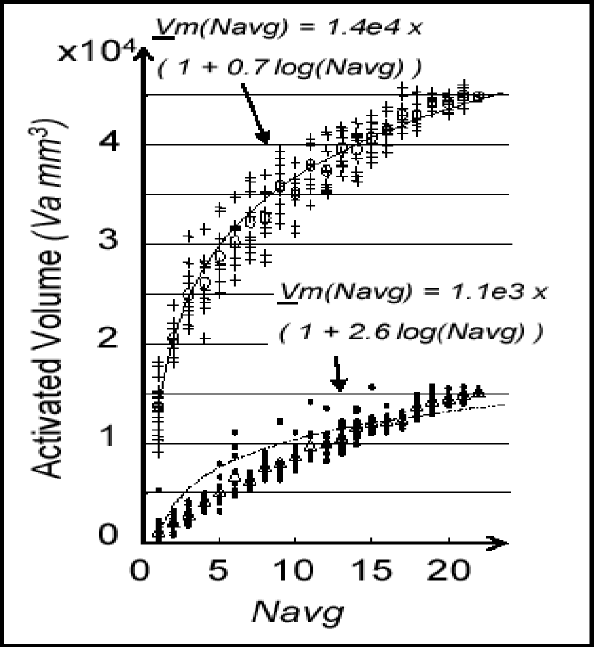
The spatial extent of the BOLD response

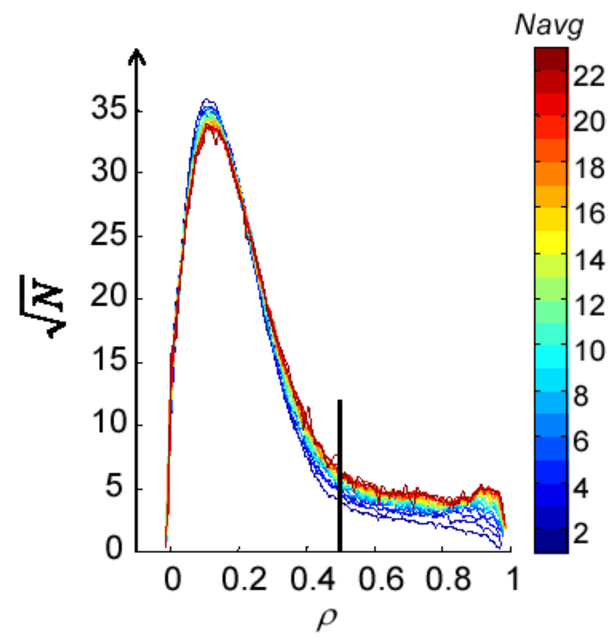
Ziad S. Saad,[a,b,*] Kristina M. Ropella,[b] Edgar A. DeYoe,[c] and Peter A. Bandettini[a]

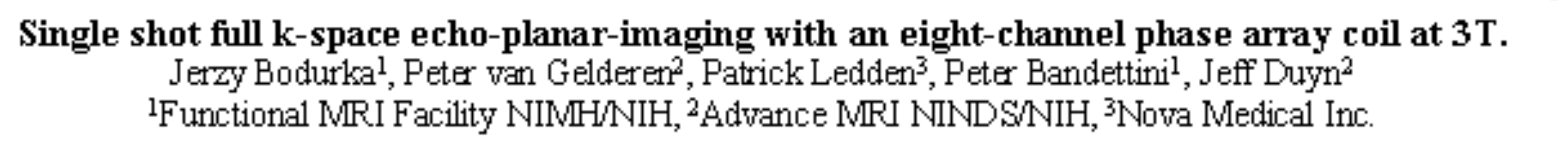
[a] *Laboratory of Brain and Cognition, National Institute of Mental Health, NIH, Bethesda, MD 20892-1148, USA*
[b] *Department of Biomedical Engineering Marquette University, Milwaukee, WI 53233, USA*
[c] *Department of Cell Biology, Neurobiology and Anatomy, Medical College of Wisconsin, Milwaukee, WI 53226, USA*

Received 16 August 2002; revised 29 October 2002; accepted 21 November 2002

NeuroImage, **19:** 132-144, (2003).







Single shot full k-space echo-planar-imaging with an eight-channel phase array coil at 3T.

Jerzy Bodurka[1], Peter van Gelderen[2], Patrick Ledden[3], Peter Bandettini[1], Jeff Duyn[2]

[1]Functional MRI Facility NIMH/NIH, [2]Advance MRI NINDS/NIH, [3]Nova Medical Inc.

Quadrature Head Coil

8 Channel Array

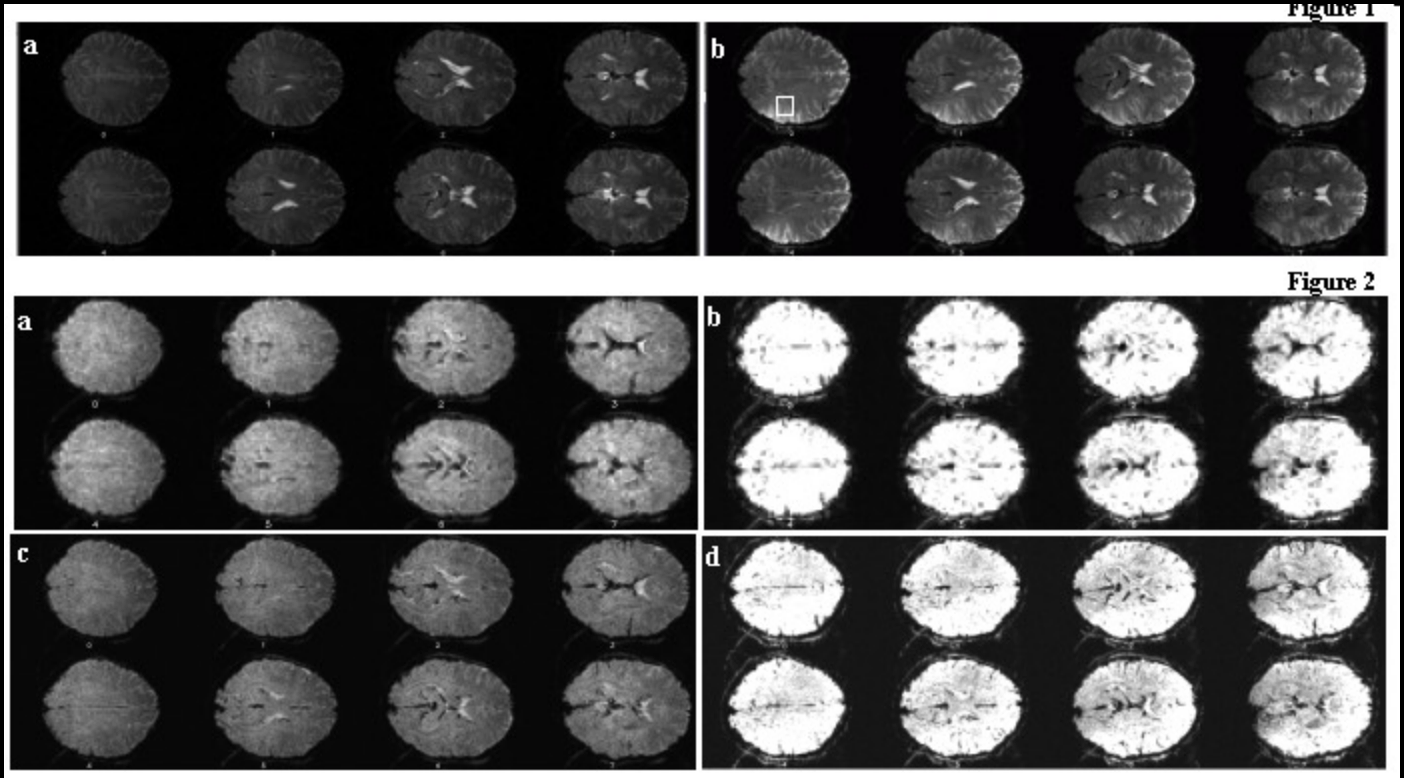
128 x 96

64 x 48

128 x 96

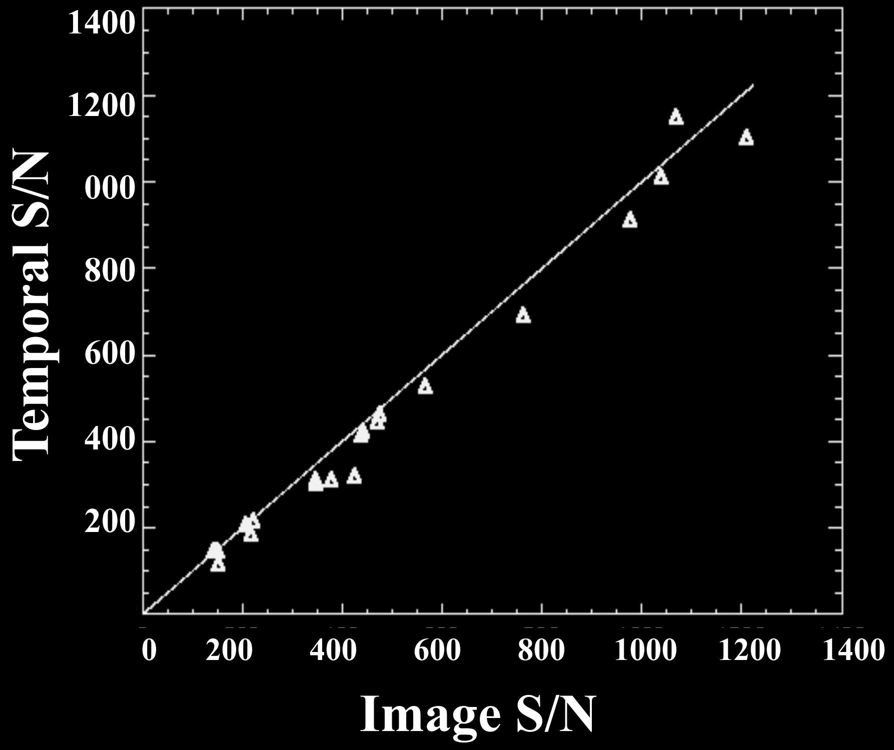
SNR

TSNR

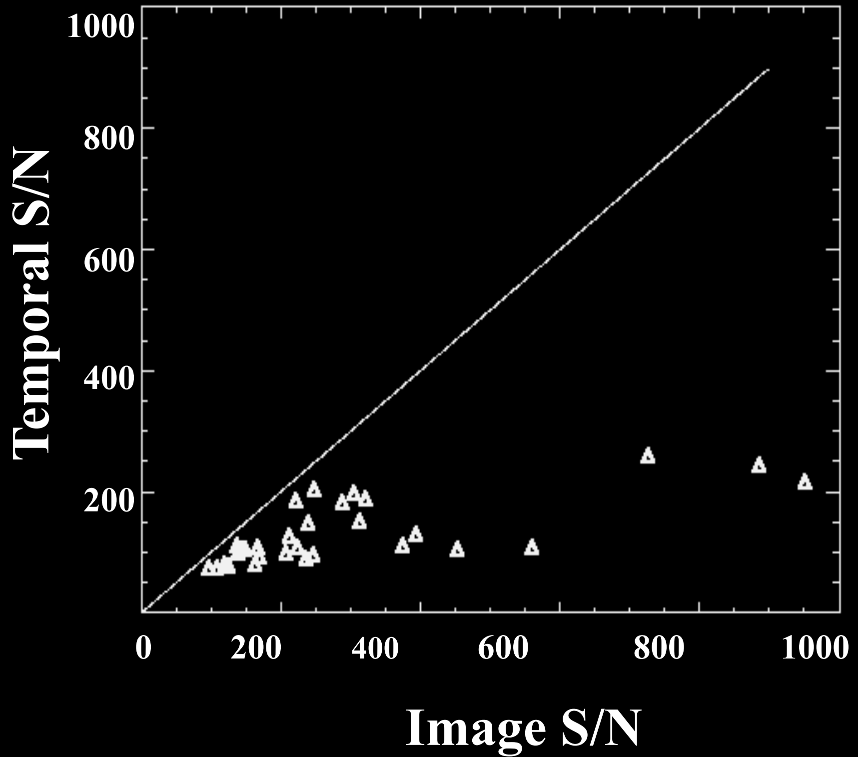


Temporal S/N vs. Image S/N

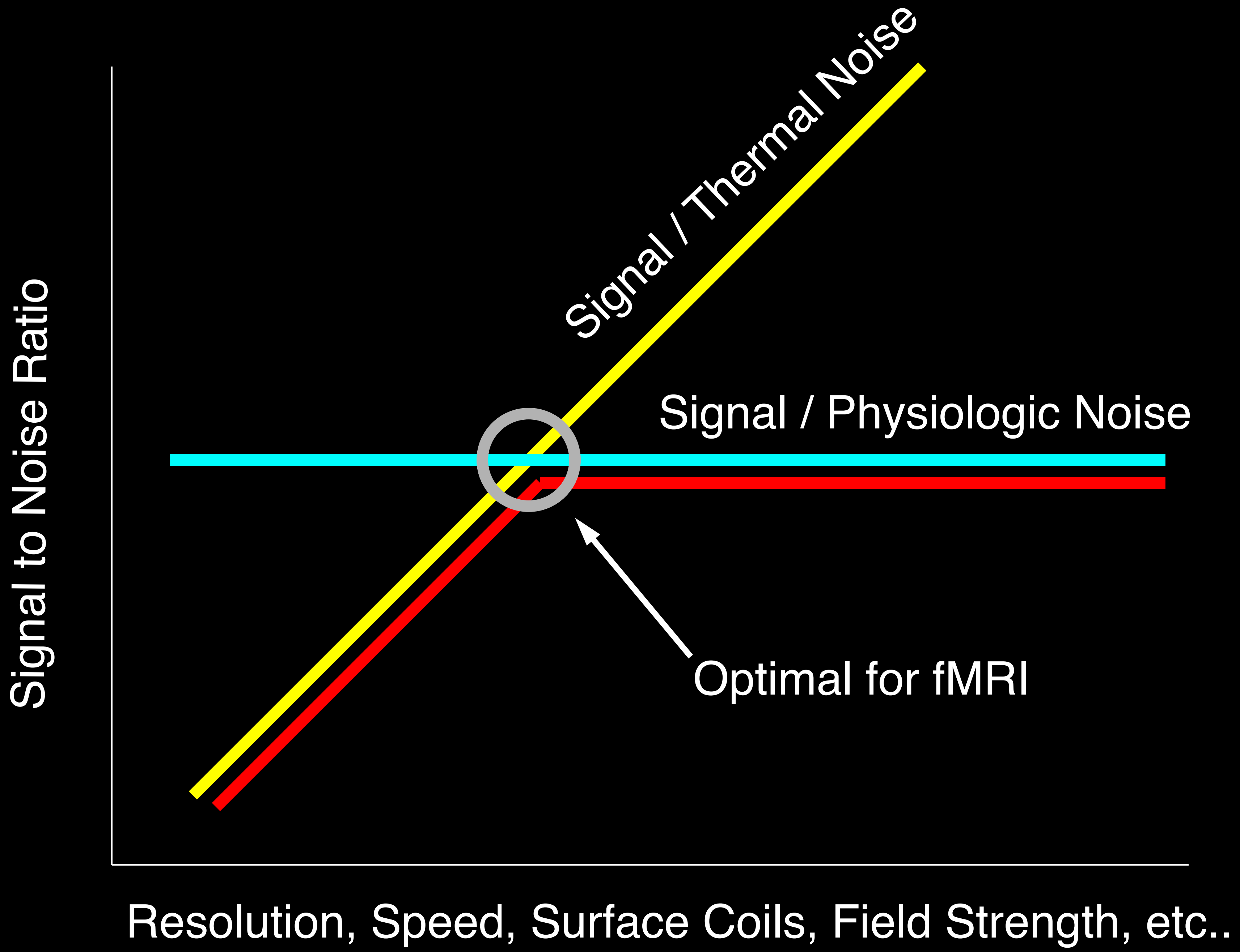
PHANTOMS



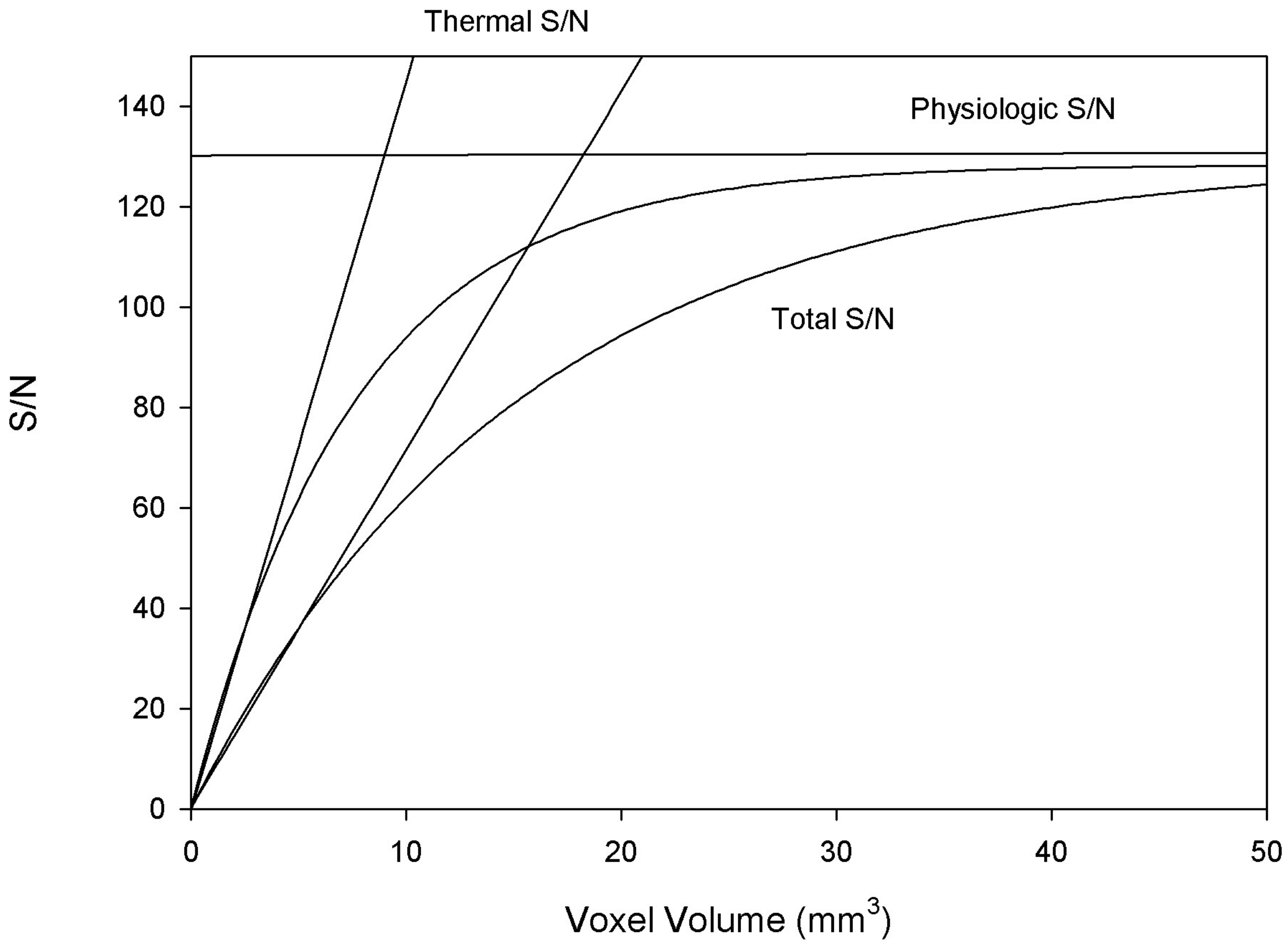
SUBJECTS



N. Petridou



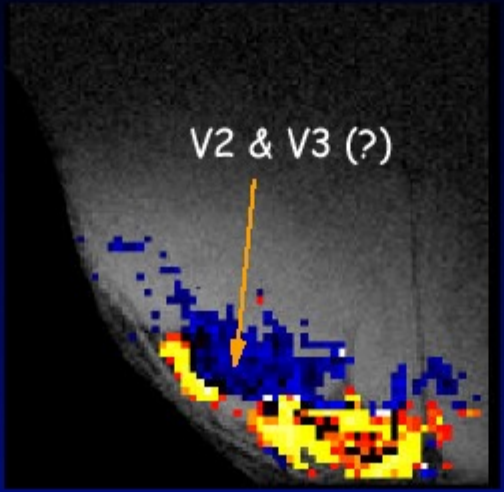
Optimal for fMRI

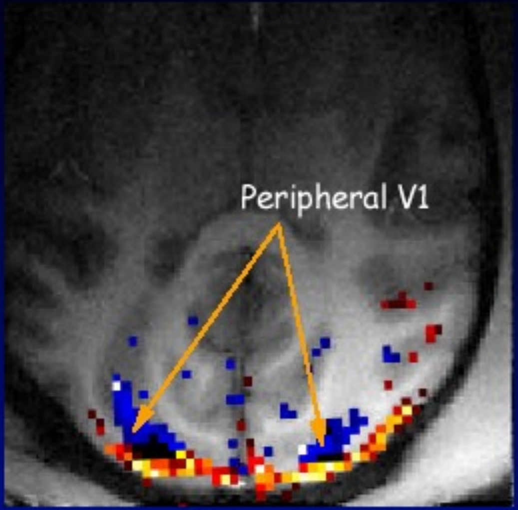

Thermal S/N
Physiologic S/N
Total S/N
S/N
Voxel Volume (mm³)
0
20
40
60
80
100
120
140
0
10
20
30
40
50

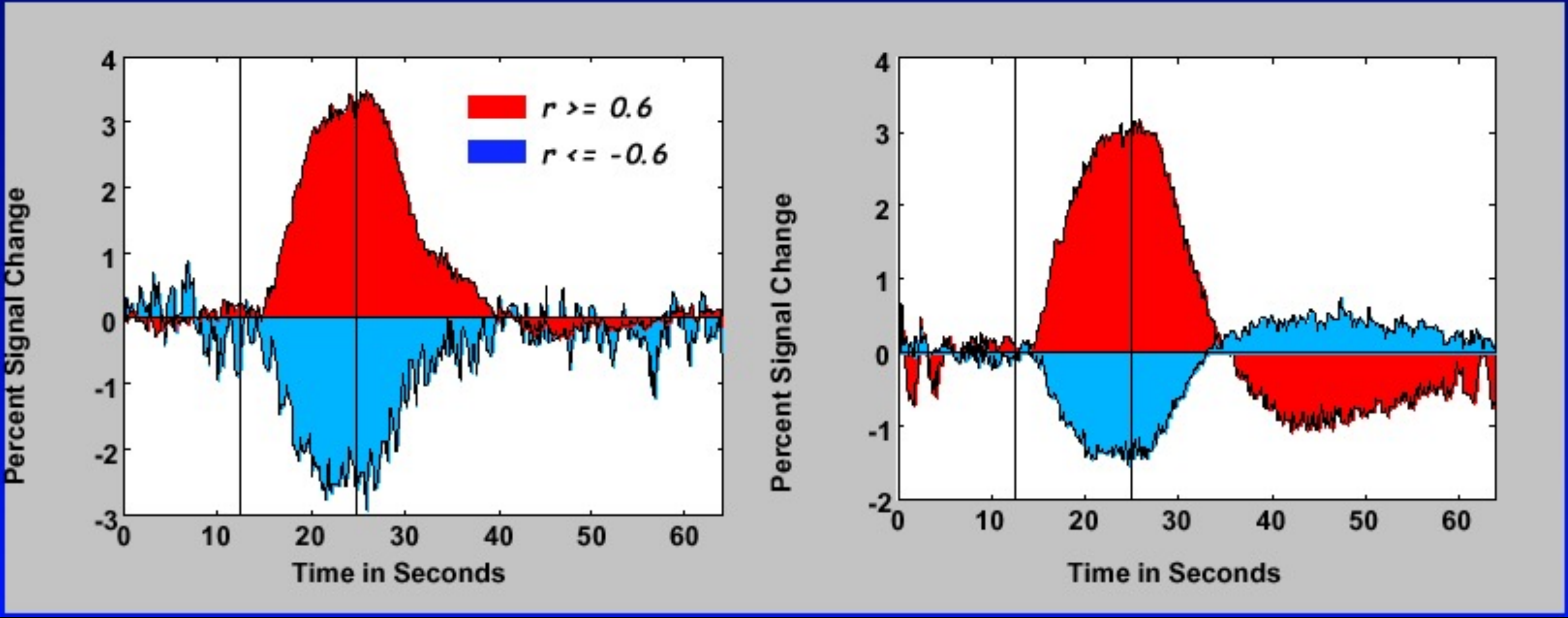
Latest Developments...

1. Temporal Resolution
2. Spatial Resolution
3. Sensitivity and Noise
4. Information Content
5. Implementation

Negative BOLD effect







HBM 2003
Poster number: 308

The Negative BOLD Response in Monkey V1 Is Associated with Decreases in Neuronal Activity

Amir Shmuel*†, Mark Augath, Axel Oeltermann, Jon Pauls, Yusuke Murayama, Nikos K. Logothetis

Figure 1

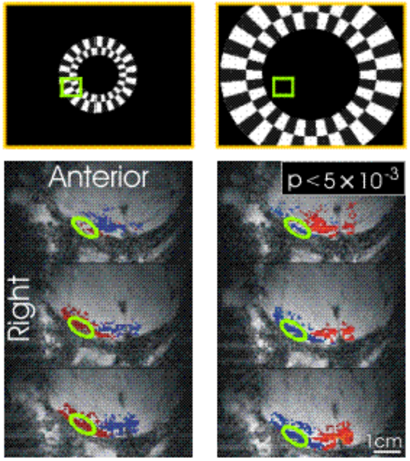


Figure 2

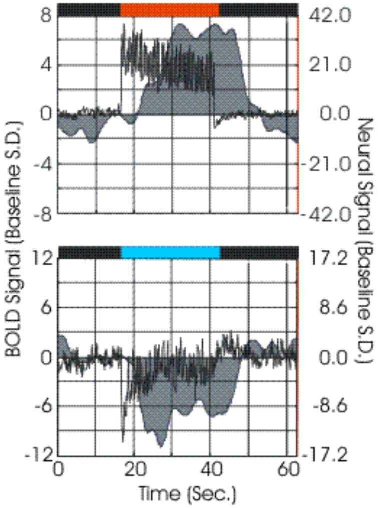
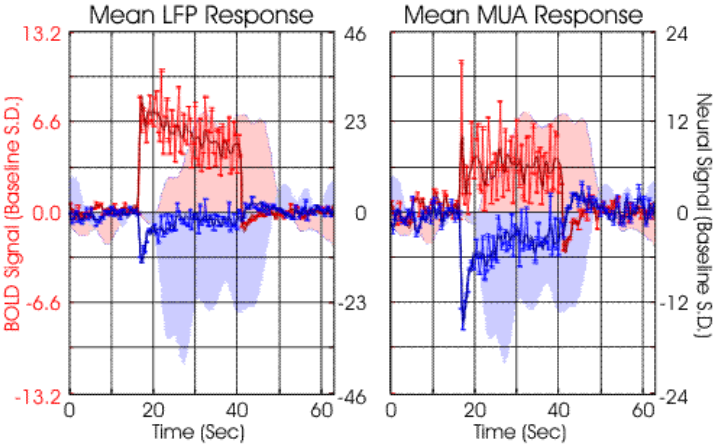
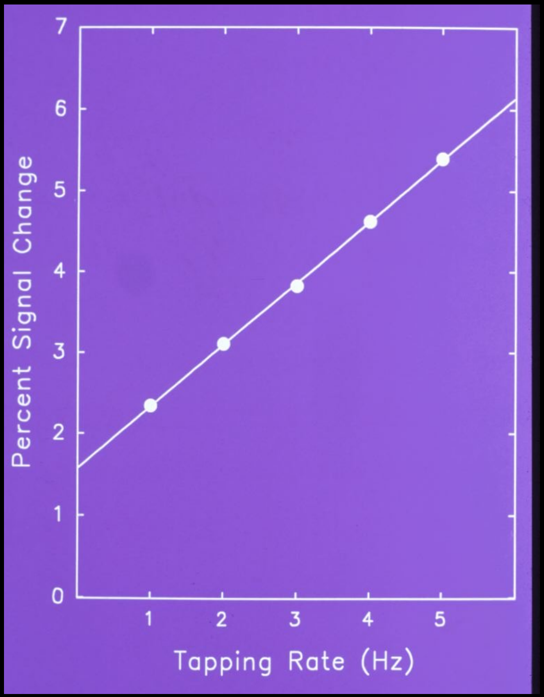


Figure 3



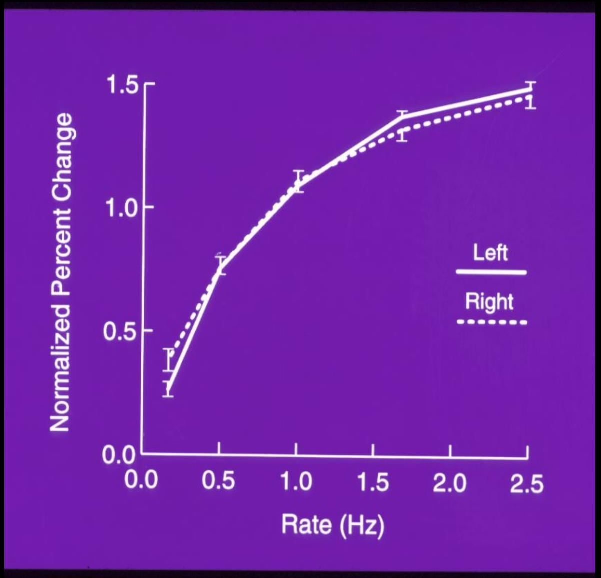
Parametric Manipulation

Motor Cortex



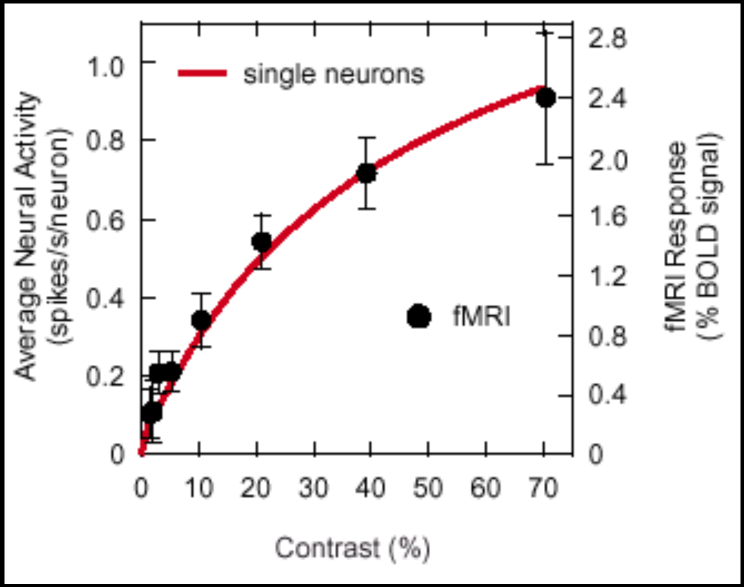
S. M. Rao et al, (1996) “Relationship between finger movement rate and functional magnetic resonance signal change in human primary motor cortex.” *J. Cereb. Blood Flow and Met.* 16, 1250-1254.

Auditory Cortex



J. R. Binder, et al, (1994). “Effects of stimulus rate on signal response during functional magnetic resonance imaging of auditory cortex.” *Cogn. Brain Res.* 2, 31-38

fMRI responses in human V1 are proportional to average firing rates in monkey V1

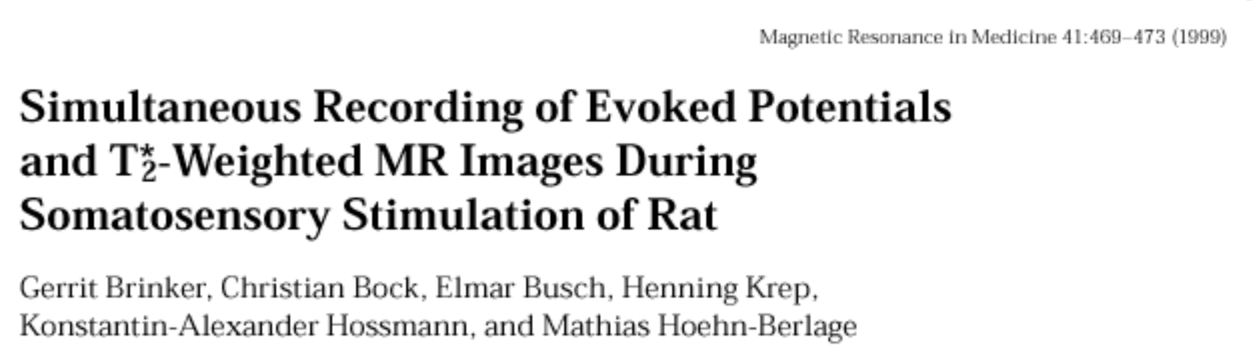


Heeger, D. J., Huk, A. C., Geisler, W. S., and Albrecht, D. G. 2000.Spikes versus BOLD: What does neuroimaging tell us about neuronal activity? *Nat. Neurosci.* **3:** 631–633.

0.4 spikes/sec -> 1% BOLD

Rees, G., Friston, K., and Koch, C. 2000. A direct quantitative relationship between the functional properties of human and macaque V5. *Nat. Neurosci.* **3:** 716–723.

9 spikes/sec -> 1% BOLD



Magnetic Resonance in Medicine 41:469–473 (1999)

Simultaneous Recording of Evoked Potentials and T_2^*-Weighted MR Images During Somatosensory Stimulation of Rat

Gerrit Brinker, Christian Bock, Elmar Busch, Henning Krep,
Konstantin-Alexander Hossmann, and Mathias Hoehn-Berlage

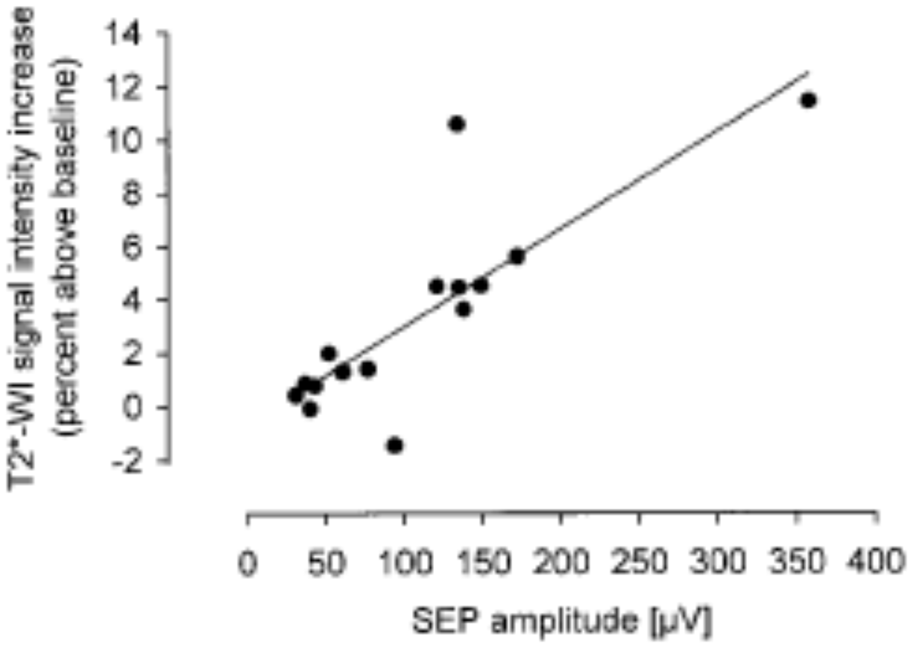
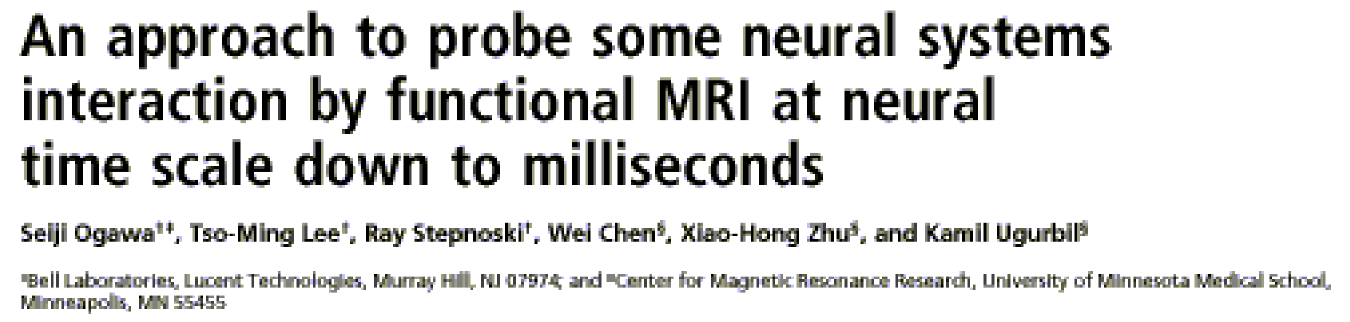


FIG. 3. Correlation of the increase of T_2^*-weighted imaging signal intensity with the peak-to-peak amplitude of the somatosensory evoked potential (SEP) during forepaw stimulation at increasing frequencies (data are from one individual animal; r = 0.82).



An approach to probe some neural systems interaction by functional MRI at neural time scale down to milliseconds

Seiji Ogawa[†‡], Tso-Ming Lee[†], Ray Stepnoski[†], Wei Chen[§], Xiao-Hong Zhu[§], and Kamil Ugurbil[§]

[†]Bell Laboratories, Lucent Technologies, Murray Hill, NJ 07974; and [§]Center for Magnetic Resonance Research, University of Minnesota Medical School, Minneapolis, MN 55455

11026–11031 PNAS **September 26, 2000** vol. 97 no. 20

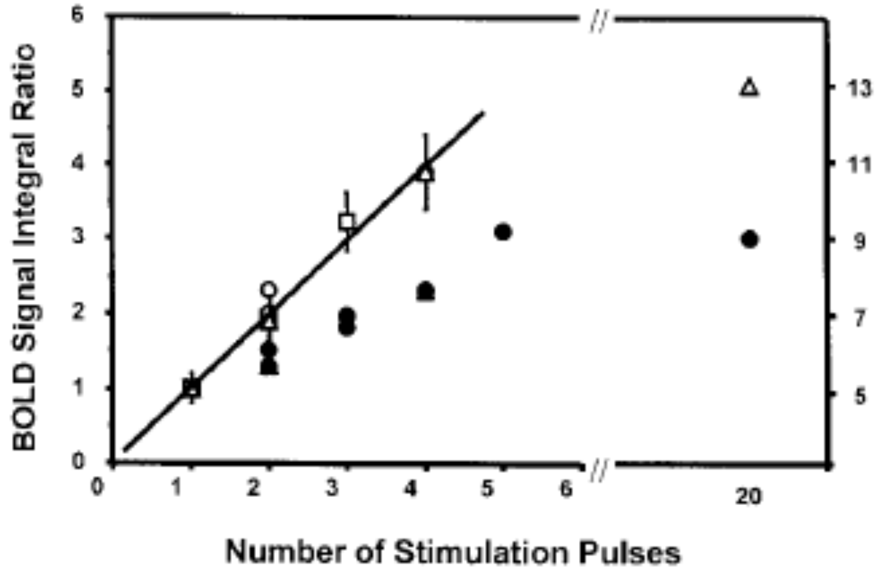
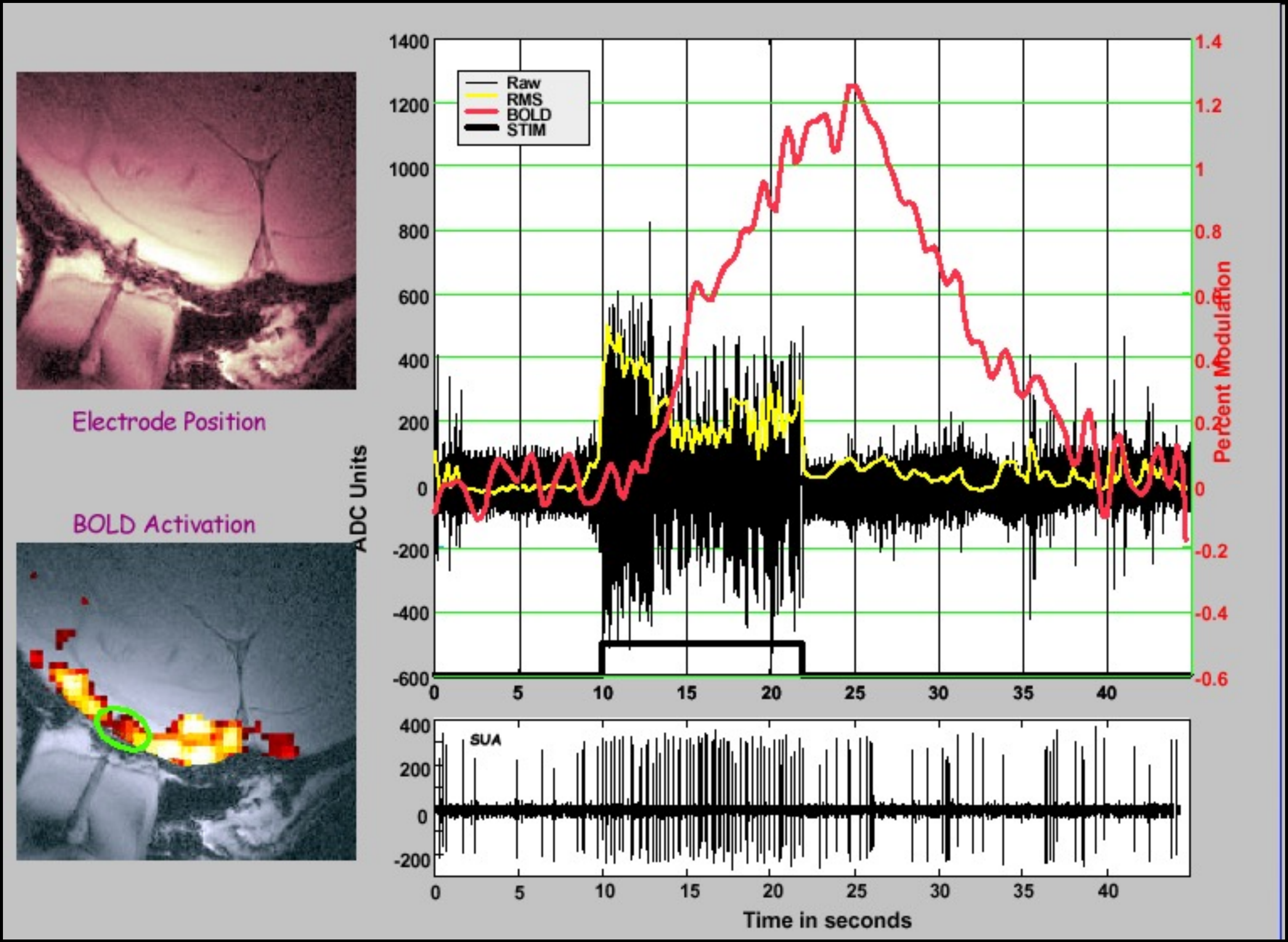
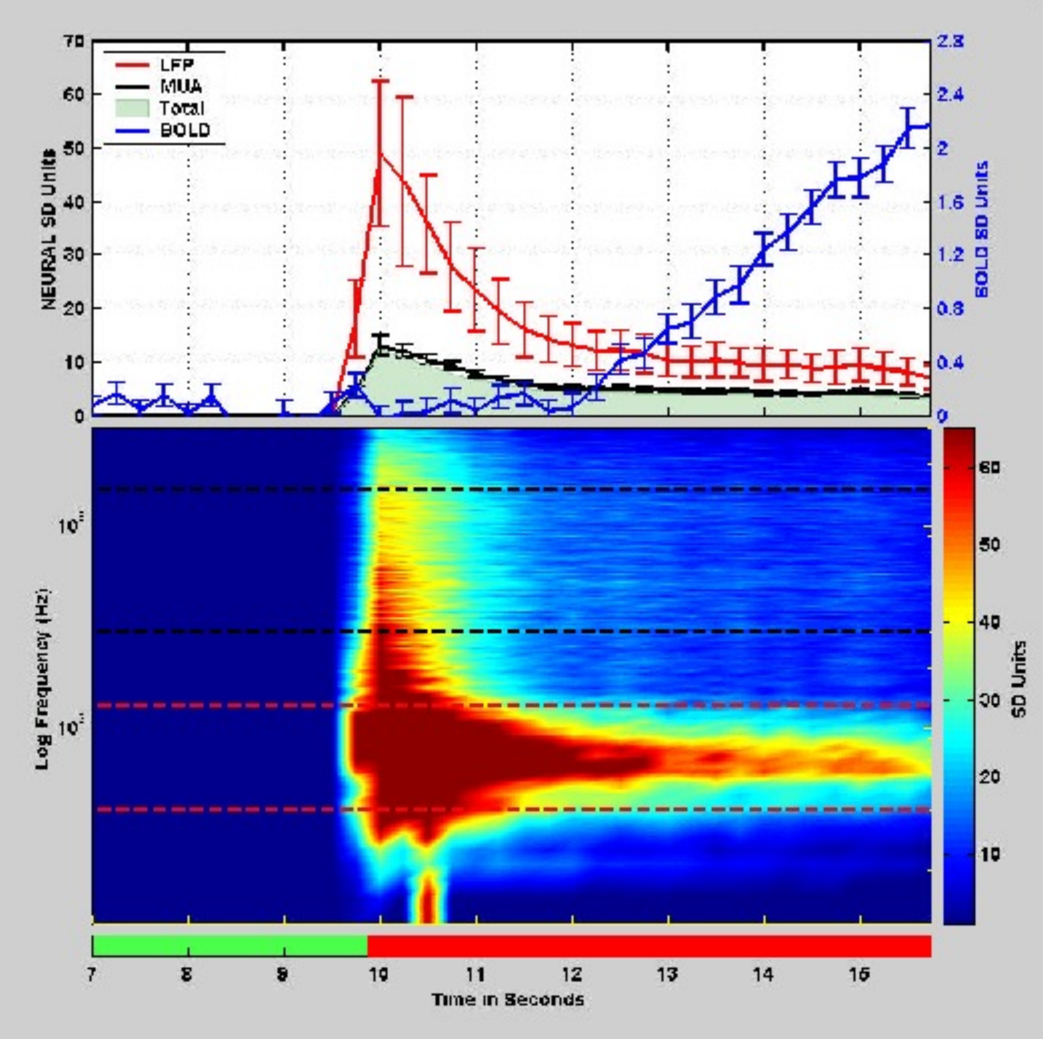


Fig. 2. BOLD responses to a number of stimulation pulses (Paradigm I) given to the rat forepaw. BOLD signal integrals (height times width at half height) relative to the signal by single stimulus (300-μsec-wide current pulse at 0.4 to 0.8 mA) are plotted as a function of the number of stimuli administered. The open symbols are those measured with 620 msec ISI. The error bars indicate the possible ranges of the uncertainty in estimating the normalized values of BOLD signal changes (four rats). The filled symbols are those with 310 msec ISI (two rats).

Logothetis et al. (2001) “Neurophysiological investigation of the basis of the fMRI signal” Nature, 412, 150-157



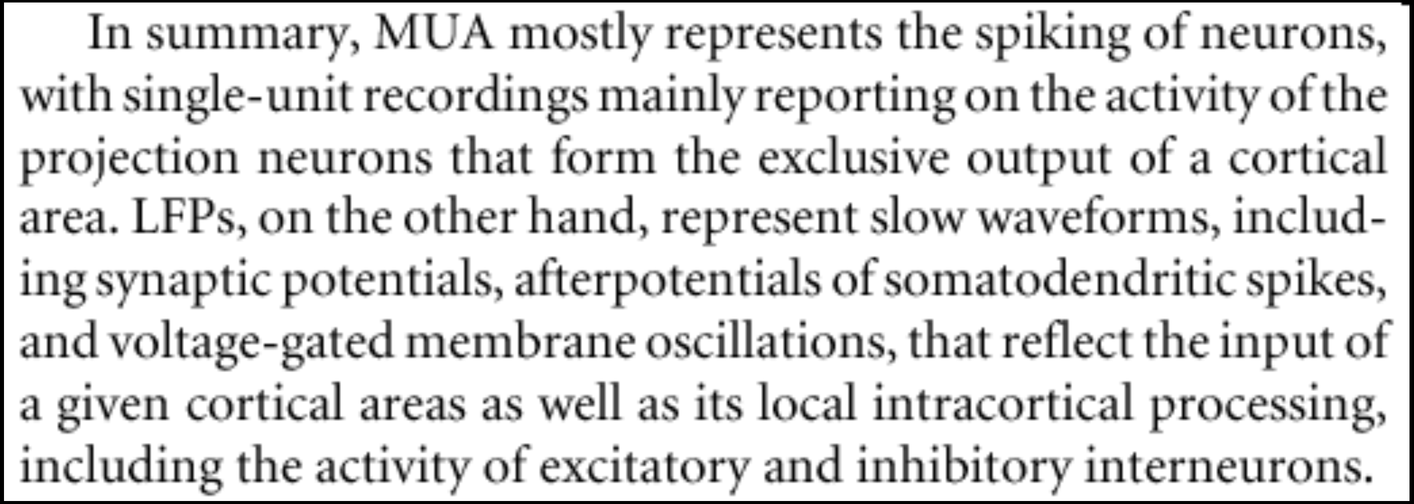
Logothetis et al. (2001) “Neurophysiological investigation of the basis of the fMRI signal” Nature, 412, 150-157



The Journal of Neuroscience, May 15, 2003 • 23(10):3963–3971 • **3963**

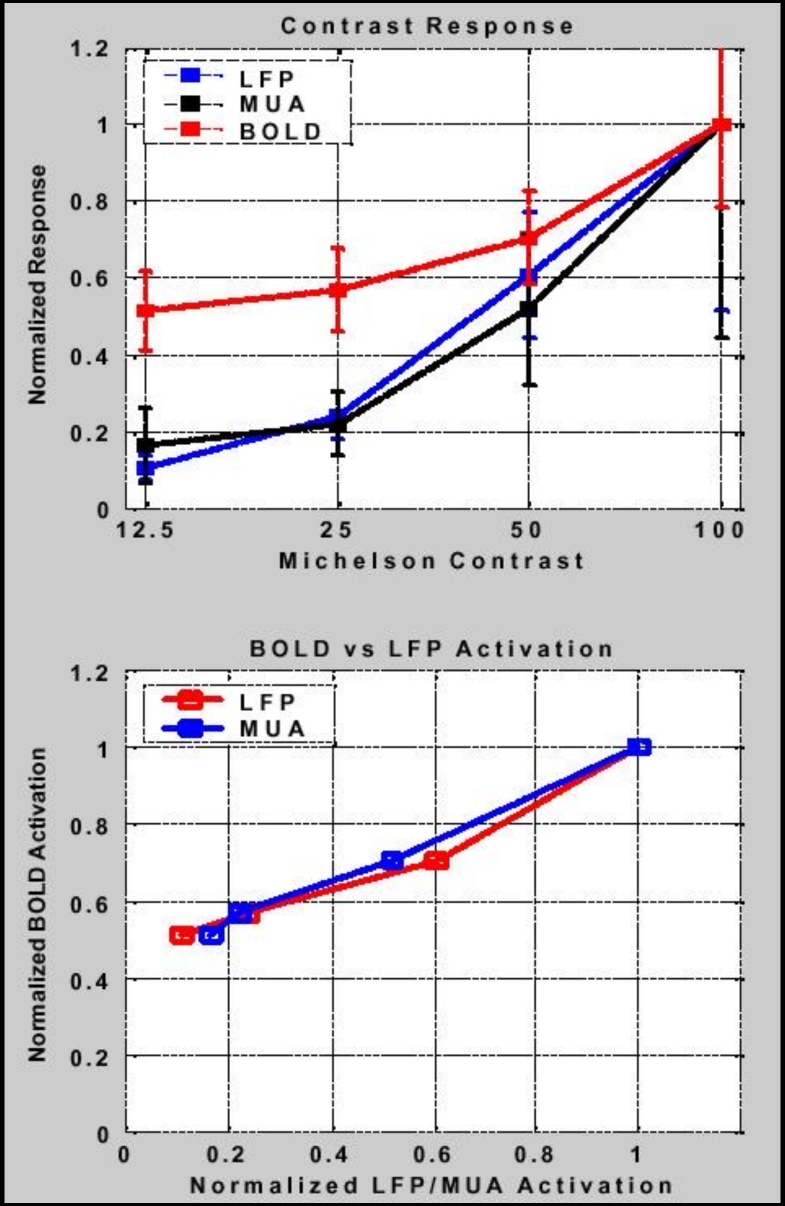
The Underpinnings of the BOLD Functional Magnetic Resonance Imaging Signal

Nikos K. Logothetis
Max Planck Institute for Biological Cybernetics, 72076 Tuebingen, Germany



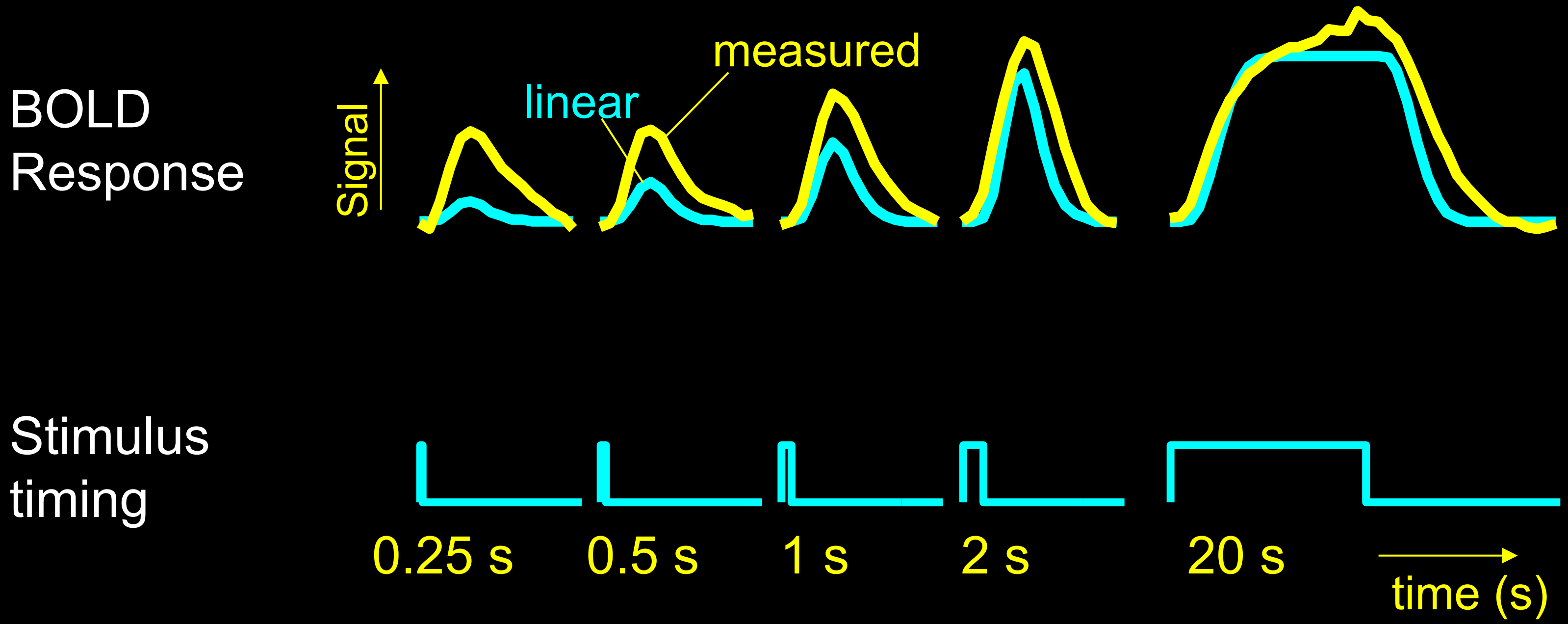
In summary, MUA mostly represents the spiking of neurons, with single-unit recordings mainly reporting on the activity of the projection neurons that form the exclusive output of a cortical area. LFPs, on the other hand, represent slow waveforms, including synaptic potentials, afterpotentials of somatodendritic spikes, and voltage-gated membrane oscillations, that reflect the input of a given cortical areas as well as its local intracortical processing, including the activity of excitatory and inhibitory interneurons.

Logothetis et al. (2001) “Neurophysiological investigation of the basis of the fMRI signal” Nature, 412, 150-157



Dynamic Nonlinearity Assessment

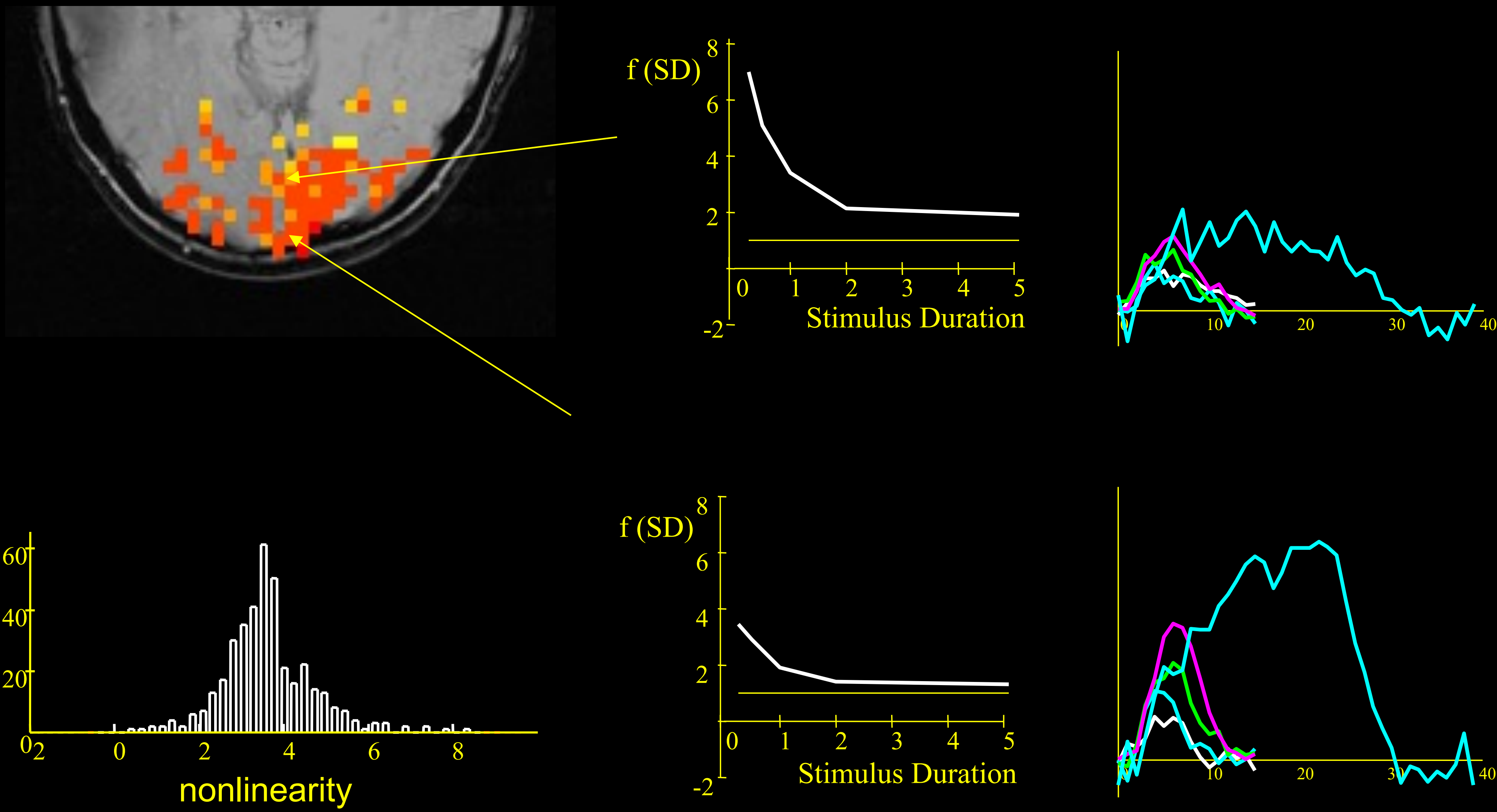
Different stimulus "ON" periods



Brief stimuli produce larger responses than expected

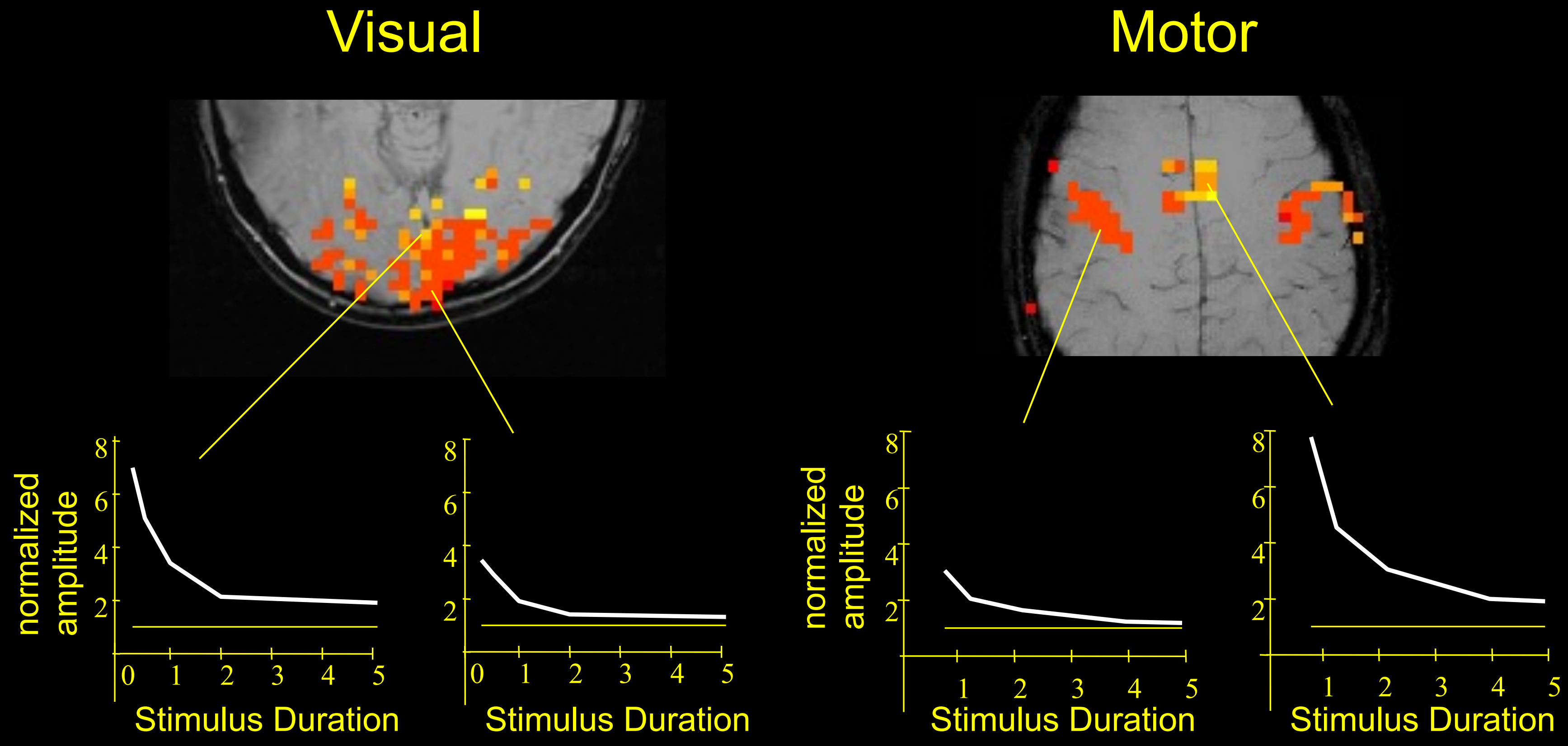
R. M. Birn, Z. Saad, P. A. Bandettini, (2001) "Spatial heterogeneity of the nonlinear dynamics in the fMRI BOLD response." ***NeuroImage*****, 14: 817-826.**

Spatial Heterogeneity of BOLD Nonlinearity



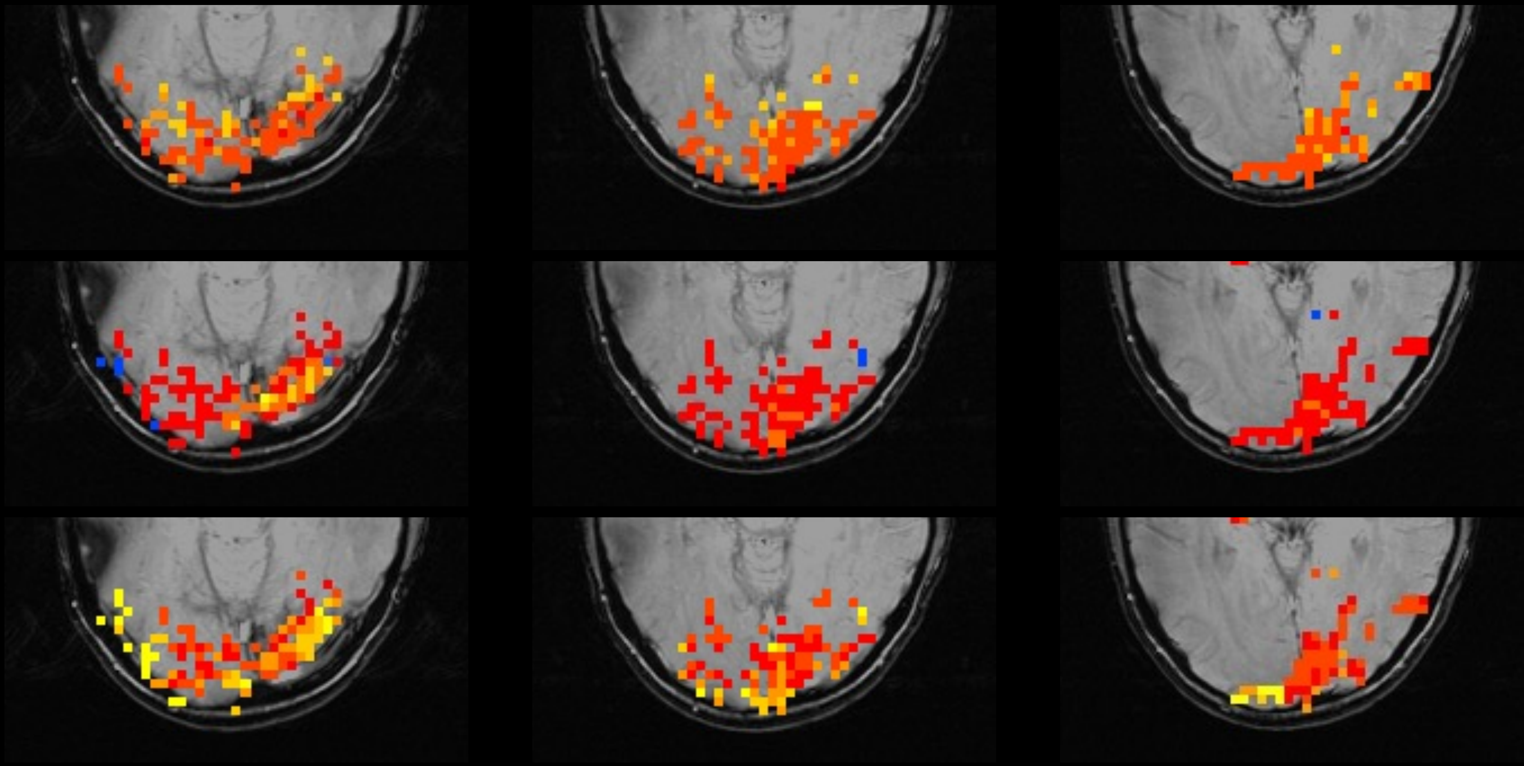
R. M. Birn, Z. Saad, P. A. Bandettini, (2001) "Spatial heterogeneity of the nonlinear dynamics in the fMRI BOLD response." *NeuroImage*, 14: 817-826.

Spatial variation of linearity



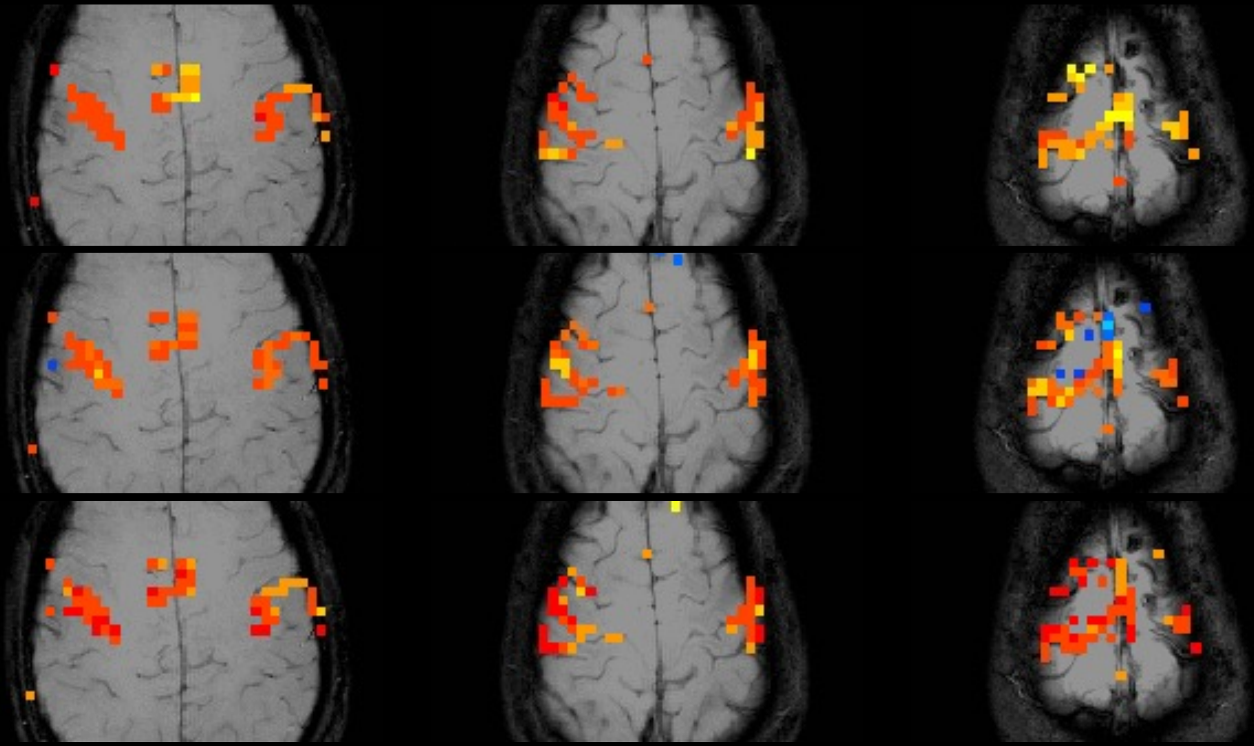
R.M. Birn, et al. Neuroimage 14, 817-26, 2001

Results – visual task



R. M. Birn, Z. Saad, P. A. Bandettini, (2001) "Spatial heterogeneity of the nonlinear dynamics in the fMRI BOLD response." ***NeuroImage*****, 14: 817-826.**

Results – motor task



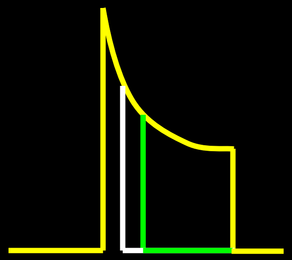
Nonlinearity

Magnitude

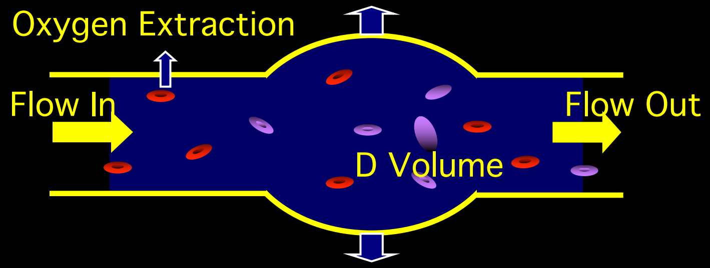
Latency

Sources of this Nonlinearity

- Neuronal

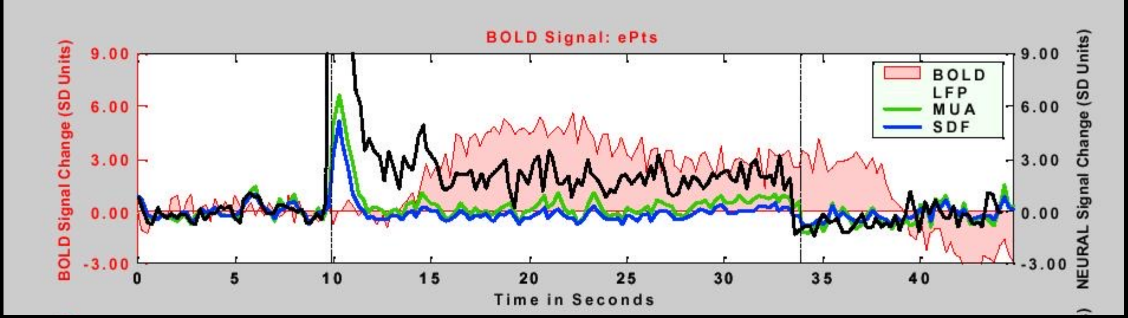


- Hemodynamic
  - Oxygen extraction
  - Blood volume dynamics

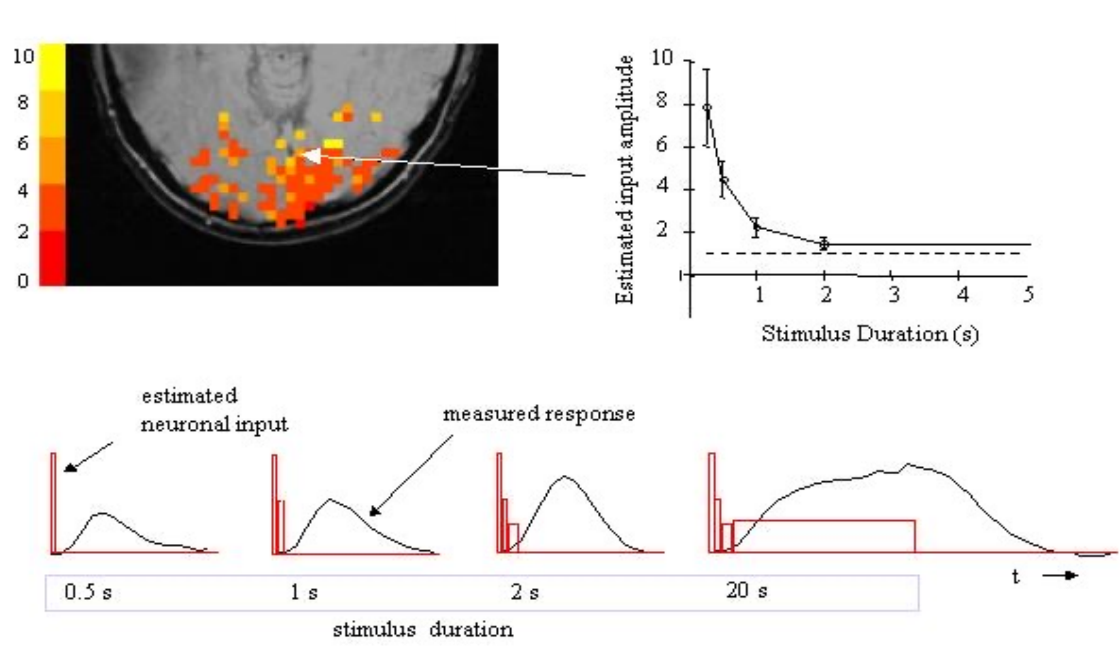


BOLD Correlation with Neuronal Activity

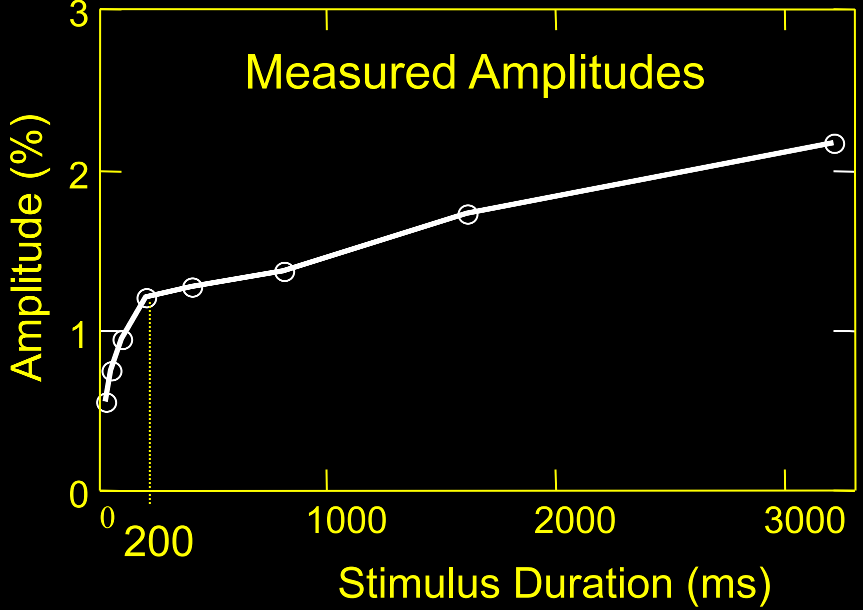
Logothetis et al. (2001) “Neurophysiological investigation of the basis of the fMRI signal” Nature, 412, 150-157.

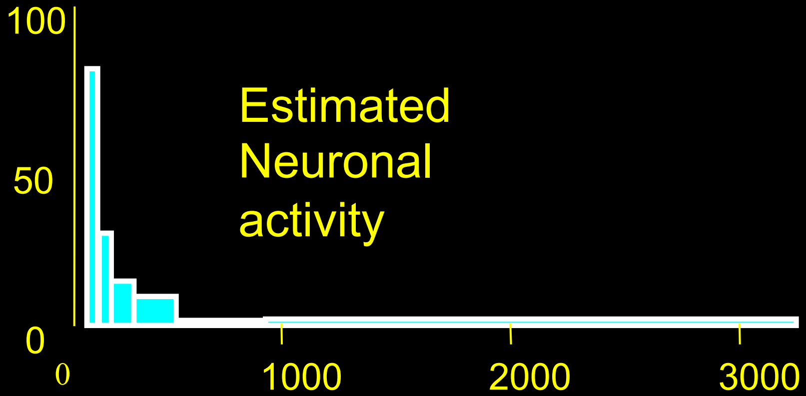


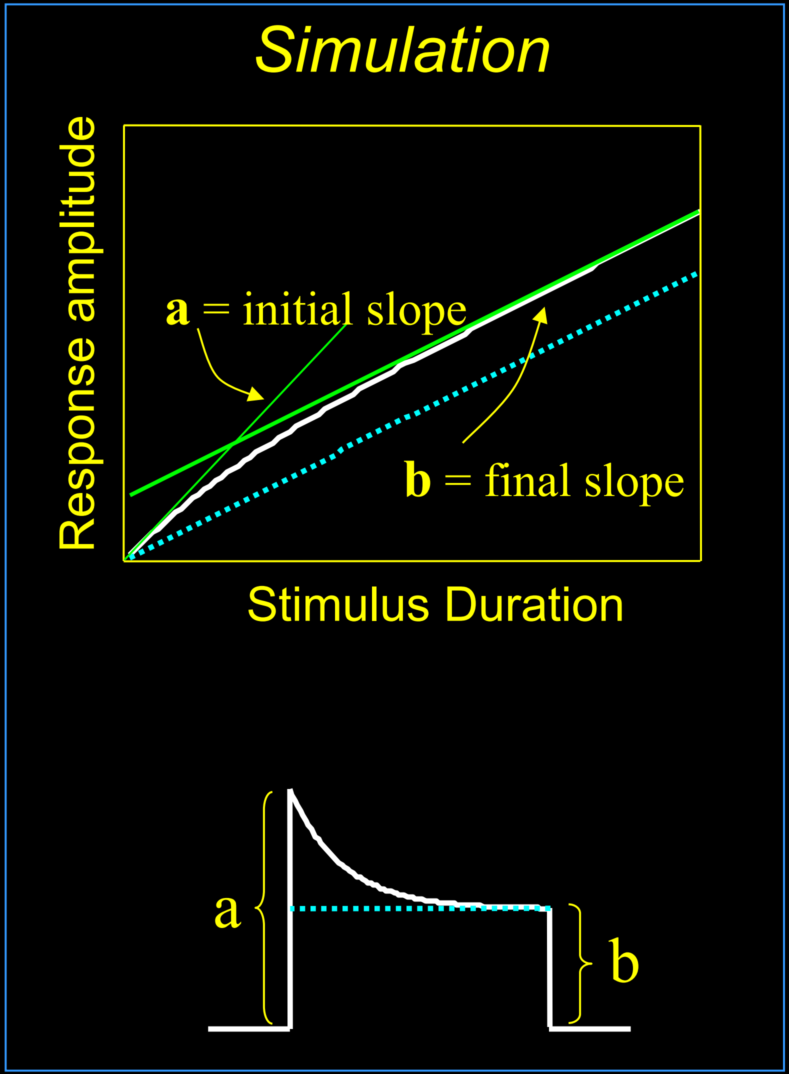
P. A. Bandettini and L. G. Ungerleider, (2001) “From neuron to BOLD: new connections.” Nature Neuroscience, 4: 864-866.



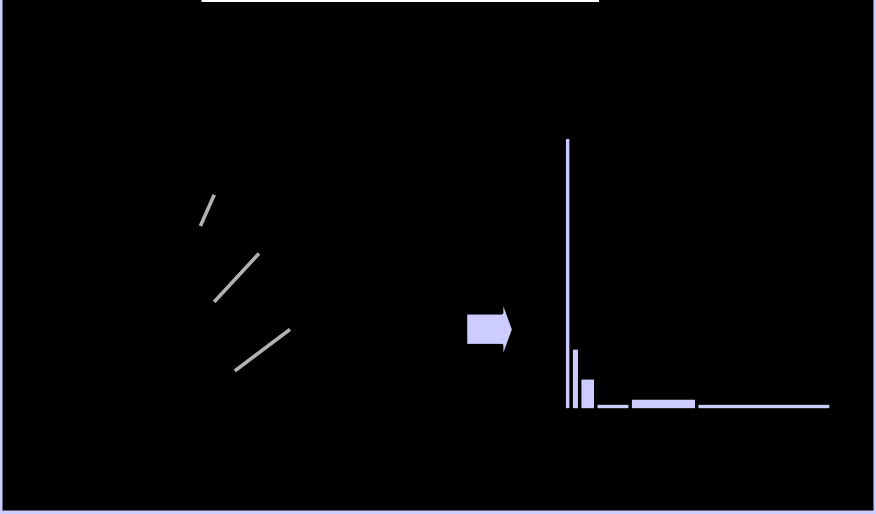
Results – constant gratings


Measured Amplitudes

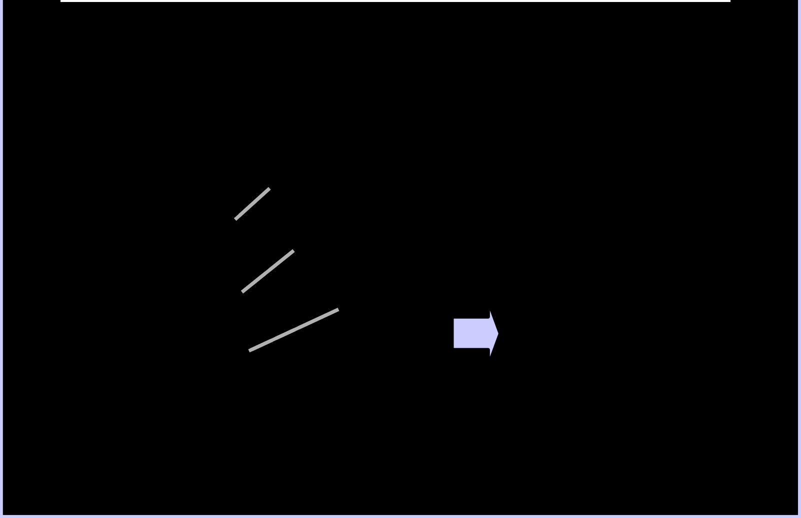

Estimated Neuronal activity


Simulation

Stationary grating

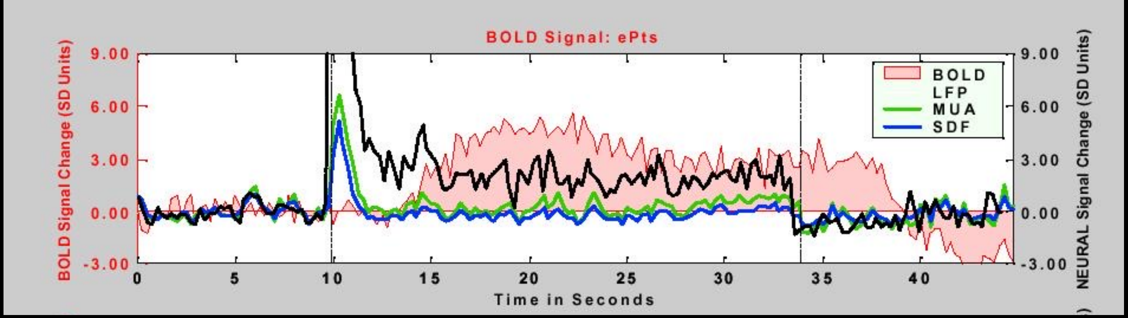


Contrast-reversing checkerboard

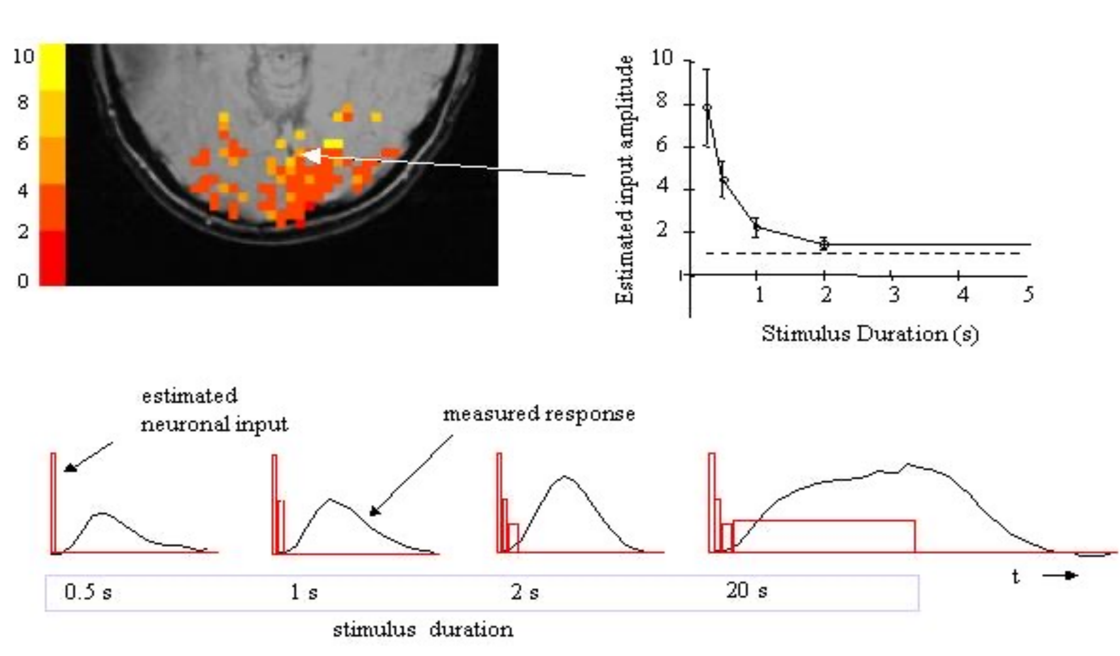


BOLD Correlation with Neuronal Activity

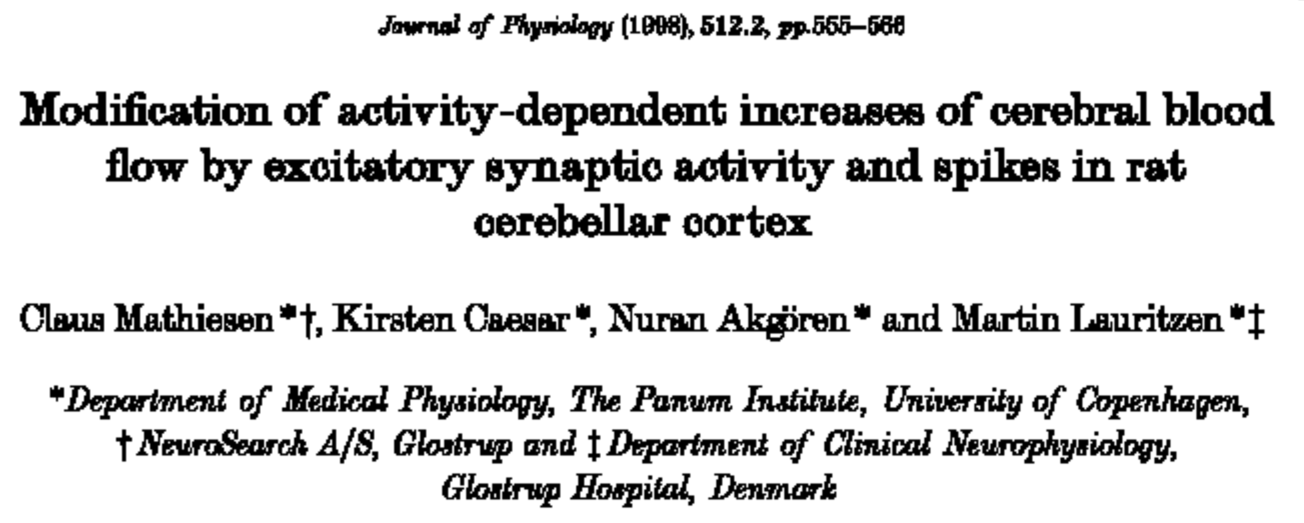
Logothetis et al. (2001) "Neurophysiological investigation of the basis of the fMRI signal" Nature, 412, 150-157.



P. A. Bandettini and L. G. Ungerleider, (2001) "From neuron to BOLD: new connections." Nature Neuroscience, 4: 864-866.



Evidence that inhibitory input produces increased blood flow



Journal of Physiology (1998), 512.2, pp.555–566

Modification of activity-dependent increases of cerebral blood flow by excitatory synaptic activity and spikes in rat cerebellar cortex

Claus Mathiesen*†, Kirsten Caesar*, Nuran Akgören* and Martin Lauritzen*‡

**Department of Medical Physiology, The Panum Institute, University of Copenhagen,*
†NeuroSearch A/S, Glostrup and ‡Department of Clinical Neurophysiology,
Glostrup Hospital, Denmark

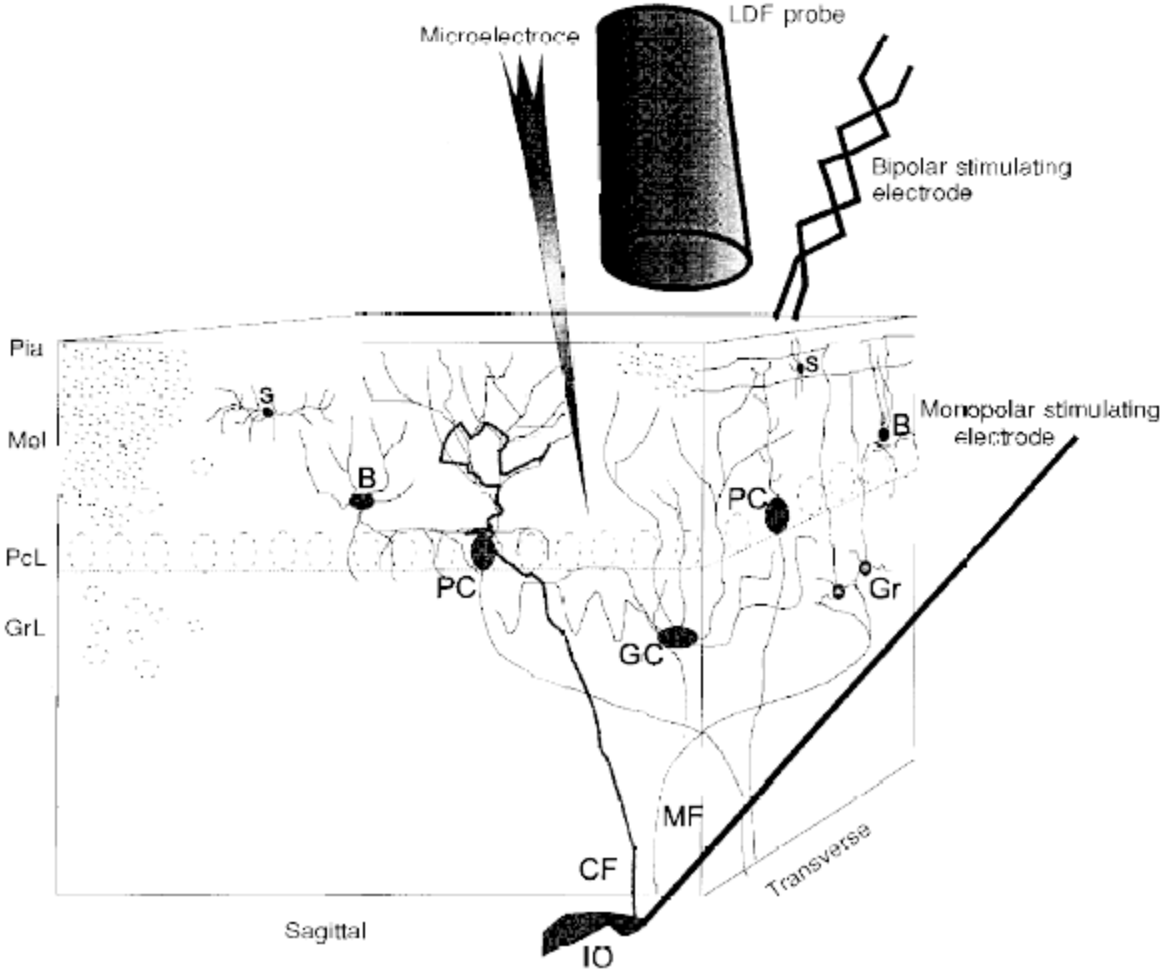
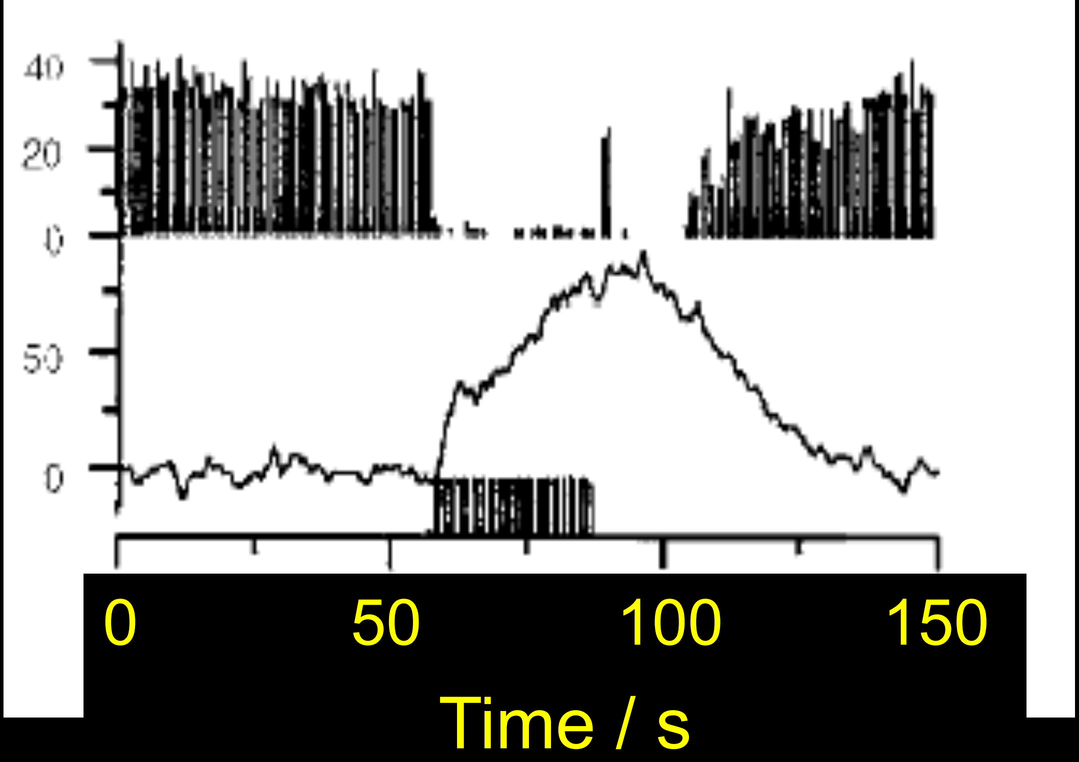


Figure 1. Schematic three-dimensional drawing of experimental set-up, including neurones of interest and position of laser Doppler probe, stimulating and recording electrodes

The positions of the three cerebellar layers, molecular (Mol, with a thickness of 400 μm), Purkinje cell (PcL, about 100 μm) and granular (GrL, 400–500 μm), are indicated. The molecular layer contains granule cell axons, called parallel fibres, the dendrites of Purkinje cells, stellate cells (S) and basket cells (B). The granule cell layer contains granule cells (Gr) and Golgi cells (GC). The superficial parallel fibres were stimulated by a bipolar stimulating electrode, while climbing fibres (CF) were stimulated by a monopolar electrode lowered into the caudal part of the inferior olive (IO). Field potentials and single unit spike activity were recorded with a glass microelectrode. CBF was recorded by a laser Doppler flowmetry (LDF) probe located 0·3–0·5 mm above the pial surface (Pia).

Divergence of spike rate and blood flow during parallel fiber stimulation



Mathiesen, Caesar, Akgören, Lauritzen (1998), J Physiol 512.2:555-566

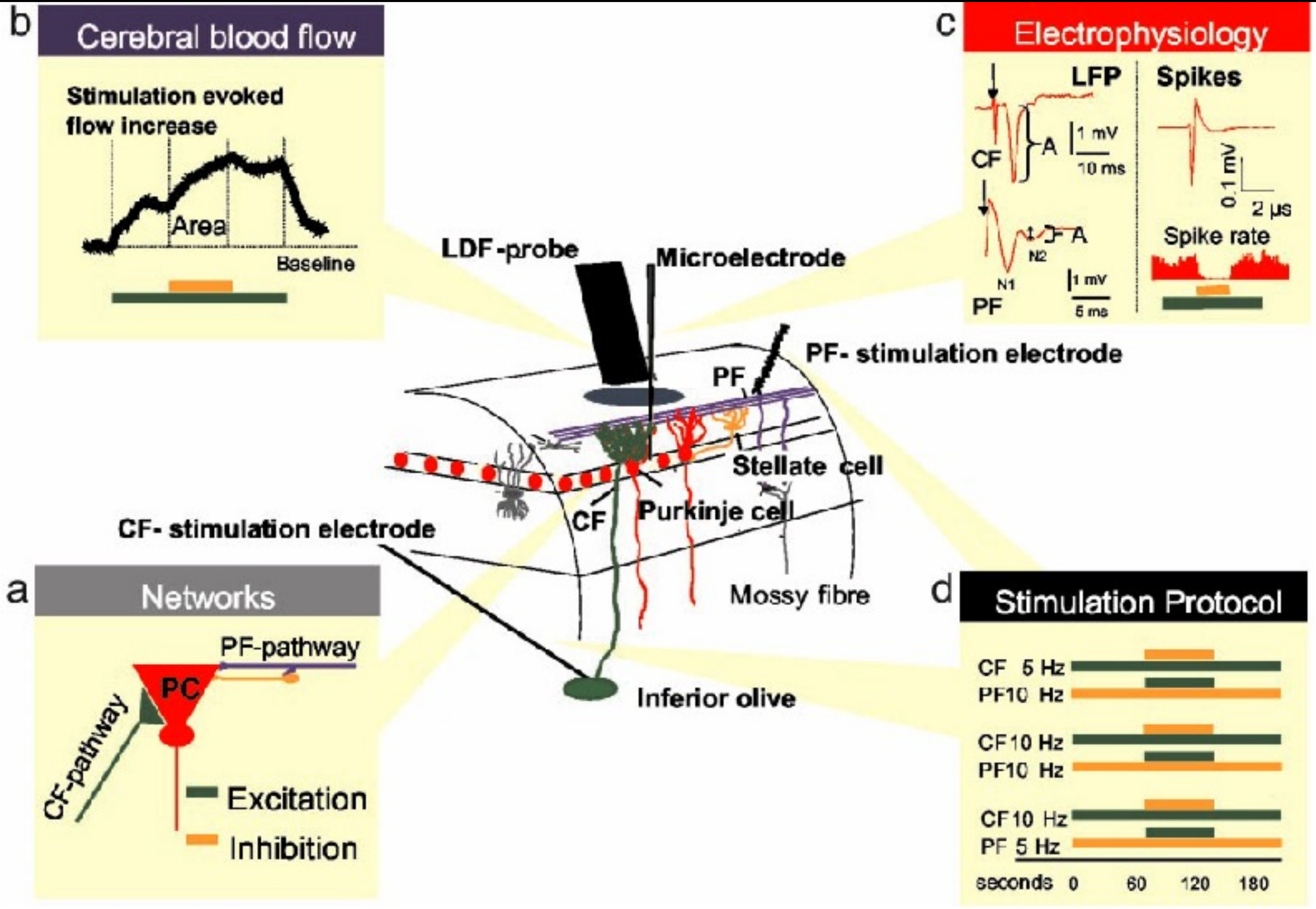
It gets more complicated...

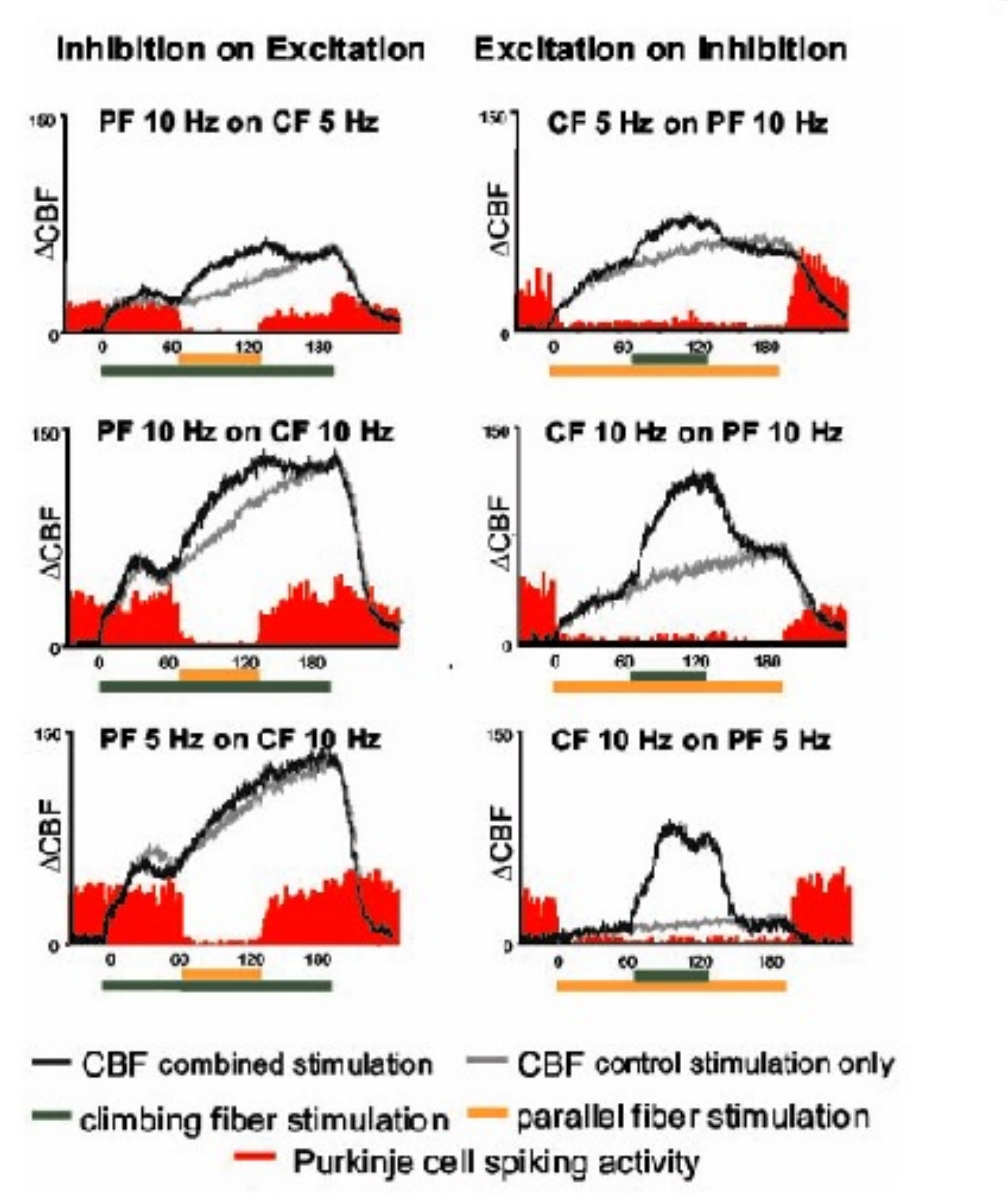
Context sensitivity of activity-dependent increases in cerebral blood flow

Kirsten Caesar*, Lorenz Gold*, and Martin Lauritzen*[†‡]

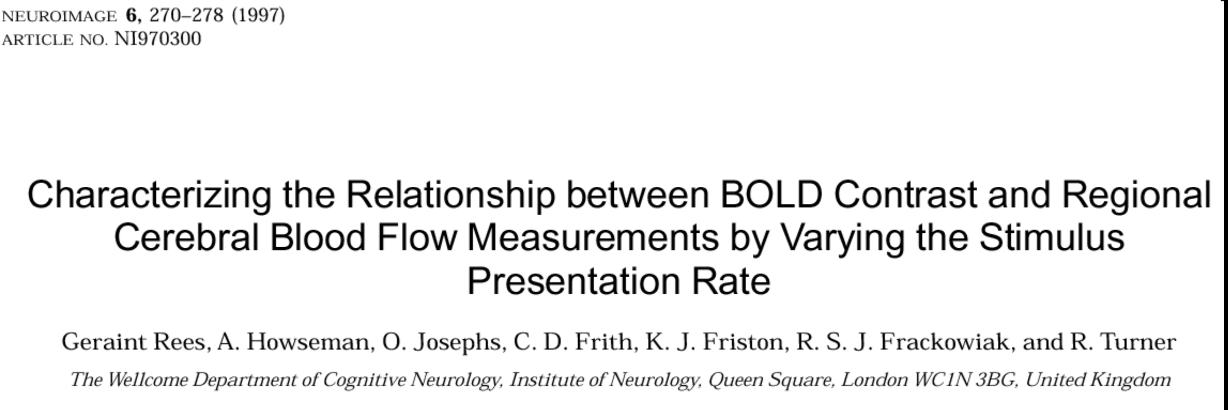
*Department of Medical Physiology, The Panum Institute, University of Copenhagen, Blegdamsvej 3, 2000 Copenhagen N, Denmark; and [†]Department of Clinical Neurophysiology, Glostrup Hospital, 2600 Glostrup, Denmark

PNAS | **April 1, 2003** | vol. 100 | no. 7 | **4239–4244**


b
Cerebral blood flow
Stimulation evoked flow increase
Area
Baseline
c
Electrophysiology
LFP
Spikes
CF
A
1 mV
10 ms
0.1 mV
2 µs
N1
N2
A
PF
1 mV
5 ms
Spike rate
LDF-probe
Microelectrode
PF- stimulation electrode
PF
Stellate cell
CF
Purkinje cell
CF- stimulation electrode
Mossy fibre
Inferior olive
a
Networks
PF-pathway
PC
CF-pathway
Excitation
Inhibition
d
Stimulation Protocol
CF 5 Hz
PF10 Hz
CF10 Hz
PF10 Hz
CF10 Hz
PF 5 Hz
seconds 0 60 120 180


Inhibition on Excitation
Excitation on Inhibition
PF 10 Hz on CF 5 Hz
CF 5 Hz on PF 10 Hz
PF 10 Hz on CF 10 Hz
CF 10 Hz on PF 10 Hz
PF 5 Hz on CF 10 Hz
CF 10 Hz on PF 5 Hz
ΔCBF
150
0
0
60
120
180
CBF combined stimulation
CBF control stimulation only
climbing fiber stimulation
parallel fiber stimulation
Purkinje cell spiking activity

?!

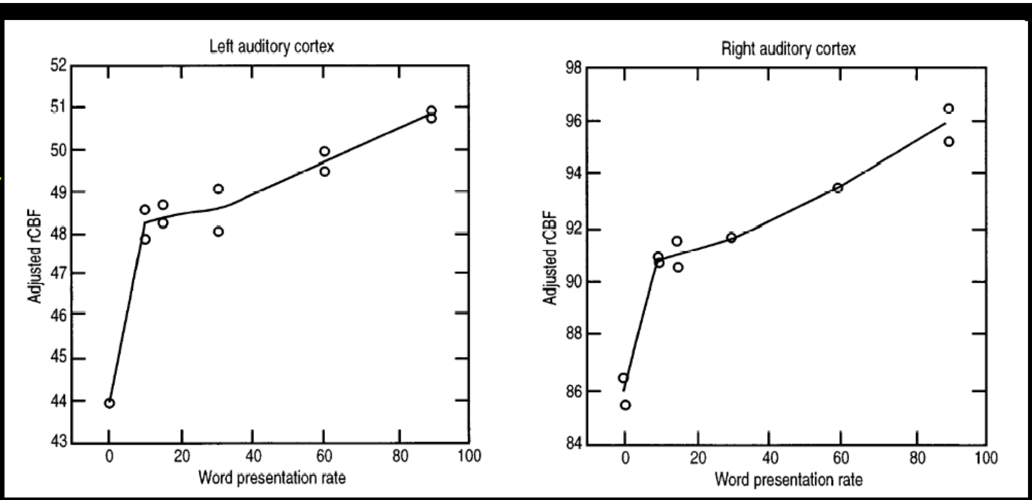


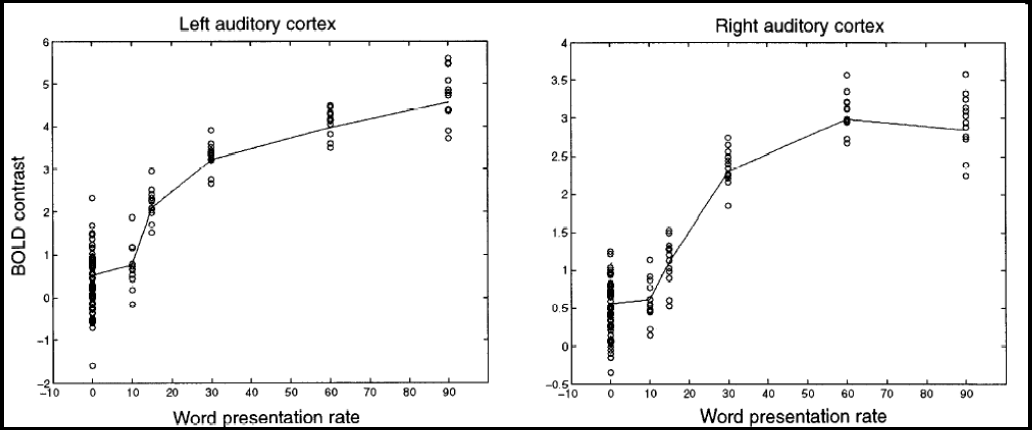
NEUROIMAGE **6,** 270–278 (1997)
ARTICLE NO. NI970300

Characterizing the Relationship between BOLD Contrast and Regional Cerebral Blood Flow Measurements by Varying the Stimulus Presentation Rate

Geraint Rees, A. Howseman, O. Josephs, C. D. Frith, K. J. Friston, R. S. J. Frackowiak, and R. Turner
The Wellcome Department of Cognitive Neurology, Institute of Neurology, Queen Square, London WC1N 3BG, United Kingdom

Flow modulation is not necessarily the same as BOLD modulation





Mediators of neurovascular coupling

There is **not just one** coupling mechanism.

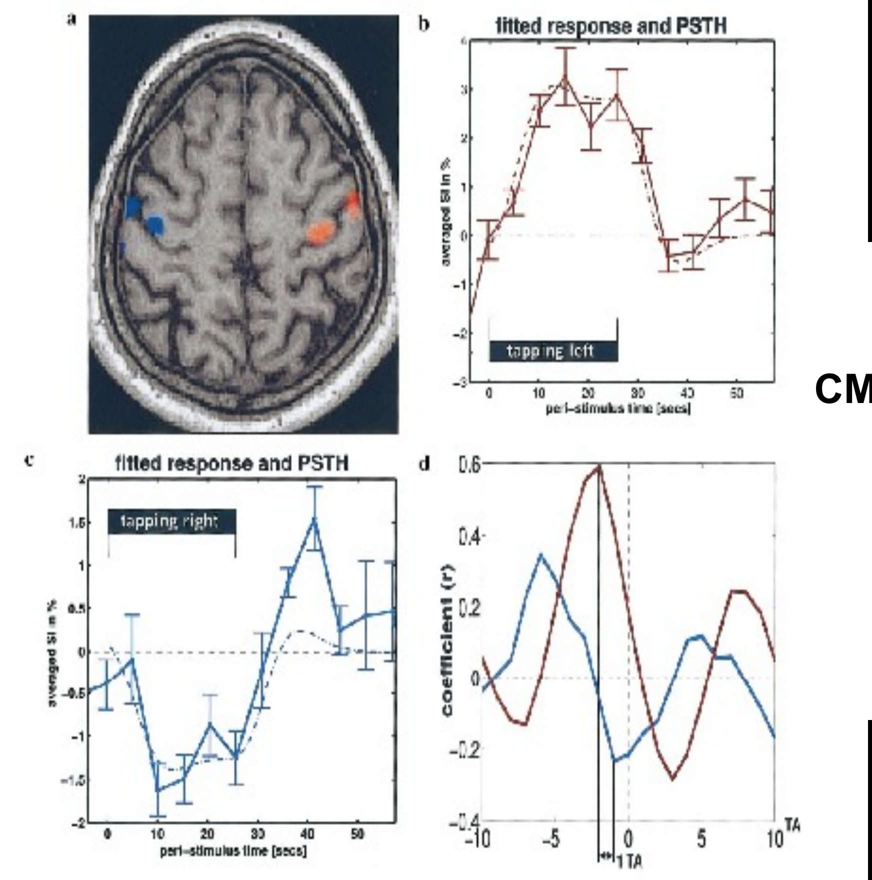
NO is a mediator in the cerebellar cortex, but only a permissive factor in the somatosensory cortex

Astrocytes may link synaptic activity to vascular response via Glutamate-induced Ca elevation and release of vasodilators at perivascular endfeets

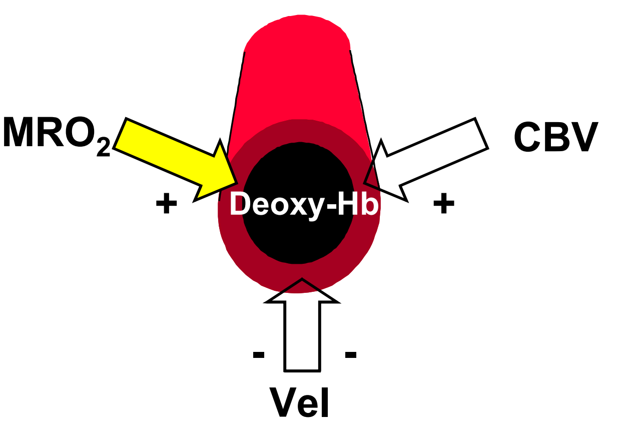
Metabolic factors (adenosine, pH, lactate, CO_2) may act posthoc for finer long-term adjustment (not much relevance for BOLD!?)

Courtesy of Arno Villringer

Negative BOLD in carotid artery disease



Röther et al. NeuroImage 2002



$CMRO_2$

CBV

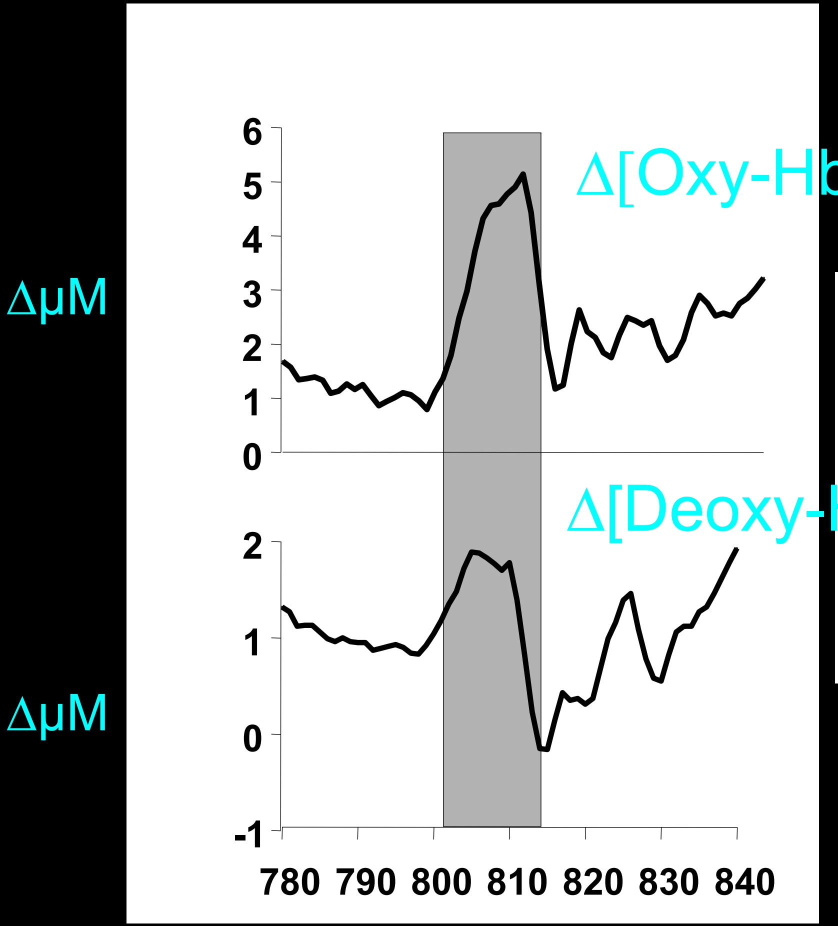
\+ Deoxy-Hb +

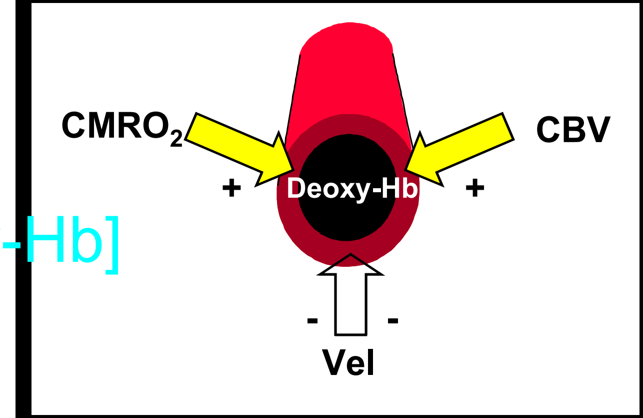
\- -

Vel

Courtesy of Arno Villringer

Increase in deoxy-Hb and oxy-Hb during focal seizure





Courtesy of Arno Villringer

Altered neurovascular coupling: Pathology, drugs

Pathologic state / Drug	**Reference**
Carotid occlusion	Röther et al. 2002
Transient global ischemia	Schmitz et al. 1998
Penumbra of cerebral ischemia	Mies et al. 1993, Wolf et al. 1997
Subarachnoid hemorrhage	Dreier et al. 2000
Trauma	Richards et al. 2001
Epilepsy	Fink et al. 1996, Brühl et al. 1998, von Pannwitz et al. 2002
Alzheimer´s disease	Hock et al. 1996, Niwa et al. 2000
Theophylline	Ko et al. 1990, Dirnagl et al. 1994
Scopolamine	Tsukada et al. 1998

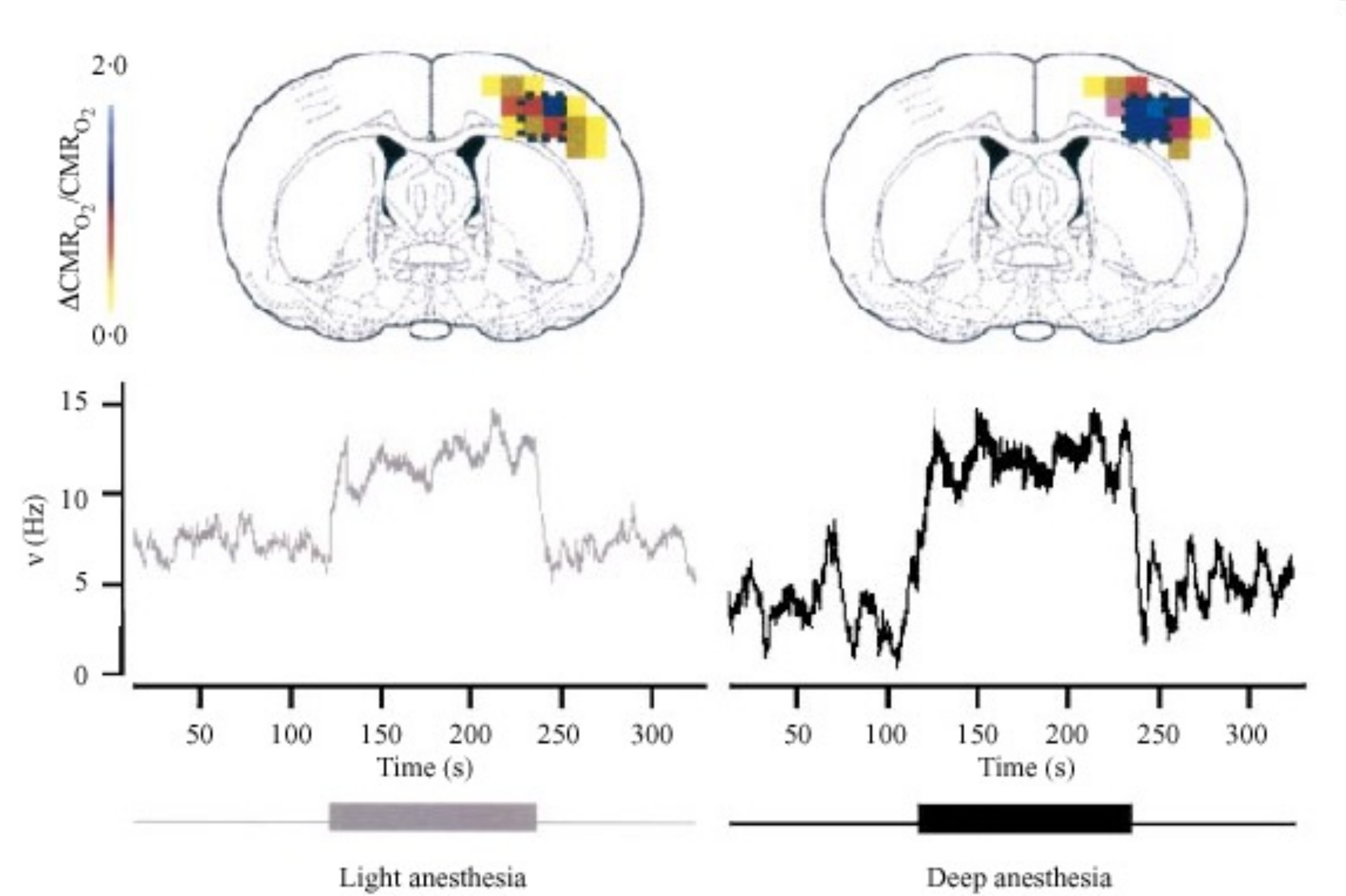
Courtesy of Arno Villringer

Quarterly Reviews of Biophysics **35**, 3 (2002), pp. 287–325. © 2002 Cambridge University Press 287
DOI: 10.1017/S0033583502003803 Printed in the United Kingdom

Biophysical basis of brain activity: implications for neuroimaging

Robert G. Shulman[1,2], Fahmeed Hyder[2,3,4] and Douglas L. Rothman[2,3,4]

Magnetic Resonance Center for Research in Metabolism and Physiology, Departments of [1] Molecular Biophysics and Biochemistry, [2] Diagnostic Radiology, [3] Biomedical Engineering, and [4] Section of Bioimaging Sciences, Yale University School of Medicine, New Haven, CT, USA



BOLD correlates with de-synchronization of MEG signal ...

NeuroImage **16,** 103–114 (2002)
doi:10.1006/nimg.2001.1050, available online at http://www.idealibrary.com on IDEAL®

Task-Related Changes in Cortical Synchronization Are Spatially Coincident with the Hemodynamic Response

Krish D. Singh,*,†,‡ Gareth R. Barnes,* Arjan Hillebrand,* Emer M. E. Forde,* and Adrian L. Williams§

**The Wellcome Trust Laboratory for MEG Studies, Neurosciences Research Institute, Aston University, Birmingham, United Kingdom; †MARIARC, Liverpool University, Liverpool, United Kingdom; ‡Walton Centre for Neurology and Neurosurgery, Liverpool, United Kingdom; and §Department of Psychology, Royal Holloway, University of London, Egham, United Kingdom*

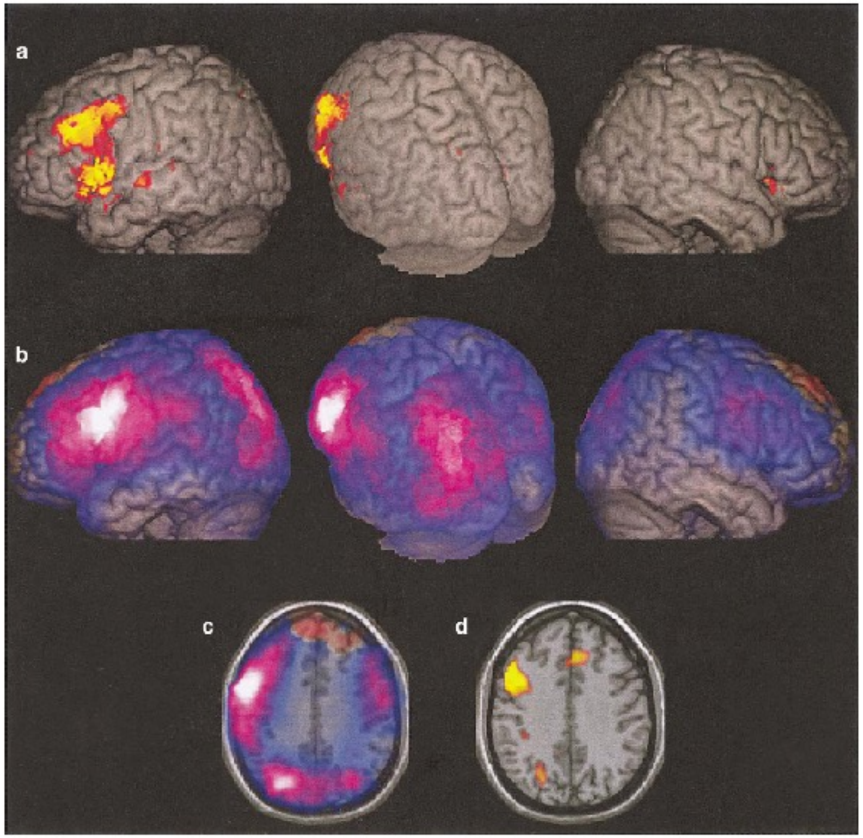


FIG. 2. The results of the group fMRI experiment and the group MEG experiment for the letter fluency task, superimposed on a template brain. The color scales are as described in the legend of Fig. 1. (a) Group fMRI data. Only those clusters significant at $P < 0.05$ (corrected) are shown. (b) The peak group SAM image. This shows the peak power increase or decrease at each voxel in the brain, irrespective of which frequency band the power change occured in. This image can be thought of as an amalgam of Figs. 1b to 1f. (c) The peak group SAM data superimposed on a slice through the template brain at an MNI Z coordinate of +36. The image shows bilateral, but strongly left biased, activation within the dorsolateral prefrontal cortex (DLPFC) and posterior parietal cortex. (d) The group fMRI data superimposed on the $Z = +36$ slice. Note the left DLPFC and left posterior parietal activation which match the group SAM results. However, there is also a small cluster in a more anterior portion of the parietal lobe, and another in the medial frontal gyri, which are visible in the group fMRI data but not in the group MEG data.

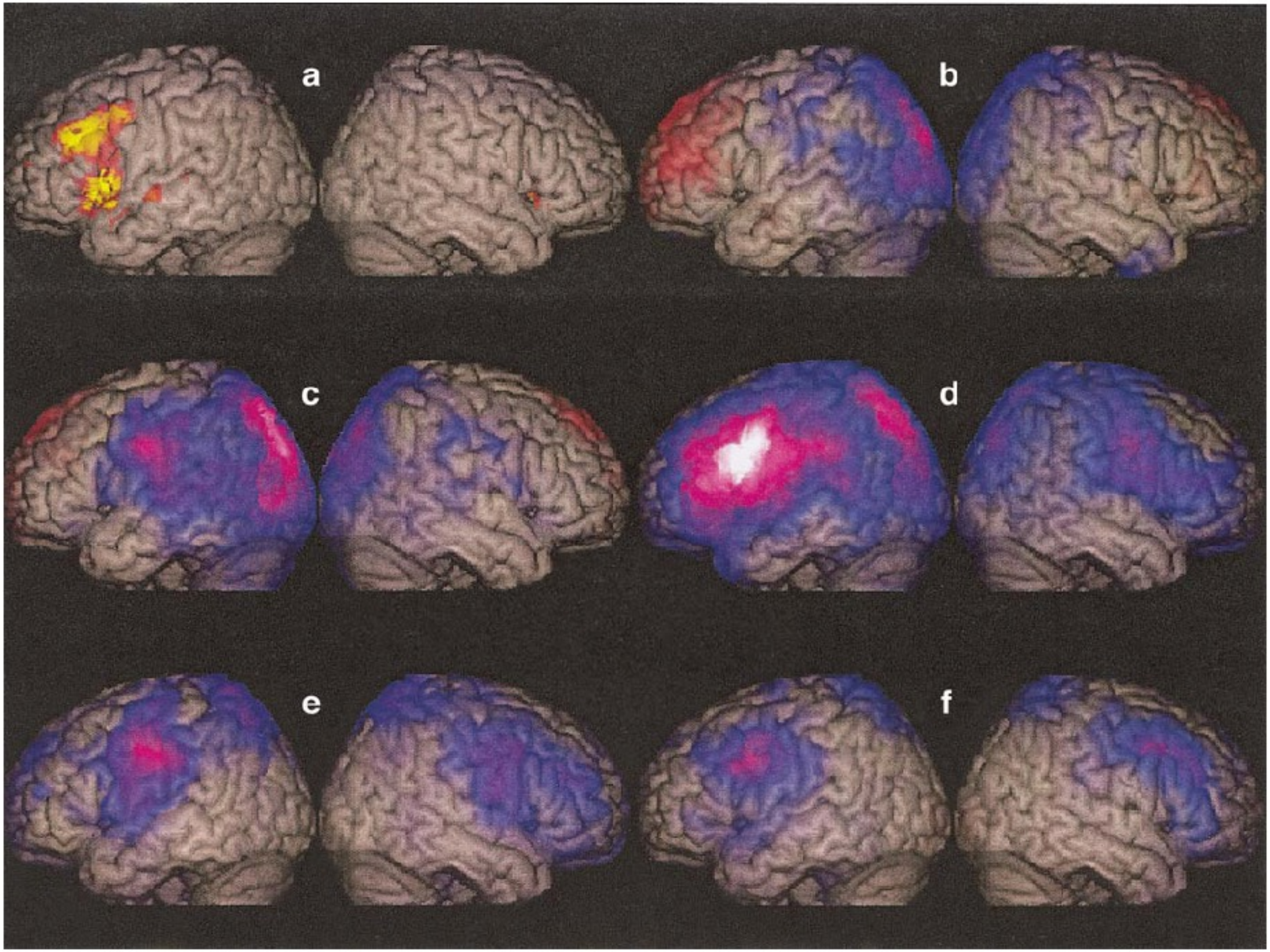
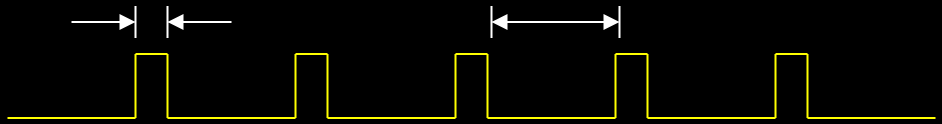


FIG. 1. The results of the group fMRI experiment and the group MEG experiment for the covert letter fluency task, superimposed on a template brain. (a) Group fMRI data. Only those clusters significant at $P < 0.05$ (corrected) are shown. The red–orange–yellow color scale depicts increasing BOLD amplitude. (b–f) The results of the group SAM analysis of the MEG data. Increases in signal power in the Active phase, compared to the Passive baseline are shown using a red–orange–yellow color scale. Decreases in signal power in the Active phase are shown using a blue–purple–white color scale. The power changes are in the following frequency bands (b) 1–10 Hz; (c) 5–15 Hz; (d) 15–25 Hz; (e) 25–35 Hz; and (f) 35–45 Hz.

Neuronal Activation Input Strategies

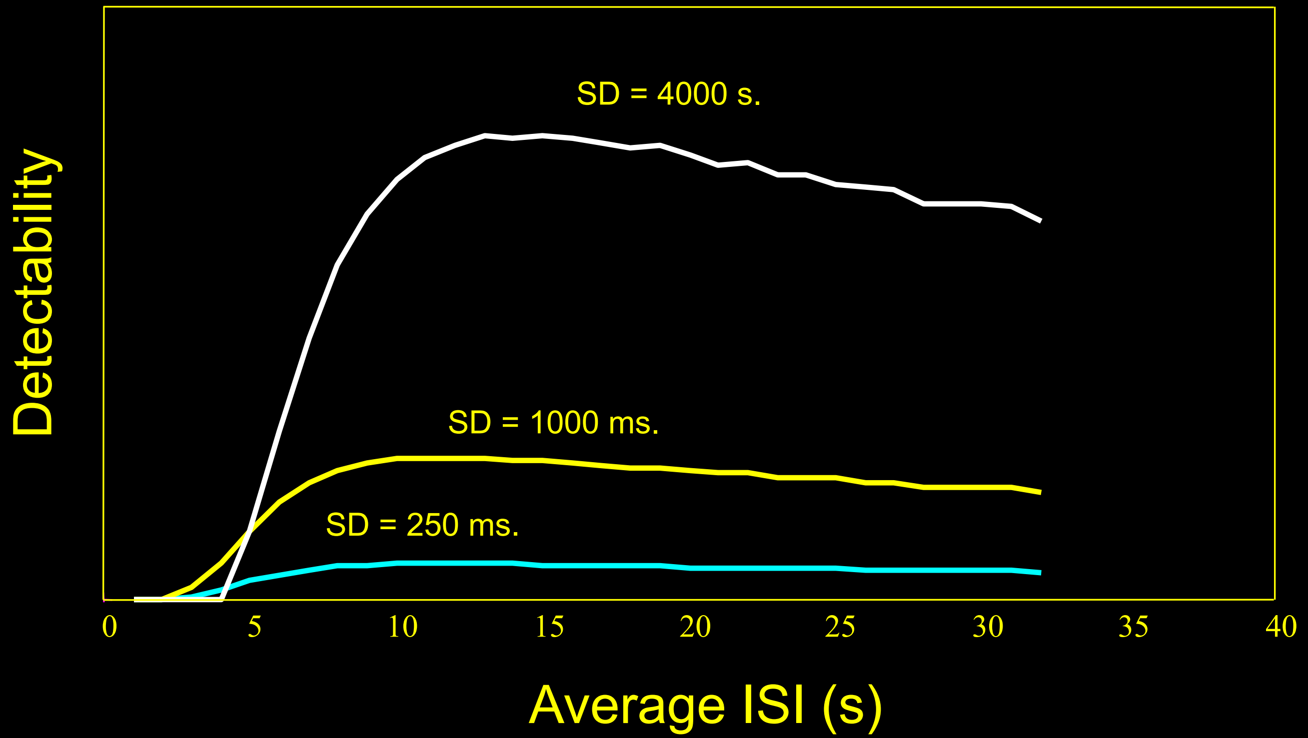
1. Block Design
2. Parametric Design
3. Frequency Encoding
4. Phase Encoding
5. Event Related
6. Orthogonal Design
7. Free Behavior Design

Detectability – constant ISI

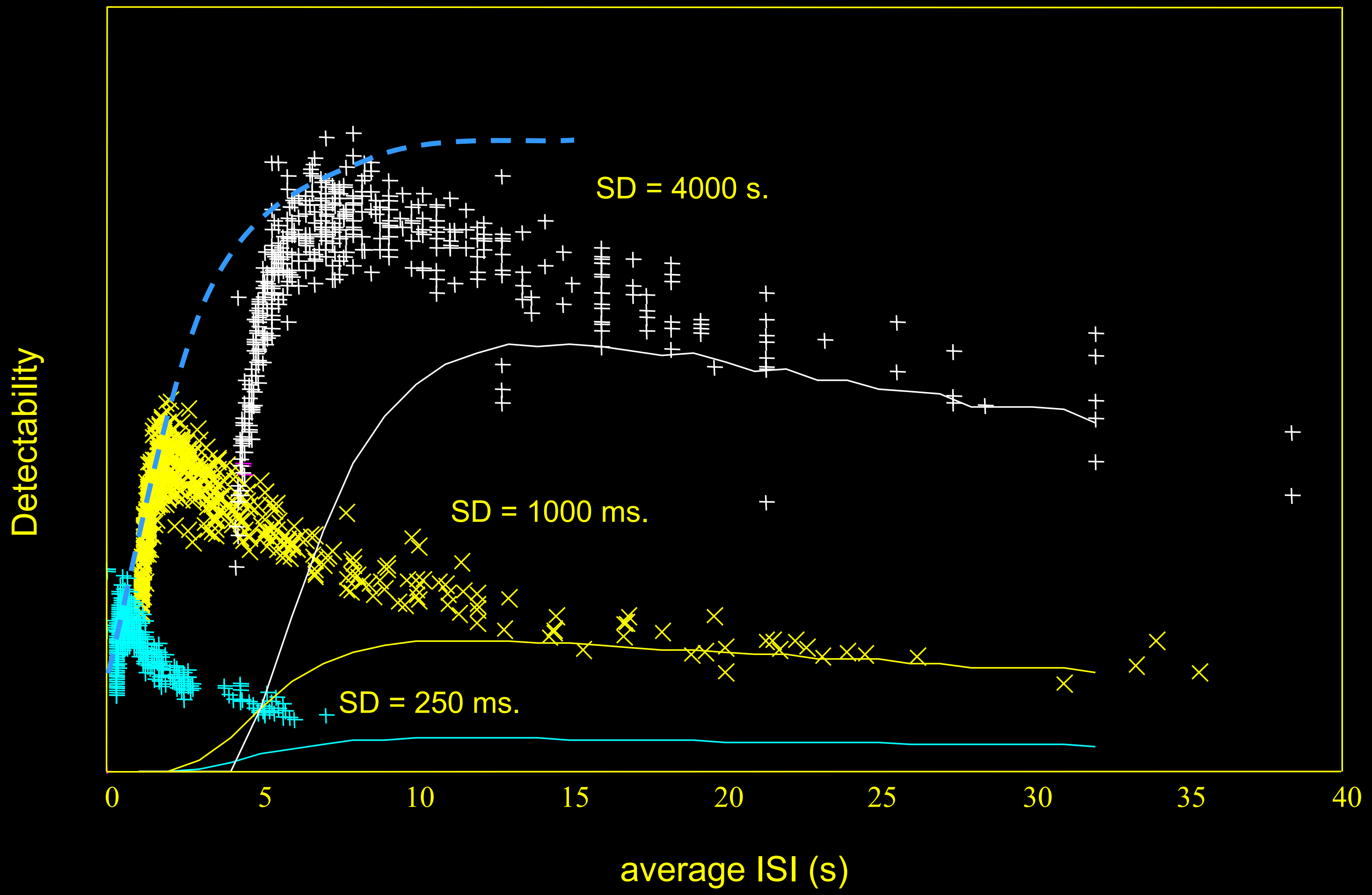


SD – stimulus duration

ISI – inter-stimulus interval

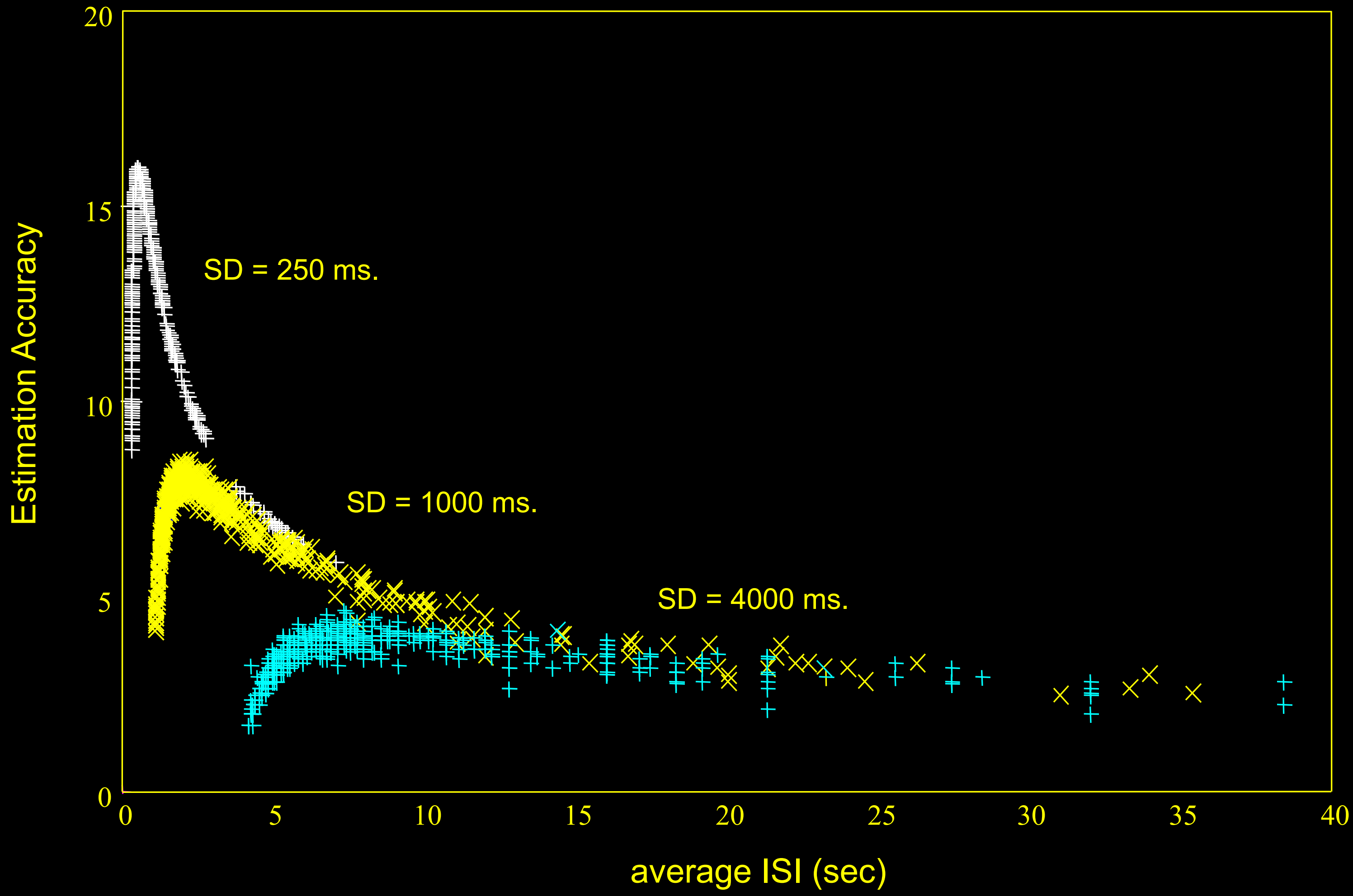


Detectability vs. Average ISI



R. M. Birn, R. W. Cox, P. A. Bandettini, Detection versus estimation in Event-Related fMRI: choosing the optimal stimulus timing. *NeuroImage* 15: 262-264, (2002).

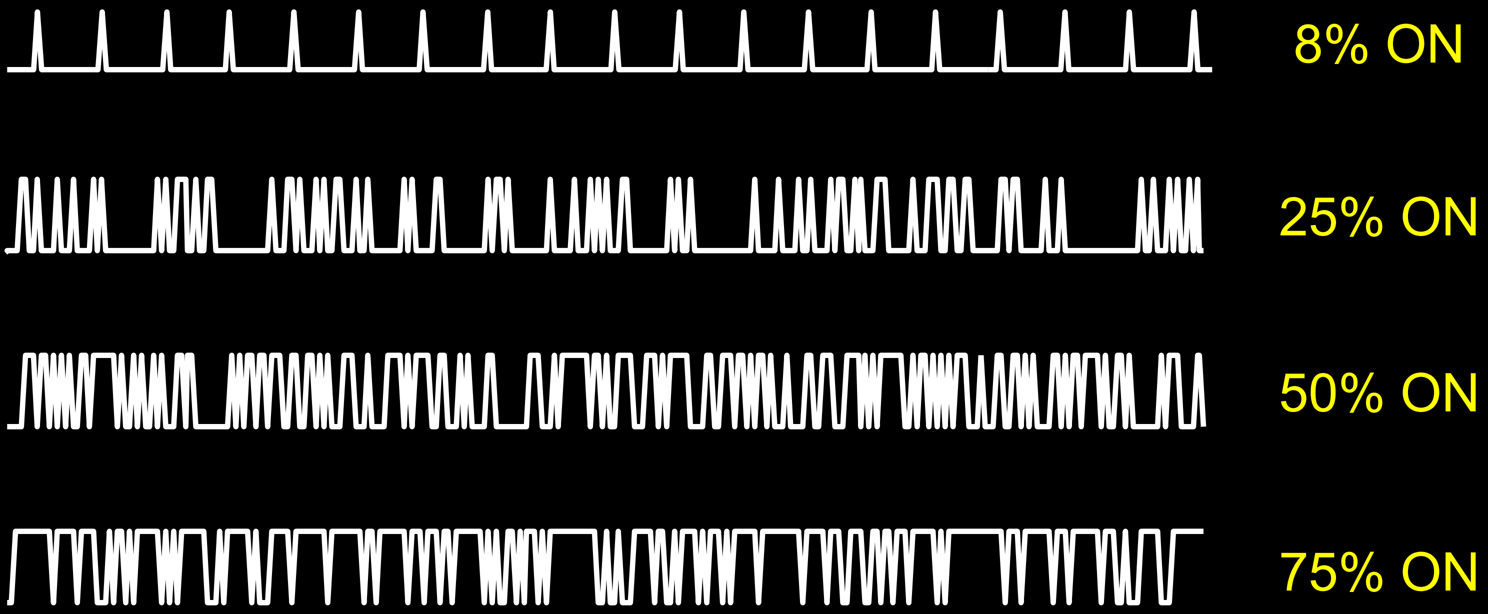
Estimation accuracy vs. average ISI



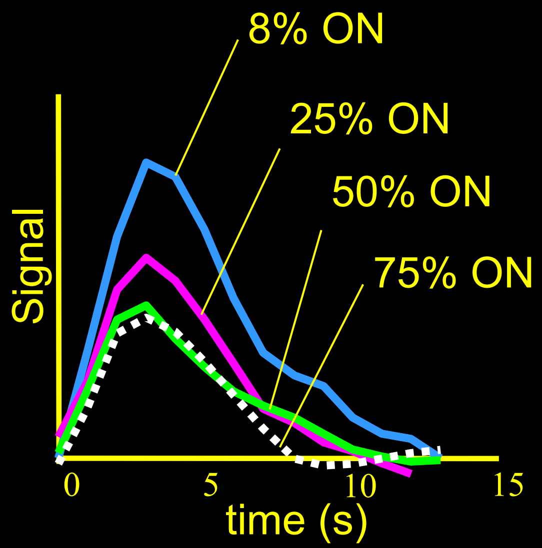
R. M. Birn, R. W. Cox, P. A. Bandettini, Detection versus estimation in Event-Related fMRI: choosing the optimal stimulus timing. *NeuroImage* 15: 262-264, (2002).

A practical implication....

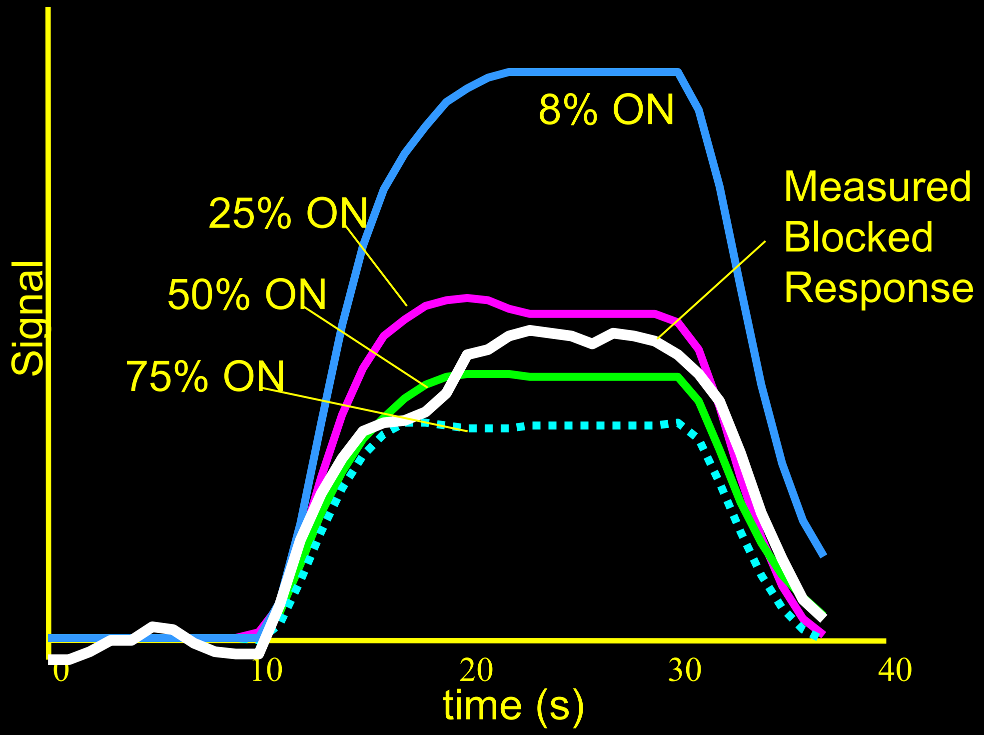
Rapid event-related design with varying ISI



Estimated Impulse Response



Predicted Responses to 20 s stimulation

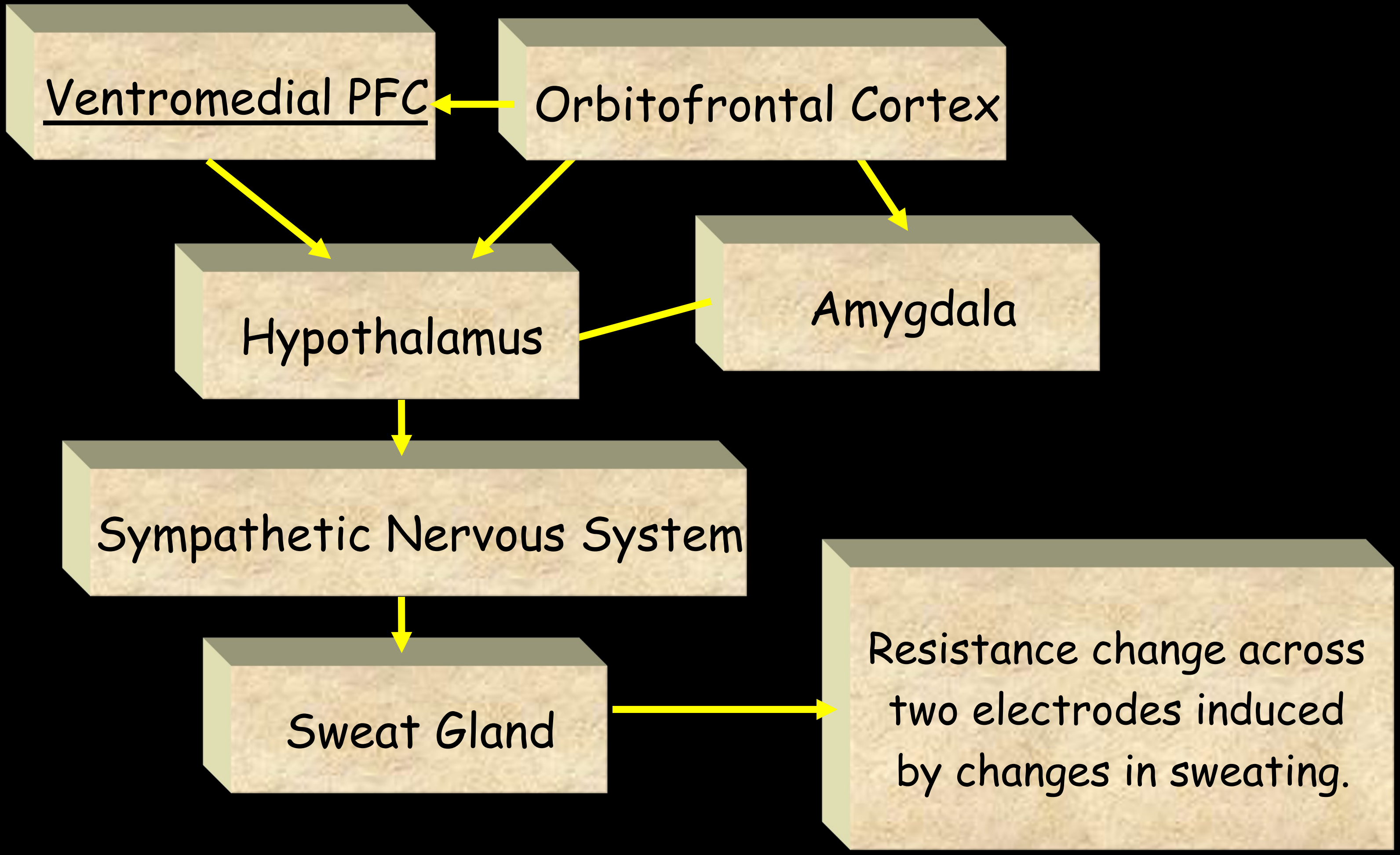


Free Behavior Design

Use a continuous measure as a reference function:

- Task performance
- Skin Conductance
- Heart, respiration rate..
- Eye position
- EEG

The Skin Conductance Response (SCR)



Ventromedial PFC

Orbitofrontal Cortex

Hypothalamus

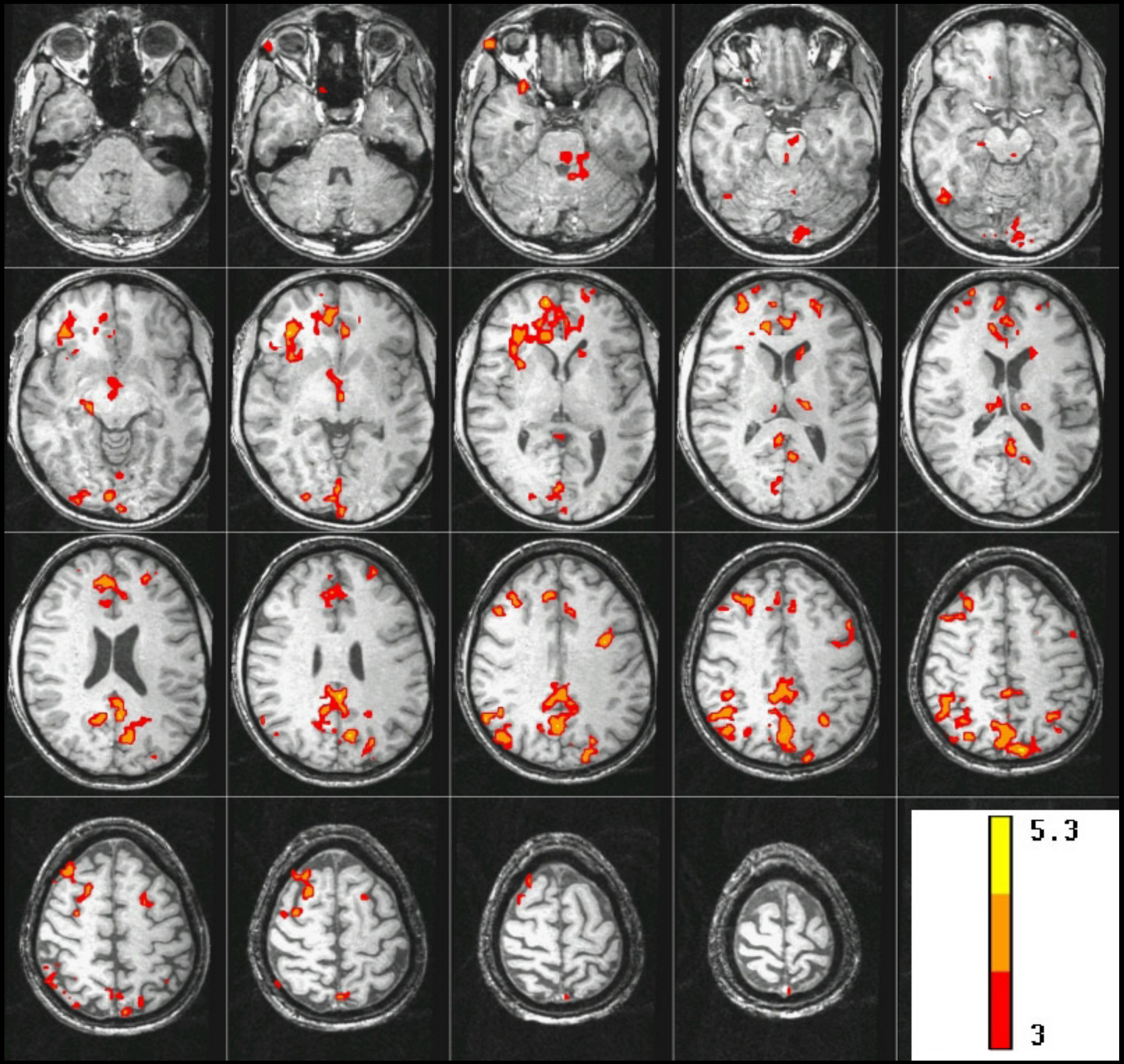
Amygdala

Sympathetic Nervous System

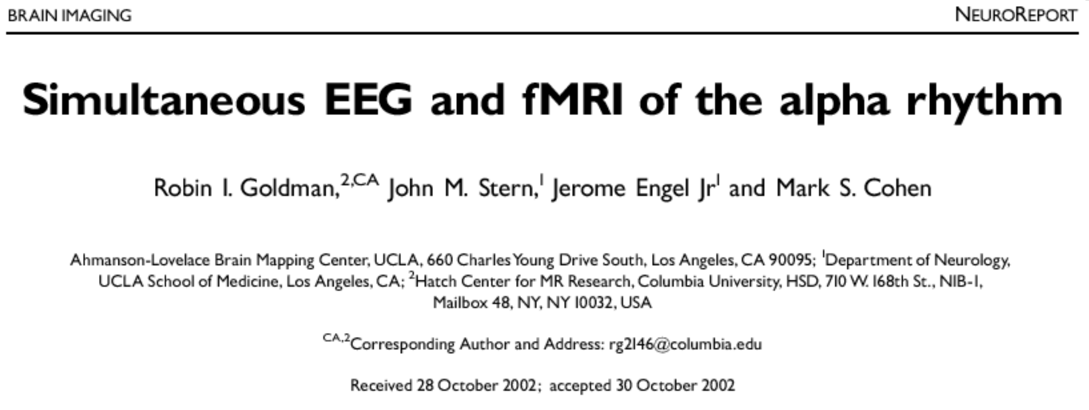
Sweat Gland

Resistance change across two electrodes induced by changes in sweating.

Brain activity correlated with SCR during "Rest"



J. C. Patterson II, L. G. Ungerleider, and P. A Bandettini, Task - independent functional brain activity correlation with skin conductance changes: an fMRI study. *NeuroImage* **17**: *1787-1806, (2002).*


BRAIN IMAGING NEUROREPORT

Simultaneous EEG and fMRI of the alpha rhythm

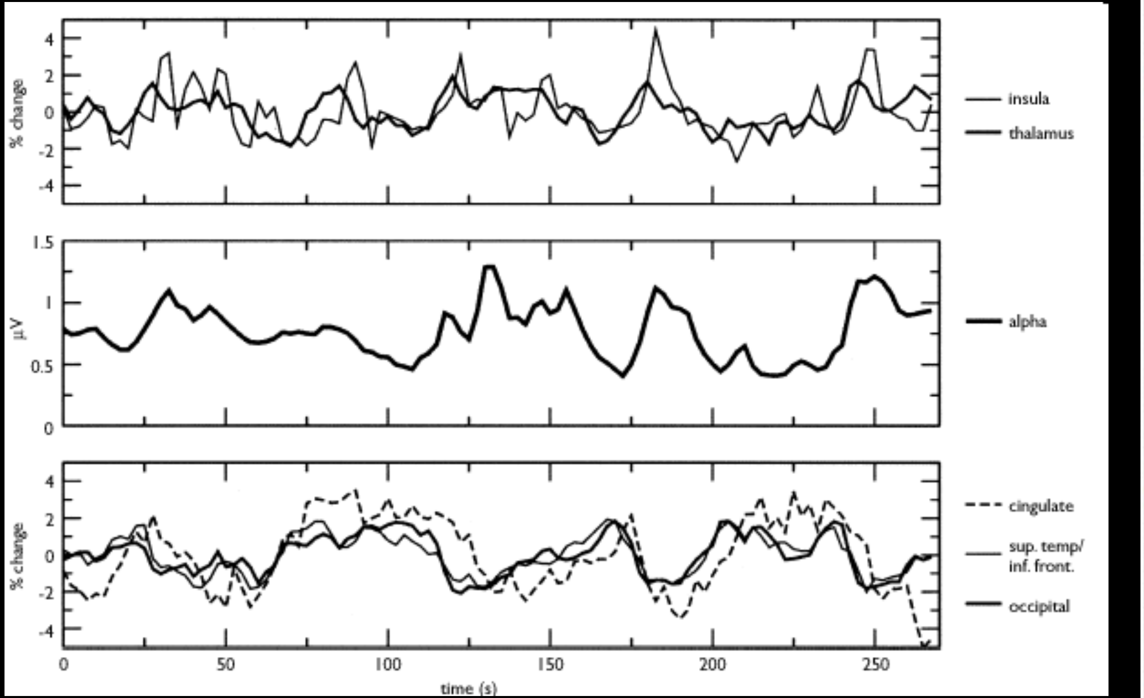
Robin I. Goldman,[2,CA] John M. Stern,[1] Jerome Engel Jr[1] and Mark S. Cohen

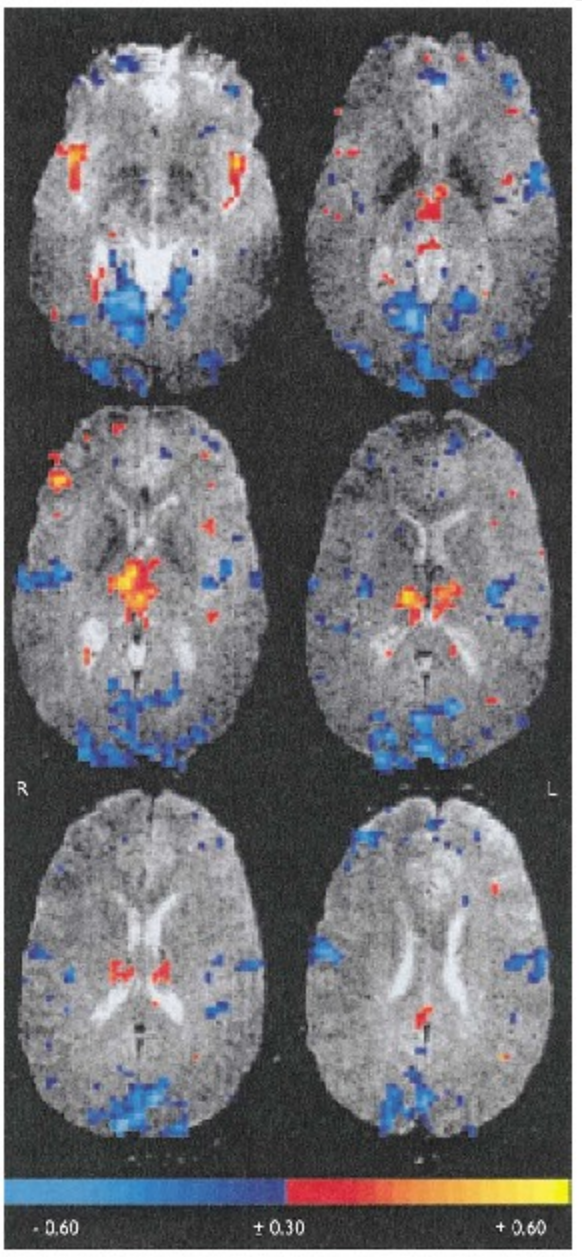
Ahmanson-Lovelace Brain Mapping Center, UCLA, 660 Charles Young Drive South, Los Angeles, CA 90095; [1]Department of Neurology, UCLA School of Medicine, Los Angeles, CA; [2]Hatch Center for MR Research, Columbia University, HSD, 710 W. 168th St., NIB-1, Mailbox 48, NY, NY 10032, USA

[CA,2]Corresponding Author and Address: rg2146@columbia.edu

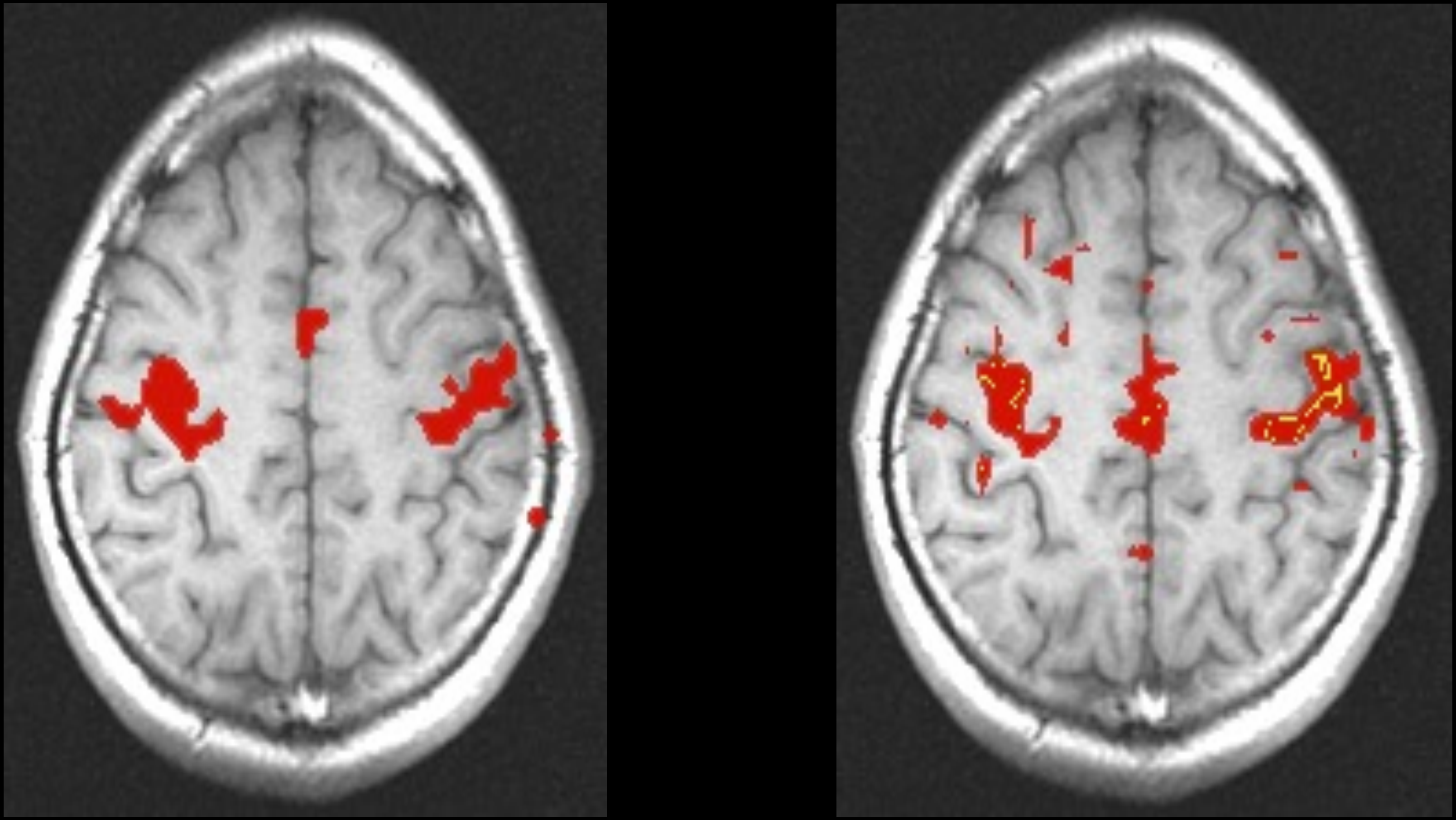
Received 28 October 2002; accepted 30 October 2002

DOI: 10.1097/01.wnr.0000047685.08940.d0





Resting State Fluctuations



B. Biswal *et al*., MRM, 34:537 (1995)

FIM Unit & FMRI Core Facility

Director:

Peter Bandettini

Staff Scientists:

Sean Marrett
Jerzy Bodurka
Frank Ye
Wen-Ming Luh

Computer Specialist:

Adam Thomas

Post Docs:

Rasmus Birn
Hauke Heekeren
David Knight
Anthony Boemio
Patrick Bellgowan
Ziad Saad

Graduate Student:

Natalia Petridou

Post-Back. IRTA Students:

Hanh Ngyun
Ilana Levy
Elisa Kapler
August Tuan
Dan Kelley

Visiting Fellows:

Sergio Casciaro
Marta Maieron
Guosheng Ding

Clinical Fellow:

James Patterson

Psychologist:

Julie Frost

Summer Students:

Allison Sanders
Julia Choi
Thomas Gallo
Jenna Gelfand
Hannah Chang
Courtney Kemps
Douglass Ruff
Carla Wettig
Kang-Xing Jin

Program Assistant:

Kay Kuhns

Scanning Technologists:

Karen Bove-Bettis
Paula Rowser
Alda Ottley