

# Latest Developments in fMRI

Peter A. Bandettini, Ph.D

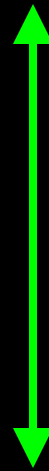
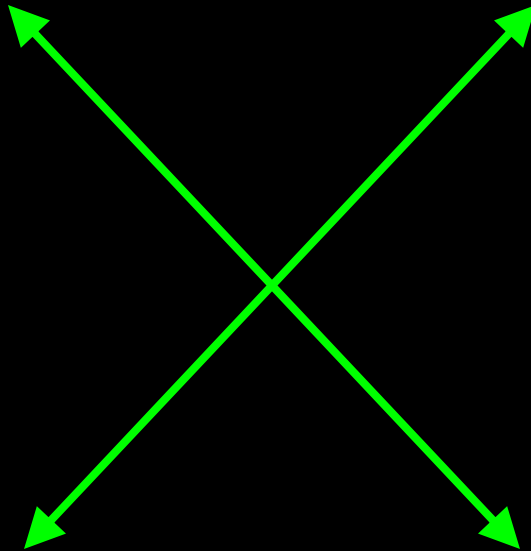
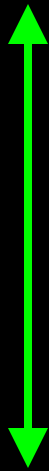
Unit on Functional Imaging Methods  
&  
3T Neuroimaging Core Facility

Laboratory of Brain and Cognition  
National Institute of Mental Health

**Technology**



**Methodology**



**Interpretation**



**Applications**

**Technology**

**Methodology**

**Engineers**

**Statisticians**

**Physicists**

**Mathematicians**

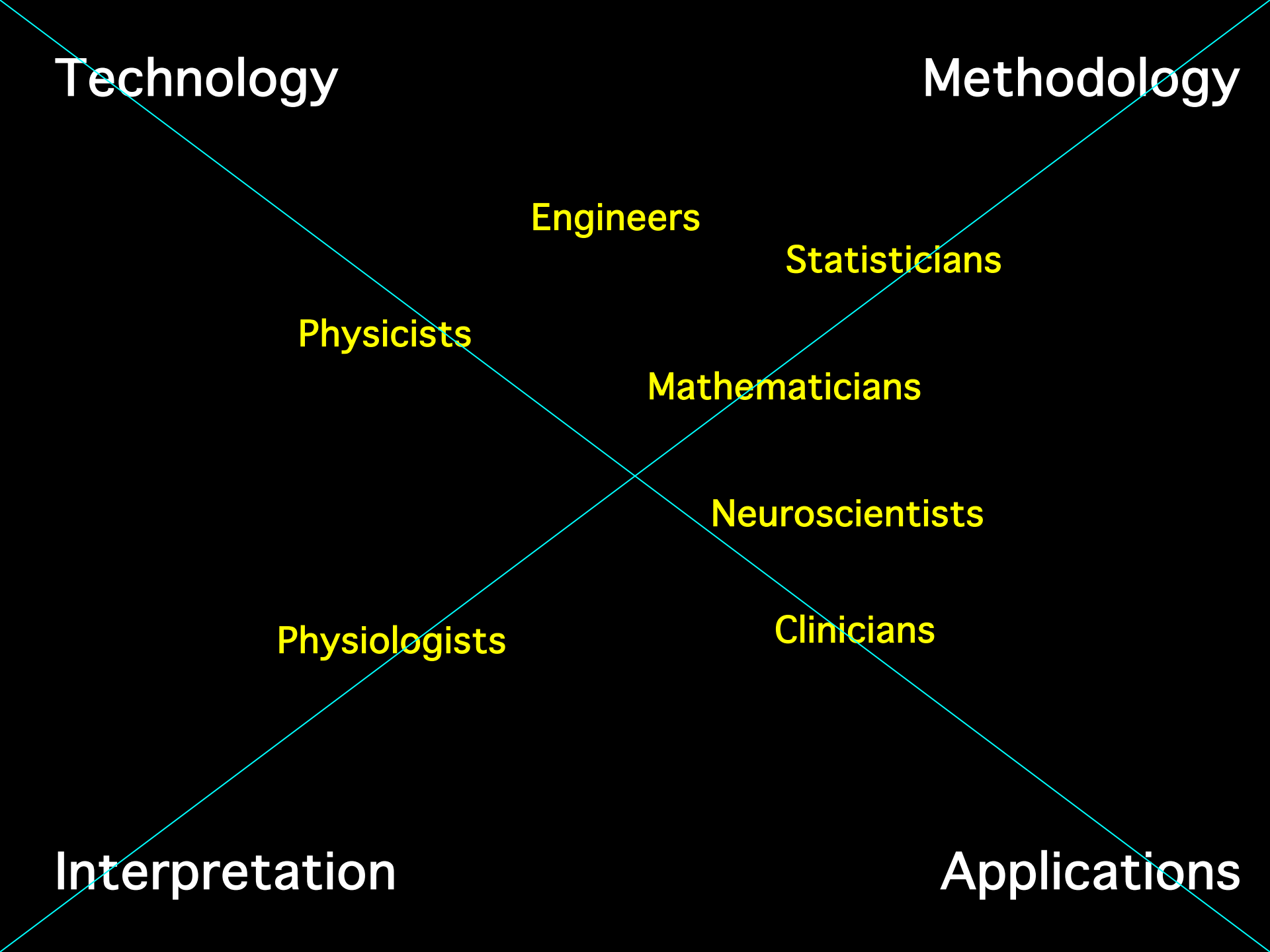
**Neuroscientists**

**Physiologists**

**Clinicians**

**Interpretation**

**Applications**



# Technology

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

# Methodology

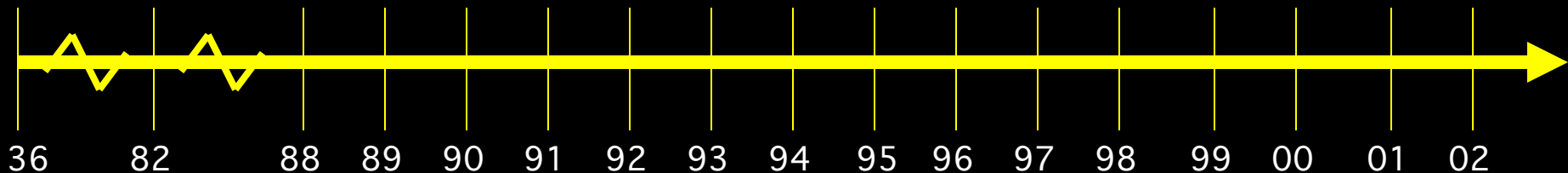
Baseline Volume  
 IVIM  
 Correlation Analysis  
 Parametric Design  
 Surface Mapping  
 Phase Mapping  
 Linear Regression  
 Event-related  
 Motion Correction  
 Multi-Modal Mapping  
 ICA  
 Free-behavior Designs  
 Mental Chronometry  
 Multi-variate Mapping  
 Deconvolution  
 Fuzzy Clustering  
 CO<sub>2</sub> Calibration

# Interpretation

Blood T2  
 Hemoglobin  
 BOLD models  
 B<sub>0</sub> dep.  
 TE dep  
 SE vs. GE  
 NIRS Correlation  
 Veins  
 PET correlation  
 IV vs EV  
 Pre-undershoot  
 Resolution Dep.  
 Post-undershoot  
 CO<sub>2</sub> effect  
 Inflow  
 ASL vs. BOLD  
 PSF of BOLD  
 Extended Stim.  
 Linearity  
 Fluctuations  
 Balloon Model  
 Metab. Correlation  
 Optical Im. Correlation  
 Electrophys. correlation

# Applications

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



# Alternating Left and Right Finger Tapping



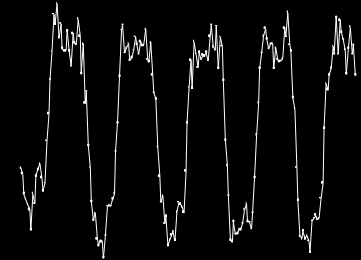
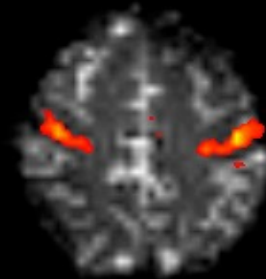
~ 1992



# The use of fMRI for the Investigation of Brain Function and Physiology

- Where?

- When?



- How much?

---

- How to do it well?

- Is there more?

# A Primary Challenge for Observing Brain Activation with fMRI:

## Brain Activation with fMRI:

...to make progressively more precise inferences without making too many assumptions about non-neuronal physiologic factors.





Neuronal  
Activation



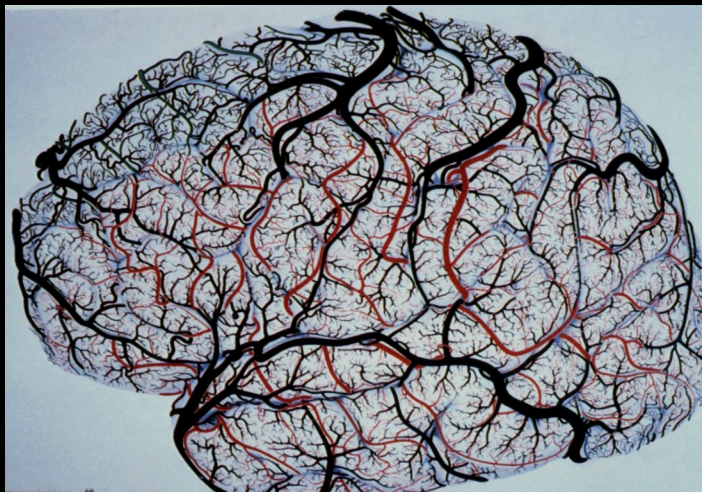
Measured  
Signal

Hemodynamics

?

?

?



Noise

# Latest Developments...

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

# Latest Developments...

1. Temporal Resolution
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4. Information Content
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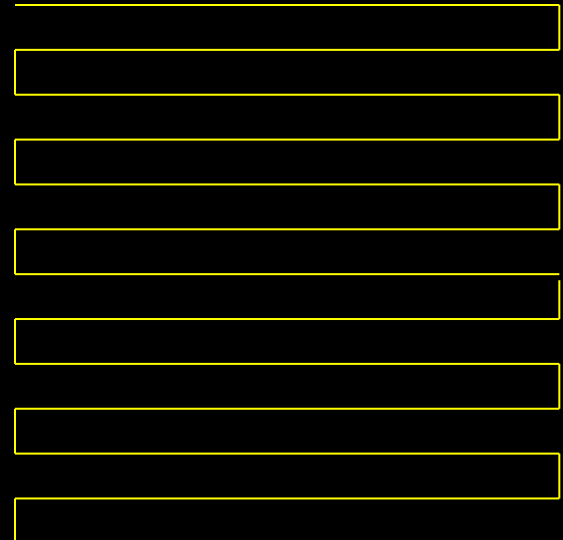
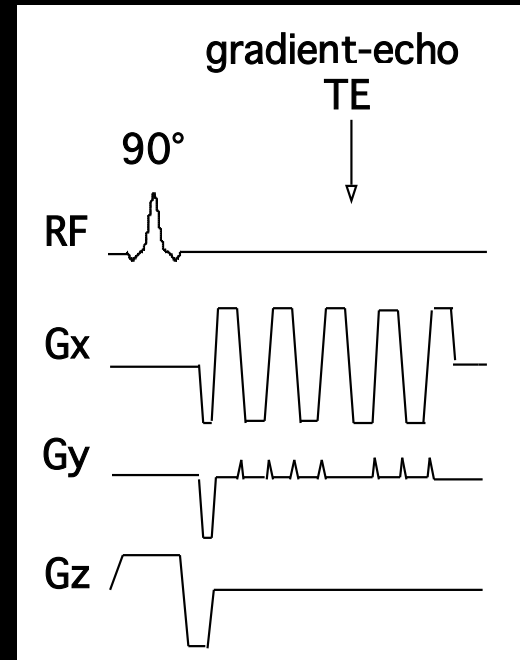
# Single Shot EPI

**T2\* decay**

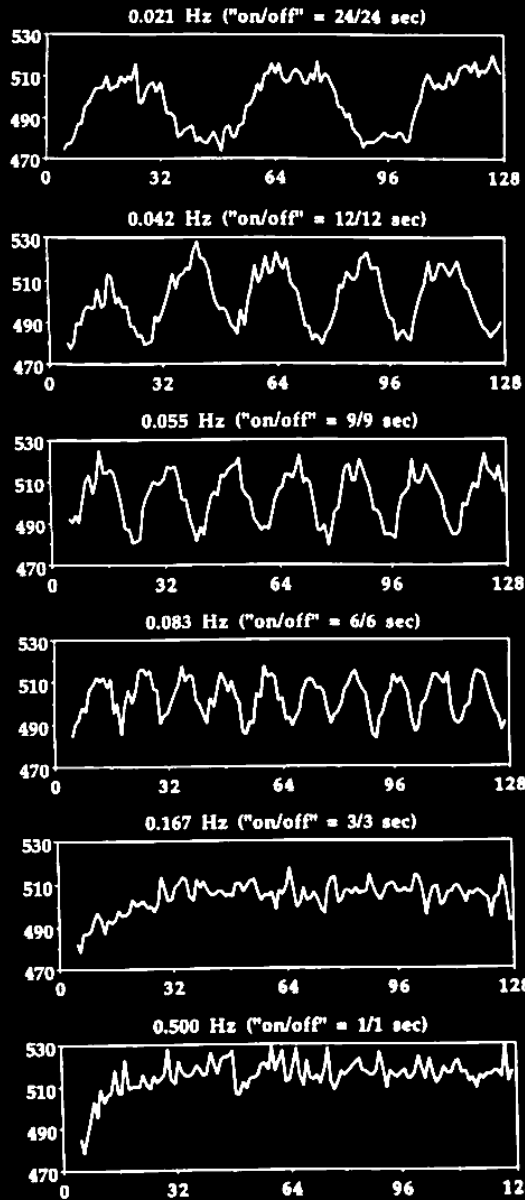


**EPI Readout Window**

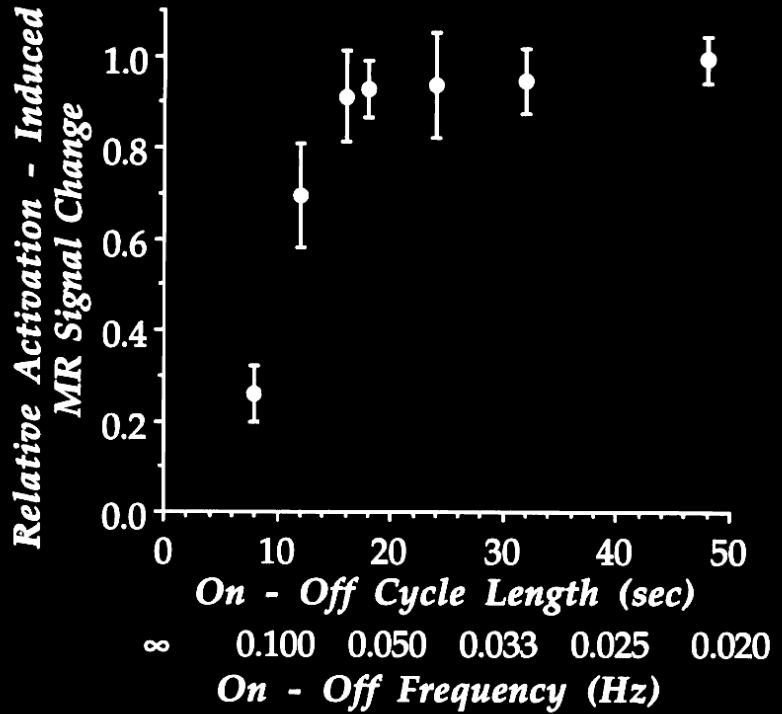
**≈ 20 to 40 ms**



MRI Signal



Time (seconds)



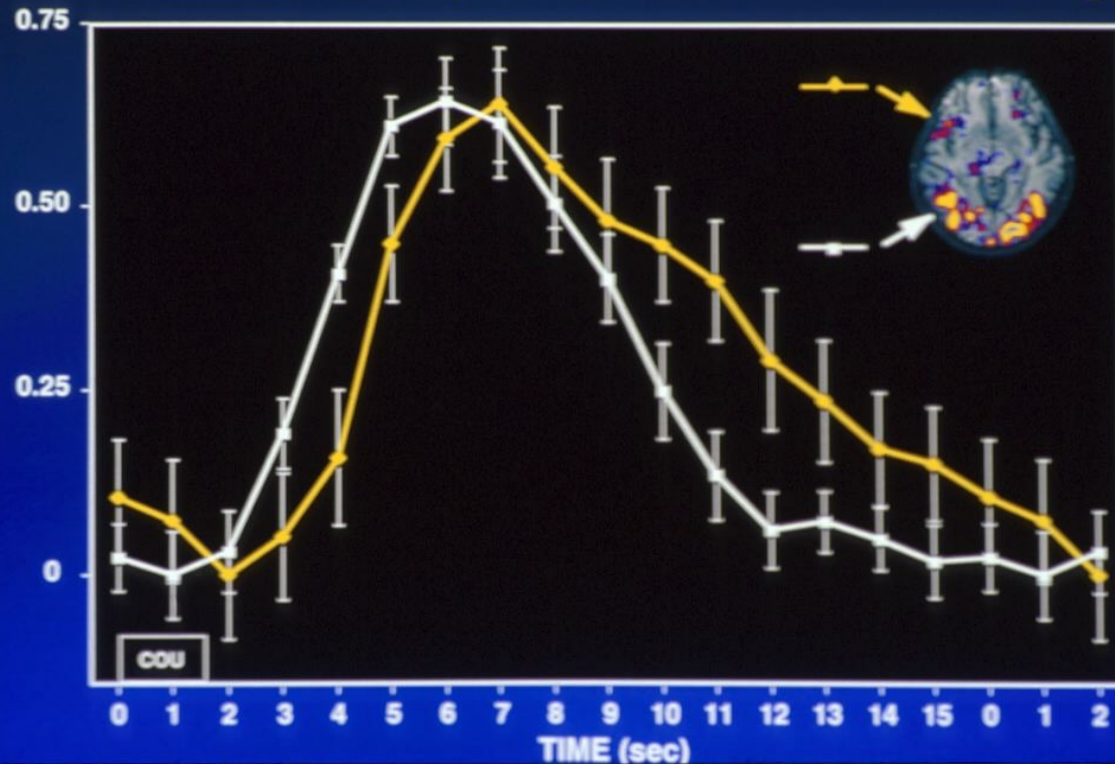
P. A. Bandettini, Functional MRI temporal resolution in "Functional MRI" (C. Moonen, and P. Bandettini., Eds.), p. 205-220, Springer - Verlag, 1999.

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

(neuroimaging/single trial/language/prefrontal)

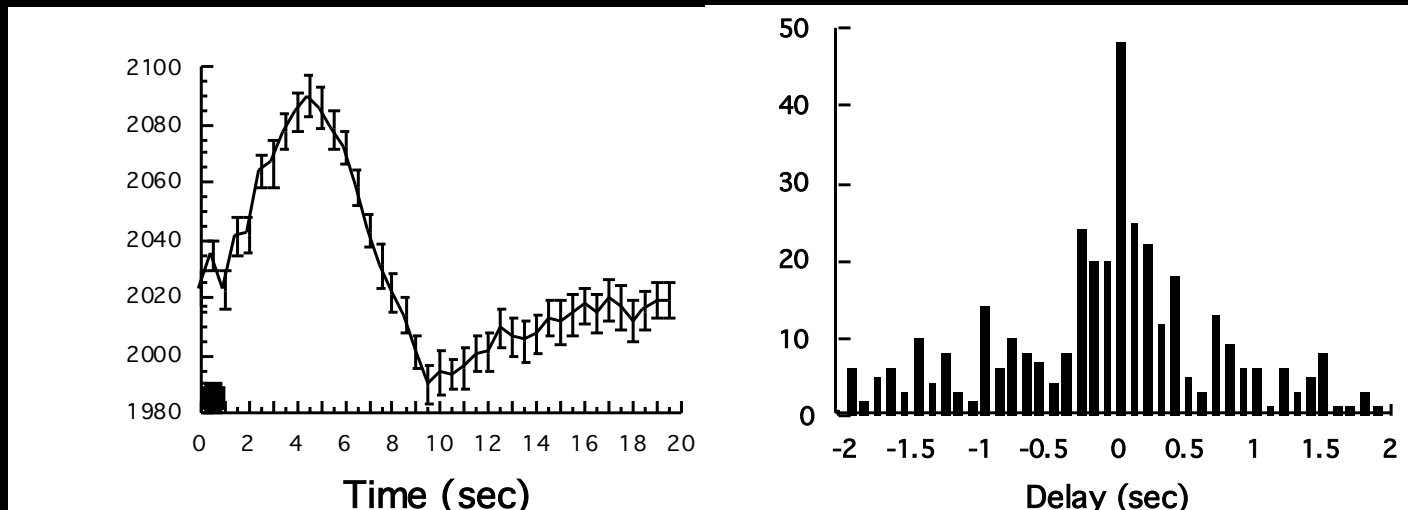
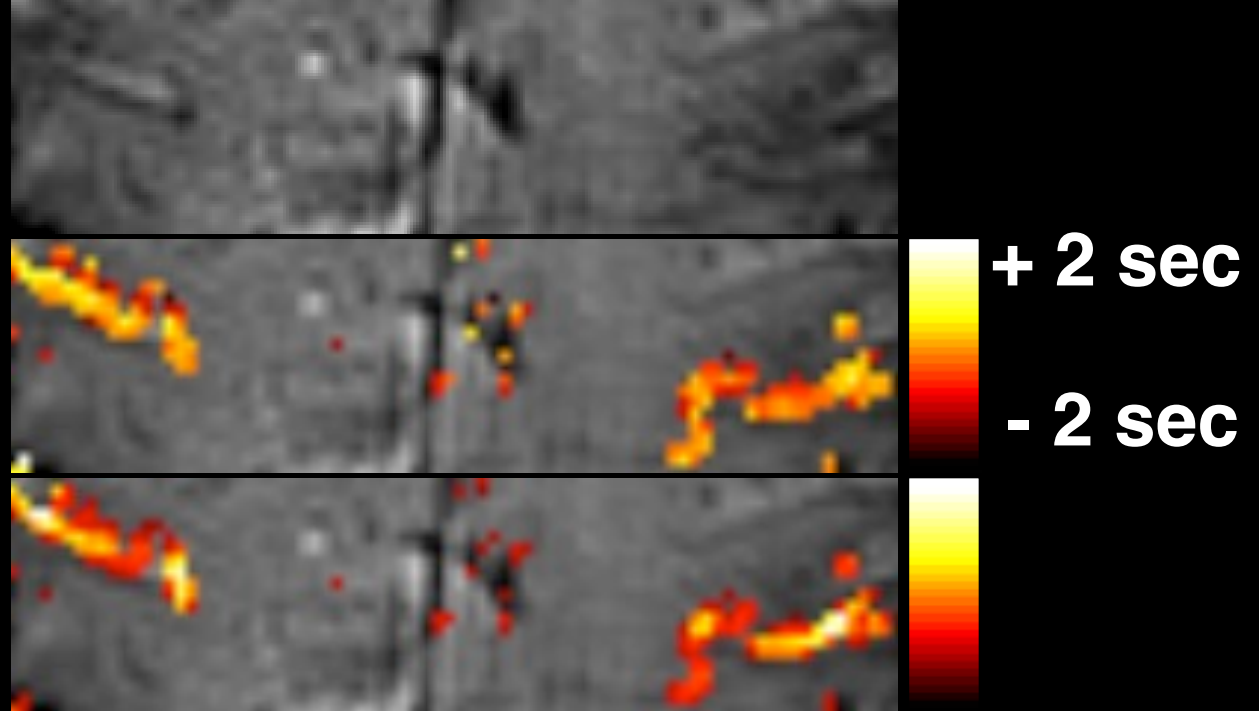
RANDY L. BUCKNER<sup>†‡§¶</sup>, PETER A. BANDETTINI<sup>†‡</sup>, KATHLEEN M. O' CRAVEN<sup>†||</sup>, ROBERT L. SAVOY<sup>†||</sup>,  
STEVEN E. PETERSEN<sup>\*\*††</sup>, MARCUS E. RAICHLE<sup>§\*\*††</sup>, AND BRUCE R. ROSEN<sup>†‡</sup>

### Time Course Comparison Across Brain Regions



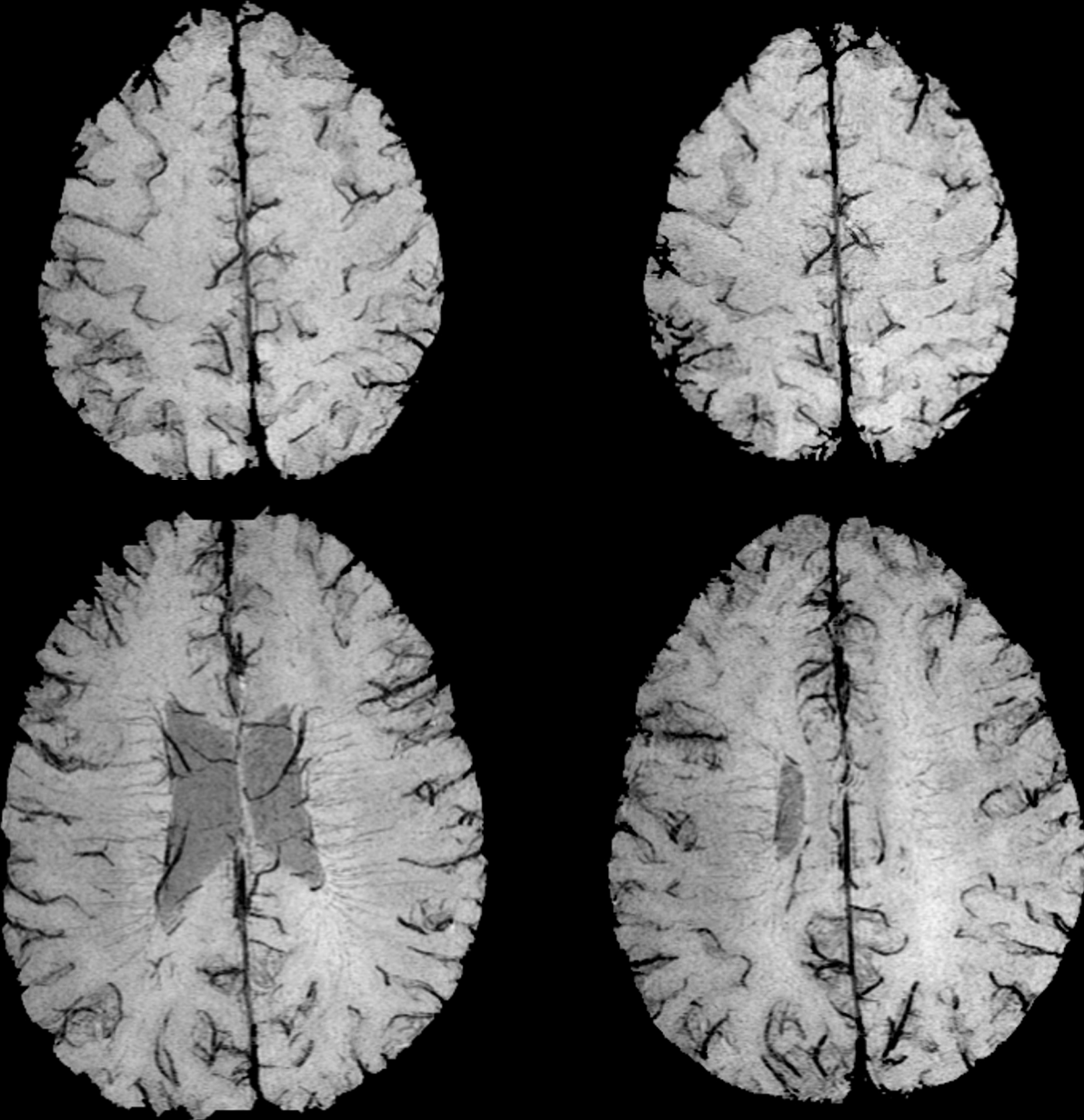
Latency

Magnitude

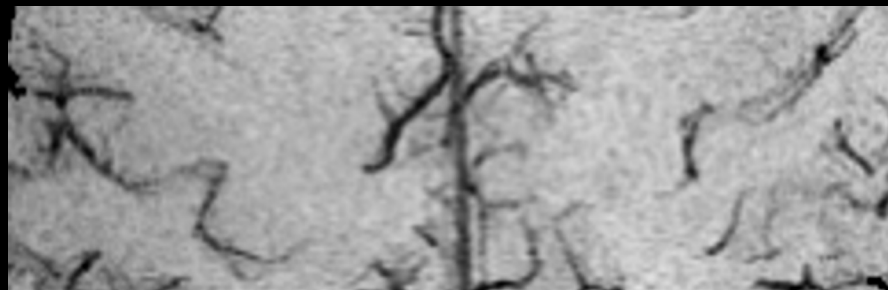
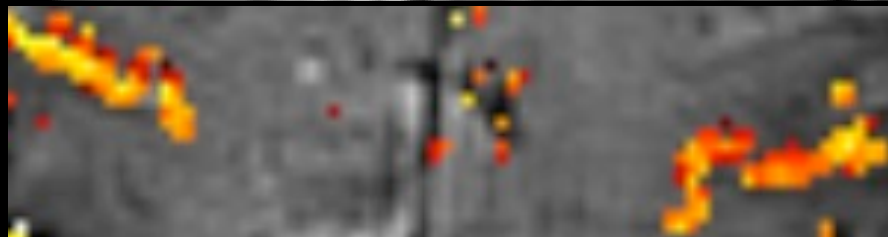
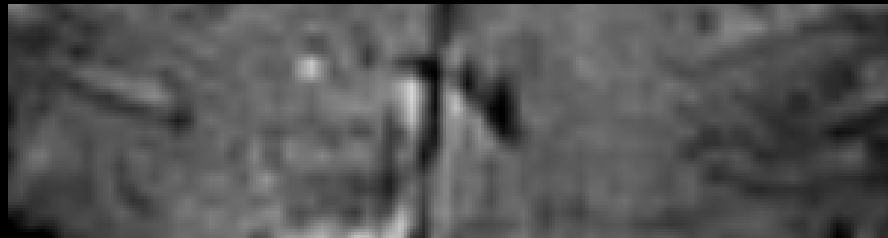


P. A. Bandettini, The temporal resolution of Functional MRI *in* "Functional MRI" (C. Moonen, and P. Bandettini., Eds.), p. 205-220, Springer - Verlag,. 1999.

# Venogram (3 Tesla)

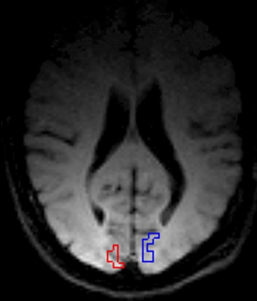




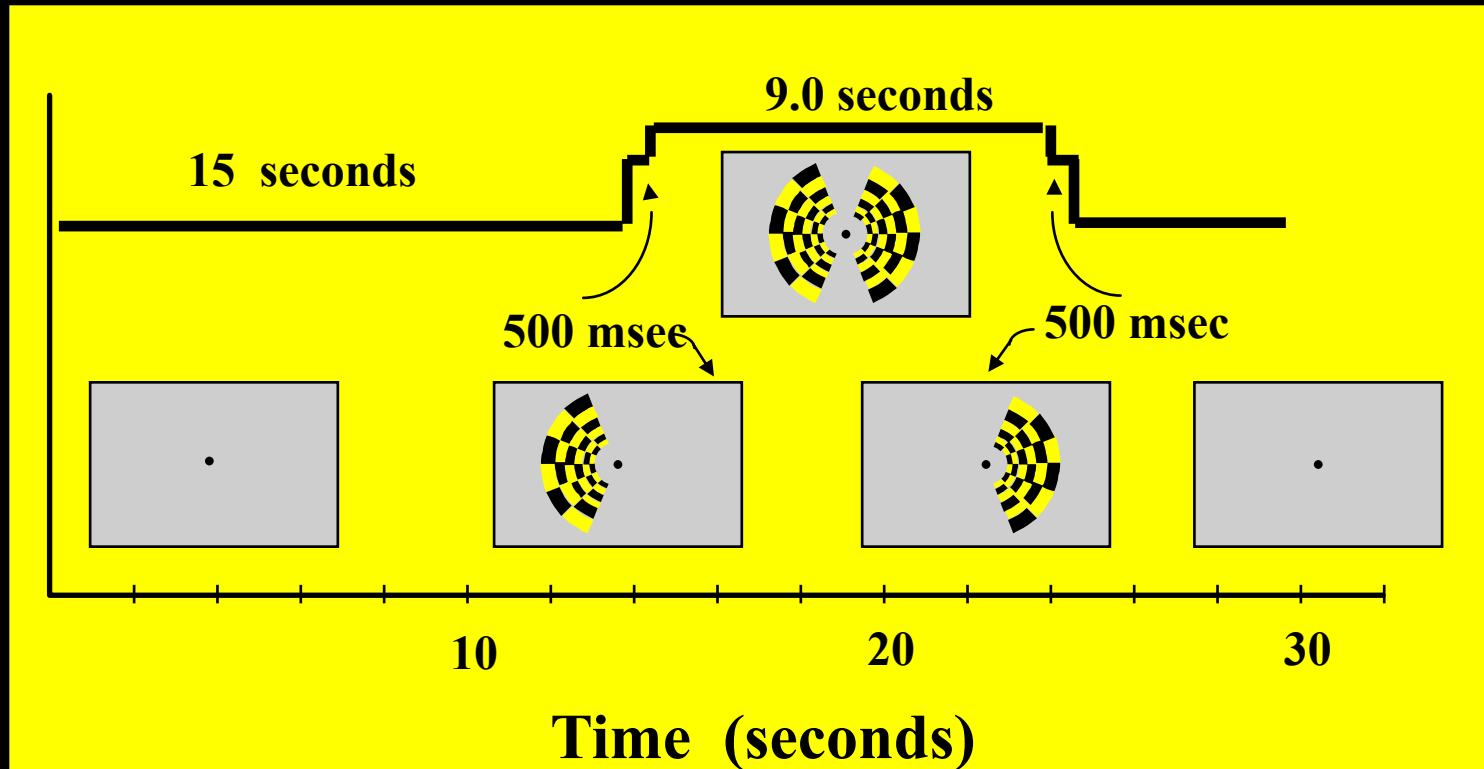


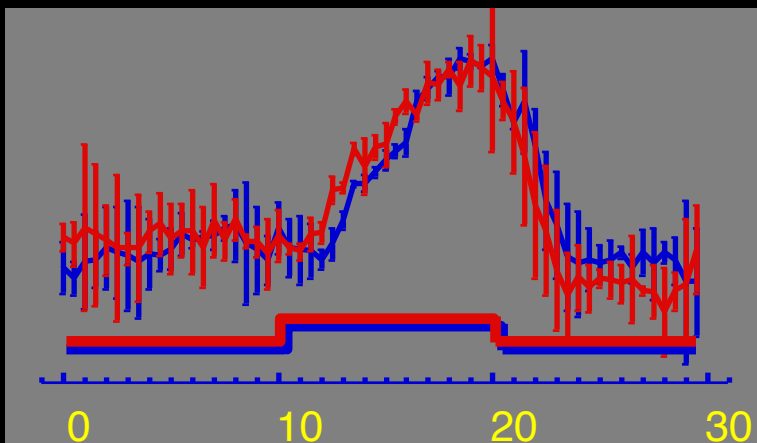
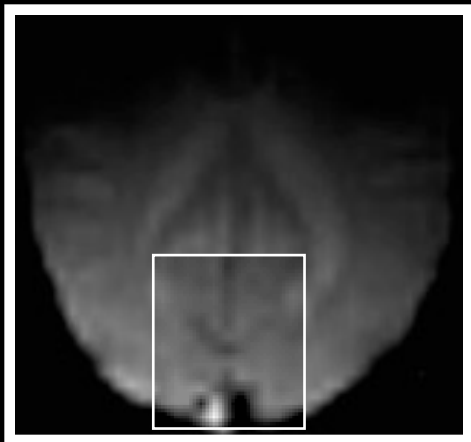
# Hemi-Field Experiment

**Right Hemisphere**



**Left Hemisphere**





500 ms



500 ms



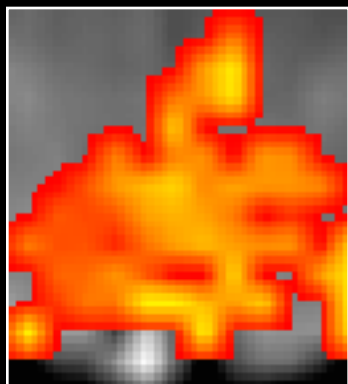
Right Hemifield

Left Hemifield

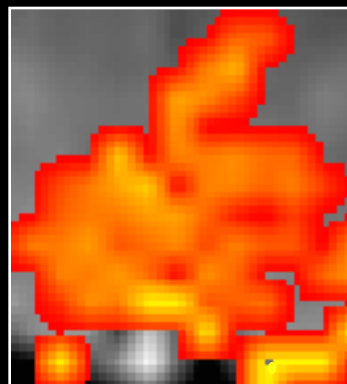
+ 2.5 s

0 s

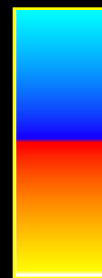
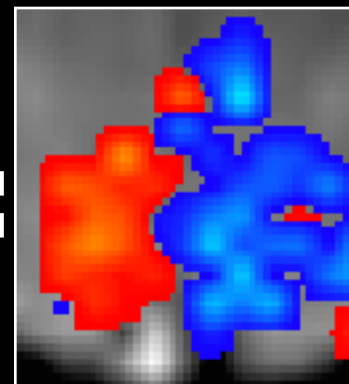
- 2.5 s



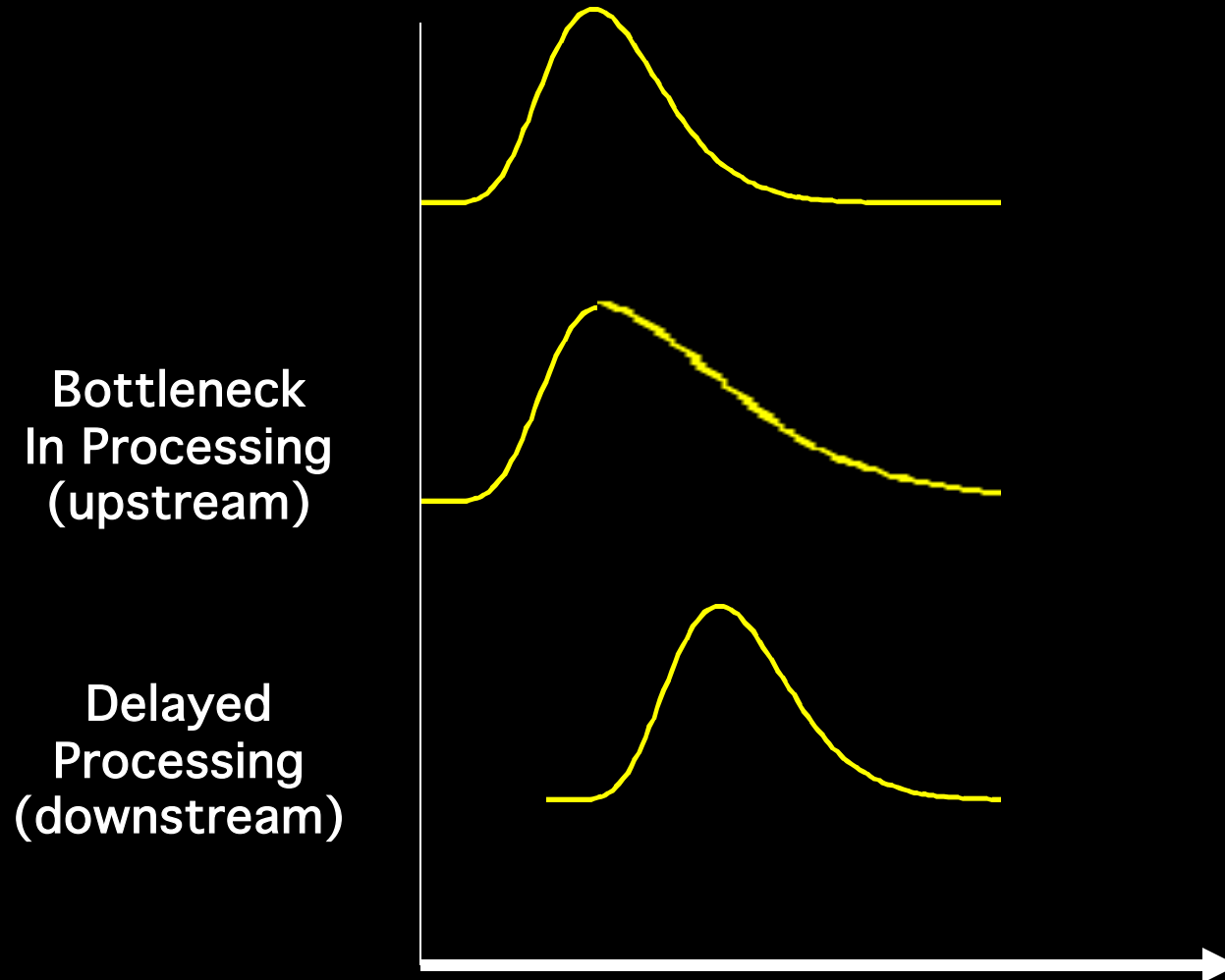
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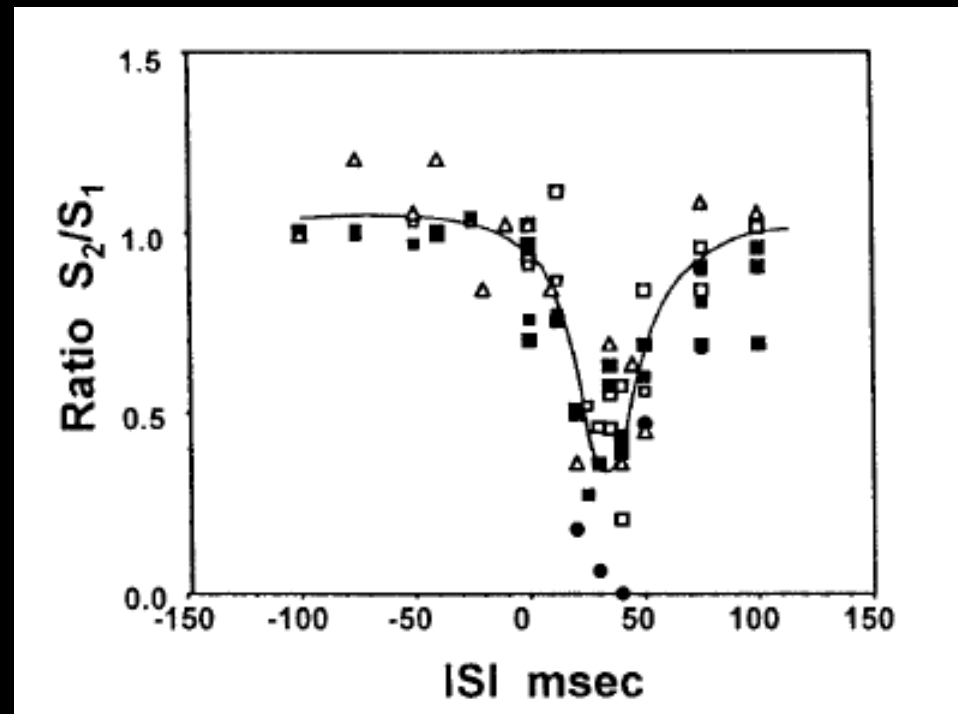


# Hemodynamic Response Modulation



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

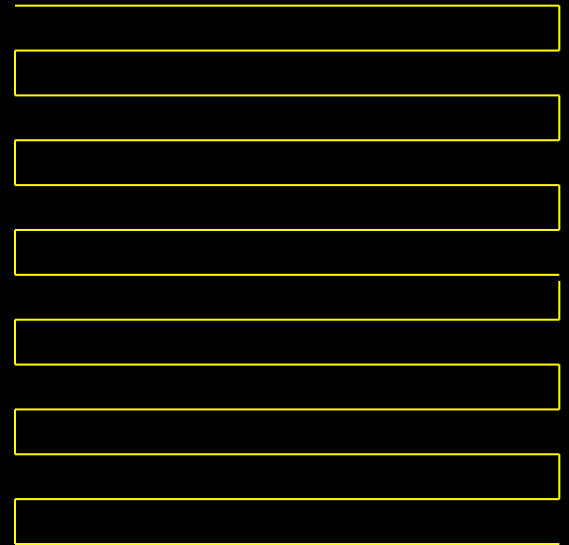
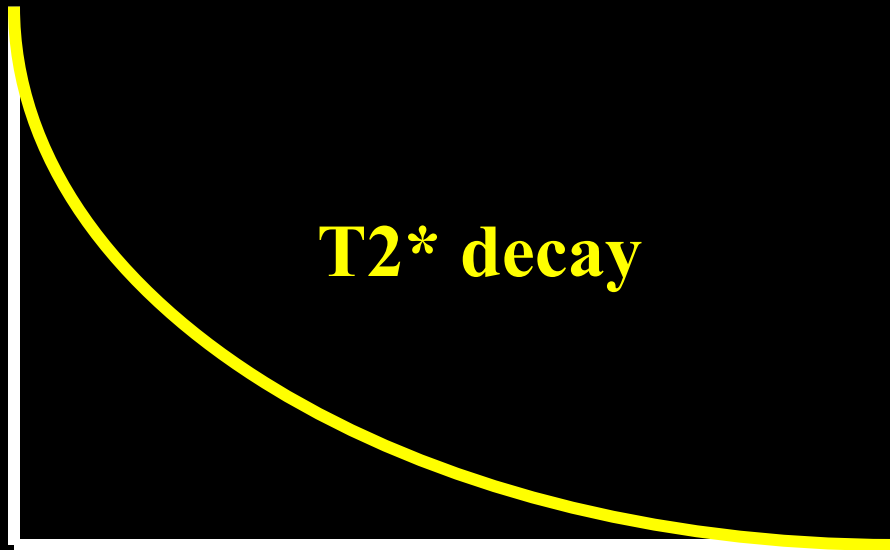
Seiji Ogawa<sup>††</sup>, Tso-Ming Lee<sup>†</sup>, Ray Stepnoski<sup>†</sup>, Wei Chen<sup>§</sup>, Xiao-Hong Zhu<sup>§</sup>, and Kamil Ugurbil<sup>§</sup>



# Latest Developments...

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

# Single Shot Imaging



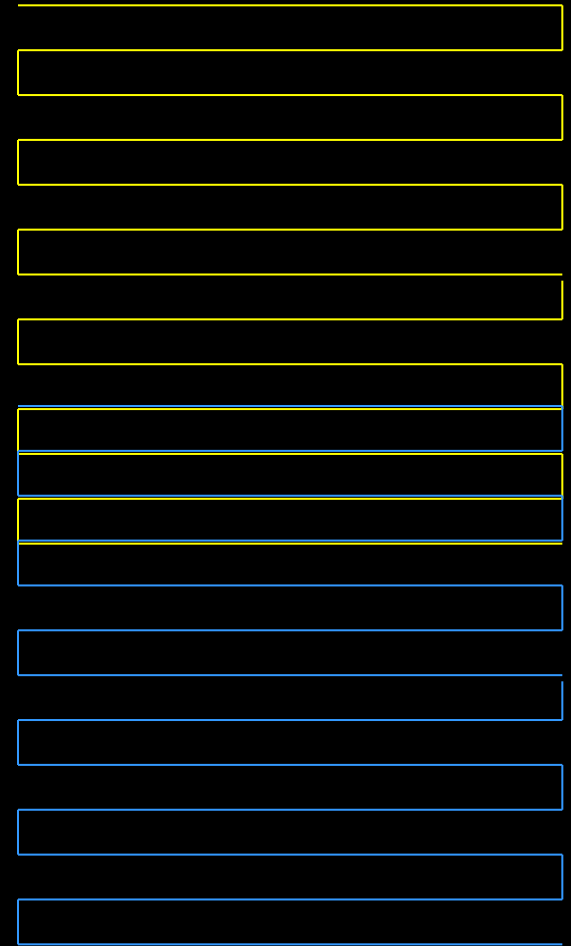
**EPI Readout Window**

**$\approx 20$  to  $40$  ms**

# Partial k-space imaging



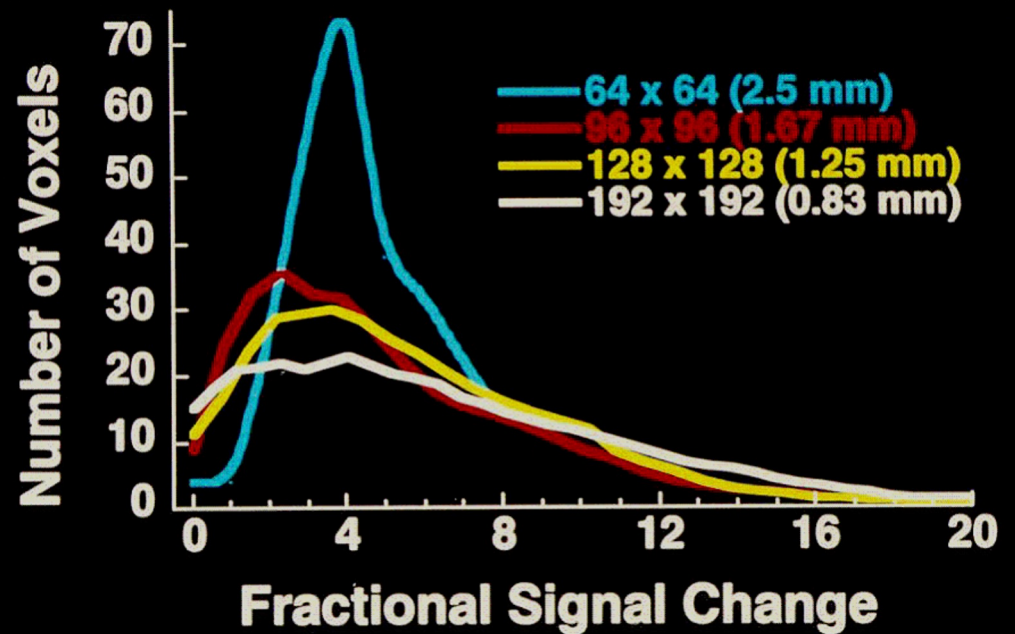
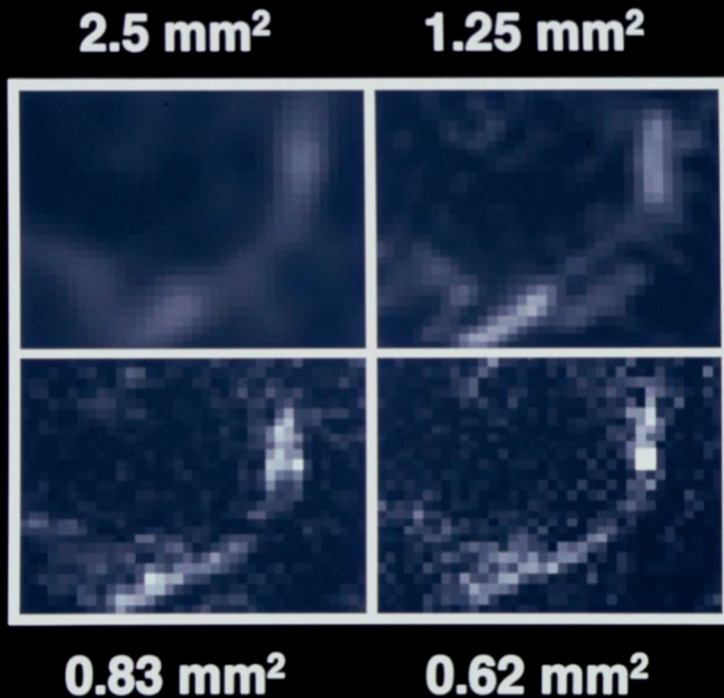
**EPI Window**





# Partial k-space imaging

## Fractional Signal Change

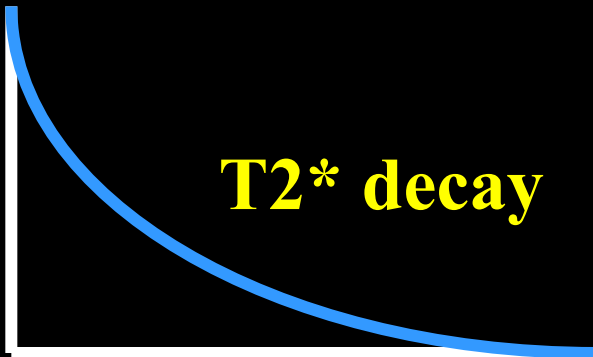


Jesmanowicz, P. A. Bandettini, J. S. Hyde, (1998) "Single shot half k-space high resolution EPI for fMRI at 3T." *Magn. Reson. Med.* 40, 754-762.

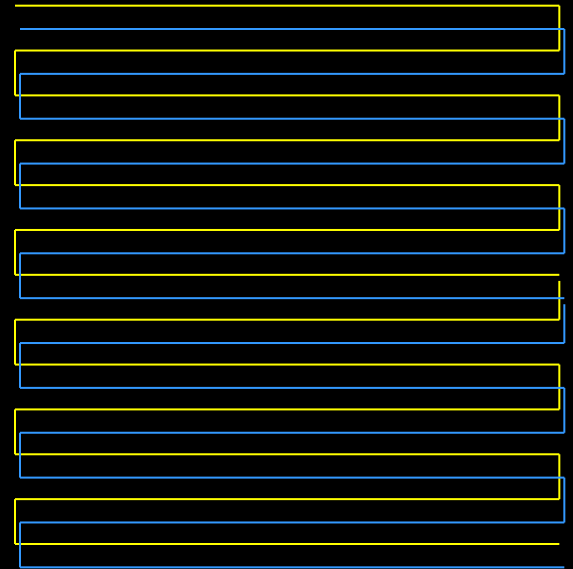
# Multishot Imaging



**EPI Window 1**



**EPI Window 2**



# Multi Shot EPI

Excitations  
Matrix Size

1

64 x 64

2

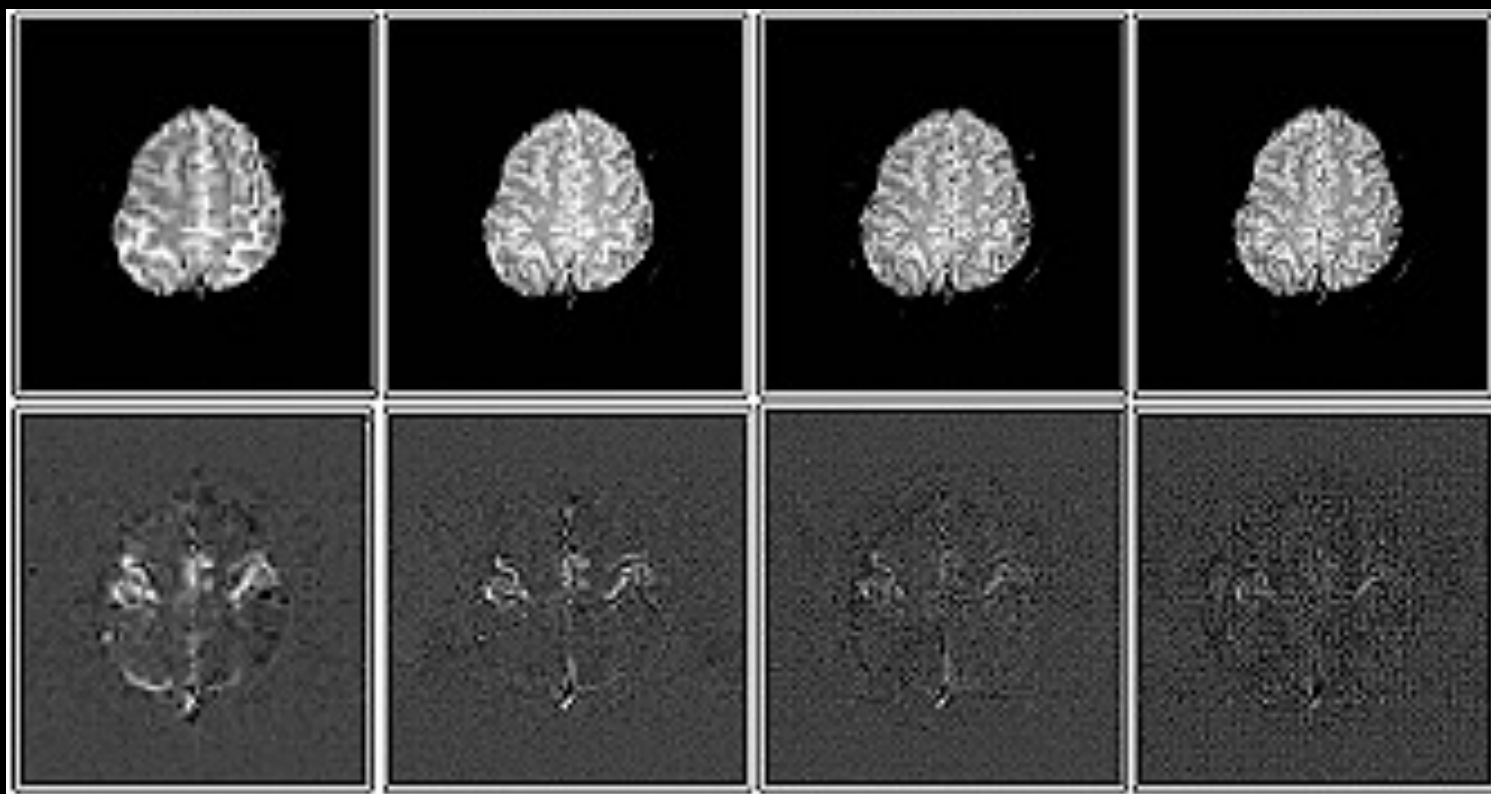
128 x 128

4

256 x 128

8

256

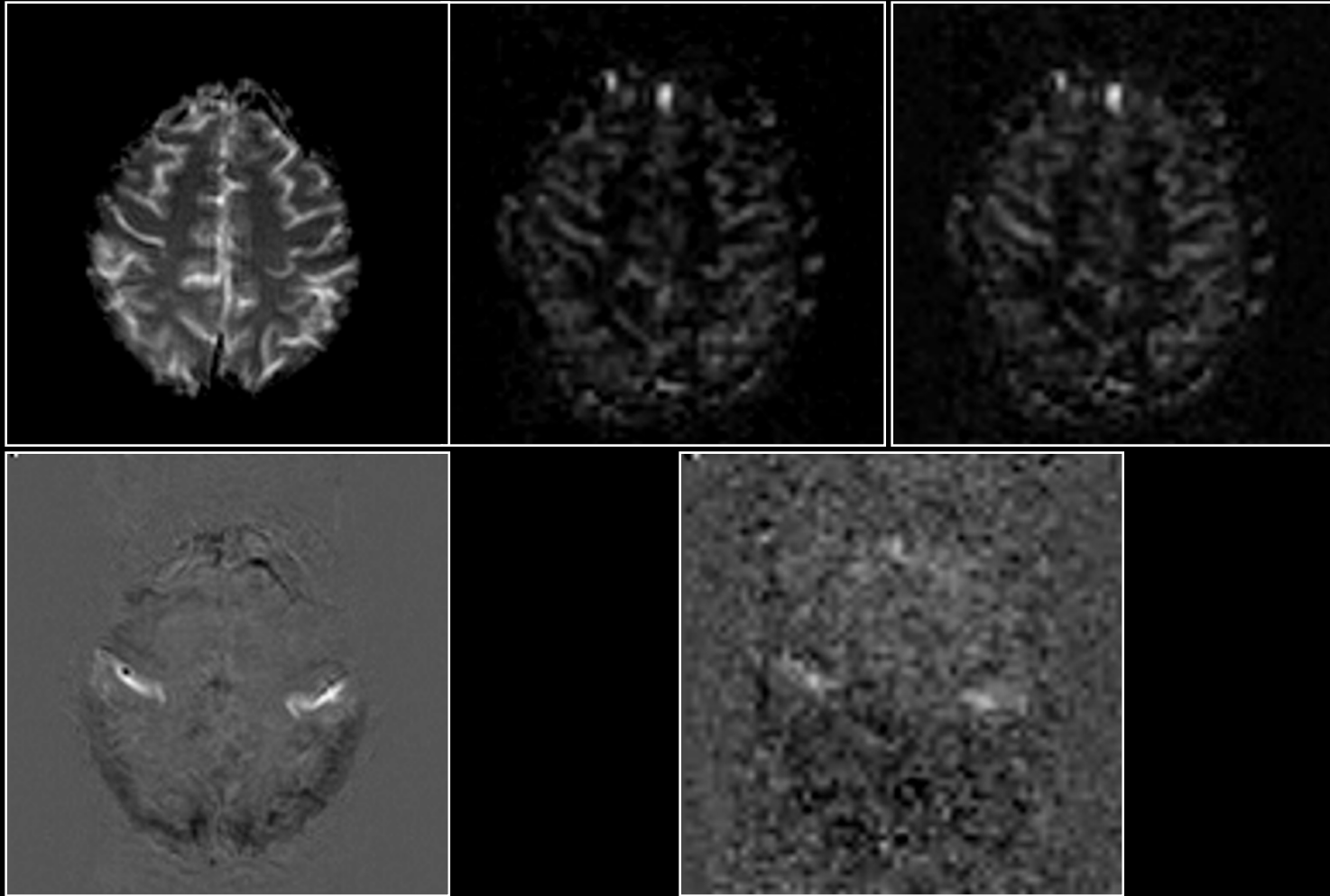


# Perfusion

**BOLD**

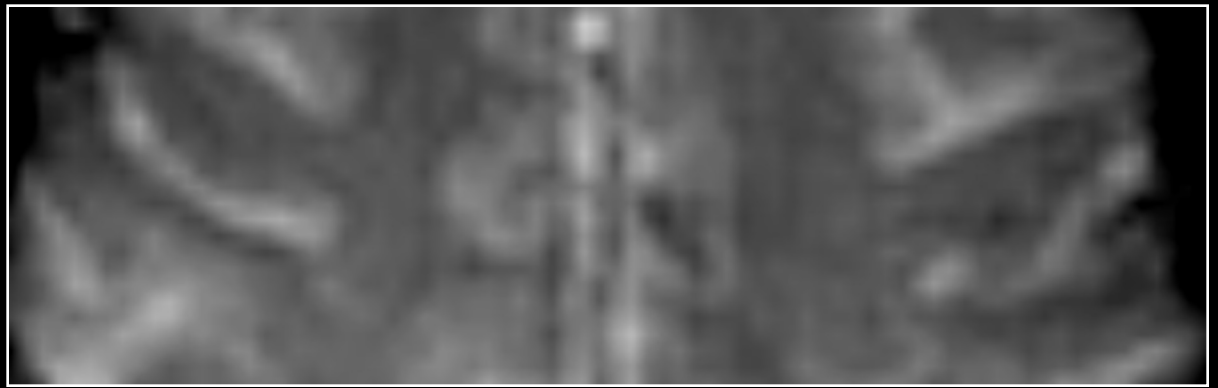
*Rest*

*Activation*

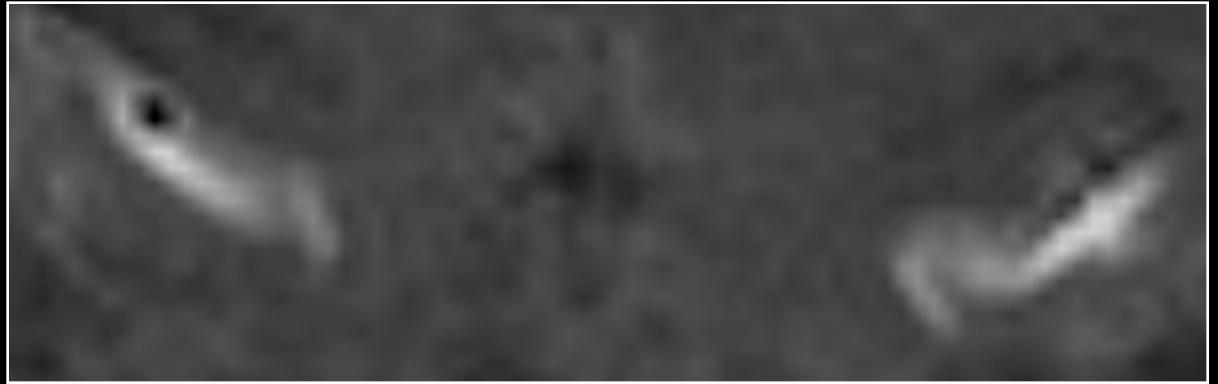


P. A. Bandettini, E. C. Wong, Magnetic resonance imaging of human brain function: principles, practicalities, and possibilities, *in* "Neurosurgery Clinics of North America: Functional Imaging" (M. Haglund, Ed.), p.345-371, W. B. Saunders Co., 1997.

**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.

Arterial inflow  
(BOLD TR < 500 ms)

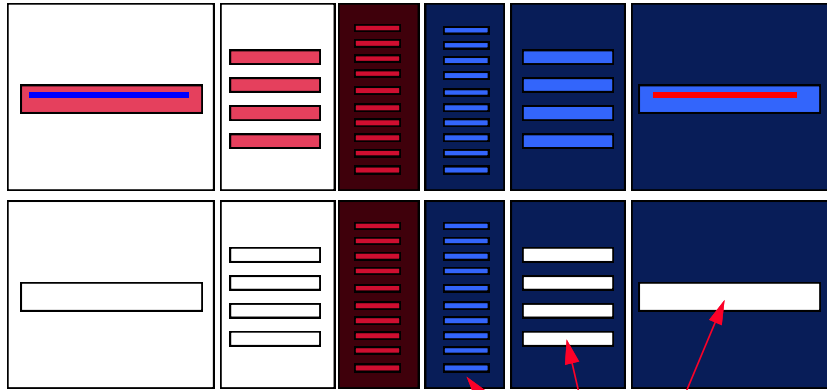
**Perfusion**

**BOLD**

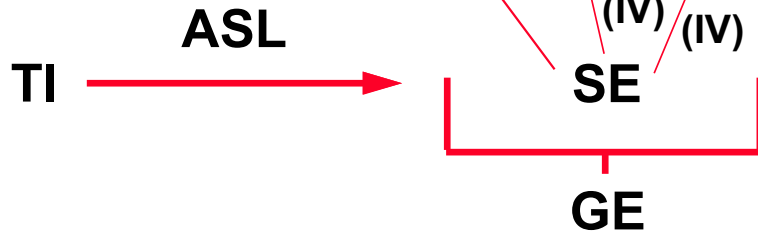
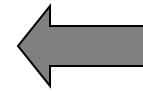
Venous inflow  
(for ASL, w/ no VN)

No  
Velocity  
Nulling

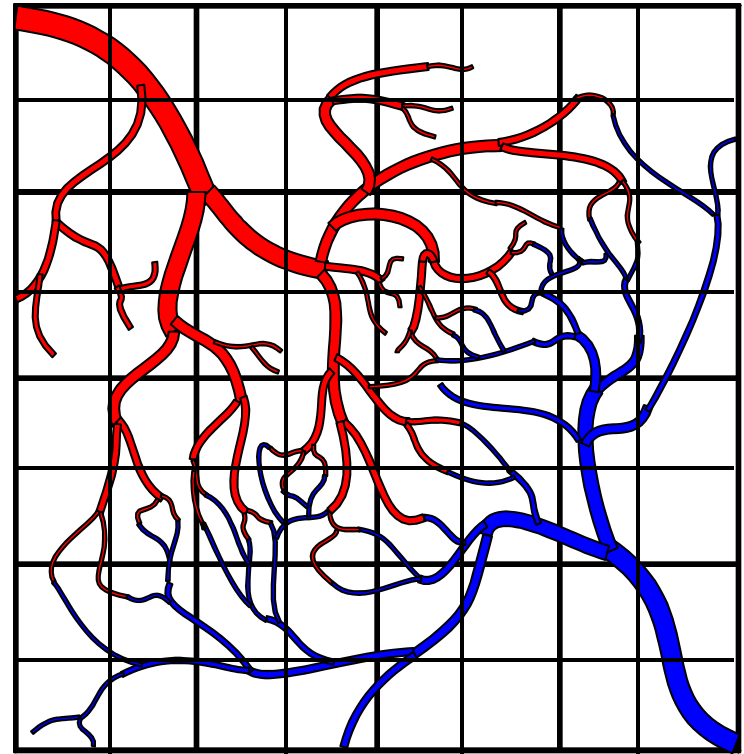
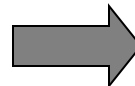
Velocity  
Nulling



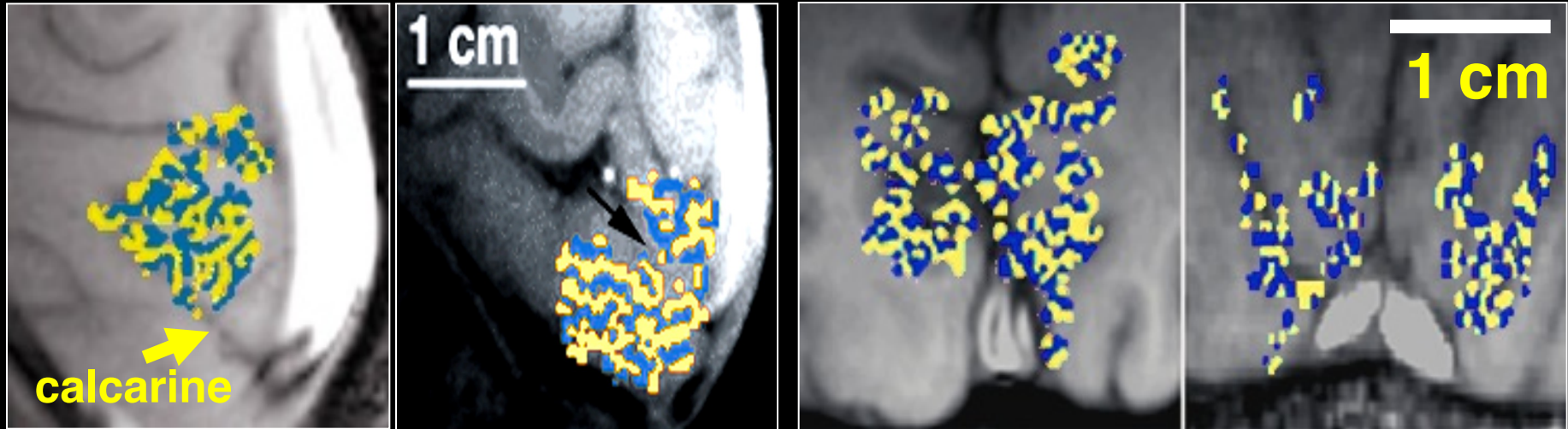
Pulse Sequence  
Sensitivity



Spatial  
Heterogeneity



# ODC Maps using fMRI



- Identical in size, orientation, and appearance to those obtained by optical imaging<sup>1</sup> and histology<sup>3,4</sup>.

<sup>1</sup>Malonek D, Grinvald A. *Science* 272, 551-4 (1996).

<sup>3</sup>Horton JC, Hocking DR. *J Neurosci* 16, 7228-39 (1996).

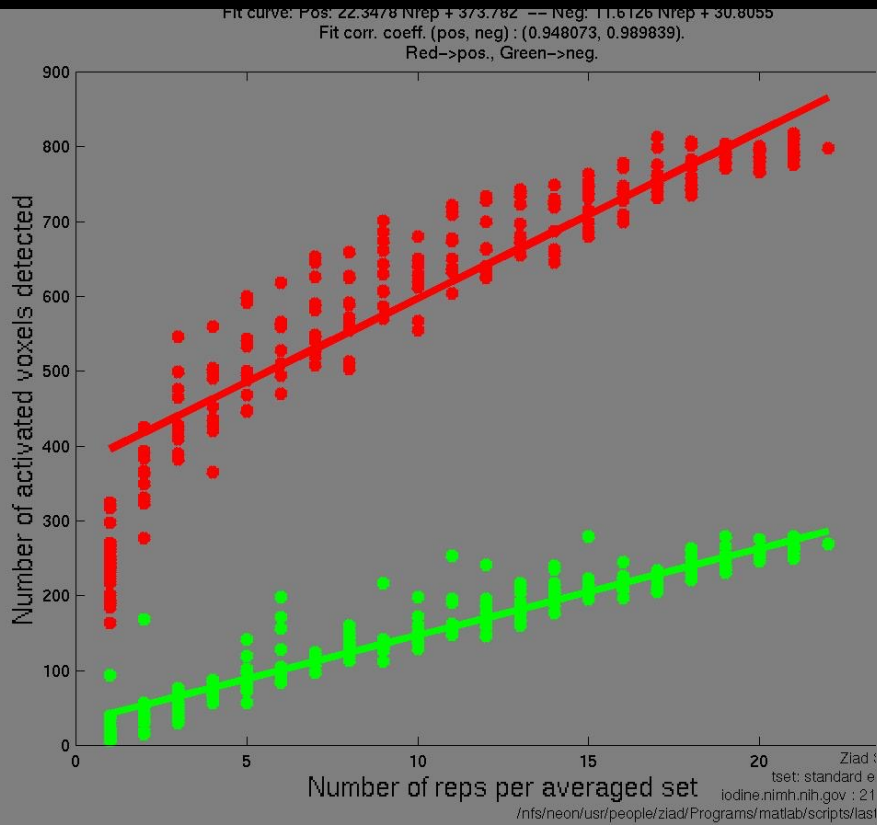
<sup>4</sup>Horton JC, et al. *Arch Ophthalmol* 108, 1025-31 (1990).

# Latest Developments...

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

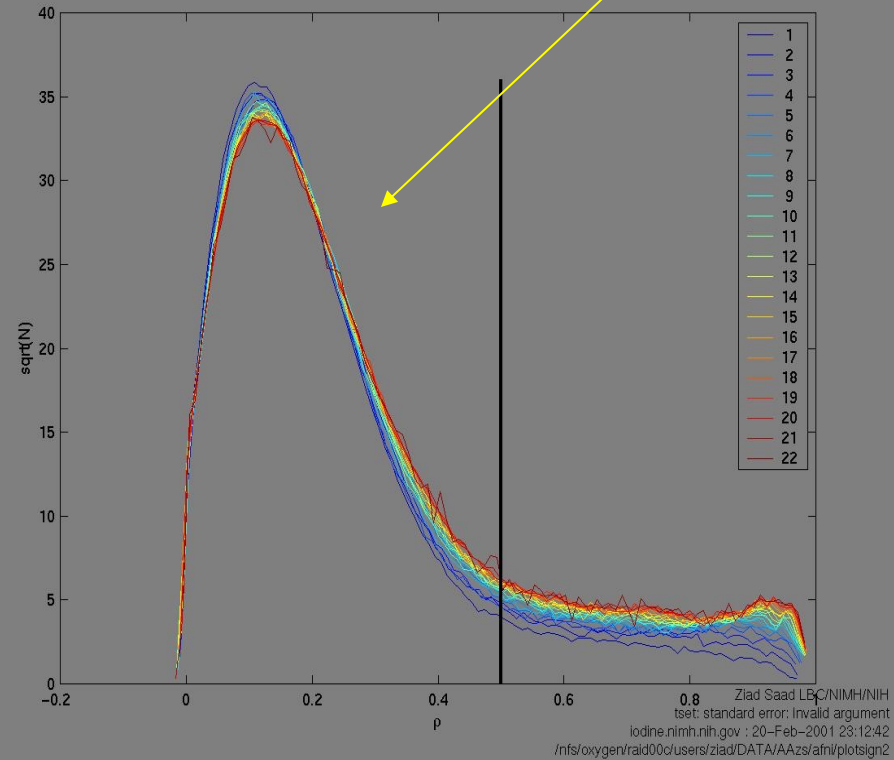


# Continuously Growing Activation Area



# CC Histogram

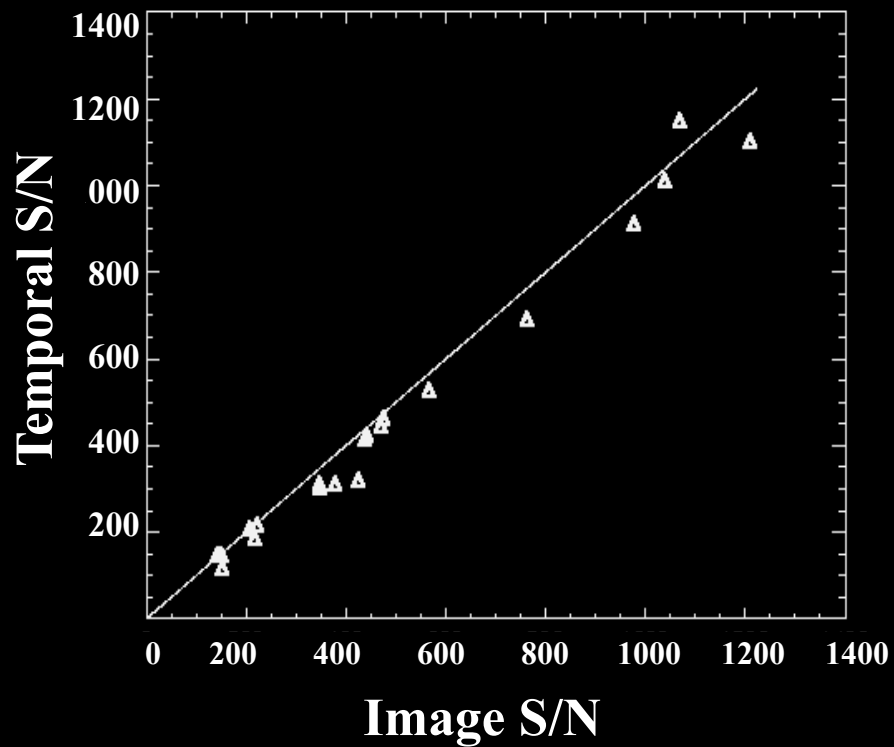
Inflection Point



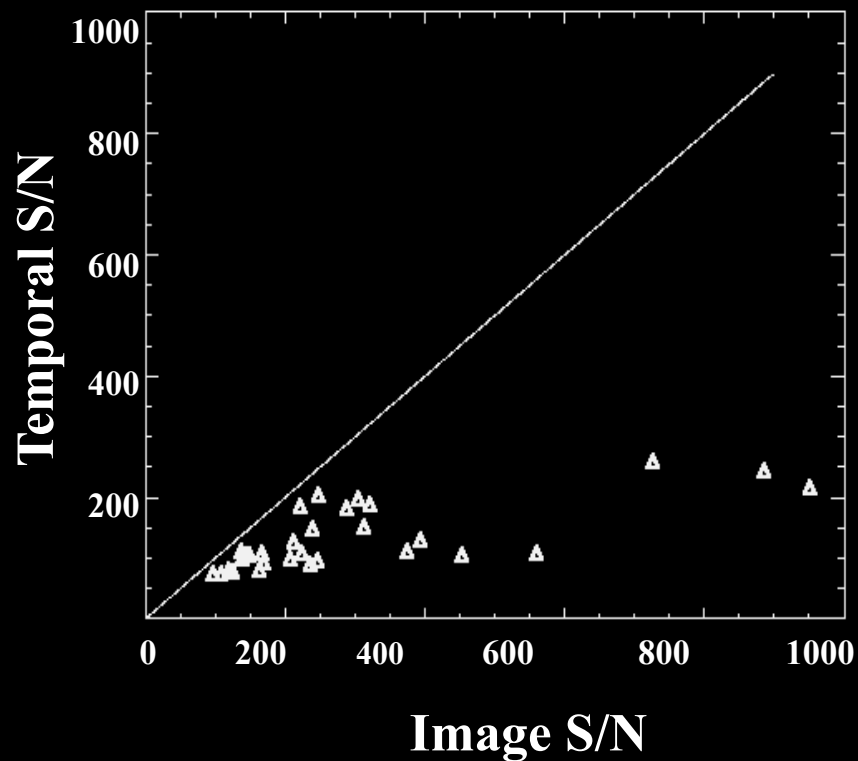
Ziad Saad, et al

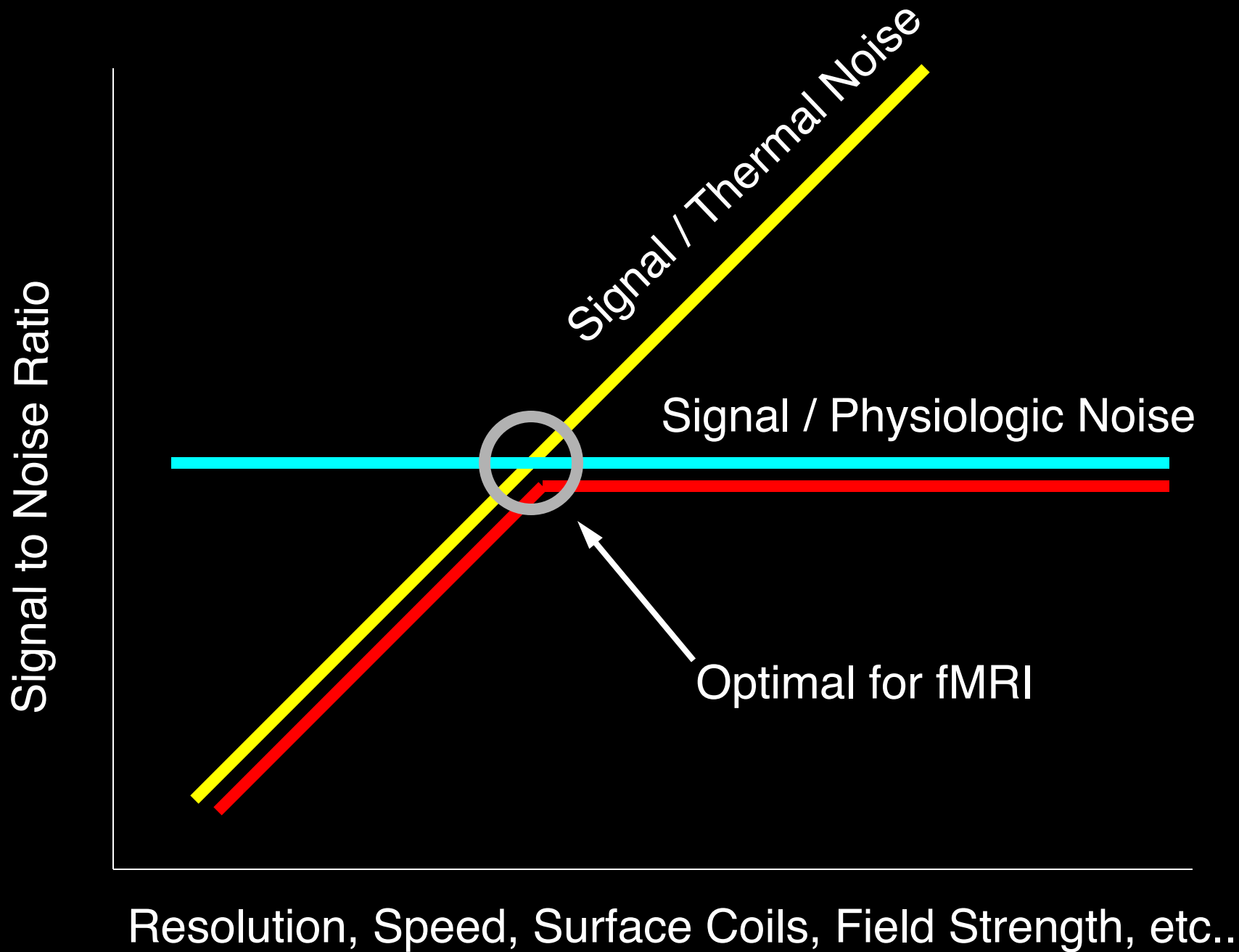
# Temporal S/N vs. Image S/N

## PHANTOMS



## SUBJECTS





# Latest Developments...

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

$\Delta$  Neuronal Activity

Number of Neurons

Local Field Potential

Spiking Coherence

Spiking Rate

$\Delta$  Metabolism

Aerobic Metabolism

Anaerobic Metabolism

$\Delta$  Hemodynamics

Blood Volume

Deoxygenated Blood

Flow Velocity

Oxygenated Blood

Perfusion

$\Delta$  BOLD Contrast

$\Delta$  Perfusion Contrast

$\Delta$  Inflow Contrast

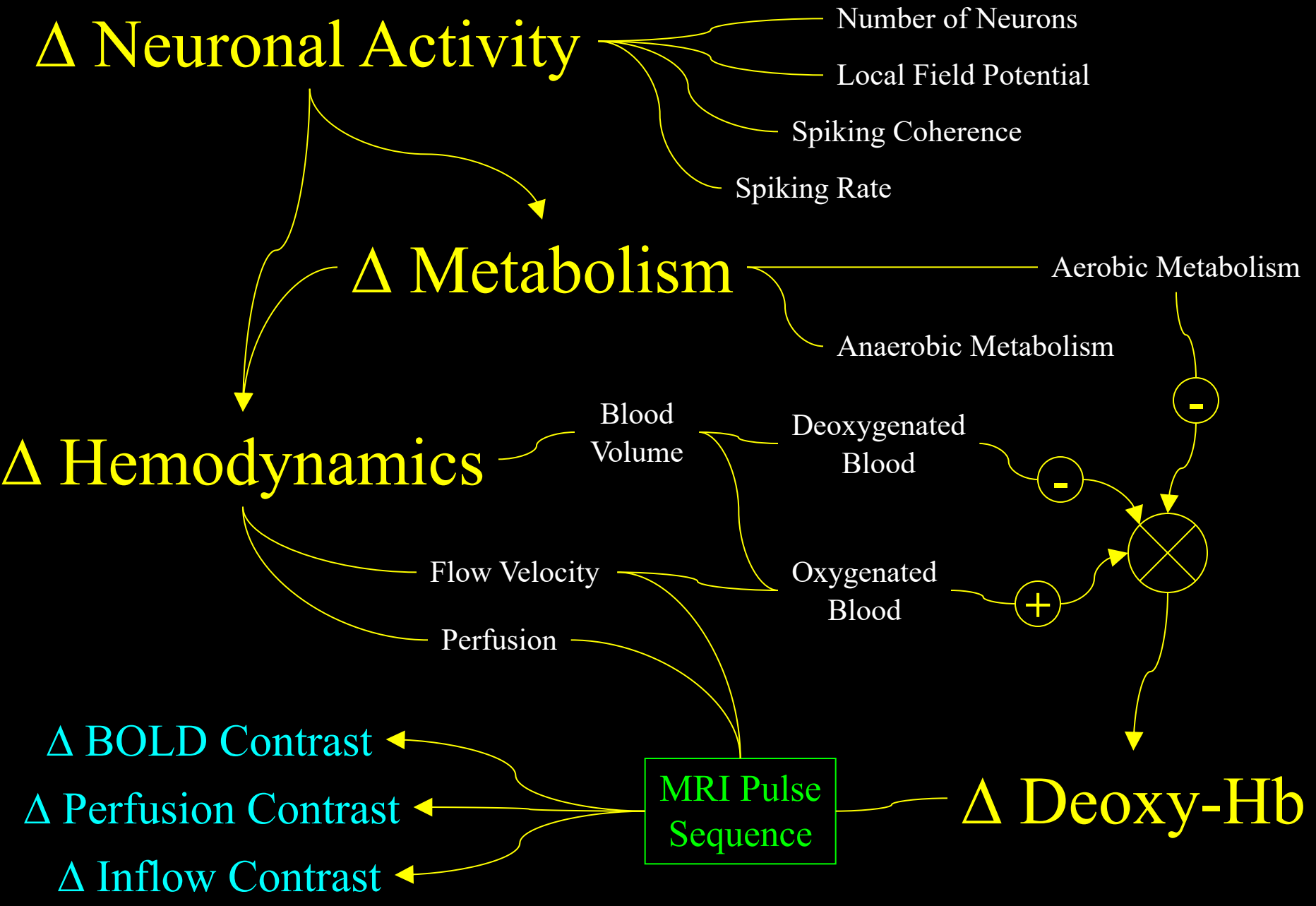
MRI Pulse Sequence

$\Delta$  Deoxy-Hb

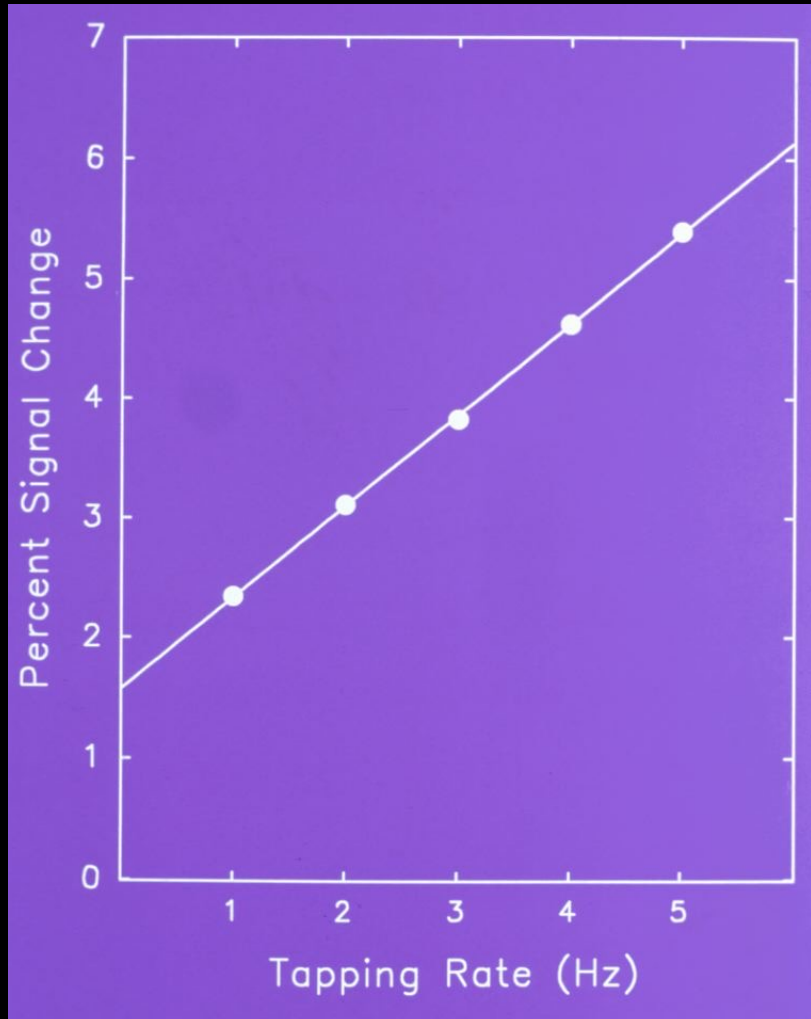
-

-

+

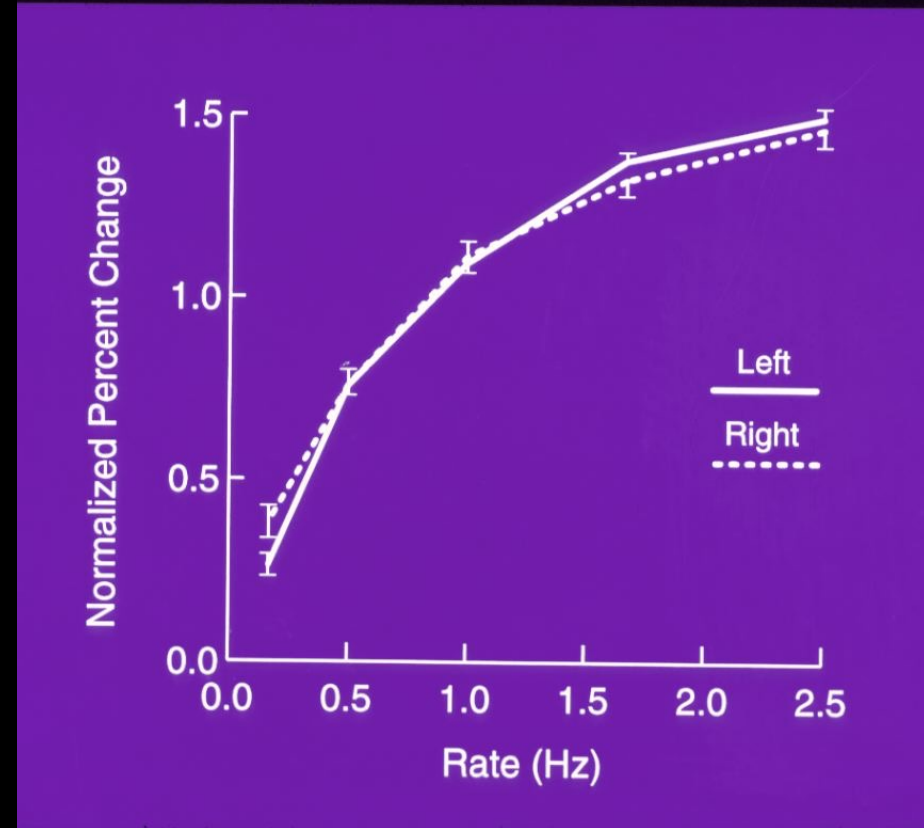


# Motor Cortex



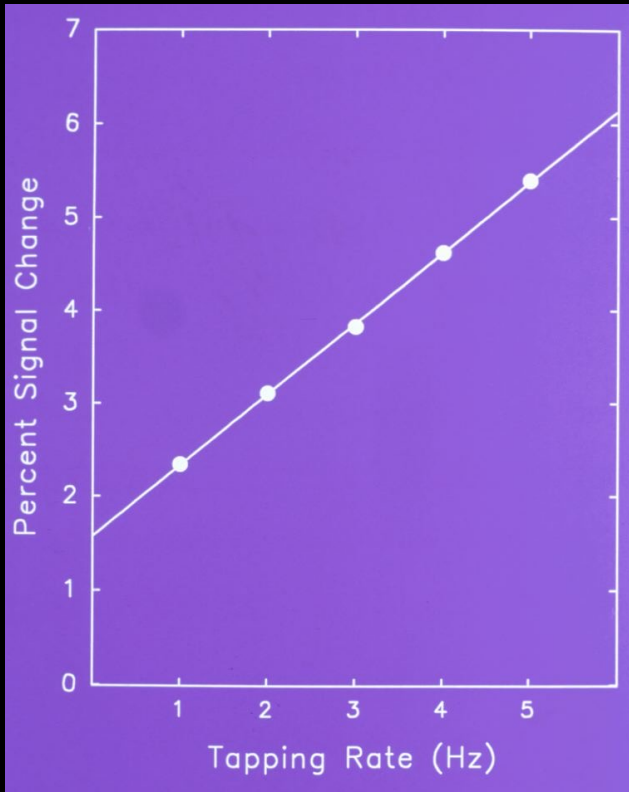
S. M. Rao et al, (1996) "Relationship between finger movement rate and functional magnetic resonance signal change in human primary motor cortex." *J. Cereb. Blood Flow and Met.* 16, 1250-1254.

# Auditory Cortex

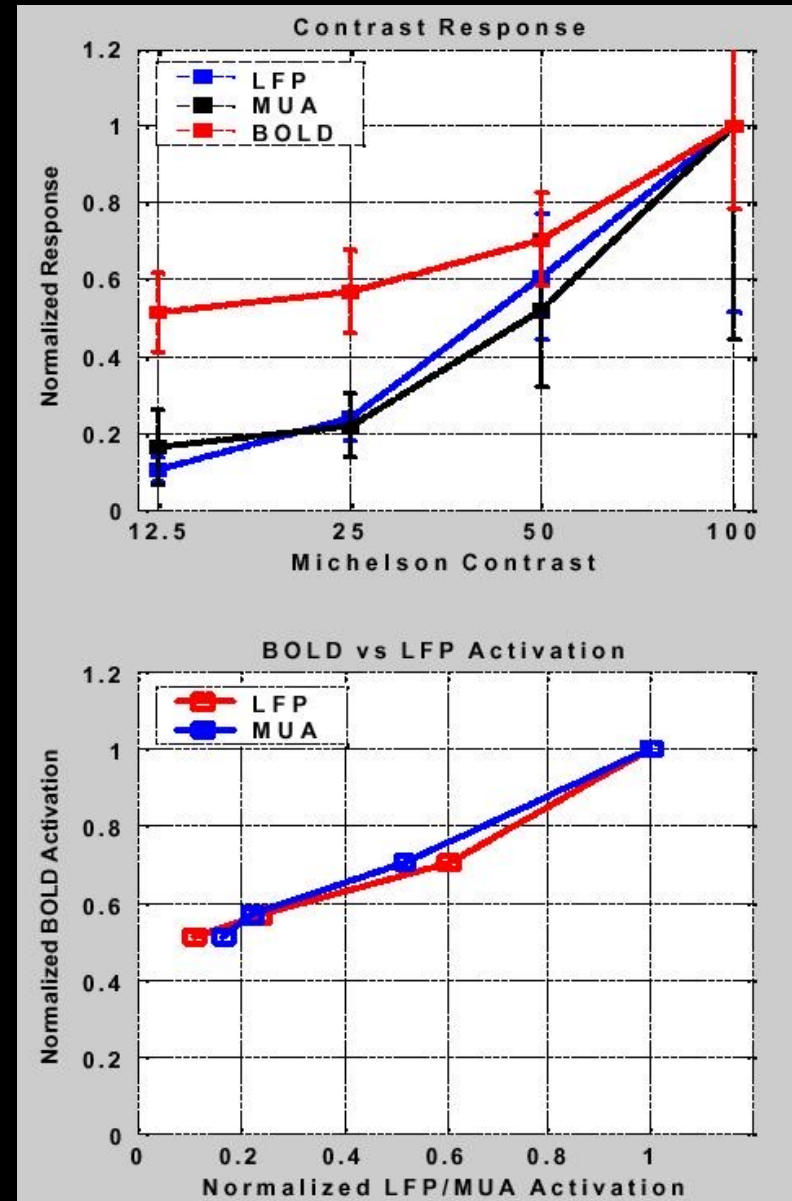


J. R. Binder, et al, (1994). "Effects of stimulus rate on signal response during functional magnetic resonance imaging of auditory cortex." *Cogn. Brain Res.* 2, 31-38

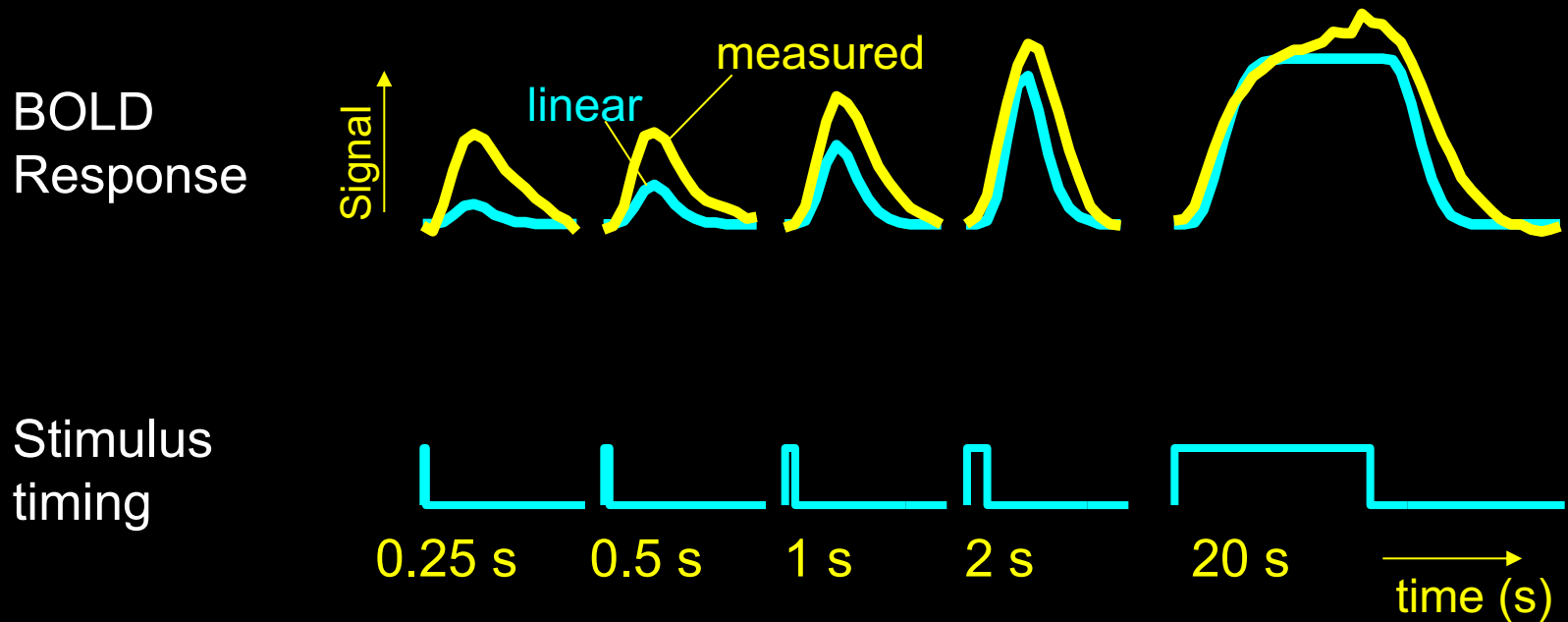
Logothetis et al. (2001) "Neurophysiological investigation of the basis of the fMRI signal" *Nature*, 412, 150-157



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.



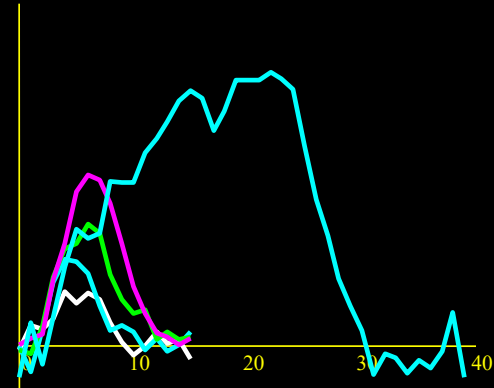
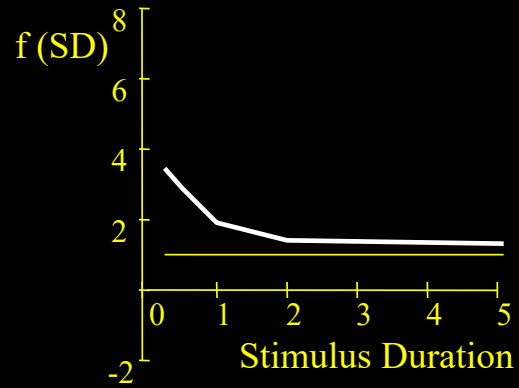
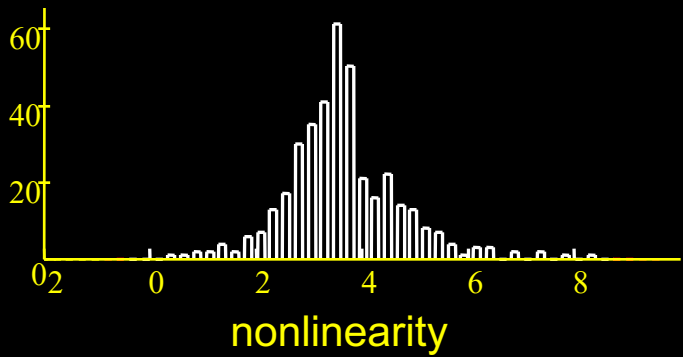
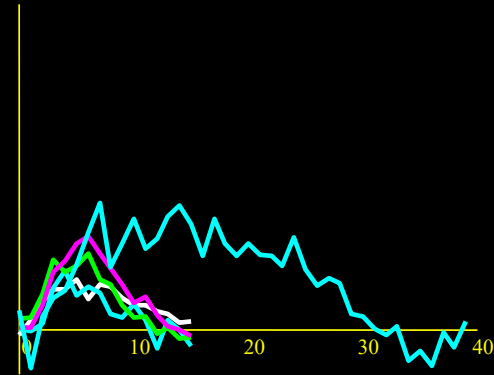
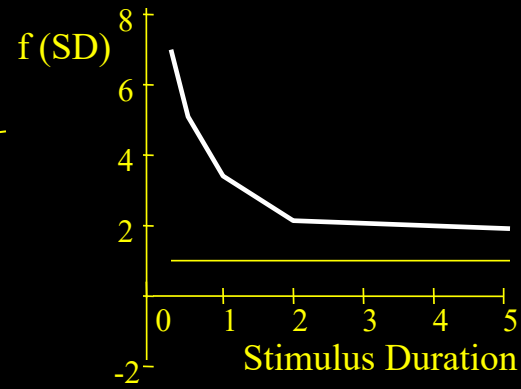
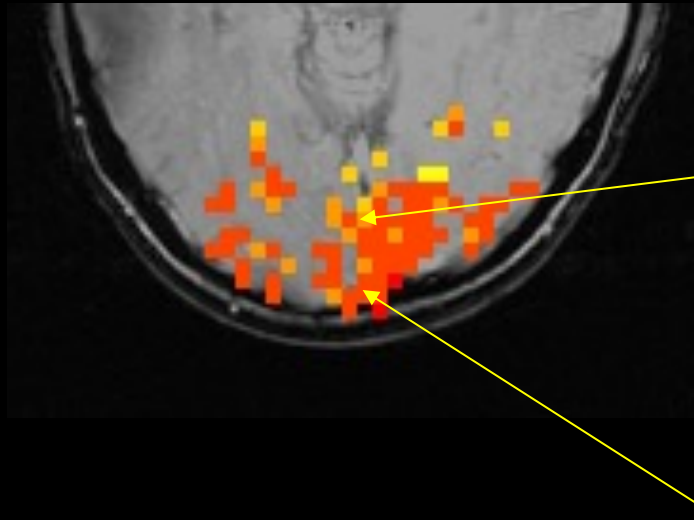
# Different stimulus “ON” periods



*Brief stimuli produce larger responses than expected*

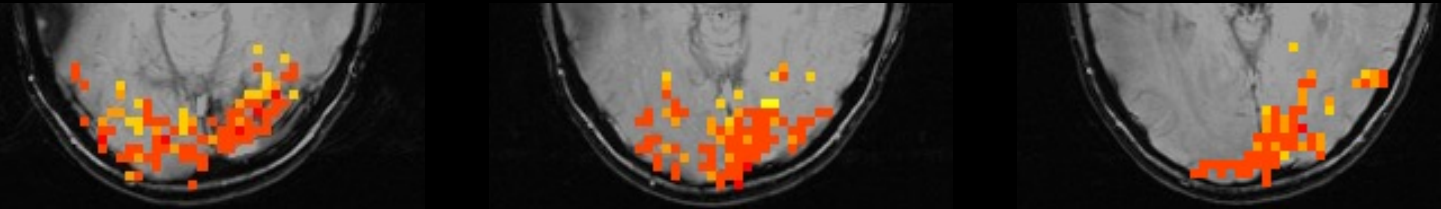


# Results — visual task

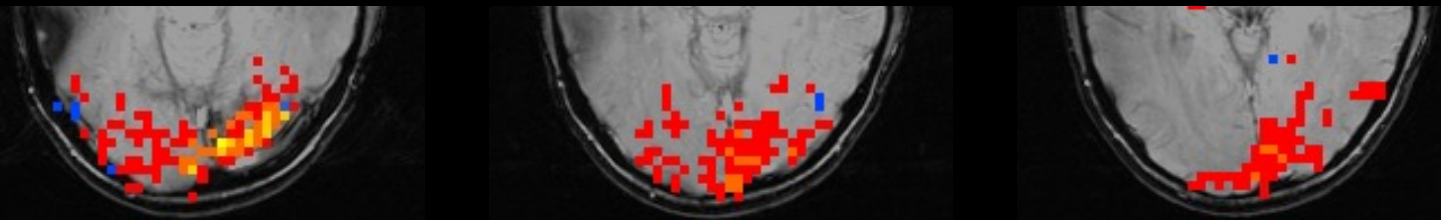


# Results – visual task

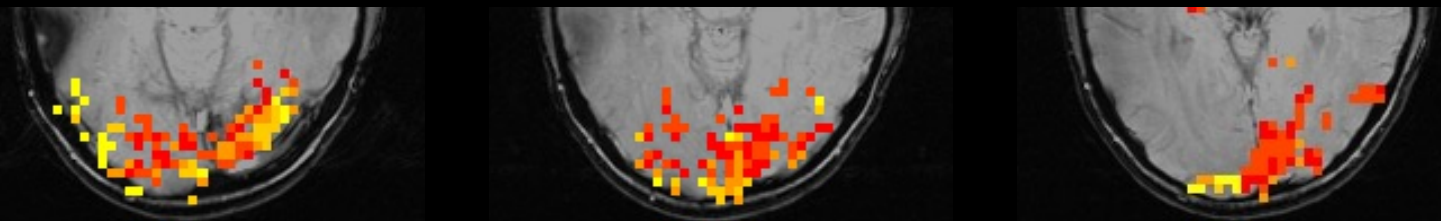
Nonlinearity



Magnitude

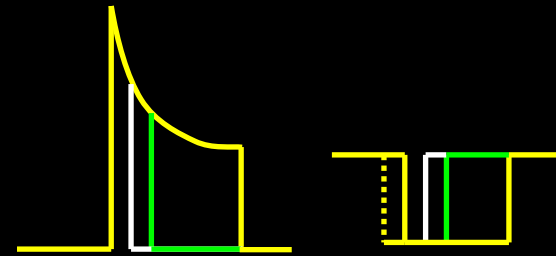
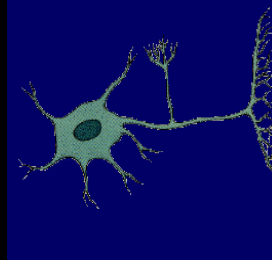


Latency



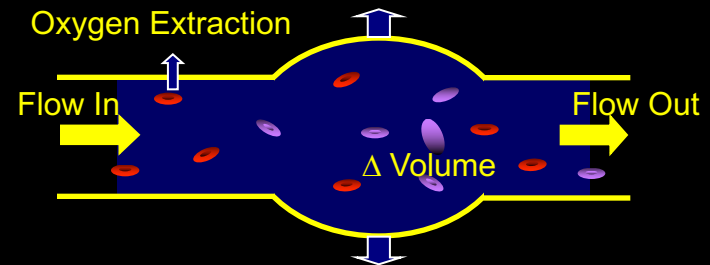
# Sources of this Nonlinearity

- Neuronal



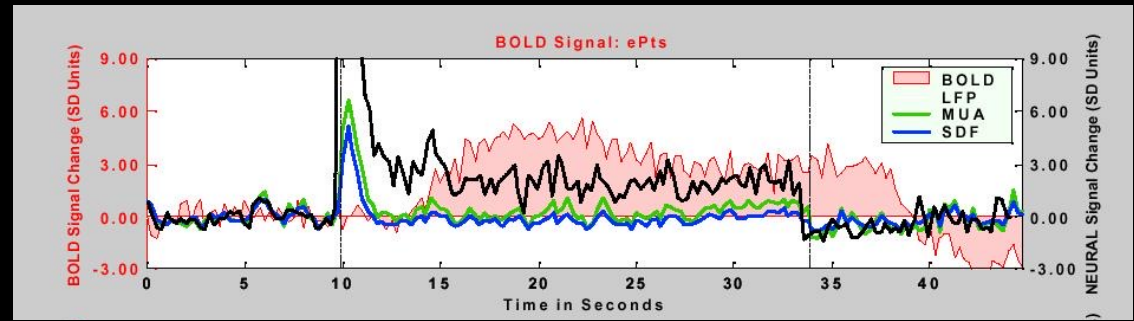
- Hemodynamic

- Oxygen extraction
- Blood volume dynamics

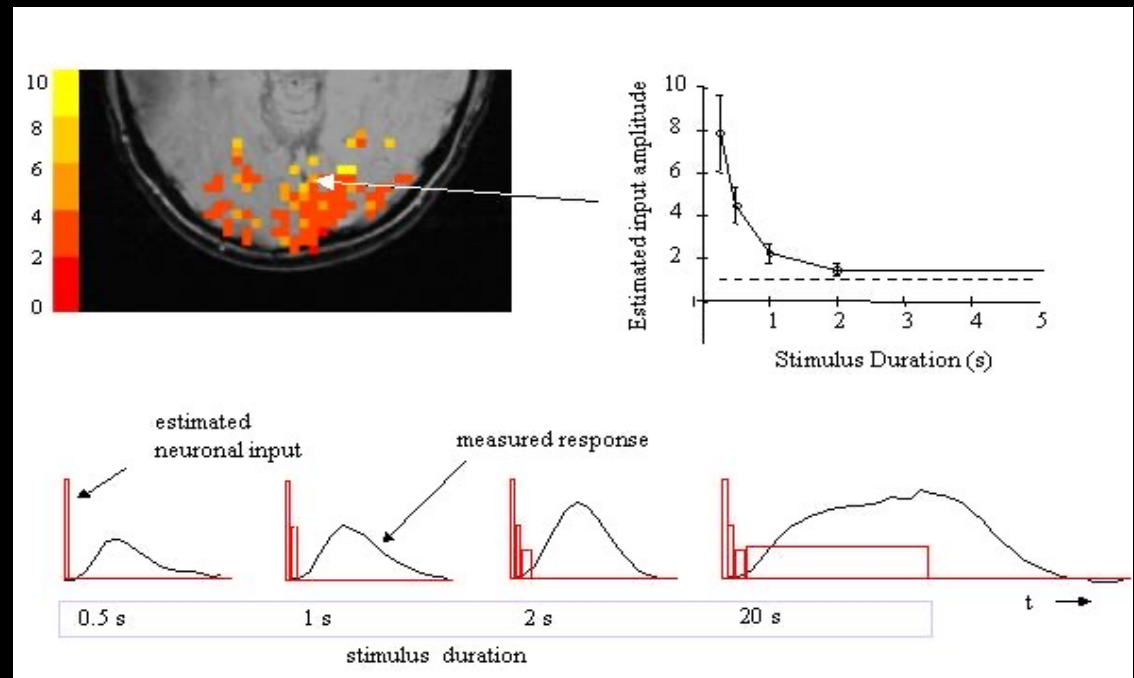


# BOLD Correlation with Neuronal Activity

**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.

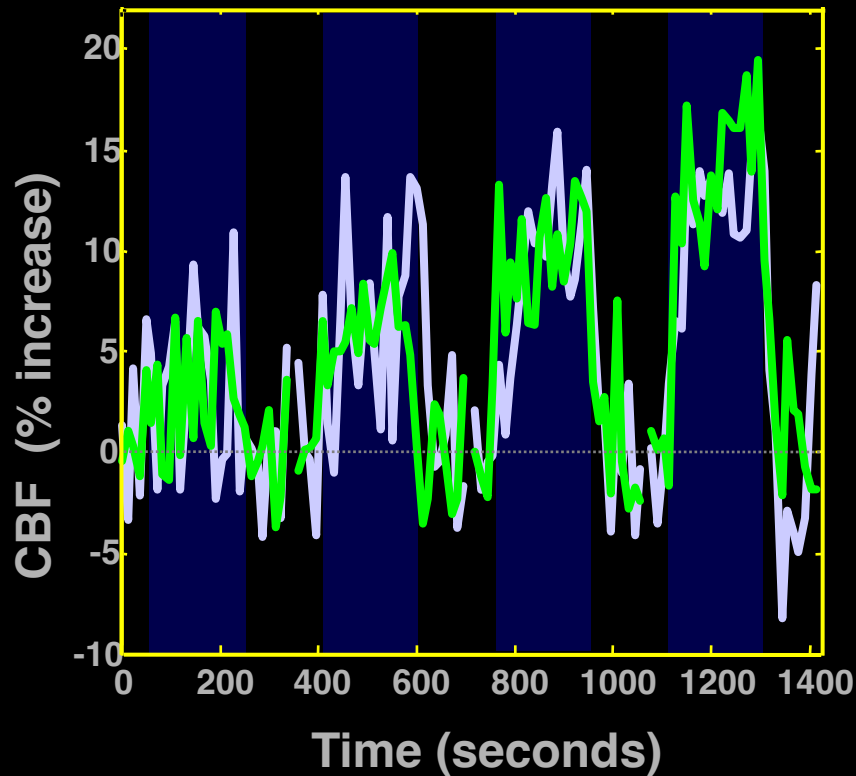


## Linear coupling between cerebral blood flow and oxygen consumption in activated human cortex

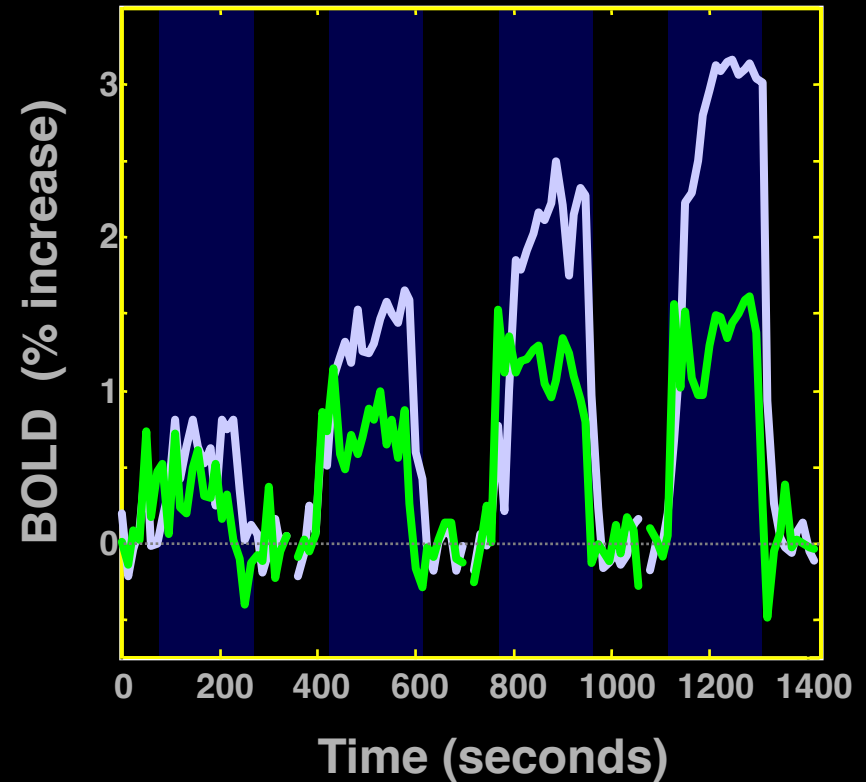
RICHARD D. HOGE<sup>\*†</sup>, JEFF ATKINSON<sup>\*</sup>, BRAD GILL<sup>\*</sup>, GÉRARD R. CRELIER<sup>\*</sup>, SEAN MARRETT<sup>‡</sup>, AND G. BRUCE PIKE<sup>\*</sup>

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

### CBF



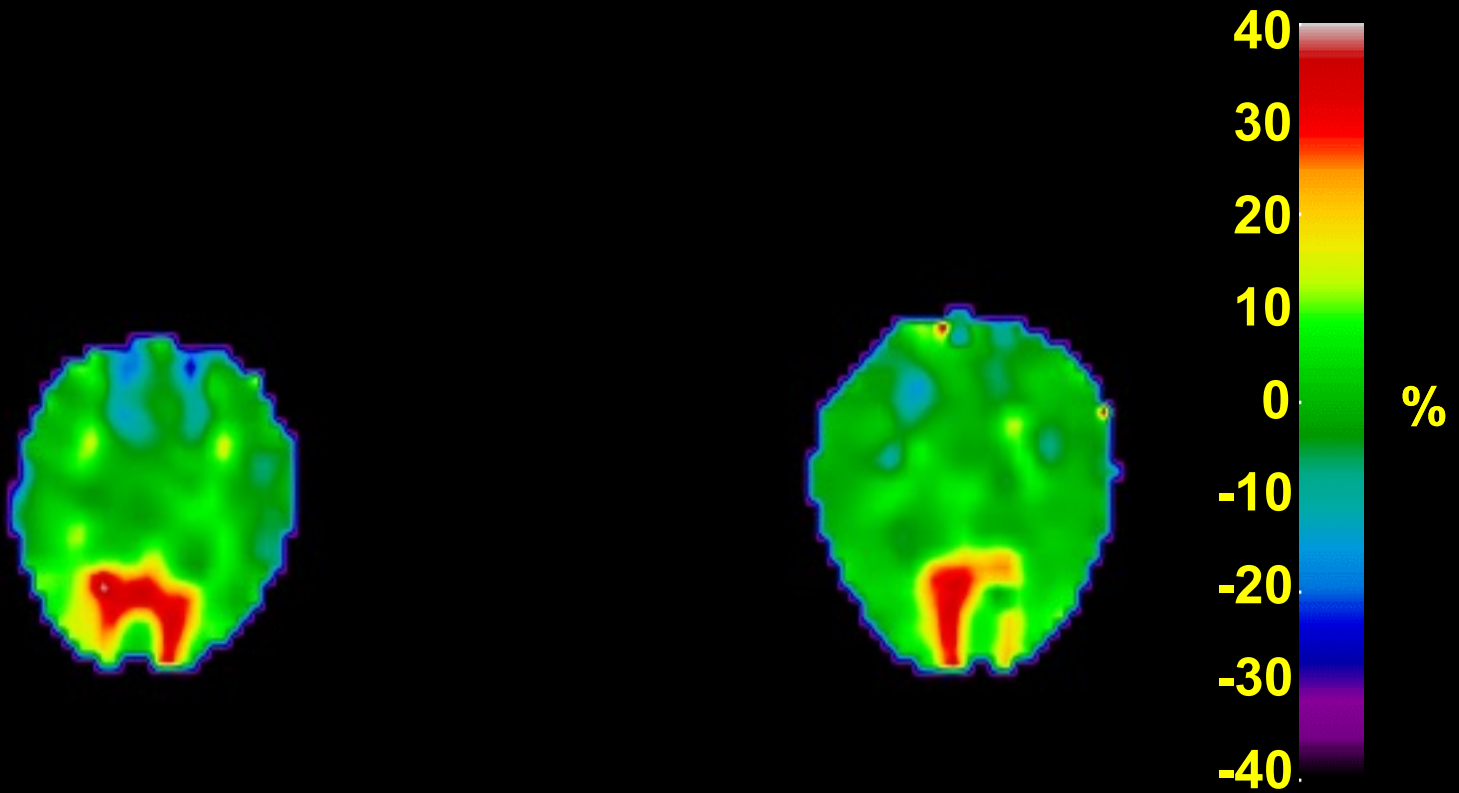
### BOLD



Simultaneous Perfusion and BOLD imaging during  
graded visual activation and hypercapnia

N=12

# Computed CMRO<sub>2</sub> Changes

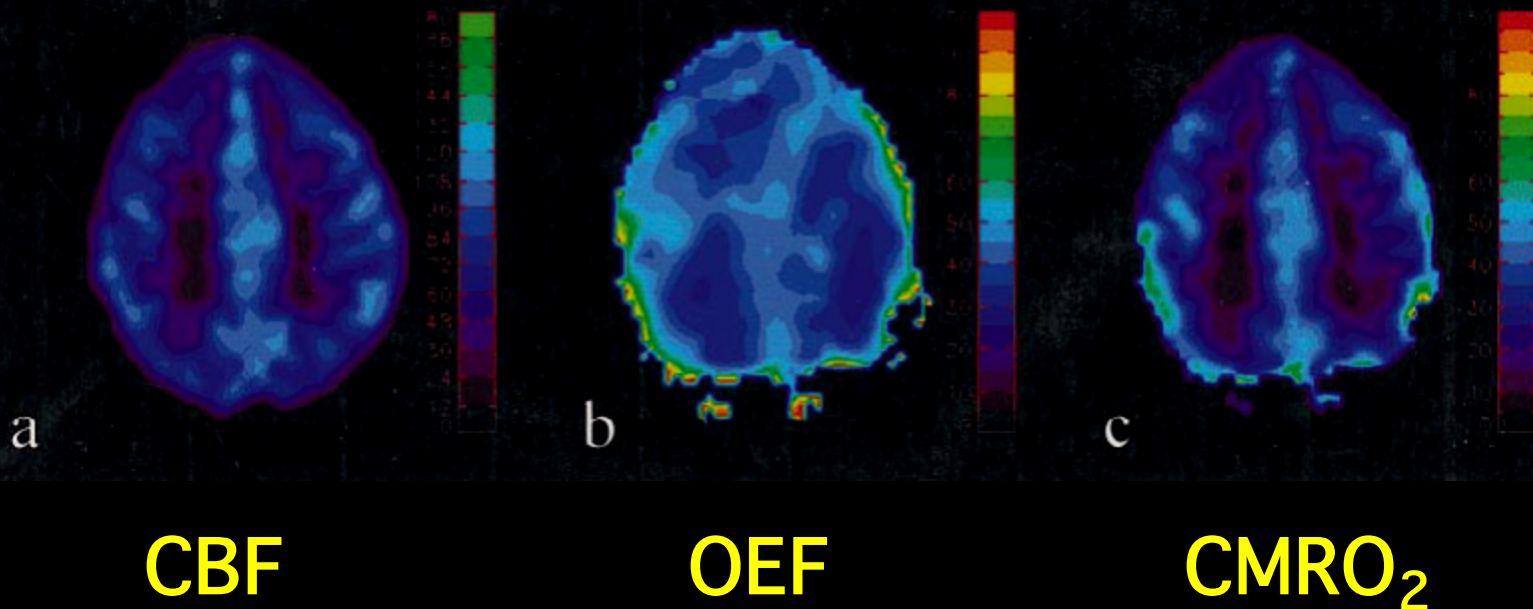


**Subject 1**

**Subject 2**

## Quantitative measurements of cerebral metabolic rate of oxygen utilization using MRI: a volunteer study

Hongyu An,<sup>1</sup> Weili Lin,<sup>2\*</sup> Azim Celik<sup>3</sup> and Yueh Z. Lee<sup>2</sup>



# Latest Developments...

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



# Neuronal Activation Input Strategies

1. Block Design

2. Parametric Design

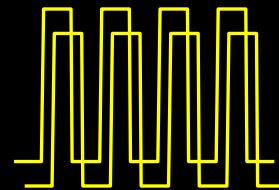
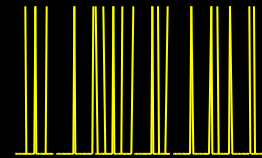
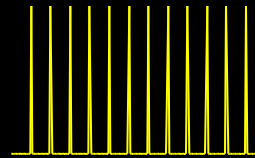
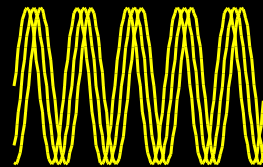
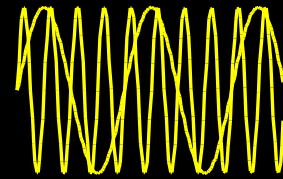
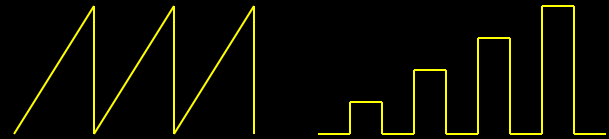
3. Frequency Encoding

4. Phase Encoding

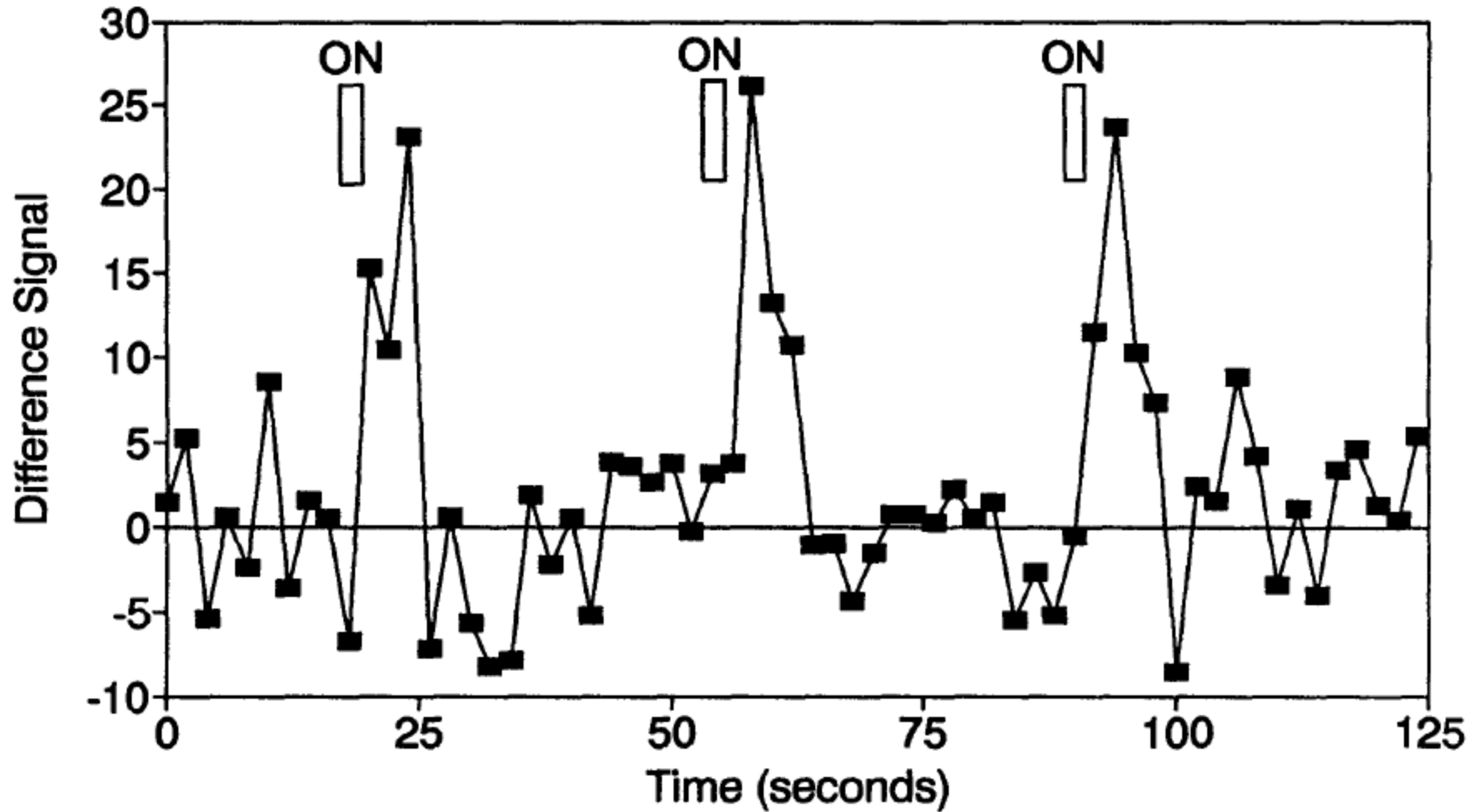
5. Event Related

6. Orthogonal Design

7. Free Behavior Design



# First Event-related fMRI Results



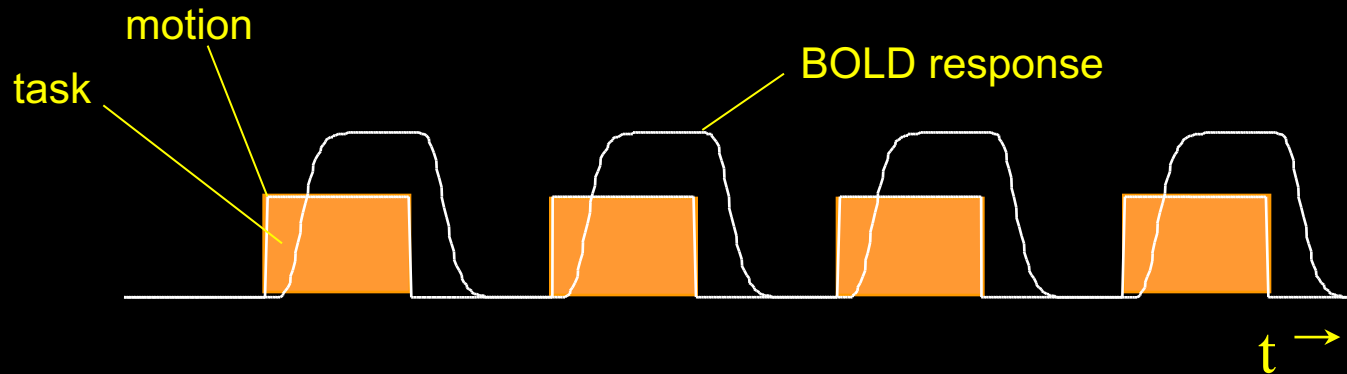
Blamire, A. M., et al. (1992). "Dynamic mapping of the human visual cortex by high-speed magnetic resonance imaging." *Proc. Natl. Acad. Sci. USA* 89: 11069-11073.

# Event Related Advantages

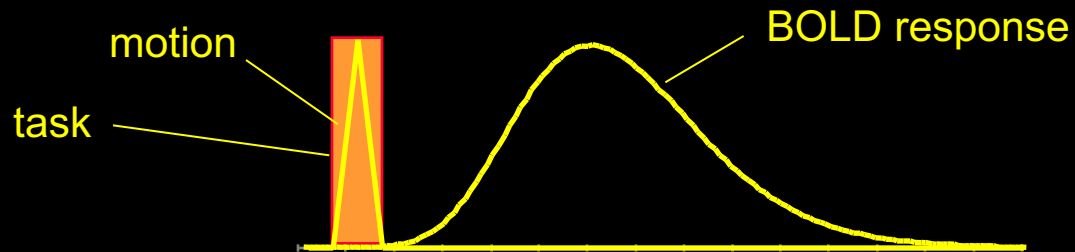
- Task Randomization
- Post acquisition, Performance-based, data binning
- Natural presentation
- Reduction of habituation effects
- Overt responses
- Reduction of scanner noise effects
- More precise estimation of hemodynamic responses

# fMRI during tasks that involve brief motion

## Blocked Design

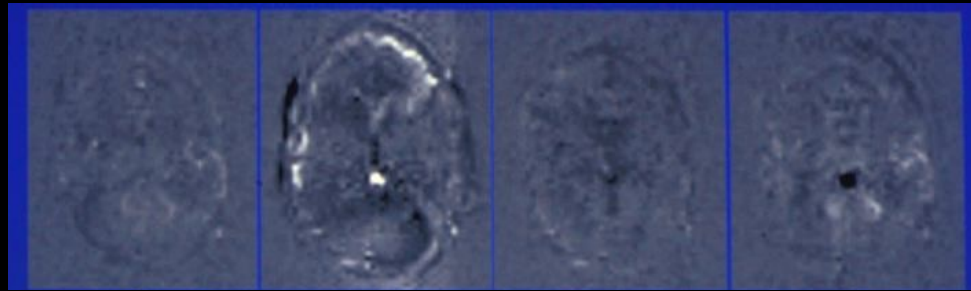


## Event-Related Design



R. M. Birn, P. A. Bandettini, R. W. Cox, R. Shaker, Event - related fMRI of tasks involving brief motion. *Human Brain Mapping* 7: 106-114 (1999).

# Overt Word Production

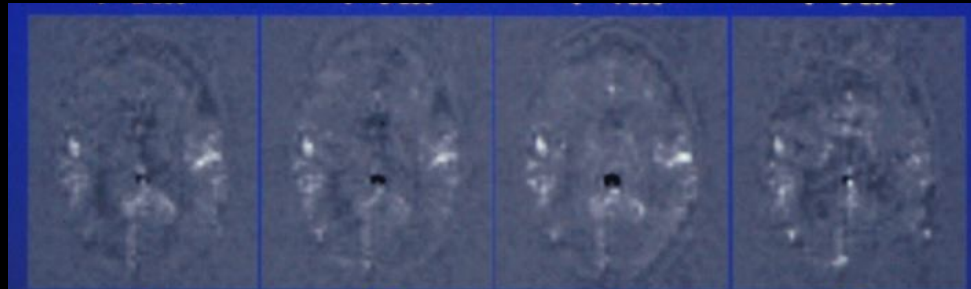


2

3

4

5

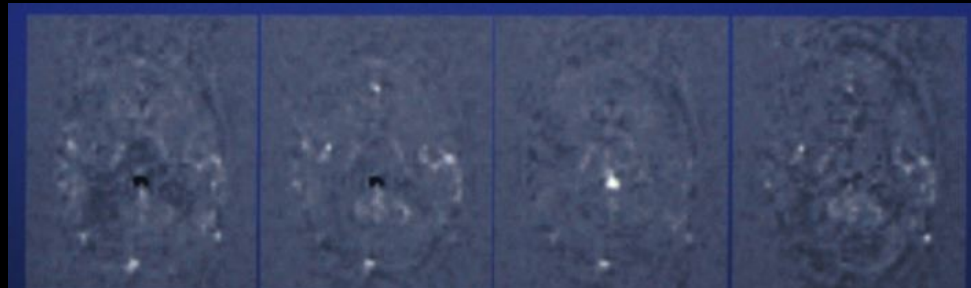


6

7

8

9



10

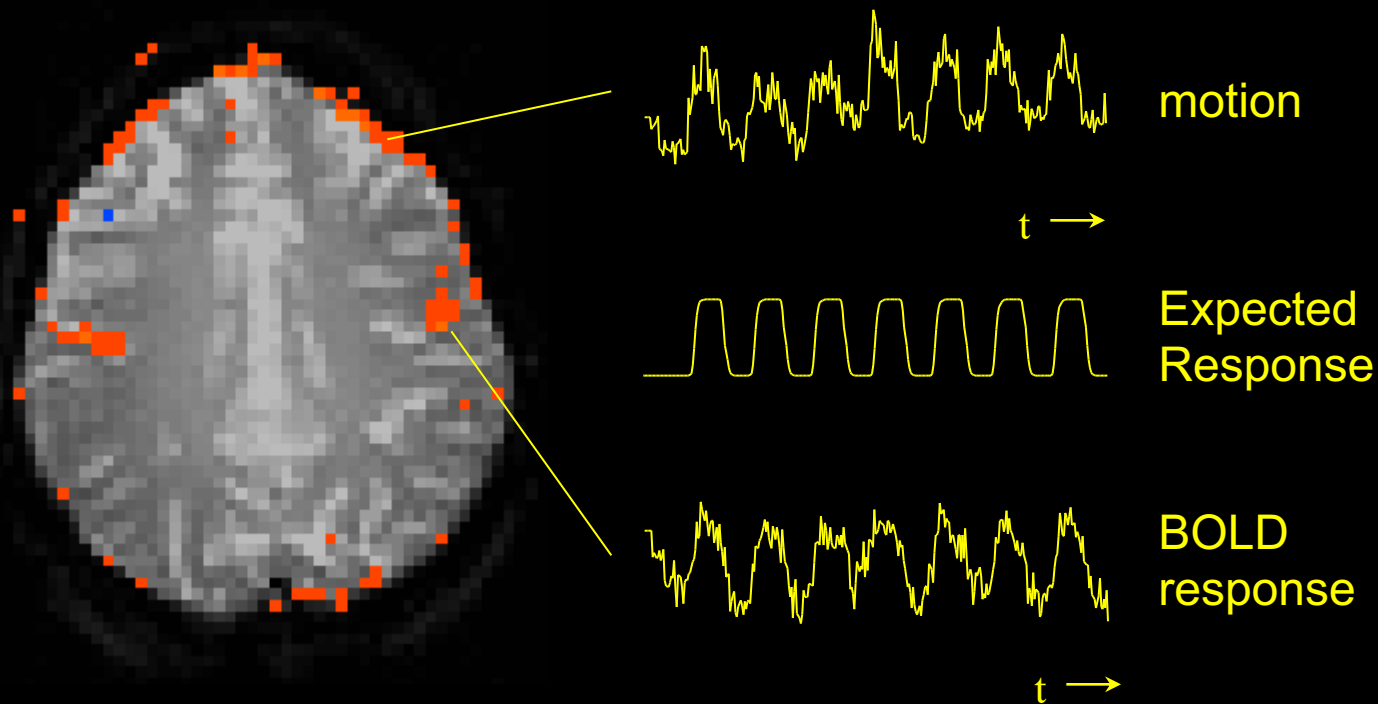
11

12

13

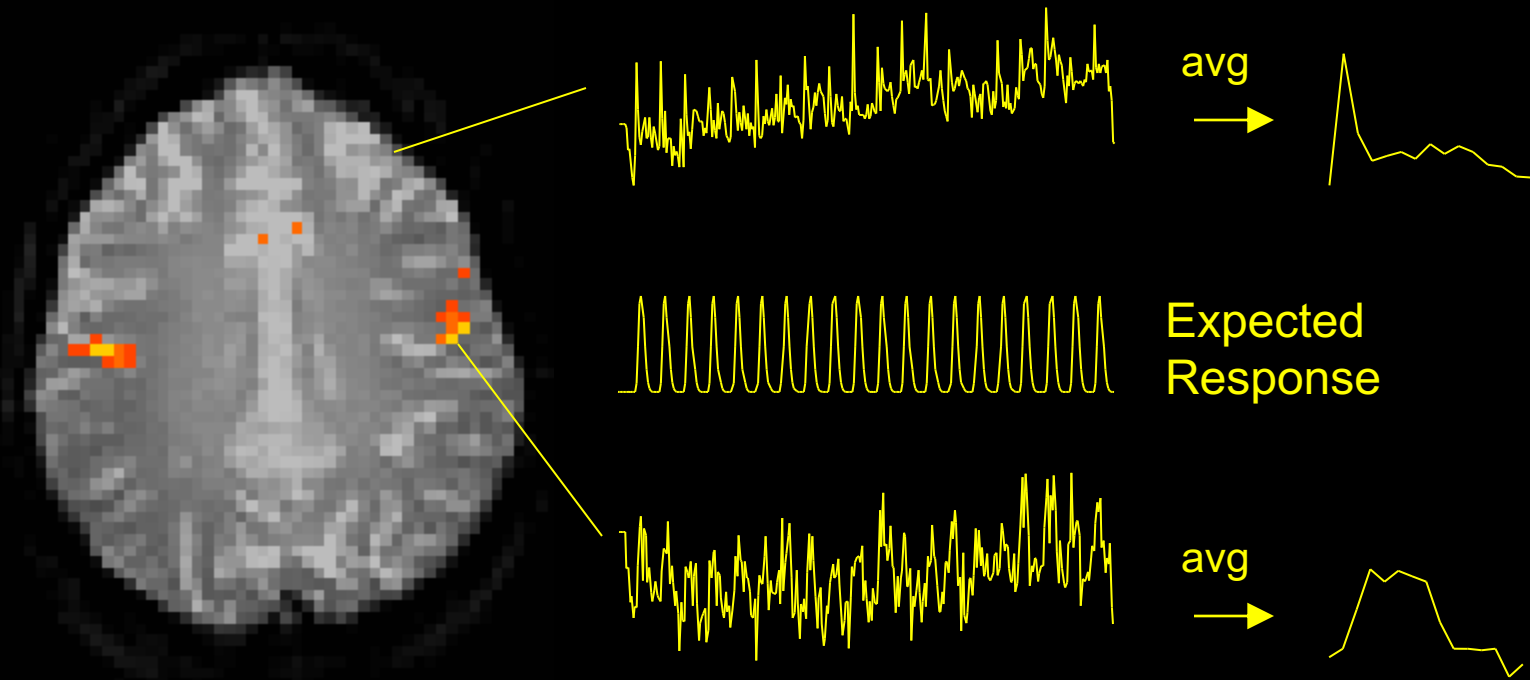
R. M. Birn, P. A. Bandettini, R. W. Cox, R. Shaker, Event - related fMRI of tasks involving brief motion. *Human Brain Mapping* 7: 106-114 (1999).

# Speaking - Blocked Trial



R. M. Birn, P. A. Bandettini, R. W. Cox, R. Shaker, Event - related fMRI of tasks involving brief motion. *Human Brain Mapping* 7: 106-114 (1999).

# Speaking - ER-fMRI

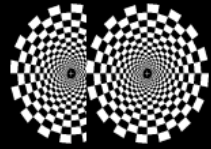


R. M. Birn, P. A. Bandettini, R. W. Cox, R. Shaker, Event - related fMRI of tasks involving brief motion. *Human Brain Mapping* 7: 106-114 (1999).



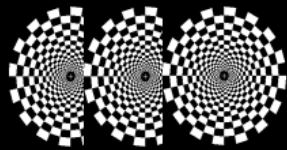
0 sec

20 sec



0 sec 2 sec

20 sec



0 sec 2 sec 4 sec

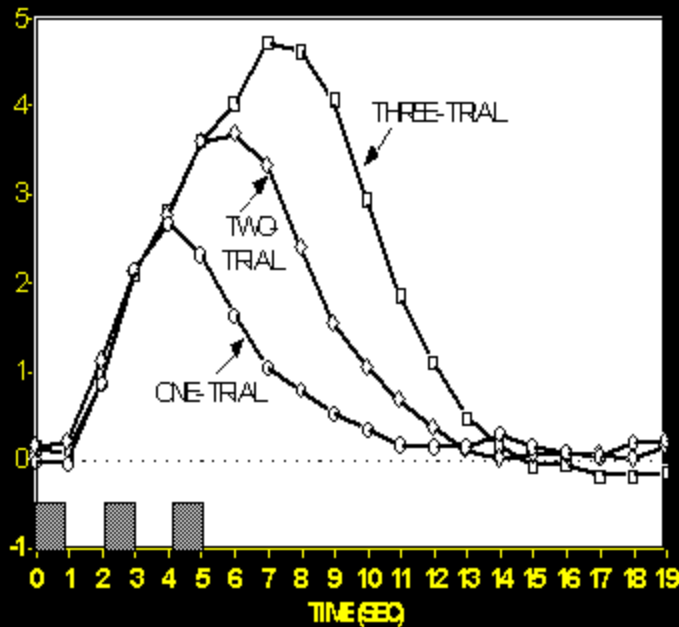
20 sec

♦ Human Brain Mapping 5:329-340(1997) ♦

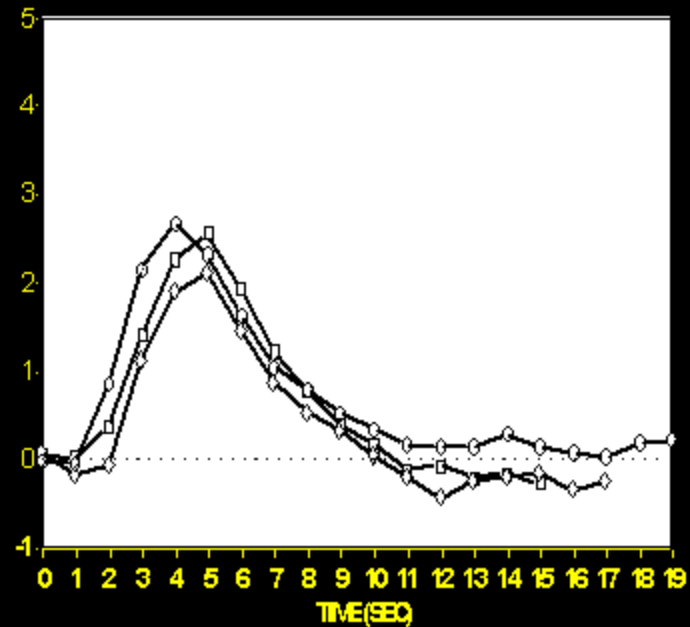
## Selective Averaging of Rapidly Presented Individual Trials Using fMRI

Anders M. Dale\* and Randy L. Buckner

### RAW DATA



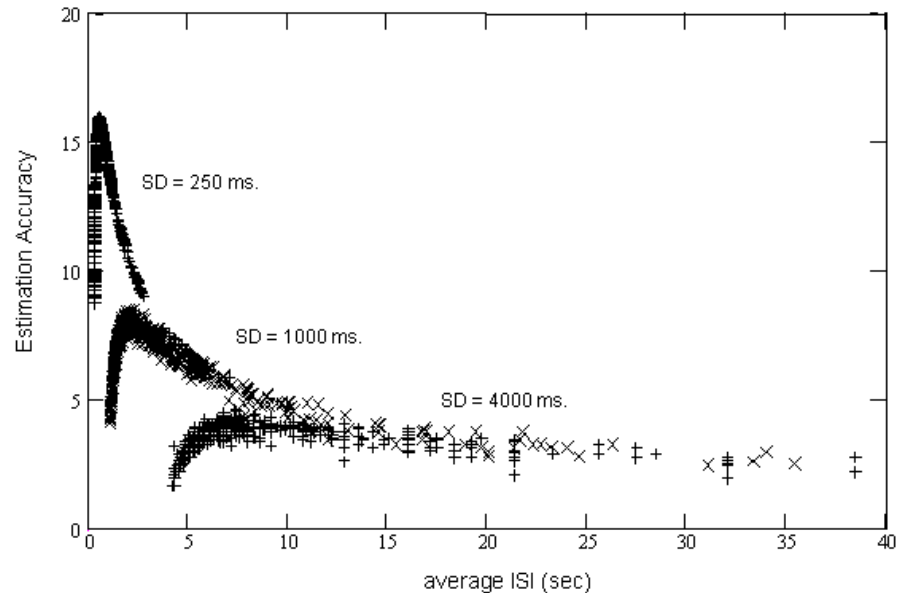
### ESTIMATED RESPONSES



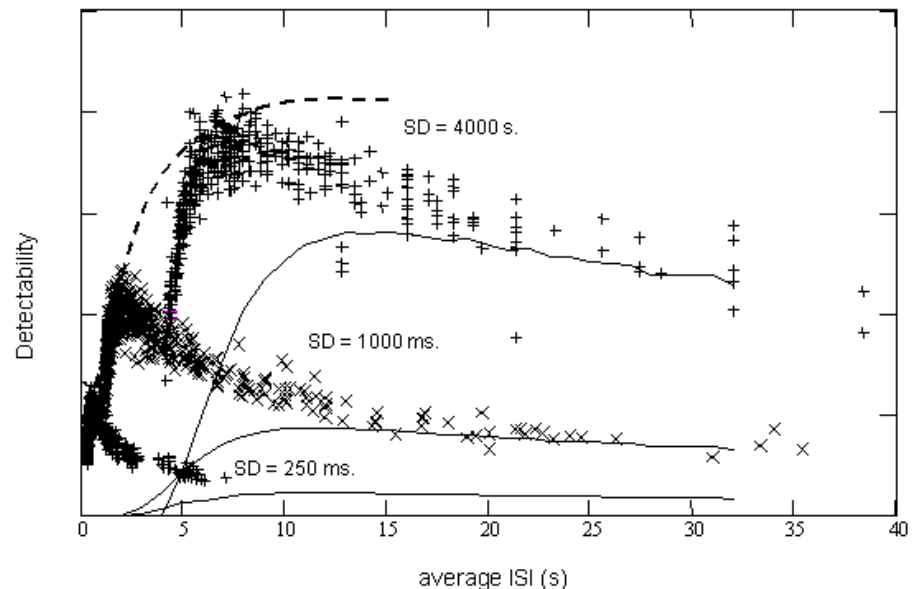


# Estimation accuracy vs. average ISI

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).



# Detectability vs. Average ISI



# Neuronal Activation Input Strategies

1. Block Design

2. Parametric Design

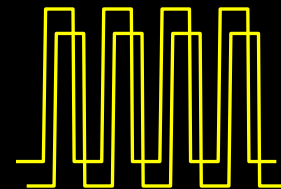
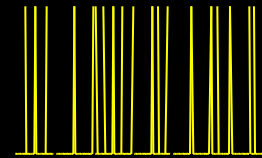
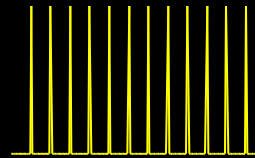
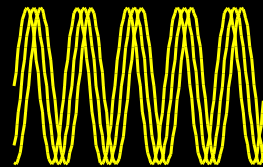
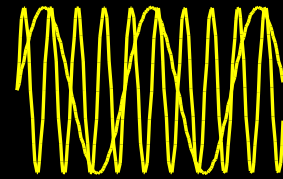
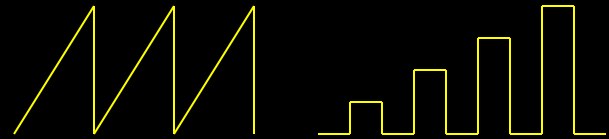
3. Frequency Encoding

4. Phase Encoding

5. Event Related

6. Orthogonal Design

7. Free Behavior Design

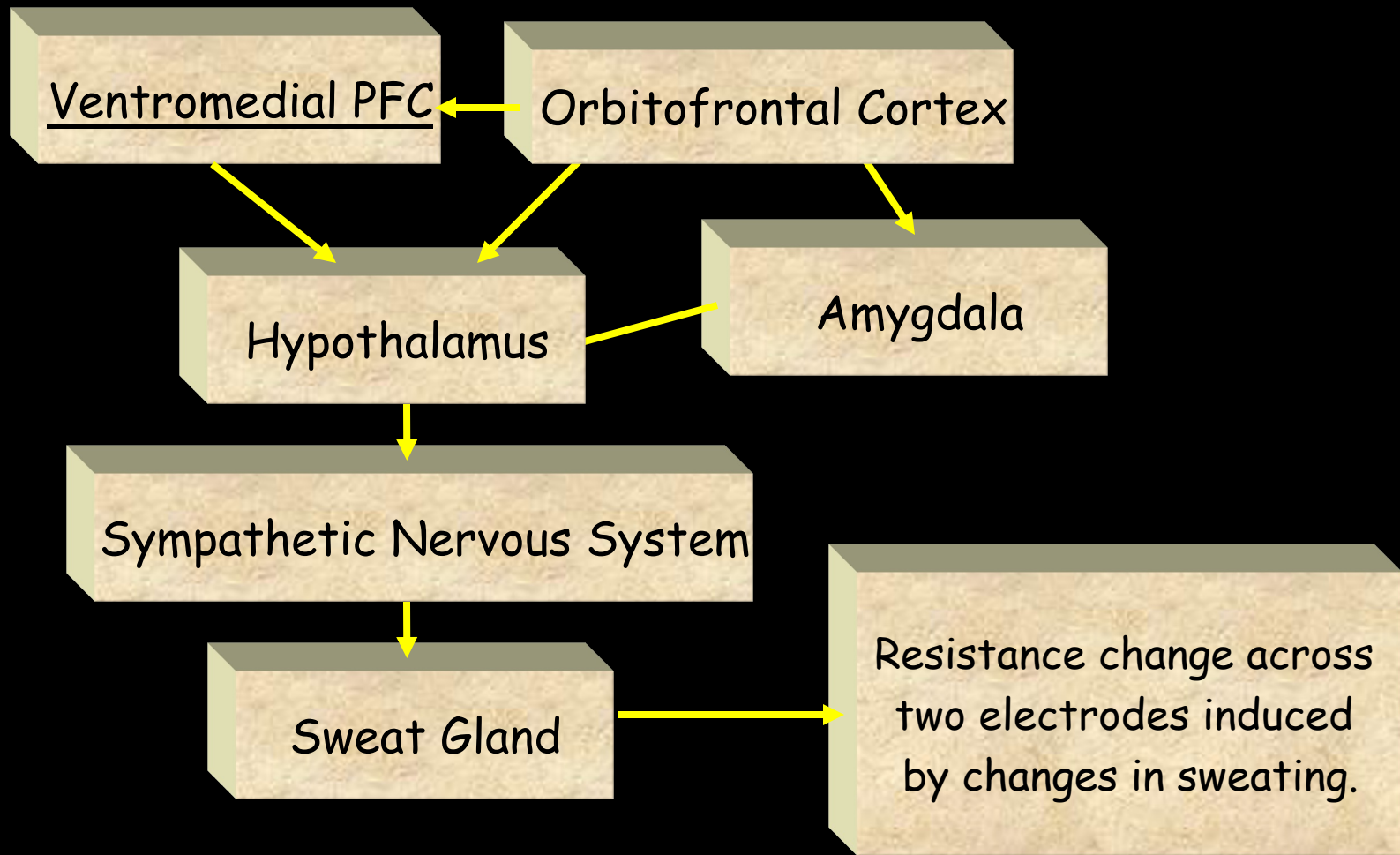


# Free Behavior Design

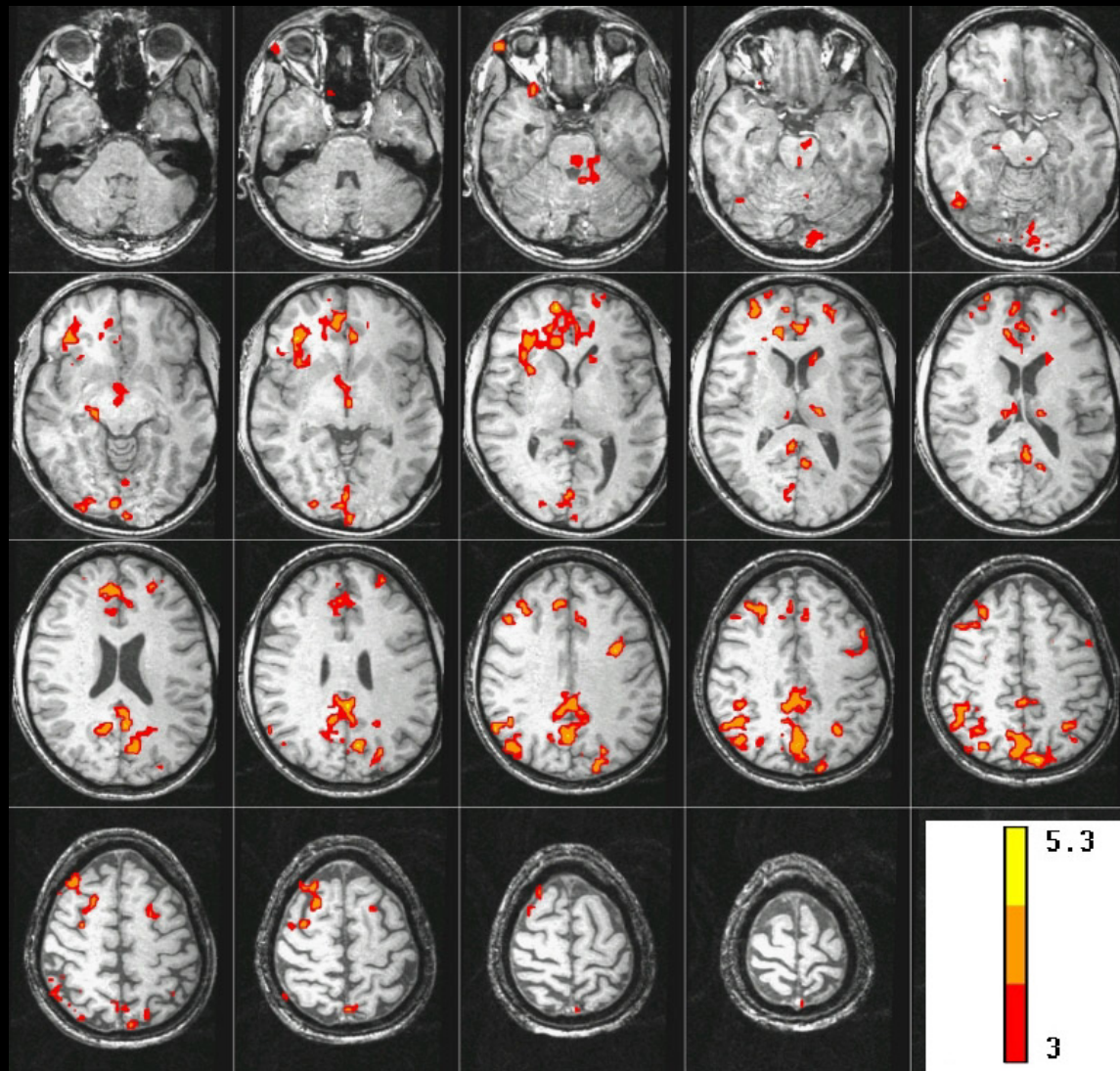
Use a continuous measure as a reference function:

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

# The Skin Conductance Response (SCR)



# Brain activity correlated with SCR during “Rest”

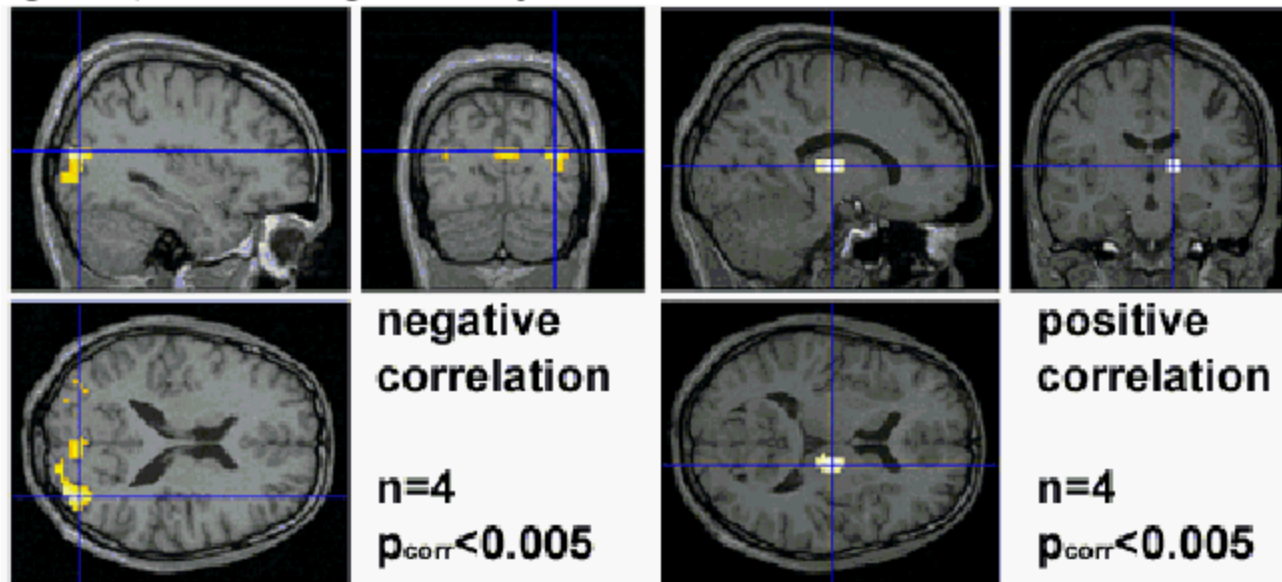


J. C. Patterson II, L. G. Ungerleider, and P. A. Bandettini, Task - independent functional brain activity correlation with skin conductance changes: an fMRI study. *NeuroImage* (in press)

## Correlates of Alpha Rhythm in BOLD-fMRI

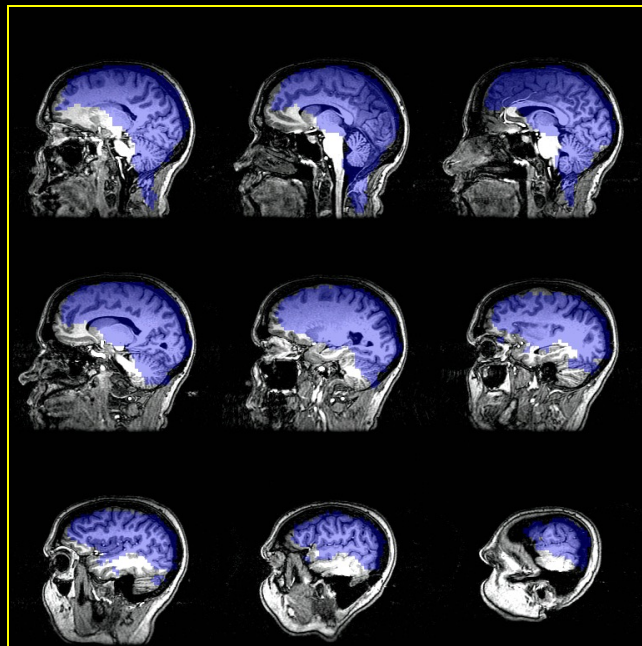
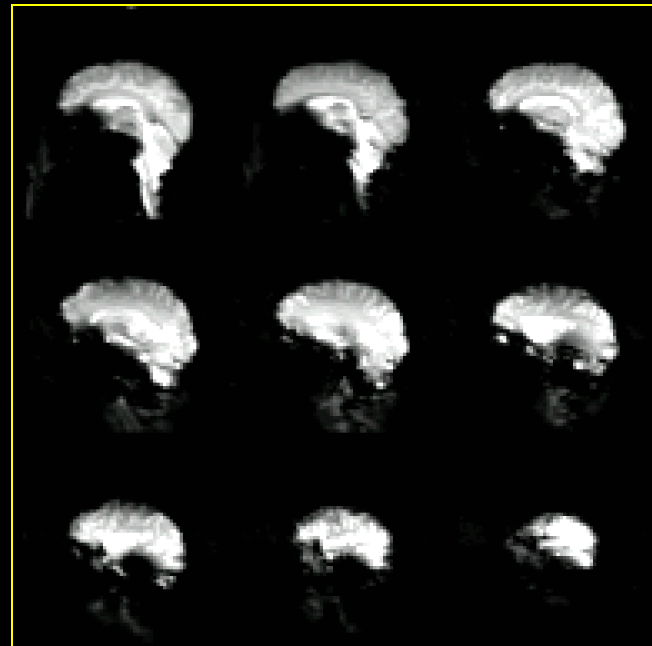
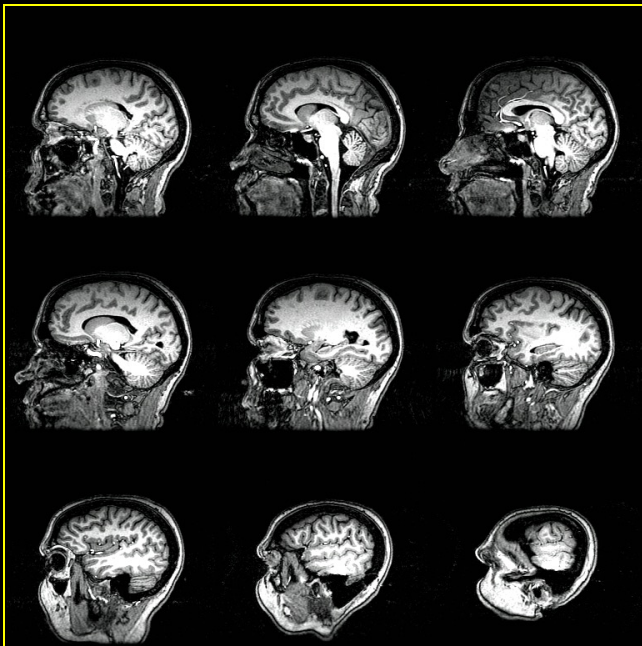
Matthias Moosmann, Petra Ritter, Andrea Brink, Ina Krastel, Sebastian Thees, Felix Blankenburg, Birol Taskin, Jan Ruben, Arno Villringer

The group analysis based on four volunteers showed a negative correlation between alpha-power and fMRI signal in the occipital cortex (figure, left side) and a positive correlation in the thalamus (figure, right side). These findings were not present for the beta band.



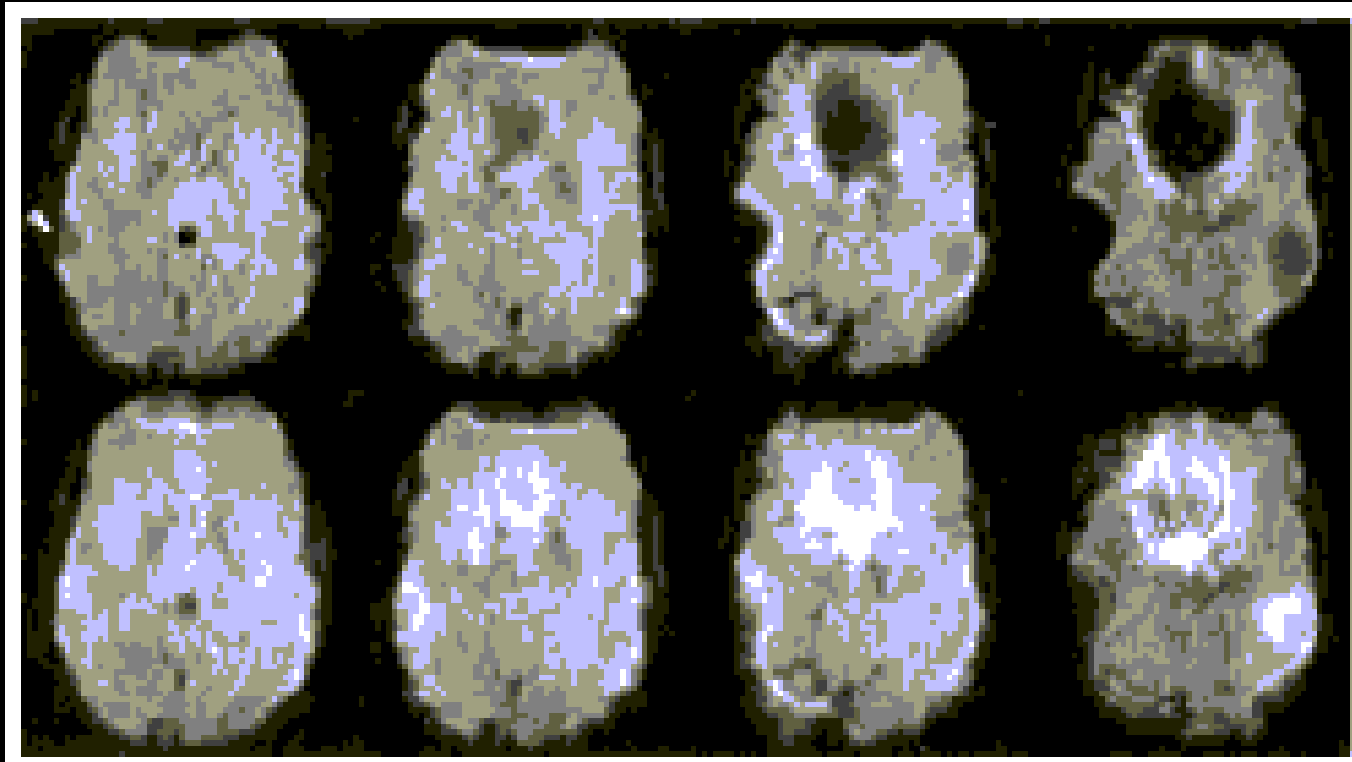
### Discussion:

Localization of alpha activity in the occipital lobe agrees with previous electrophysiological findings. The negative correlations of fMRI signal and alpha suggests less energy consumption with higher degrees of synchronization. Positive correlations in the thalamus suggest the thalamus to be an active energy consuming generator of alpha synchronization. Our results are in concordance with findings recently reported by other groups, showing deactivations in the occipital pole and activations in the thalamus or in the brain stem using PET (Sadato et al. 1998) and fMRI (Goldman et al. 2001).



## 3D z-Shim Method for Reduction of Susceptibility Effects in BOLD fMRI

Gary H. Glover\*





- Shimming
- Acoustic Noise
- Multishot Techniques
- Increased Gradient Performance
- Higher Field Strengths
- Surface Coil Arrays
- Calibration / Quantification
- Embedded Functional Contrast
- Noise / Fluctuations
- Direct Neuronal Current Imaging
- Clinical Populations
- Neuronal, Vascular, and Metabolic Information

# 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

Patrick Bellgowan

Ziad Saad

## Graduate Student:

Natalia Petridou

## Post-Back. IRTA Students:

Elisa Kapler

August Tuan

Dan Kelley

## Visiting Fellows:

Sergio Casciaro

Marta Maieron

Guosheng Ding

## Clinical Fellow:

James Patterson

## Psychologist:

Julie Frost

## Summer Students:

Hannah Chang

Courtney Kemps

Douglass Ruff

Carla Wettig

Kang-Xing Jin

## Program Assistant:

Kay Kuhns

## Scanning Technologists:

Karen Bove-Bettis

Paula Rowser

