

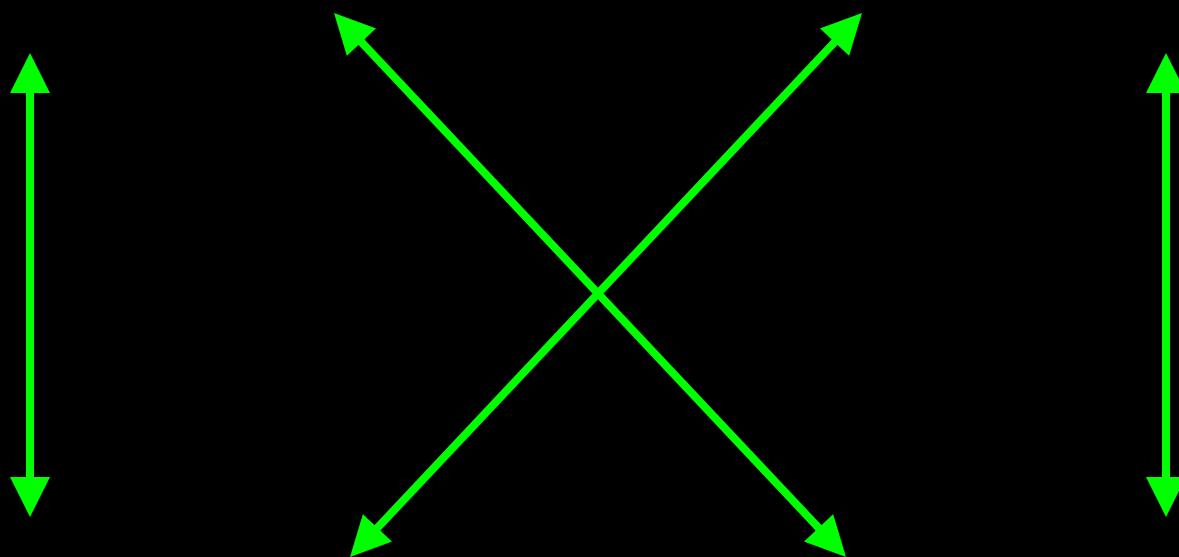
# Functional MRI: Past, Present, Future

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

# Methodology

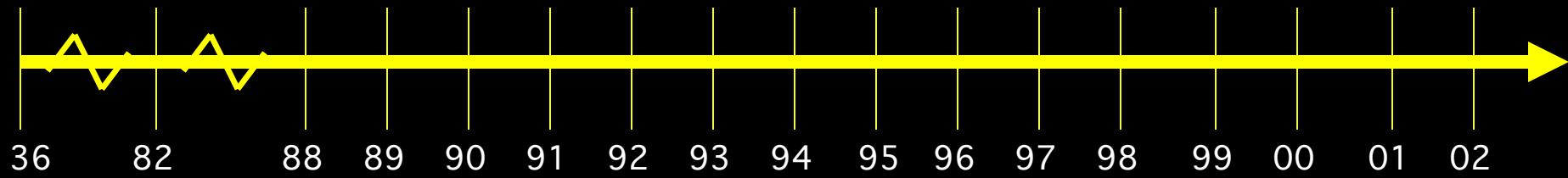
Baseline Volume	Correlation Analysis		CO <sub>2</sub> Calibration
	Motion Correction		Mixed ER and Blocked
	Parametric Design		Multi-Modal Mapping
IVIM	Surface Mapping	ICA	Free-behavior Designs
	Phase Mapping		
Linear Regression		Mental Chronometry	
	Event-related	Deconvolution	Fuzzy Clustering
			Multi-variate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

# Interpretation

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

# Applications

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





**L. Pauling, C. D. Coryell, (1936) "The magnetic properties and structure of hemoglobin, oxyhemoglobin, and carbonmonoxyhemoglobin."** Proc.Natl. Acad. Sci. USA 22, 210-216.

**Thulborn, K. R., J. C. Waterton, et al. (1982). "Oxygenation dependence of the transverse relaxation time of water protons in whole blood at high field."** Biochim. Biophys. Acta. 714: 265-270.

**S. Ogawa, T. M. Lee, A. R. Kay, D. W. Tank, (1990) "Brain magnetic resonance imaging with contrast dependent on blood oxygenation."** Proc. Natl. Acad. Sci. USA 87, 9868-9872.

**R. Turner, D. LeBihan, C. T. W. Moonen, D. Despres, J. Frank, (1991). Echo-planar time course MRI of cat brain oxygenation changes.** Magn. Reson. Med. 27, 159-166.

# Functional MRI Methods

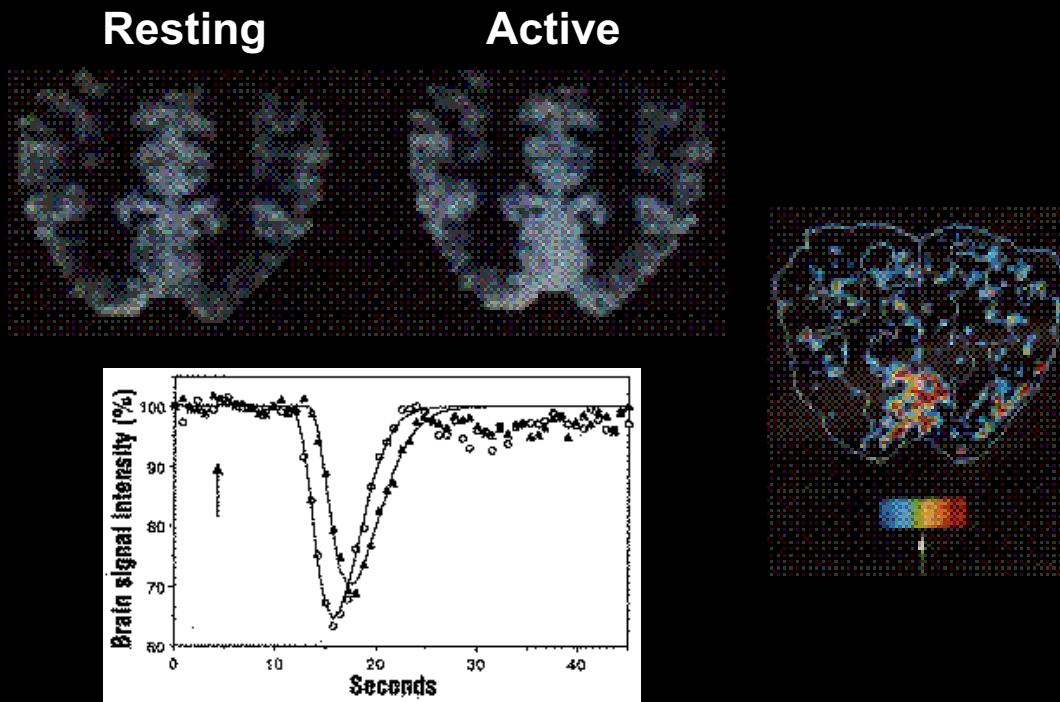
Blood Volume Imaging

BOLD Contrast

Arterial Spin Labeling

# Blood Volume Imaging

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



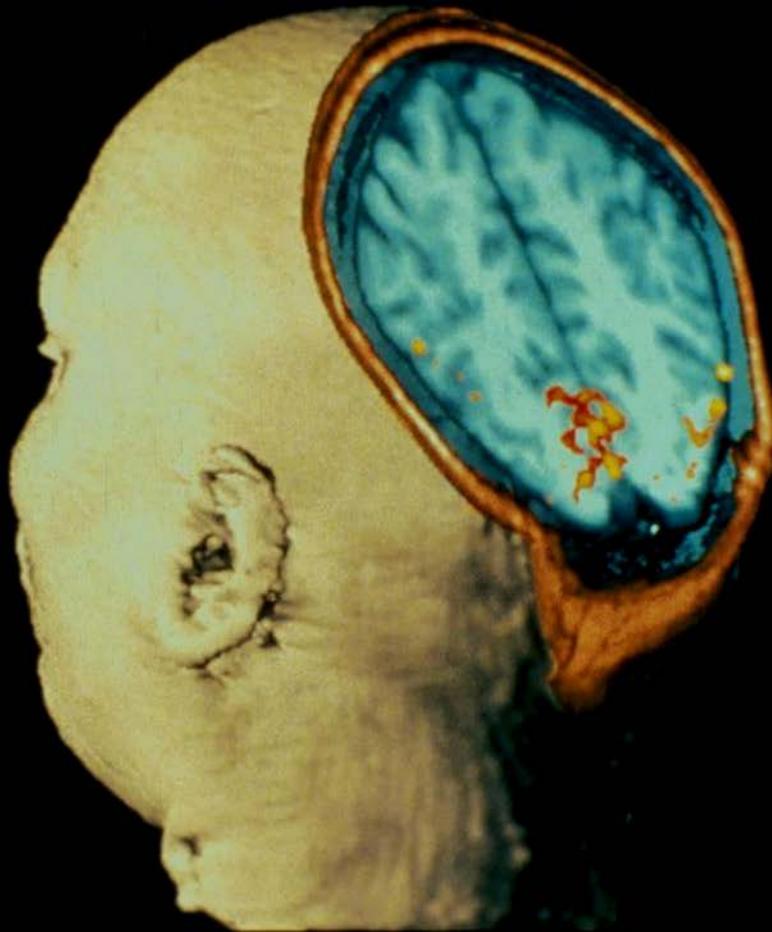
# Blood Volume

**Photic  
Stimulation**

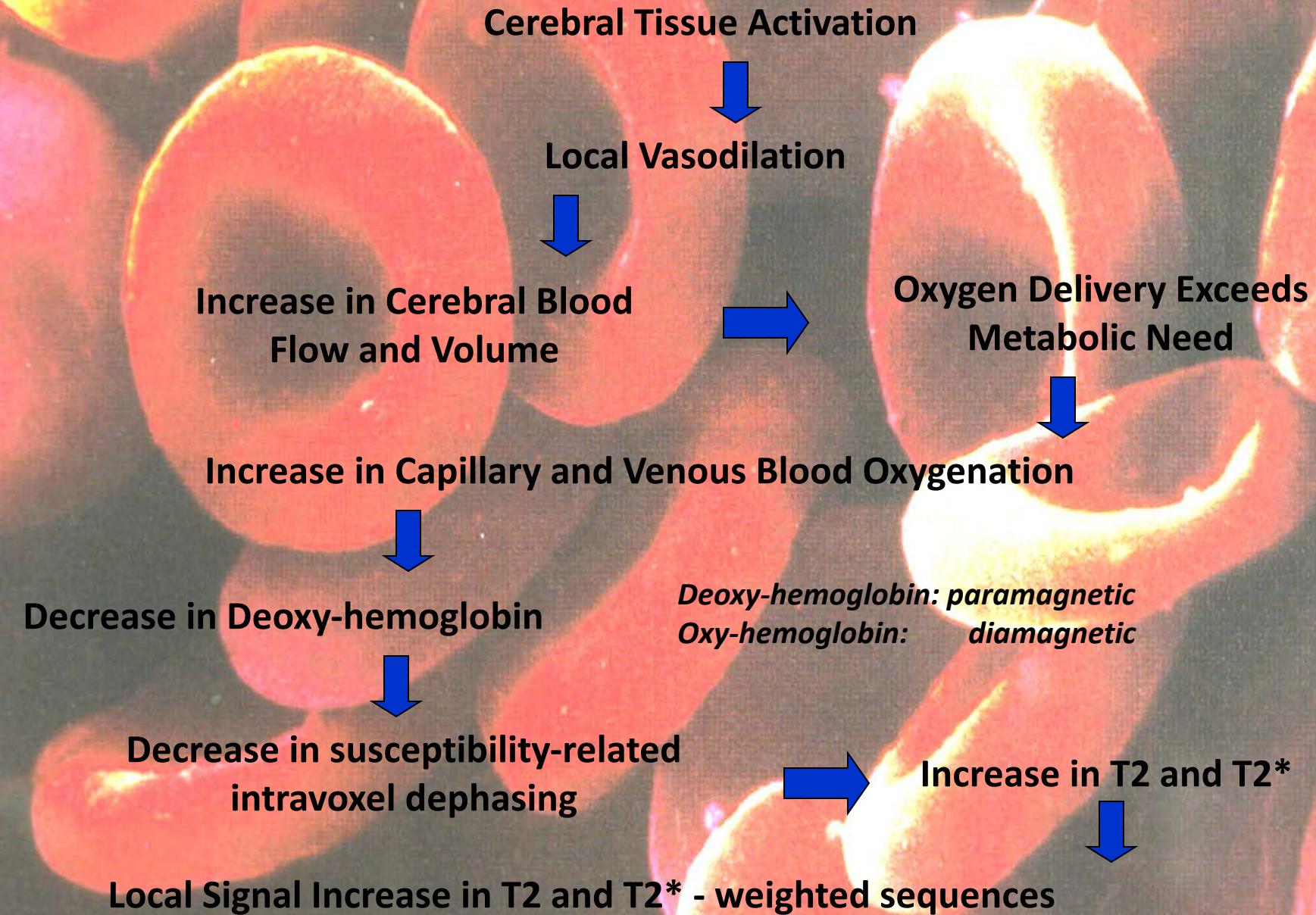
**MRI Image showing  
activation of the  
Visual Cortex**

**From Belliveau, et al.  
Science Nov 1991**

**MSC - perfusion**



# BOLD Contrast in the Detection of Neuronal Activity



# Alternating Left and Right Finger Tapping



~ 1992

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.

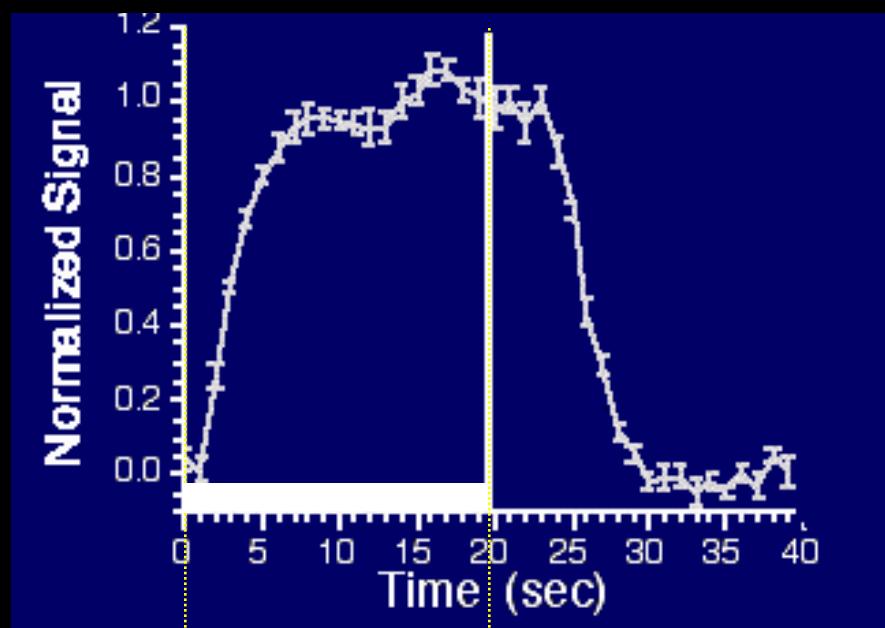
Blamire, A. M., et al. (1992). “Dynamic mapping of the human visual cortex by high-speed magnetic resonance imaging.” Proc. Natl. Acad. Sci. USA 89: 11069-11073.



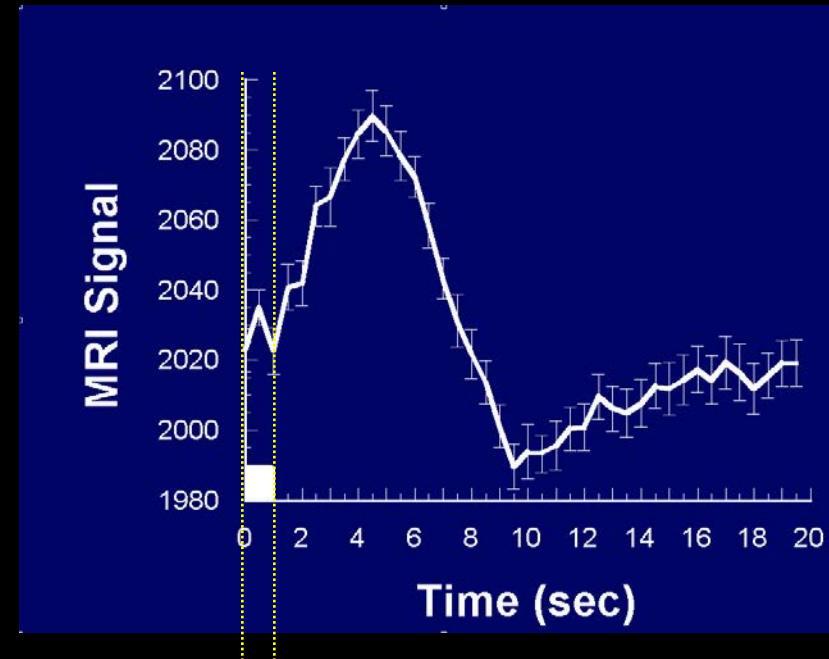
- Correlation analysis, Fourier analysis, t-test, f-test...
- SPM, AFNI, brain voyager, FIASCO, FSL, free surfer...

# The BOLD Signal

Blood Oxxygenation Level Dependent (BOLD) signal changes

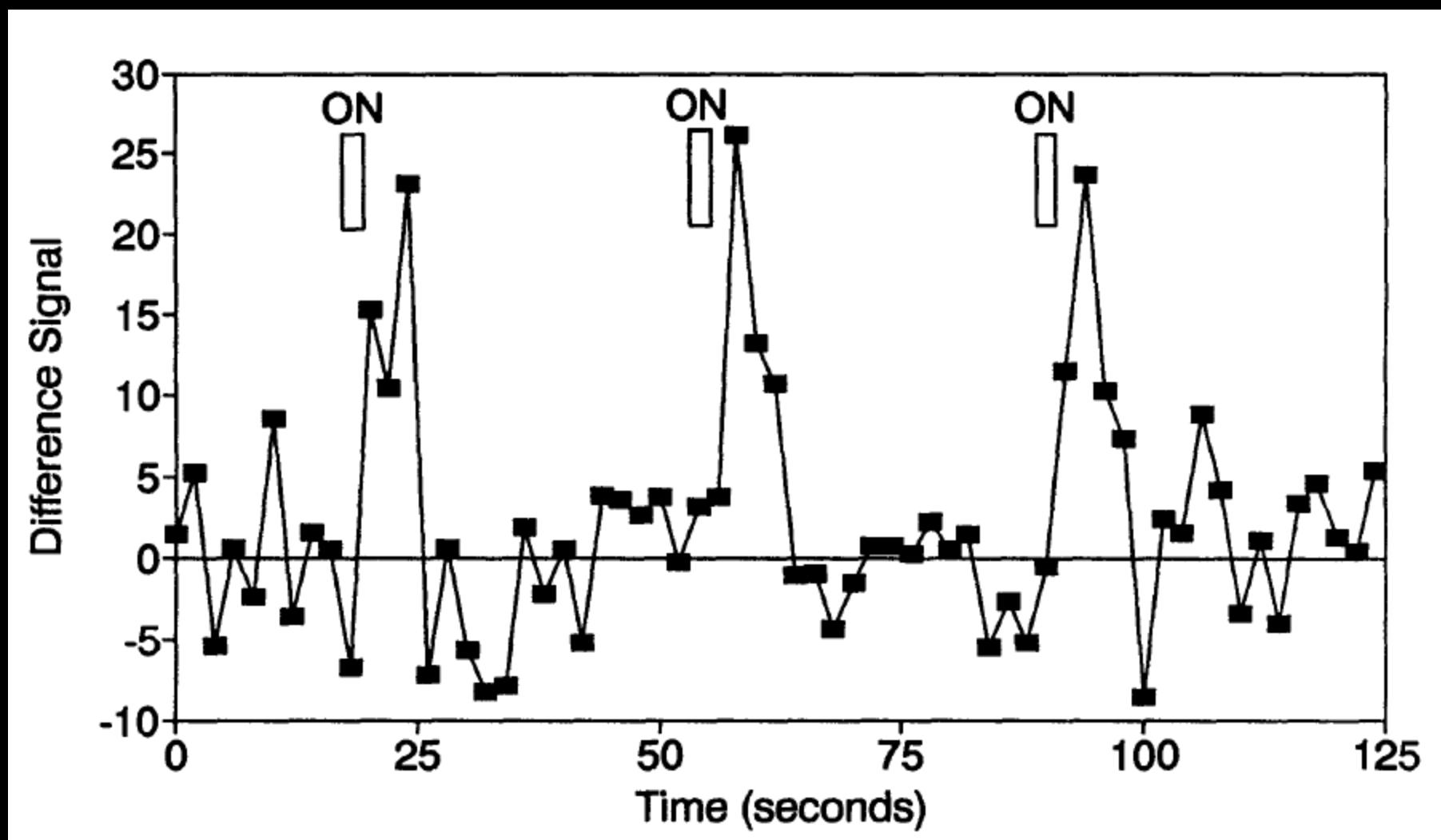


*task*

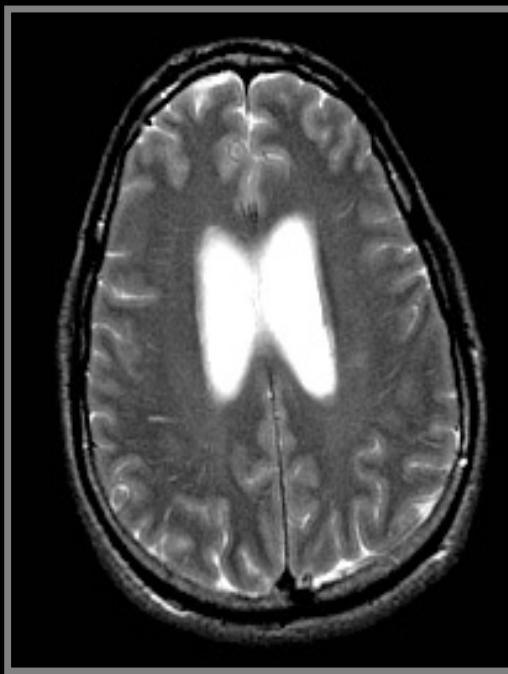


*task*

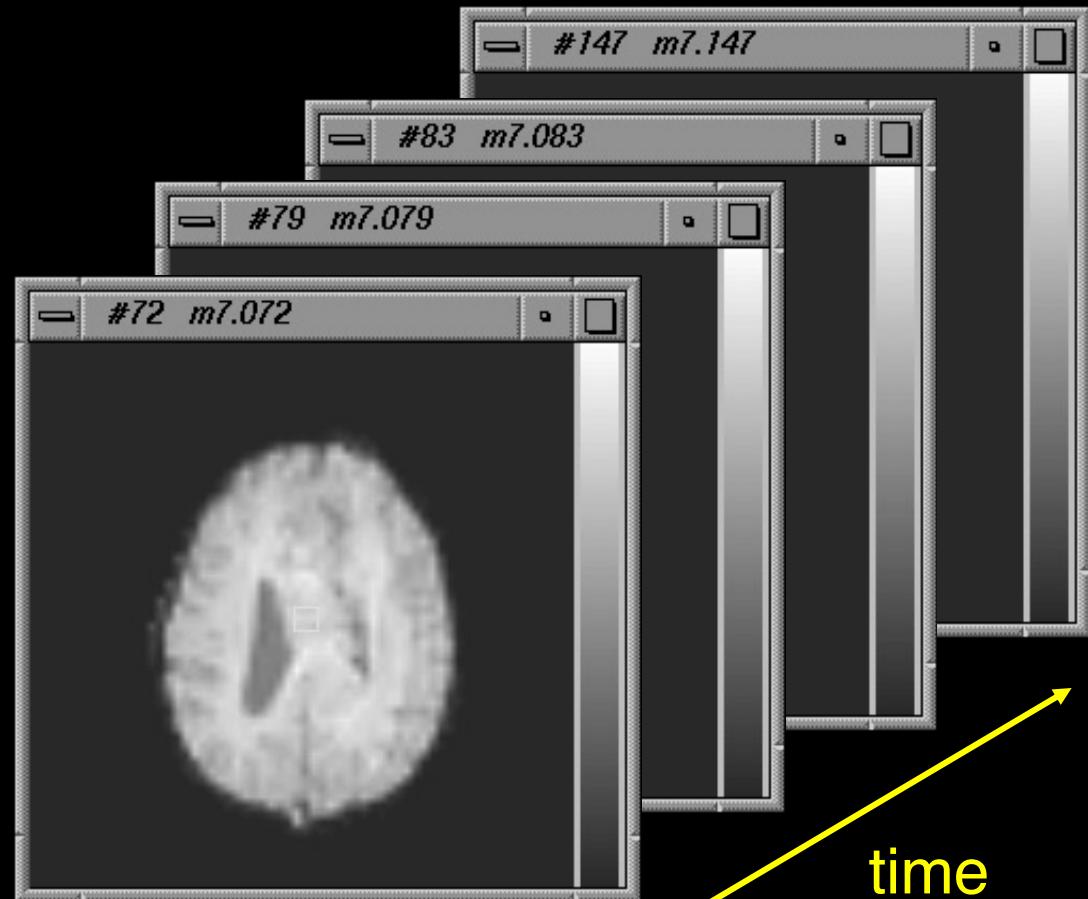
# First Event-related fMRI Results



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.



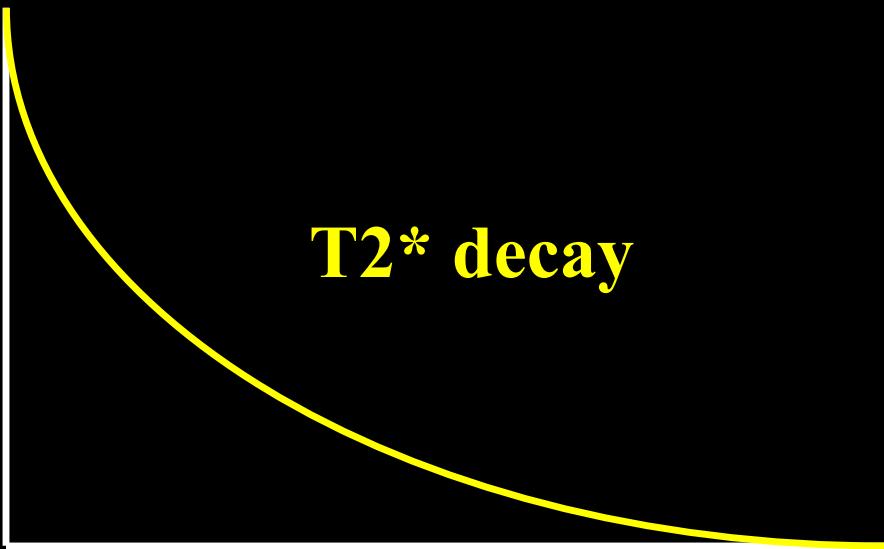
Anatomic



Functional

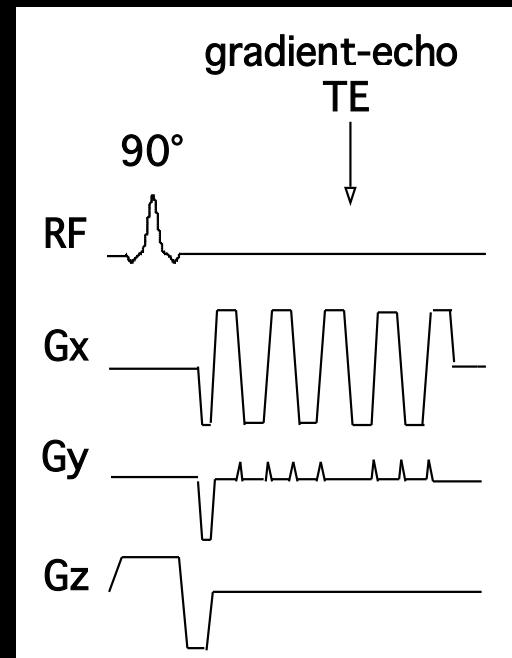
time

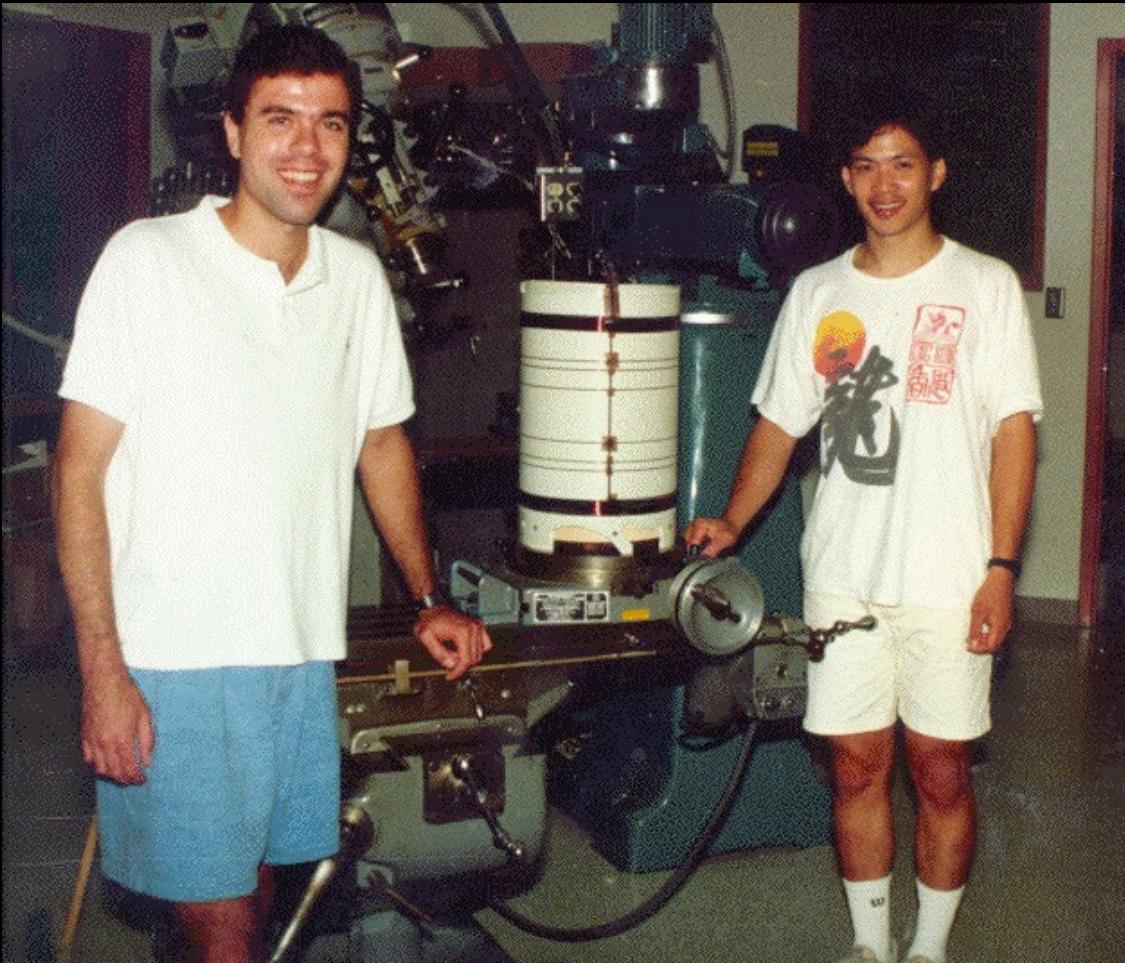
# Single Shot EPI



EPI Readout Window

$\approx 20$  to 40 ms





August, 1991

**1991-1992**



**1992-1999**

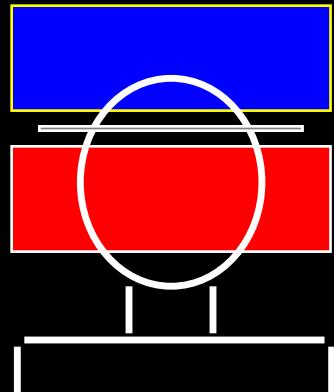


# General Electric 3 Tesla Scanner

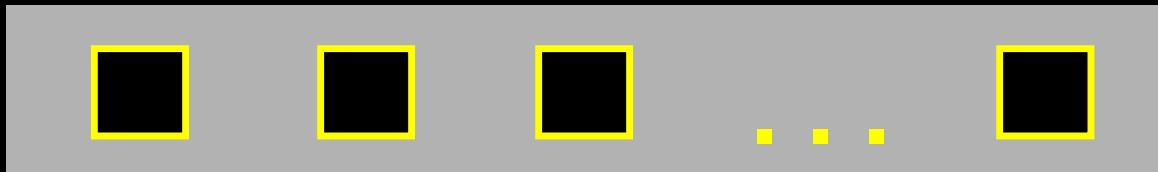
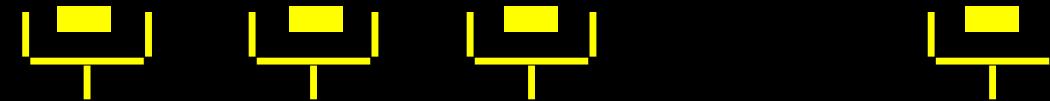
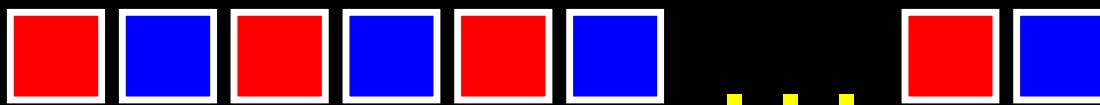
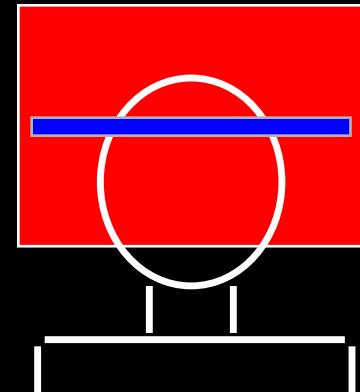


# Blood Perfusion

EPISTAR



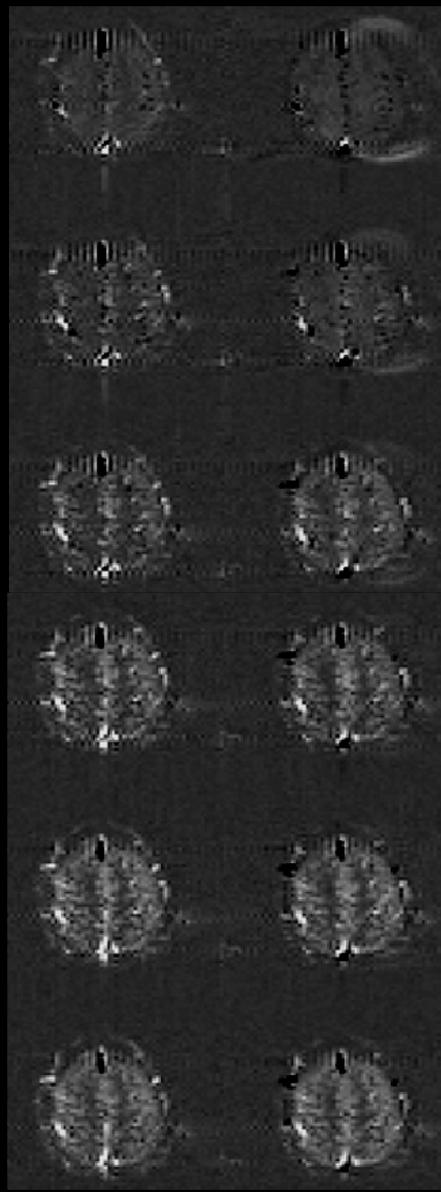
FAIR



Perfusion  
Time Series

**TI (ms) FAIR EPISTAR**

**200**



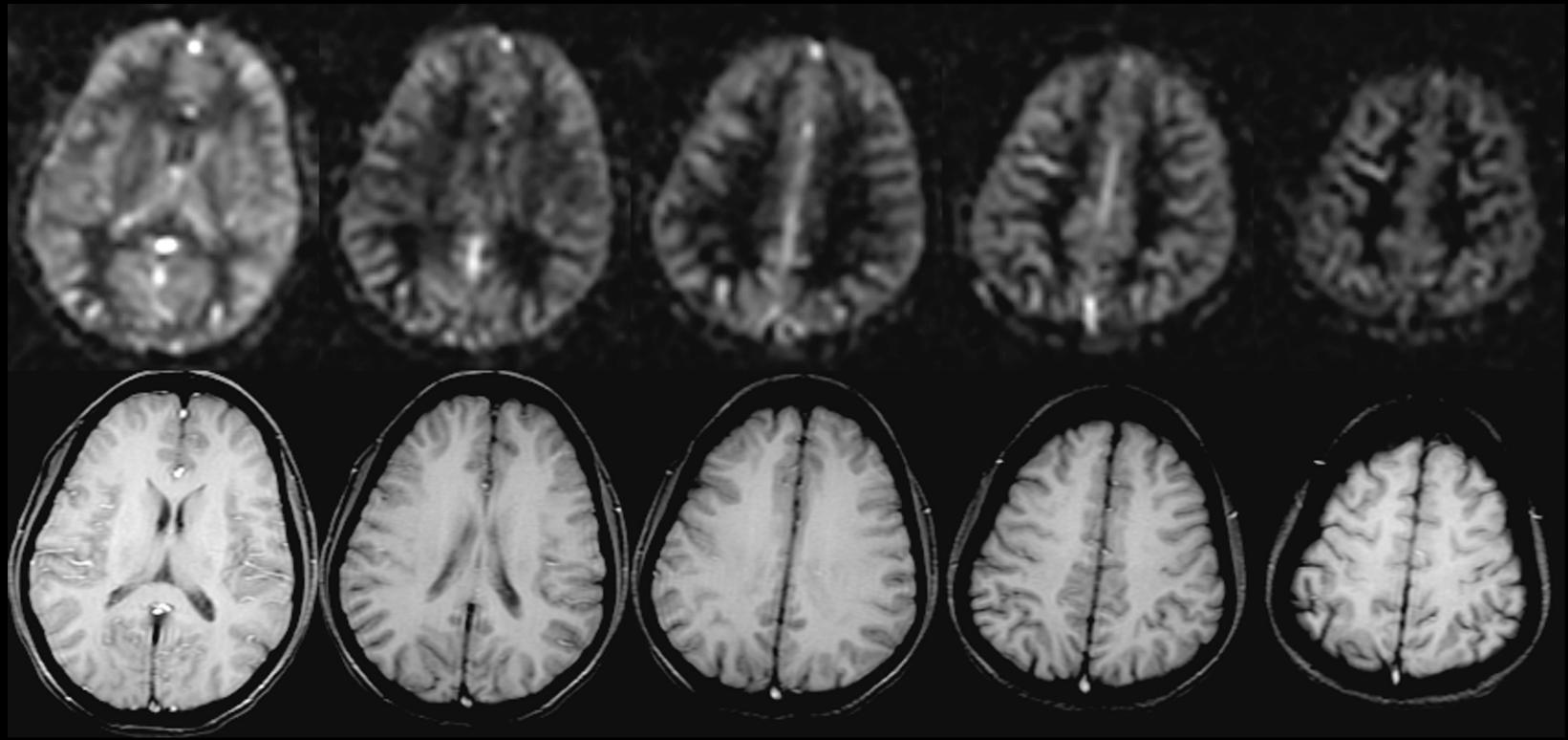
**400**

**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 and 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.

# Refinements

BOLD Contrast Interpretation

Paradigm Design and Processing

# Technology

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

# Methodology

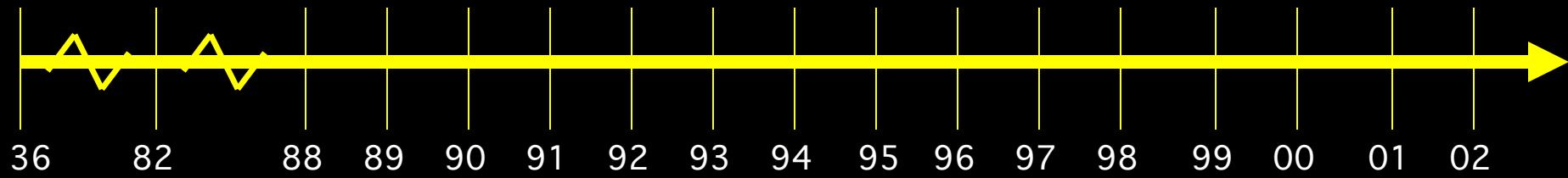
Baseline Volume	Correlation Analysis		CO <sub>2</sub> Calibration
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	Phase Mapping		
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	Resolution Dep.			
Hemoglobin	Post-undershoot	Extended Stim.		
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	CO <sub>2</sub> effect	Fluctuations	Optical Im. Correlation	
	NIRS Correlation	Balloon Model	Electophys. correlation	
	Veins	Inflow		

# Applications

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



# Refinements

BOLD Contrast Interpretation

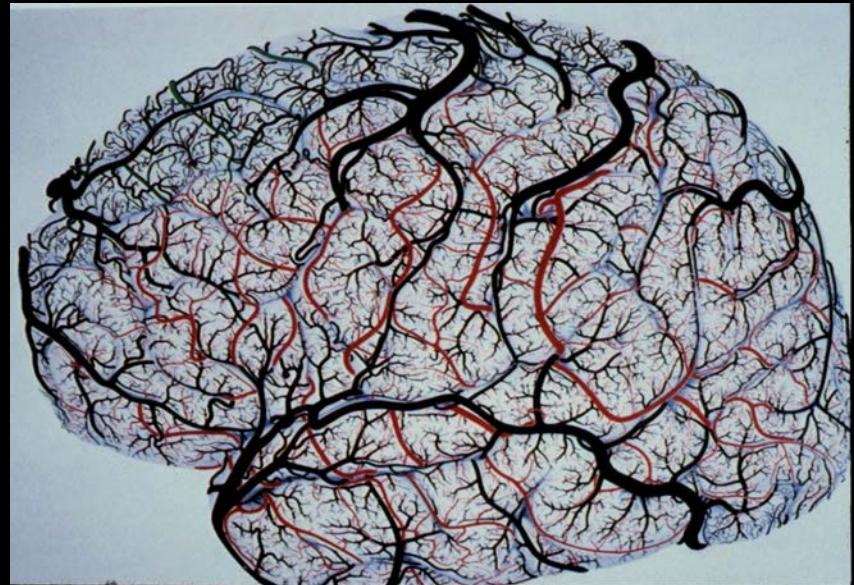
Paradigm Design and Processing

# A challenge in using fMRI:

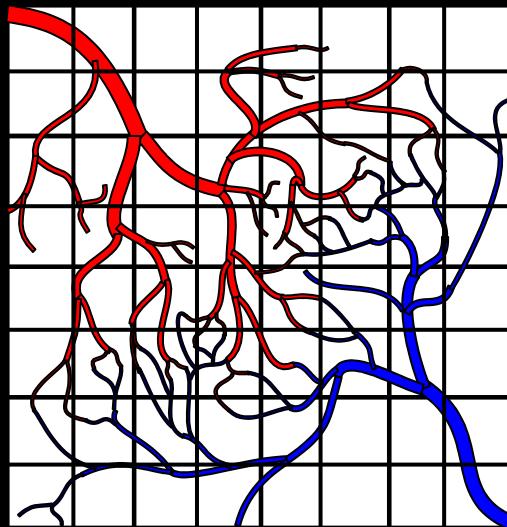
...to make progressively more precise inferences using fMRI without making too many assumptions about non-neuronal physiologic factors.



FIG. 43. Middle temporal gyrus. Female, 60 years. (1) Principal intracortical vein. The branches length regularly decreases from deep towards superficial cortical regions, thus the vascular territory of the principal vein has a conical appearance (dotted line) ( $\times 28$ )



Neuronal  
Activation



Measured  
Signal

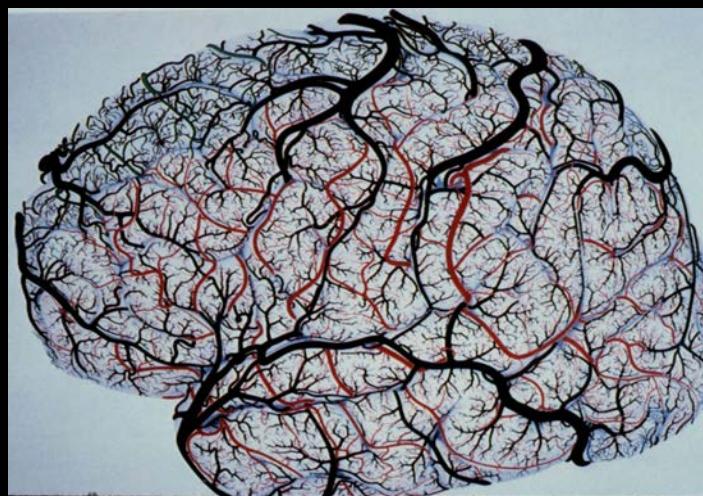
Hemodynamics

?

?

?

Noise



# BOLD Contrast: Strategies for Better Interpretation

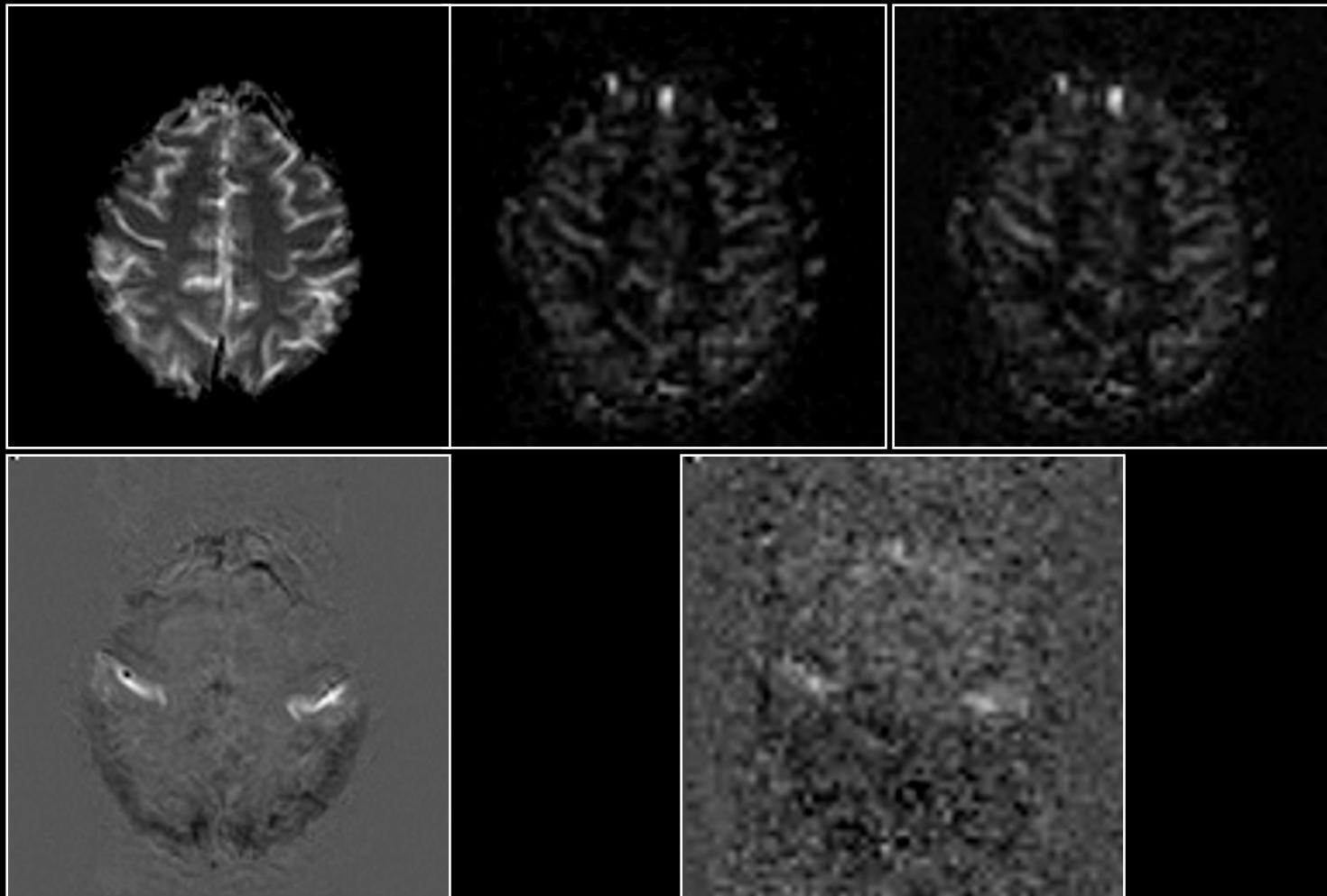
- Pulse sequence modulation
- Neuronal activation modulation
- Alternative measurement comparison

**BOLD**

*Rest*

**Perfusion**

*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

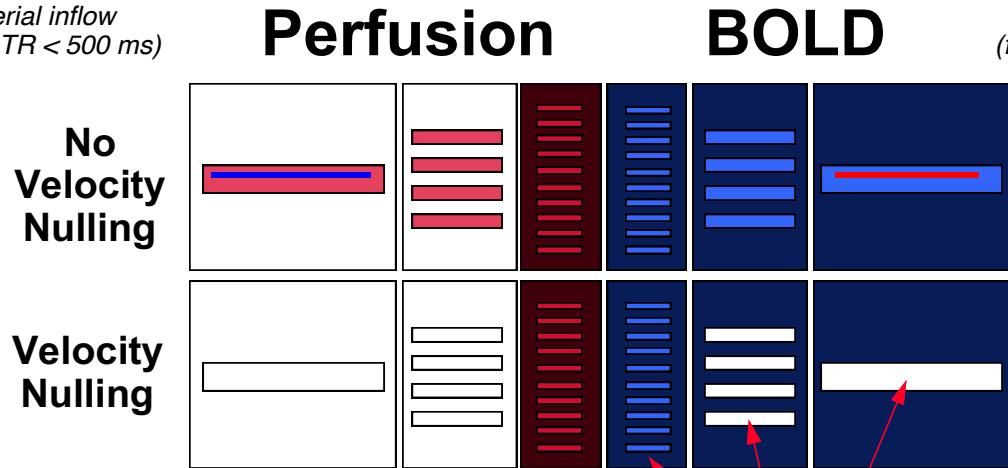


# Perfusion



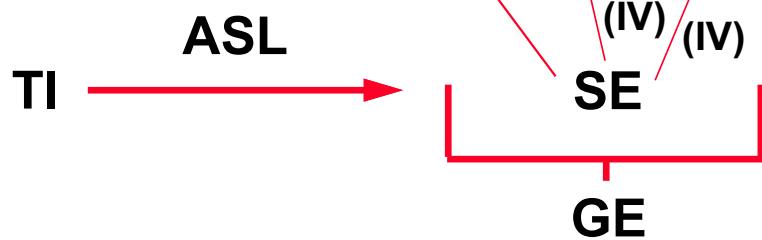
P. A. Bandettini, E. C. Wong, Magnetic resonance imaging of human brain function: principles, practicalities, and possibilities, in "Neurosurgery Clinics of North America: Functional Imaging" (M. Haglund, Ed.), p.345-371, W. B. Saunders Co., 1997.

*Arterial inflow*  
(*BOLD TR < 500 ms*)

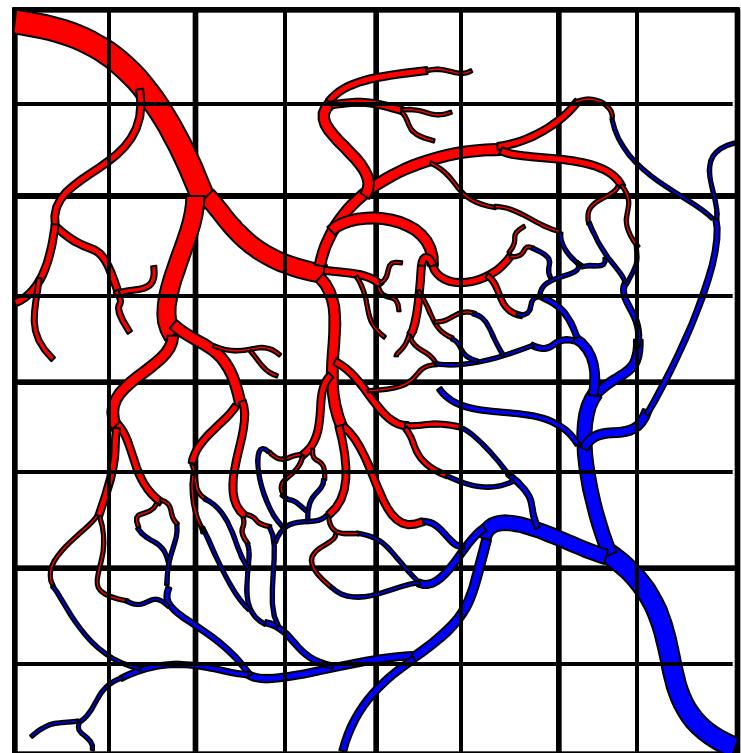


*Venous inflow*  
(for ASL, w/ no VN)

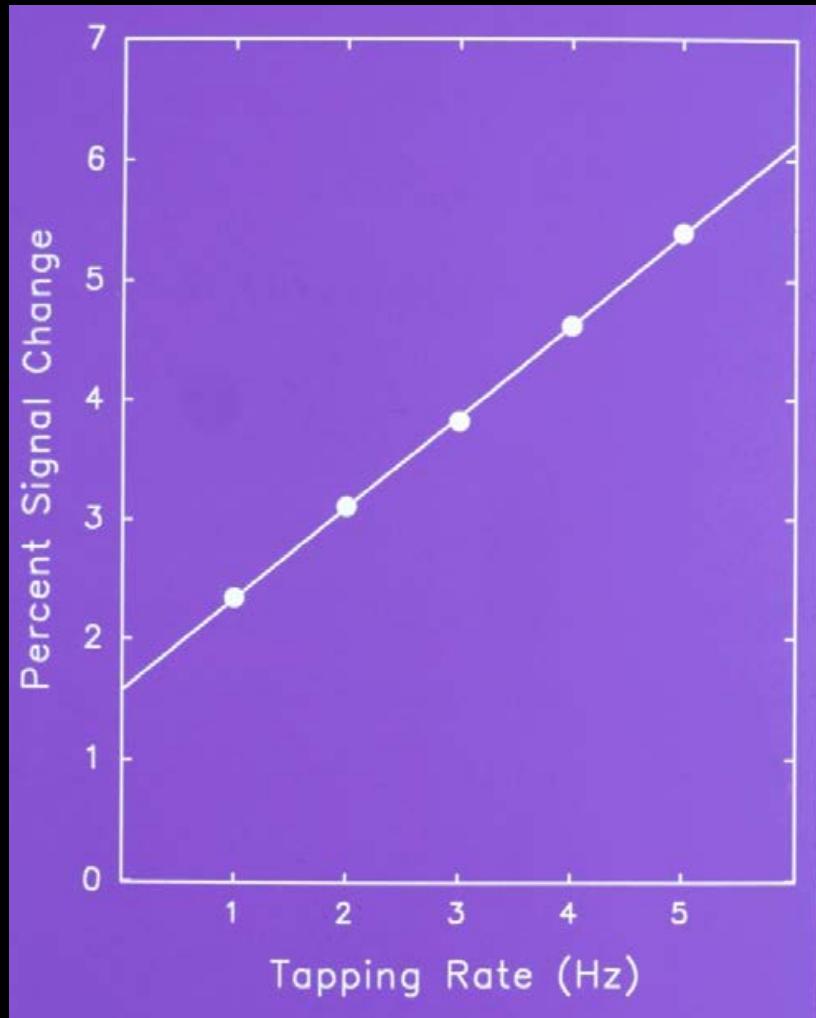
Pulse Sequence  
Sensitivity



Spatial  
Heterogeneity

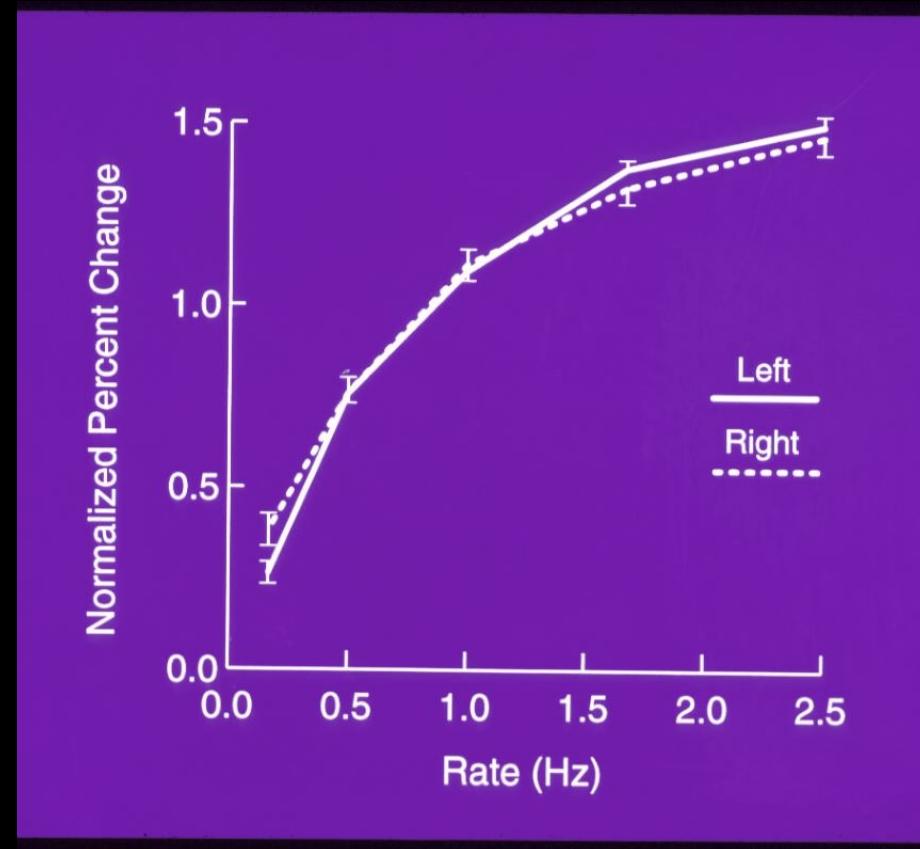


# Motor Cortex



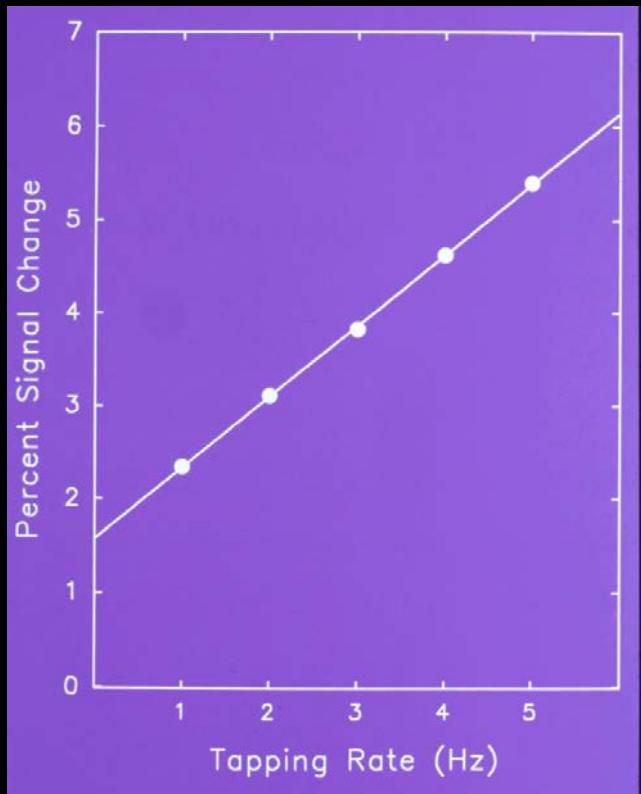
S. M. Rao et al, (1996) “Relationship between finger movement rate and functional magnetic resonance signal change in human primary motor cortex.” *J. Cereb. Blood Flow and Met.* 16, 1250-1254.

# Auditory Cortex

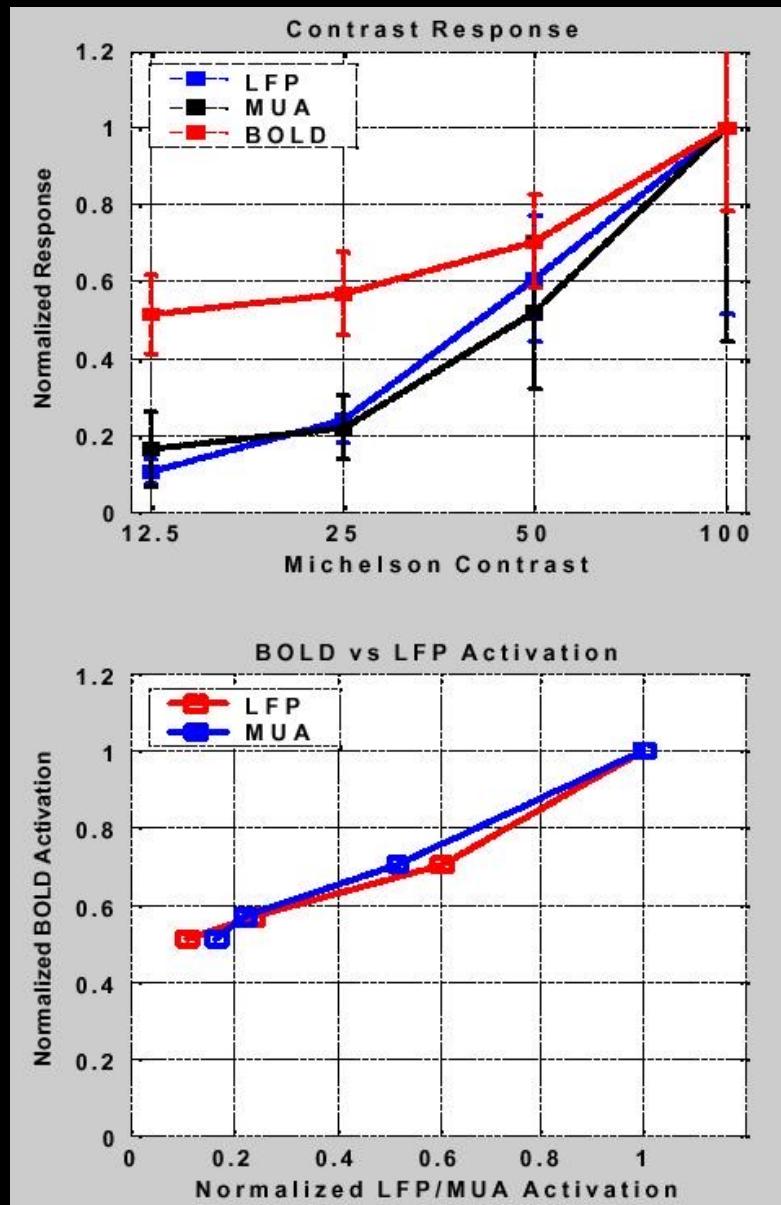


J. R. Binder, et al, (1994). “Effects of stimulus rate on signal response during functional magnetic resonance imaging of auditory cortex.” *Cogn. Brain Res.* 2, 31-38

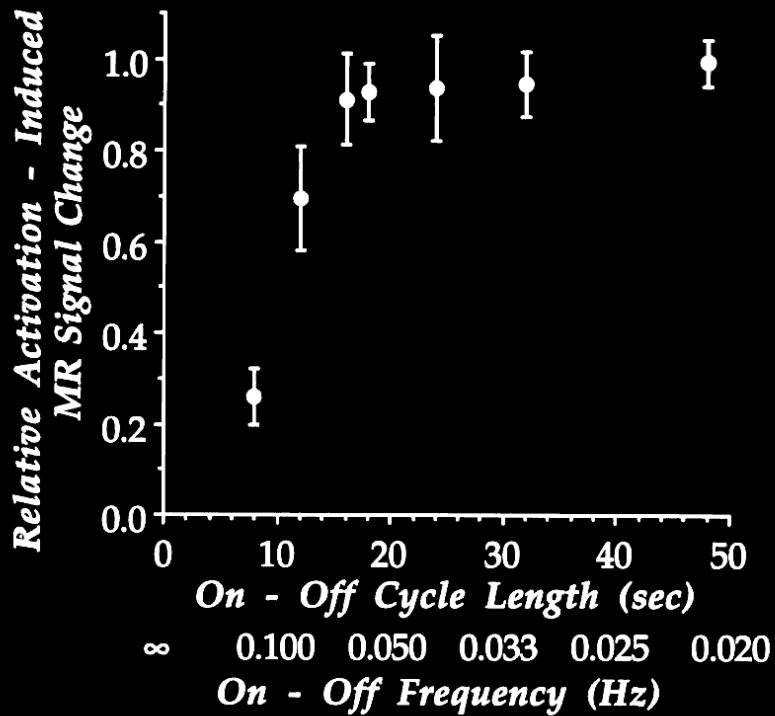
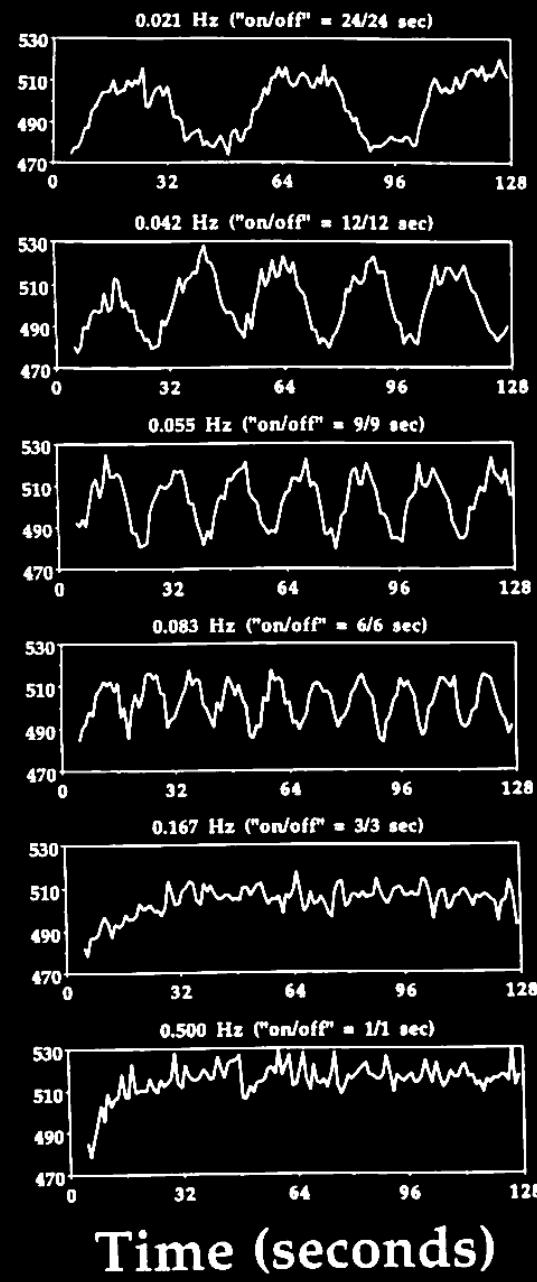
Logothetis et al. (2001) "Neurophysiological investigation of the basis of the fMRI signal" Nature, 412, 150-157



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.

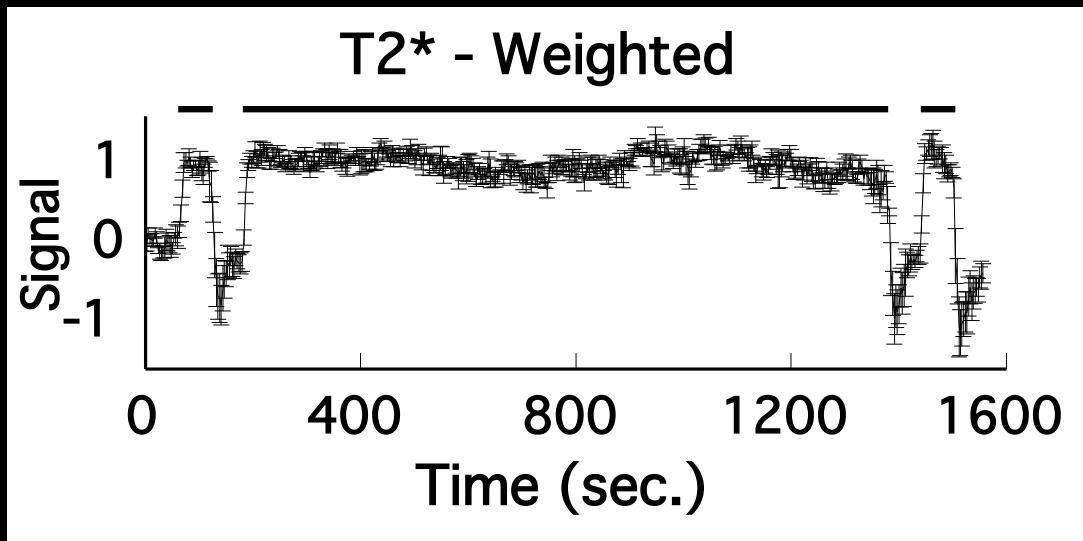


# MRI Signal

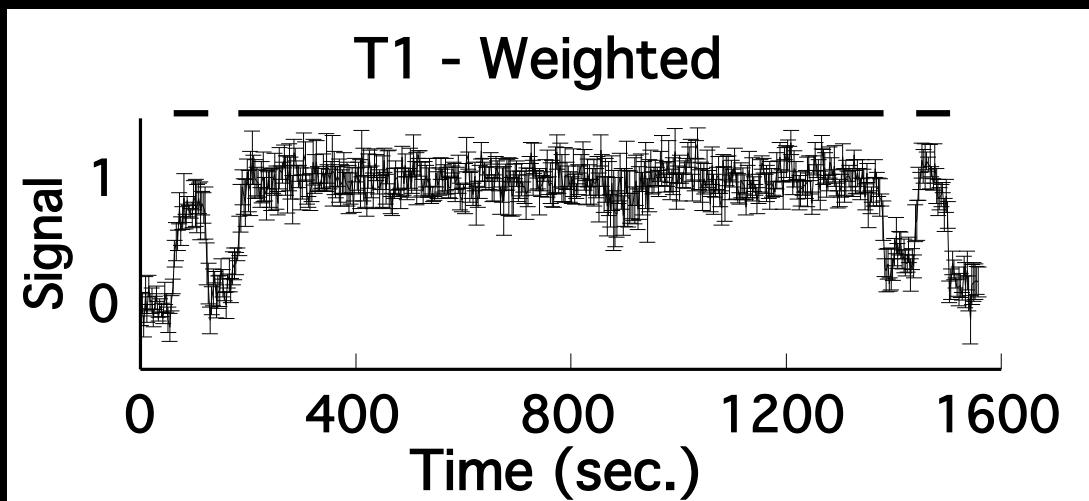


P. A. Bandettini, Functional MRI  
temporal resolution in "Functional  
MRI" (C. Moonen, and P. Bandettini.,  
Eds.), p. 205-220, Springer - Verlag.,  
1999.

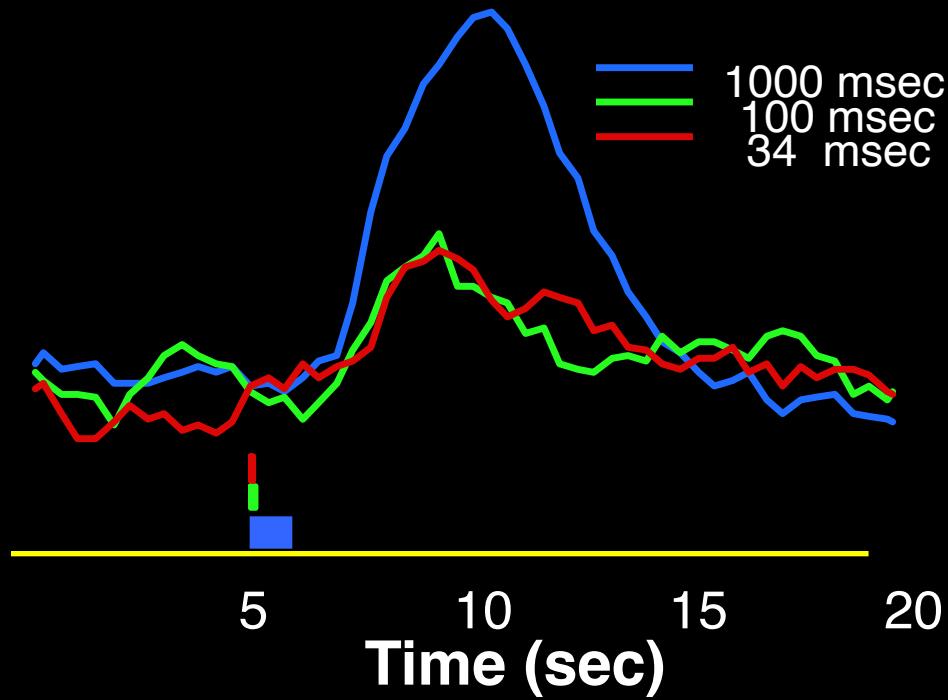
BOLD



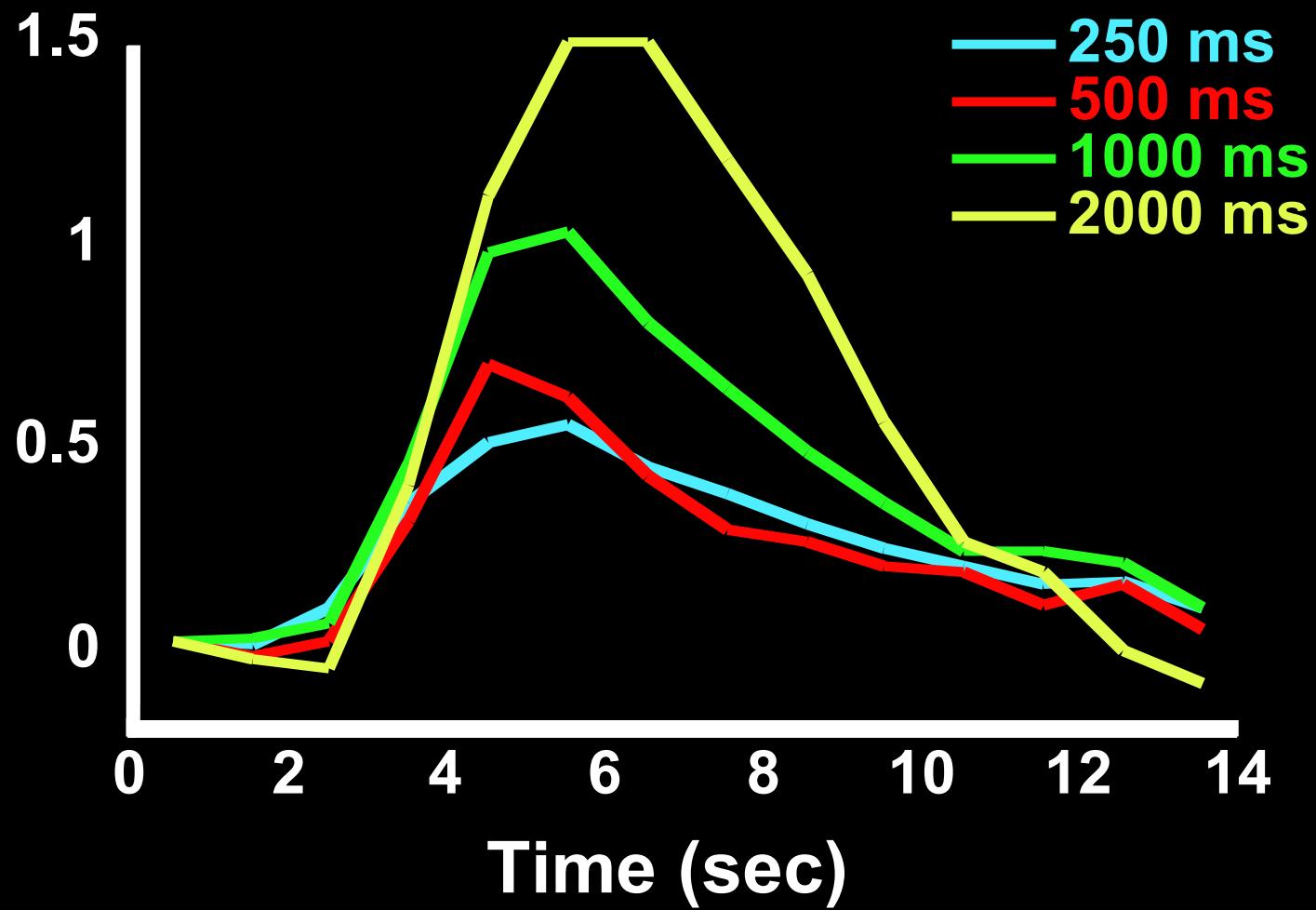
Flow



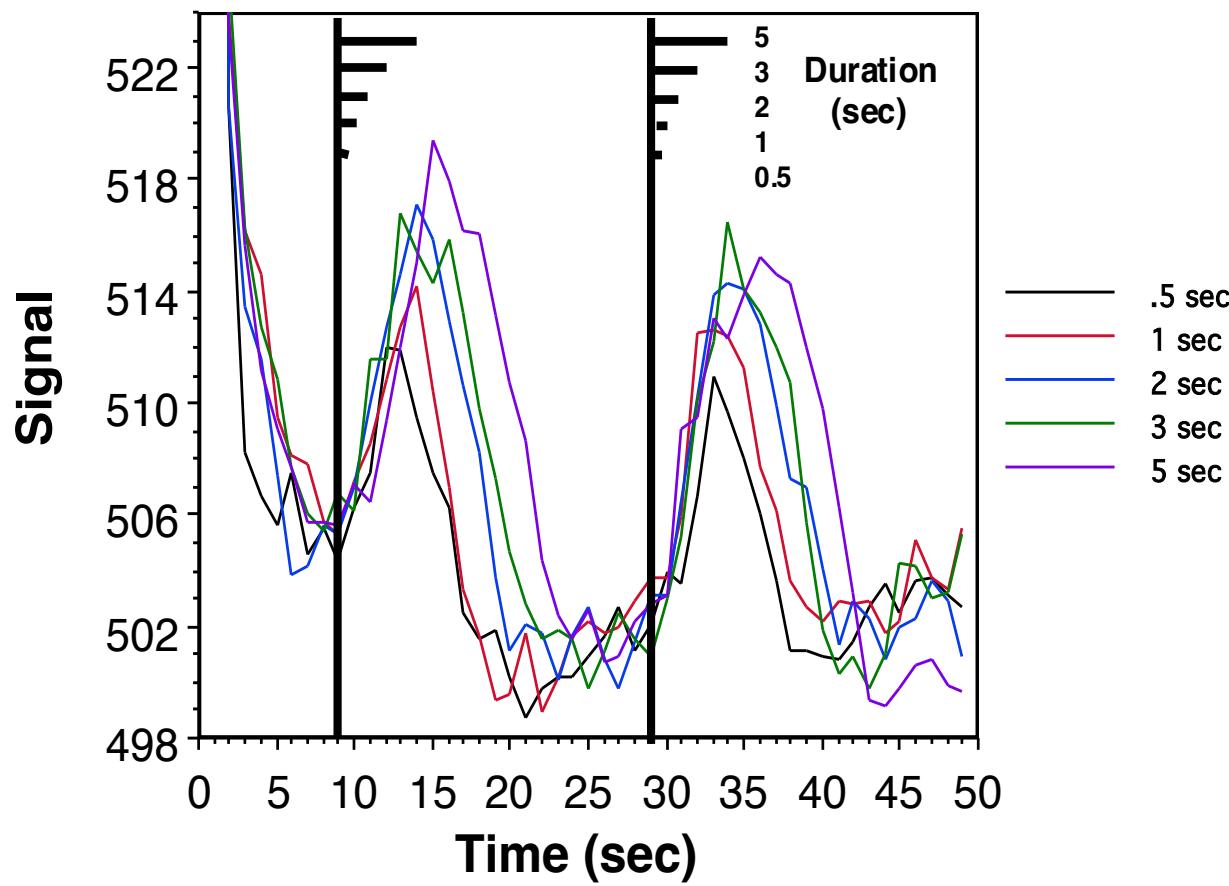
P. A. Bandettini, K. K. Kwong, T. L. Davis, R. B. H. Tootell, E. C. Wong, P. T. Fox, J. W. Belliveau, R. M. Weisskoff, B. R. Rosen, (1997). “Characterization of cerebral blood oxygenation and flow changes during prolonged brain activation.” *Human Brain Mapping* 5, 93-109.



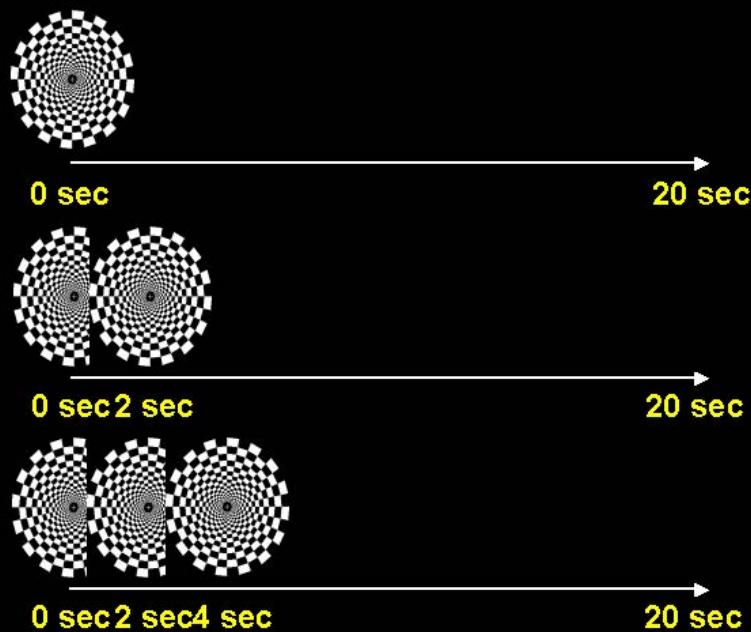
R. L. Savoy, et al., Pushing the temporal resolution of fMRI: studies of very brief visual stimuli, onset variability and asynchrony, and stimulus-correlated changes in noise [oral], 3'rd Proc. Soc. Magn. Reson., Nice, p. 450. (1995).



## Motor Cortex



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).

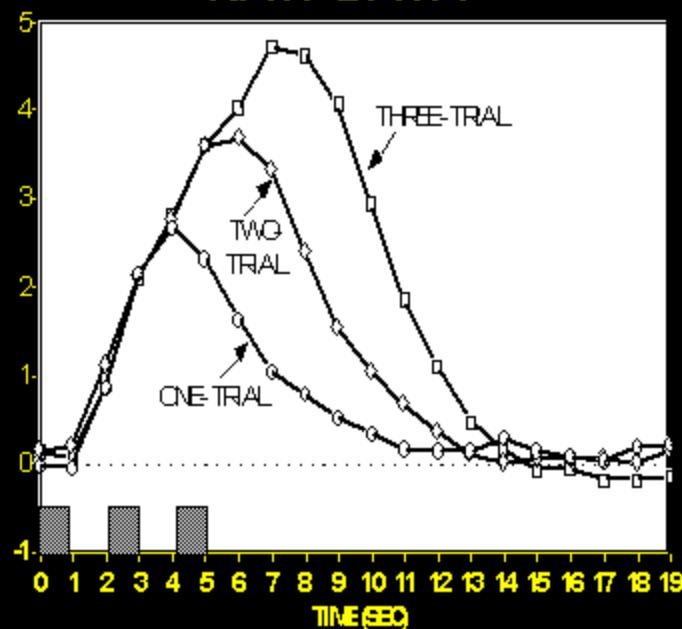


♦ Human Brain Mapping 5:329–340(1997)

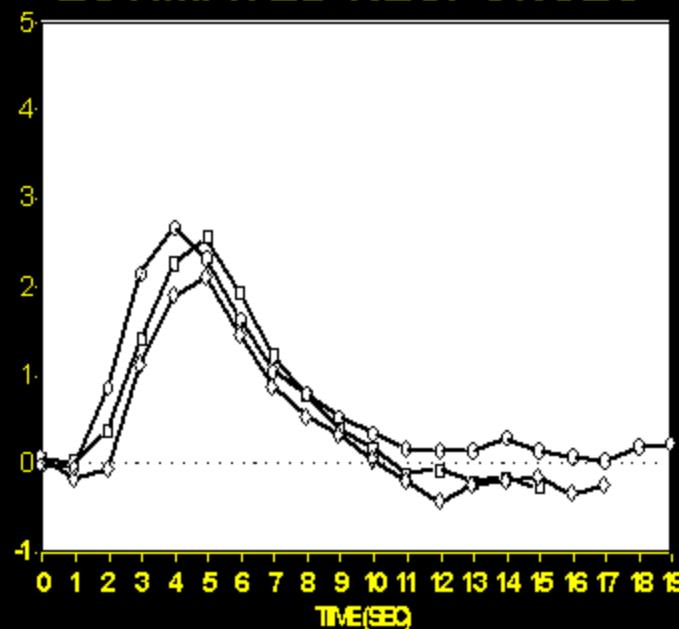
## Selective Averaging of Rapidly Presented Individual Trials Using fMRI

Anders M. Dale\* and Randy L. Buckner

### RAW DATA

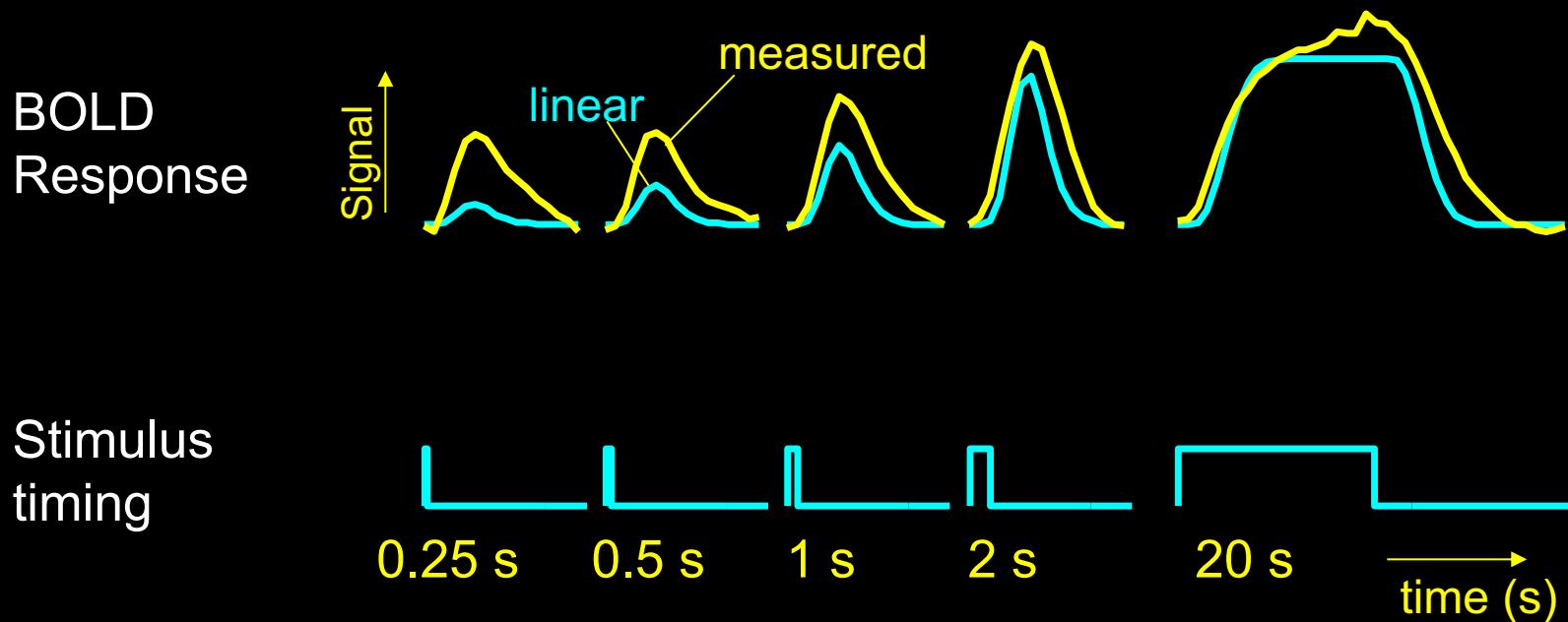


### ESTIMATED RESPONSES



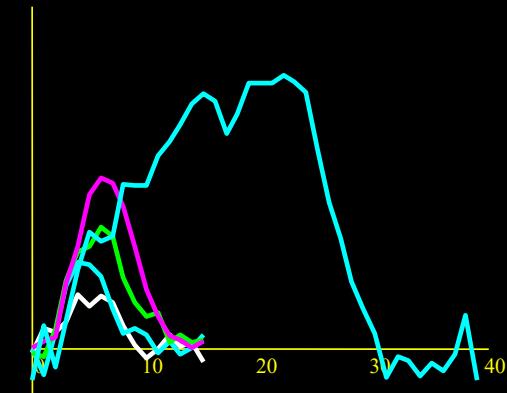
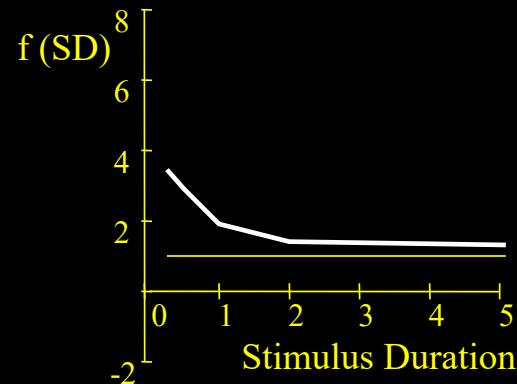
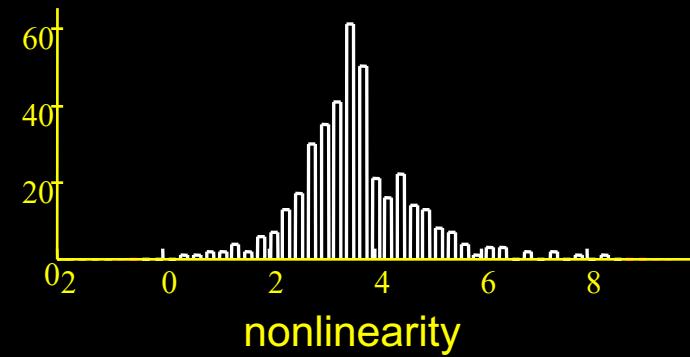
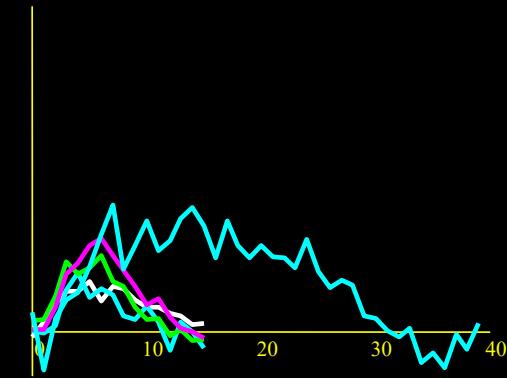
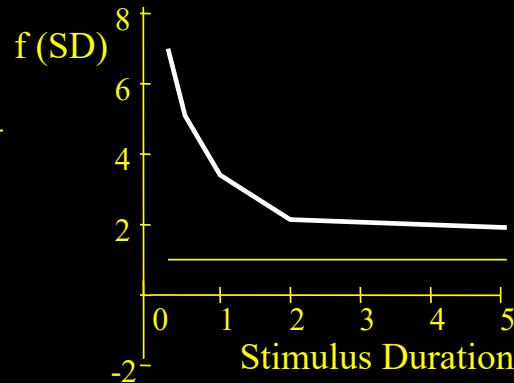
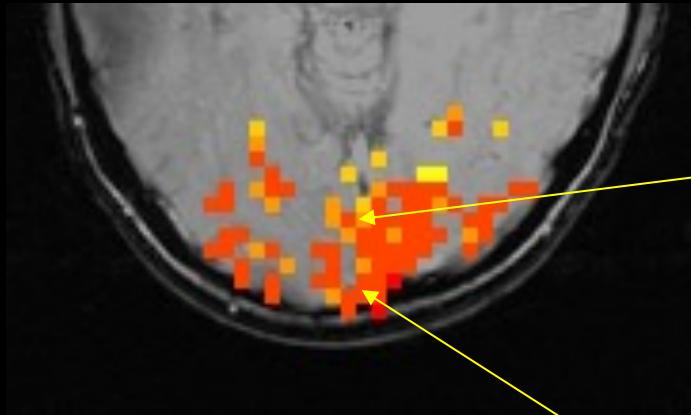
# Dynamic Nonlinearity Assessment

Different stimulus “ON” periods



*Brief stimuli produce larger responses than expected*

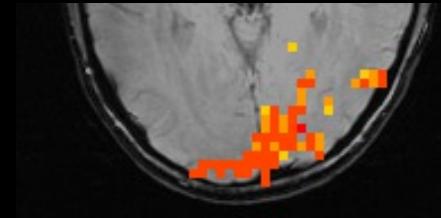
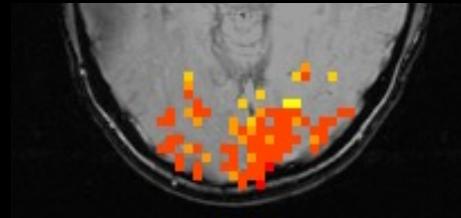
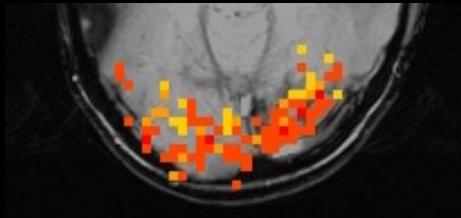
# Spatial Heterogeneity of BOLD Nonlinearity



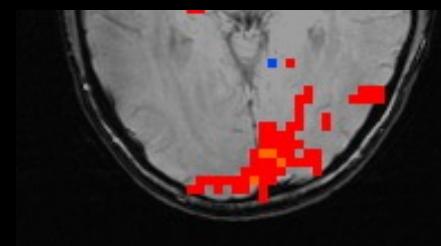
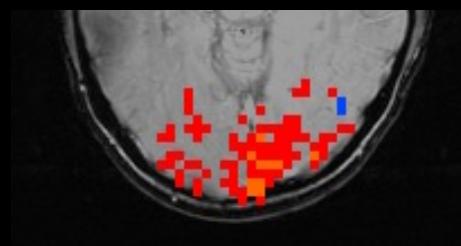
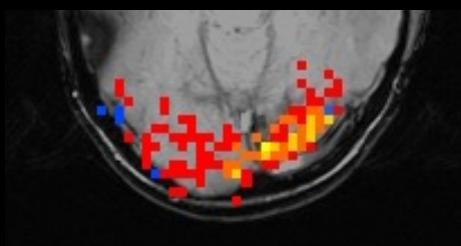
R. M. Birn, Z. Saad, P. A. Bandettini, (2001) “Spatial heterogeneity of the nonlinear dynamics in the fMRI BOLD response.” *NeuroImage*, 14: 817-826.

# Results – visual task

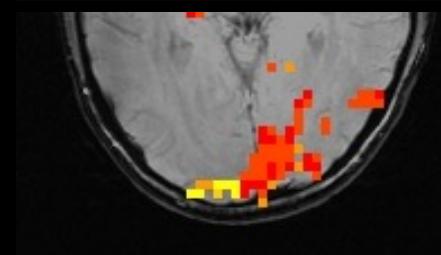
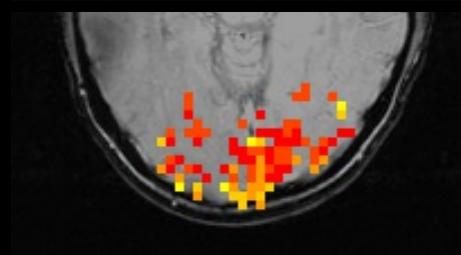
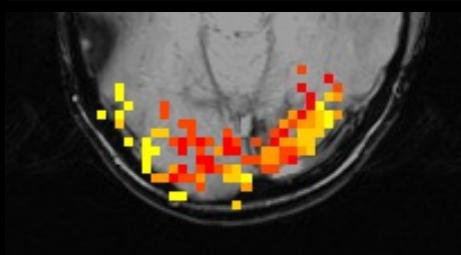
Nonlinearity



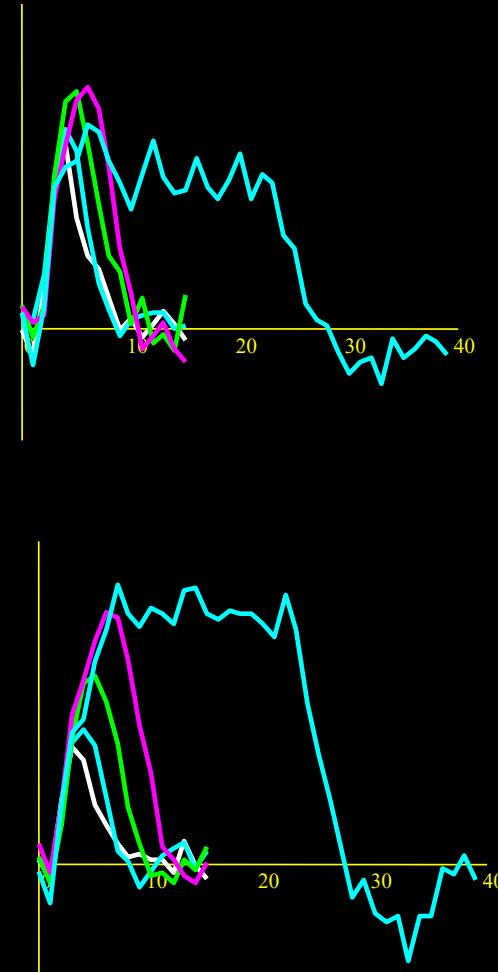
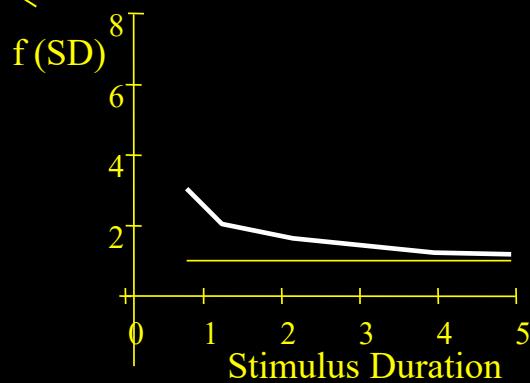
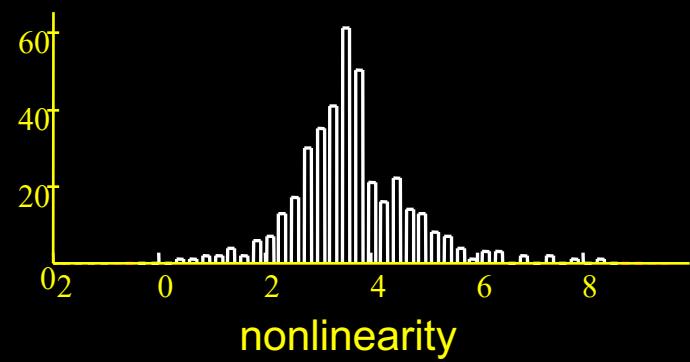
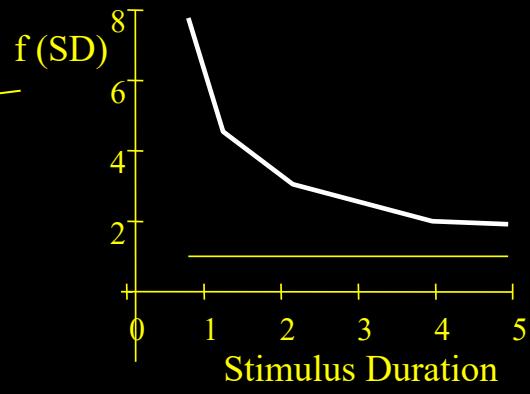
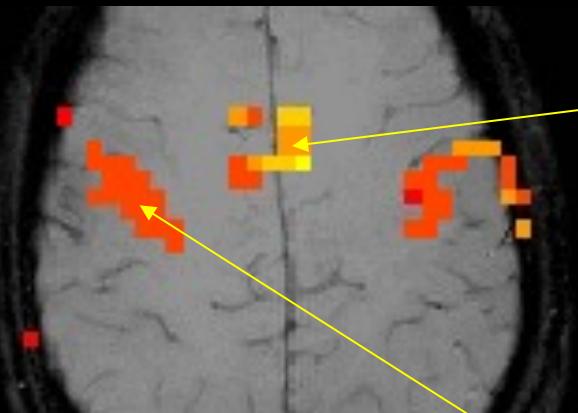
Magnitude



Latency

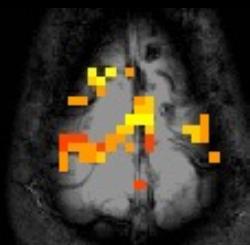
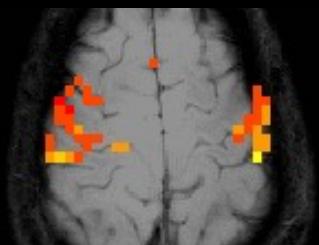
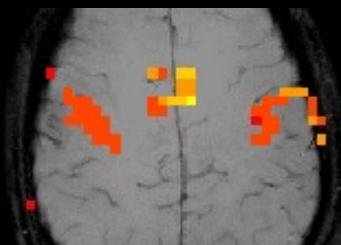


# Results – motor task

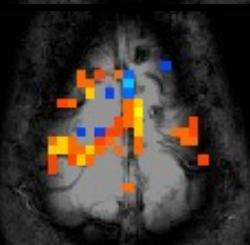
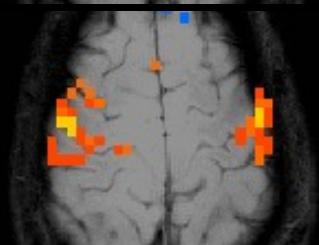
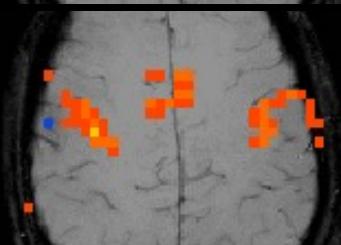


# Results – motor task

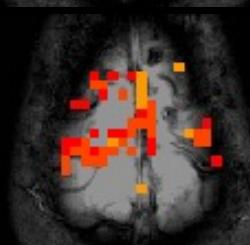
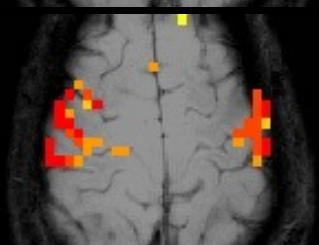
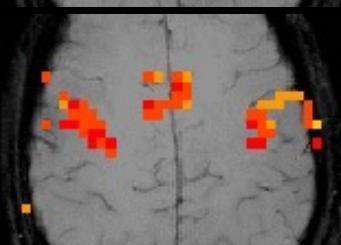
Nonlinearity



Magnitude

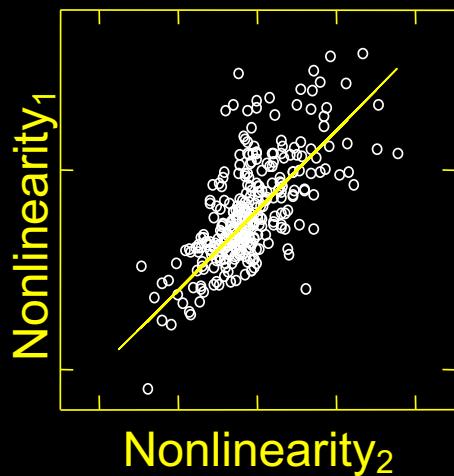


Latency

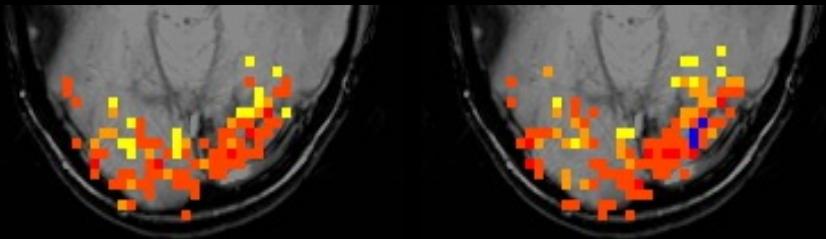
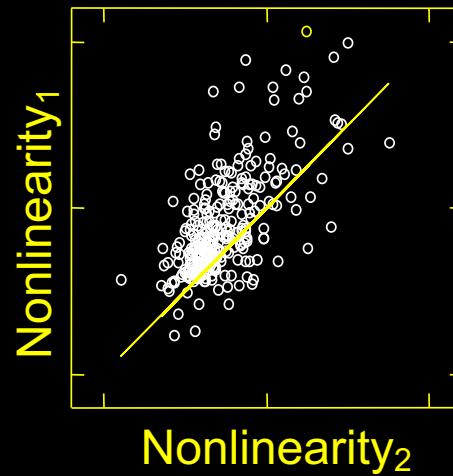


# Reproducibility

*Visual task*

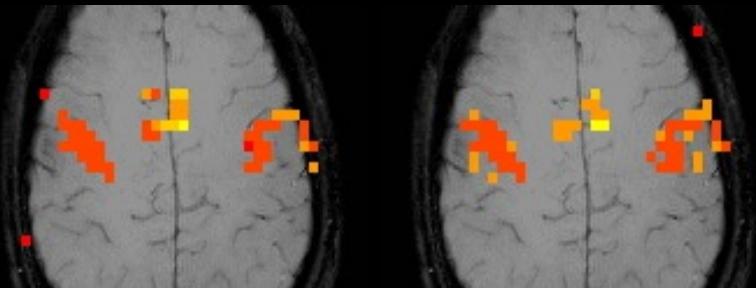


*Motor task*



Experiment 1

Experiment 2

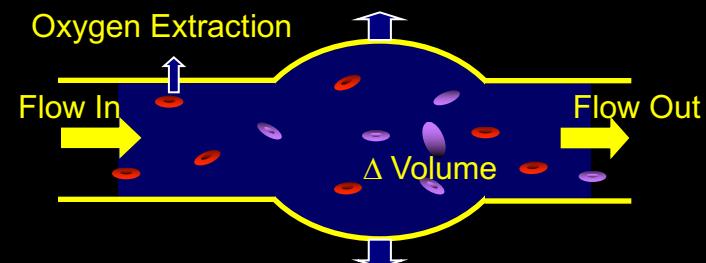
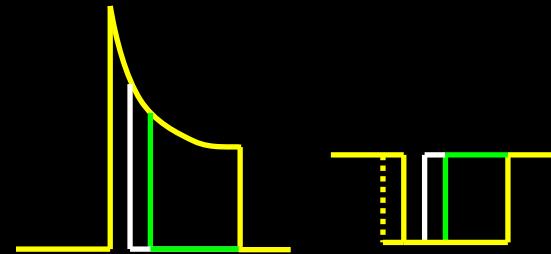
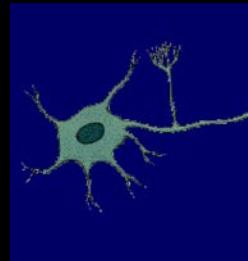


Experiment 1

Experiment 2

# Sources of this Nonlinearity

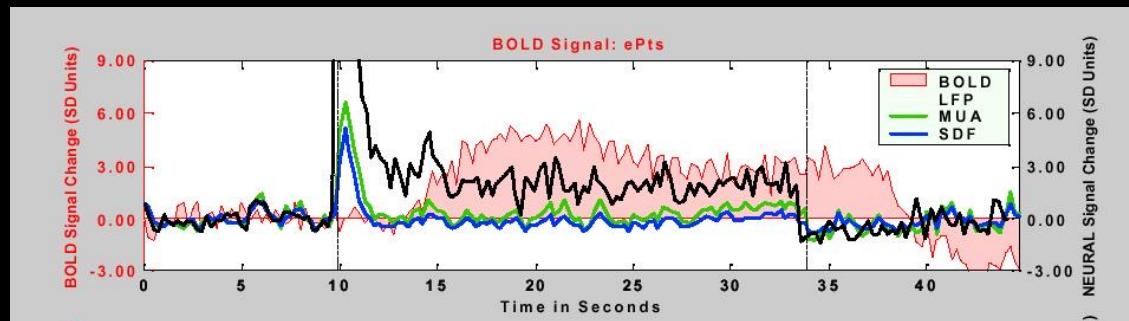
- Neuronal
- Hemodynamic
  - Oxygen extraction
  - Blood volume dynamics



# BOLD Correlation with Neuronal Activity

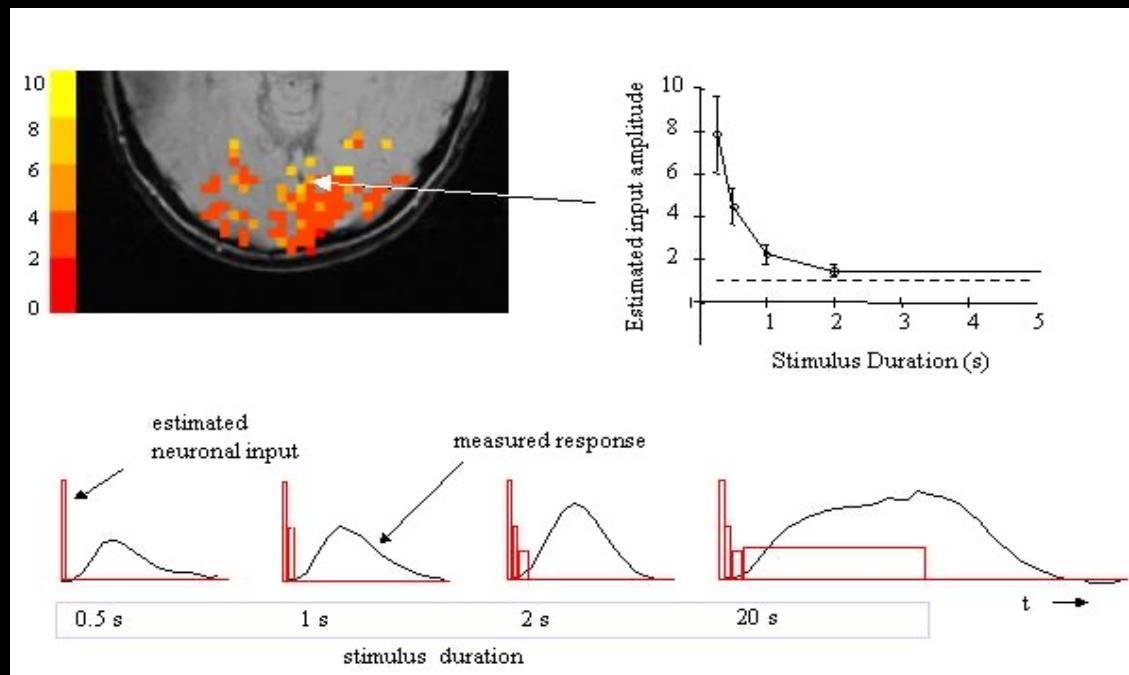
Logothetis et al. (2001)

“Neurophysiological investigation  
of the basis of the fMRI signal”  
Nature, 412, 150-157.



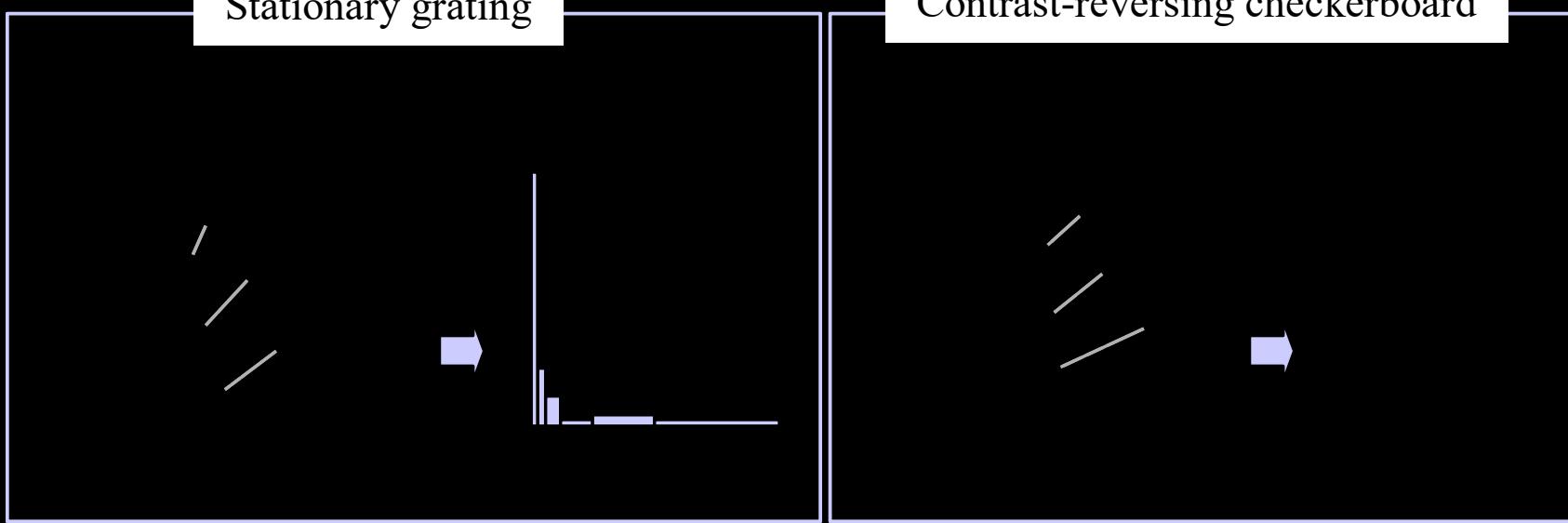
P. A. Bandettini and L. G.

Ungerleider, (2001) “From neuron  
to BOLD: new connections.”  
Nature Neuroscience, 4: 864-866.

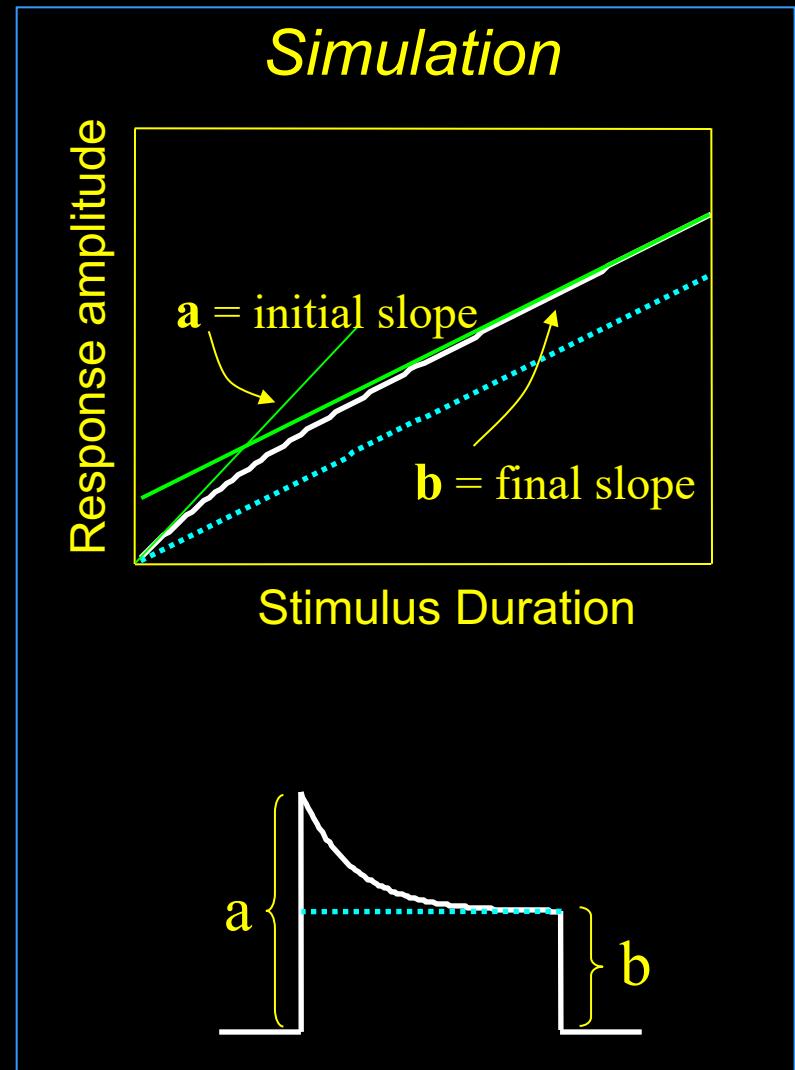
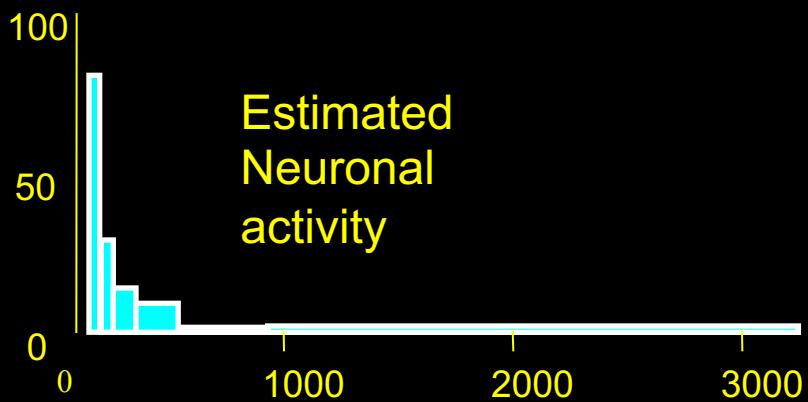
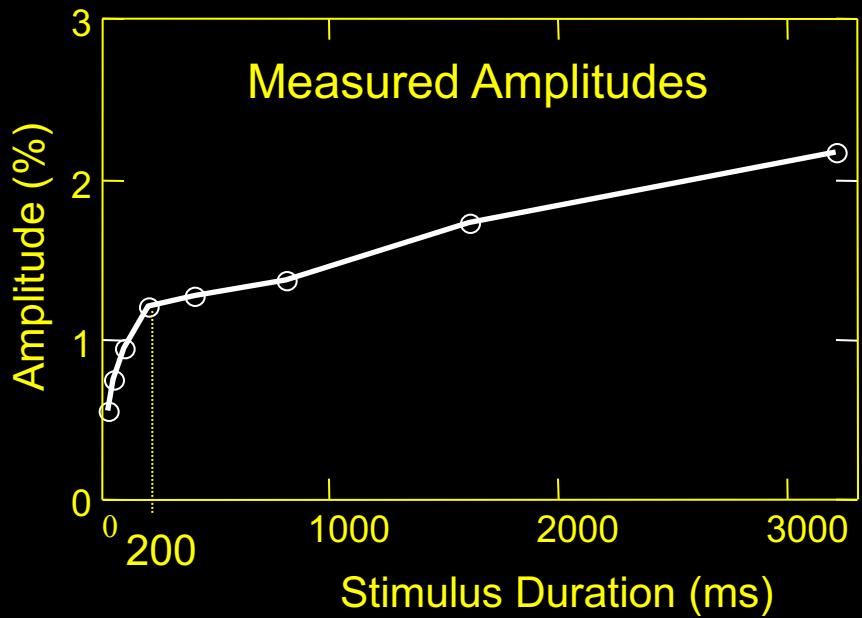


Stationary grating

Contrast-reversing checkerboard



# Results – constant gratings

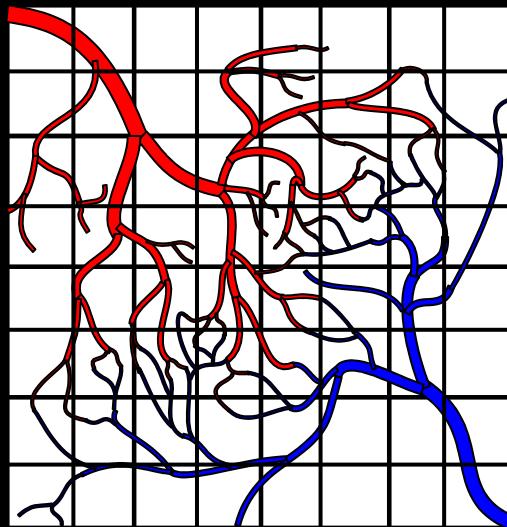


# Refinements

BOLD Contrast Interpretation

Paradigm Design and Processing

Neuronal  
Activation



Measured  
Signal

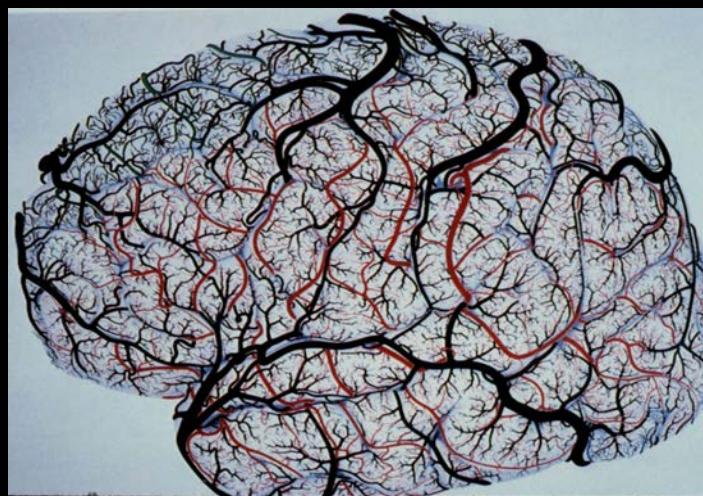
Hemodynamics

?

?

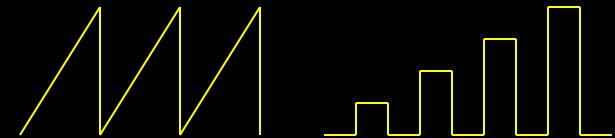
?

Noise

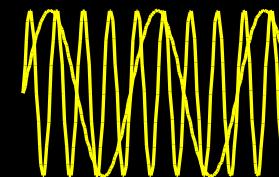


# Neuronal Activation Input Strategies

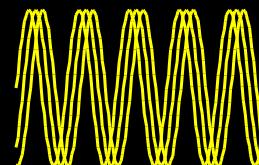
1. Block Design



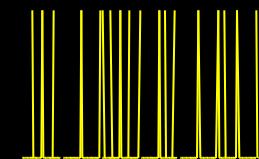
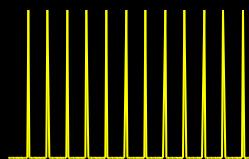
2. Parametric Design



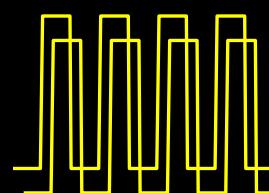
3. Frequency Encoding



4. Phase Encoding



5. Event Related

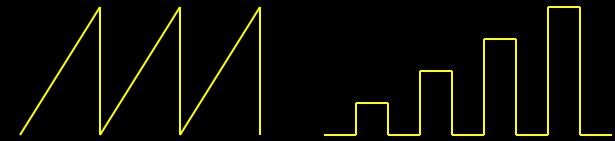


6. Orthogonal Design

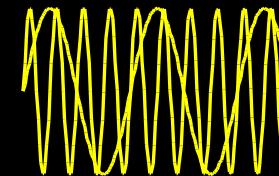
7. Free Behavior Design

# Neuronal Activation Input Strategies

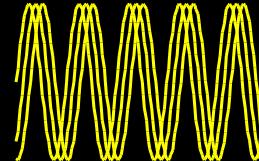
1. Block Design



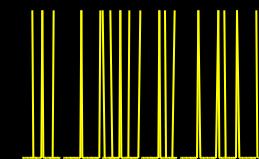
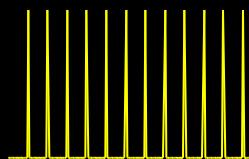
2. Parametric Design



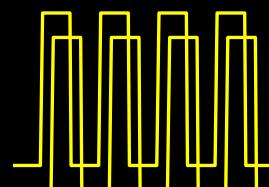
3. Frequency Encoding



4. Phase Encoding

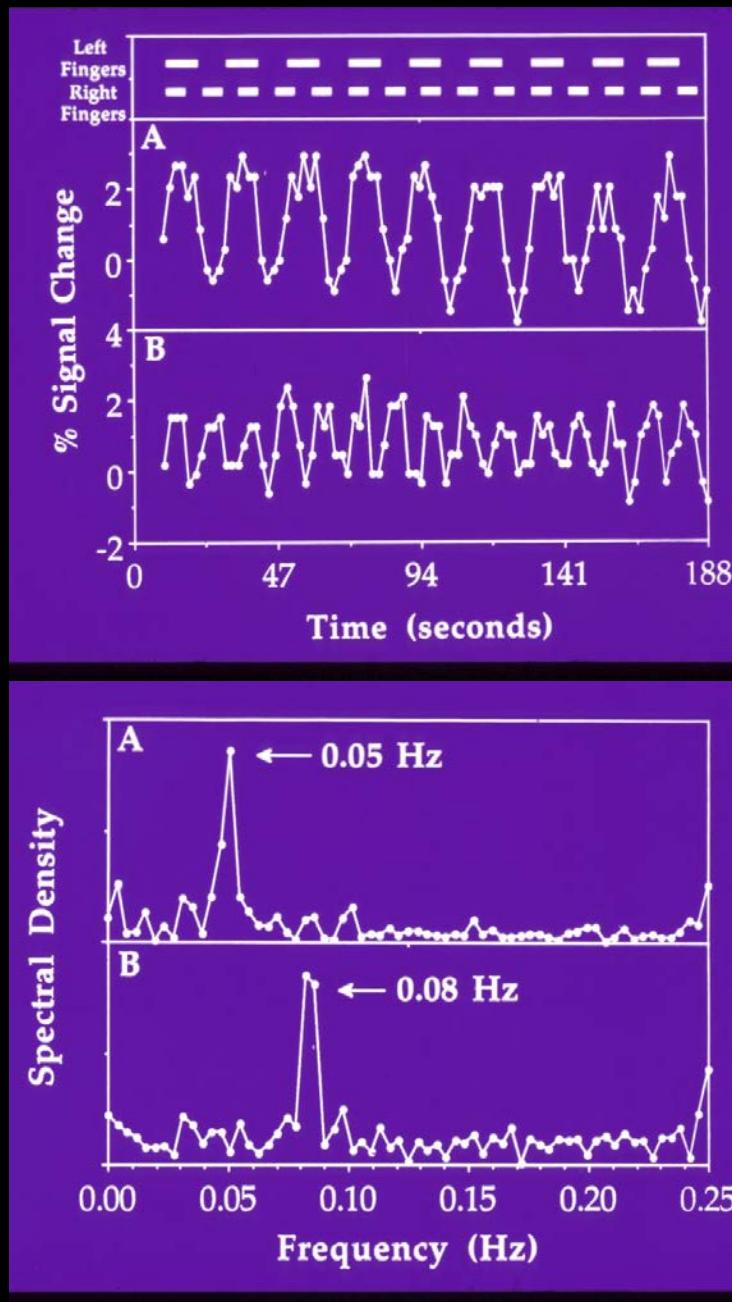
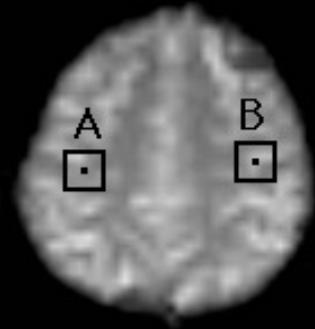


5. Event Related



6. Orthogonal Design

7. Free Behavior Design



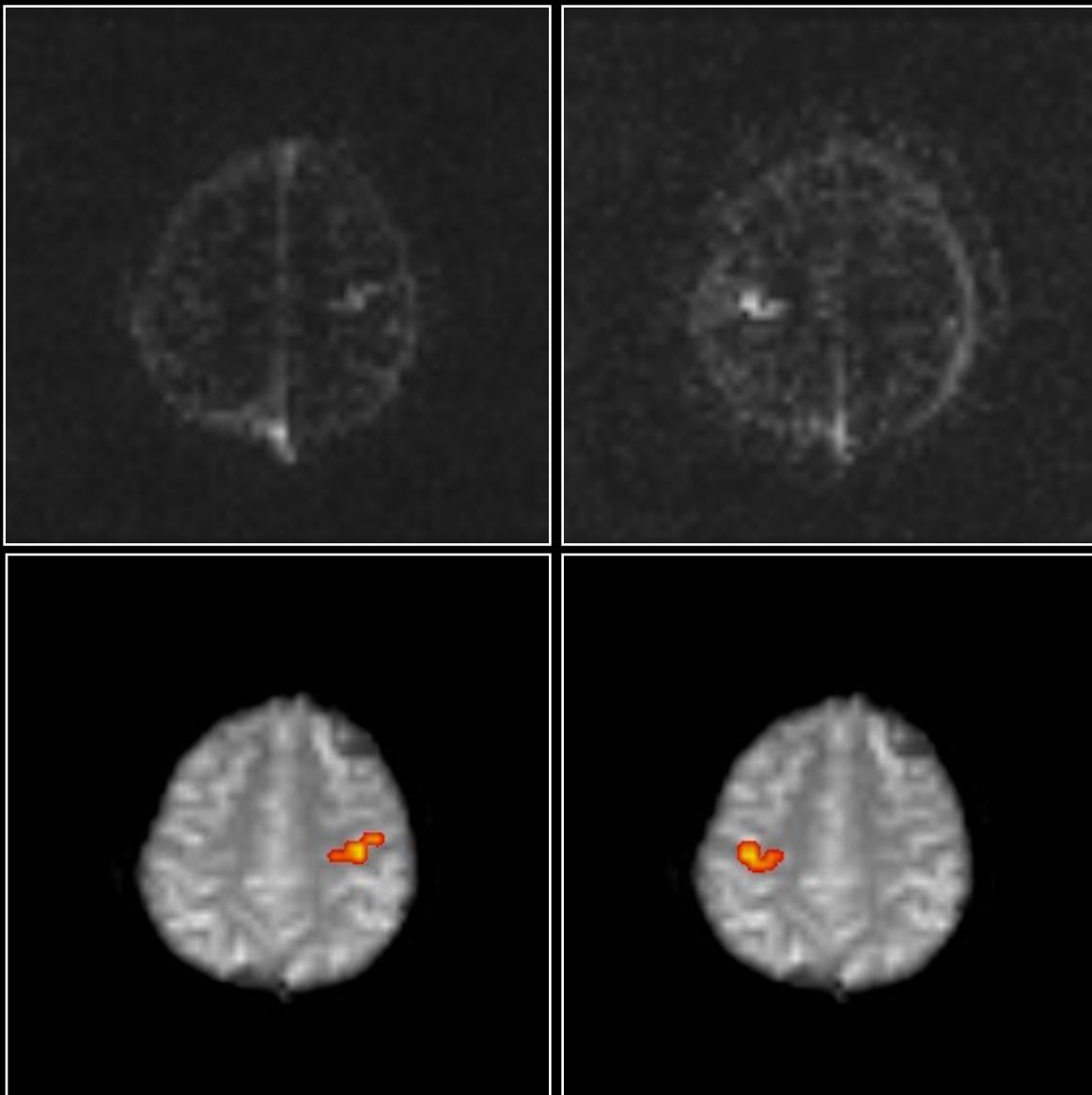
P. A. Bandettini, A. Jesmanowicz, E. C. Wong, J. S. Hyde, Processing strategies for time-course data sets in functional MRI of the human brain. *Magn. Reson. Med.* 30, 161-173 (1993).

**0.08 Hz**

**0.05 Hz**

**spectral  
density**

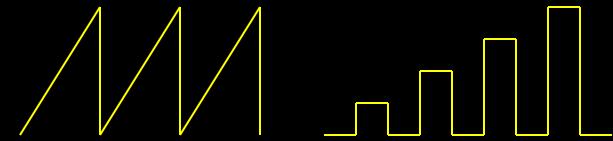
**c.c. > 0.5  
with spectra**



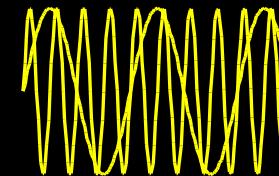
P. A. Bandettini, A. Jesmanowicz, E. C. Wong, J. S. Hyde, Processing strategies for time-course data sets in functional MRI of the human brain. *Magn. Reson. Med.* 30, 161-173 (1993).

# Neuronal Activation Input Strategies

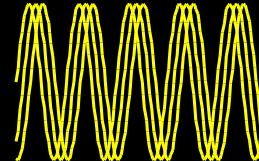
1. Block Design



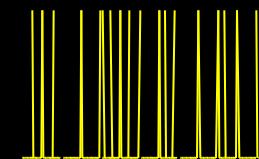
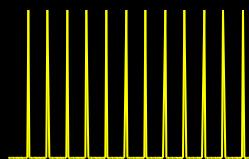
2. Parametric Design



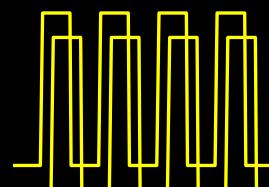
3. Frequency Encoding



4. Phase Encoding



5. Event Related

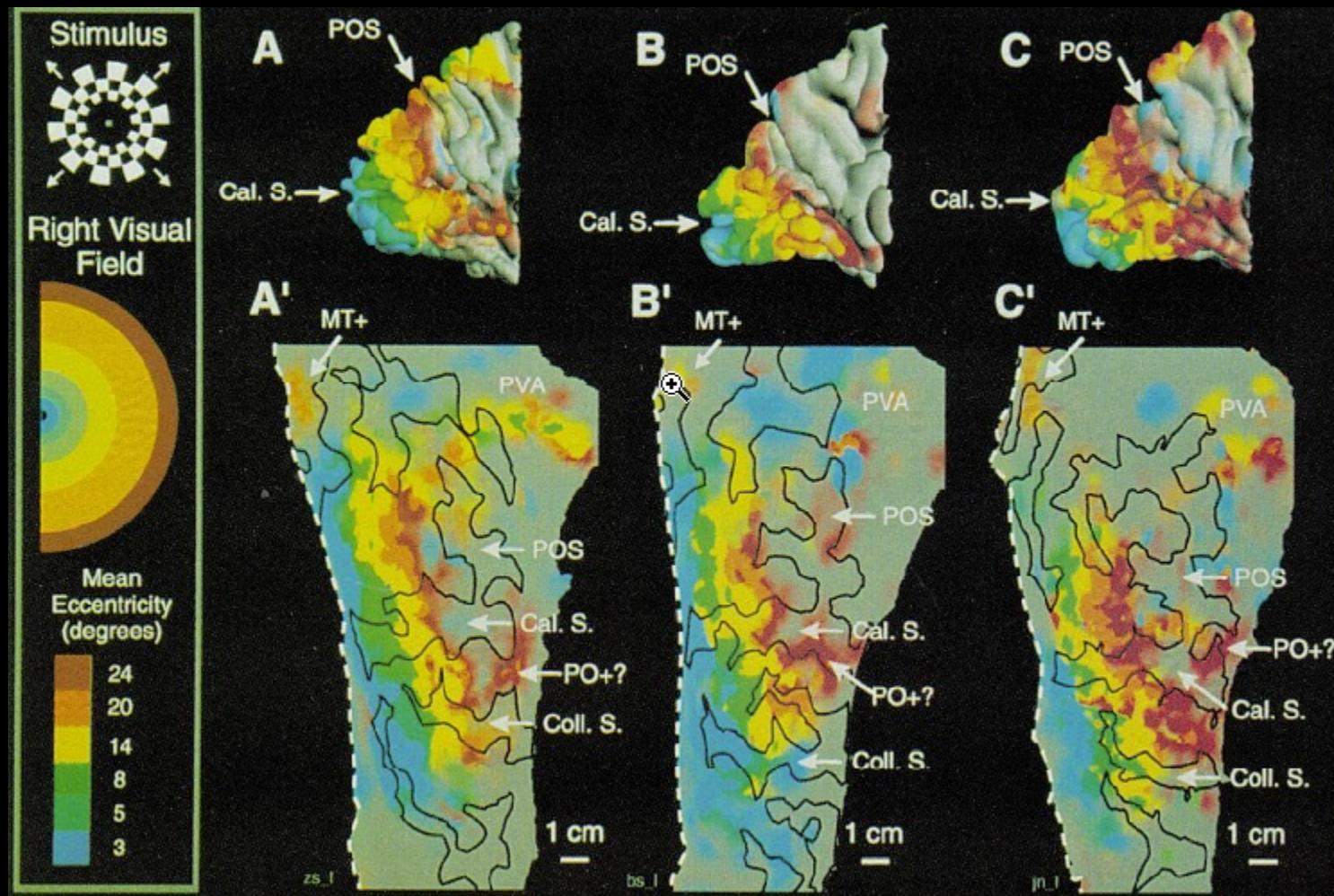


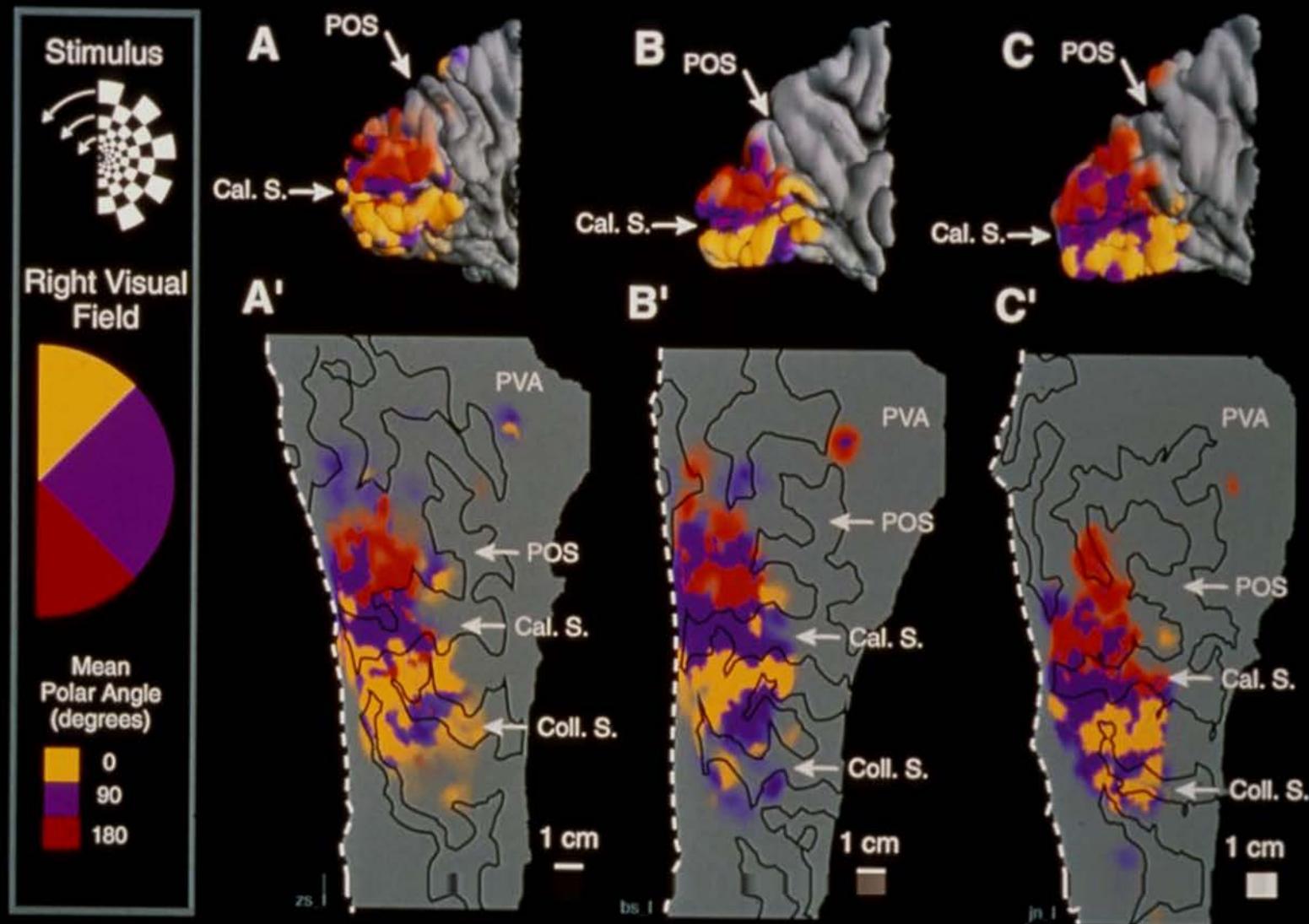
6. Orthogonal Design

7. Free Behavior Design

## Mapping striate and extrastriate visual areas in human cerebral cortex

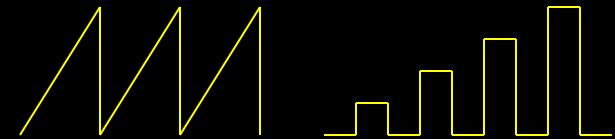
EDGAR A. DEYOE\*, GEORGE J. CARMAN†, PETER BANDETTINI‡, SETH GLICKMAN\*, JON WIESER\*, ROBERT COX§,  
DAVID MILLER¶, AND JAY NEITZ\*



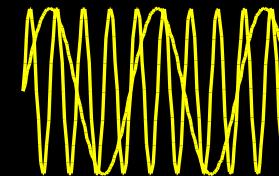


# Neuronal Activation Input Strategies

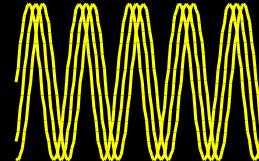
1. Block Design



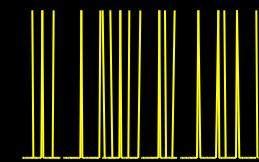
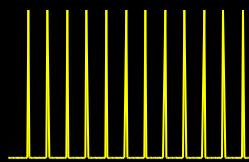
2. Parametric Design



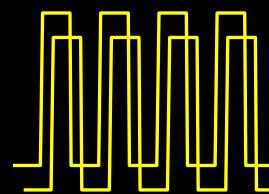
3. Frequency Encoding



4. Phase Encoding



5. Event Related



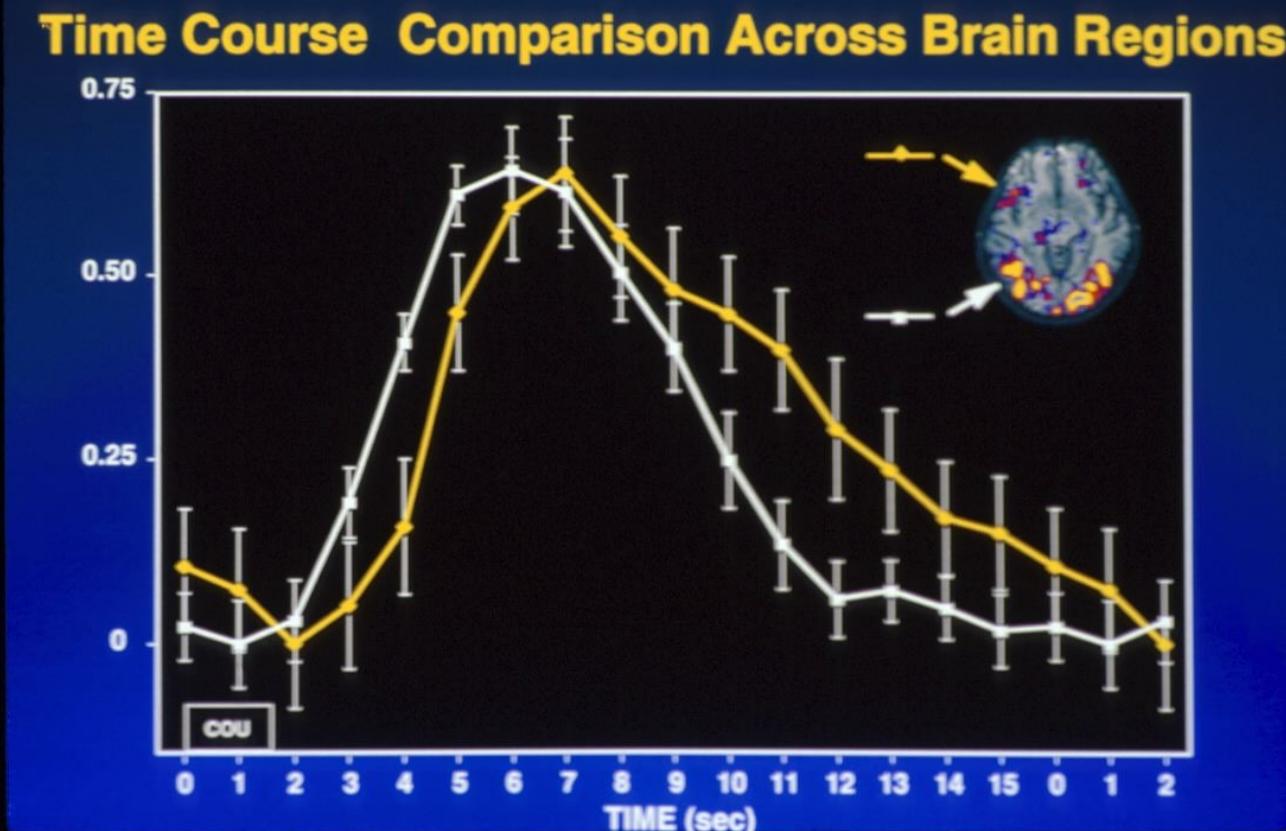
6. Orthogonal Design

7. Free Behavior Design

## 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>

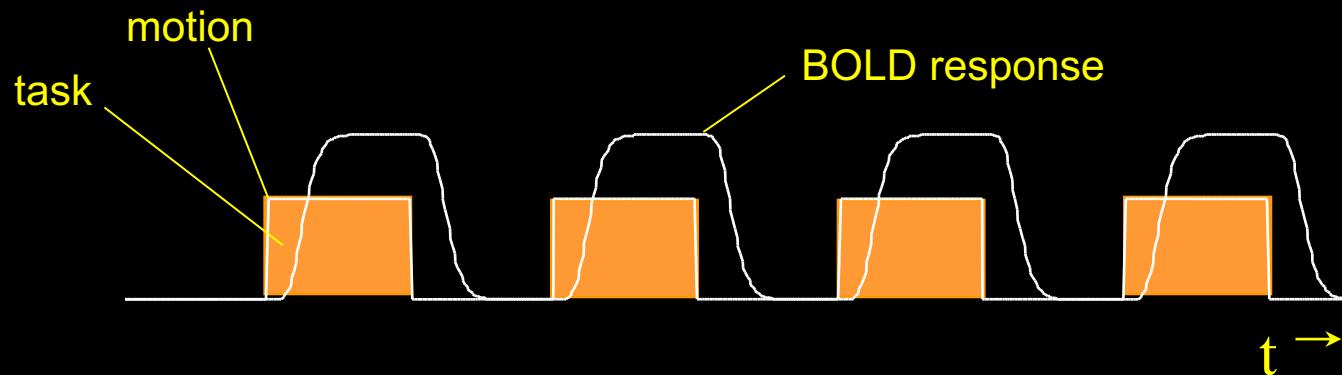


# Event Related Advantages

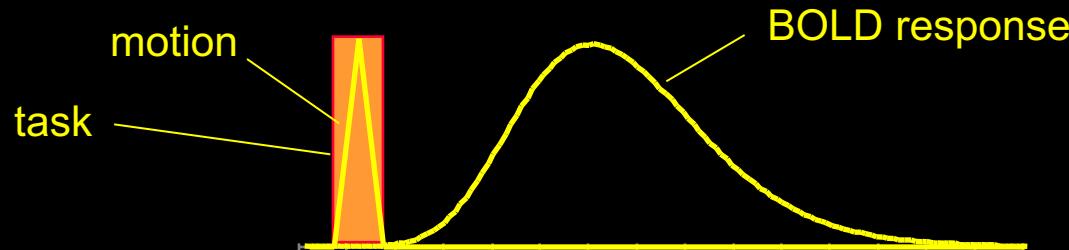
- Task Randomization
- Post acquisition, Performance-based, data binning
- Natural presentation
- Reduction of habituation effects
- Overt responses
- Reduction of scanner noise effects
- More precise estimation of hemodynamic responses

# fMRI during tasks that involve brief motion

## Blocked Design

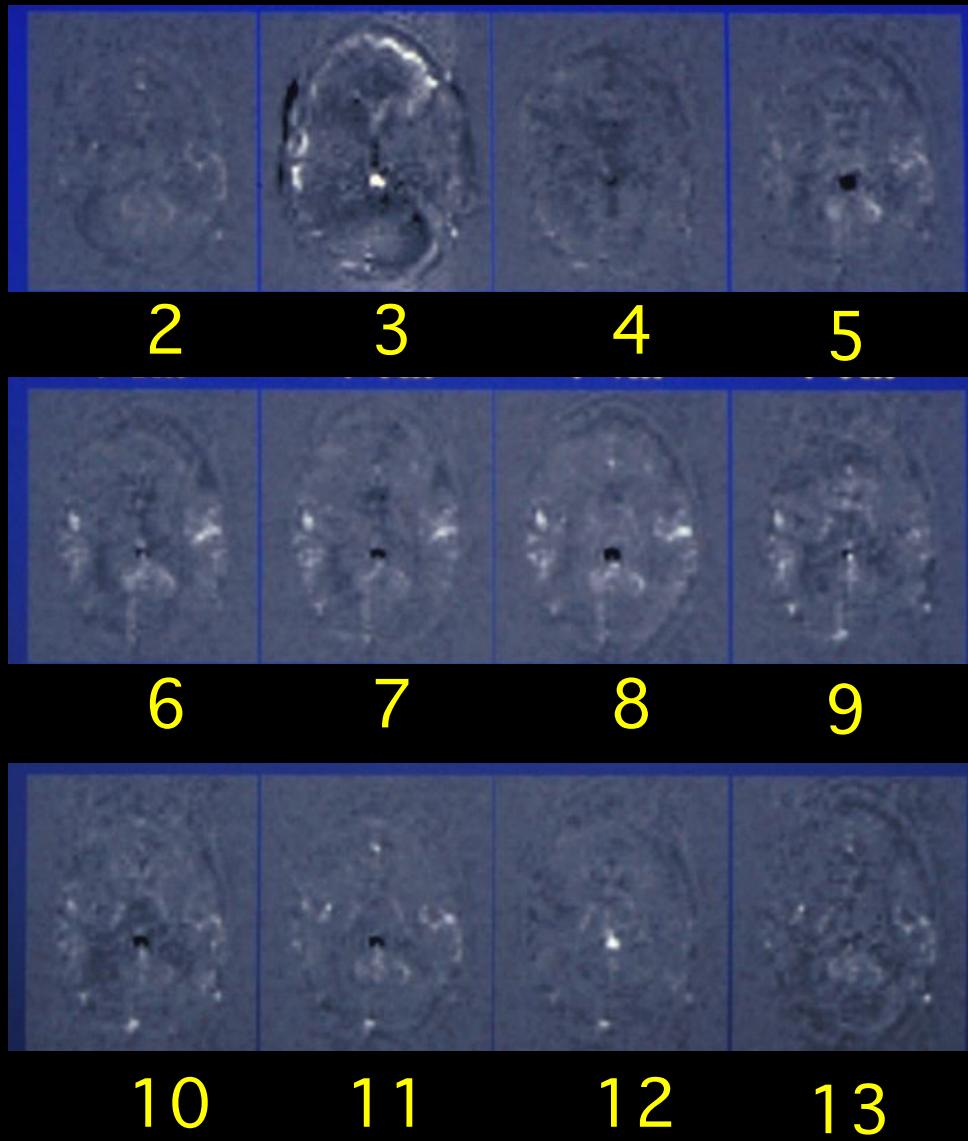


## Event-Related Design



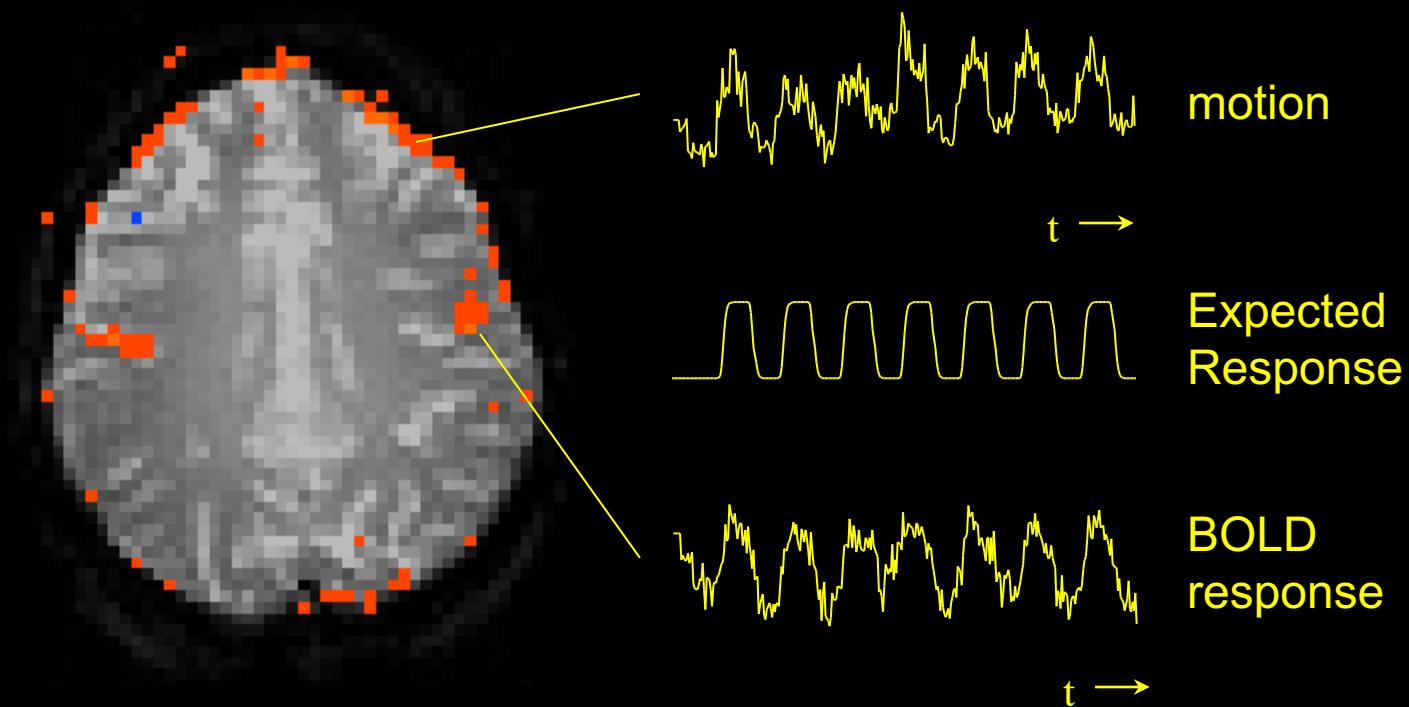
R. M. Birn, P. A. Bandettini, R. W. Cox, R. Shaker, Event - related fMRI of tasks involving brief motion. *Human Brain Mapping* 7: 106-114 (1999).

# Overt Word Production



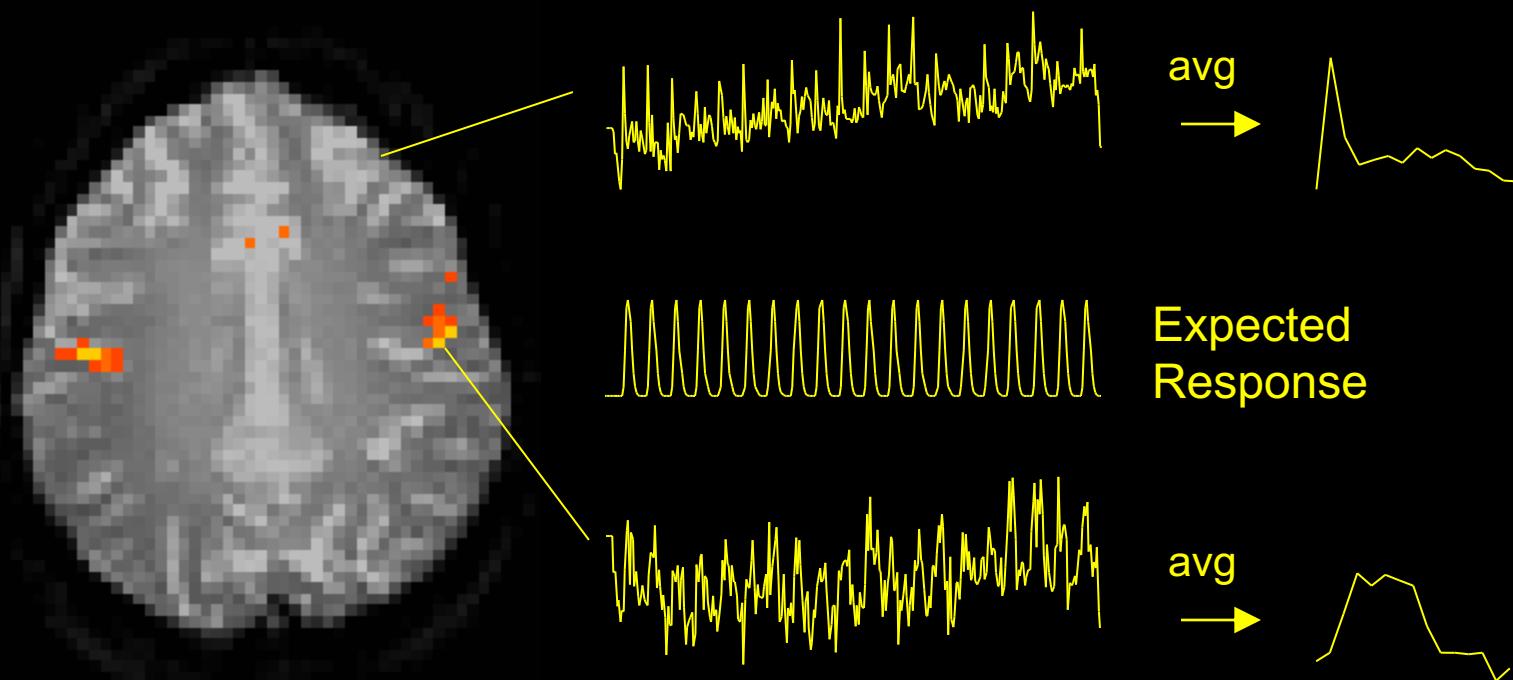
R. M. Birn, P. A. Bandettini, R. W. Cox, R. Shaker, Event - related fMRI of tasks involving brief motion. *Human Brain Mapping* 7: 106-114 (1999).

# Speaking - Blocked Trial



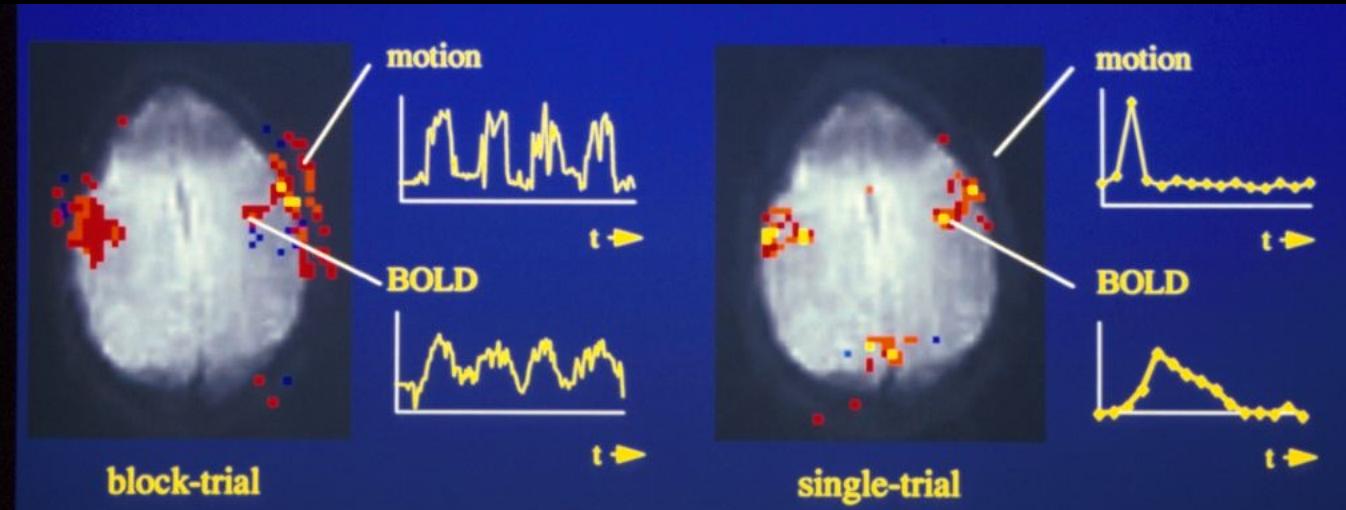
R. M. Birn, P. A. Bandettini, R. W. Cox, R. Shaker, Event - related fMRI of tasks involving brief motion. *Human Brain Mapping* 7: 106-114 (1999).

# Speaking - ER-fMRI

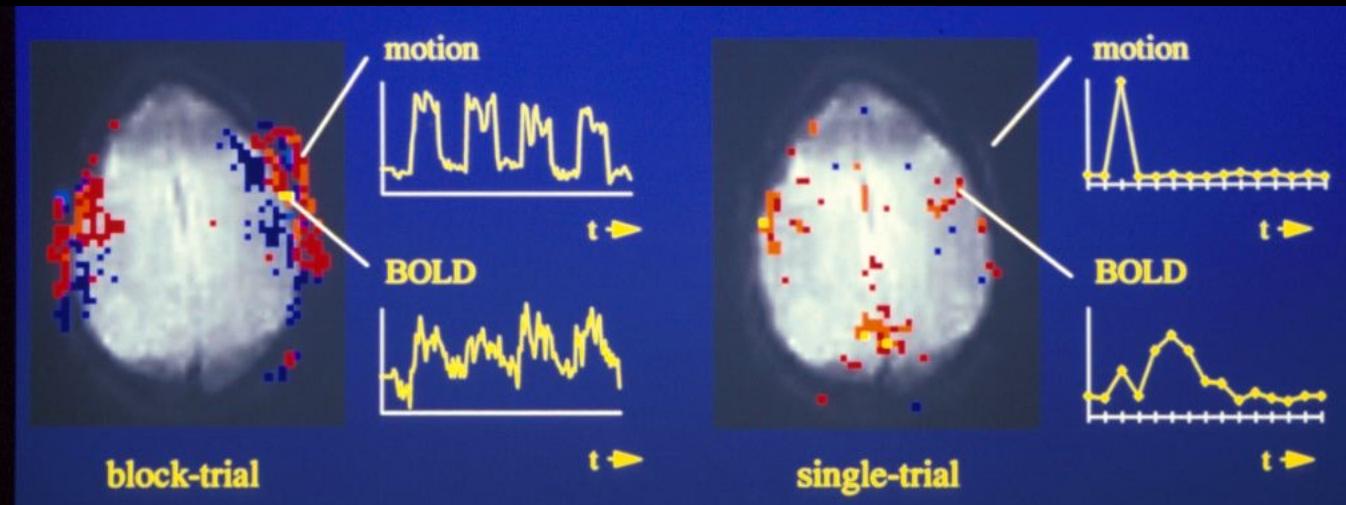


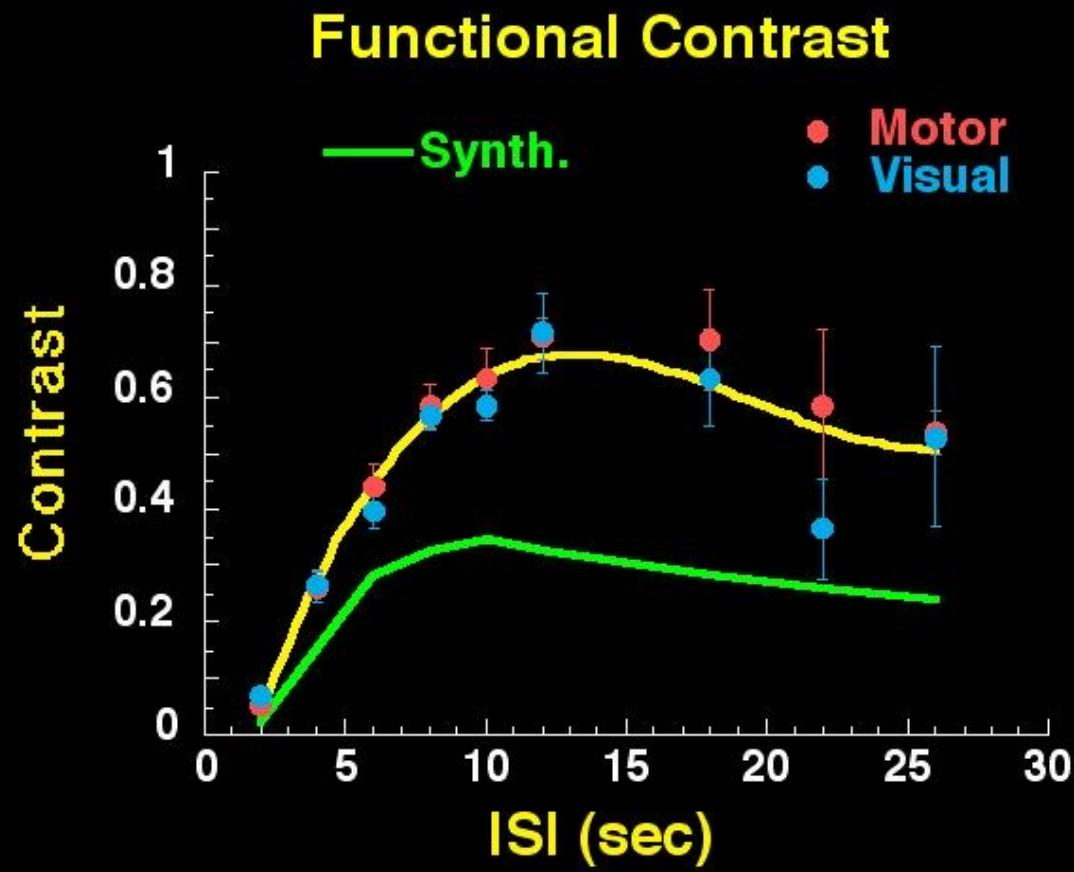
R. M. Birn, P. A. Bandettini, R. W. Cox, R. Shaker, Event - related fMRI of tasks involving brief motion. *Human Brain Mapping* 7: 106-114 (1999).

# Tongue Movement



# Jaw Clenching





( Block design = 1 )

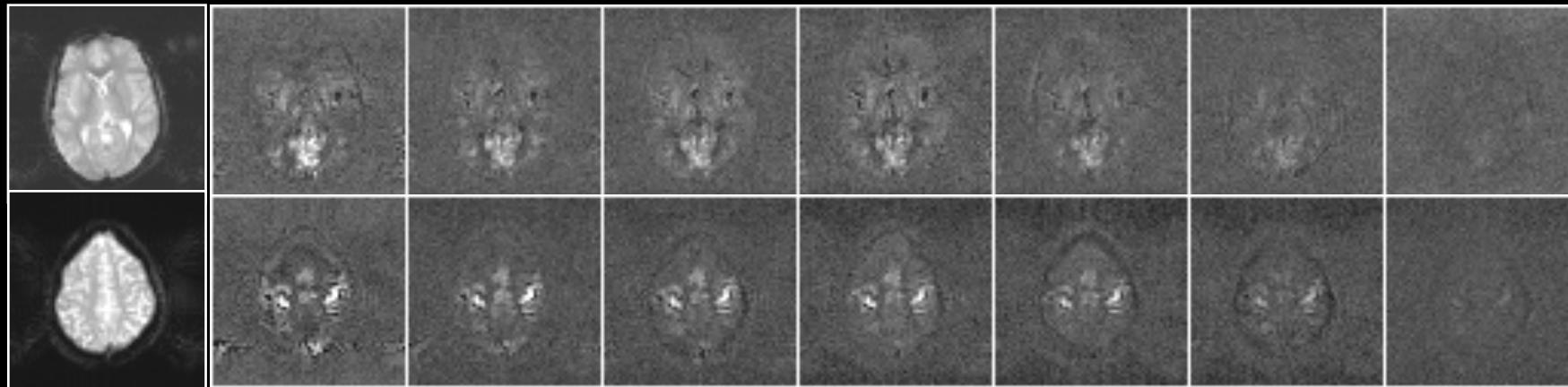
P. A. Bandettini, R. W. Cox. Functional contrast in constant interstimulus interval event - related fMRI: theory and experiment. *Magn. Reson. Med.* 43: 540-548 (2000).

# Contrast to Noise Images

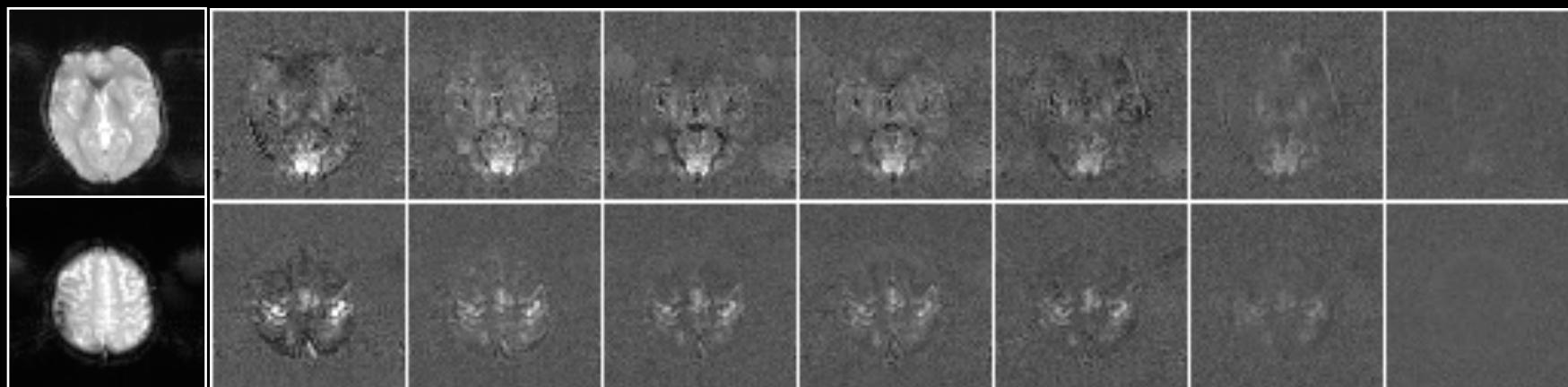
( ISI, SD )

20, 20    12, 2    10, 2    8, 2    6, 2    4, 2    2, 2

S1



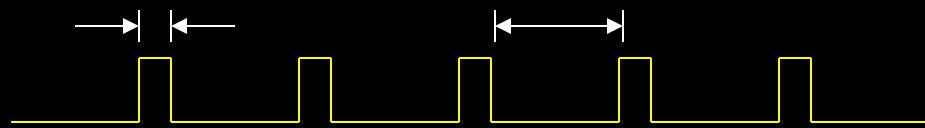
S2



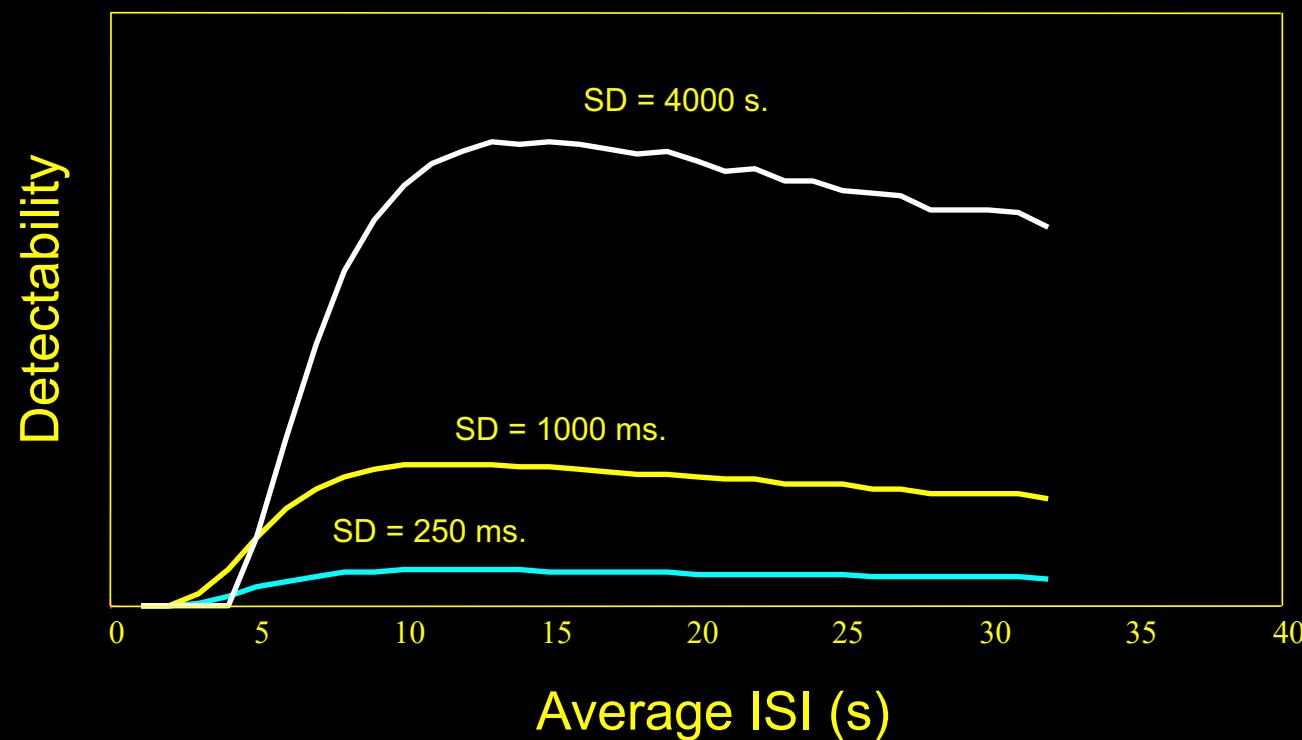
P. A. Bandettini, R. W. Cox. Functional contrast in constant interstimulus interval event - related fMRI: theory and experiment. *Magn. Reson. Med.* 43: 540-548 (2000).

# Detectability – constant ISI

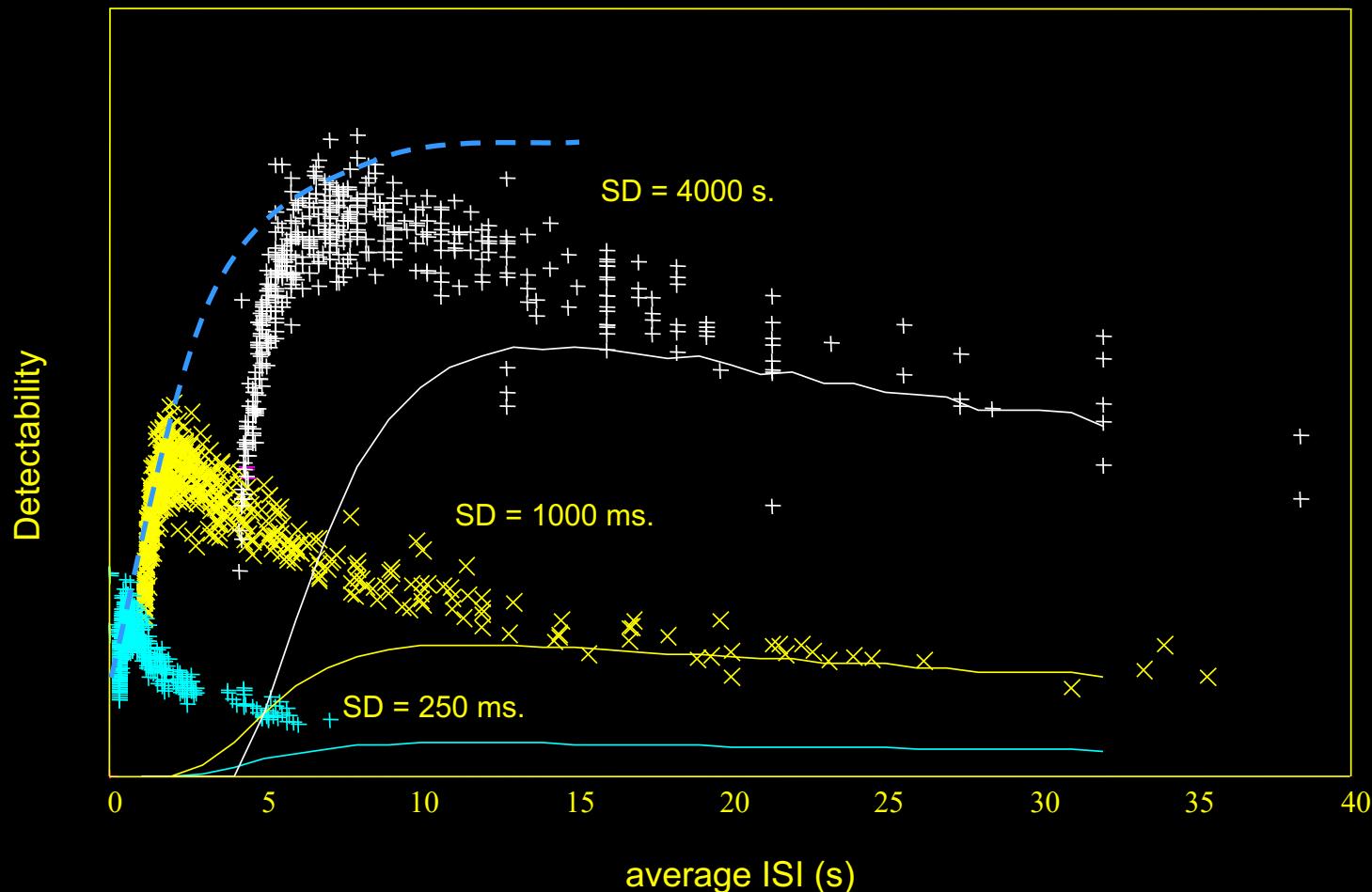
SD – stimulus duration



ISI – inter-stimulus interval

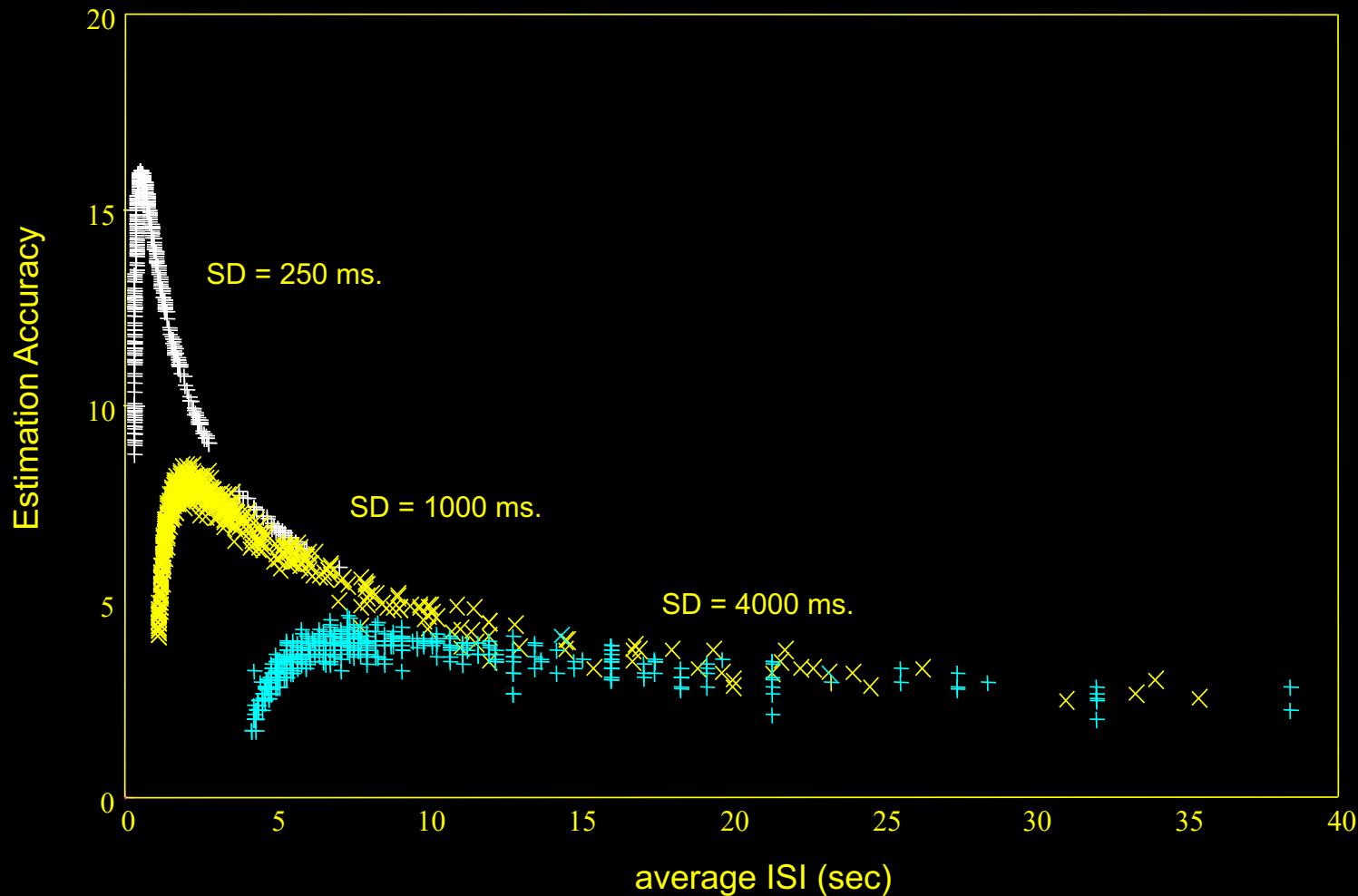


# Detectability vs. Average ISI



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).

# Varying “ON” and “OFF” periods

- *Rapid event-related design with varying ISI*



8% ON



25% ON

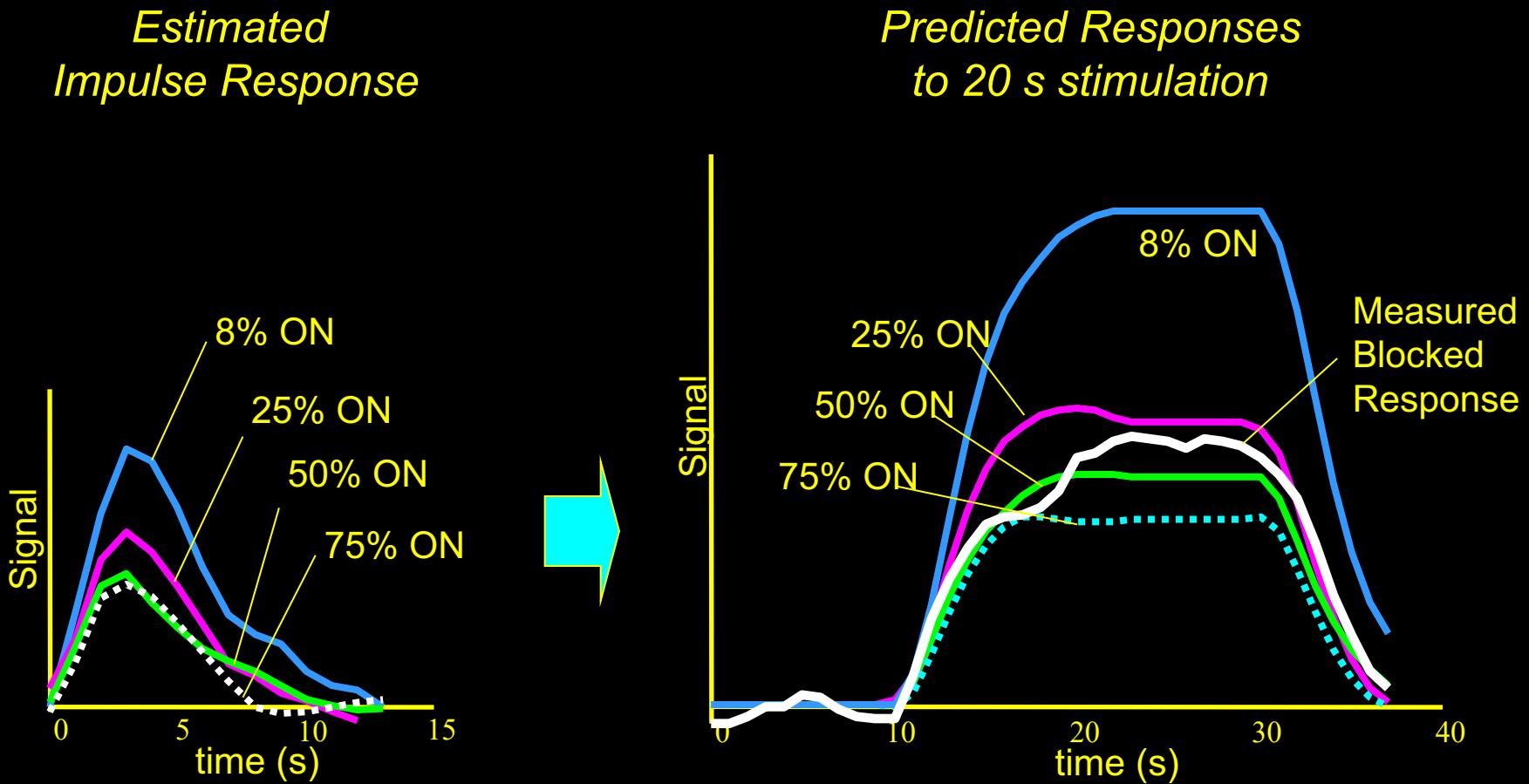


50% ON



75% ON

# Varying “ON” and “OFF” periods

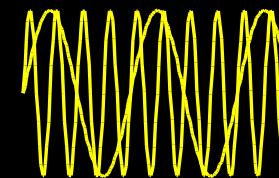


# Neuronal Activation Input Strategies

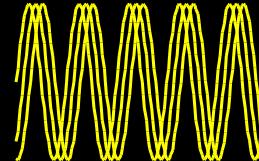
1. Block Design



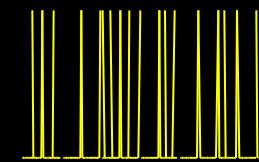
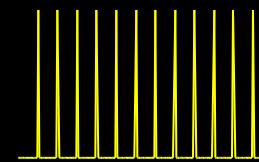
2. Parametric Design



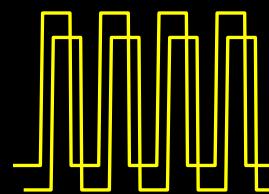
3. Frequency Encoding



4. Phase Encoding



5. Event Related



6. Orthogonal Design

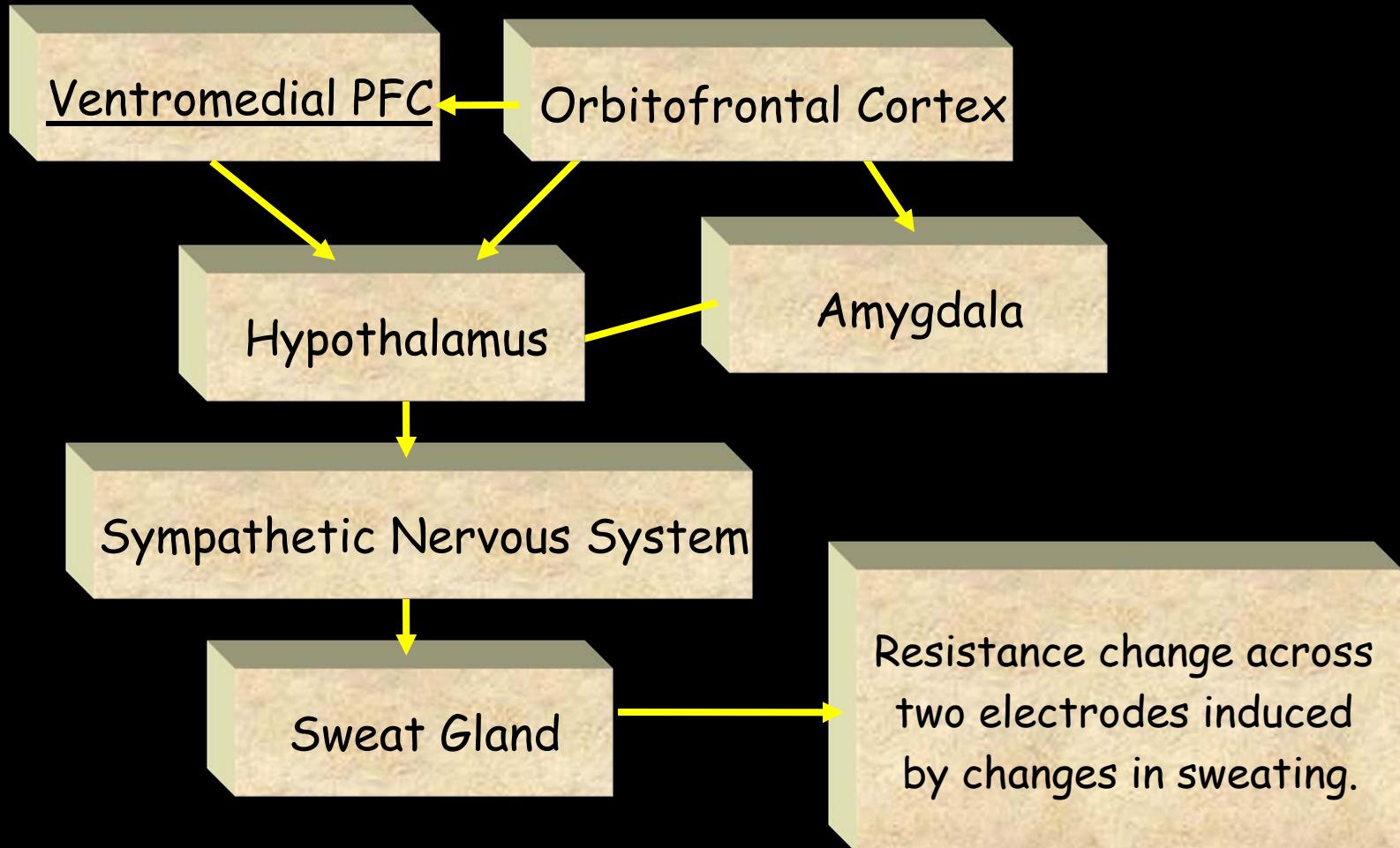
7. Free Behavior Design

# Free Behavior Design

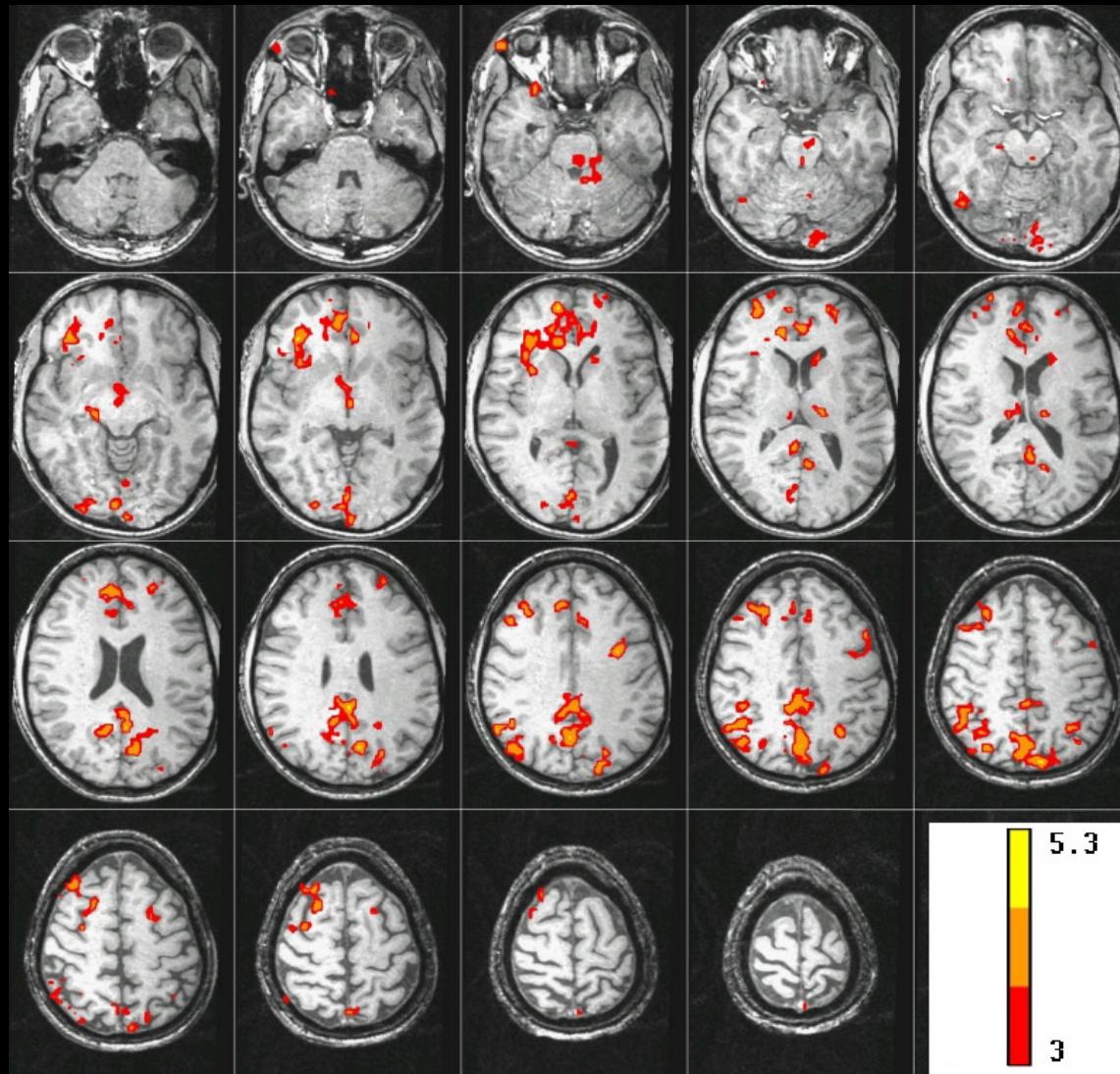
Use a continuous measure as a reference function:

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

# The Skin Conductance Response (SCR)



# Brain activity correlated with SCR during “Rest”

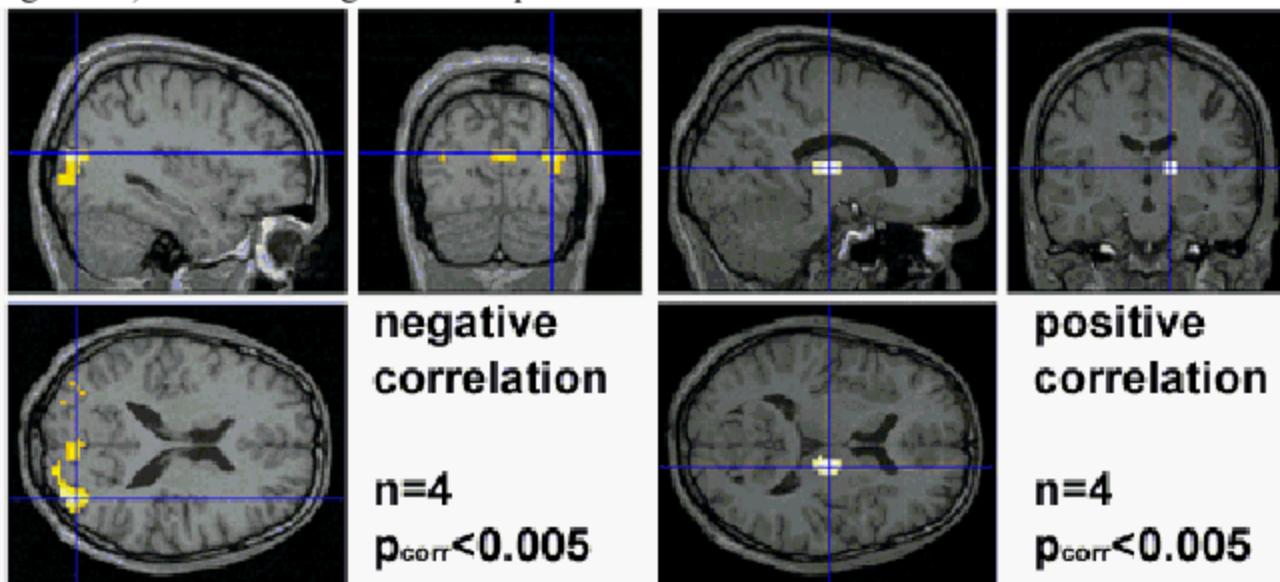


J. C. Patterson II, L. G. Ungerleider, and P. A. Bandettini, Task - independent functional brain activity correlation with skin conductance changes: an fMRI study. *NeuroImage* (in press)

## 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

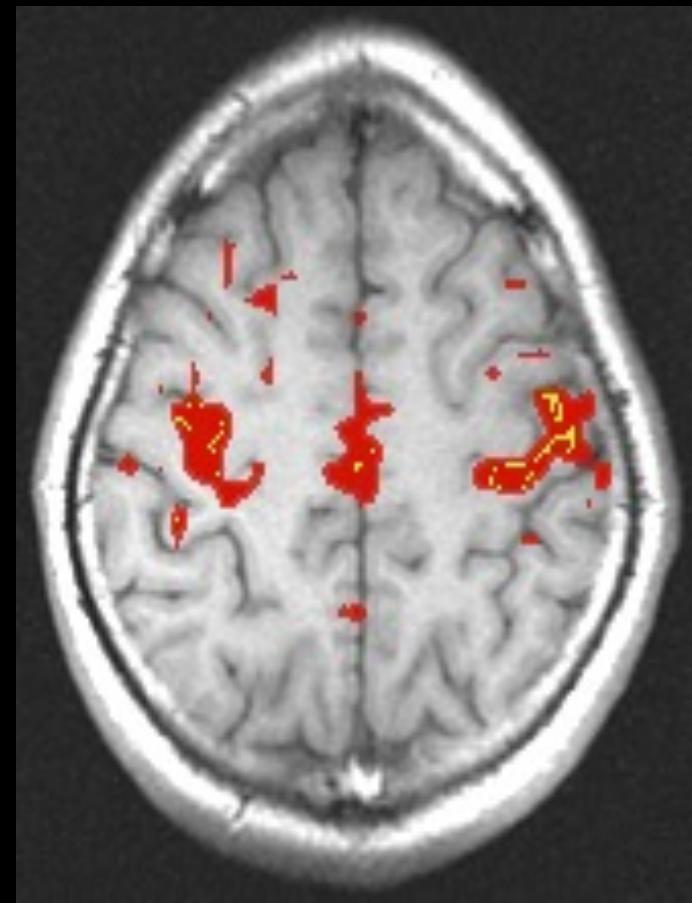
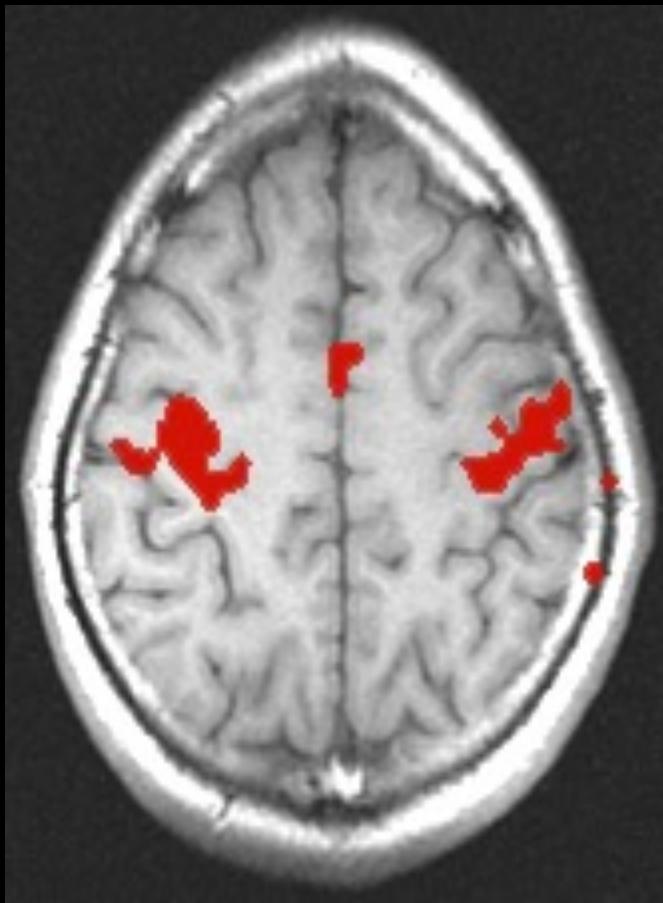
The group analysis based on four volunteers showed a negative correlation between alpha-power and fMRI signal in the occipital cortex (figure, left side) and a positive correlation in the thalamus (figure, right side). These findings were not present for the beta band.



### 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).

# Resting Hemodynamic Autocorrelations



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

# Where Are We Going?

- Interpretation
- Temporal Resolution
- Spatial Resolution

- Interpretation
- Temporal Resolution
- Spatial Resolution

# $\Delta$ Neuronal Activity

Number of Neurons  
Local Field Potential  
Spiking Coherence  
Spiking Rate

# $\Delta$ Metabolism

Aerobic Metabolism

Anaerobic Metabolism

Blood Volume

Deoxygenated Blood

Oxygenated Blood

Flow Velocity

Perfusion

# $\Delta$ Hemodynamics

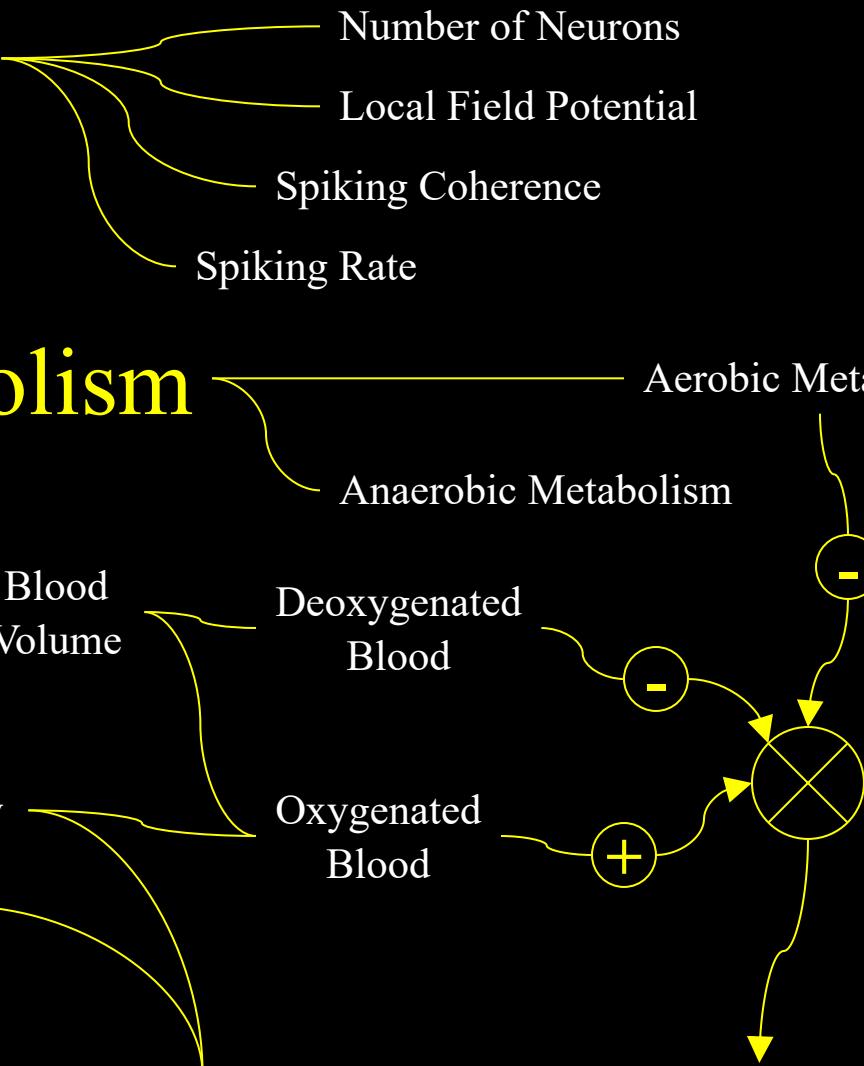
$\Delta$  BOLD Contrast

$\Delta$  Perfusion Contrast

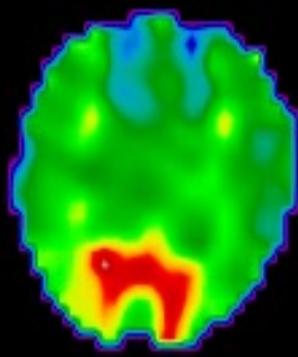
$\Delta$  Inflow Contrast

MRI Pulse Sequence

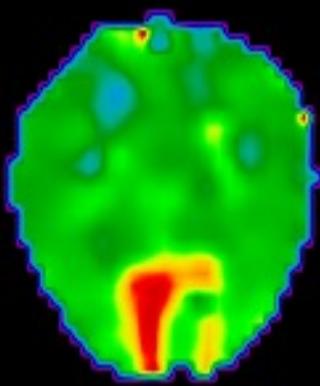
$\Delta$  Deoxy-Hb



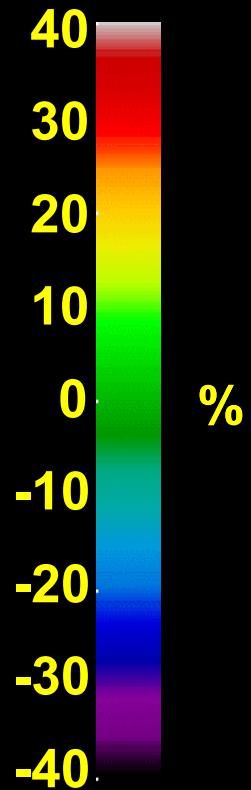
# Computed CMRO<sub>2</sub> Changes



**Subject 1**



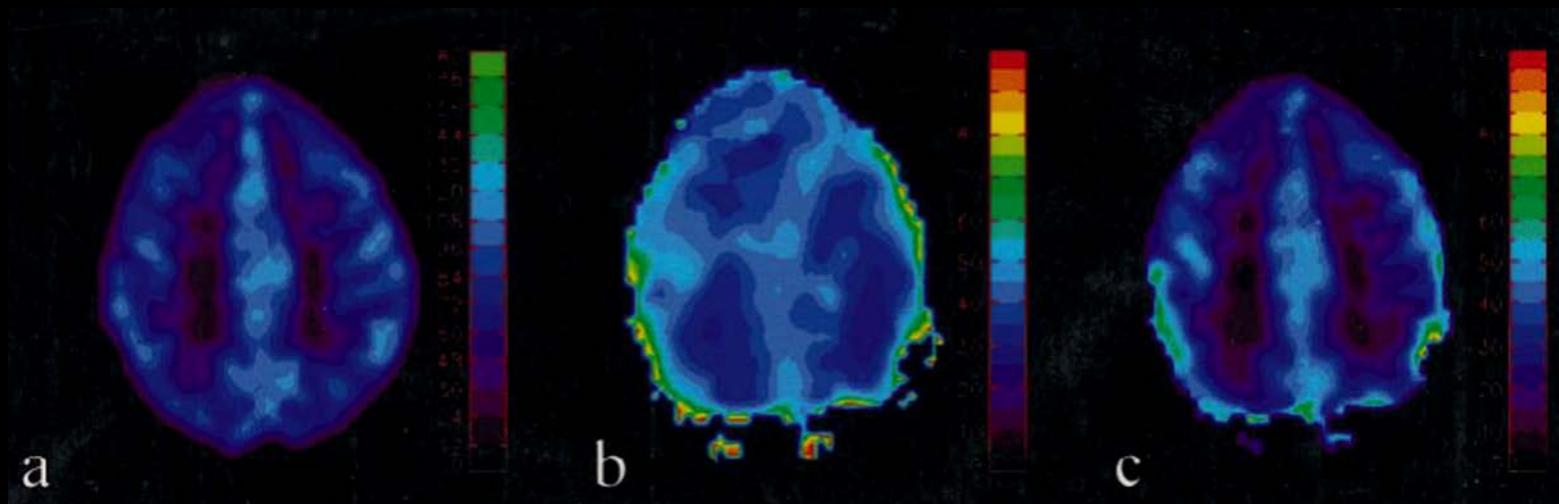
**Subject 2**



%

## 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>



CBF

OEF

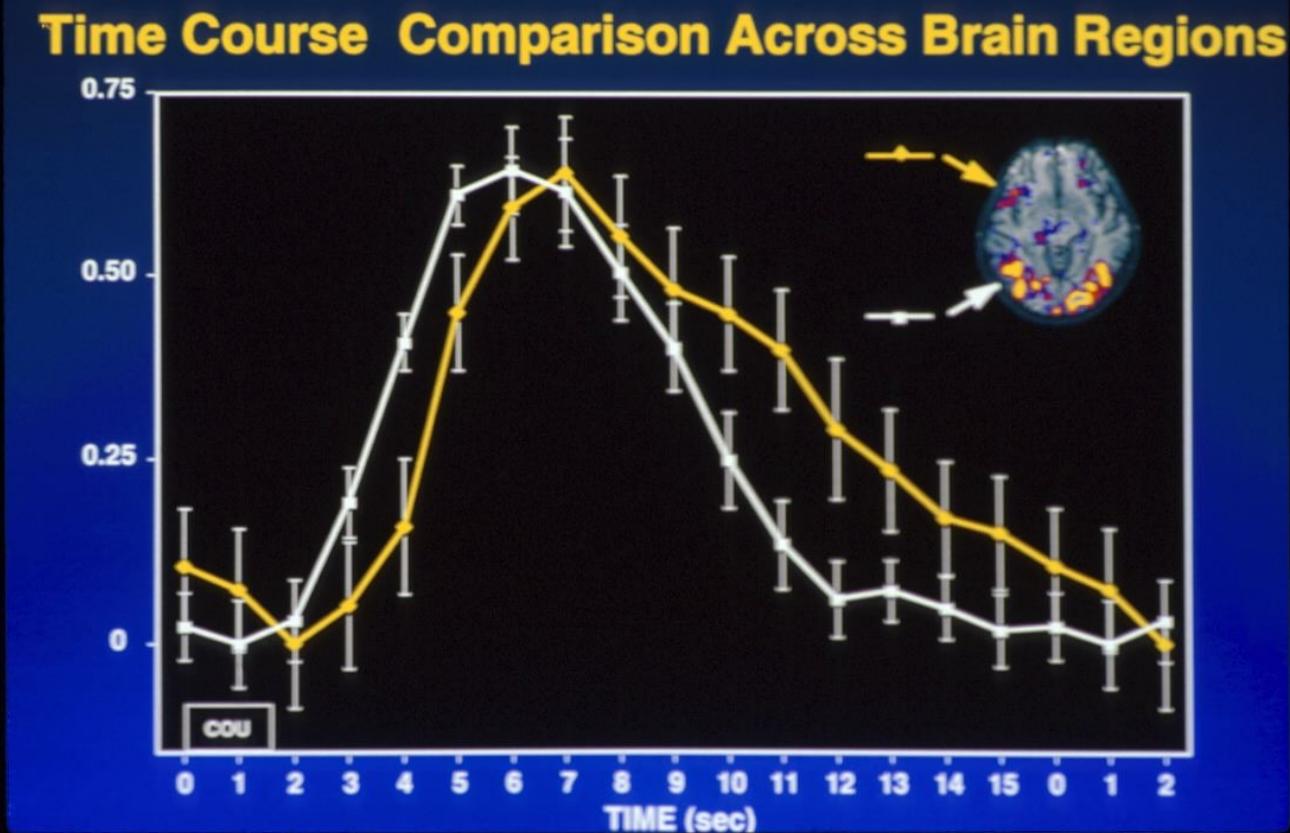
CMRO<sub>2</sub>

- Interpretation
- Temporal Resolution
- Spatial Resolution

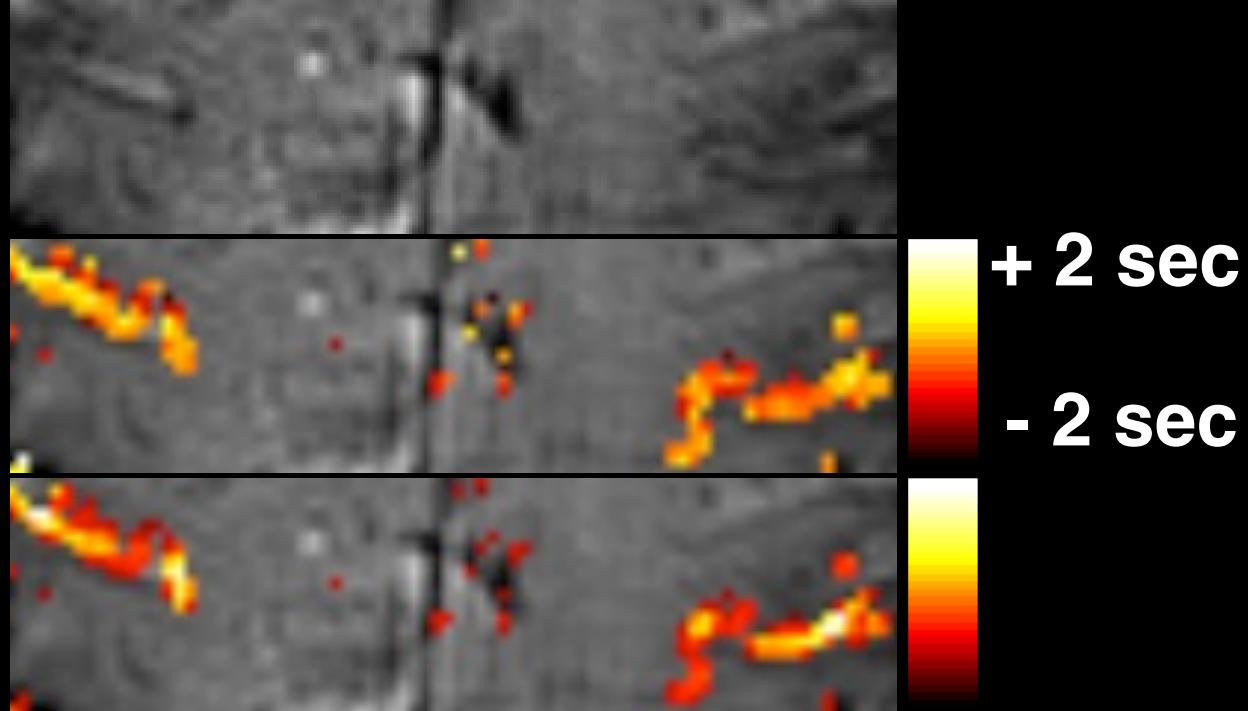
## Detection of cortical activation during averaged single trials of a cognitive task using functional magnetic resonance imaging

(neuroimaging/single trial/language/prefrontal)

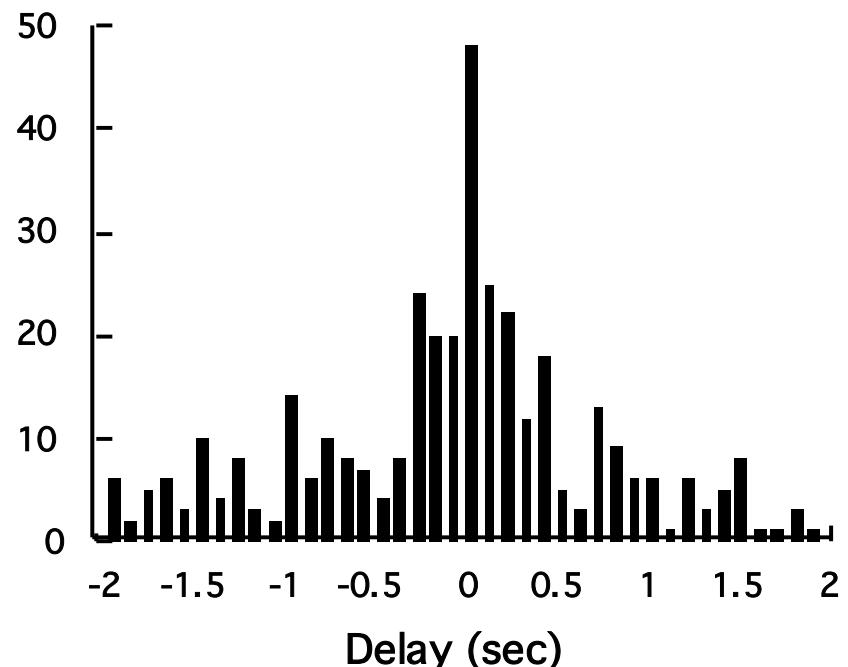
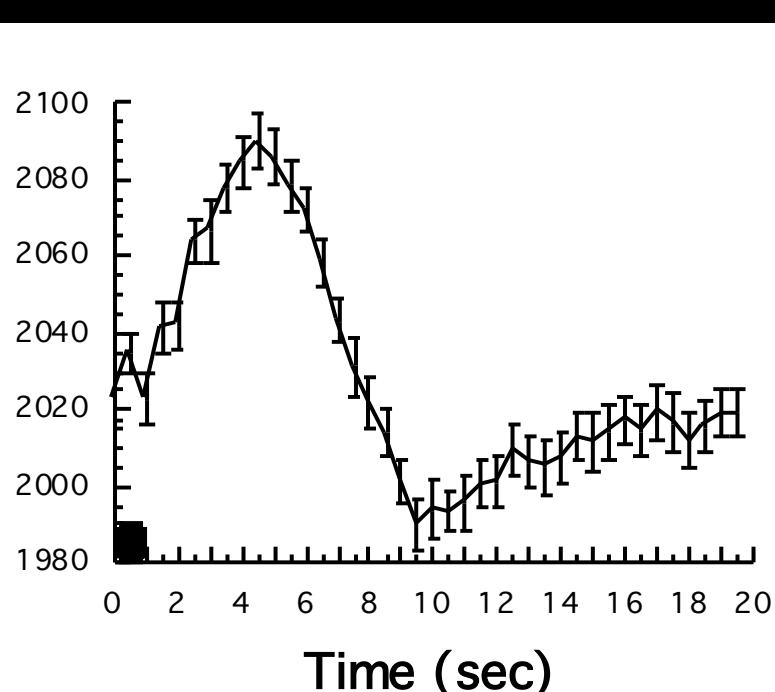
RANDY L. BUCKNER<sup>†‡§¶||</sup>, PETER A. BANDETTINI<sup>†‡</sup>, KATHLEEN M. O'CRAVEN<sup>†||</sup>, ROBERT L. SAVOY<sup>†||</sup>,  
STEVEN E. PETERSEN<sup>\*++††</sup>, MARCUS E. RAICHLE<sup>§++††</sup>, AND BRUCE R. ROSEN<sup>†‡</sup>



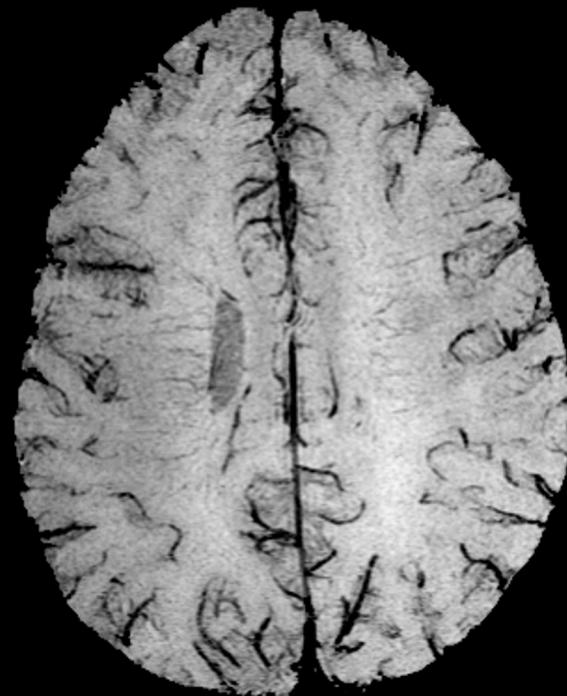
# Latency

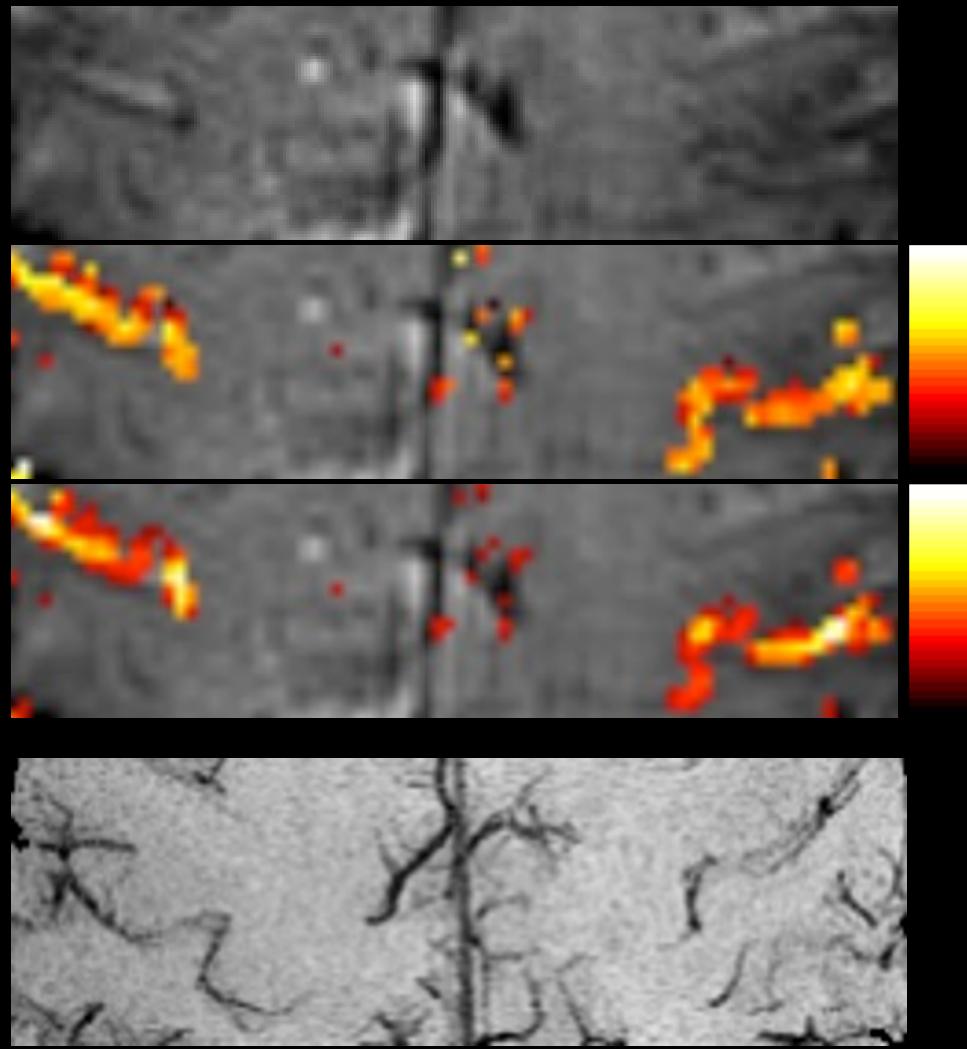


# Magnitude



# Venograms (3T)

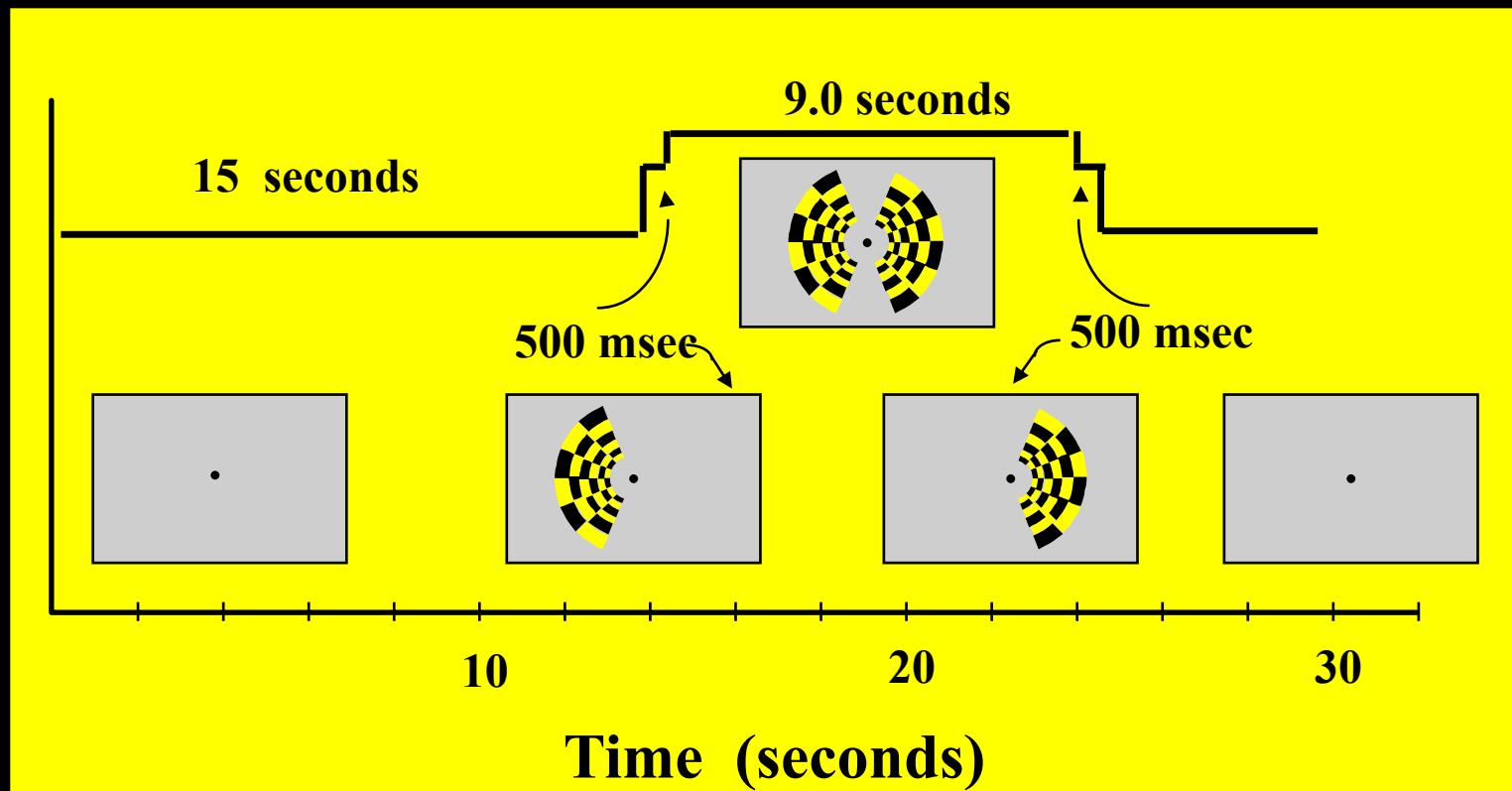


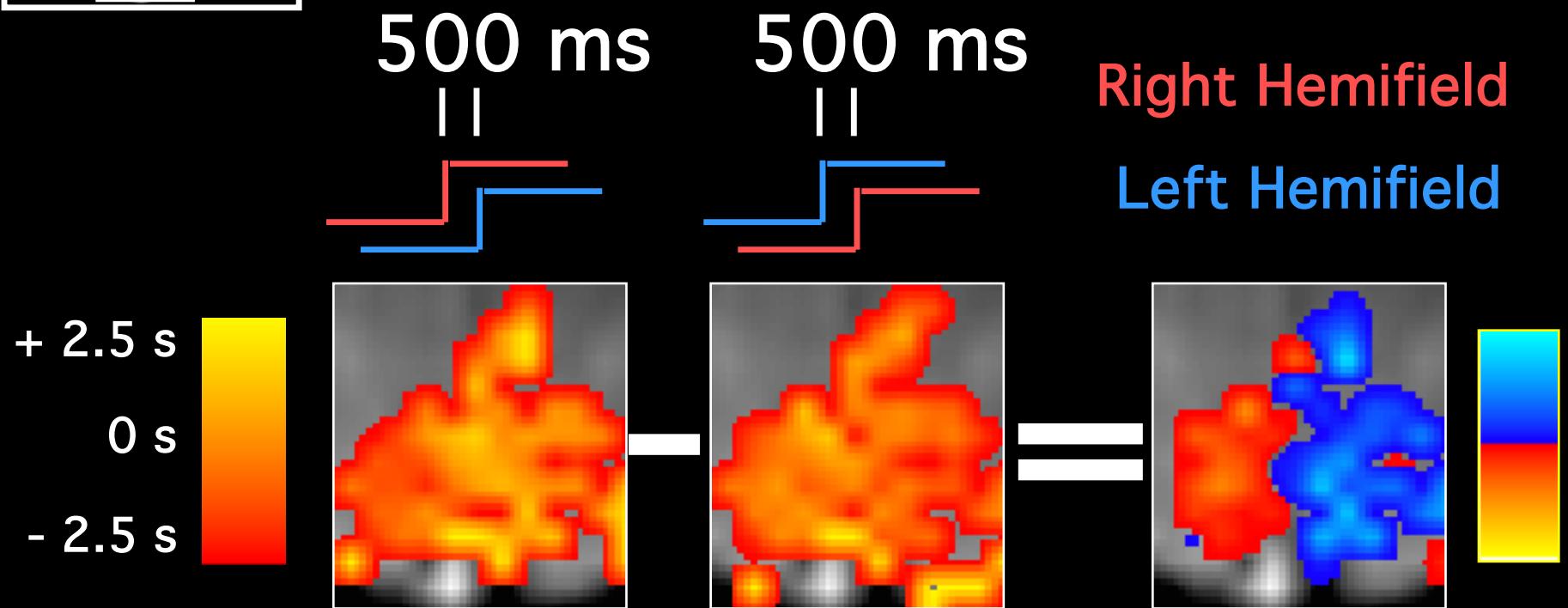
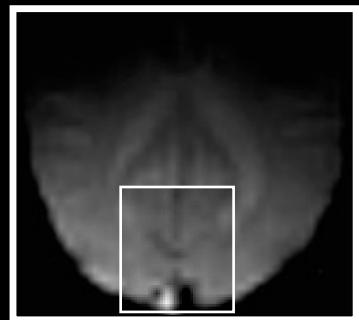


# Hemi-Field Experiment

**Left  
Hemisphere**

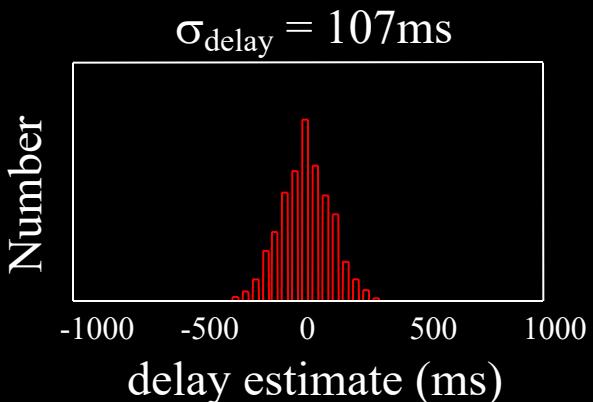
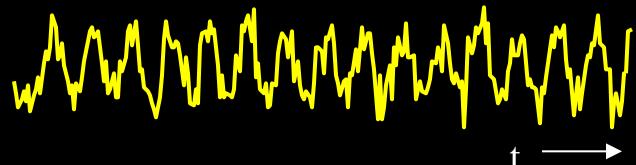
**Right  
Hemisphere**



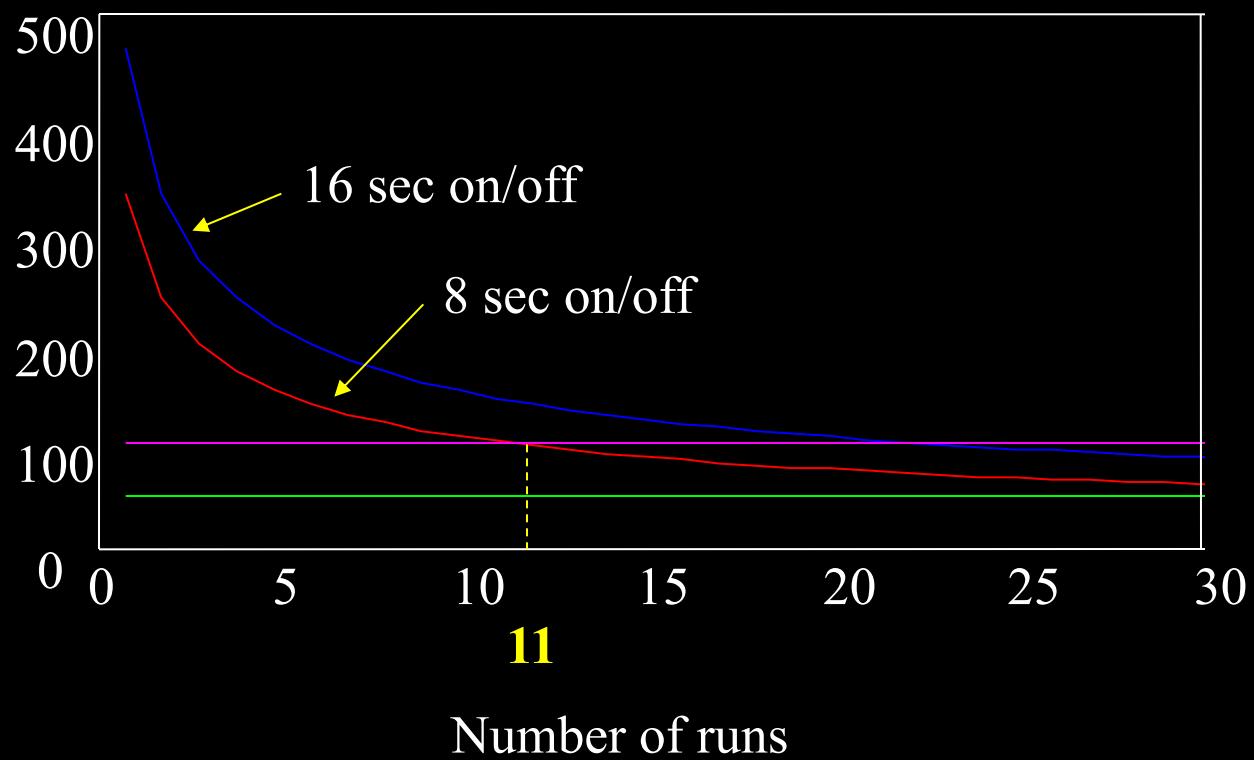


1 run:

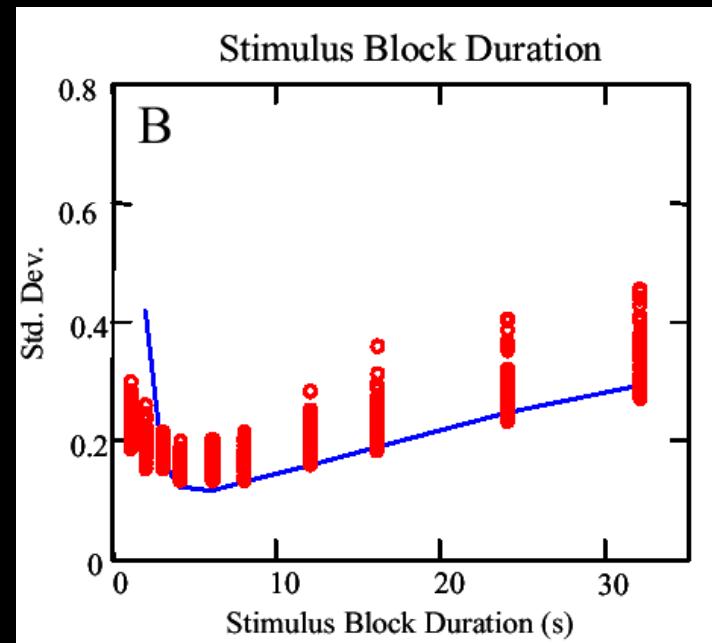
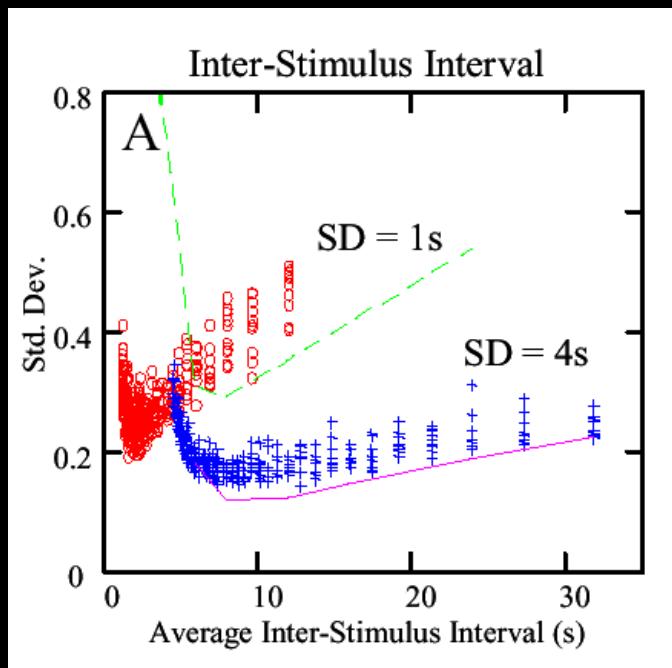
1% Noise  
4% BOLD  
256 time pts /run  
1 second TR



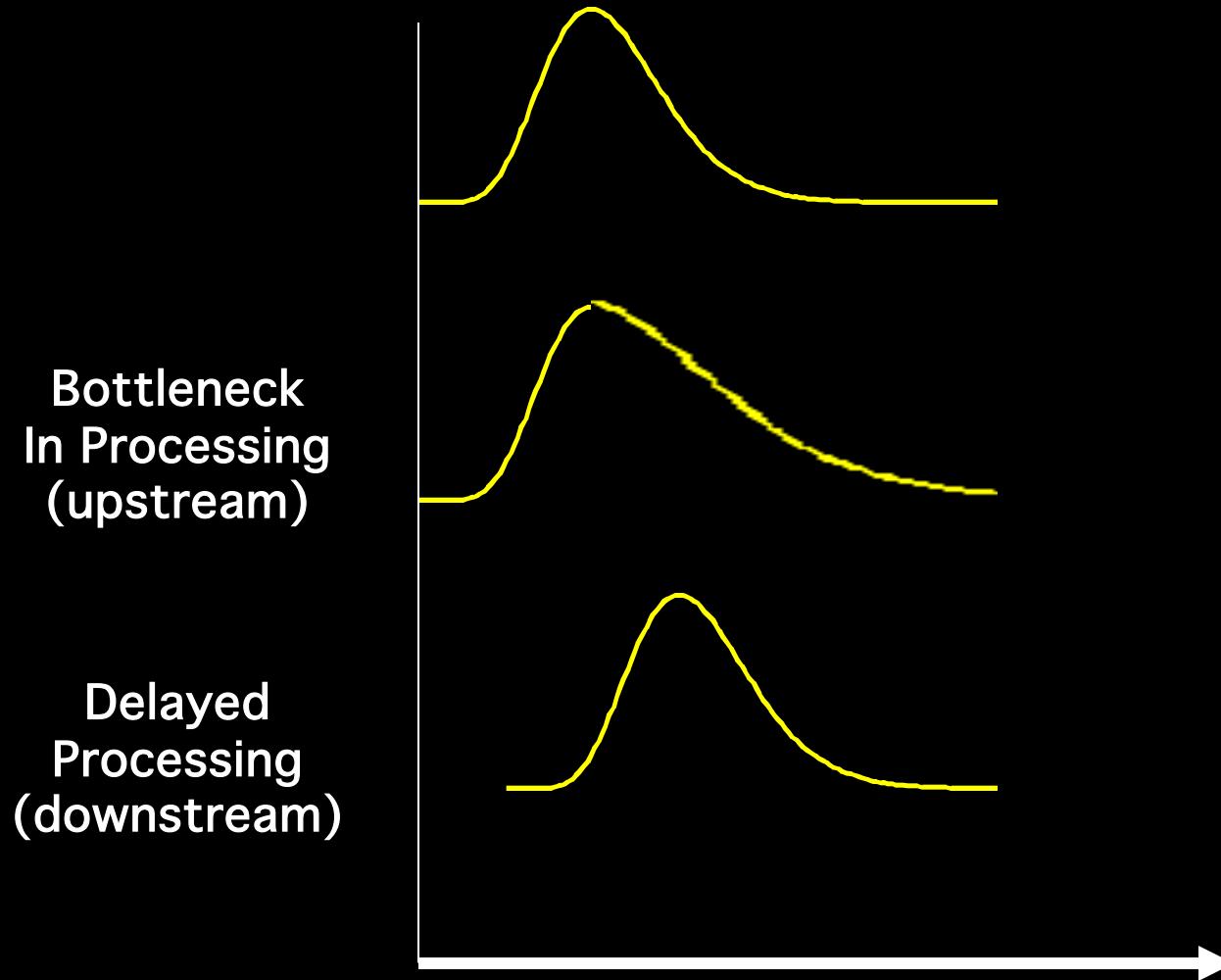
Smallest latency  
Variation Detectable  
(ms) ( $p < 0.001$ )



# Optimal Detection of Hemodynamic Latency



## Hemodynamic Response Modulation



# Use of Task Timing Modulation to Extract Processing Streams

Stimuli - Six-letter English words and pronounceable non-words.

Each word or non-word was rotated either 0, 60, or 120 degrees

Task - Lexical Decision (word / non-word).

Dependent Measures - Percent Correct and Reaction Time.

Hypotheses :

1) **Stimulus rotation of 120 degrees will result in:**

- a) Longer Reaction Times
- b) Stimulus rotation demands a change in perceptual perspective prior to linguistic processing. This will result in a delayed IRF onset in areas involved in Lexical and Pre-Lexical processing.

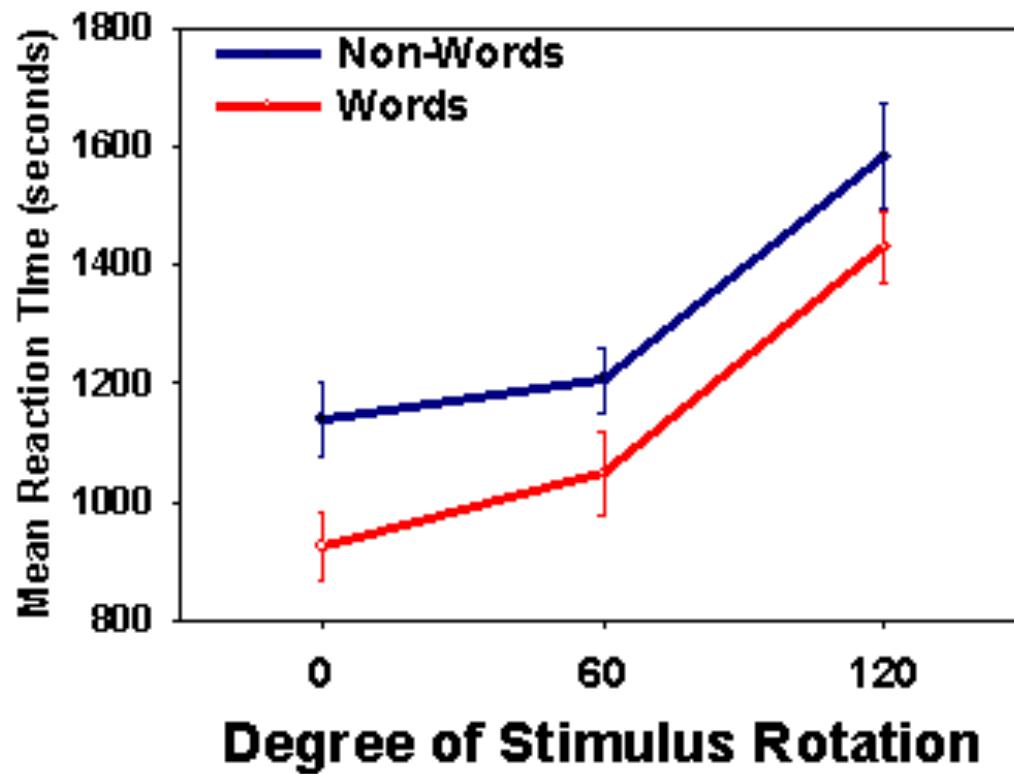
2) **Lexical discrimination will result in :**

- a) Longer Reaction Times for non-words due to increased Pre-Lexical processing demands.
- b) Wider IRF in Inferior Frontal cortex for non-words
- c) Delayed IRF onset in Left Middle Frontal Cortex

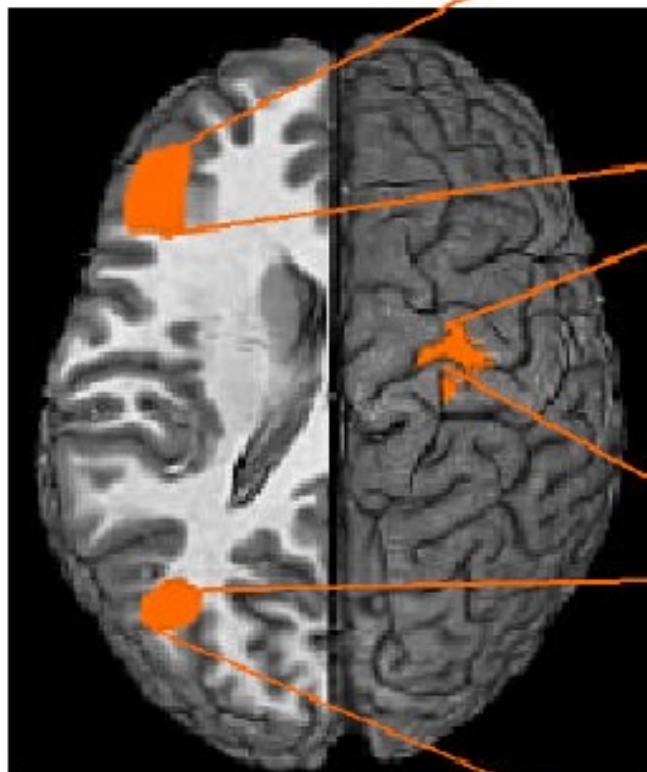
# Lexical Delay

Words	Non-Words	Mean Reaction Time
smudge	dierts	823 ms
frolic	cuhlos	891 ms
slooch	gdeamus	1446 ms
Mean Reaction Time	986 ms	1219 ms

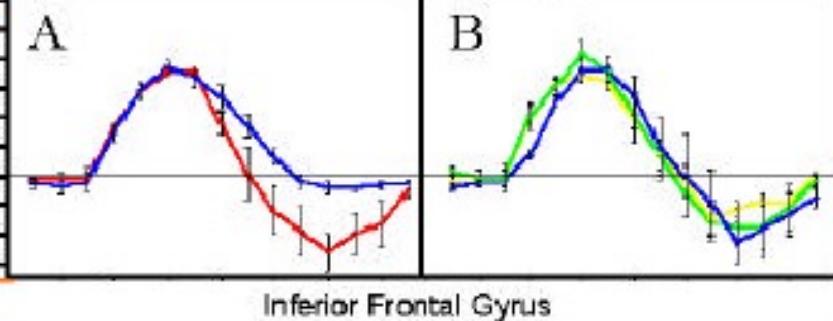
### **Response Times for each Stimulus Type**



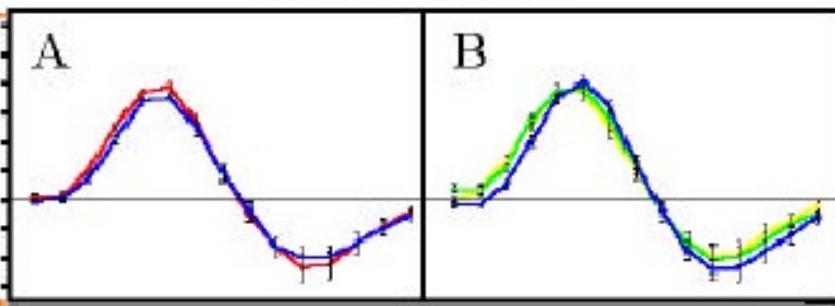
### Regions of Interest



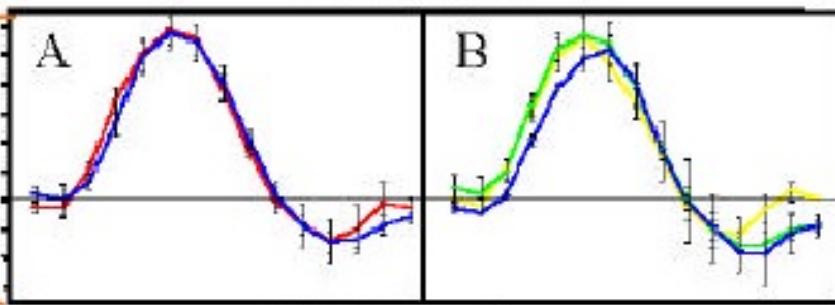
Word vs. Non-word 0°, 60°, 120° Rotation



Inferior Frontal Gyrus

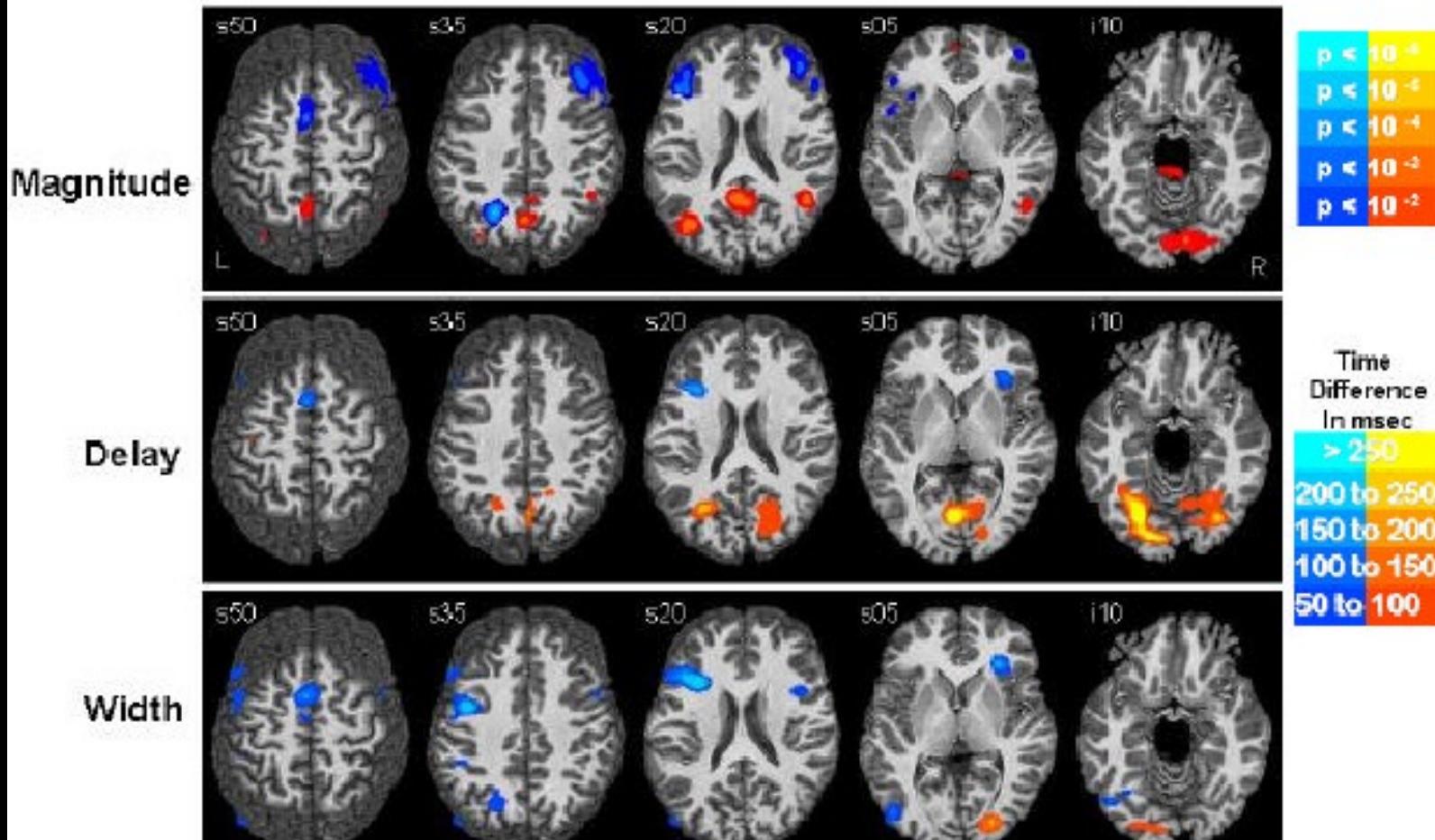


Precentral Gyrus



Middle Temporal Gyrus

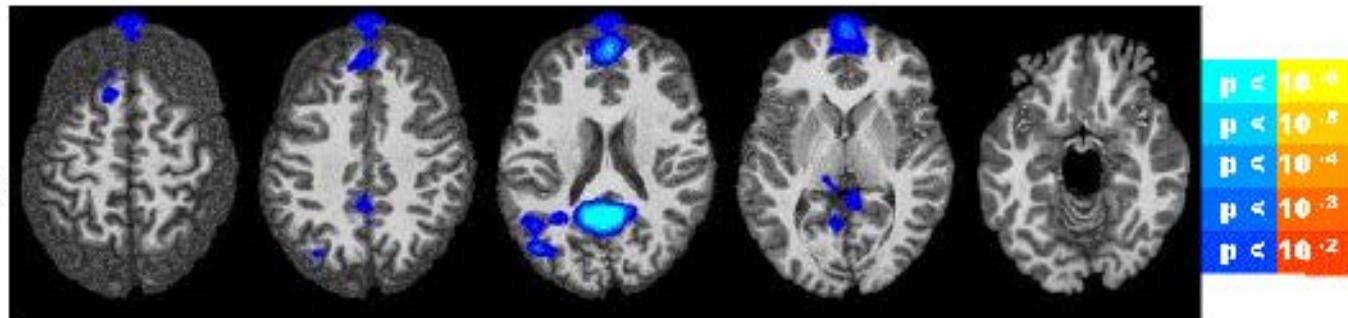
## Lexical effect maps



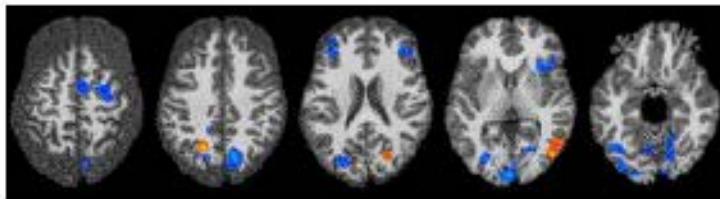
Warm colors are areas where Words > Non-words. Cool colors (blues) are areas where Non-words > words.

## Rotational effect maps

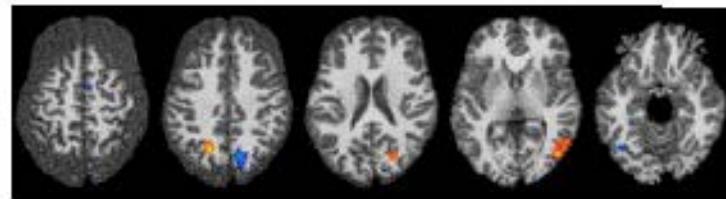
Magnitude



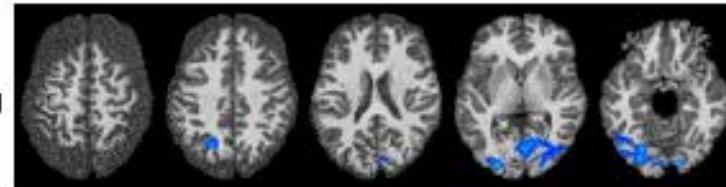
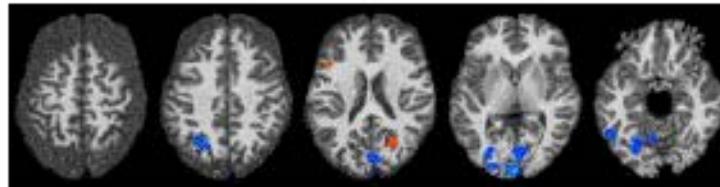
Non-rotated vs. 120° rotated



Delay

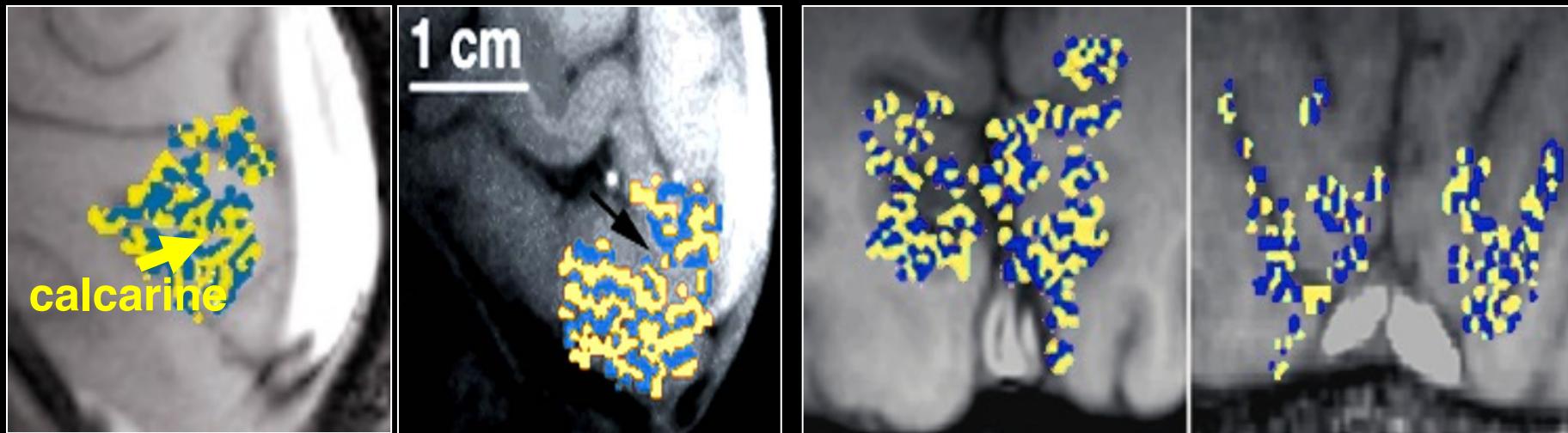


Width

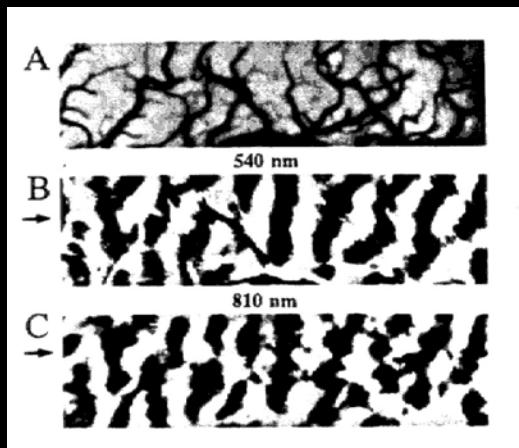


- Interpretation
- Temporal Resolution
- **Spatial Resolution**

# Ocular Dominance Column Mapping using fMRI

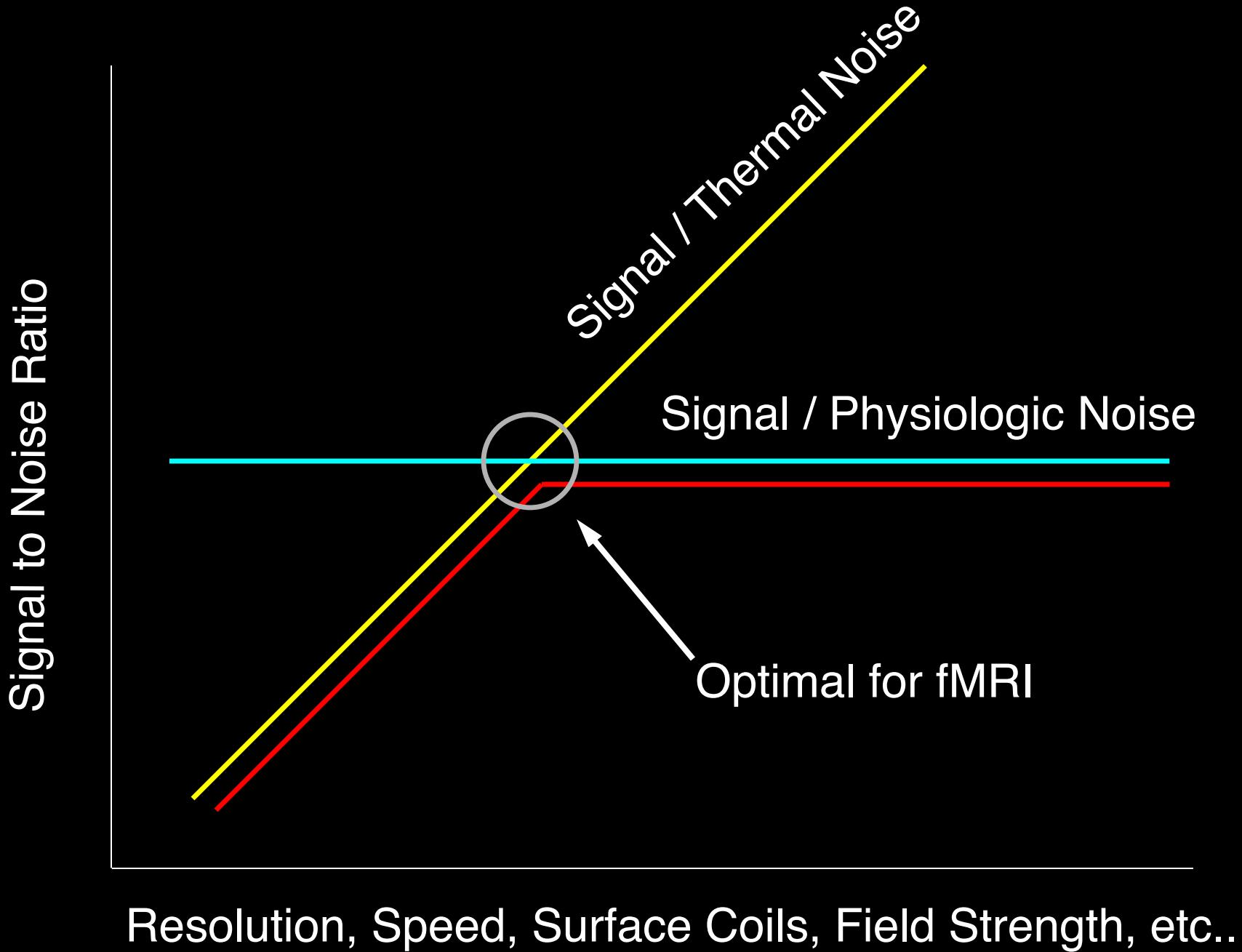


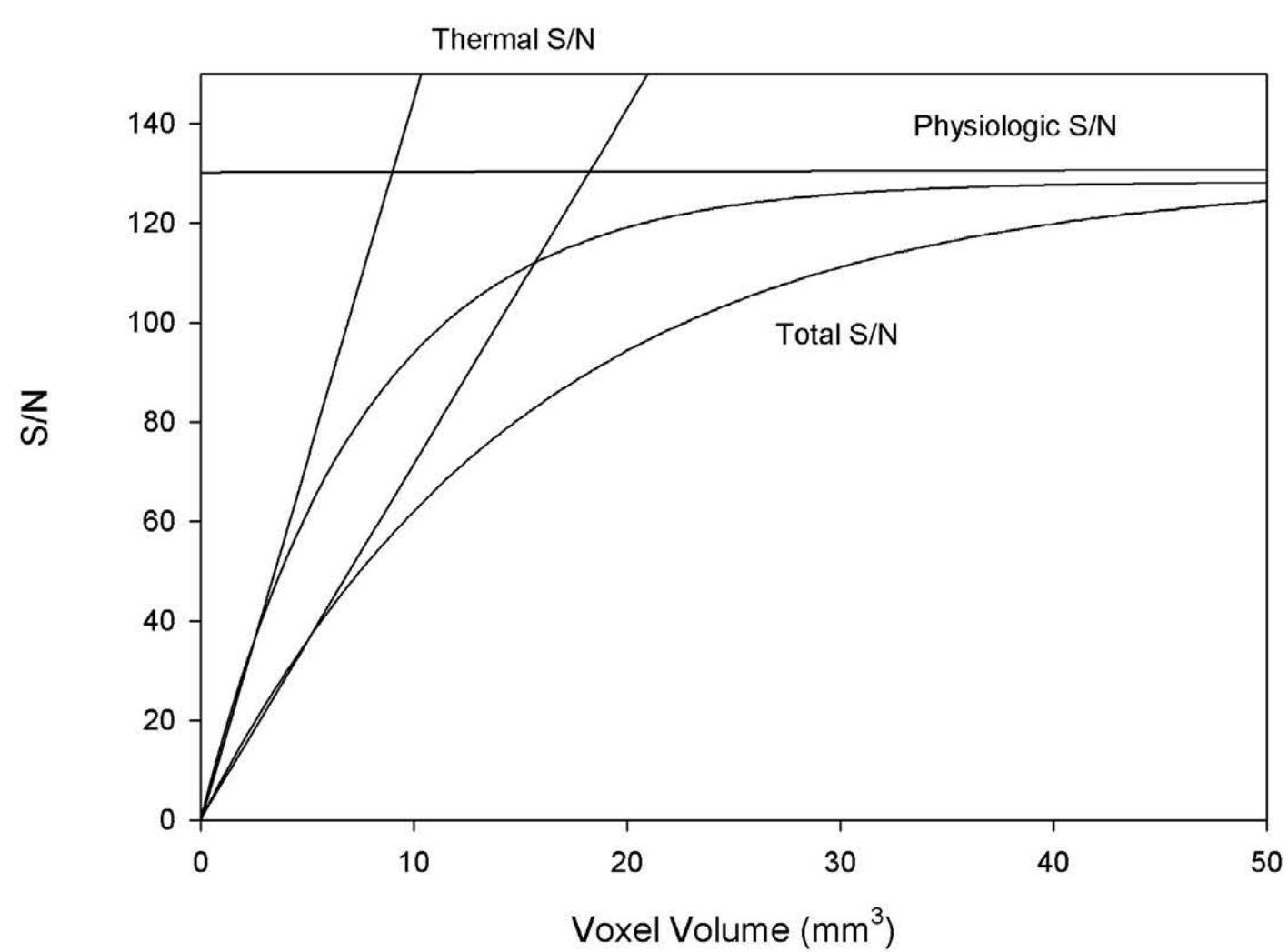
Menon, R. S., S. Ogawa, et al. (1997). "Ocular dominance in human V1 demonstrated by functional magnetic resonance imaging." *J Neurophysiol* 77(5): 2780-7.



Optical Imaging

R. D. Frostig et. al, PNAS 87: 6082-6086, (1990).





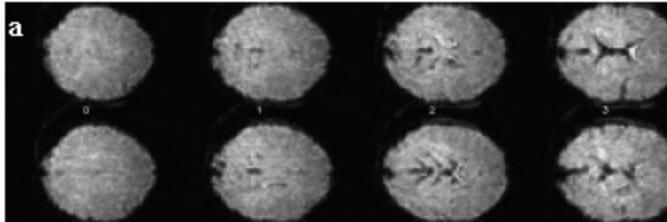
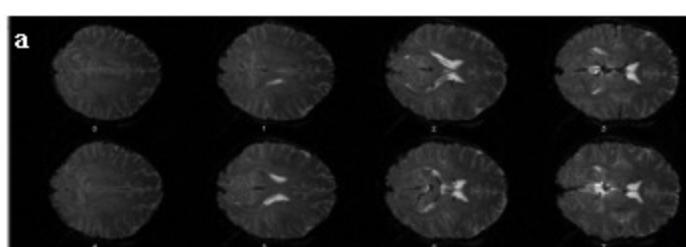
**Single shot full k-space echo-planar-imaging with an eight-channel phase array coil at 3T.**

Jerzy Bodurka<sup>1</sup>, Peter van Gelderen<sup>2</sup>, Patrick Ledden<sup>3</sup>, Peter Bandettini<sup>1</sup>, Jeff Duyn<sup>2</sup>

<sup>1</sup>Functional MRI Facility NIMH/NIH, <sup>2</sup>Advance MRI NINDS/NIH, <sup>3</sup>Nova Medical Inc.

**Quadrature Head Coil**

128 x 96



64 x 48

128 x 96

**8 Channel Array**

Figure 1

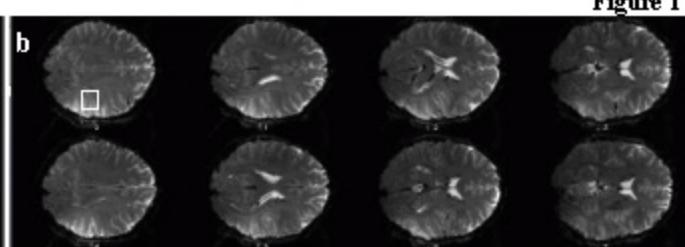
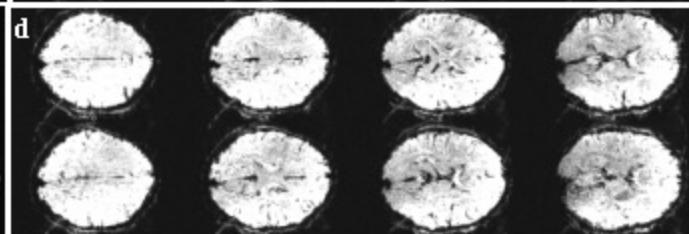
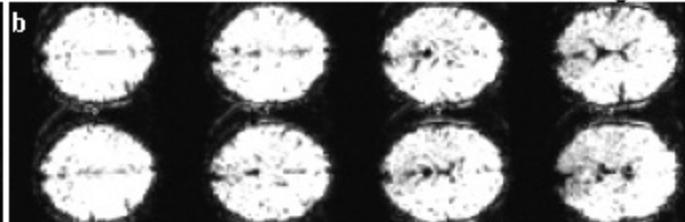


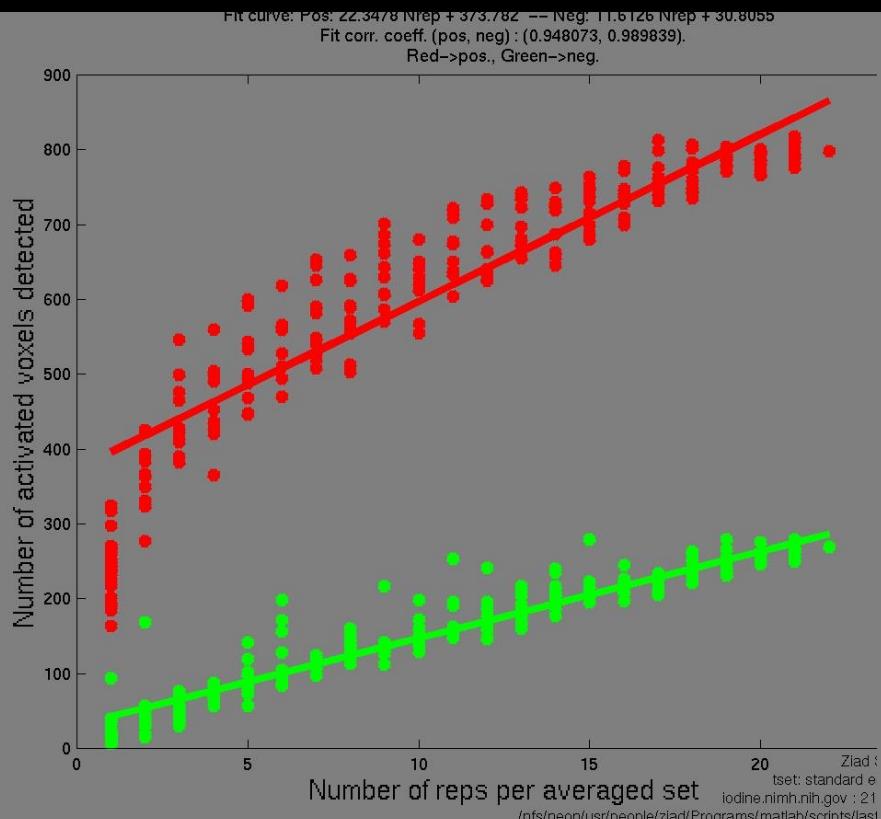
Figure 2



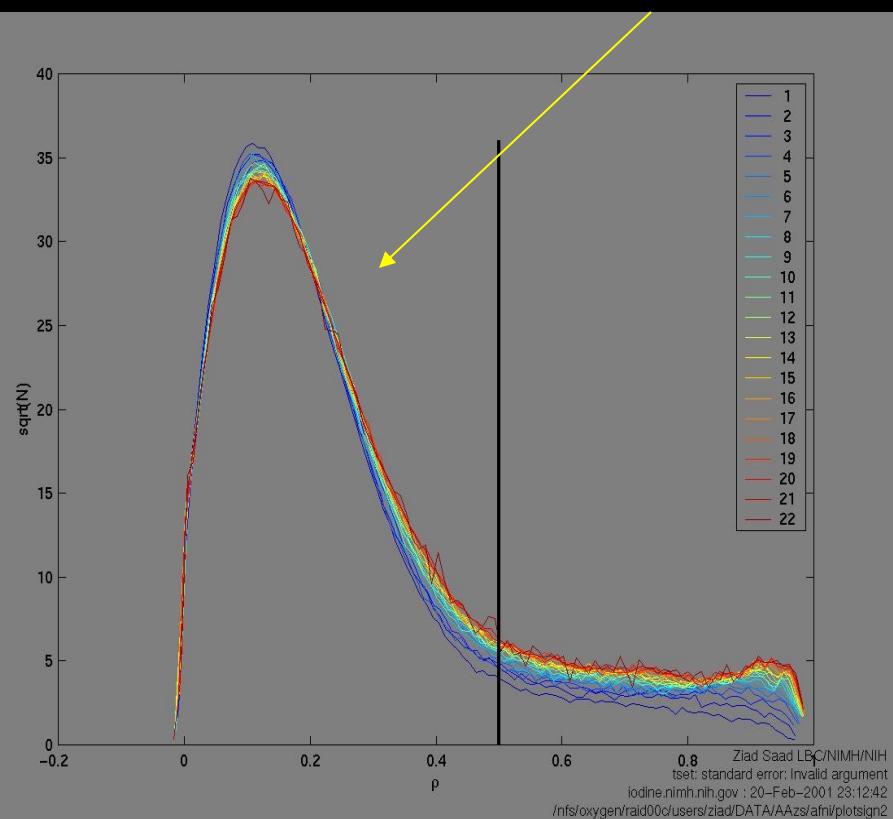
**SNR**

**TSNR**

# Continuously Growing Activation Area



# CC Histogram Inflection Point



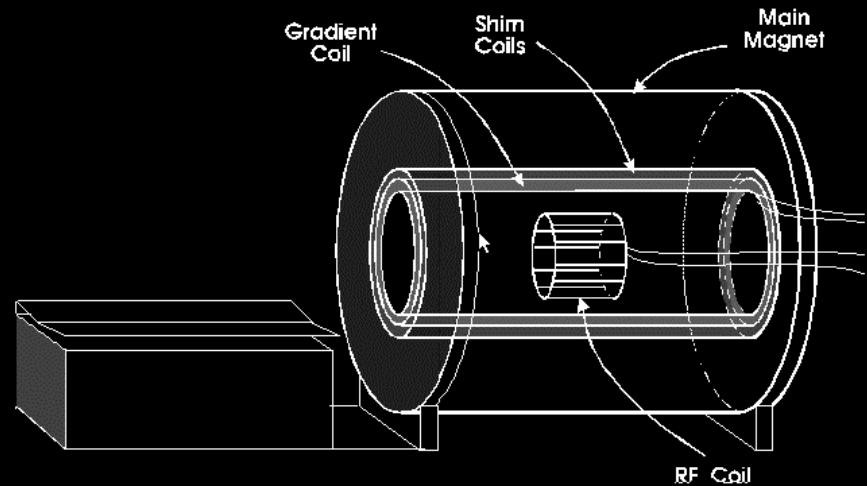
Ziad Saad, et al (Submitted)

- 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

2 G/cm, 350 T/m/s



4 G/cm, 150 T/m/s



10 G/cm, 1000 T/m/s



Diffusion imaging  
Faster imaging  
Higher resolution

# Neuronal Current Imaging

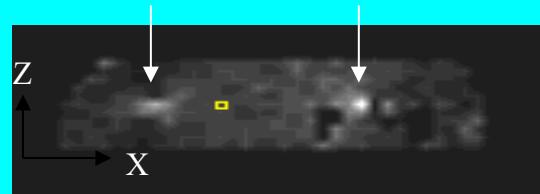
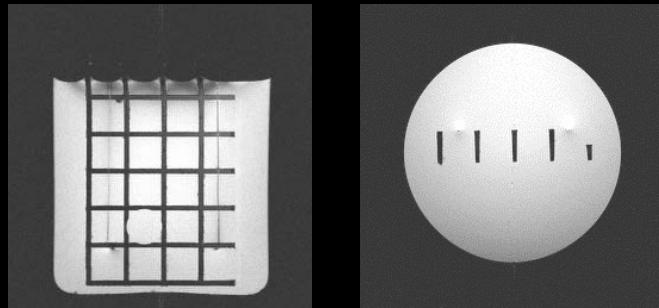
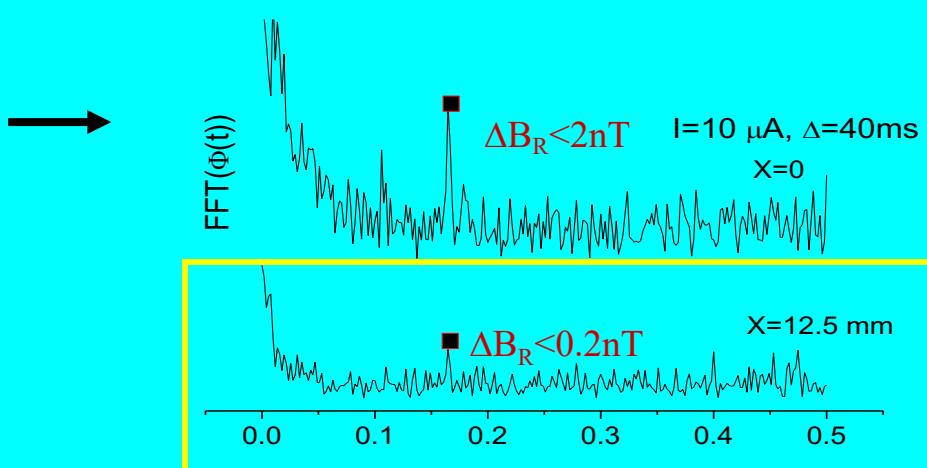
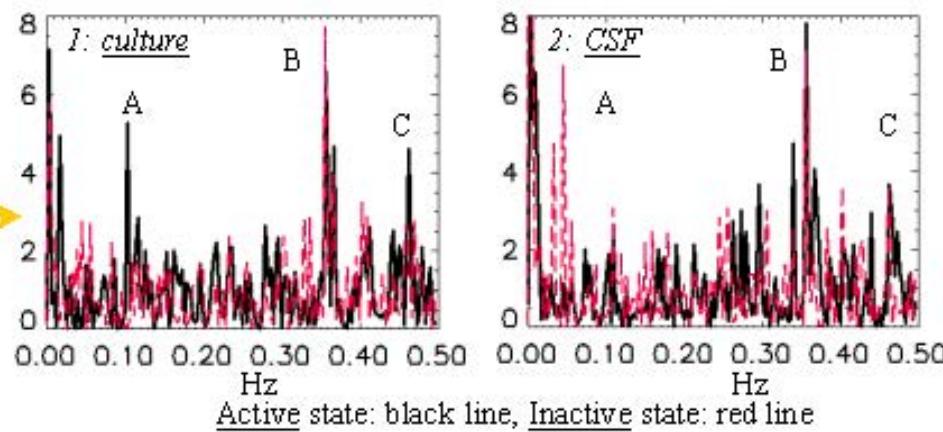
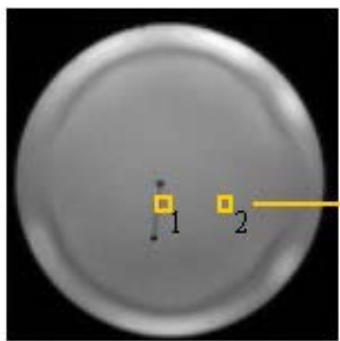
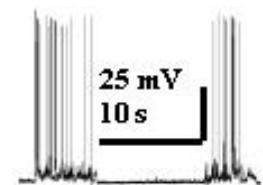


Figure 1





A: activity, on-off frequency  
(see trace)  
B: scanner noise (cooling-pump)  
C: activity



Typical  
Electrophysiology trace

# Technology

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

# Methodology

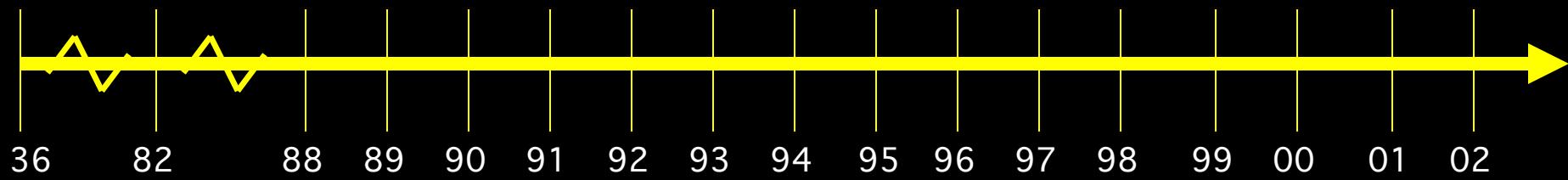
Baseline Volume	Correlation Analysis		CO <sub>2</sub> Calibration
	Motion Correction		Mixed ER and Blocked
	Parametric Design		Multi-Modal Mapping
IVIM	Surface Mapping	ICA	Free-behavior Designs
	Phase Mapping		
Linear Regression		Mental Chronometry	
	Event-related	Deconvolution	Fuzzy Clustering
			Multi-variate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

# Interpretation

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

# Applications

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



# 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 Maierov

Guosheng Ding

**Clinical Fellow:**

James Patterson

**Psychologist:**

Julie Frost

**Summer Students:**

Hannah Chang

Courtney Kemps

Douglass Ruff

Carla Wettig

Kang-Xing Jin

**Program Assistant:**

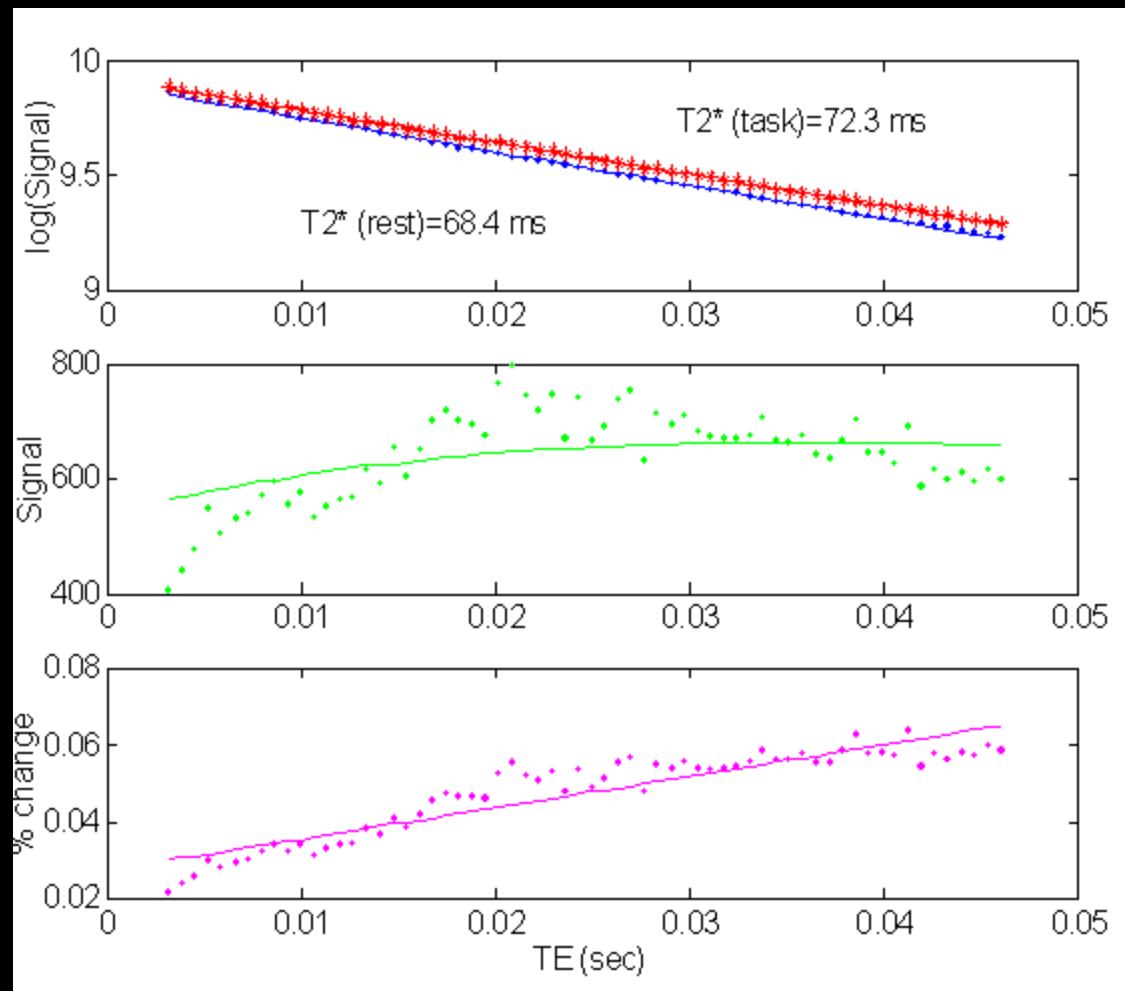
Kay Kuhns

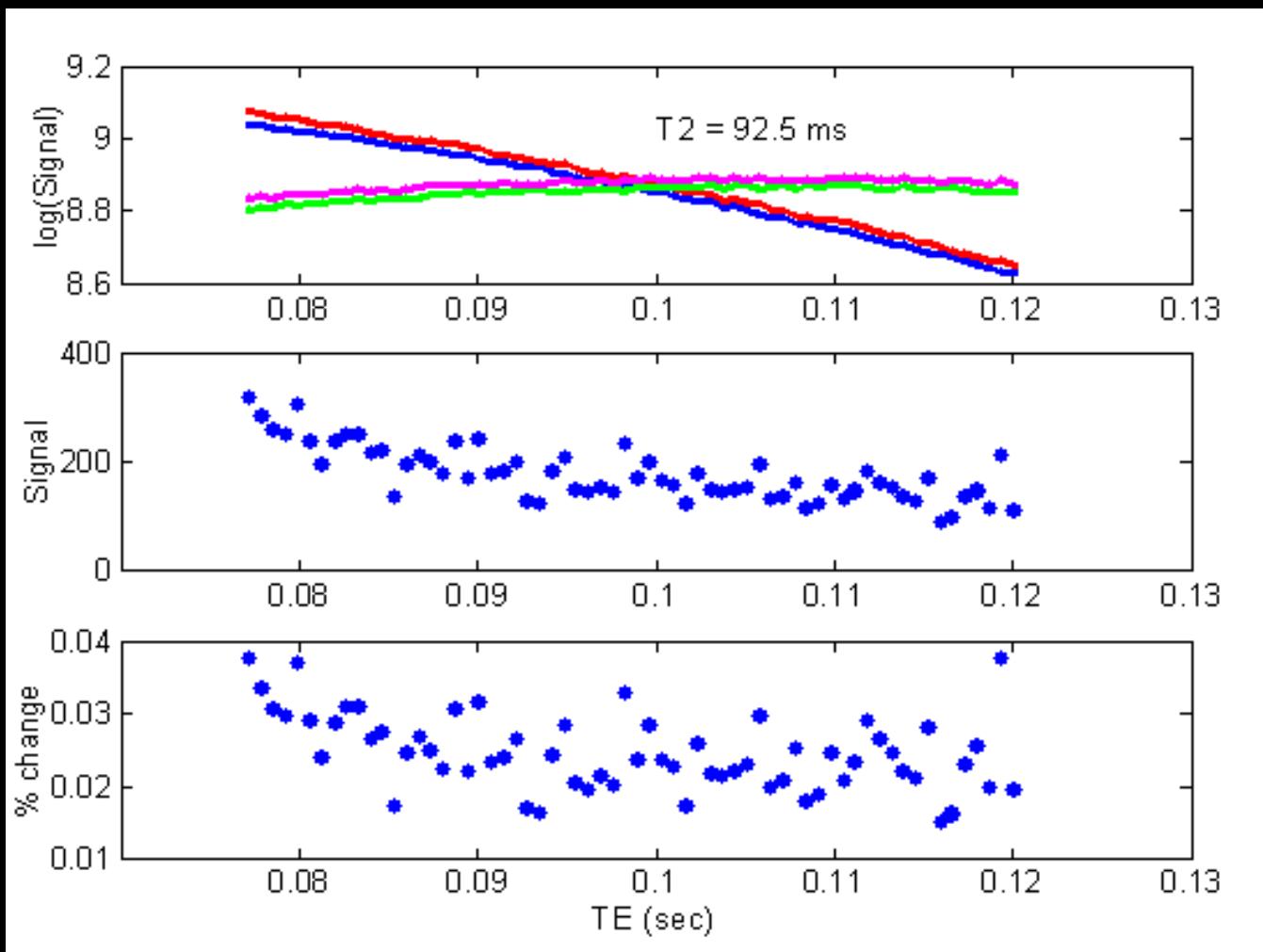
**Scanning Technologists:**

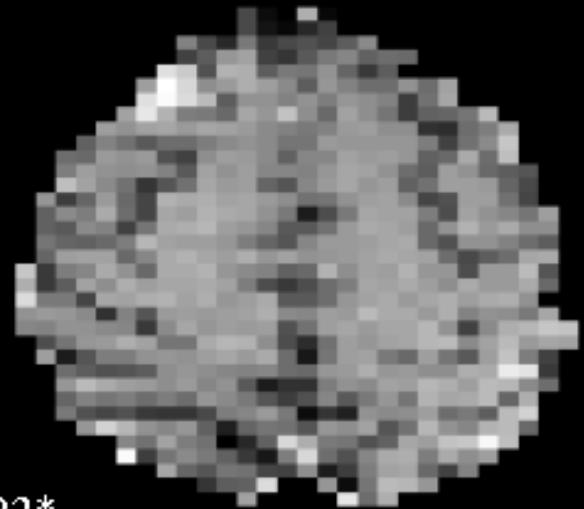
Karen Bove-Bettis

Paula Rowser

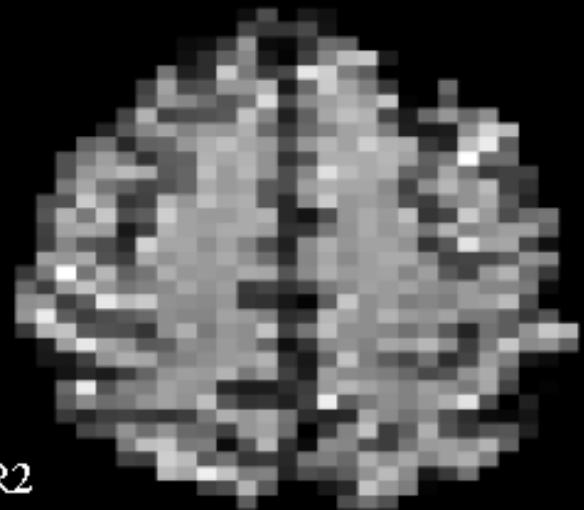




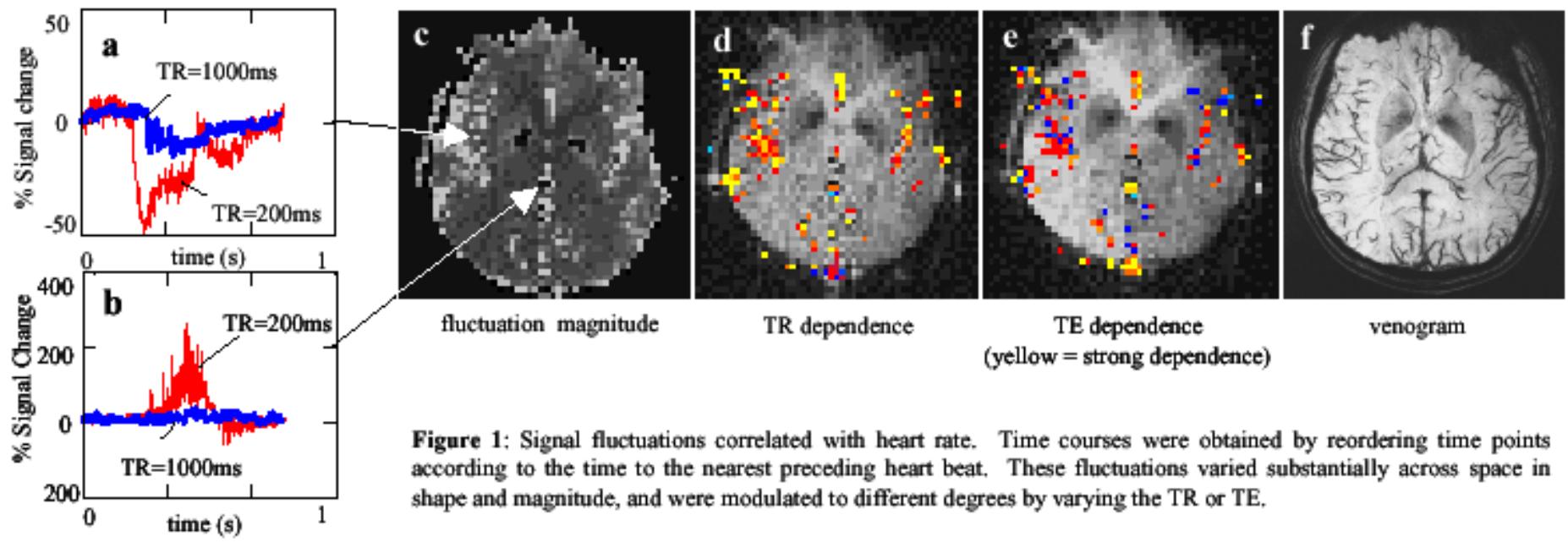




R2\*



R2



**Figure 1:** Signal fluctuations correlated with heart rate. Time courses were obtained by reordering time points according to the time to the nearest preceding heart beat. These fluctuations varied substantially across space in shape and magnitude, and were modulated to different degrees by varying the TR or TE.