

# Spatial, Temporal, and Interpretative Limits of fMRI

Peter A. Bandettini, Ph.D.

Section on Functional Imaging Methods

<http://fim.nimh.nih.gov>

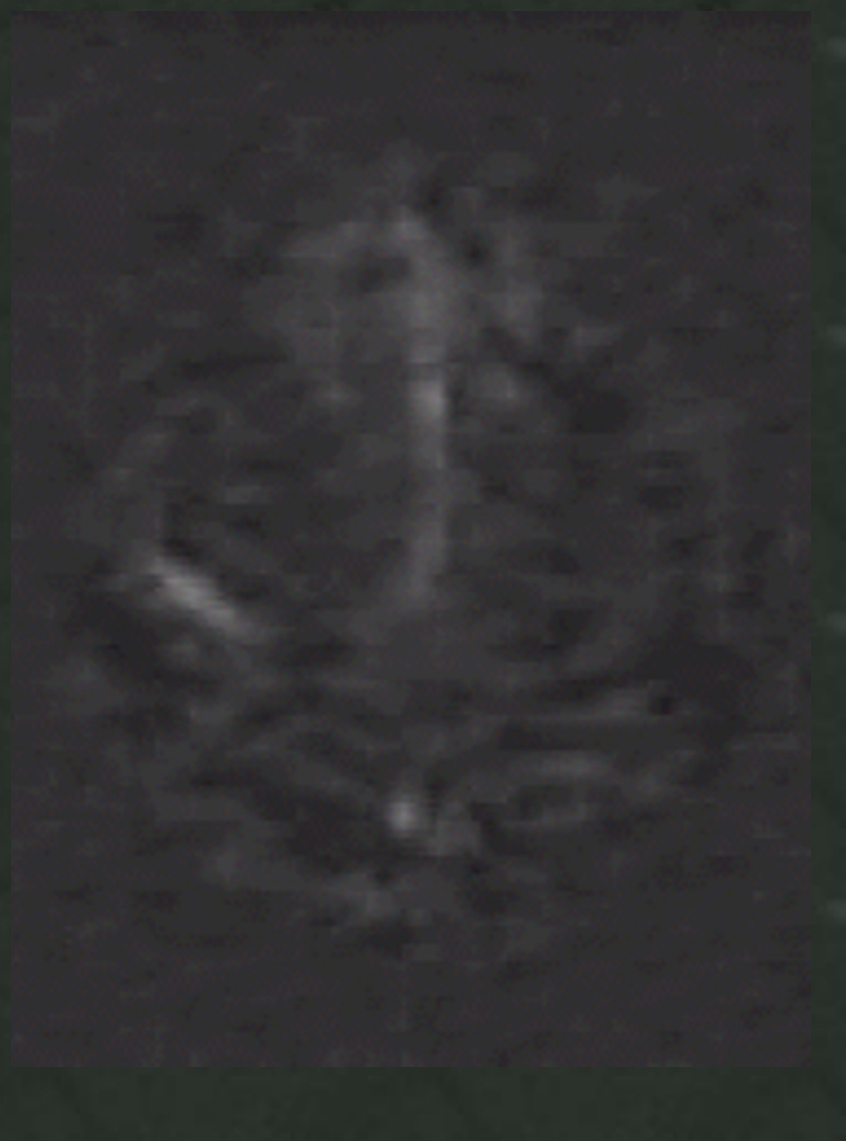
Laboratory of Brain and Cognition

&

Functional MRI Facility

<http://fmrif.nimh.nih.gov>





1991

# What really limits fMRI ?

- Imaging Methodology
- Hemodynamic Response Function

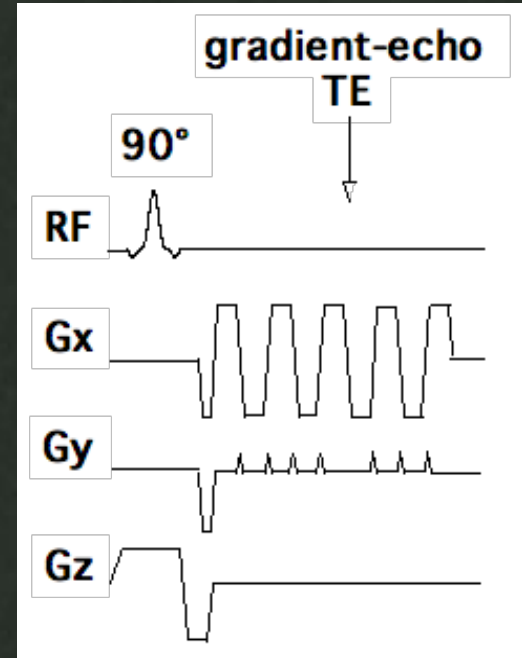
We can typically image faster and at higher resolution than the functional resolution that is determined by the hemodynamic response function.

# Single Shot Echo Planar Imaging (EPI)



EPI Readout Window

$\approx 20$  to  $40$  ms

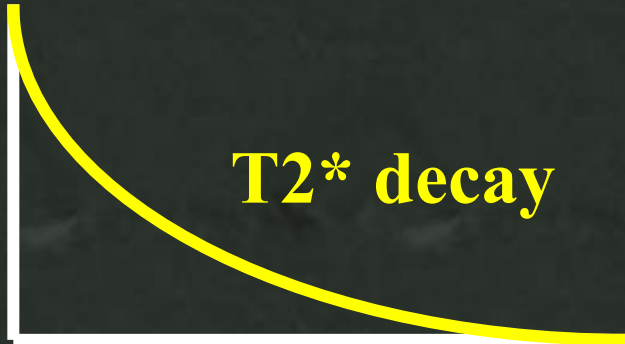


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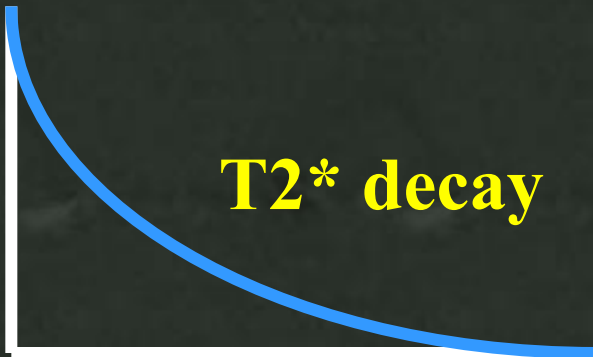
## How might we improve things?

- Multi-shot imaging
- Partial k-space imaging
- RF coils
- SENSE imaging
- Higher field strength

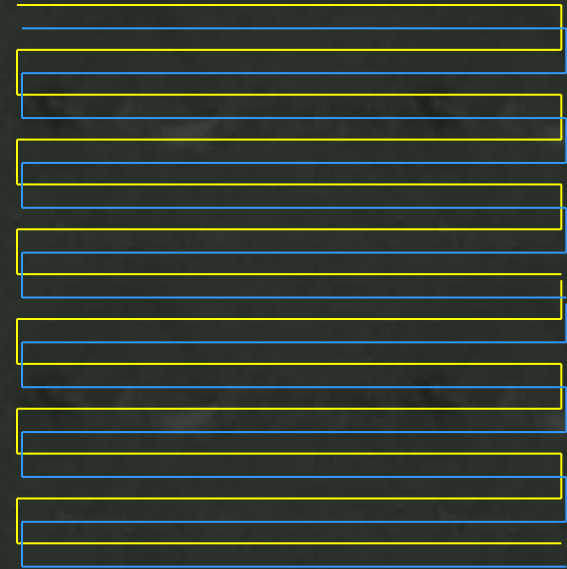
# Multi-shot imaging



EPI Window 1



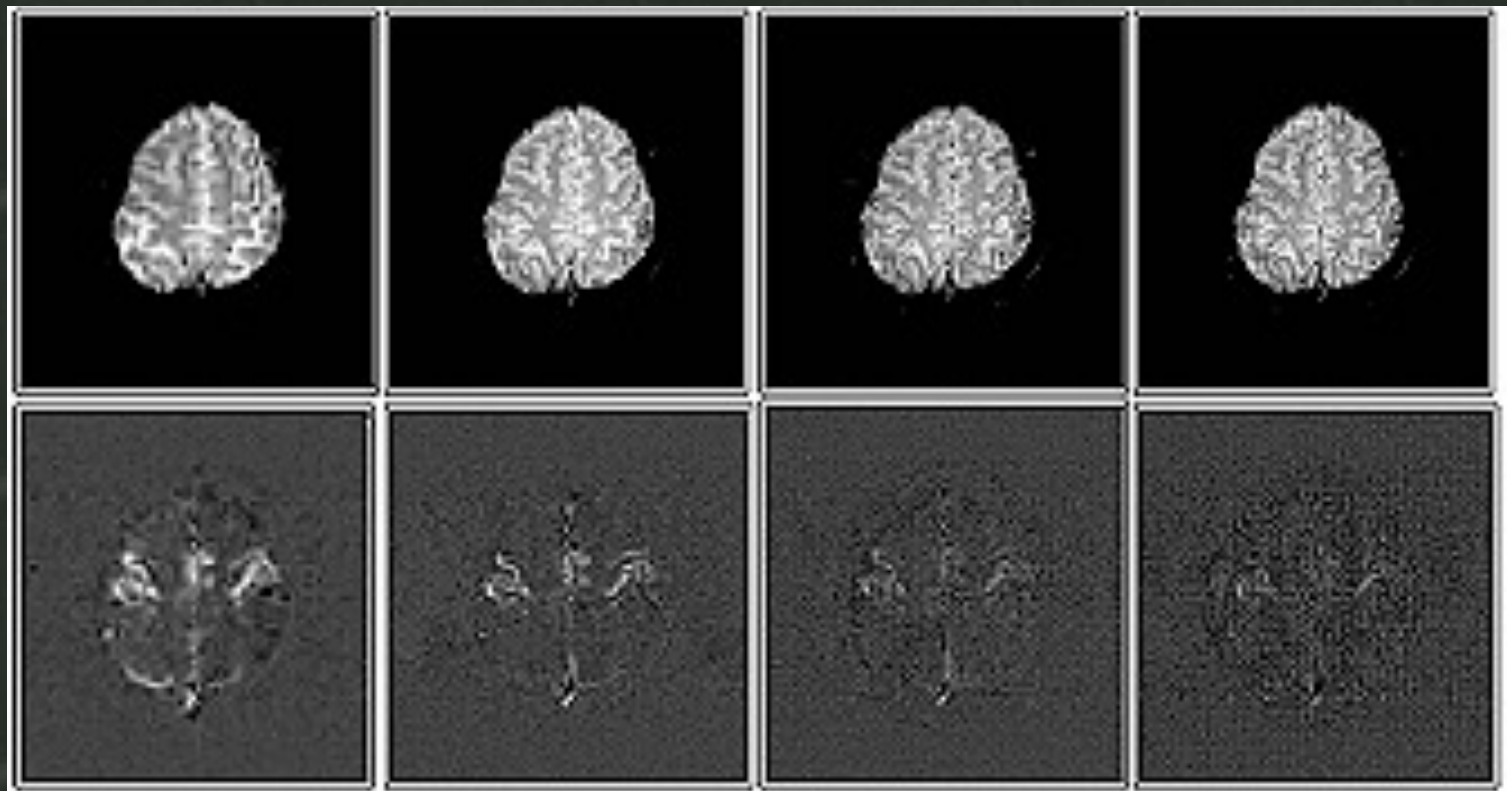
EPI Window 2



- Requires navigator pulses
- Temporal resolution and stability tradeoff

# Multi-shot imaging

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



# Partial k-space imaging



**EPI Window**

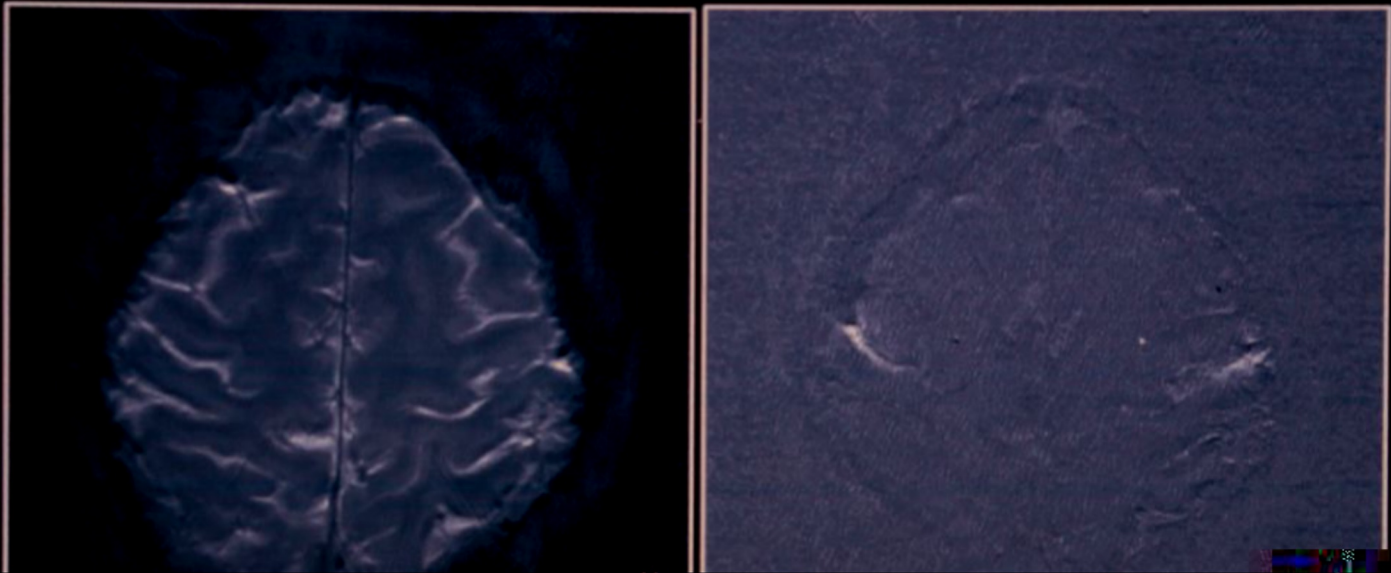


- More warping
- Lower image SNR
- Improvement in one dimension



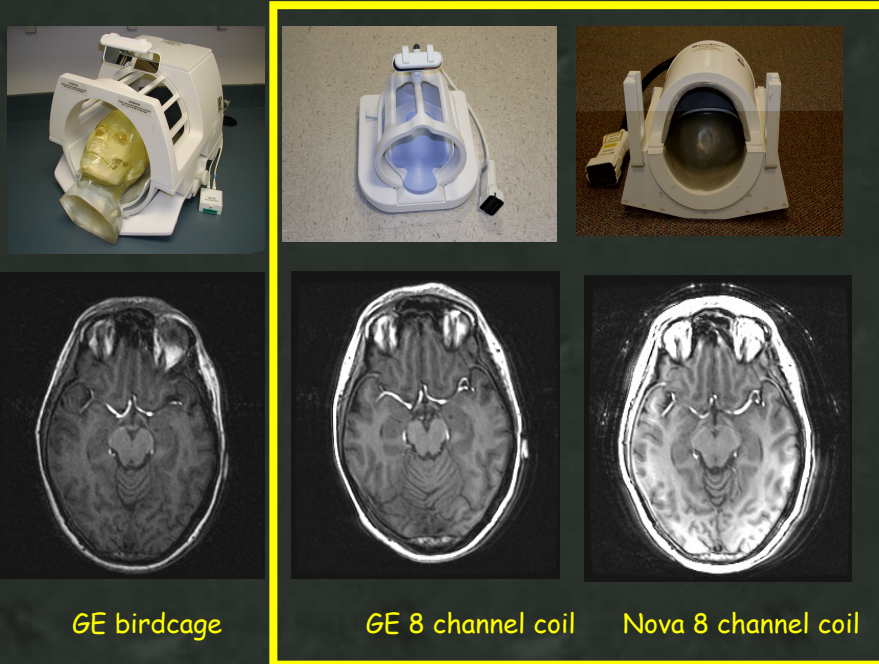
# Partial k-space imaging

**Single - Shot EPI at 3T:  
Half NEX, 256 x 256, 16 cm FOV**

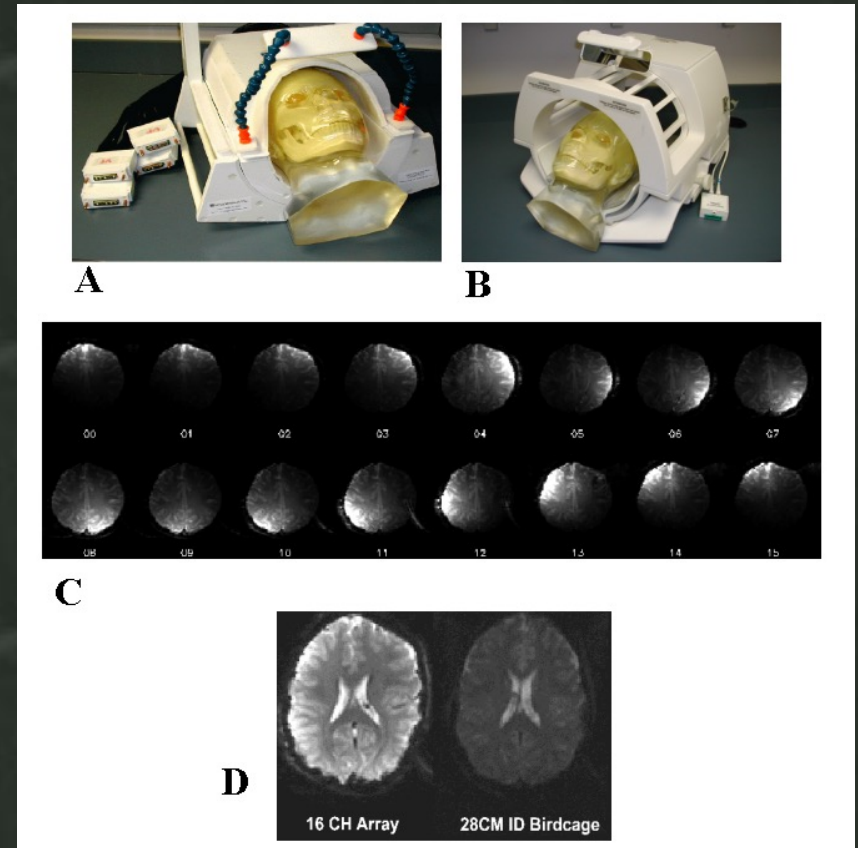


# RF coils

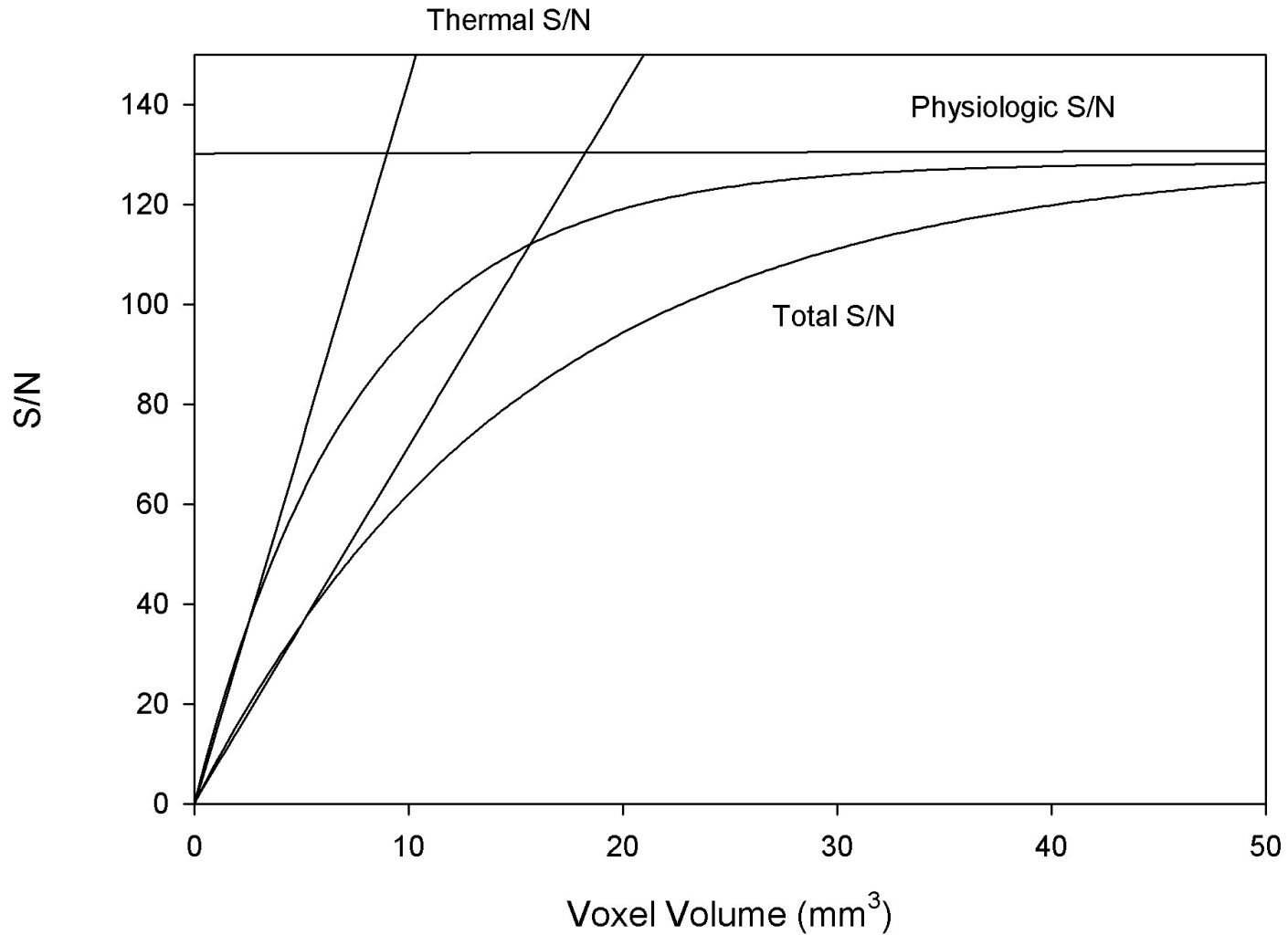
8 channel parallel receiver coil



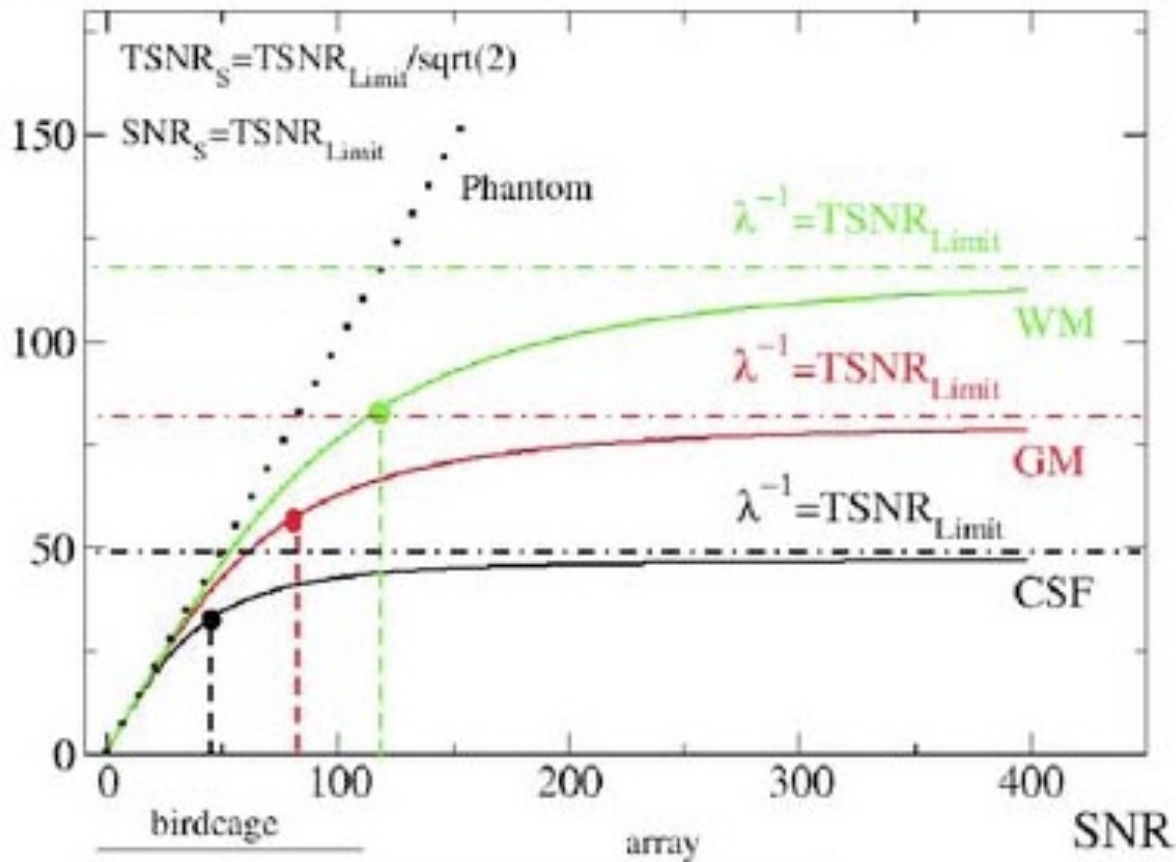
16 channel parallel receiver coil



## Simulated gains in TNSR with doubling sensitivity

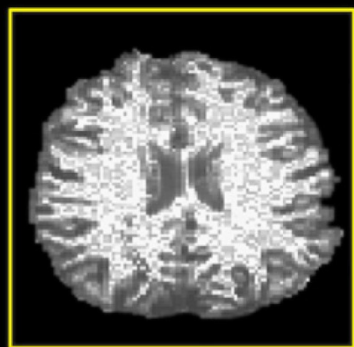


## TSNR

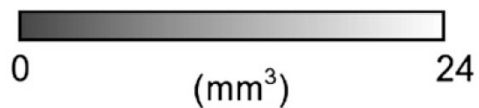
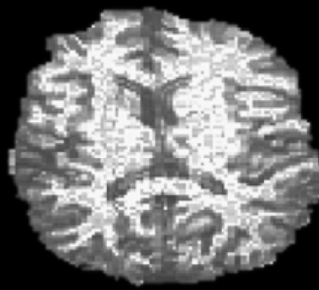


J. Bodurka, F. Ye, N Petridou, P. A. Bandettini, Mapping the MRI voxel volume in which thermal noise matches physiological noise - implications for fMRI. *NeuroImage*, 34, 542-549 (2007)

# Finding the "Suggested resolution"



**GM: 9.5 +/- 5.3 mm<sup>3</sup>; WM: 14.0 +/- 6.1 mm<sup>3</sup>; CSF: 3.1 +/- 2.1mm<sup>3</sup>**





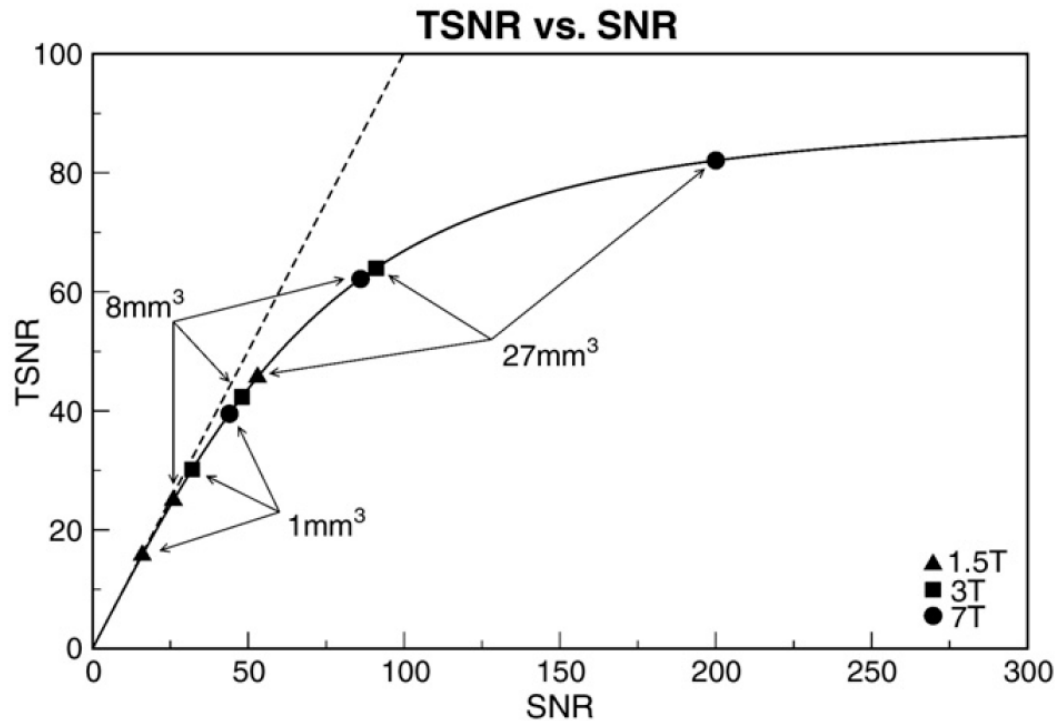
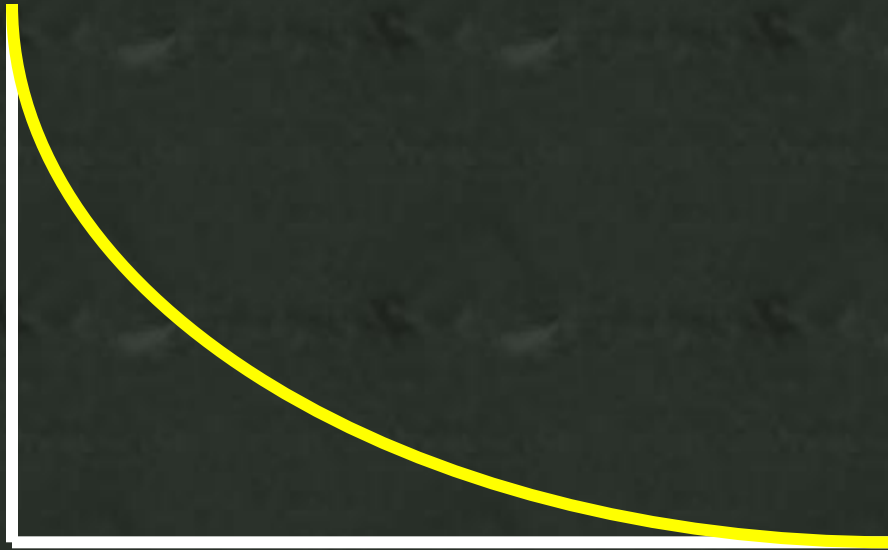


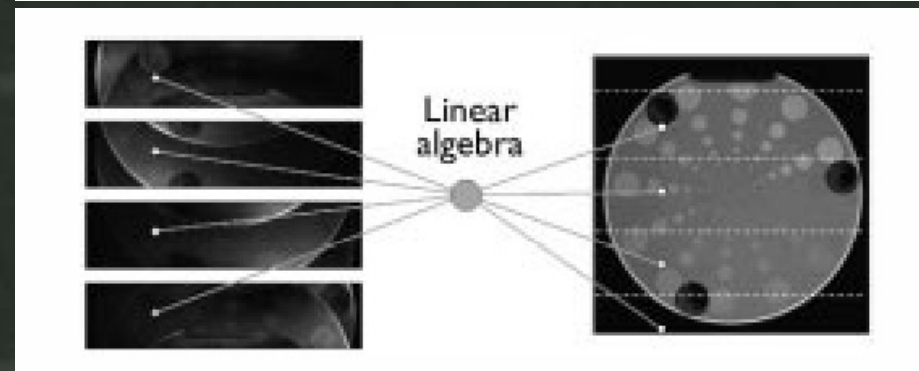
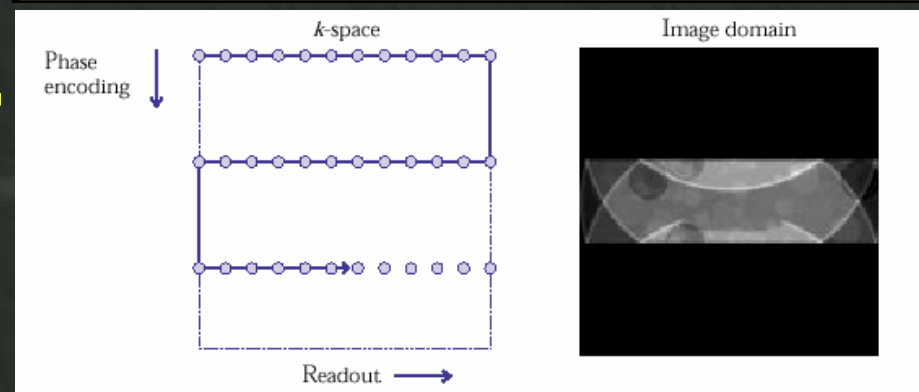
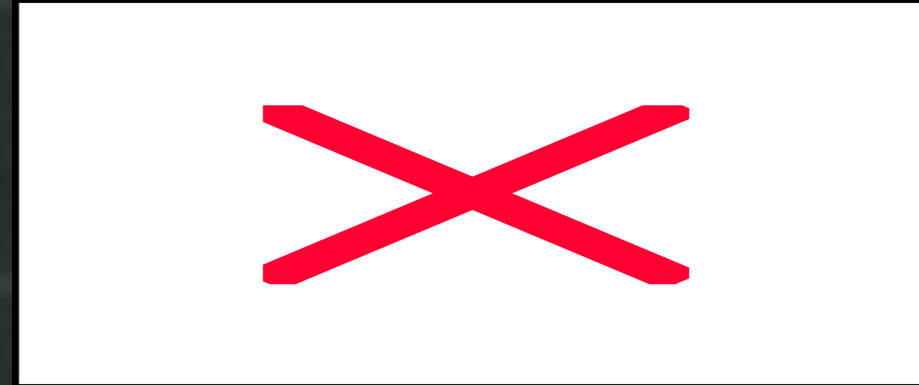
Fig. 1. A schematic of the relationship between TSNR and SNR in gray matter is shown. The dashed line represents this relationship in the absence of physiological noise. In vivo, gains in TSNR are limited by physiological noise as SNR is increased and this relationship is displayed with the solid line. For gray matter, the TSNR limit is approximately 87 (Bodurka et al., 2005). Using values derived from those reported by Triantafyllou et al. (2005), estimates of SNR for 1.5 T, 3 T and 7 T scanners equipped with standard head coils are shown for voxel sizes of  $1 \times 1 \times 1 \text{ mm}^3 = 1 \text{ mm}^3$ ,  $2 \times 2 \times 2 \text{ mm}^3 = 8 \text{ mm}^3$  and  $3 \times 3 \times 3 \text{ mm}^3 = 27 \text{ mm}^3$ .

# SENSE Imaging



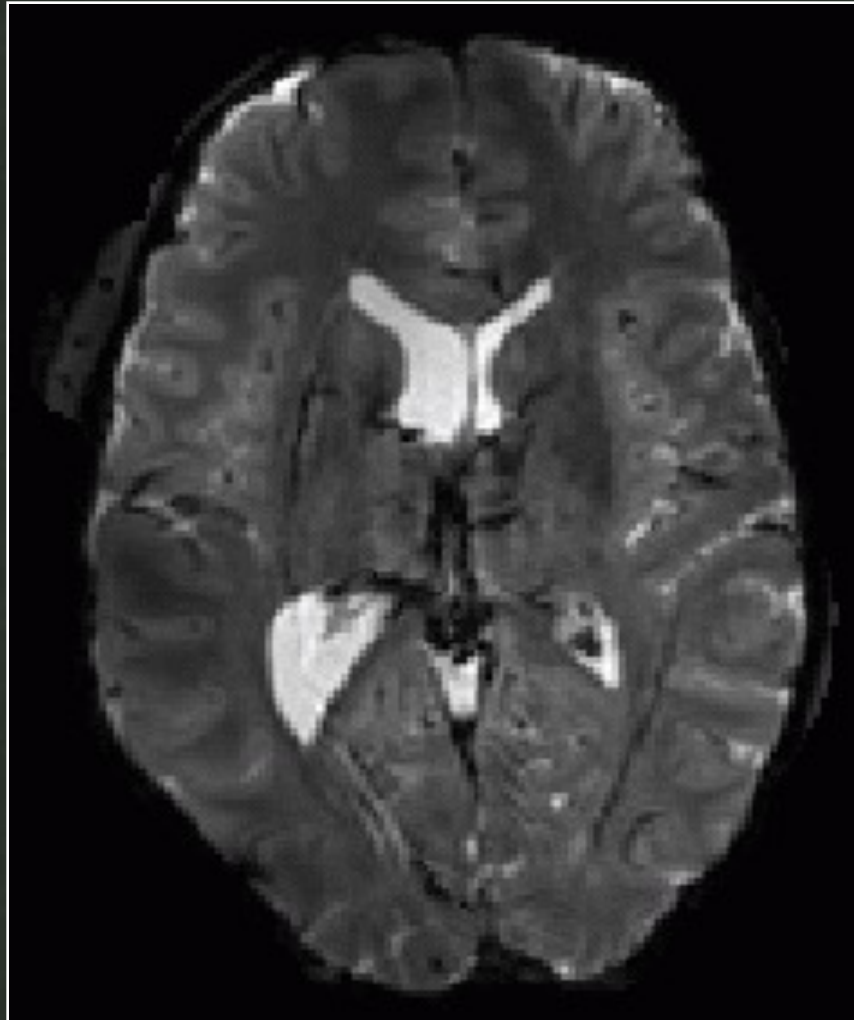
≈ 5 to 30 ms

- Gain in resolution per window width
- If shorter readout window is used:
- Small gain in #slices per TR
- Reduced distortions
- Reduced Image SNR



Pruessmann, et al.

# SENSE Imaging



3T single-shot SENSE EPI using 16 channels: 1.25x1.25x2mm

Bodurka et al.



# The Hemodynamic Response Function

Neuronal Activation

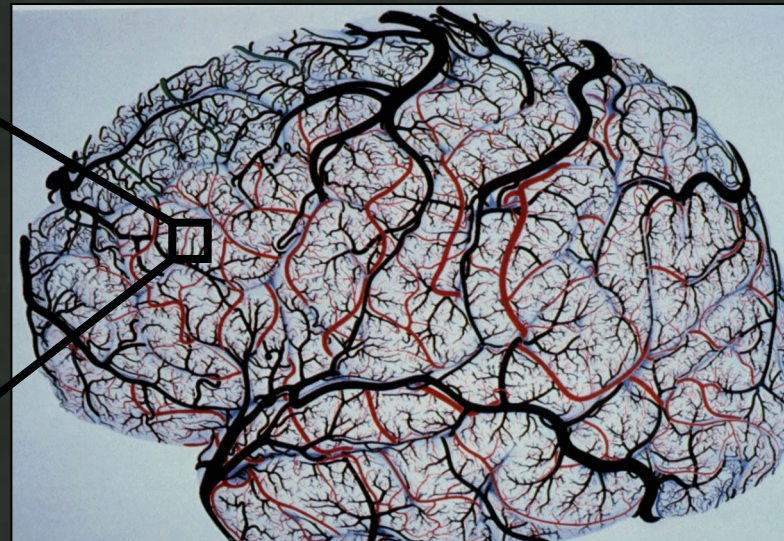
Measured Signal



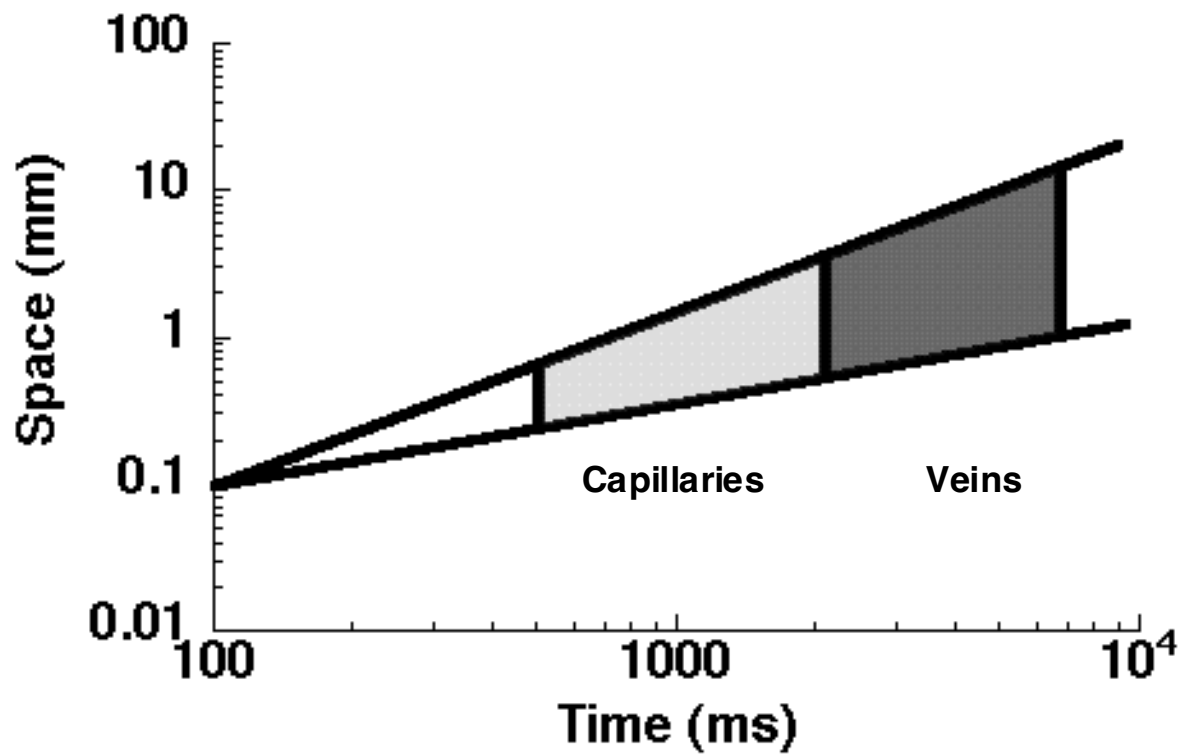
Hemodynamics



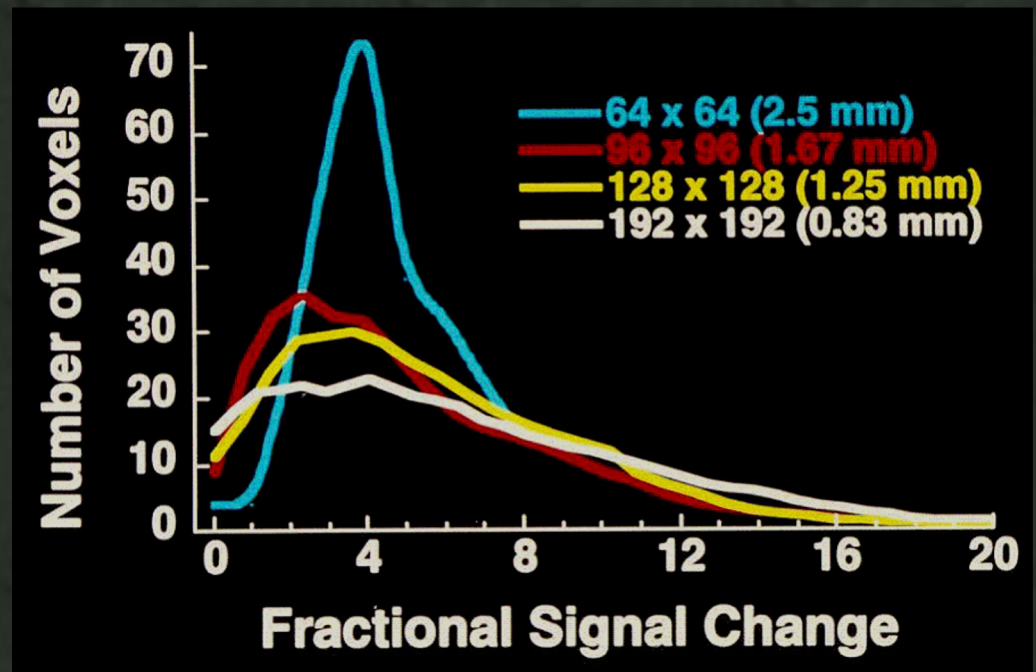
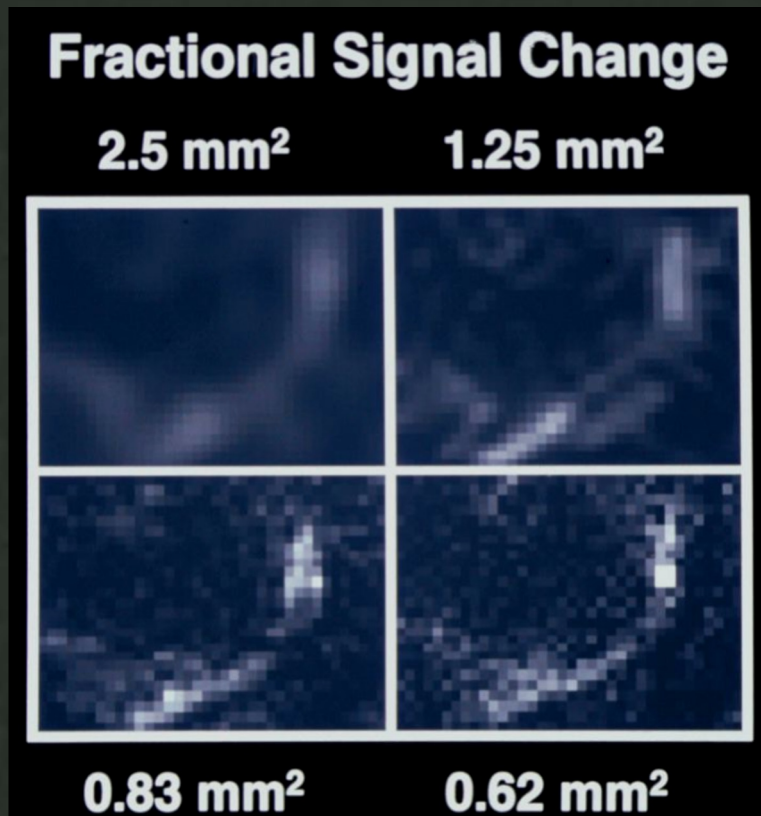
Noise



## Hemodynamic Latency and Variability Following Neuronal Activation

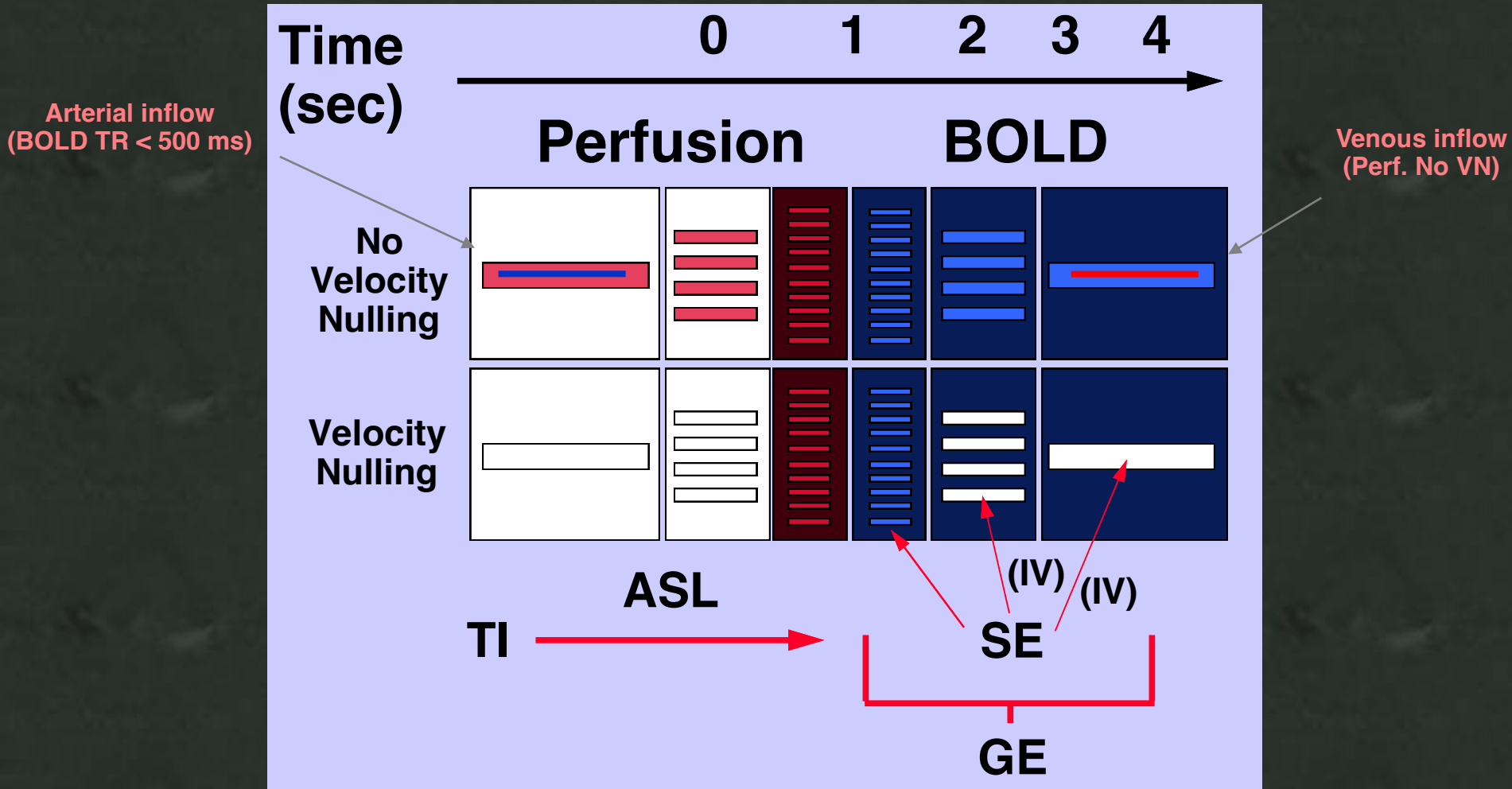


# The effect of increasing spatial resolution



Large vessel effects tend to be amplified...

# Hemodynamic Specificity

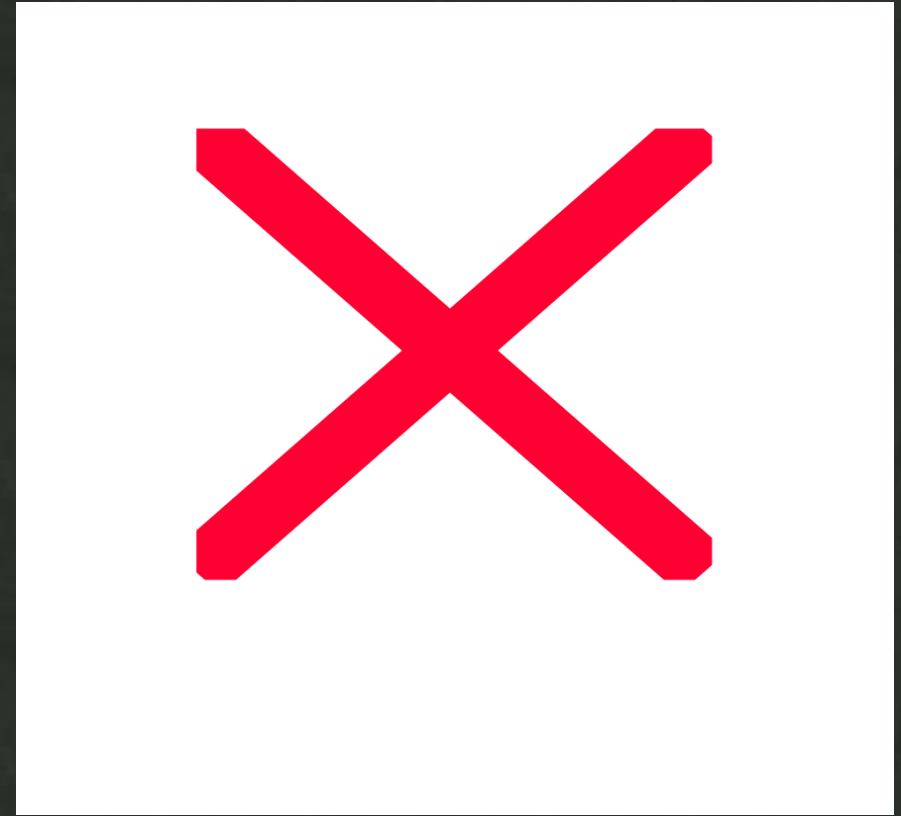
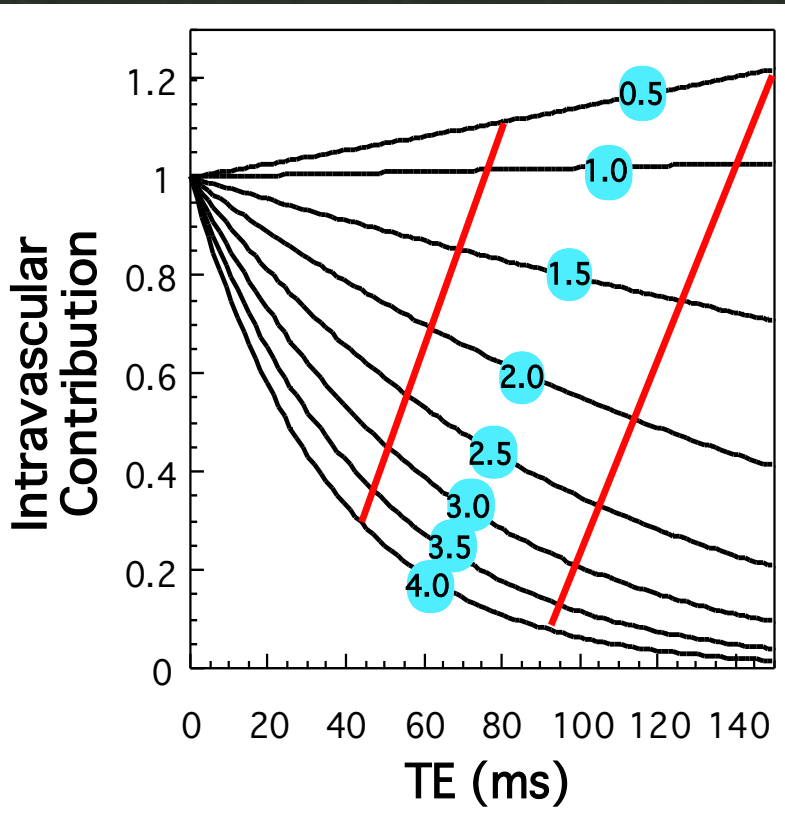


Some pulse sequence strategies..

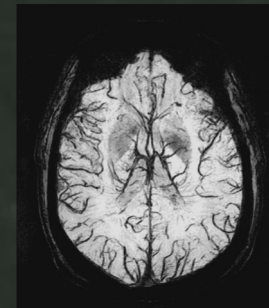
# Field strength dependence of intravascular effects

Spin-echo, %HbO<sub>2</sub> = 60

Gradient-echo, %HbO<sub>2</sub> = 60

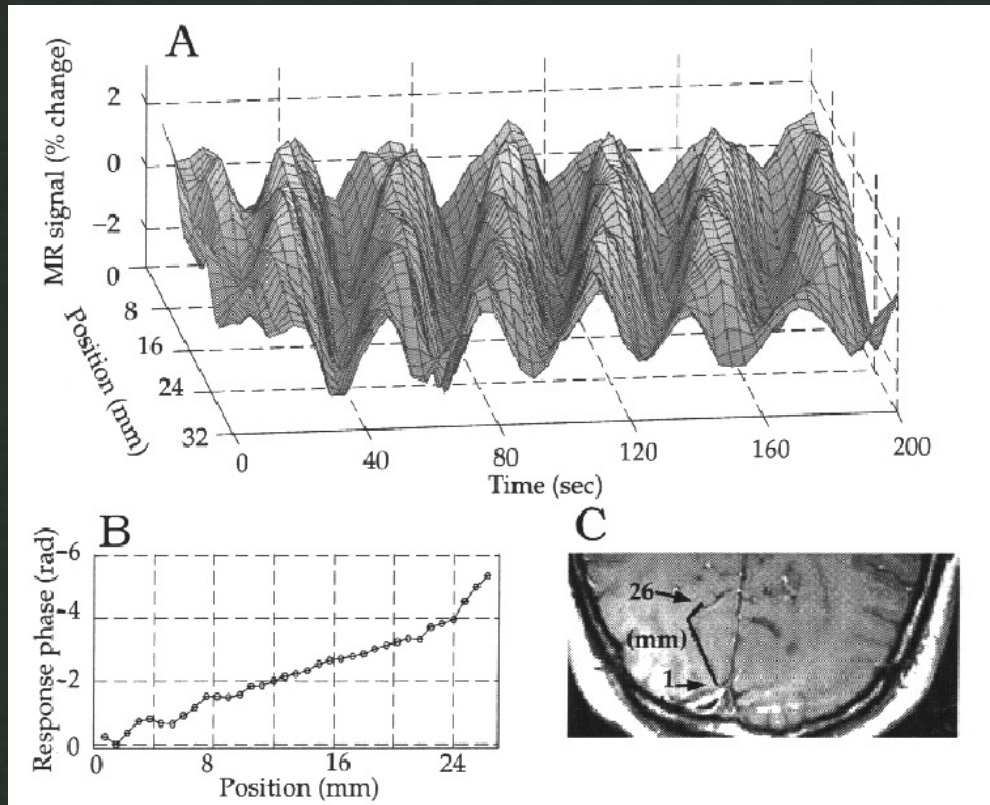


Source of contrast in venograms..





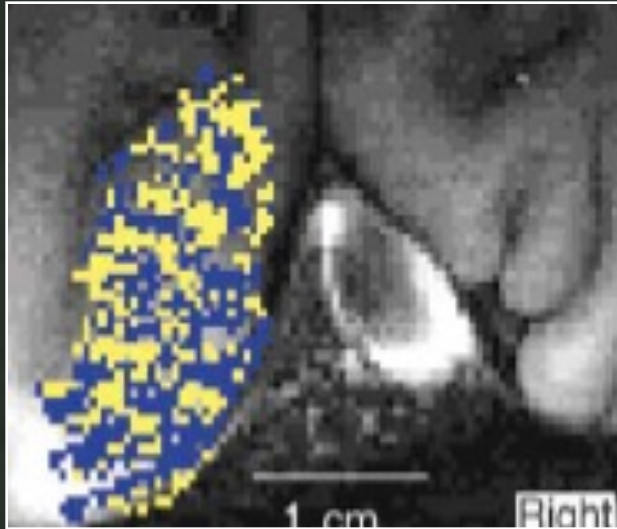
PSF FWHM = 3.5mm



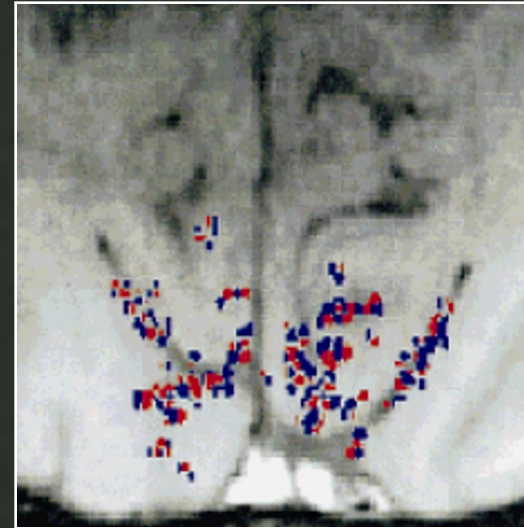
S.A. Engel, et al. Investigative Ophthalmology & Visual Science 35 (1994) 1977-1977.

## Detailed structure is extractable

0.47 x 0.47 in plane resolution



0.54 x 0.54 in plane resolution

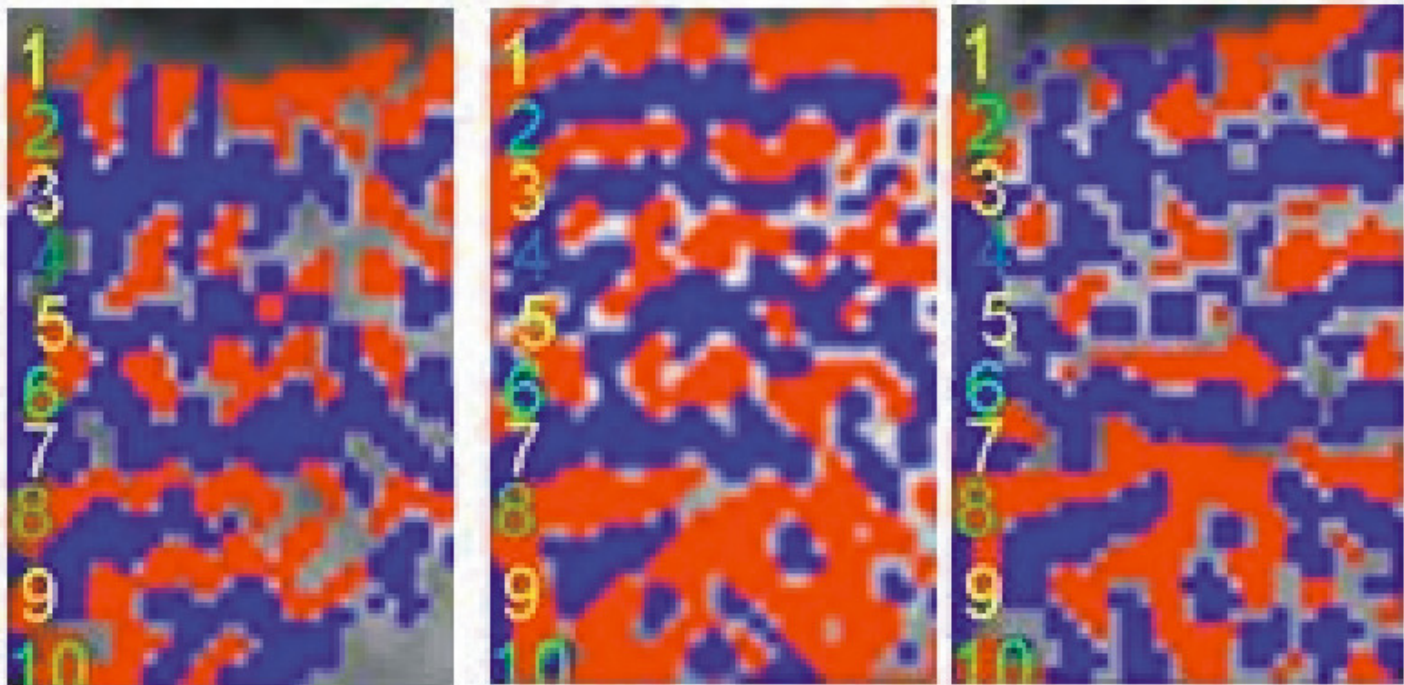


Cheng, et al. (2001) Neuron,32:359-374    Menon et al, (1999) MRM 41 (2): 230-235

Multi-shot with navigator pulse

# HSE-BOLD demonstration of ocular dominance columns

human, 7T,  $0.5 \times 0.5 \times 3 \text{ mm}^3$



day 1

day 2

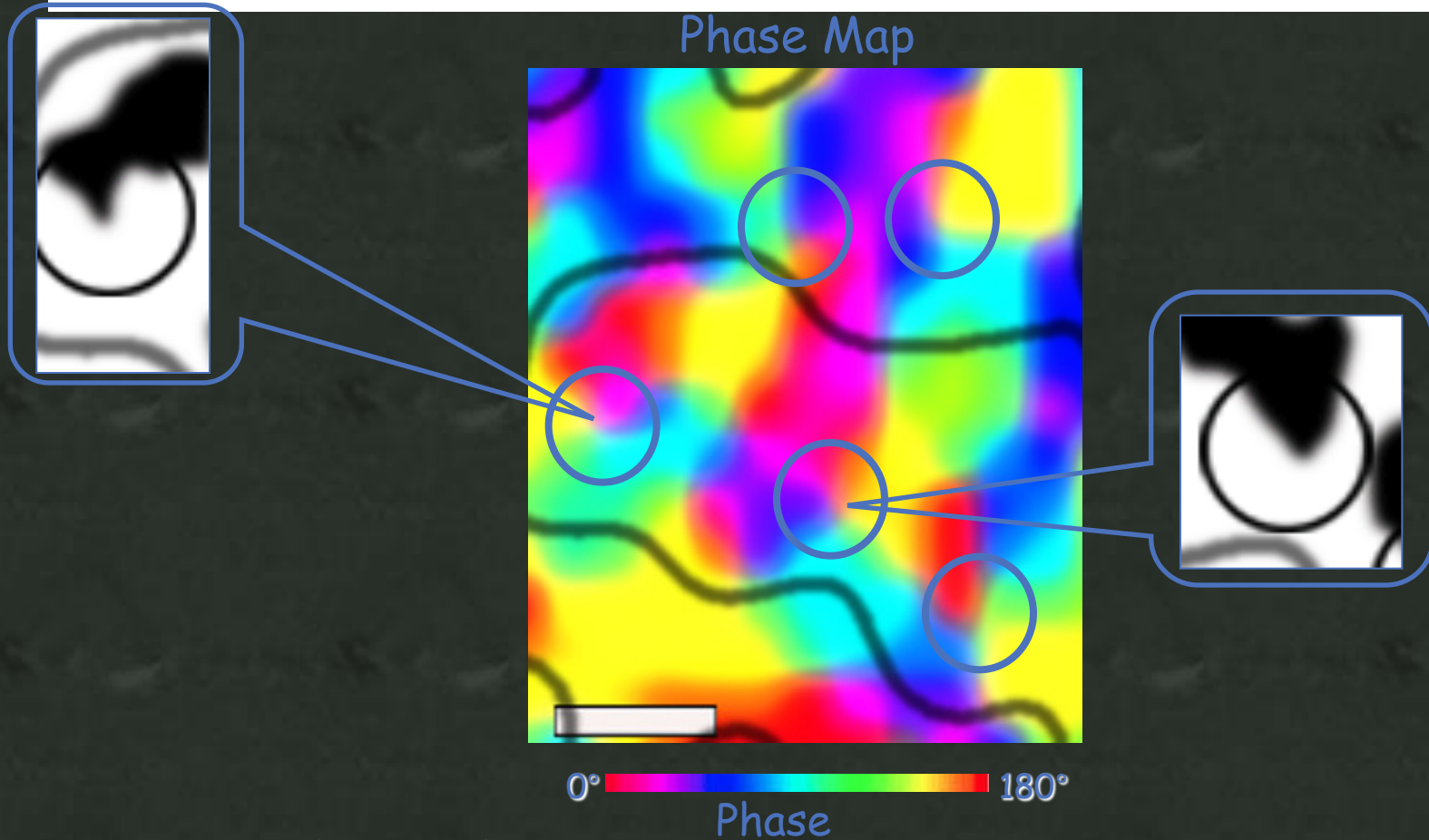
day 3

Yacoub et al: differential maps contrasting stimulation of the left and right eye



# Orientation Columns in Human V1 as Revealed by fMRI at 7T

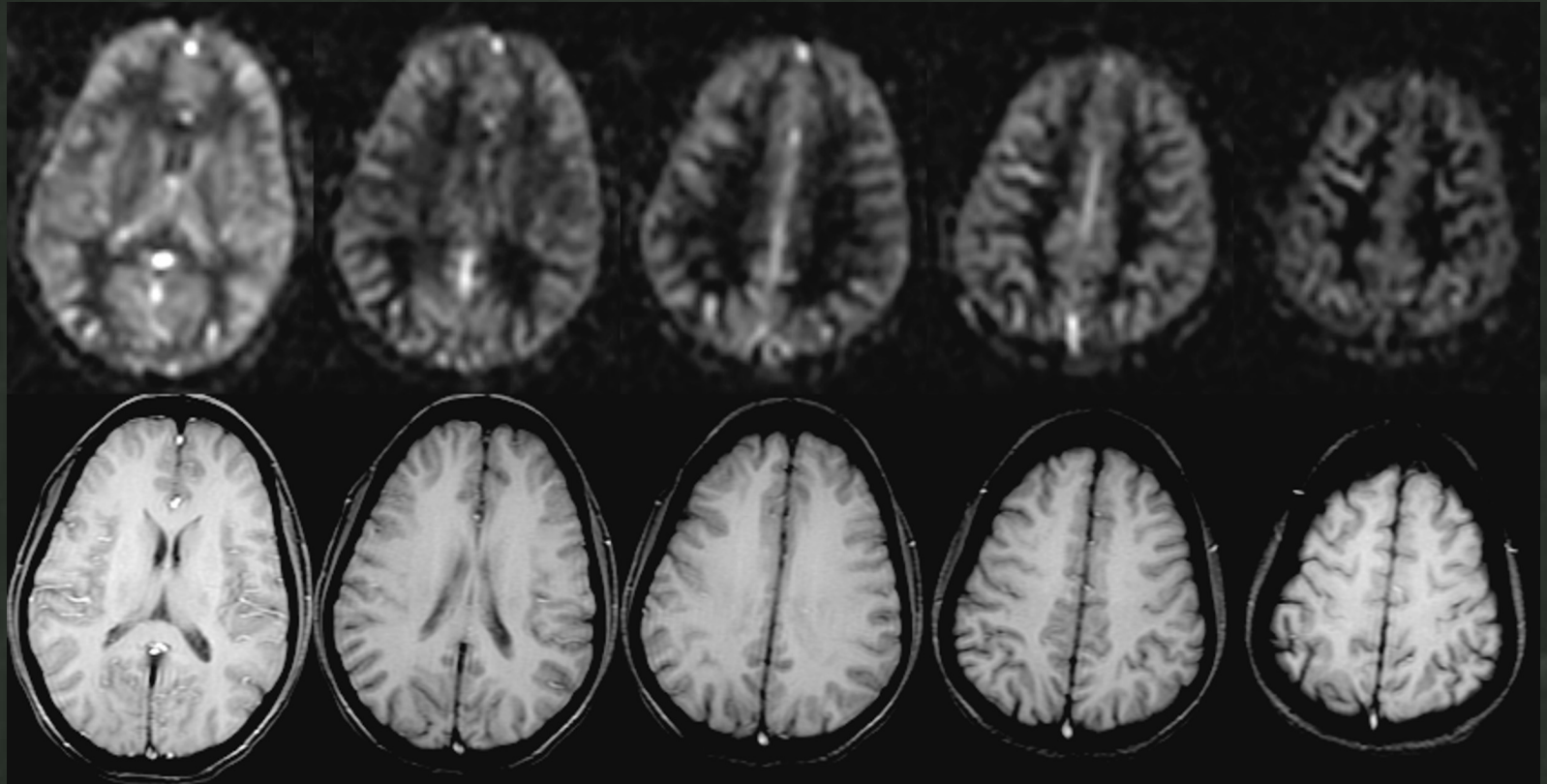
Phase Map



Yacoub, Ugurbil & Harel  
University of Minnesota / CMRR  
HBM 2006

Scalebar = 0.5 mm

# Perfusion (ASL)



# Simultaneous BOLD and Perfusion



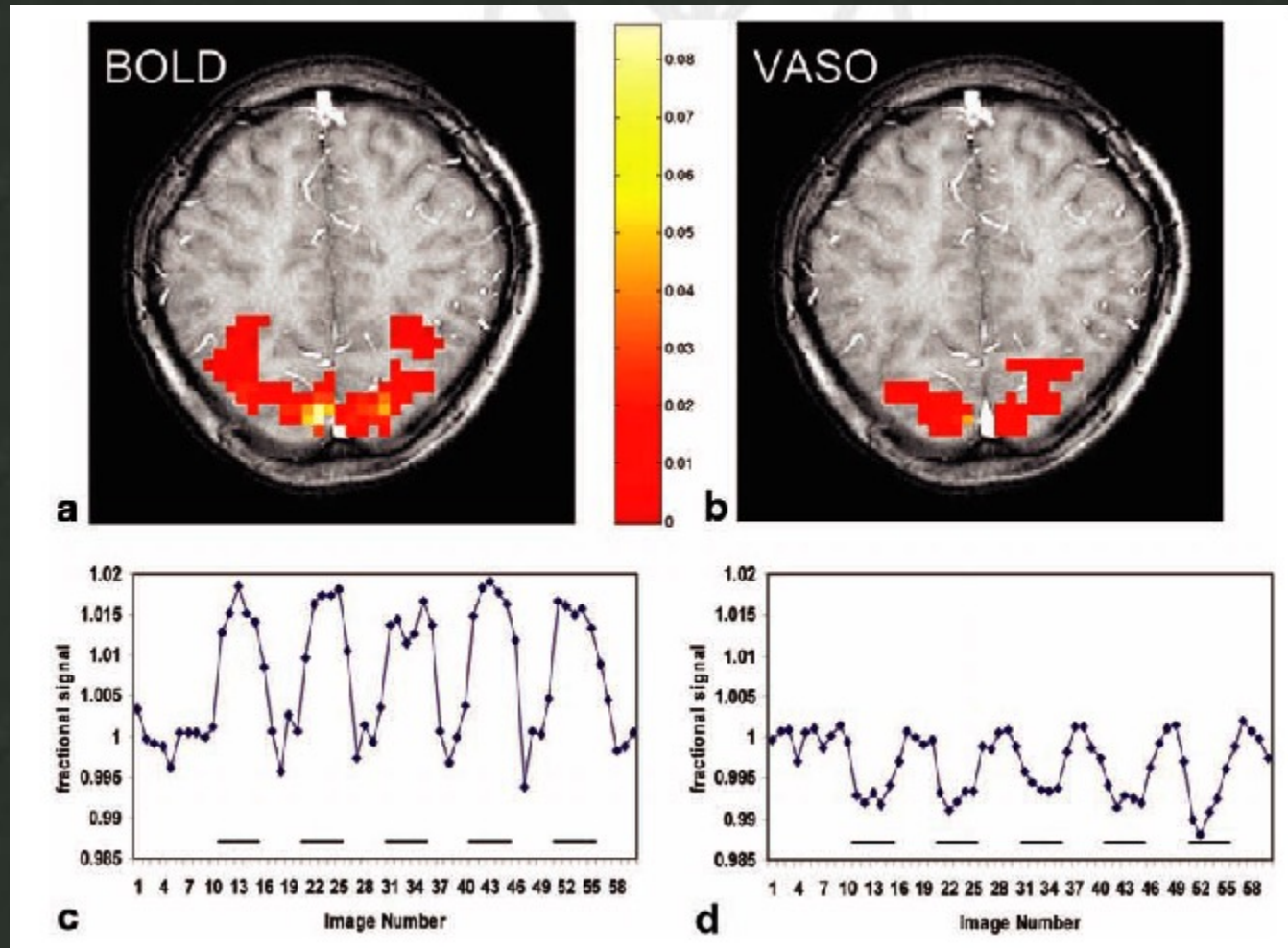
**BOLD**



**Perfusion**

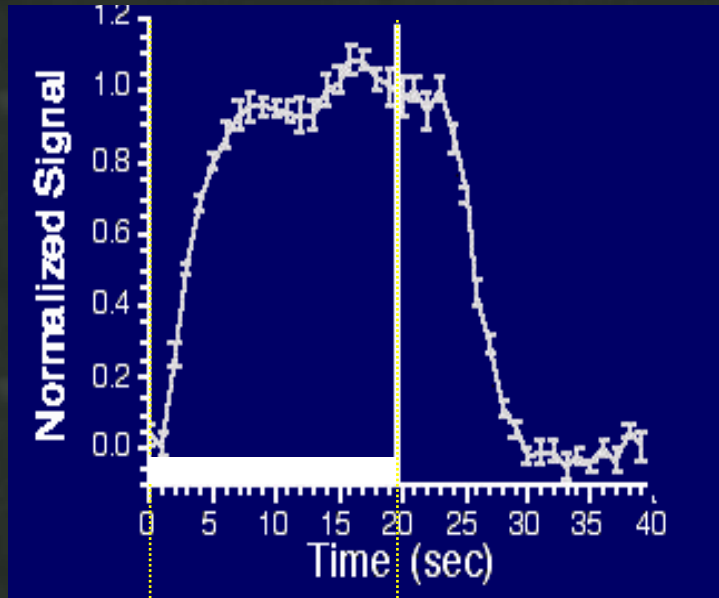


## Is Vascular Space Occupancy Imaging (VASO) more specific?

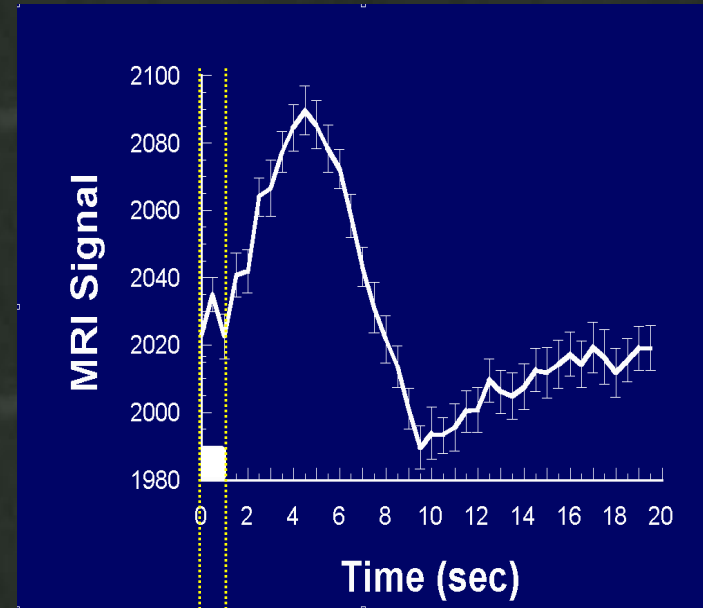


Lu et al, MRM 50 (2): 263-274 (2003)

# Temporal resolution



*task*

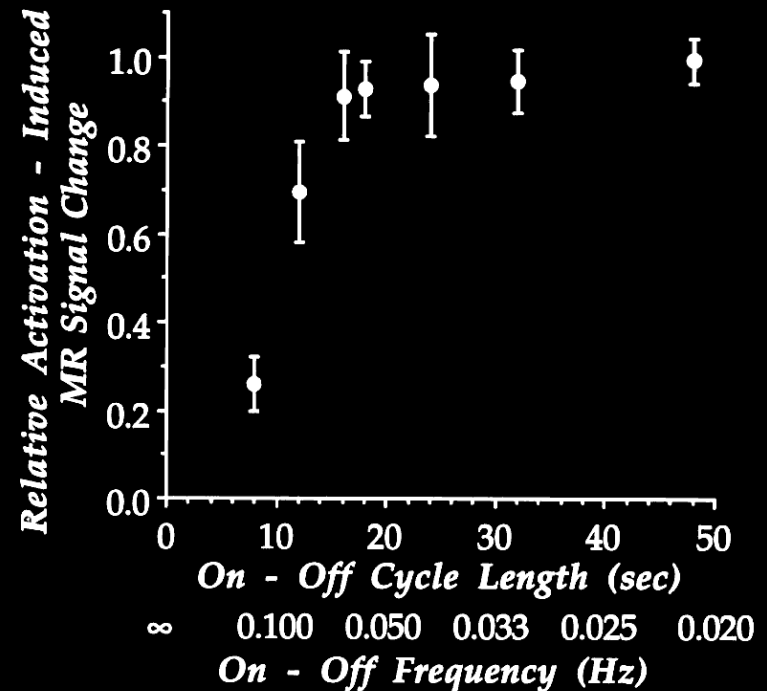
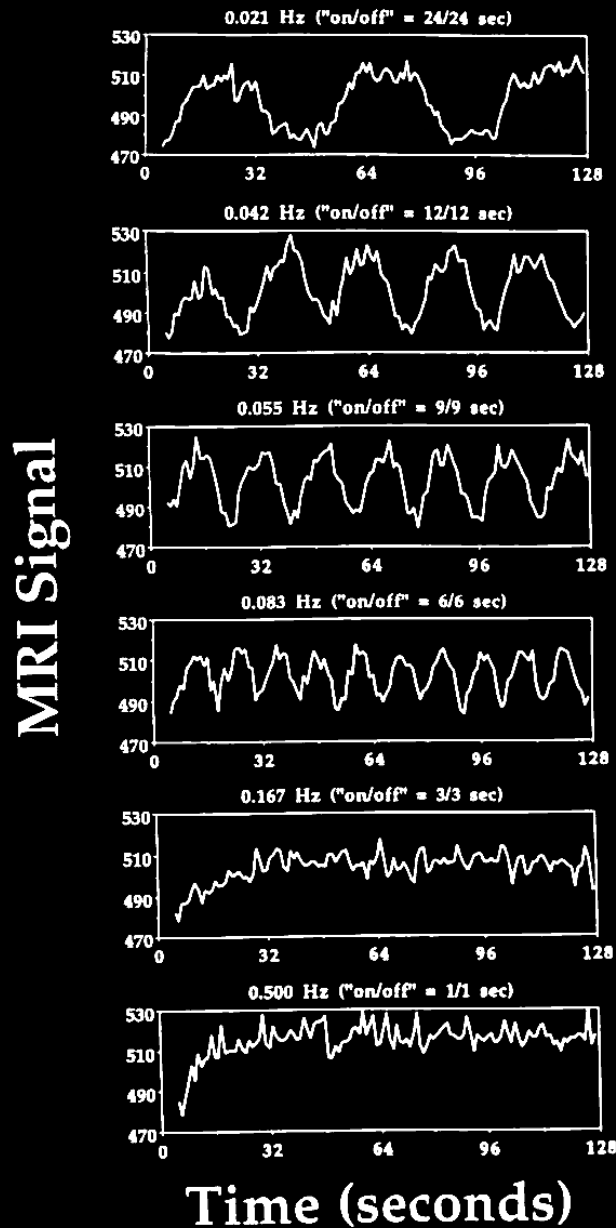


*task*



# Temporal Resolution

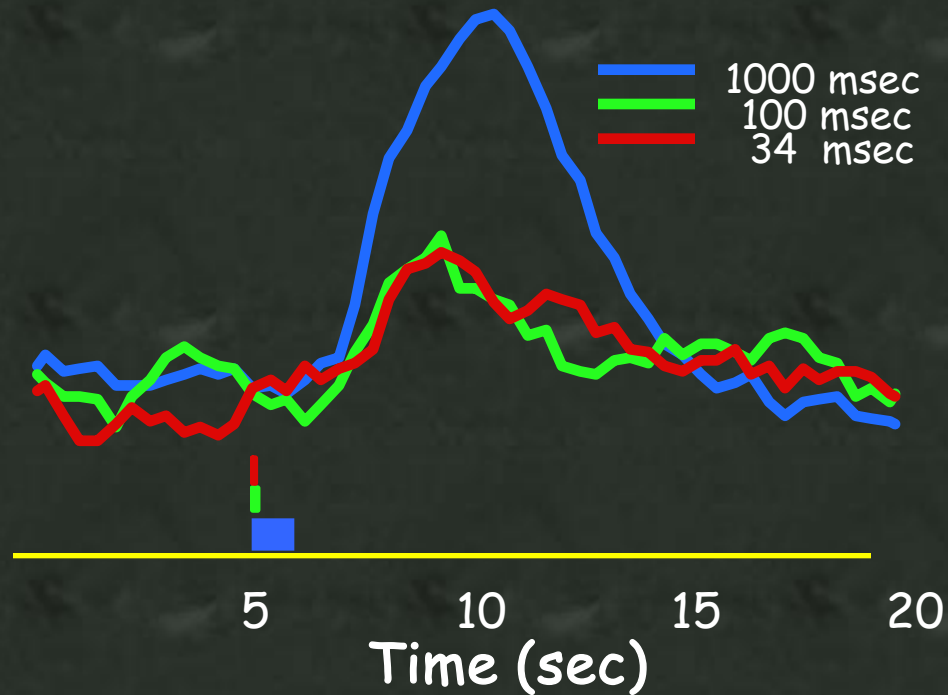
How rapidly can one switch on and off?



P. A. Bandettini,, Functional MRI using the BOLD approach: dynamic characteristics and data analysis methods, in "Diffusion and Perfusion: Magnetic Resonance Imaging" (D. L. Bihan, Ed.), p.351-362, Raven Press, New York, 1995.

# Temporal Resolution

How brief of a stimulus can one give?



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, 3<sup>rd</sup> Proc. Soc. Magn. Reson., Nice, p. 450. (1995).

# Temporal Resolution

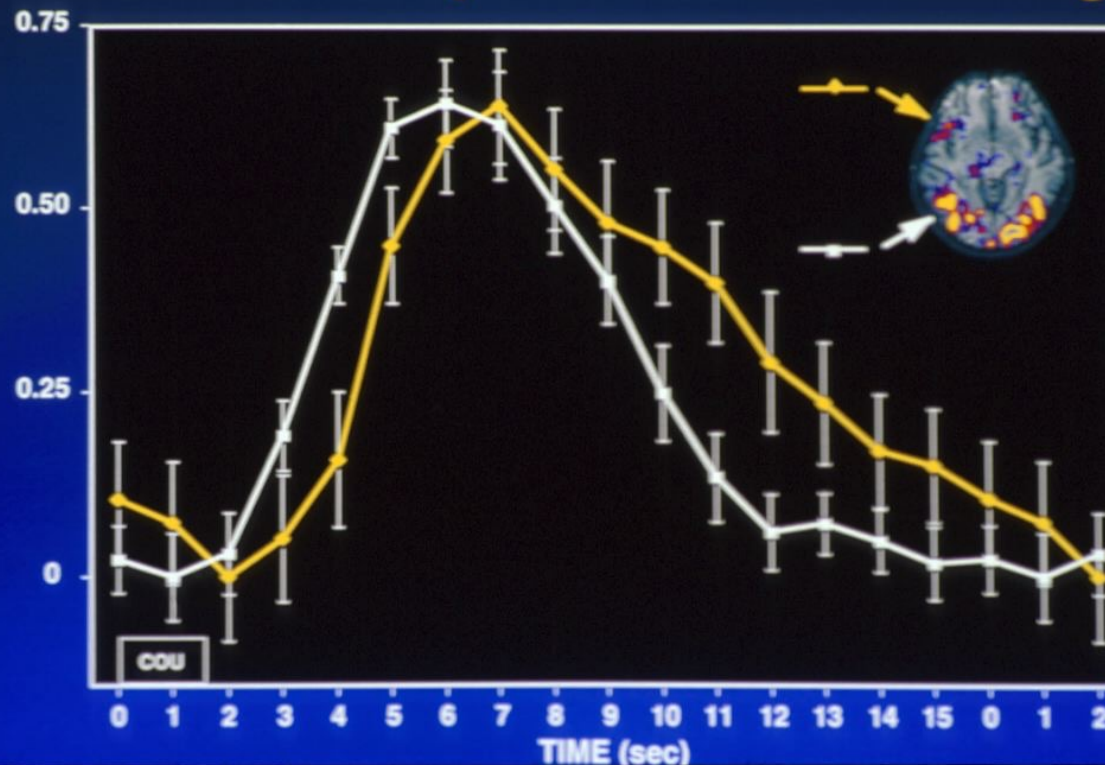
*Proc. Natl. Acad. Sci. USA*  
Vol. 93, pp. 14878–14883, December 1996  
Neurobiology

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

(neuroimaging/single trial/language/prefrontal)

RANDY L. BUCKNER<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. RAICHEL<sup>§\*\*††</sup>, AND BRUCE R. ROSEN<sup>†‡</sup>

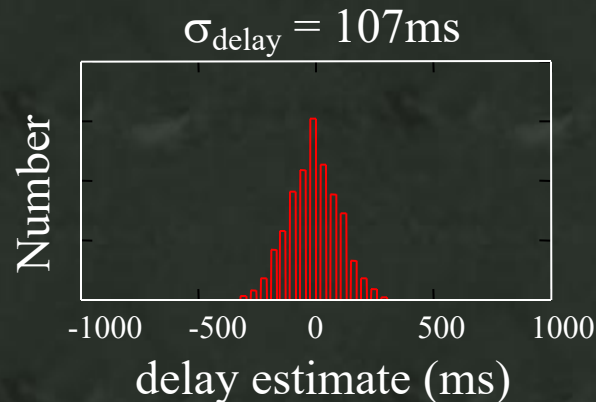
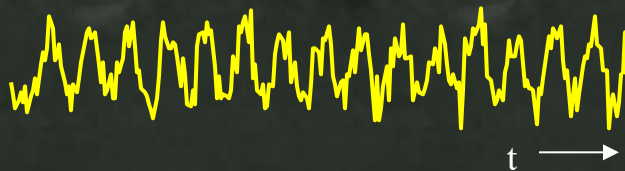
### Time Course Comparison Across Brain Regions



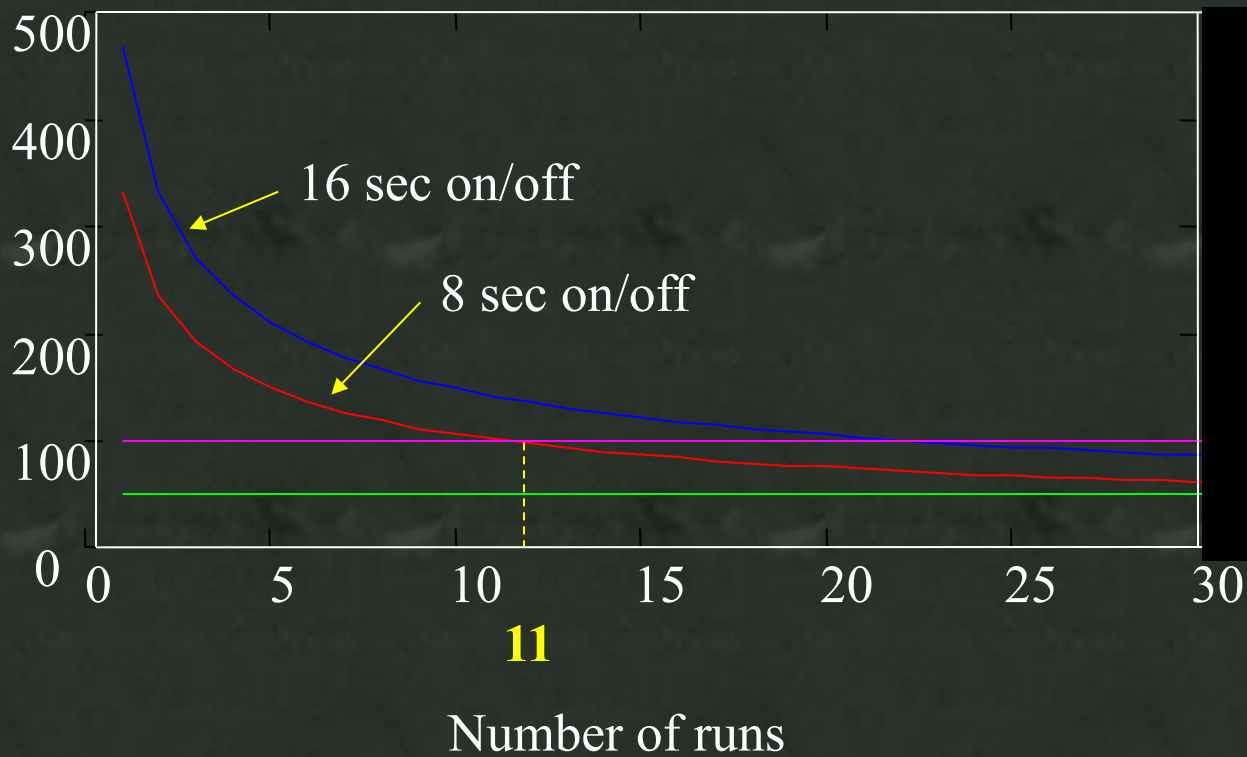


1 run:

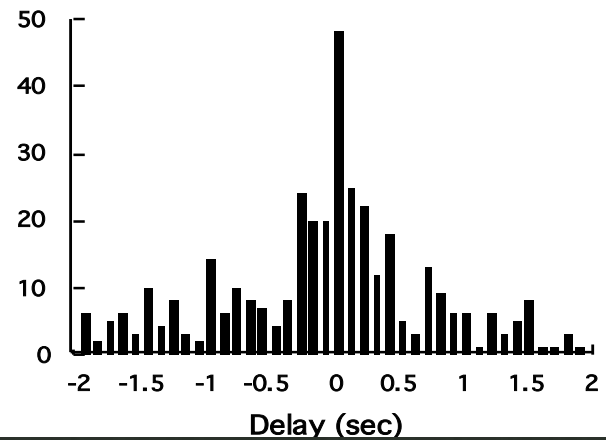
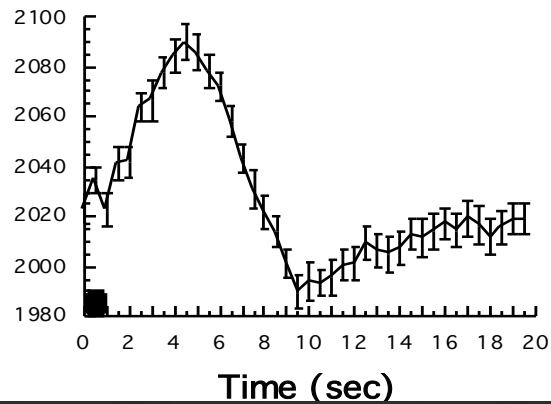
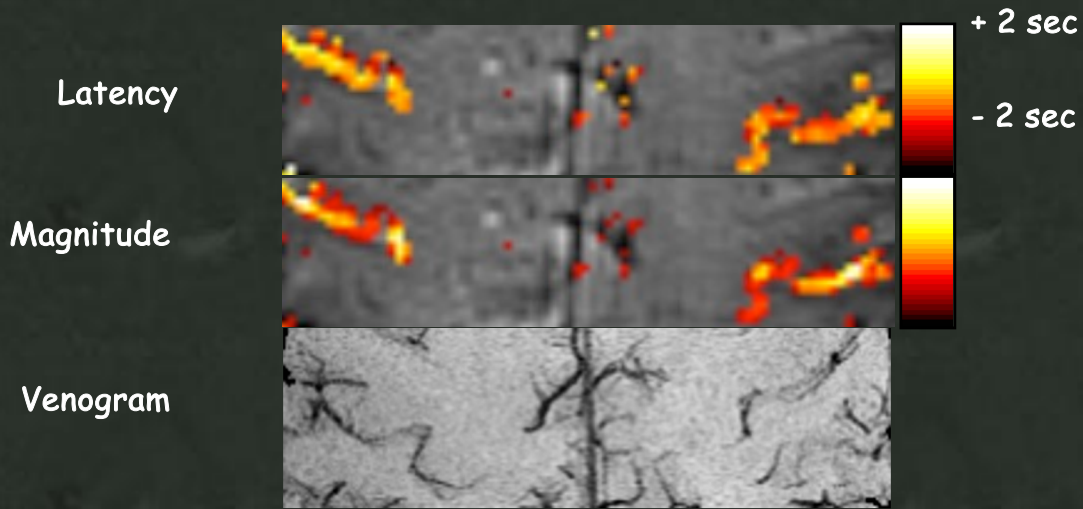
1% Noise  
4% BOLD  
256 time pts /run  
1 second TR



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



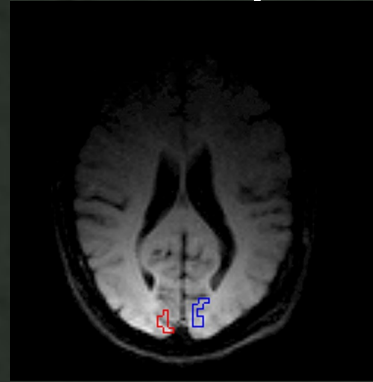
## Latency Variation...



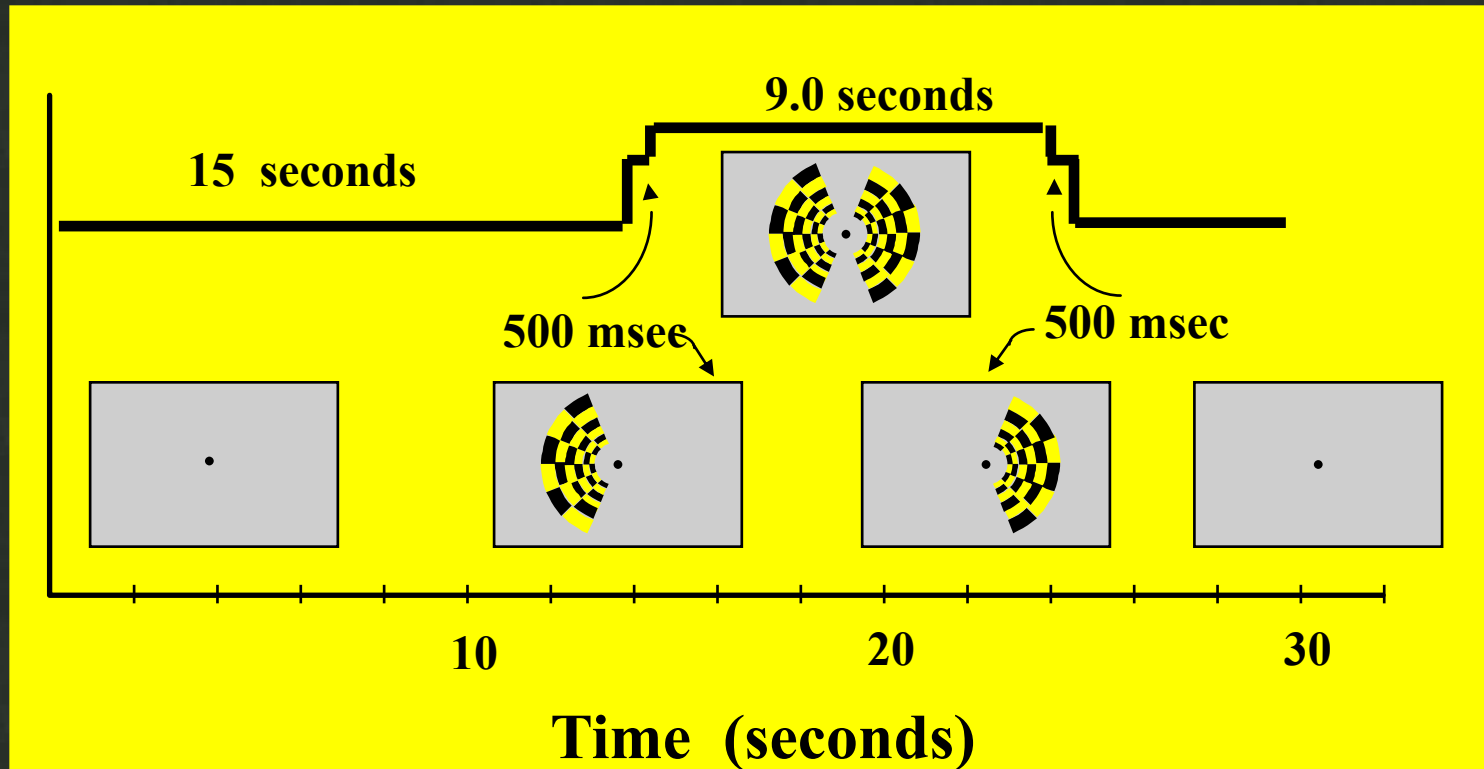
P. A. Bandettini, (1999) "Functional MRI" 205-220.

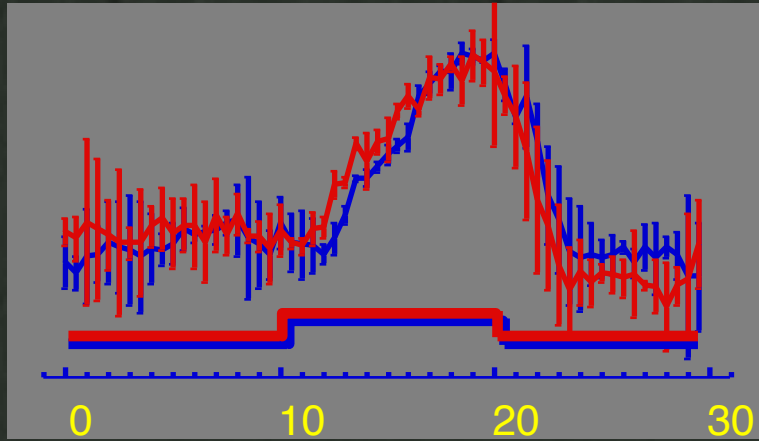
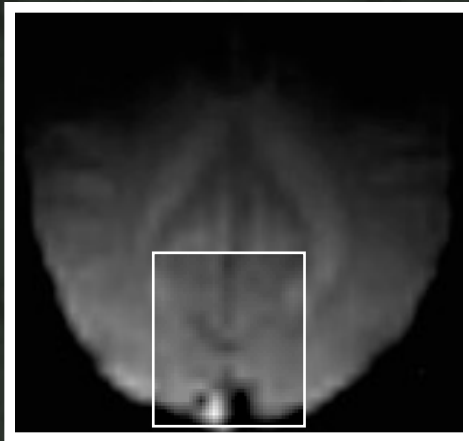
# Hemi-Field Experiment

Right Hemisphere



Left Hemisphere





500 ms



500 ms



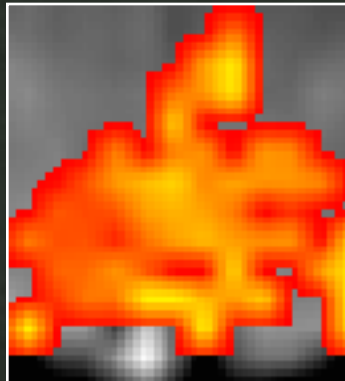
Right Hemifield

Left Hemifield

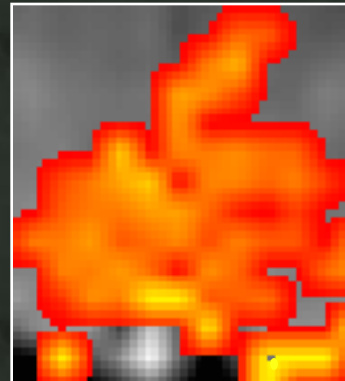
+ 2.5 s

0 s

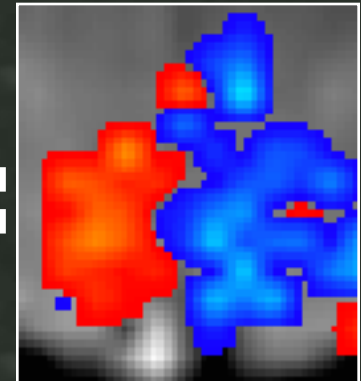
- 2.5 s



-



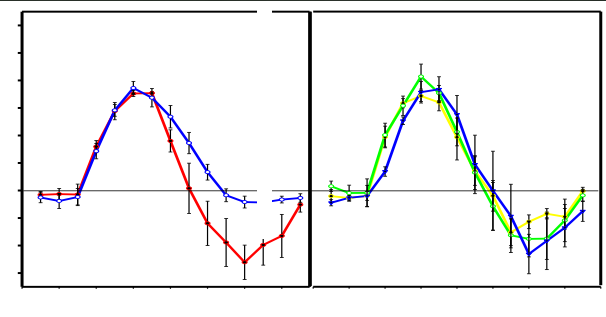
=



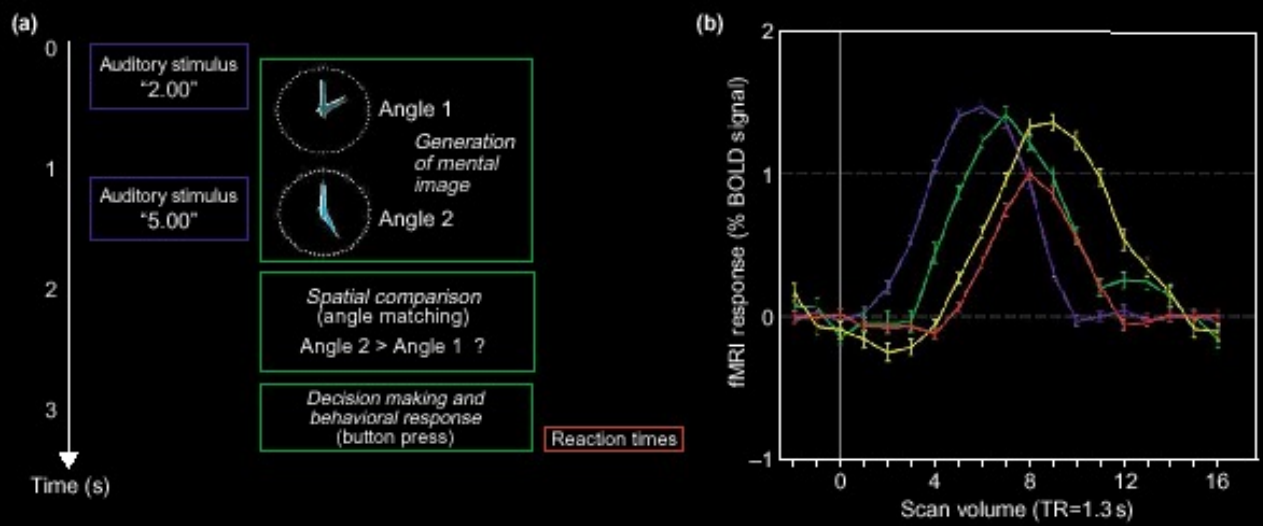
# Task timing modulation

Word vs. Non-word

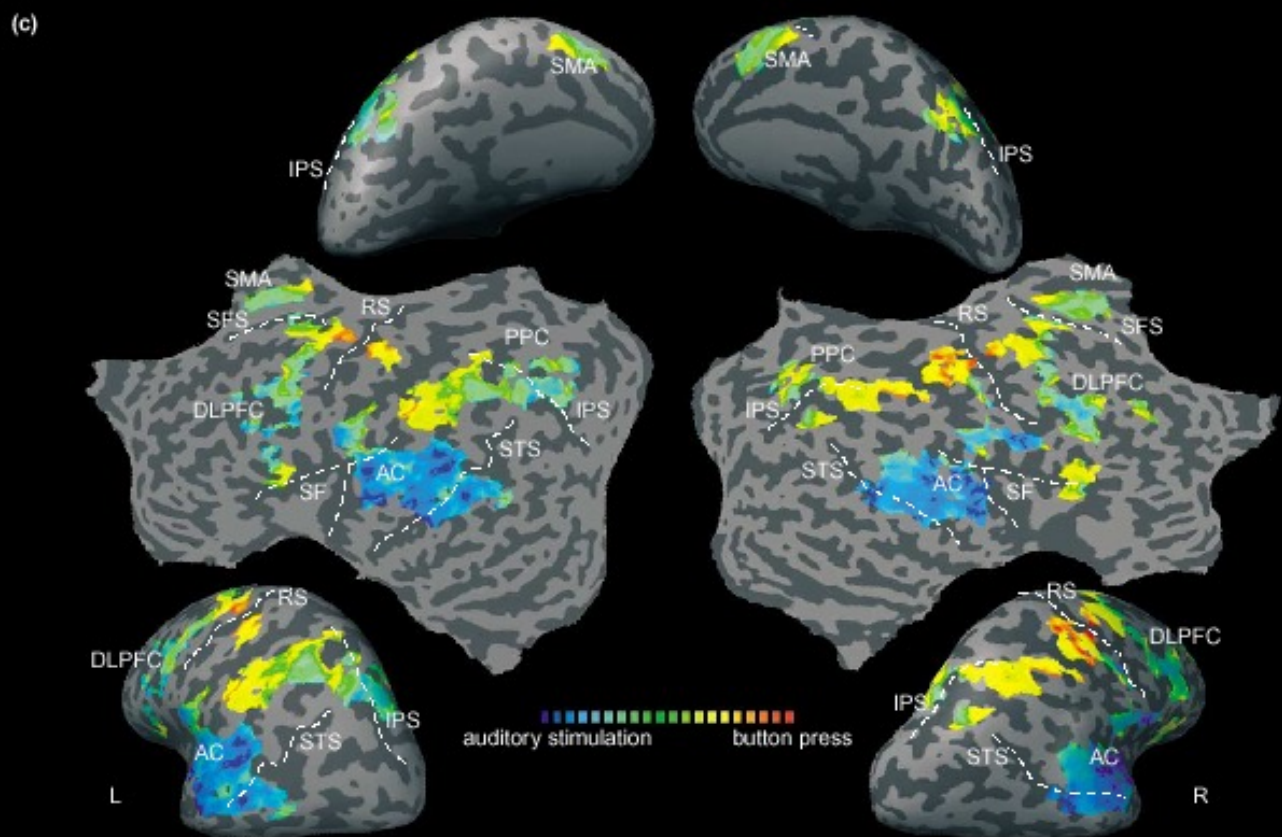
0°, 60°, 120° Rotation



Rotational Delay	Lexical Delay		Mean Reaction Time
	Words	Non-Words	
0°	smudge	dierts	823 ms
60°	frollic	cuhlos	891 ms
120°	slouch	gednus	1446 ms
Mean Reaction Time	986 ms	1219 ms	



# No calibration



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



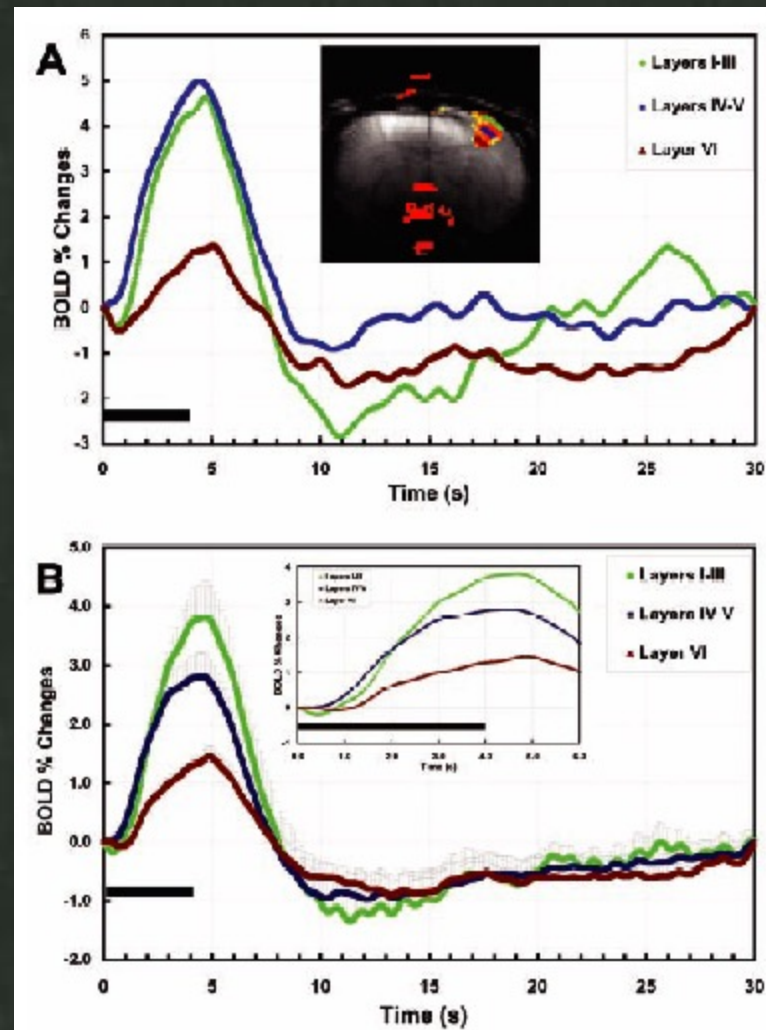
# Laminar specificity of functional MRI onset times during somatosensory stimulation in rat

Afonso C. Silva\* and Alan P. Koretsky

Laboratory of Functional and Molecular Imaging, National Institute of Neurological Disorders and Stroke, Bethesda, MD 20892

15182-15187 | PNAS | November 12, 2002 | vol. 99 | no. 23

No calibration



11.7 T

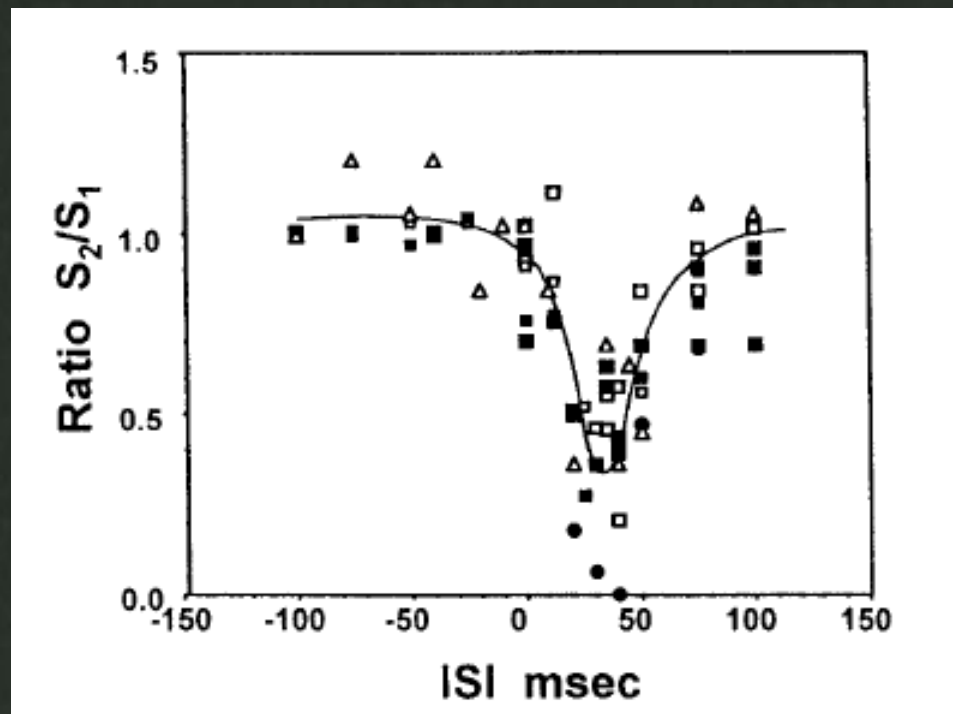
Temporal resolution factors	Values for each factor
Fastest image acquisition rate	≈64 images/s
Minimum time for signal to significantly deviate from baseline	≈3 s
Fastest on-off rate in which amplitude-is not compromised	≈8 s on, 8 s off
Fastest on-off rate in which hemodynamic response keeps up	≈2 s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

P. A. Bandettini, (1999) "Functional MRI" 205-220.



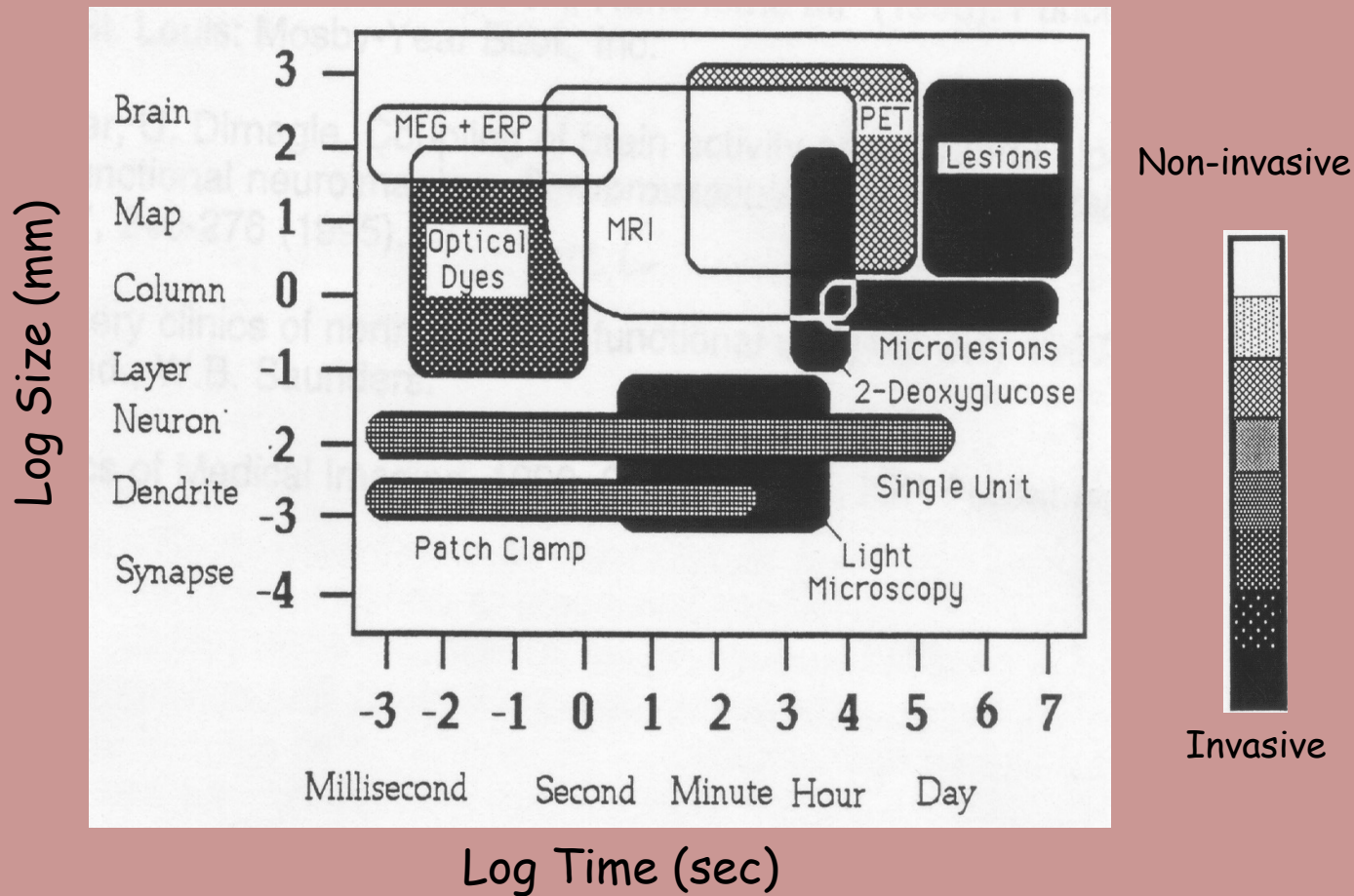
# An approach to probe some neural systems interaction by functional MRI at neural time scale down to milliseconds

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



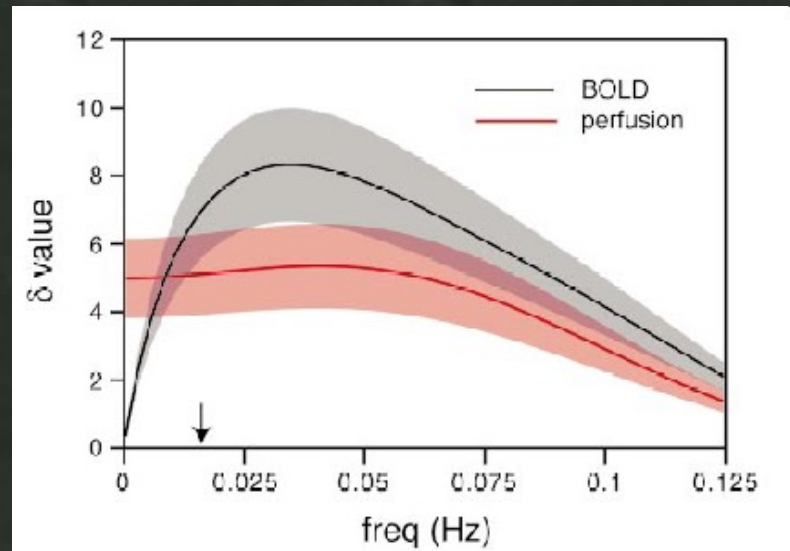
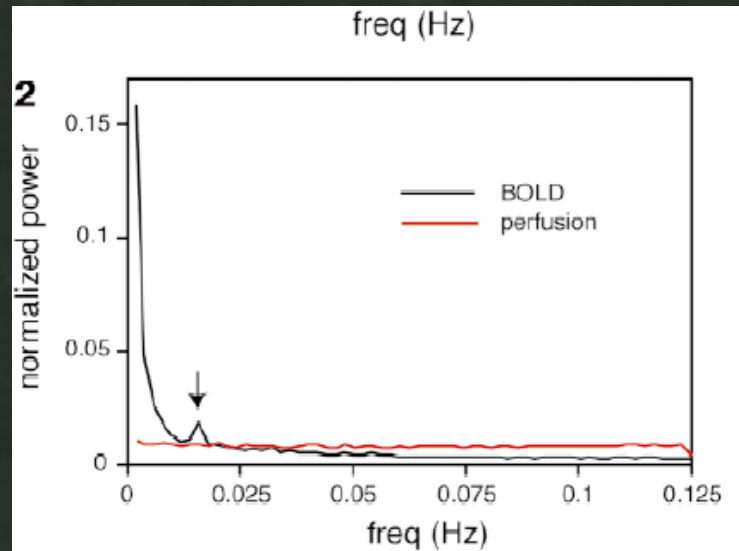
11026–11031 PNAS September 26, 2000 vol. 97 no. 20

# Functional Neuroimaging Techniques



# Slow Limits...

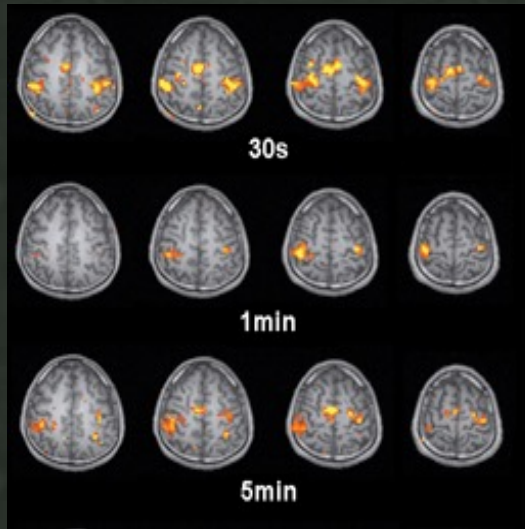
Perfusion is better than BOLD for slow "state change" comparisons..



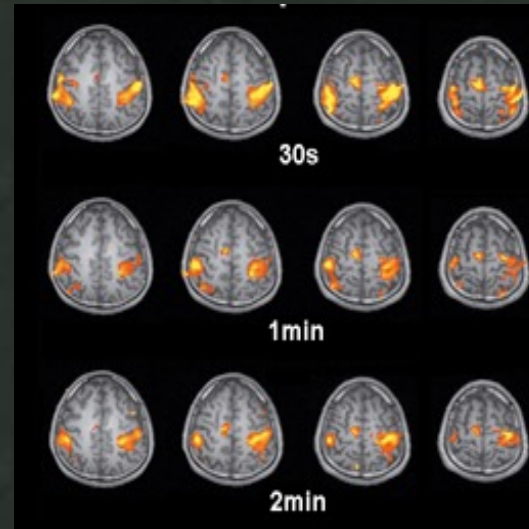
GK Aguirre et al, (2002) NeuroImage 15 (3): 488-500

# Perfusion vs. BOLD: Low Task Frequency

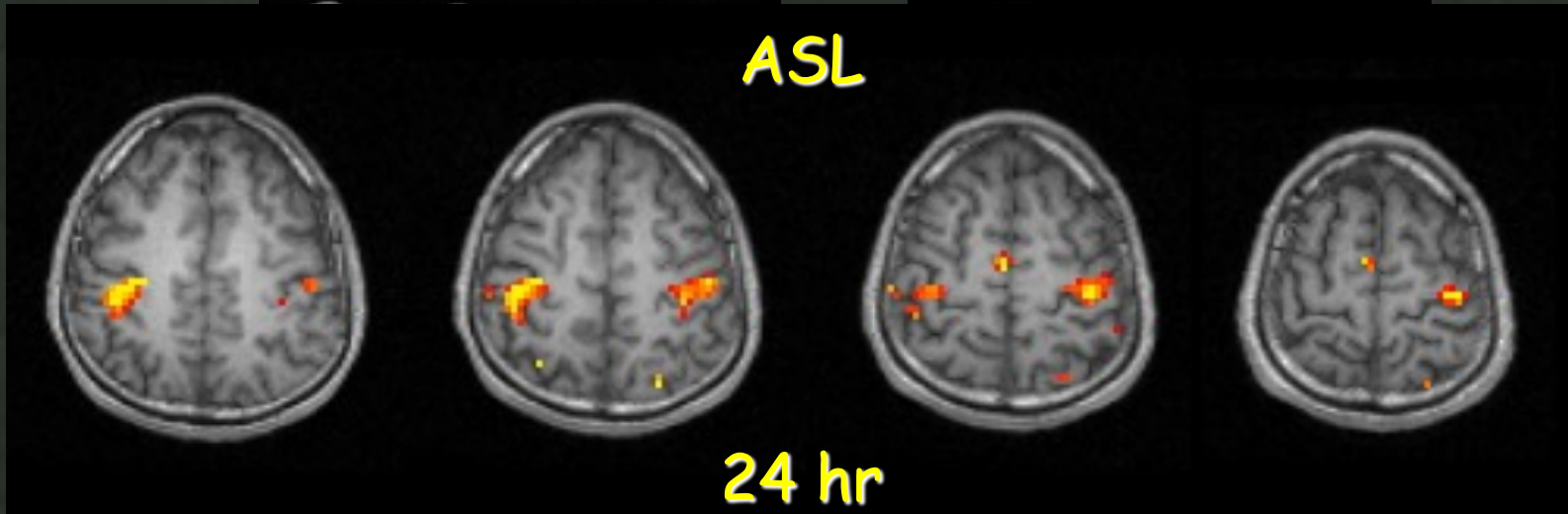
Perfusion

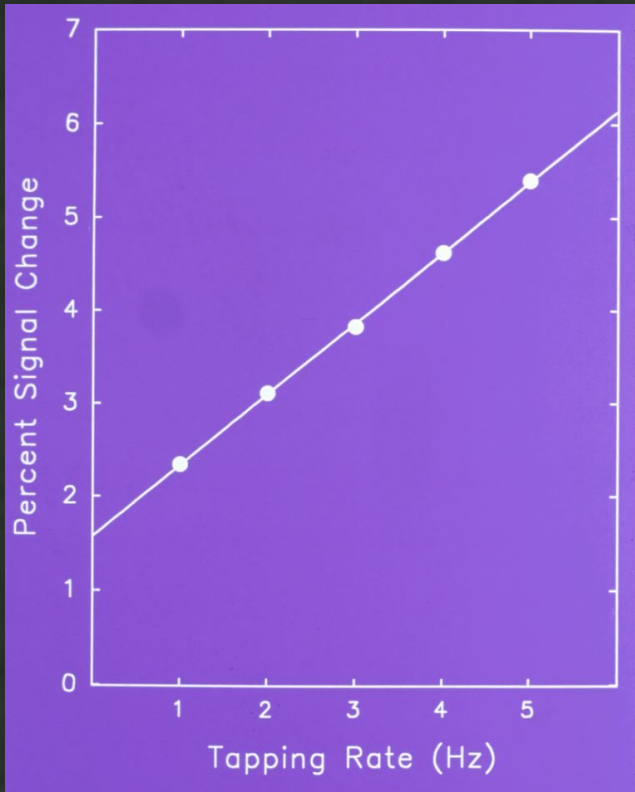


BOLD

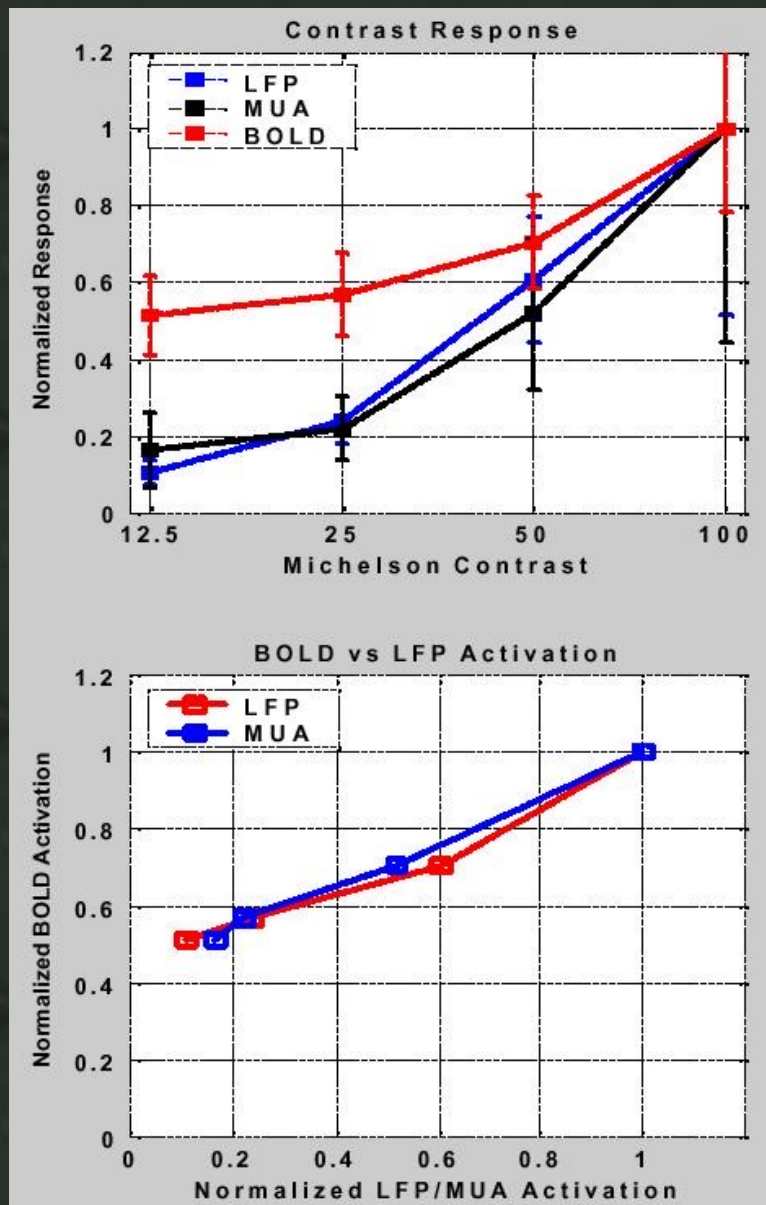


ASL





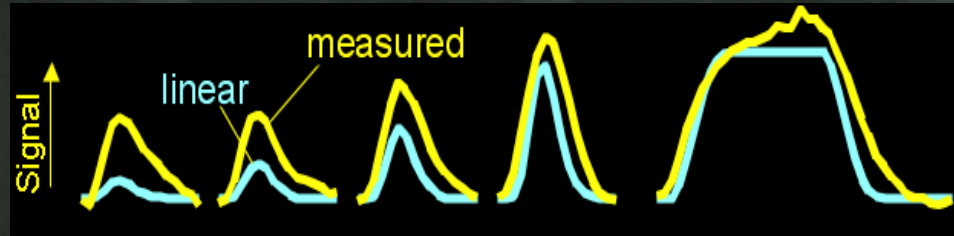
S. M. Rao et al, (1996) "Relationship between finger movement rate and functional magnetic resonance signal change in human primary motor cortex." *J. Cereb. Blood Flow and Met.* 16, 1250-1254.



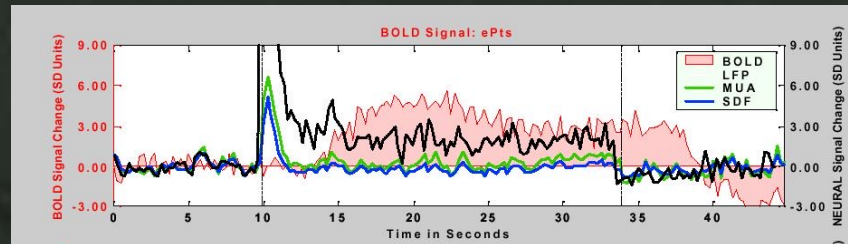
Logothetis et al. (2001) "Neurophysiological investigation of the basis of the fMRI signal" *Nature*, 412, 150-157



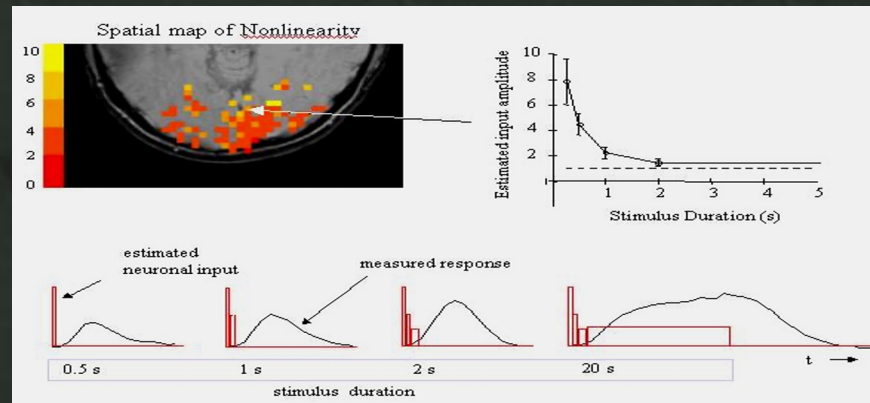
# Linearity



R. M. Birn, (2001) NeuroImage, 14: 817-826.



Logothetis et al. (2001) Nature, 412, 150-157.

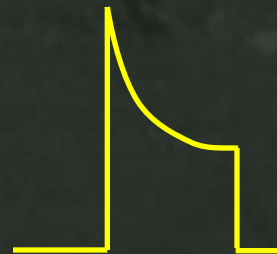
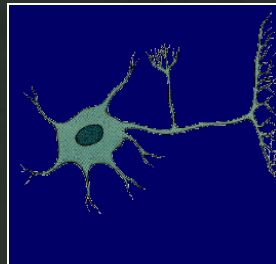


P. A. Bandettini et al, (2001) Nature Neuroscience, 4: 864-866.

R. M. Birn, et. al, (2001) NeuroImage, 14: 817-826.

## Sources of this Nonlinearity

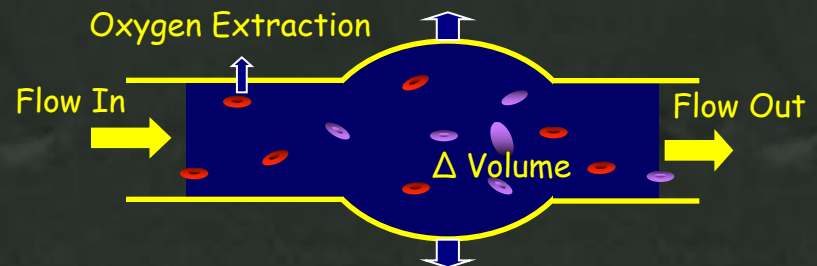
- Neuronal



- Hemodynamic

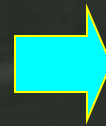
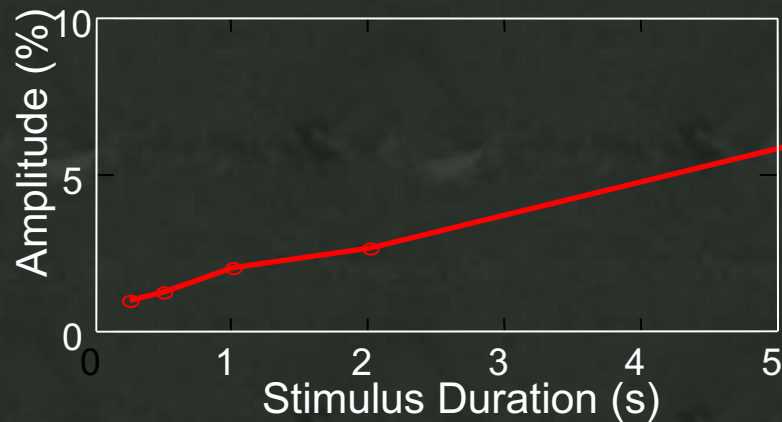
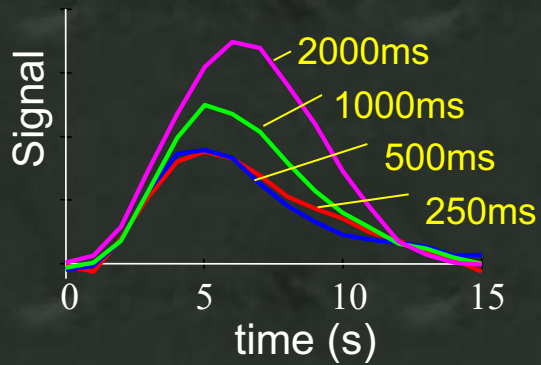
- Oxygen extraction

- Blood volume dynamics

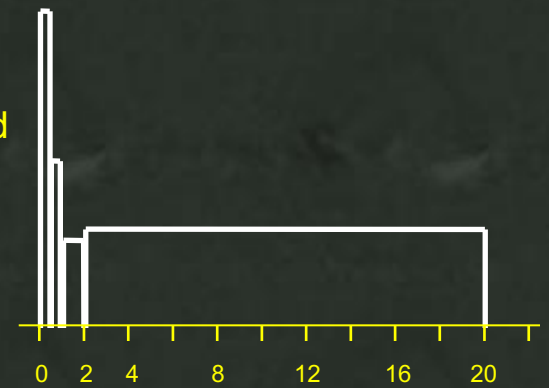


# Linearity

## Contrast Reversing Checkerboard

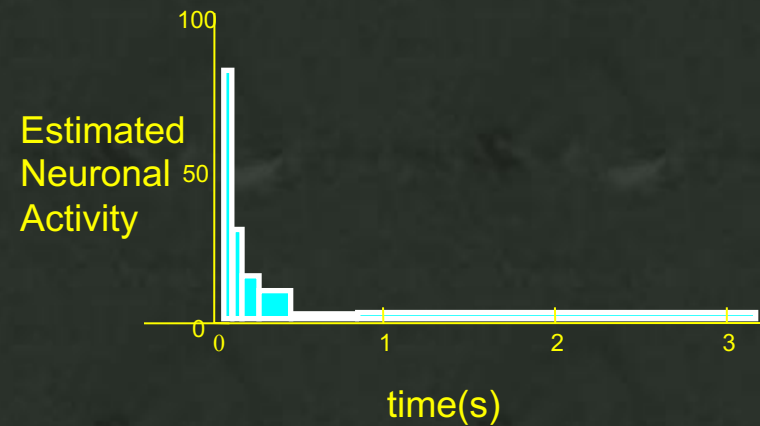
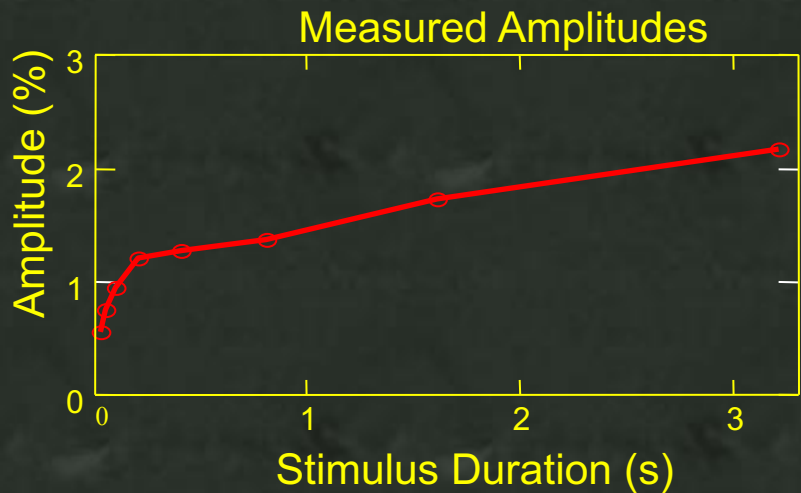
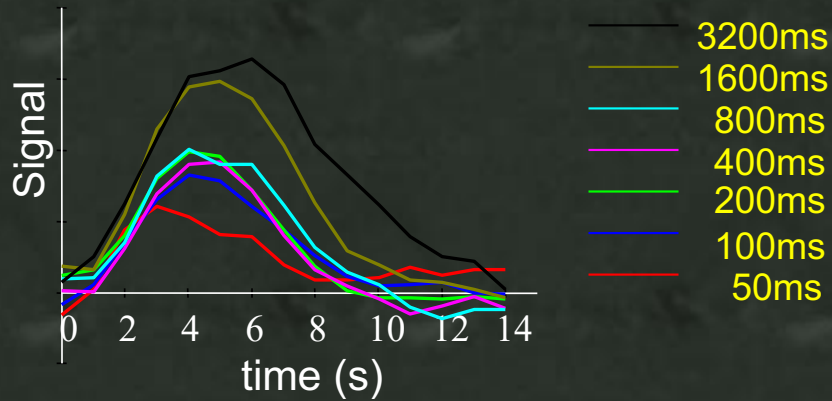


Estimated  
Neuronal  
Activity



# Linearity

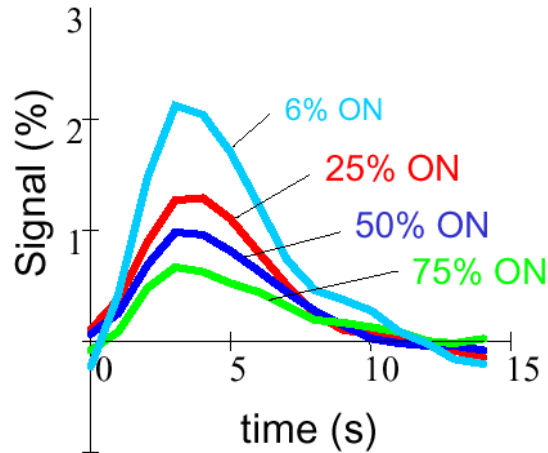
## Static Grating



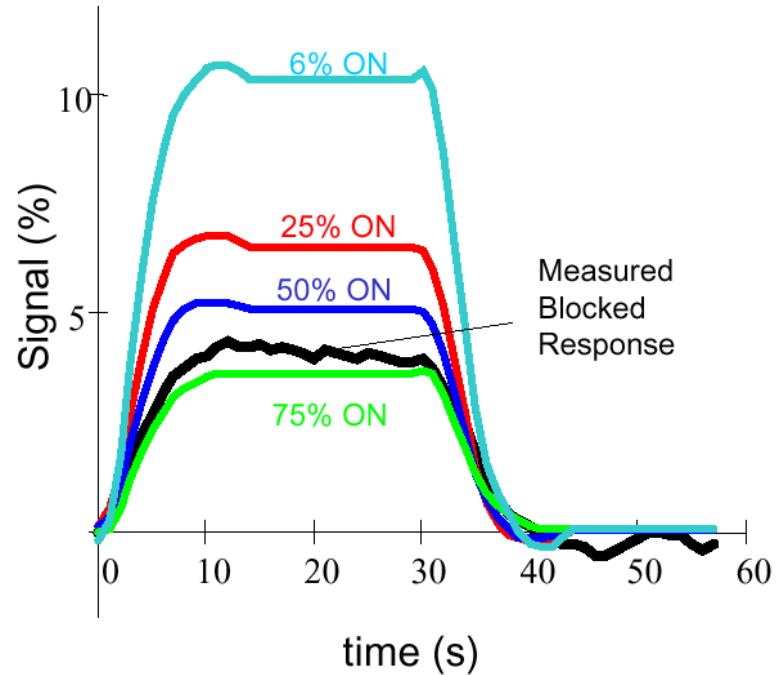
# Linearity

# Duty Cycle Effects

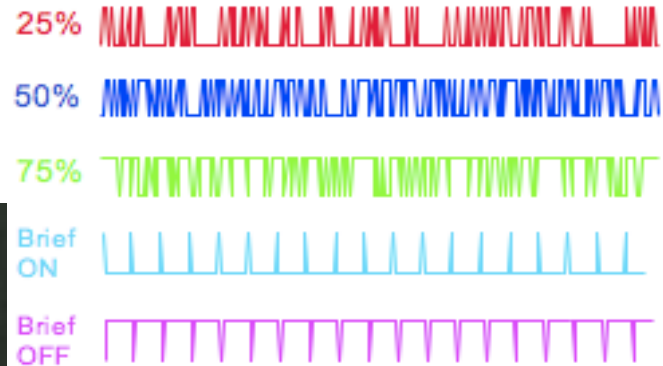
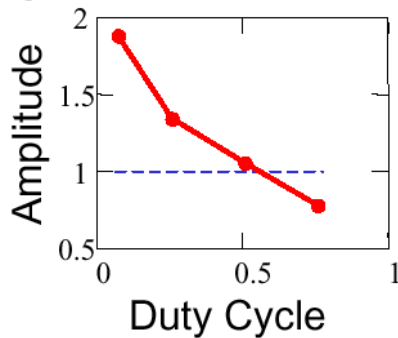
**a** Measured Event-related Responses



**b** Predicted Blocked Responses



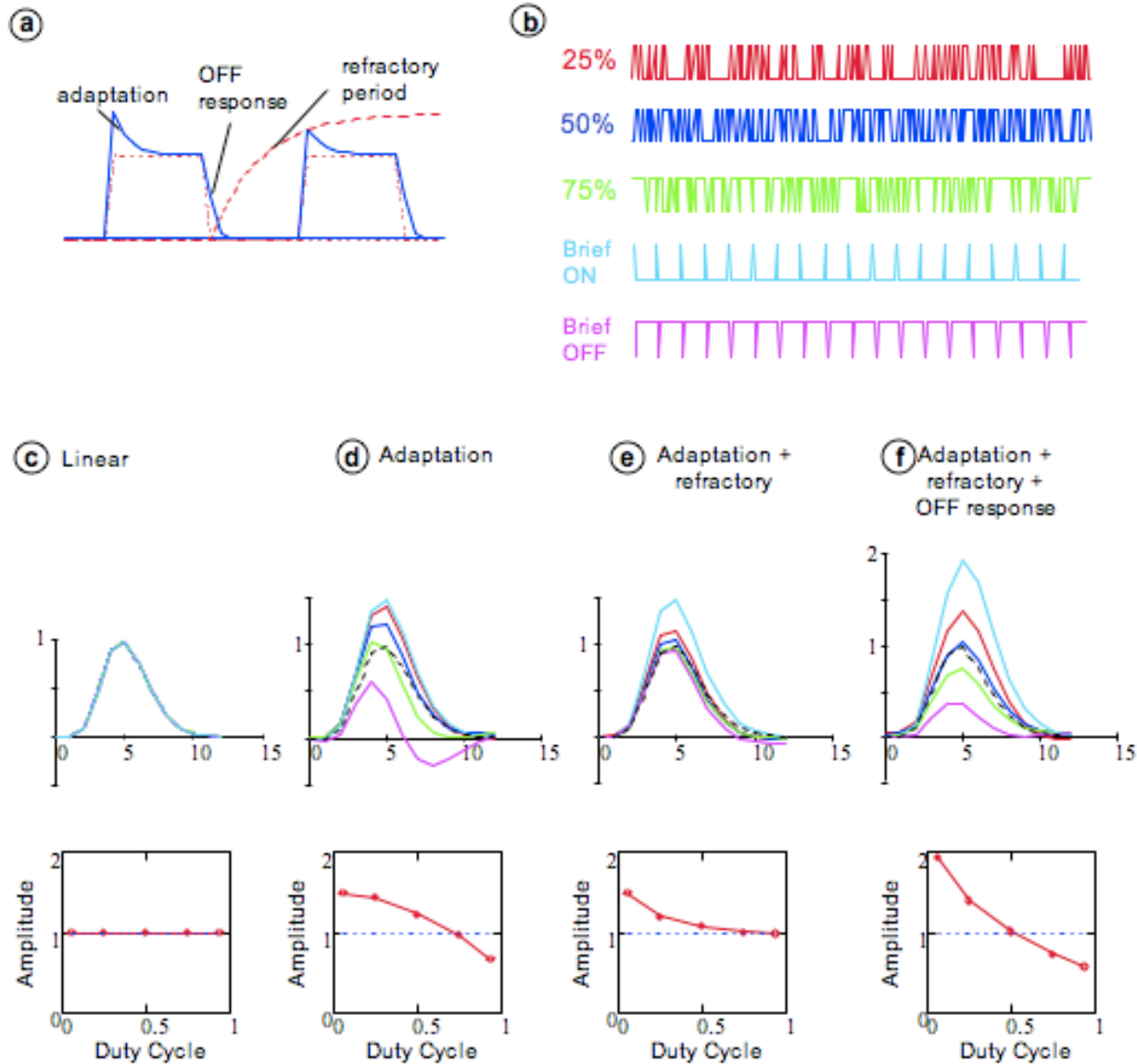
**c**



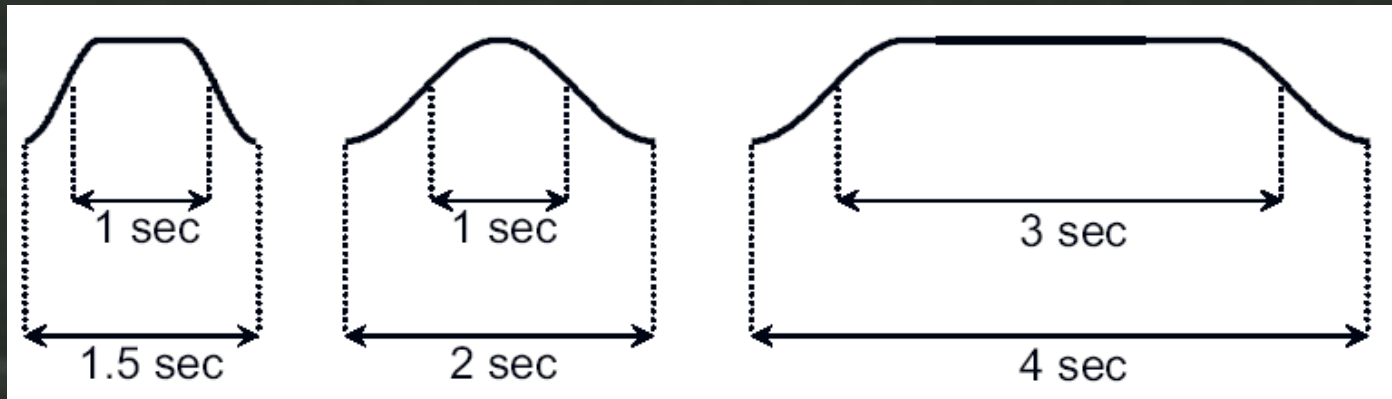
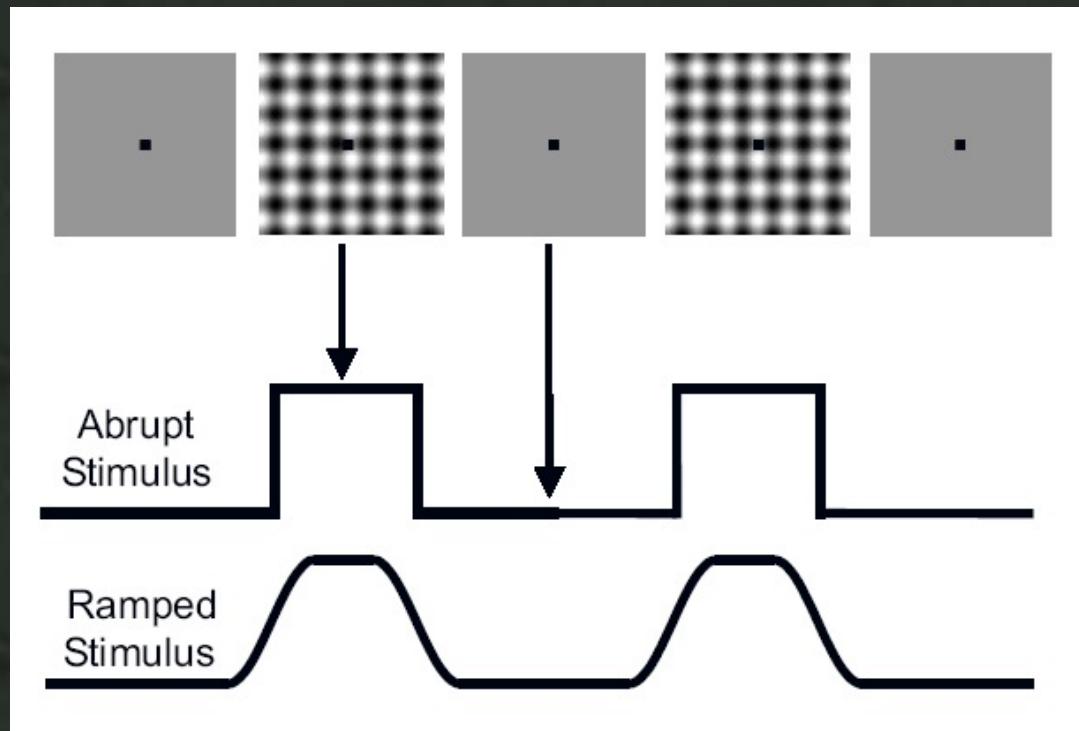


# Linearity

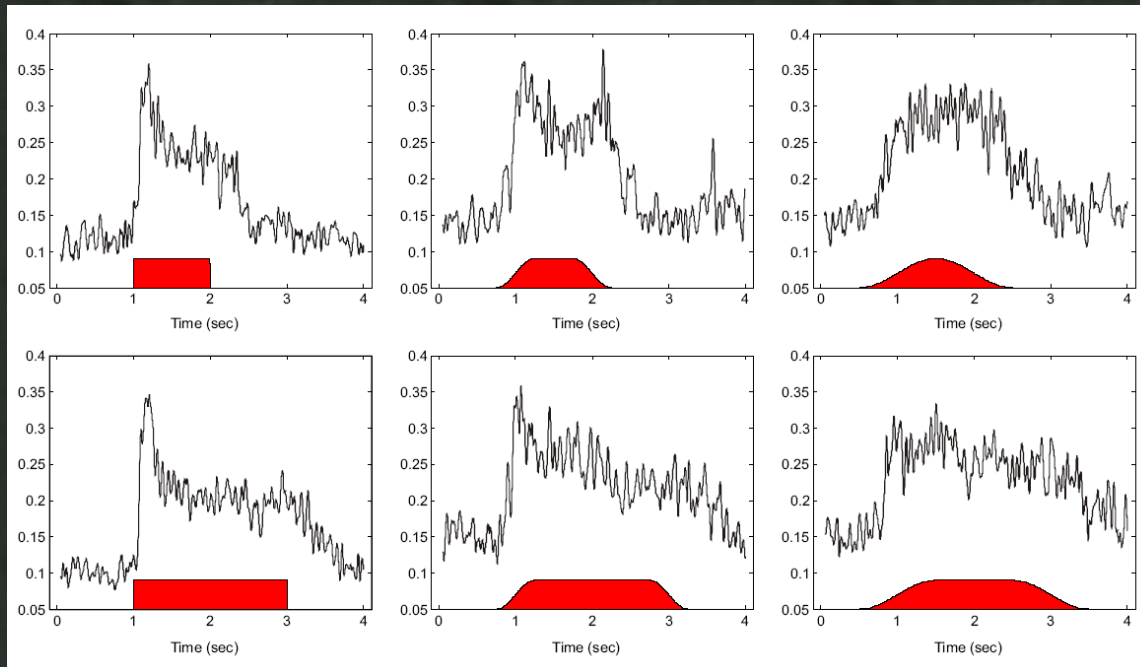
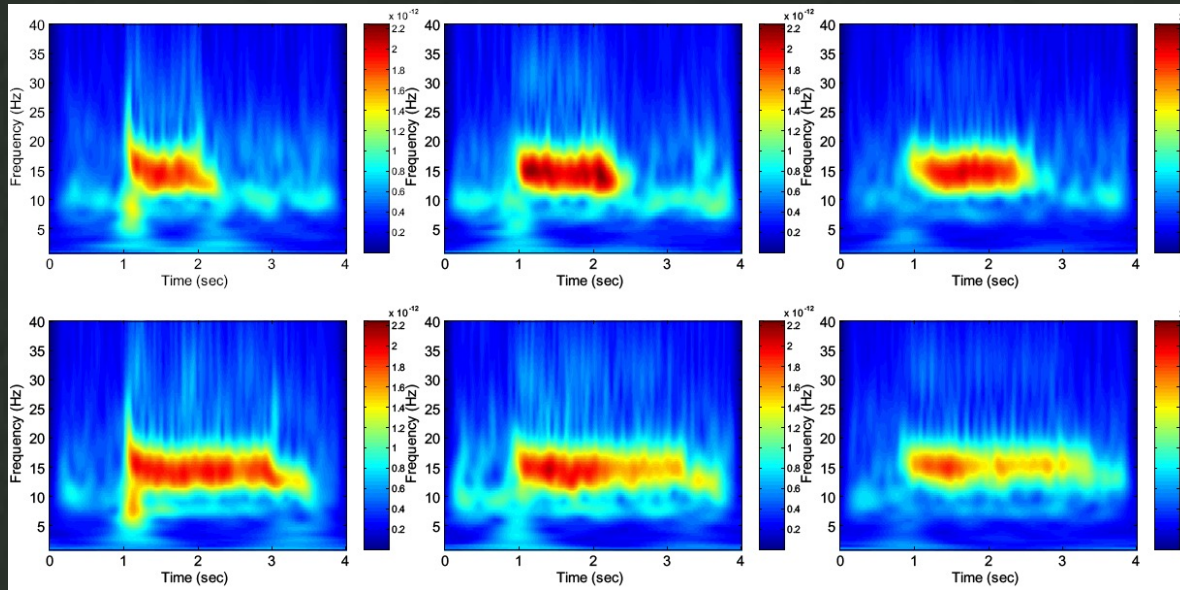
## duty cycle effects



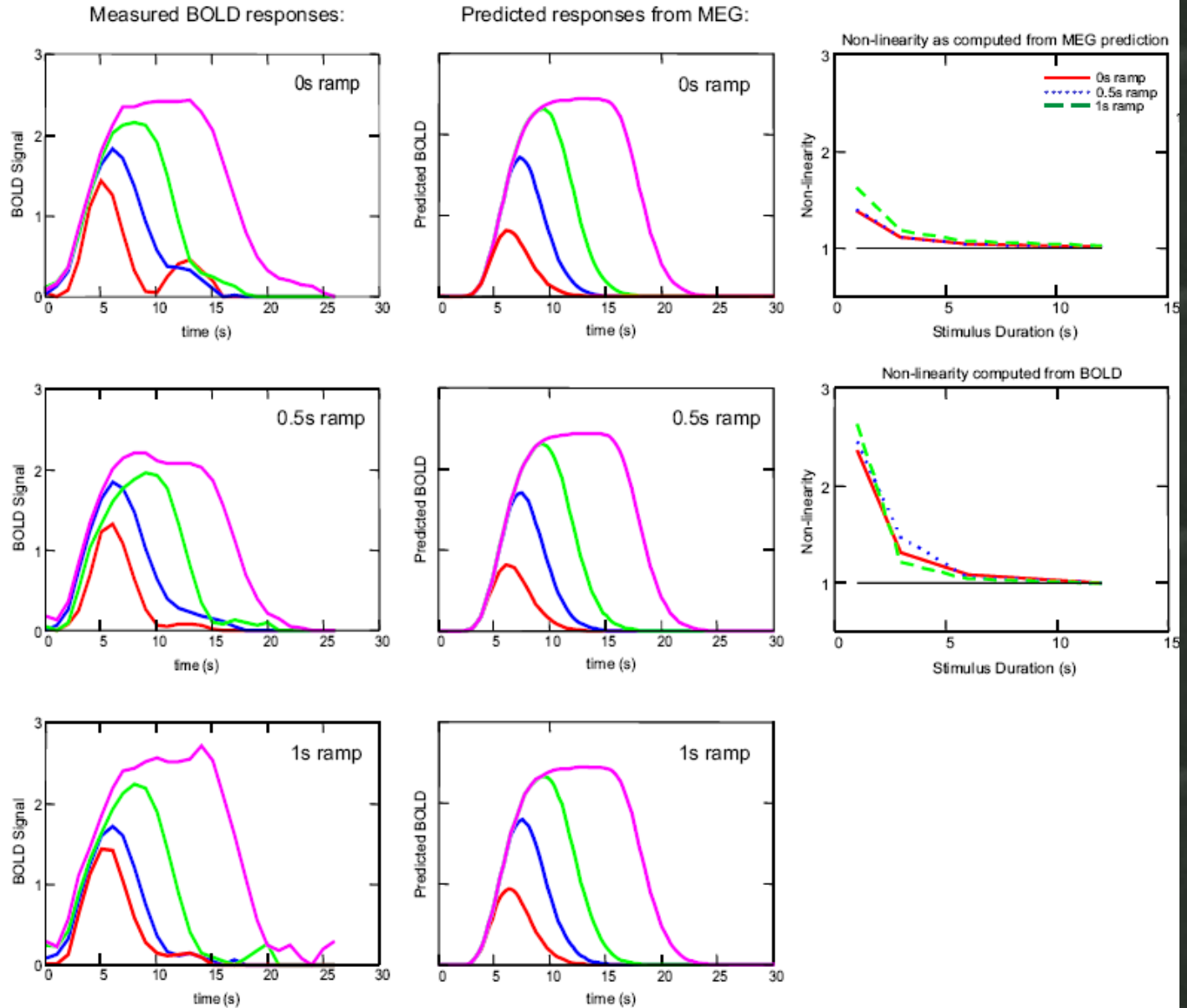
# Linearity



# Linearity

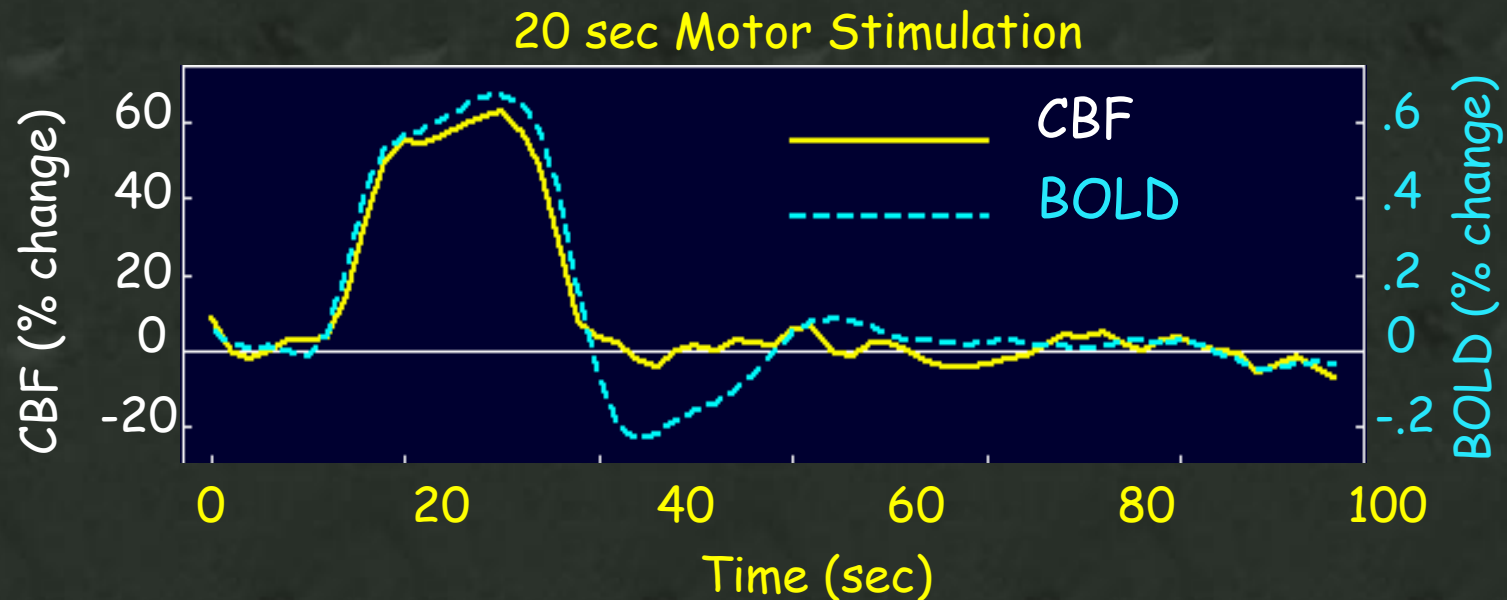


# Linearity



## Post Undershoot

# BOLD post-stimulus undershoot

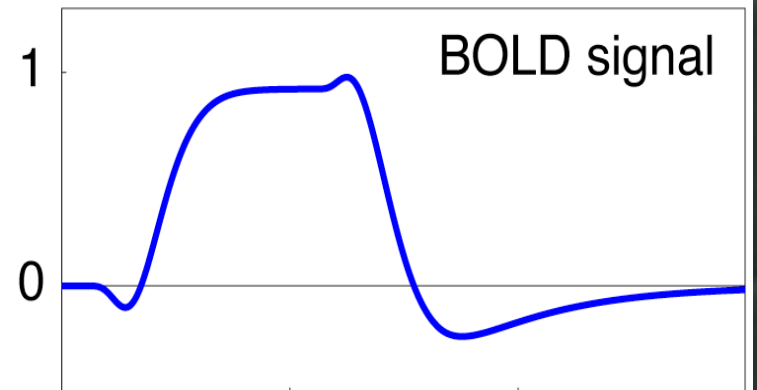
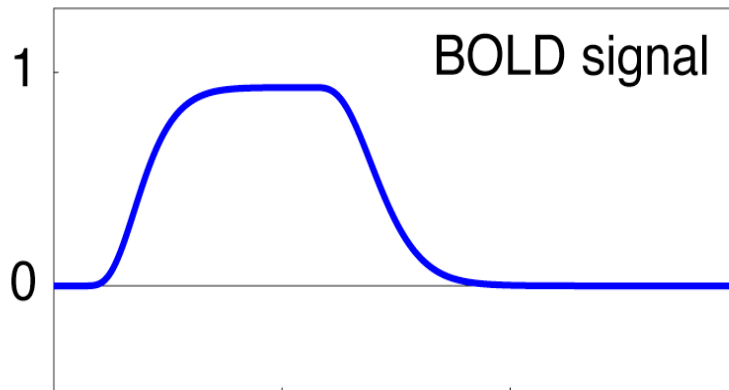
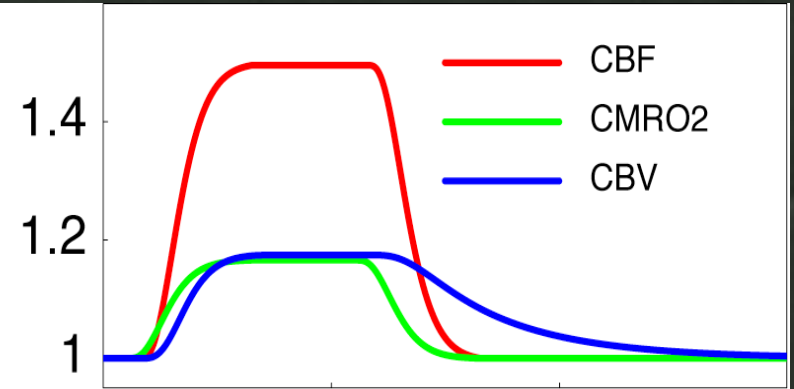
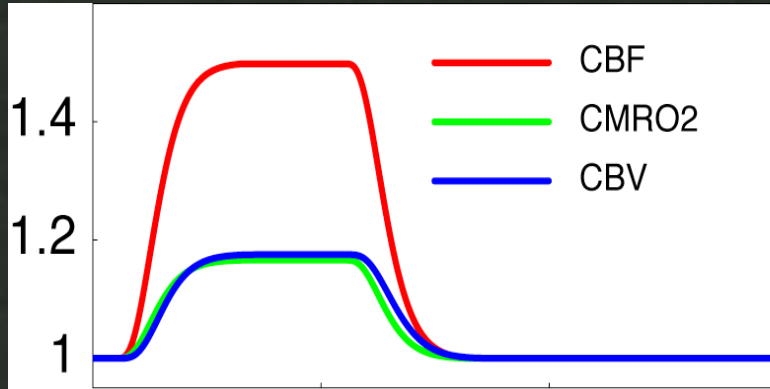


A BOLD undershoot without a CBF undershoot could be due to a slow return to baseline of either CBV or  $CMRO_2$

Courtesy Rick Buxton



# Post Undershoot Simulated BOLD Signal Dynamics



Time (s)

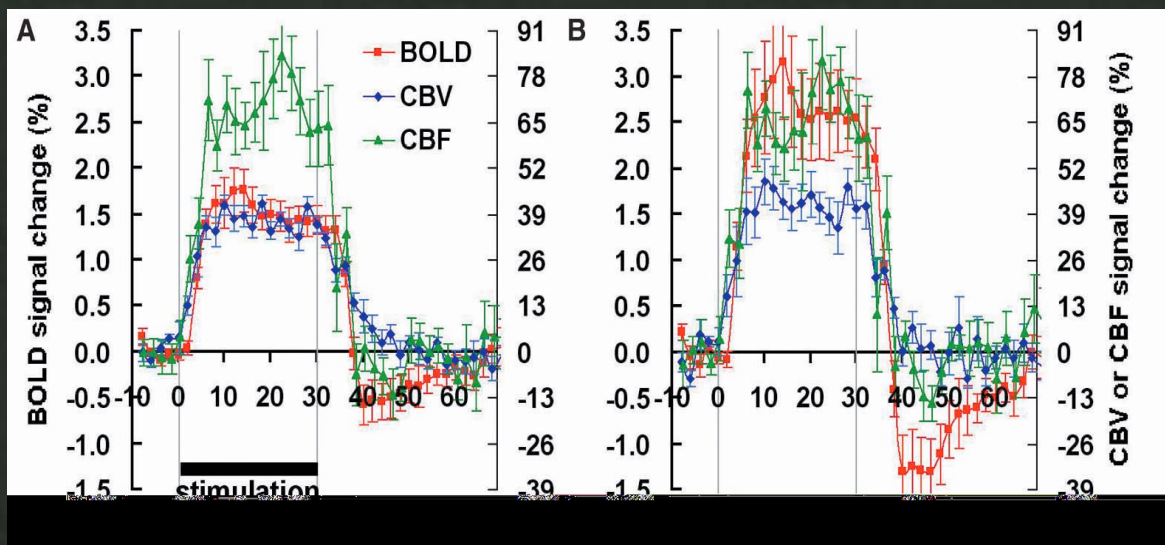
Time (s)

Courtesy Rick Buxton

# Post Undershoot

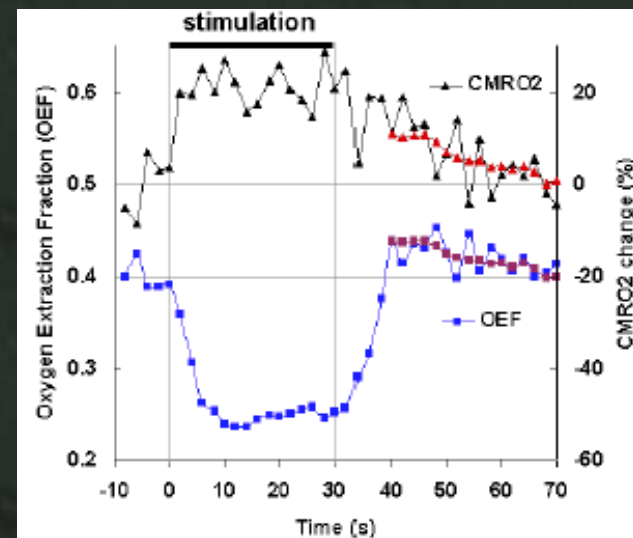
## VASO (Vascular Space Occupancy)

Evidence for sustained elevated  $CMRO_2$   
(VASO indicates fast return of CBV despite BOLD undershoot)



All activated voxels

Overlapped voxels



Lu, et al: JCBF+M 24:764, 2004

# Section on Functional Imaging Methods & Functional MRI Facility Jan 19, 2007



Back row: Wenming Luh, Niko Kriegeskorte, Rasmus Birn, Tyler Jones, Sean Marrett

Middle row: Jon West, Kay Kuhns, Anthony Boemio, Peter Bandettini, Joey Dunsmoor, Doug Ruff, Kevin Murphy

Front row: Dorian Van Tassel, Jerzy Bodurka, Adam Thomas, Marieke Mur, David Knight