I have no conflicts to disclose with regard to this presentation.

The Absolute Beginners Guide to fMRI

Peter A. Bandettini, Ph.D.

Section on Functional Imaging Methods
Laboratory of Brain and Cognition
http://fim.nimh.nih.gov

&

Functional MRI Facility
http://fmrif.nimh.nih.gov

The Absolute Beginners Guide to fMRI

1. History

2. Functional Contrast

3. Interpretation Issues

The Absolute Beginners Guide to fMRI

1. History

2. Functional Contrast

3. Interpretation Issues

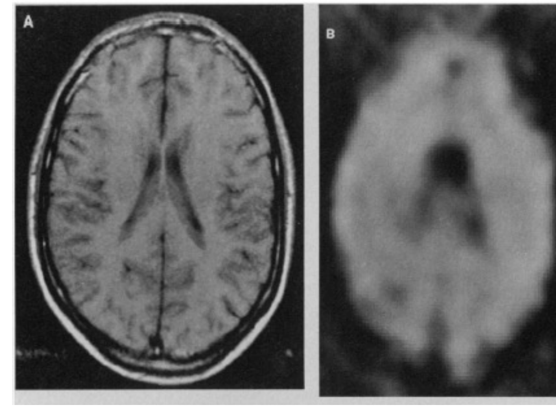
History

Functional Magnetic Resonance Imaging in Medicine and Physiology

Chrit T. W. Moonen, Peter C. M. van Zijl, Joseph A. Frank, Denis Le Bihan, Edwin D. Becker

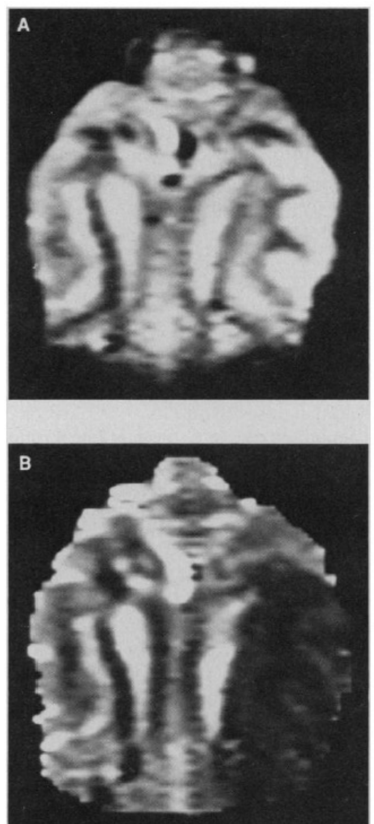
(1990) *Science*, 250, 53-61.

metabolic imaging (NAA)

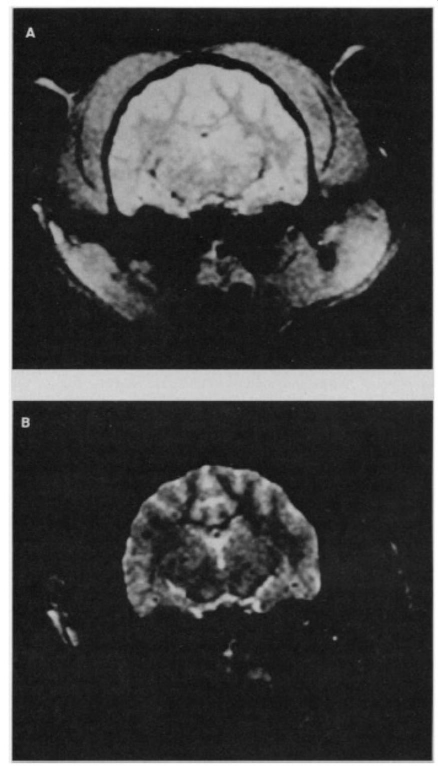


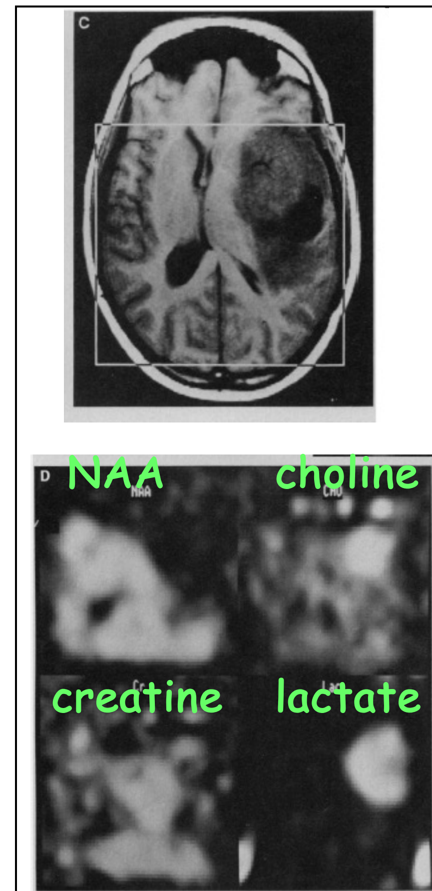
angiography

Diffusion

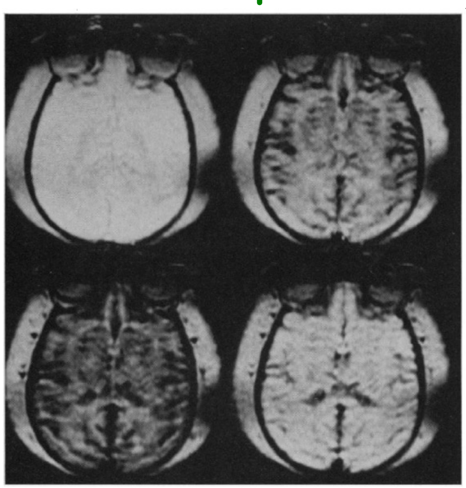


magnetization transfer





Gadolinium perfusion

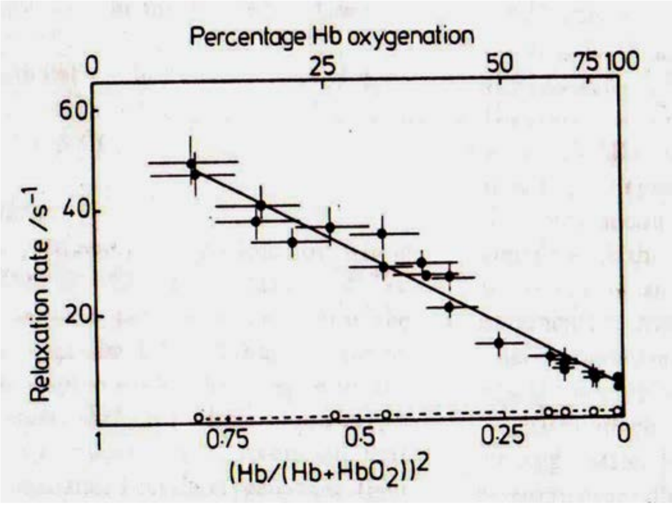


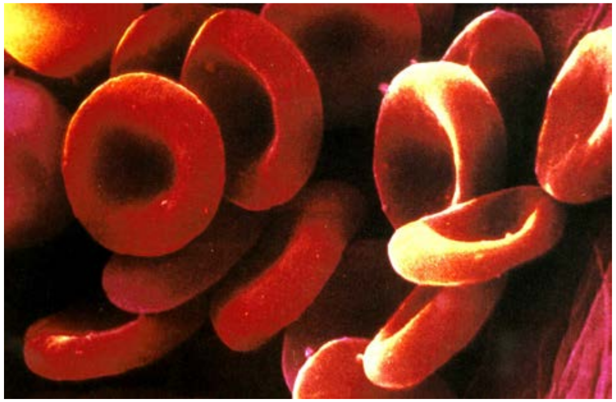
History

Magnetic Properties of Blood

L. Pauling, C. D. Coryell, *Proc.Natl. Acad. Sci. USA 22, 210-216*, **1936**.

K.R. Thulborn, J. C. Waterton, et al., *Biochim. Biophys. Acta. 714: 265-270*, **1982**.

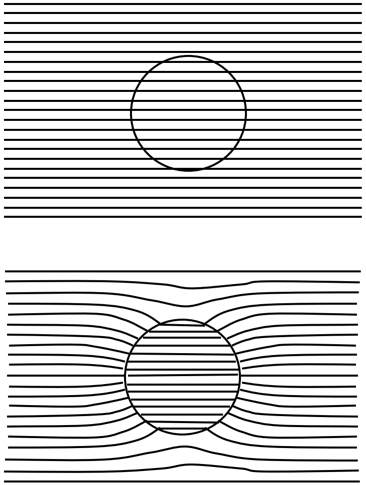




red blood cells

oxygenated

deoxygenated

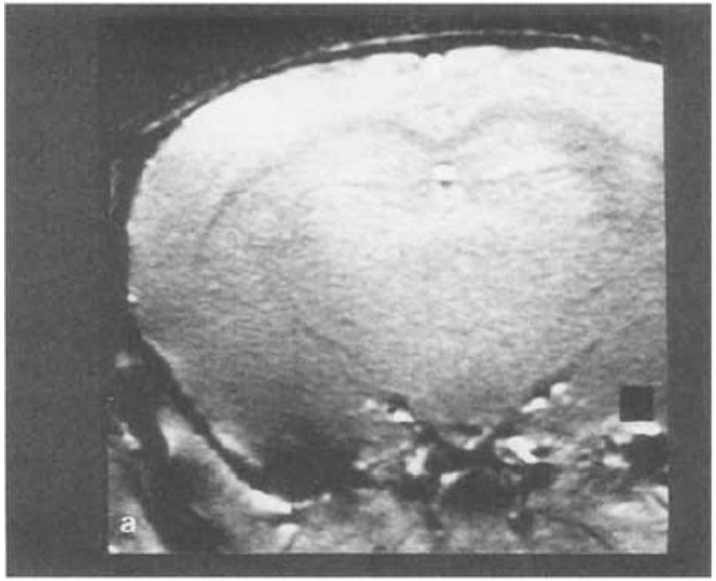


History

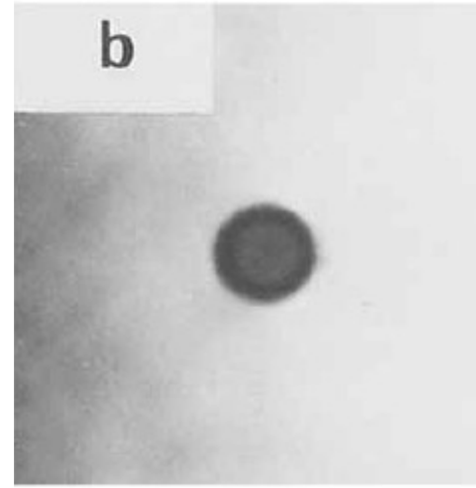
in vivo

in vitro

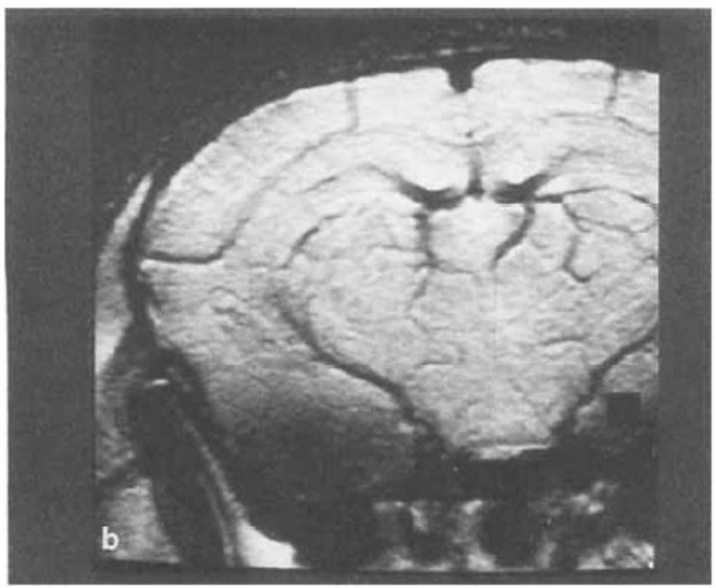
100% O_2



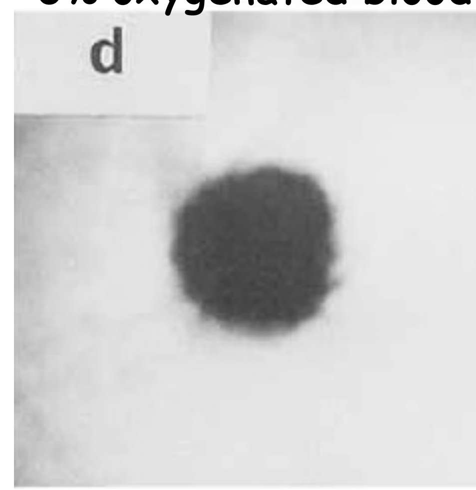
100% oxygenated blood



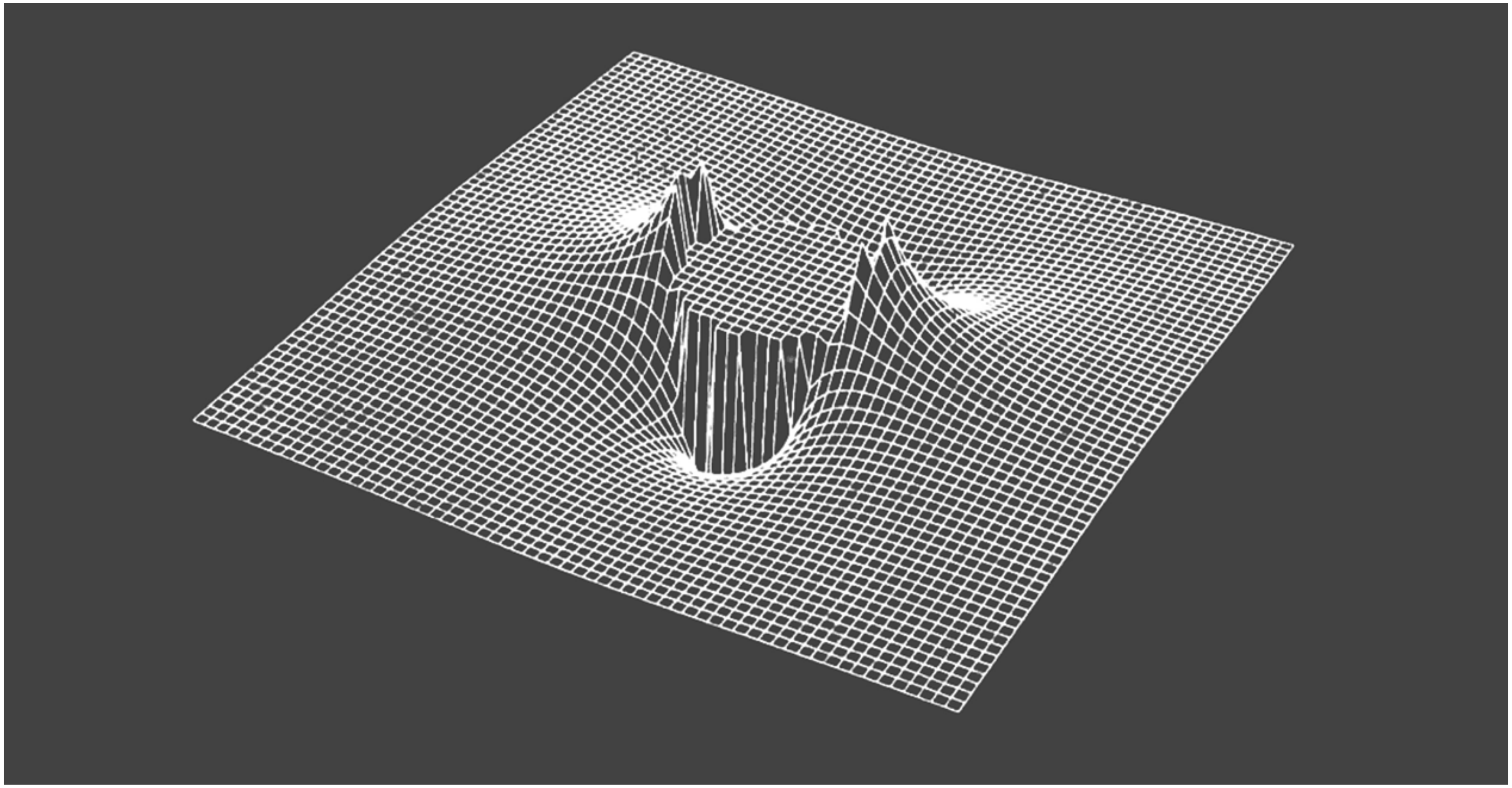
20% O_2



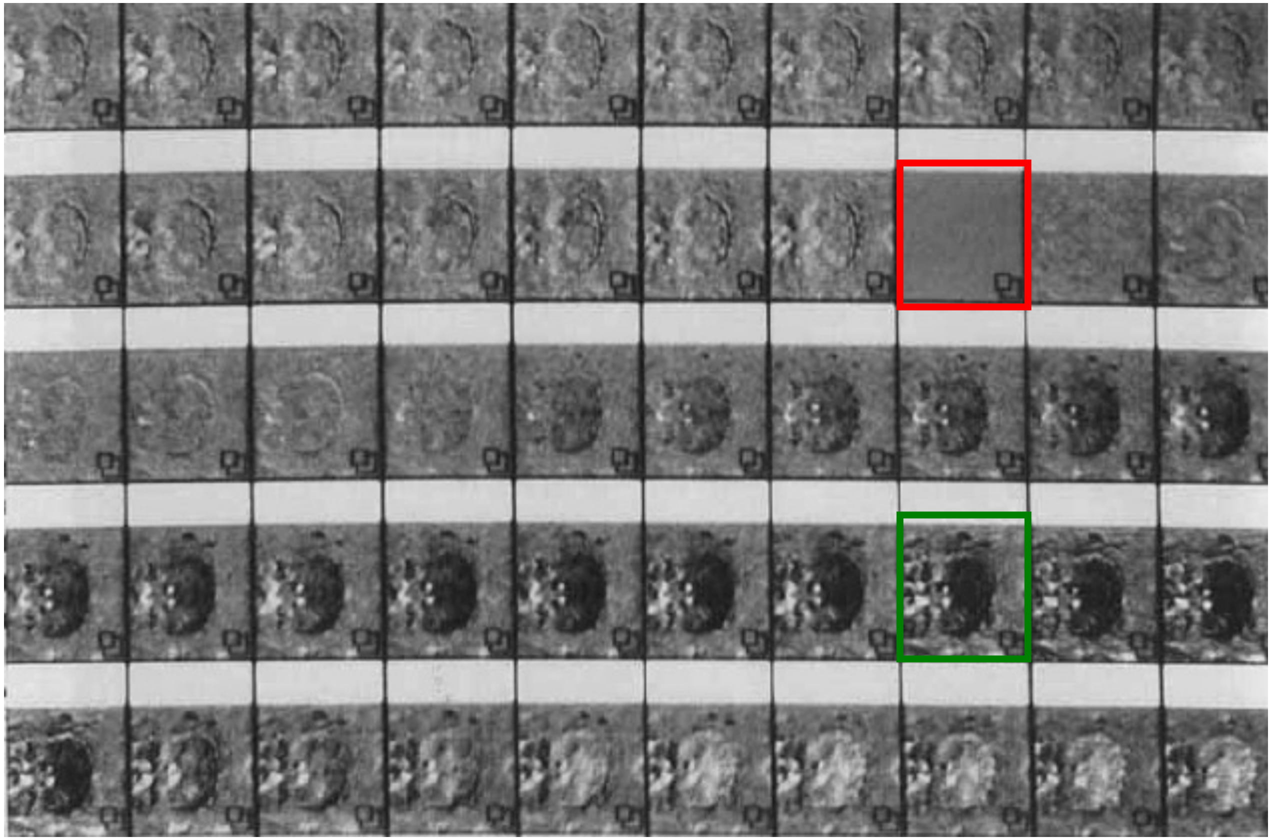
0% oxygenated blood

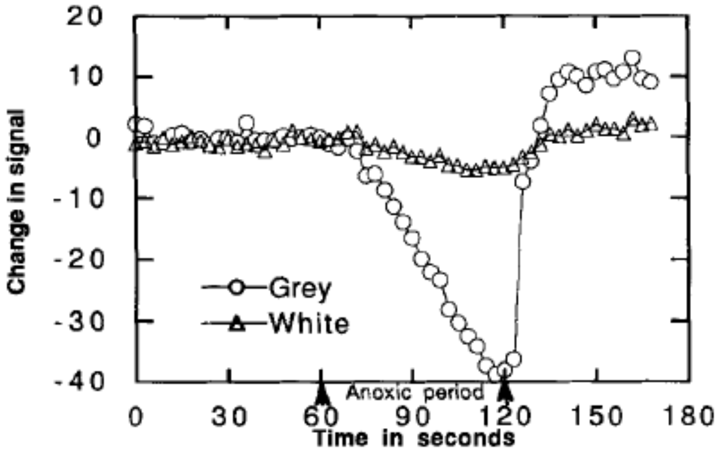


S. Ogawa, T.-M. Lee, A. S. Nayak, P. Glynn, Magn. Reson. Med, 14, 68-78 (1990)



History





R. Turner, D. LeBihan, C.T.W. Moonen, D. Despres, J. Frank, Magn. Reson. Med, 22, 159-166 (1991)

“BOLD contrast adds to…functional MRI methodologies that are likely to be complementary to PET imaging in the study of regional brain activity.”

Ogawa, S., Lee, T. M., Kay, A. R. and Tank, D. W. (1990) *Proceedings of the National Academy of Sciences of the United States of America,* **87**, **9868-9872.**

The Absolute Beginners Guide to fMRI

1. History
2. Functional Contrast
3. Interpretation Issues

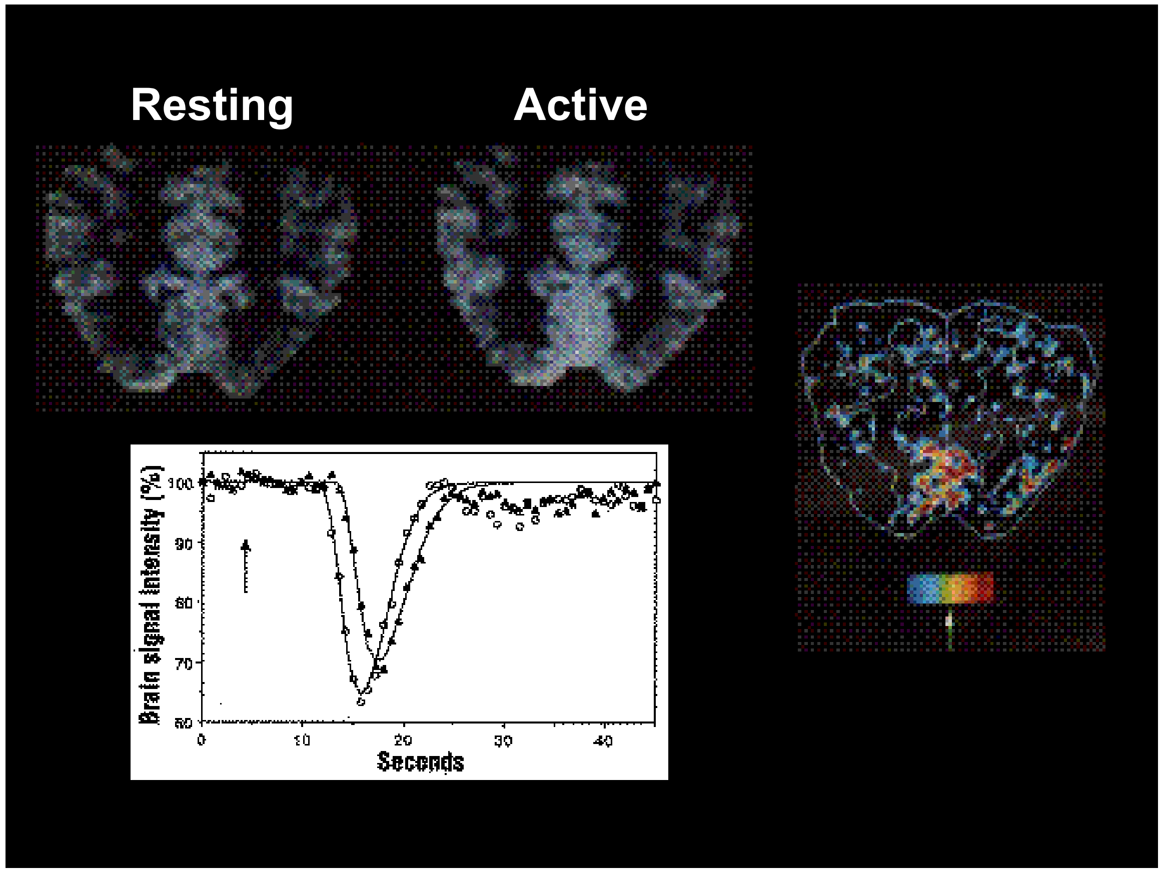
Functional Contrast

- Volume (gadolinium)
- BOLD
- Perfusion (ASL)
- $\Delta CMRO_2$
- ΔVolume (VASO)
- Neuronal Currents
- Diffusion coefficient
- Temperature

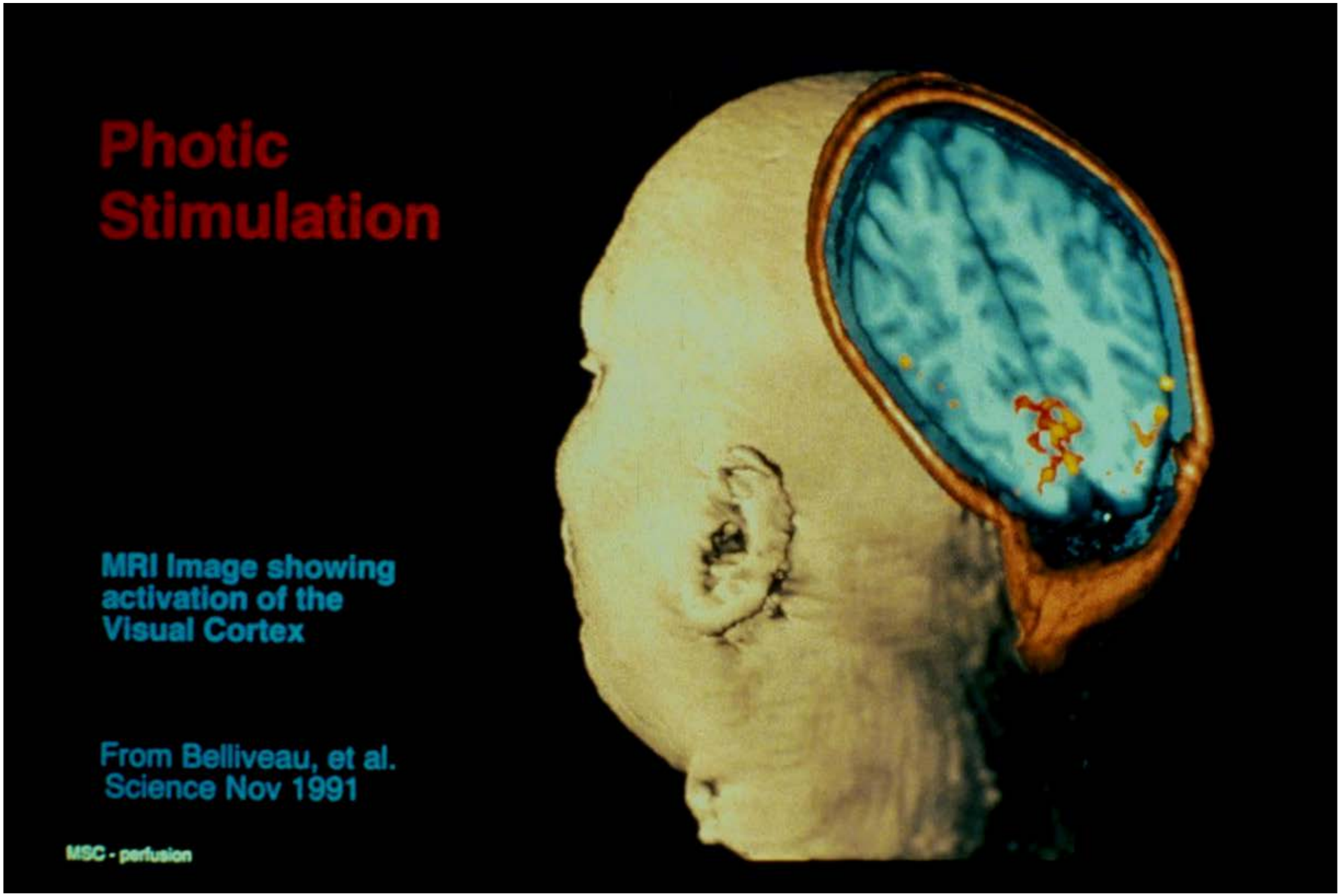
Functional Contrast

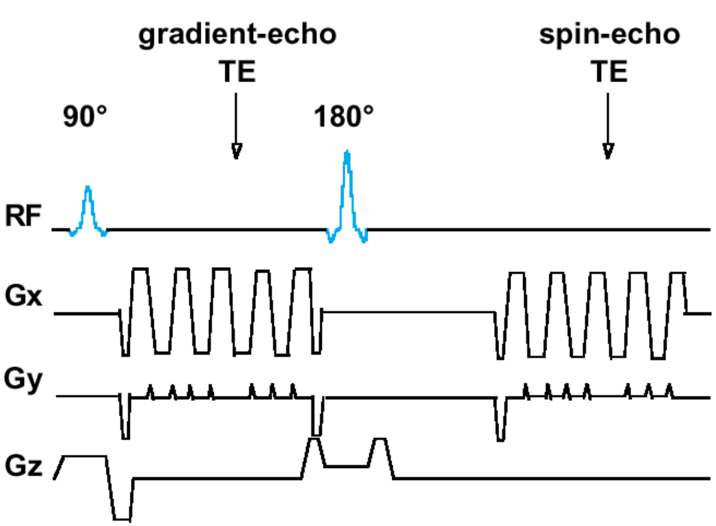
- Volume (gadolinium)
- Blood oxygenation (BOLD)
- Perfusion (ASL)
- $\Delta CMRO_2$
- ΔVolume (VASO)
- Neuronal Currents
- Diffusion coefficient
- Temperature

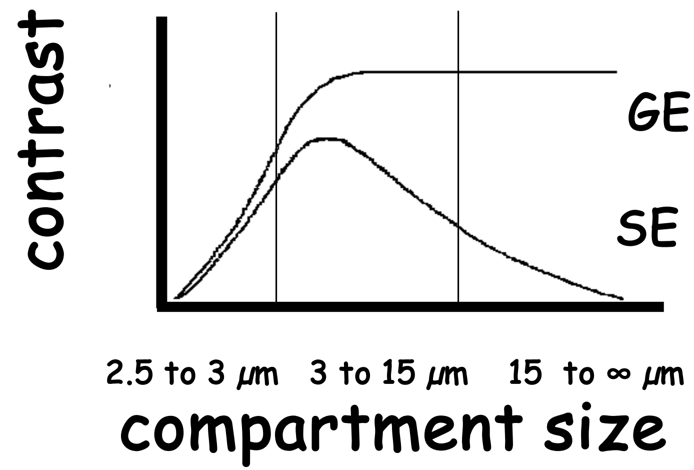
Blood Volume Contrast (Gadolinium)



Activation-Induced Blood Volume Change

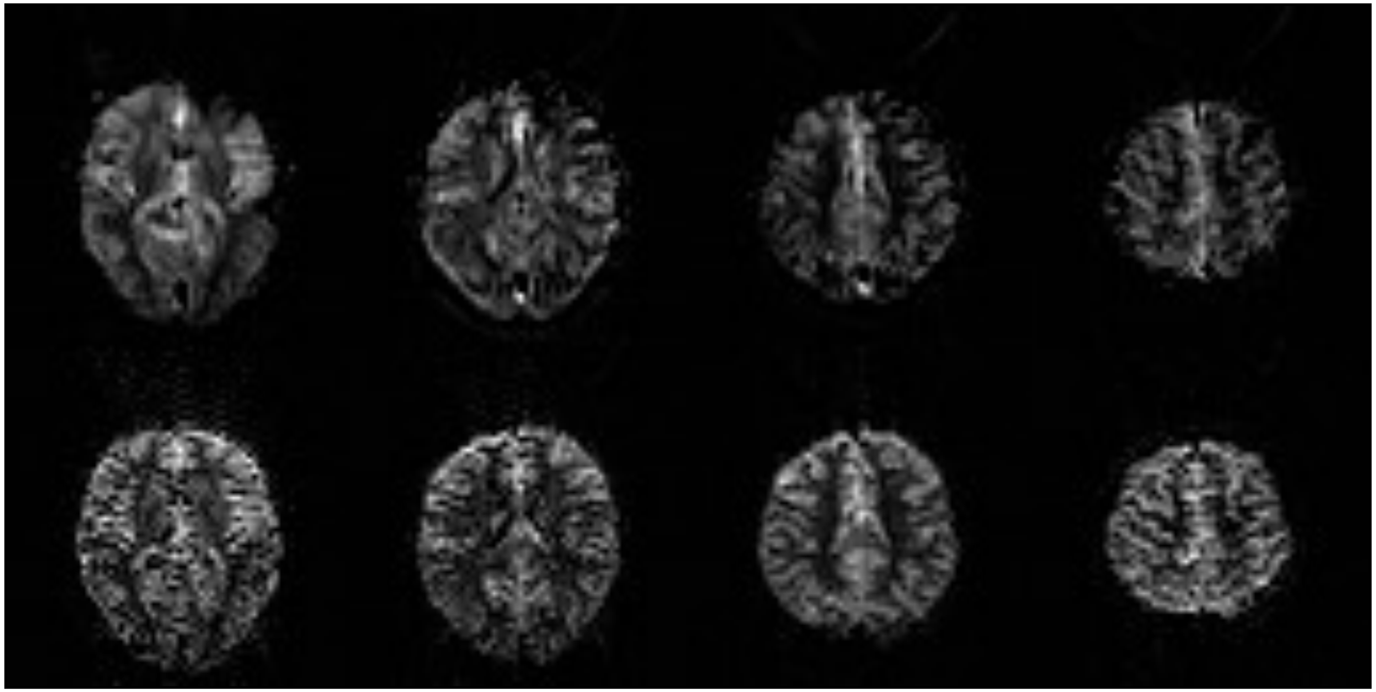






GE
TE = 30 ms

SE
TE = 110 ms



Blood Oxygenation Level Dependent Contrast (BOLD)

Cerebral Tissue Activation

↓

Local Vasodilatation

↓

Increase in Cerebral Blood Flow and Volume → Oxygen Delivery Exceeds Metabolic Need

↓

Increase in Capillary and Venous Blood Oxygenation

↓

Decrease in Deoxy-hemoglobin

Deoxy-hemoglobin: paramagnetic
Oxy-hemoglobin: diamagnetic

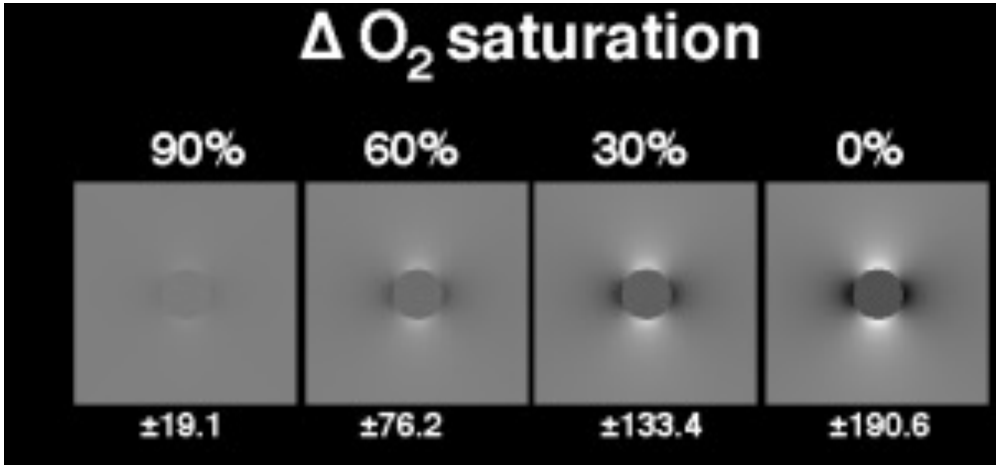
↓

Decrease in susceptibility-related intravoxel dephasing → Increase in T2 and T2*

↓

Local Signal Increase in T2 and T2* - weighted sequences

Blood Oxygenation



1992…BOLD

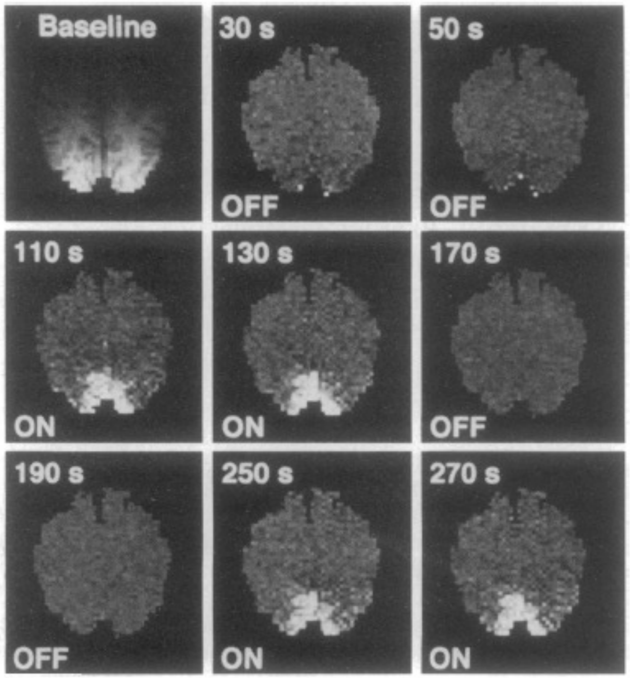
K. K. Kwong, et al, (1992) "Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation." **Proc. Natl. Acad. Sci. USA. 89, 5675-5679.**

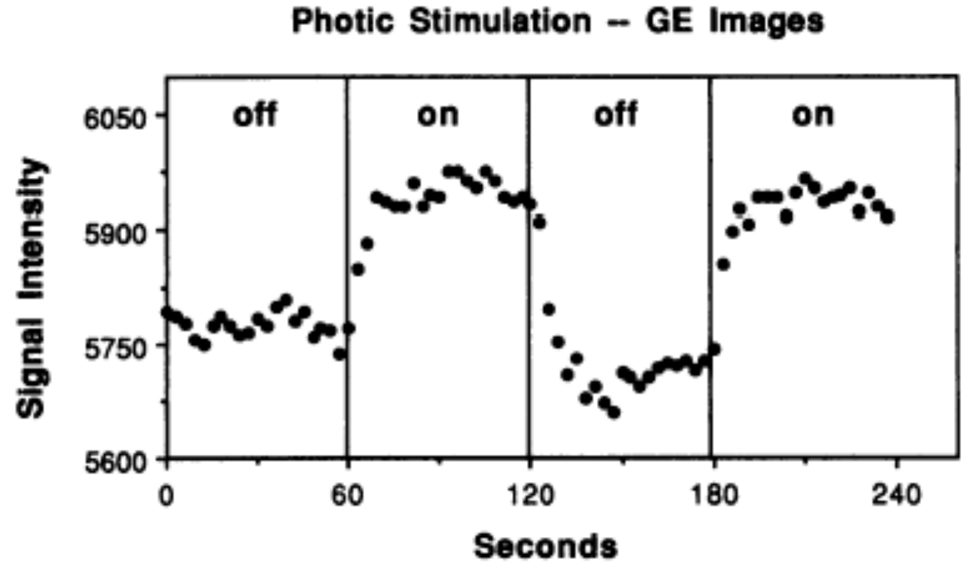
S. Ogawa, et al., (1992) "Intrinsic signal changes accompanying sensory stimulation: functional brain mapping with magnetic resonance imaging." **Proc. Natl. Acad. Sci. USA. 89, 5951-5955.**

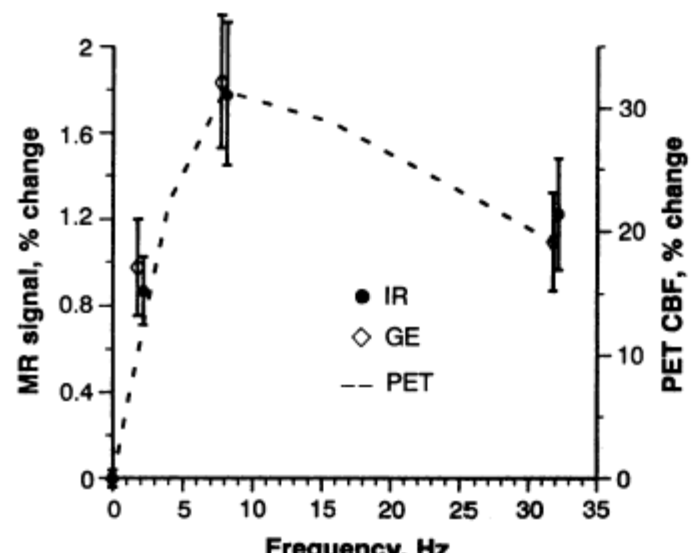
P. A. Bandettini, et al., (1992) "Time course EPI of human brain function during task activation." **Magn. Reson. Med 25, 390-397.**

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.**

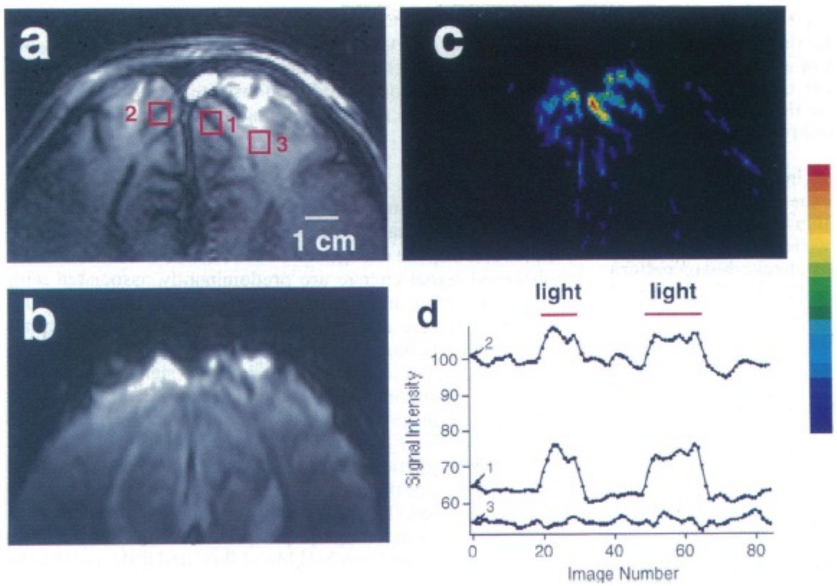
Frahm, J., et al (1992) "Dynamic MR Imaging of Human Brain Oxygenation During Rest and Photic-Stimulation." **Journal of Magnetic Resonance Imaging, 2, 501-505.**



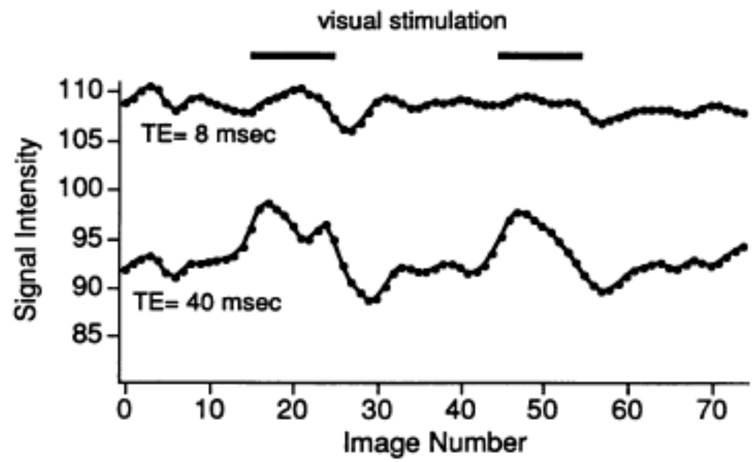


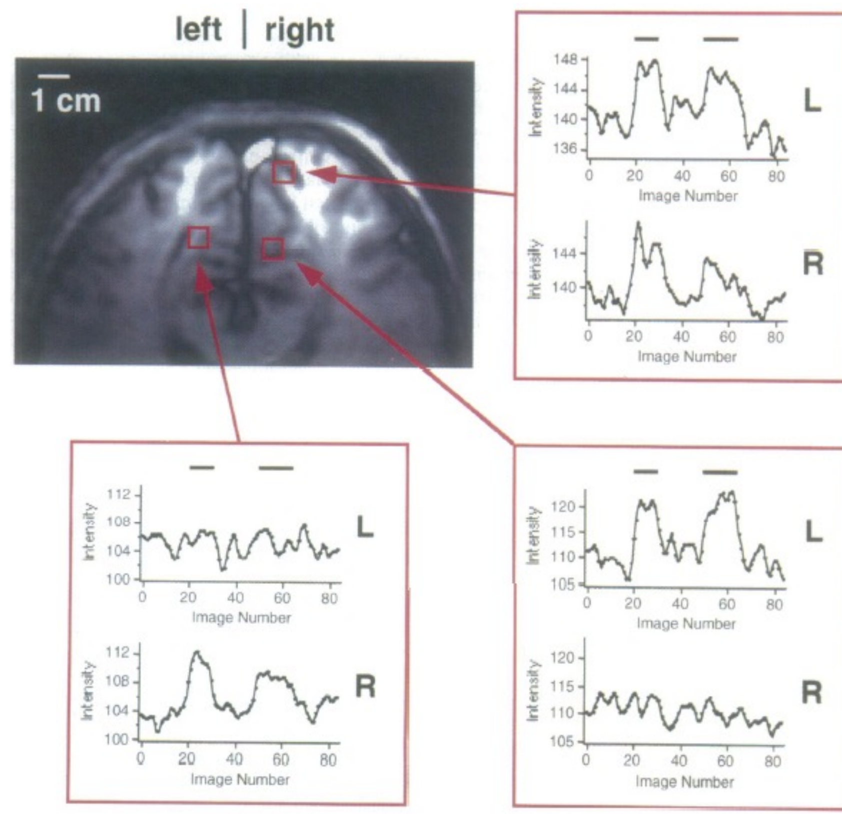


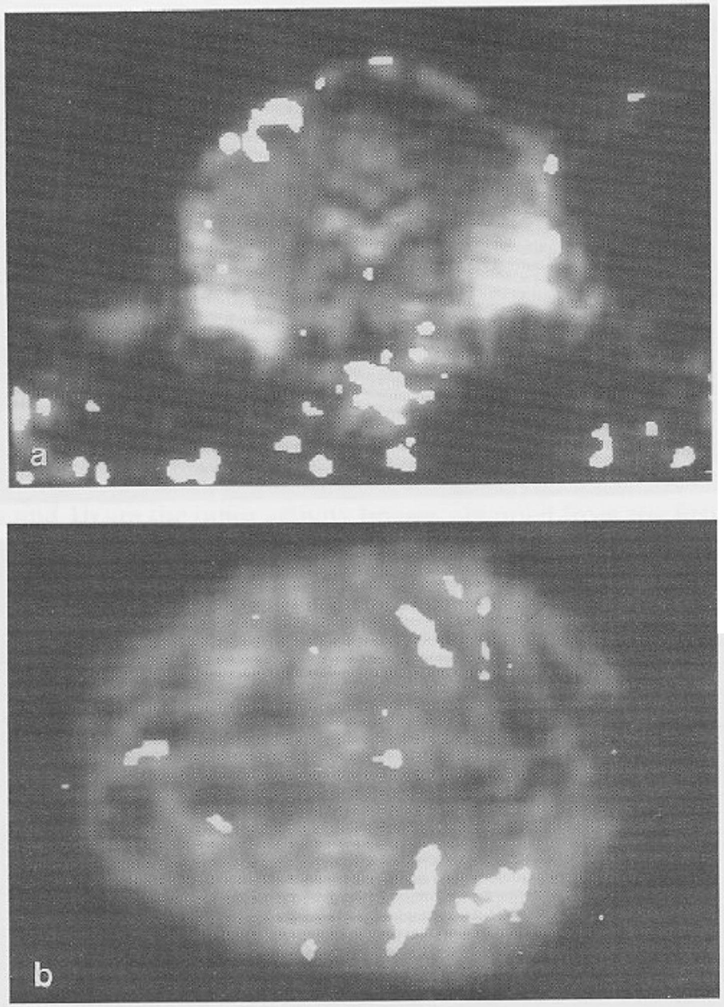
K. K. Kwong, et al, (1992) "Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation." Proc. Natl. Acad. Sci. USA. 89, 5675-5679.

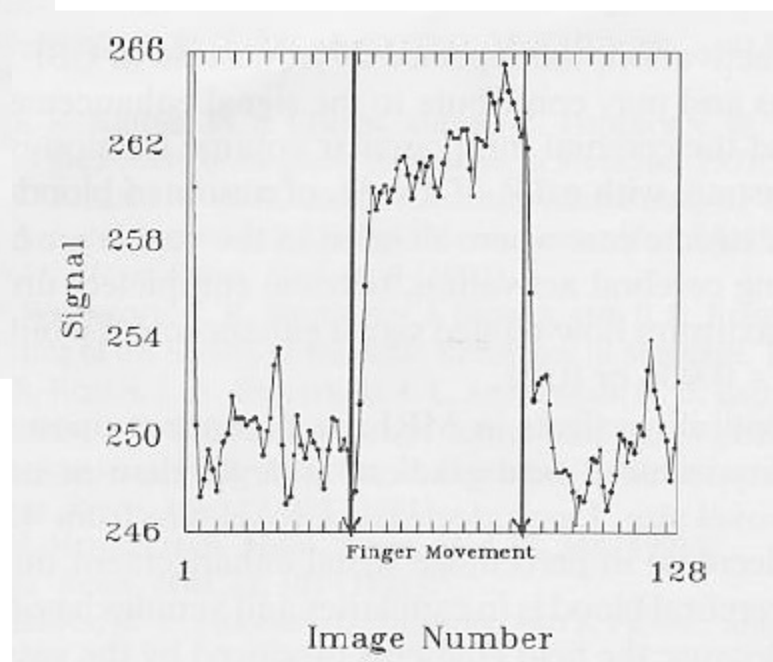


S. Ogawa, et al., (1992) “Intrinsic signal changes accompanying sensory stimulation: functional brain mapping with magnetic resonance imaging.” **Proc. Natl. Acad. Sci. USA. 89, 5951-5955.**

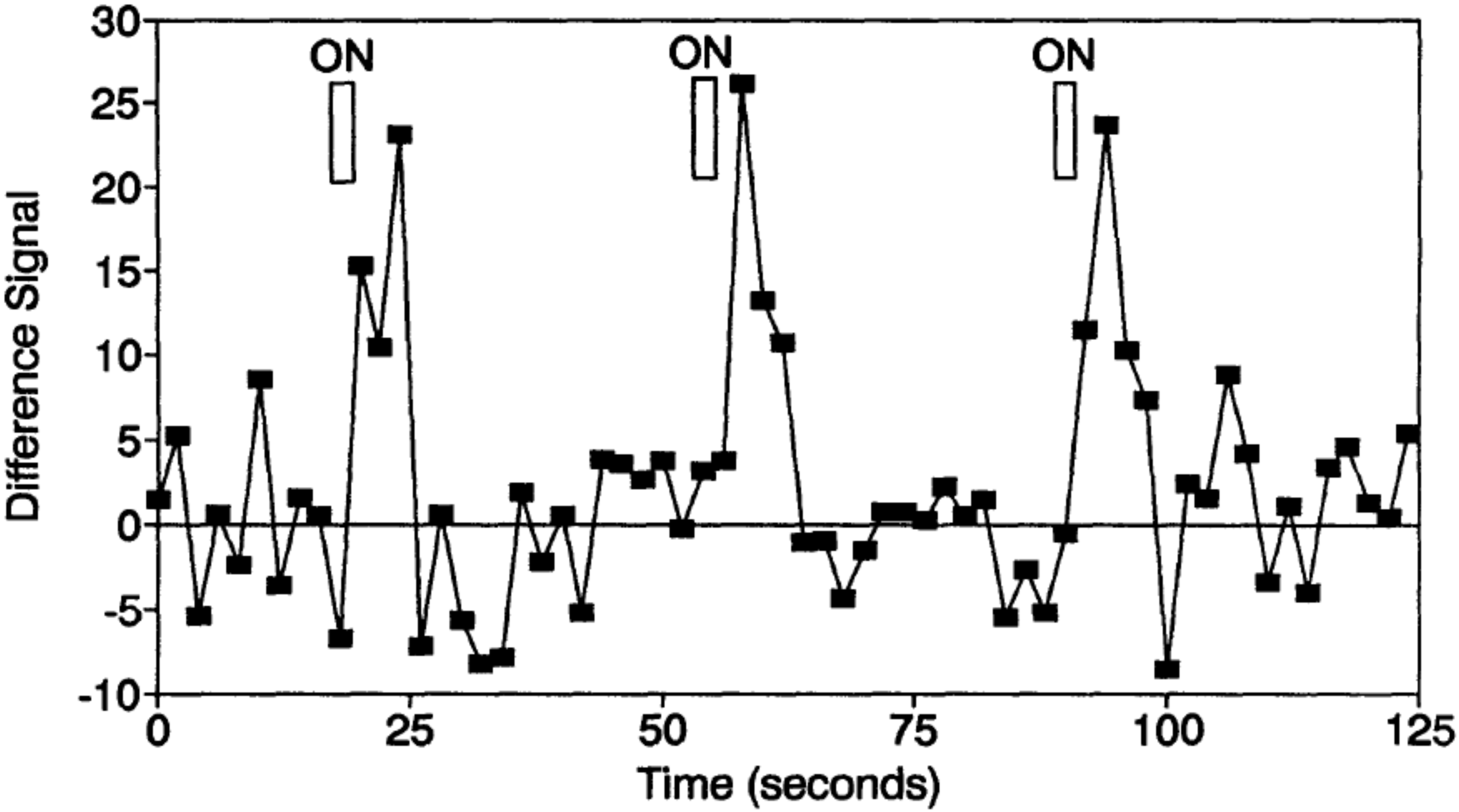






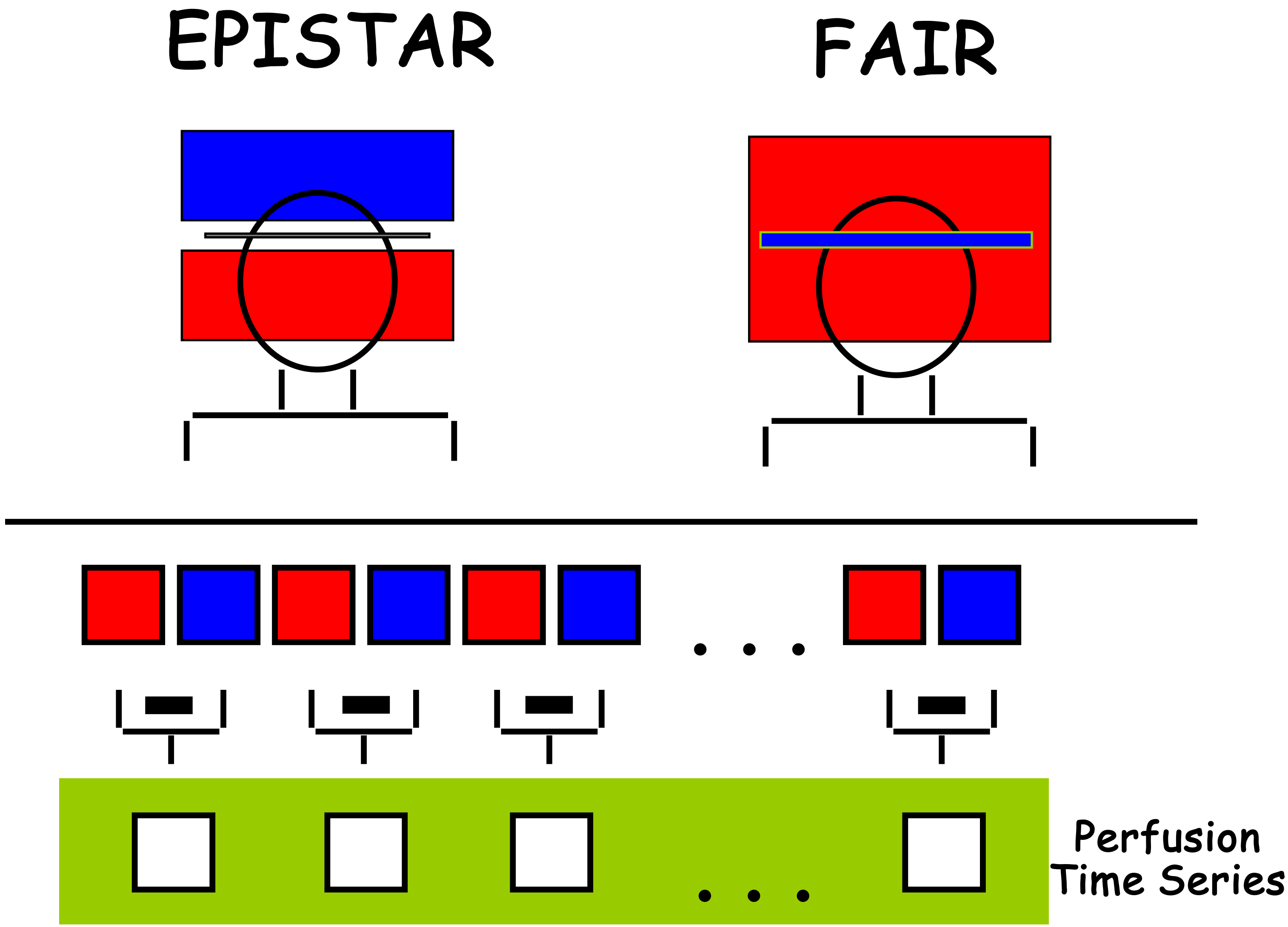


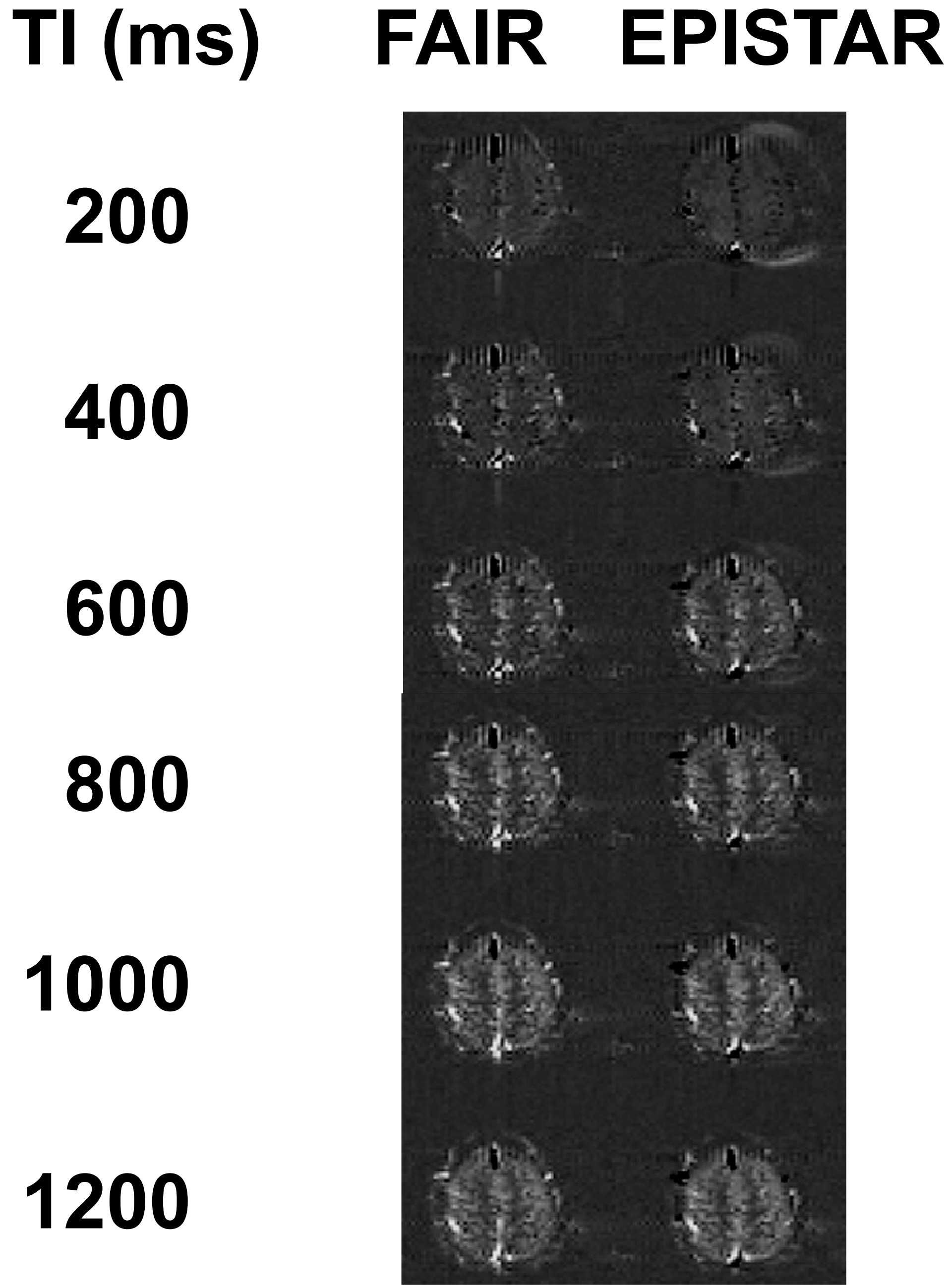
P. A. Bandettini, et al., (1992)
"Time course EPI of human brain function during task activation."
Magn. Reson. Med 25, 390-397.

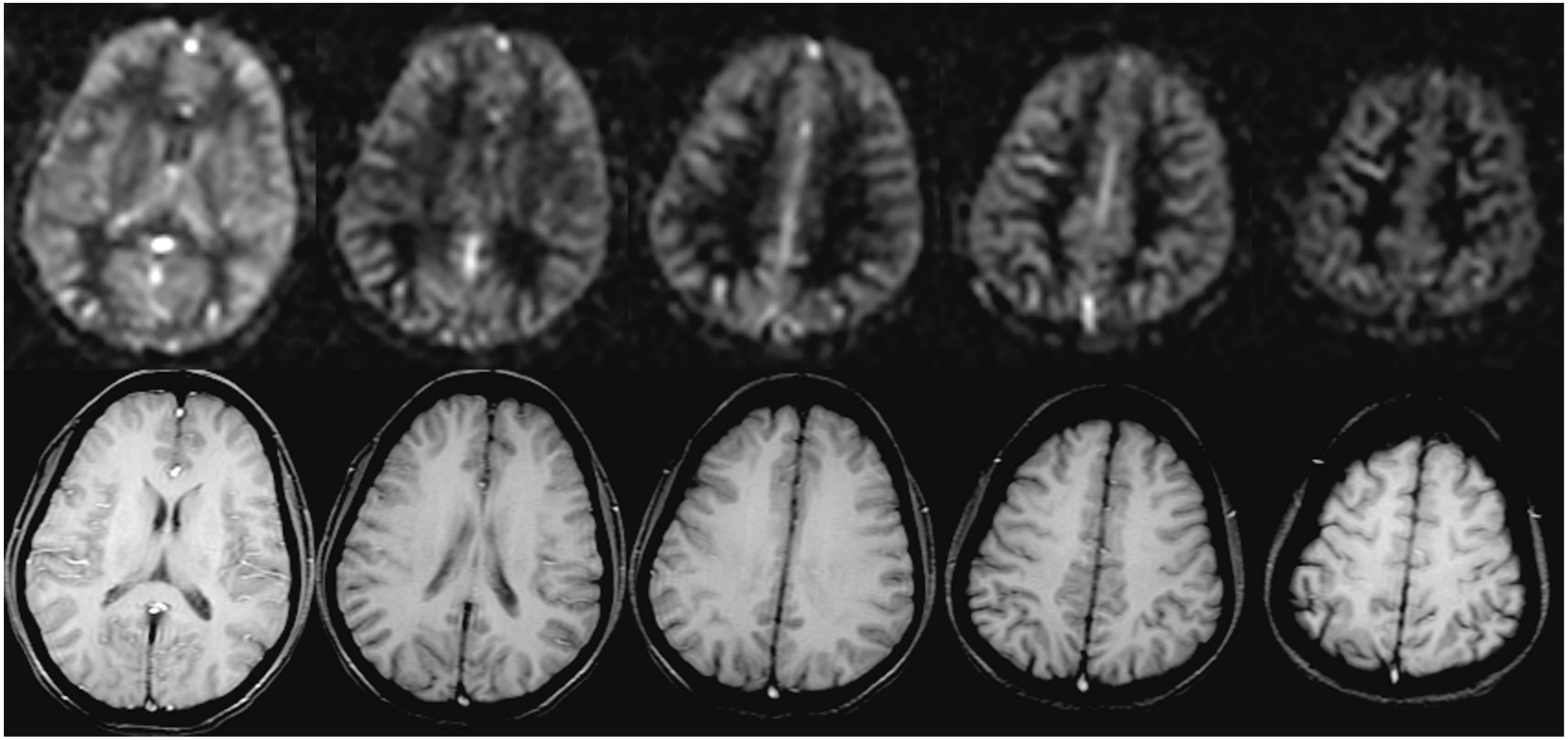


Blamire, A. M., et al. (1992).
"Dynamic mapping of the human visual cortex by high-speed magnetic resonance imaging."
Proc. Natl. Acad. Sci. USA 89: 11069-11073.

Blood Perfusion Contrast




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



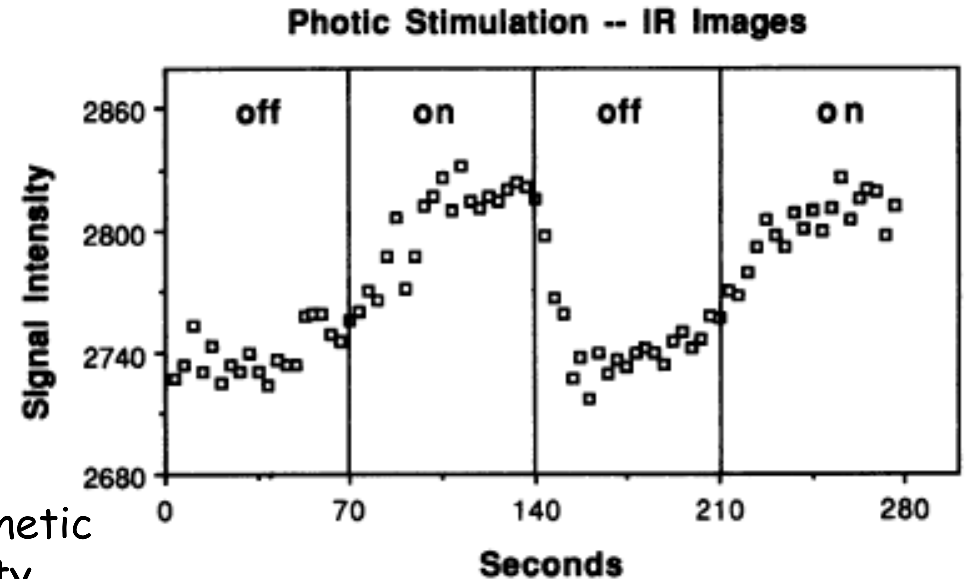
Williams, D. S., Detre, J. A., Leigh, J. S. & Koretsky, A. S. (1992) "Magnetic resonance imaging of perfusion using spin-inversion of arterial water." Proc. Natl. Acad. Sci. USA 89, 212-216.

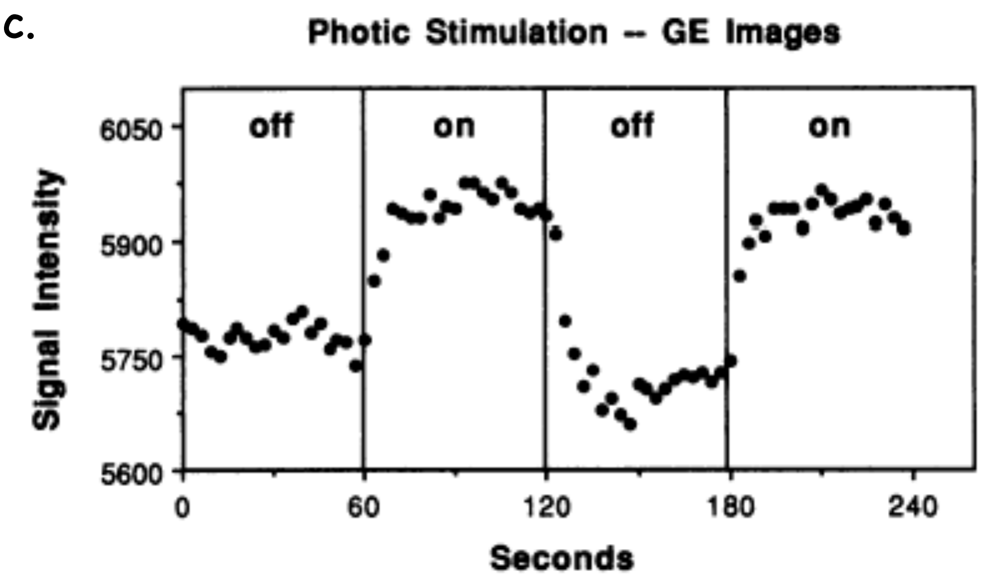
Edelman, R., Siewert, B. & Darby, D. (1994) "Qualitative mapping of cerebral blood flow and functional localization with echo planar MR imaging ans signal targeting with alternating radiofrequency (EPISTAR)." Radiology **192**, 1-8.

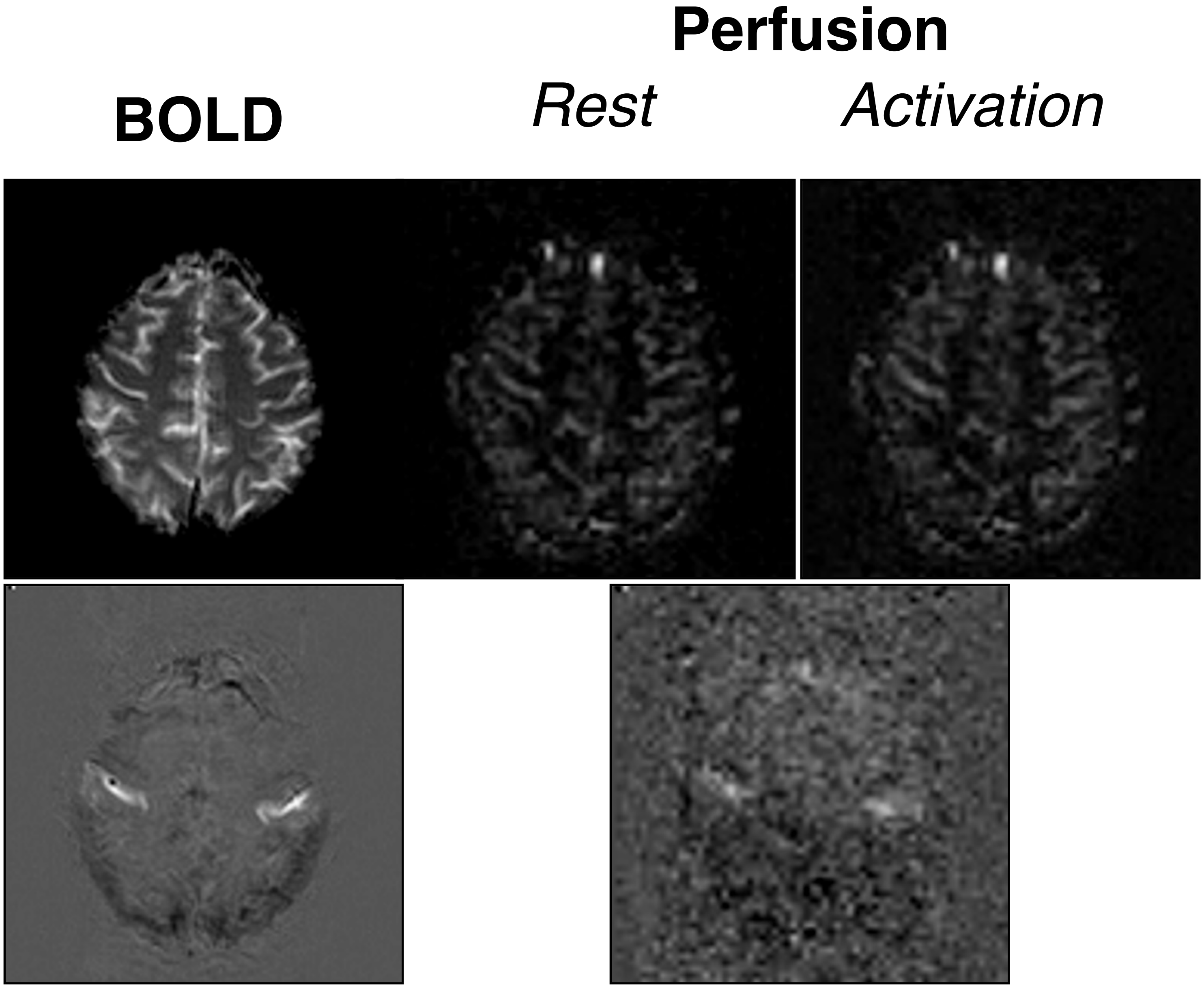
Kim, S.-G. (1995) "Quantification of relative cerebral blood flow change by flow-sensitive alternating inversion recovery (FAIR) technique: application to functional mapping." Magn. Reson. Med. **34**, 293-301.

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

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.

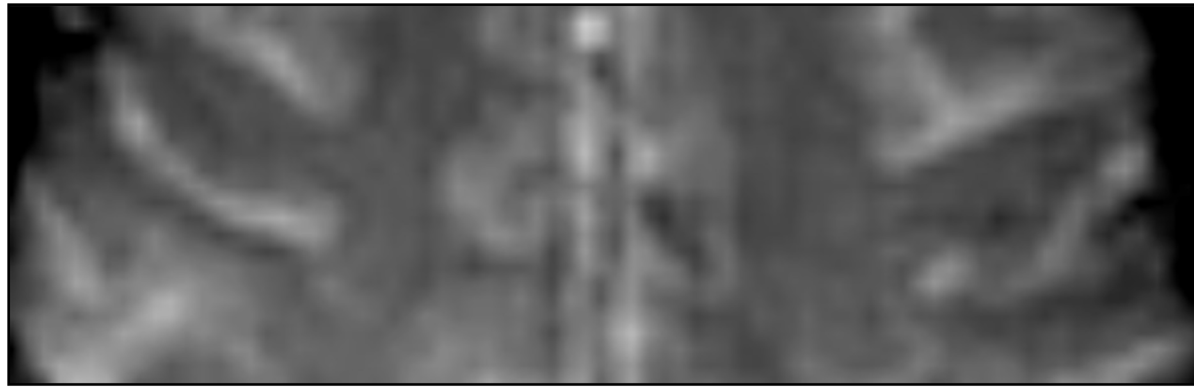




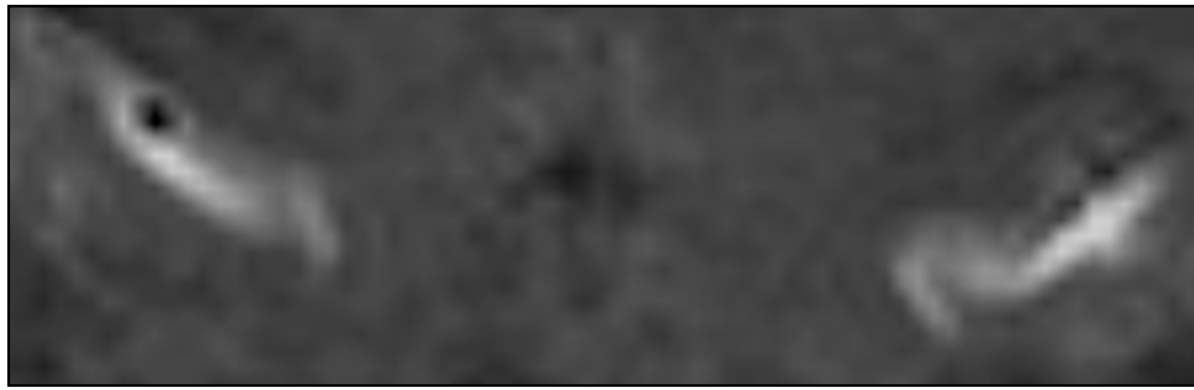


P. A. Bandettini, E. C. Wong, Magnetic resonance imaging of human brain function: principles, practicalities, and possibilities, *in* "Neurosurgery Clinics of North America: Functional Imaging" (M. Haglund, Ed.), p.345-371, W. B. Saunders Co., 1997.

Anatomy



BOLD

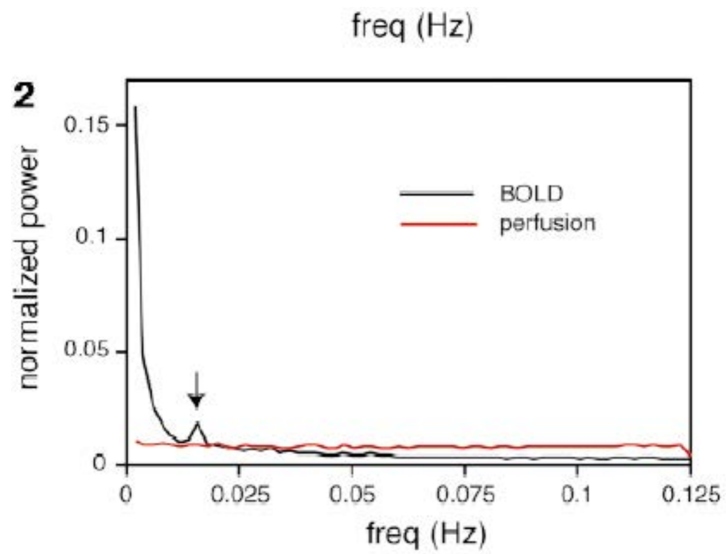


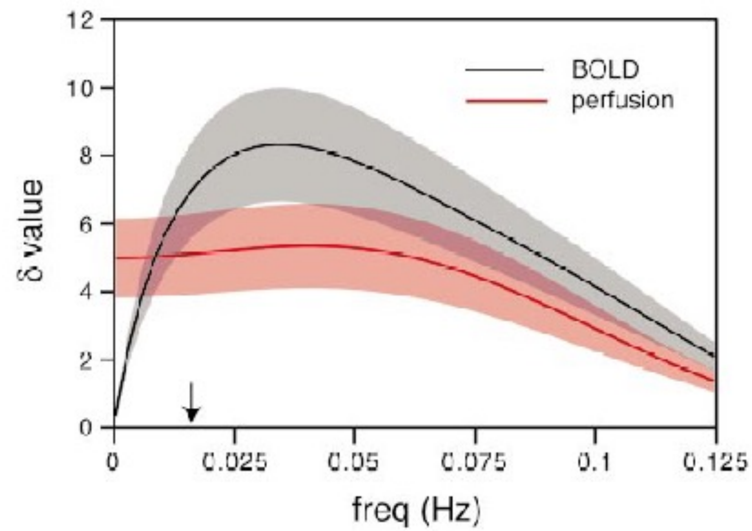
Perfusion

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.

Stability of Perfusion Imaging

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

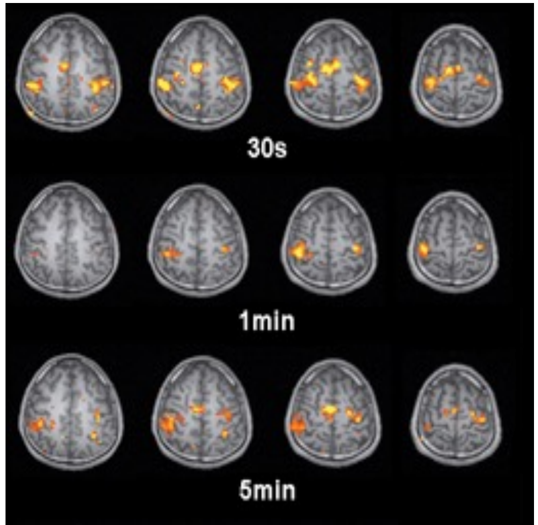




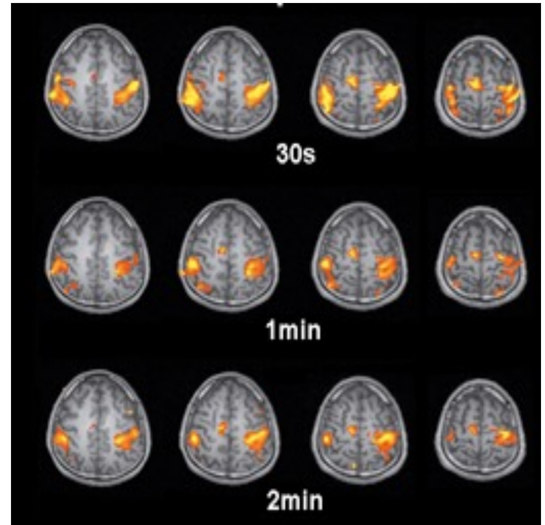
GK Aguirre et al, (2002) NeuroImage 15 (3): 488-500

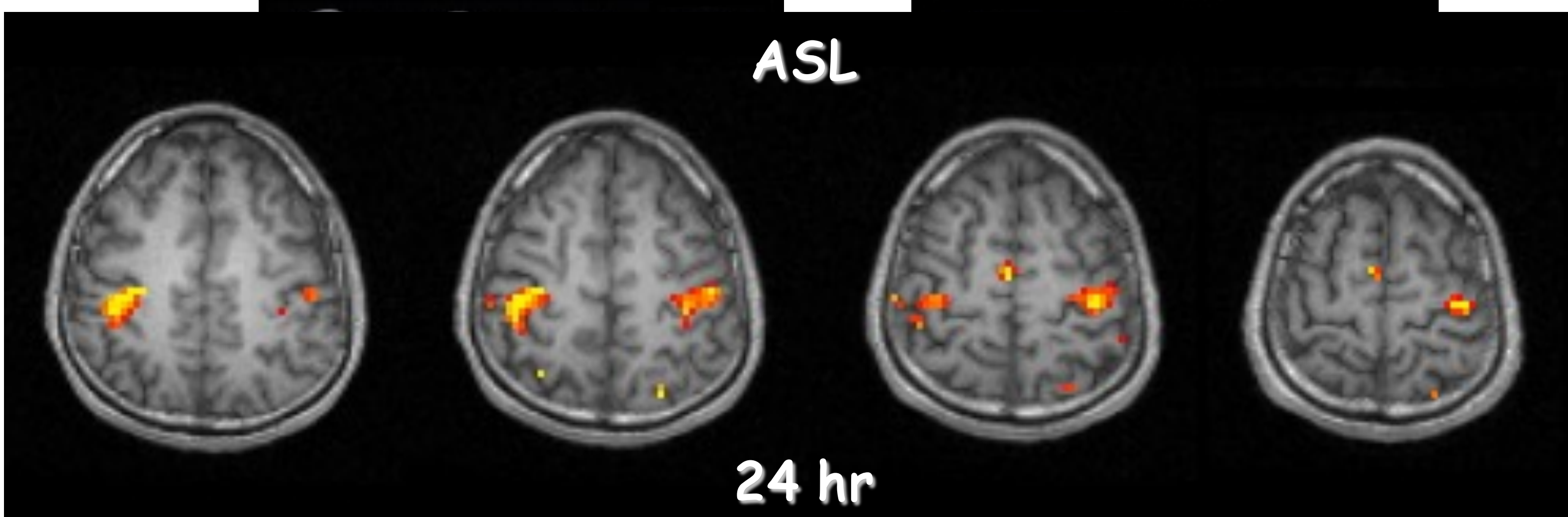
Perfusion vs. BOLD: Low Task Frequency

Perfusion



BOLD





The Absolute Beginners Guide to fMRI

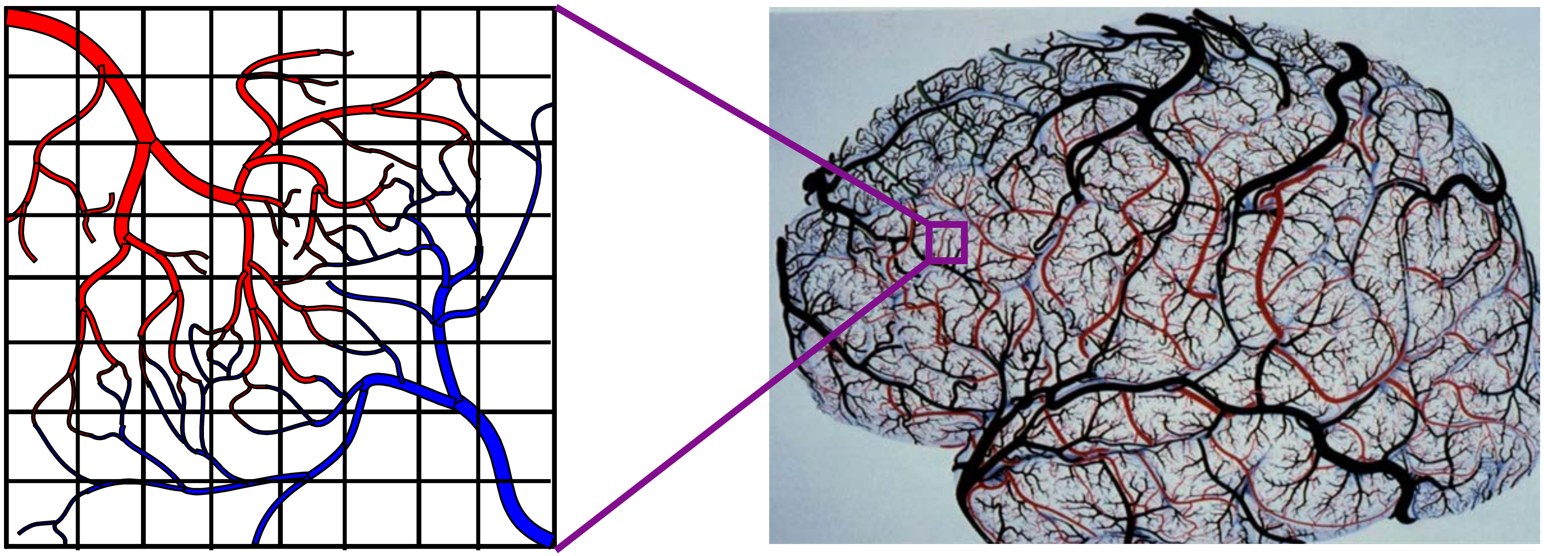
1. History
2. Functional Contrast
3. Interpretation Issues

Interpretation Issues

Neuronal Activation → ? → Measured Signal

Neuronal Activation → ? → Hemodynamics → ? → Measured Signal

Noise → ? → Measured Signal



Interpretation Issues

Temporal Resolution

Spatial Resolution

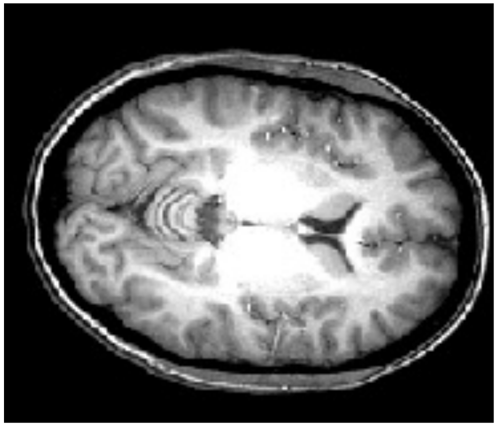
Relationship to Neuronal Activity

Noise and Fluctuations

MRI vs. fMRI

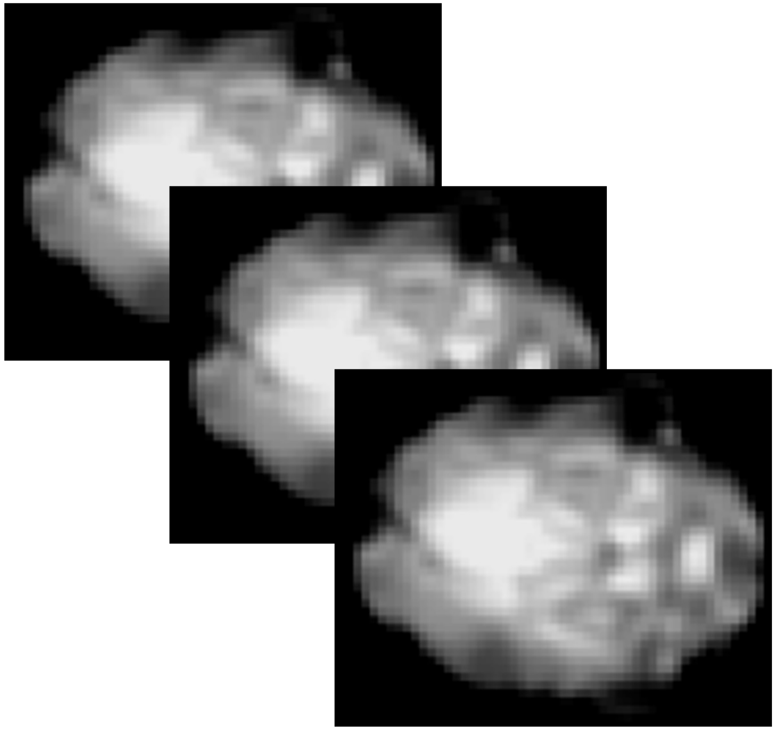
MRI

high resolution
(1 mm)



one image

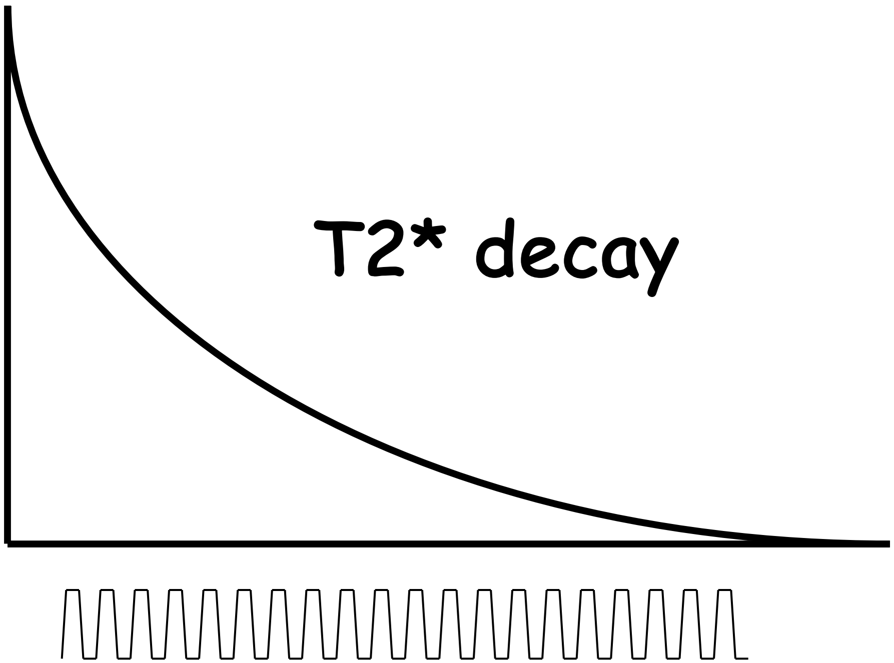
fMRI



...

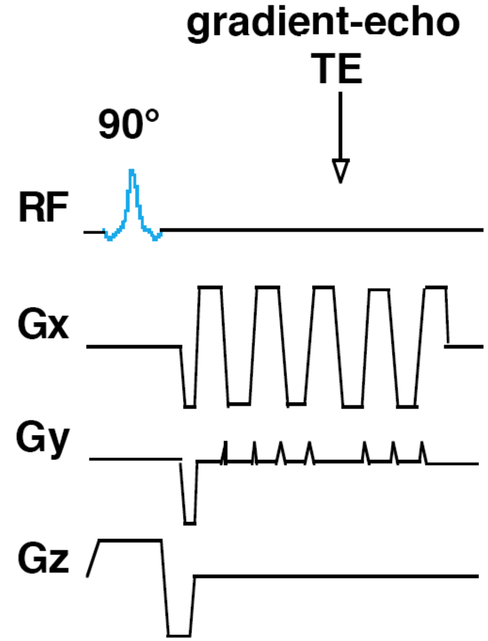
many images
(e.g., every 2 sec for 5 mins)

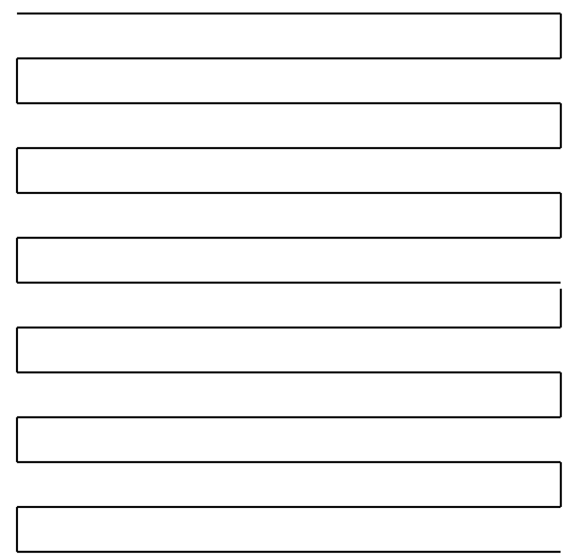
Single Shot Echo Planar Imaging (EPI)

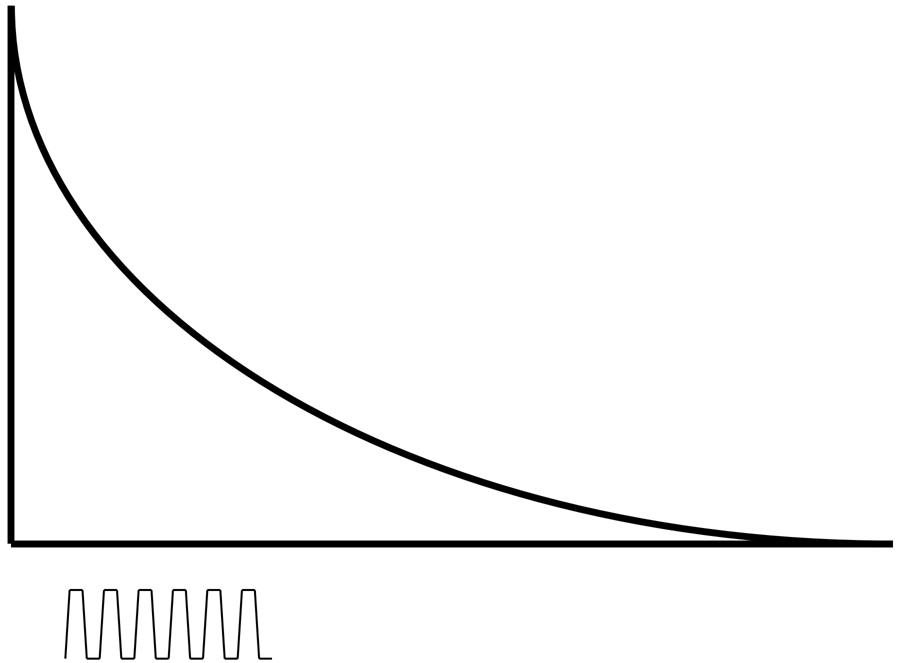


EPI Readout Window

≈ 20 to 40 ms

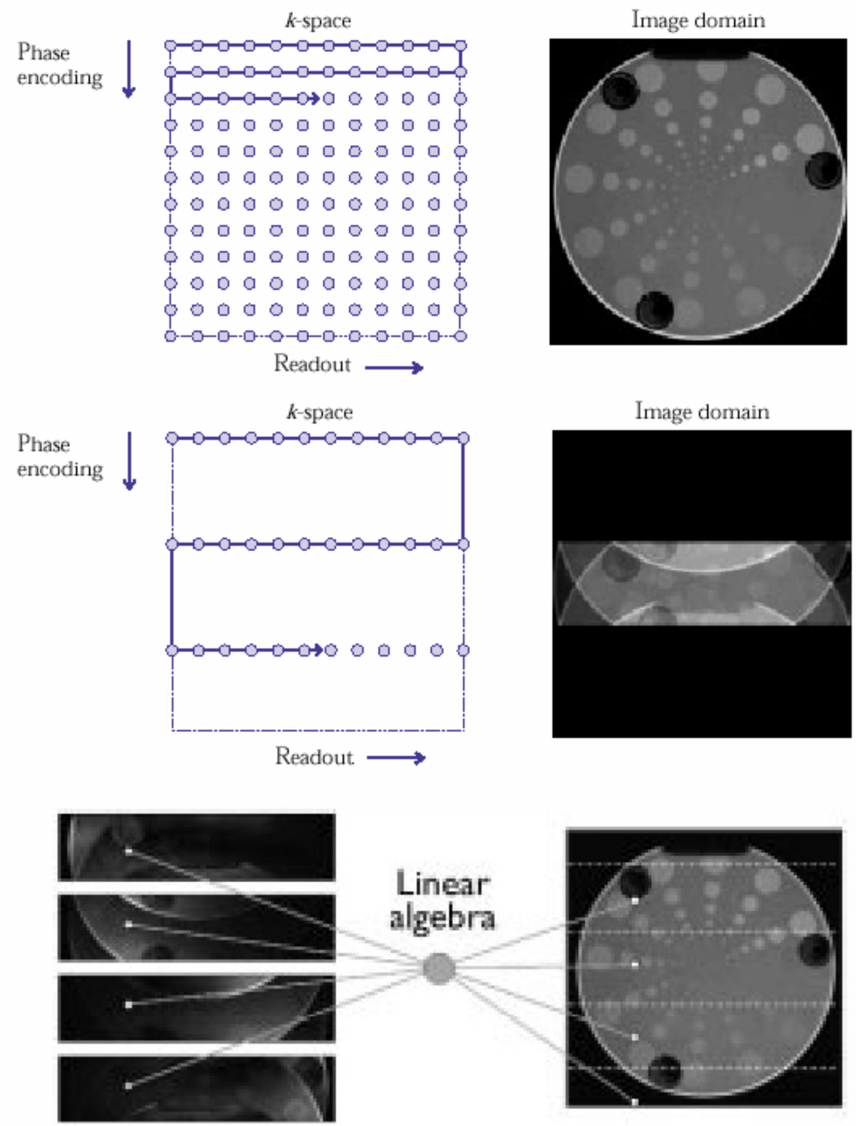




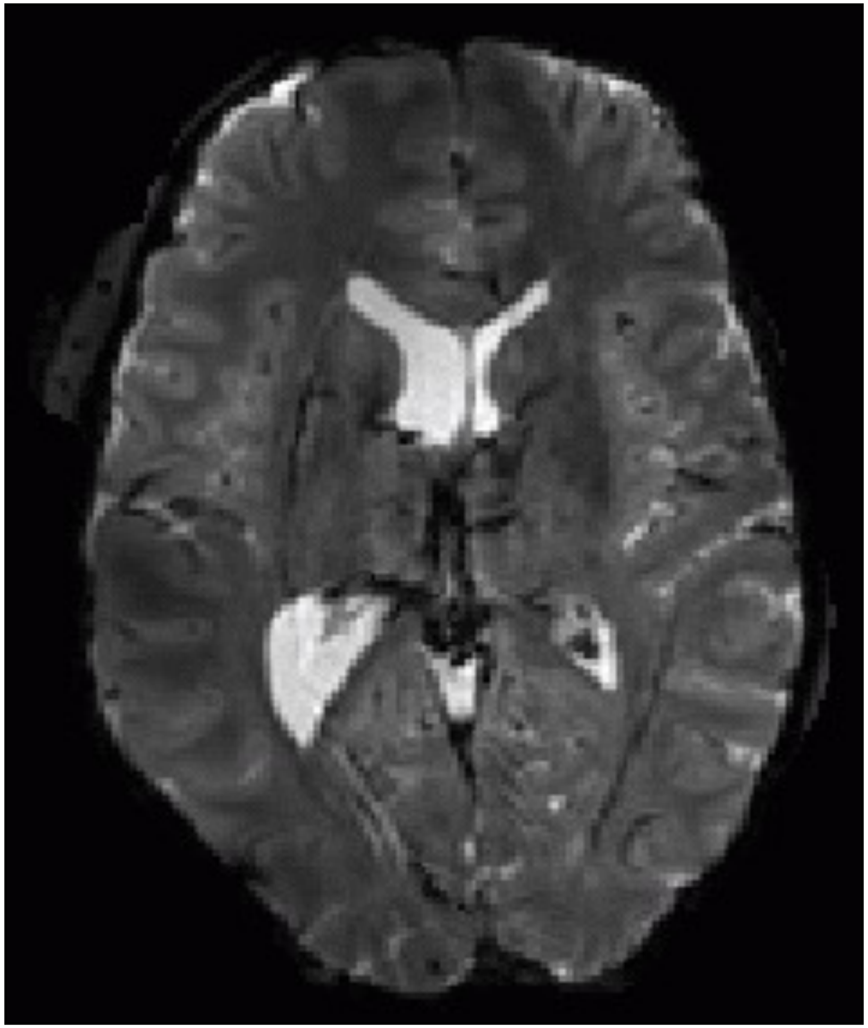


≈ 5 to 30 ms

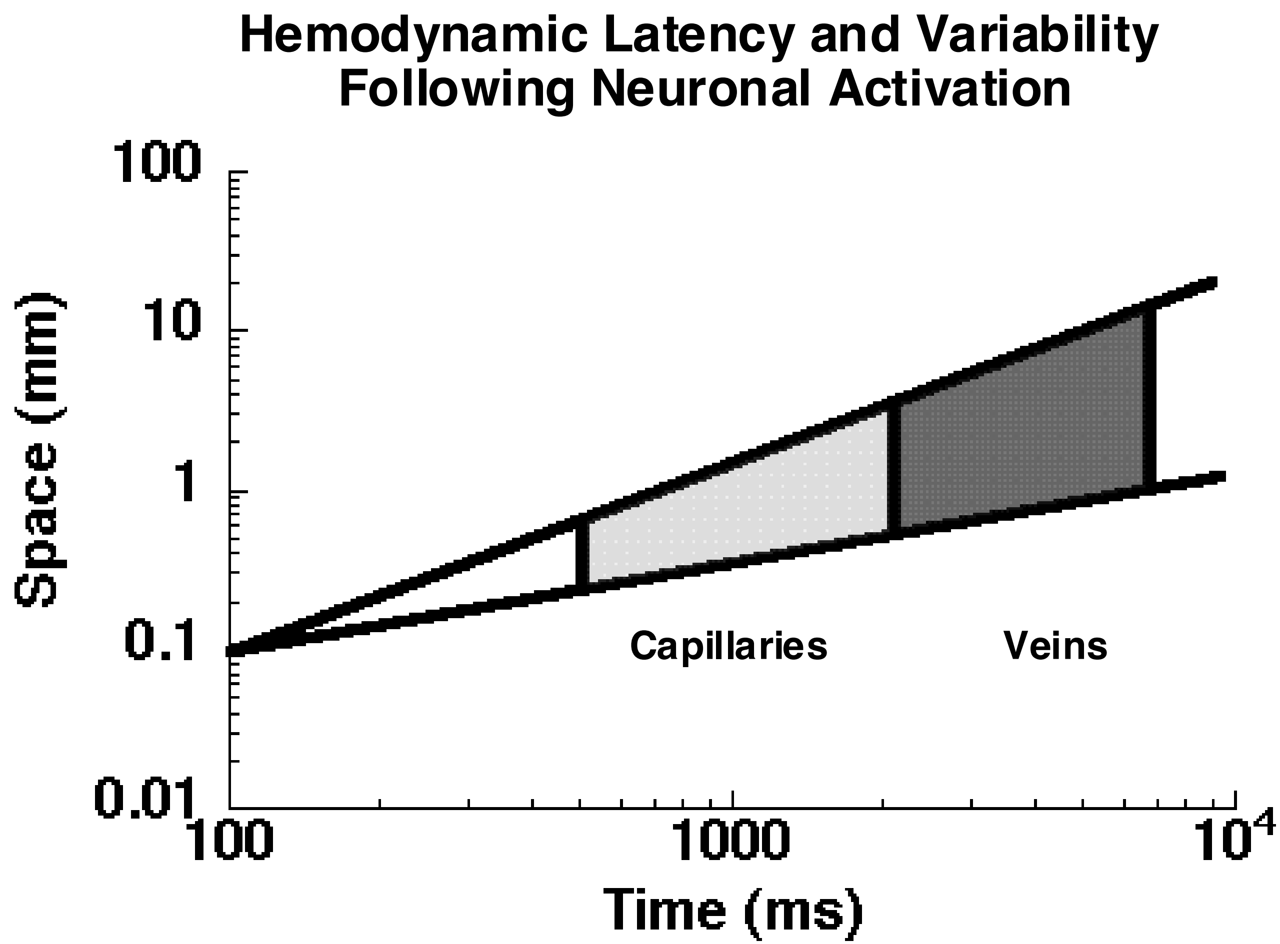
SENSE Imaging



Pruessmann, et al.



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


Hemodynamic Latency and Variability
Following Neuronal Activation
Space (mm)
100
10
1
0.1
0.01
100
1000
10^4
Time (ms)
Capillaries
Veins

Interpretation Issues

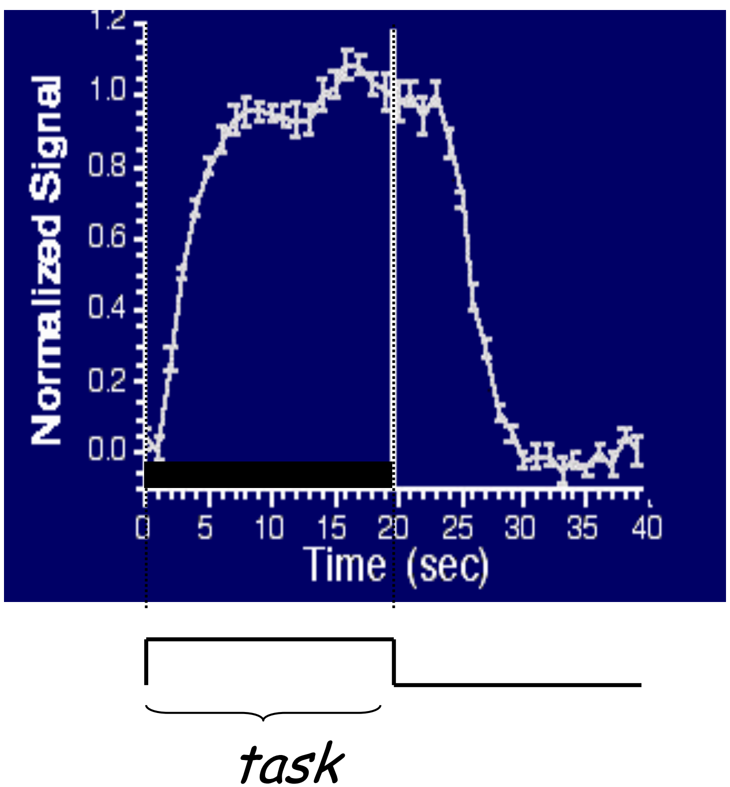
Temporal Resolution

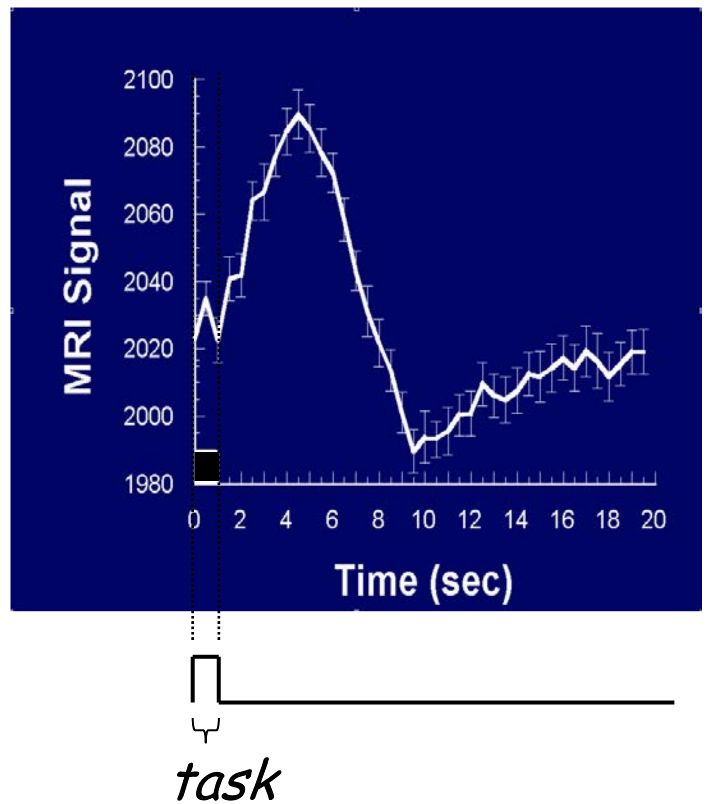
Spatial Resolution

Relationship to Neuronal Activity

Noise and Fluctuations

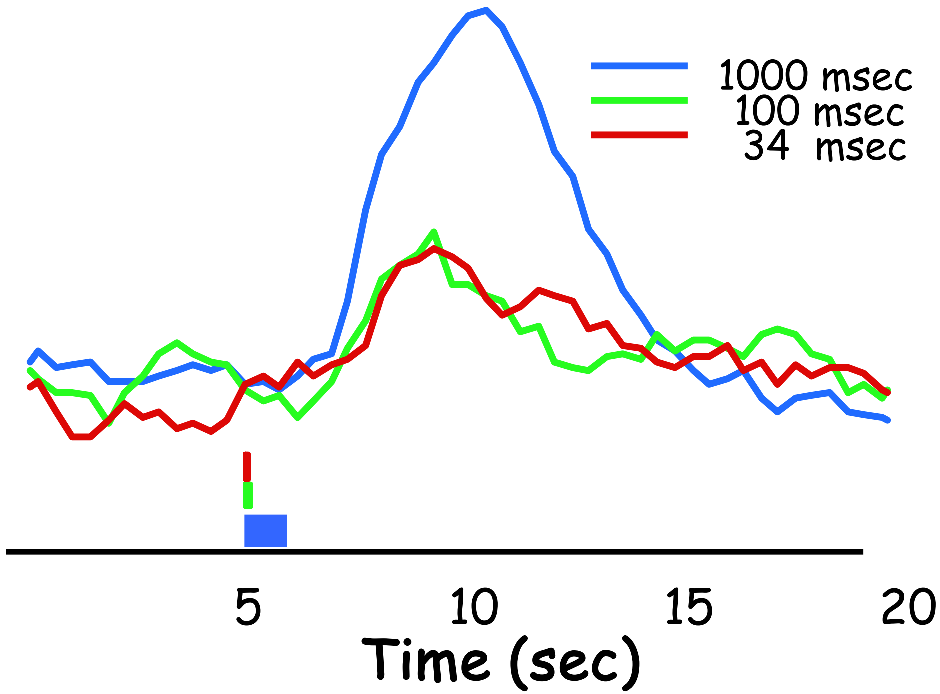
Temporal resolution





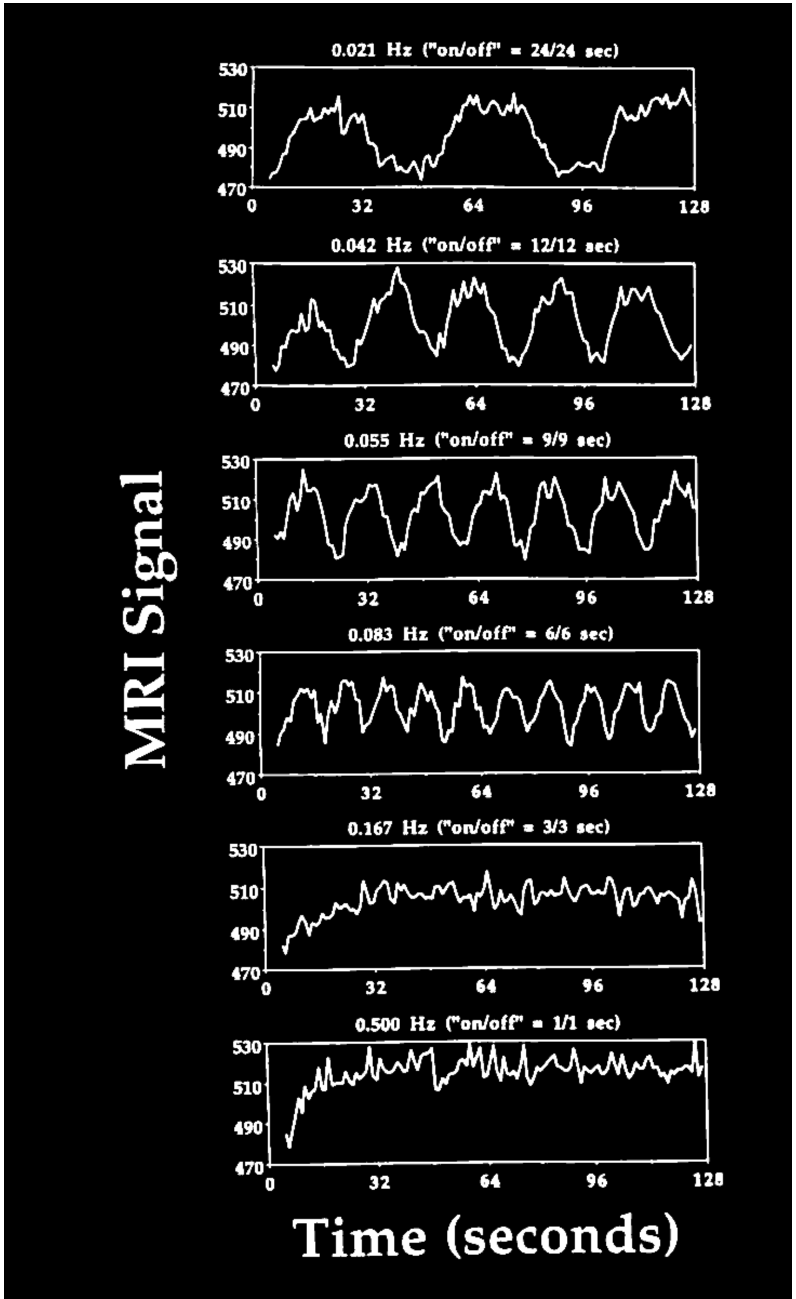
Temporal Resolution

How brief of a stimulus can one give?

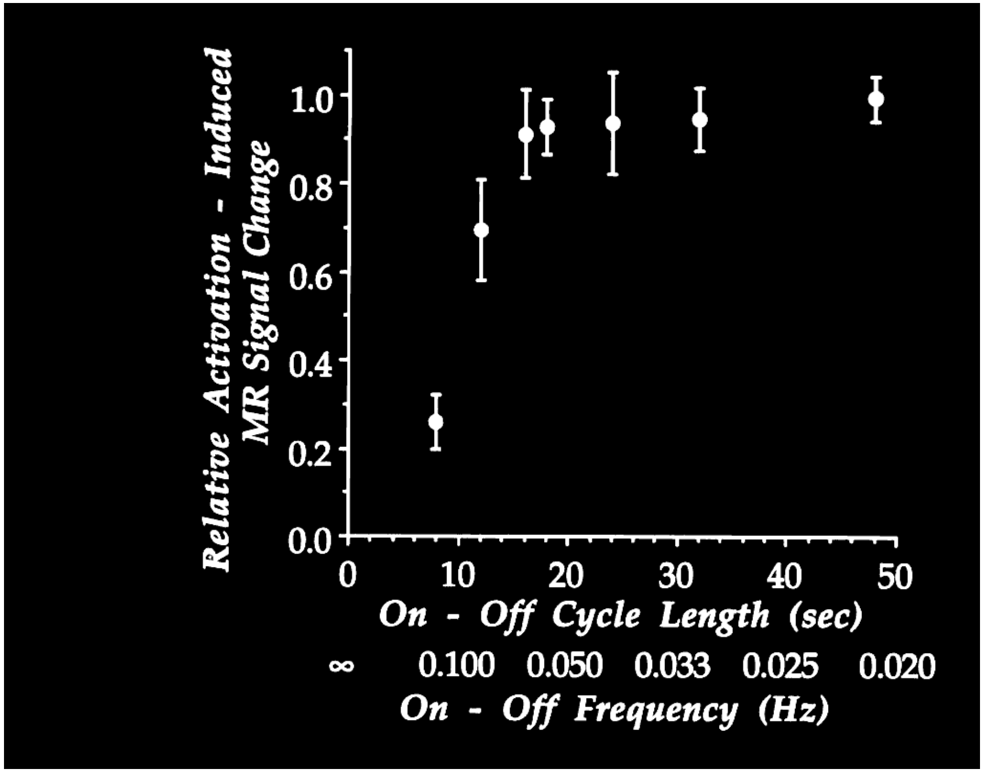


R. L. Savoy, et al., Pushing the temporal resolution of fMRI: studies of very brief visual stimuli, onset variability and asynchrony, and stimulus-correlated changes in noise, 3'rd Proc. Soc. Magn. Reson., Nice, p. 450. (1995).

Temporal Resolution



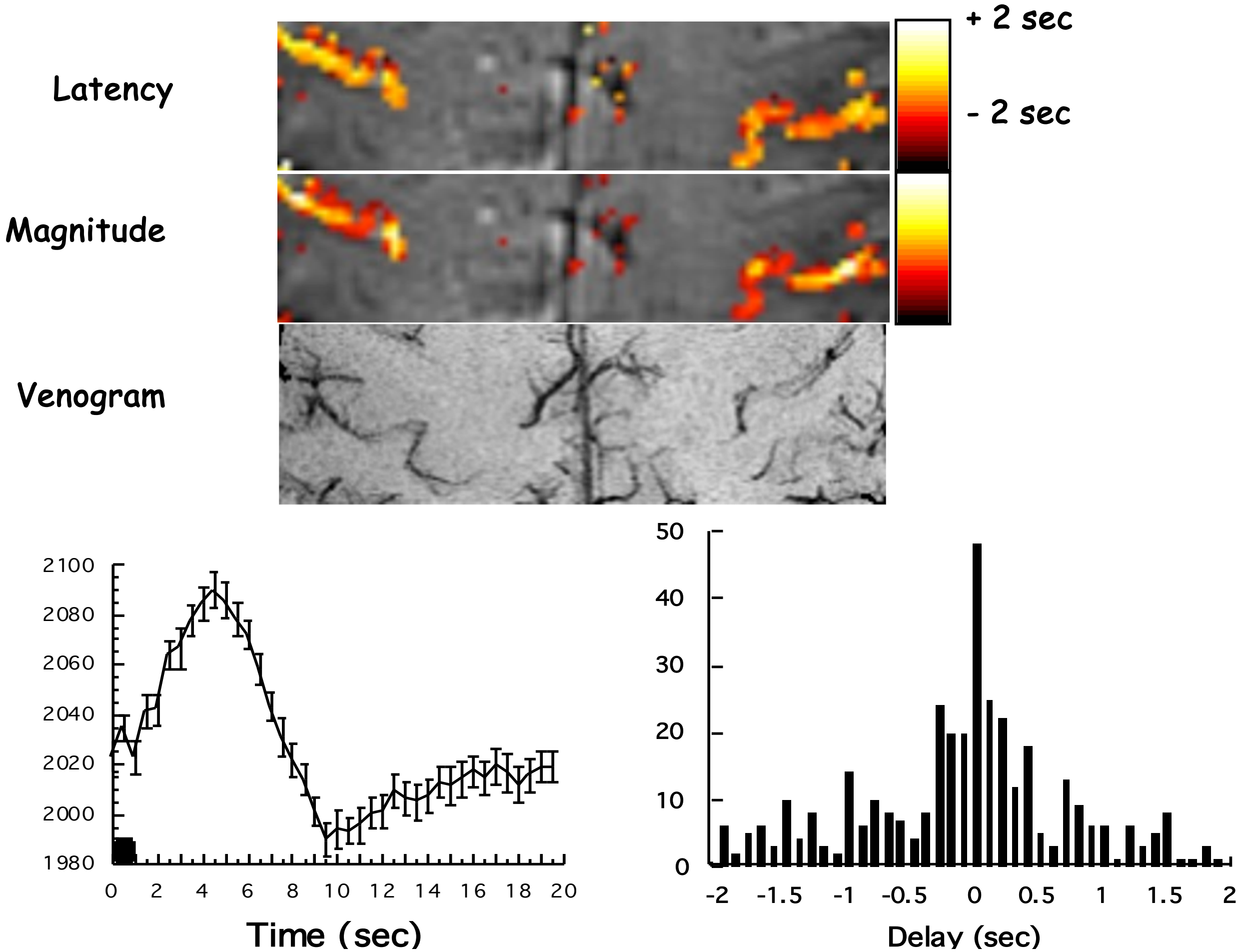
How rapidly can one switch on and off?



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

Latency Variation...

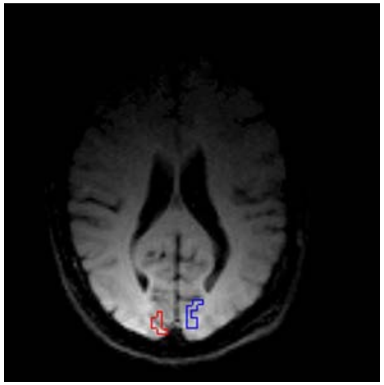


P. A. Bandettini, (1999) "Functional MRI" 205-220.

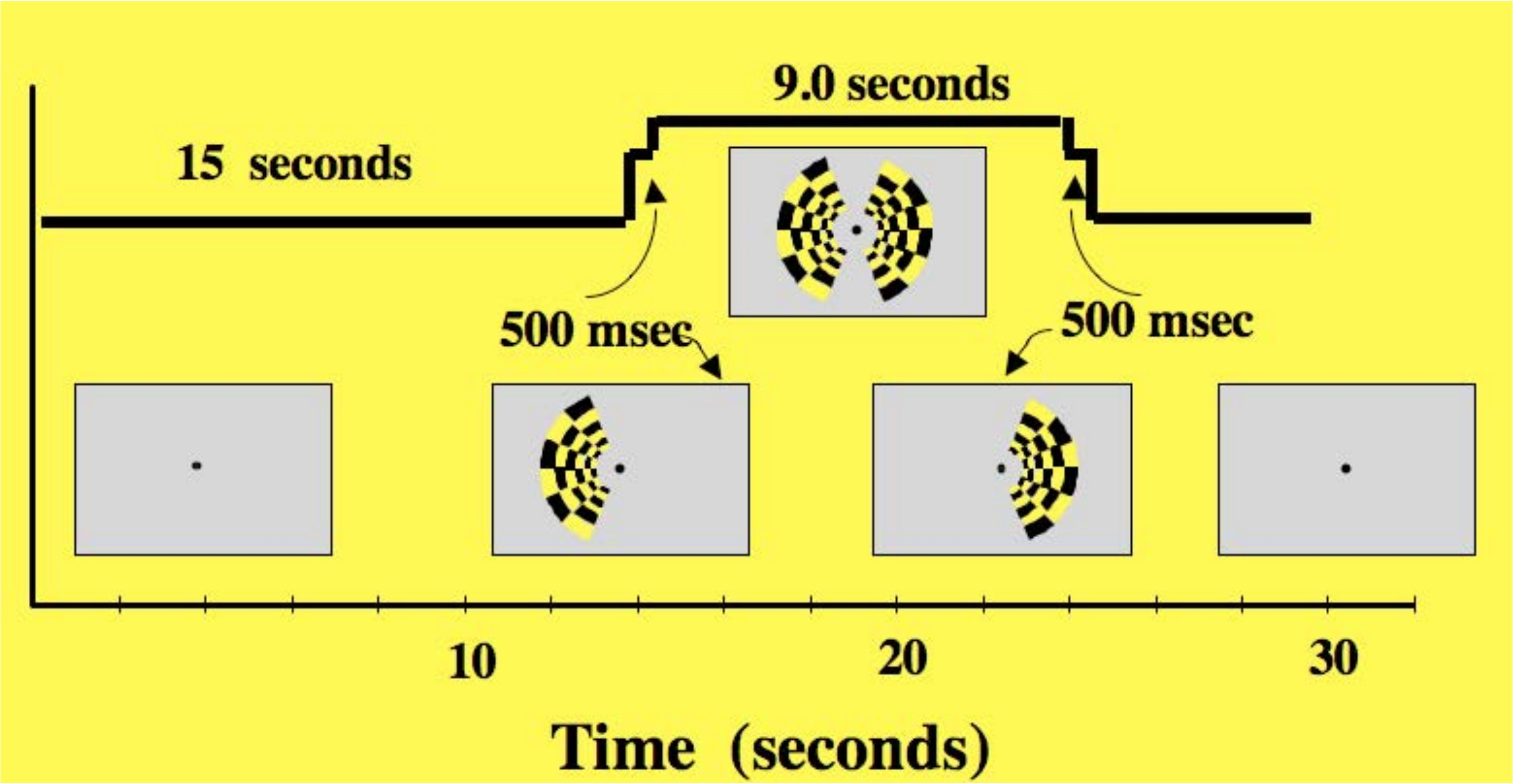
Temporal Resolution

Hemi-Field Experiment

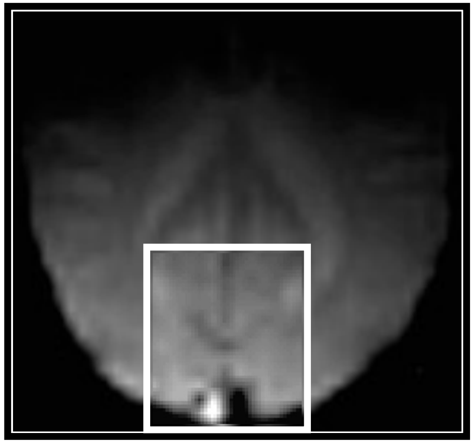
Right Hemisphere

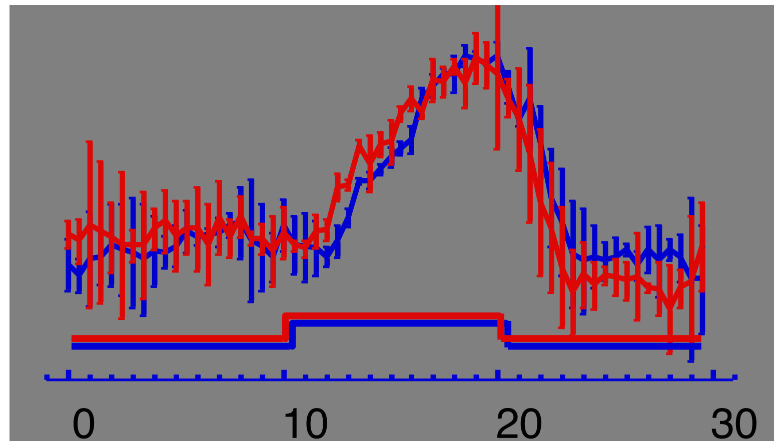


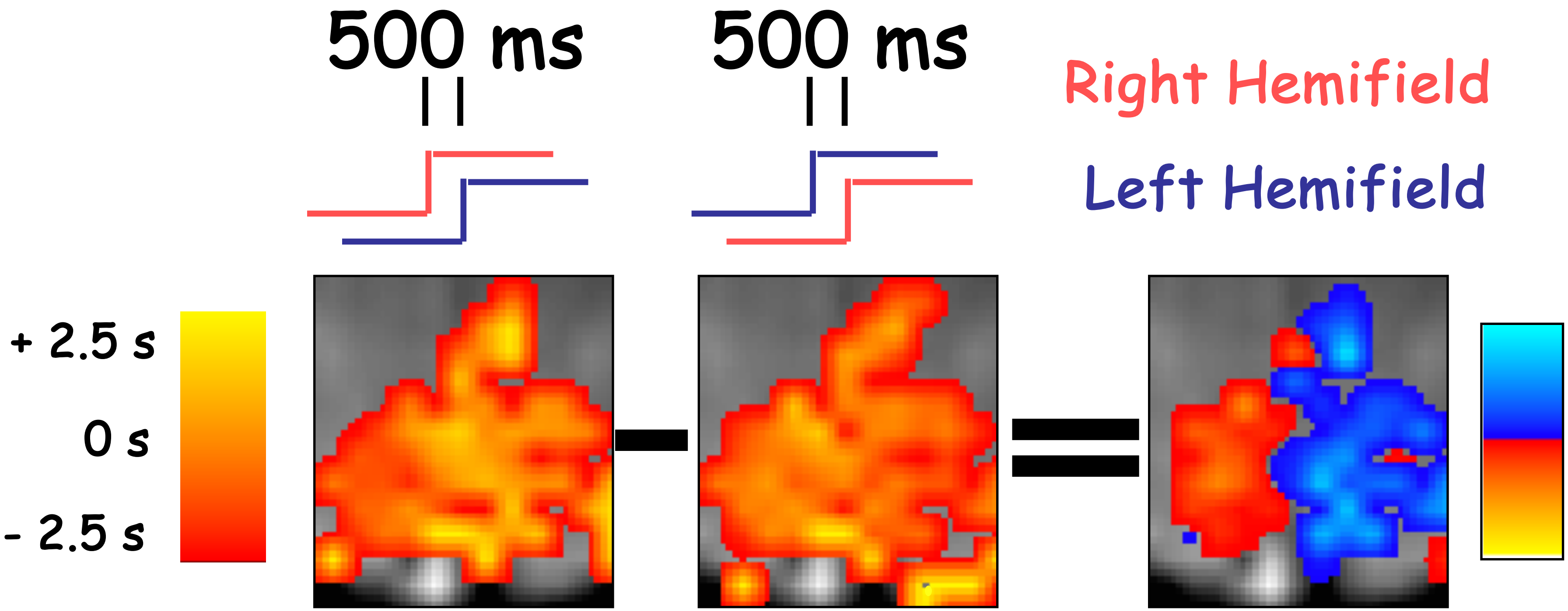
Left Hemisphere



Temporal Resolution



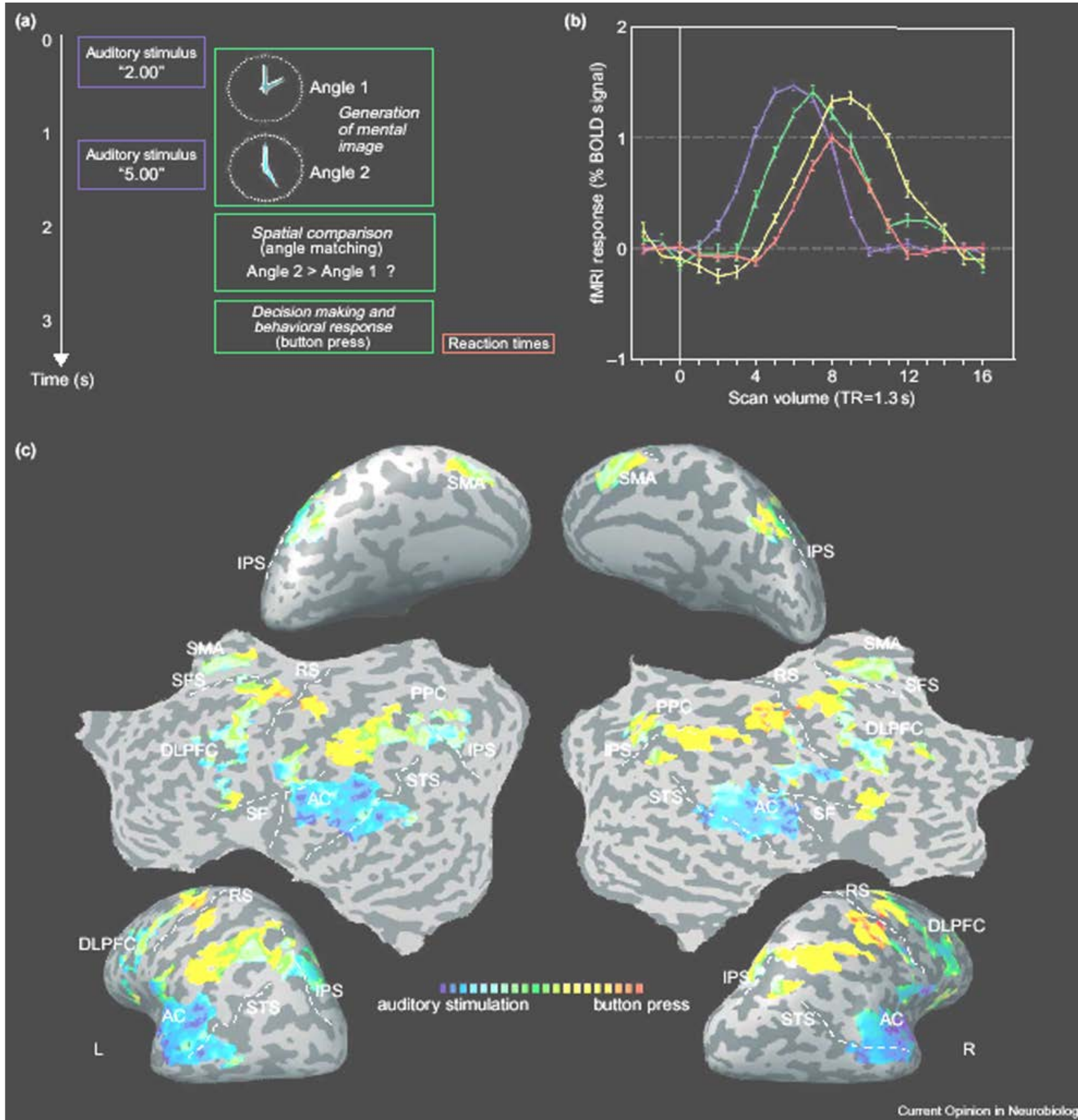




Temporal Resolution

No calibration

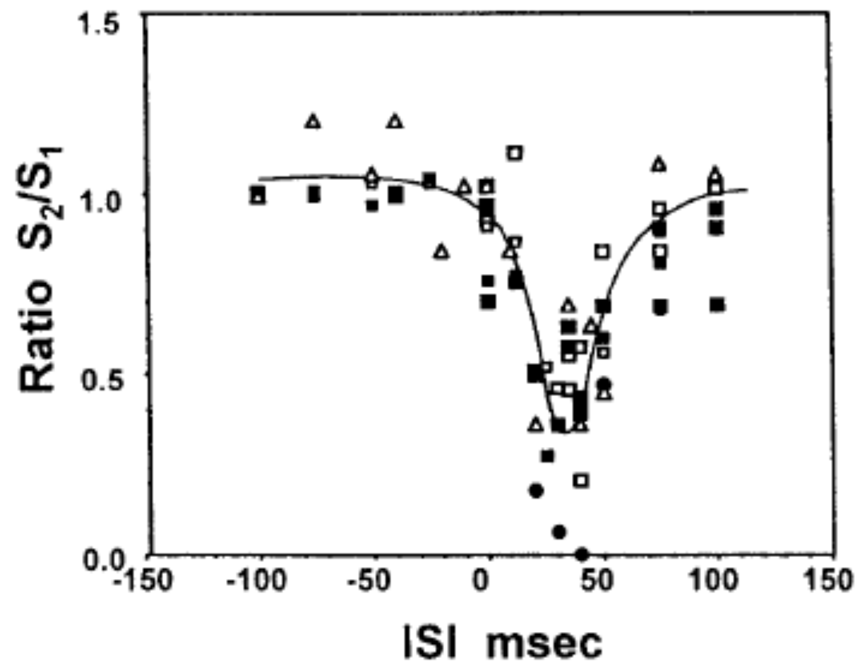
Formisano, E. and R. Goebel, *Tracking cognitive processes with functional MRI mental chronometry.* Current Opinion in Neurobiology, 2003. **13**: p. 174-181.



Temporal Resolution

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

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



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

Interpretation Issues

Temporal Resolution

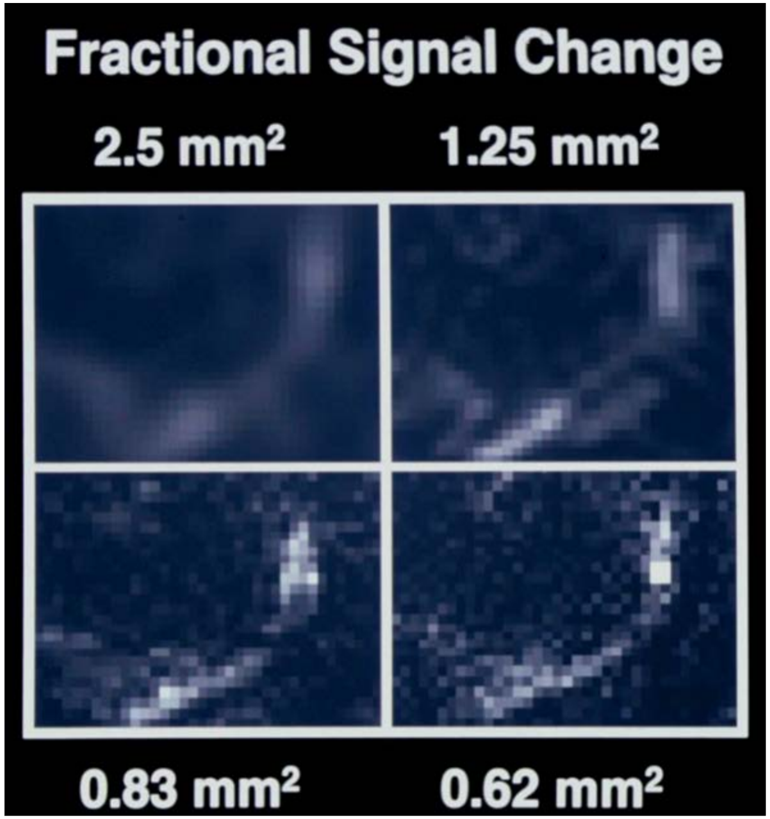
Spatial Resolution

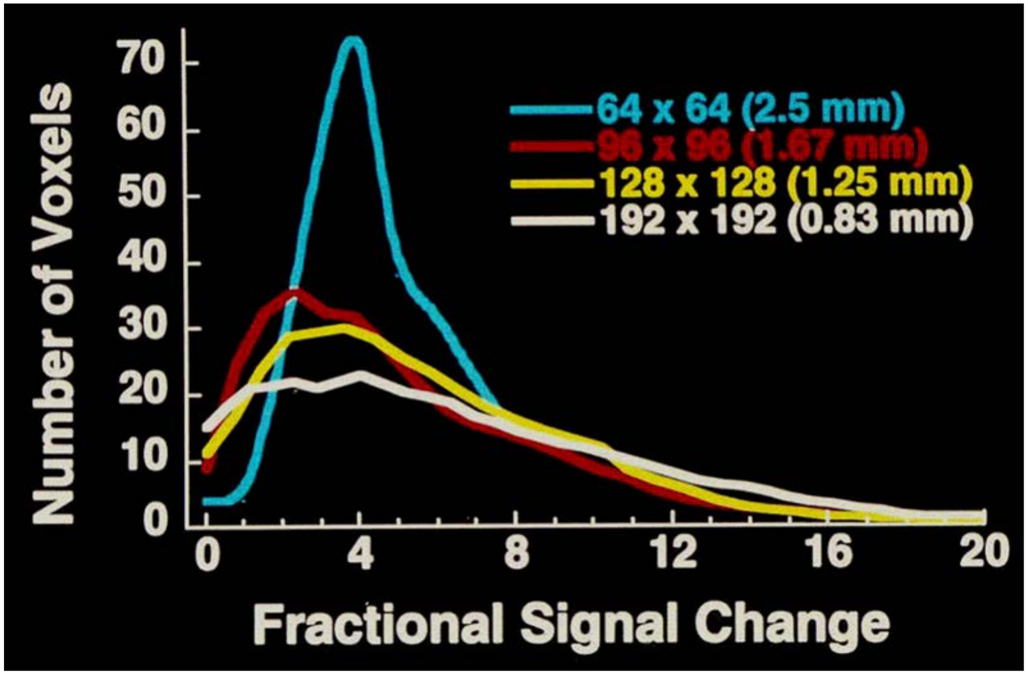
Relationship to Neuronal Activity

Noise and Fluctuations

Temporal Resolution

The effect of increasing spatial resolution

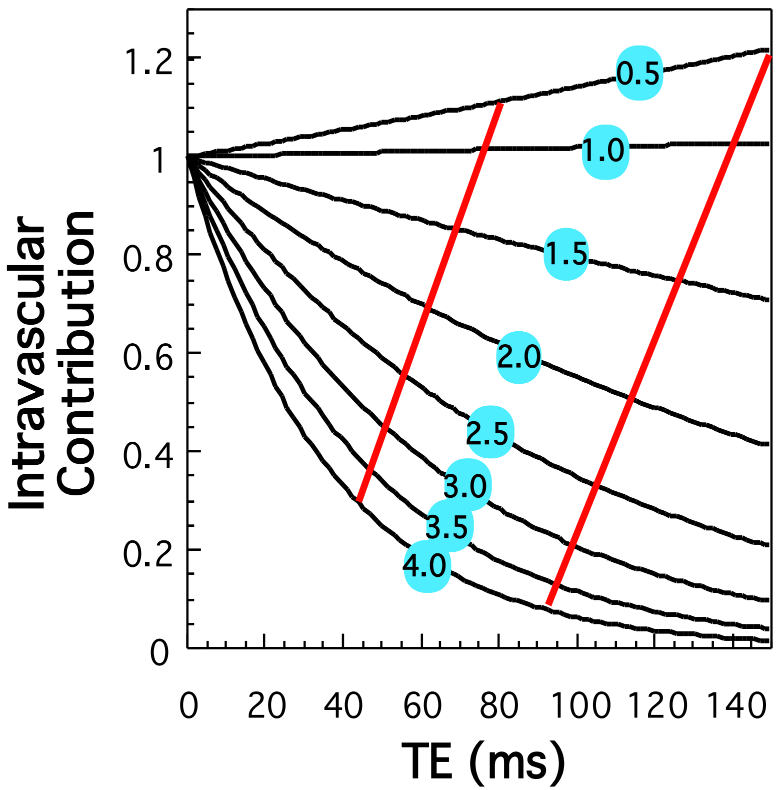




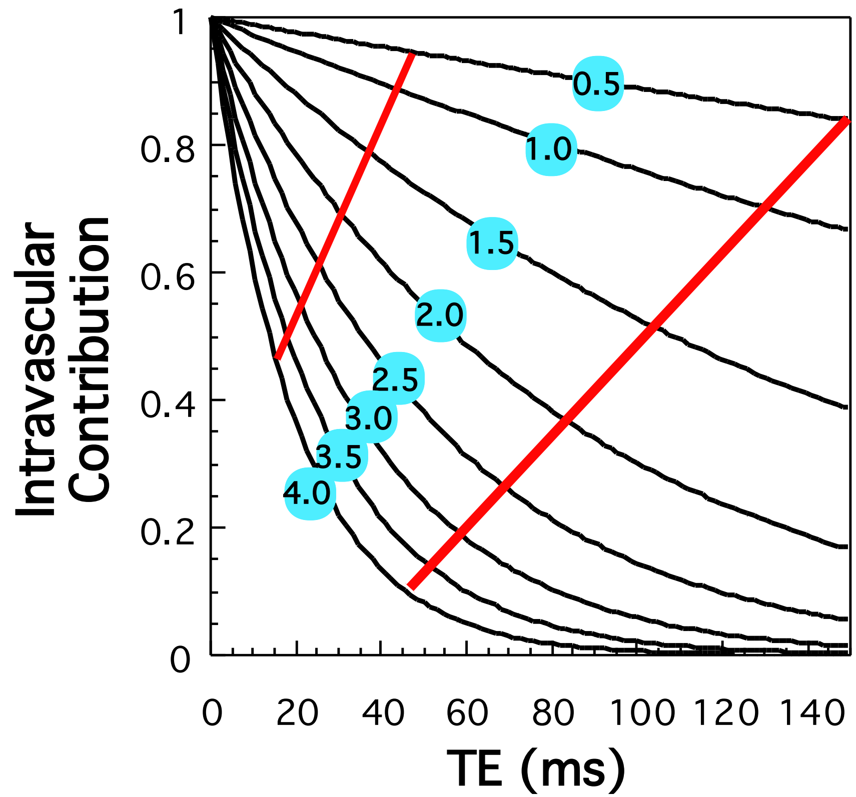
Large vessel effects tend to be amplified…

Field strength dependence of intravascular signal

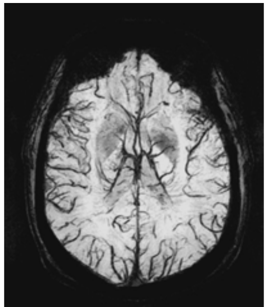
Spin-echo, %HbO_2 = 60



Gradient-echo, %HbO_2 = 60

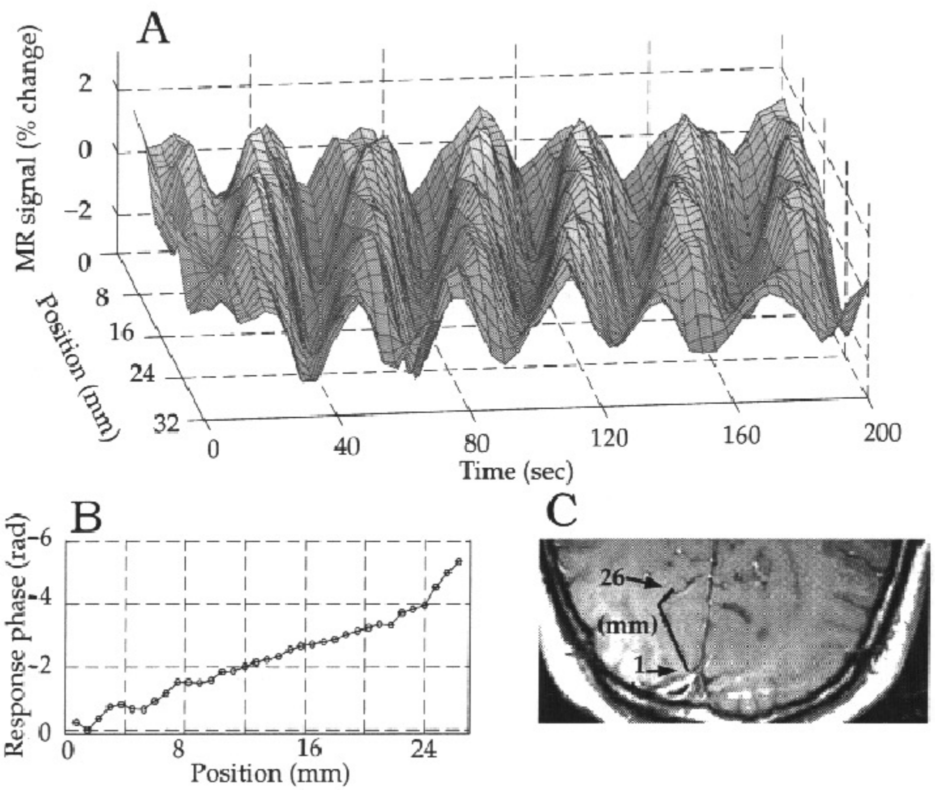


Source of contrast in venograms..



Spatial Resolution

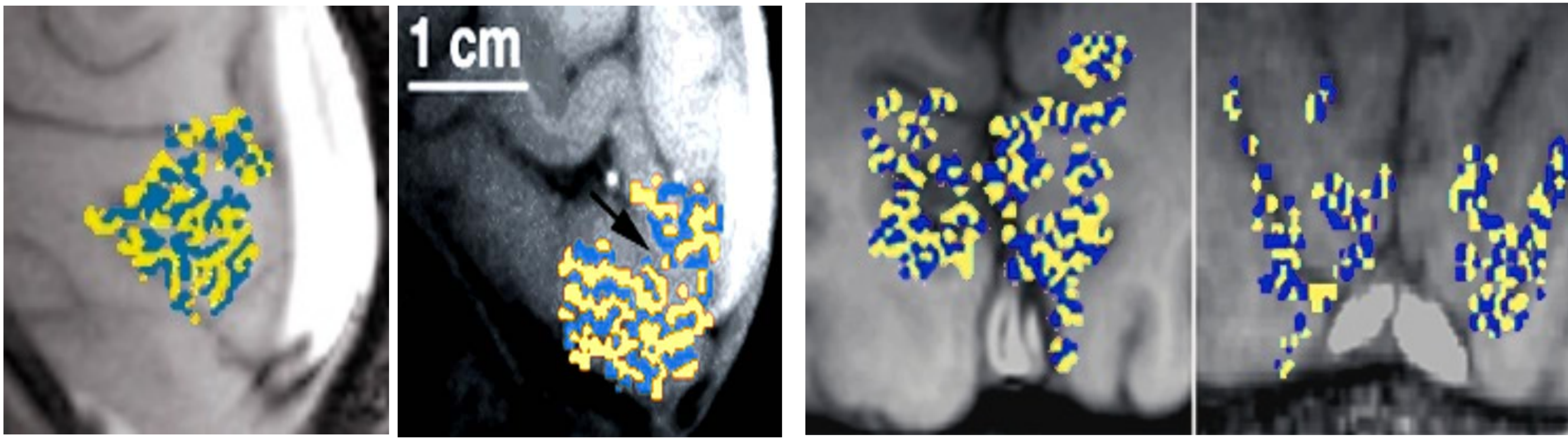
PSF FWHM = 3.5mm



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

Spatial Resolution

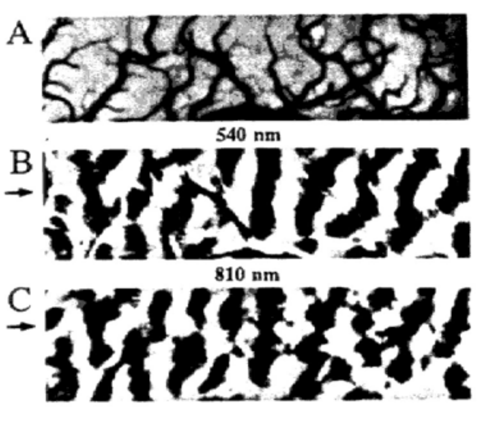
Ocular Dominance Column Mapping



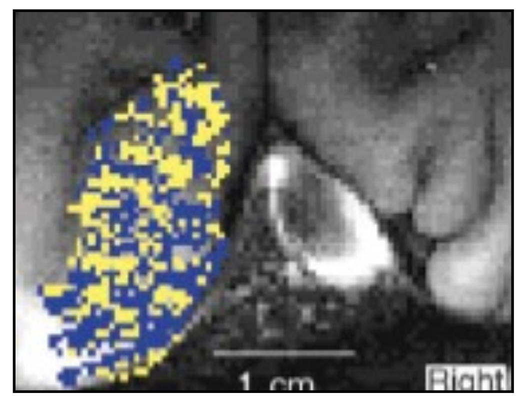
Menon, R. S., S. Ogawa, et al. (1997). J Neurophysiol 77(5): 2780-7.

0.54 x 0.54 in plane resolution

Optical Imaging



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

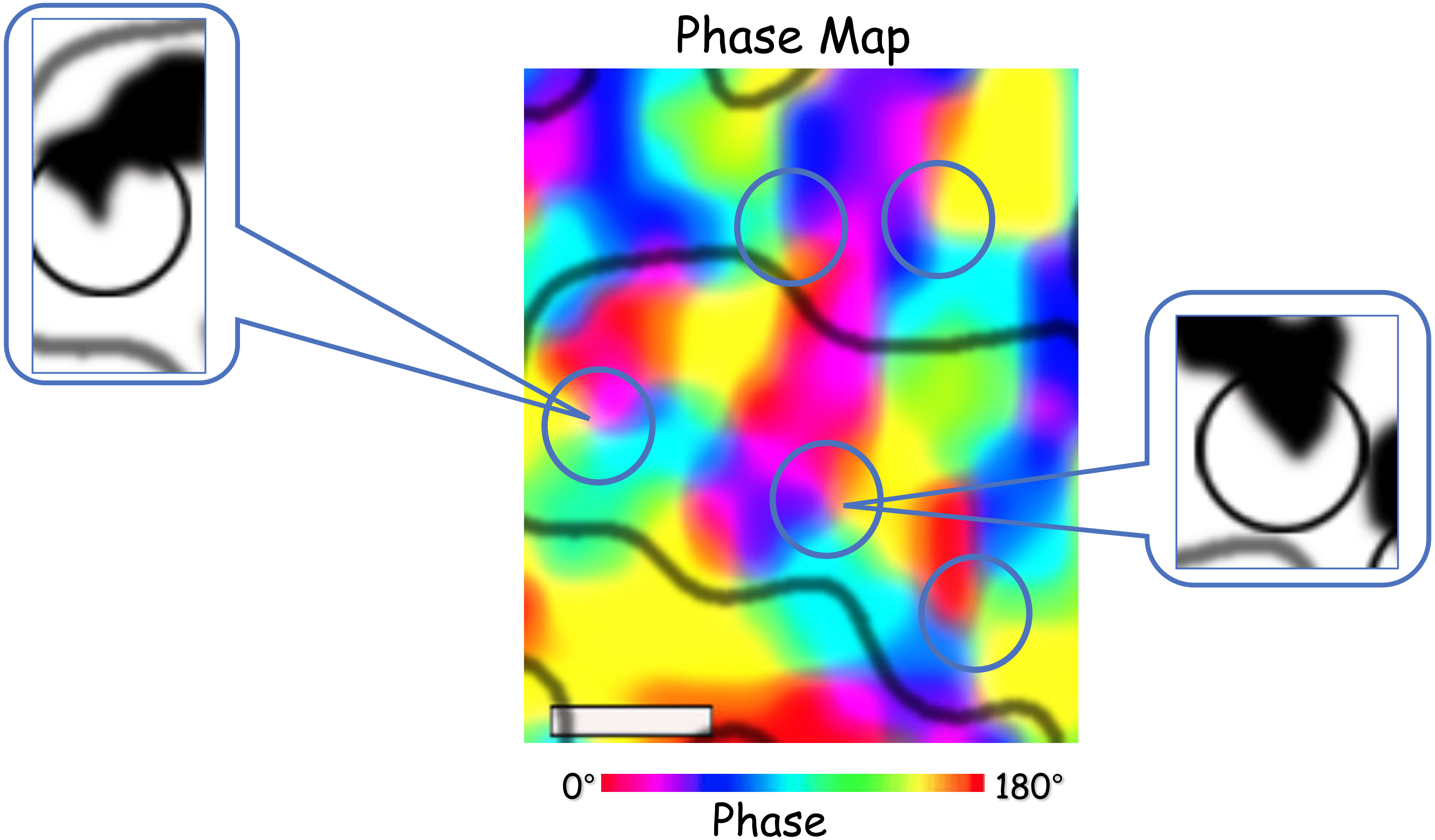


Cheng, et al. (2001)
Neuron,32:359-374

0.47 x 0.47 in plane resolution

Spatial Resolution

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

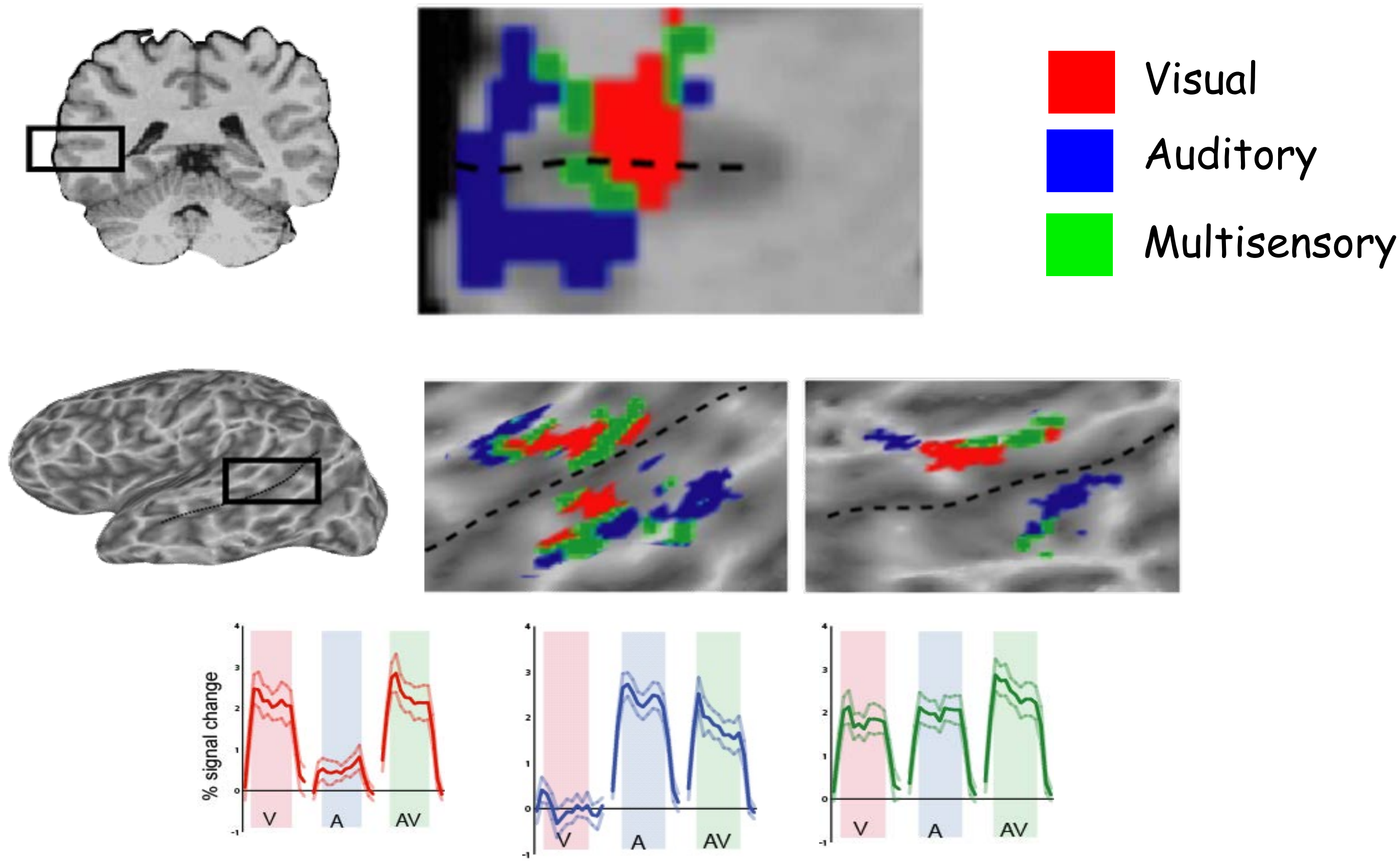


Yacoub, Ugurbil & Harel
University of Minnesota / CMRR
In press

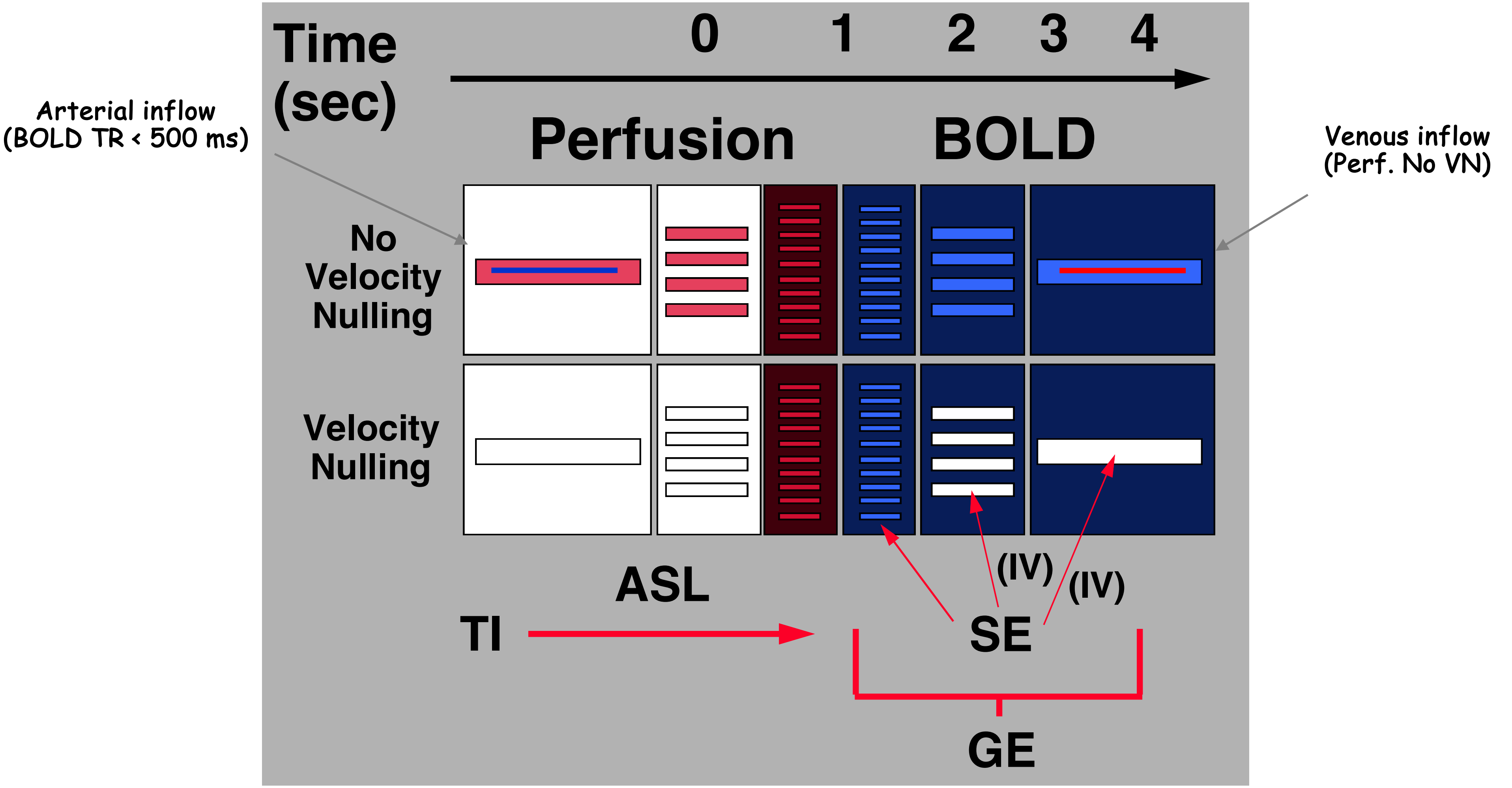
Scalebar = 0.5 mm

Multi-sensory integration

M.S. Beauchamp et al.,



Hemodynamic Specificity



Pulse sequence strategies..

Interpretation Issues

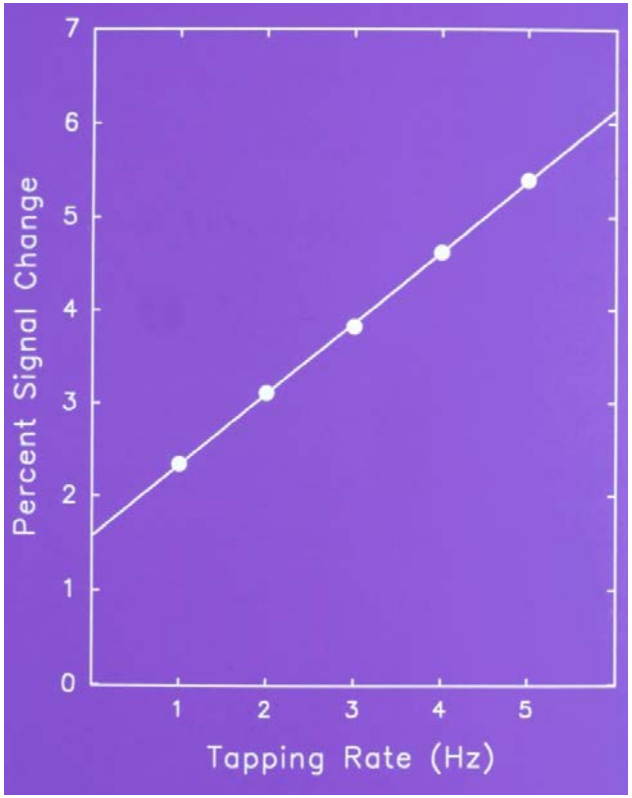
Temporal Resolution

Spatial Resolution

Relationship to Neuronal Activity

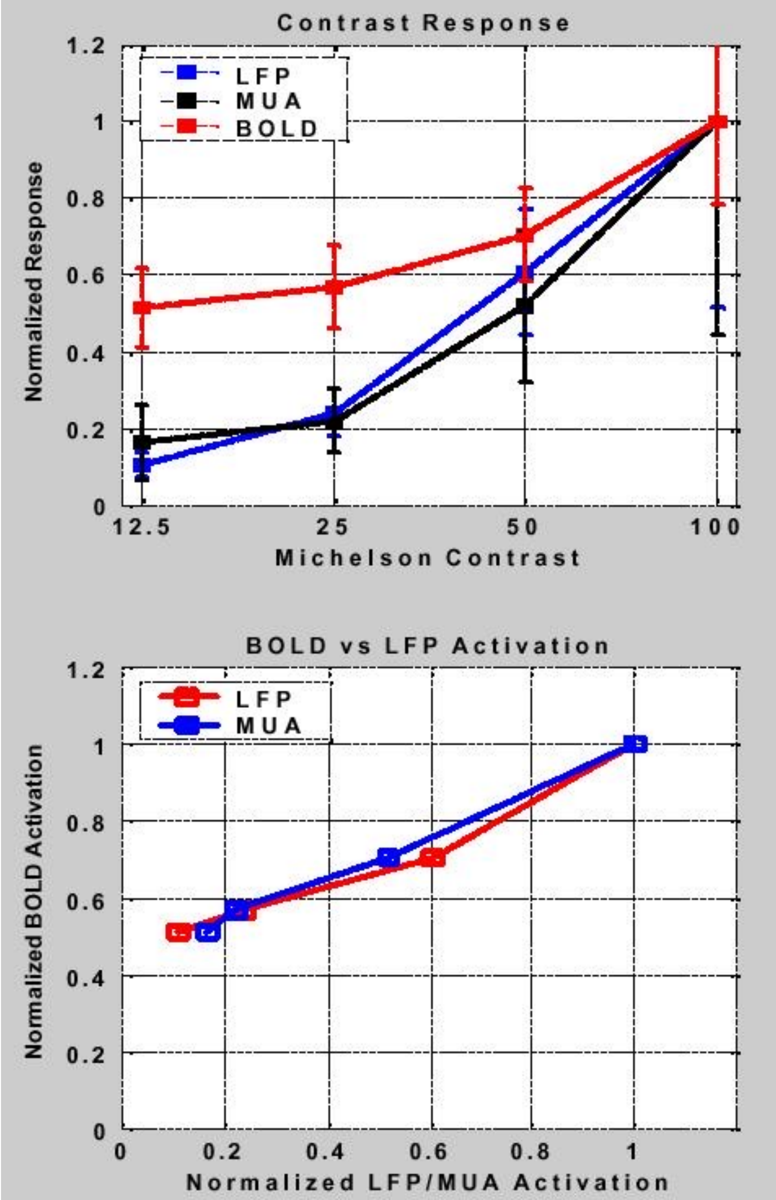
Noise and Fluctuations

Relationship to Neuronal Activity

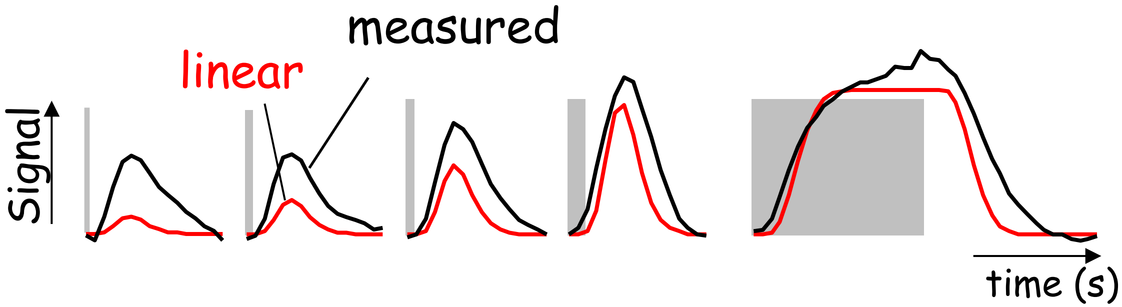


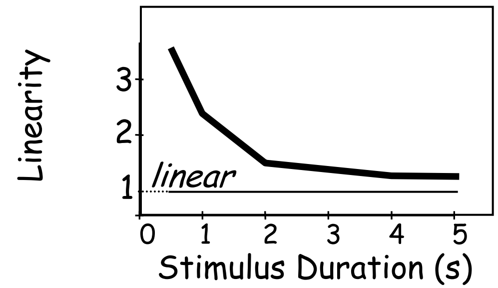
S. M. Rao et al, (1996) "Relationship between finger movement rate and functional magnetic resonance signal change in human primary motor cortex." *J. Cereb. Blood Flow and Met.* 16, 1250-1254.

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



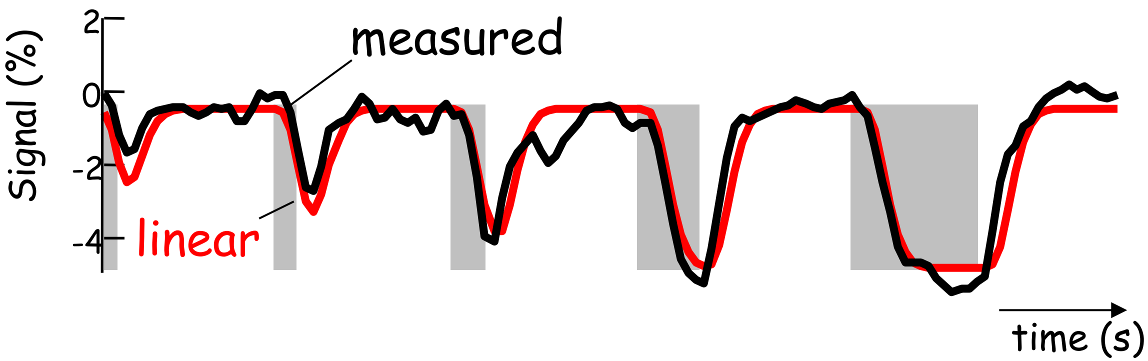
Brief "on" periods produce larger increases than expected.

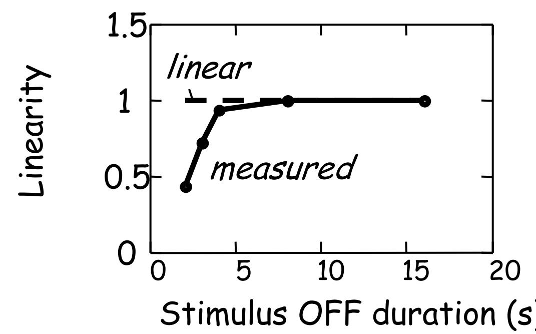




R. M. Birn, Z. Saad, P. A. Bandettini, NeuroImage, 14: 817-826, (2001)

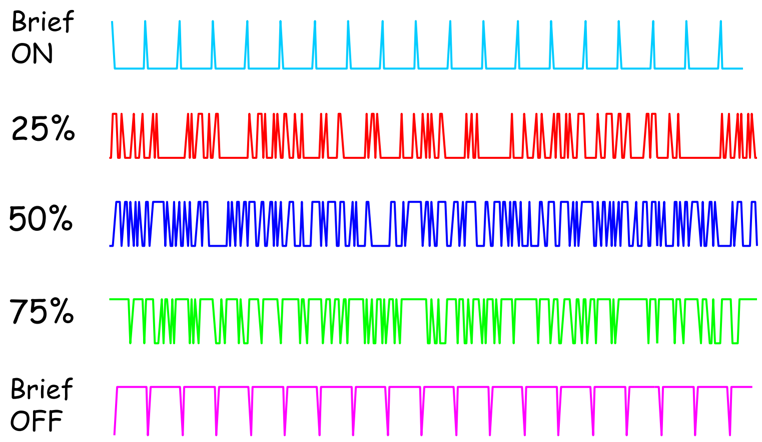
Brief "off" periods produce smaller decreases than expected.

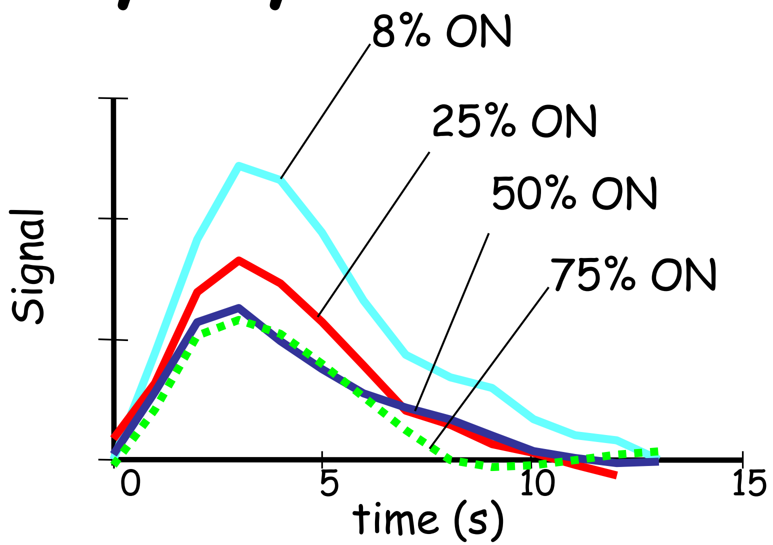




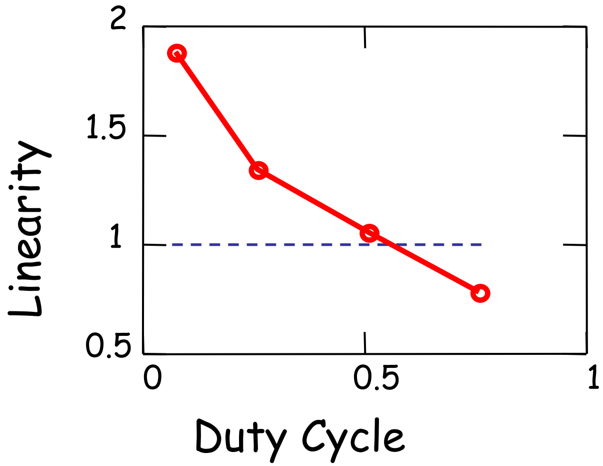
R.M. Birn, P. A. Bandettini, NeuroImage, 27, 70-82 (2005)

Varying the Duty Cycle



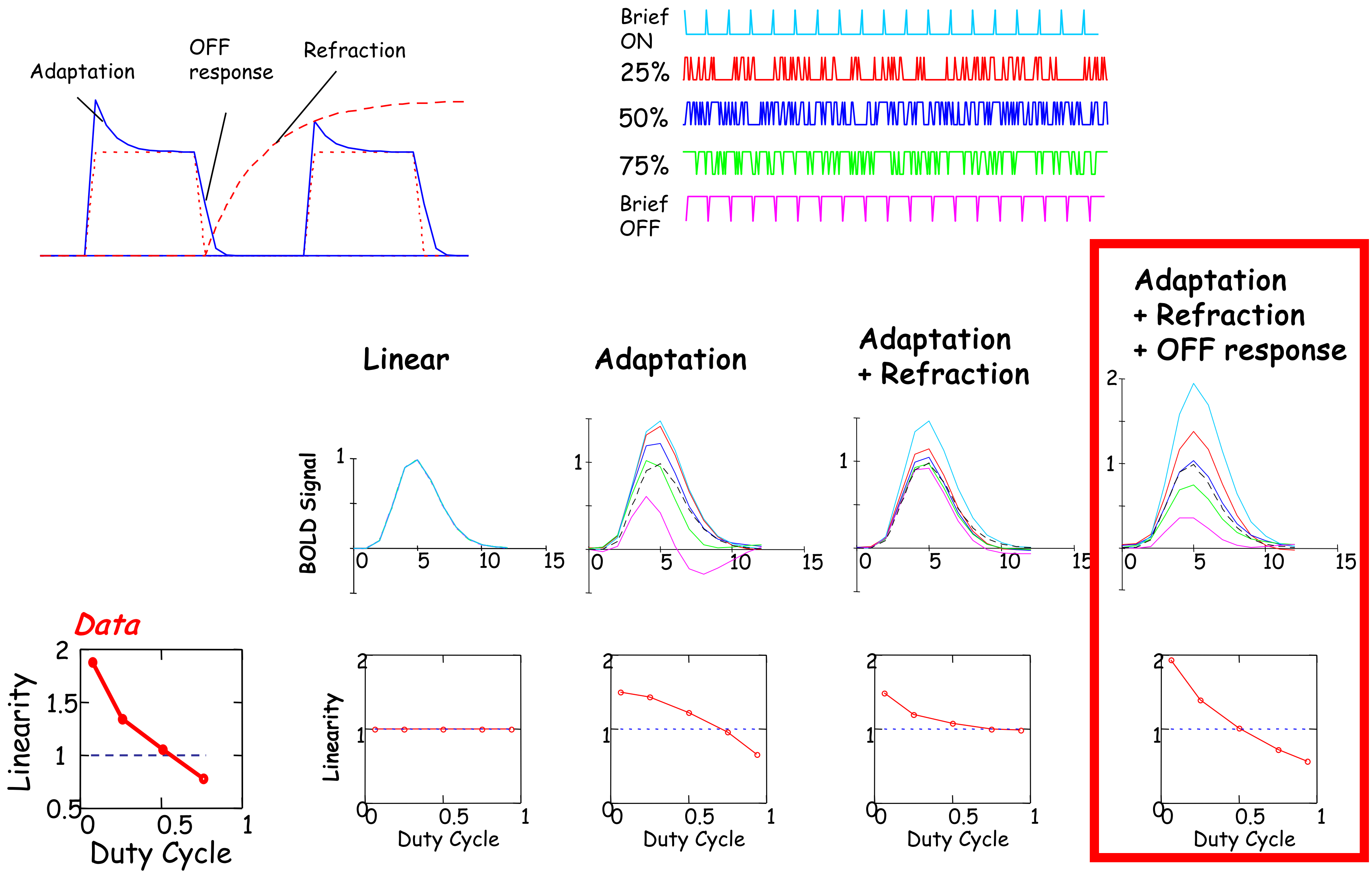


Deconvolved Response



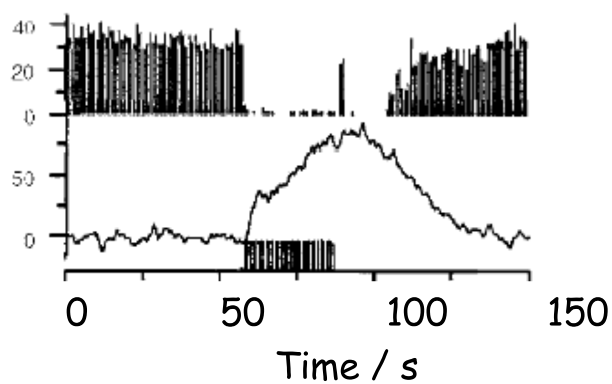
R.M. Birn, P. A. Bandettini, *NeuroImage*, 27, 70-82 (2005)

Simulation of Neuronal Mechanisms



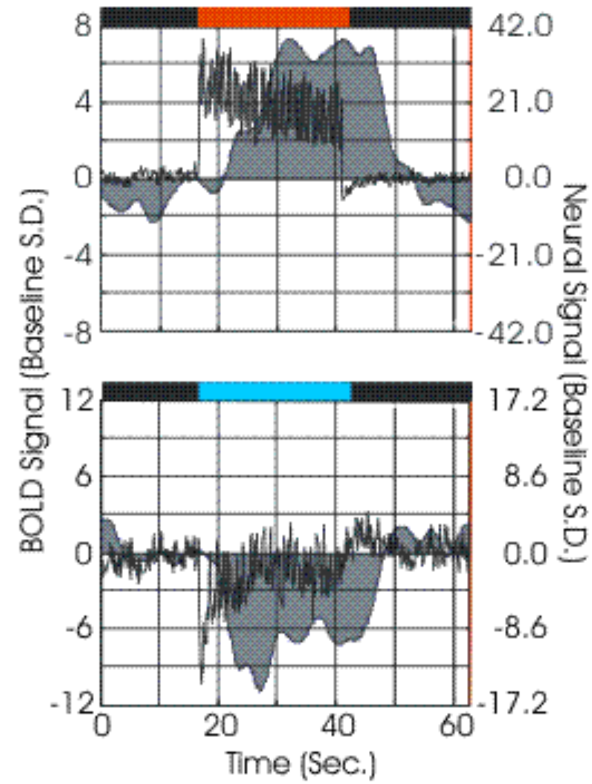
Relationship to Neuronal Activity

Inhibition



Mathiesen, et al (1998), J Physiol 512.2:555-566

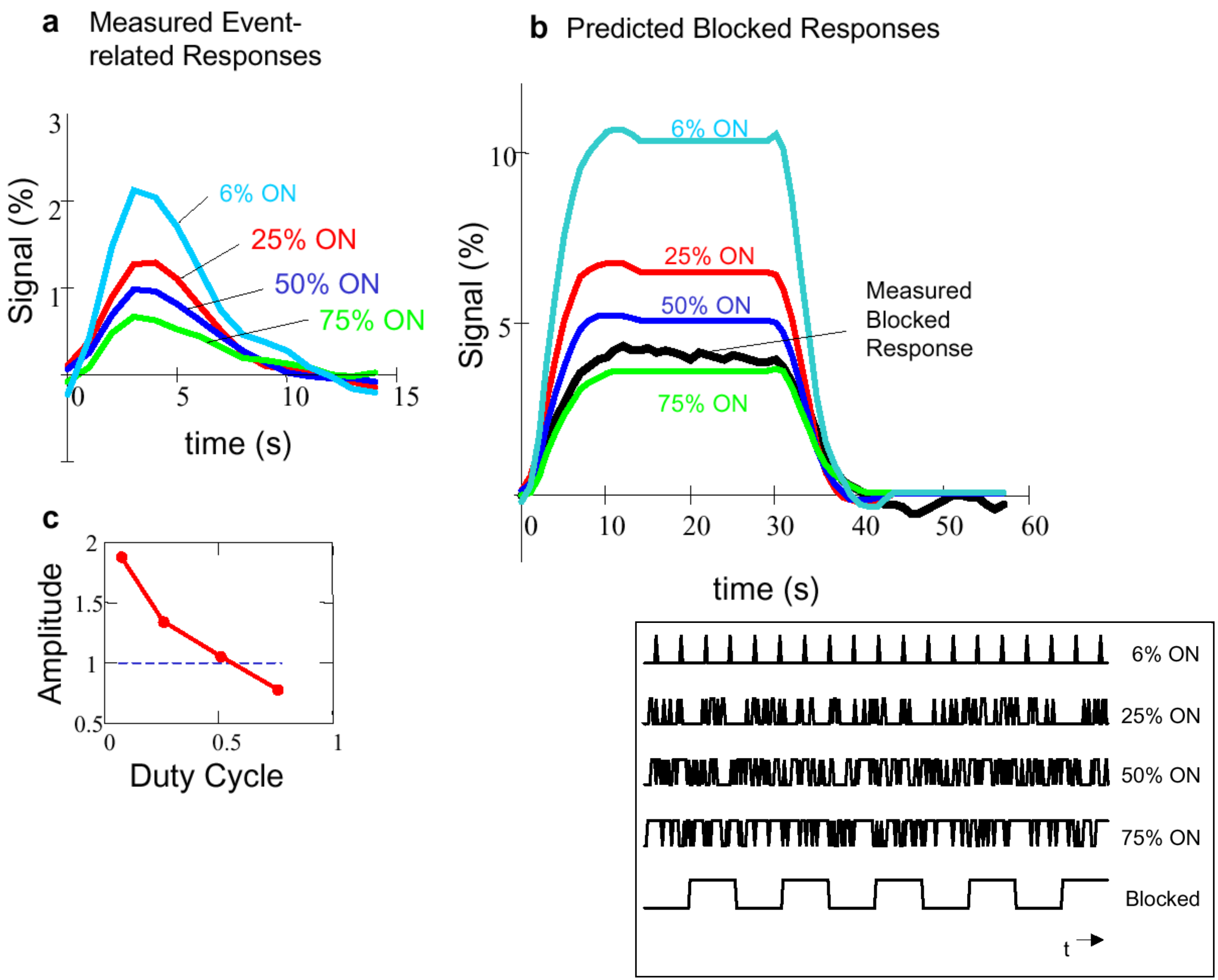
Neg. BOLD



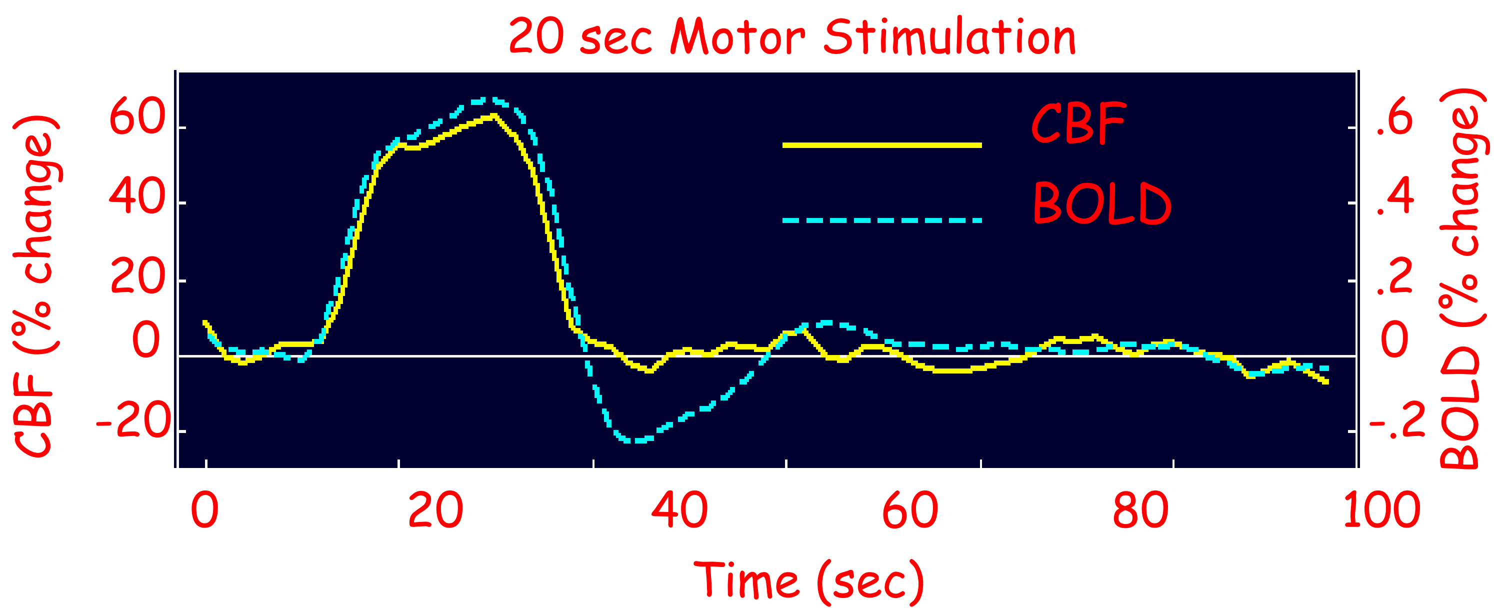
Schmuel et al.

Relationship to Neuronal Activity

Duty Cycle Effects



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

Interpretation Issues

Temporal Resolution

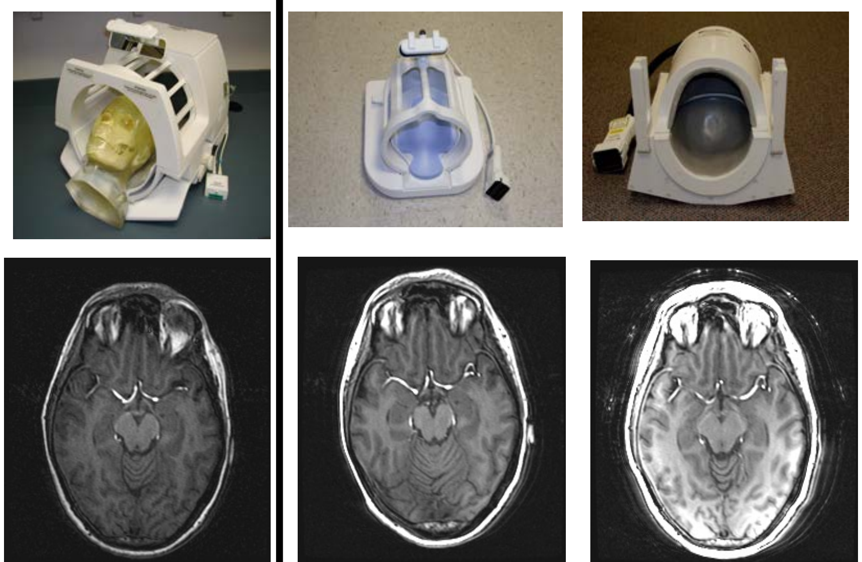
Spatial Resolution

Relationship to Neuronal Activity

Noise and Fluctuations

Noise and Fluctuations

8 channel parallel receiver coil

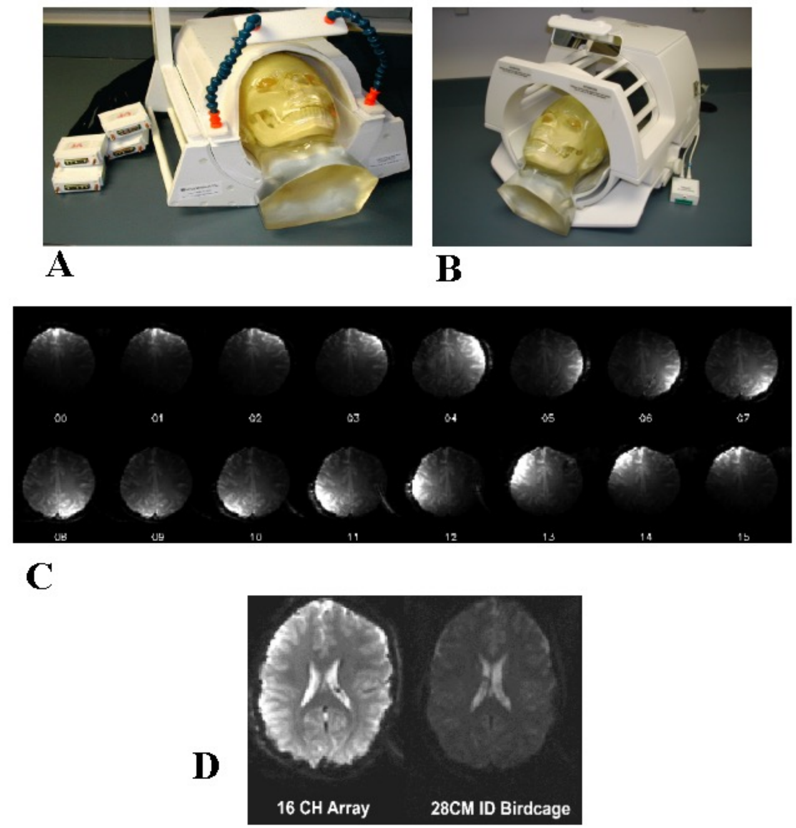


GE birdcage

GE 8 channel coil

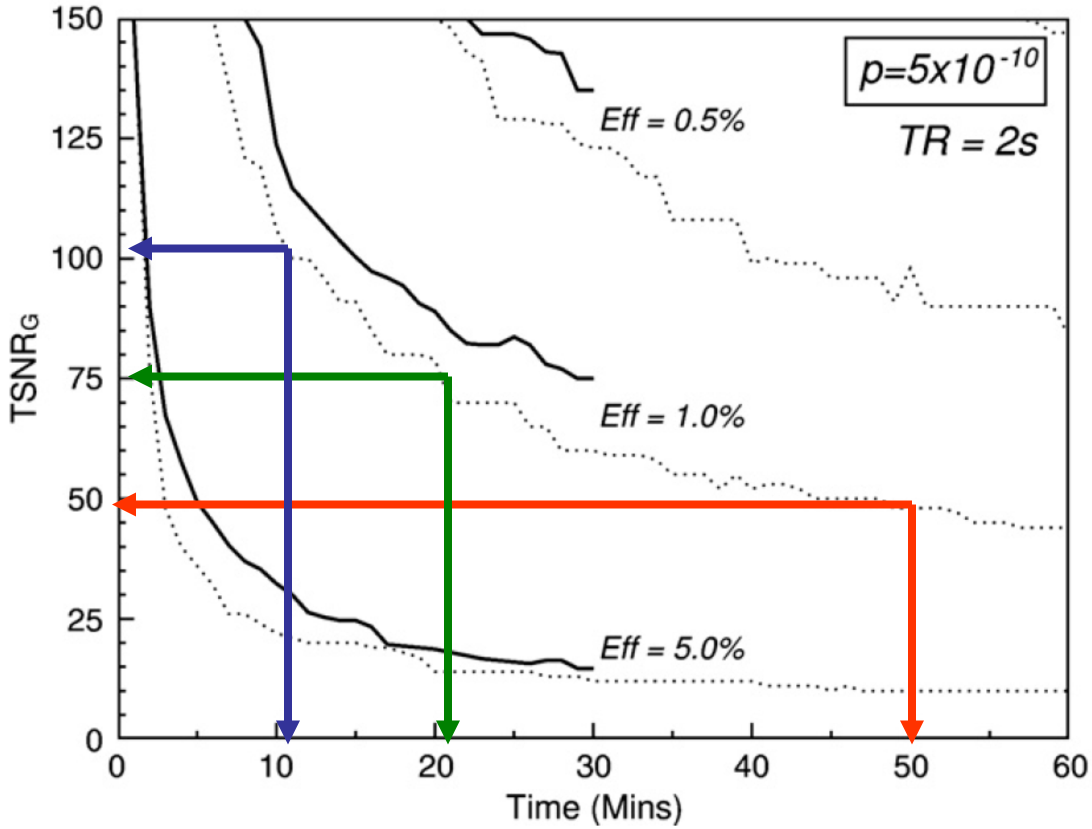
Nova 8 channel coil

16 channel parallel receiver coil



J. Bodurka, et al, Magnetic Resonance in Medicine 51 (2004) 165-171.

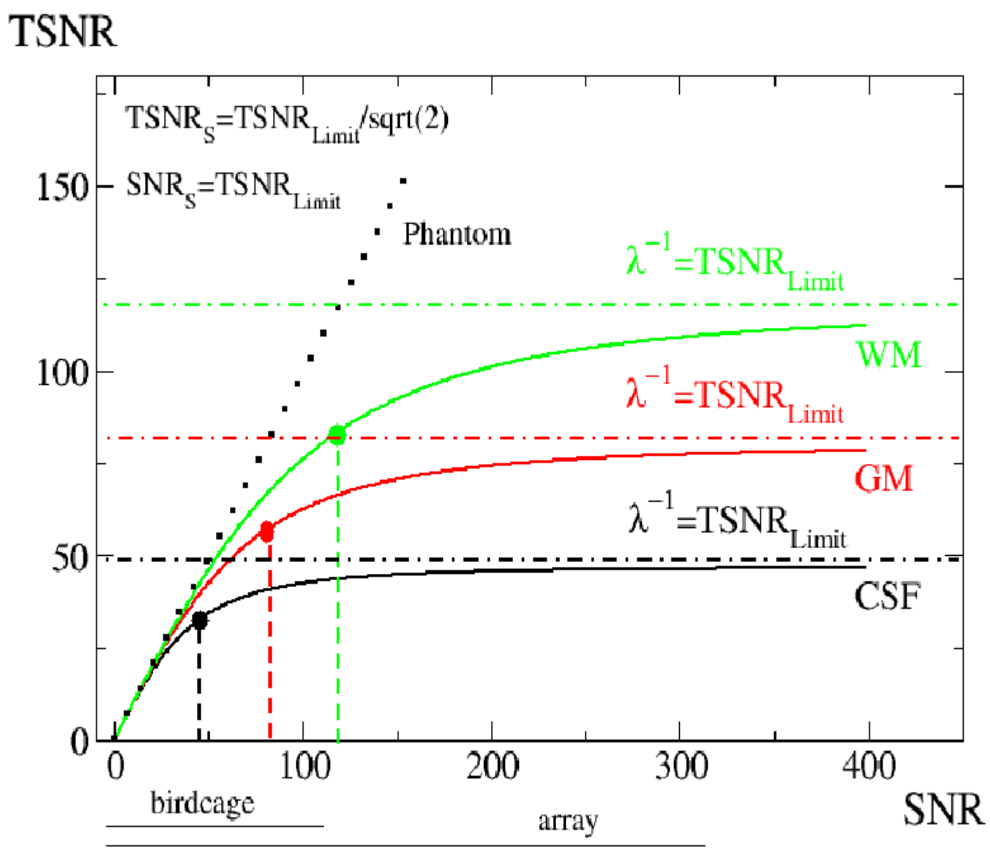
Noise and Fluctuations



K. Murphy, J. Bodurka, P. A. Bandettini, How long to scan? The relationship between fMRI temporal signal to noise and the necessary scan duration. *NeuroImage*, 34, 565-574 (2007)

Noise and Fluctuations

Temporal Signal to Noise Ratio (TSNR) vs. Signal to Noise Ratio (SNR)



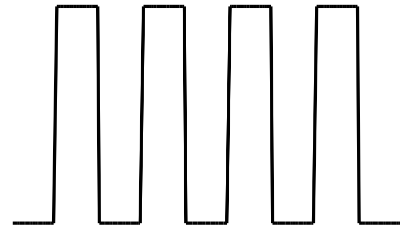
suggested voxel volume

3T, birdcage:	2.5 mm^3
3T, 16 channel:	1.8 mm^3
7T, 16 channel:	1.4 mm^3

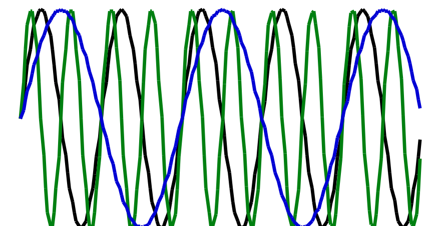
J. Bodurka, F. Ye, N Petridou, K. Murphy, P. A. Bandettini, *NeuroImage,* 34, 542-549 (2007)

Neuronal Activation Input Strategies

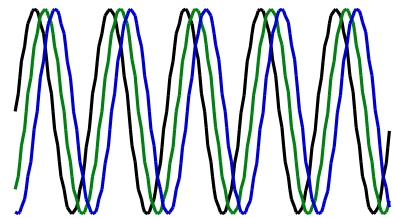
1. Block Design



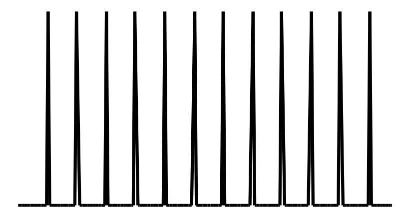
2. Frequency Encoding



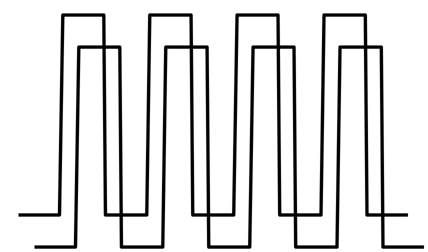
3. Phase Encoding



4. Event-Related

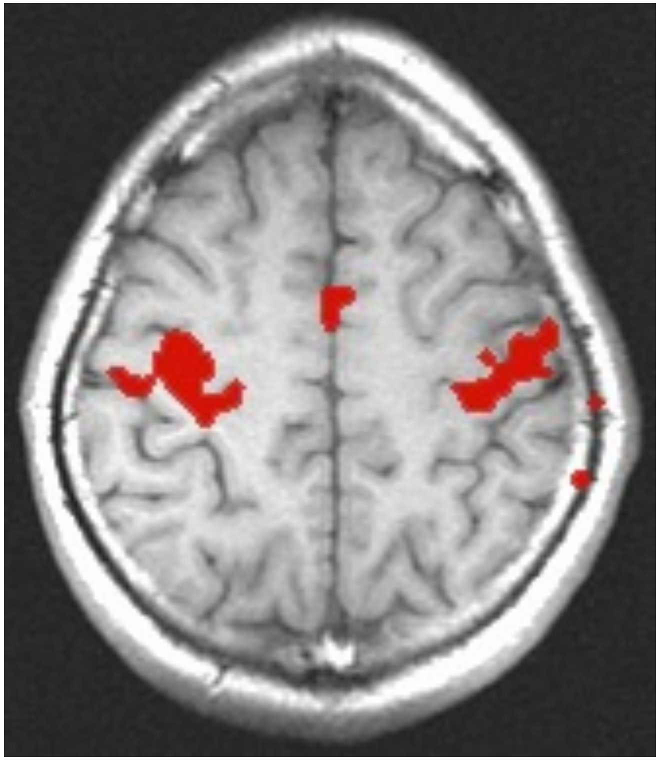


5. Orthogonal Block Design

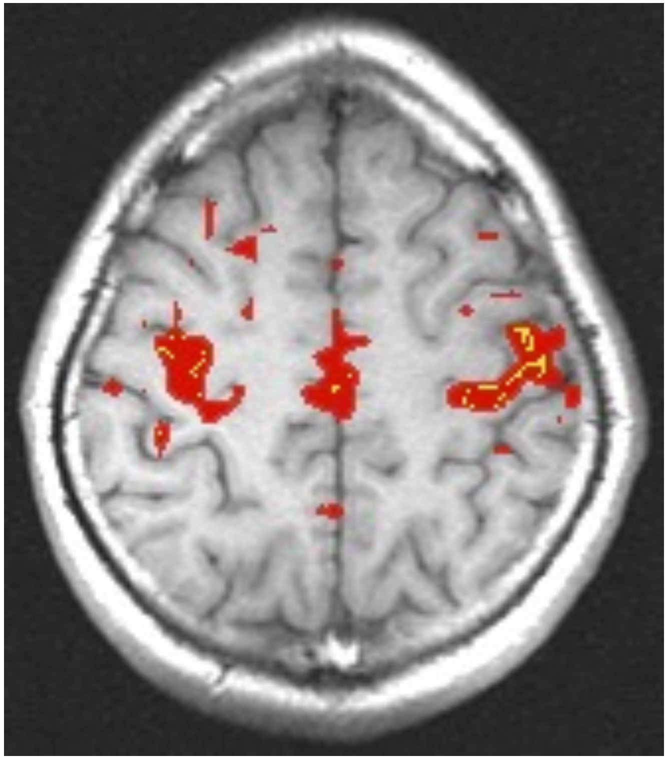


6. Free Behavior Design.

Resting State Correlations



Activation:
correlation with reference function

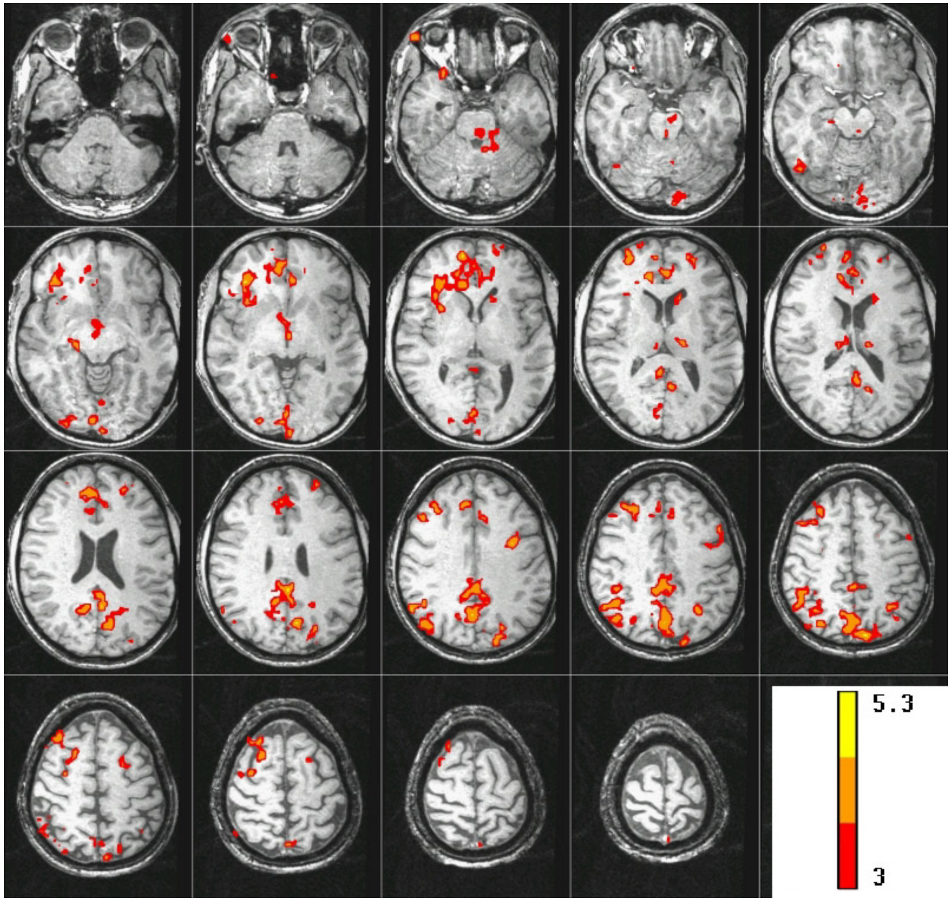


Rest:
seed voxel in motor cortex

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

Noise and Fluctuations

BOLD correlated with SCR during "Rest"

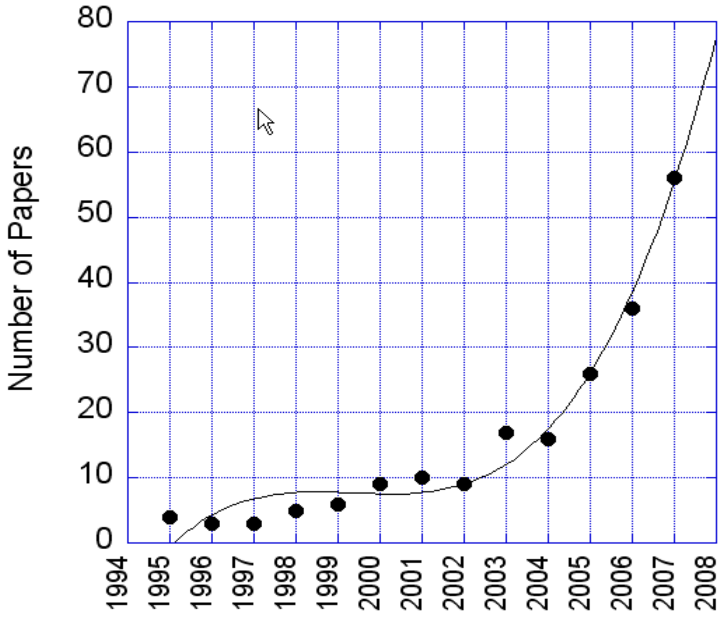


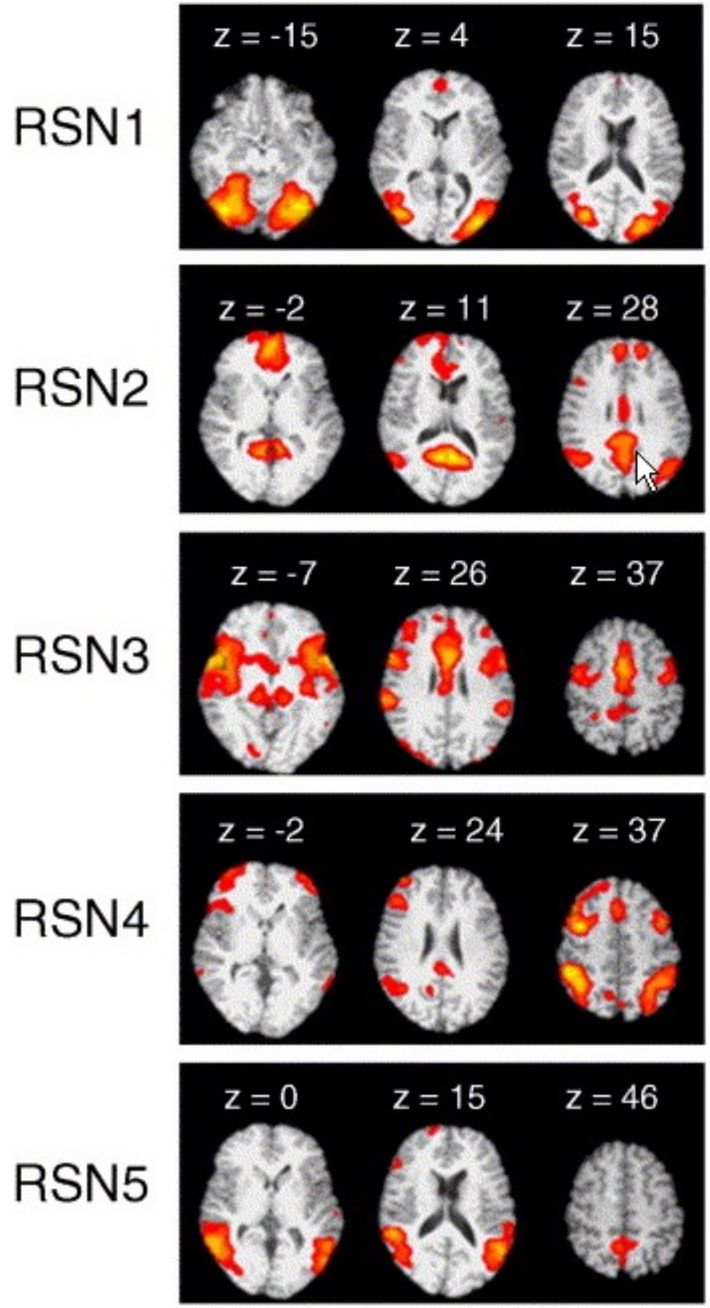
J. C. Patterson II, L. G. Ungerleider, and P. A Bandettini, *NeuroImage 17: 1787-1806, (2002).*

Noise and Fluctuations

Resting state networks identified with ICA

M. DeLuca, C.F. Beckmann, N. De Stefano, P.M. Matthews, S.M. Smith, fMRI resting state networks define distinct modes of long-distance interactions in the human brain. NeuroImage, 29, 1359-1367





Noise and Fluctuations

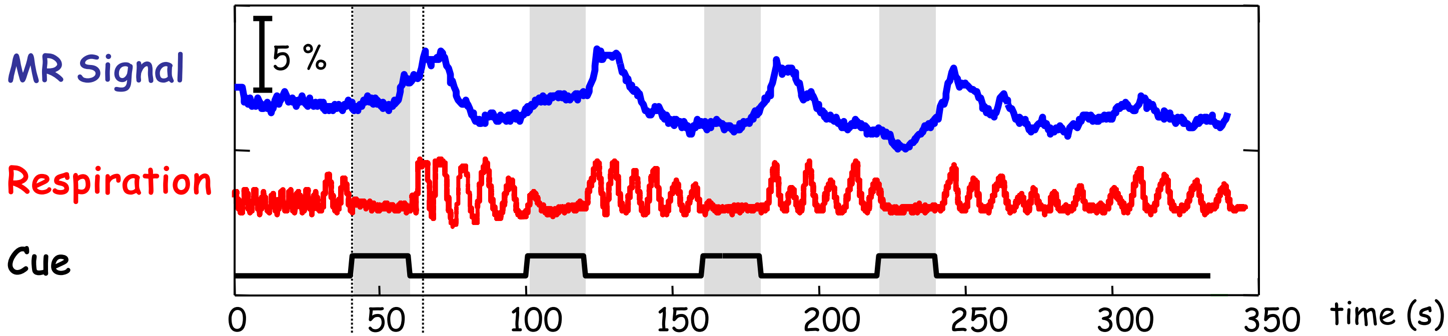
Sources of time series fluctuations:

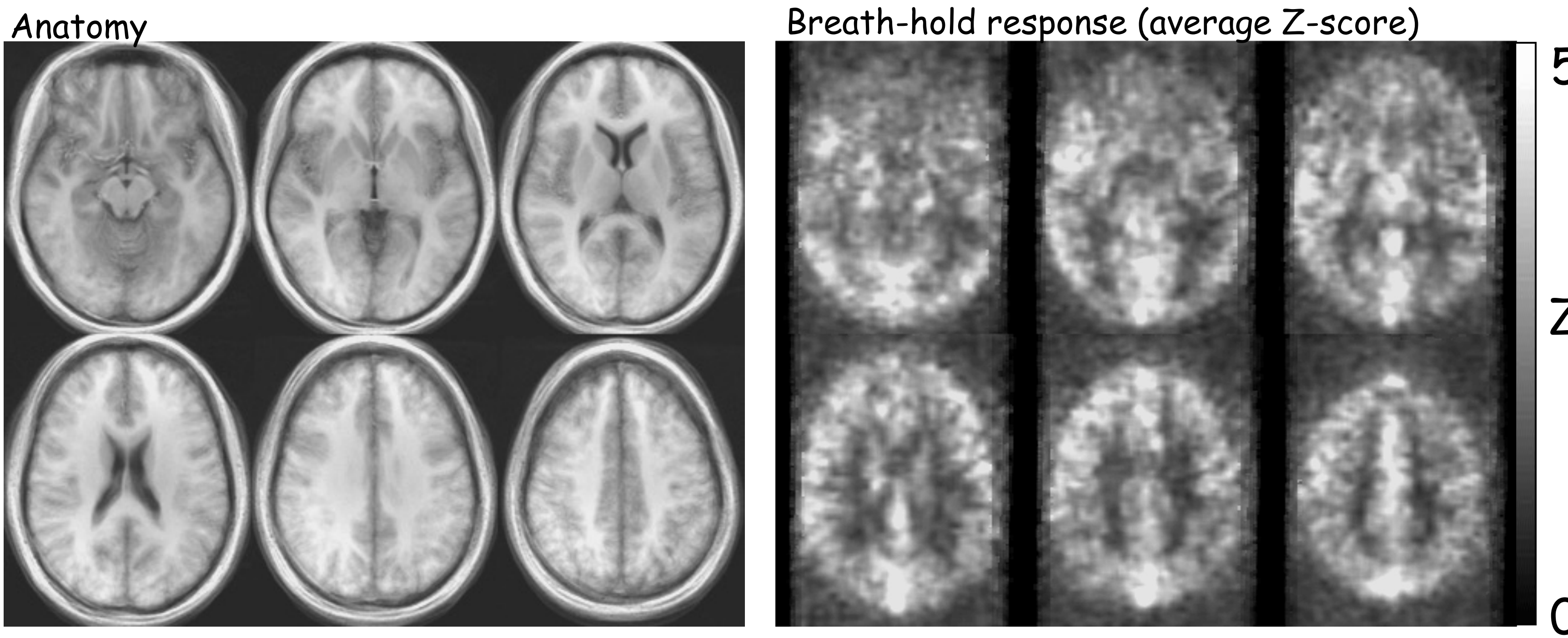
- Blood, brain and CSF pulsation
- Vasomotion
- Breathing cycle (B_0 shifts with lung expansion)
- Bulk motion
- Scanner instabilities
- Changes in blood CO_2 (changes in breathing)
- Spontaneous neuronal activity

Noise and Fluctuations

Breath-holding

Group Maps (N = 7)

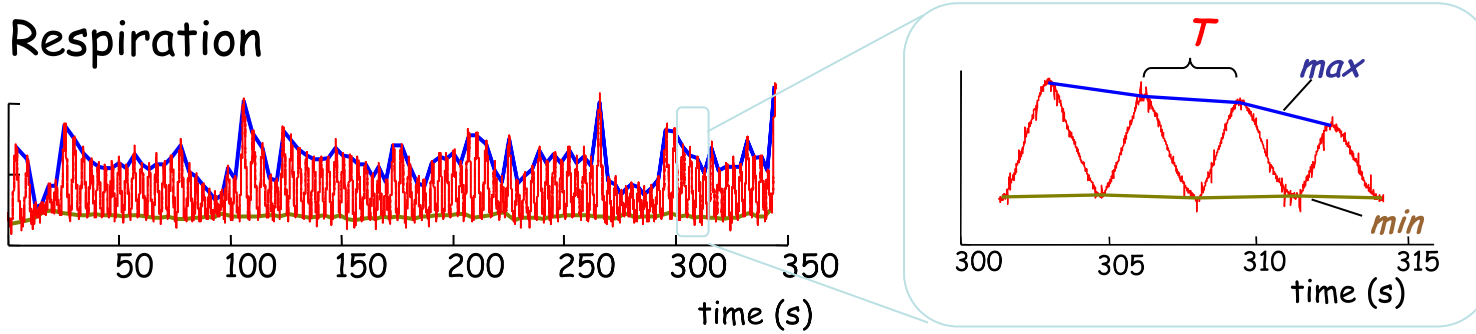




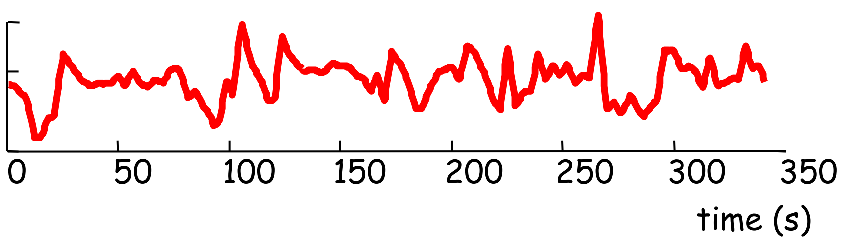
R.M. Birn, J. A. Diamond, M. A. Smith, P. A. Bandettini, *NeuroImage*, 31, 1536-1548

Estimating respiration volume changes

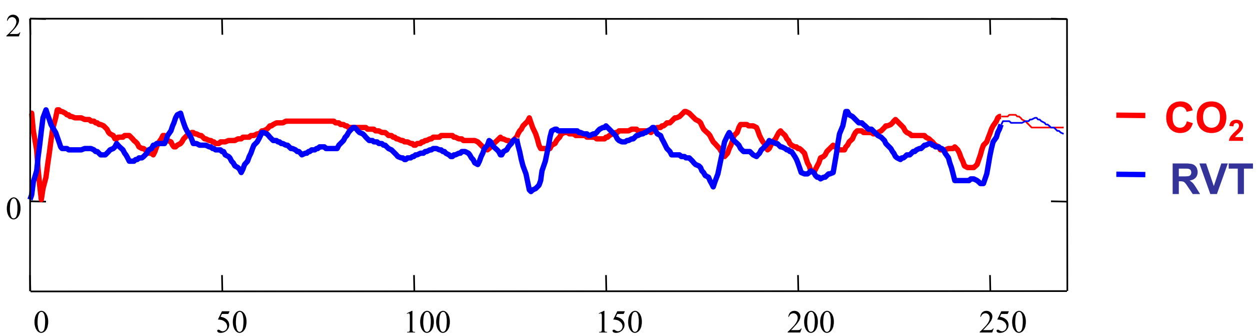
Respiration

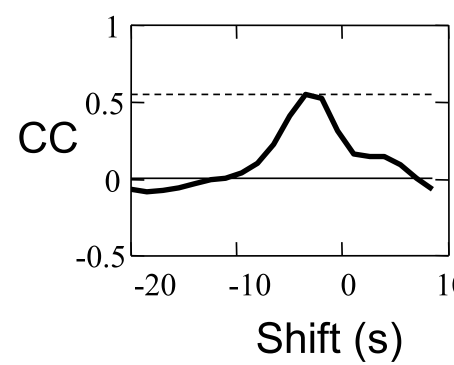


Respiration Volume / Time (RVT)



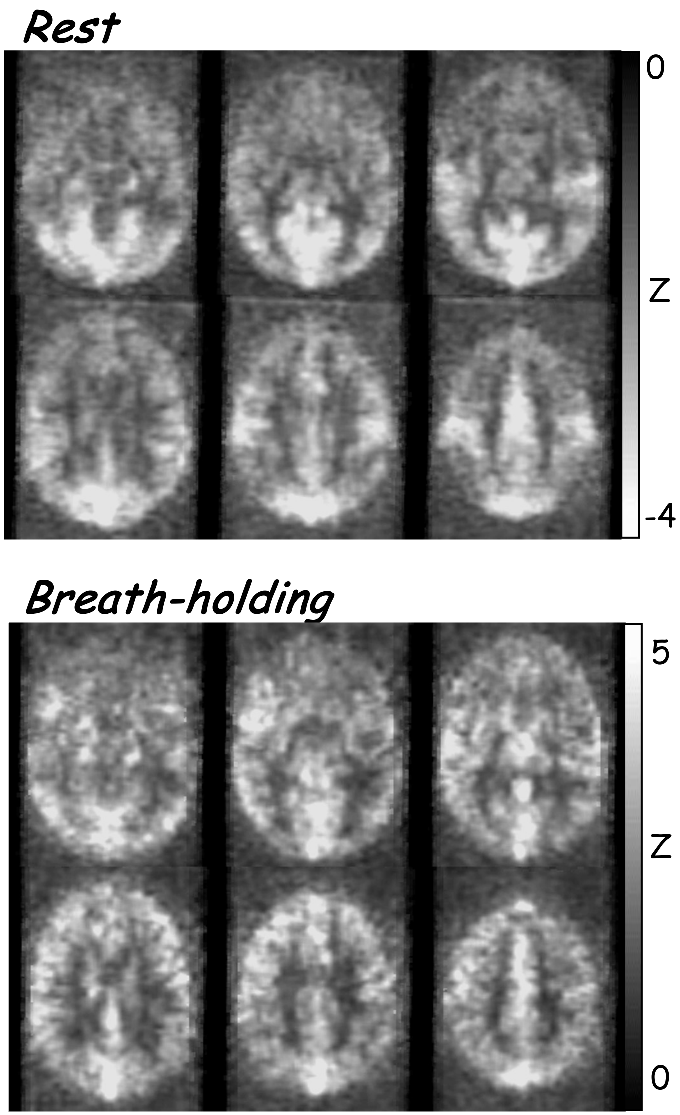
$$\mathrm{RVT} = \frac{\max - \min}{T}$$

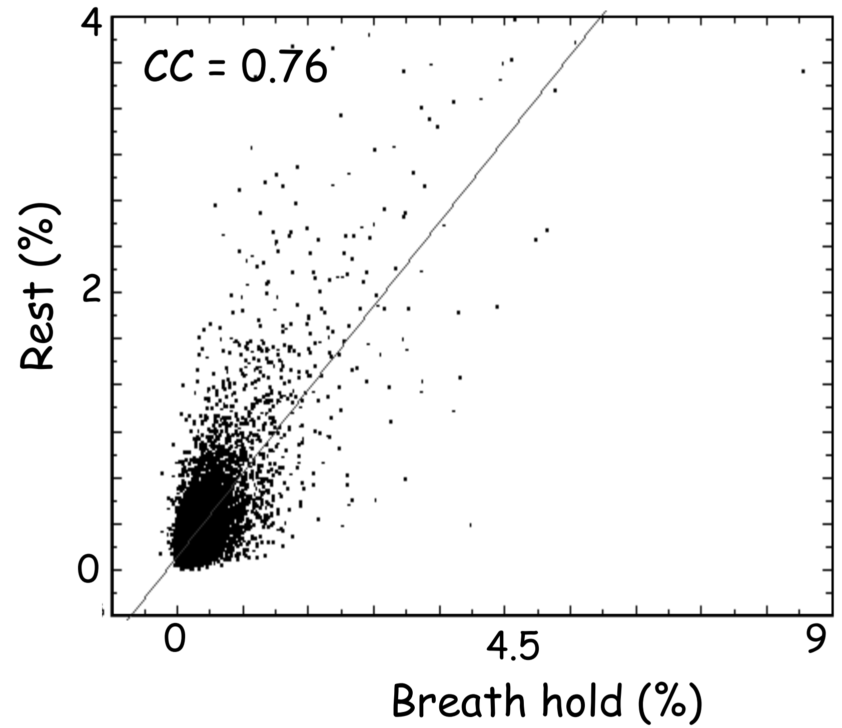




RVT precedes end tidal CO_2 by 5 sec.

Respiration induced signal changes



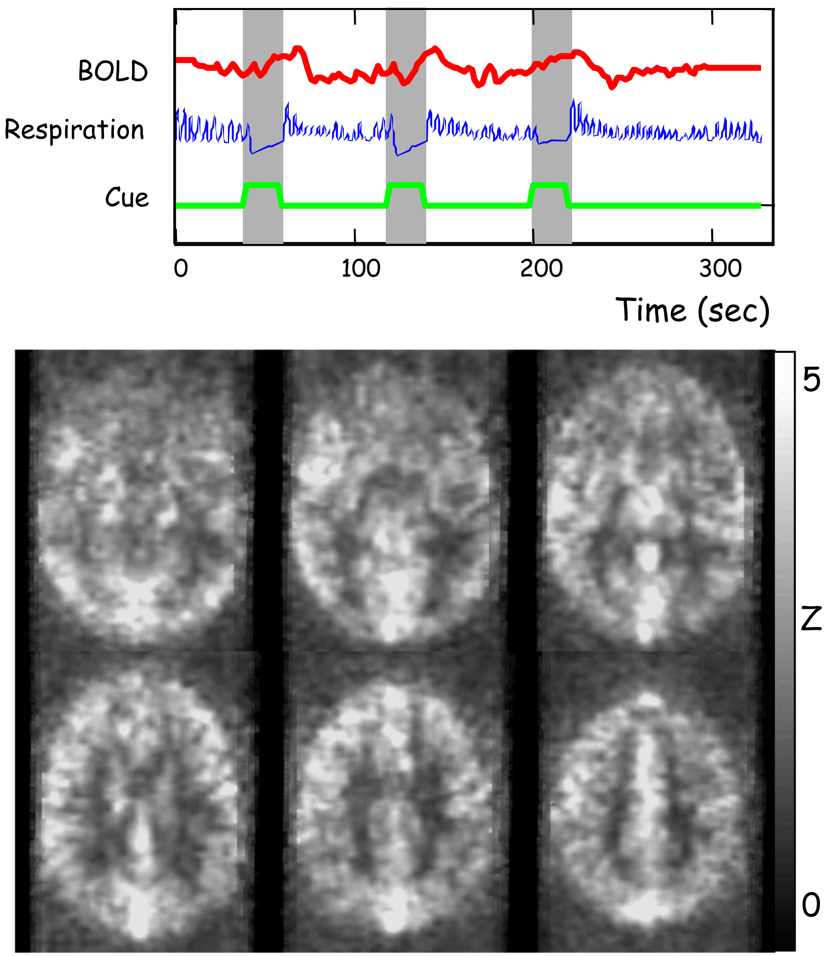


(N=7)

Noise and Fluctuations

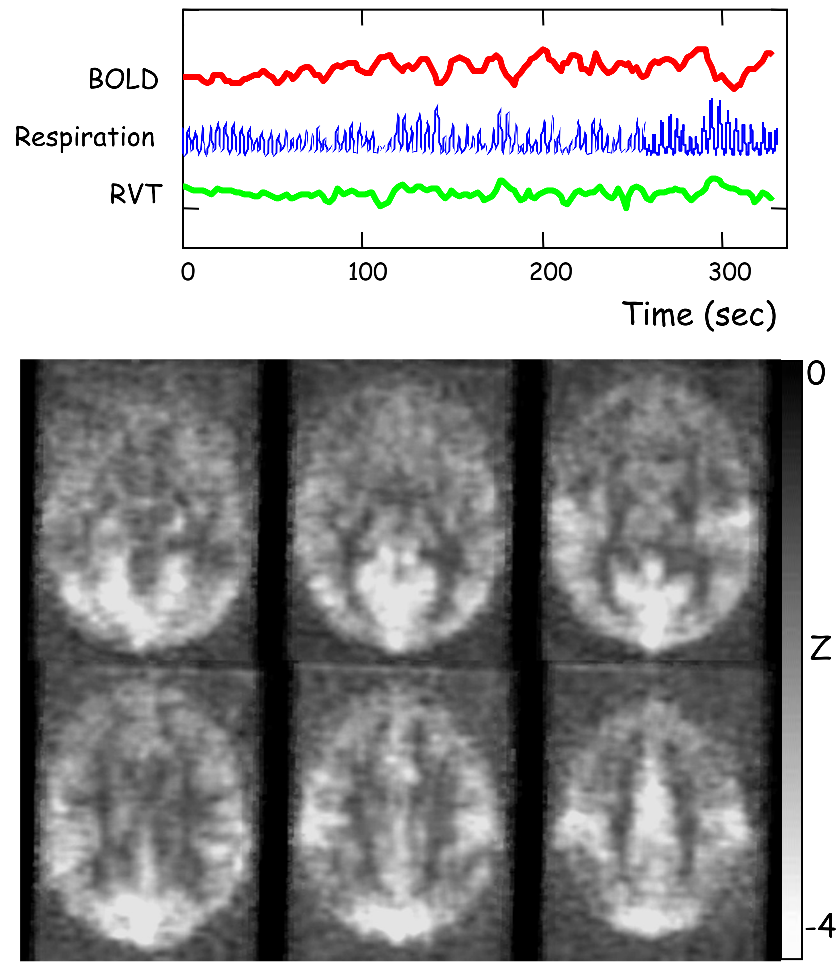
Respiration induced signal changes

Breath-holding



(N=7)

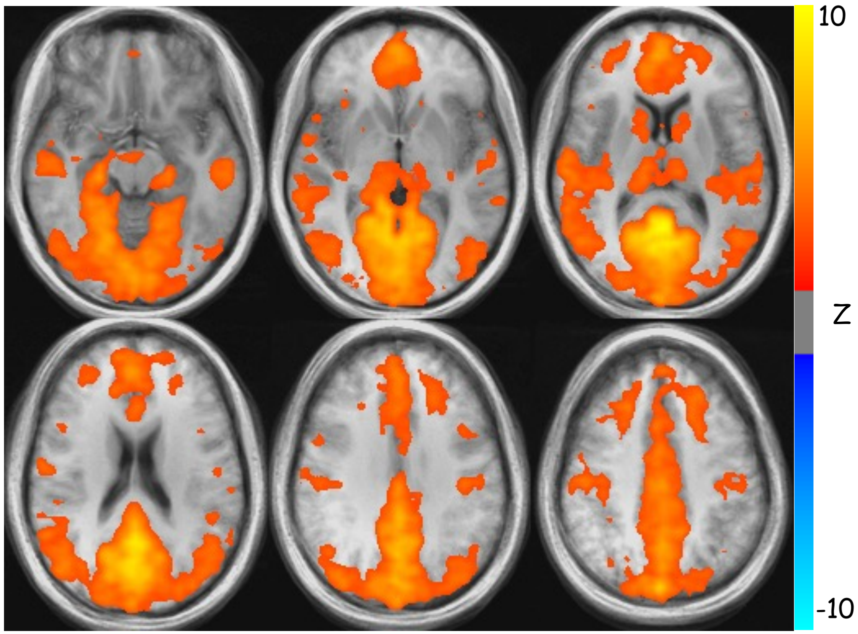
Rest



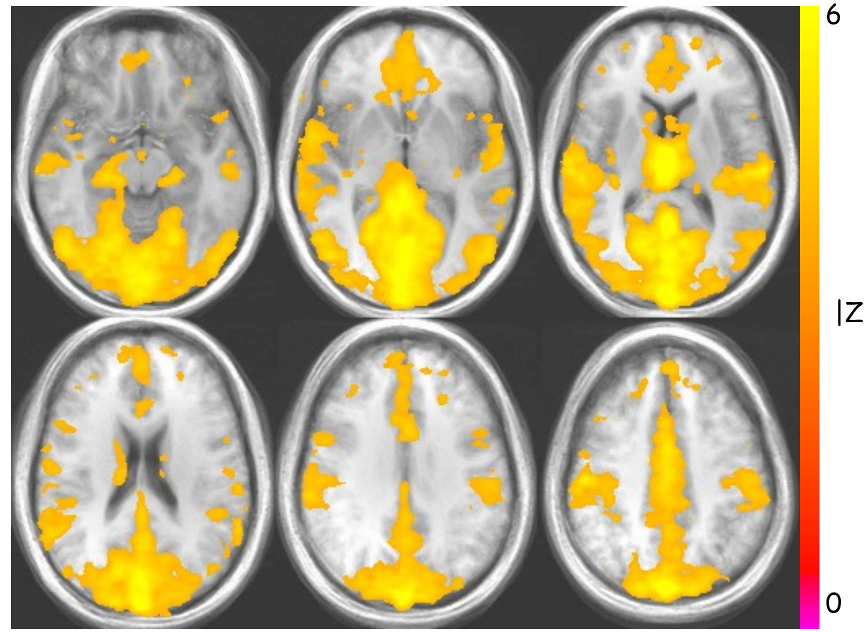
R.M. Birn, J. A. Diamond, M. A. Smith, P. A. Bandettini, *NeuroImage*, 31, 1536-1548 (2006)

RVT Correlation Maps & Functional Connectivity Maps

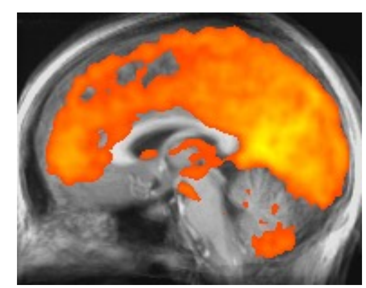
Resting state correlation with signal from posterior cingulate



Resting state correlation with RVT signal

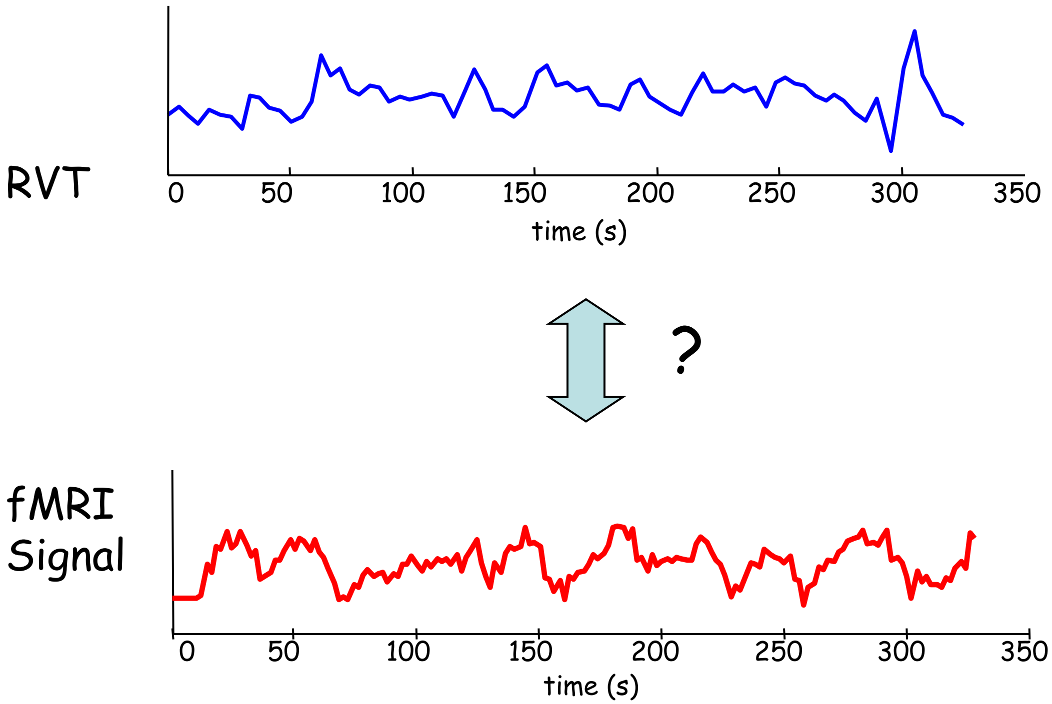


Group (n=10)



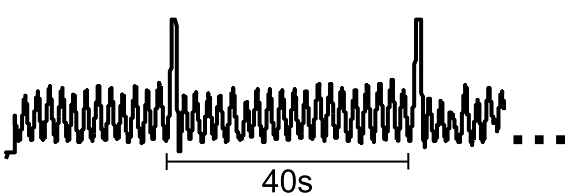
Respiration Changes vs. BOLD

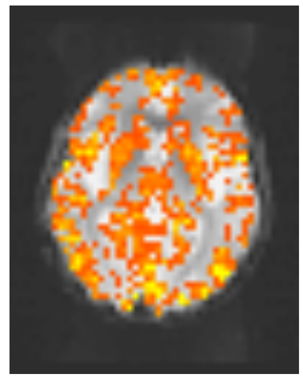
How are the BOLD changes related to respiration variations?

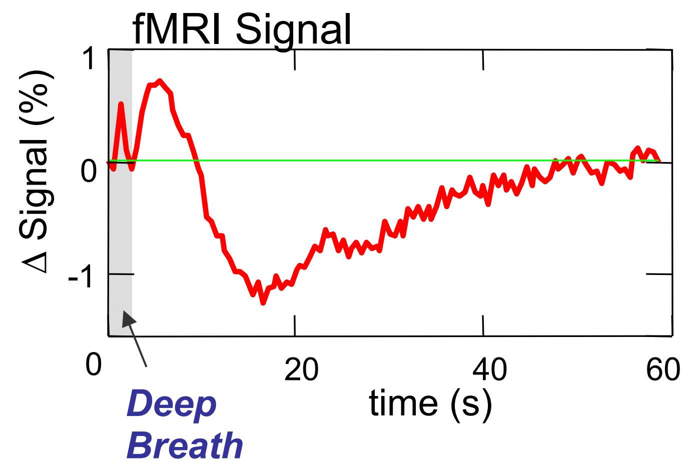


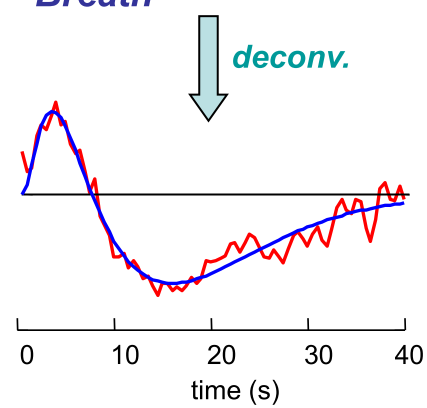
fMRI response to a single Deep Breath

Respiration







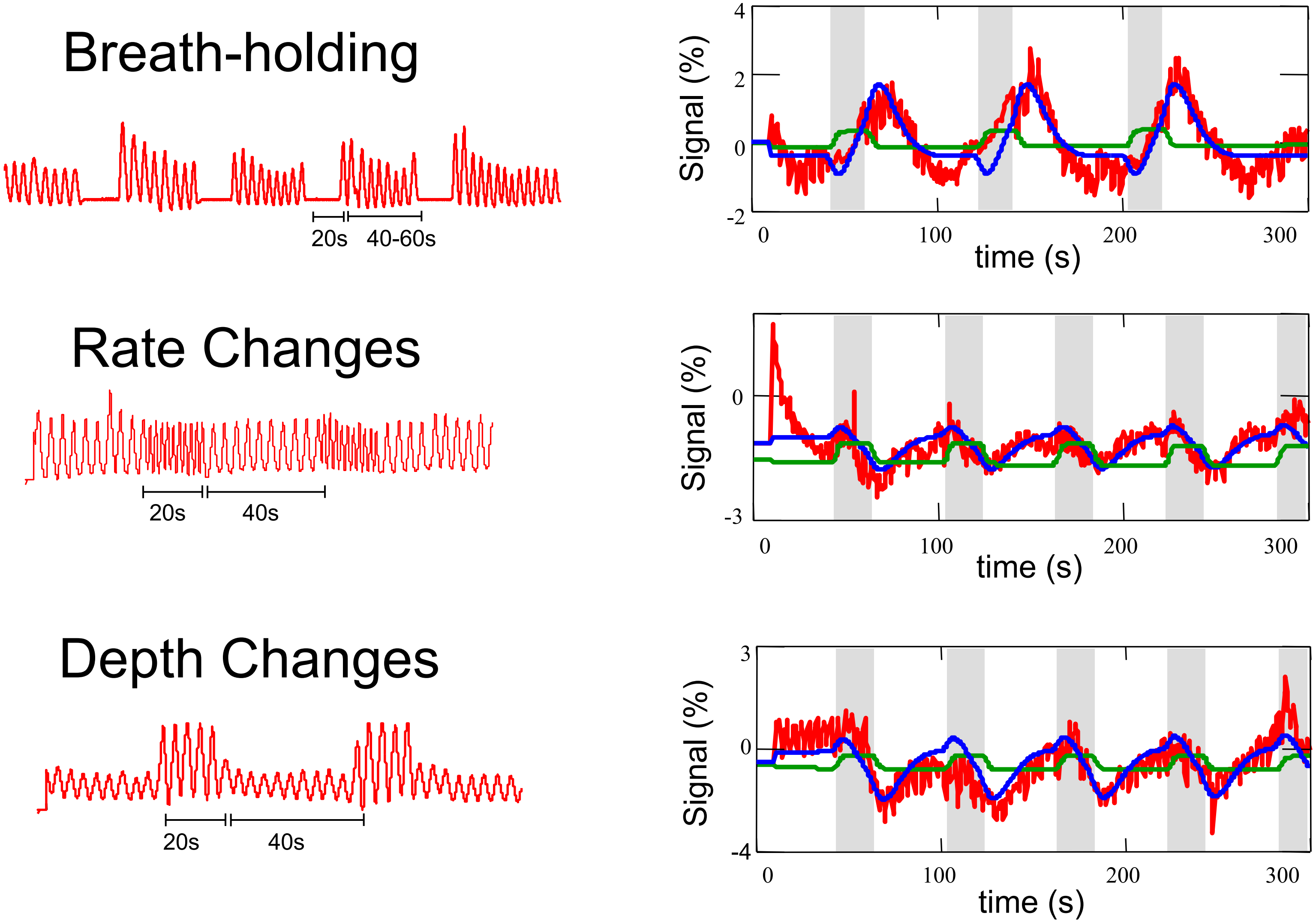


Respiration Response Function (**RRF**)

$$\mathrm{RRF}(t) = 0.6\, t^{2.1} e^{\frac{t}{1.6}} - 0.0023\, t^{3.54} e^{\frac{t}{4.25}}$$

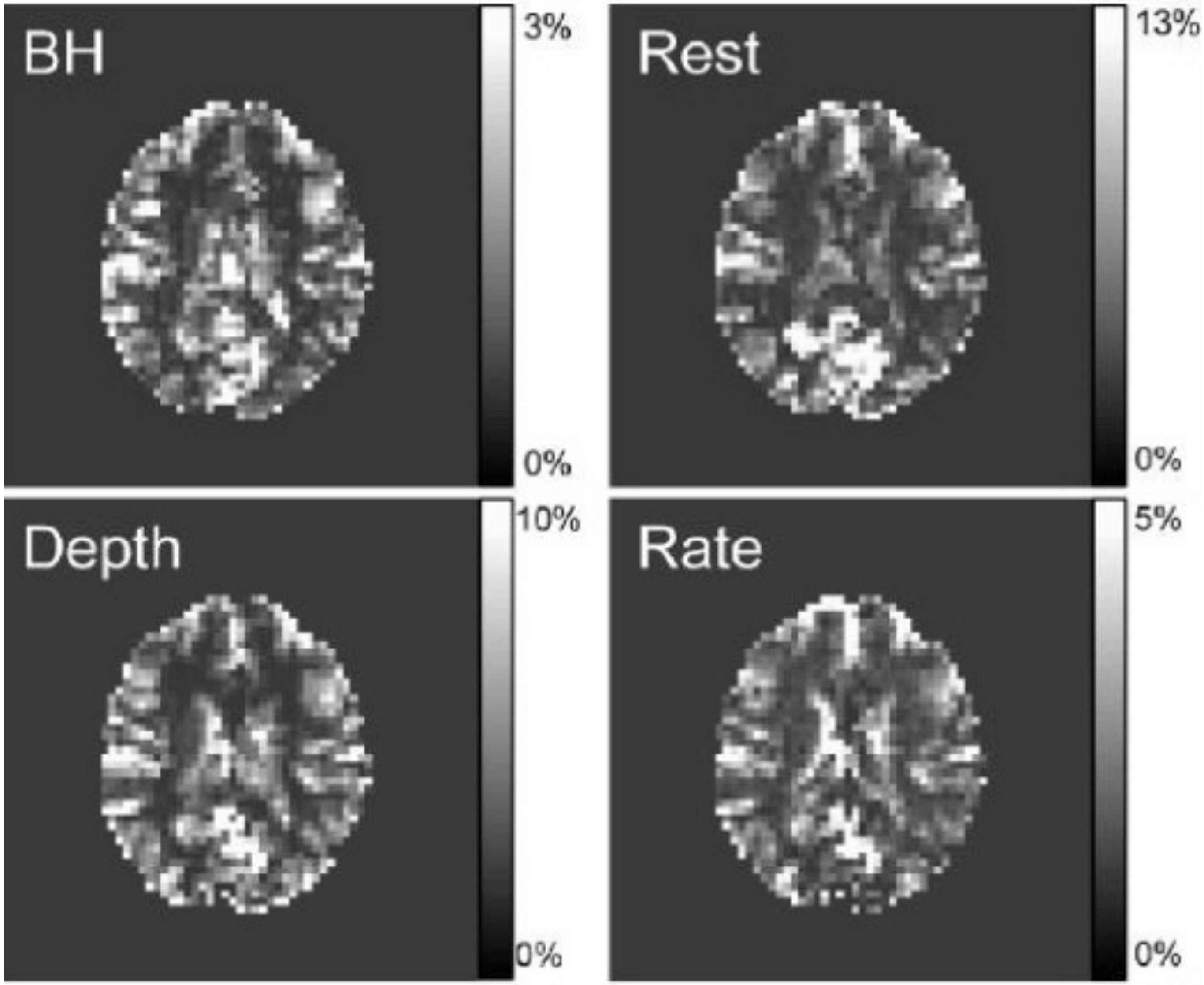
R.M. Birn, M. A. Smith, T. B. Jones, P. A. Bandettini, *NeuroImage*, 40, 644-654 (2008)

Respiration response function predicts BOLD signal associated with breathing changes better than activation response function.



R.M. Birn, M. A. Smith, T. B. Jones, P. A. Bandettini, *NeuroImage*, 40, 644-654 (2008)

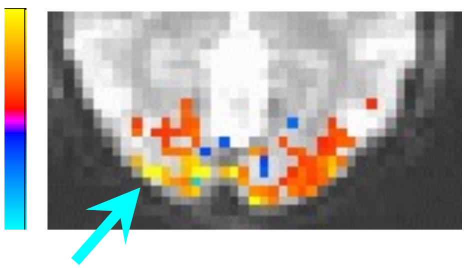
Noise and Fluctuations



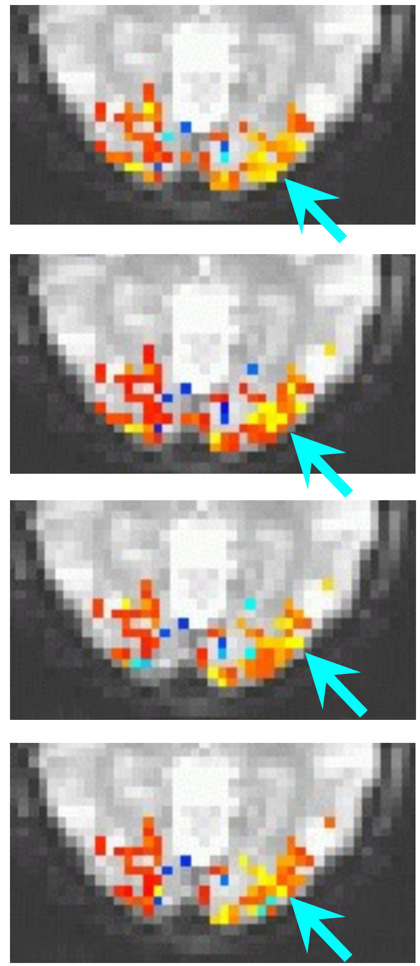
R.M. Birn, M. A. Smith, T. B. Jones, P. A. Bandettini, *NeuroImage*, 40, 644-654 (2008)

BOLD magnitude calibration

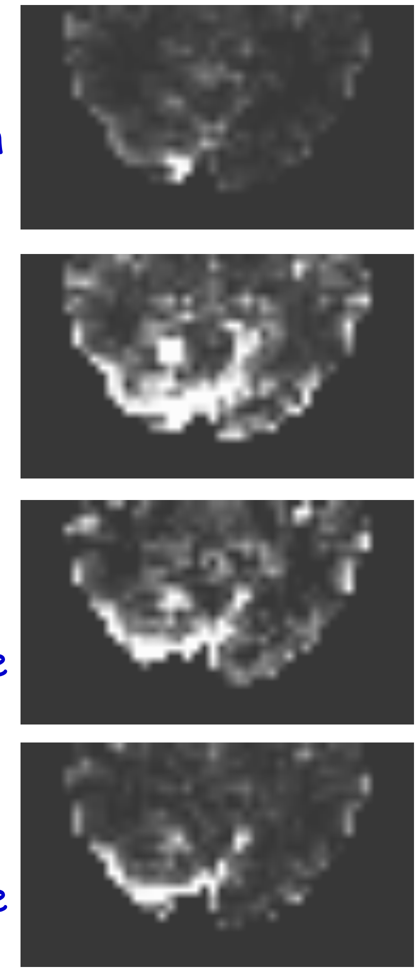
Before Calibration



After Calibration



Respiration-induced ΔS



Breath Hold

Rest

Depth Change

Rate Change

$$\mathrm{BOLD_{calib}} = \frac{\%\Delta S\ (\mathrm{BOLD})}{\%\Delta S\ (\mathrm{Resp})}$$

R.M. Birn, M. A. Smith, T. B. Jones, P. A. Bandettini, *NeuroImage*, 40, 644-654 (2008)

The Absolute Beginners Guide to fMRI

1. History

2. Functional Contrast

3. Interpretation Issues