Beyond Spatial, Temporal, and Interpretative Limits of fMRI

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Section on Functional Imaging Methods

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&

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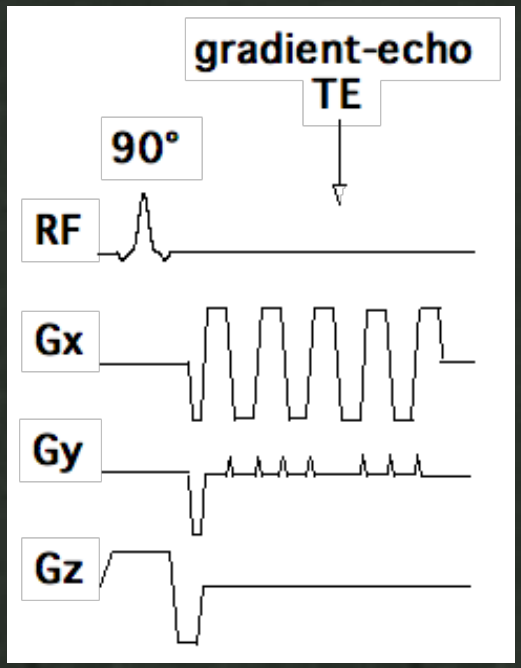
What really limits fMRI ?

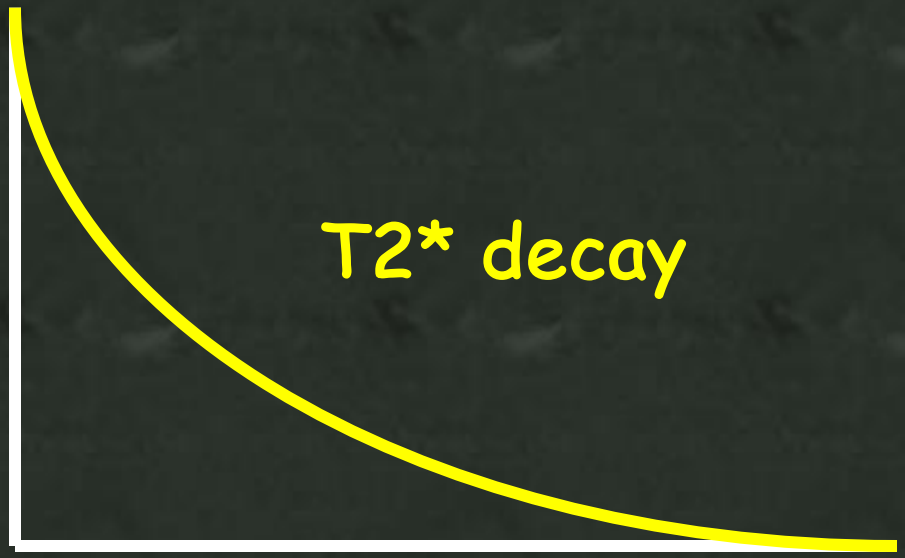
- Imaging Methodology
- Hemodynamic Response Function

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

Imaging Methodology

Single Shot Echo Planar Imaging (EPI)





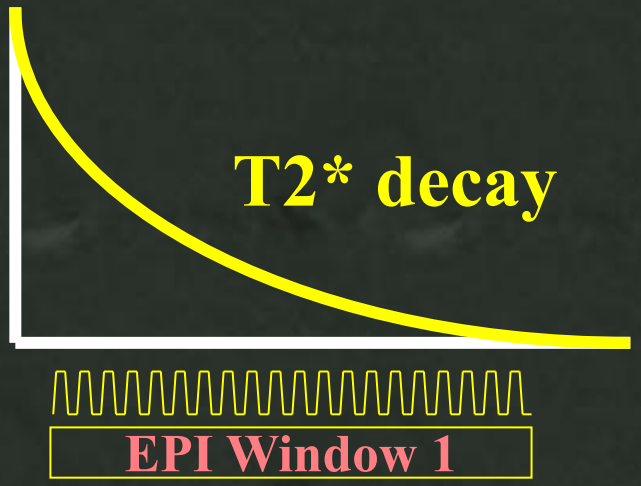
EPI Readout Window

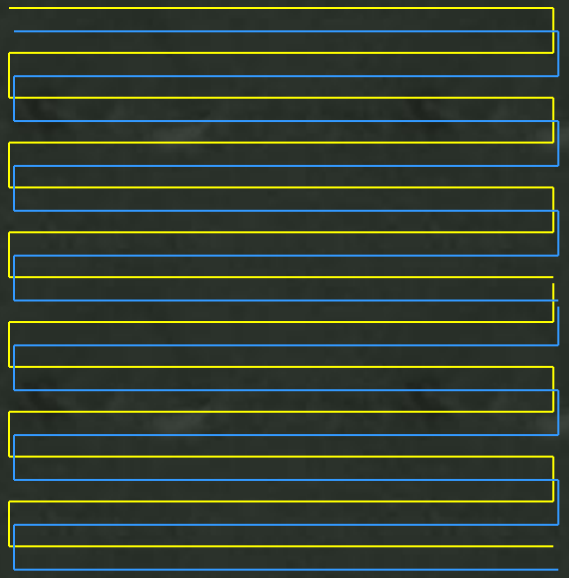
≈ 20 to 40 ms

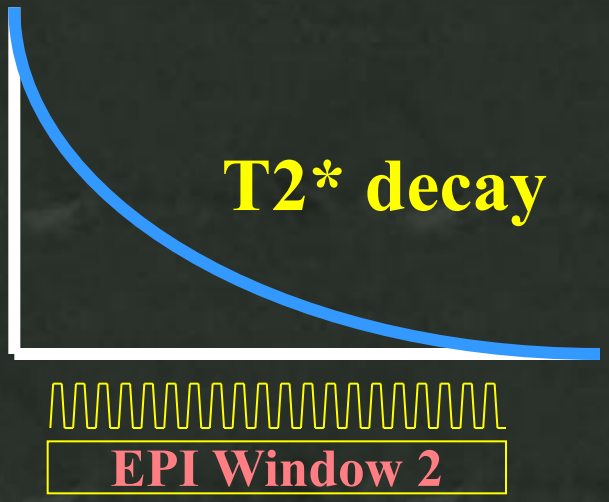
How do we improve things?

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

Multi-shot imaging



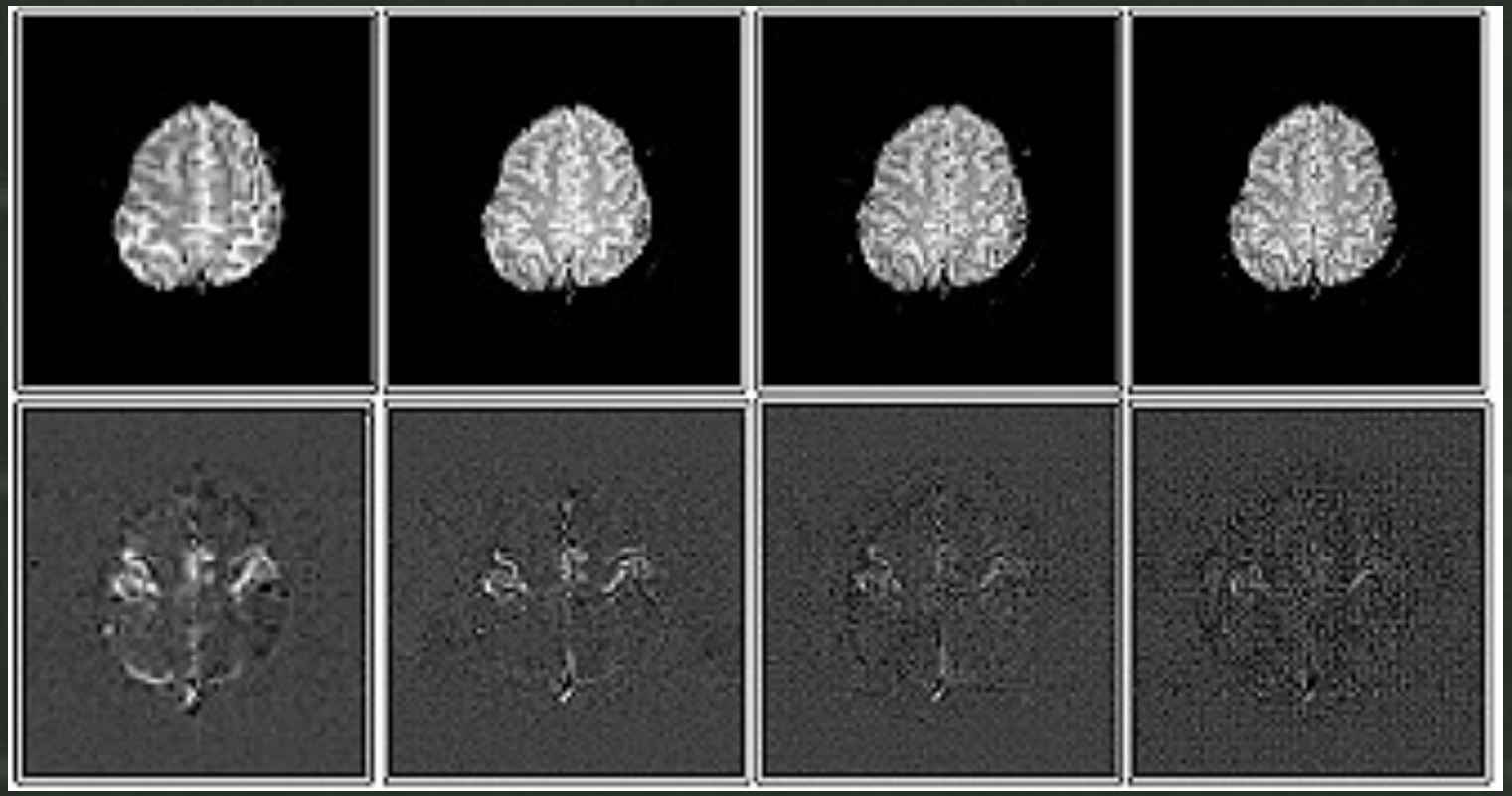




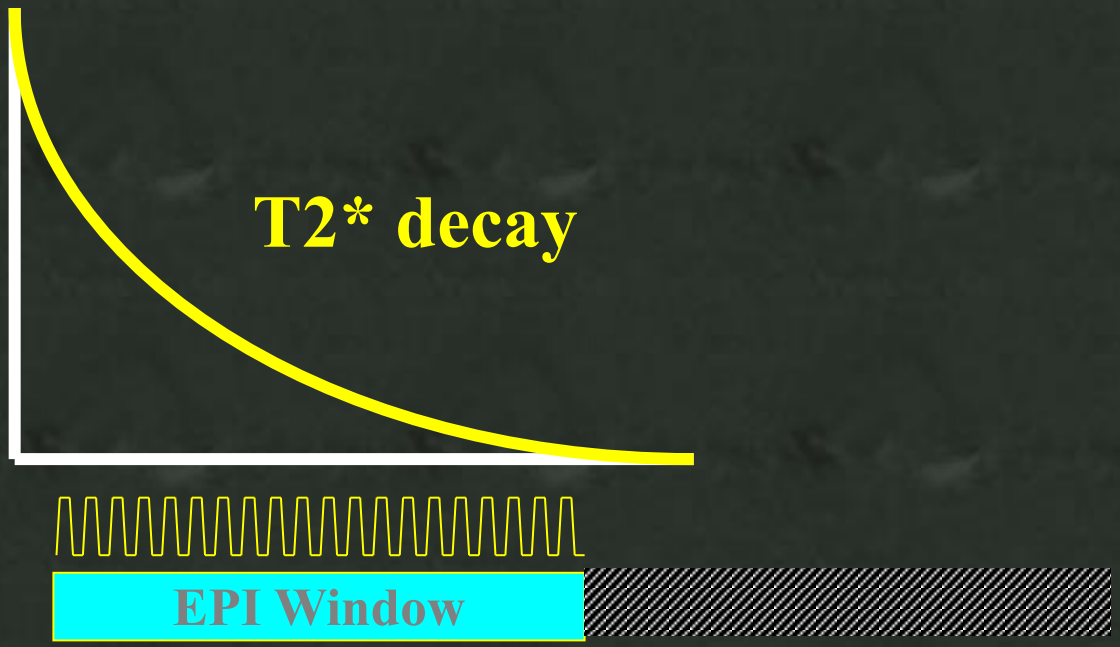
- Requires navigator pulses
- Temporal resolution and stability tradeoff

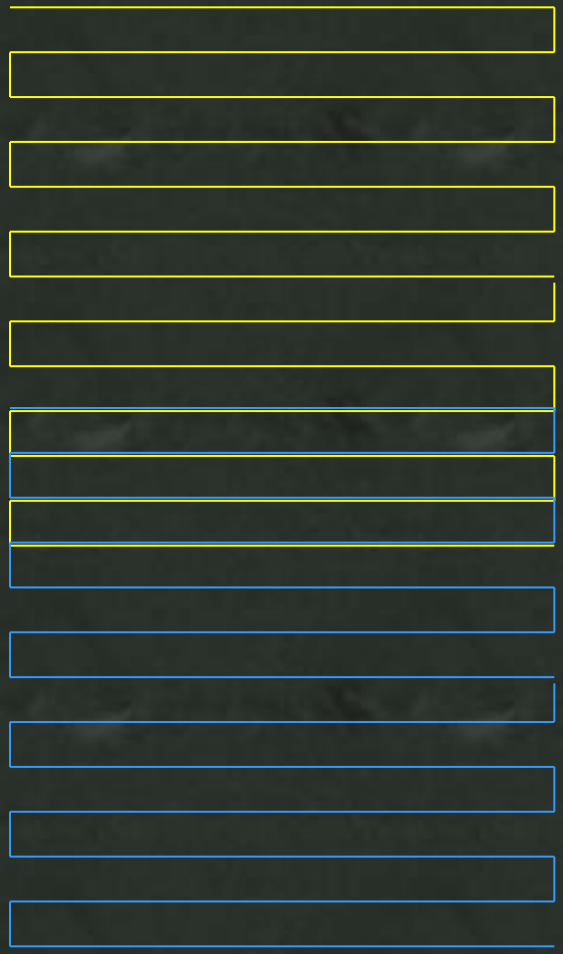
Multi-shot imaging

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



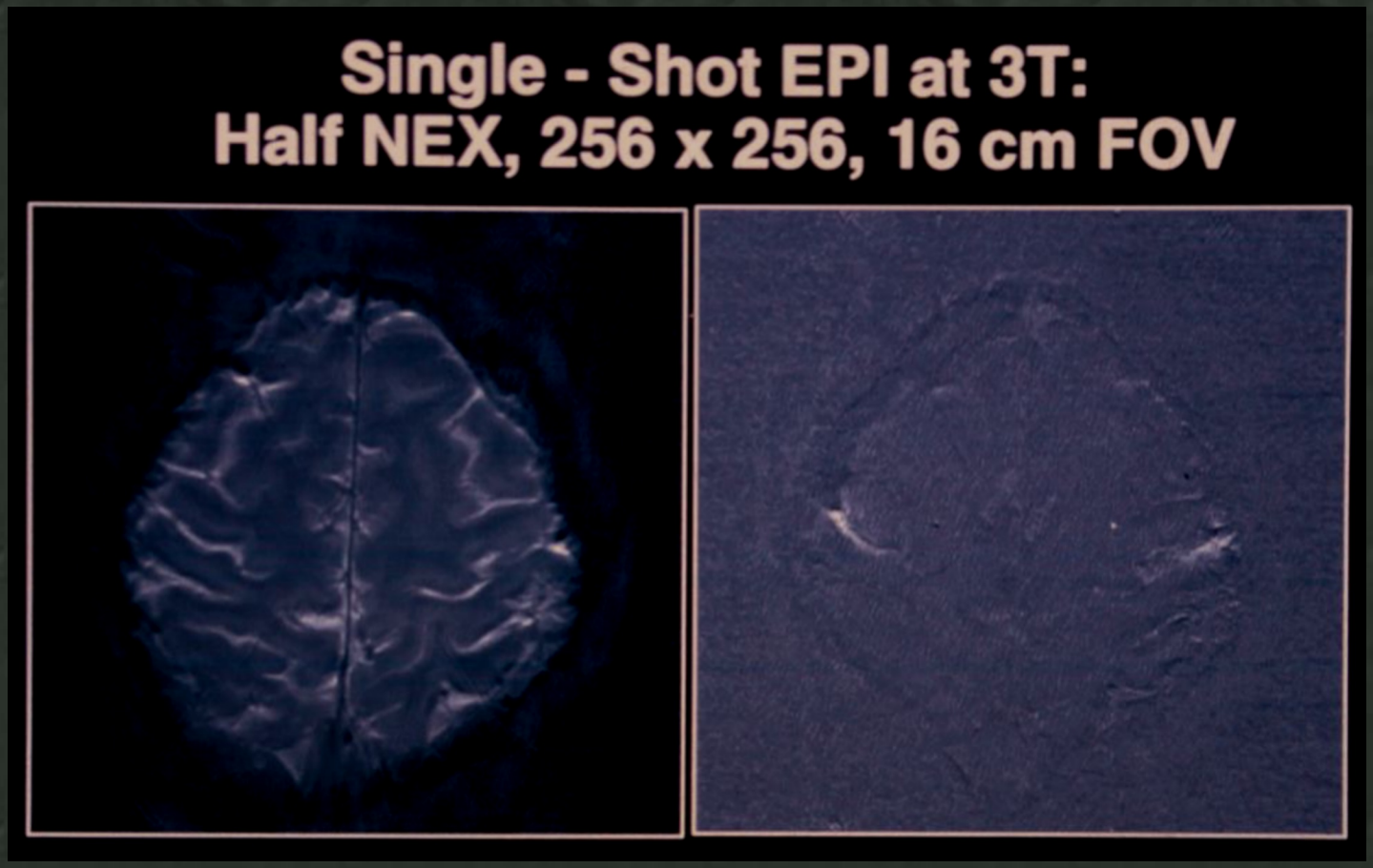
Partial k-space imaging





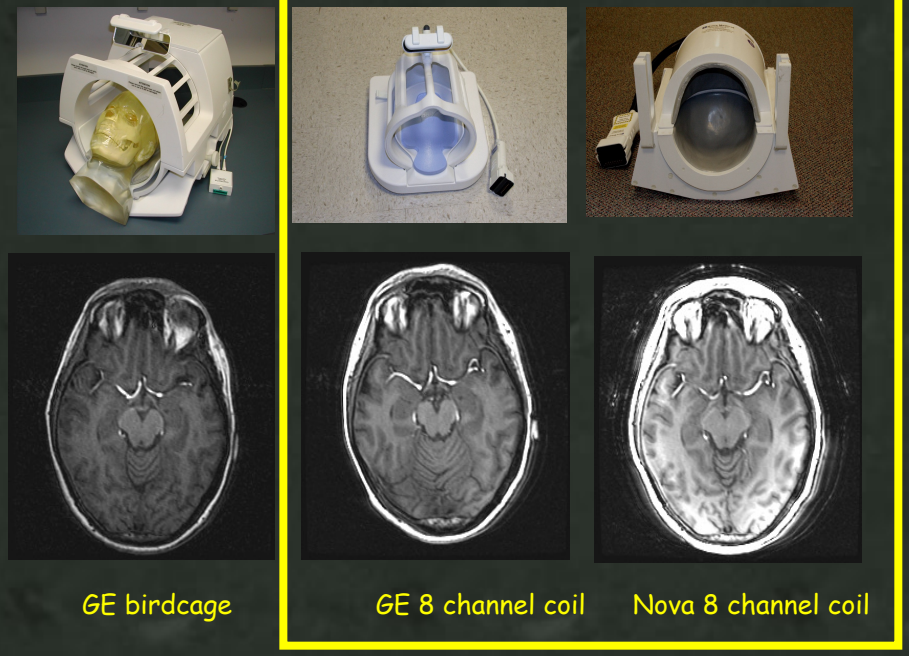
- More warping
- Lower image SNR
- Improvement in one dimension

Partial k-space imaging

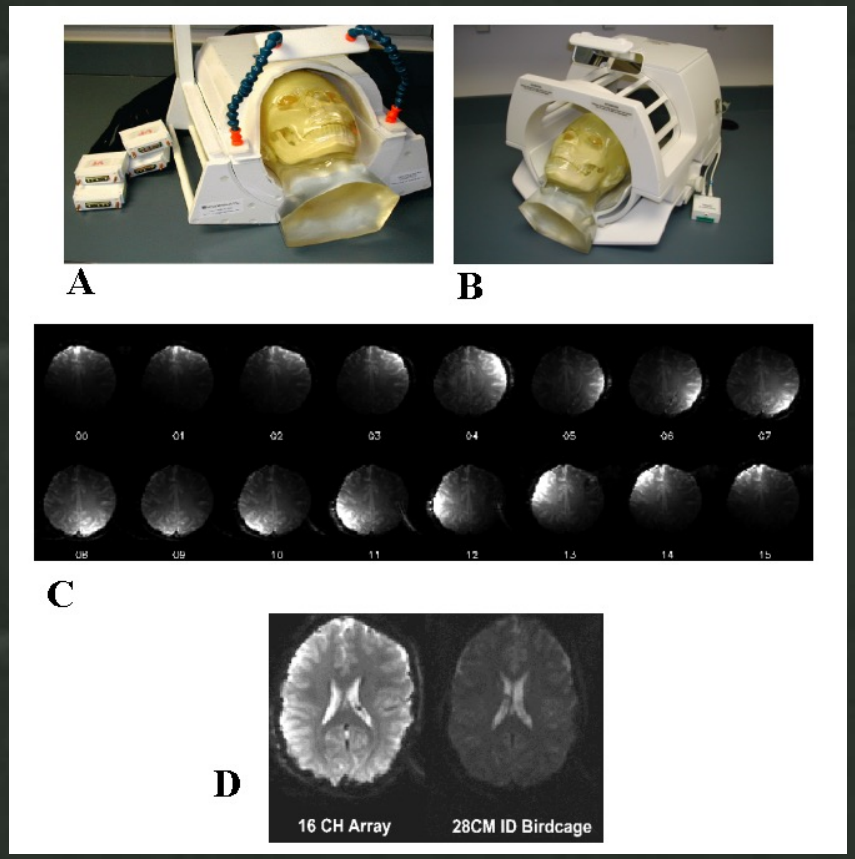


RF coils

8 channel parallel receiver coil

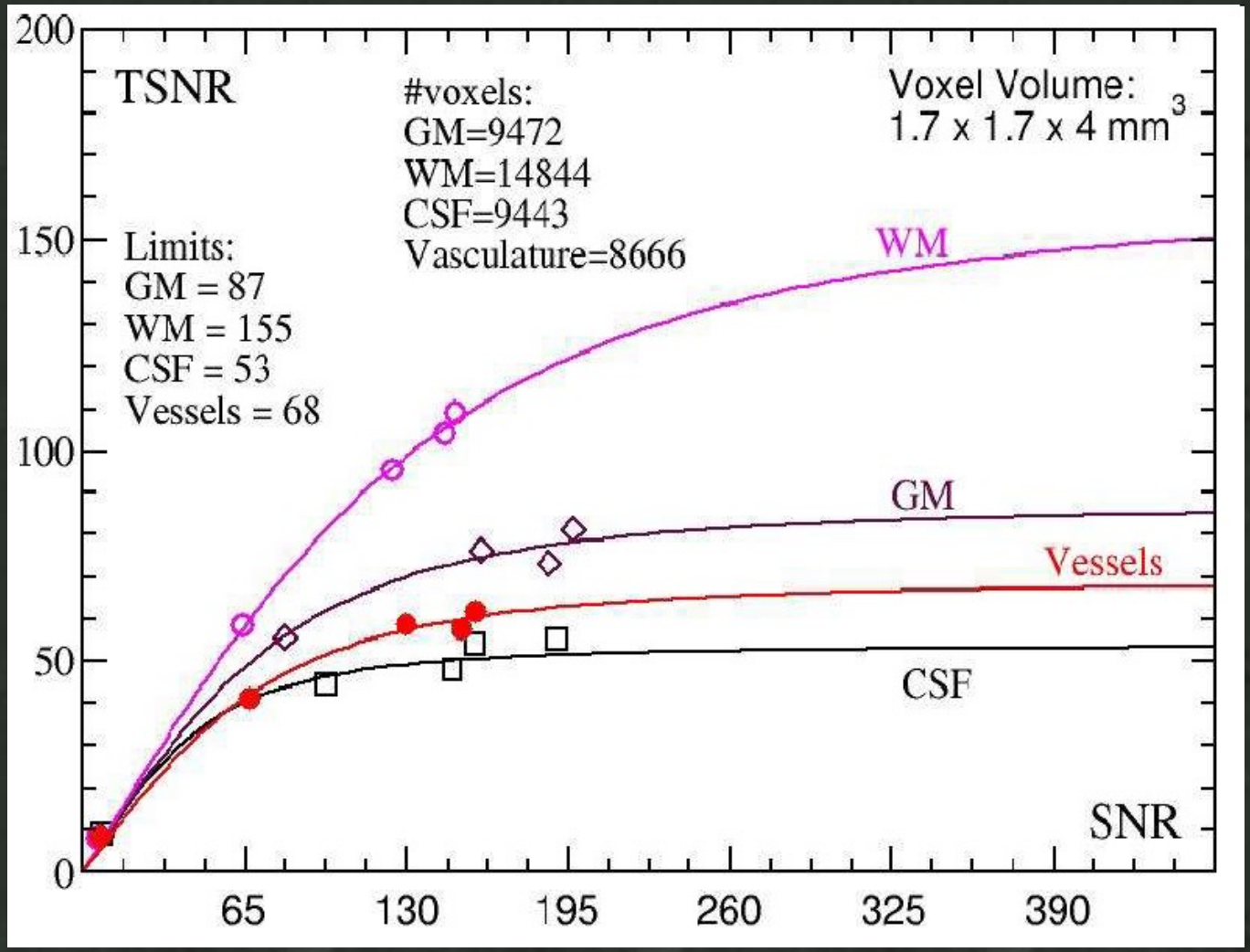


16 channel parallel receiver coil

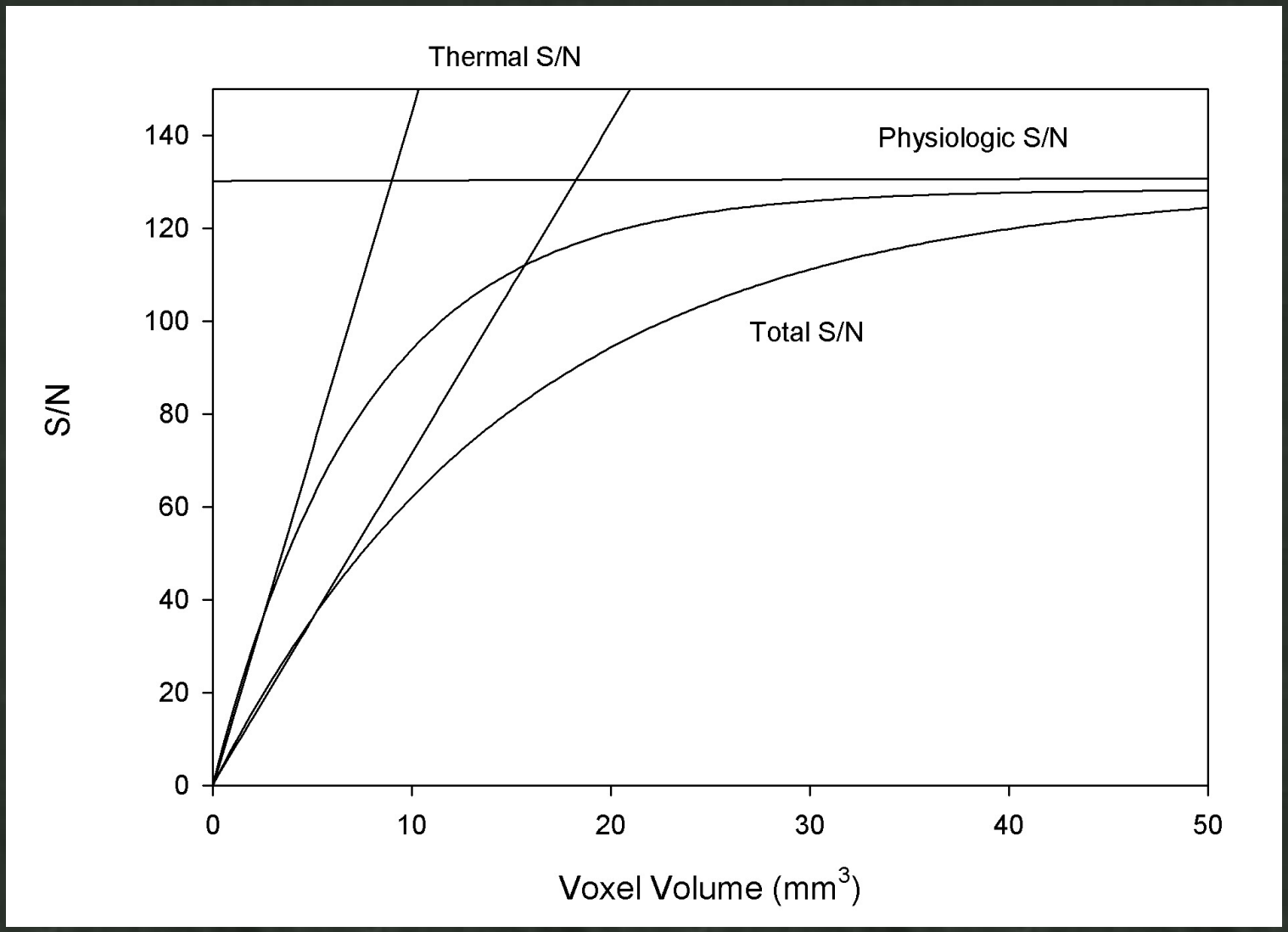


J. Bodurka, et al, MRM 51 (2004) 165-171.

Gain in SNR has diminishing returns

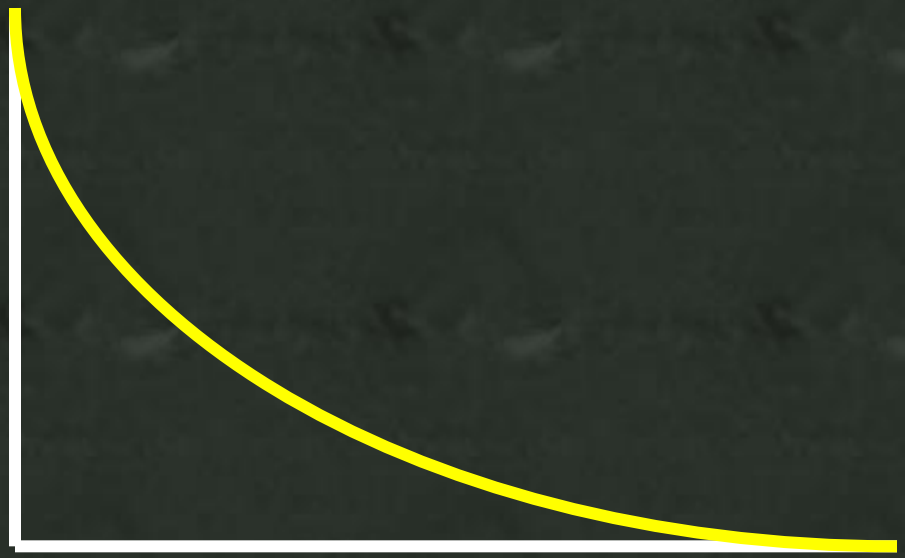


Simulated gains in TNSR with doubling sensitivity



Imaging Methodology

SENSE Imaging



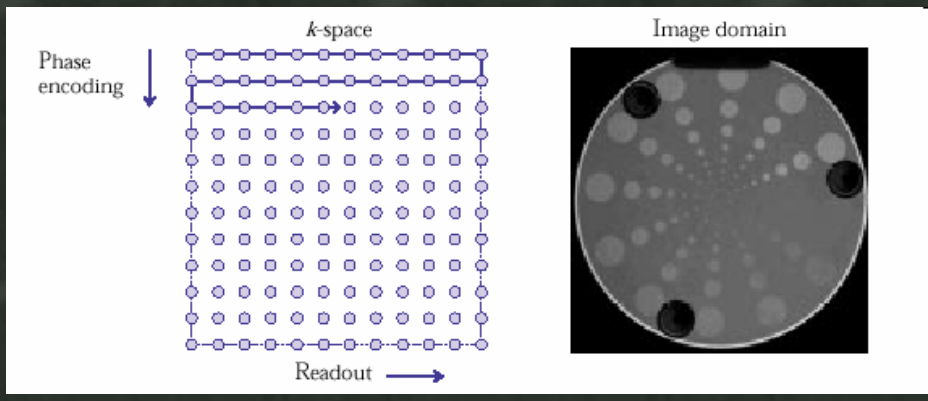
≈ 5 to 30 ms

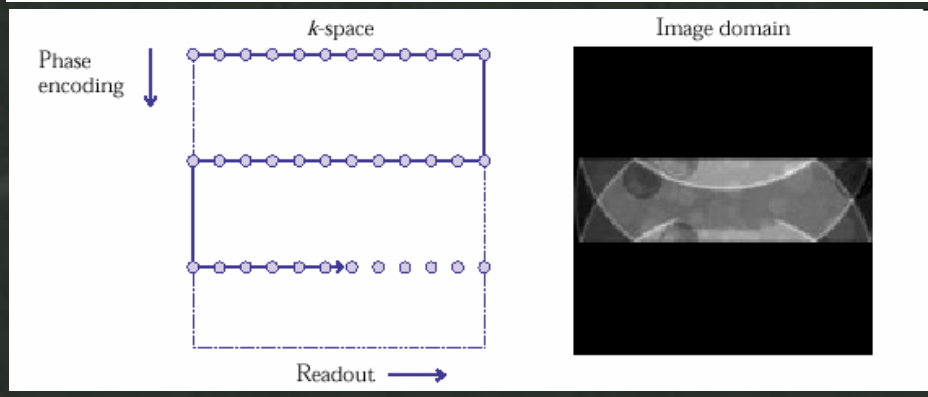
- Gain in resolution per window width

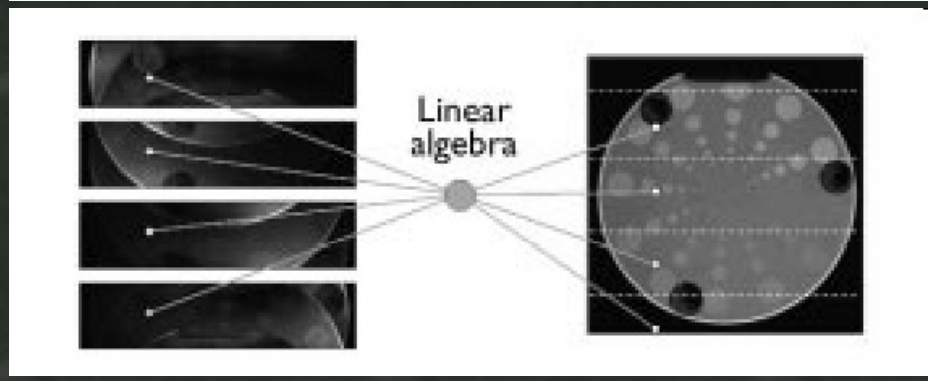
If shorter readout window is used:

- Small gain in #slices per TR
- Reduced distortions

- Reduced Image SNR







Pruessmann, et al.

SENSE Imaging

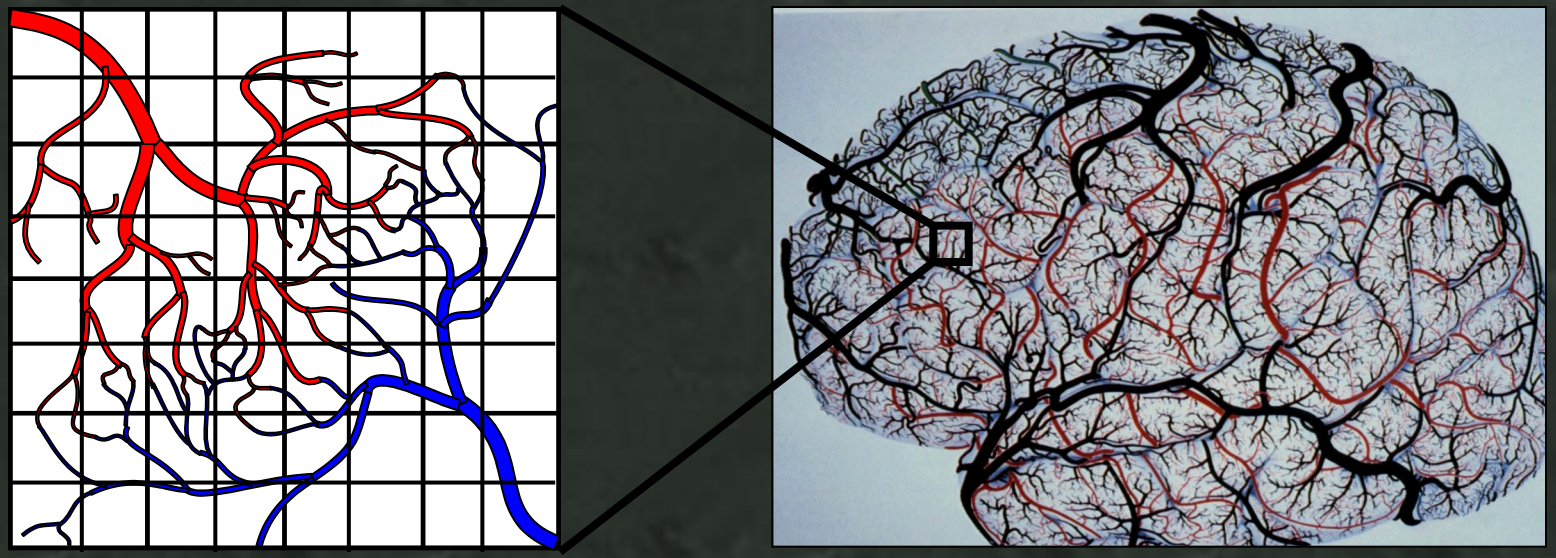
3T single-shot SENSE EPI using 16 channels: 1.25x1.25x2mm

Bodurka et al.

The Hemodynamic Response Function

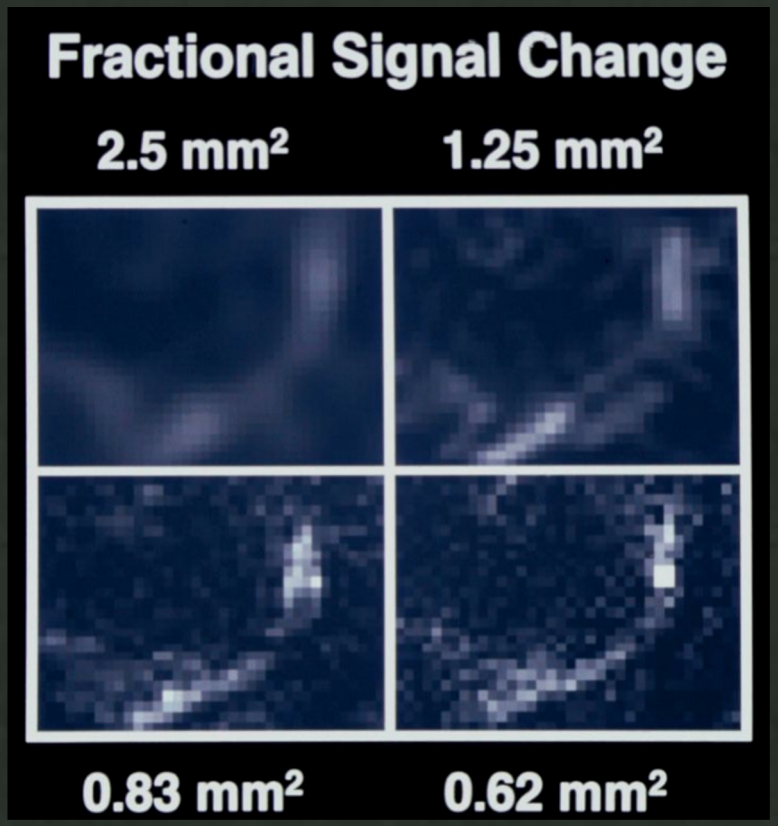
Neuronal Activation → ? → Hemodynamics → ? → Measured Signal

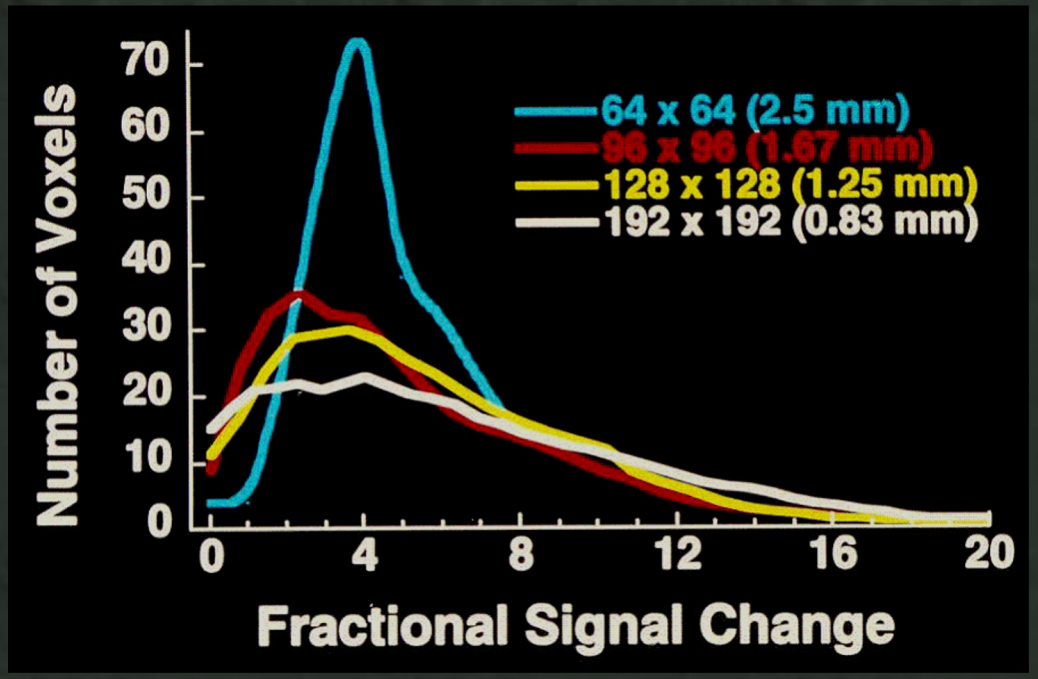
Noise → ? → Measured Signal



The HRF

The effect of increasing spatial resolution

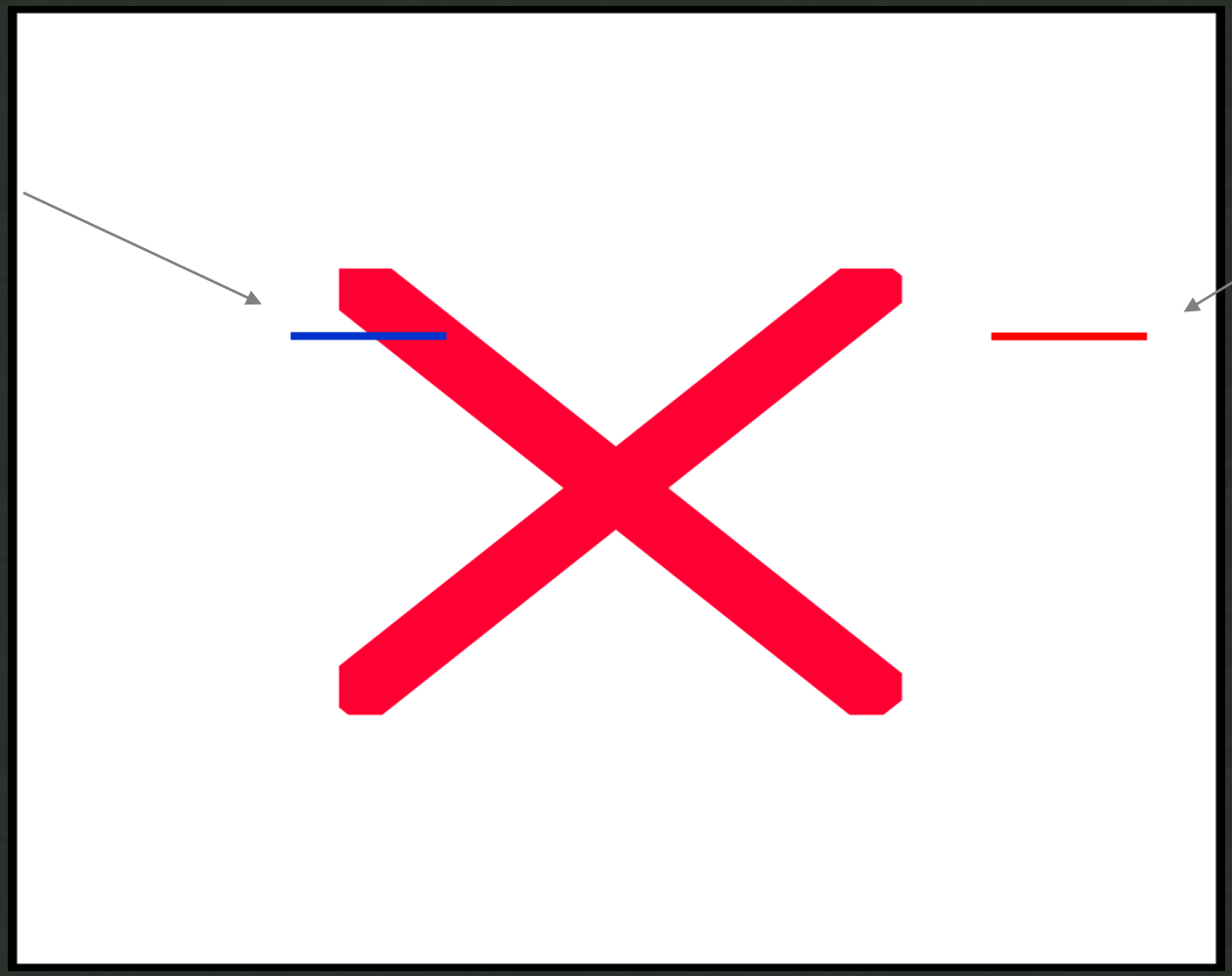




Large vessel effects tend to be amplified…

Hemodynamic Specificity

Arterial inflow
(BOLD TR < 500 ms)



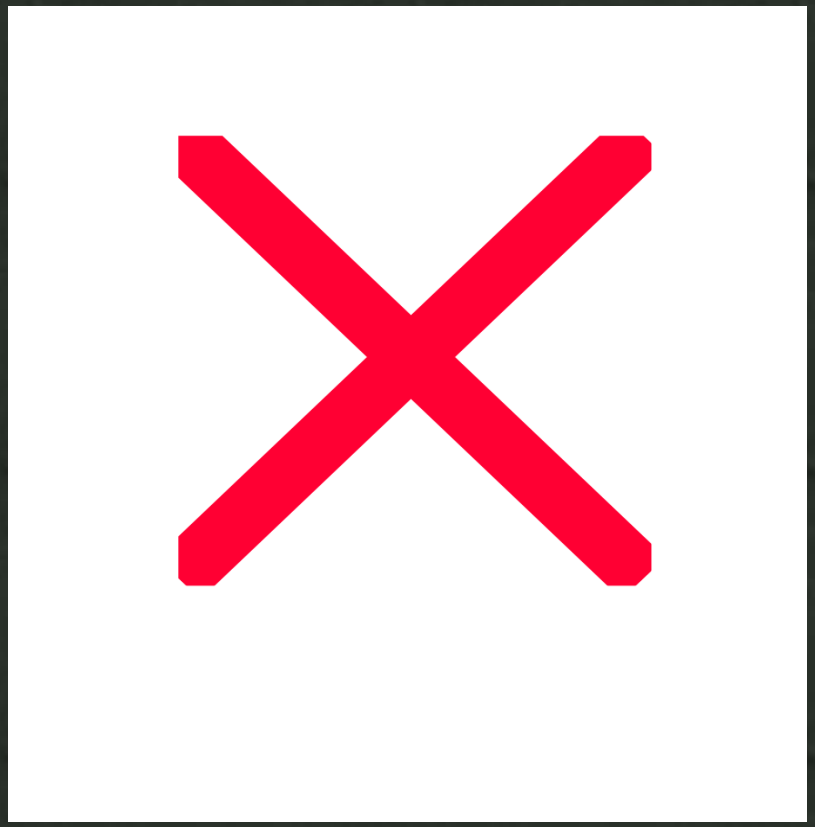
Venous inflow
(Perf. No VN)

Some pulse sequence strategies..

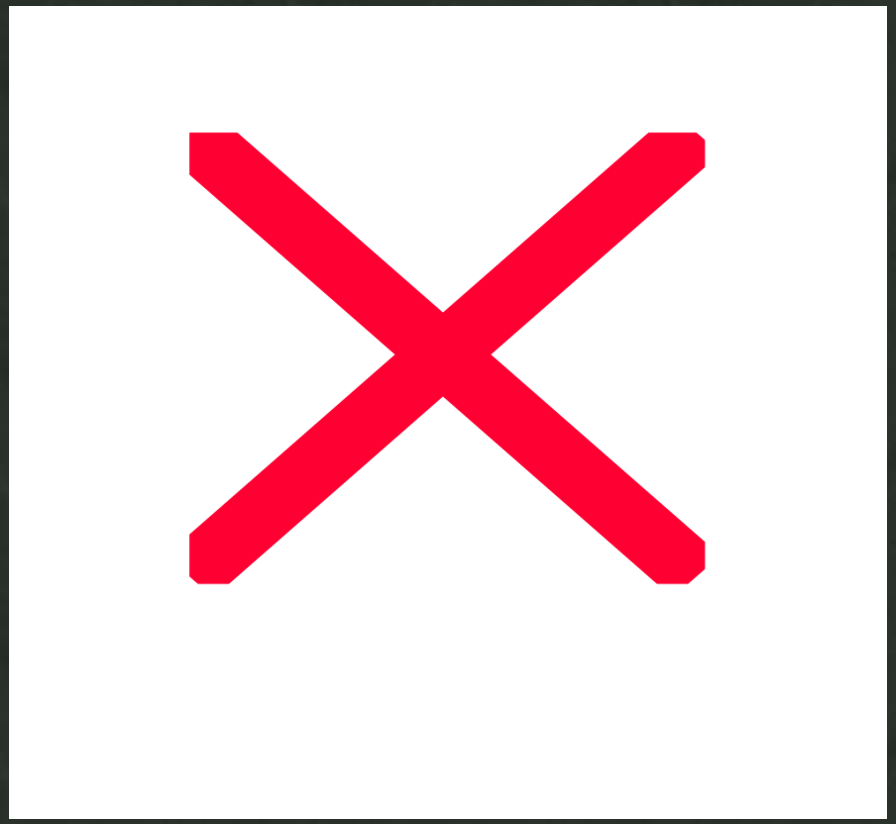
The HRF

Field strength dependence of intravascular effects

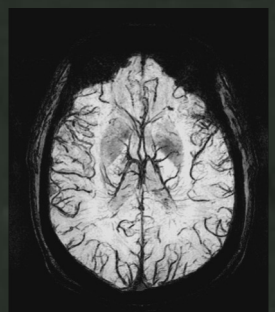
Spin-echo, $\%HbO_2 = 60$



Gradient-echo, $\%HbO_2 = 60$

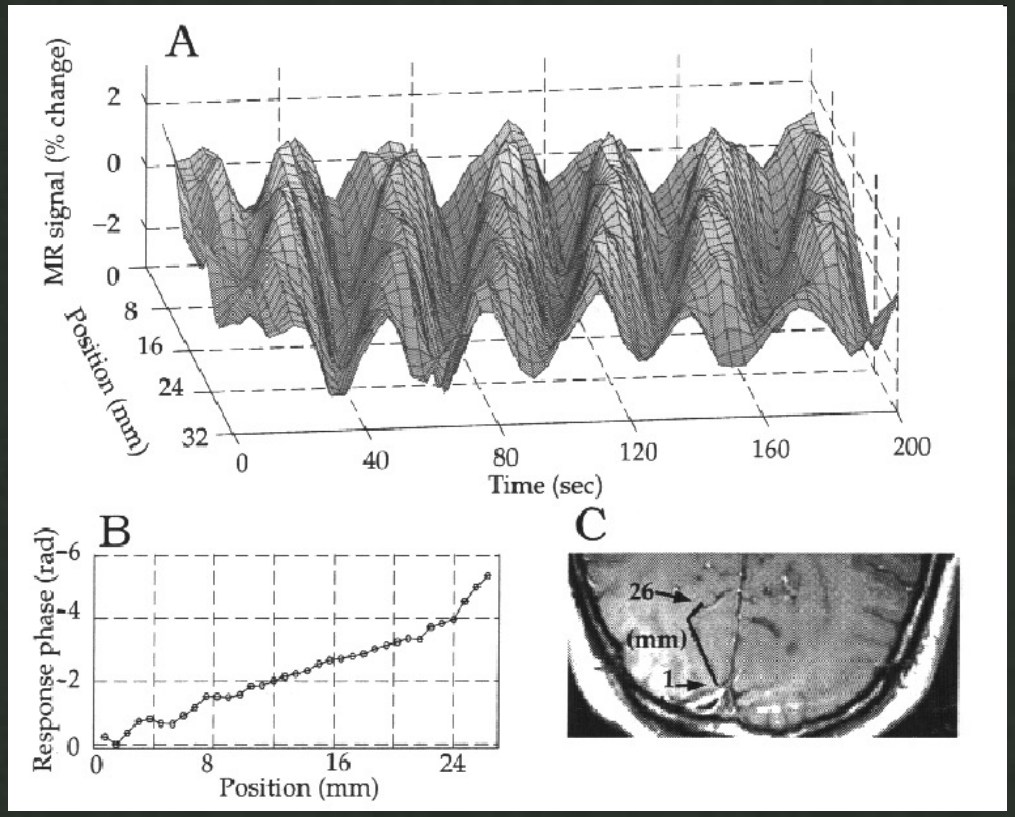


Source of contrast in venograms..



The HRF

PSF FWHM = 3.5mm

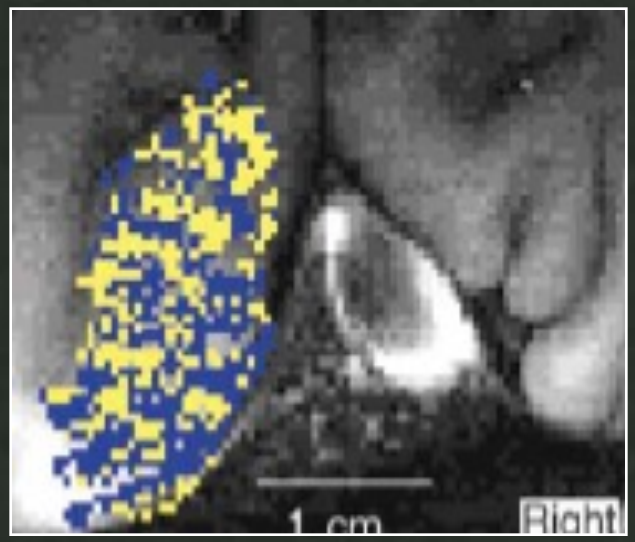


S.A. Engel, et al. Investigative Ophthalmology & Visual Science 35 (1994) 1977-1977.

The HRF

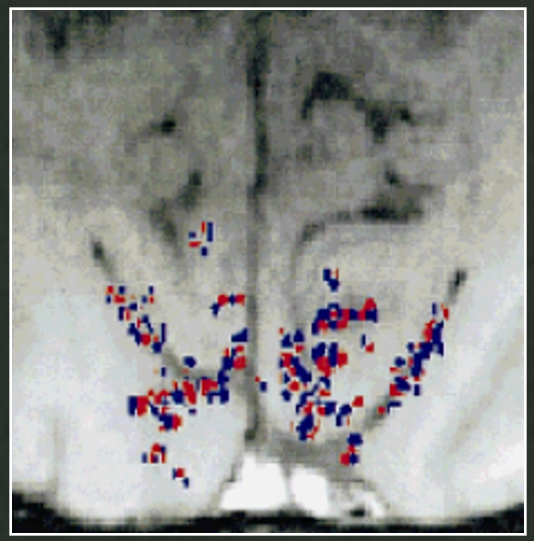
Detailed structure is extractable

0.47 x 0.47 in plane resolution



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

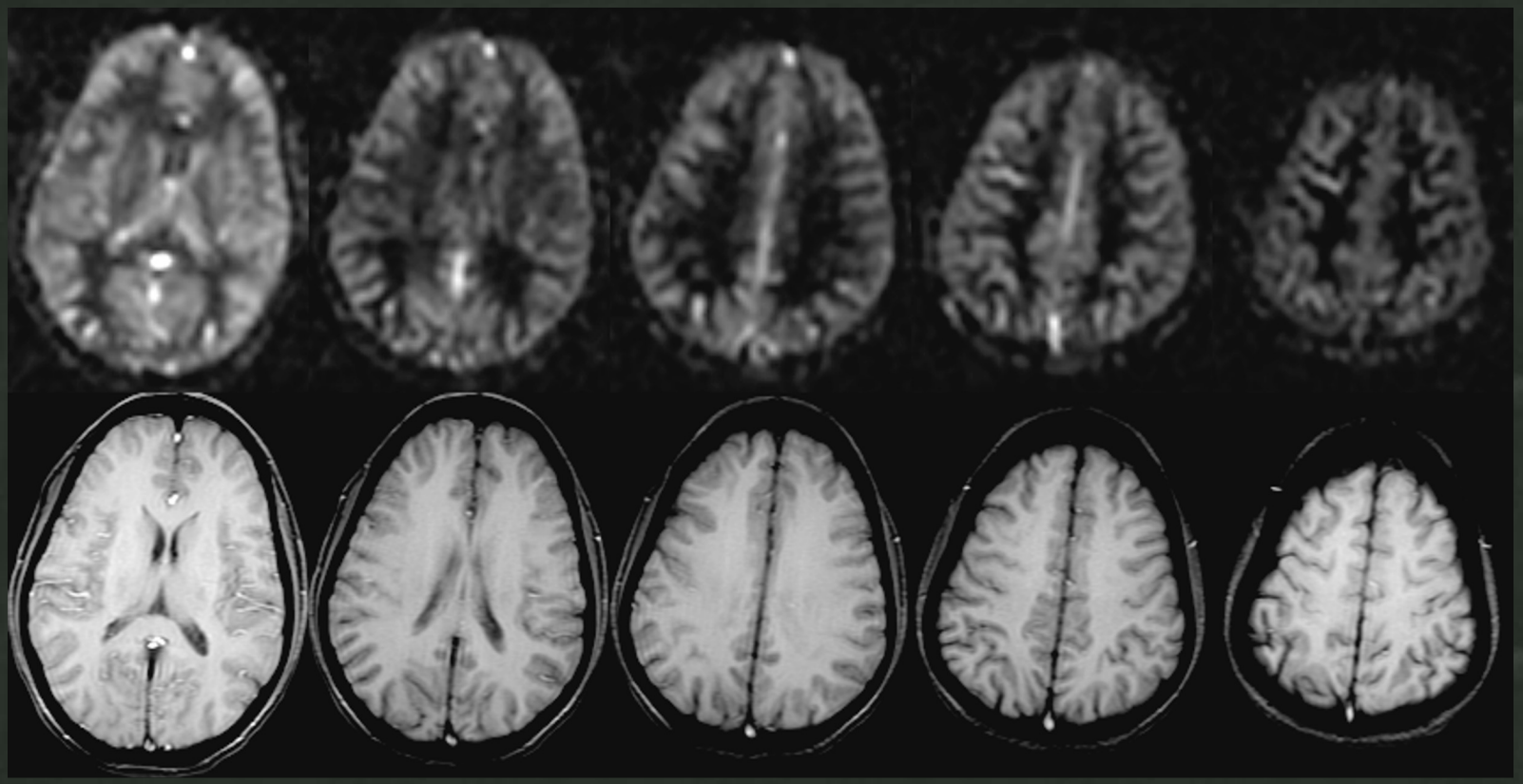
0.54 x 0.54 in plane resolution



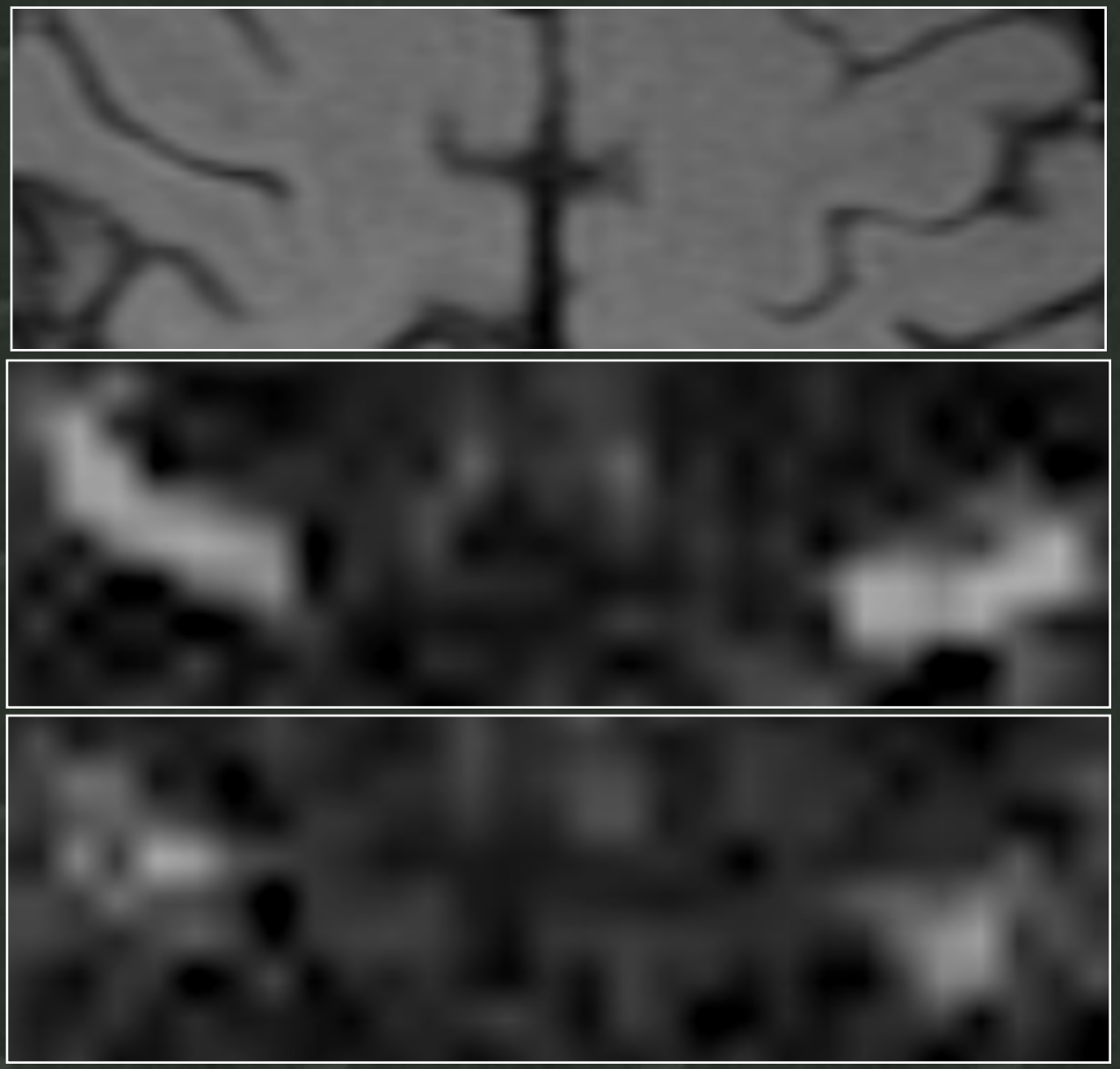
Menon et al, (1999) MRM 41 (2): 230-235

Multi-shot with navigator pulse

Perfusion (ASL)



Simultaneous BOLD and Perfusion

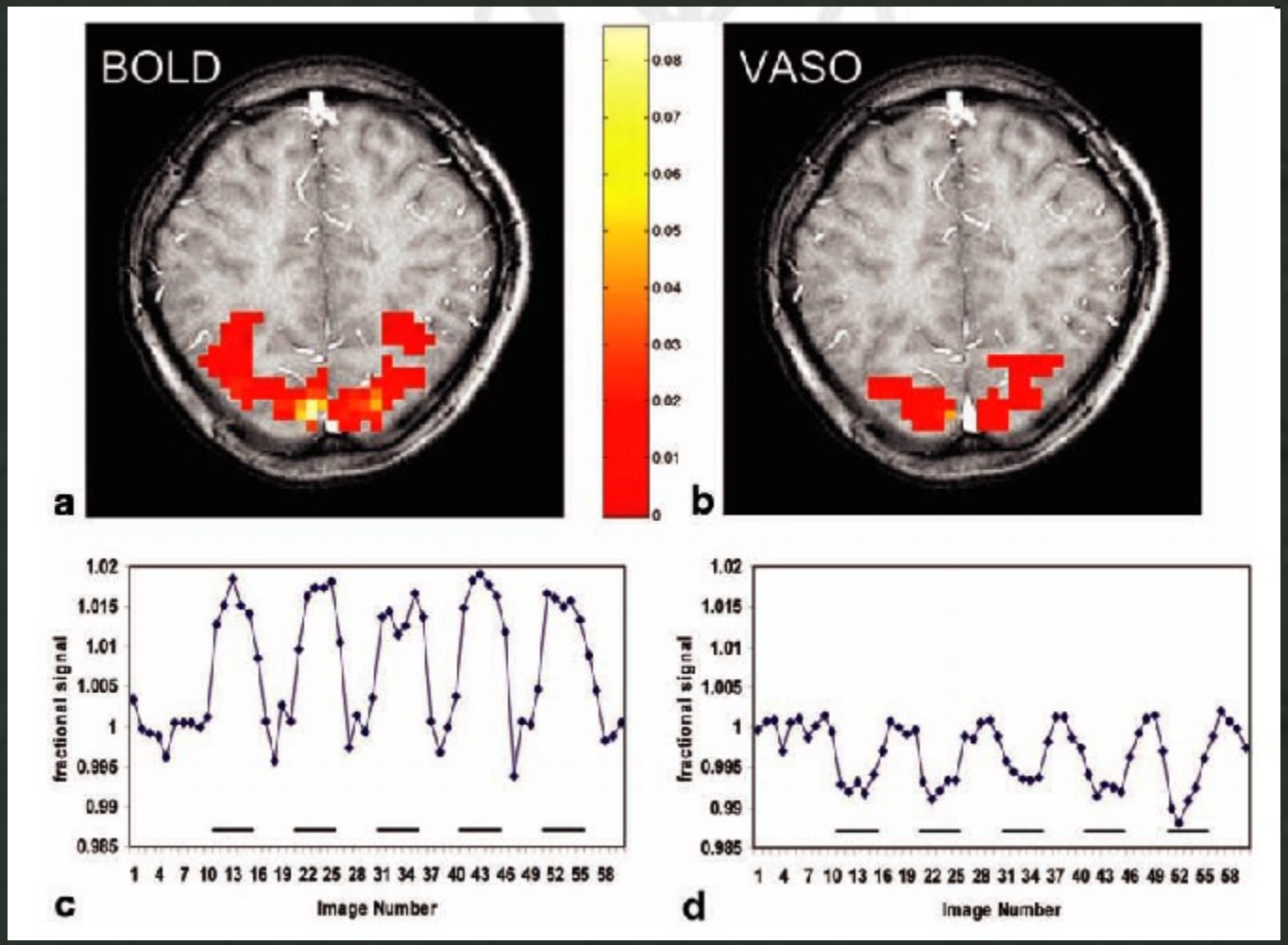


BOLD

Perfusion

The HRF

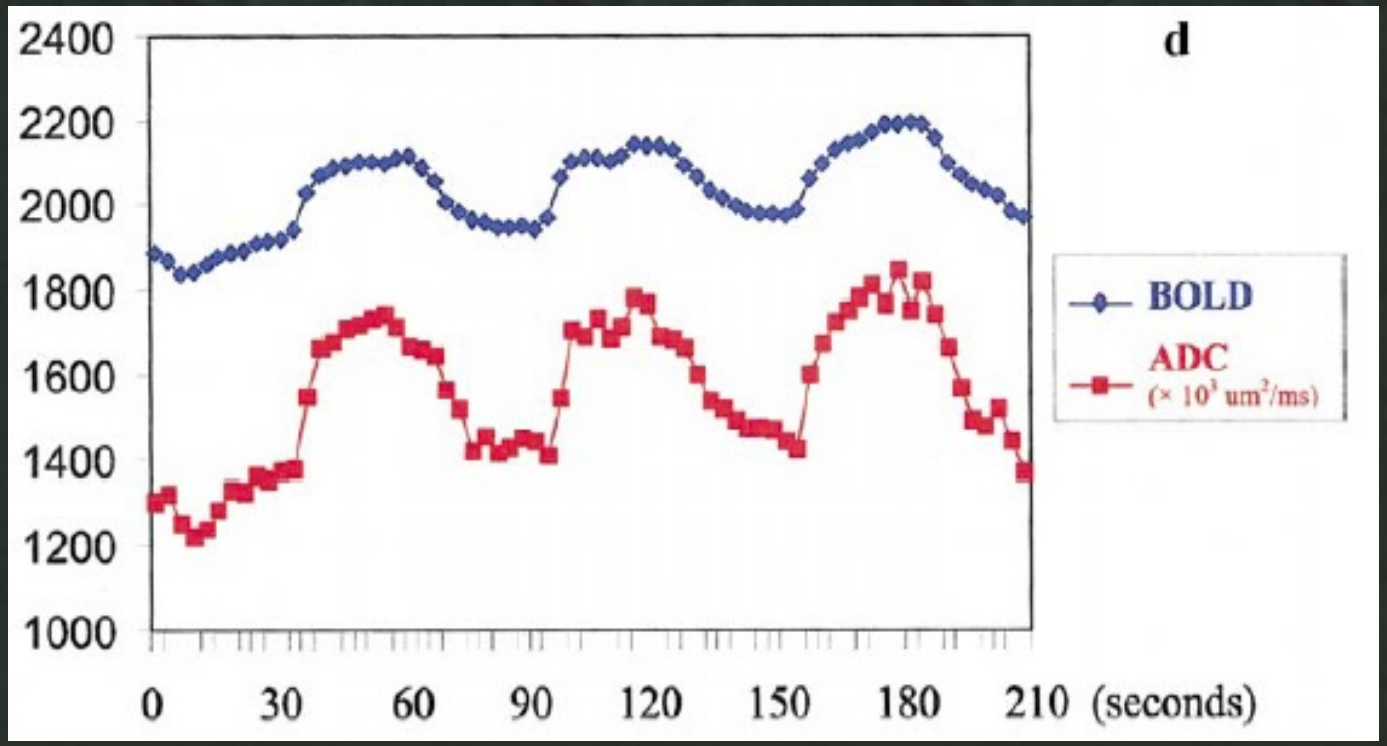
Is Vascular Space Occupancy Imaging (VASO) more specific?



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

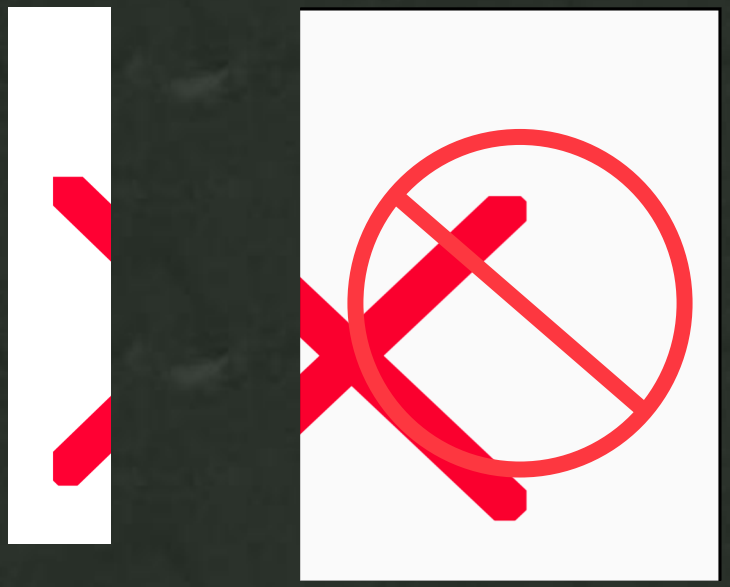
Other techniques?

Activation-induced changes in ADC (low b)

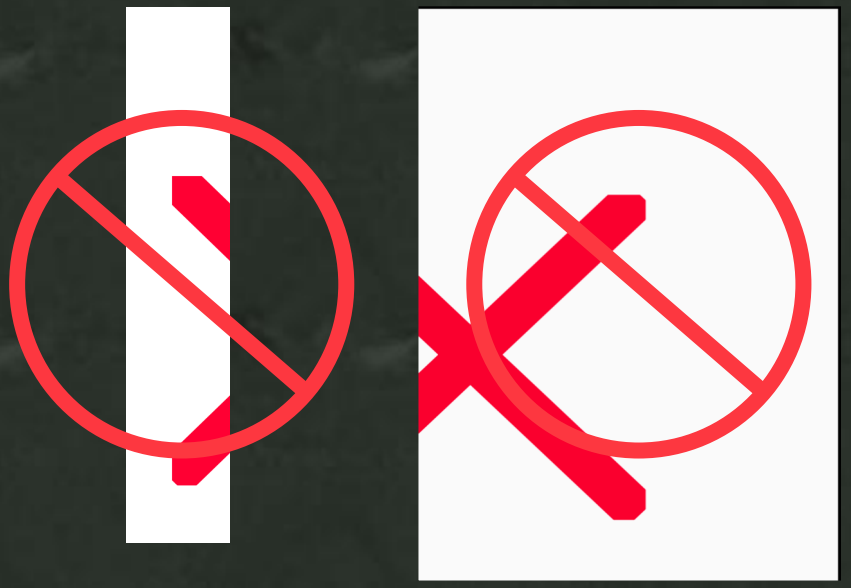


A. Song, et al (2002), NeuroImage 17, 742-750

Hypothesized mechanism for ADC change



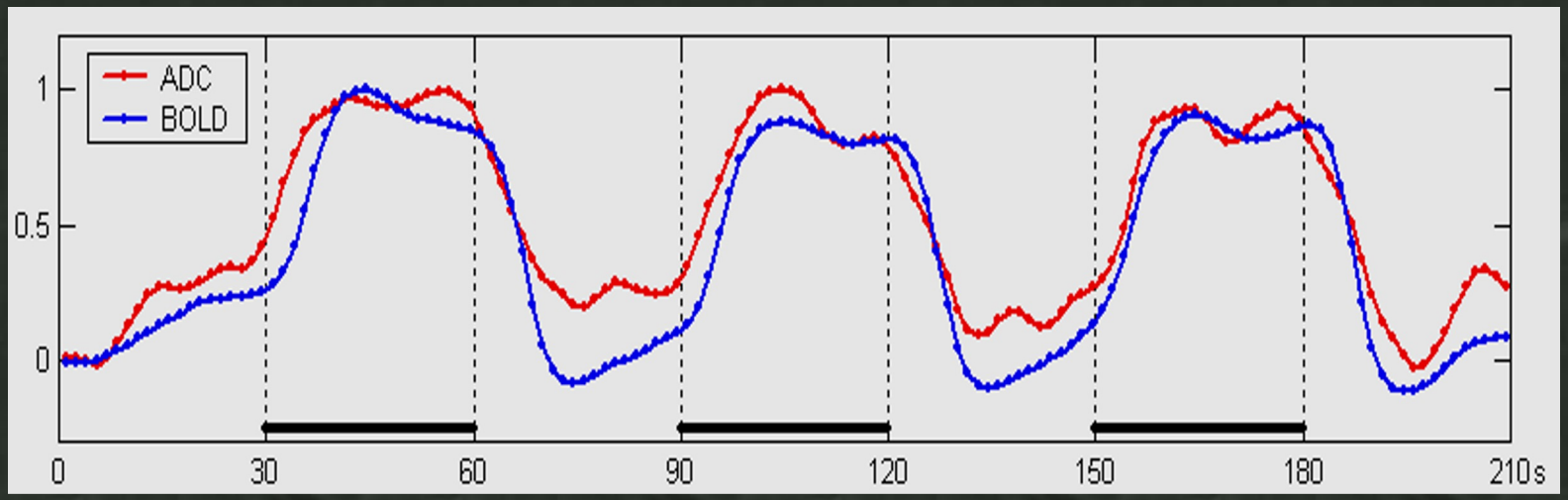
rest

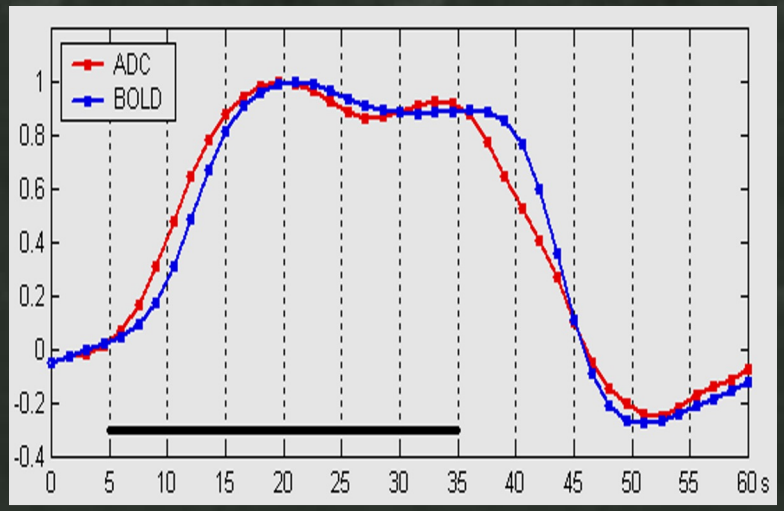


activation

The HRF

Averaged ADC time course precedes the BOLD time course

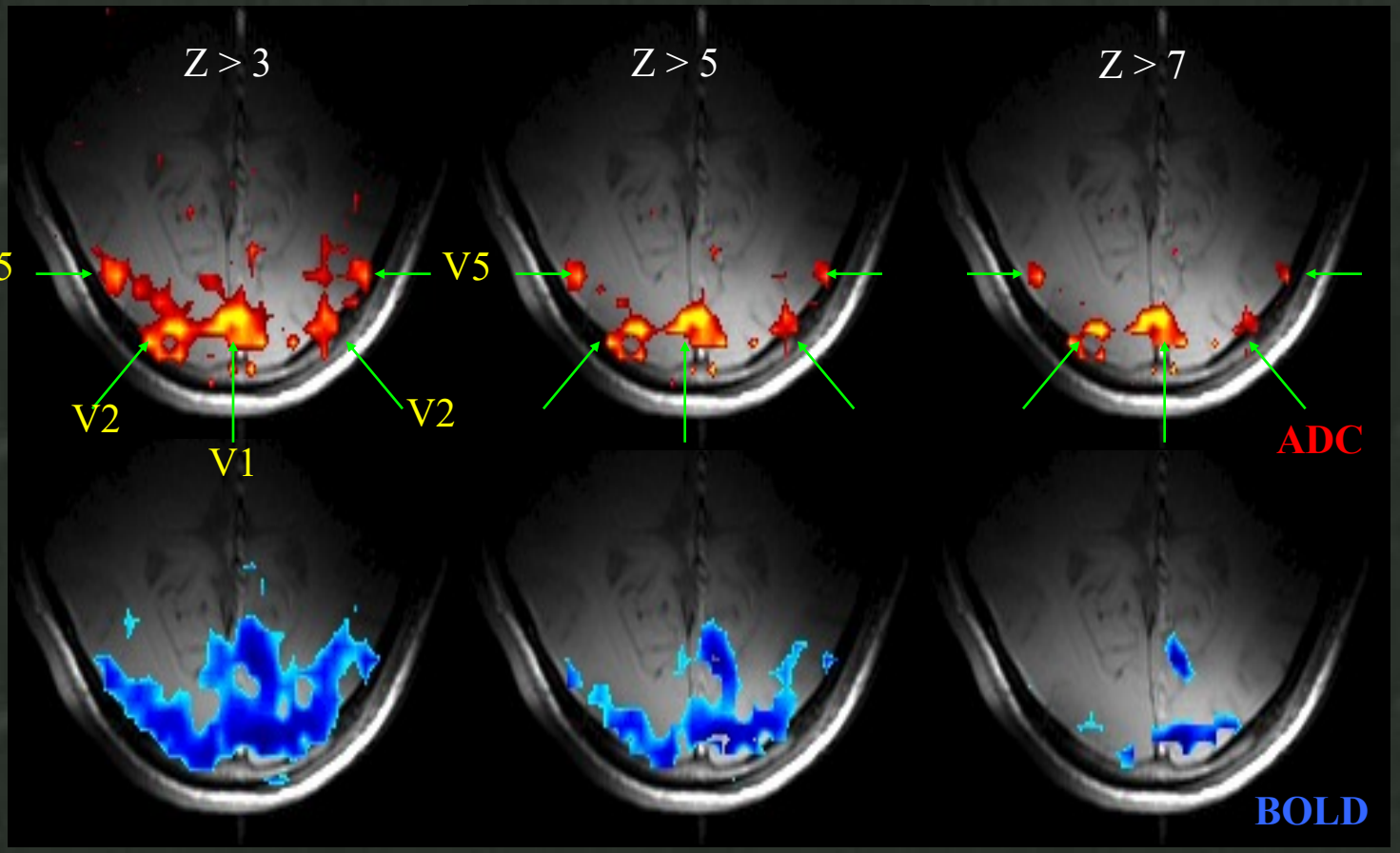




Gangstead and Song, MRM 48, 385-388, 2002

The HRF

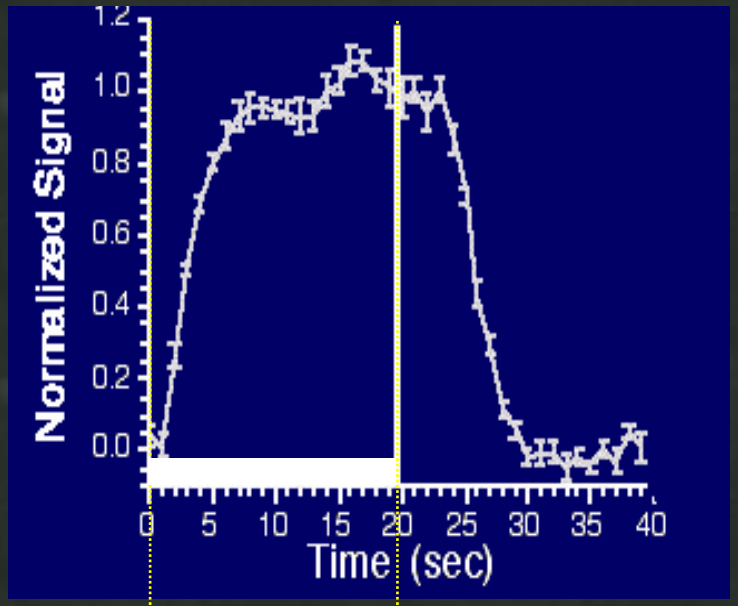
ADC changes appear to be more specific

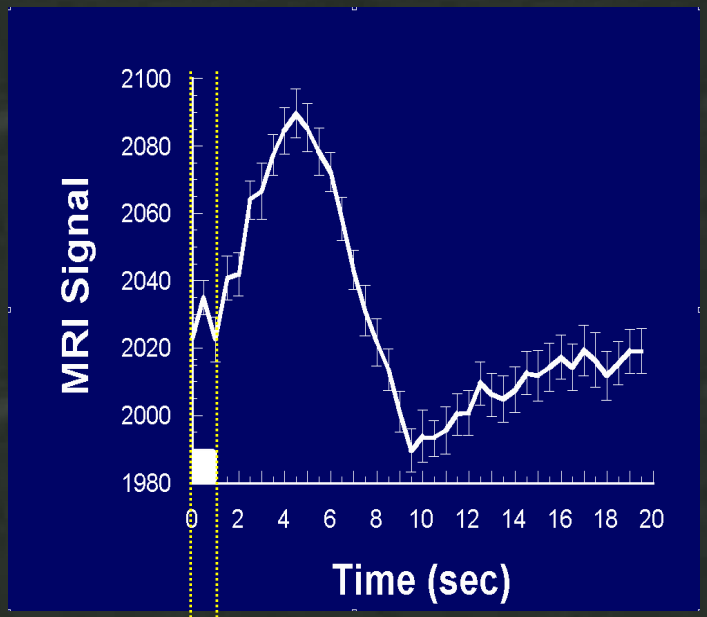


Visual Stimulation: Flashing and Rotating Checkerboard, 12° Angle

Song et al., NeuroImage, 20, 955-961, 2003.

Temporal resolution

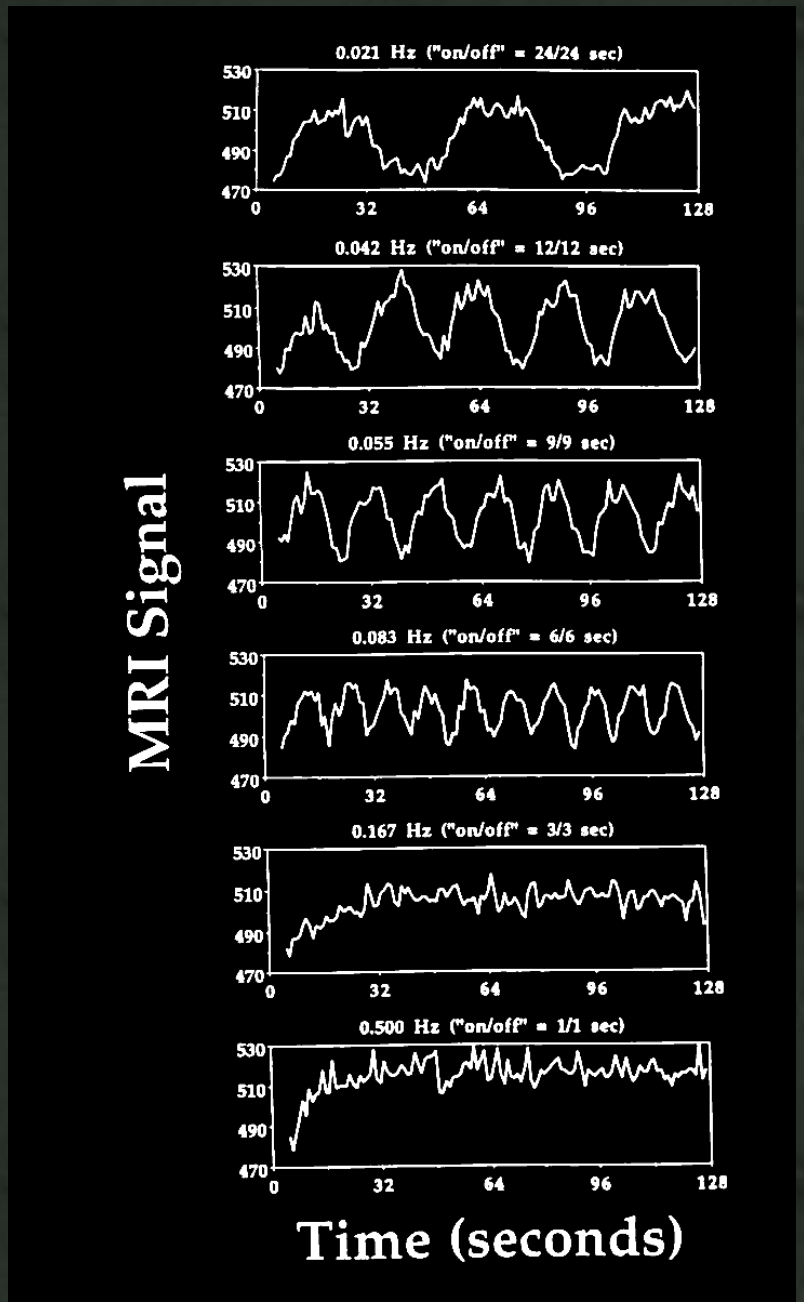




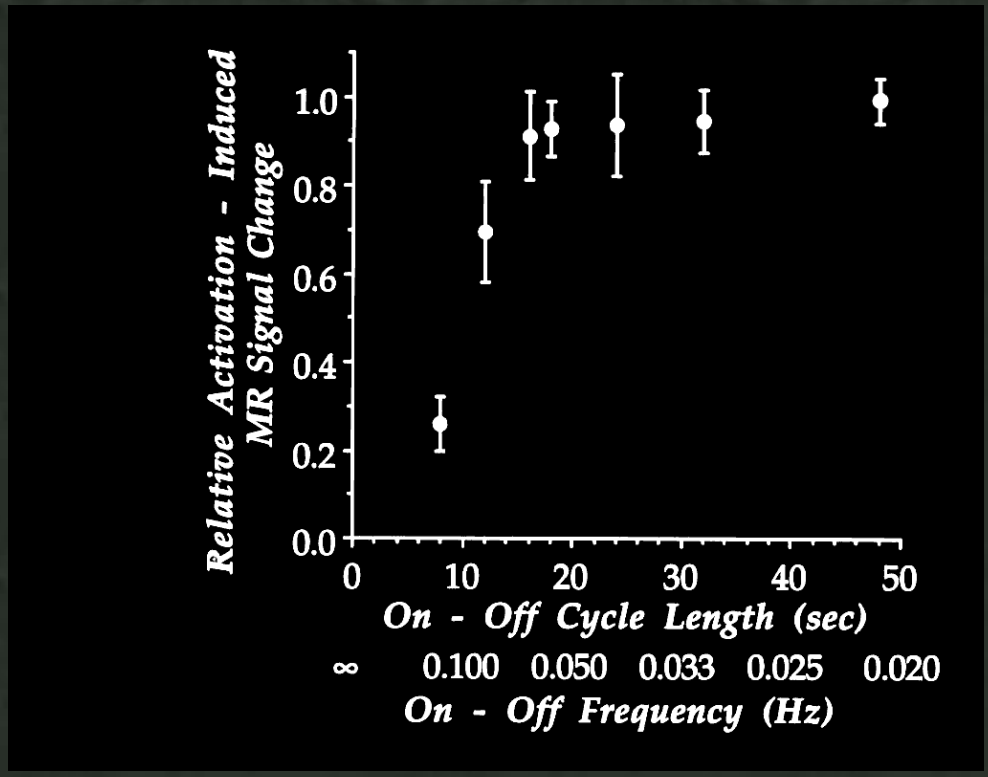
task

task

Temporal Resolution



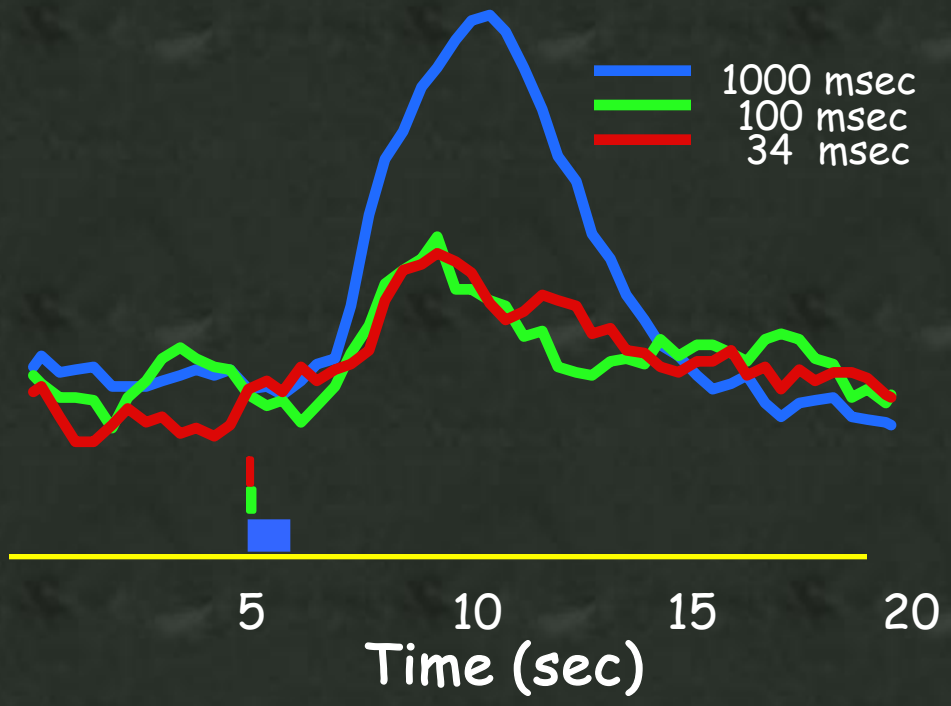
How rapidly can one switch on and off?



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'rd Proc. Soc. Magn. Reson., Nice, p. 450. (1995).

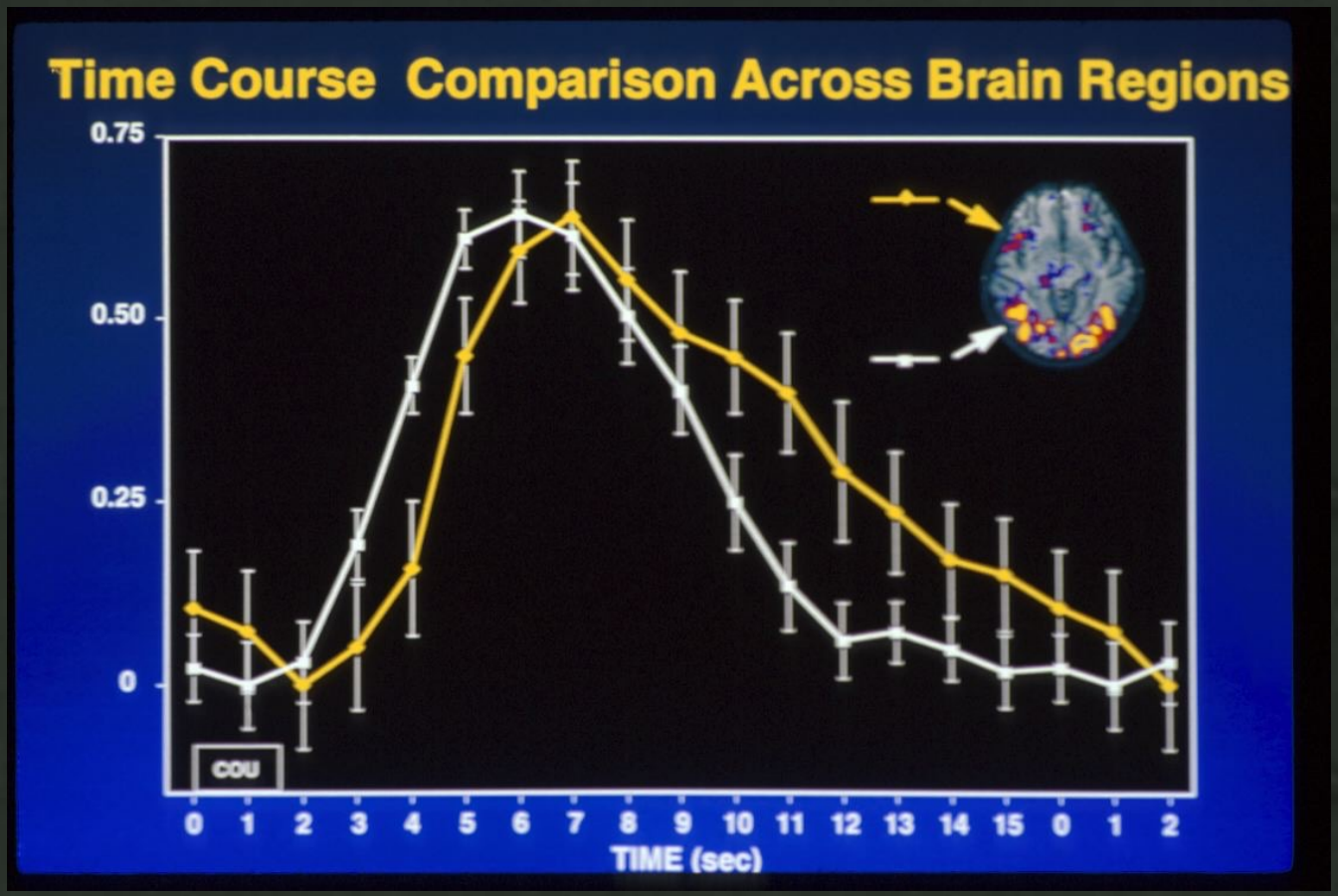
Temporal Resolution

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

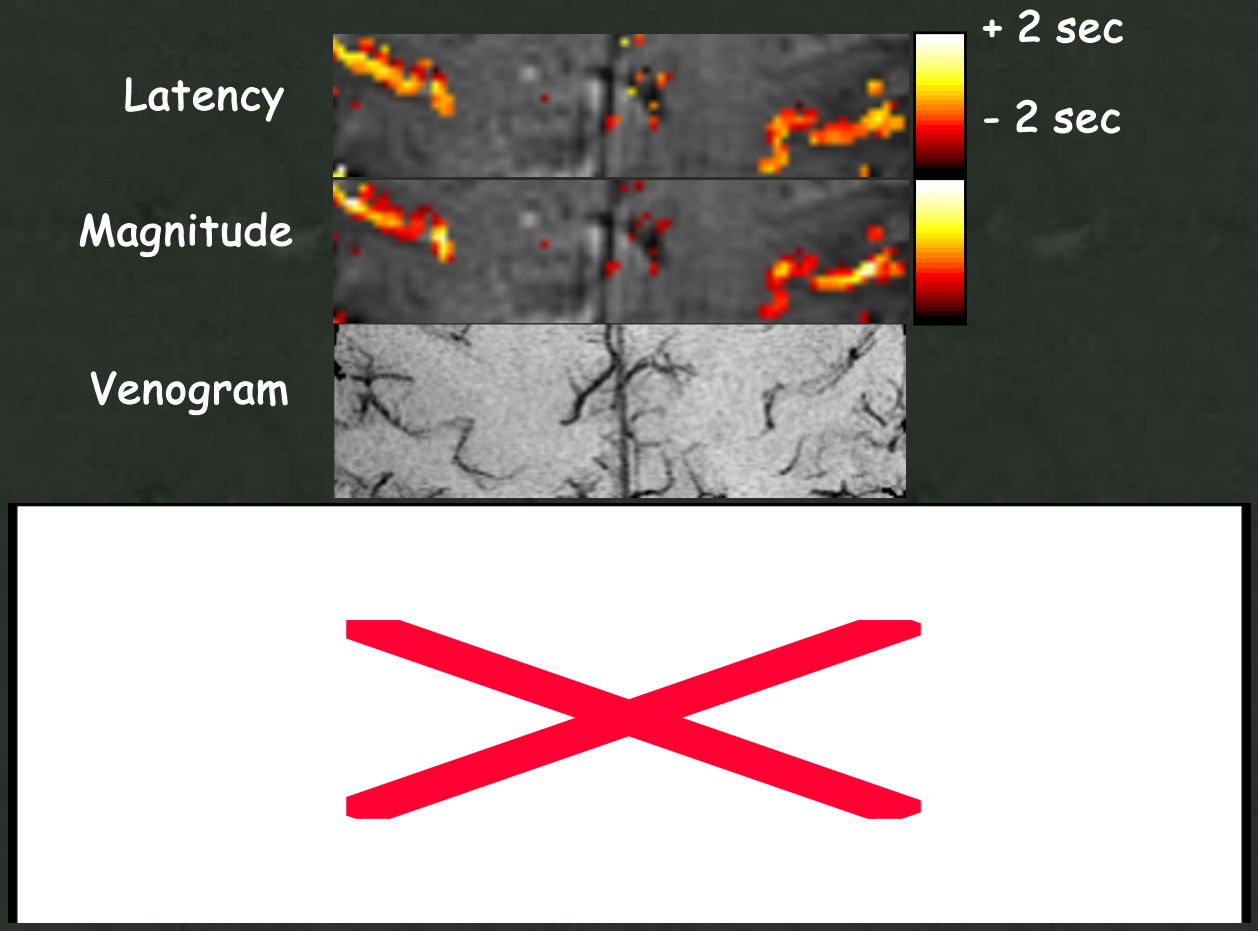
(neuroimaging/single trial/language/prefrontal)

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



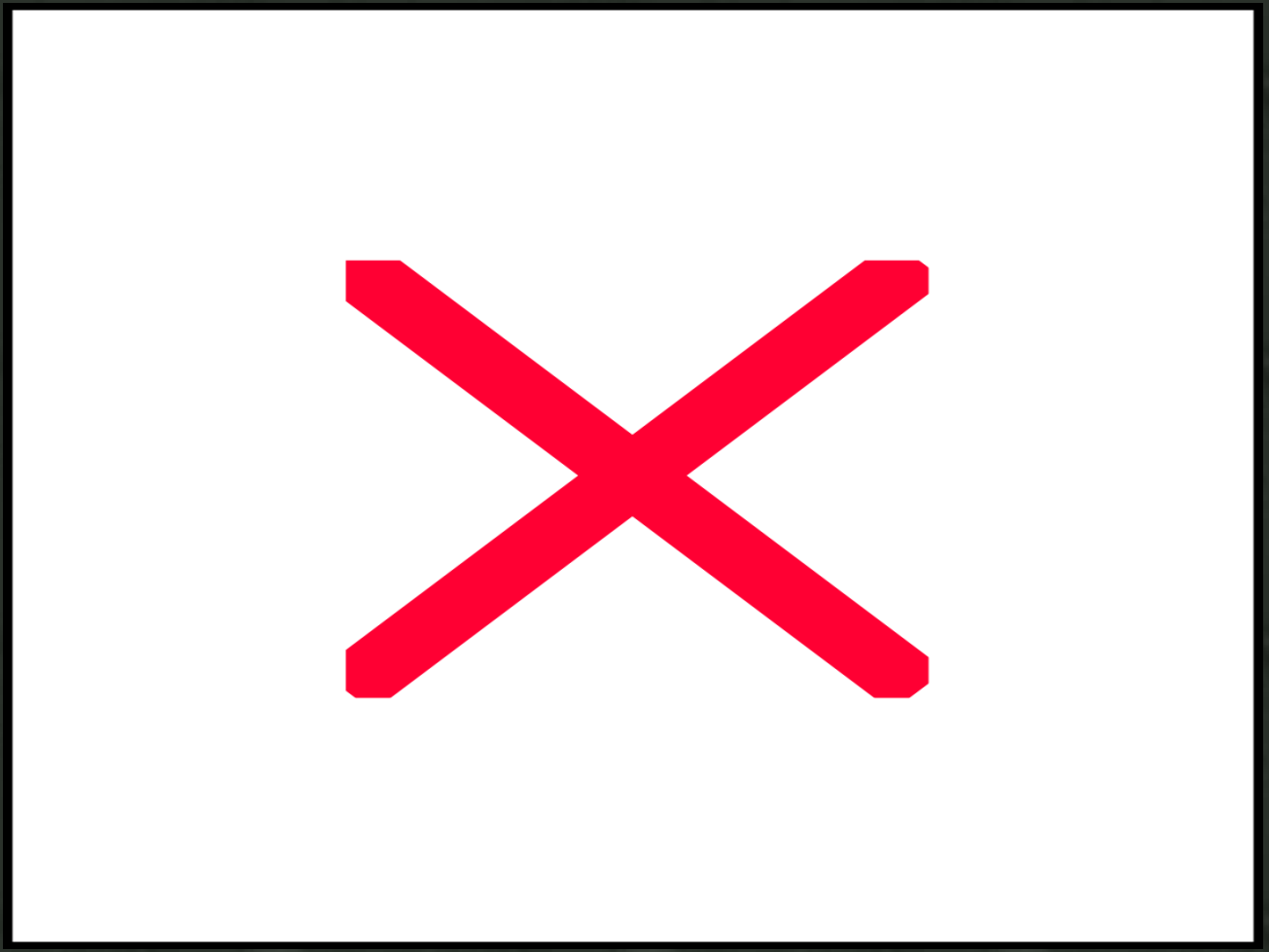
The HRF

Latency variation over space…is huge



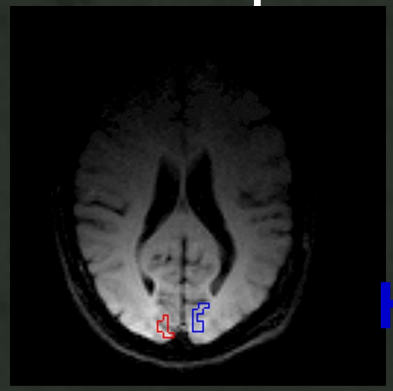
P. A. Bandettini, (1999) "Functional MRI" 205-220.

The Hemodynamic Response Function

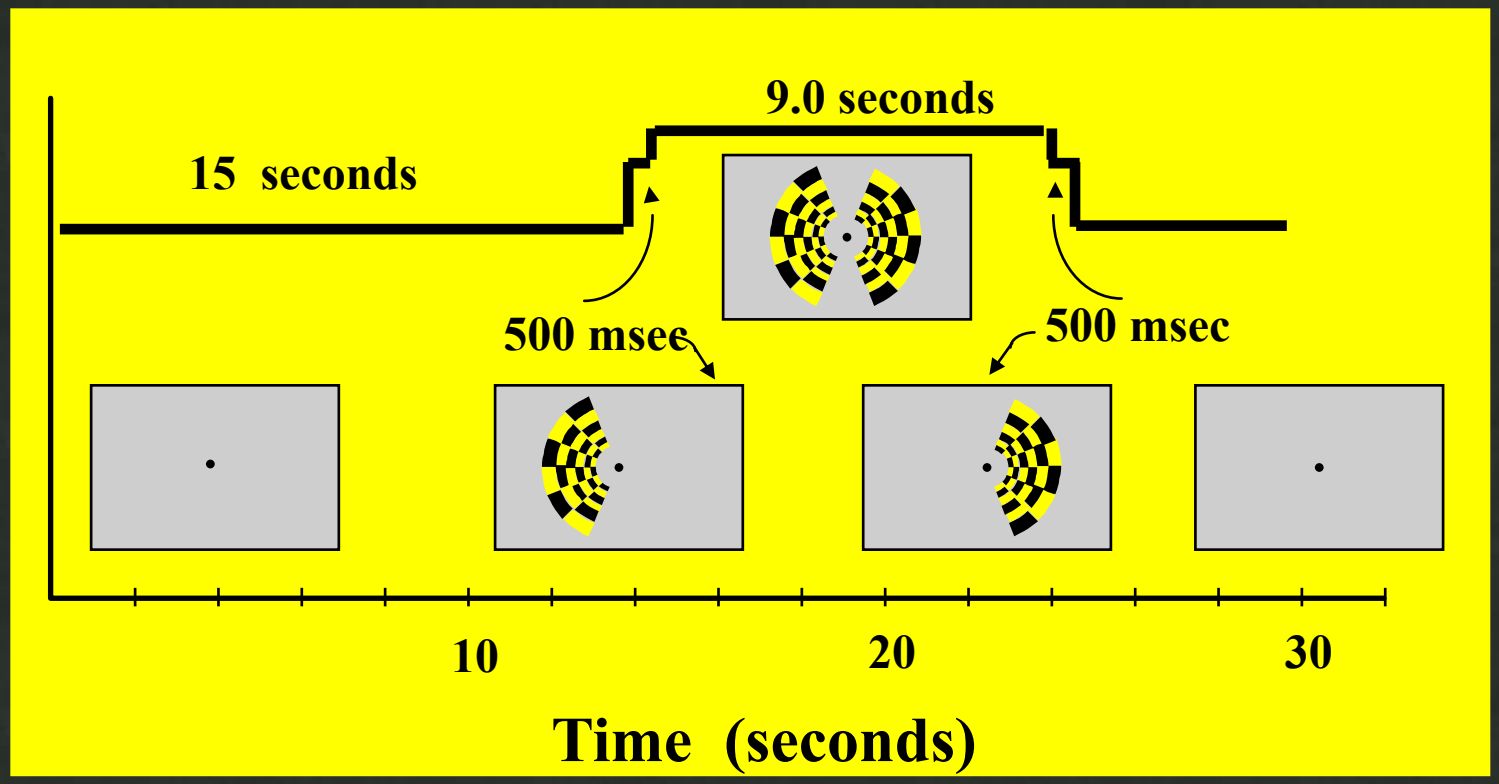


Hemi-Field Experiment

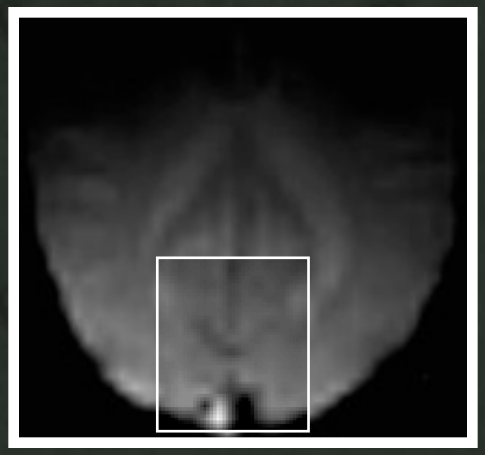
Right Hemisphere

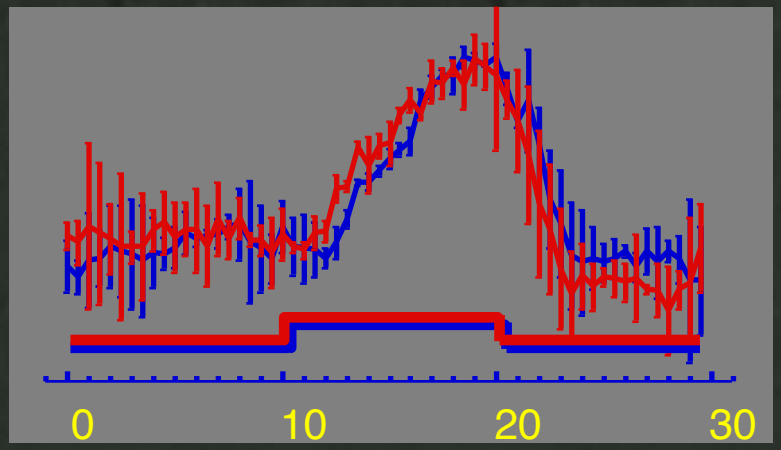


Left Hemisphere



The HRF



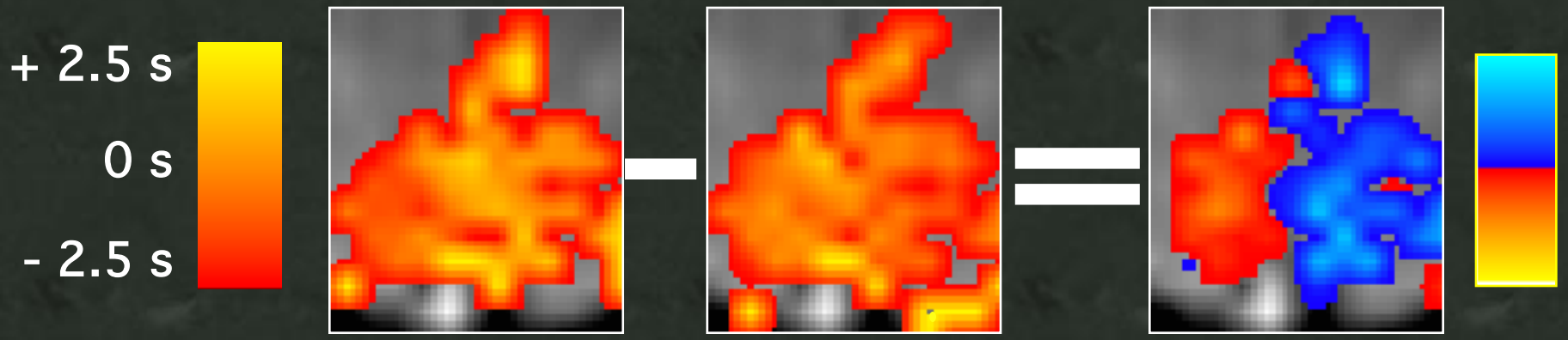


500 ms

500 ms

Right Hemifield

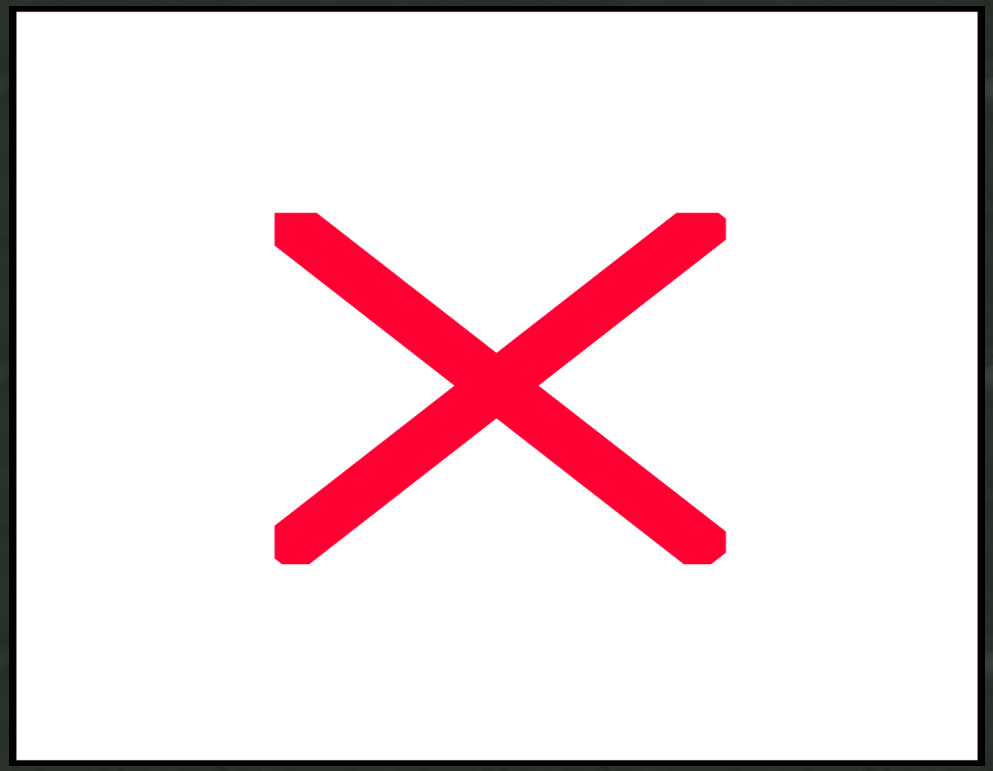
Left Hemifield

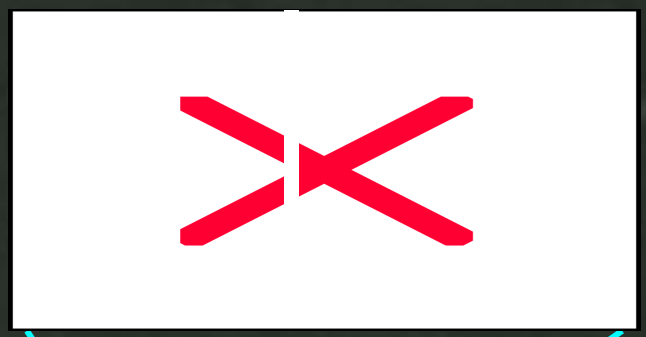


Task timing modulation

Word vs. Non-word

0°, 60°, 120° Rotation

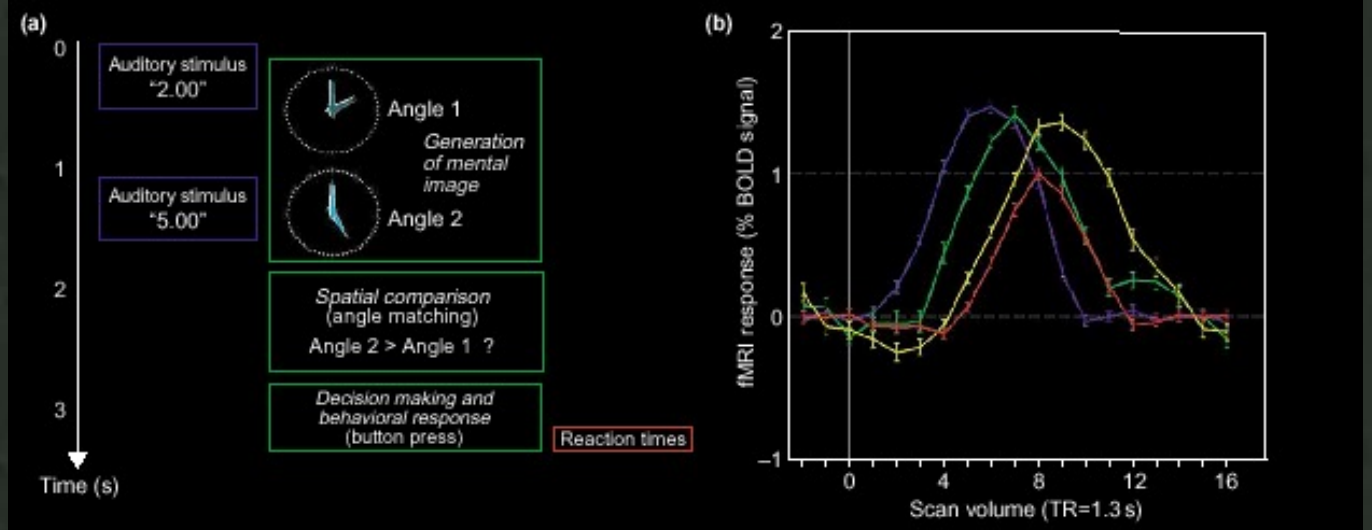


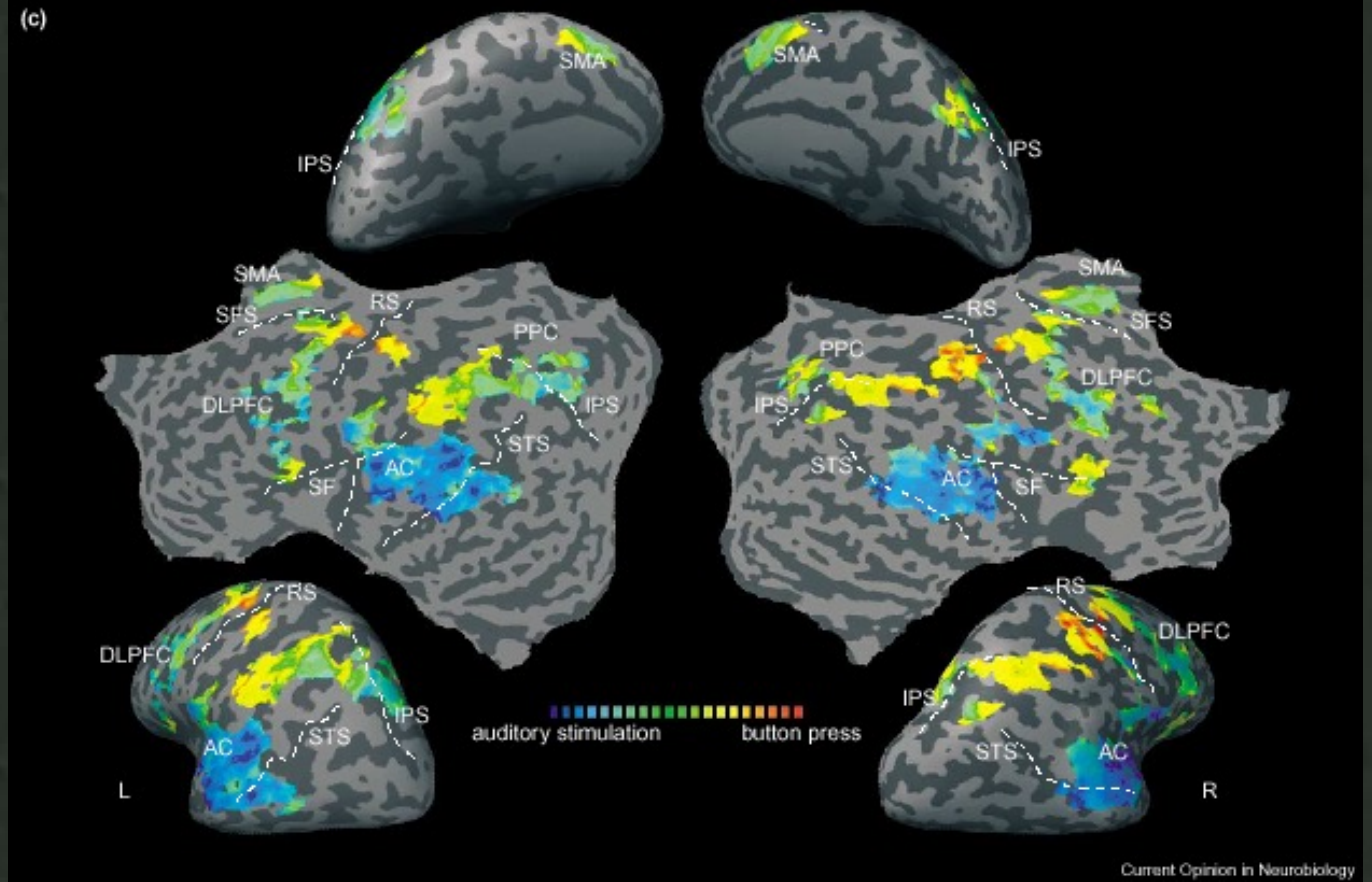


Bellgowan, et al (2003), PNAS 100, 15820–15283

The HRF

No calibration





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

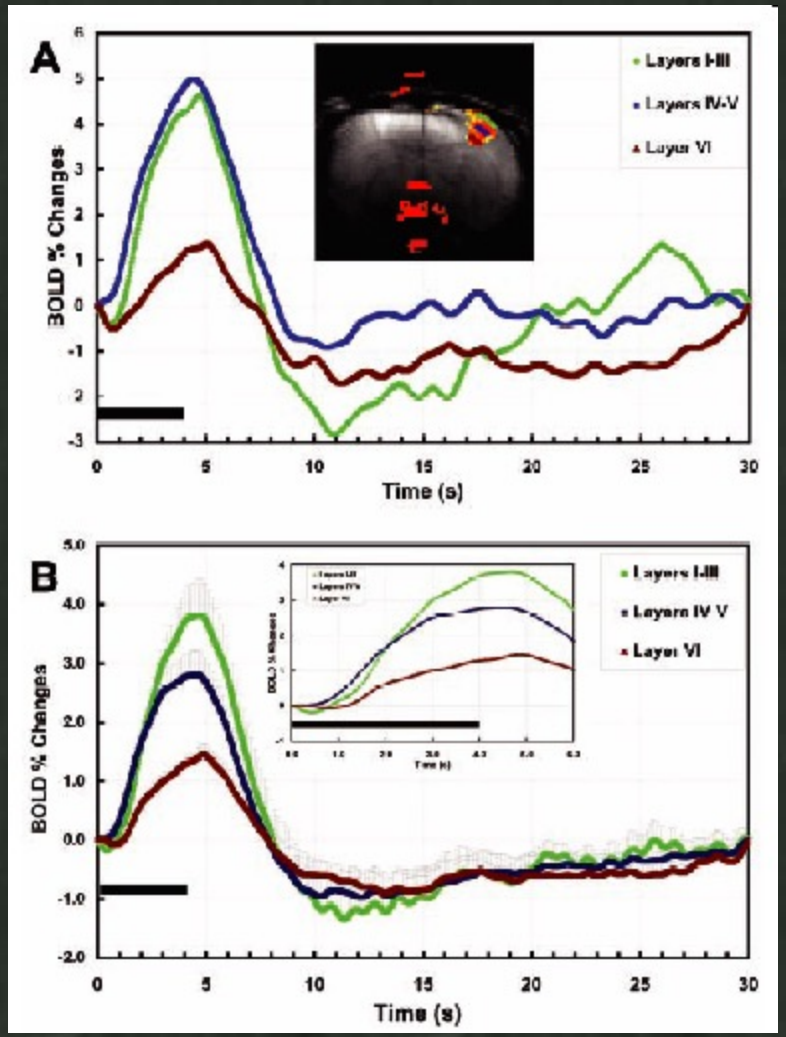
The HRF

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

5182–15187 | PNAS | November 12, 2002 | vol. 99 | no. 23



No calibration

11.7 T

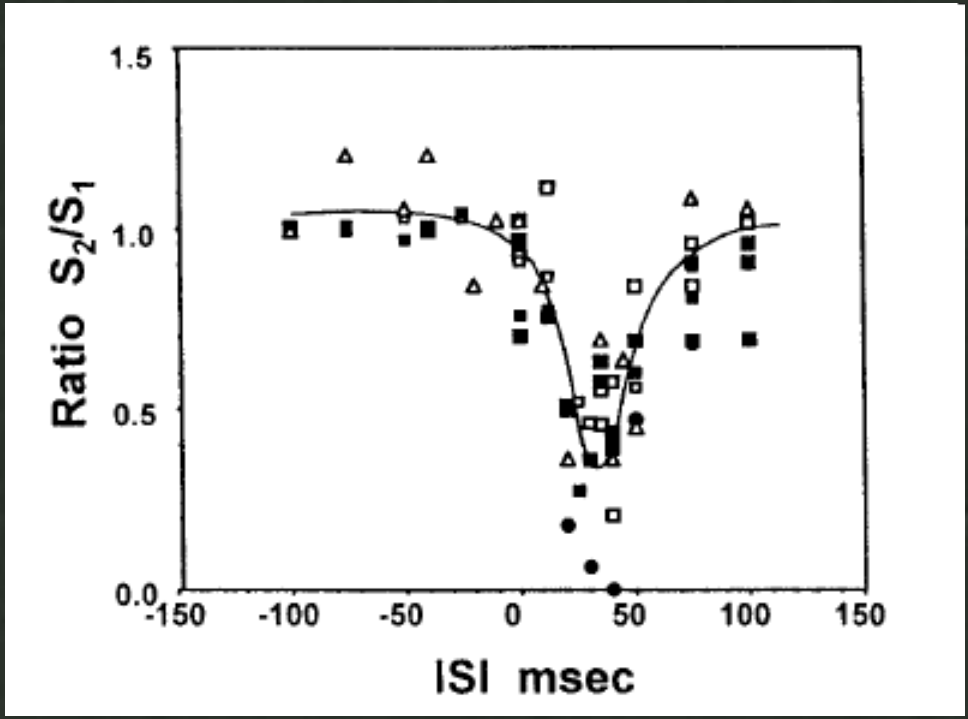
The HRF

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.

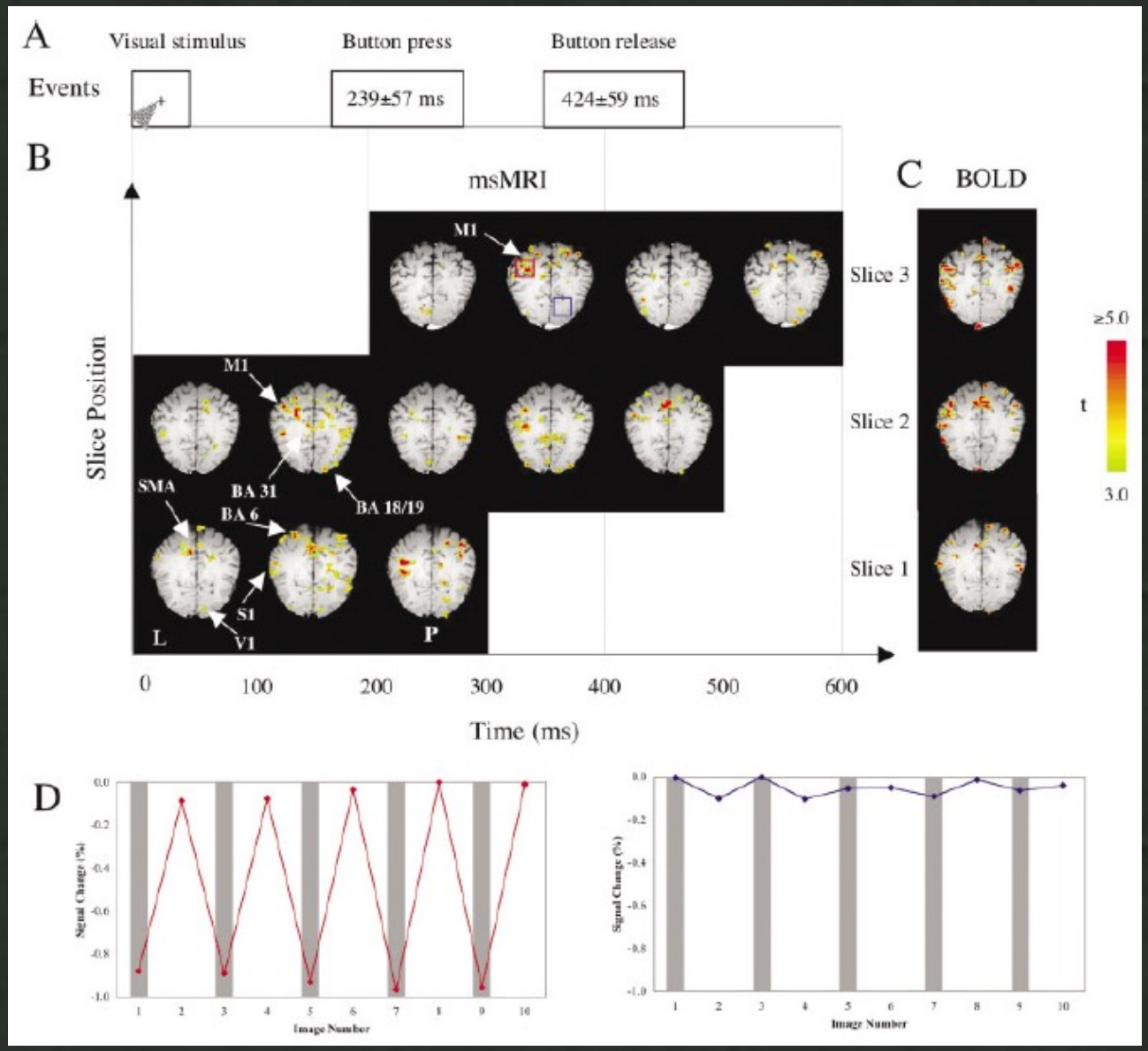
An approach to probe some neural systems interaction by functional MRI at neural time scale down to milliseconds

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



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

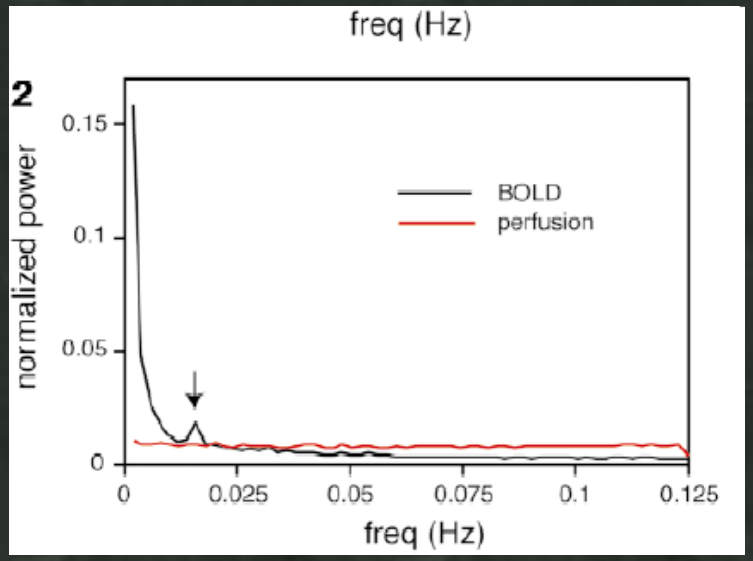
Neuronal Currents

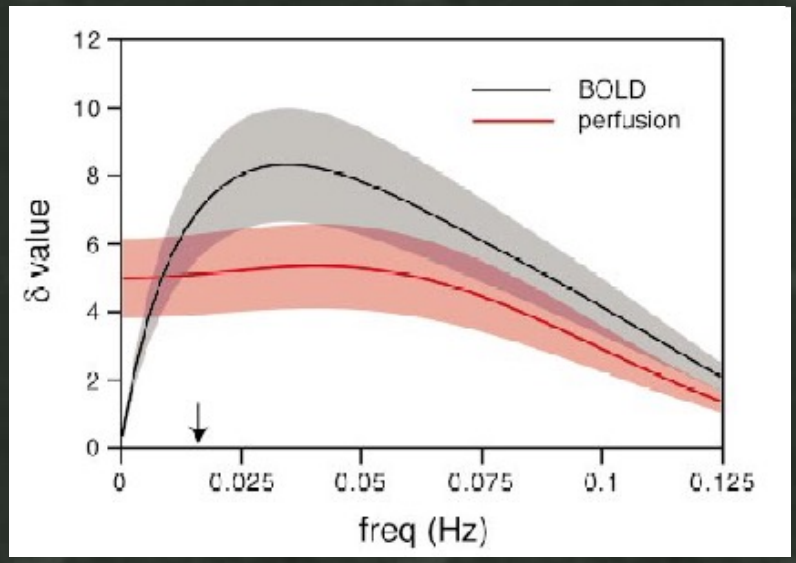


J. Xiong, P. T. Fox, J.-H. Gao, *Direct MRI Mapping of neuronal activity.* Human Brain Mapping, 20: 41-49, (2003)

Slow Limits…

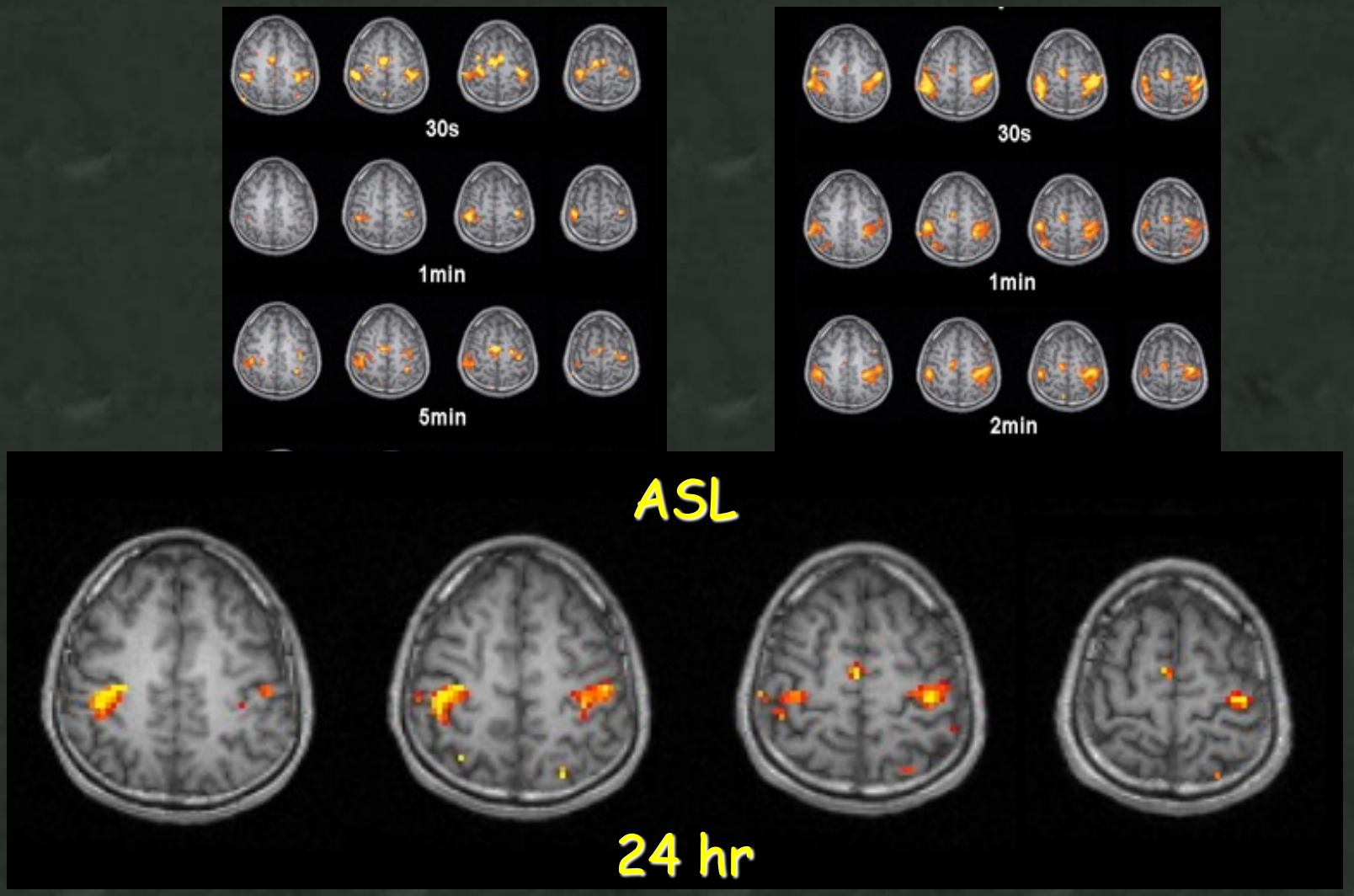
Perfusion is better than BOLD for slow "state change" comparisons..





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

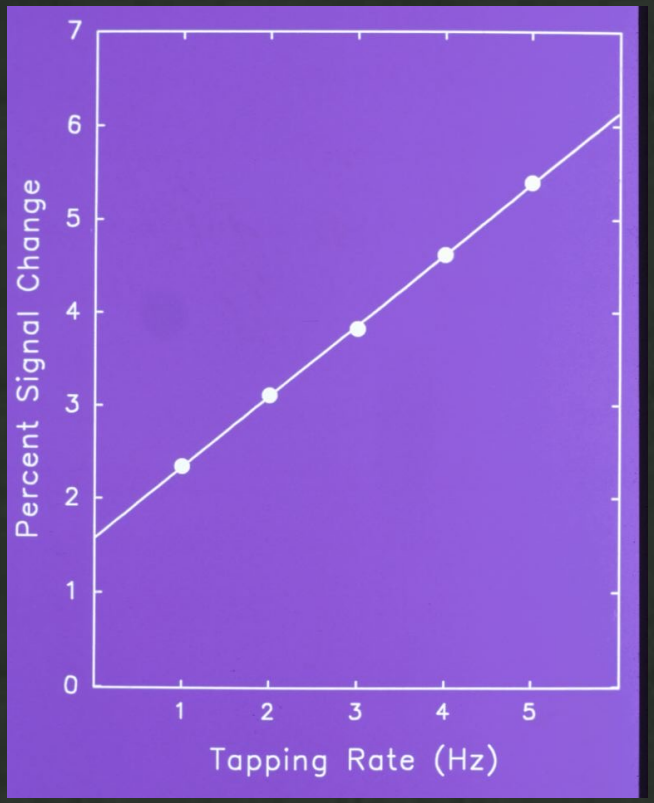
Perfusion vs. BOLD: Low Task Frequency



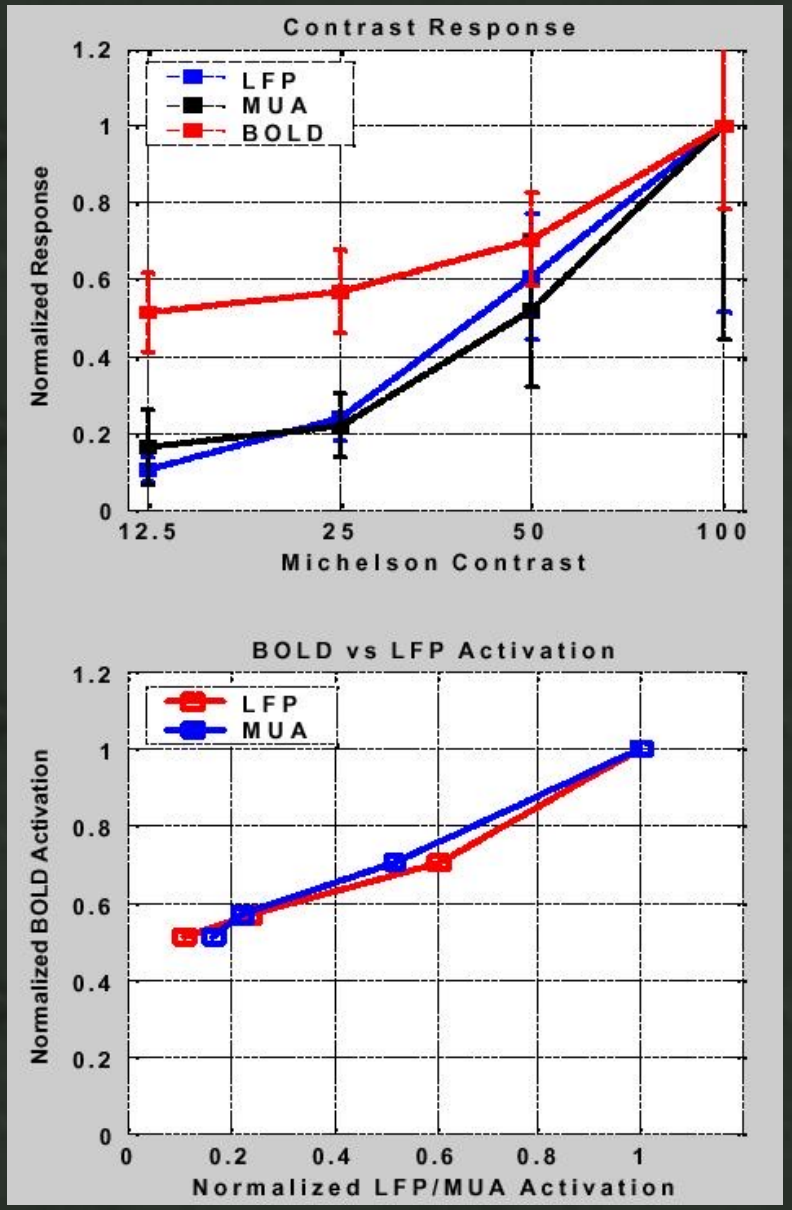
Wang et al., 2002

Interpretation

Linearity



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.

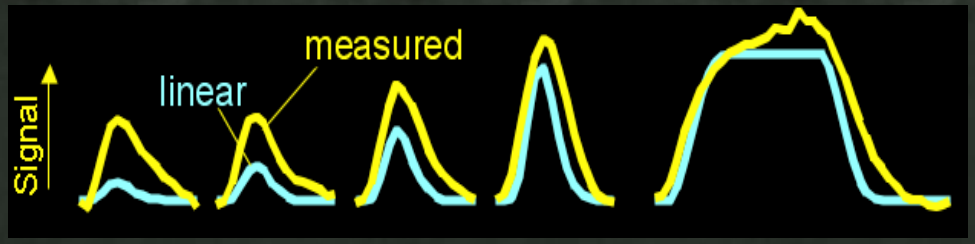


Logothetis et al. (2001) "Neurophysiological investigation of the basis of the fMRI signal" Nature, 412, 150-157

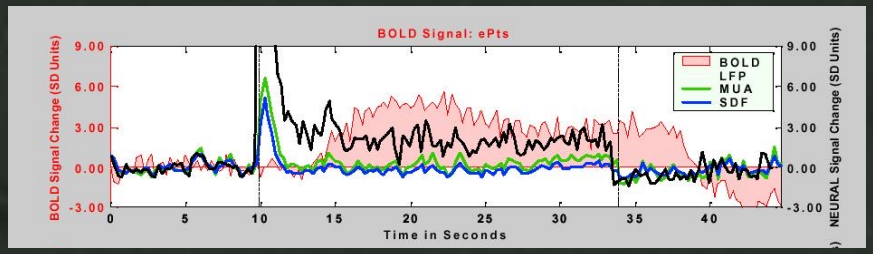
Interpretation

Linearity

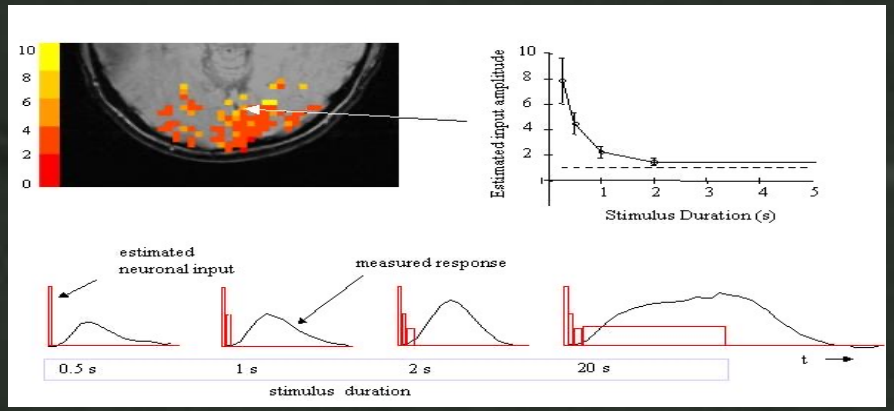
Increases: linearity



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



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

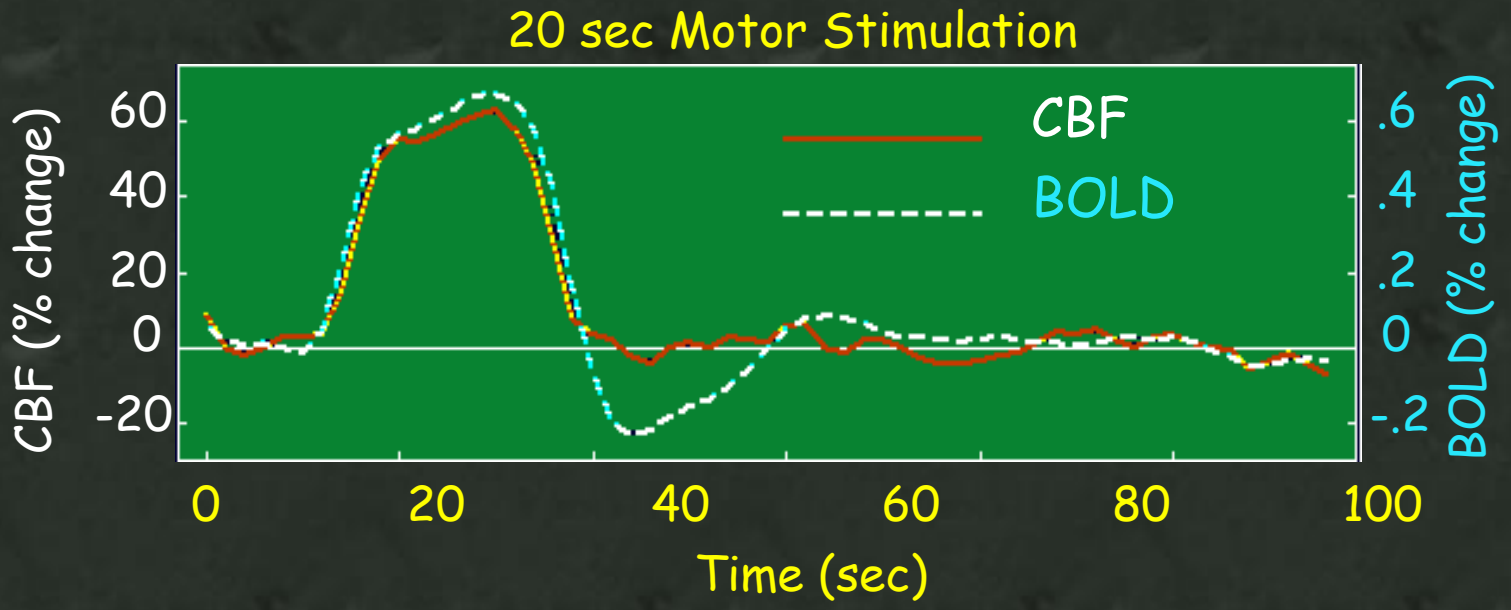


P. A. Bandettini et al, (2001) Nature Neuroscience, 4: 864-866.

Interpretation

Post Undershoot

BOLD post-stimulus undershoot



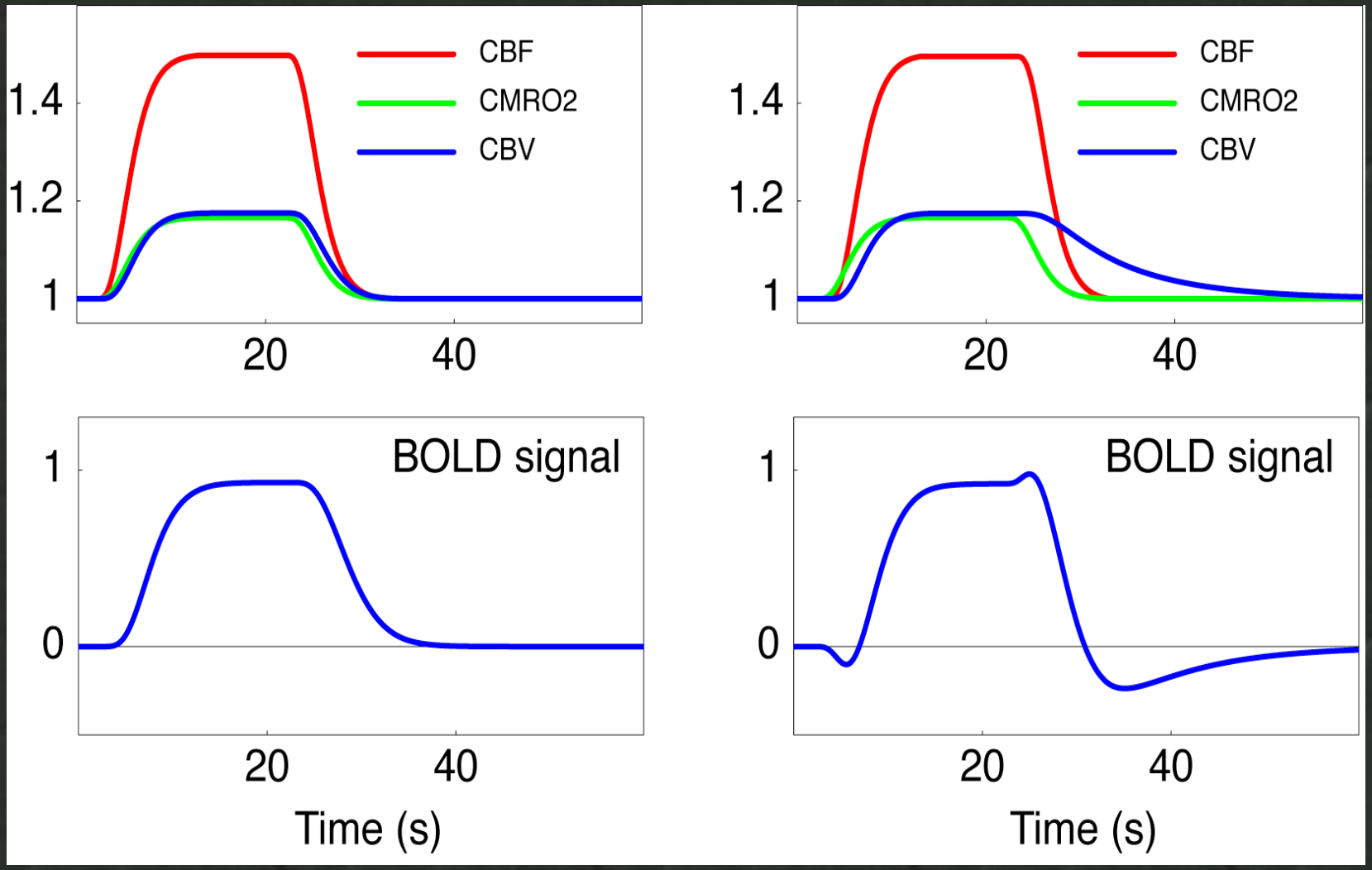
A BOLD undershoot without a CBF undershoot could be due to a slow return to baseline of either CBV or $CMRO_2$

Courtesy Rick Buxton

Interpretation

Post Undershoot

Simulated BOLD Signal Dynamics



Courtesy Rick Buxton

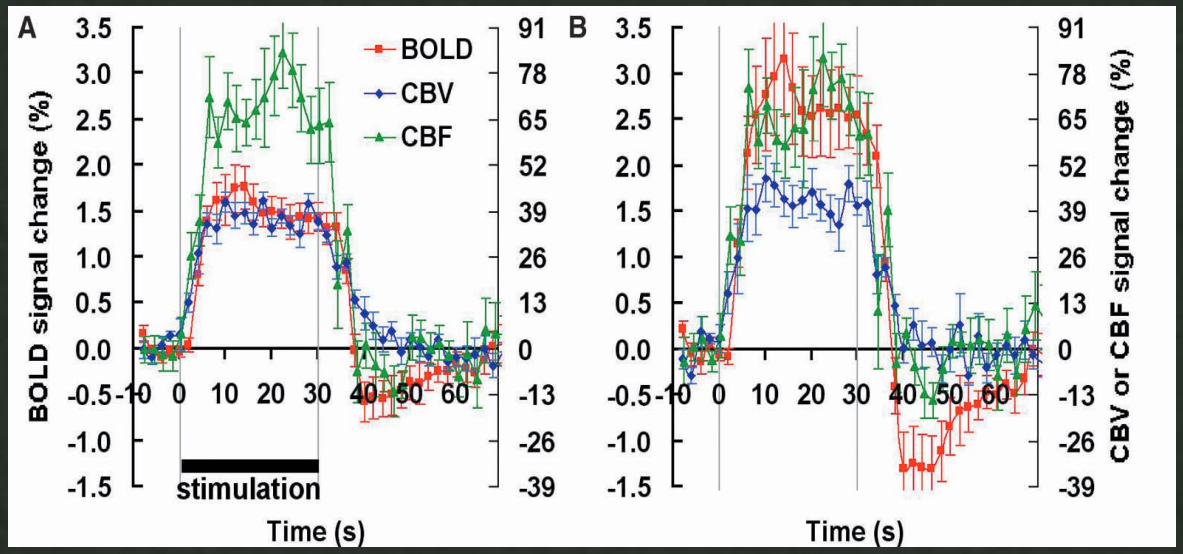
Interpretation

Post Undershoot

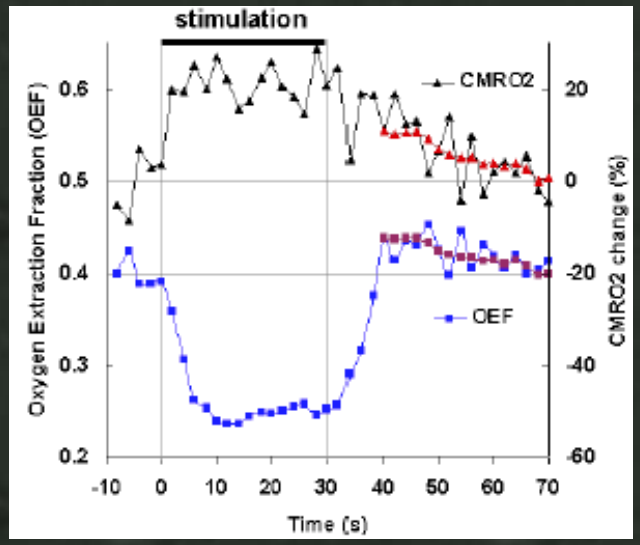
VASO (Vascular Space Occupancy)

Evidence for sustained elevated $CMRO_2$

(VASO indicates fast return of CBV despite BOLD undershoot)



All activated voxels

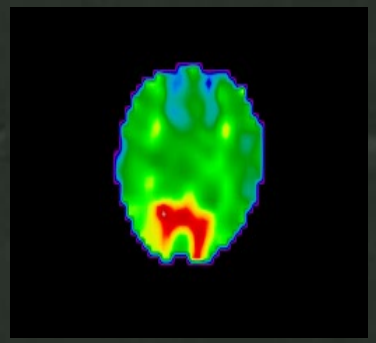


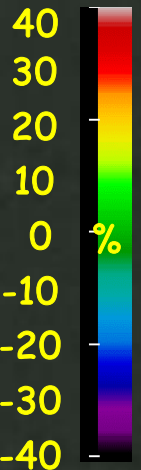
Overlapped voxels

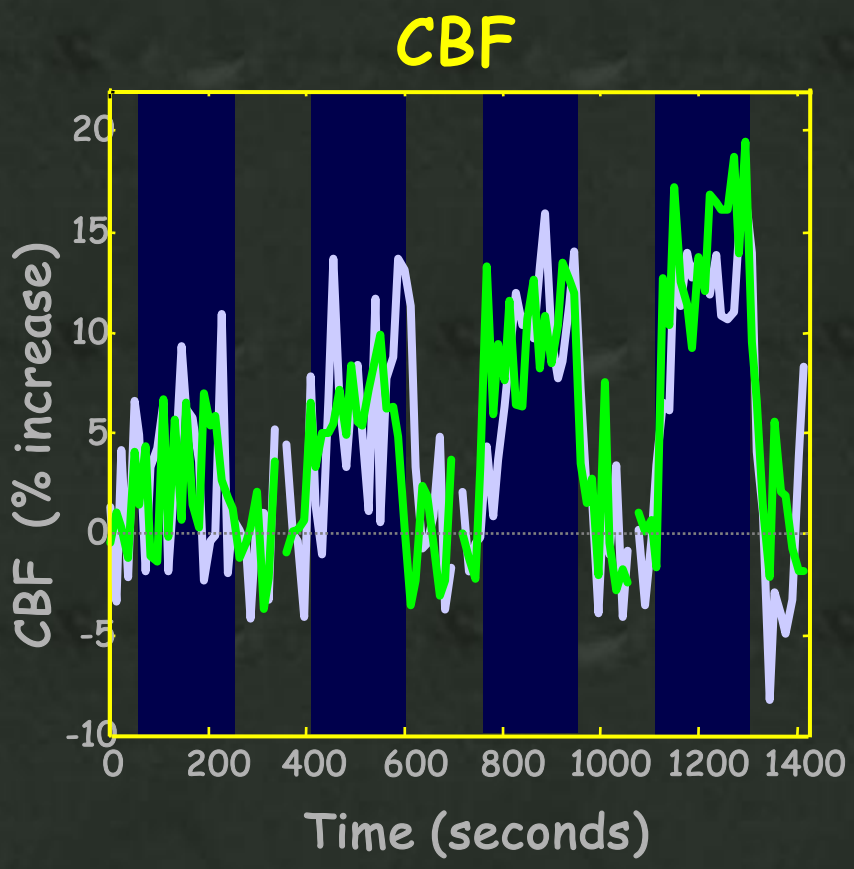
Lu, et al: JCBF+M 24:764, 2004

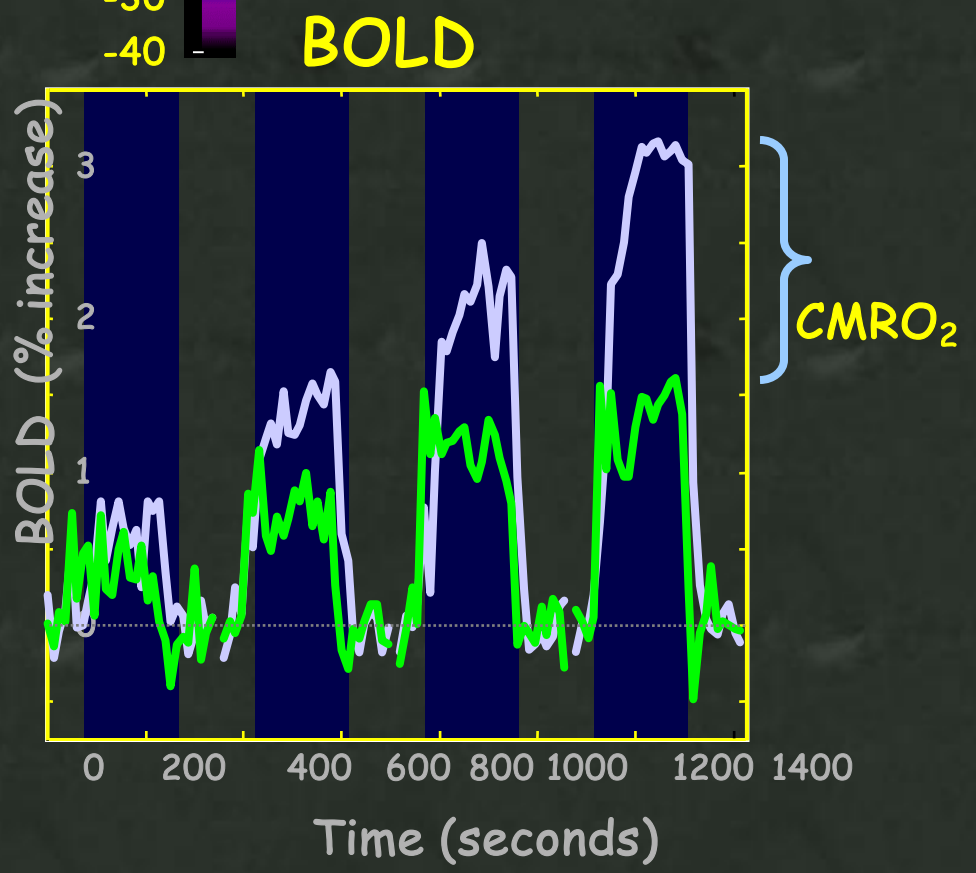
Interpretation

$\Delta CMRO_2$









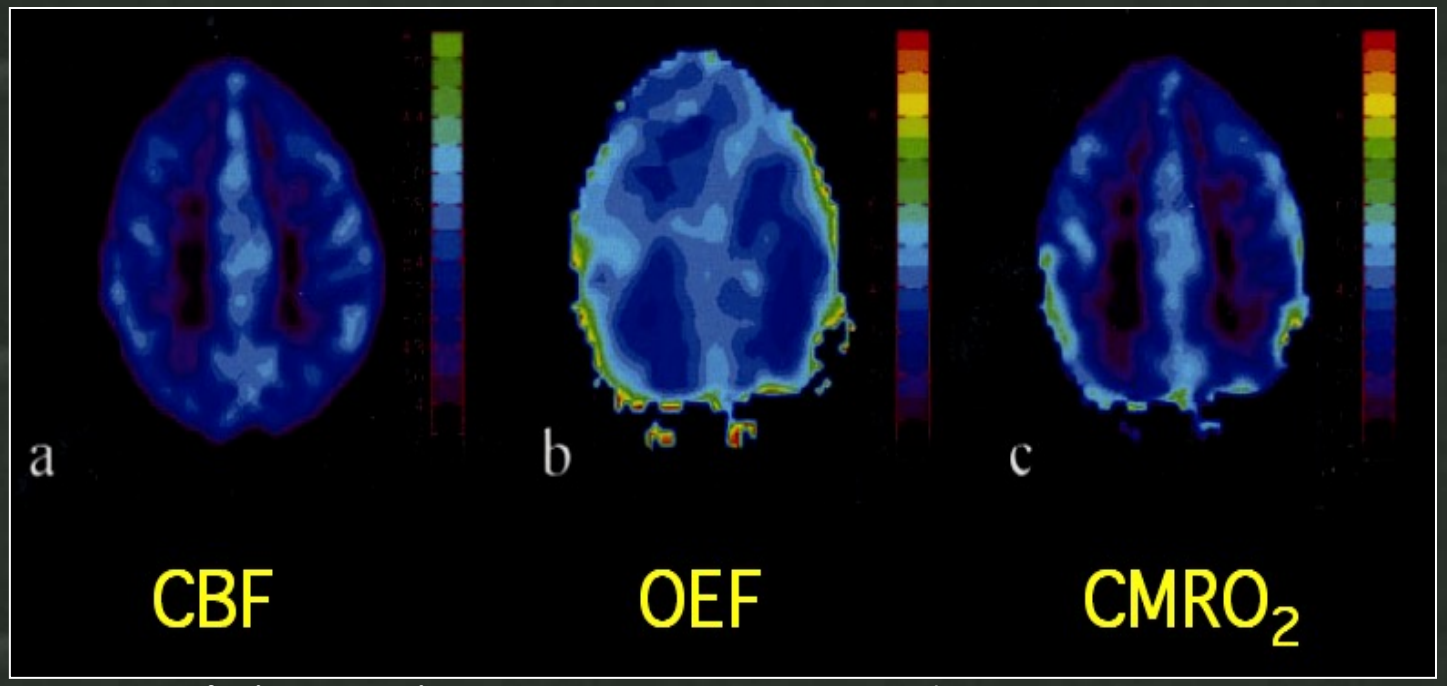
Simultaneous Perfusion and BOLD imaging during graded visual activation and hypercapnia

Hoge et al, PNAS 96: 9403-9408 (1999)

Interpretation

Baseline $CMRO_2$?

Potential for baseline OEF and $CMRO_2$ information?

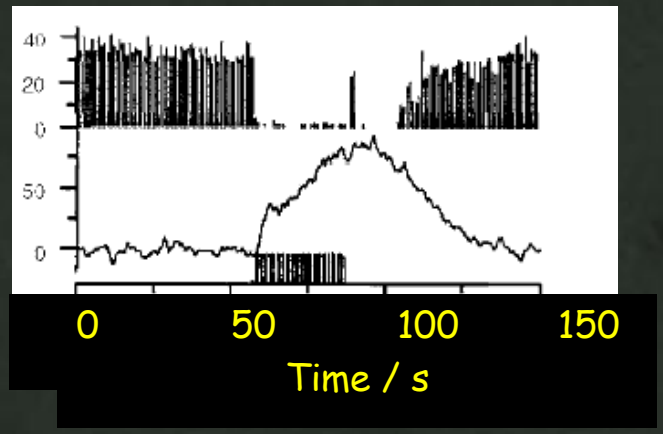


An, et al (2001), NMR in Biomedicine 14:441-447

Interpretation

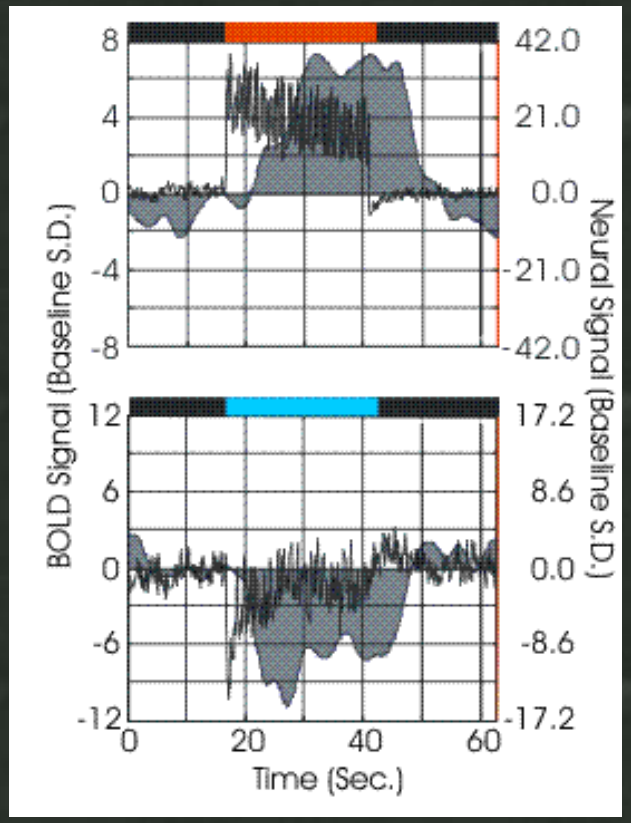
Inhibition and Decreases

Inhibition



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

Neg. BOLD



Schmuel et al. (2003) OHBM, 308

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