fMRI Course 2019: The Challenges and Controversies : Sheet1

Week	Week dates	Lecture Date	Time	Lecture 1 of week	Lecture 1 speaker	Lecture Date	Time	Lecture 2 of week	Lecture 2 speaker
3	June 17-27	June 18 (bldg 40)	2:00 PM	Hemodynamic Controversies and Challenges	Peter Bandettini	June 20 (bldg 40)	2:00 PM	Curious contrasts other than BOLD	Peter Bandettini
4	June 24-28	June 25 (bldg 40)	2:00 PM	The strategies, problems and challenges of noise removal: Why is noise removal so hard to solve?	Dan Handwerker	June 27 (bldg 40)	2:00 PM	The strategies, problems and challenges of fMRI noise removal: Figuring out the least bad ways to remove noise	Dan Handwerker
5	July 1-5	July 2 (bldg 40)	2:00 PM	Real time fMRI: challenges and uses	Michal Ramot			July 4th Holiday	
6	July 8-12	July 9 (bldg 40)	2:00 PM	The crisis of reproducibility in neuroimaging (small N vs big N)	Adam Thomas, Peter Bandettini	July 11 (bldg 40)	2:00 PM	Deep sources and other things you are not supposed to see with MEG	Fred Carver
7	July 15-19	July 16 (bldg 40)	2:00 PM	The clustering catastrophe & dead salmon controversey	Bob Cox	July 18 (bldg 49)	2:00 PM	Voodoo correlations and double dipping	Chris Baker
8	July 22-26	July 23 (bldg 40)	2:00 PM	What can high field do for fMRI and MRI? What can't it do?	Peter Bandettini	July 25 (bldg 40)	2:00 PM	Does TMS, tDCS, etc..really work?	Eric Wassermann
9	July 29-Aug 2	July 30 (bldg 40)	4:00 PM	Why isn't fMRI more clinically useful?	Peter Bandettini	Aug 1 (bldg 40)	10:00 AM	Why do we need to go back to local head gradient coils?	Andy Derbyshire
10	Aug 5-8	Aug 6 (bldg 40)	2:00 PM	Can we extract individual differences with fMRI? Can we go on to create "biomarkers?"	Emily Finn	Aug 8 (bldg 40)	2:00 PM	"Functional Connectivity:" What do BOLD correlations tell us about brain connectivity?	David Jangraw
11	Aug 12-16	Aug 13 (bldg 40)	2:00 PM	Is multi-modal integration really useful? If so, how?	Pete Molfese	Aug 15 (bldg 49)	2:00 PM	Do we have to deal with multiple comparisons in neuroimaging?	Gang Chen
12	Aug 19-23	Aug 20 (bldg 49)	2:00 PM	Motion correction in structural and diffusion MRI: How has it and how could it help?	Joelle Sarlls	Aug 22 (bldg 49)	2:00 PM	The use of diffusion MRI for brain morphometry	Carlo Pierpaoli
13	Aug 26-30	Aug 27 (bldg 40)	1:00 PM	TBD	TBD	Sept 3 (bldg 40)	2:00 PM	Dynamic connectivity: Is it real? Is it useful? How do we extract information?	Javier Gonzalez-Castillo
14	Sept 2-6	Sept 3 (bldg 40)	2:00 PM	Is fMRI just cartography? Can we really understand the brain with fMRI?	Peter Bandettini	Sept 5 (bldg 40)	10:00 AM	The brain initiative and understanding the brain: where is it taking us and how can it be better?	Peter Bandettini, Francisco Pereira, and others

Hemodynamic Controversies and Challenges

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

BOLD Contrast

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

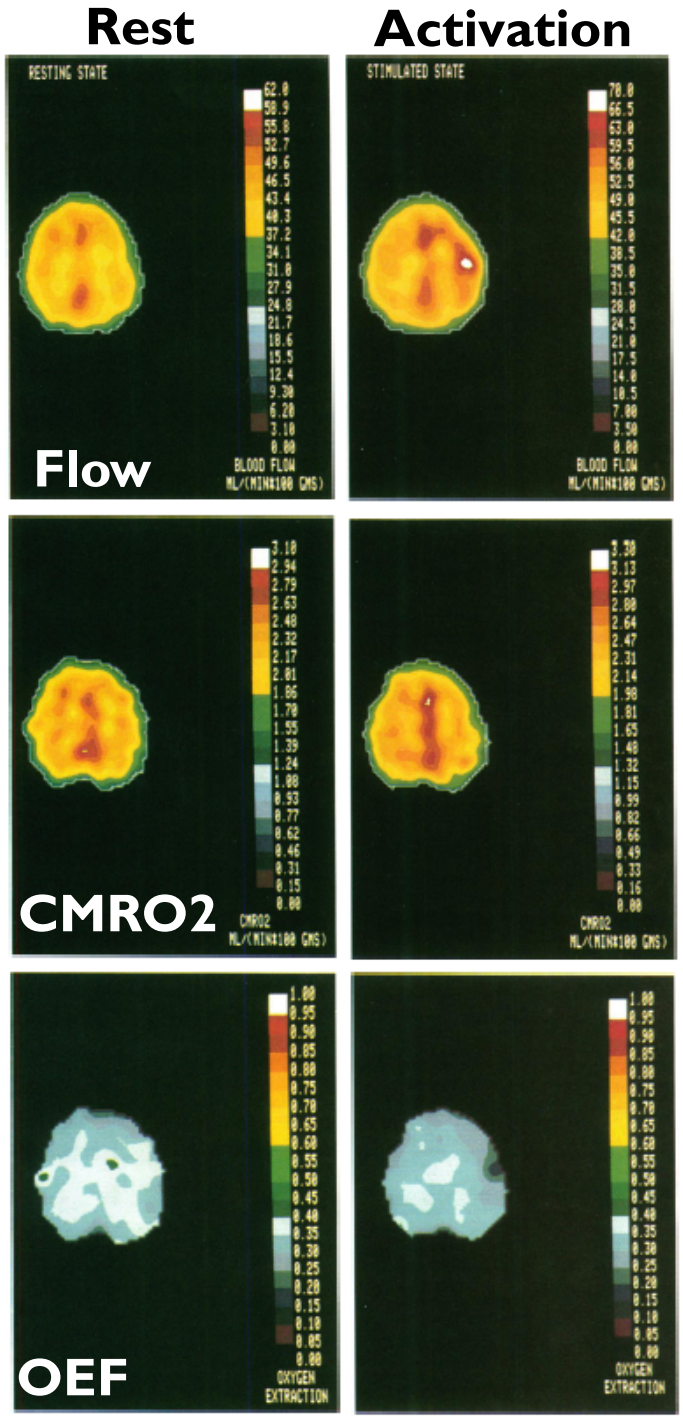
Deoxy-hemoglobin: paramagnetic
Oxy-hemoglobin: diamagnetic

↓

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

↓

Local Signal Increase in T2 and T2* - weighted sequences



Proc. Natl. Acad. Sci. USA
Vol. 83, pp. 1140–1144, February 1986
Neurobiology

Mechanisms of BOLD

Focal physiological uncoupling of cerebral blood flow and oxidative metabolism during somatosensory stimulation in human subjects

(positron emission tomography)

PETER T. FOX*†‡ AND MARCUS E. RAICHLE*†

*Department of Neurology and Neurological Surgery (Neurology), †Department of Radiology (Radiation Sciences), and The McDonnell Center for Studies of Higher Brain Function, Washington University School of Medicine, St. Louis, MO 63110

Communicated by Oliver H. Lowry, October 7, 1985

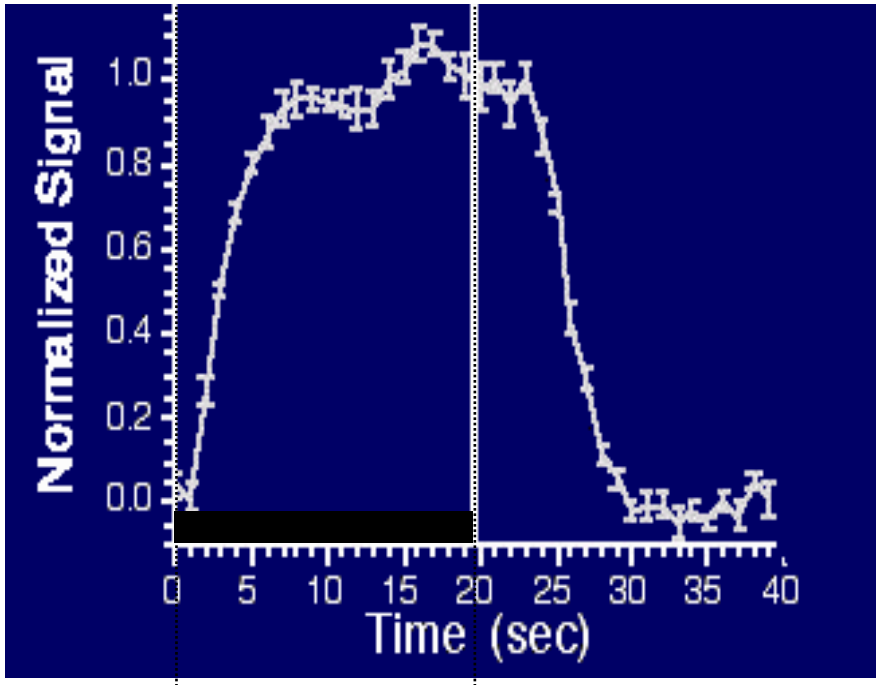
FIG. 1. Physiological uncoupling of brain blood flow and metabolism. (*Left*) Resting-state measurements. (*Right*) Stimulated-state measurements (unilateral vibrotactile stimulation of the fingers). All images are from a single subject's scanning session and pass through the same brain plane. Color scales are linear with the maxima set at a fixed multiple (1.6) of the global average, to facilitate visual comparisons (16). During specific somatosensory stimulation a marked focal increase in CBF (29% of mean, nine subjects, three trials per subject) was produced in the contralateral sensorimotor cortex. The observed increase in the $CMRO_2$ was much smaller (5% of mean, nine subjects, three trials per subject) and failed to attain significance. This physiological uncoupling of CBF and $CMRO_2$ flow produced a highly significant decrease in the local OEF (−19% of mean), indicating that tissue Po_2 (and probably pH) rose during stimulation. Note that, although the data were analyzed as contralateral/ipsilateral ratios (see text and Tables 1–4), the disparity between blood flow and metabolism was evident from the raw data and was not dependent on a particular strategy of analysis.

OEF ↓

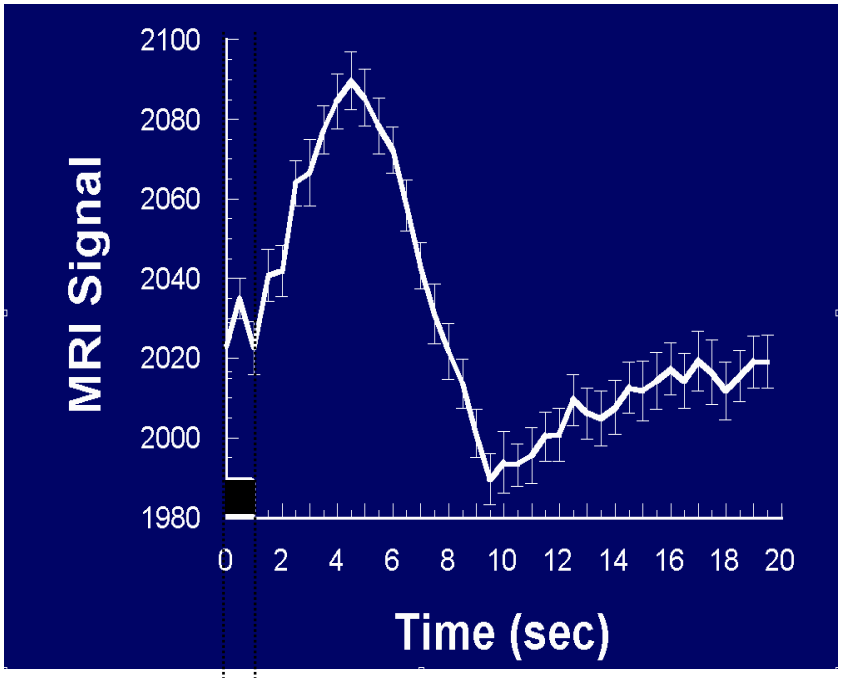
Therefore…

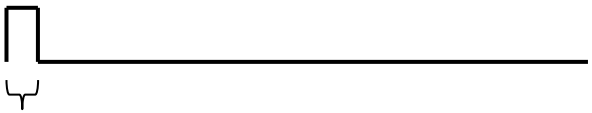
Blood PO_2 ↑

Controversy

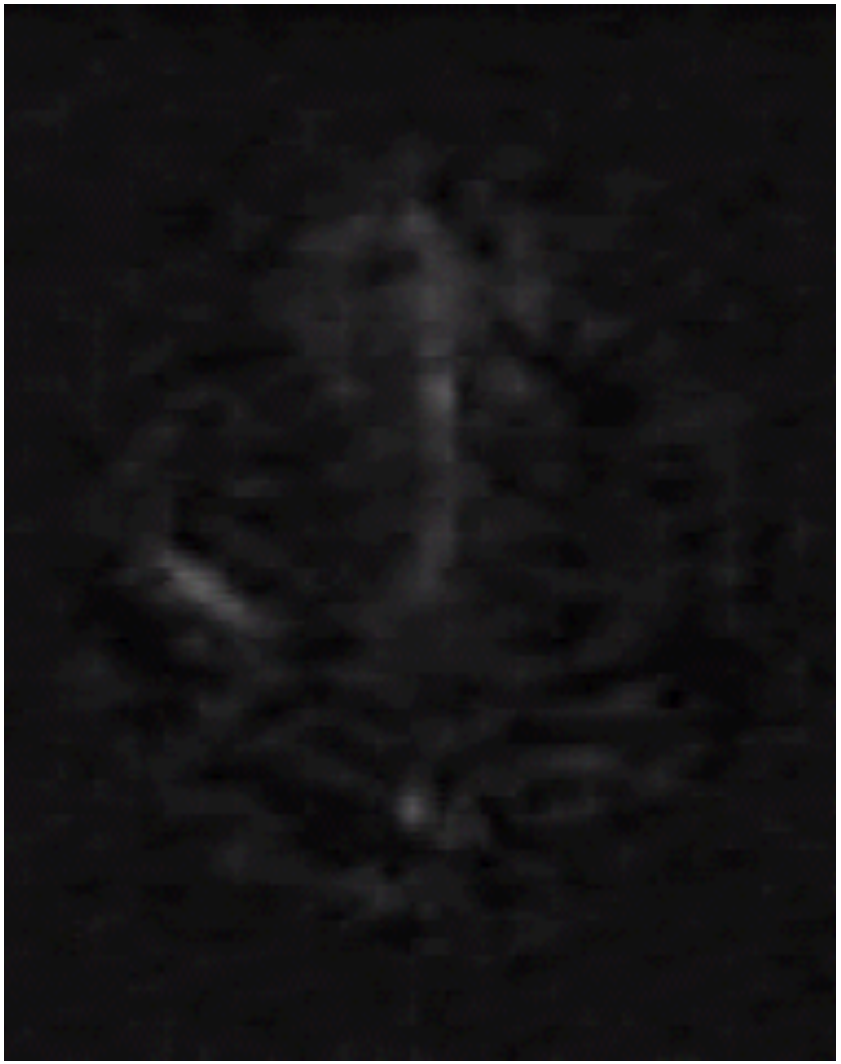

Normalized Signal
1.0
0.8
0.6
0.4
0.2
0.0
0
5
10
15
20
25
30
35
40
Time (sec)

task


MRI Signal
2100
2080
2060
2040
2020
2000
1980
0
2
4
6
8
10
12
14
16
18
20
Time (sec)

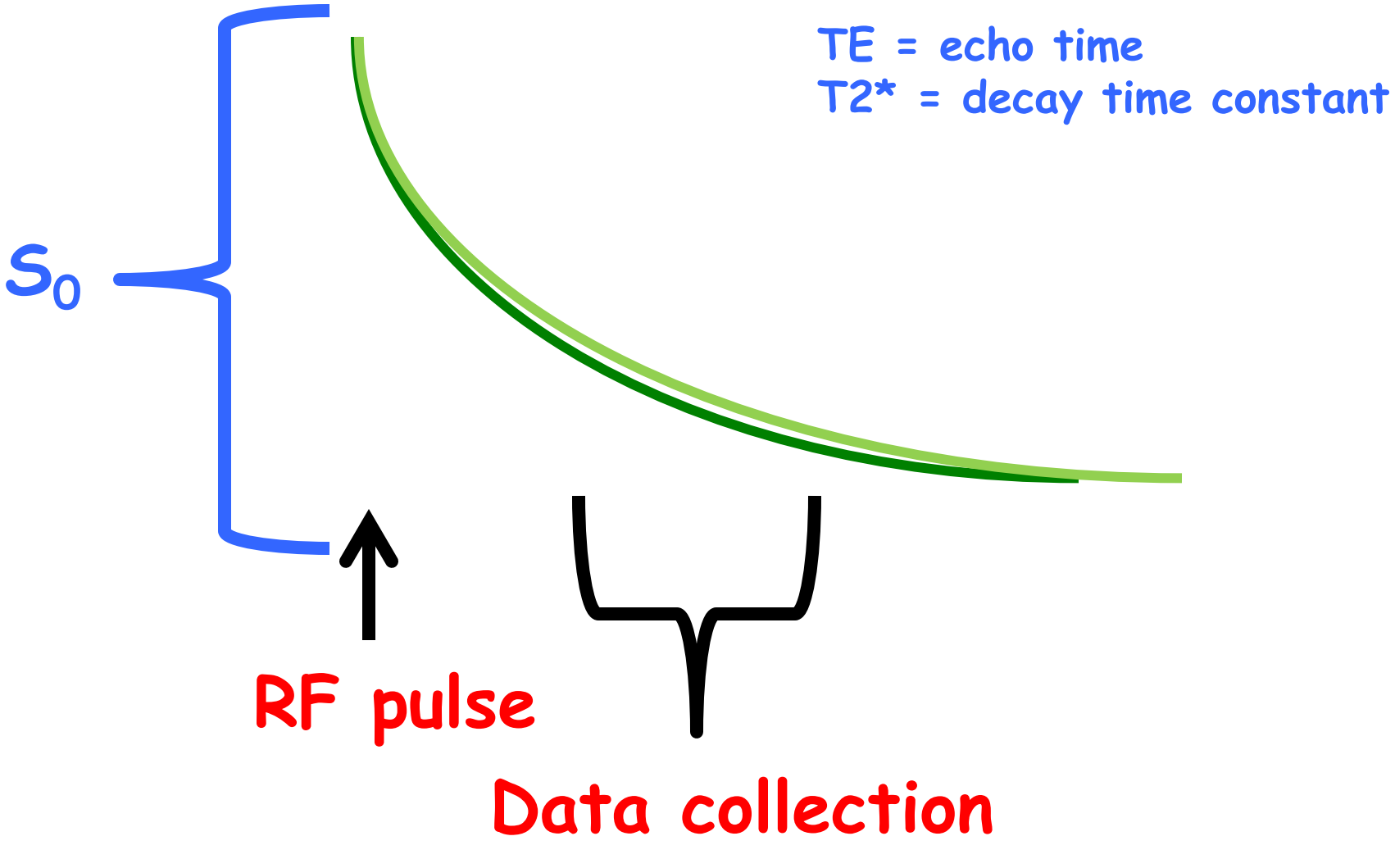


task

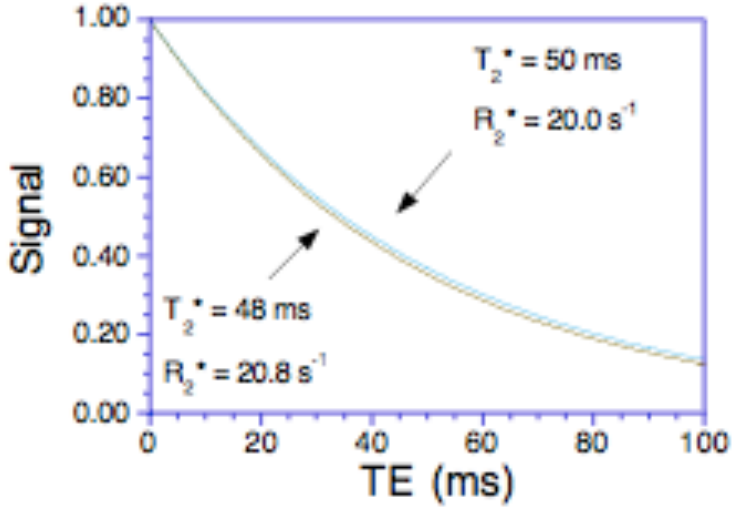


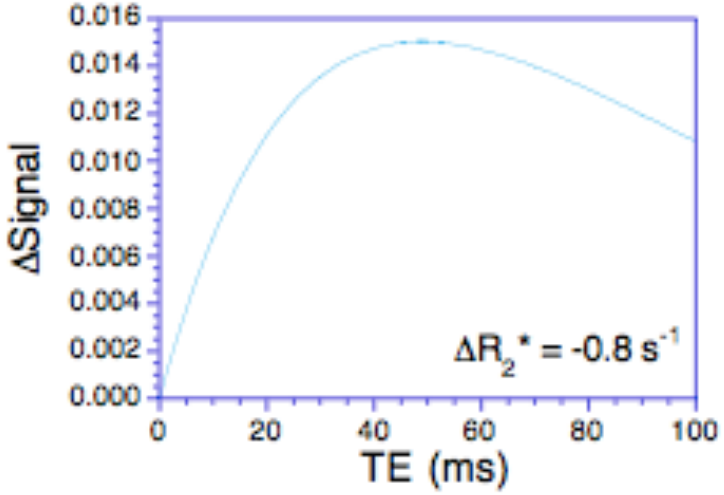
1991

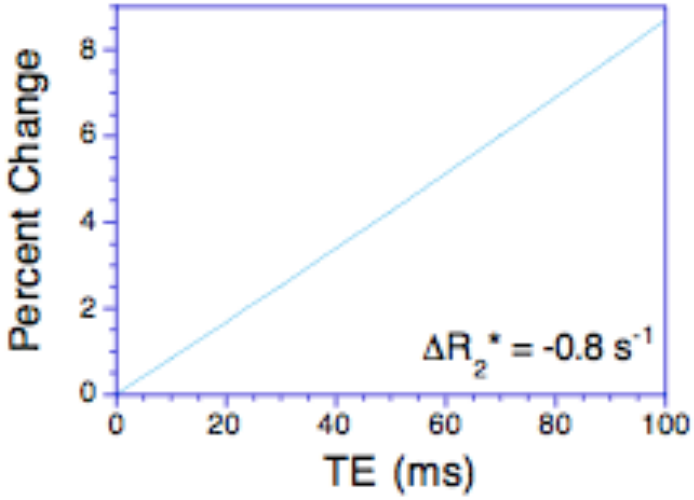
$$\text{Signal} = S_0 \, e^{-TE/T2^*}$$



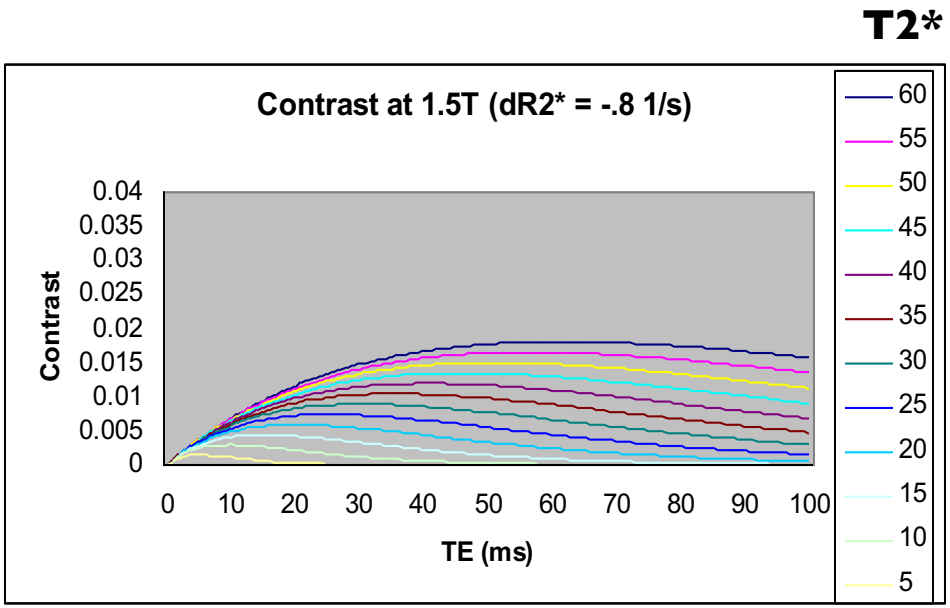
Characteristics of the BOLD signal: T2* effect.

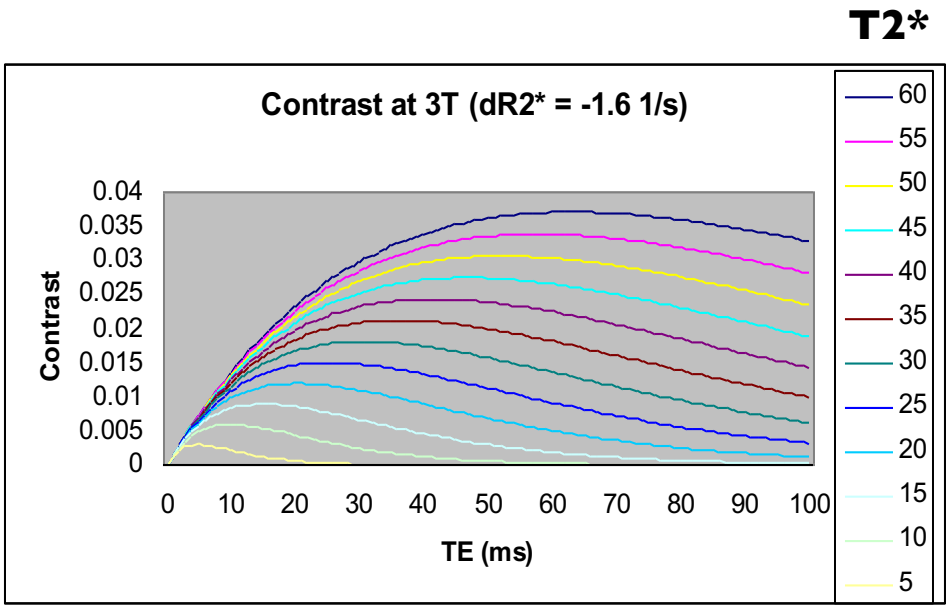


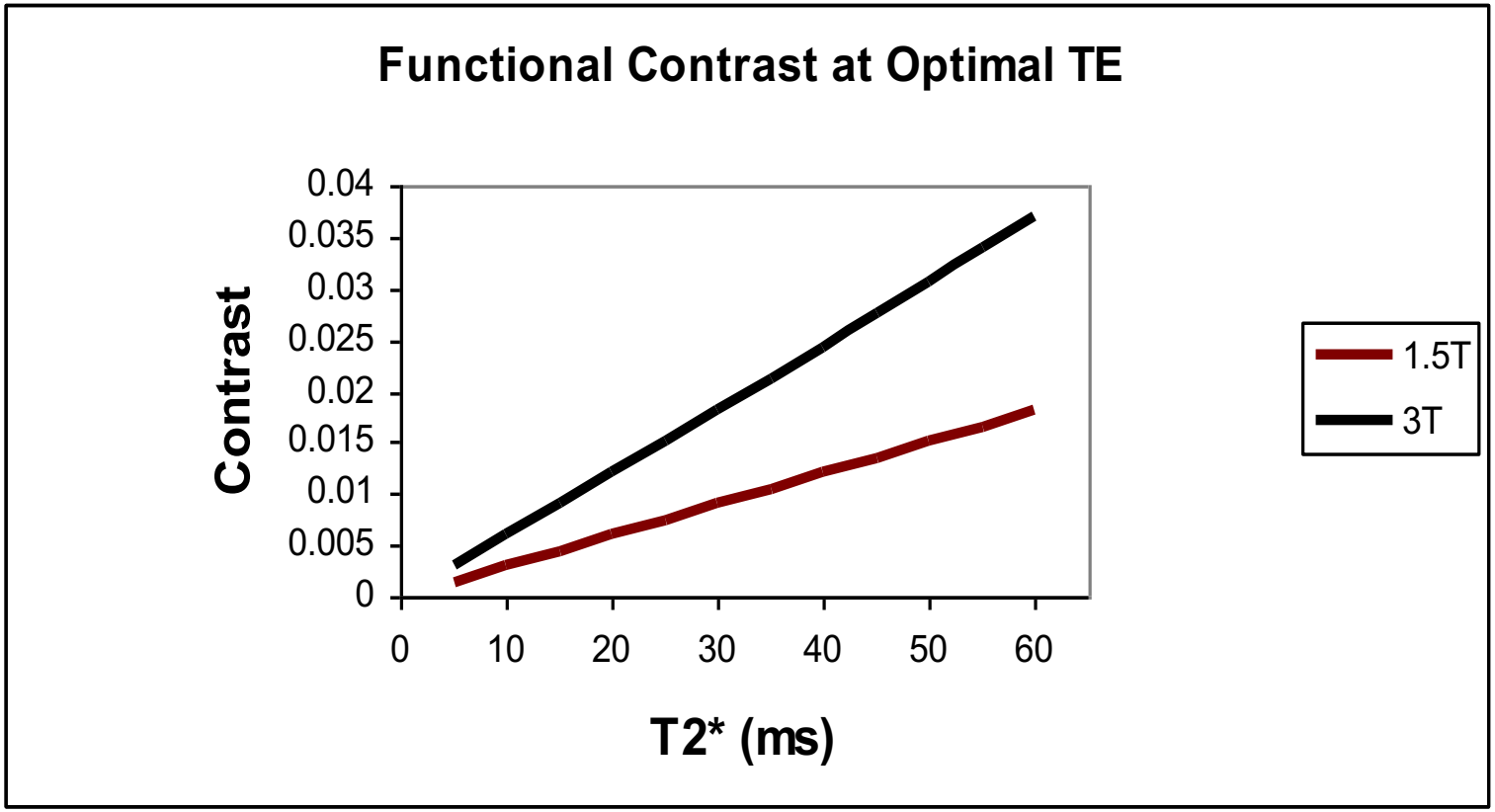




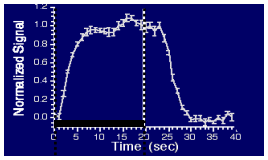
Contrast depends on:
activation-induced changes in T2* *and* resting T2*

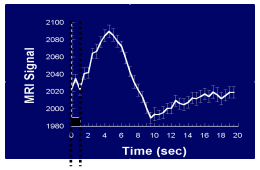





Functional Contrast at Optimal TE
Contrast
0.04
0.035
0.03
0.025
0.02
0.015
0.01
0.005
0
0
10
20
30
40
50
60
T2* (ms)
1.5T
3T

Inhibition
Excitation
Frequencies
Transients
Spontaneous Activity





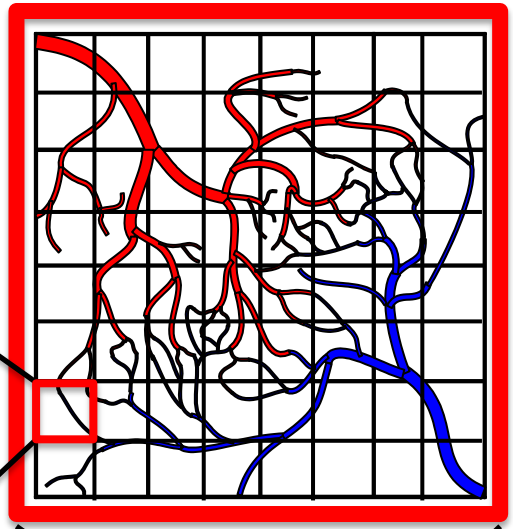
Magnitudes
Latencies
Correlations
Fluctuations
Transients
Undershoots

Neuronal Activation

Hemodynamics

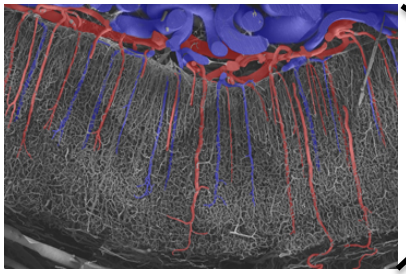
Measured Signal

voxel



tSNR ≅ 100
fCNR ≅ 10 to < 1

layer



Noise

Thermal
System
Motion
Physiologic
Respiration
Cardiac

region

Challenge

Hemodynamic Controversies and Challenges

Pulse sequence dependence

Temporal resolution

Nonlinearity

Pre and post undershoots

Negative signal changes

What are we missing?

Hemodynamic Controversies and Challenges

Pulse sequence dependence

Temporal resolution

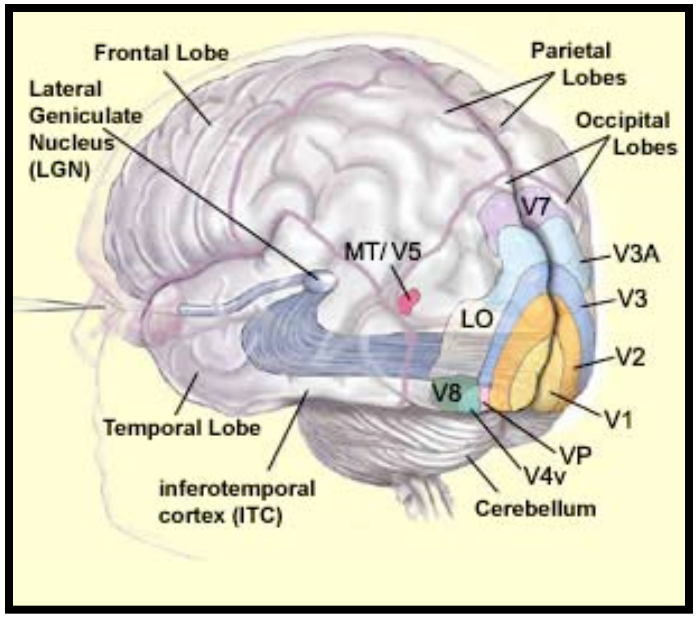
Nonlinearity

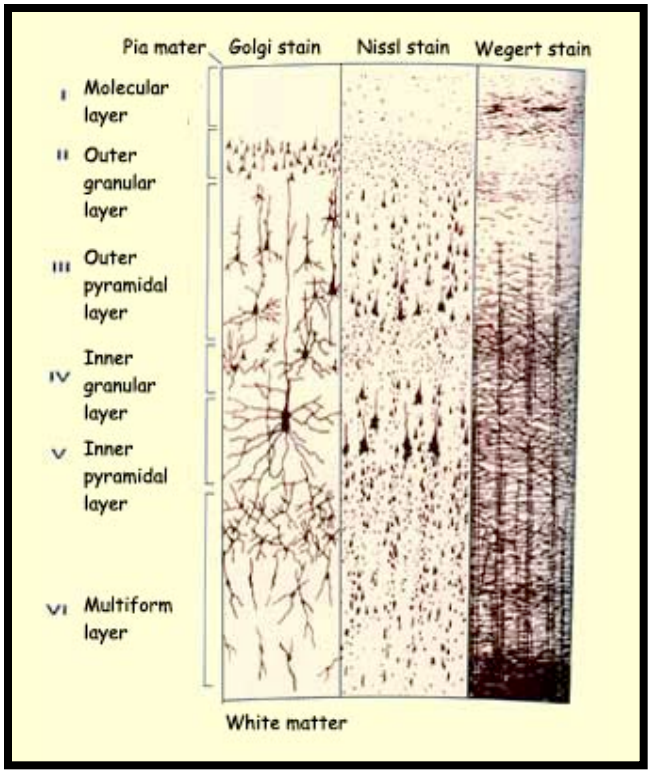
Pre and post undershoots

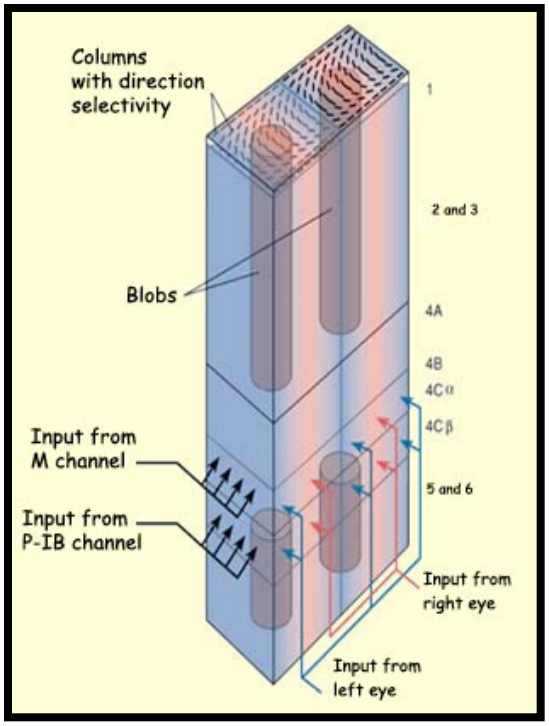
Negative signal changes

What are we missing?

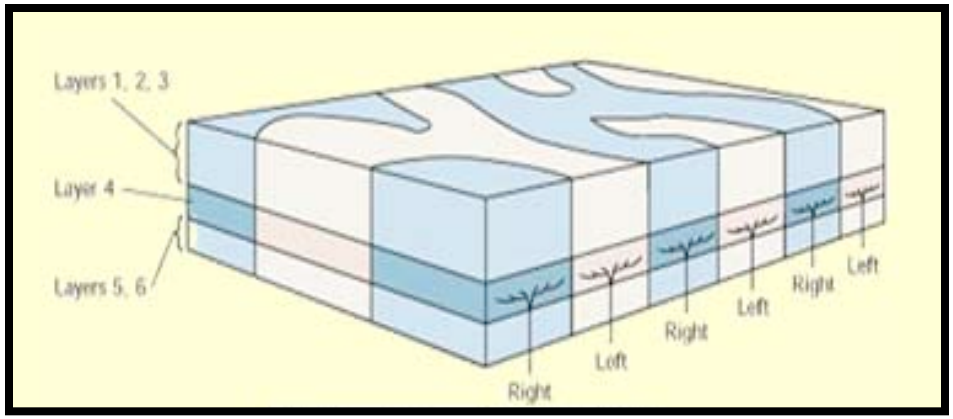
Visual Cortex Organization



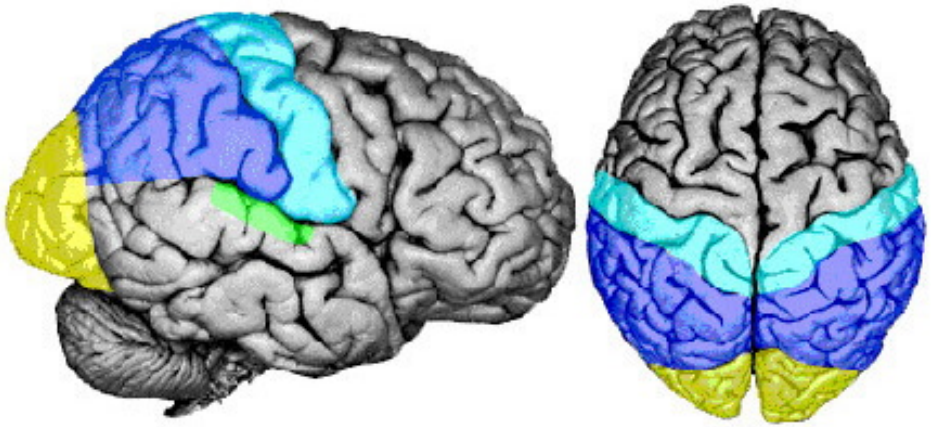




http://www.thebrain.mcgill.ca



BOLD

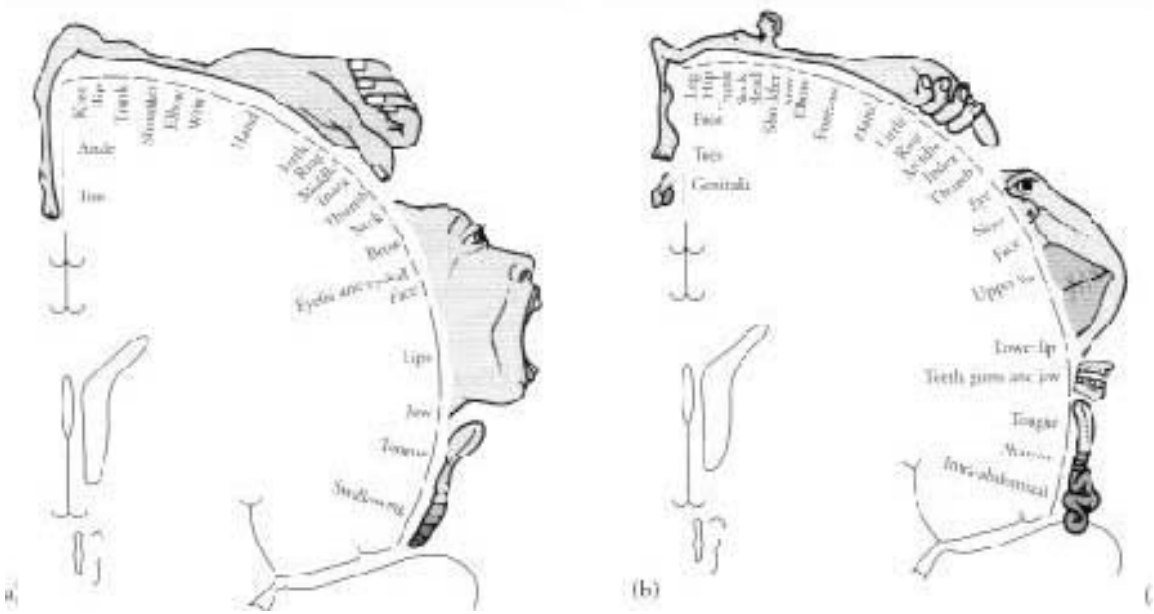


Parietal/
Somatosensory

Occipital/Vision

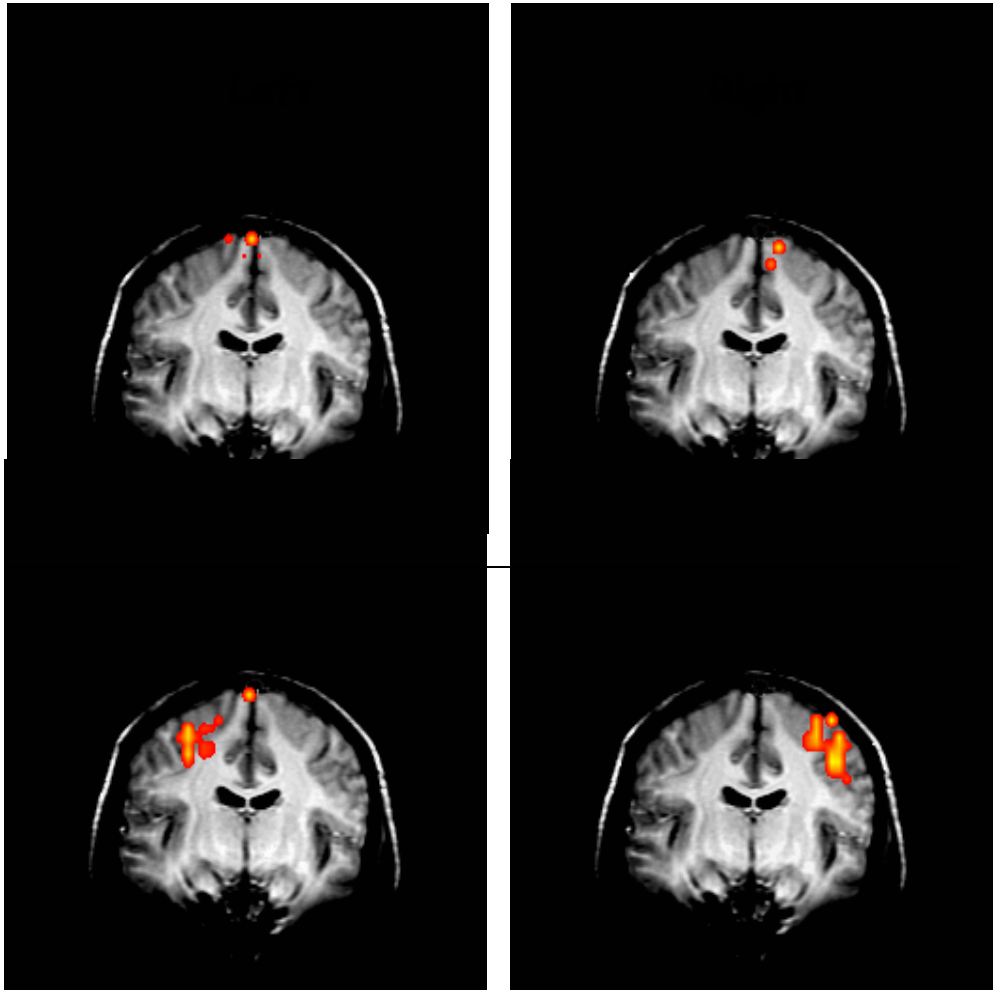
Parietal/
Association Area

Auditory

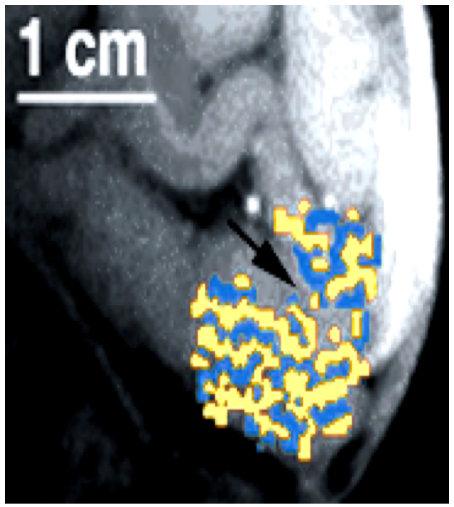


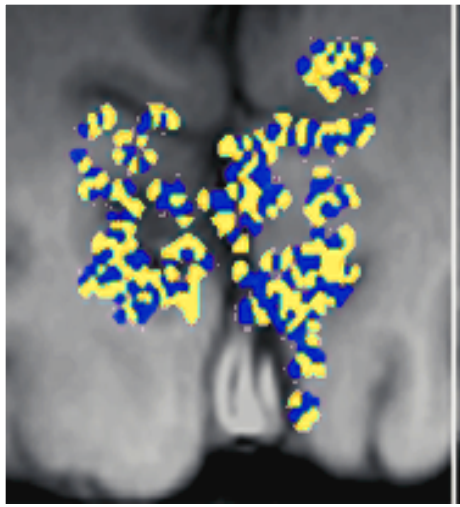
Toe movement

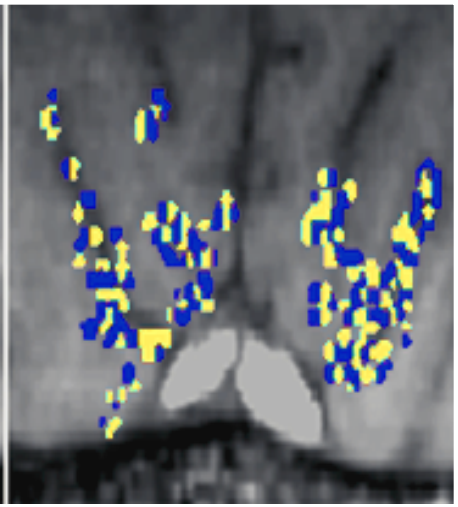
Finger movement



Ocular Dominance Column Mapping



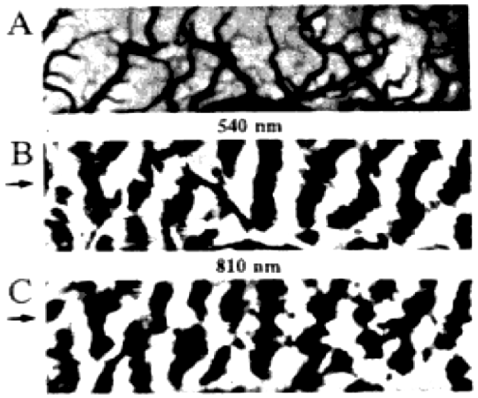




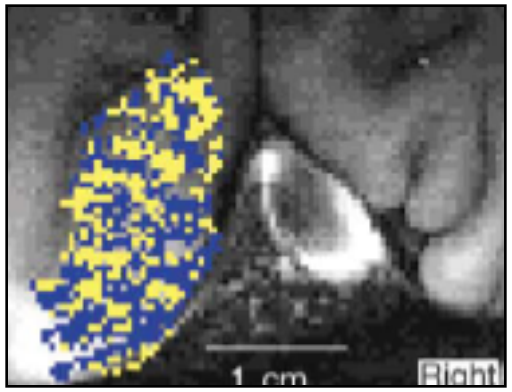
Menon, R. S., S. Ogawa, et al. (1997). J Neurophysiol 77(5): 2780-7.

0.54 x 0.54 in plane resolution

Optical Imaging



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



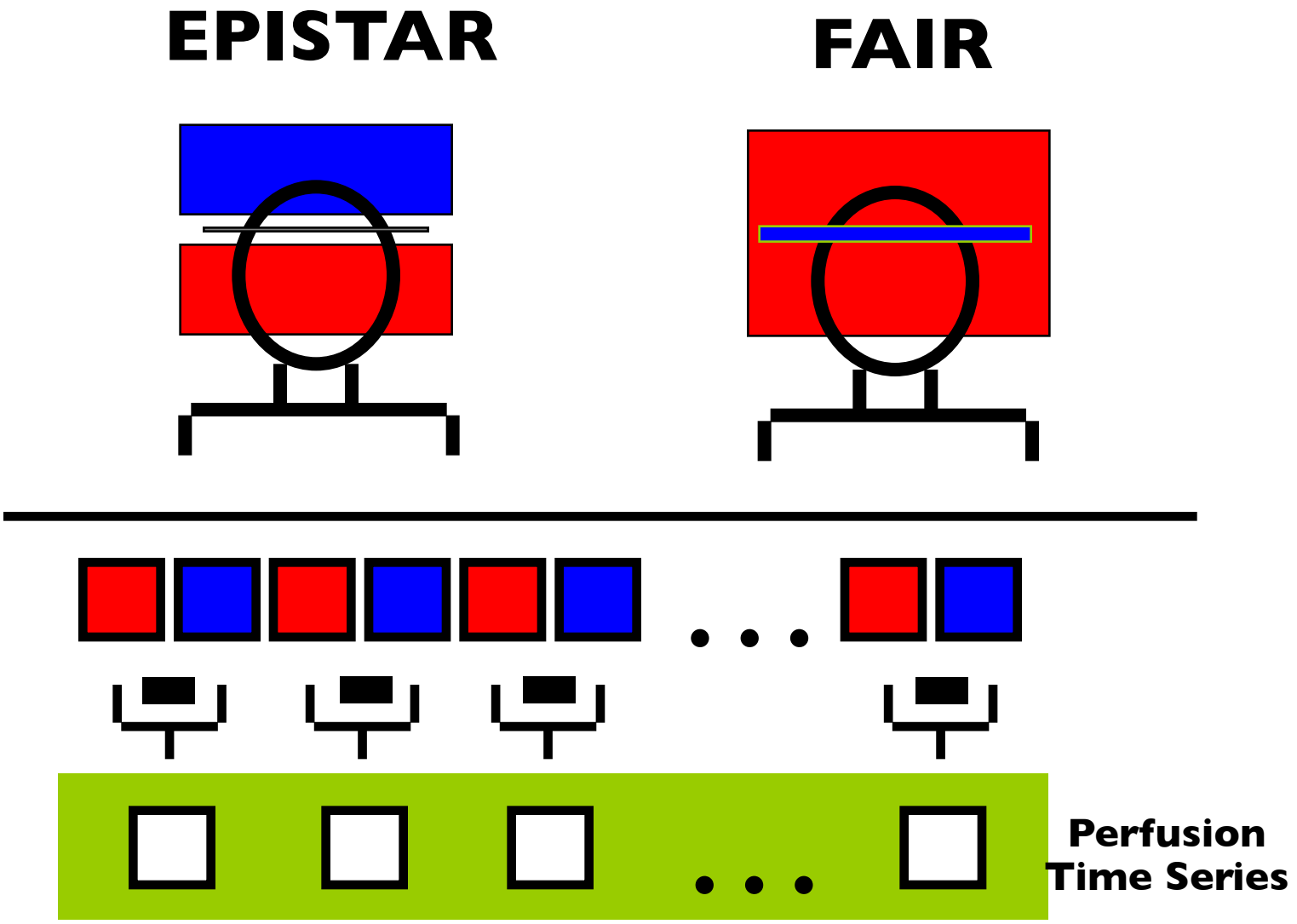
Cheng, et al. (2001) Neuron,32:359-374

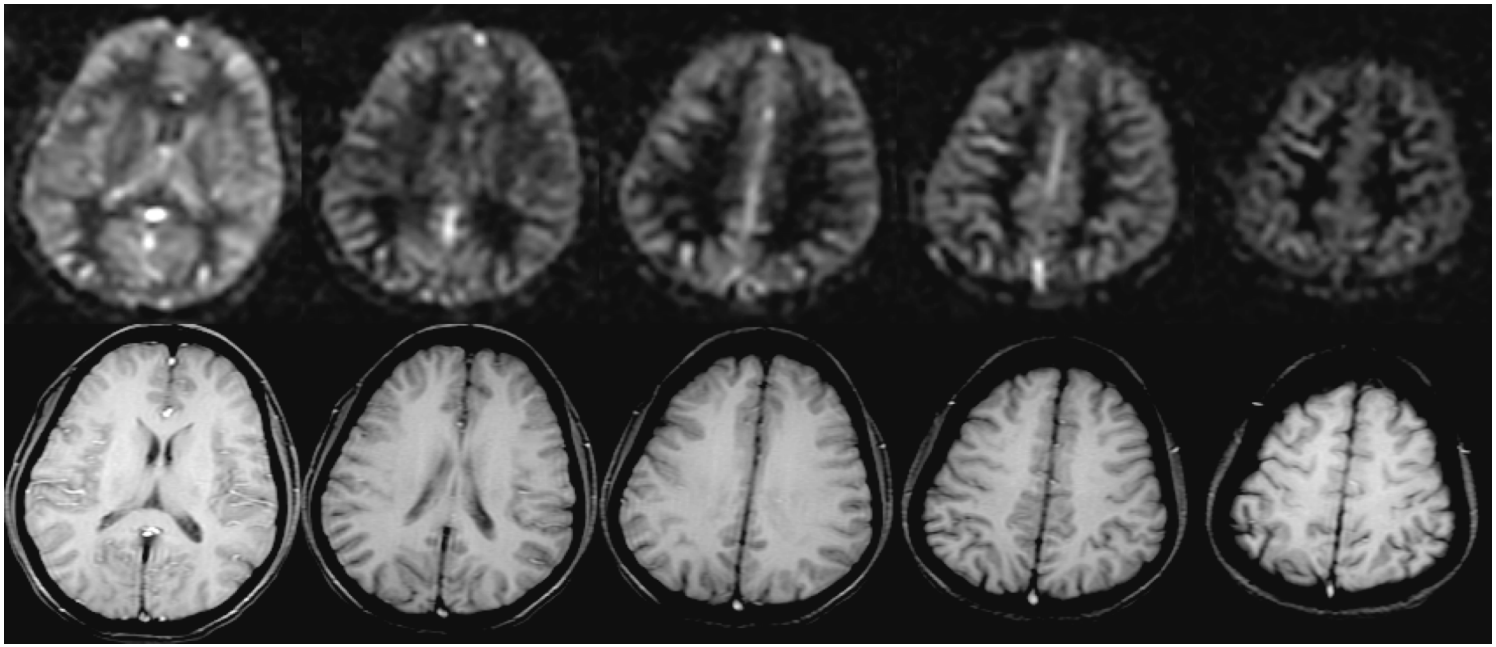
0.47 x 0.47 in plane resolution

Controversy

Perfusion

Perfusion Contrast





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.**

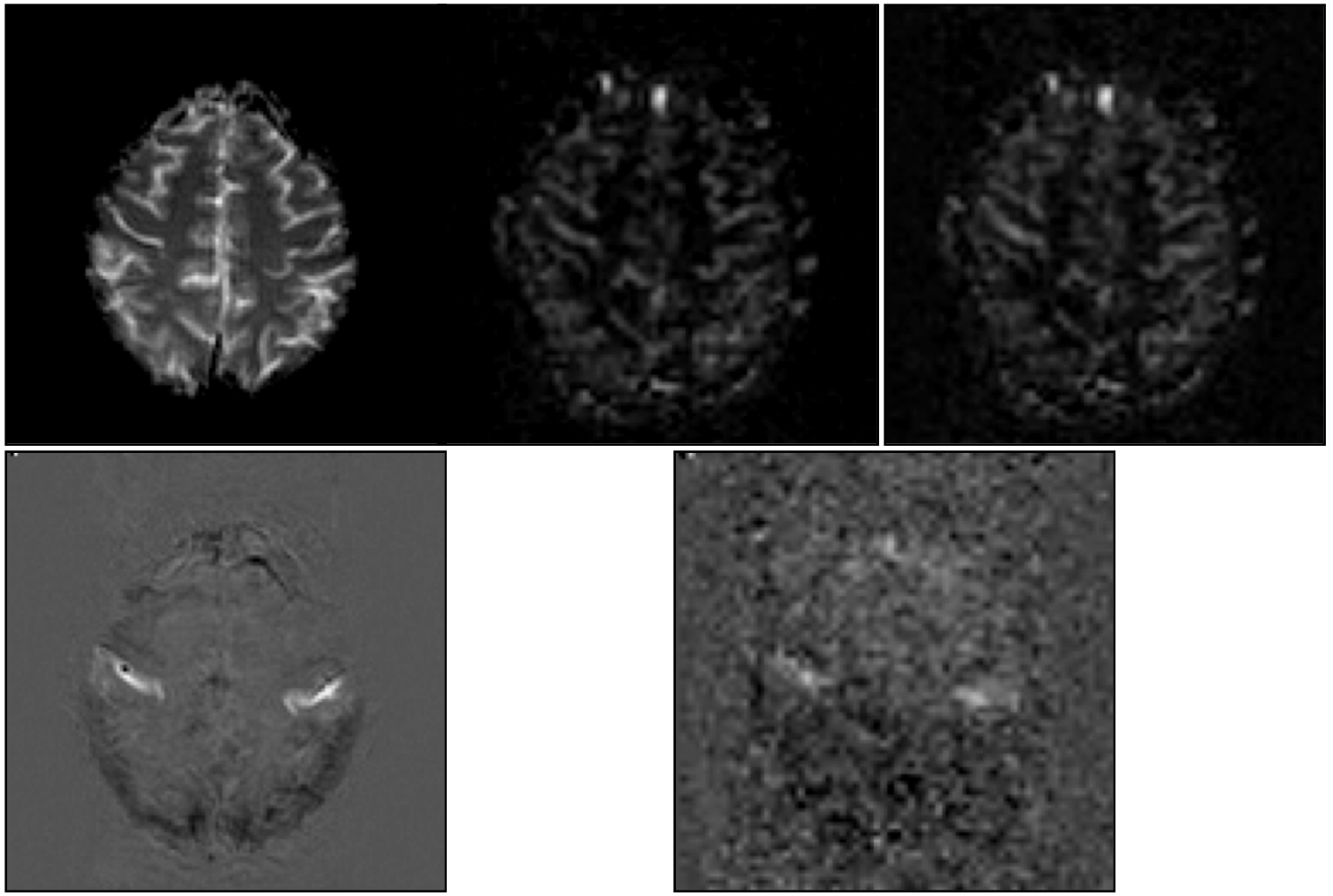
Edelman, R., Siewert, B. & Darby, D. (1994) "Qualitative mapping of cerebral blood flow and functional localization with echo planar MR imaging ans signal targeting with alternating radiofrequency (EPISTAR)." **Radiology 192, 1-8.**

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.**

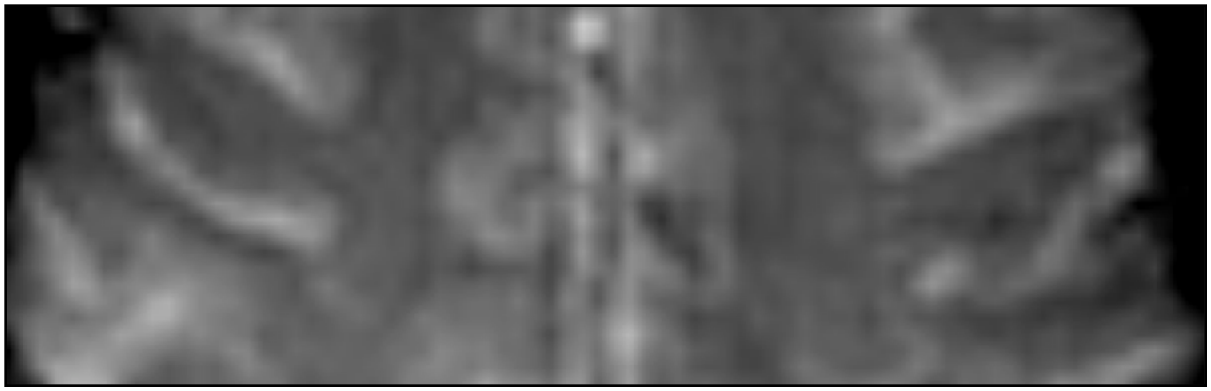
Perfusion

BOLD *Rest* *Activation*

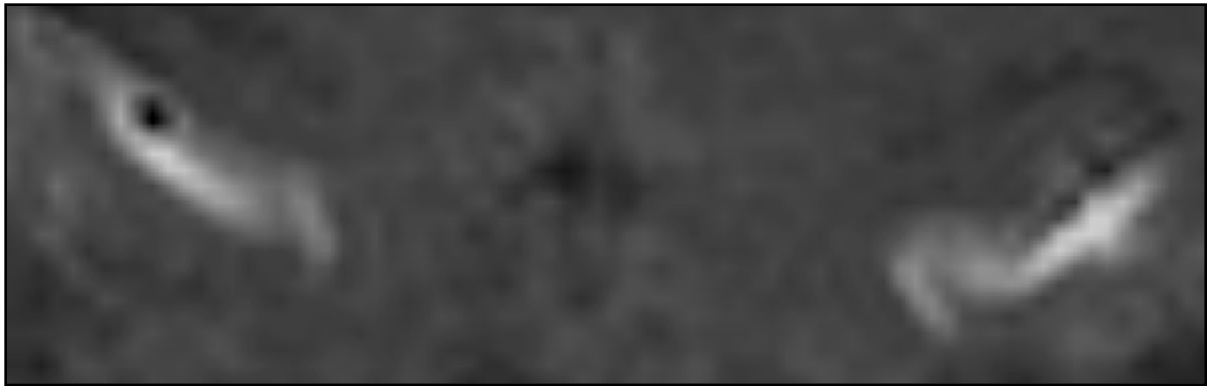


P. A. Bandettini, E. C. Wong, Magnetic resonance imaging of human brain function: principles, practicalities, and possibilities, *in* "Neurosurgery Clinics of North America: Functional Imaging" (M. Haglund, Ed.), p.345-371, W. B. Saunders Co., 1997.

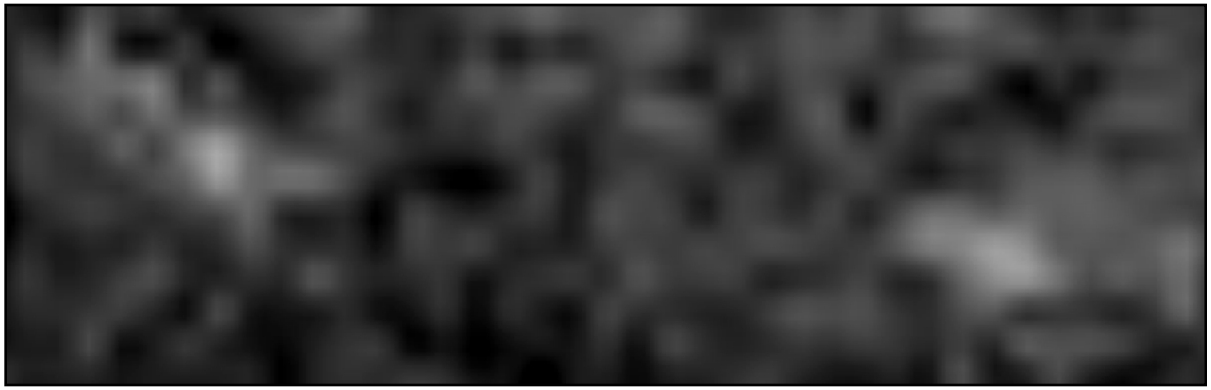
Anatomy



BOLD

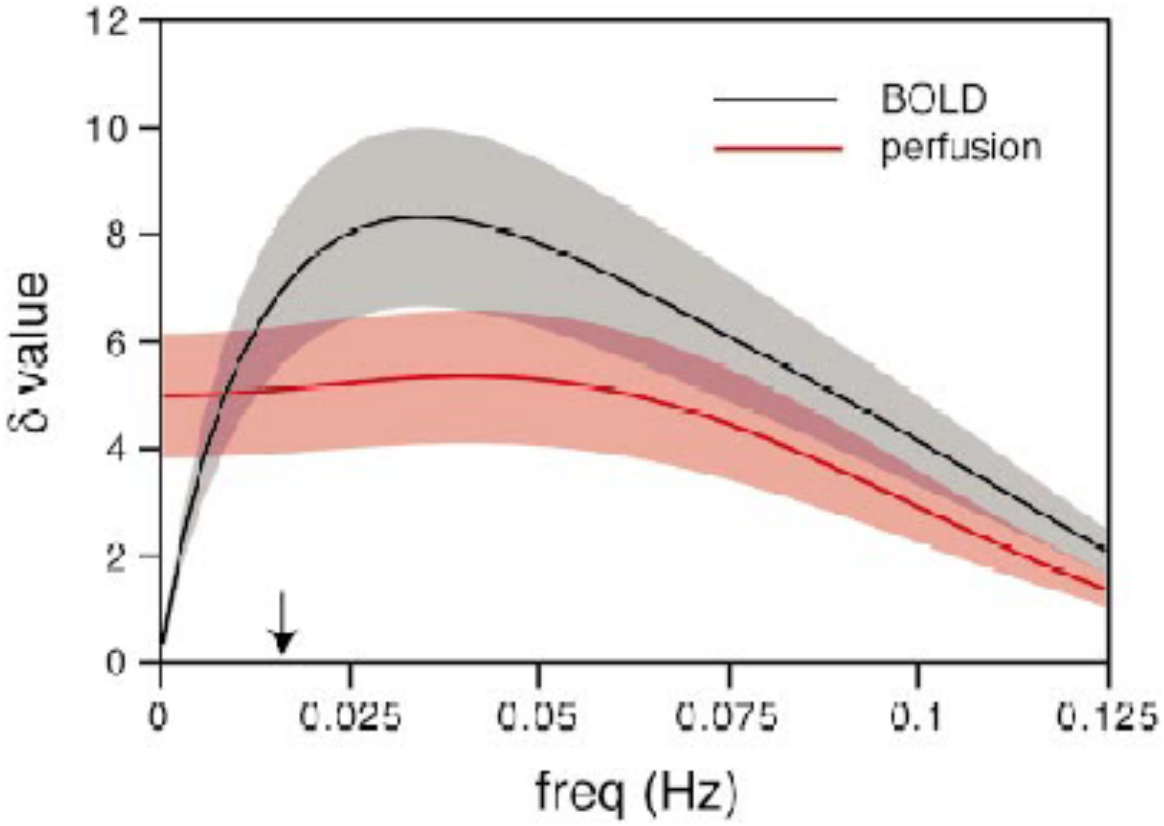


Perfusion



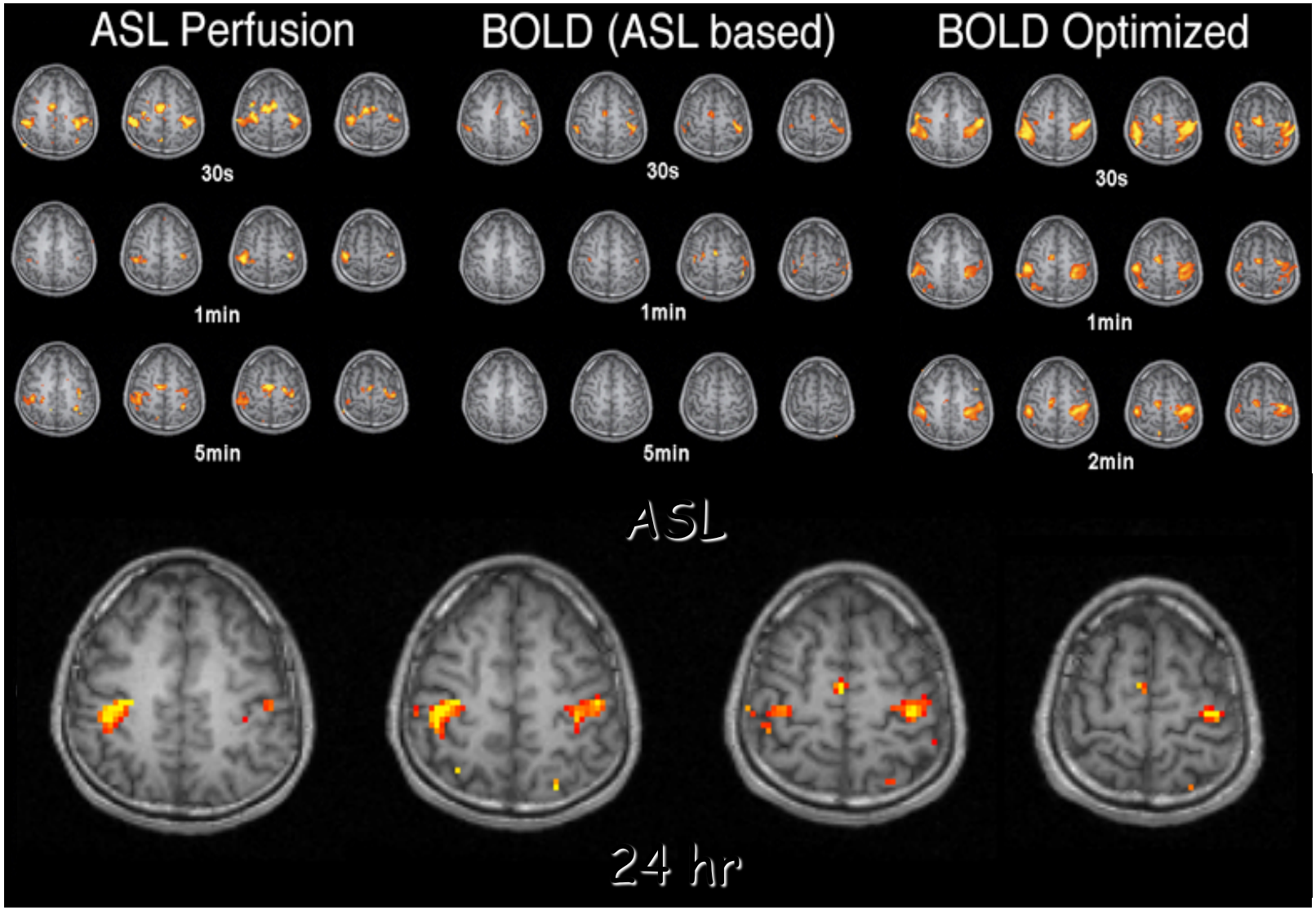
P. A. Bandettini, E. C. Wong, Magnetic resonance imaging of human brain function: principles, practicalities, and possibilities, *in* "Neurosurgery Clinics of North America: Functional Imaging" (M. Haglund, Ed.), p.345-371, W. B. Saunders Co., 1997.

Better than BOLD for long duration activation…



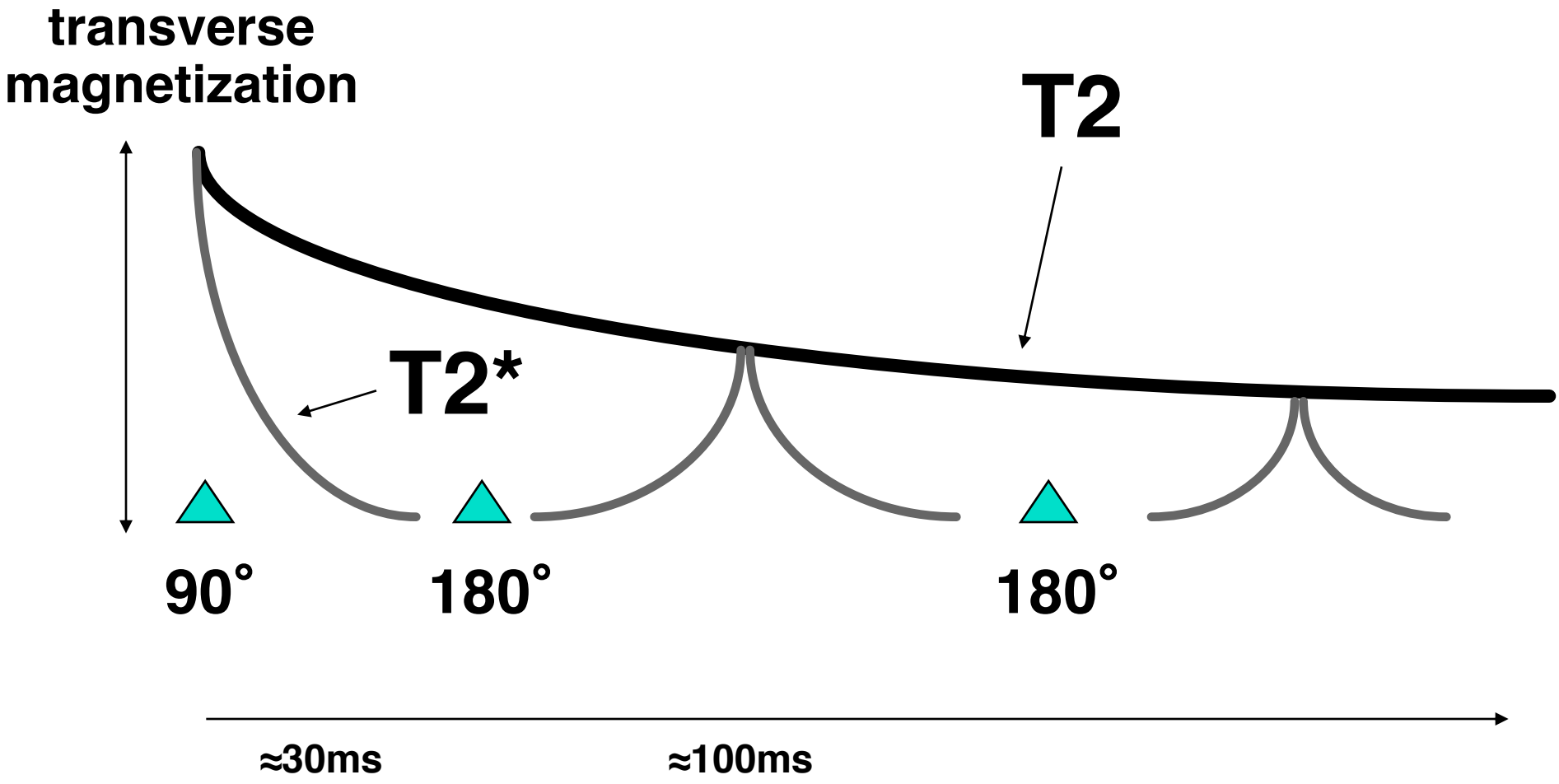
GK Aguirre et al, (2002) NeuroImage 15 (3): 488-500

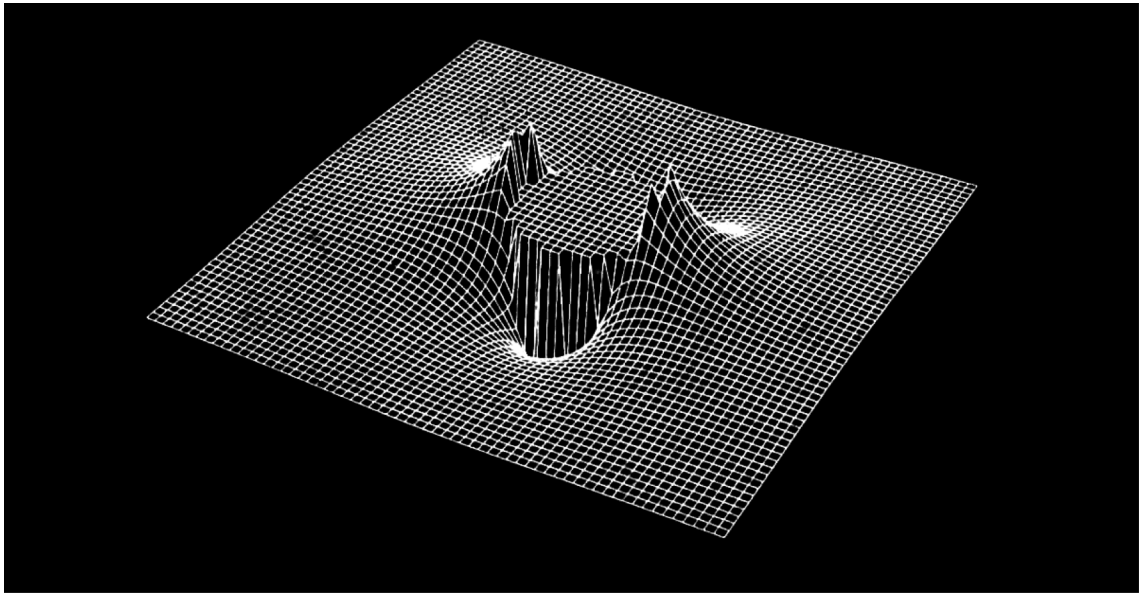
Perfusion vs. BOLD: Low Task Frequency

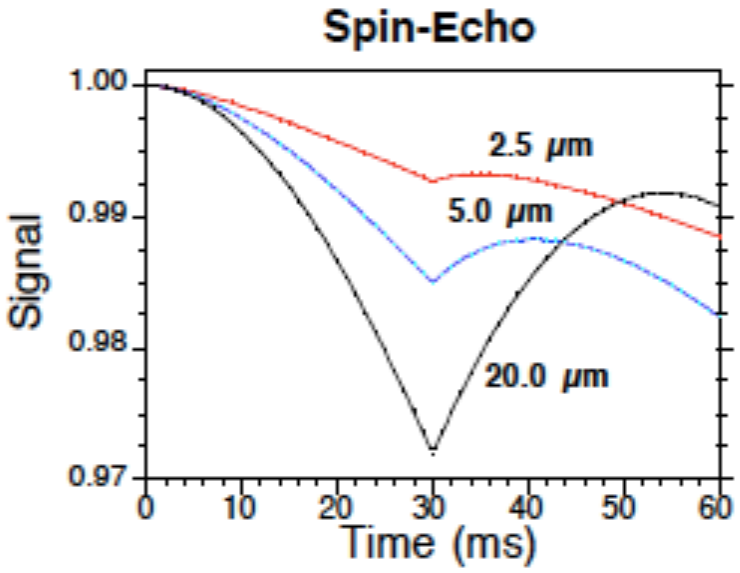


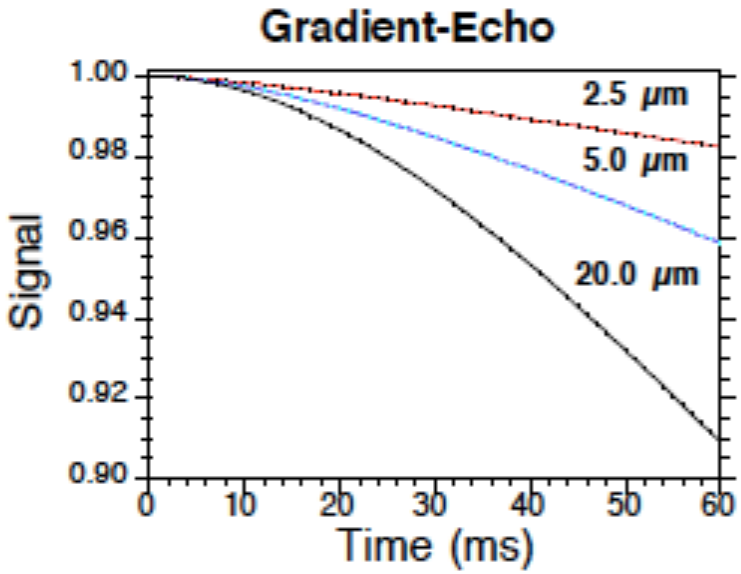
Spin-echo

Spin-echo vs Gradient-echo

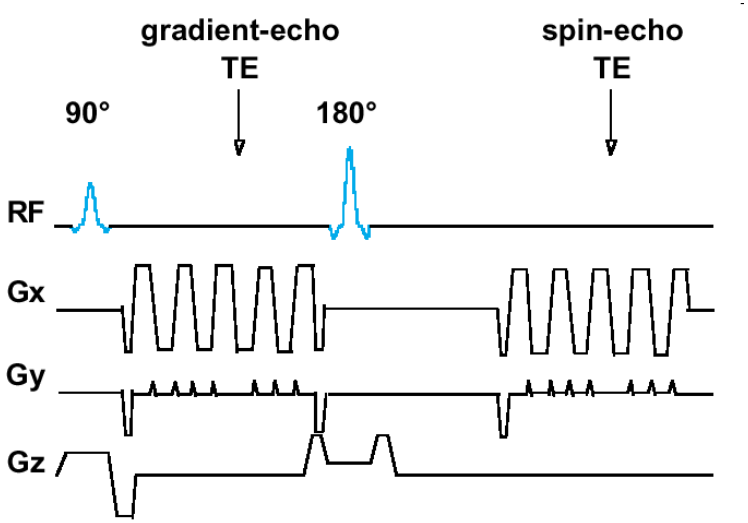


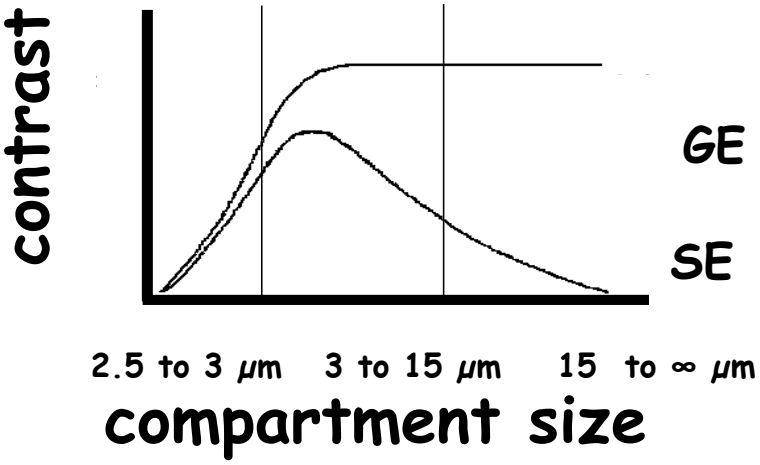



Spin-Echo
Signal
1.00
0.99
0.98
0.97
0
10
20
30
40
50
60
Time (ms)
2.5 μm
5.0 μm
20.0 μm


Gradient-Echo
Signal
1.00
0.98
0.96
0.94
0.92
0.90
0
10
20
30
40
50
60
Time (ms)
2.5 μm
5.0 μm
20.0 μm

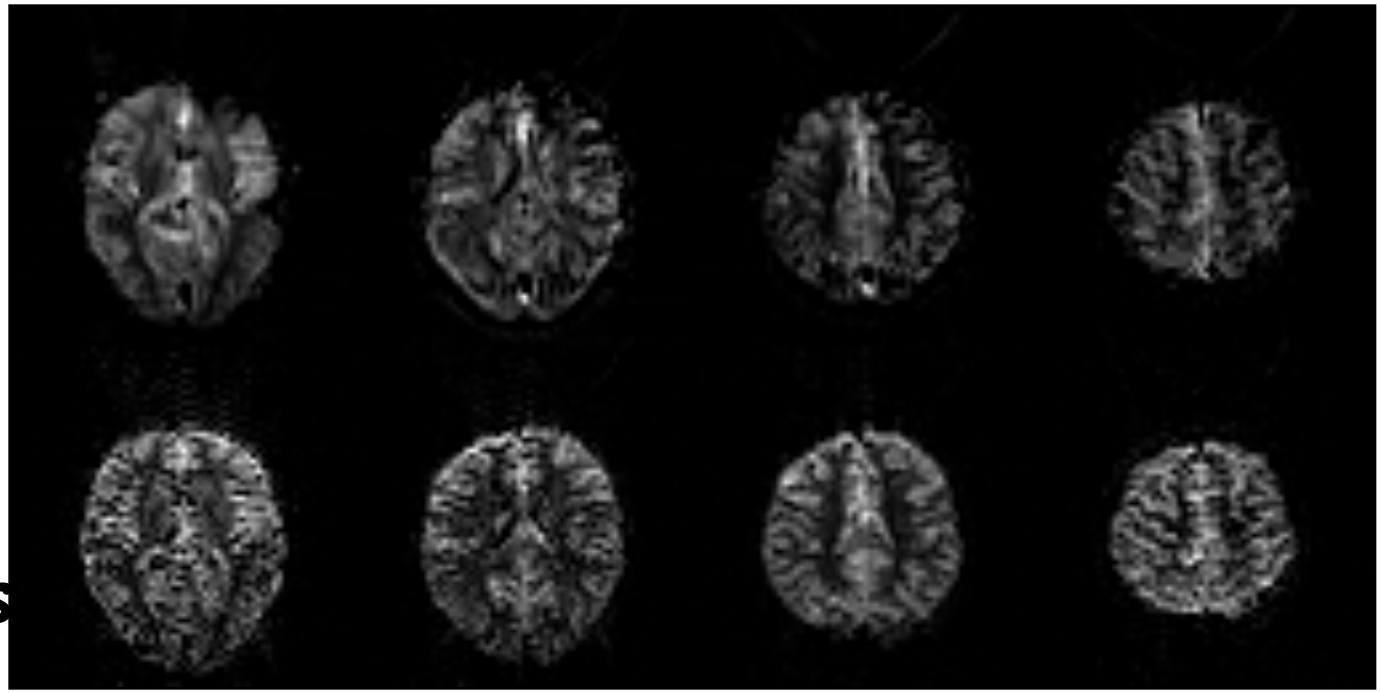
Bolus Injection of Gadolinium

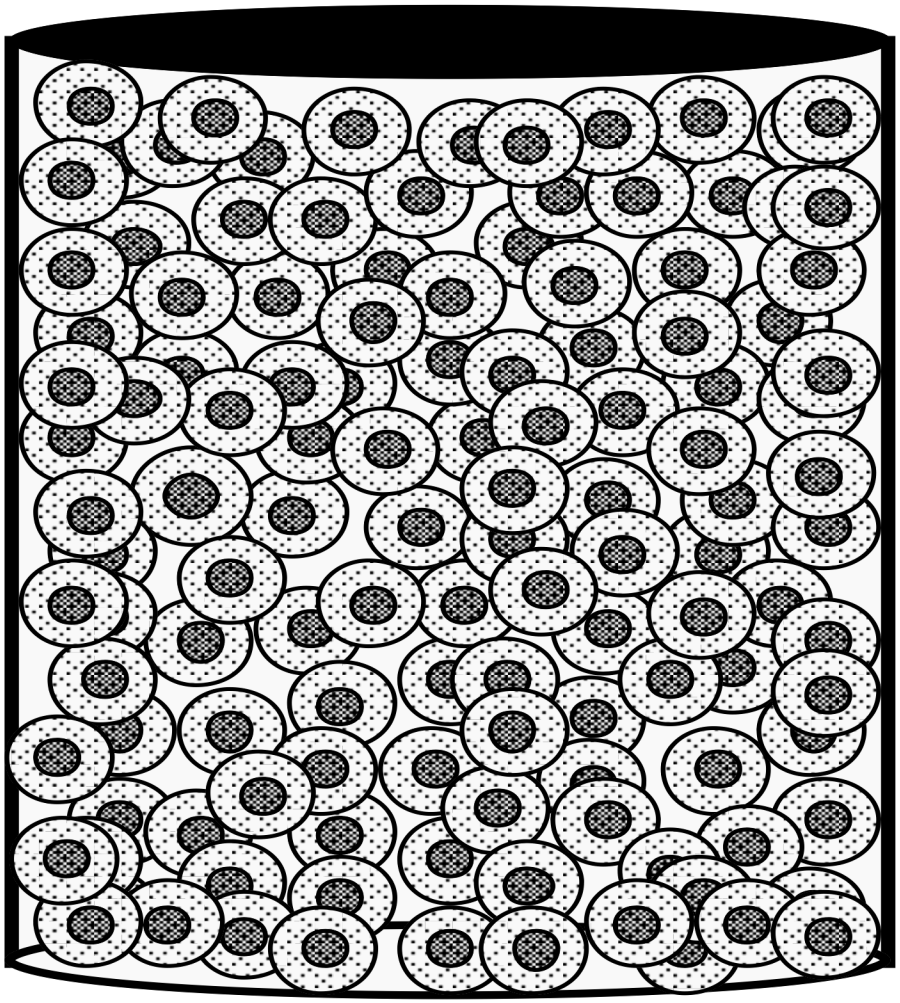




GE
TE = 30 ms

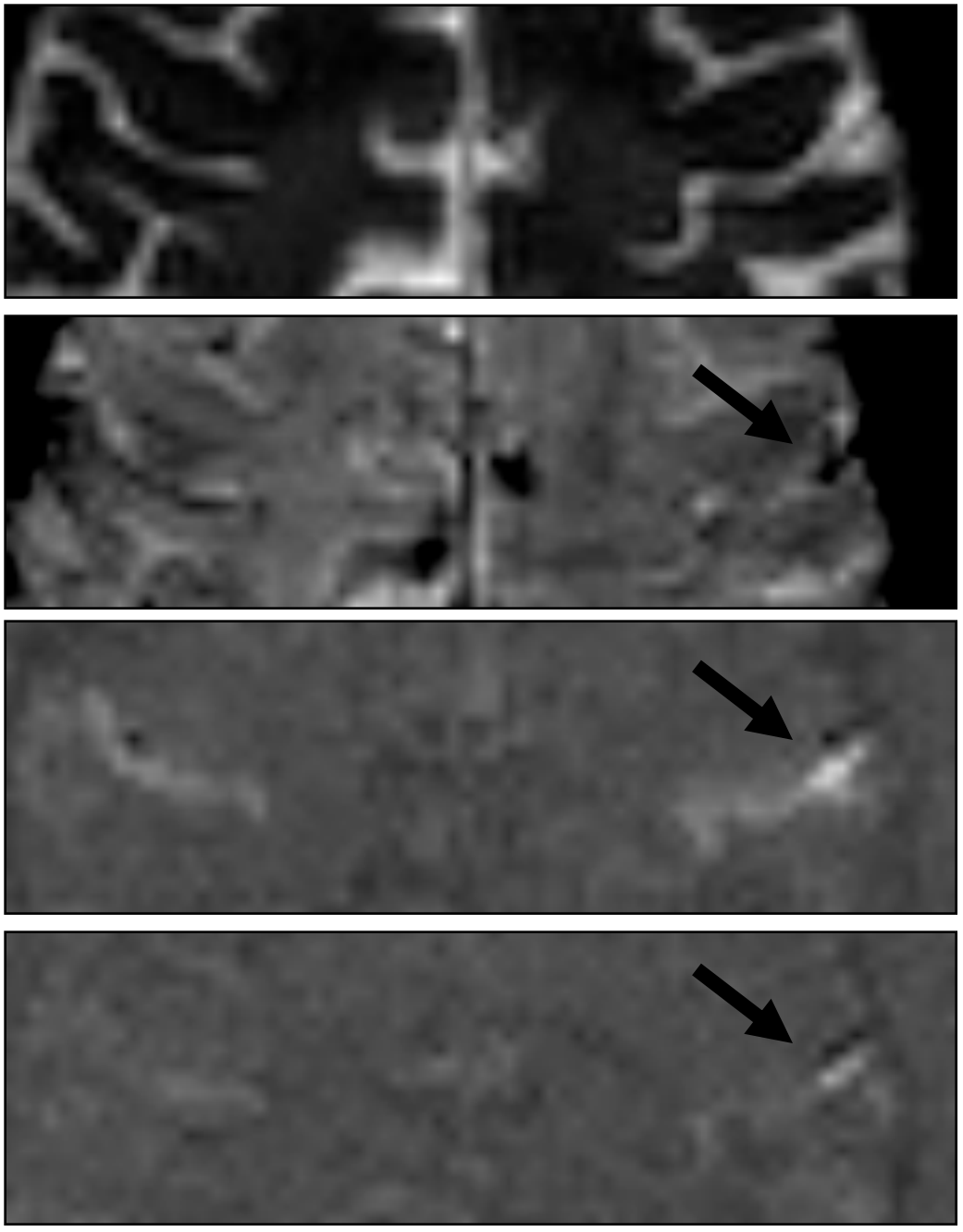
SE
TE = 110 ms





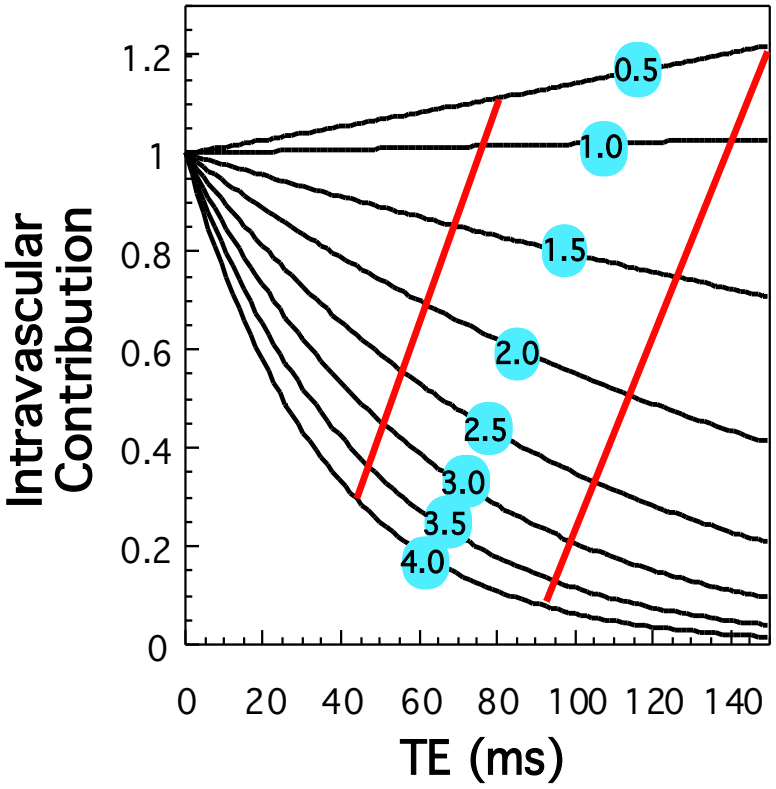
Controversy

3T

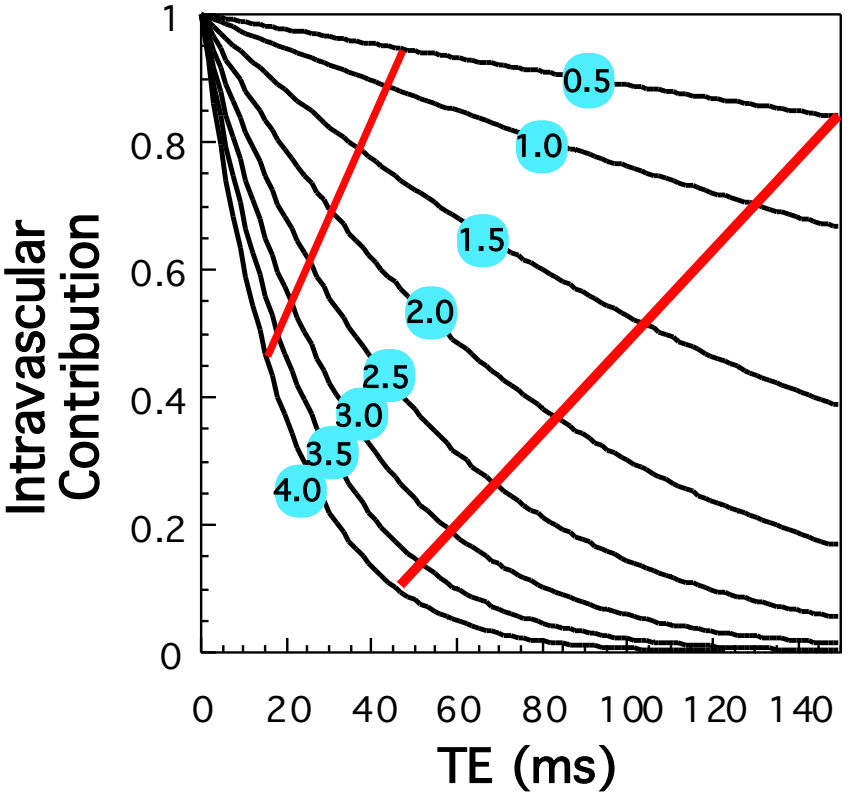

Spin-Echo
TE = 105 ms
TR = ∞
Gradient-Echo
TE = 50 ms
Gradient-Echo
functional
TE = 50 ms
Spin-Echo
functional
TE = 105 ms

Field strength dependence of intravascular signal

Spin-echo, %HbO_2 = 60



Gradient-echo, %HbO_2 = 60



Source of most contrast in venograms..

Pros and Cons of Spin-Echo

- Increased specificity (esp at high fields where IV signal is low)
- Less sensitive to rapidly flowing blood
- Less signal dropout.

- Less slices per TR
- Lower fCNR by x 2 to 4.
- Acquisition window still T2*
- Very large IV signal still present at most field strengths.

I would only use 3D SE at 7T if also imaging at high resolution and interested in something like columns or layers.

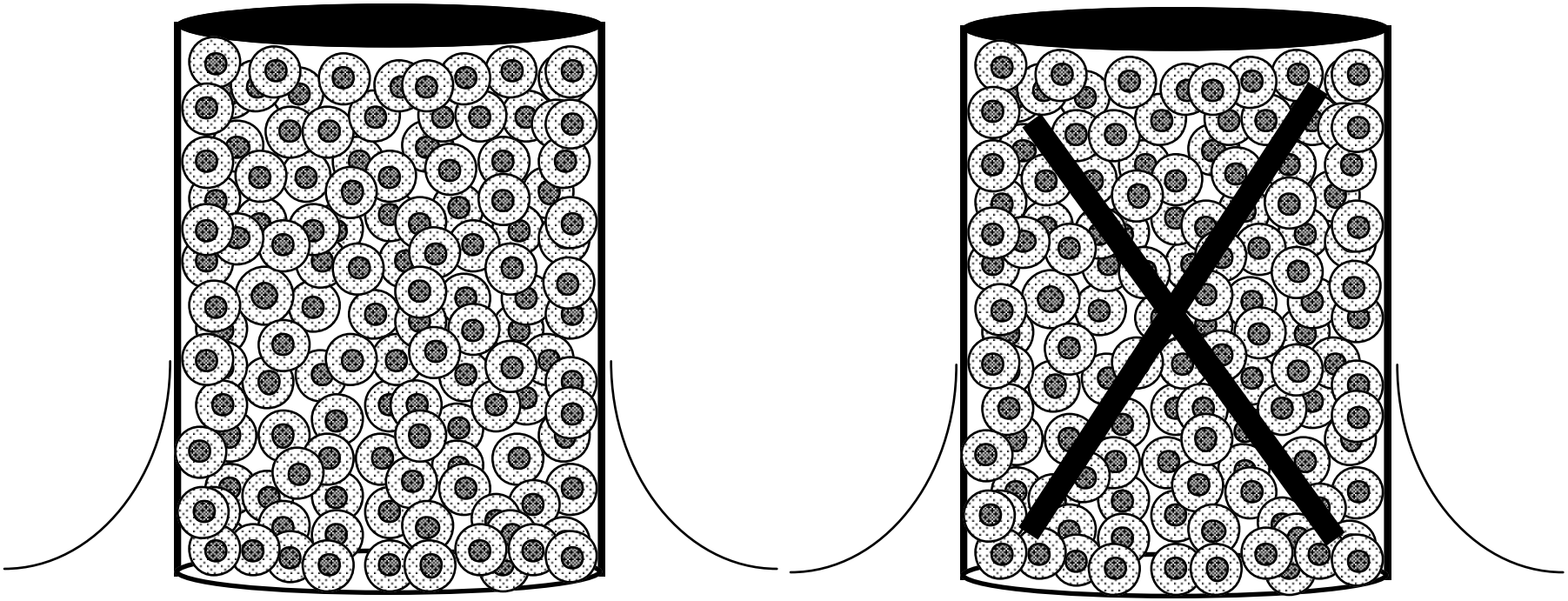
Velocity Nulling

…so let's remove the intravascular signal...

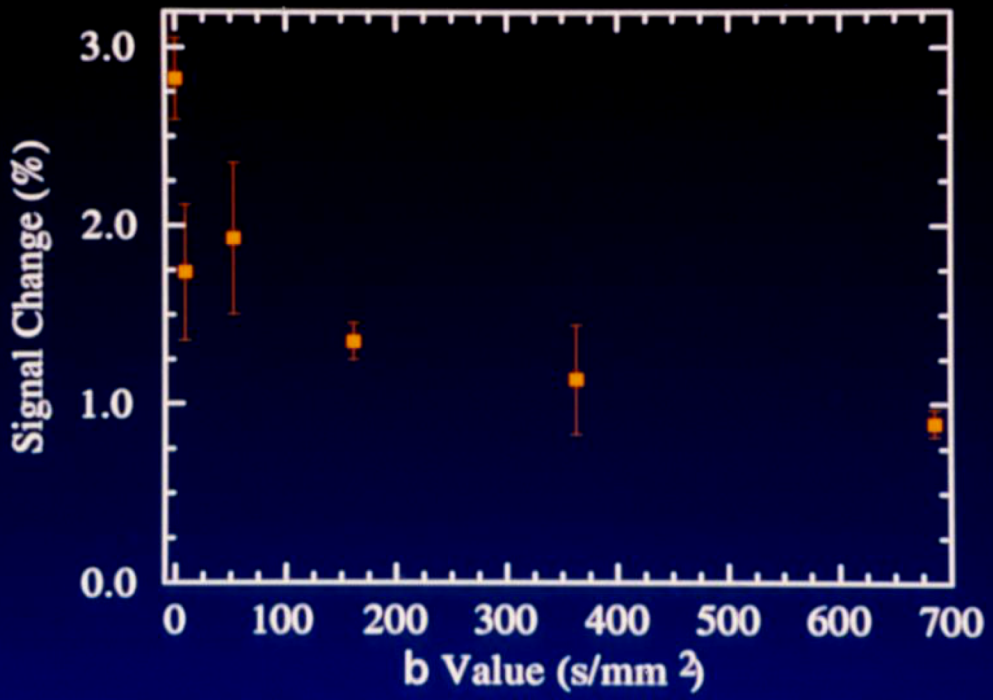
Velocity Nulled (or diffusion weighted) fMRI.

no diffusion weighting

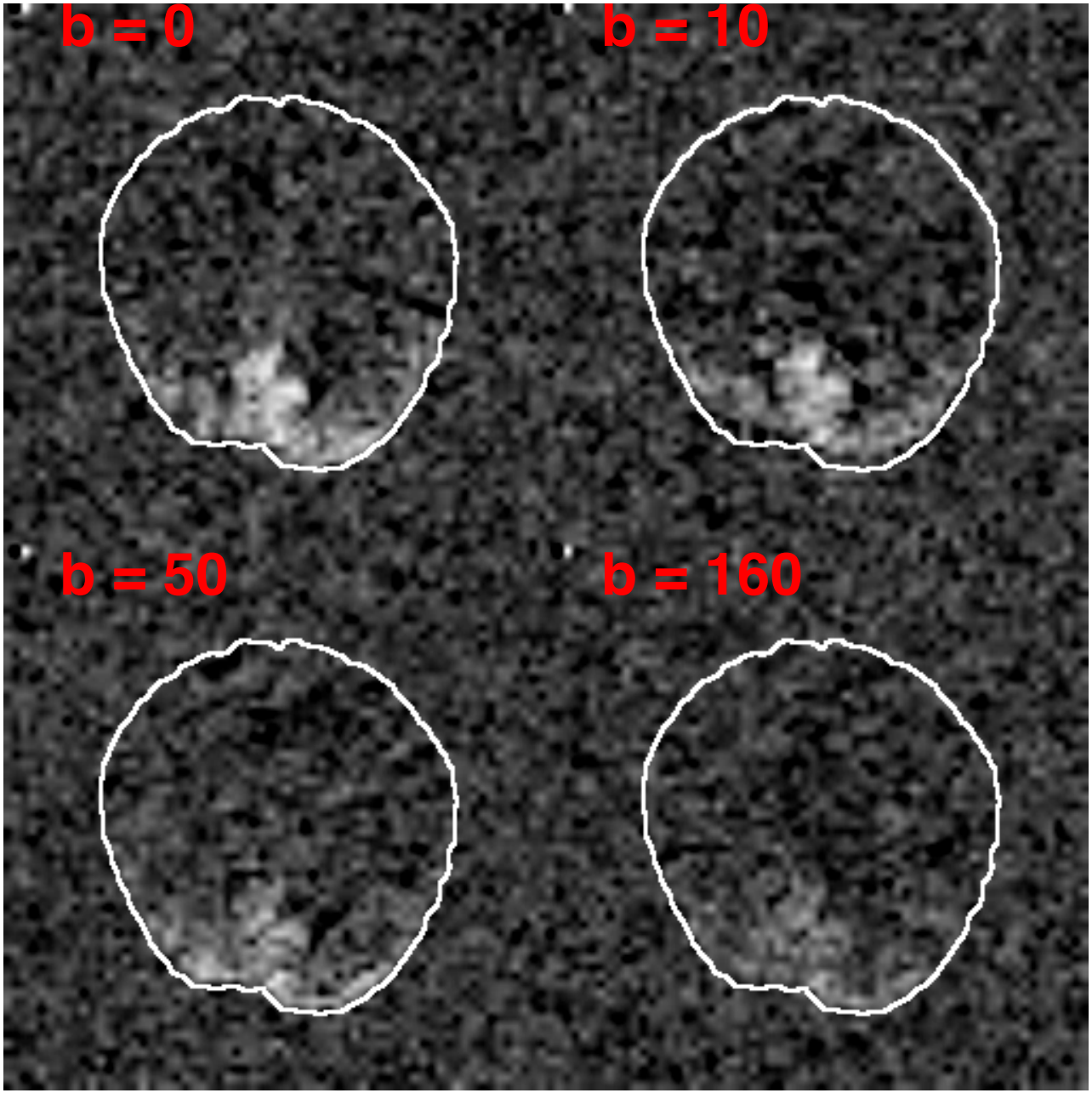
diffusion weighting



Summary of Diffusion-Weighted fMRI Data



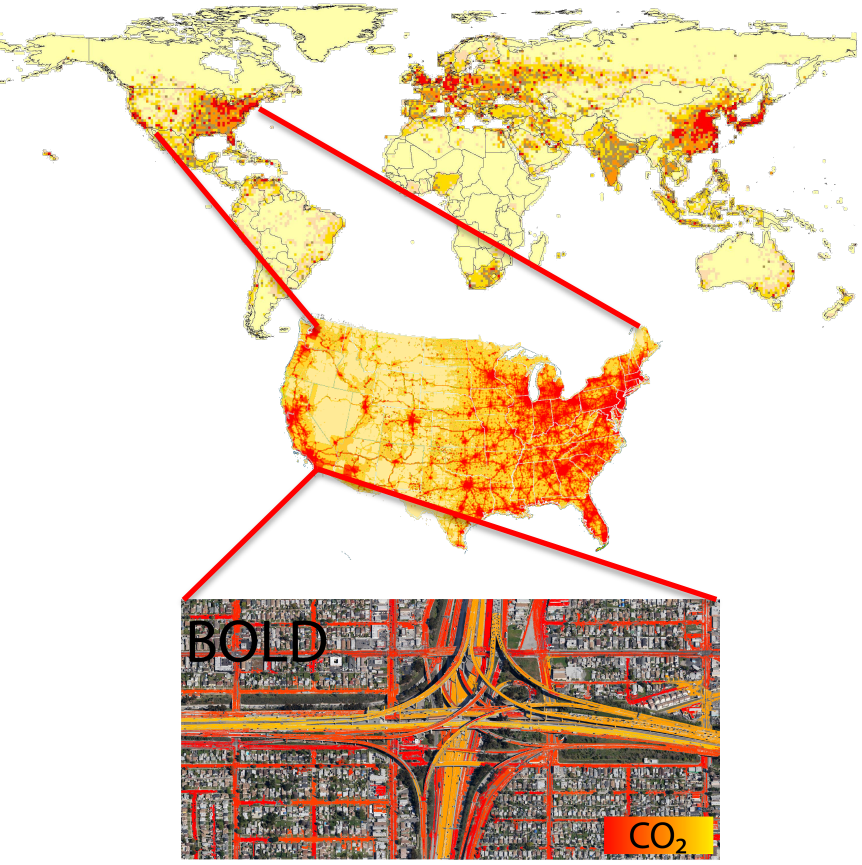
J. L. Boxerman, P. A. Bandettini, K. K. Kwong, J. R. Baker, T. L. Davis, B. R. Rosen, R. M. Weisskoff, The intravascular contribution to fMRI signal change: monte carlo modeling and diffusion - weighted studies in vivo. *Magn. Reson. Med.* 34, 4-10 (1995).

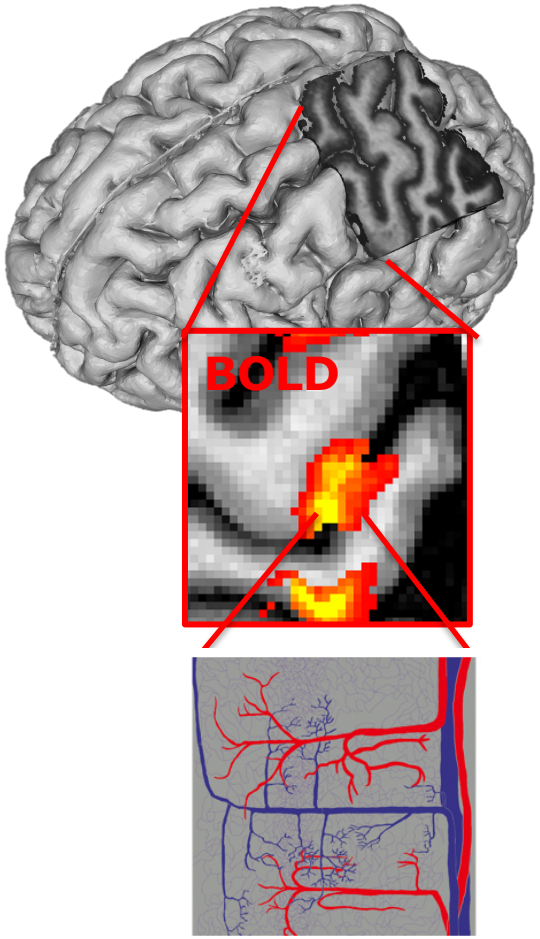

b = 0
b = 10
b = 50
b = 160

VASO

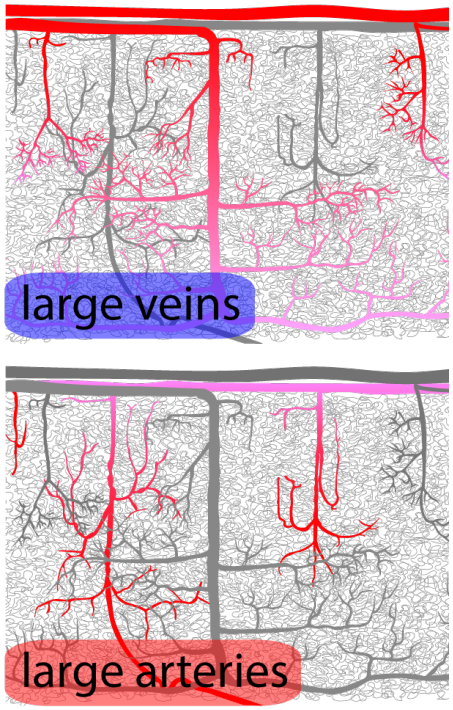
local specificity - highway metaphor

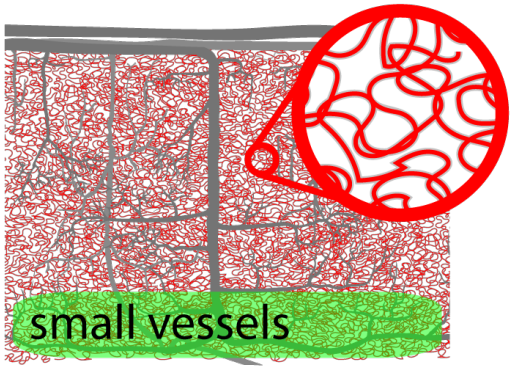
CO_2-emission:

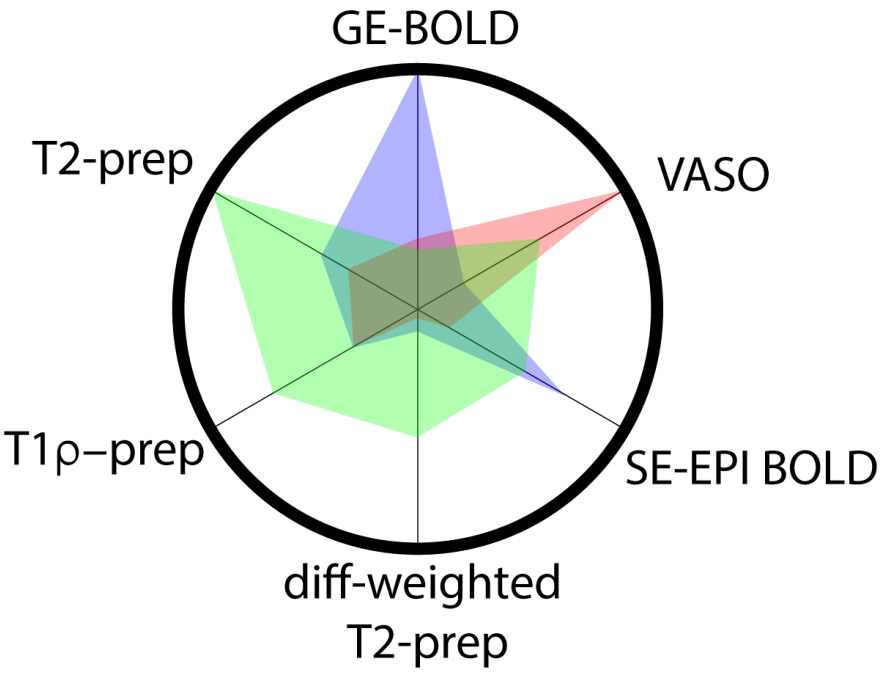




specific contrast candidates

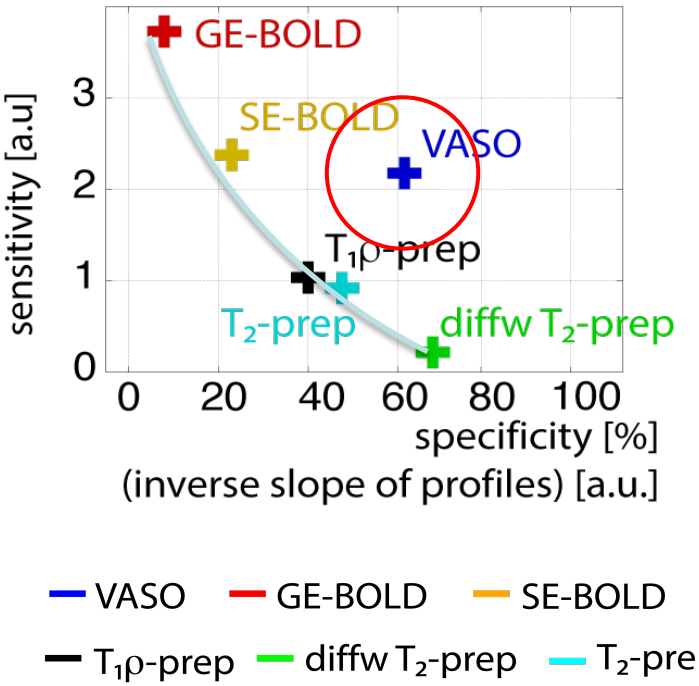




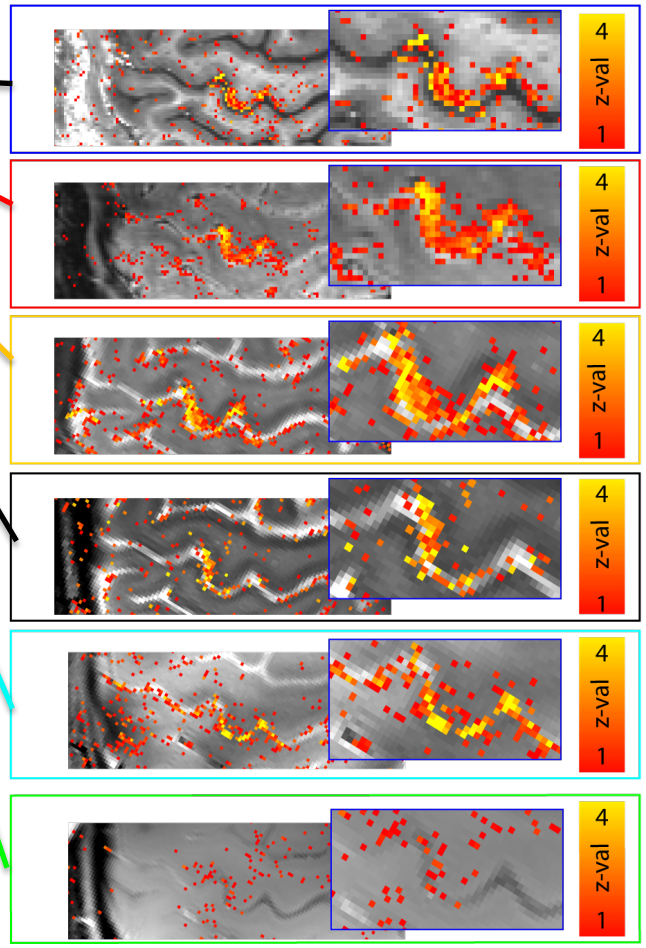


graphical depiction of review articles [Uludağ and Blinder 2017] and [Huber et al., 2017]

drawn based on Duvernoy, 1981 Brain Res

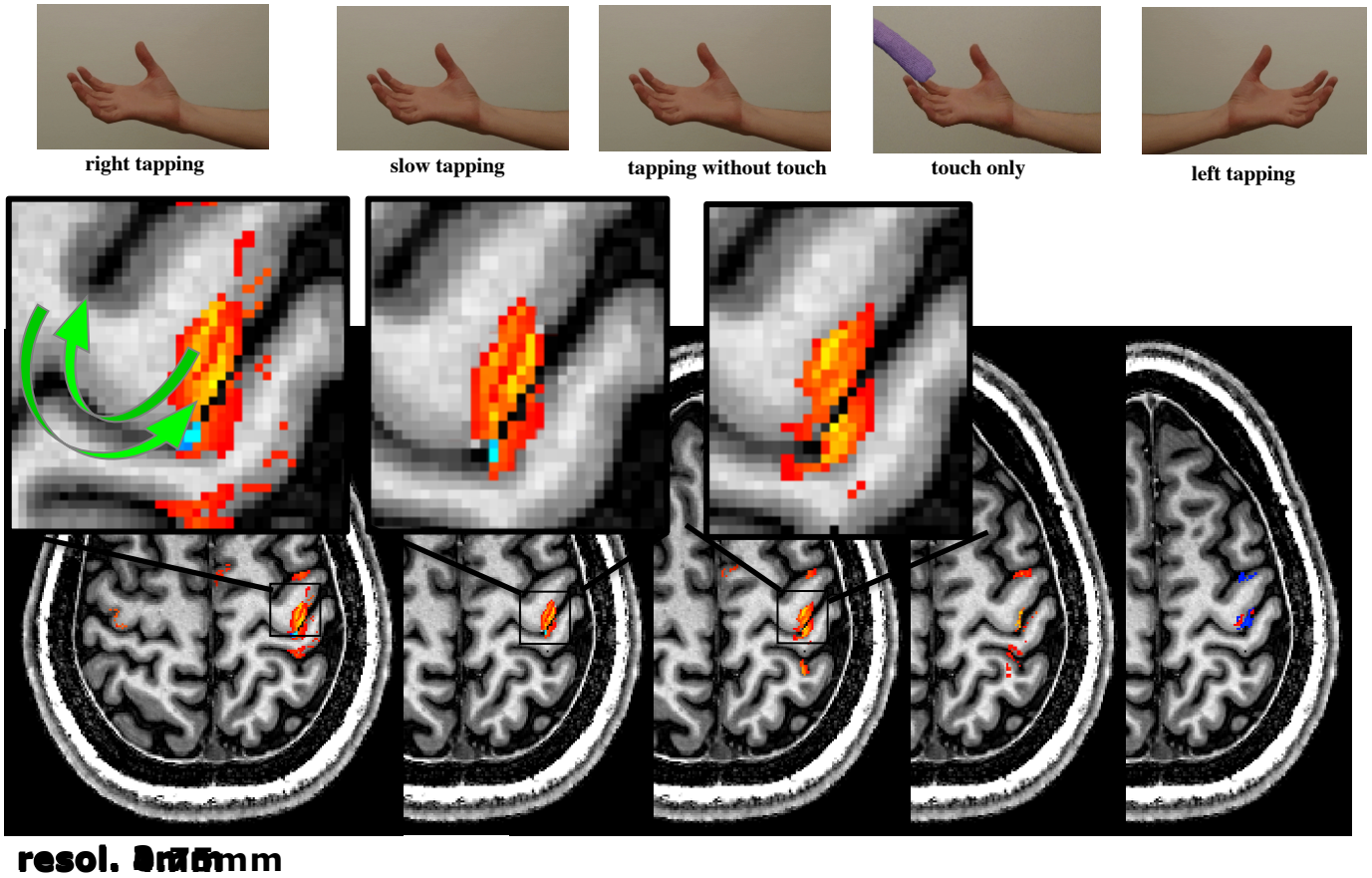


functional response

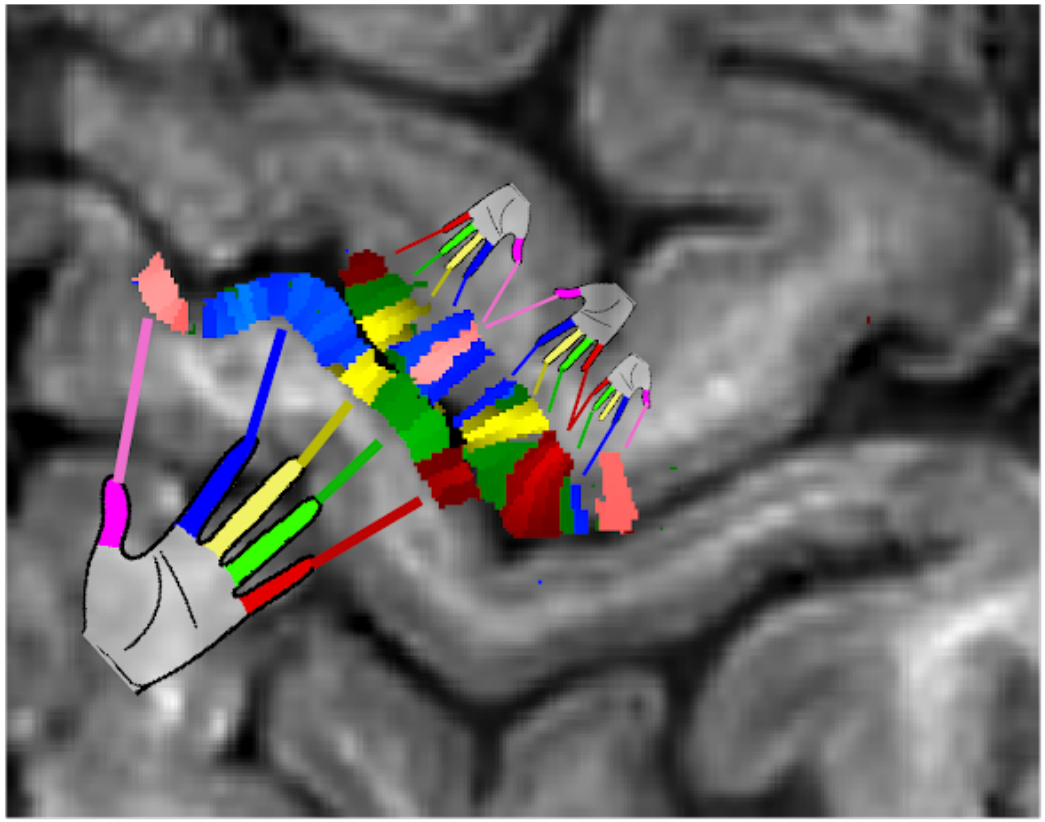


[Huber et al., ISMRM, 2017]

additional information in layer fMRI



Finger Mapping in Motor and Sensory Cortex with VASO



index finger tapping (0.75 Hz)
middle finger tapping (0.75 Hz)
ring finger tapping (0.75 Hz)
little finger tapping (0.75 Hz)
thumb tapping (0.75 Hz)

Hemodynamic Controversies and Challenges

Pulse sequence dependence

Temporal resolution

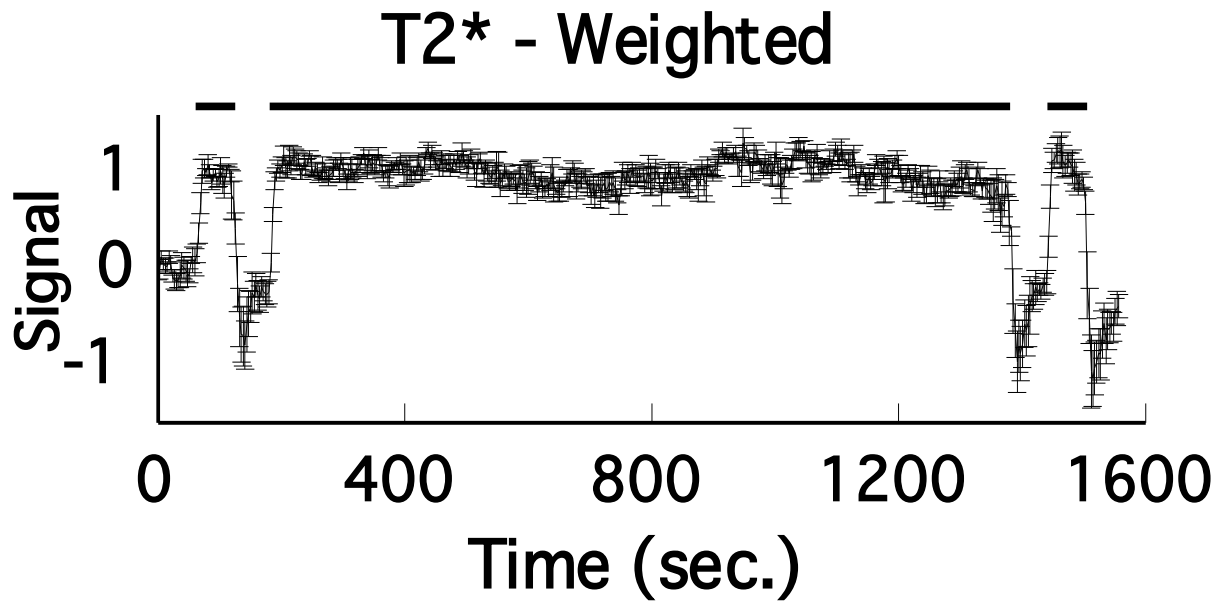
Nonlinearity

Pre and post undershoots

Negative signal changes

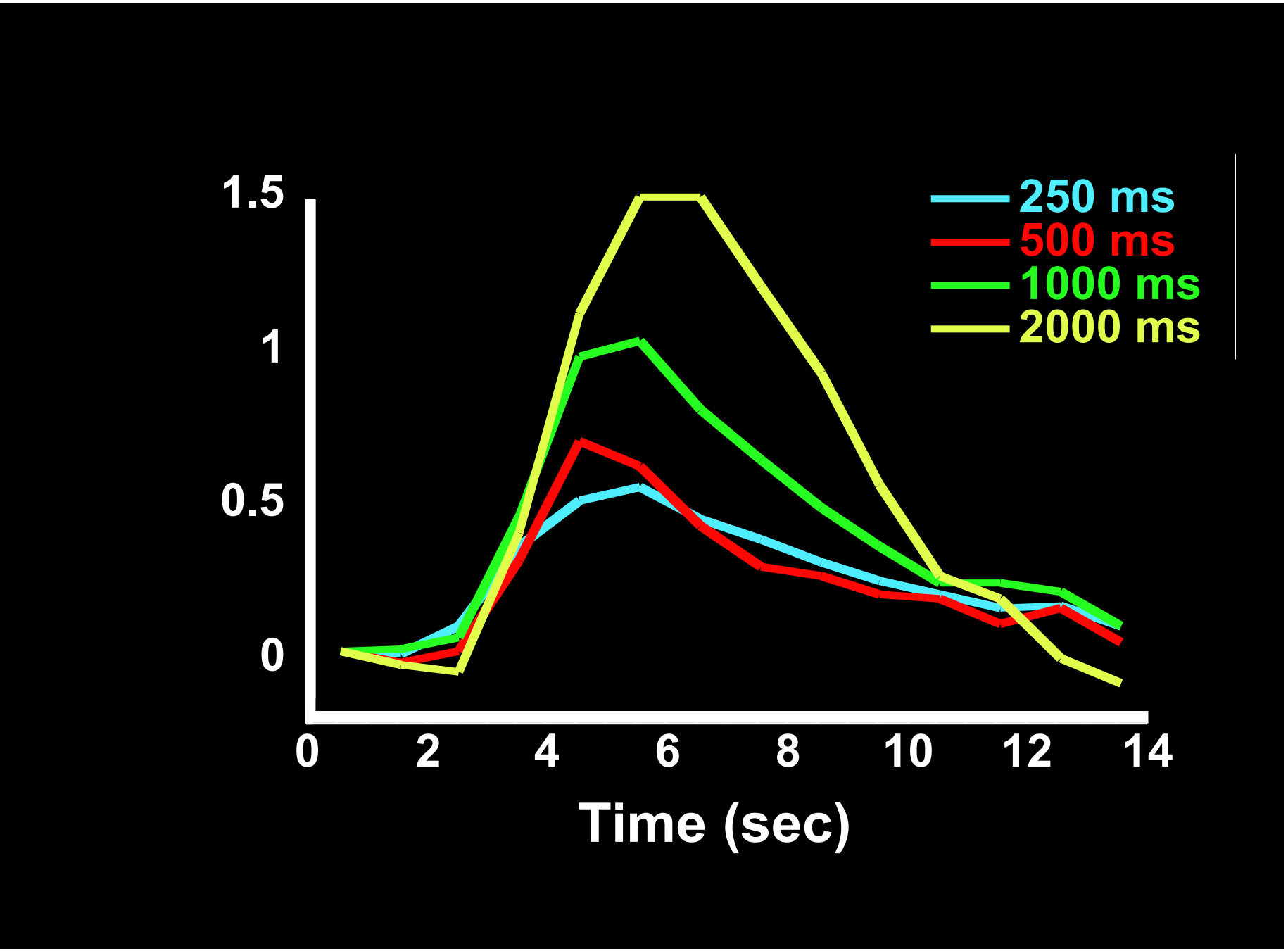
What are we missing?

20 minutes continuous activation

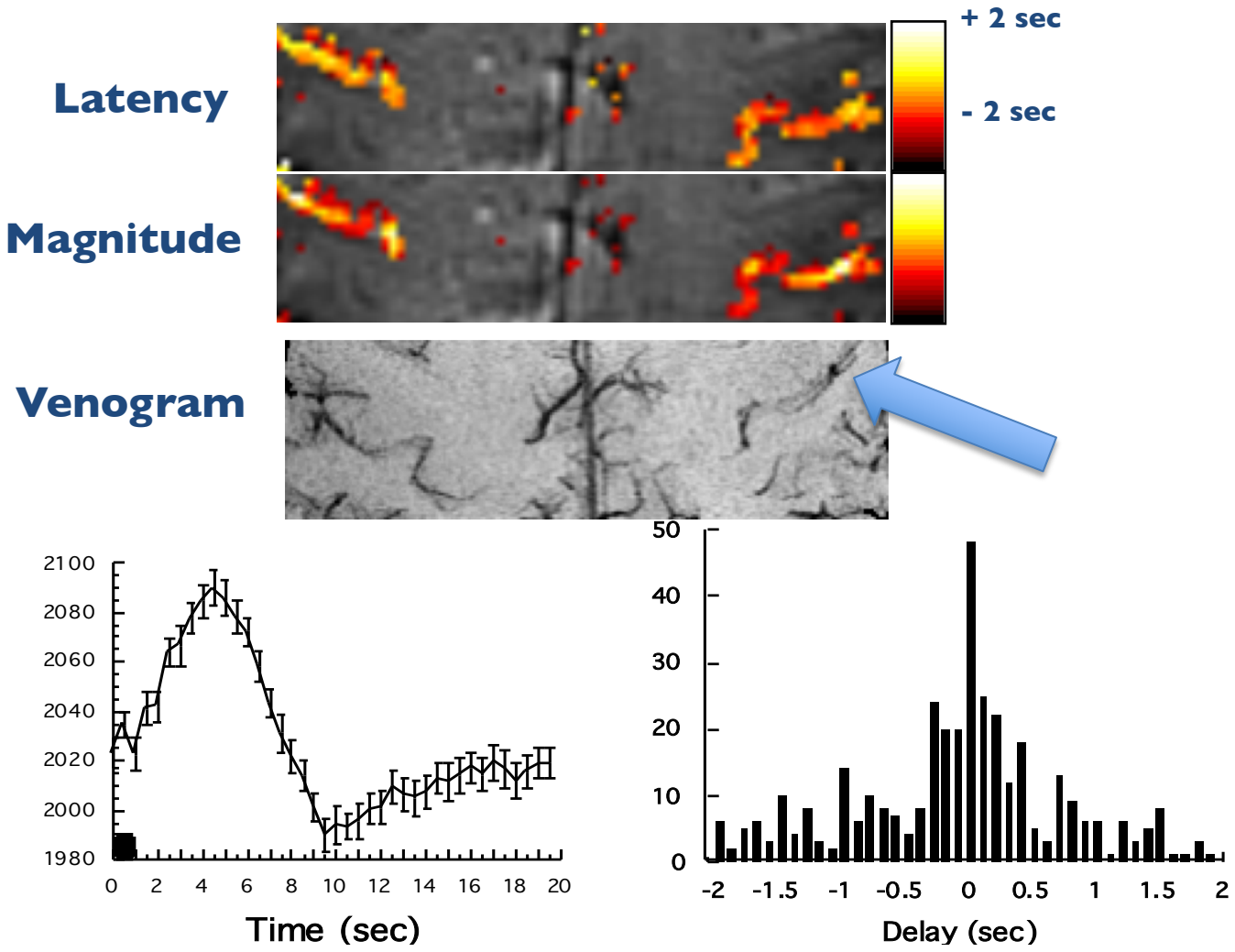


P.A. Bandettini, K. K. Kwong, T. L. Davis, R. B. H. Tootell, E. C. Wong, P.T. Fox, J.W. Belliveau, R. M. Weisskoff, B. R. Rosen, (1997). "Characterization of cerebral blood oxygenation and flow changes during prolonged brain activation." *Human Brain Mapping* 5, 93-109.

Controversy

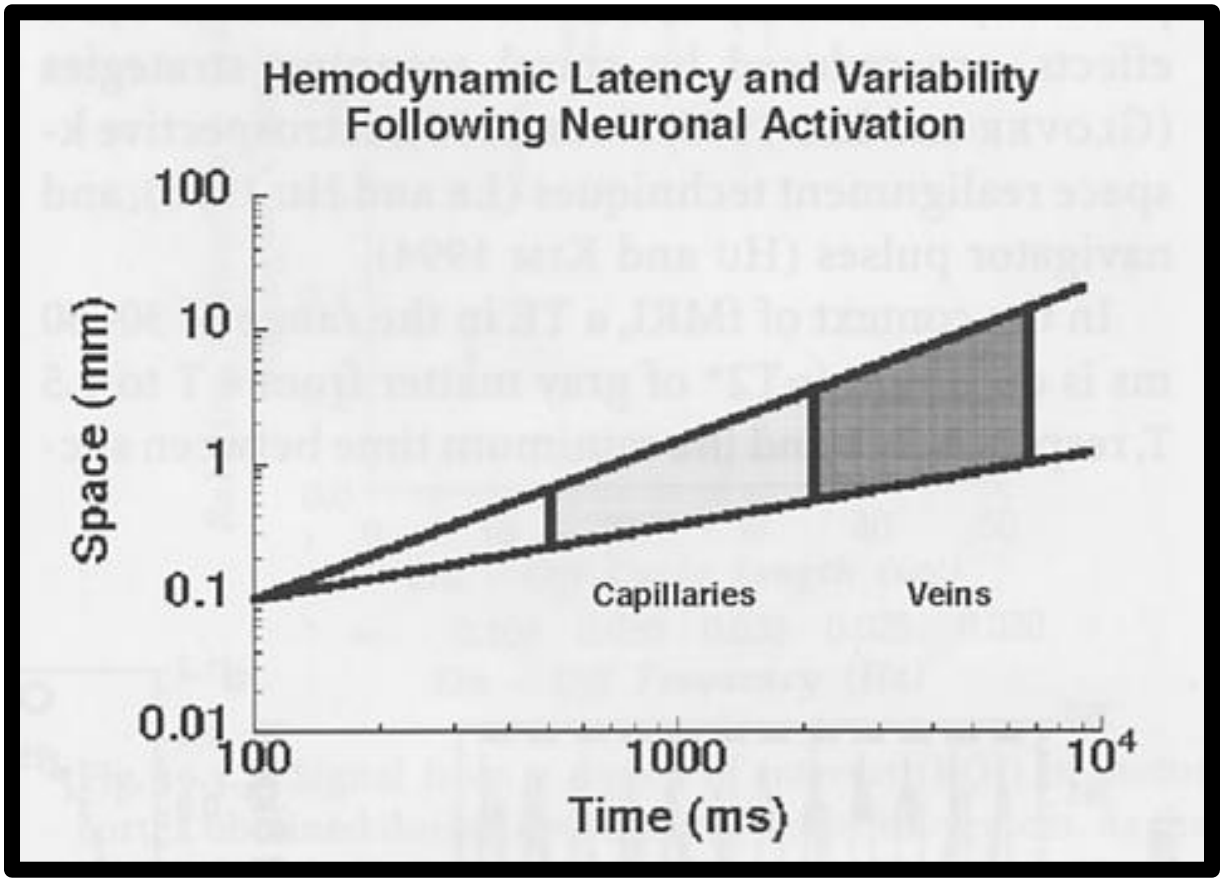

1.5
1
0.5
0
0
2
4
6
8
10
12
14
Time (sec)
250 ms
500 ms
1000 ms
2000 ms

Latency Variation... DRAINING VEIN EFFECTS!



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

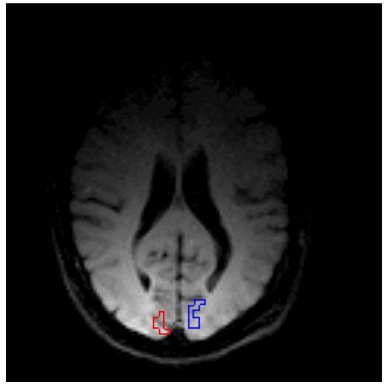
Controversy


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

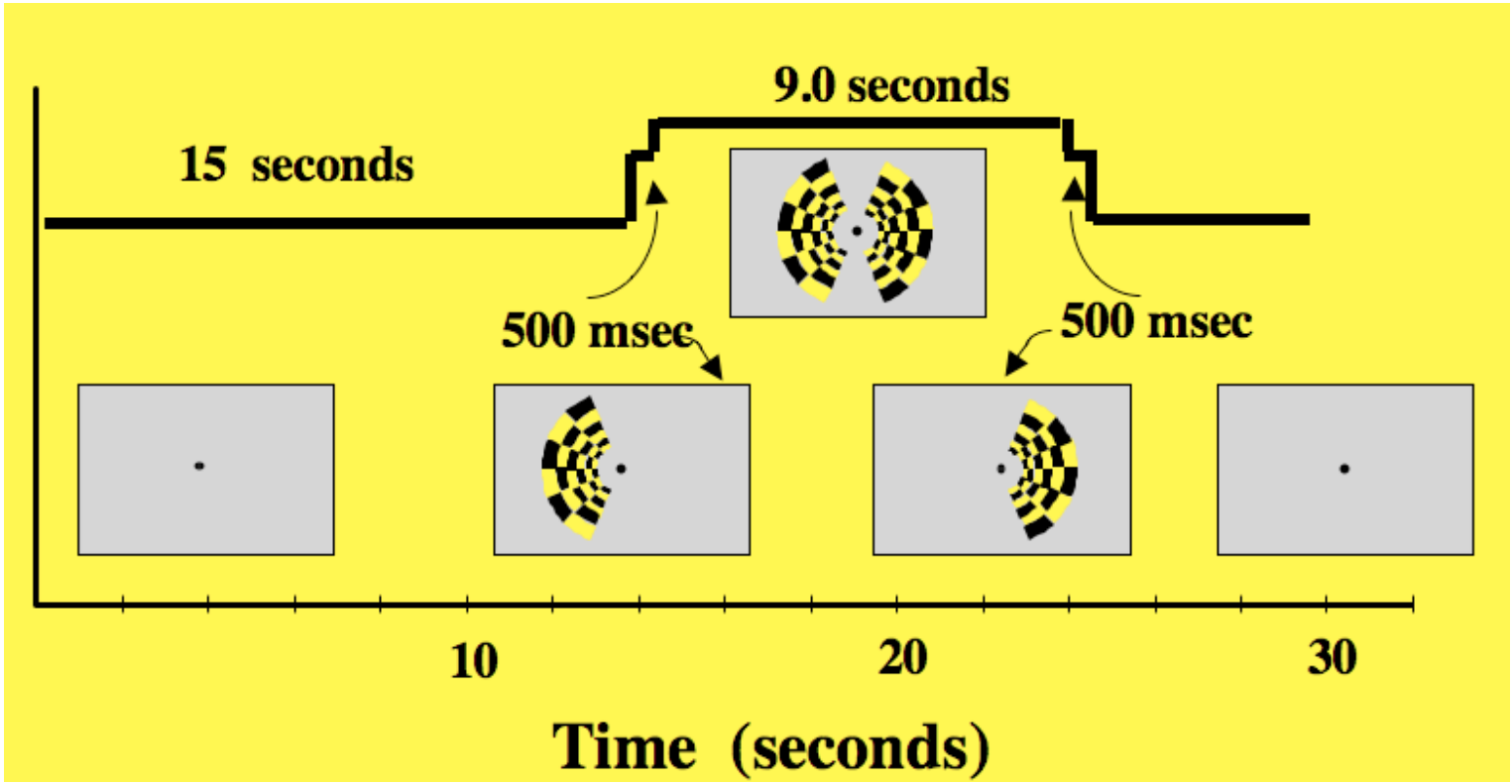
Temporal resolution factors	Values for each factor
Fastest image acquisition rate	≈64 images/s
Minimum time for signal to significantly deviate from baseline	≈3 s
Fastest on-off rate in which amplitude-is not compromised	≈8 s on, 8 s off
Fastest on-off rate in which hemodynamic response keeps up	≈2 s 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

Hemi-Field Experiment

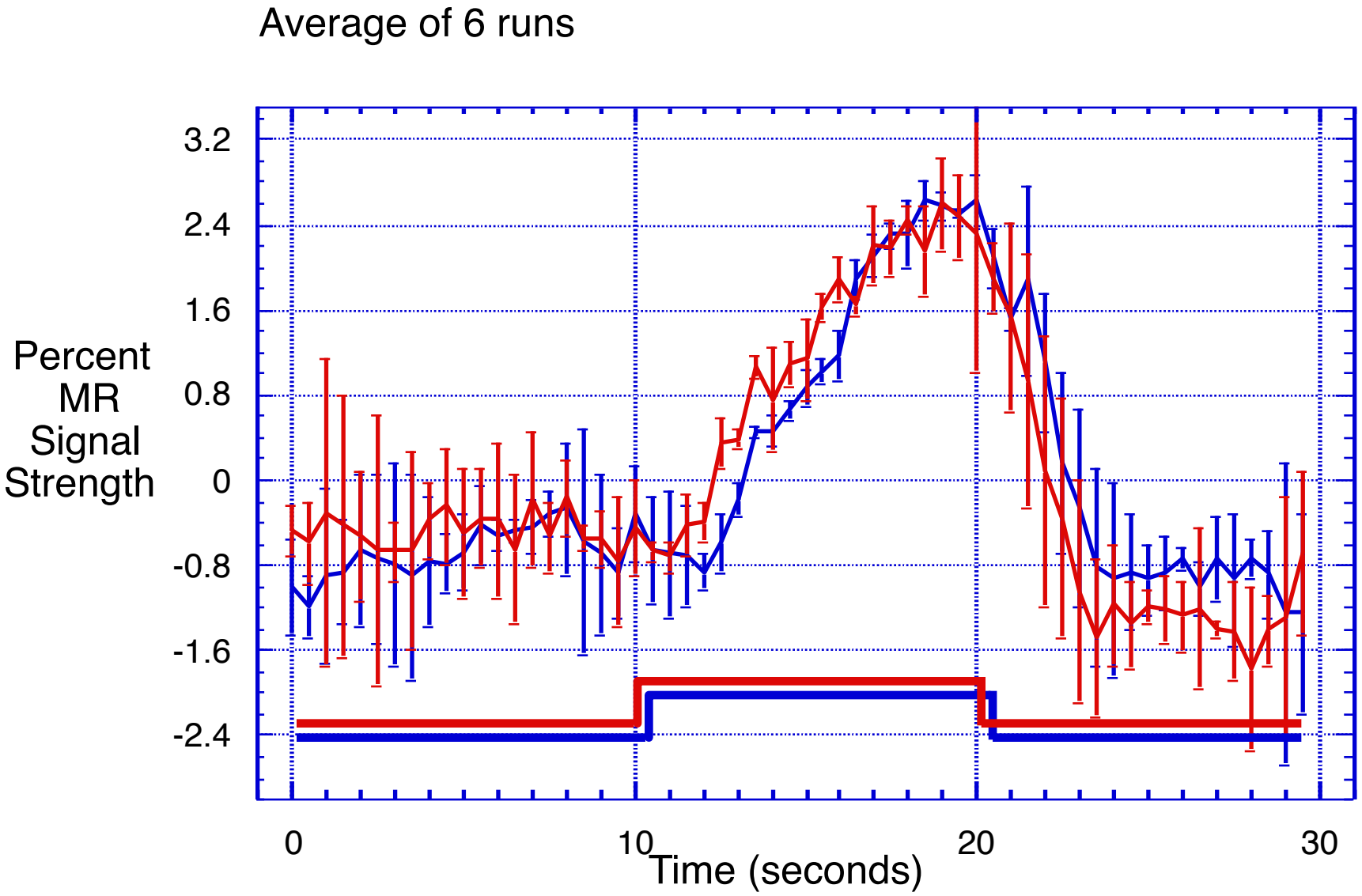
Right Hemisphere

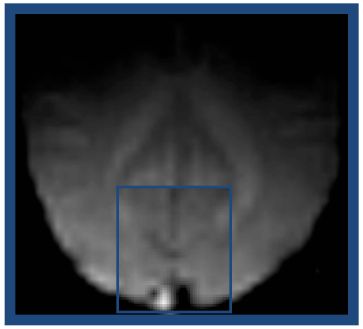


Left Hemisphere



Hemi-field with 500 msec asynchrony





Timing

500 ms

500 ms

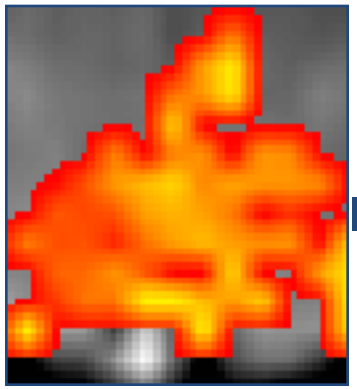
Right Hemifield

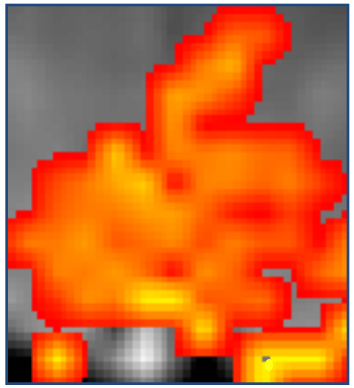
Left Hemifield

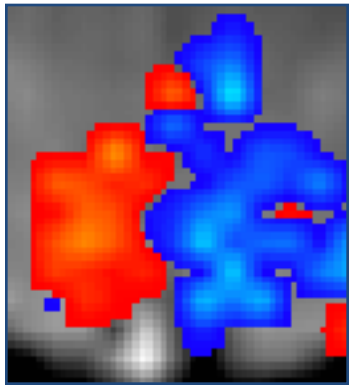
+ 2.5 s

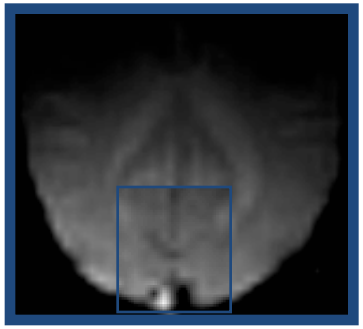
0 s

- 2.5 s









Timing

250 ms

250 ms

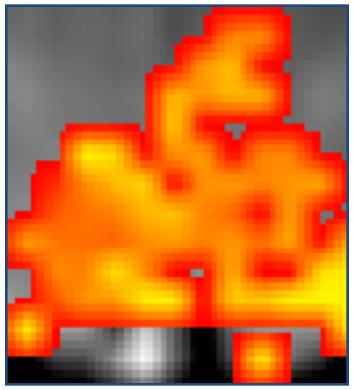
Right Hemifield

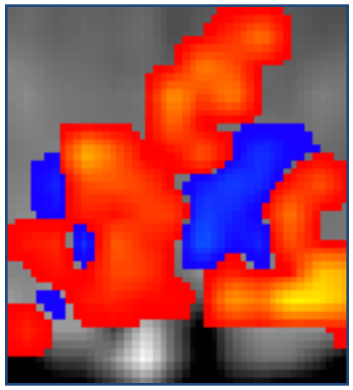
Left Hemifield

+ 2.5 s

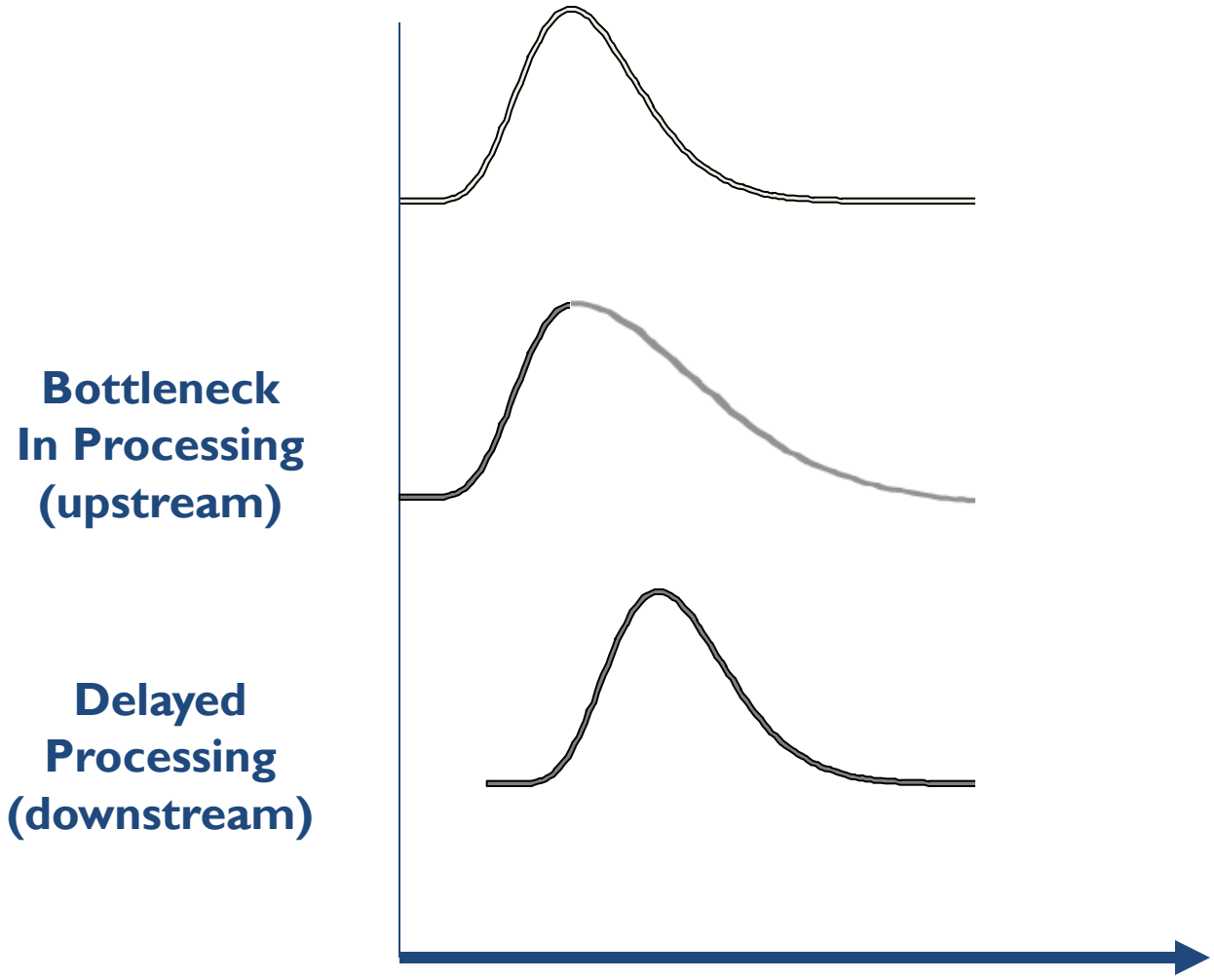
0 s

- 2.5 s





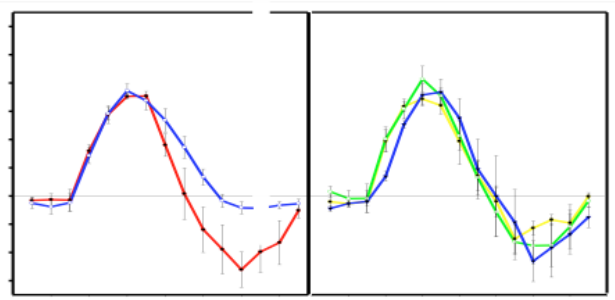
Hemodynamic Response Modulation



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

Word vs. Non-word

0°, 60°, 120° Rotation



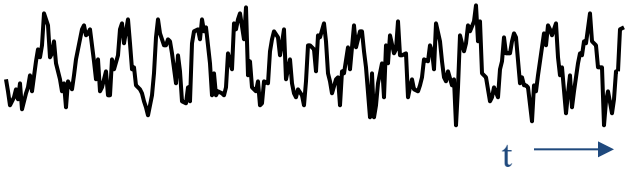
Bellgowan, et al (2003), PNAS 100, 15820–15283

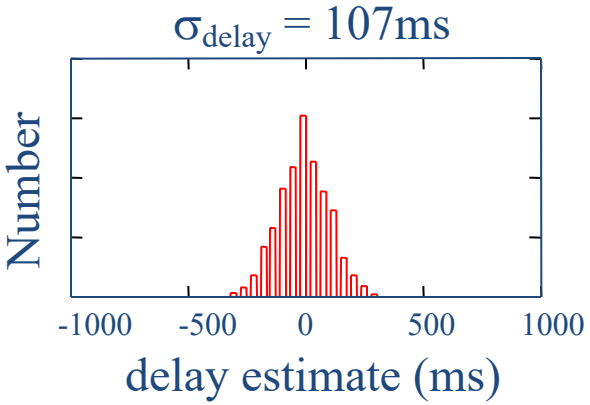
Controversy

Even if no hemodynamic variability exists…

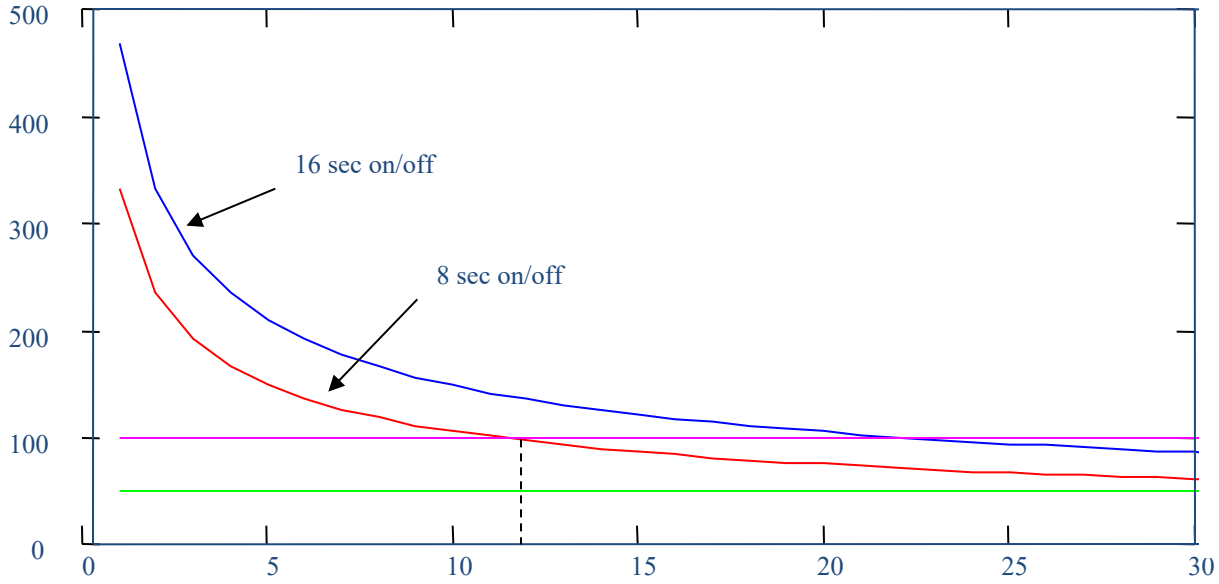
1 run:

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



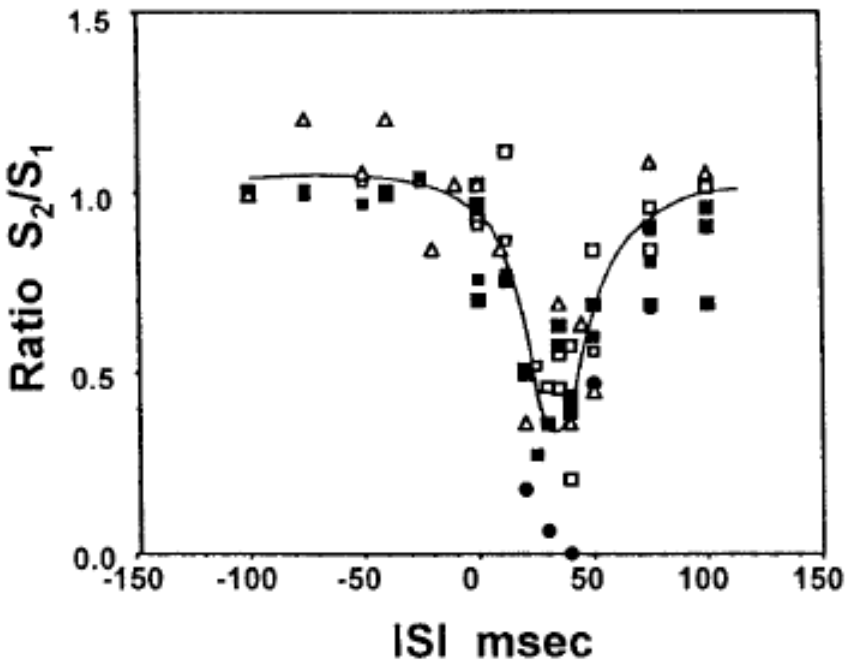


Smallest latency
Variation Detectable
(ms) (p < 0.001)



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

Hemodynamic Controversies and Challenges

Pulse sequence dependence

Temporal resolution

Nonlinearity

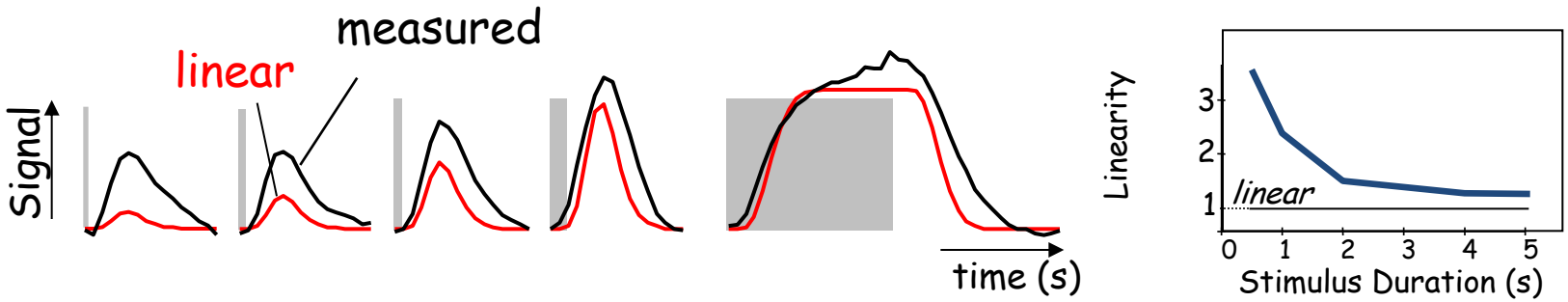
Pre and post undershoots

Negative signal changes

What are we missing?

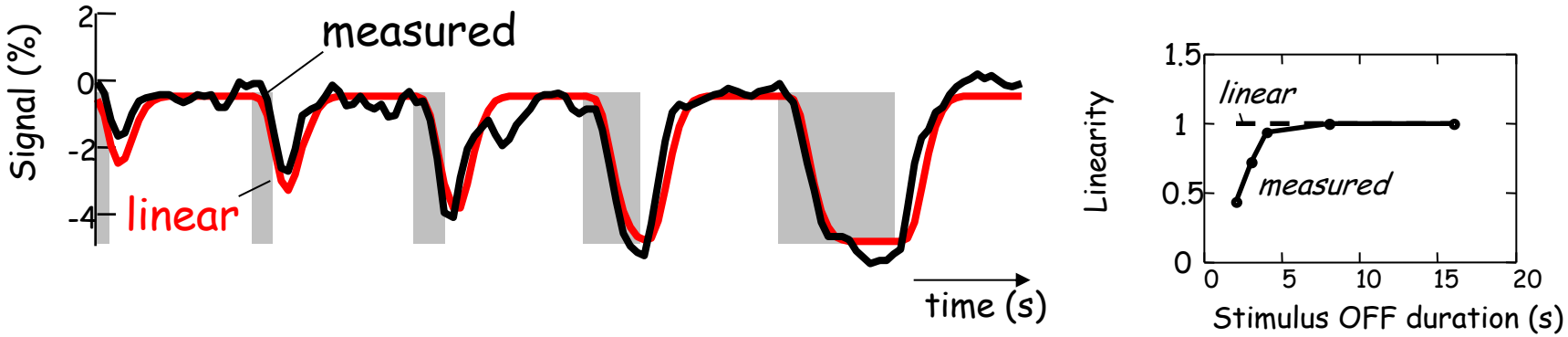
Linearity

Brief "on" periods produce **larger** increases than expected.



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

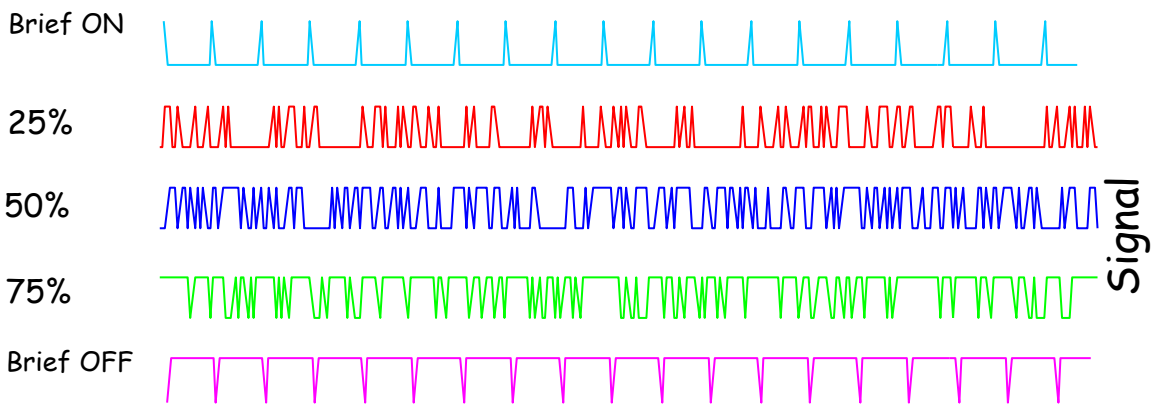
Brief "off" periods produce **smaller** decreases than expected.

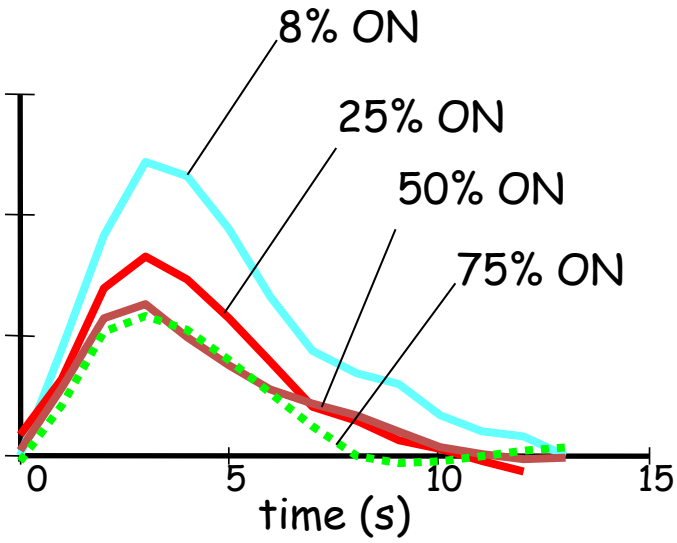


R.M. Birn, P. A. Bandettini, NeuroImage, 27, 70-82 (2005)

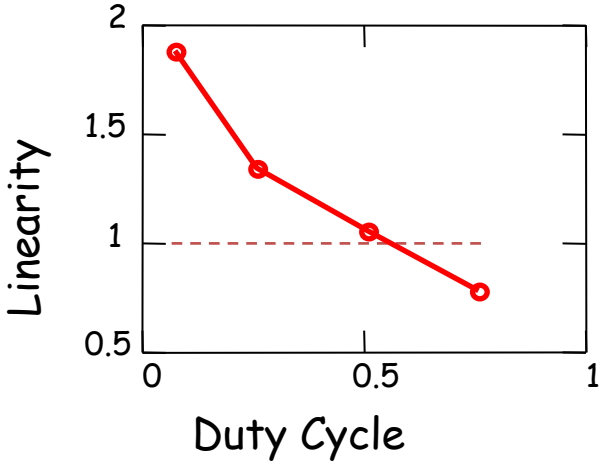
Challenge

Varying the Duty Cycle



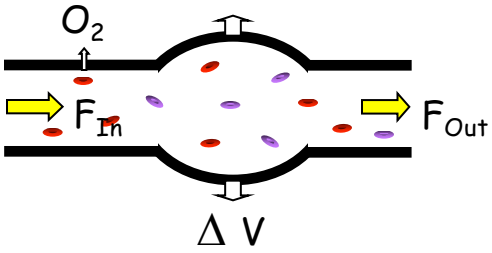


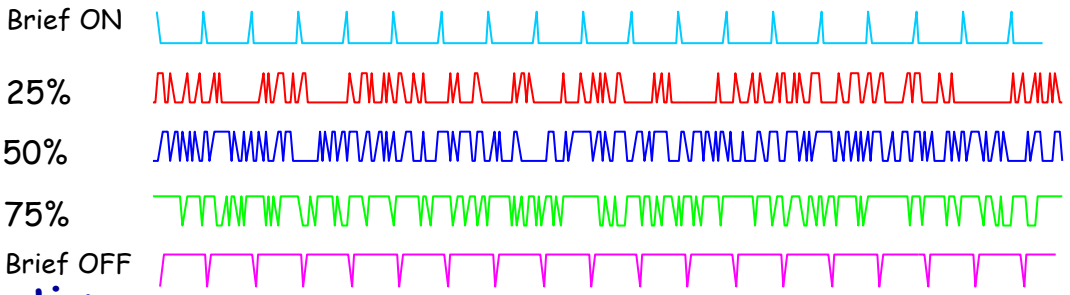
Deconvolved Response



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

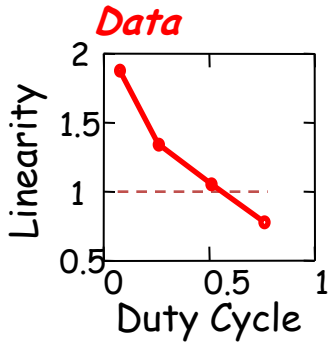
Simulation of Hemodynamic Mechanisms *(Balloon model)*

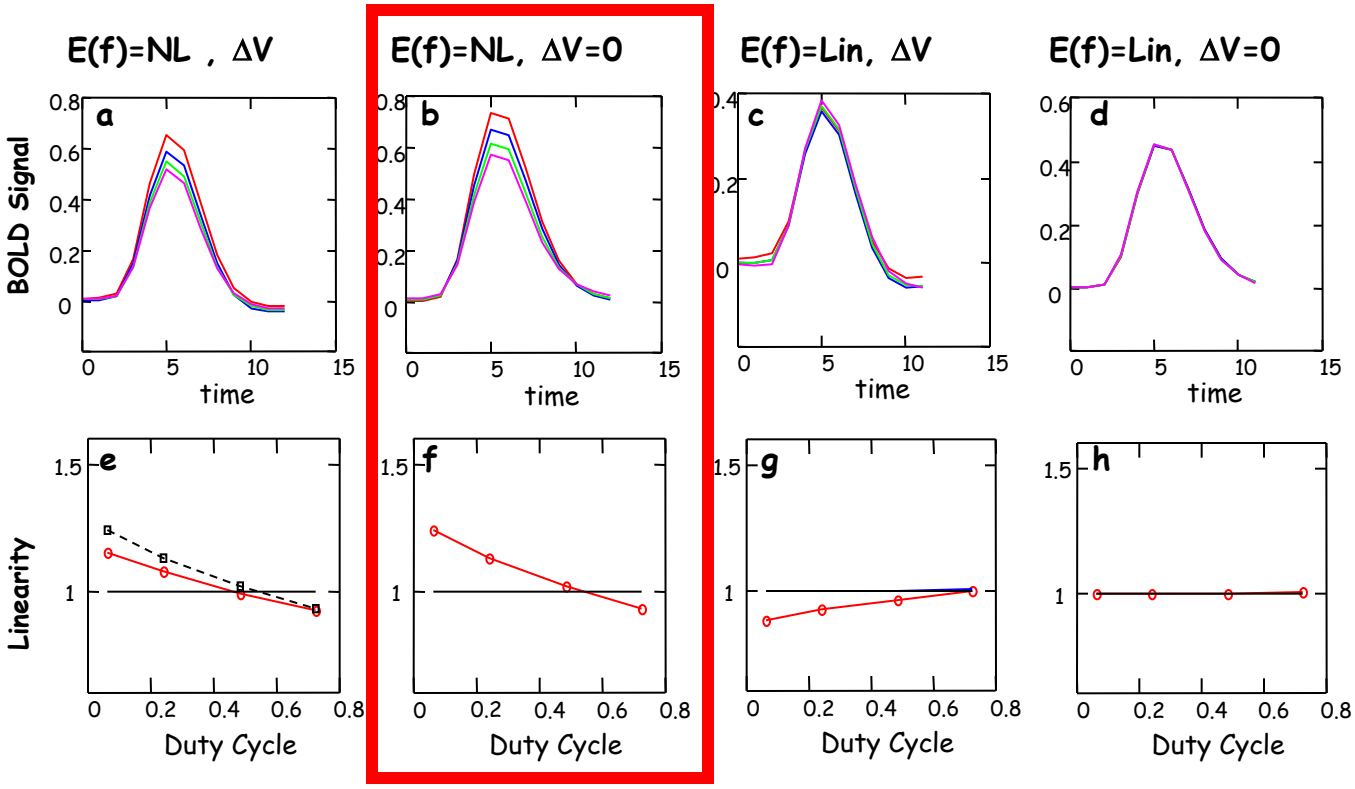




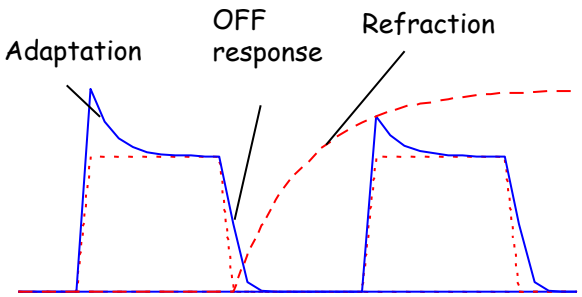
E(f) = oxygen extraction fraction

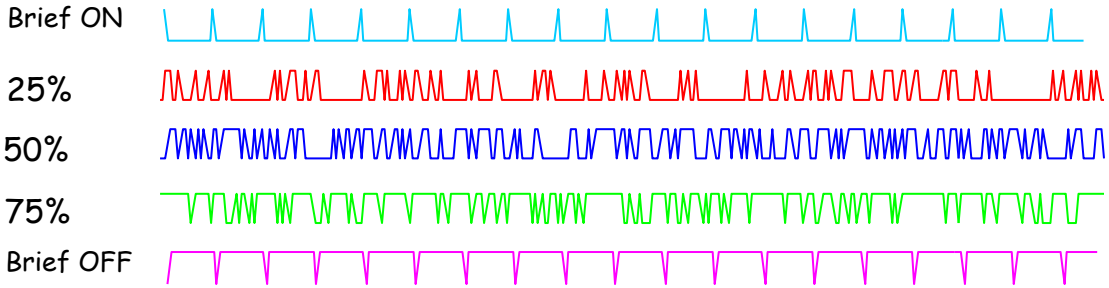
V = blood volume

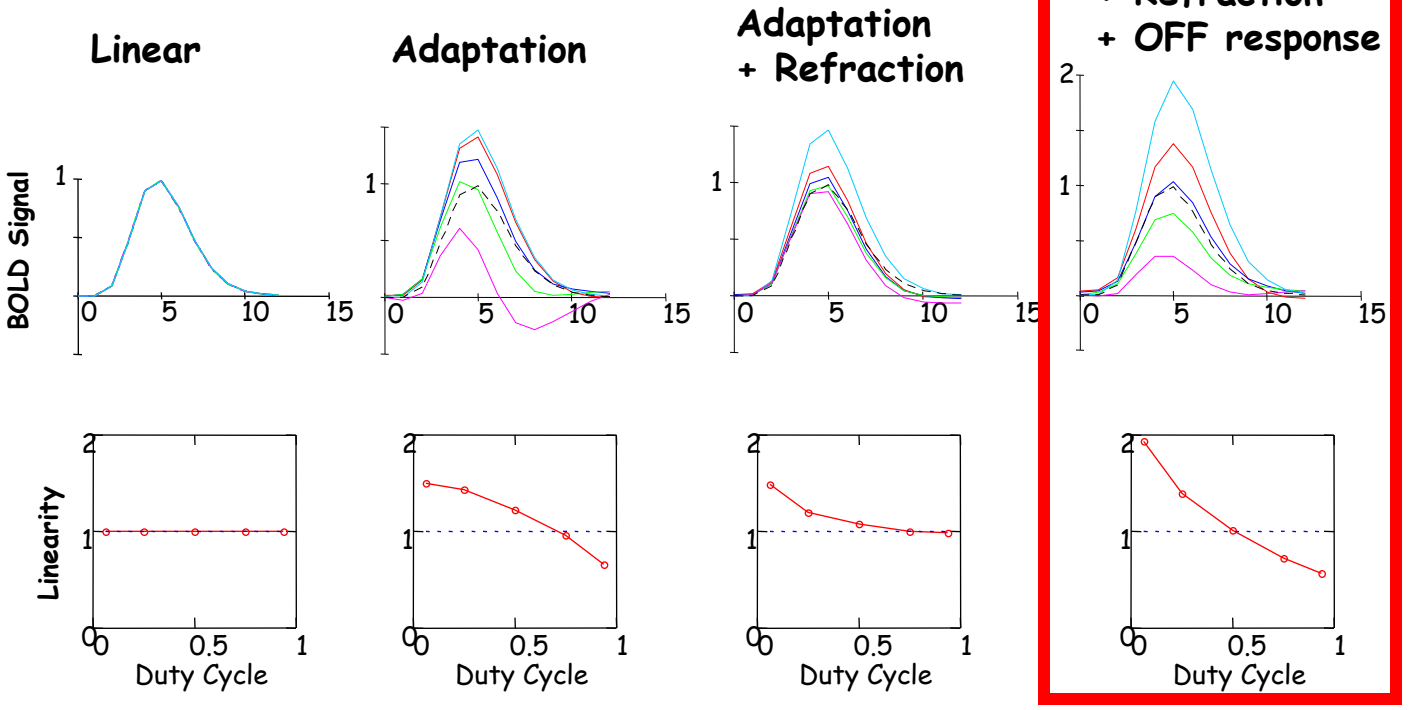




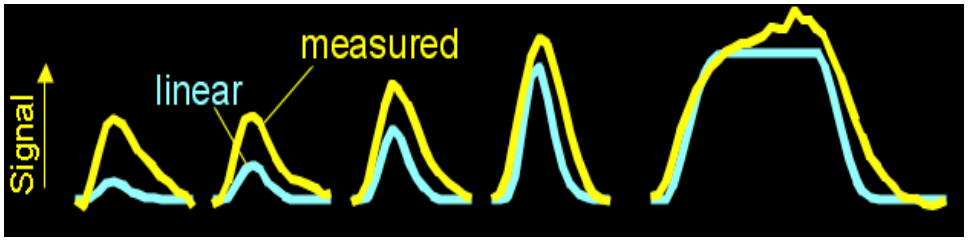
Simulation of Neuronal Mechanisms



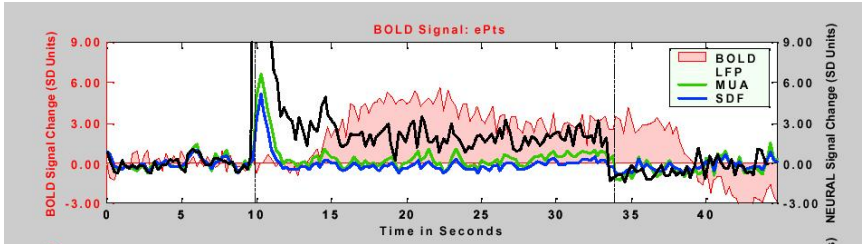




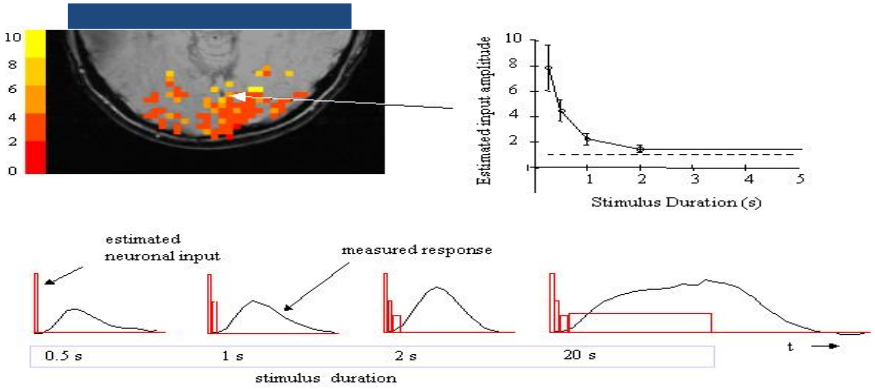
Brief stimuli produce larger responses than expected



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



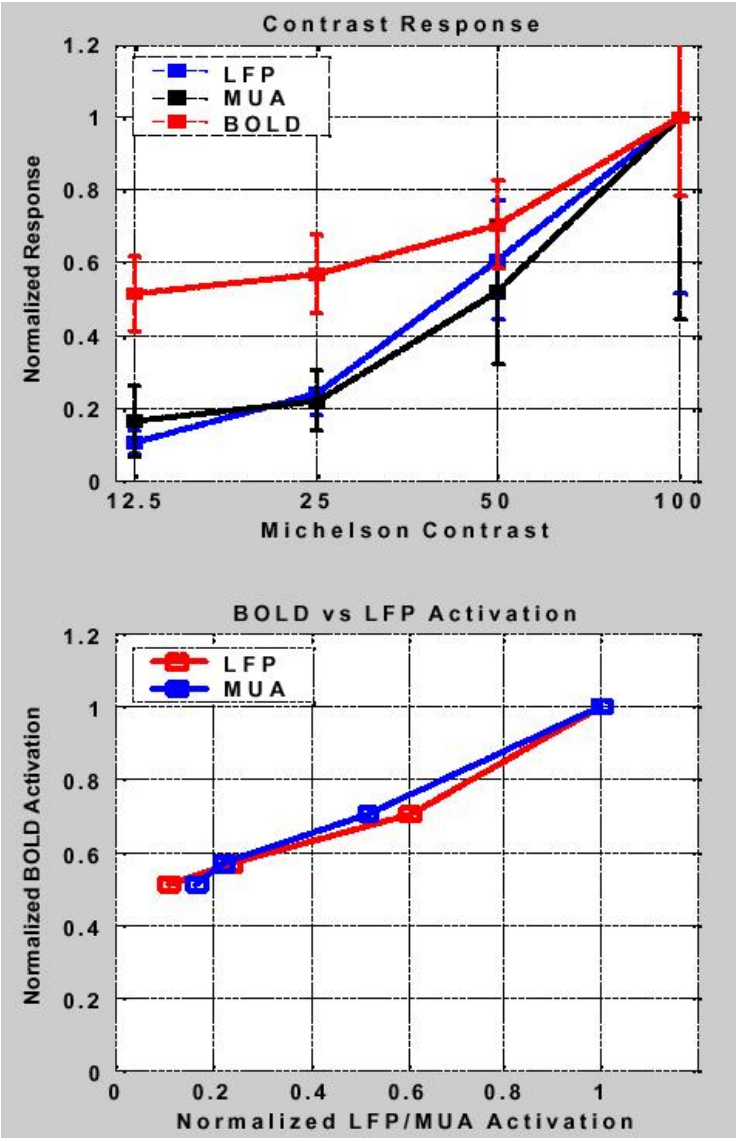
Logothetis et al. (2001) Nature, 412, 150-157.



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

Controversy

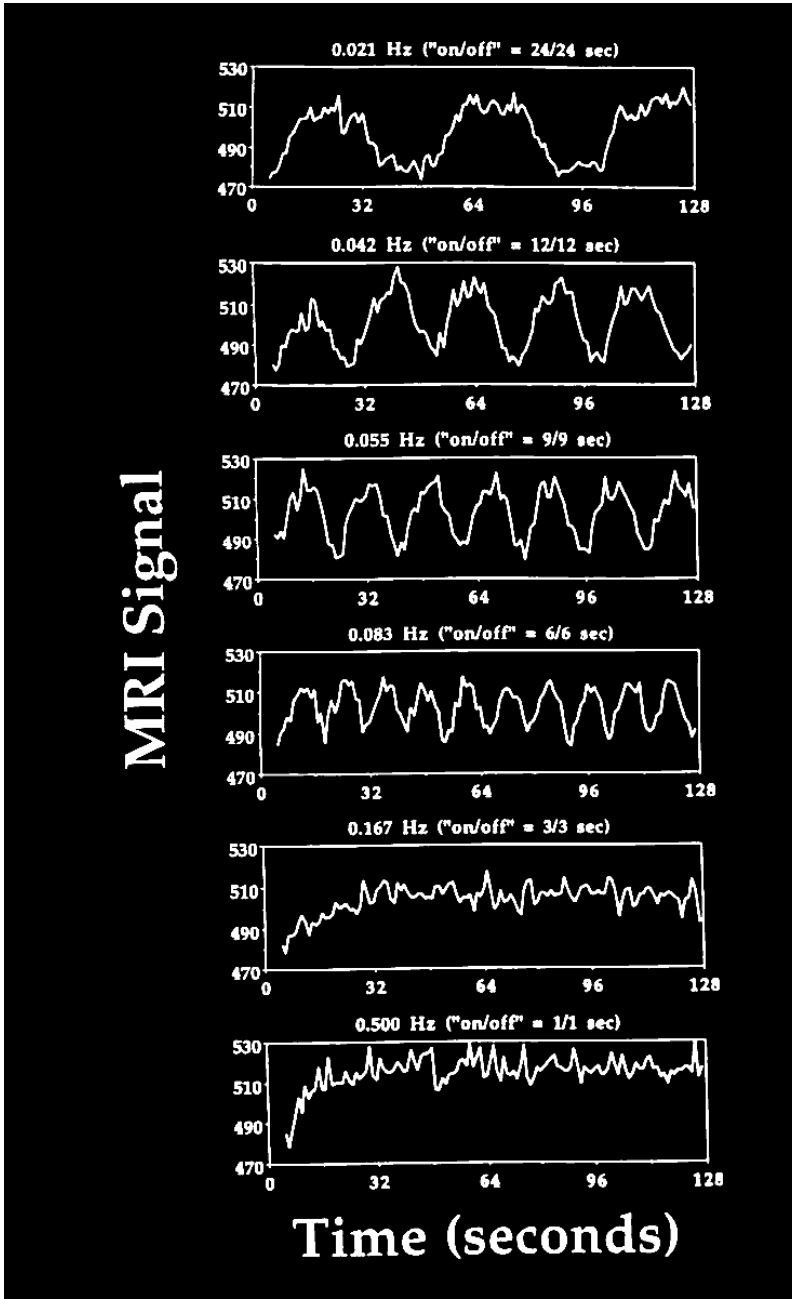
Mechanisms of BOLD: Neuronal Correlates

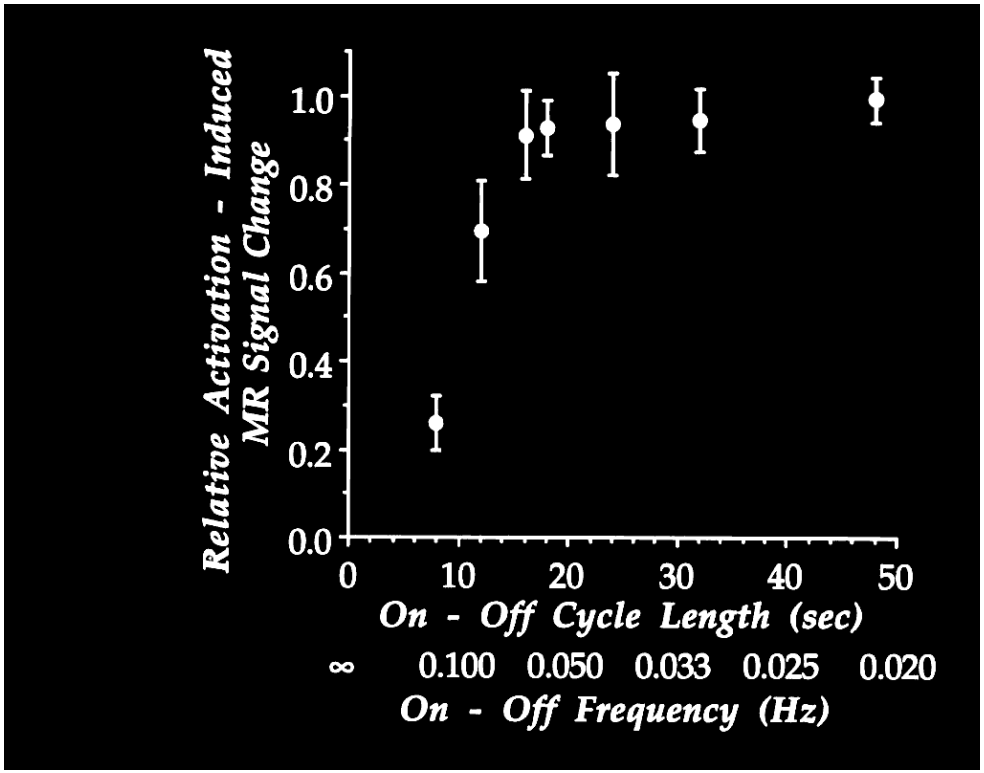


Logothetis et al. (2001) "Neurophysiological investigation of the basis of the fMRI signal" Nature, 412, 150-157

Controversy

How rapidly can one switch on and off?



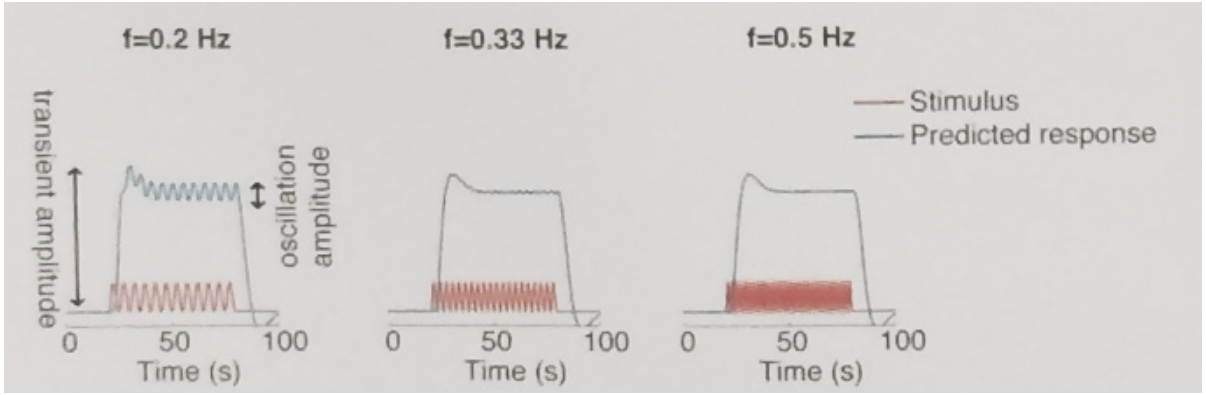


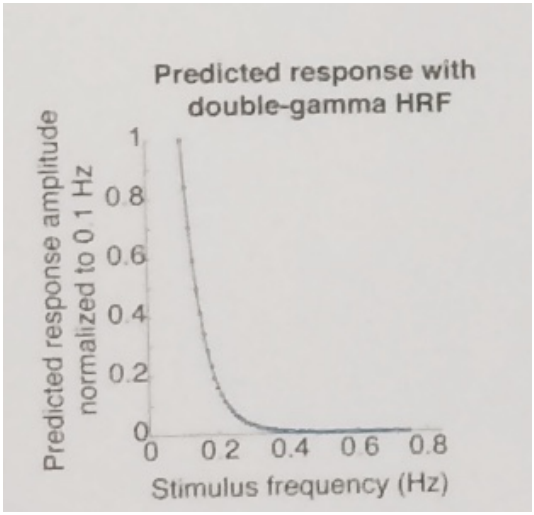
P. A. Bandettini,, Functional MRI using the BOLD approach: dynamic characteristics and data analysis methods, in "Diffusion and Perfusion: Magnetic Resonance Imaging" (D. L. Bihan, Ed.), p.351-362, Raven Press, New York, 1995.

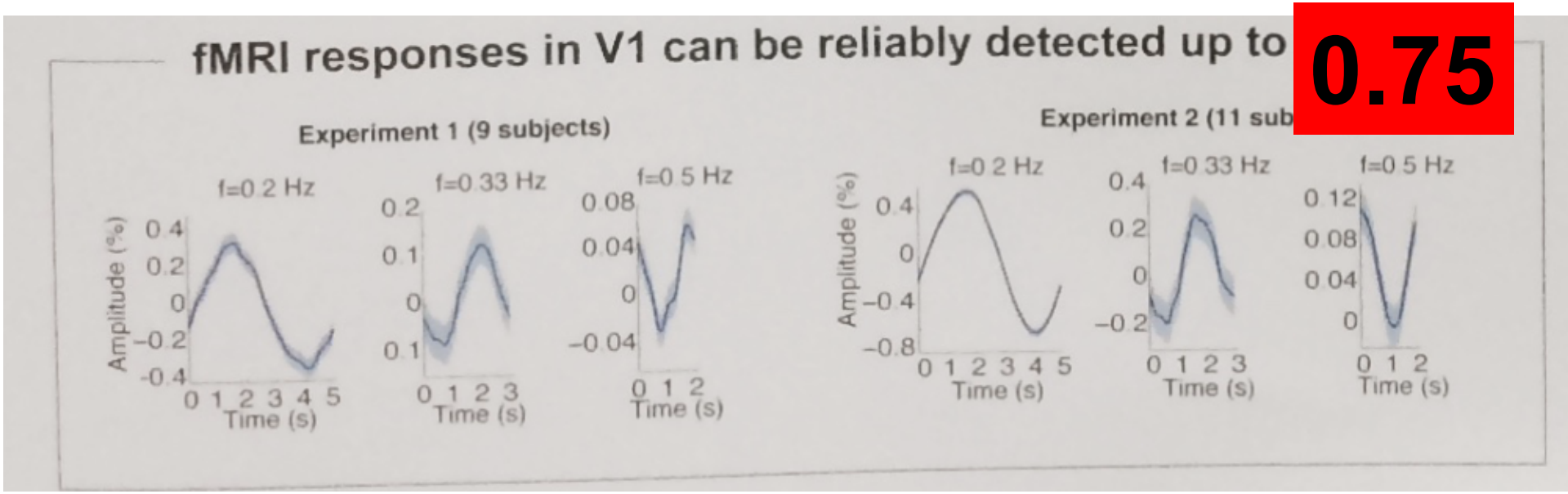
Detection of delta-band oscillations in visual cortex using fast fMRI and simultaneous EEG-fMRI

Laura D. Lewis, Kawin Setsompop, Bruce R. Rosen, Jonathan R. Polimeni

OHBM 2015







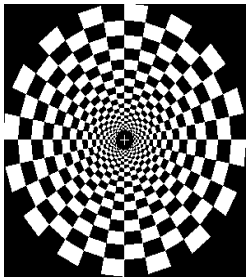
Challenge

◆ Human Brain Mapping 5:329–340(1997) ◆

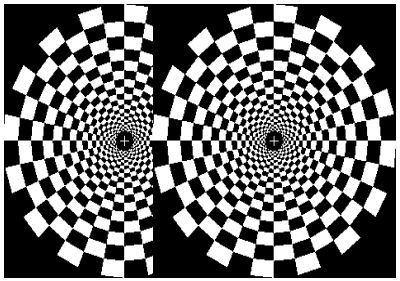
Selective Averaging of Rapidly Presented Individual Trials Using fMRI

Anders M. Dale* **and Randy L. Buckner**

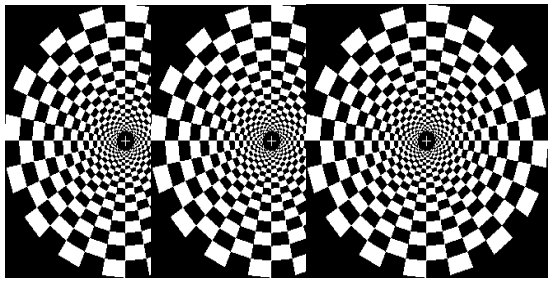
Massachusetts General Hospital Nuclear Magnetic Resonance Center and the Department of Radiology, Harvard Medical School, Boston, Massachusetts 02129



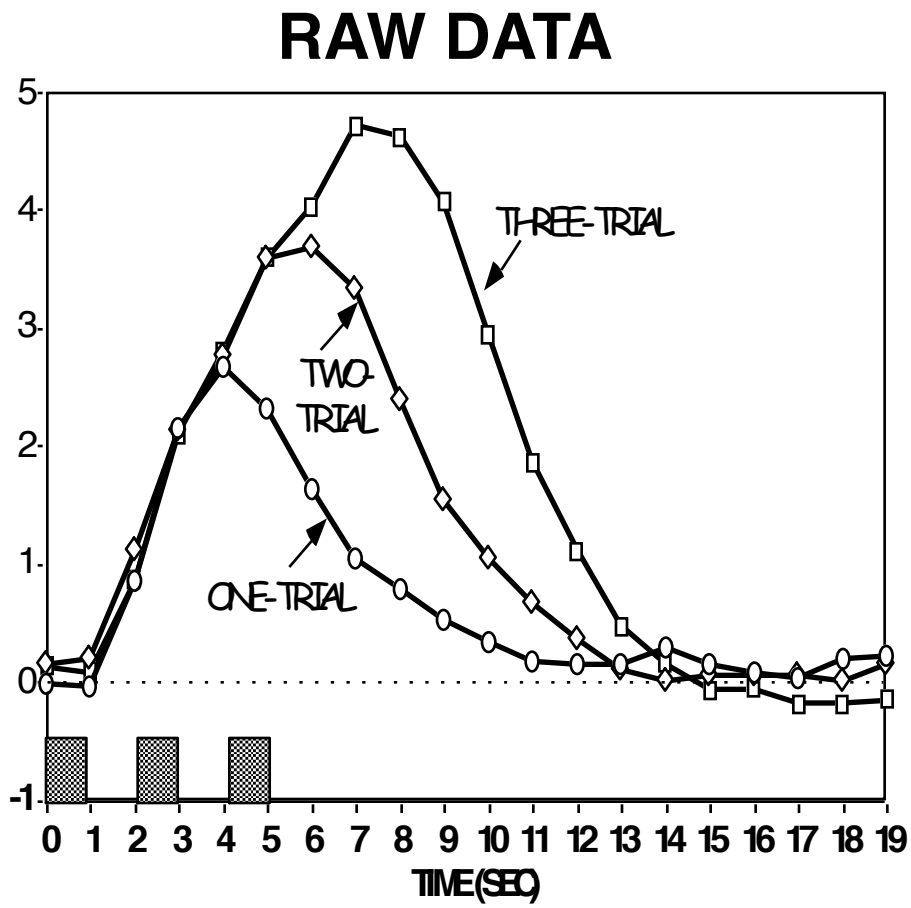
0 sec 20 sec

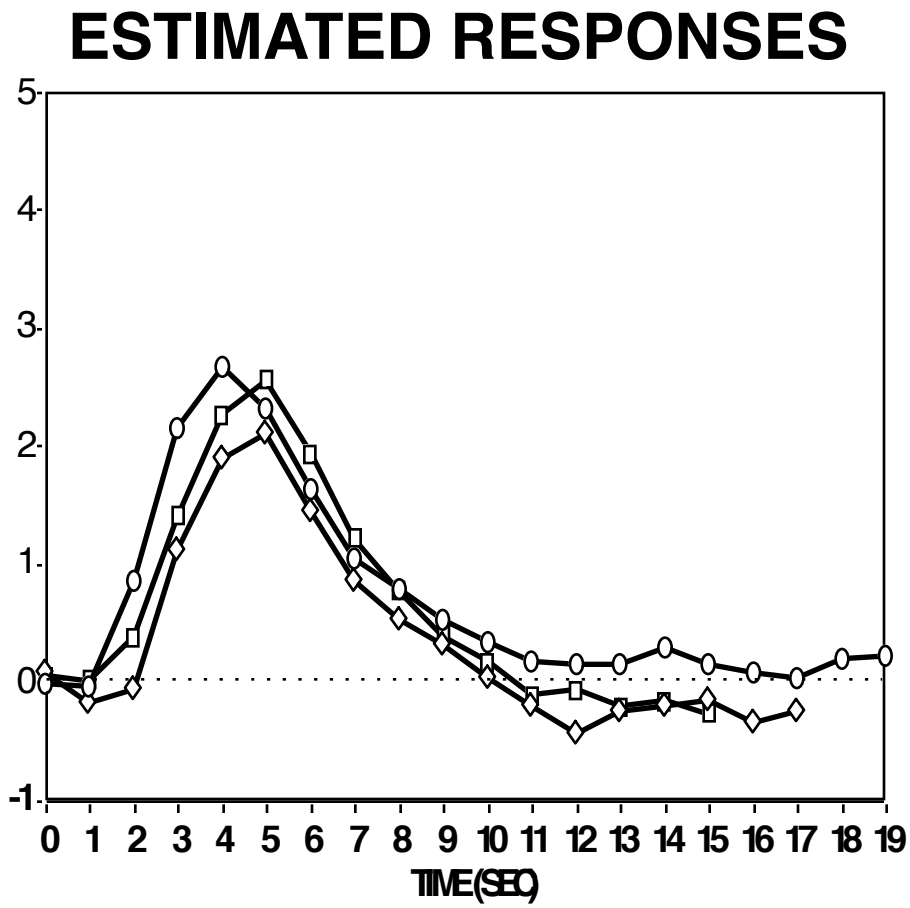


0 sec2 sec 20 sec



0 sec2 sec4 sec 20 sec


RAW DATA
THREE-TRIAL
TWO-TRIAL
ONE-TRIAL
5
4
3
2
1
0
-1
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
TIME (SEC)


ESTIMATED RESPONSES
5
4
3
2
1
0
-1
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
TIME (SEC)

Hemodynamic Controversies and Challenges

Pulse sequence dependence

Temporal resolution

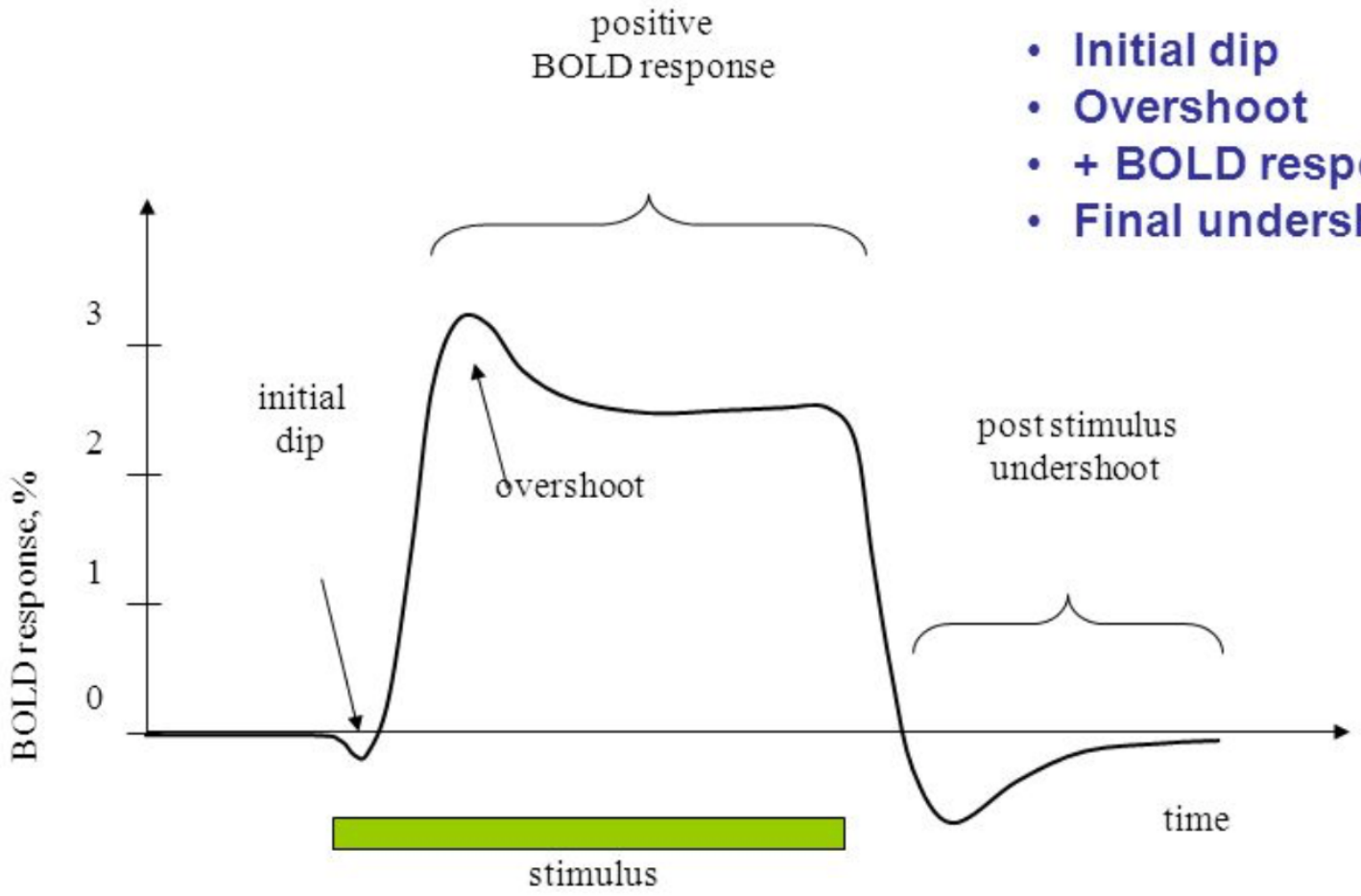
Nonlinearity

Pre and post undershoots

Negative signal changes

What are we missing?

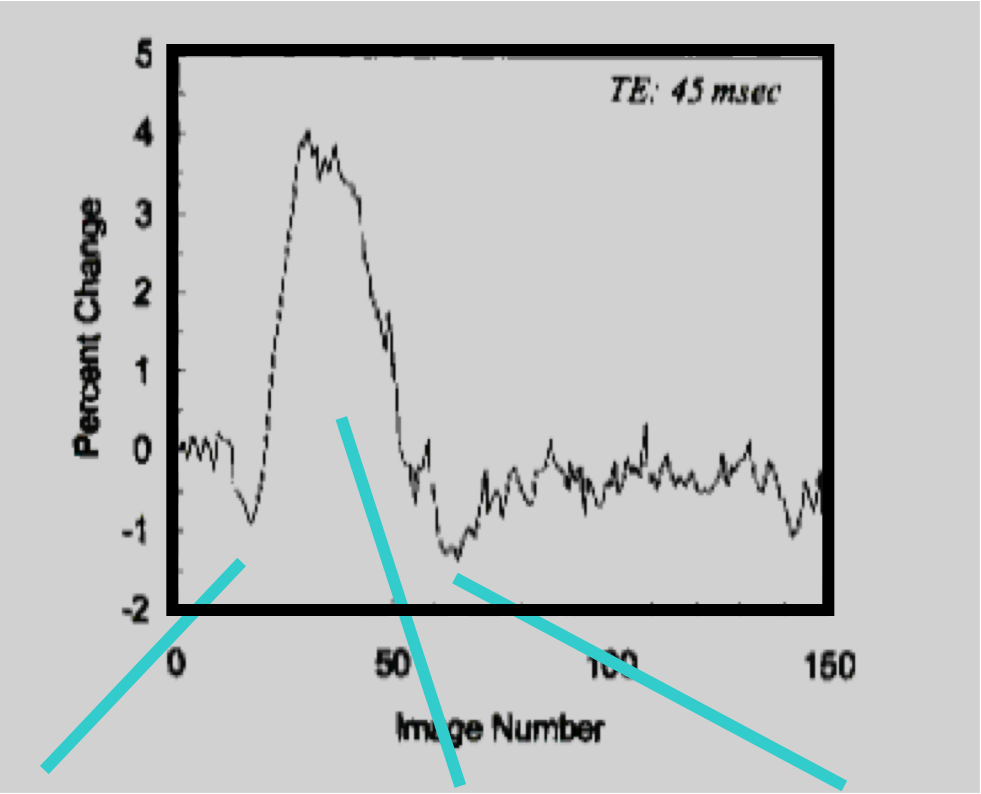
fMRI Bold Response Model



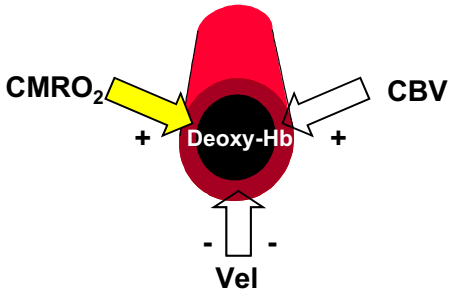
- **Initial dip 0.5-1sec**
- **Overshoot peak 5-8 sec**
- **+ BOLD response 2-3%**
- **Final undershoot variable**

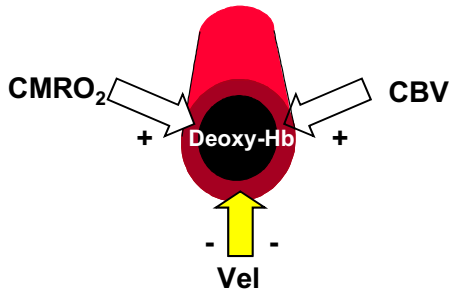
Controversy

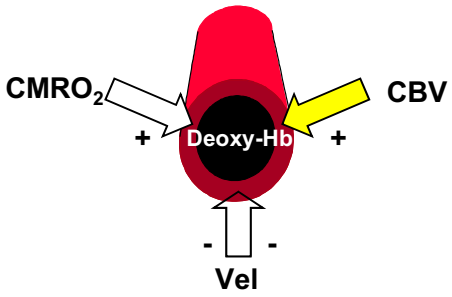
The Undershoots



Yacoub E, Le TH, Ugurbil K, Hu X (1999) Magn Res Med 41(3):436-41

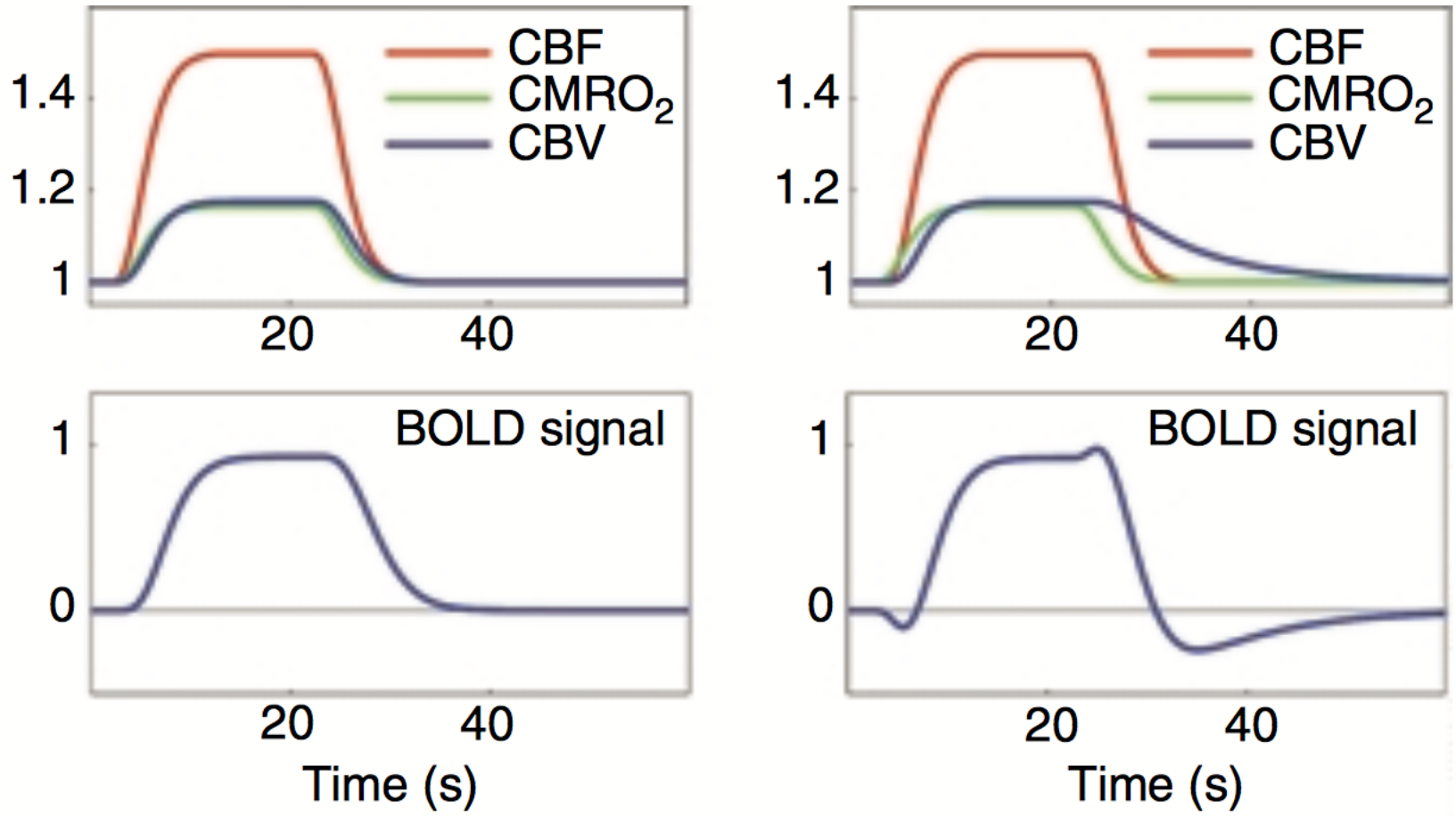






Courtesy of Arno Villringer

Controversy



Controversy

Origins of evoked BOLD response

- Large (2-4%; 3.0T) sustained positive response due to mismatch in increases in CBF and CMRO2 during elevated brain activity

- Initial dip
  - May be due to temporal mismatch in increase in CMRO2 and CBF
  - May be due to early increase in CBV relative to CBF
  - Some think it doesn't exist at all

- Post-stimulus undershoot
  - Sustained elevation in $CMRO_2$
  - Sustained elevation in CBV ("balloon model")
  - Reduction in CBF
  - All my be operational to different extents

Hemodynamic Controversies and Challenges

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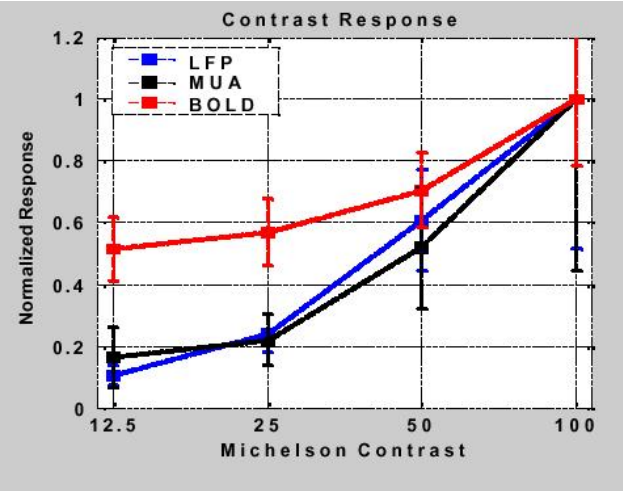
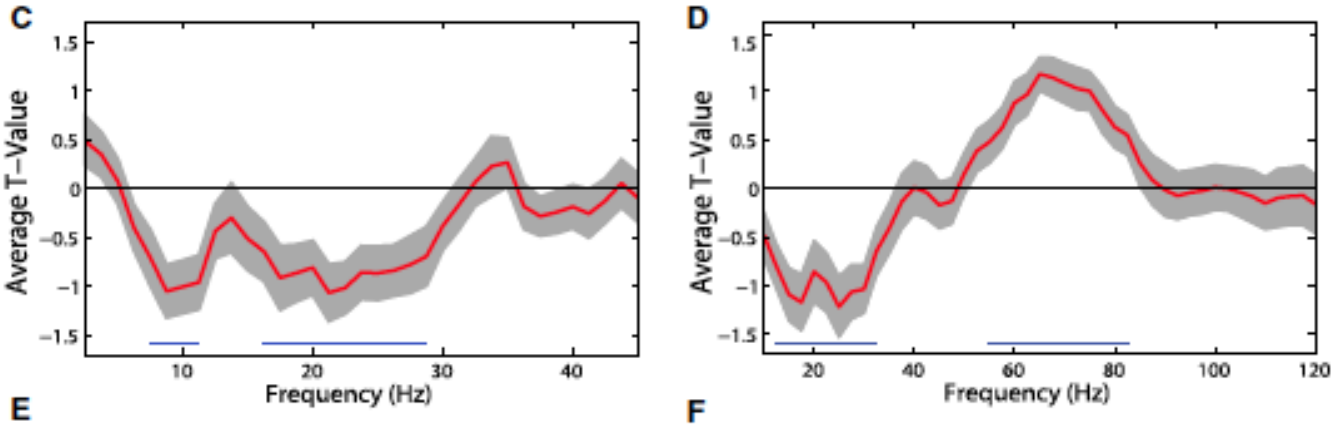
What are we missing?



Logothetis et al, Nature, 412, 150-157, 2001

-Activation causes enhanced high frequency and decreased low frequency oscillations

EEG-BOLD RELATION



R. Scheeringa, et al. Neuron, 69: 572-583, 2011

Controversy

Multiple ways to get a BOLD signal change

Positive BOLD Effect	↑ CBF	↑ CBV	↑ $CMRO_2$
	↑ CBF	↑ CBV	— $CMRO_2$
	↑ CBF	↑ CBV	↓ $CMRO_2$
Negative BOLD Effect	— CBF	↑ CBV	— $CMRO_2$
	— CBF	— CBV	↑ $CMRO_2$
	↓ CBF	— CBV	— $CMRO_2$
	↓ CBF	↑ CBV	↑ $CMRO_2$

Hemodynamic Controversies and Challenges

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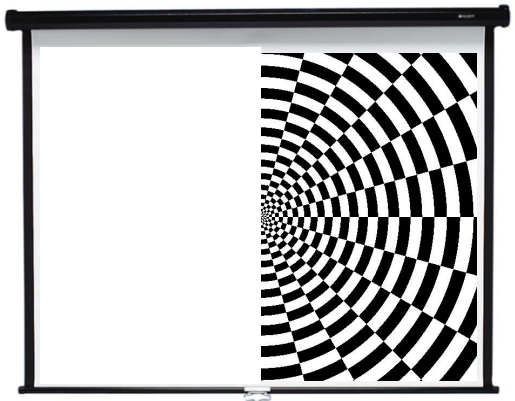
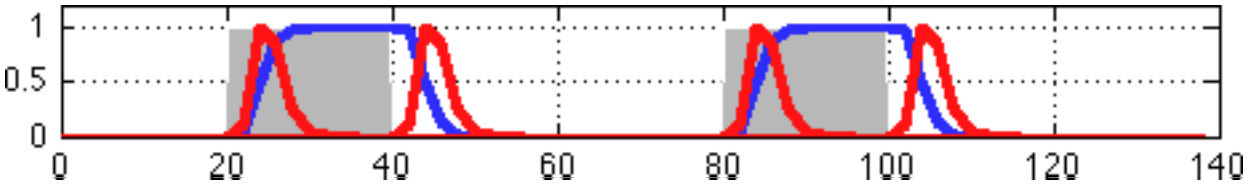
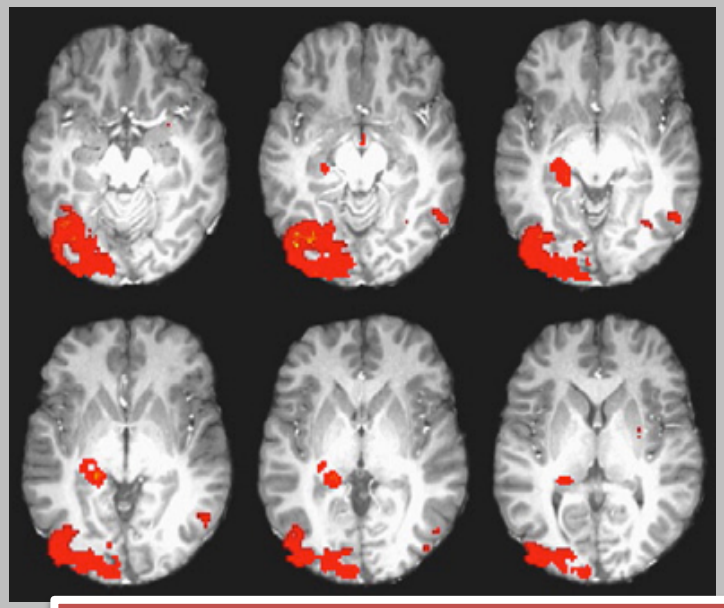
Predictive Response Model effect on fMRI Results (III)



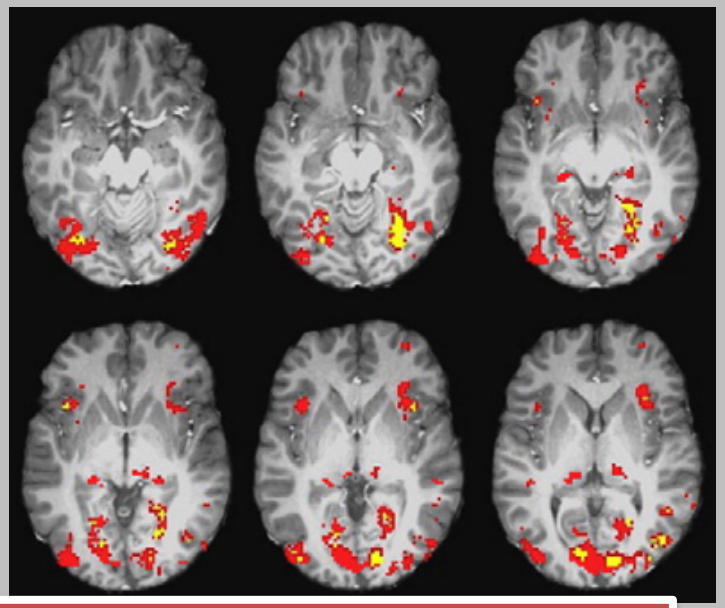
BLOCK DESIGN & HEMIFIELD VISUAL STIMULATION



SUSTAINED RESPONSE MODEL



ONSET/OFFSET RESPONSE MODEL

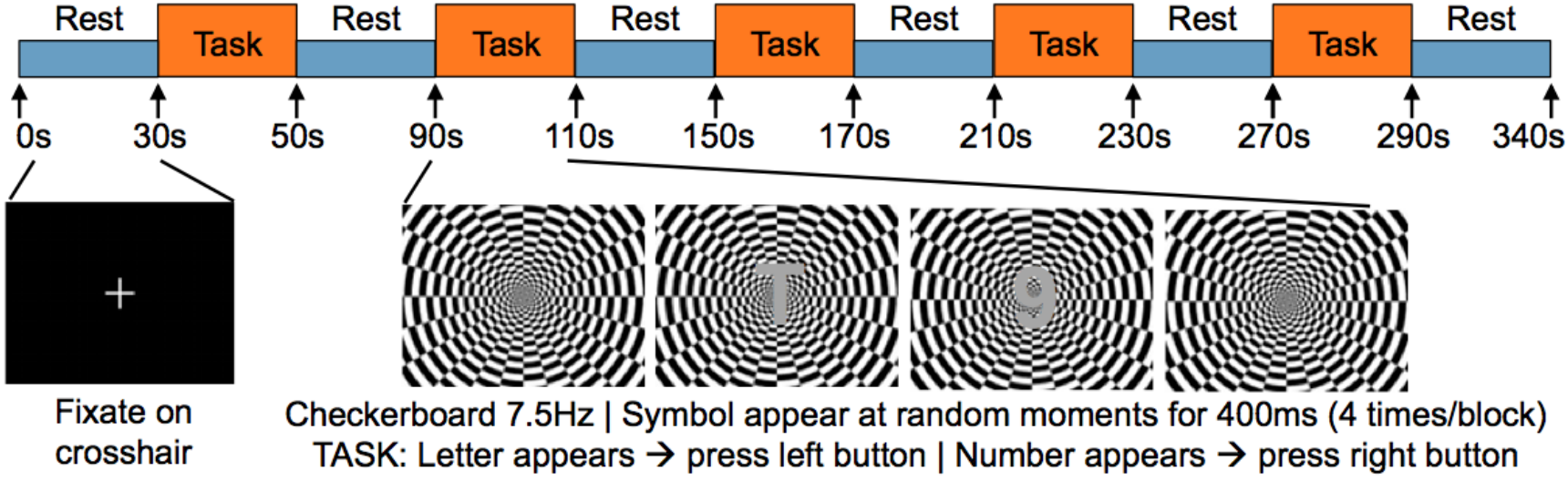


DIFFERENT RESPONSE SHAPES ARE PRESENT ACROSS DIFFERENT REGIONS OF THE BRAIN FOR A SINGLE STIMULUS TYPE

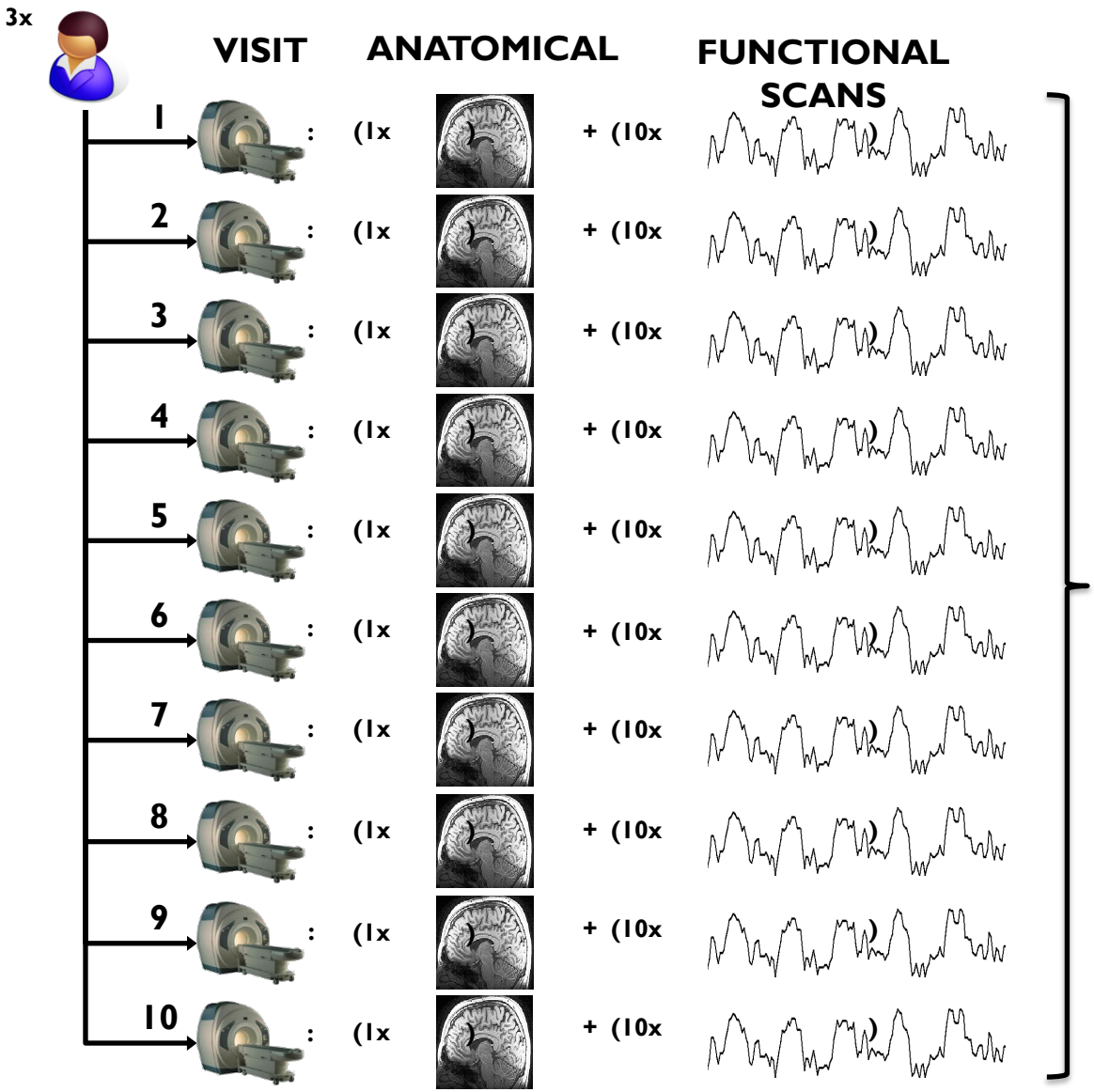
Uludag et al. Magn Reson Imaging. 2008 Sep;26(7):8

Experimental Methods (I)

- 3 Healthy Volunteers: 1M/2F; Age = 27 ± 2.5
- 3T GE Signa HDx
- Anatomical Scan: MPRAGE | .9x.9x1.2 mm^3 | 192 Slices
- Functional Scans: GRE-EPI
  - TR/TE = 2s/30ms
  - In-Plane Res = 64x64
  - #Slices = 32 Oblique
  - **FOV = 240mm**
  - **Slice Thickness = 3.8 mm**
  - **Flip Angle = 75°**



Experimental Methods (II)



100 FUNCTIONAL RUNS/SUBJECT

=

500 TRIALS/SUBJECT

=

9 HOURS OF DATA/SUBJECT

X 100
(QA Axial EPIs)

Data Analysis

DATA PRE-PROCESSING

Remove Physiological Noi

Slice Timing Correction

Head Motion Corre

Inter-run Coregistra

Discard Initial 5 Vol

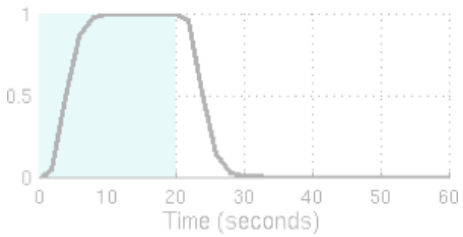
Remove Motion & 1

Intensity Normaliz

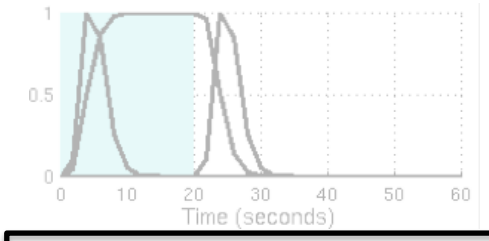
DATA AVERAGING

$N_{avg} = 1$ < -- > $N_{avg} = 100$

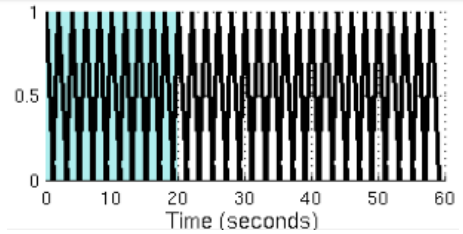
STATISTICAL ANALYSIS



SUSTAINED RESPONSE ONLY (SUS)

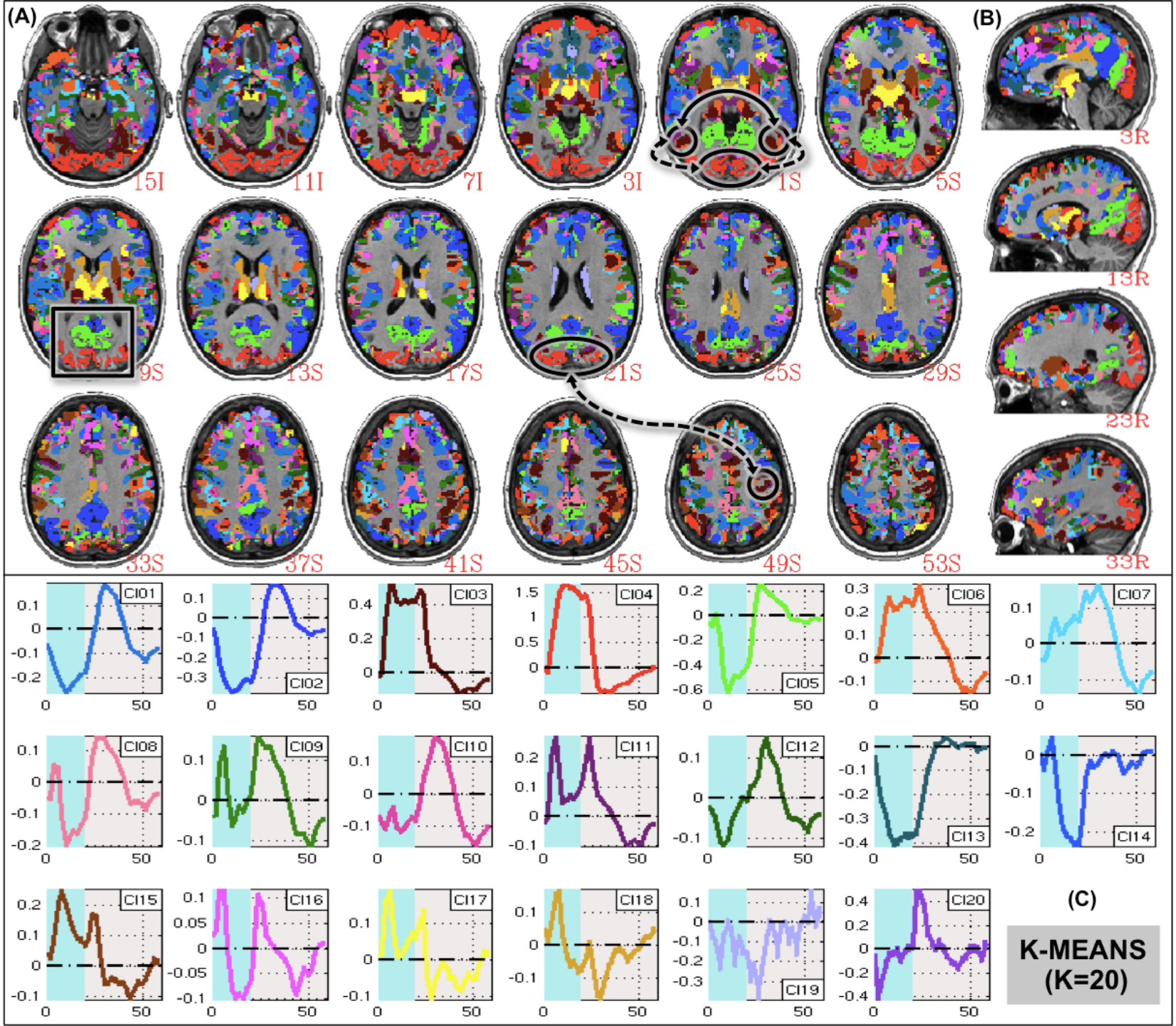


ONSET + SUSTAINED + OFFSET RESPONSE (SUS)

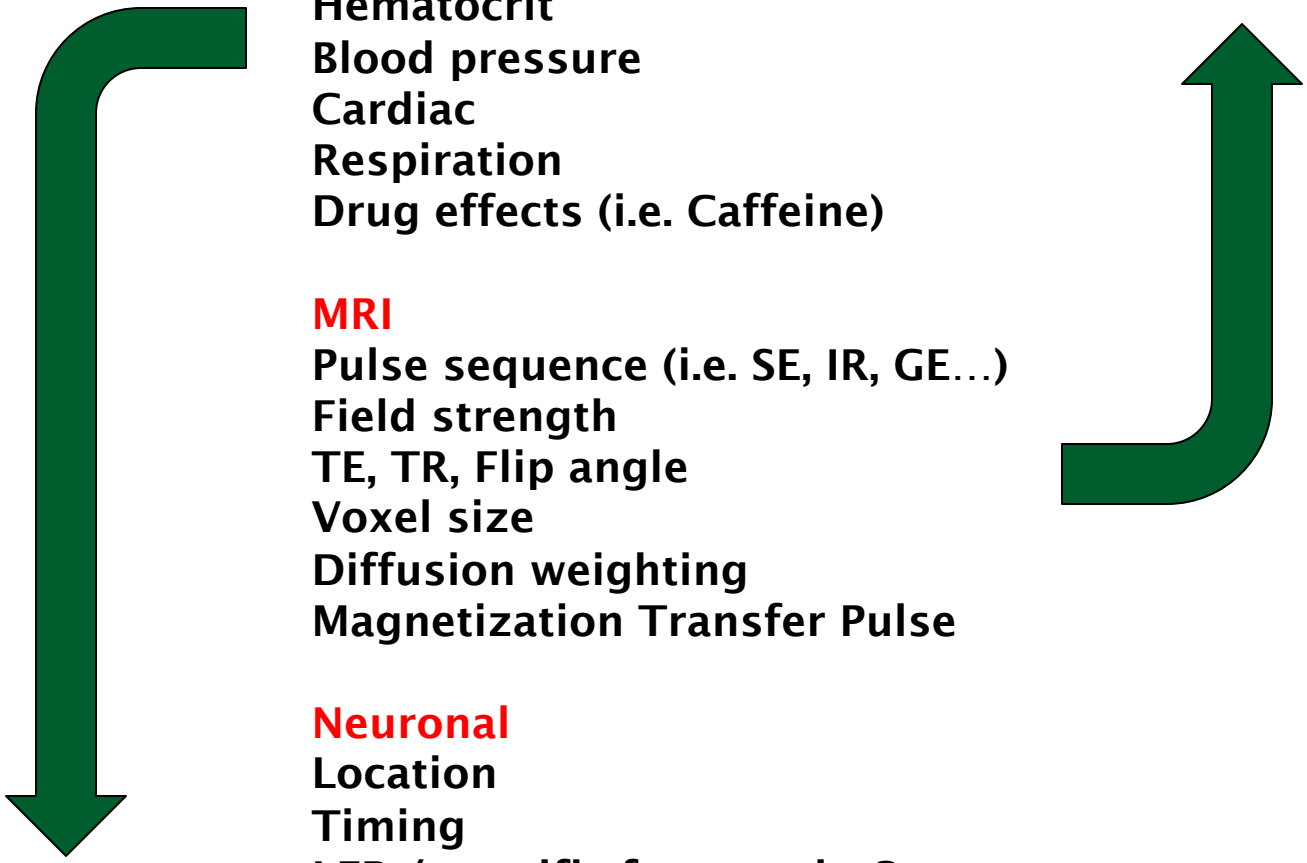


UNCONSTRAINED MODEL (UNC)

CLUSTERING ANALYSIS


(A)
15I
11I
7I
3I
1S
5S
9S
13S
17S
21S
25S
29S
33S
37S
41S
45S
49S
53S
(B)
3R
13R
23R
33R
CI01
CI02
CI03
CI04
CI05
CI06
CI07
CI08
CI09
CI10
CI11
CI12
CI13
CI14
CI15
CI16
CI17
CI18
CI19
CI20
(C)
K-MEANS
(K=20)

What factors influence the fMRI signal magnitude and timing?



Physiologic

Baseline: flow, oxygenation, volume, vessel size, metabolism

Change: flow, oxygenation, volume, vessel size, metabolism

Hematocrit

Blood pressure

Cardiac

Respiration

Drug effects (i.e. Caffeine)

MRI

Pulse sequence (i.e. SE, IR, GE…)

Field strength

TE, TR, Flip angle

Voxel size

Diffusion weighting

Magnetization Transfer Pulse

Neuronal

Location

Timing

LFP / specific frequencies?

Number / Coherence of Neurons ?

Inhibition/Excitation?

Neurotransmitter concentrations?

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