Functional MRI Contrast and Limits of Spatial and Temporal Resolution

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&

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http://fmrif.nimh.nih.gov

Functional Contrast

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

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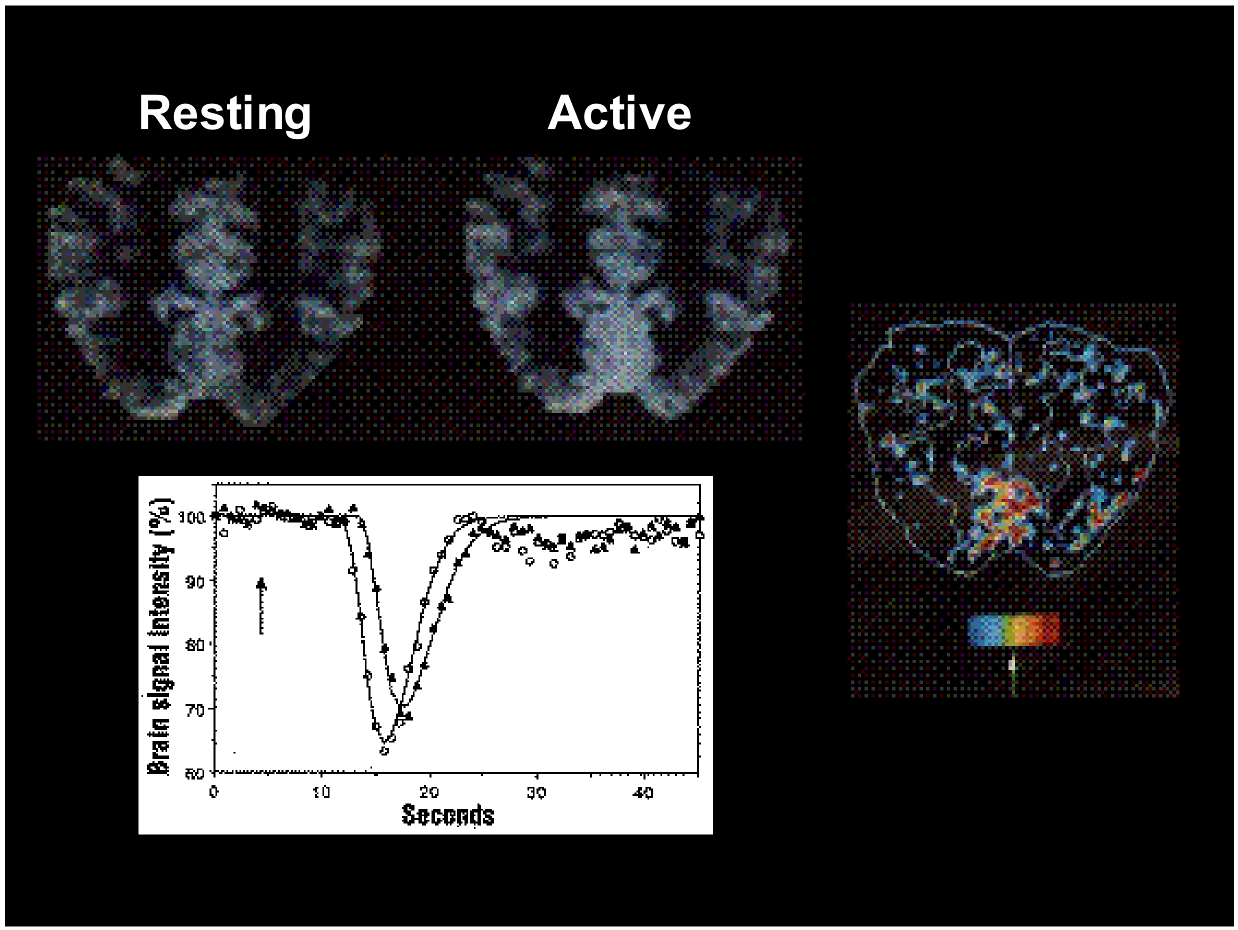
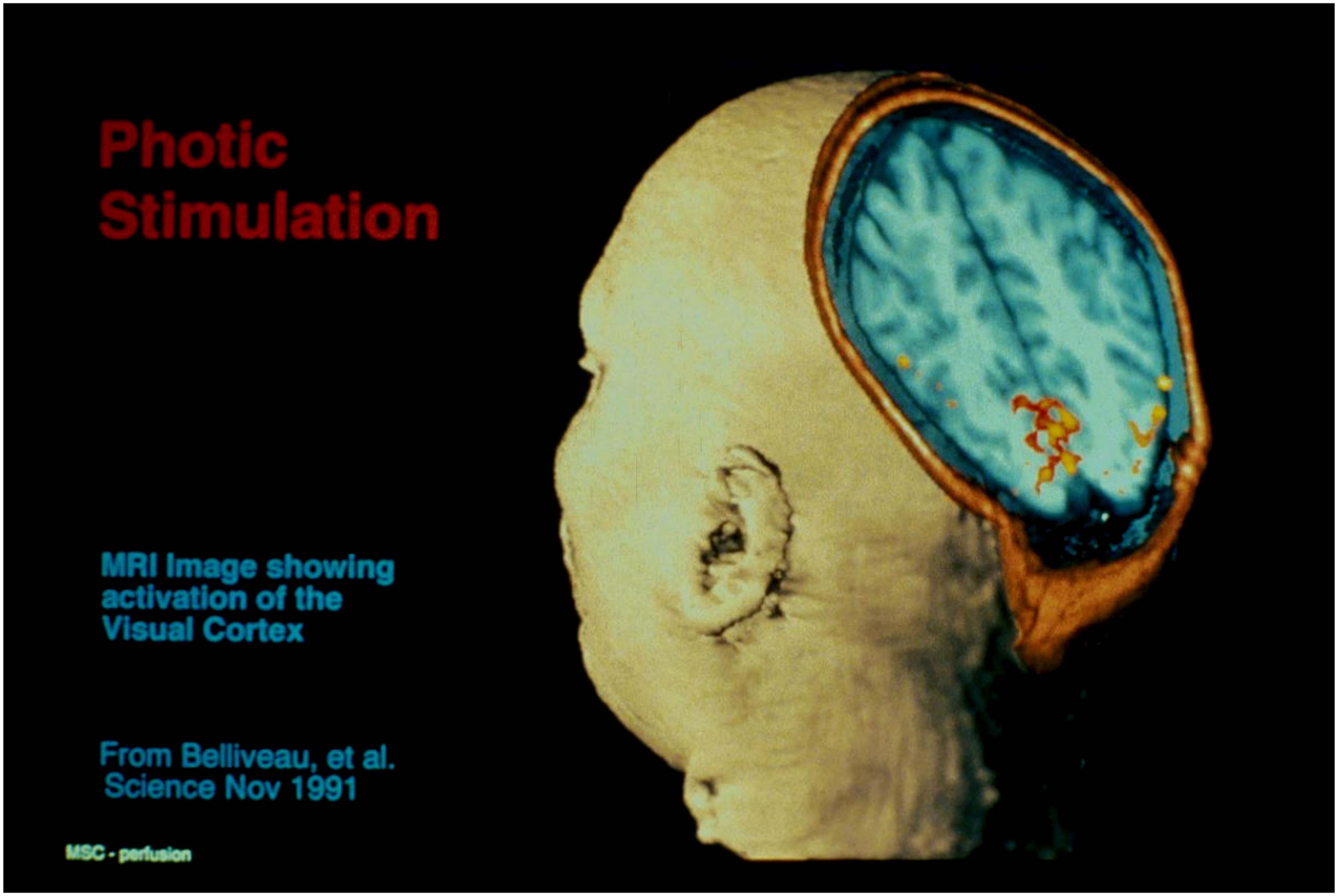
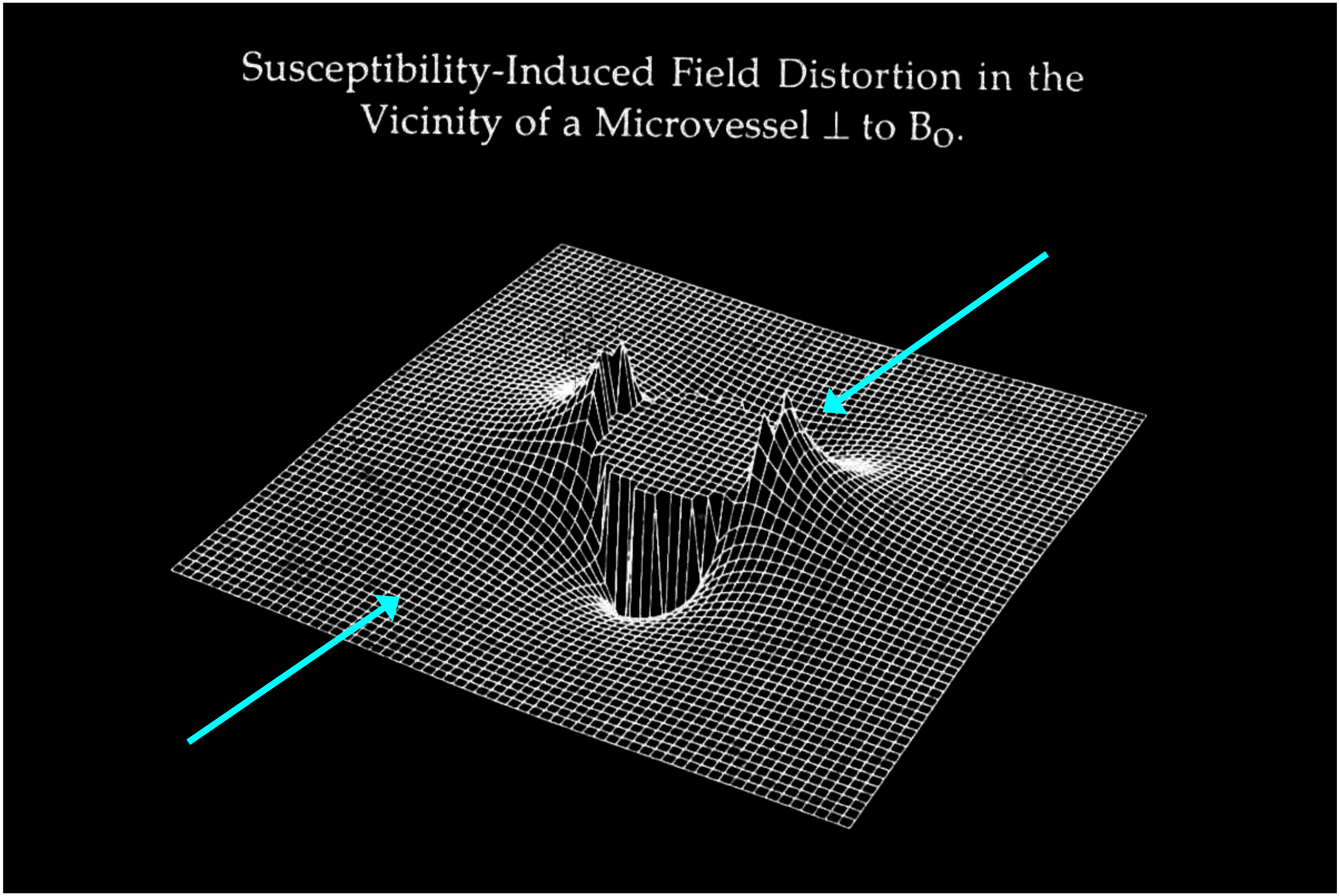
Blood Volume Imaging

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

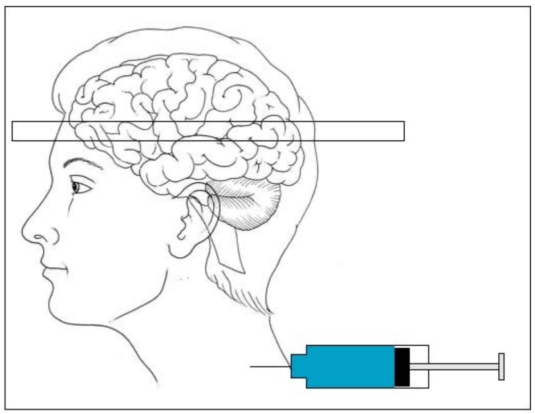


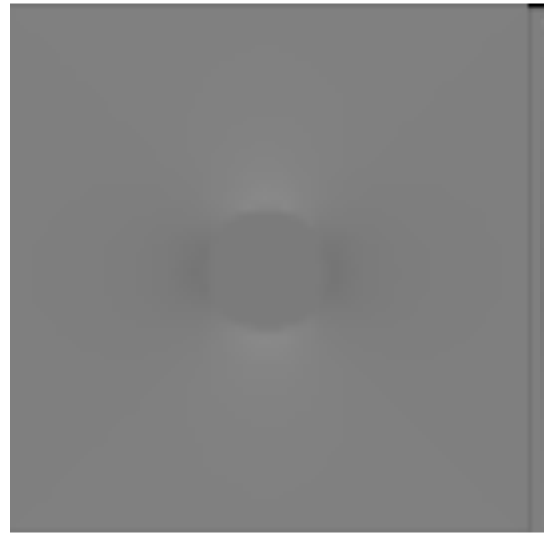

Photic
Stimulation
MRI Image showing
activation of the
Visual Cortex
From Belliveau, et al.
Science Nov 1991
MSC - perfusion

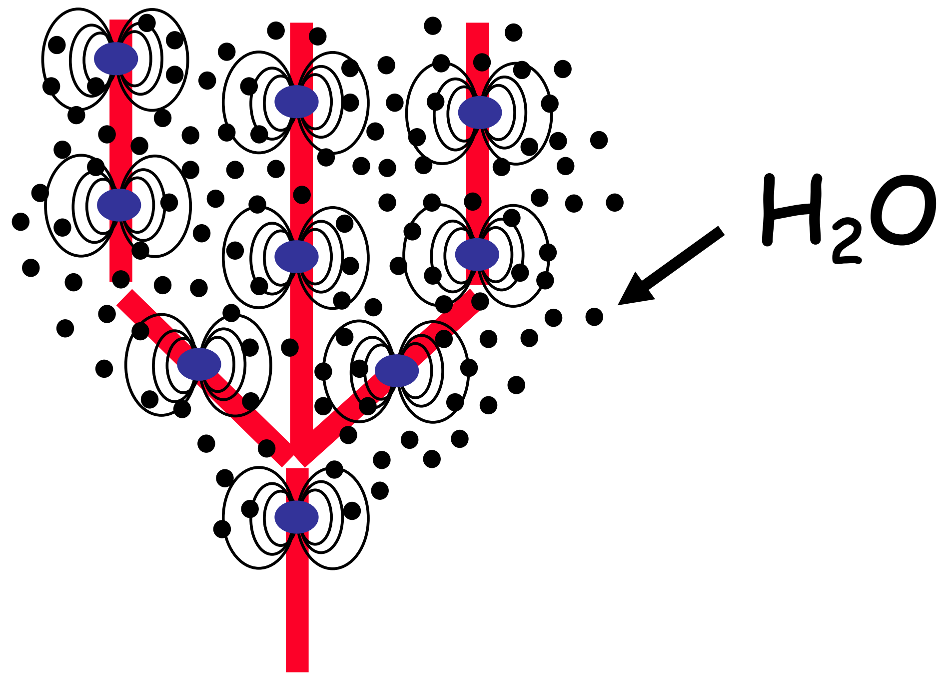
Susceptibility Contrast



Addition of paramagnetic compound to blood







Courtesy Larry Wald

Functional Contrast

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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

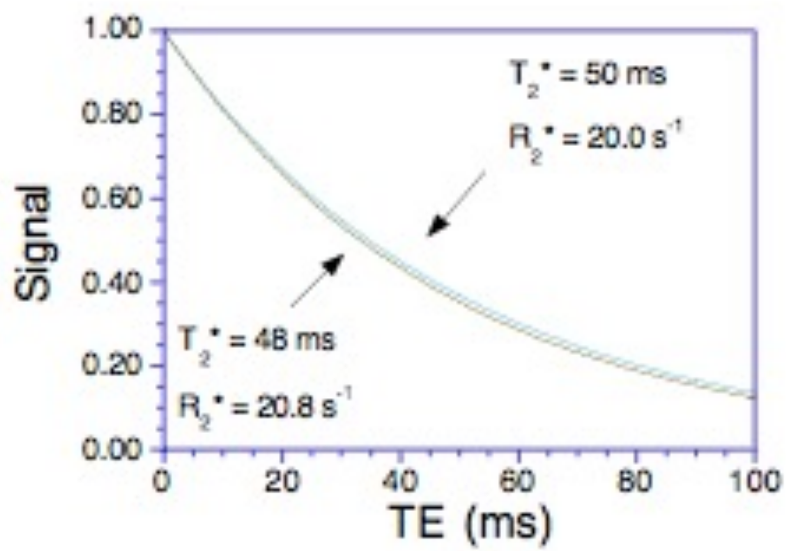
Deoxy-hemoglobin: paramagnetic
Oxy-hemoglobin: diamagnetic

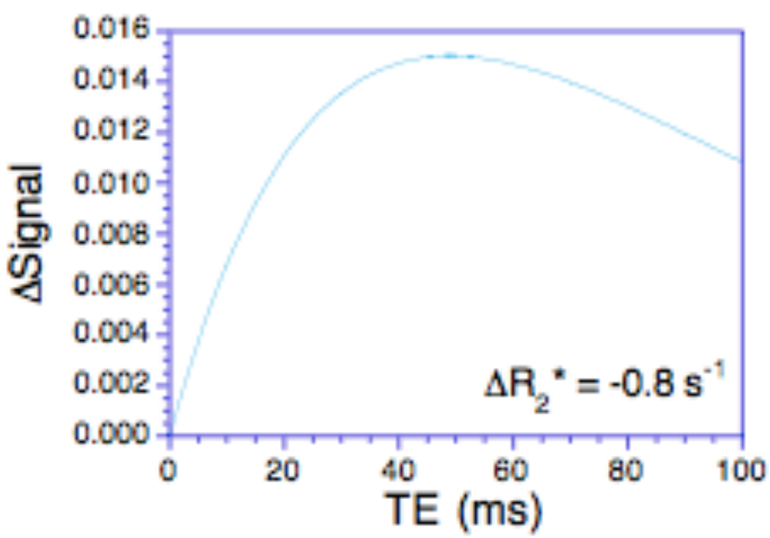
Decrease in susceptibility-related intravoxel dephasing

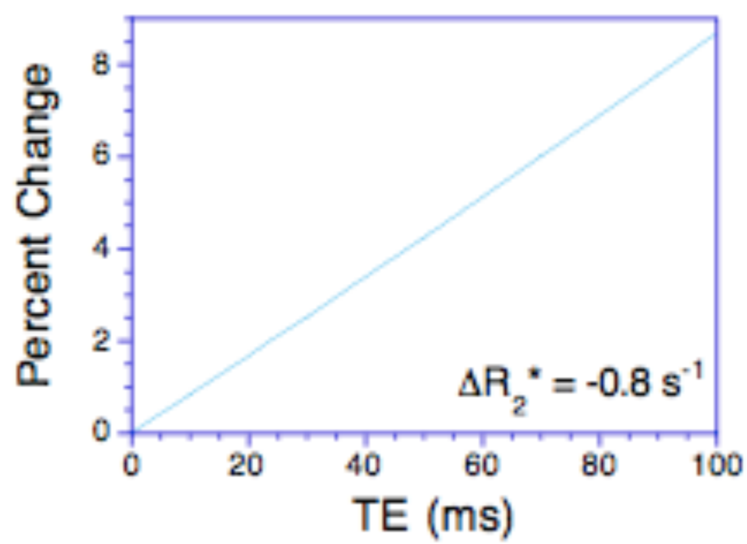
Increase in T2 and T2*

Local Signal Increase in T2 and T2* - weighted sequences

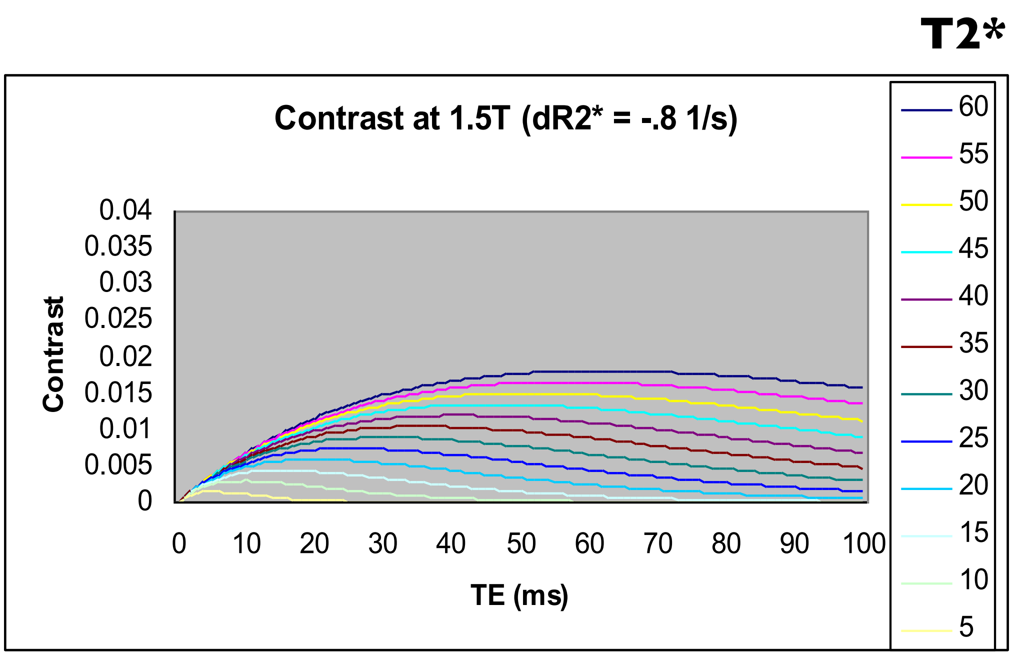
Characteristics of the BOLD signal: T2* effect.

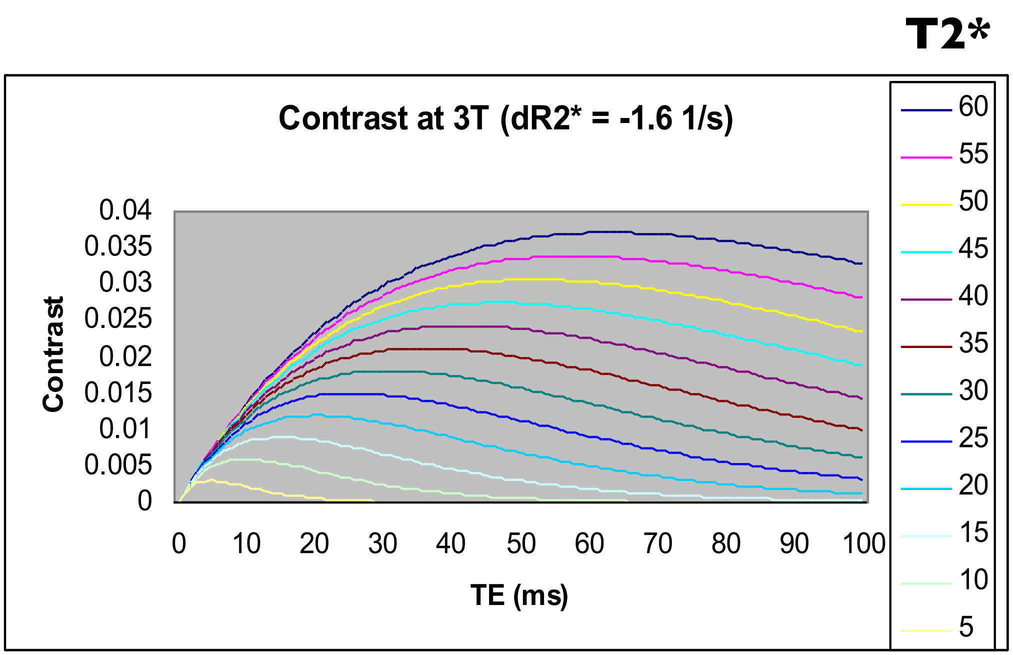


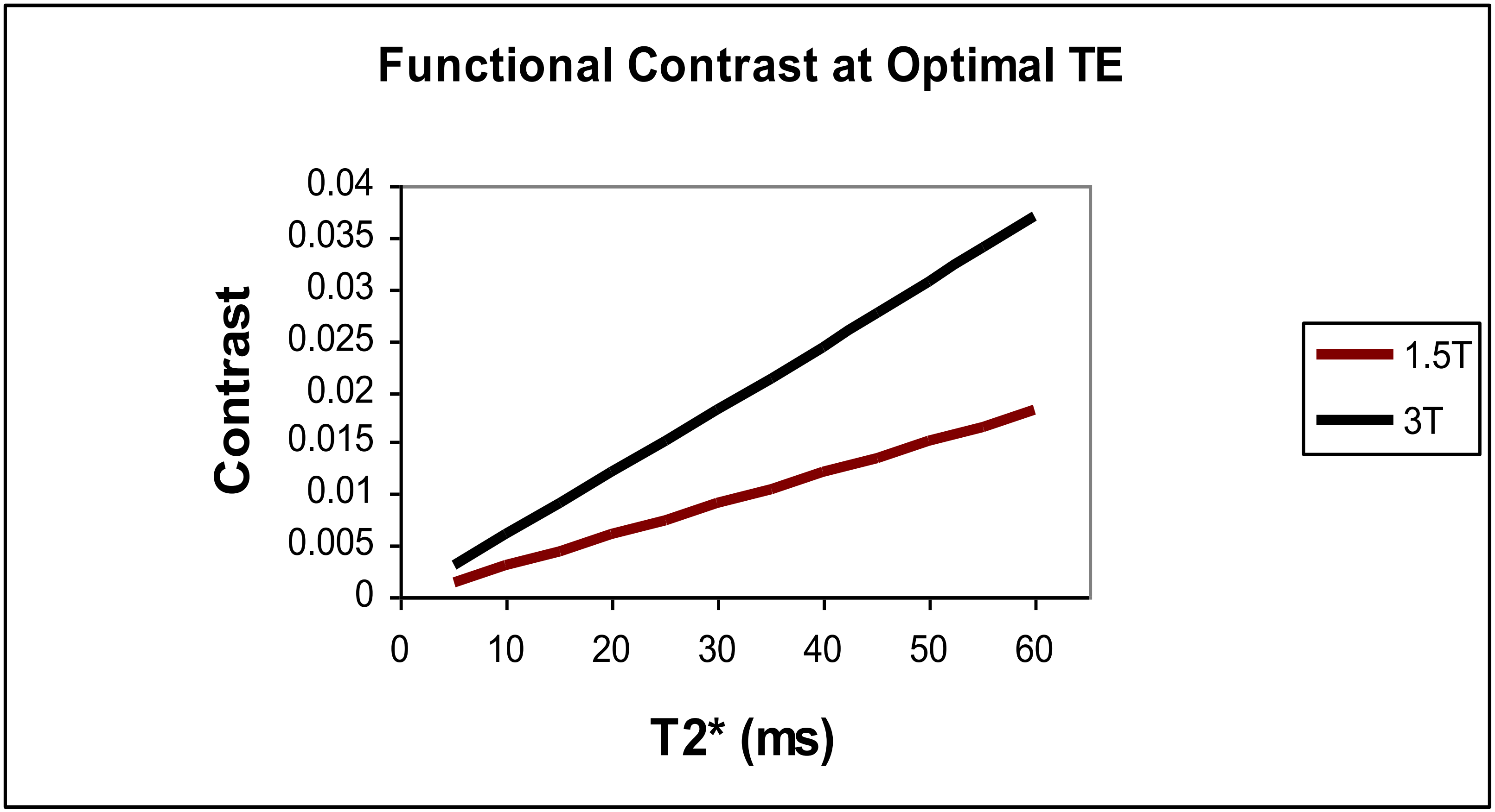




Contrast depends on:
activation-induced changes in T2* *and* resting T2*





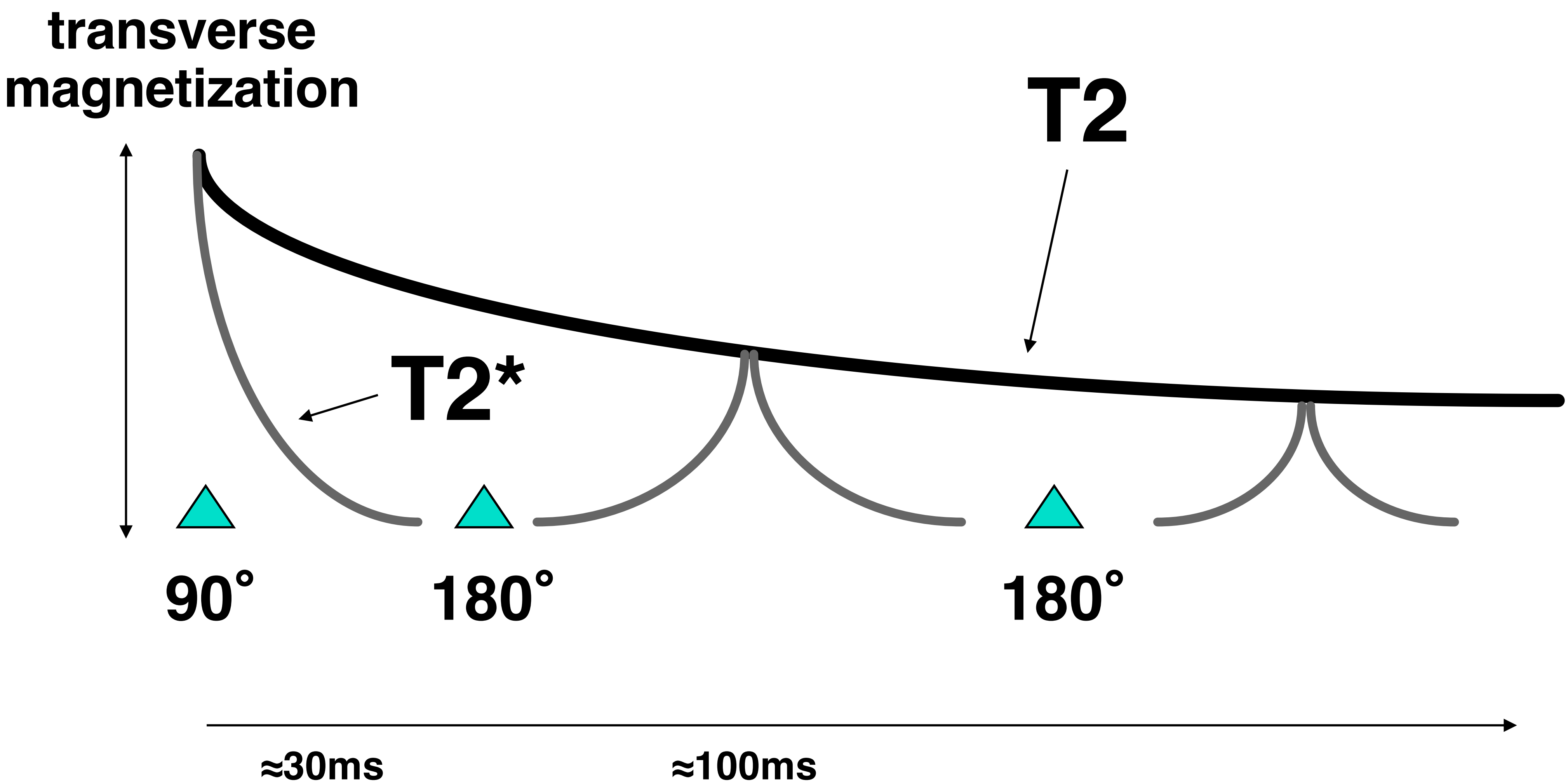


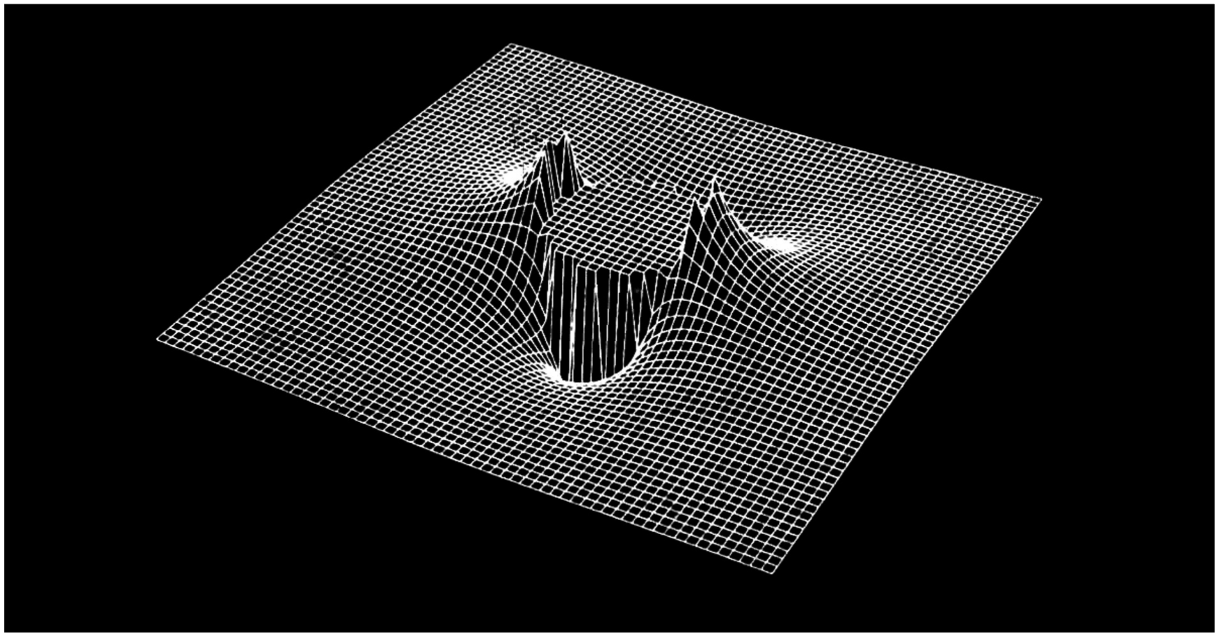
Functional Contrast at Optimal TE
Contrast
0.04
0.035
0.03
0.025
0.02
0.015
0.01
0.005
0
0
10
20
30
40
50
60
T2* (ms)
1.5T
3T

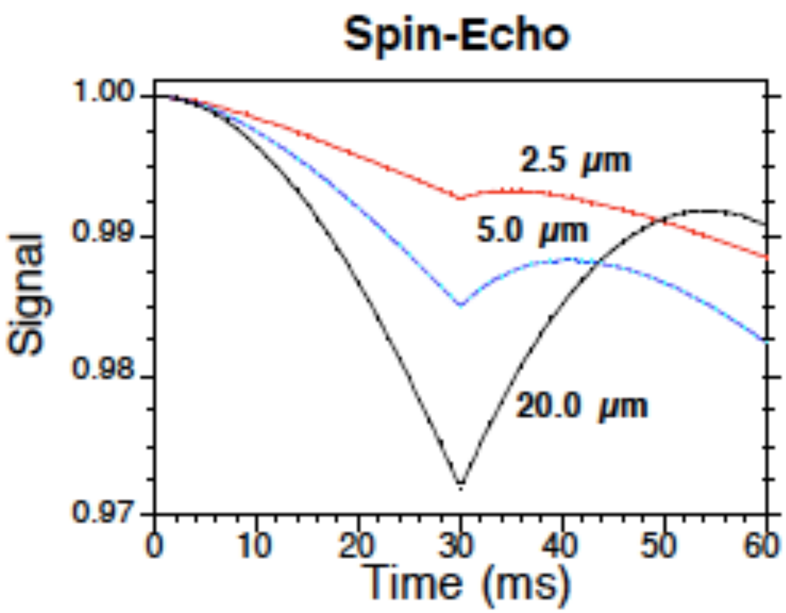
Spin-Echo vs. Gradient-Echo

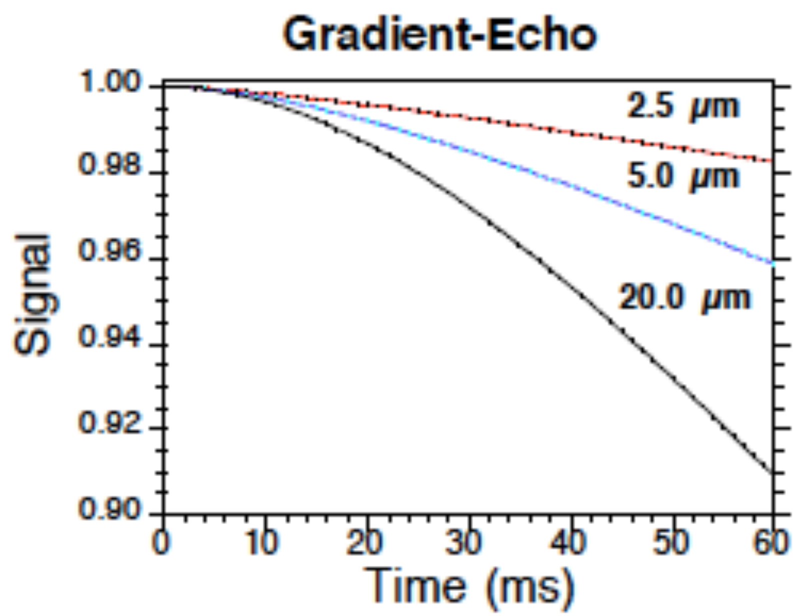
fMRI

Transverse Relaxation

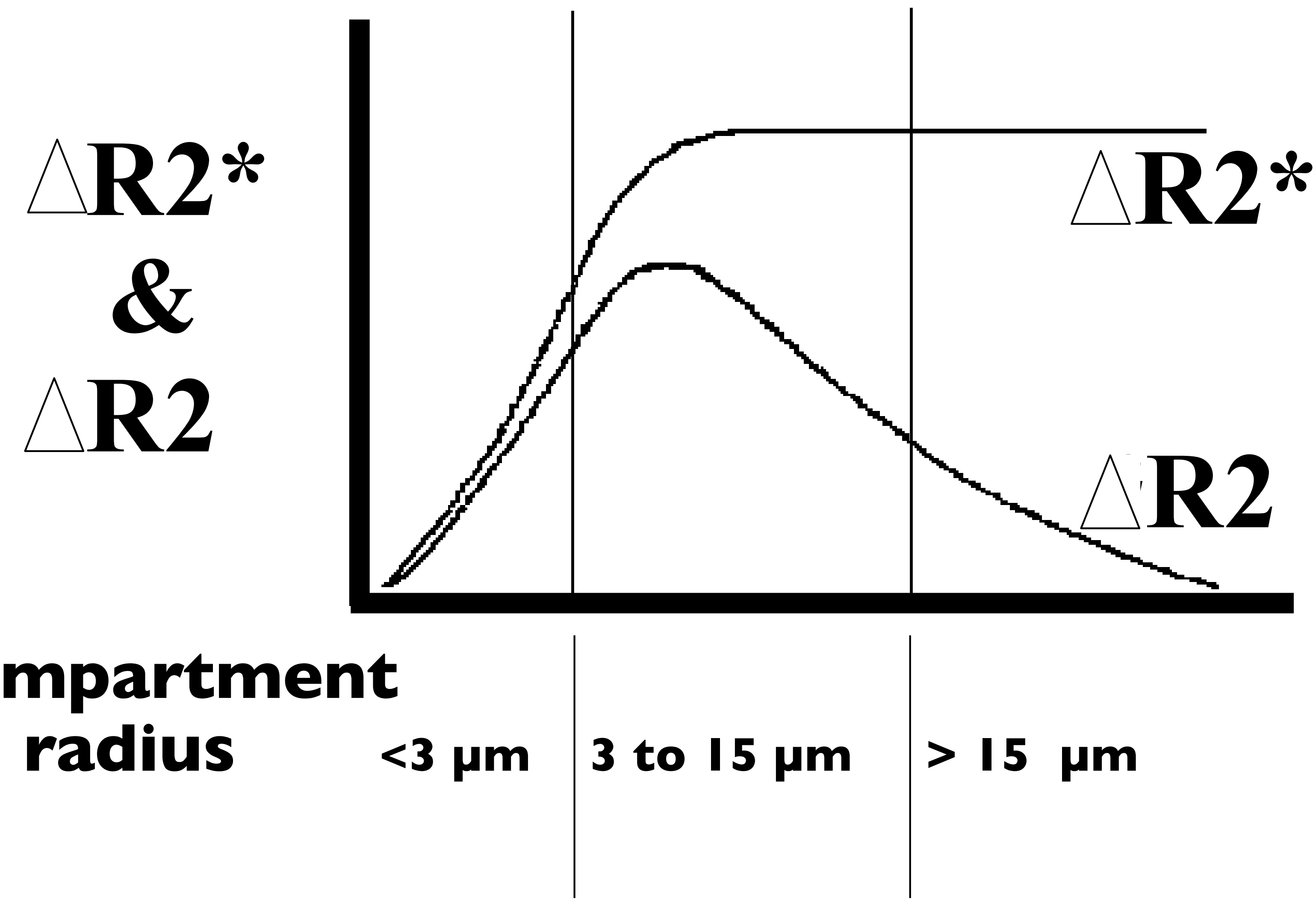




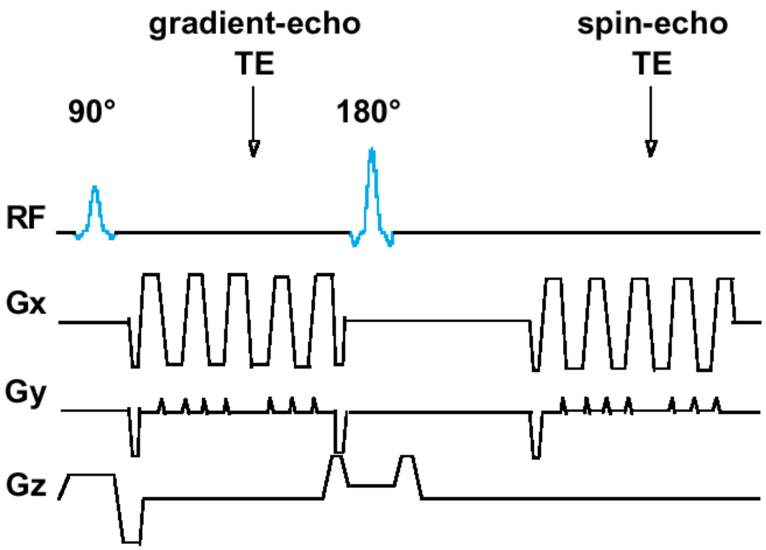

Spin-Echo
Signal
Time (ms)
1.00
0.99
0.98
0.97
0
10
20
30
40
50
60
2.5 μm
5.0 μm
20.0 μm

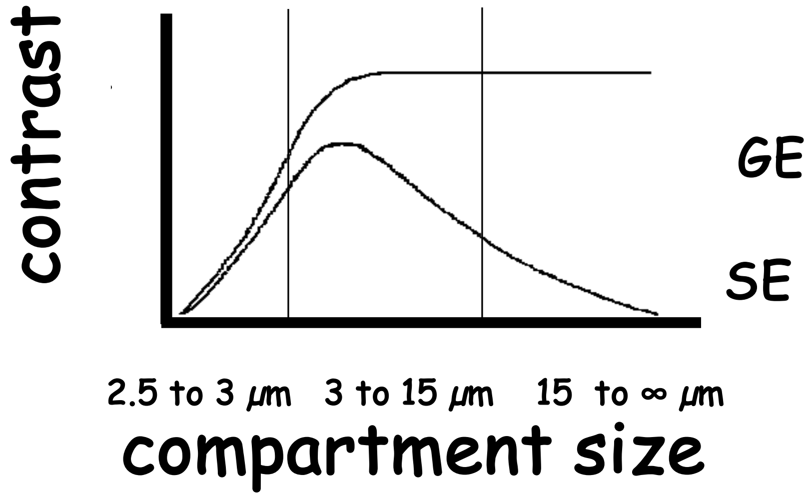

Gradient-Echo
Signal
Time (ms)
1.00
0.98
0.96
0.94
0.92
0.90
0
10
20
30
40
50
60
2.5 μm
5.0 μm
20.0 μm

Spin echo vs. Gradient echo



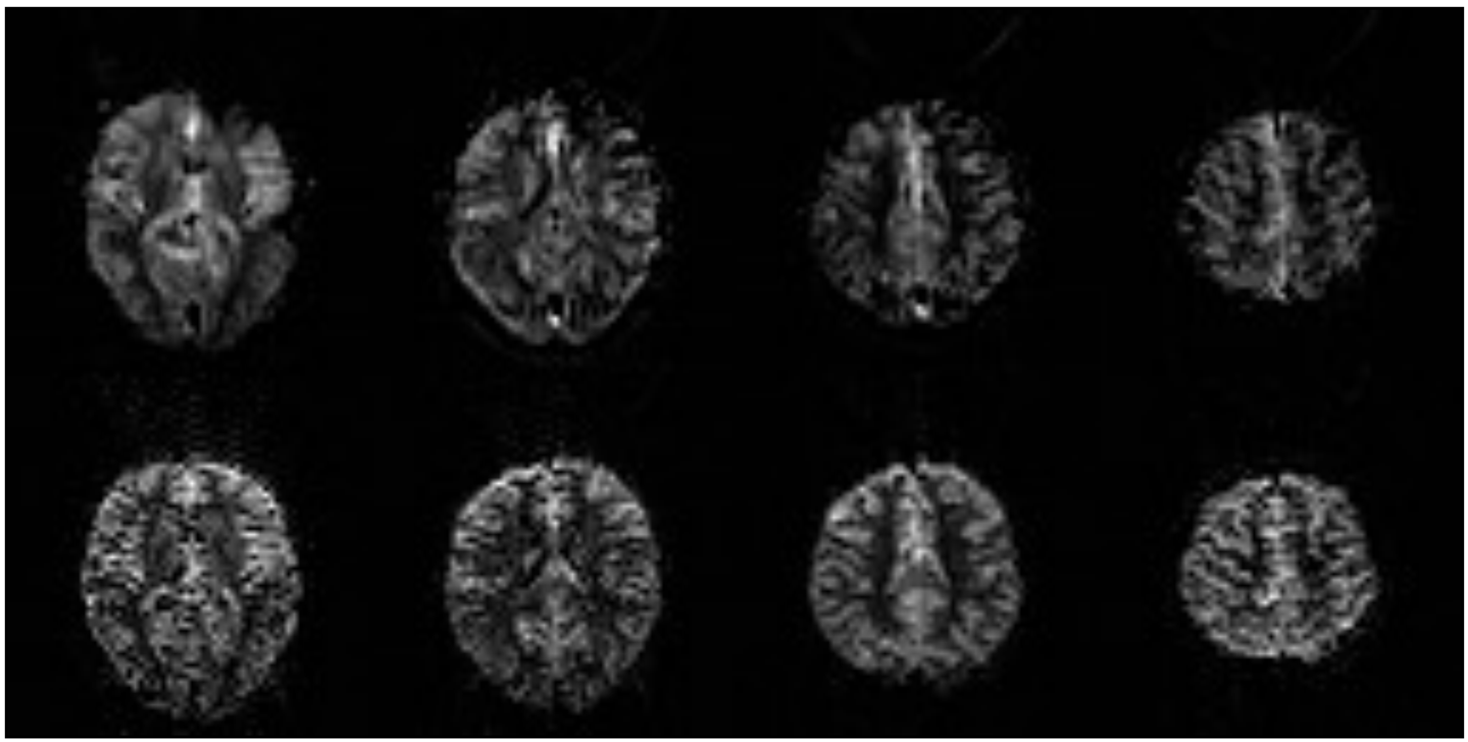
Bolus Injection of Gadolinium

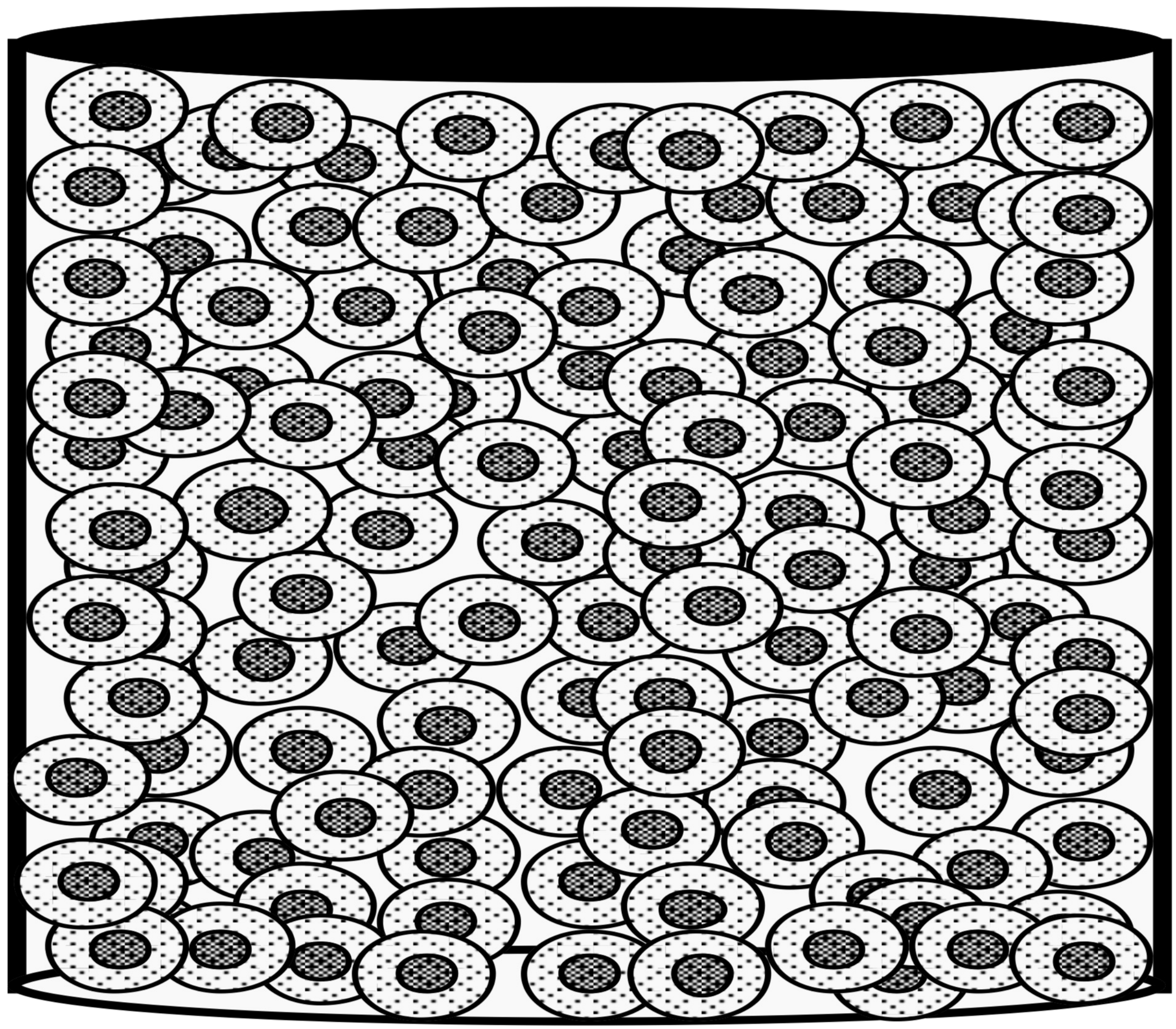


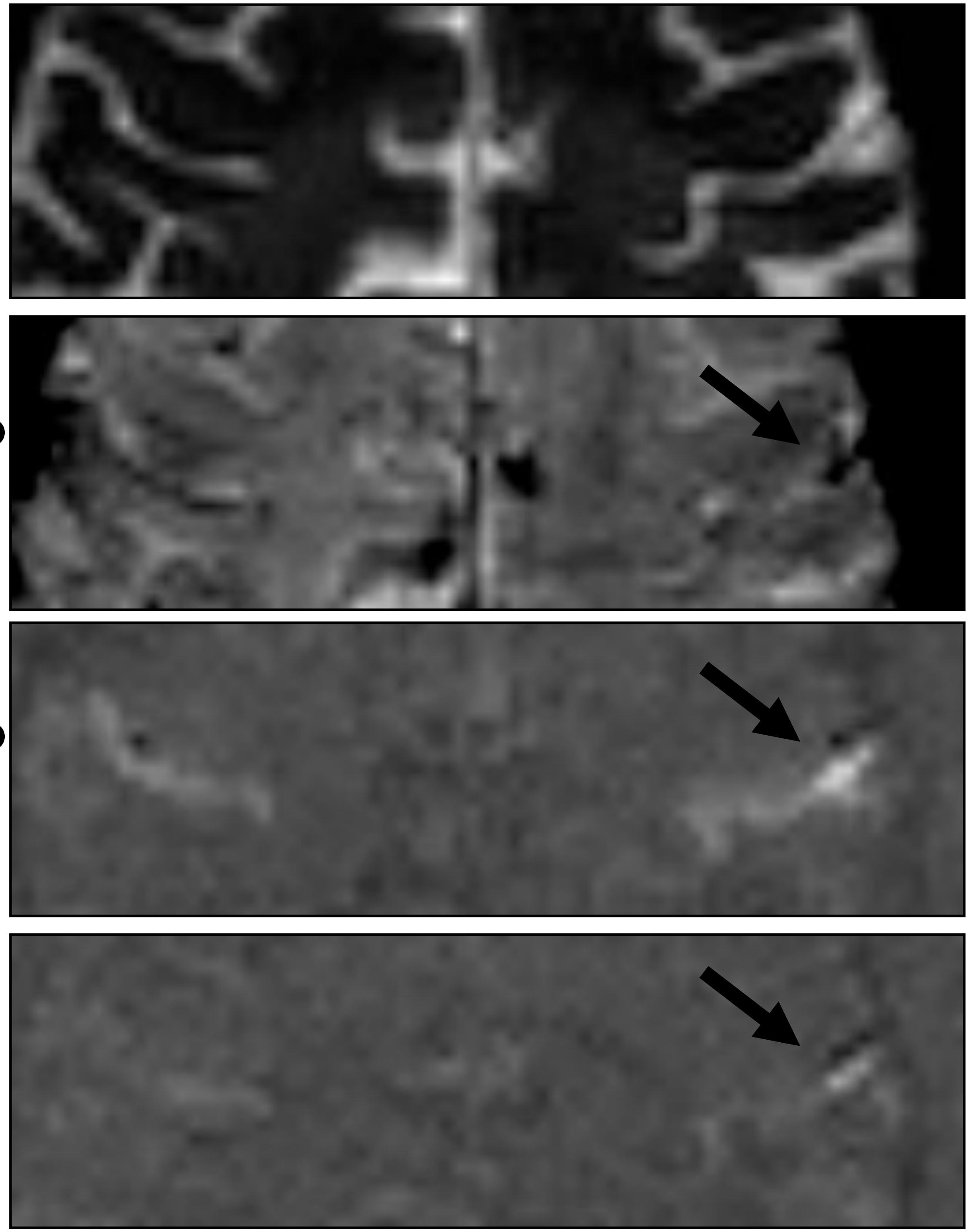


GE
TE = 30 ms

SE
TE = 110 ms

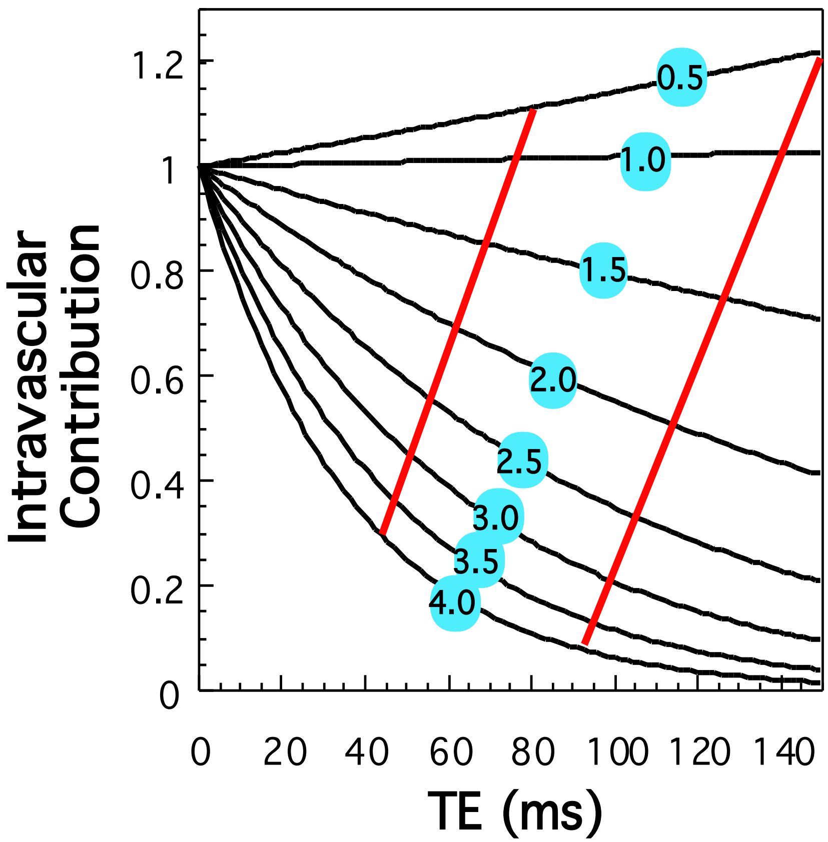




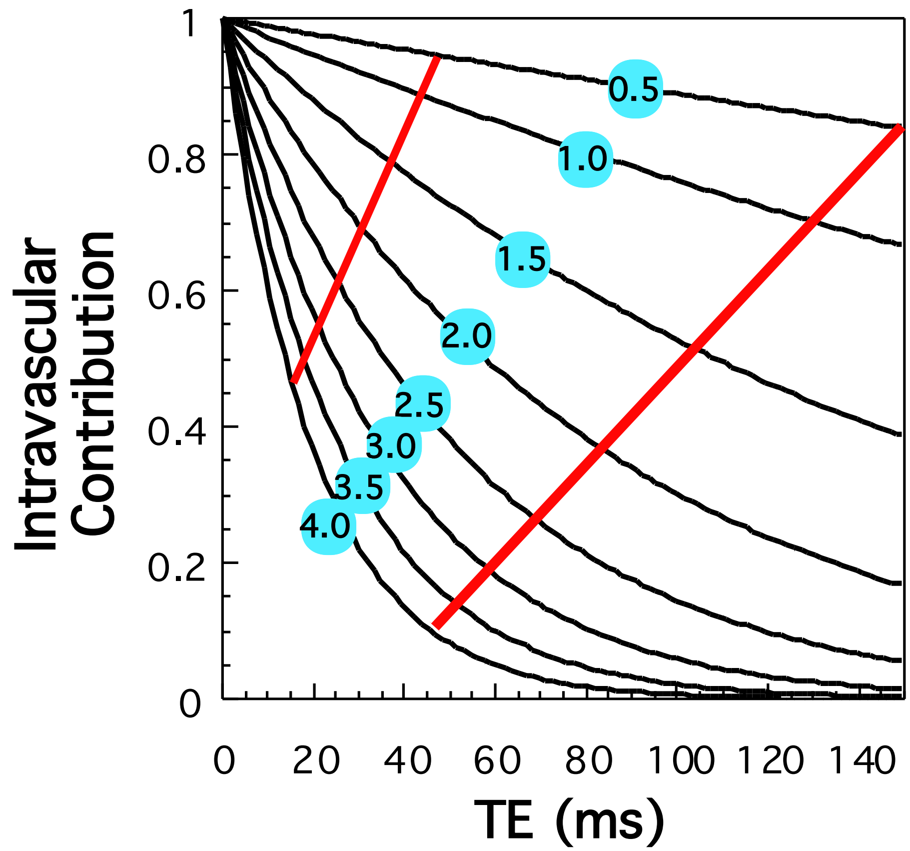

3T
Spin-Echo
TE = 105 ms
TR = ∞
Gradient-Echo
TE = 50 ms
Gradient-Echo
functional
TE = 50 ms
Spin-Echo
functional
TE = 105 ms

Field strength dependence of intravascular signal

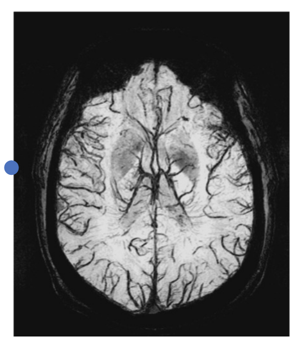
Spin-echo, $\%HbO_2$ = 60



Gradient-echo, $\%HbO_2$ = 60



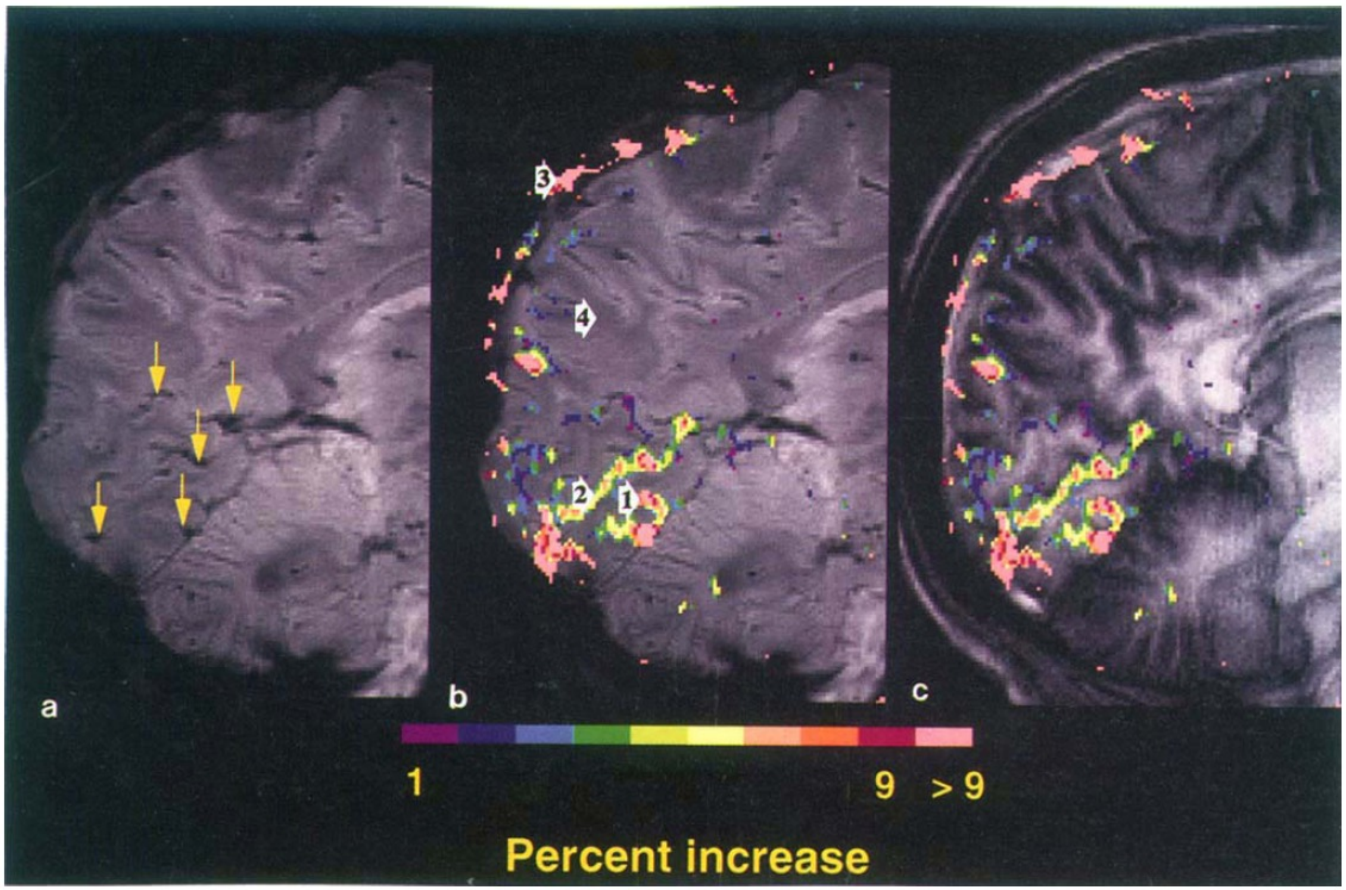
Source of most contrast in venograms..

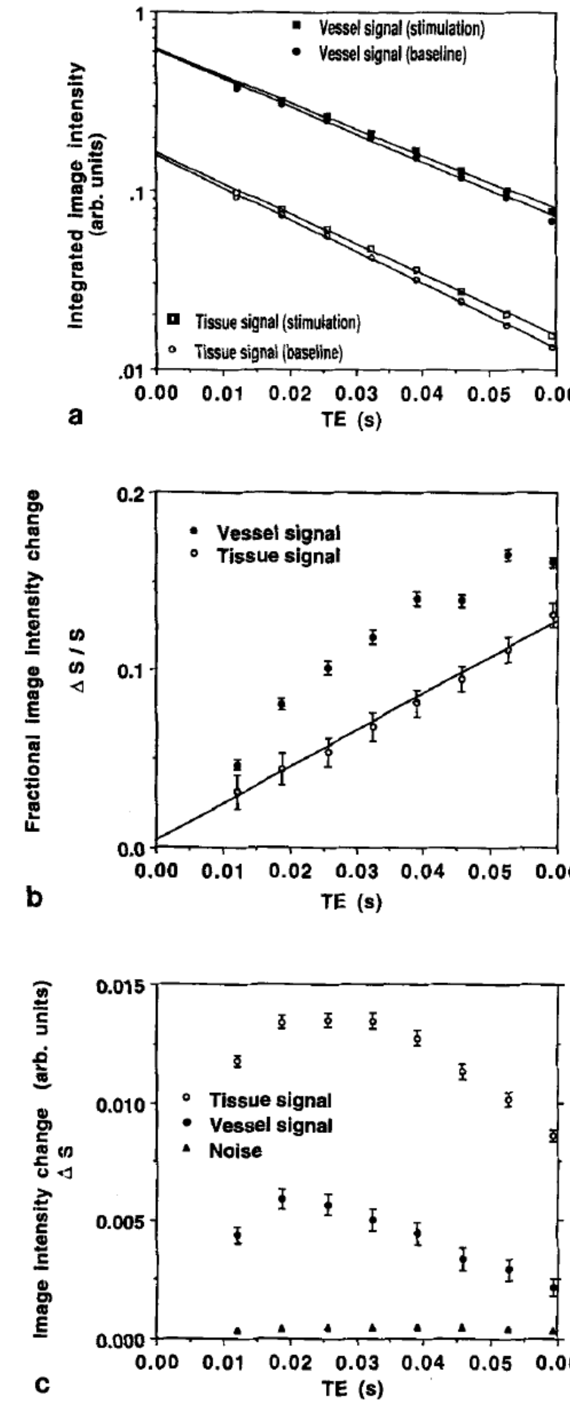


MRM 30:380-386 (1993)

4 Tesla Gradient Recalled Echo Characteristics of Photic Stimulation-Induced Signal Changes in the Human Primary Visual Cortex

Ravi S. Menon, Seiji Ogawa, David W. Tank, Kâmil Uğurbil





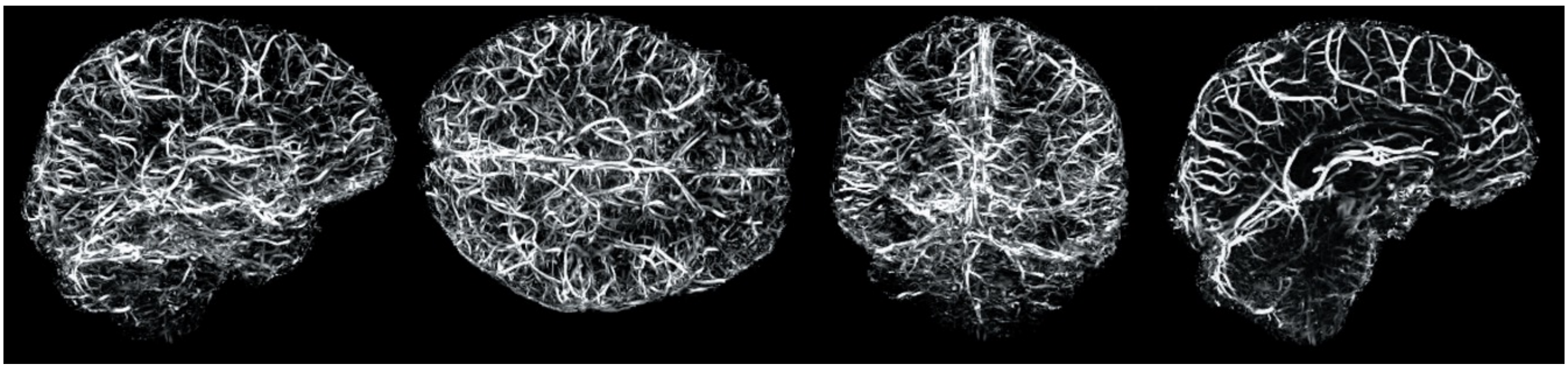
Magnetic Resonance in Medicine 52:612–618 (2004)

Susceptibility Weighted Imaging (SWI)

E. Mark Haacke,[1-4*] Yingbiao Xu,[1,2] Yu-Chung N. Cheng,[1] and Jürgen R. Reichenbach[5]

a

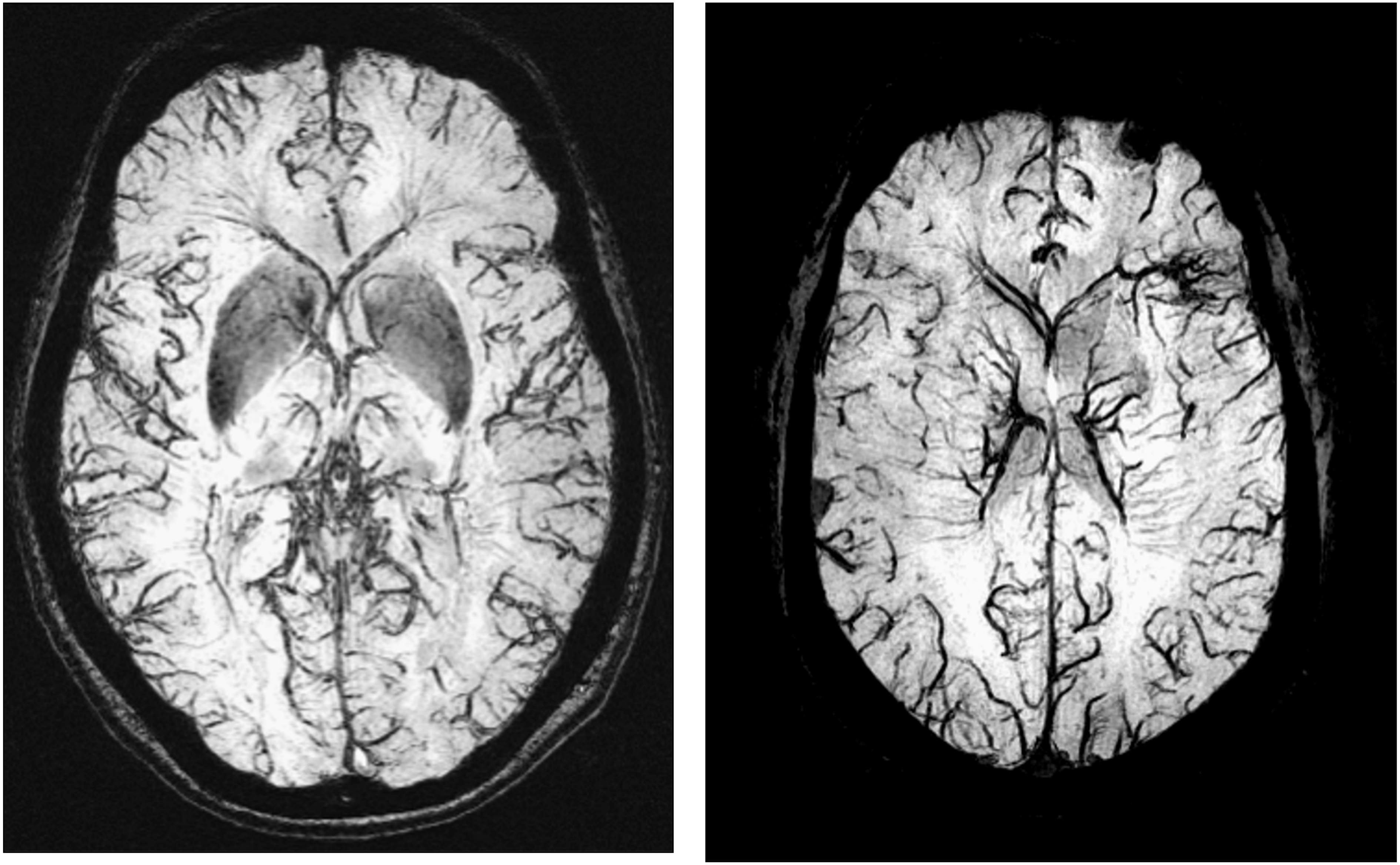
SWI: Susceptibility Weighted Imaging



David Norris,
Marcus Barth

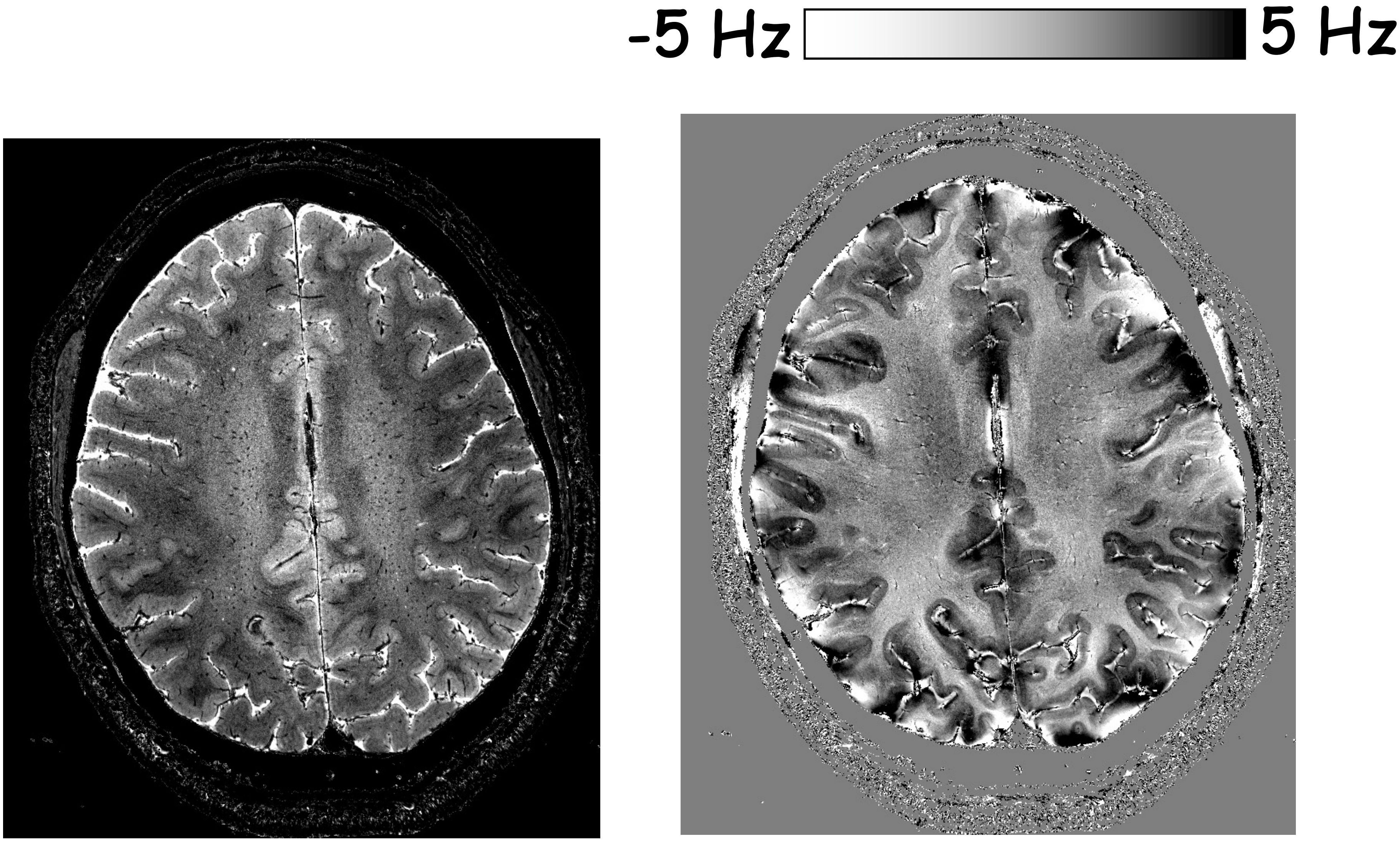
7T
Hahn Institute

BOLD effect to highlight veins: 3 Tesla



Bove-Bettis, et al (2004), SMRT

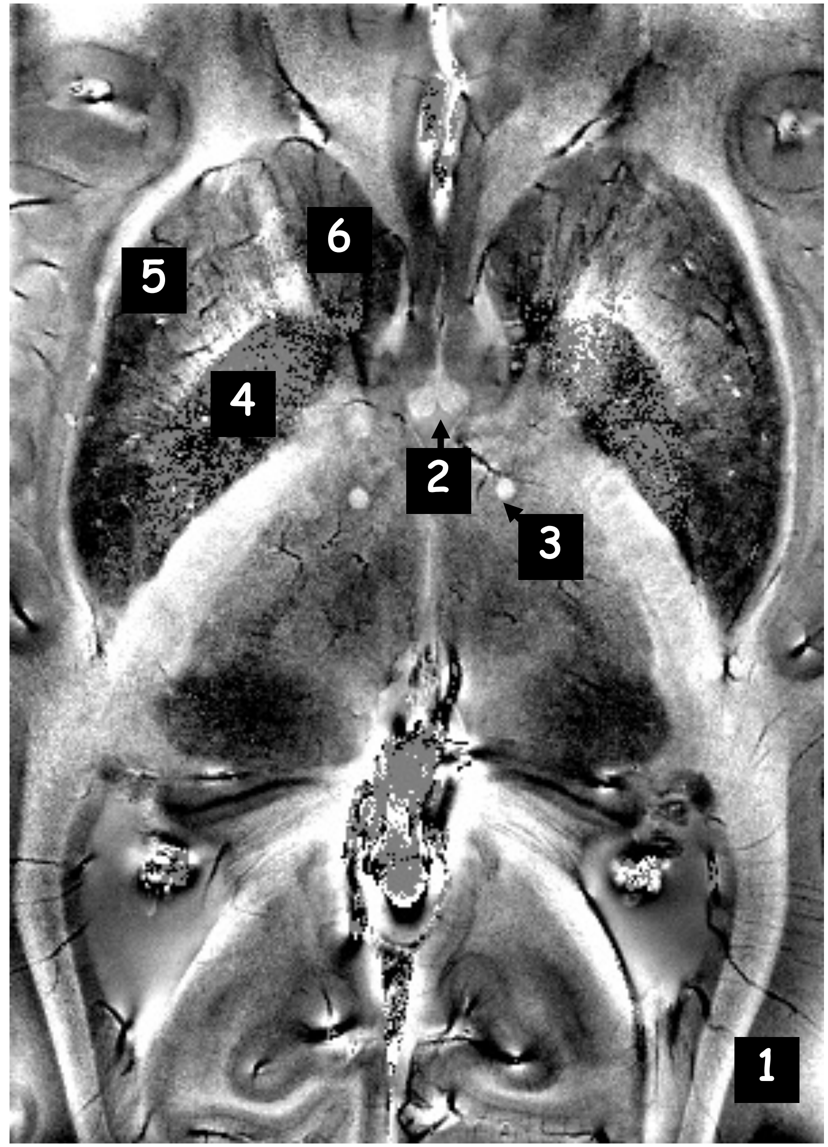
Phase versus Magnitude Contrast



Courtesy :P. Van Geldern and J. Duyn

GRE, magnitude

GRE, phase



1. veins crossing the optic radiations; 2. anterior column, fornix; 3. cross-section of the mamillothalamic tract; 4. globuspallidus; 5. putamen; 6. head of the caudate nucleus.

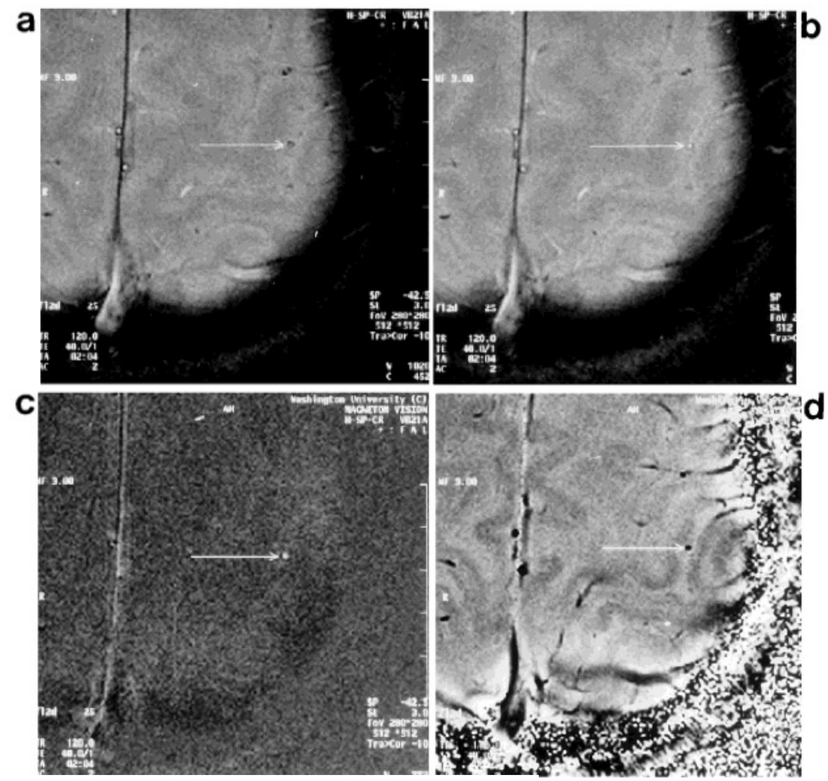
Courtesy :P. Van Gelderen and J. Duyn

What information can we extract using MRI / fMRI?

Baseline and Activation-induced Changes in Oxygenation

-assumptions on Hct, geometry
-limited to picking out vessels

E. M. Haacke, et al, HBM 5: 341-346, 1997



◆ MRI of Blood Oxygen Saturation ◆

TABLE I. Results of phase, susceptibility, oxygenation, and velocity changes in pial veins in 5 volunteers upon motor cortex activation*

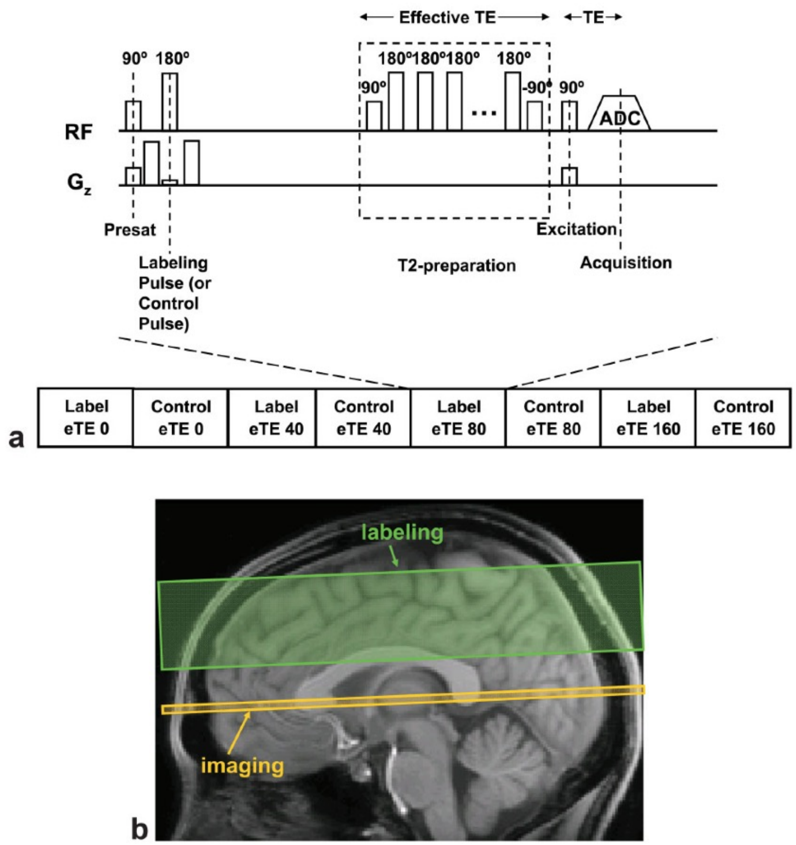
Volunteer number	TE (msec)	$\Delta\phi_{rest-act}$ (deg)	$\Delta\chi_{rest-act}$ (ppm)	ΔY_{susc}	v_{rest} (cm/sec)	v_{act} (cm/sec)	ΔY_{flow}
1	60	20	0.008	0.11	3.1	4.1	0.13
2	40	36	0.012	0.165	3.0	3.7	0.08
3	60	19	0.009	0.13	4.8	7.4	0.16
4	40	42	0.011	0.15	1.2	2.0	0.19
5	40	45	0.012	0.16	1.5	2.3	0.15
Mean ± SD		32.4 ± 12.2	0.01 ± 0.001	0.14 ± 0.02	2.72 ± 1.44	3.90 ± 1.91	0.14 ± 0.04

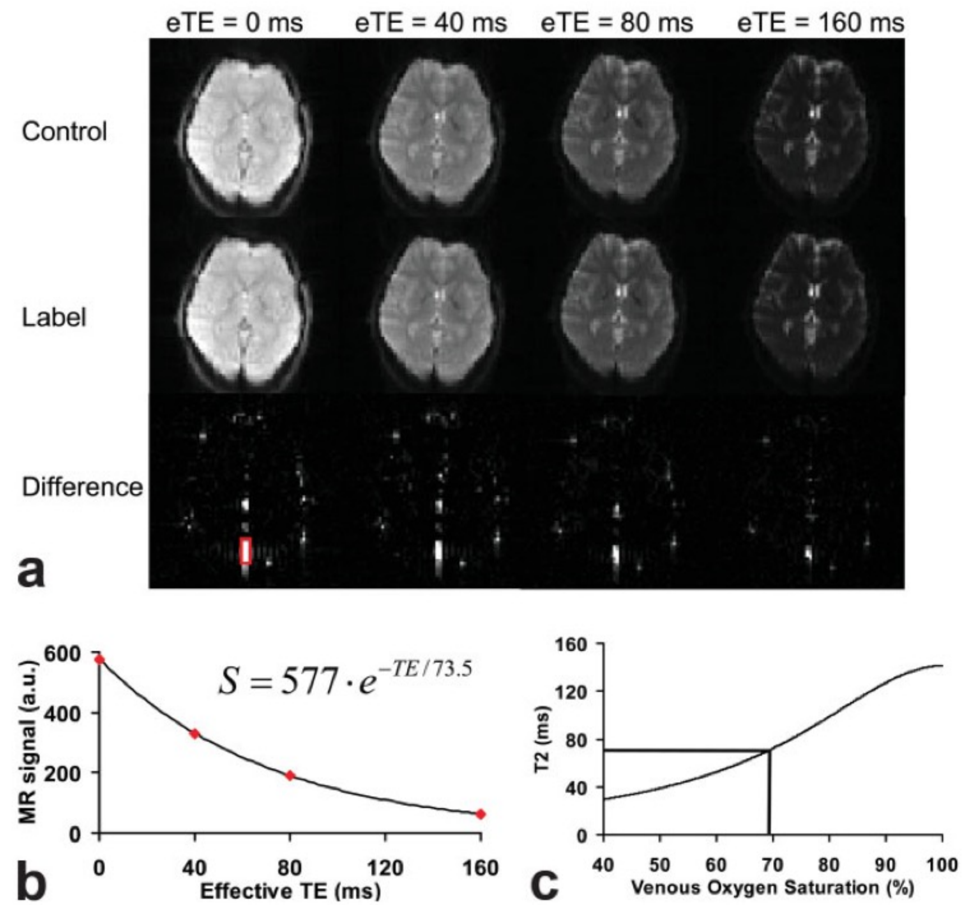
*Where TE is echo time, $\Delta\phi_{rest-act}$ the phase difference fo flow-compensated acquisition. $\Delta\chi_{rest-act}$ and ΔY_{uss} the susceptibility change and corresponding oxygen saturation change extracted from $\Delta\phi_{rest-act}$, while ΔY_{flow} is the oxygen saturation change extracted from the change of flow velocity, i.e., from v_{rest} in the resting state to v_{act} in the activation state.

What information can we extract using MRI / fMRI?

Baseline oxygenation with fewer assumptions

-measurement of T2 of ASL- tagged blood
-assumptions of Hct, accuracy of calibration plot





T2-Relaxation-Under-Spin-Tagging
"TRUST" MRI

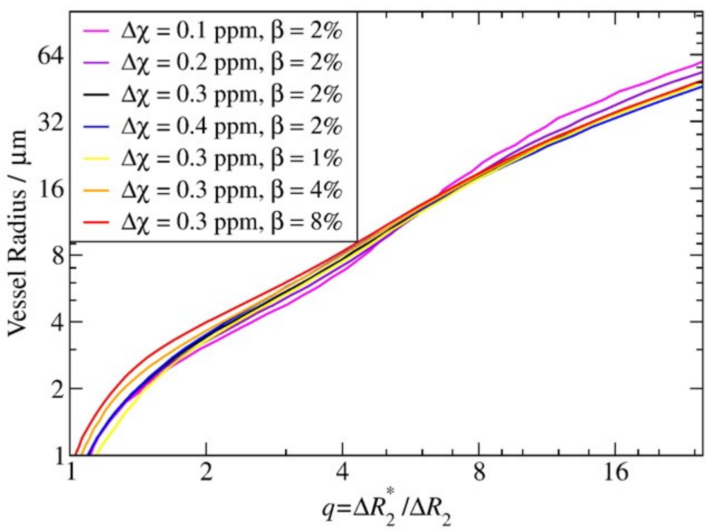
H. Lu, MRM, 60:357-363, 2008

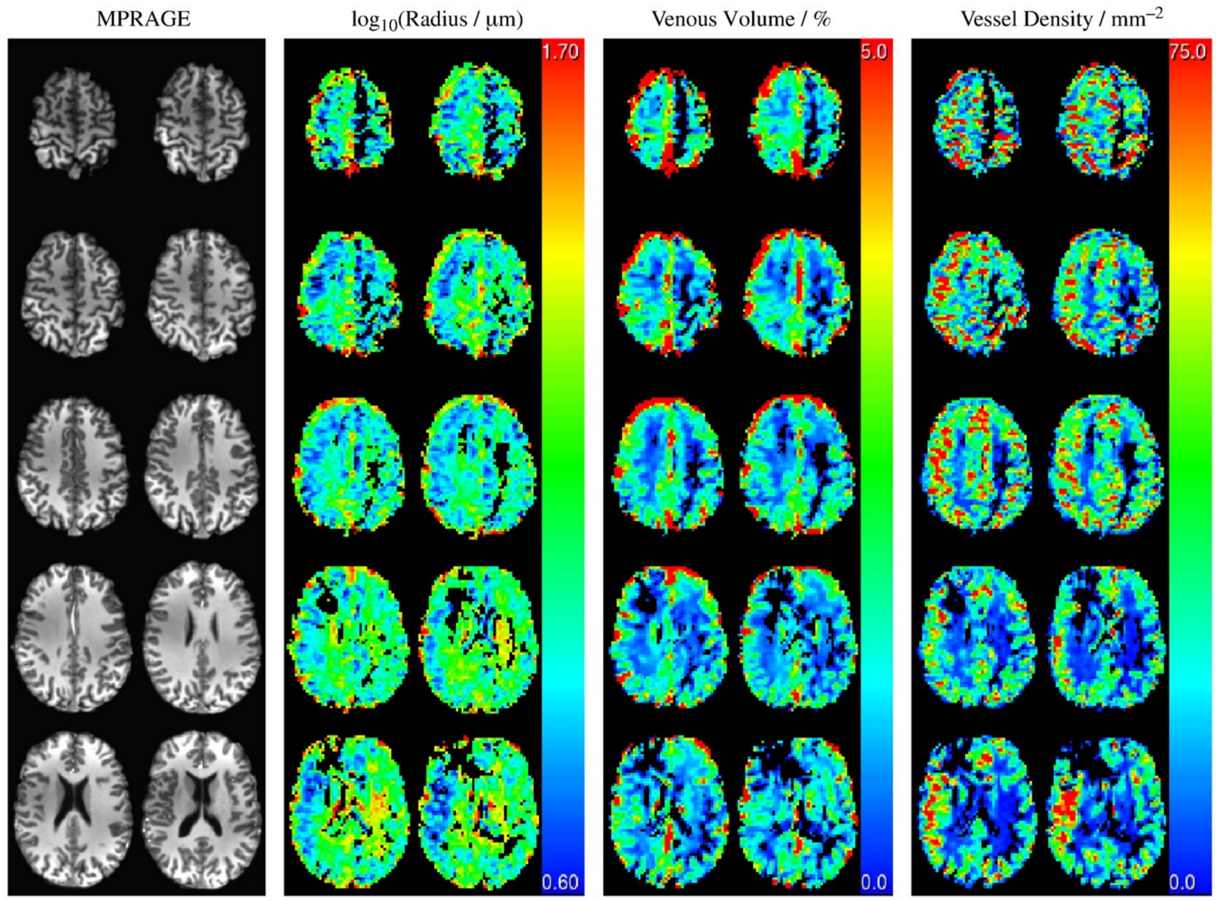
What information can we extract using MRI / fMRI?

*Ve*ssel Parameter Mapping

-SE/GE ratio -> vessel radius

-GE signal change with global stress
-> blood volume





T. H. Jochimsen, et al. NeuroImage, 51: 765-774 (2010)

Pros and Cons of Spin-Echo

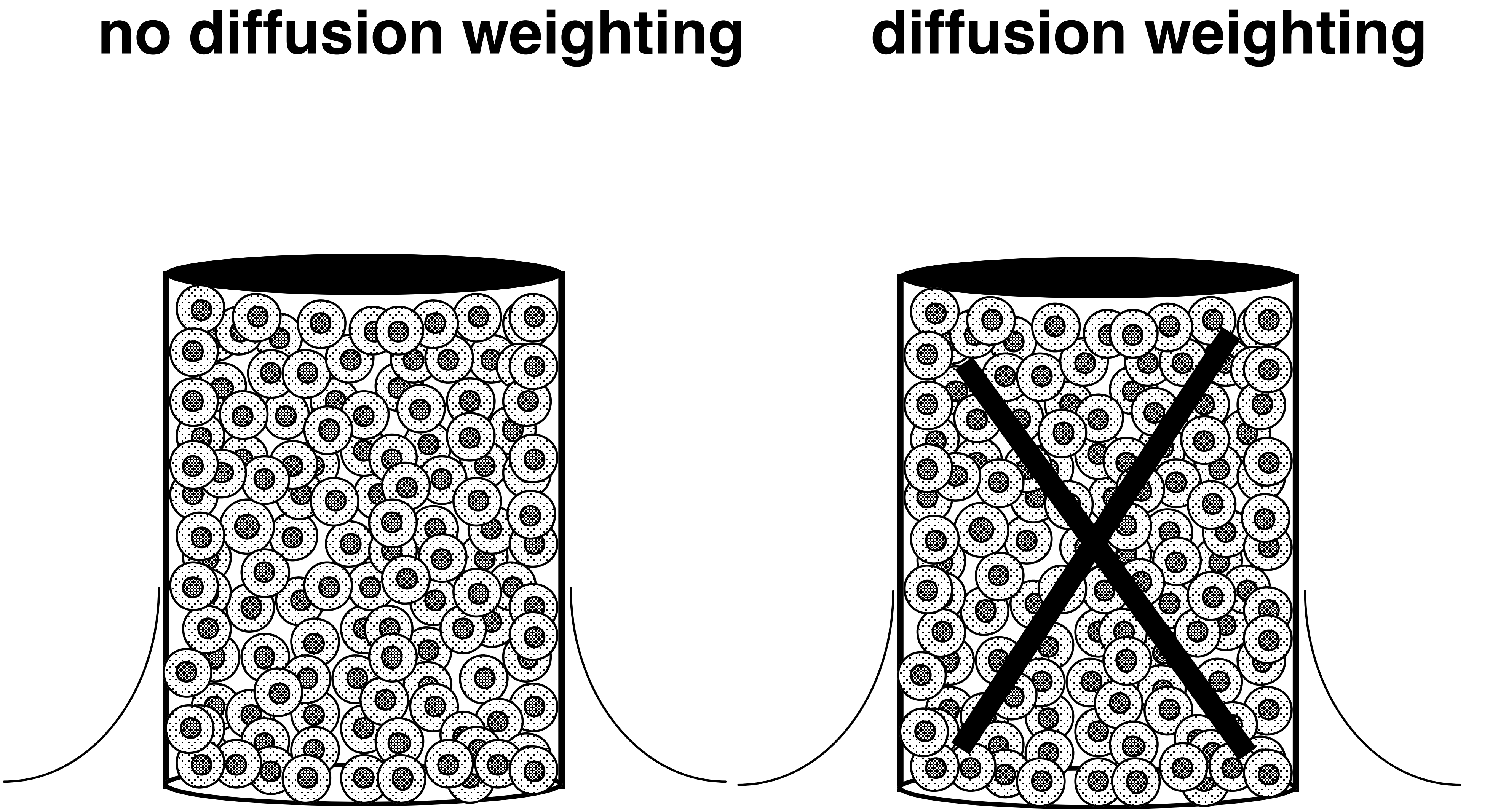
- Increased specificity (esp at high fields where IV signal is low)
- Less sensitive to rapidly flowing blood
- Less signal dropout.

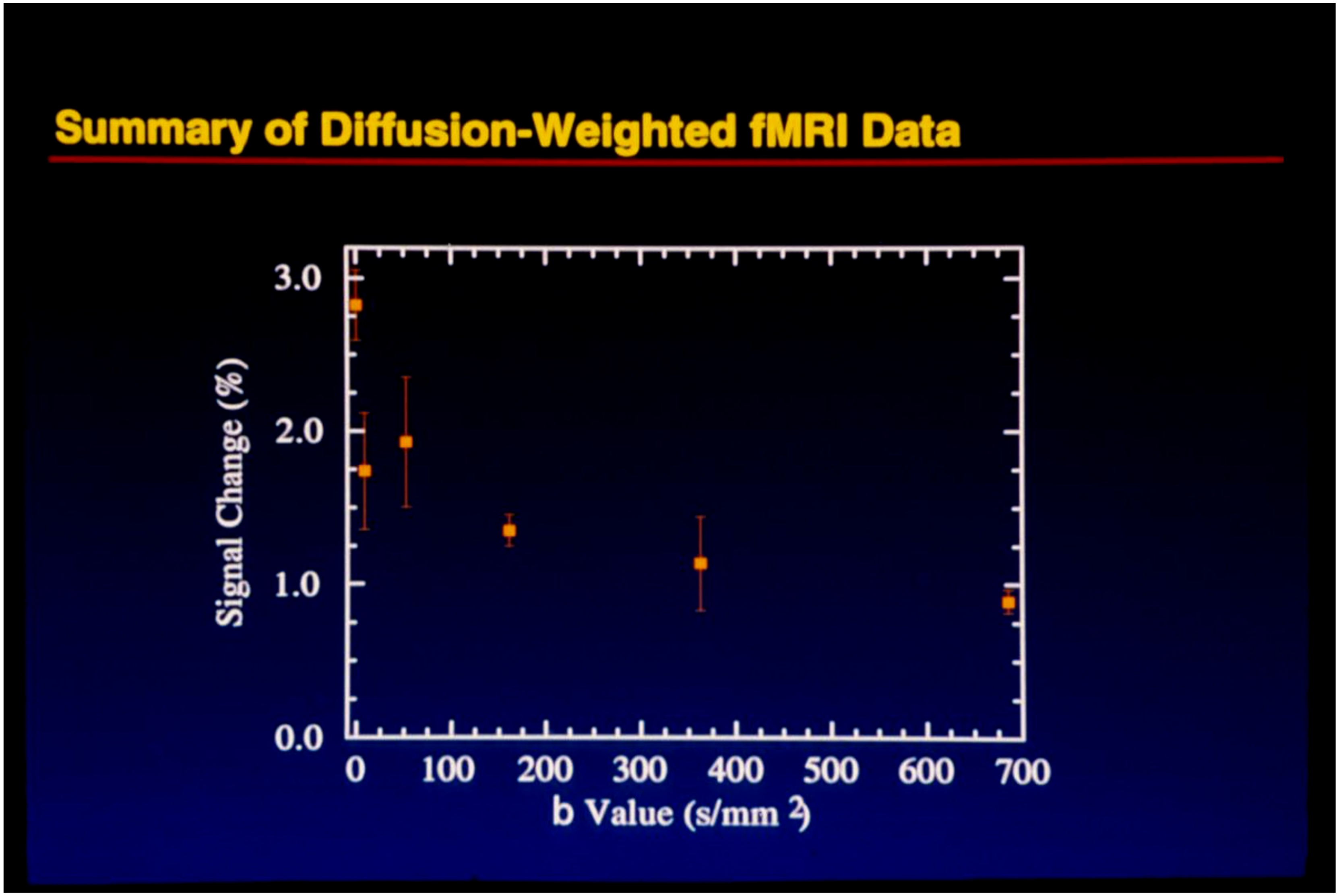
- Less slices per TR
- Lower fCNR by x 2 to 4.
- Acquisition window still T2*
- Very large IV signal still present at most field strengths.

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

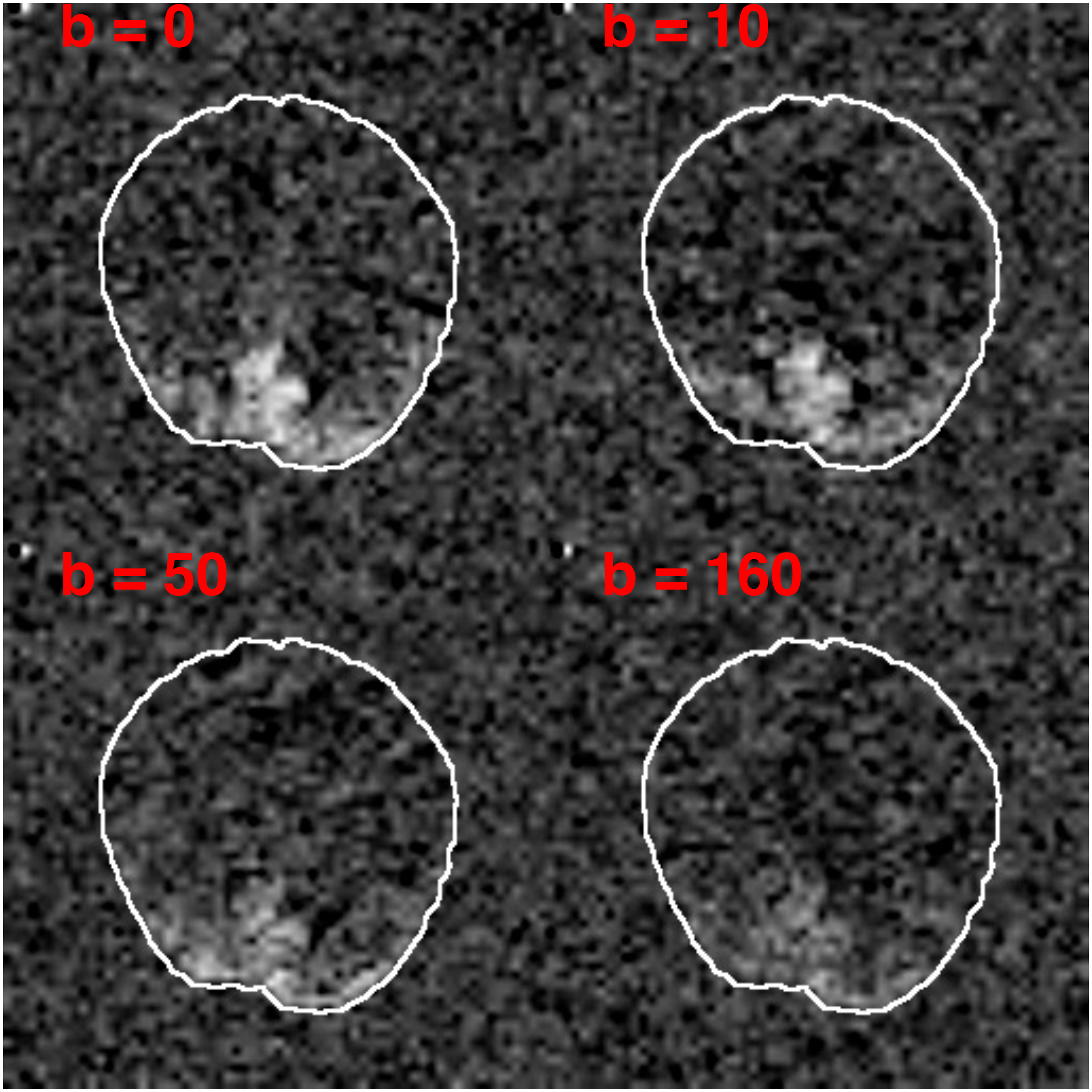
…so let’s remove the intravascular signal...

Velocity Nulled (or diffusion weighted) fMRI.

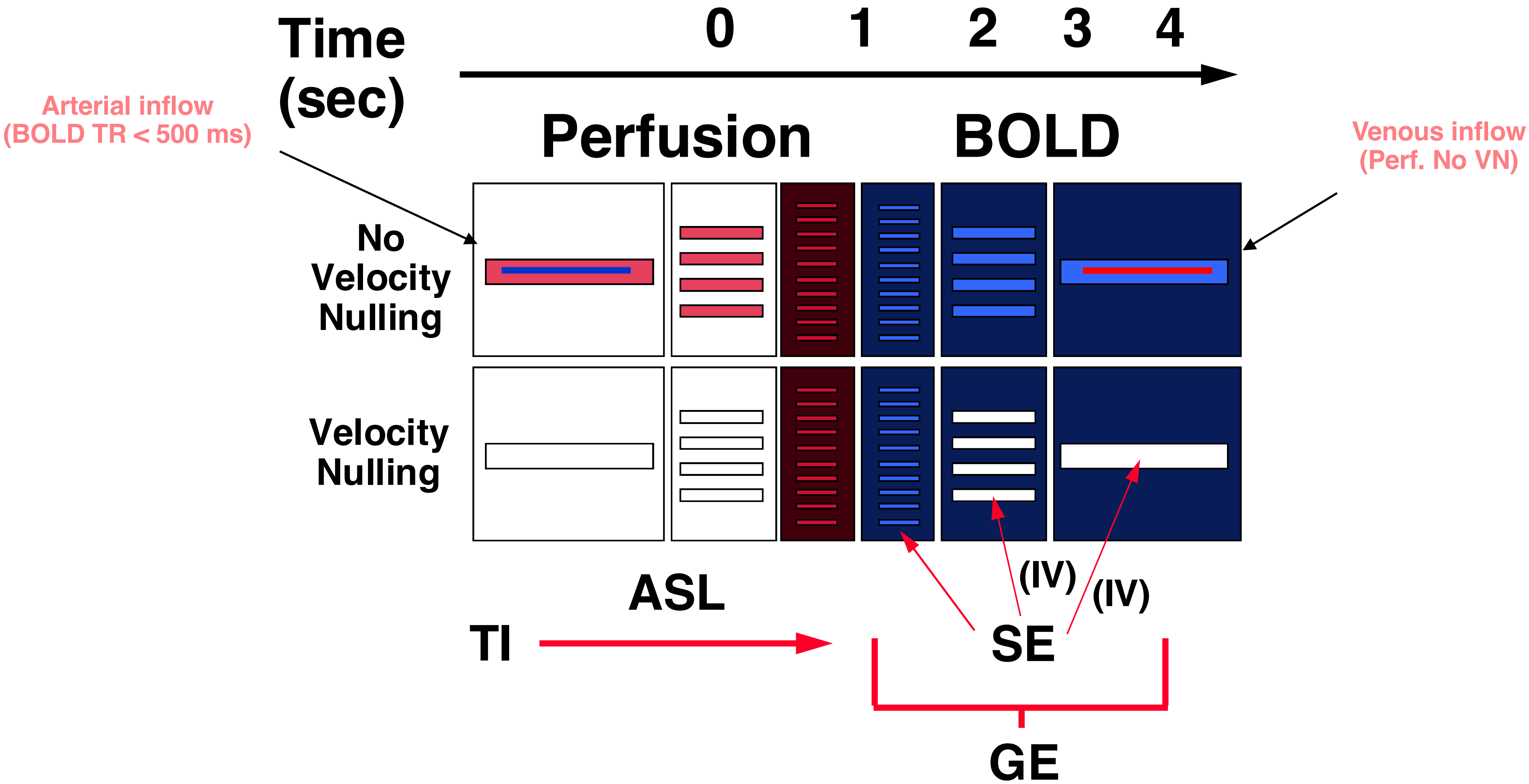

no diffusion weighting
diffusion weighting



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

Hemodynamic Specificity



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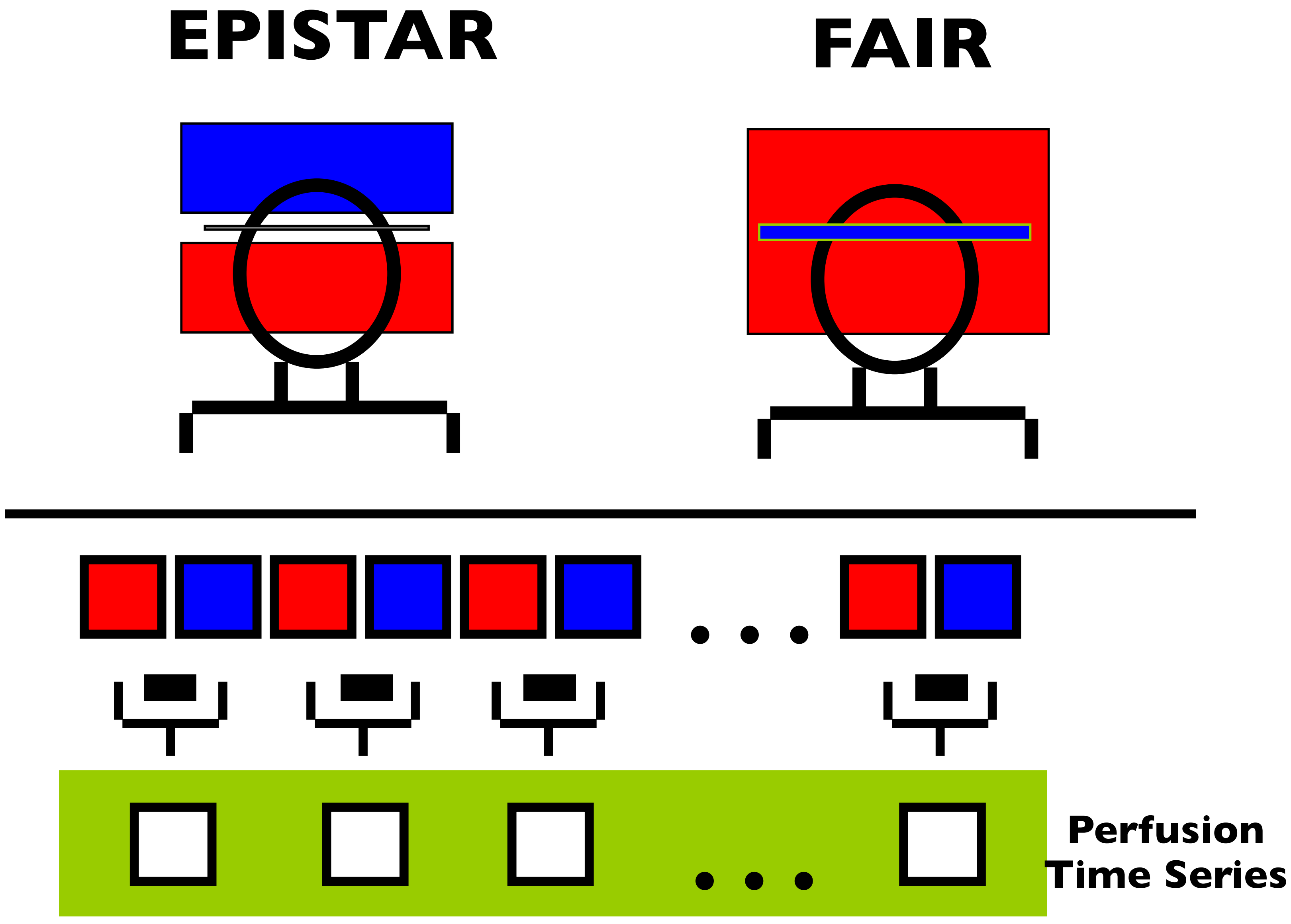
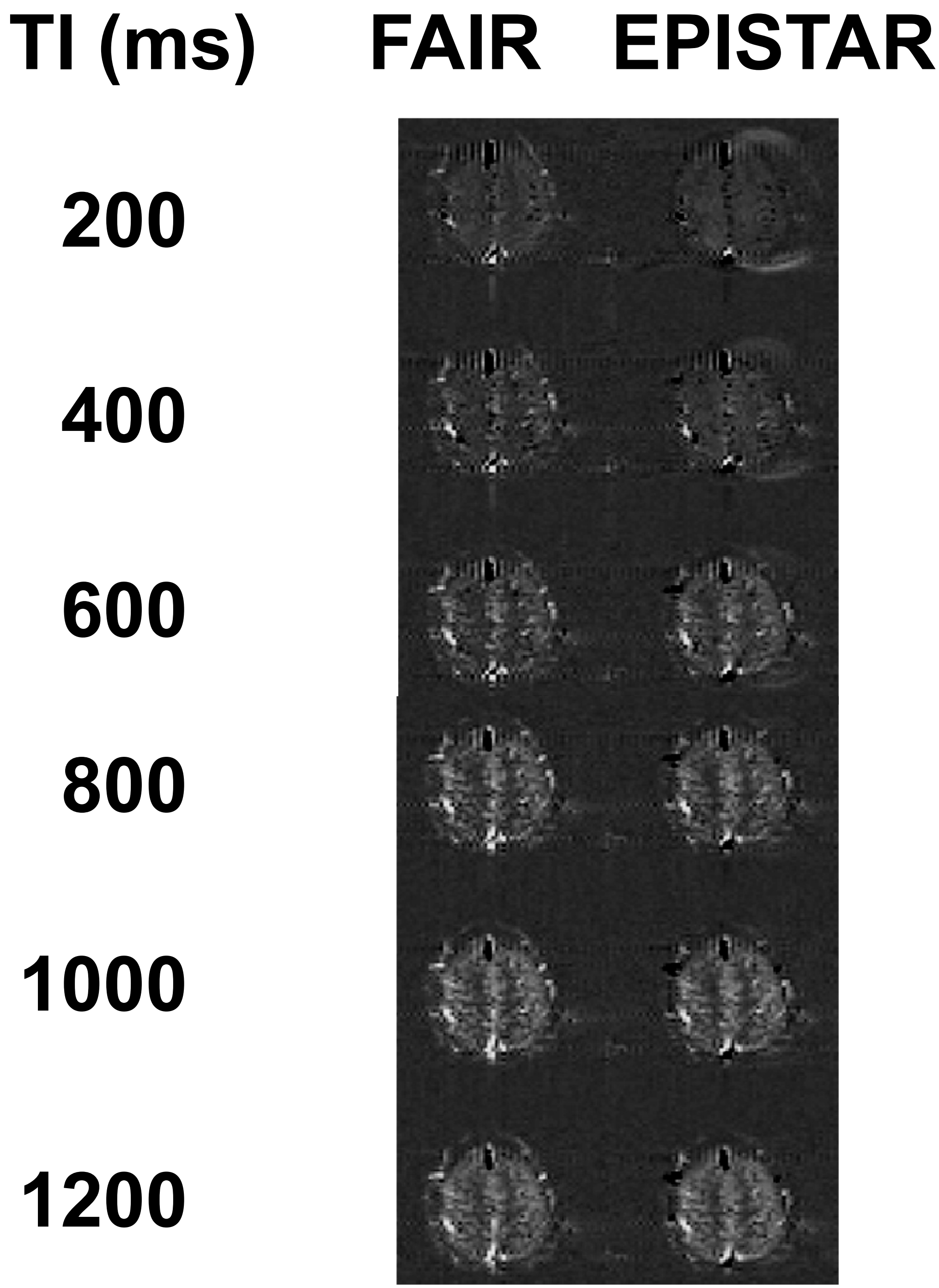
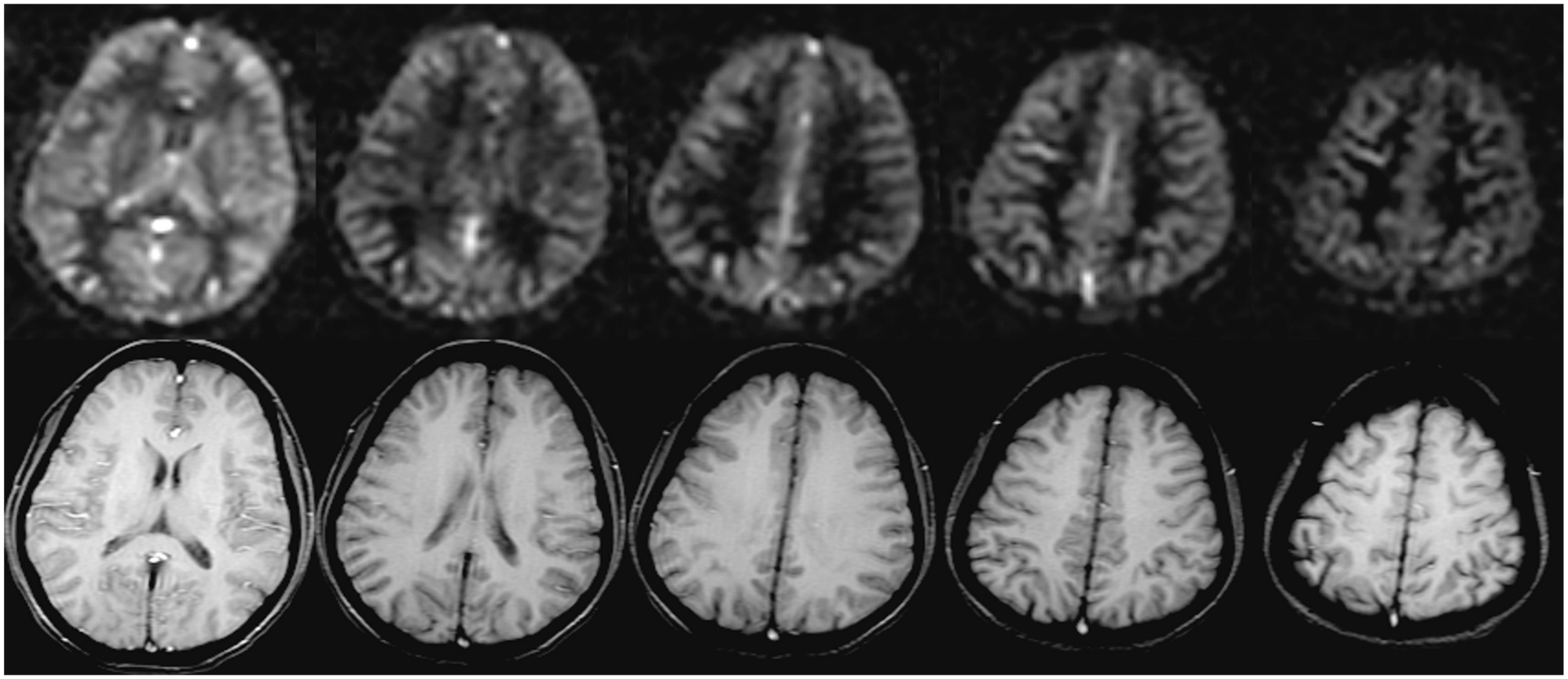
Perfusion Contrast




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

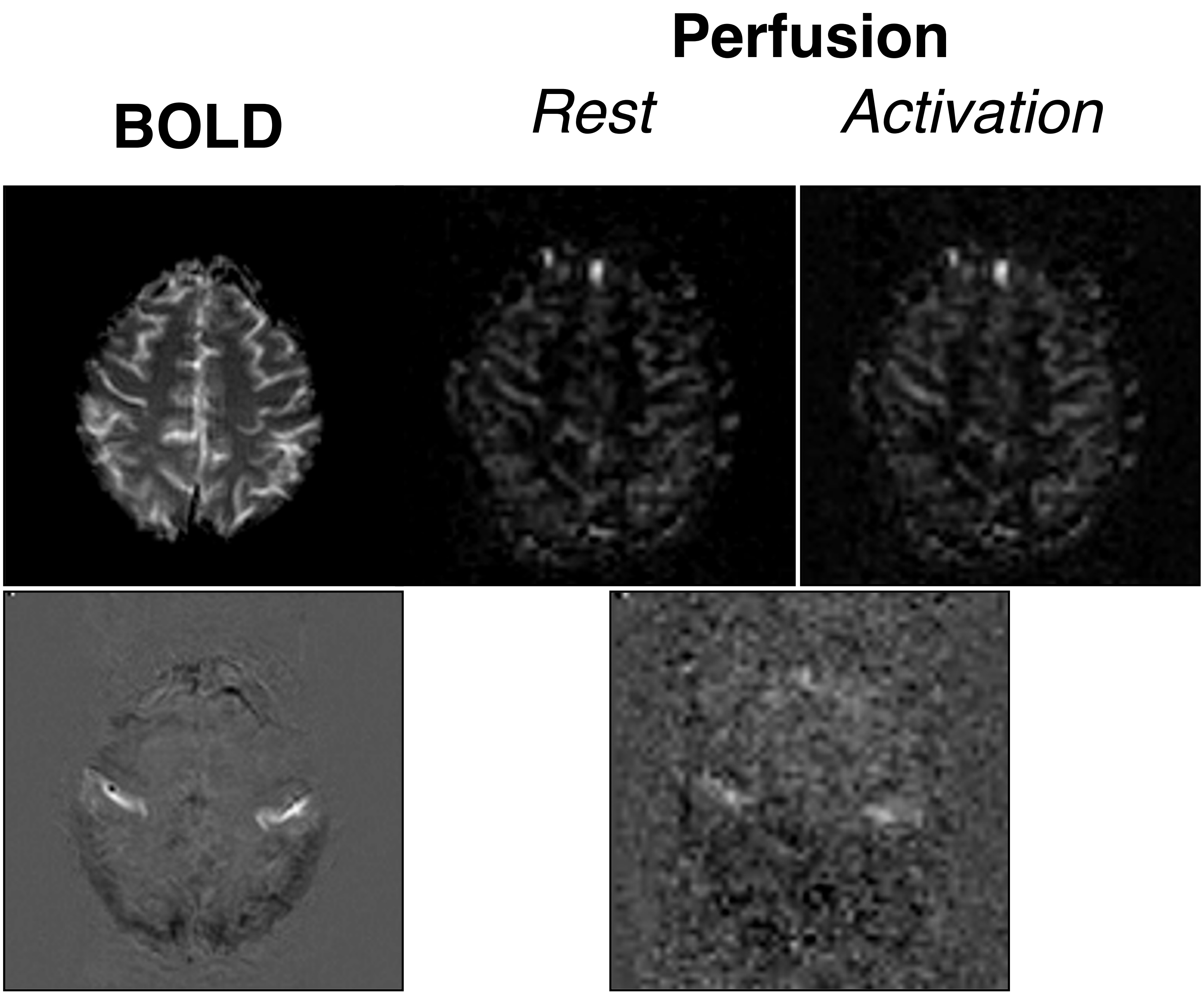


Williams, D. S., Detre, J. A., Leigh, J. S. & Koretsky, A. S. (1992) “Magnetic resonance imaging of perfusion using spin-inversion of arterial water.” **Proc. Natl. Acad. Sci. USA 89, 212-216.**

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.**

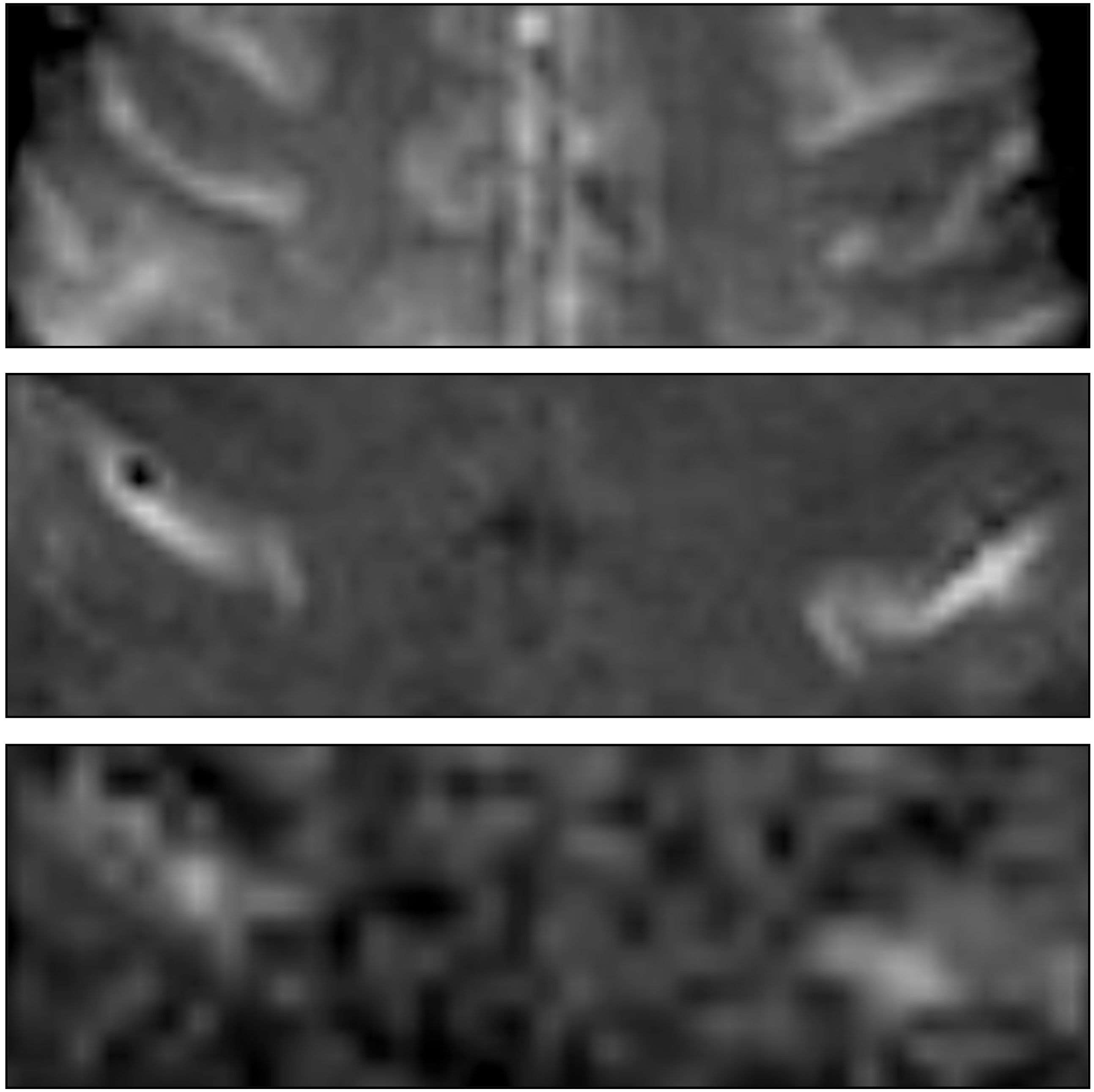


P. A. Bandettini, E. C. Wong, Magnetic resonance imaging of human brain function: principles, practicalities, and possibilities, *in* "Neurosurgery Clinics of North America: Functional Imaging" (M. Haglund, Ed.), p.345-371, W. B. Saunders Co., 1997.

Anatomy

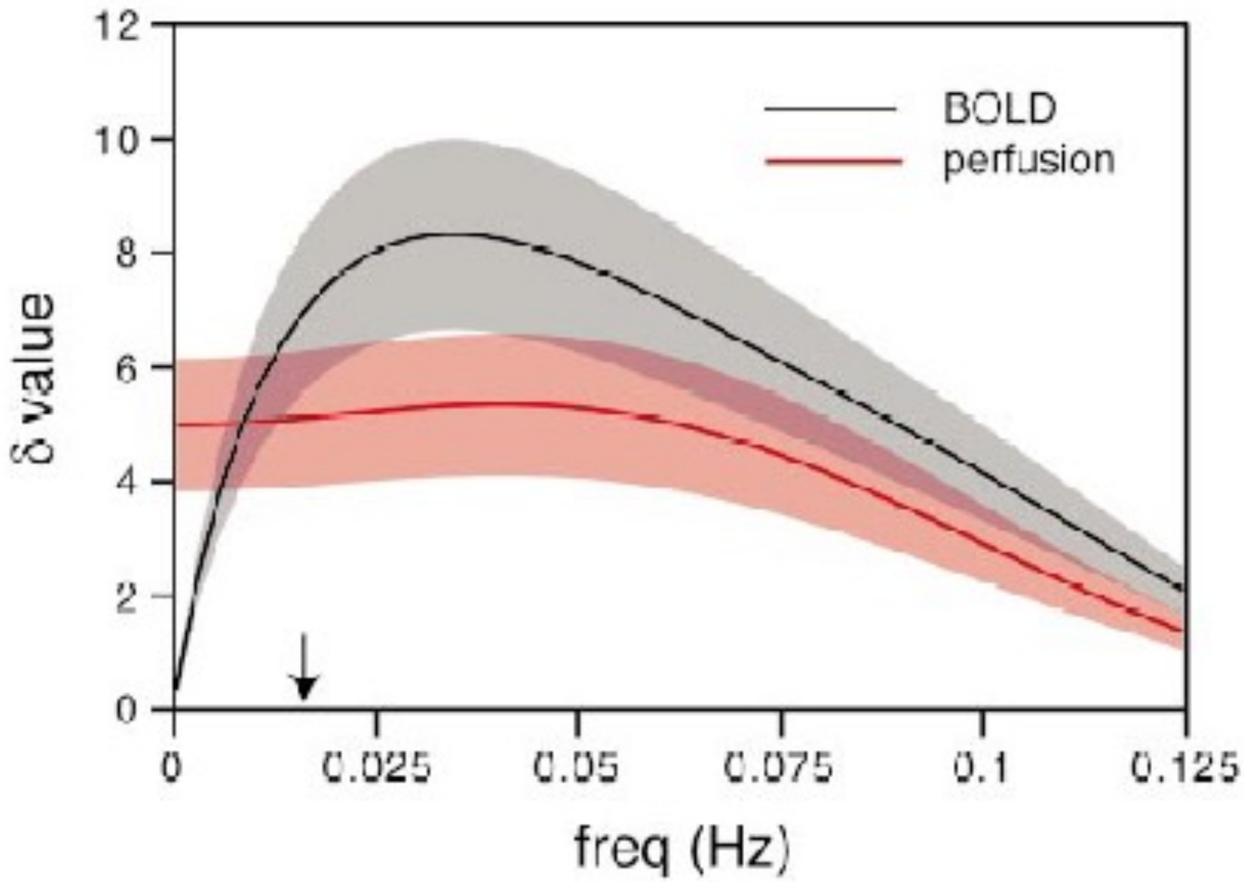
BOLD

Perfusion



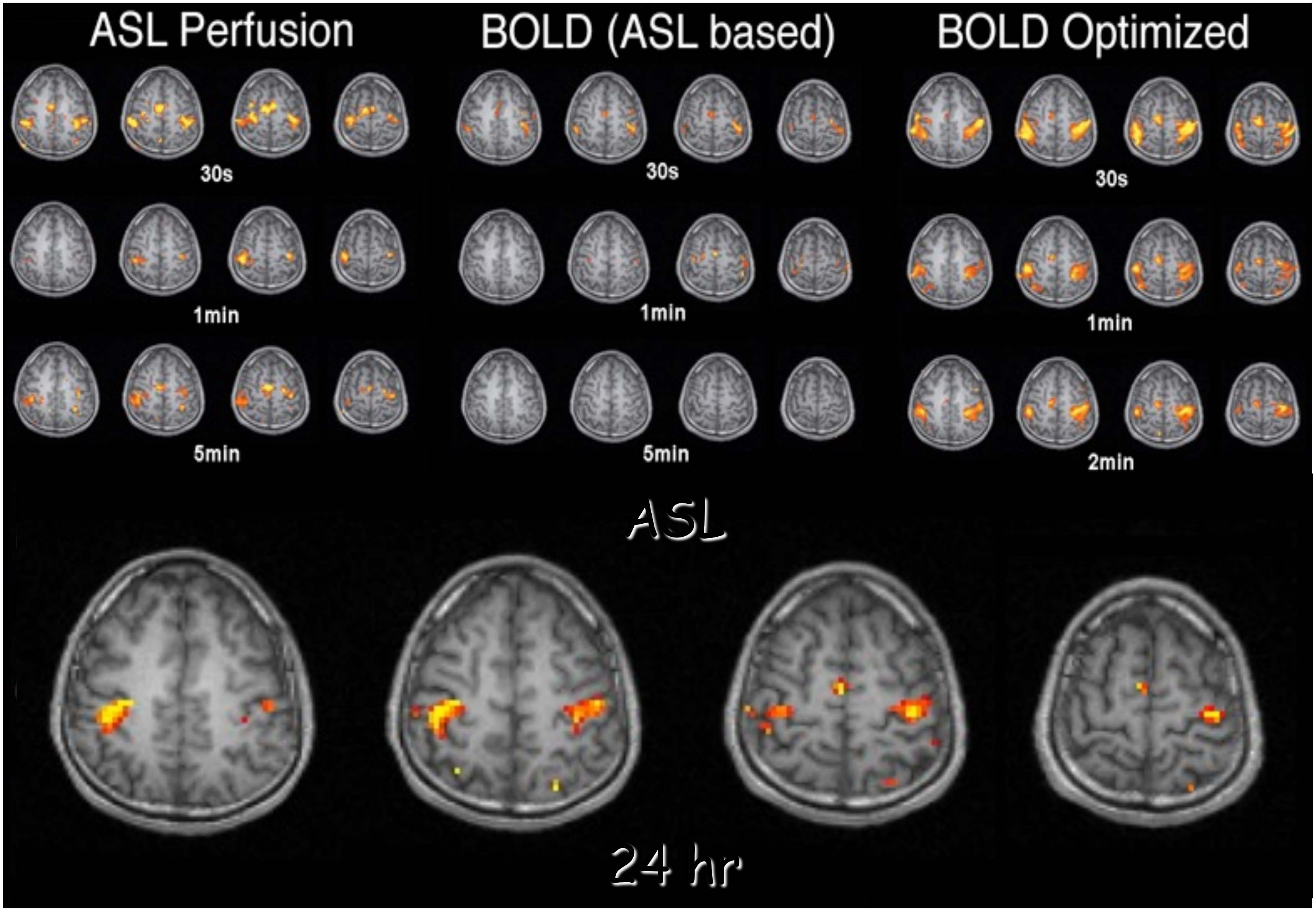
P. A. Bandettini, E. C. Wong, Magnetic resonance imaging of human brain function: principles, practicalities, and possibilities, *in* "Neurosurgery Clinics of North America: Functional Imaging" (M. Haglund, Ed.), p.345-371, W. B. Saunders Co., 1997.

Better than BOLD for long duration activation…

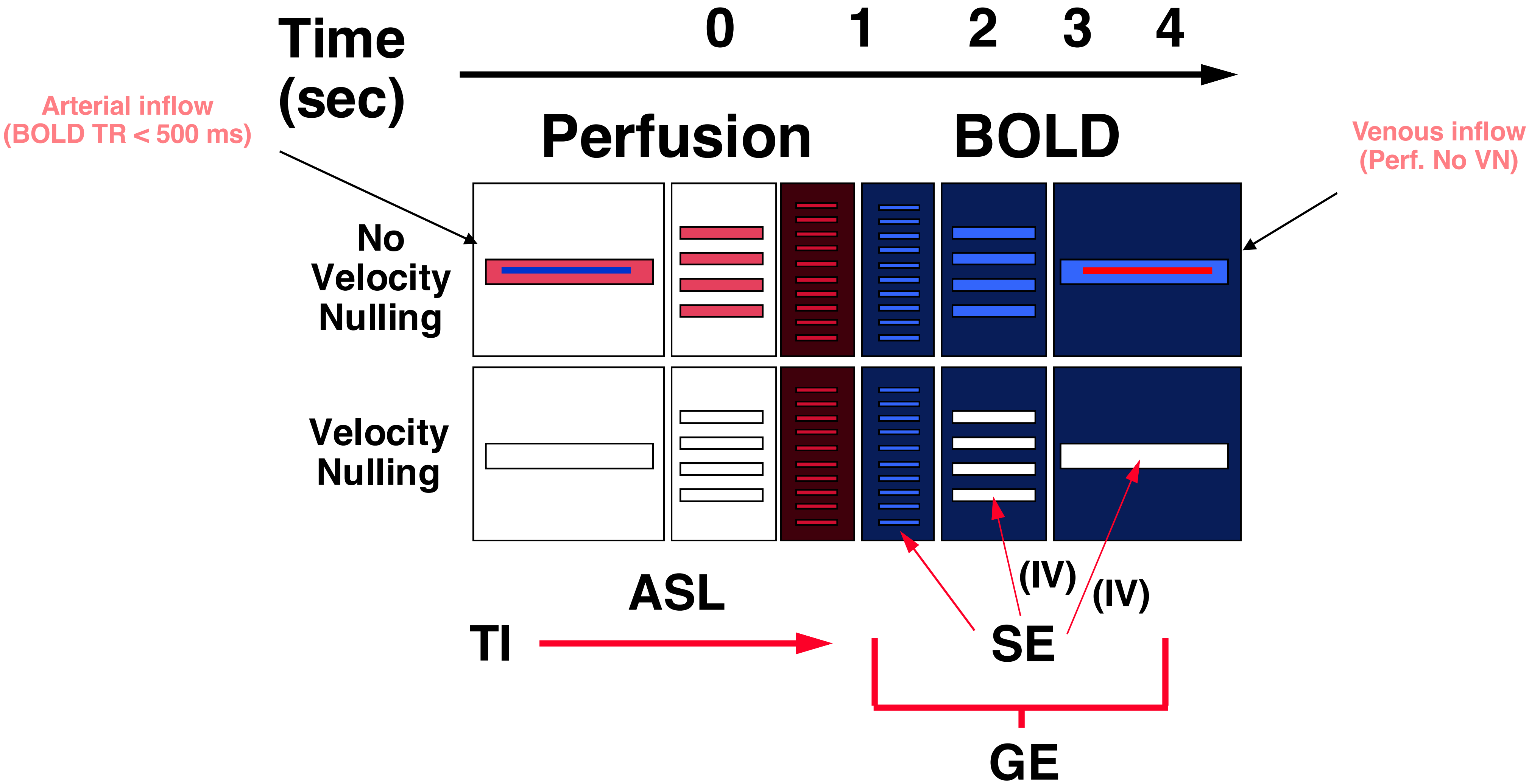


GK Aguirre et al, (2002) NeuroImage 15 (3): 488-500

Perfusion vs. BOLD: Low Task Frequency



Hemodynamic Specificity



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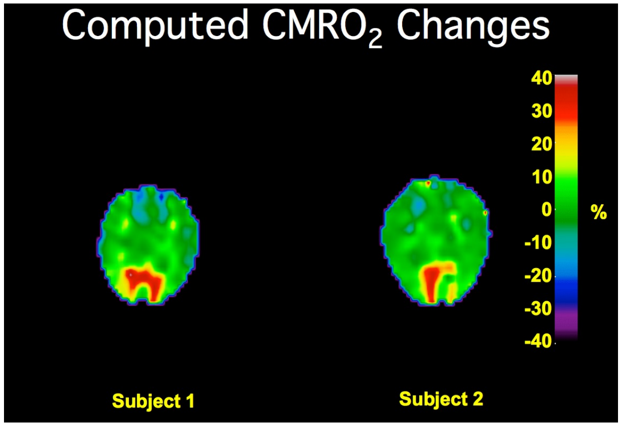
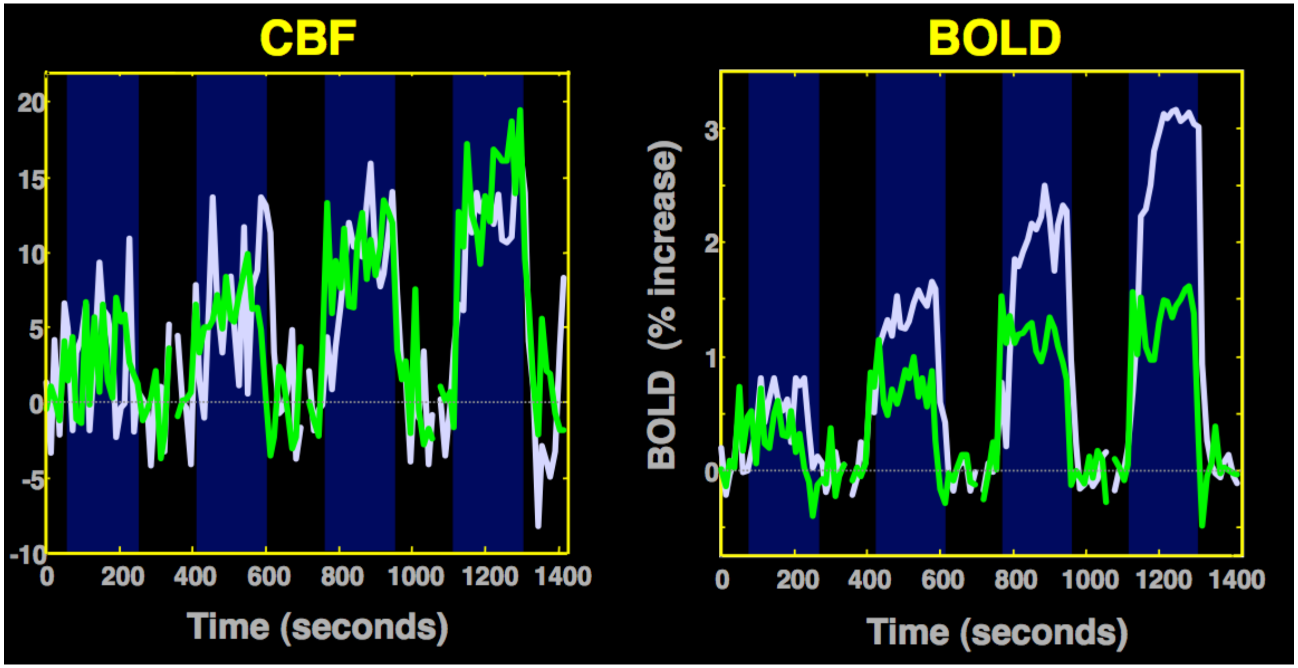
Activation-induced $CMRO_2$ changes



-requires a global hemodynamic stress
-assumption is that $CMRO_2$ unchanged with global stress
-requires simultaneous flow and BOLD collection

R. D. Hoge, et al, PNAS 96: 9403-9408, 1999



Visual = green
Hypercapnia = white

Functional Contrast

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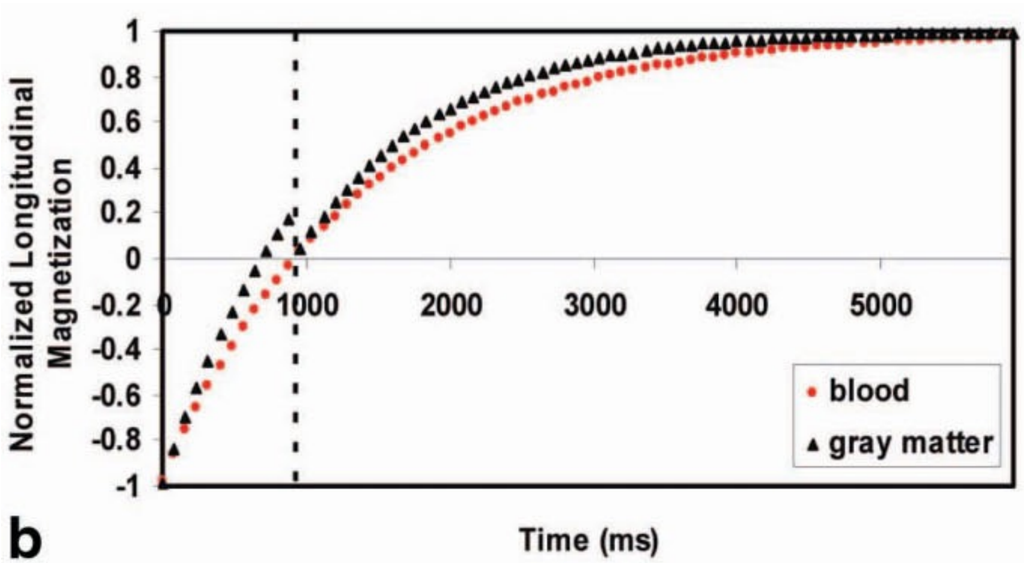
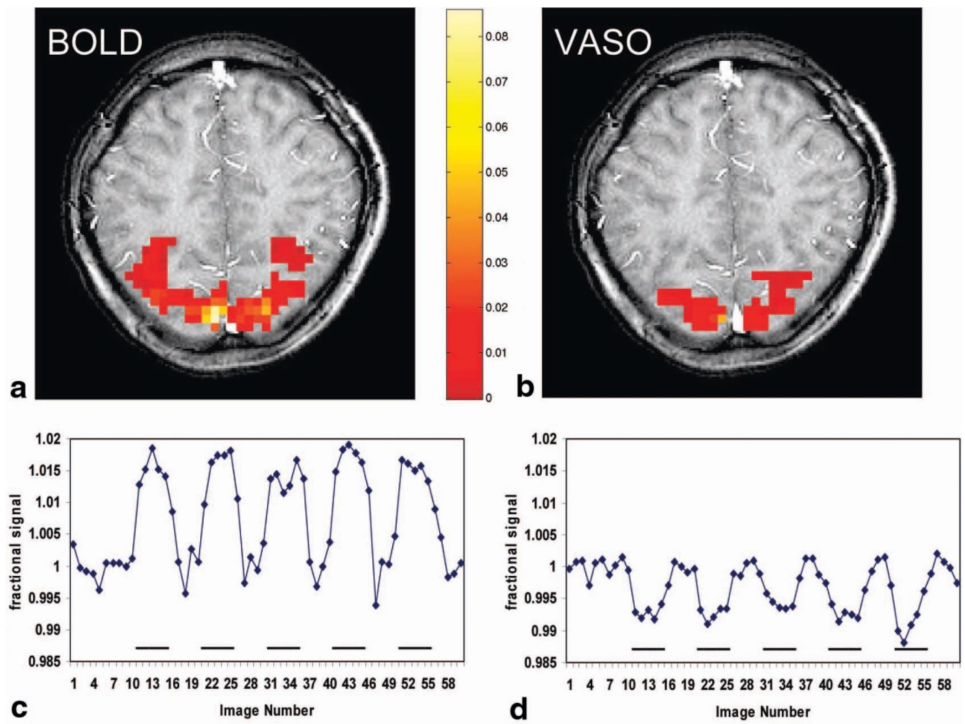
- ΔVolume (VASO)
- Neuronal Currents
- Diffusion coefficient
- Temperature

Activation-induced Blood Volume Changes: "VASO"

H. Lu, et al, MRM 50: 263-274, 2003



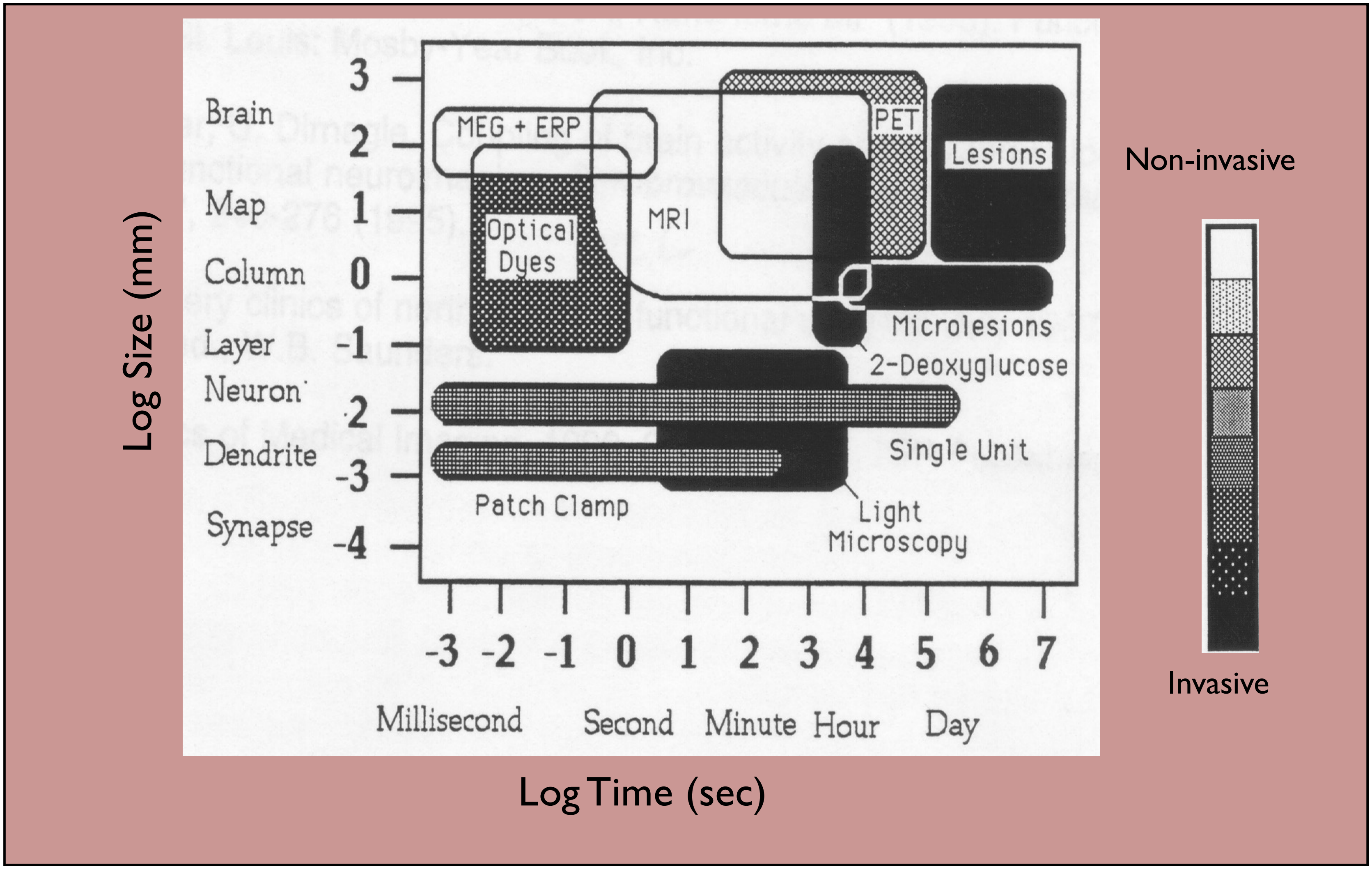


Null blood based on T1 difference between blood and tissue
..more blood -> less signal.

Extracting Information from the fMRI Signal:

- Spatial Resolution
- Temporal Resolution
- Sensitivity

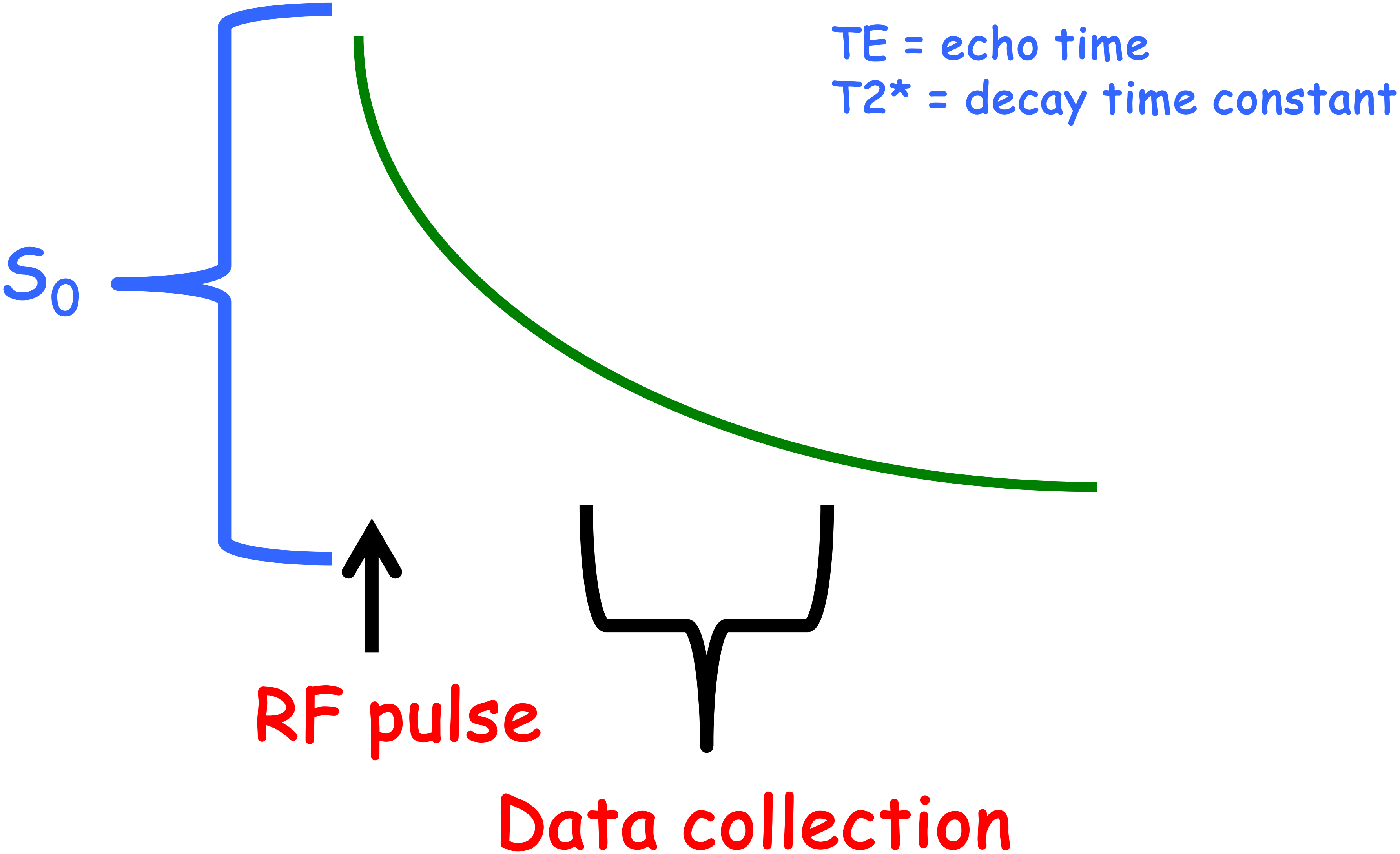
Functional Neuroimaging Techniques

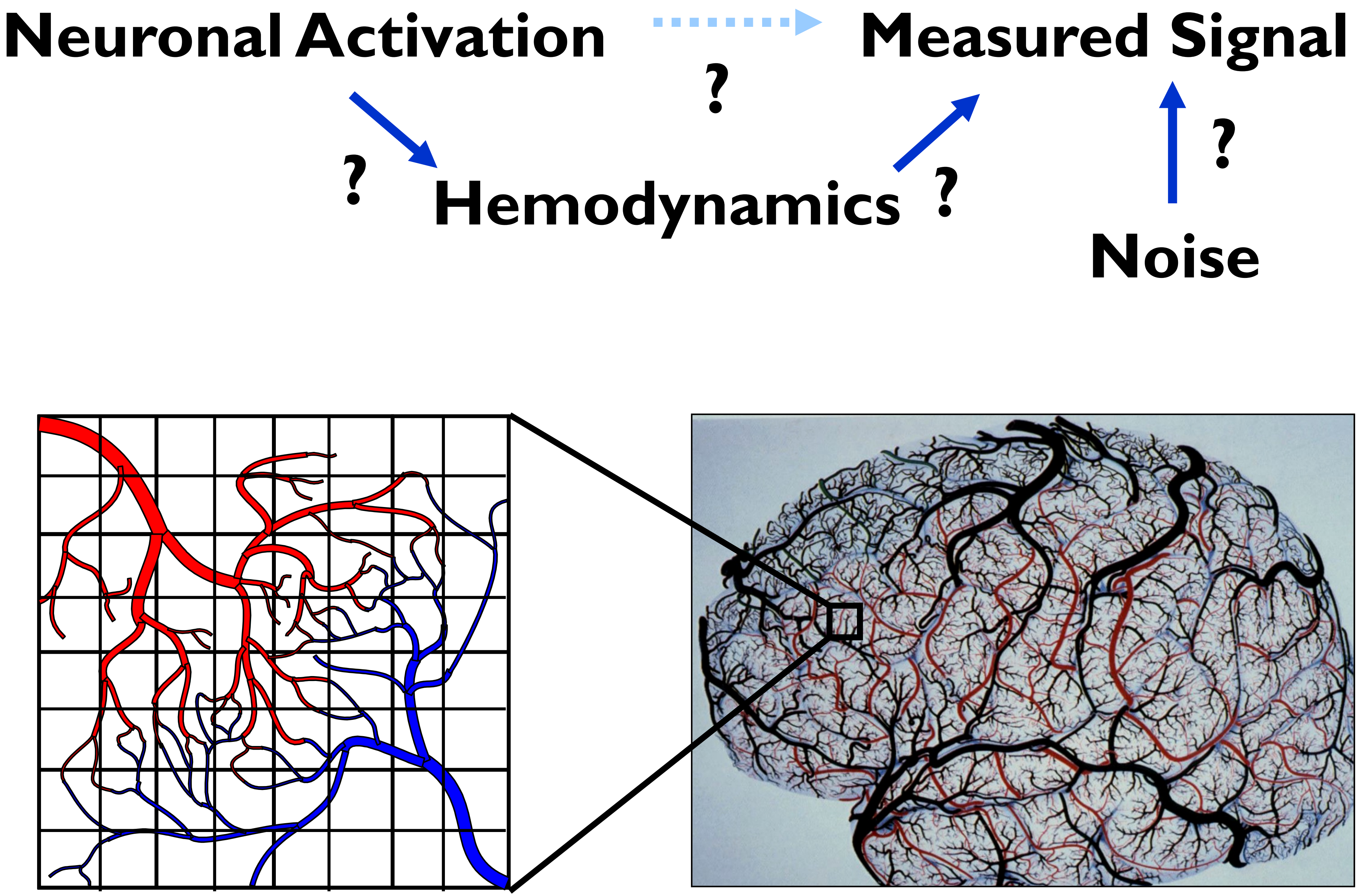


Extracting Information from the fMRI Signal:

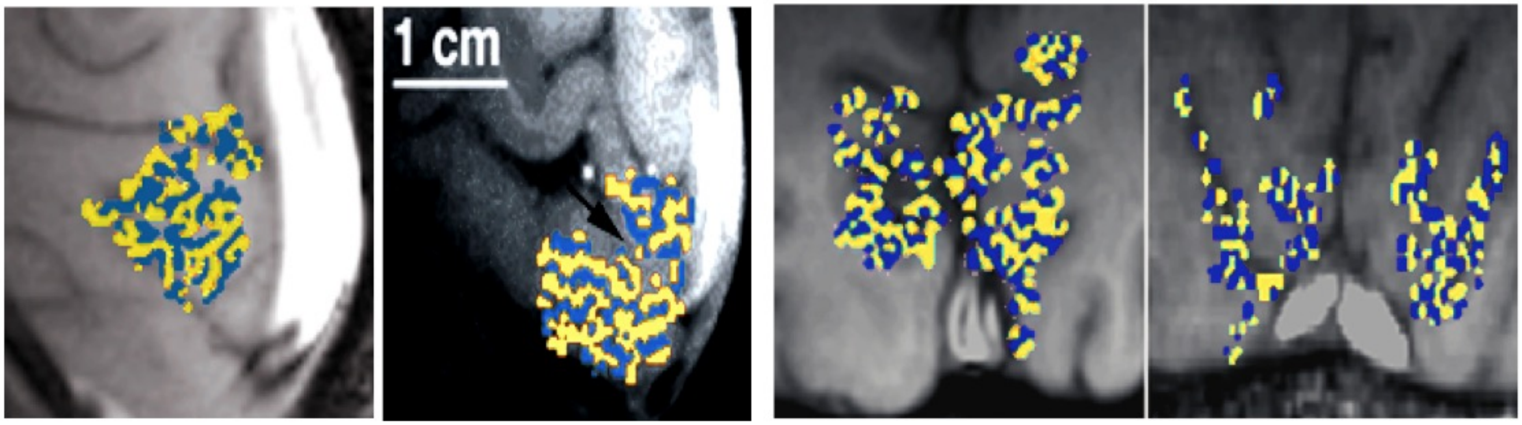
- Spatial Resolution
- Temporal Resolution
- Sensitivity

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




Neuronal Activation
Measured Signal
?
?
Hemodynamics
?
?
Noise

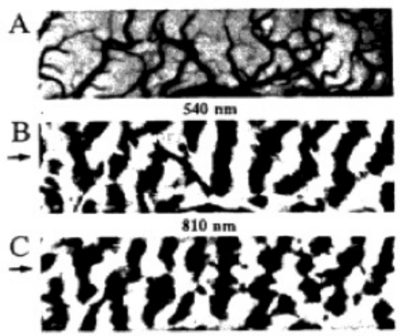
Ocular Dominance Column Mapping



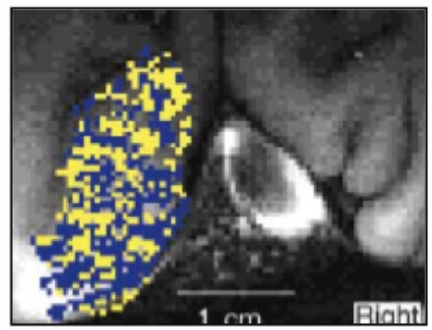
Menon, R. S., S. Ogawa, et al. (1997). J Neurophysiol 77(5): 2780-7.

0.54 x 0.54 in plane resolution

Optical Imaging



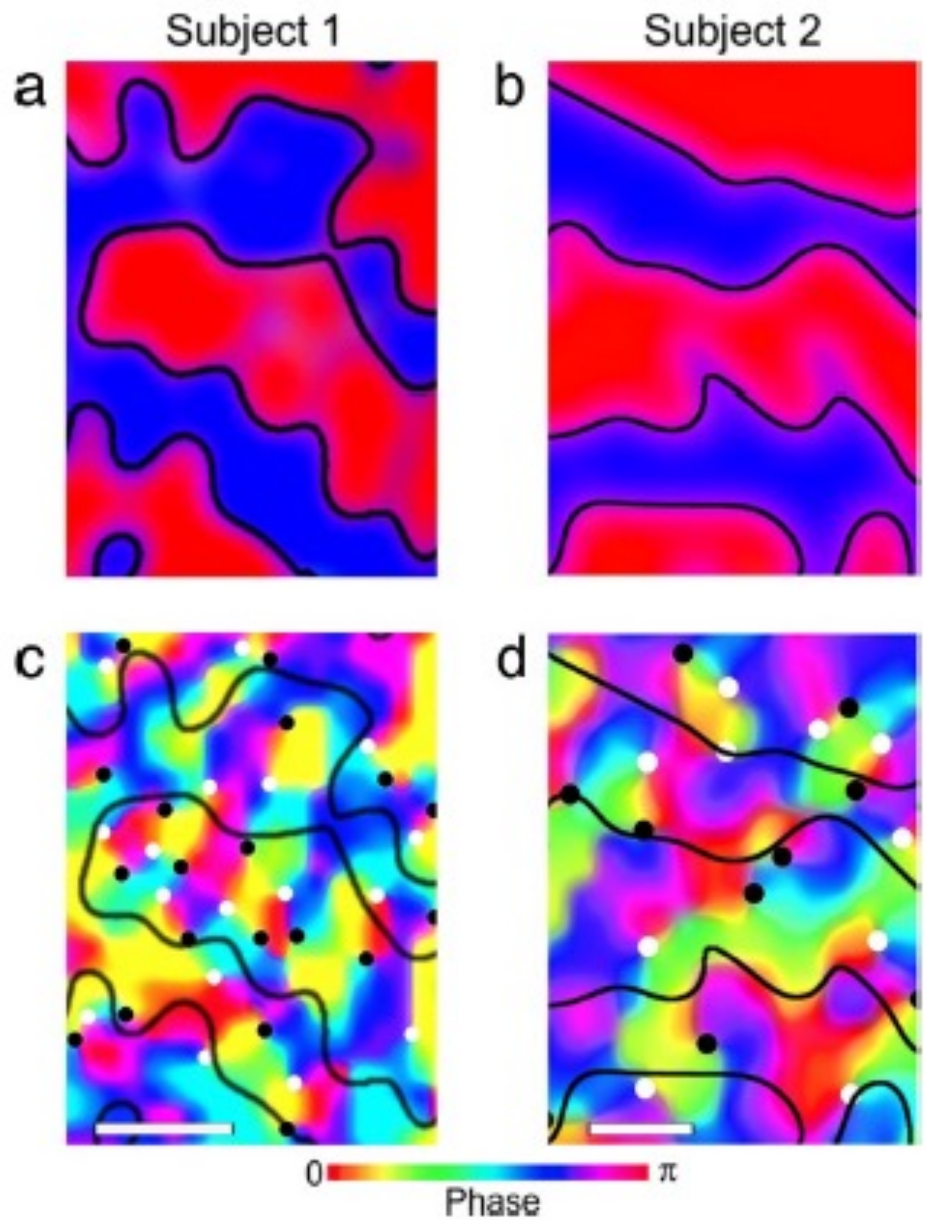
R. D. Frostig et. al, PNAS
87: 6082-6086, (1990).



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

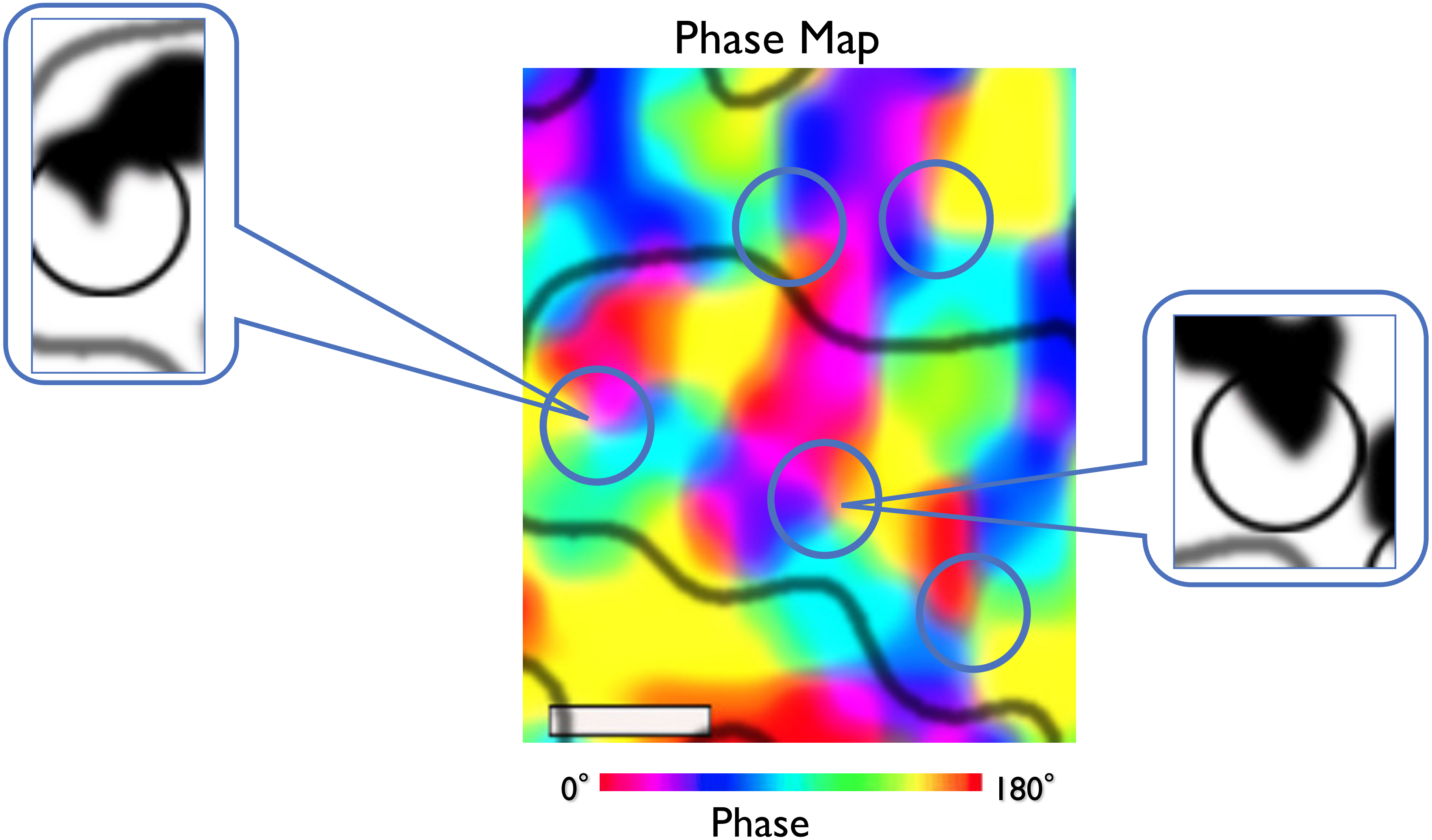
0.47 x 0.47 in plane resolution

3.5mm at 1.5T (S. Engel et al - 1994)
3.9mm (GE), 3.4mm (SE) at 3T (L. Parkes et al - 2005)
2.3 mm at 7T (A. Schmuel et al - 2007)



Yacoub et al. PNAS 2008

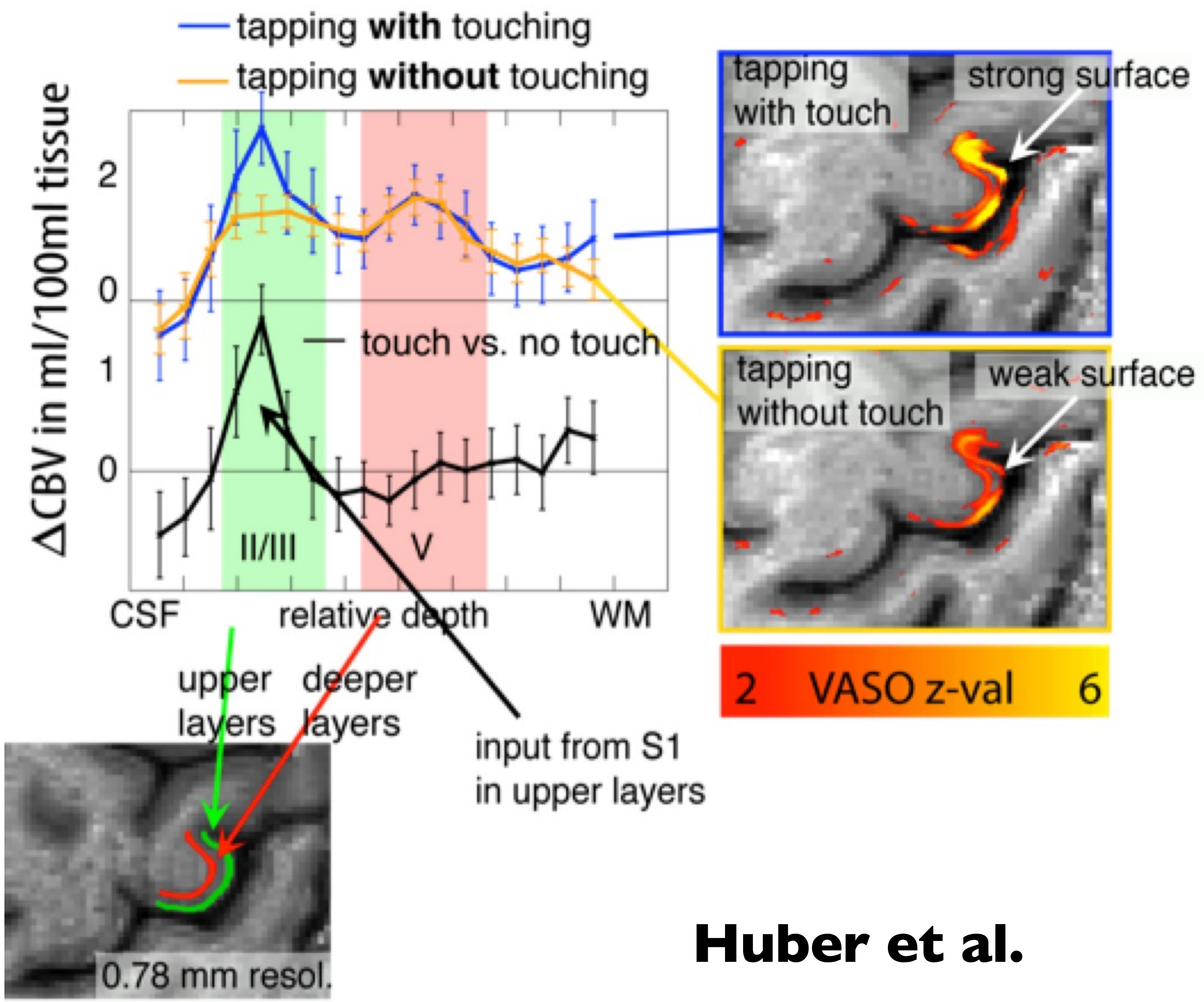
Orientation Columns in Human V1 as Revealed by fMRI at 7T



Scalebar = 0.5 mm

Yacoub et al. PNAS 2008

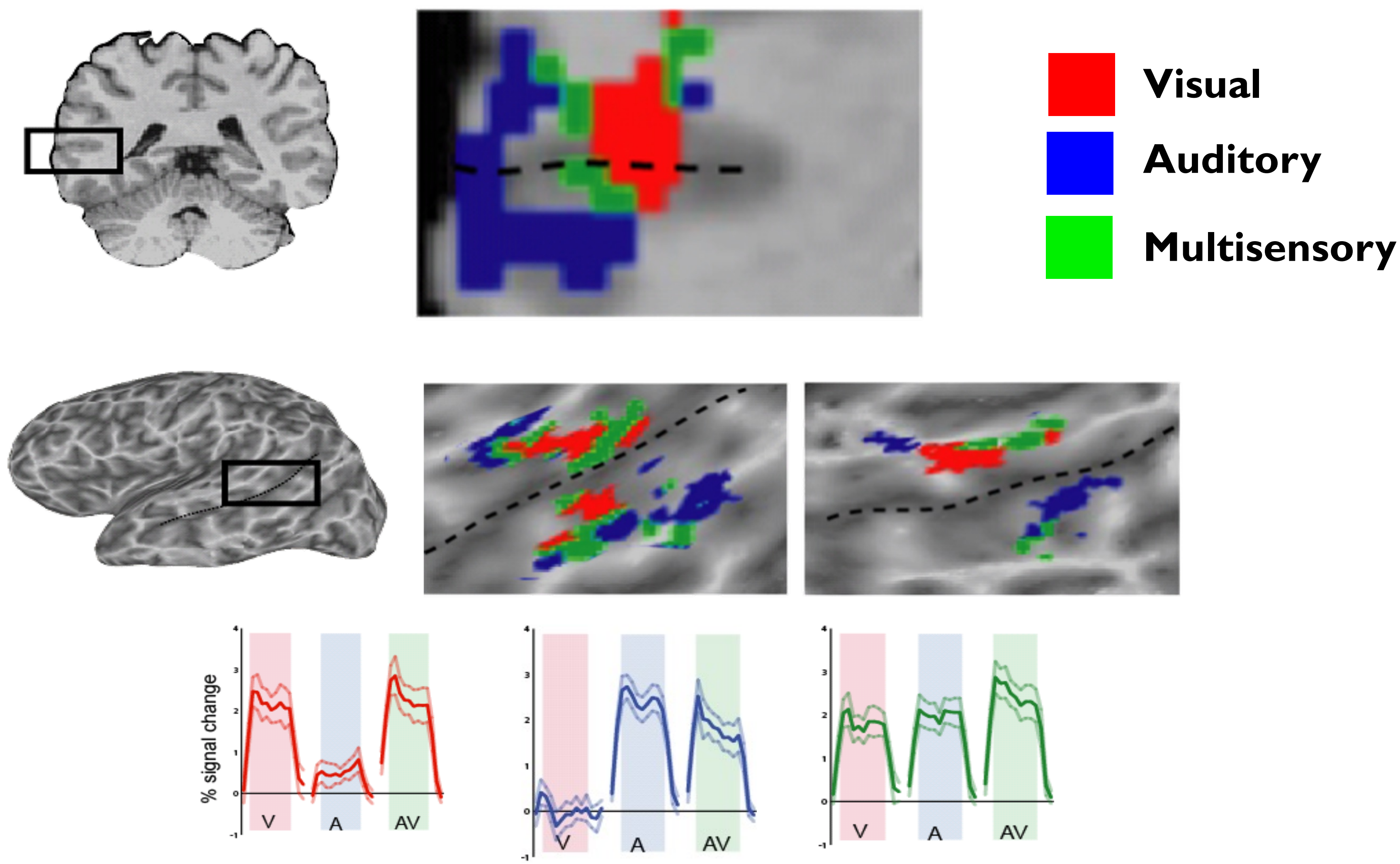
Layer Dependent Activity



Huber et al.

Multi-sensory integration

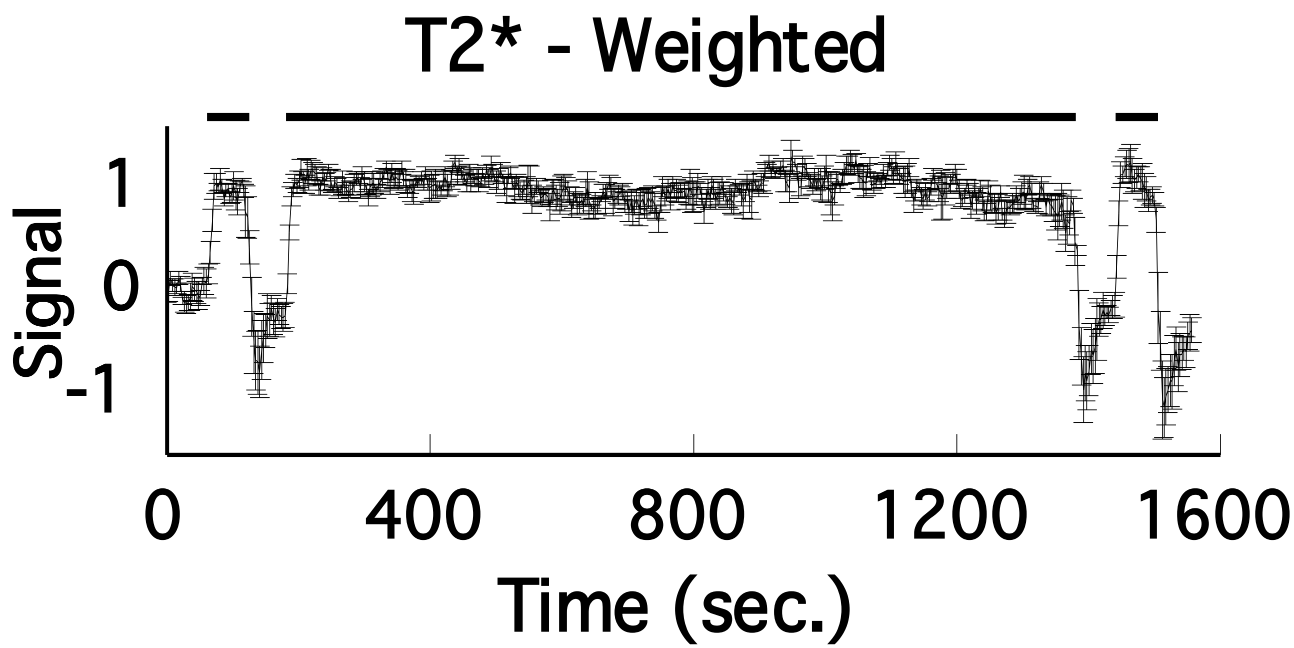
M.S. Beauchamp et al.,



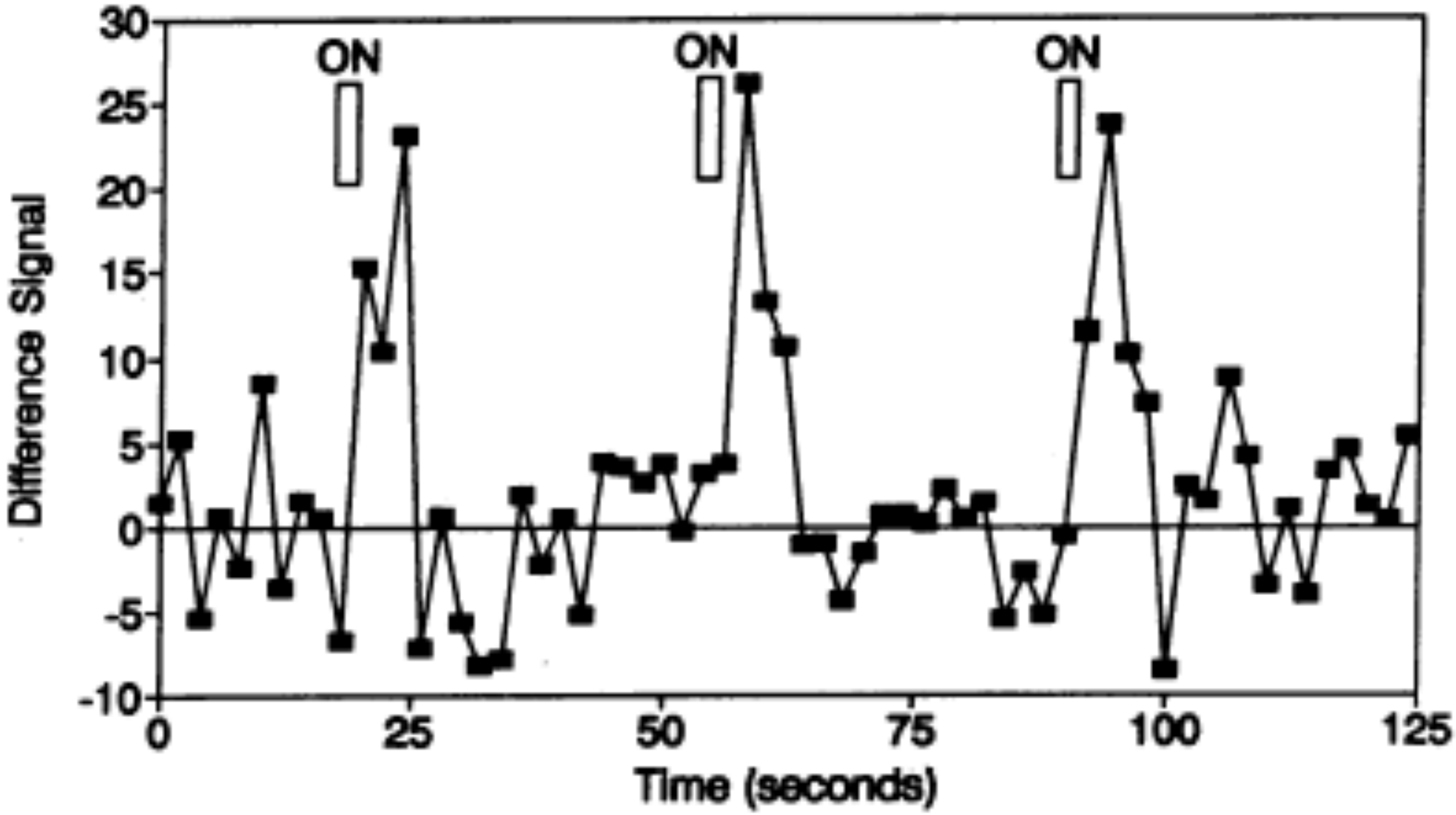
Extracting Information from the fMRI Signal:

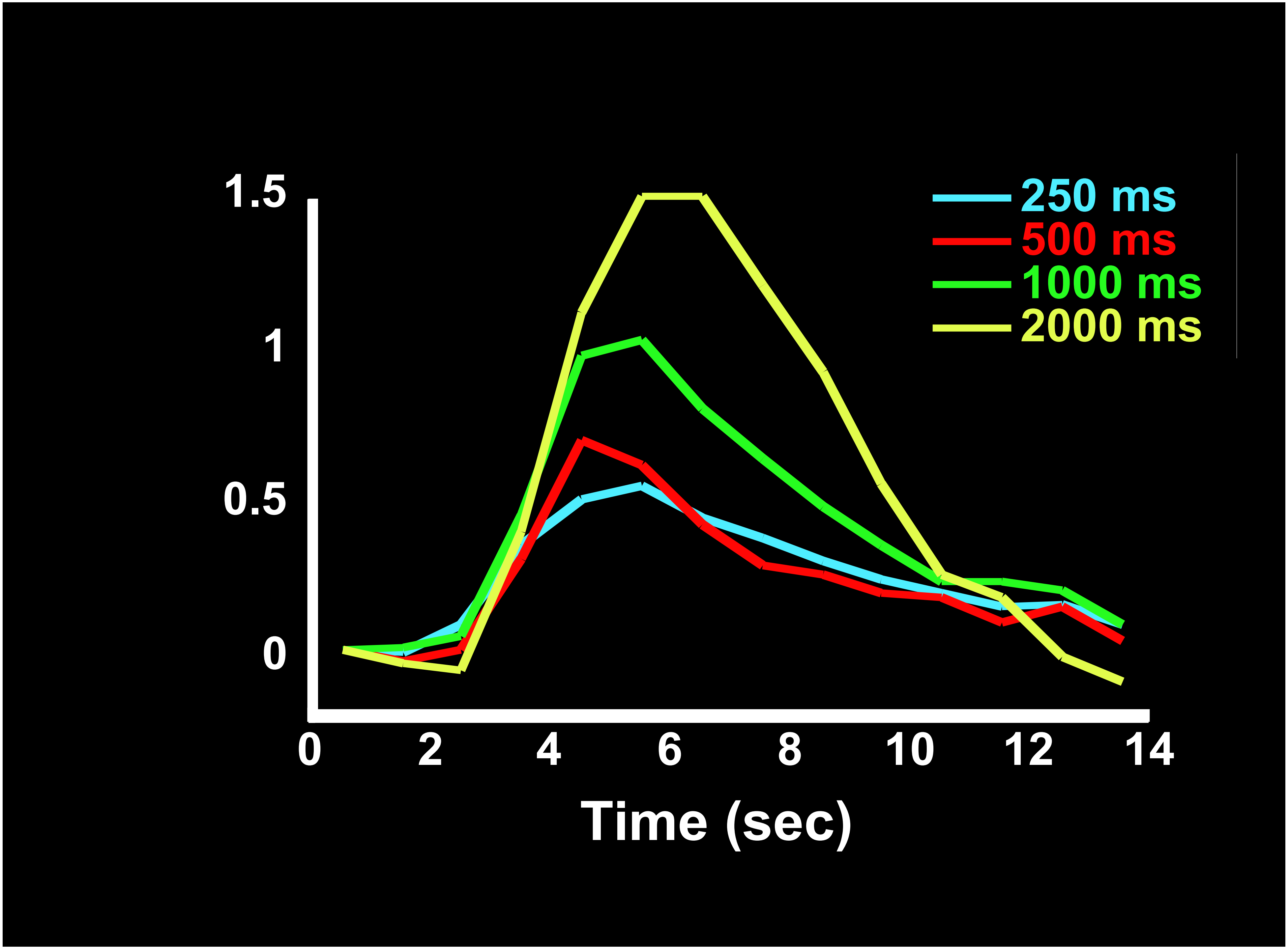
- Spatial Resolution
- Temporal Resolution
- Sensitivity

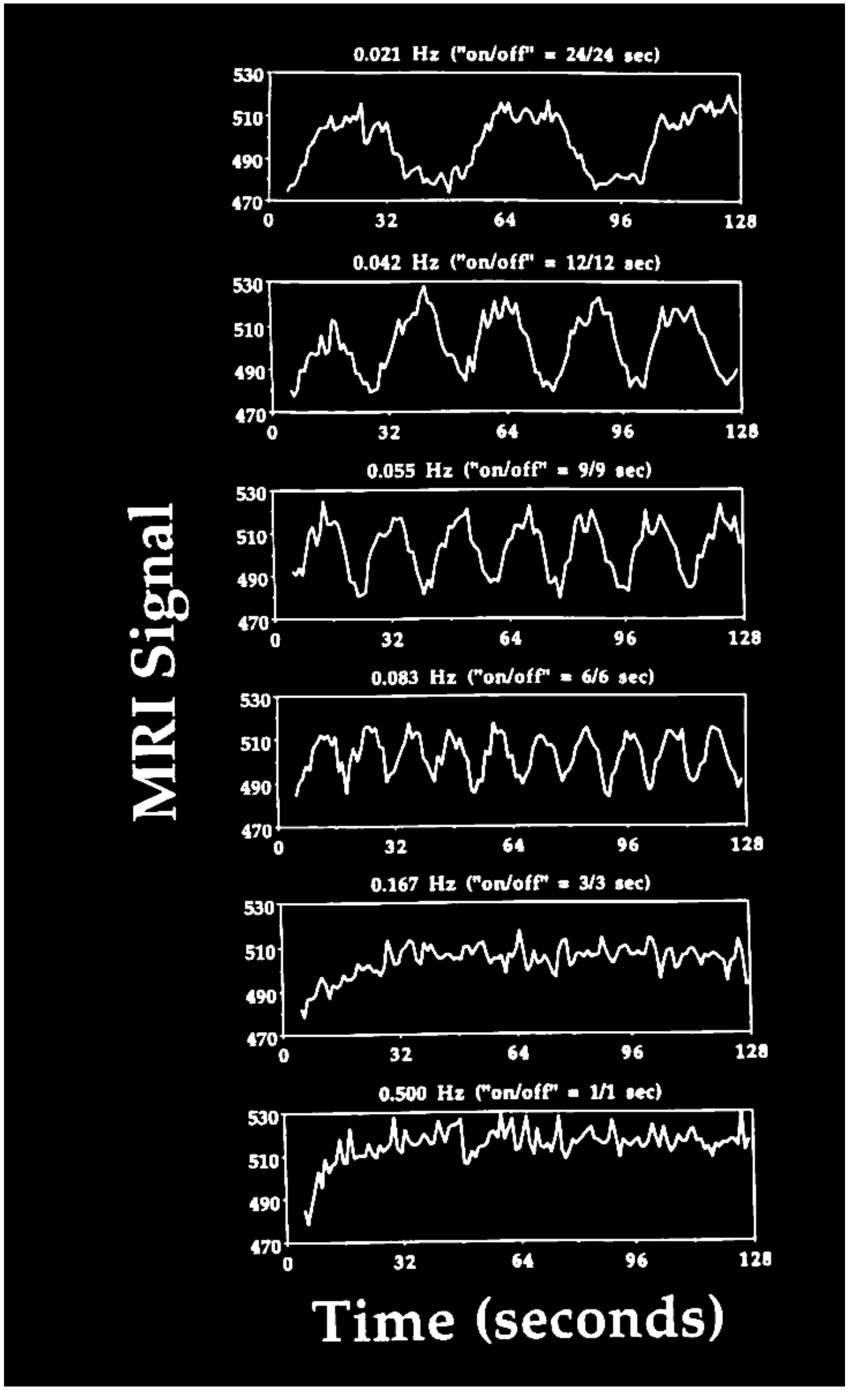
20 minutes continuous activation



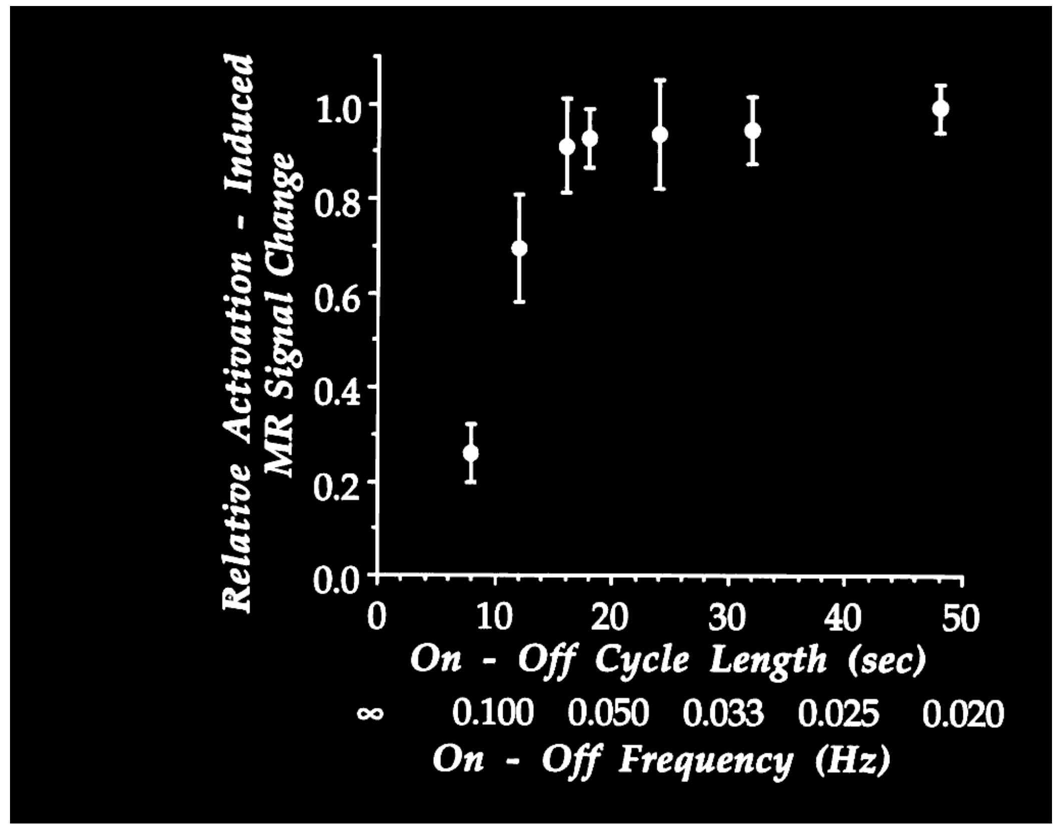
P. A. Bandettini, K. K. Kwong, T. L. Davis, R. B. H. Tootell, E. C. Wong, P. T. Fox, J. W. Belliveau, R. M. Weisskoff, B. R. Rosen, (1997). "Characterization of cerebral blood oxygenation and flow changes during prolonged brain activation." ***Human Brain Mapping*** **5, 93-109.**


ON
ON
ON
30
25
20
15
10
5
0
-5
-10
Difference Signal
0
25
50
75
100
125
Time (seconds)


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



How rapidly can one switch on and off?

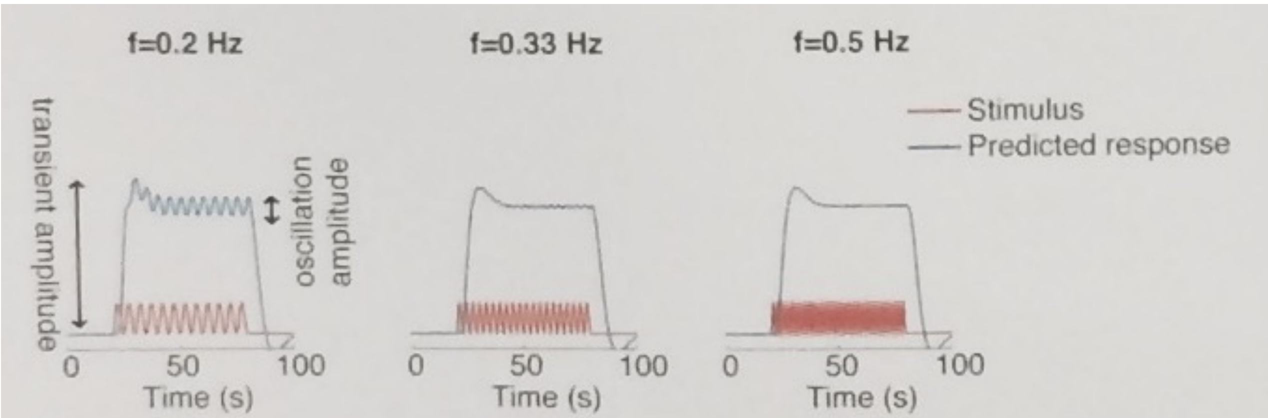


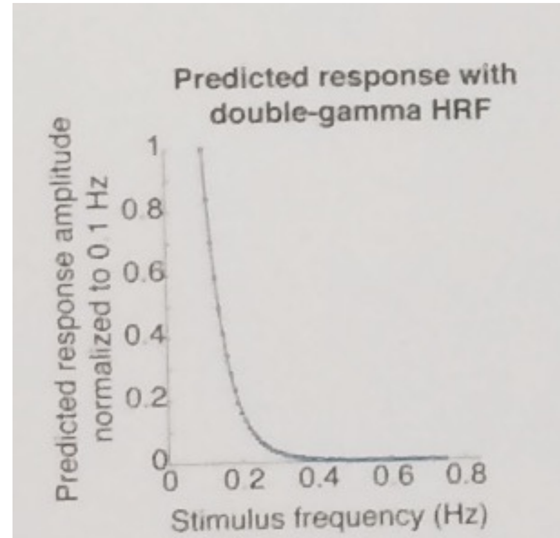
P. A. Bandettini,, Functional MRI using the BOLD approach: dynamic characteristics and data analysis methods, in "Diffusion and Perfusion: Magnetic Resonance Imaging" (D. L. Bihan, Ed.), p.351-362, Raven Press, New York, 1995.

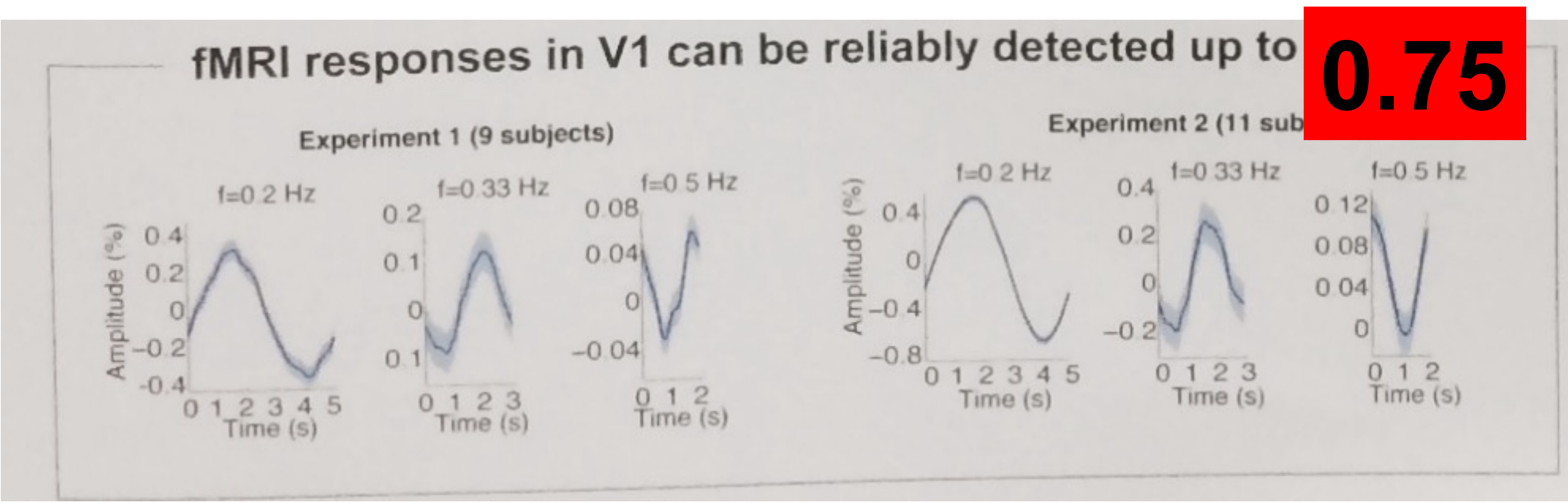
Detection of delta-band oscillations in visual cortex using fast fMRI and simultaneous EEG-fMRI

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

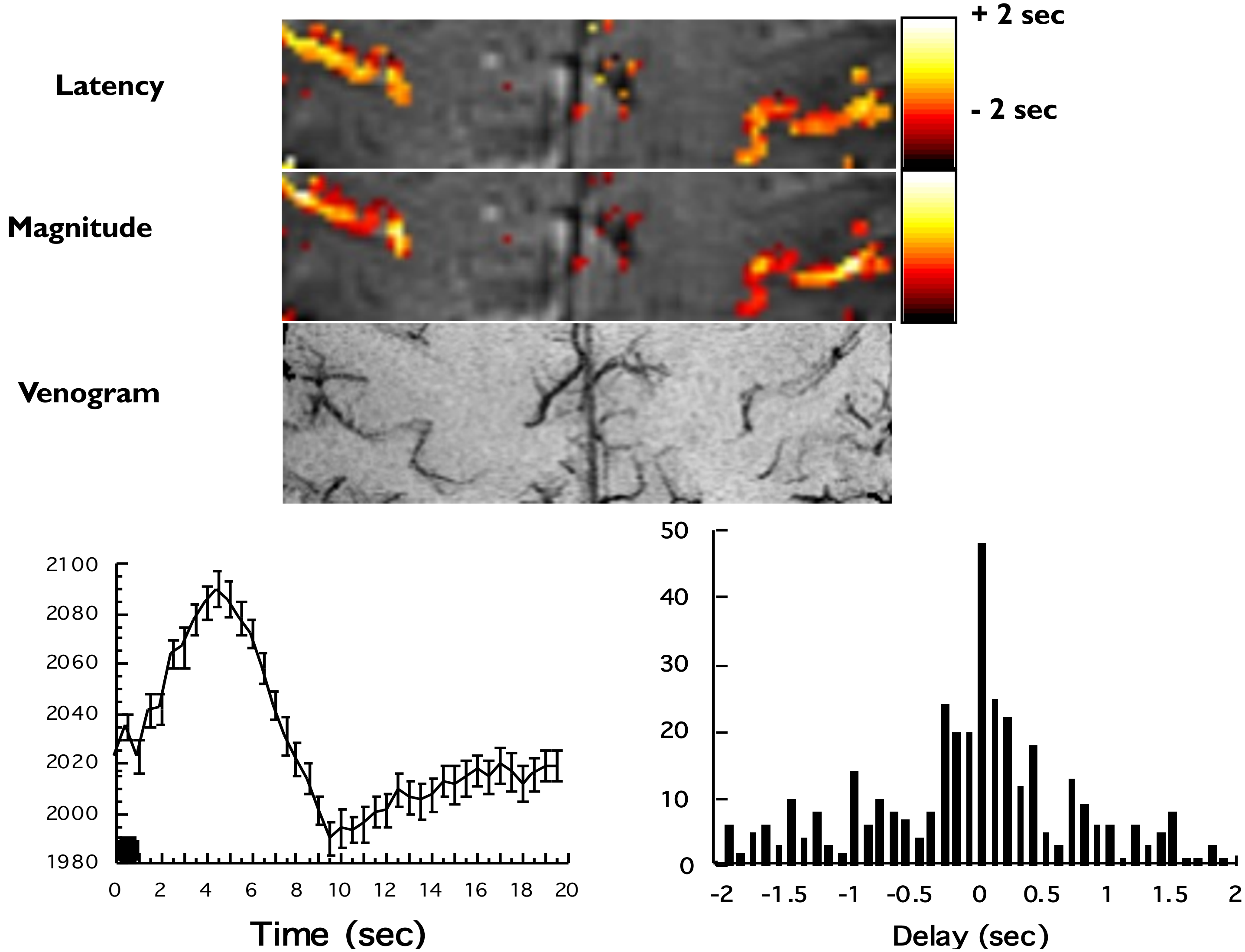
OHBM 2015







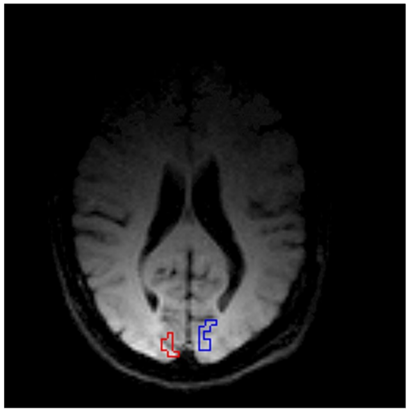
Latency Variation...



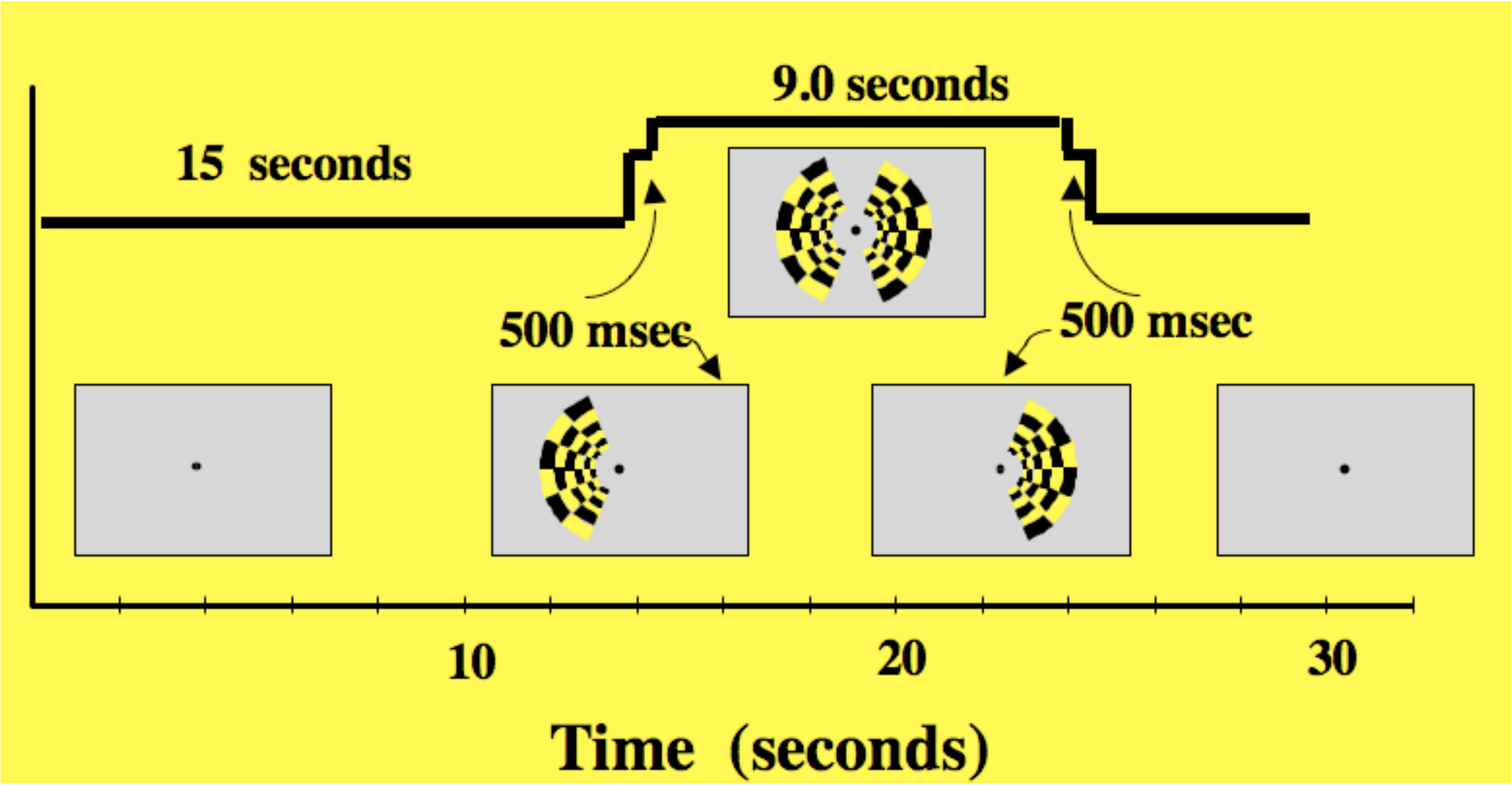
P.A. Bandettini, (1999) "Functional MRI" 205-220.

Hemi-Field Experiment

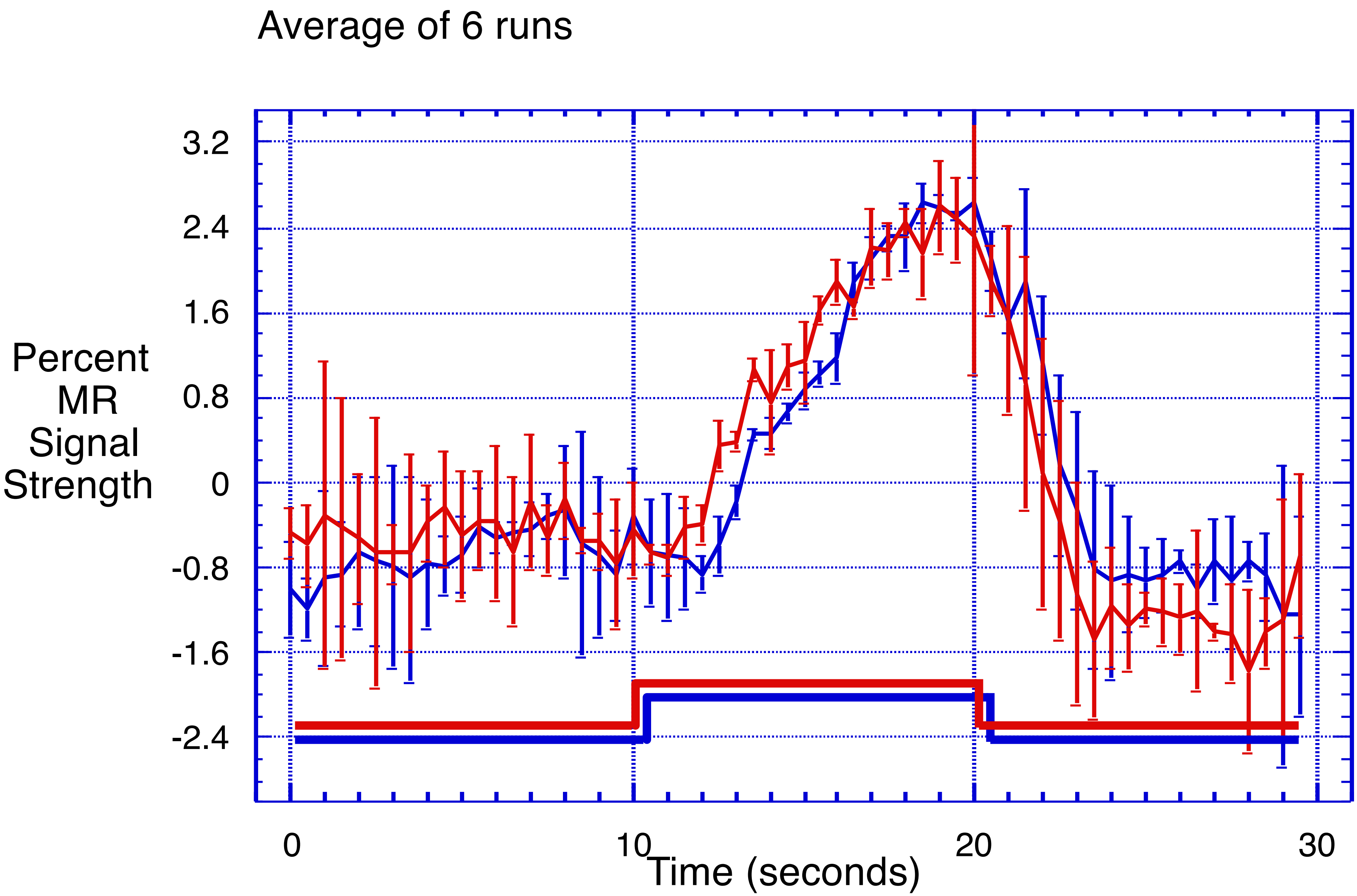
Right Hemisphere

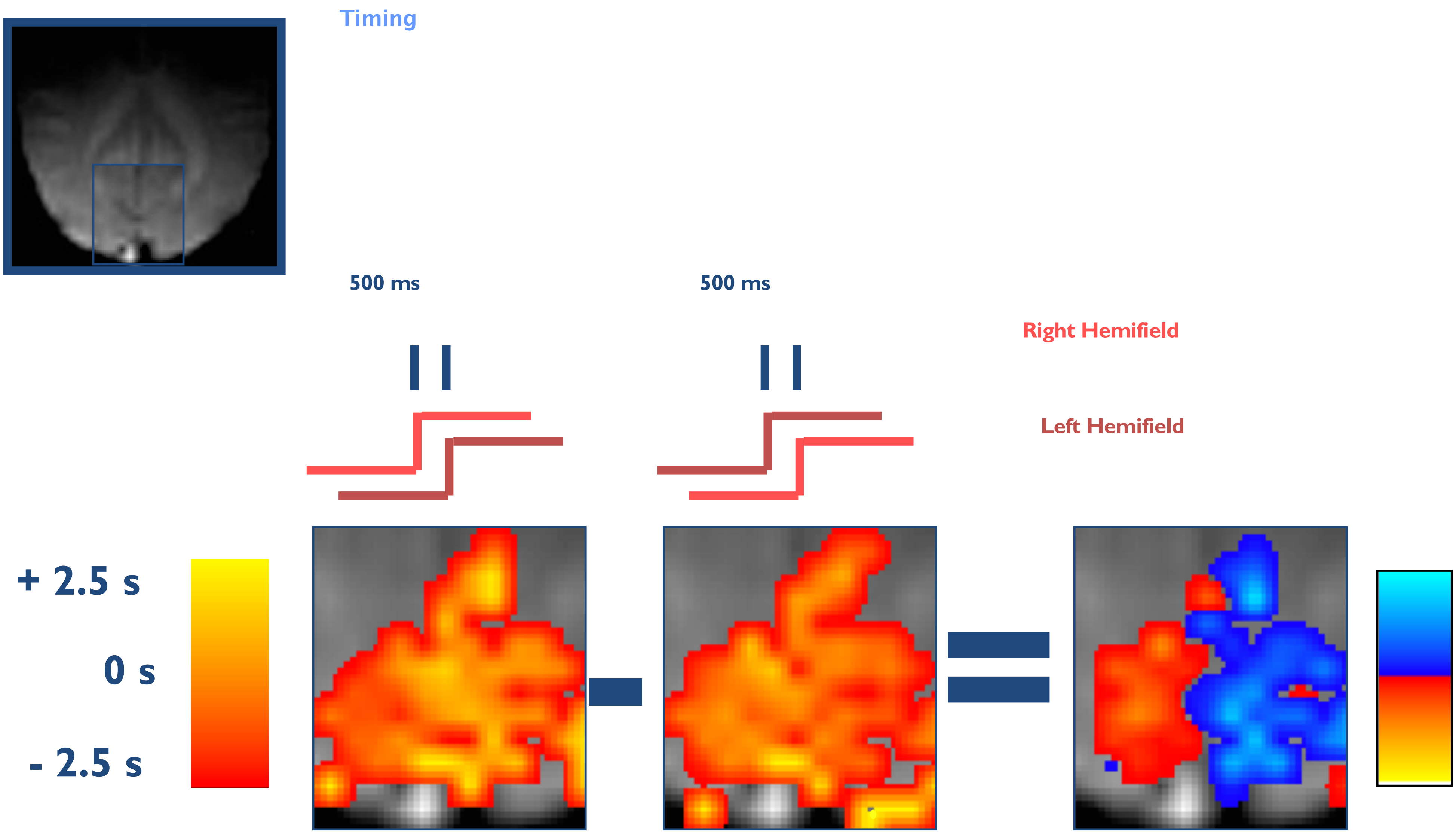


Left Hemisphere

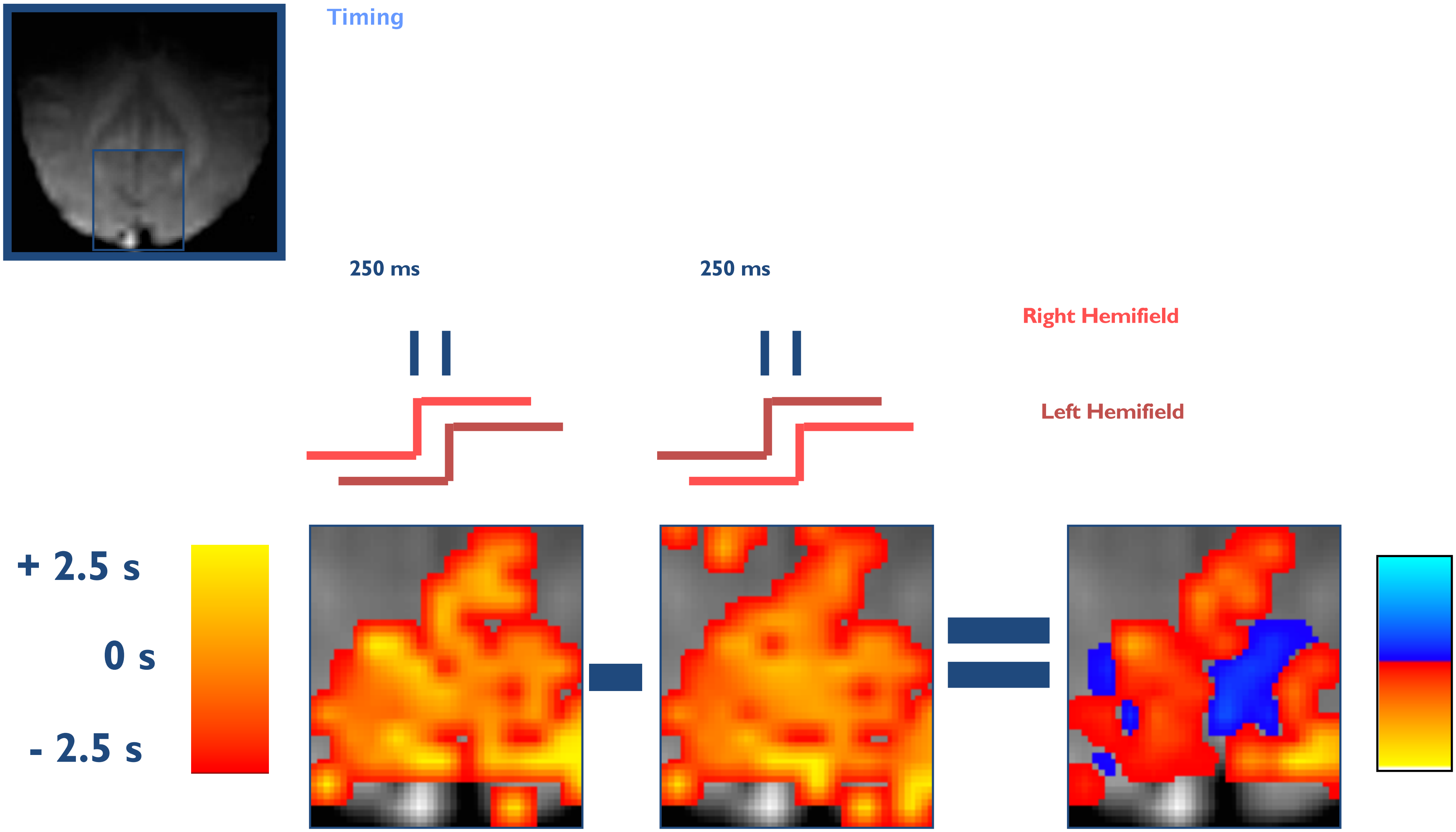


Hemi-field with 500 msec asynchrony




Timing
500 ms
500 ms
Right Hemifield
Left Hemifield
+ 2.5 s
0 s
- 2.5 s

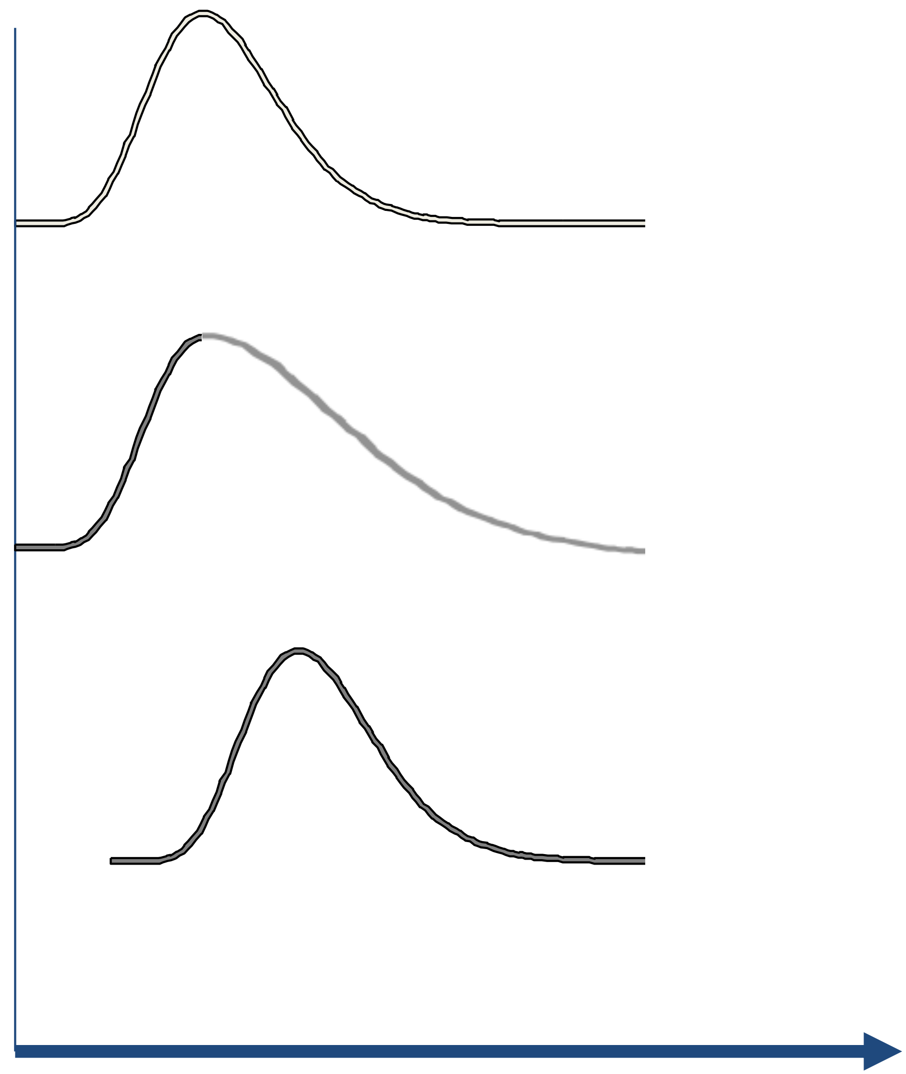
Timing

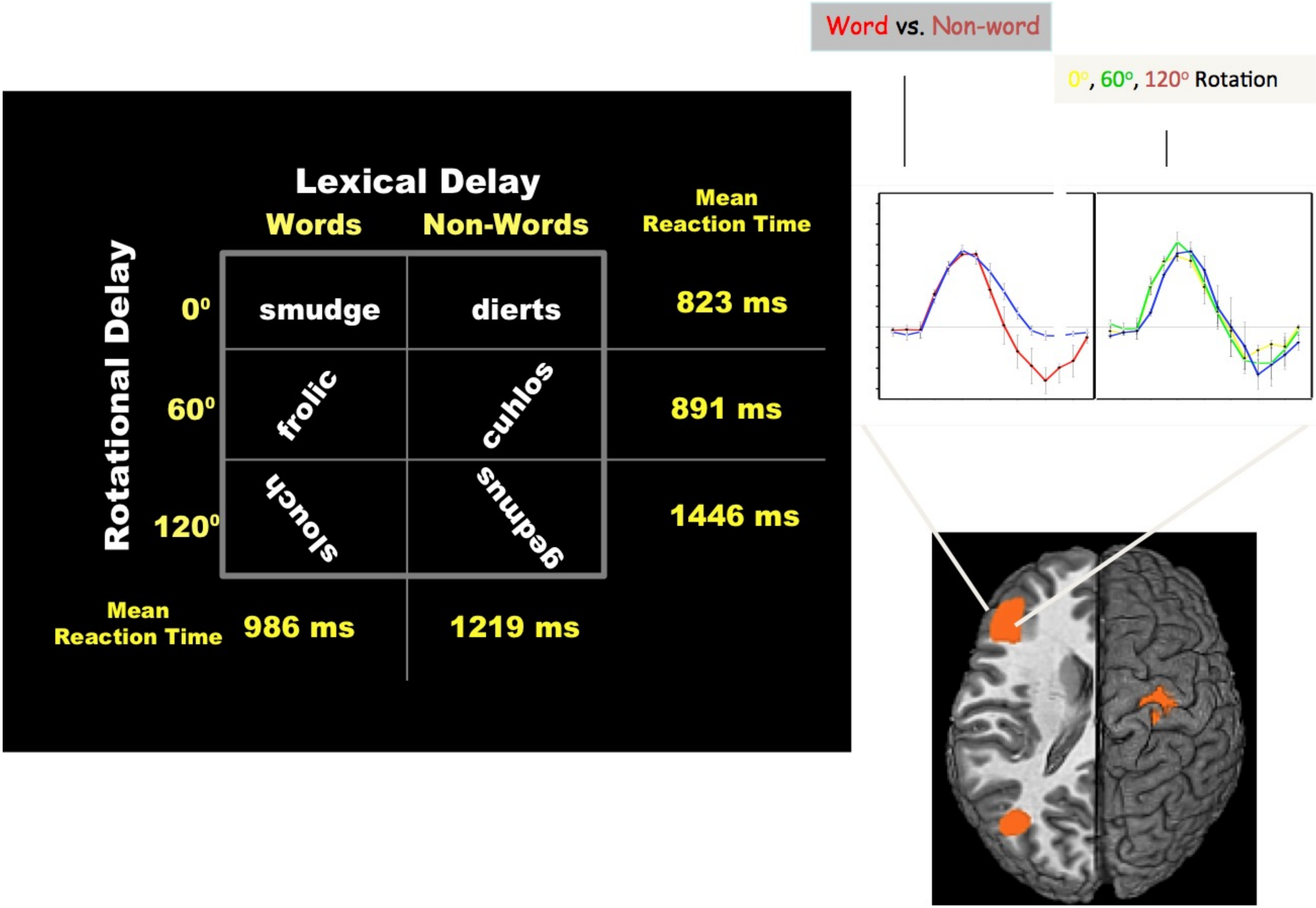


Hemodynamic Response Modulation

Bottleneck In Processing (upstream)

Delayed Processing (downstream)



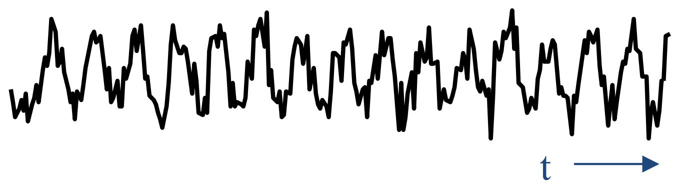


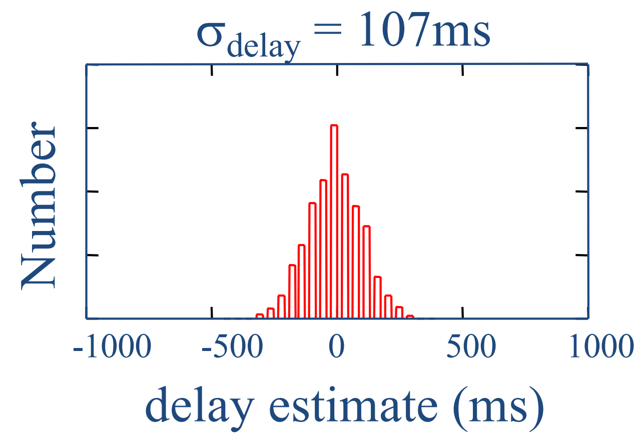
Bellgowan, et al (2003), PNAS 100, 15820–15283

Even if no hemodynamic variability exists…

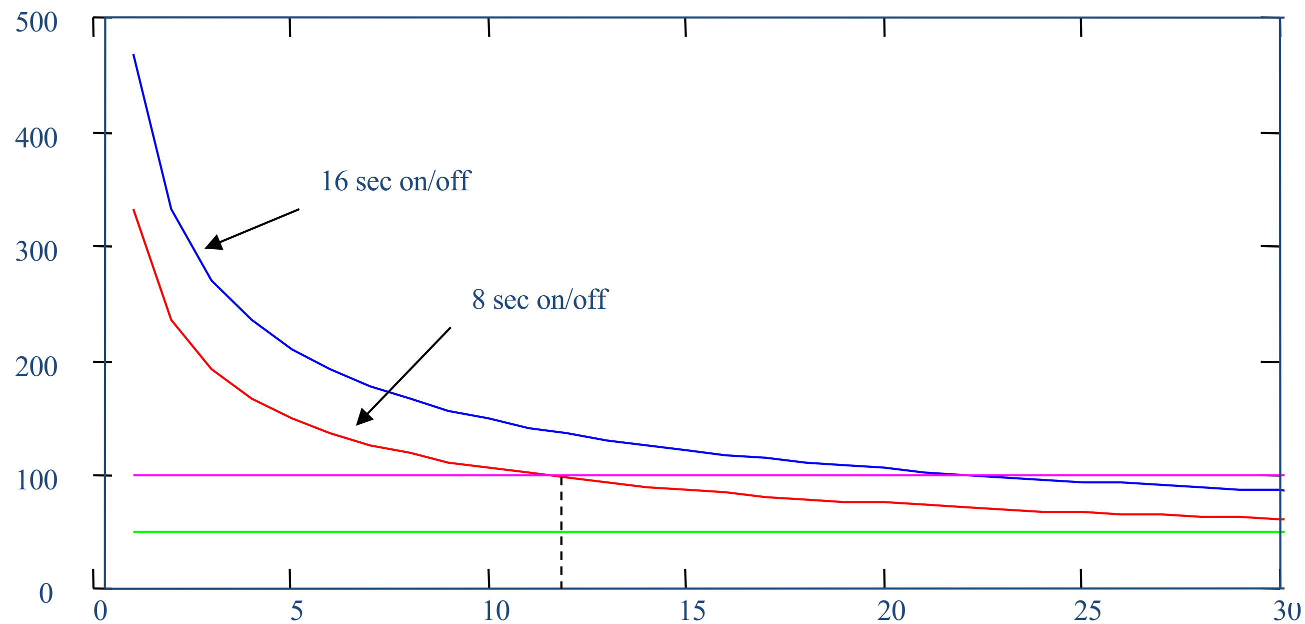
1 run:

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





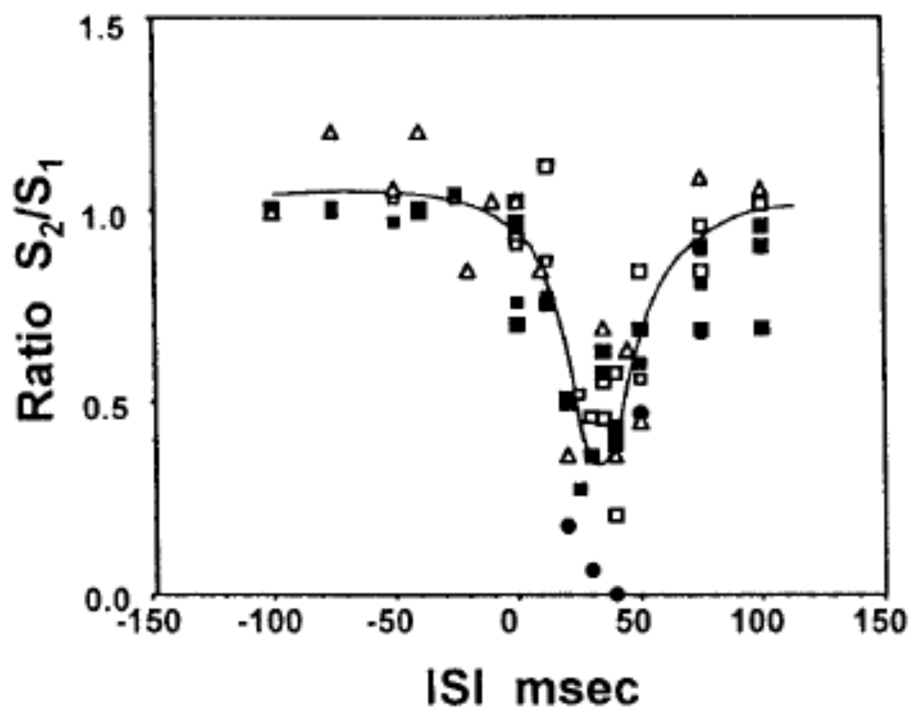
Smallest latency
Variation Detectable
(ms) ($p < 0.001$)



Number of runs

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

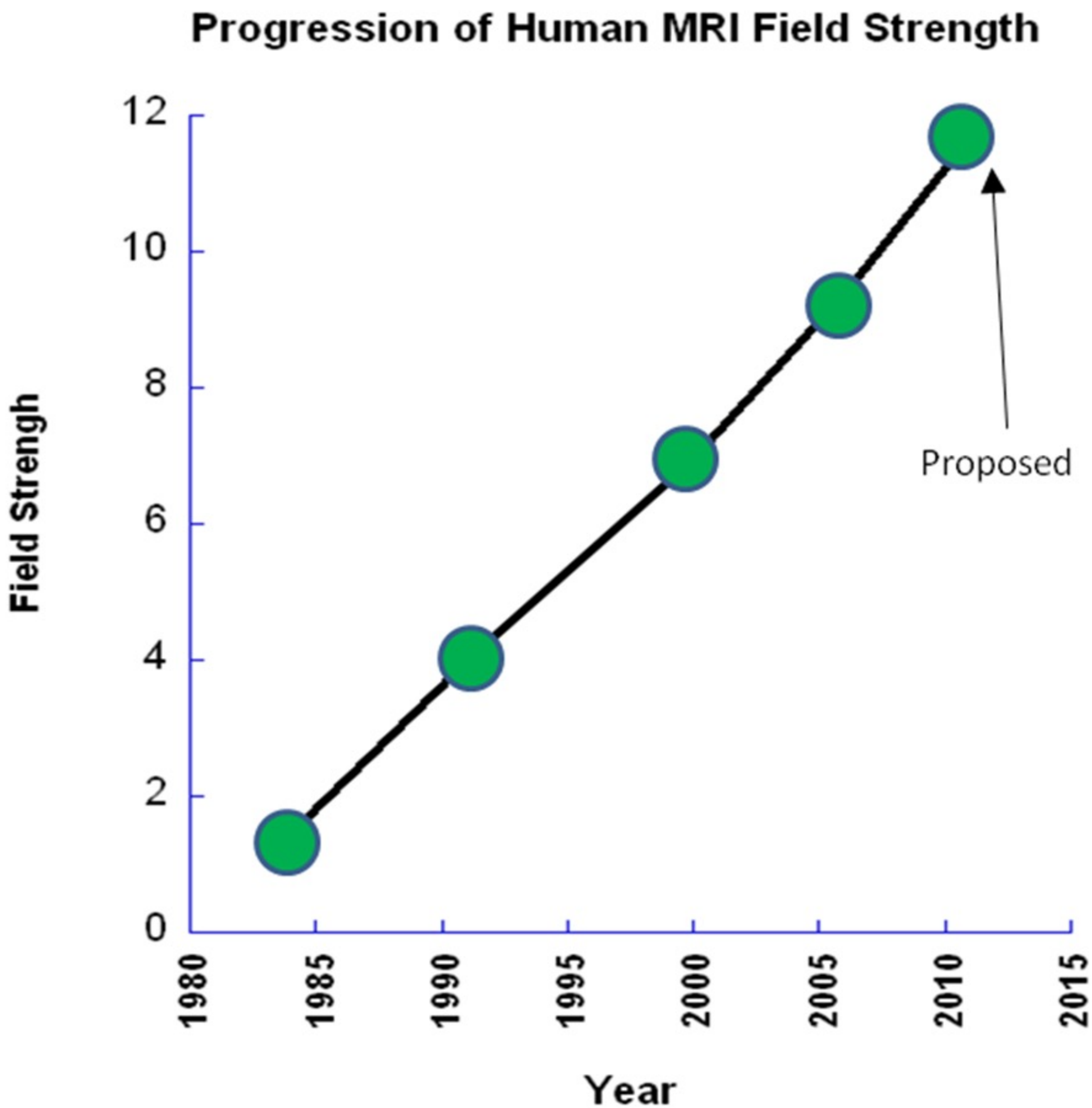
Seiji Ogawa[†‡], Tso-Ming Lee[†], Ray Stepnoski[†], Wei Chen[§], Xiao-Hong Zhu[§], and Kamil Ugurbil[§]



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

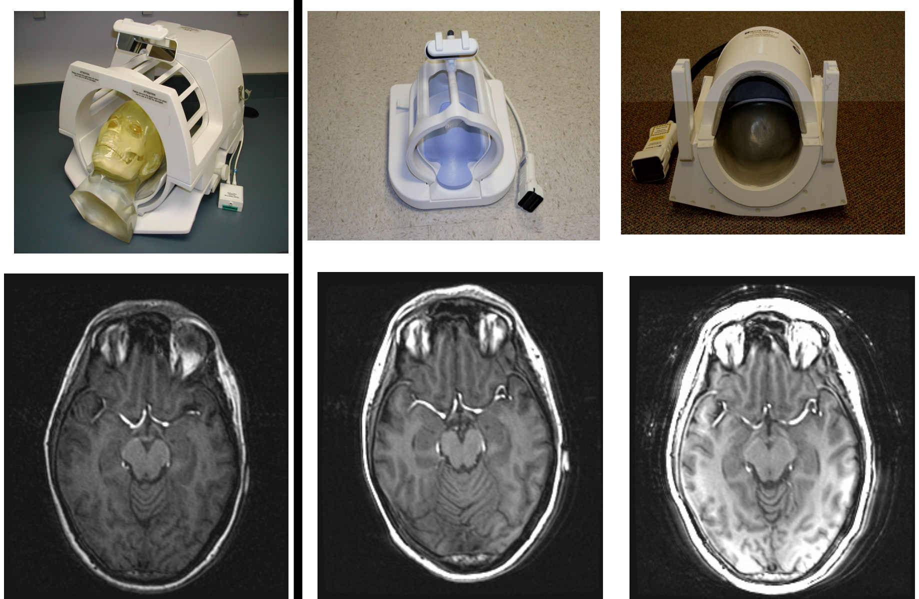
Extracting Information from the fMRI Signal:

- Spatial Resolution
- Temporal Resolution
- Sensitivity



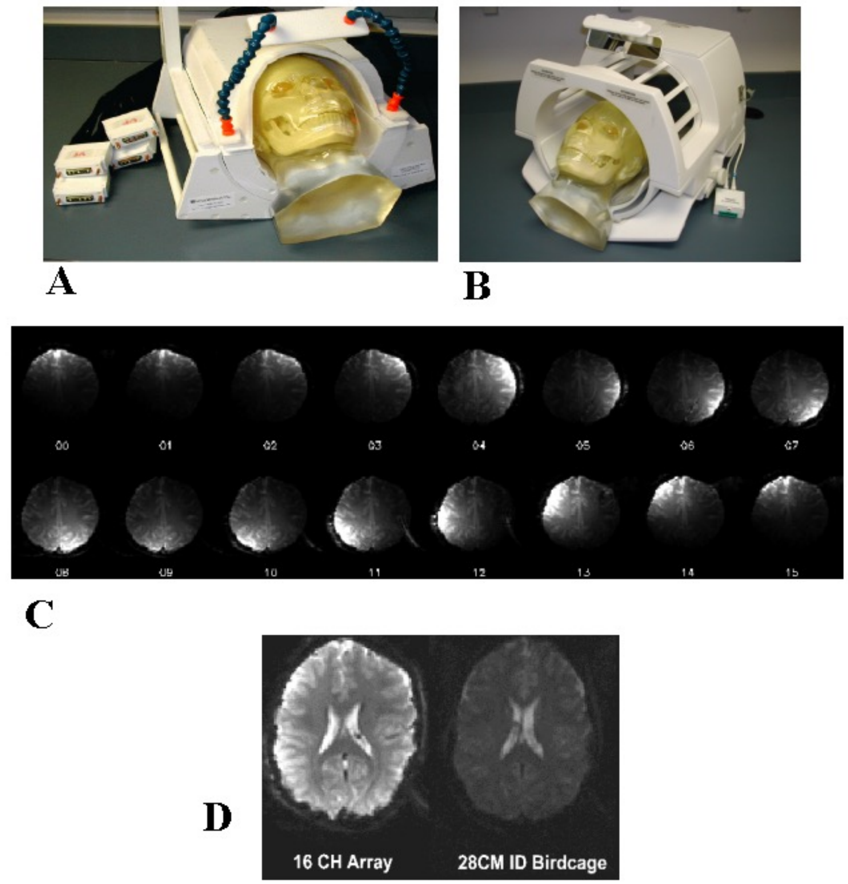
Progression of Human MRI Field Strength
Field Strengh
Year
0
2
4
6
8
10
12
1980
1985
1990
1995
2000
2005
2010
2015
Proposed

8 channel parallel receiver coil



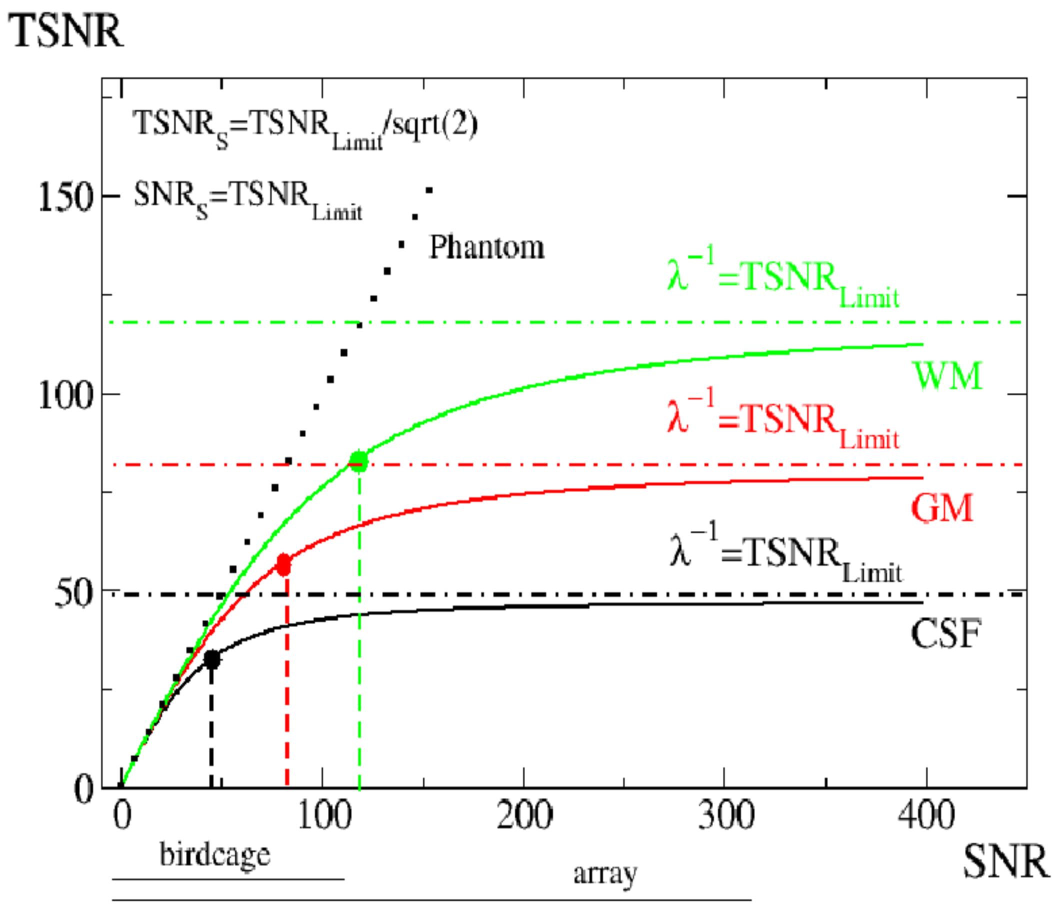
GE birdcage | GE 8 channel coil | Nova 8 channel coil

16 channel parallel receiver coil



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

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

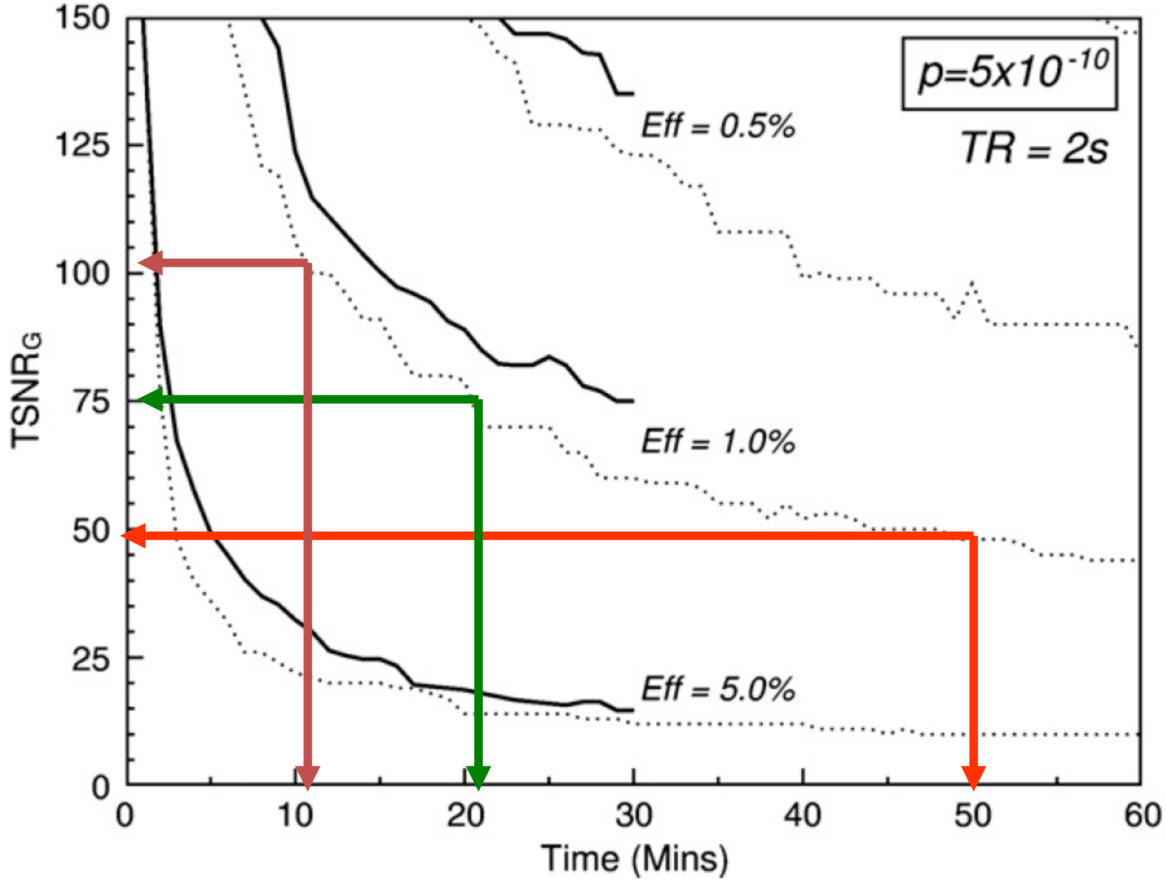


J. Bodurka, F. Ye, N Petridou, K. Murphy, P.A. Bandettini, *NeuroImage,* 34, 542-549 (2007)

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

Sensitivity, Scan Time, and Temporal Signal to Noise

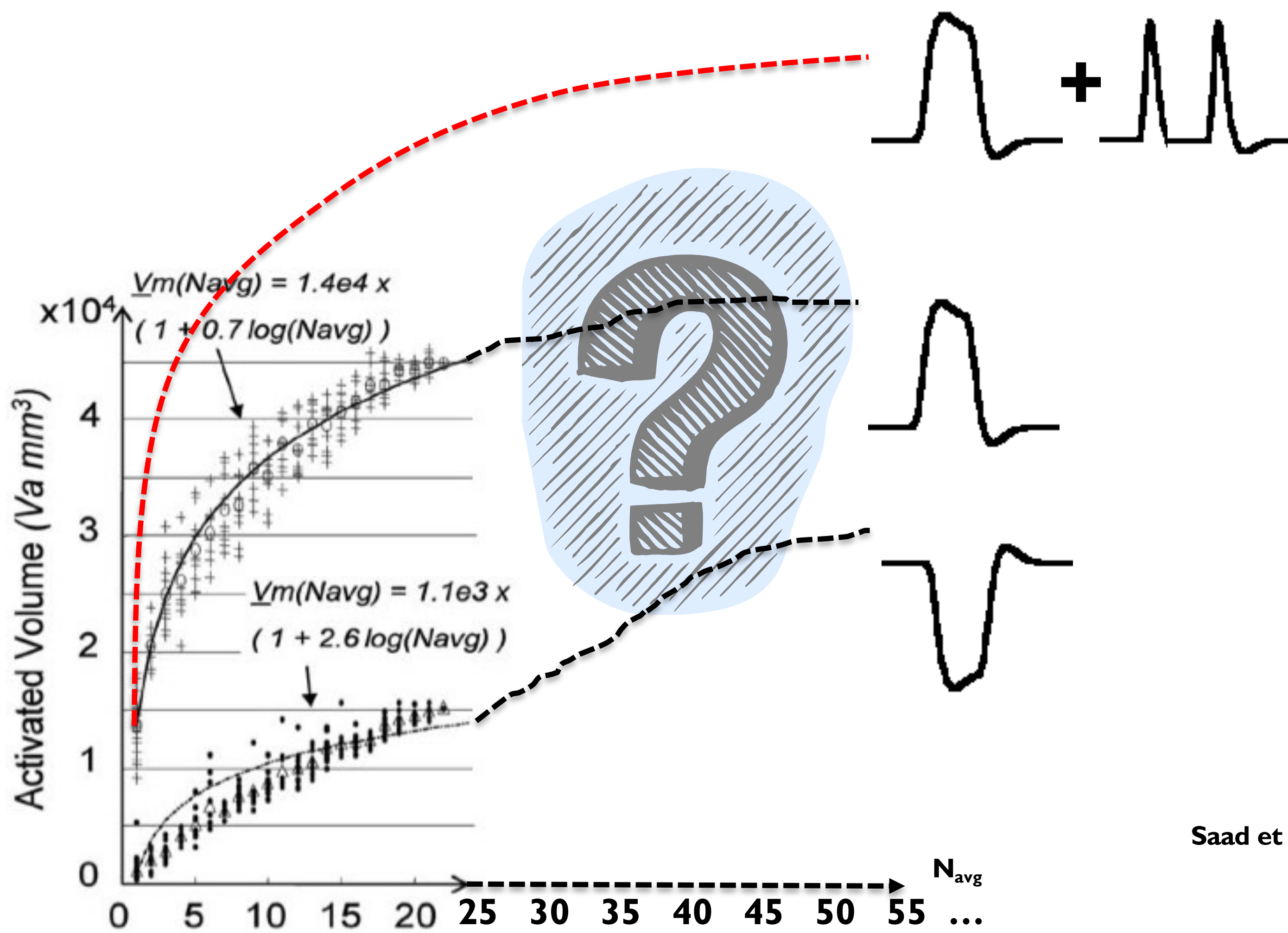


K. Murphy, J. Bodurka, P.A. Bandettini, *NeuroImage*, 34, 565-574 (2007)

IS THE SPARSENESS OF FMRI ACTIVATIONS REAL?

OR

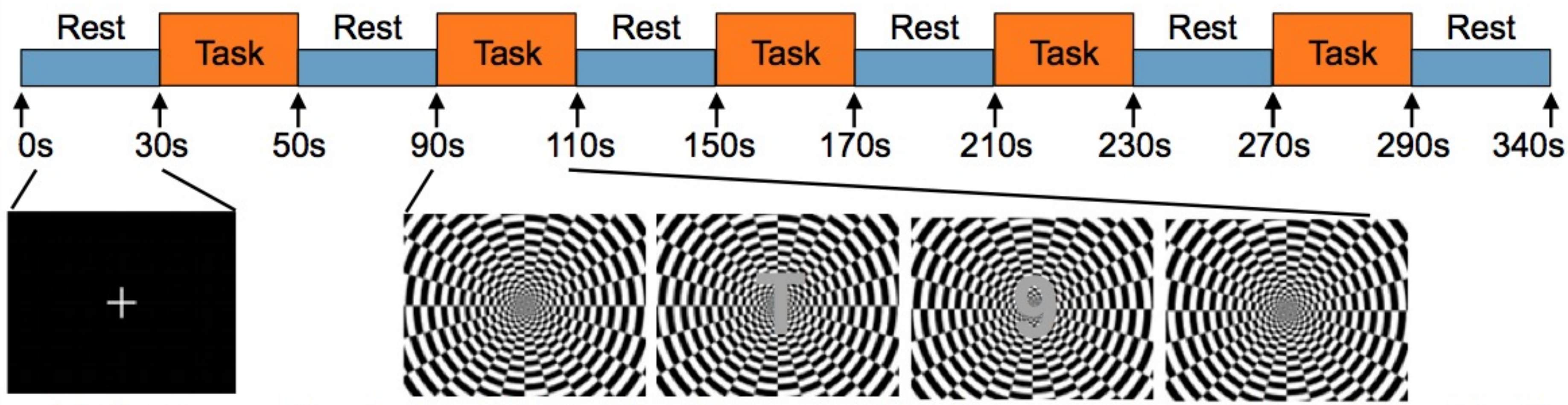
IS IT THE RESULT OF INSUFFICIENT TSNR + OVERLY STRICT RESPO



Saad et al

Experimental Methods (I)

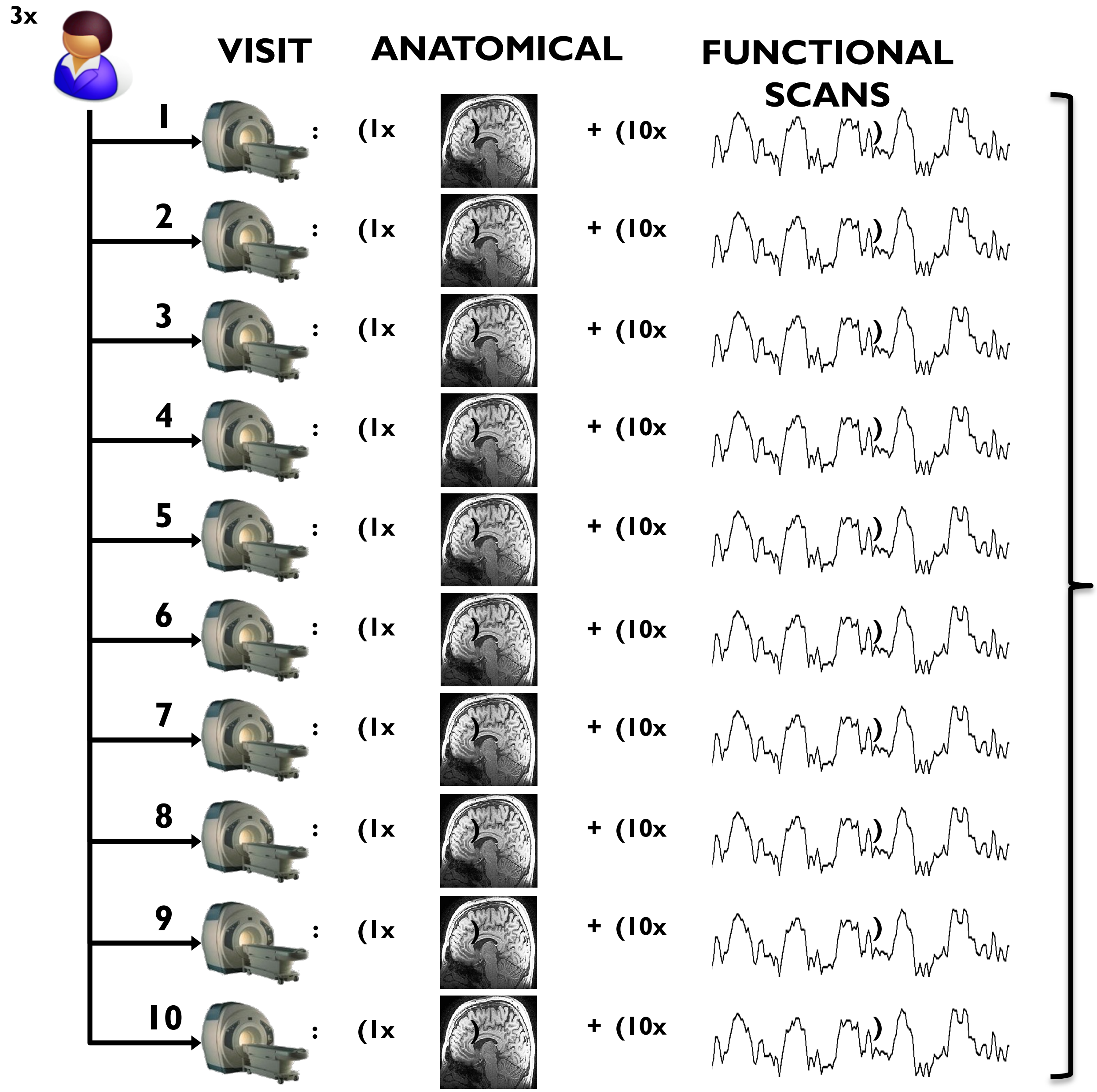
- 3 Healthy Volunteers: 1M/2F; Age = 27 ± 2.5
- 3T GE Signa HDx
- Anatomical Scan: MPRAGE | .9x.9x1.2 mm^3 | 192 Slices
- Functional Scans: GRE-EPI
  - TR/TE = 2s/30ms
  - In-Plane Res = 64x64
  - #Slices = 32 Oblique
  - **FOV = 240mm**
  - **Slice Thickness = 3.8 mm**
  - **Flip Angle = 75°**



Fixate on crosshair

Checkerboard 7.5Hz | Symbol appear at random moments for 400ms (4 times/block)
TASK: Letter appears → press left button | Number appears → press right button

Experimental Methods (II)



100 FUNCTIONAL RUNS/SUBJECT

=

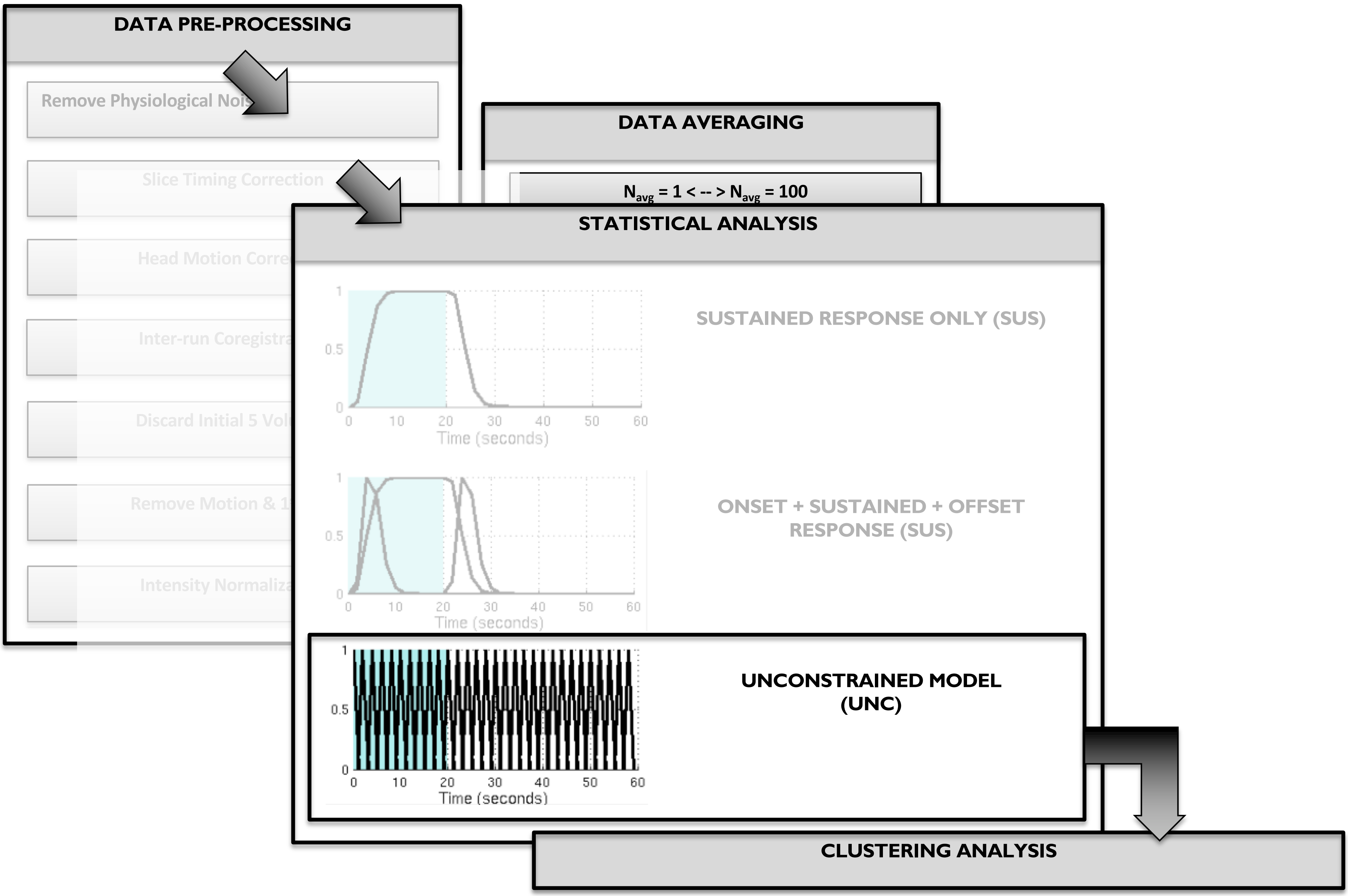
500 TRIALS/SUBJECT

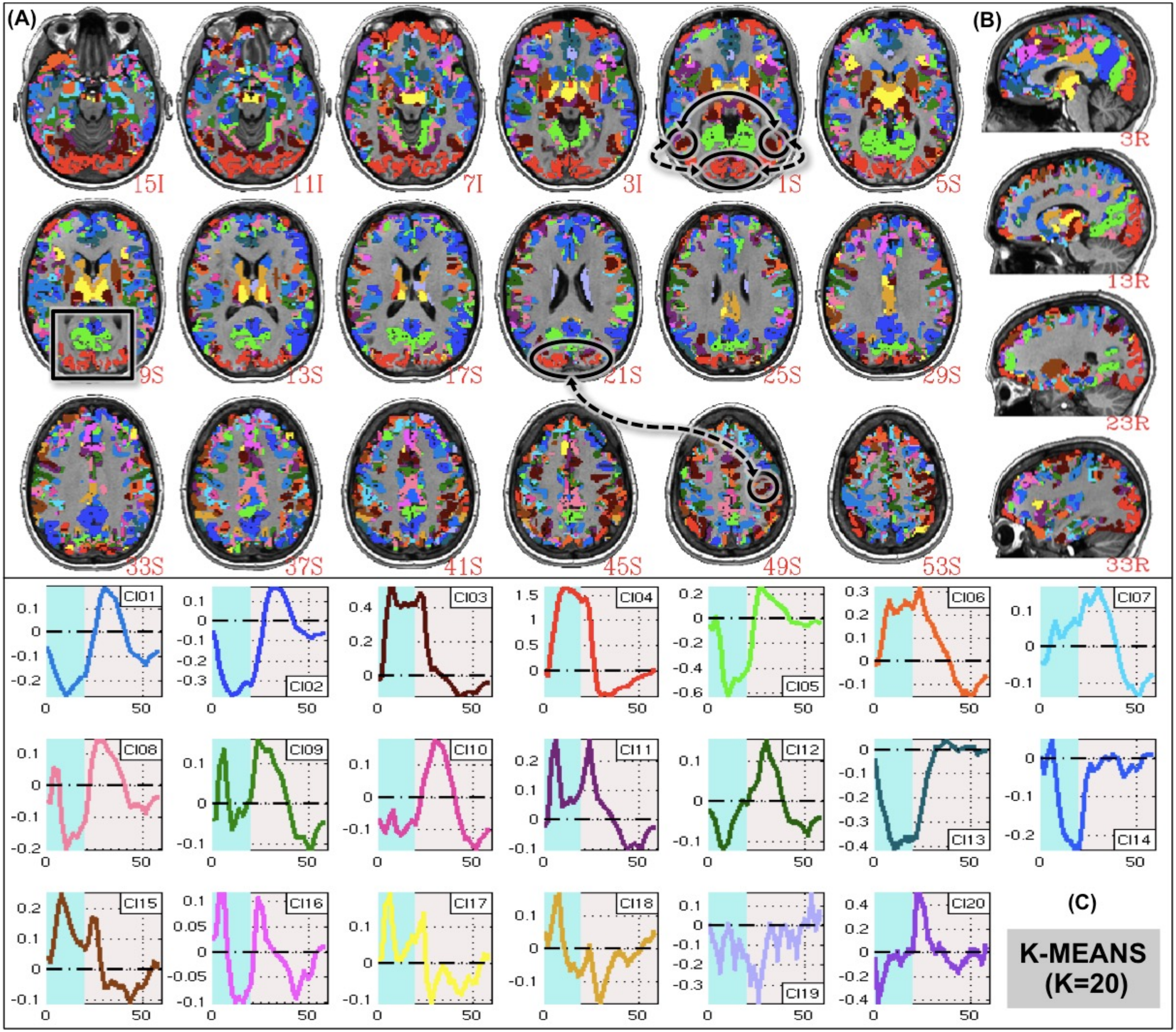
=

9 HOURS OF DATA/SUBJECT

X 100
(QA Axial EPIs)

Data Analysis




(A)
(B)
15I
11I
7I
3I
1S
5S
9S
13S
17S
21S
25S
29S
33S
37S
41S
45S
49S
53S
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)