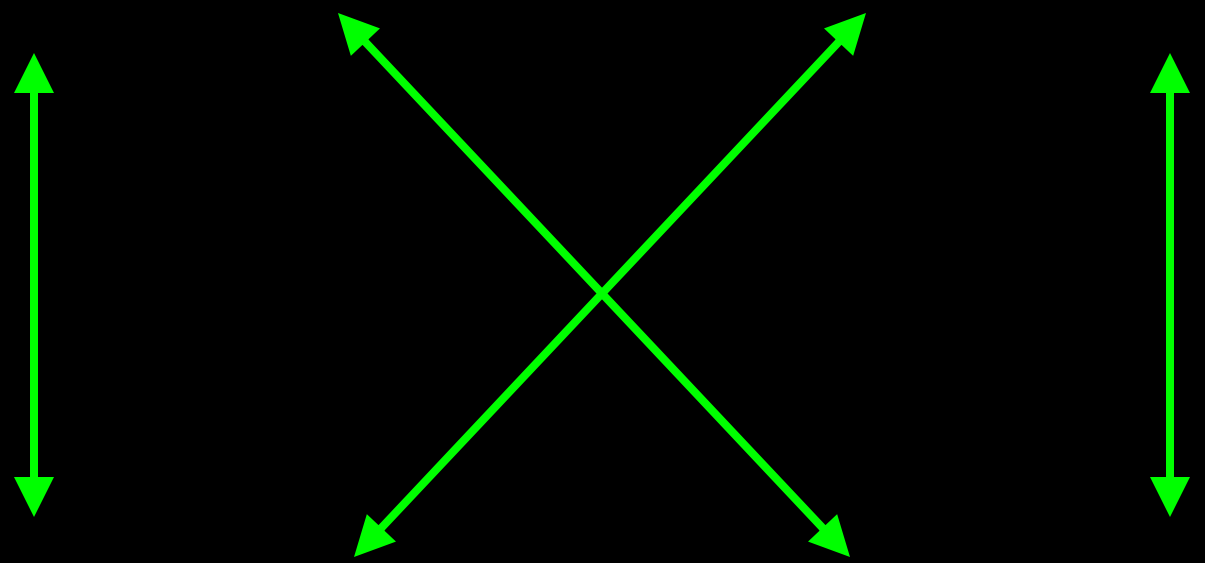
fMRI: Past, Present, and Future
Limits of Spatial Resolution, Temporal Resolution and Interpretation

Peter A. Bandettini, Ph.D

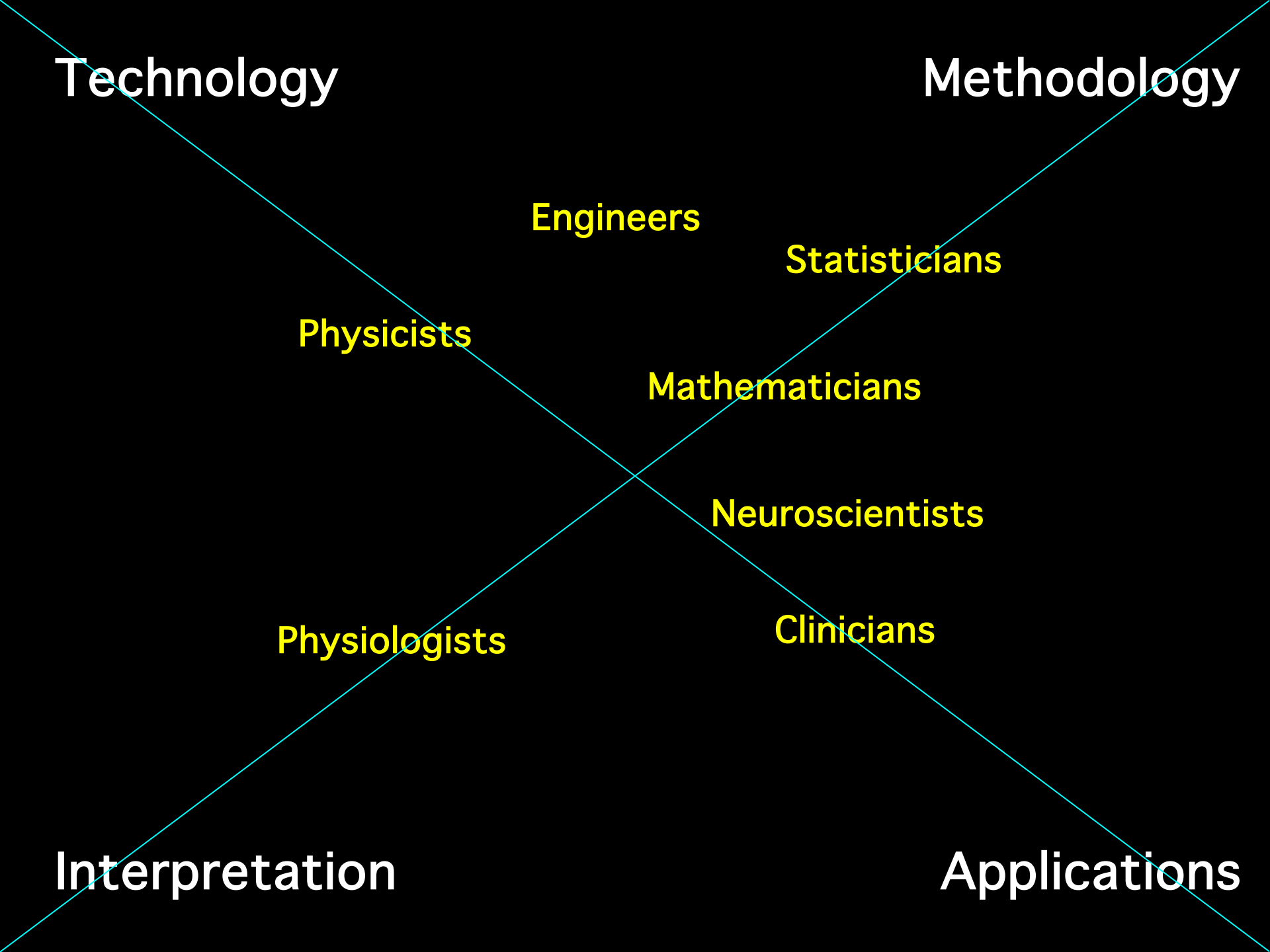
Unit on Functional Imaging Methods
&
3T Neuroimaging Core Facility

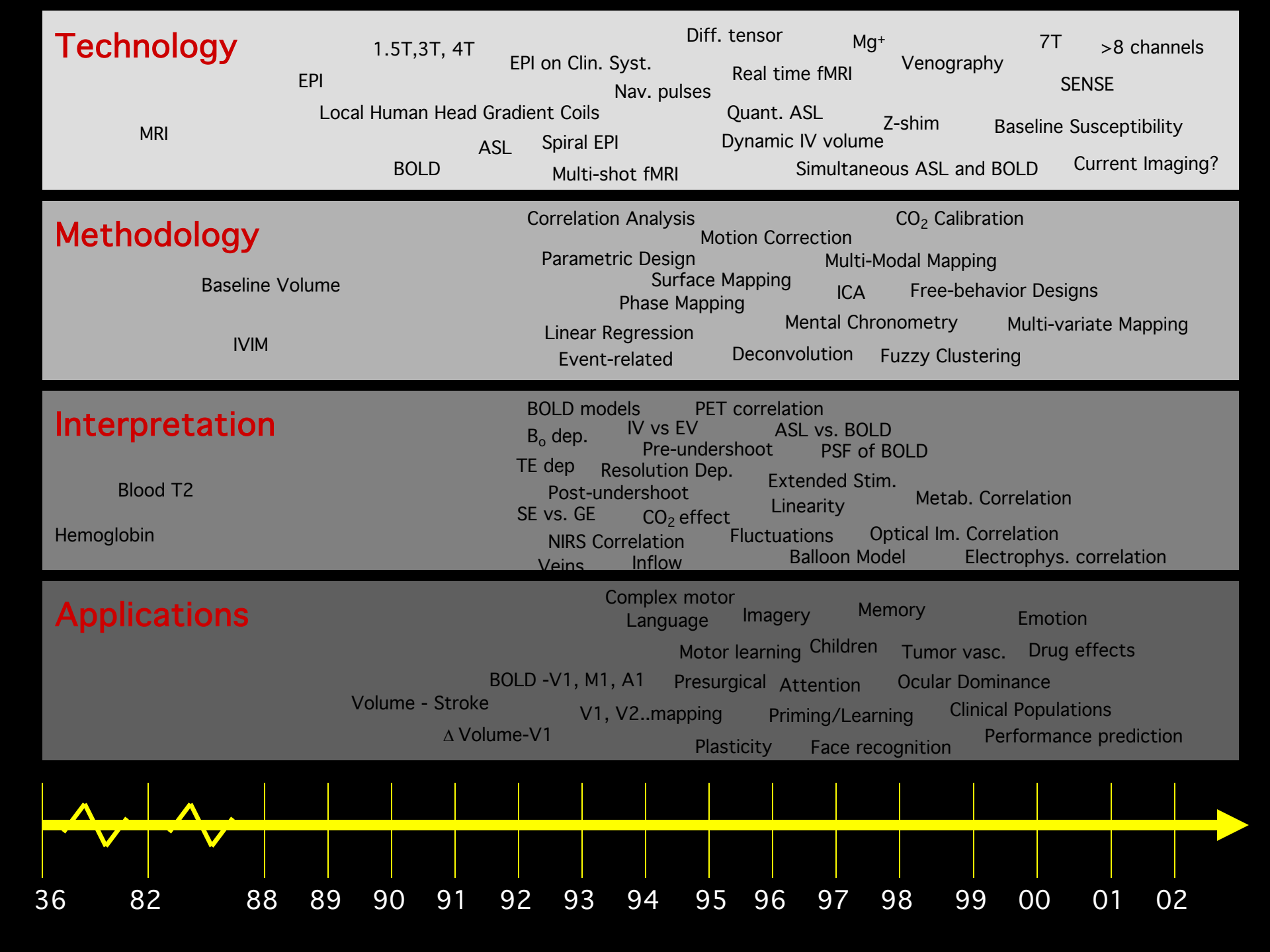
Laboratory of Brain and Cognition
National Institute of Mental Health

Technology ↔ Methodology



Interpretation ↔ Applications


Technology
Methodology
Engineers
Statisticians
Physicists
Mathematicians
Neuroscientists
Physiologists
Clinicians
Interpretation
Applications


Technology
1.5T,3T, 4T
Diff. tensor
Mg+
7T
>8 channels
EPI on Clin. Syst.
Venography
EPI
Real time fMRI
SENSE
Nav. pulses
Local Human Head Gradient Coils
Quant. ASL
Z-shim
Baseline Susceptibility
MRI
Dynamic IV volume
ASL
Spiral EPI
BOLD
Multi-shot fMRI
Simultaneous ASL and BOLD
Current Imaging?
Methodology
Correlation Analysis
CO2 Calibration
Motion Correction
Parametric Design
Multi-Modal Mapping
Surface Mapping
Baseline Volume
ICA
Free-behavior Designs
Phase Mapping
Mental Chronometry
Multi-variate Mapping
Linear Regression
IVIM
Deconvolution
Fuzzy Clustering
Event-related
Interpretation
BOLD models
PET correlation
IV vs EV
B0 dep.
ASL vs. BOLD
Pre-undershoot
PSF of BOLD
TE dep
Resolution Dep.
Extended Stim.
Blood T2
Post-undershoot
Metab. Correlation
Linearity
SE vs. GE
CO2 effect
Hemoglobin
Fluctuations
Optical Im. Correlation
NIRS Correlation
Balloon Model
Electrophys. correlation
Veins
Inflow
Applications
Complex motor
Language
Imagery
Memory
Emotion
Motor learning
Children
Tumor vasc.
Drug effects
BOLD -V1, M1, A1
Presurgical
Attention
Ocular Dominance
Volume - Stroke
V1, V2..mapping
Priming/Learning
Clinical Populations
Δ Volume-V1
Plasticity
Face recognition
Performance prediction
36
82
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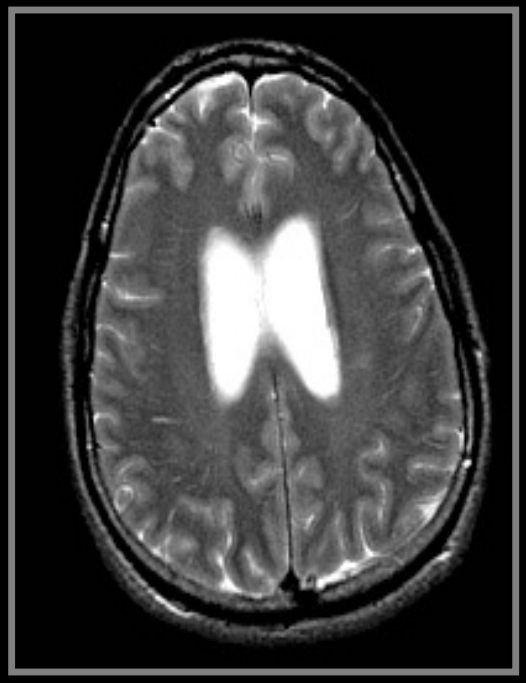
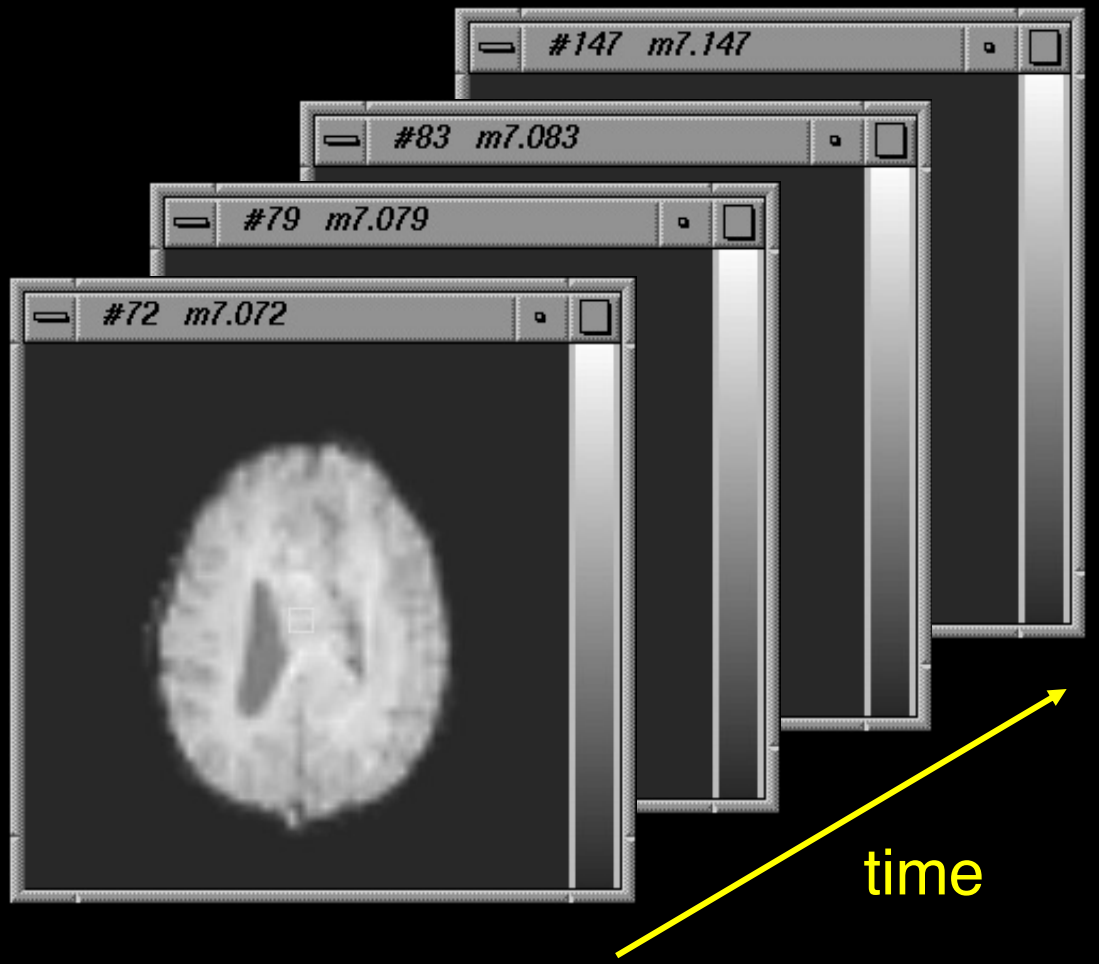
L. Pauling, C. D. Coryell, (1936) “The magnetic properties and structure of hemoglobin, oxyhemoglobin, and carbonmonoxyhemoglobin.” Proc.Natl. Acad. Sci. USA 22, 210-216.

Thulborn, K. R., J. C. Waterton, et al. (1982).“Oxygenation dependence of the transverse relaxation time of water protons in whole blood at high field.” Biochim. Biophys. Acta. 714: 265-270.

S. Ogawa, T. M. Lee, A. R. Kay, D. W. Tank, (1990) “Brain magnetic resonance imaging with contrast dependent on blood oxygenation.” Proc. Natl. Acad. Sci. USA 87, 9868-9872.

R. Turner, D. LeBihan, C. T. W. Moonen, D. Despres, J. Frank, (1991). Echo-planar time course MRI of cat brain oxygenation changes. Magn. Reson. Med. 27, 159-166.

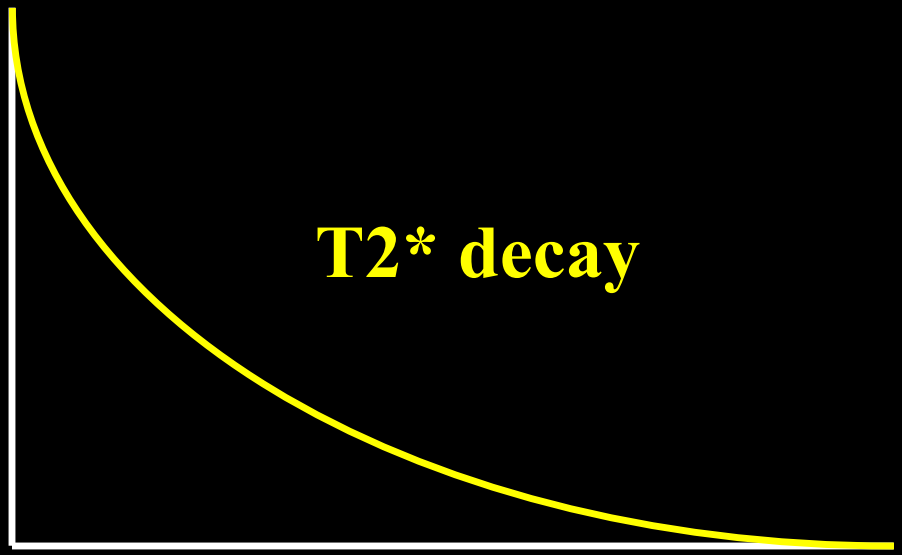


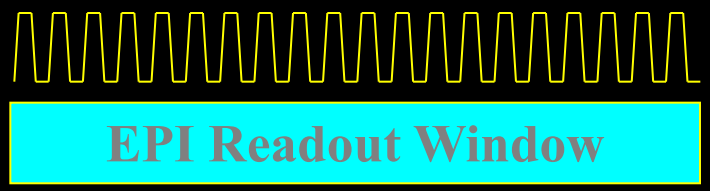


Anatomic

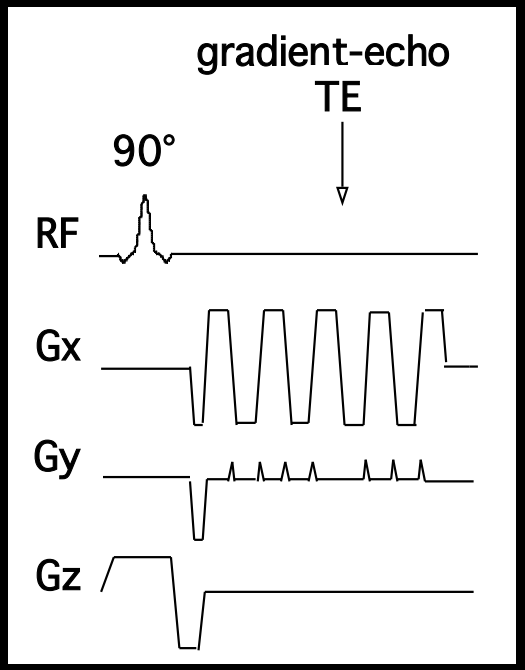
Functional

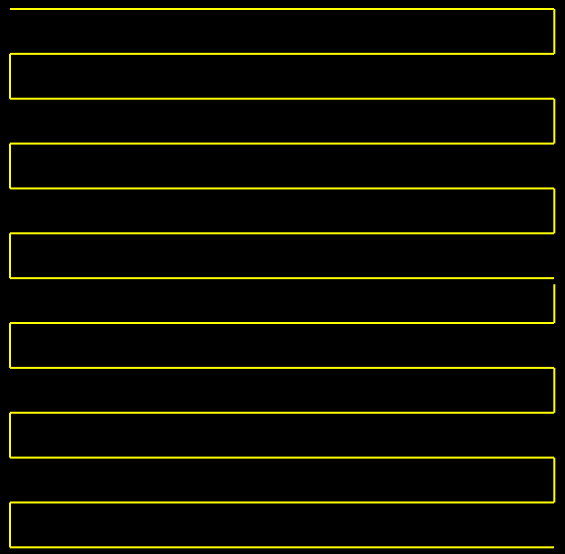
Single Shot EPI



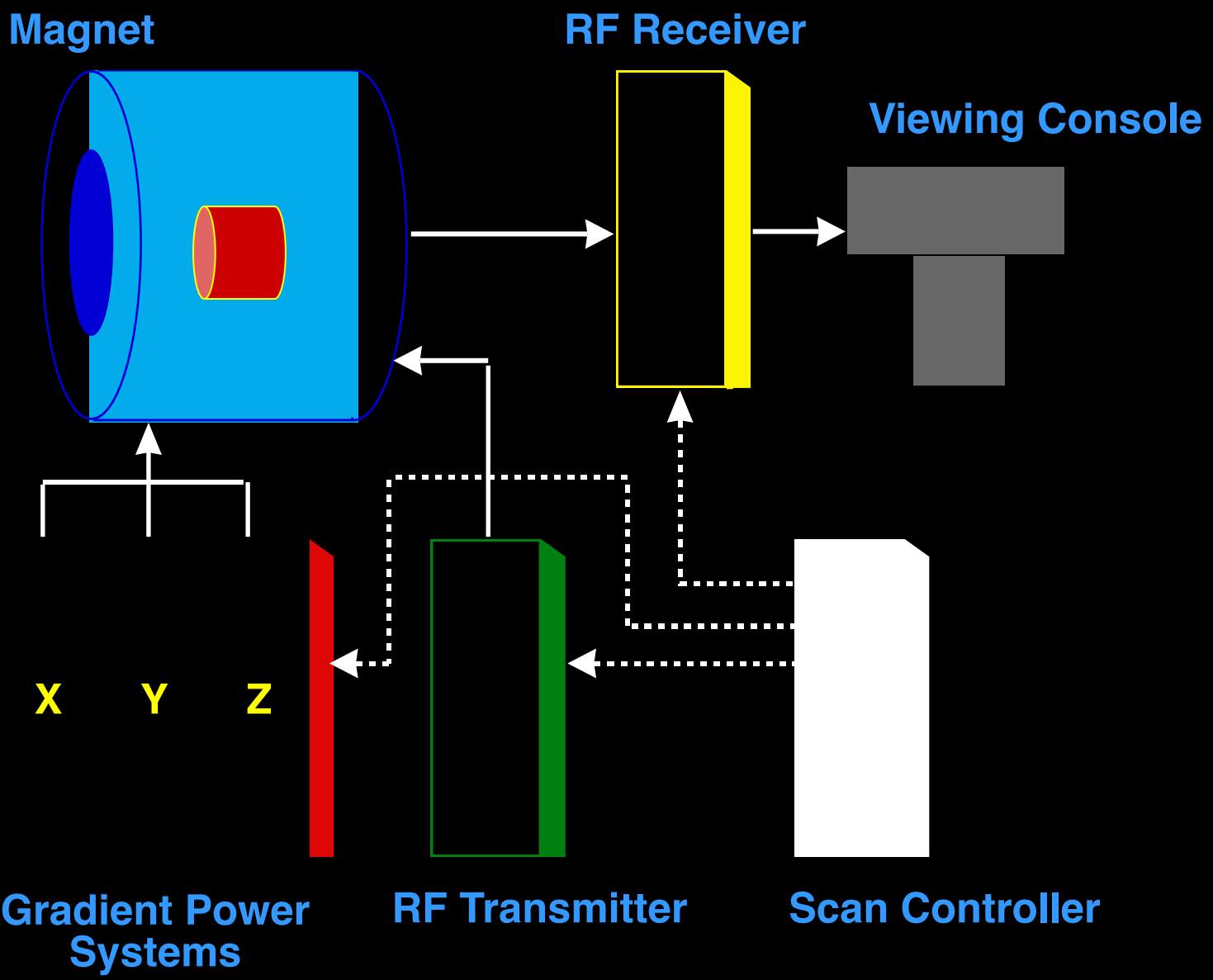


≈ 20 to 40 ms

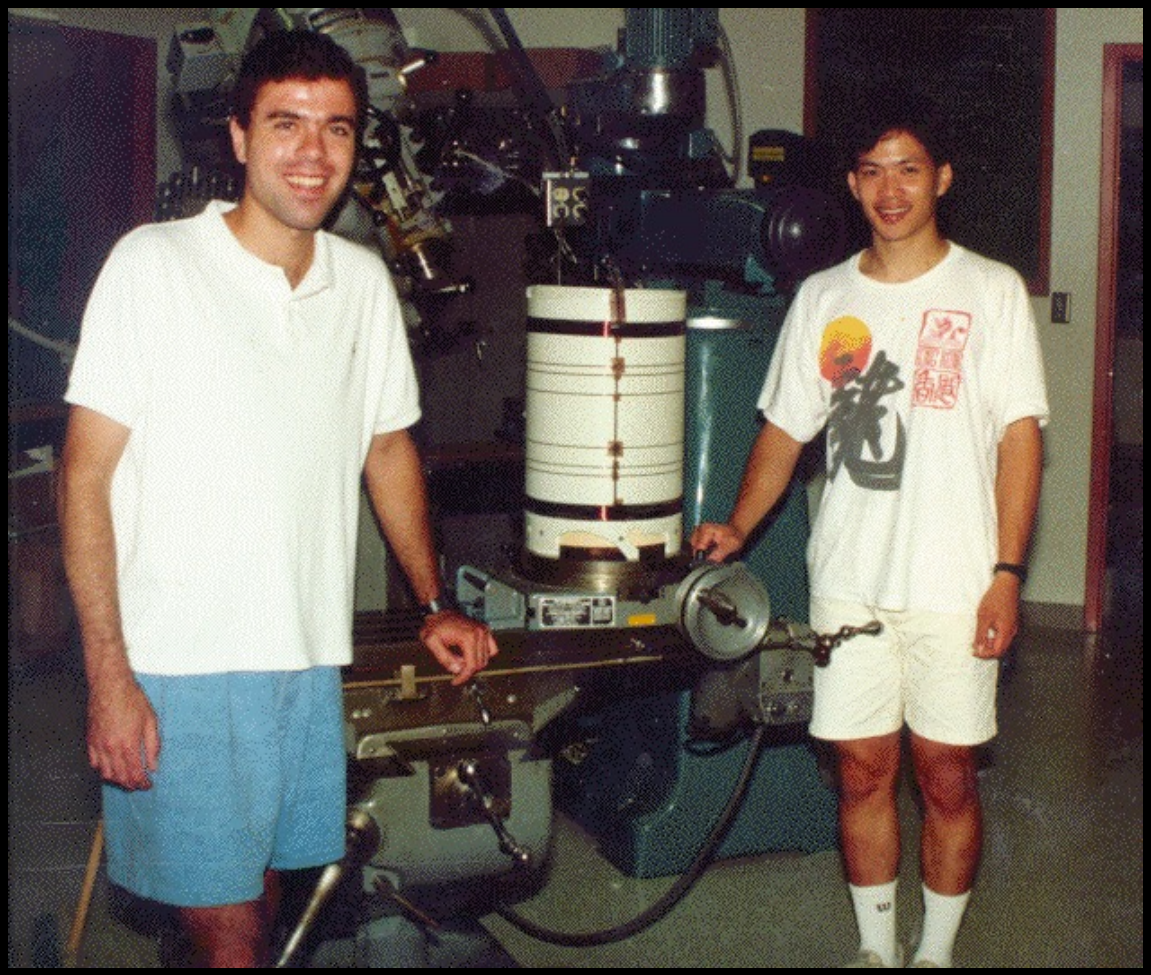




Imaging System Components



Local gradients solved the problem

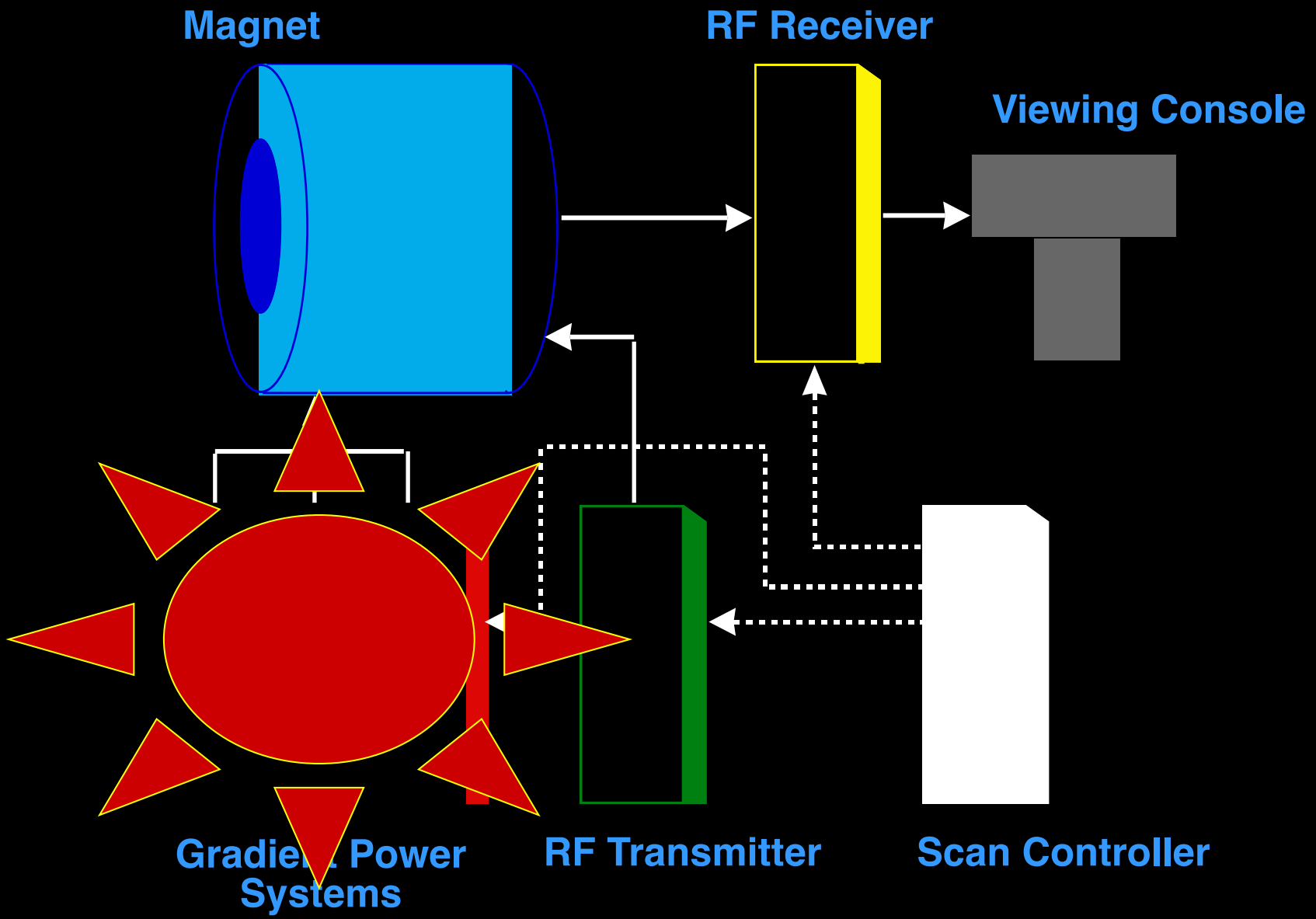


August, 1991

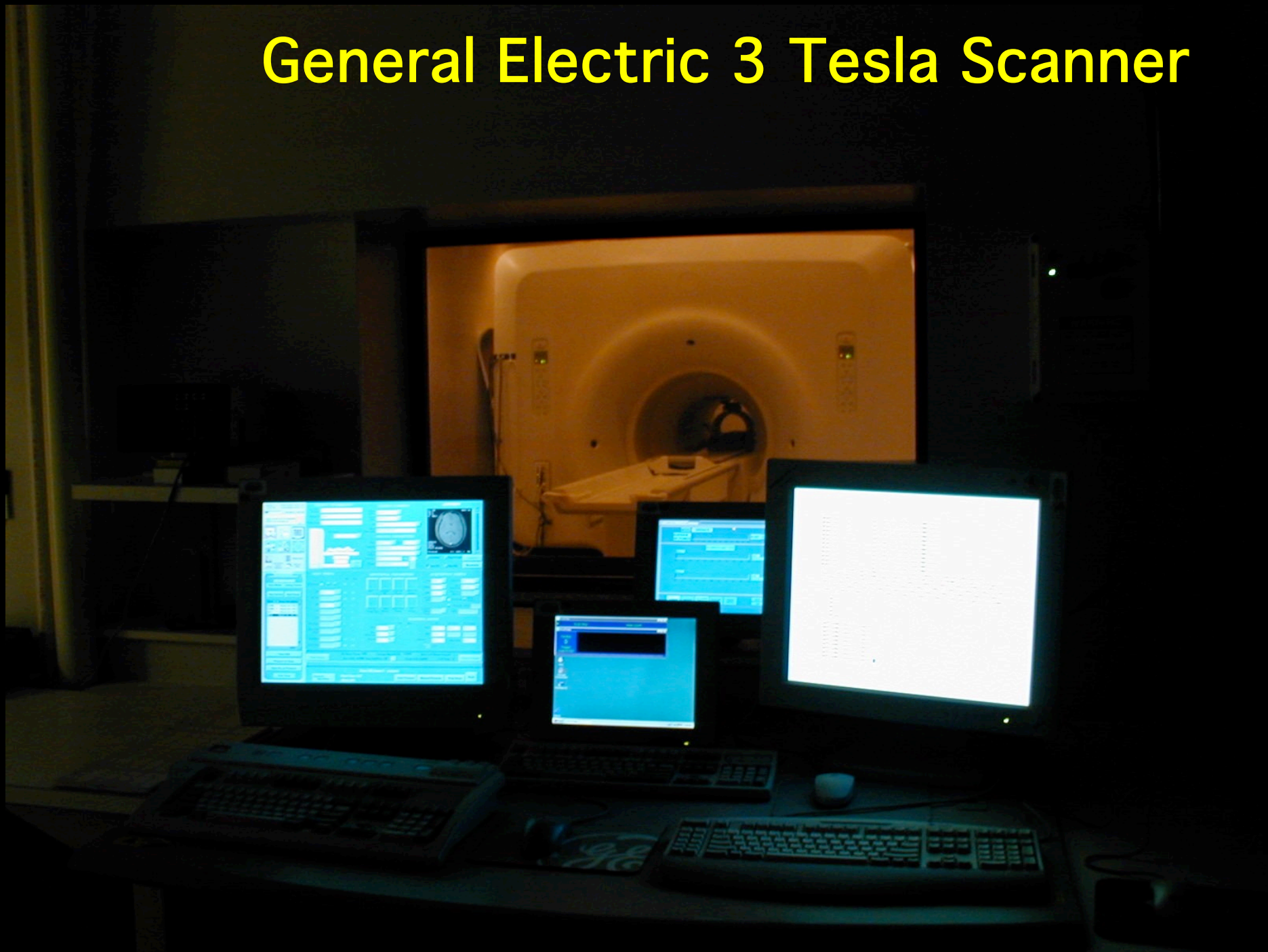
1991-1992

1992-1999

Imaging System Components



General Electric 3 Tesla Scanner



Functional MRI Methods

Blood Volume Imaging

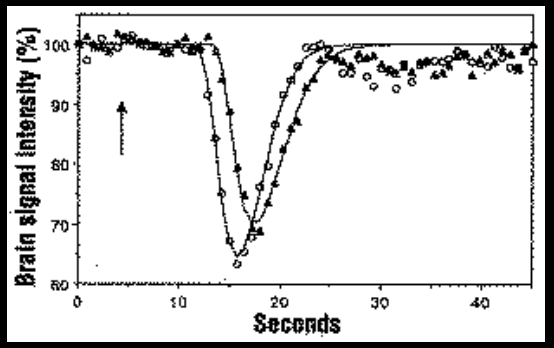
BOLD Contrast

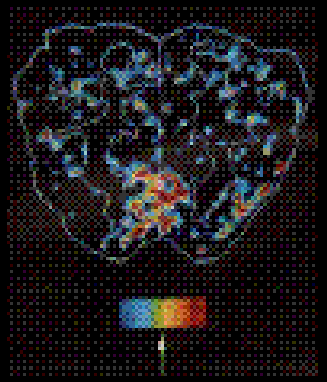
Arterial Spin Labeling

Blood Volume Imaging

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

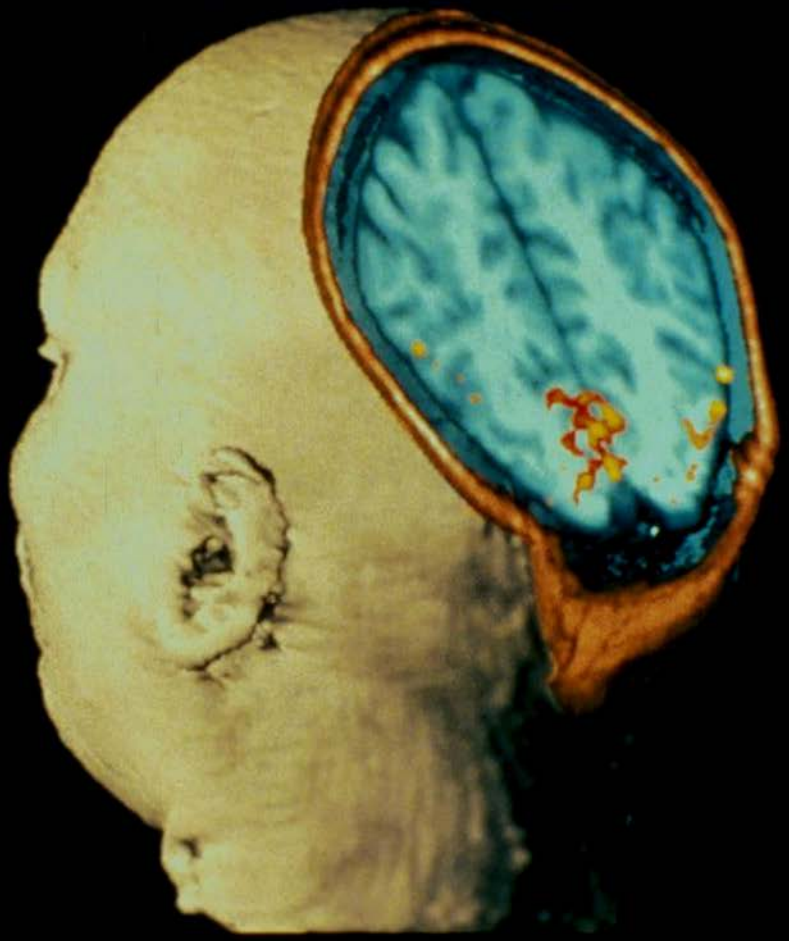
Resting Active





Blood Volume

Photic Stimulation

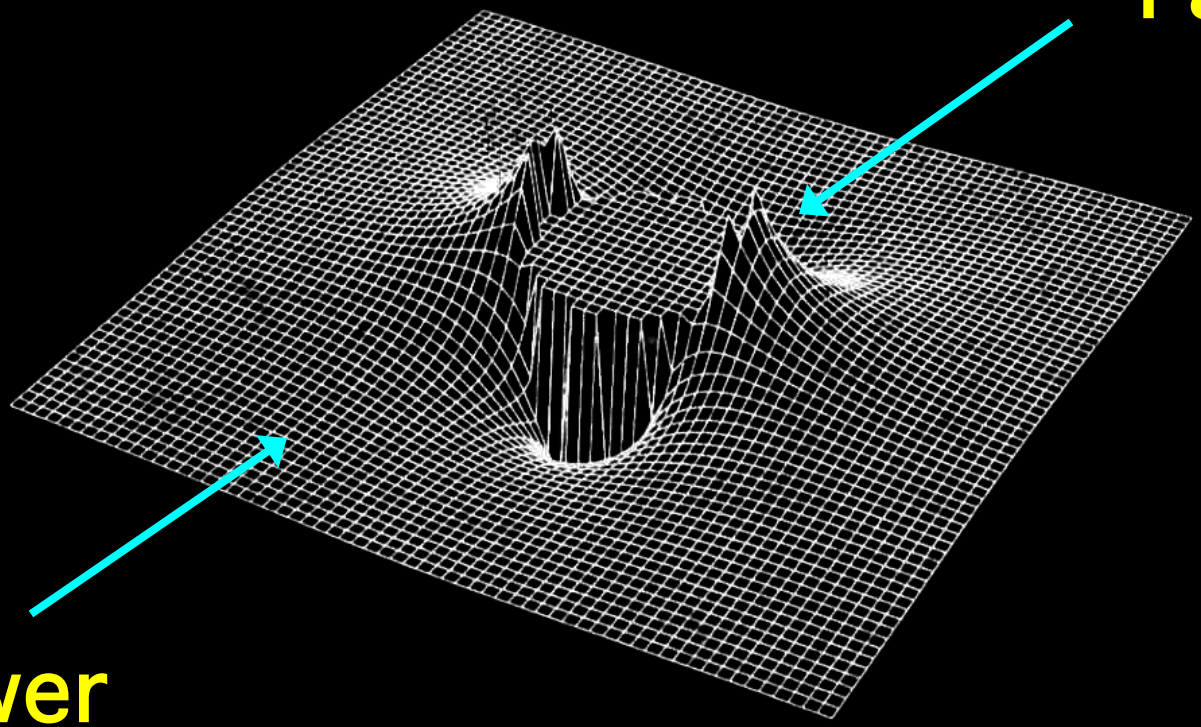


MRI Image showing activation of the Visual Cortex

From Belliveau, et al. Science Nov 1991

Susceptibility Contrast

Susceptibility-Induced Field Distortion in the Vicinity of a Microvessel $\perp$ to B_o.



BOLD Contrast in the Detection of Neuronal Activity

Cerebral Tissue Activation

↓

Local Vasodilation

↓

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

↓

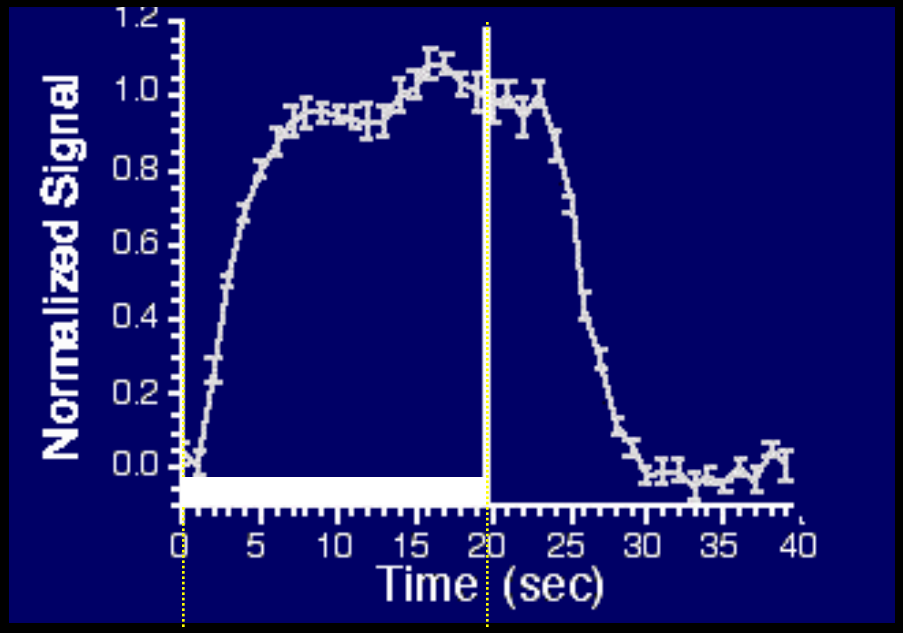
Decrease in susceptibility-related intravoxel dephasing → Increase in T2 and T2*

↓

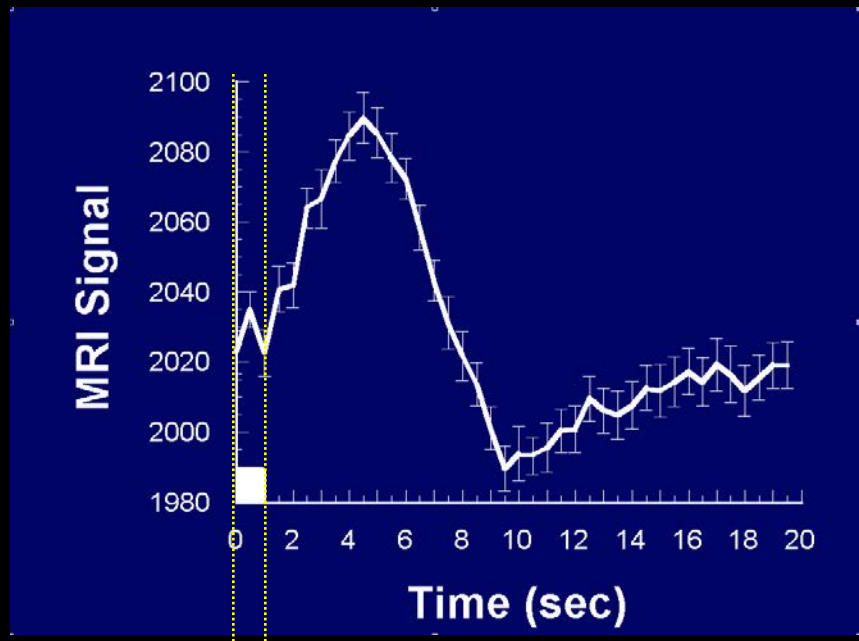
Local Signal Increase in T2 and T2* - weighted sequences

The BOLD Signal

Blood Oxygenation Level Dependent (BOLD) signal changes



task



task

Alternating Left and Right Finger Tapping

~ 1992

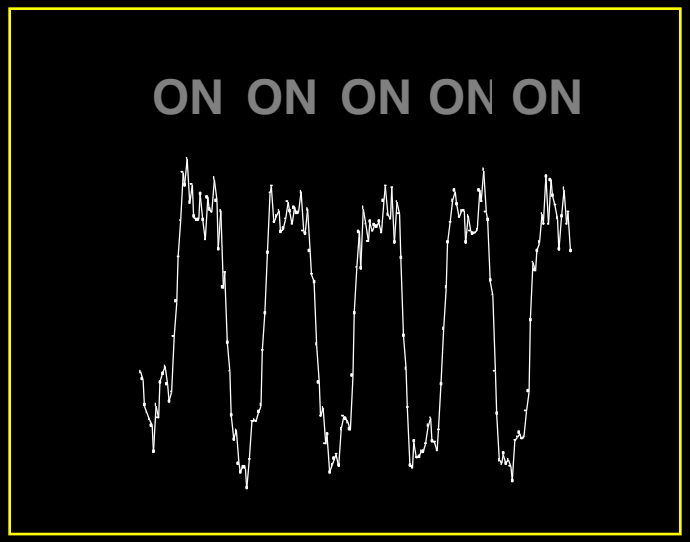
K. K. Kwong, et al, (1992) "Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation." Proc. Natl. Acad. Sci. USA. 89, 5675-5679.

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

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

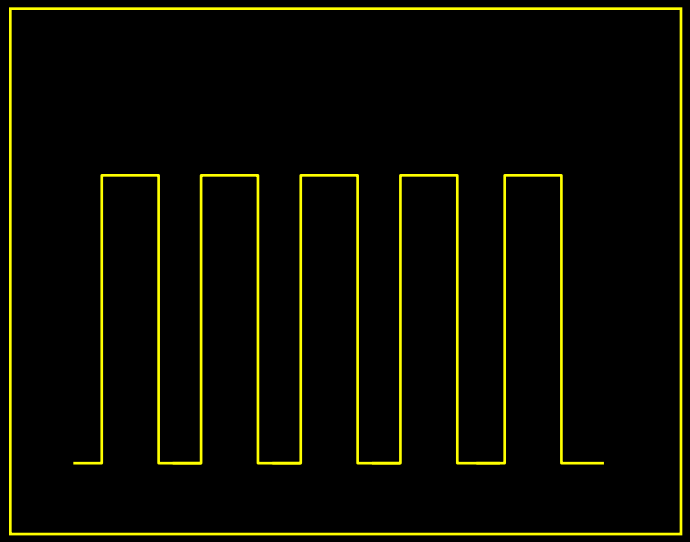
Blamire, A. M., et al. (1992). "Dynamic mapping of the human visual cortex by high-speed magnetic resonance imaging." Proc. Natl. Acad. Sci. USA 89: 11069-11073.

Creating a Functional Image



Signal Time Course

X

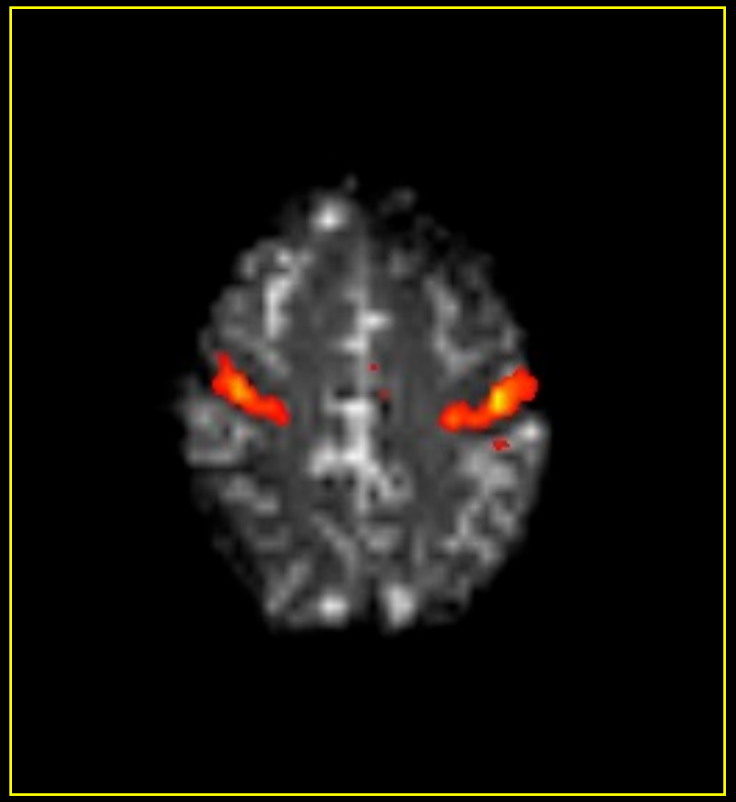


Reference Function

=

P. A. Bandettini, A. Jesmanowicz, E. C. Wong, J. S. Hyde, Processing strategies for time-course data sets in functional MRI of the human brain. *Magn. Reson. Med.* **30, 161-173 (1993).**

Cross Correlation Image



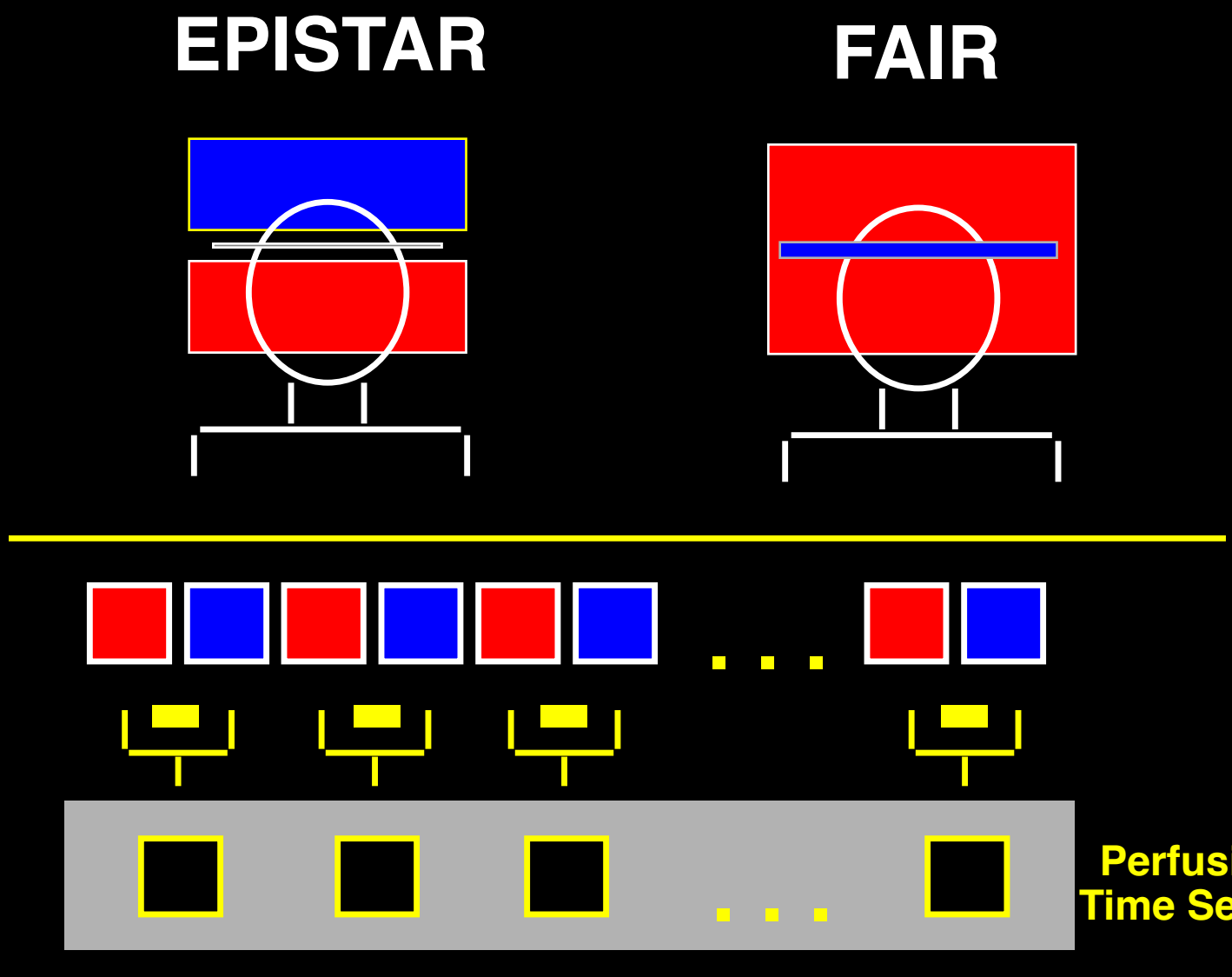
$$\frac{\text{Cross Correlation Image}}{\text{Anatomical Image}}$$

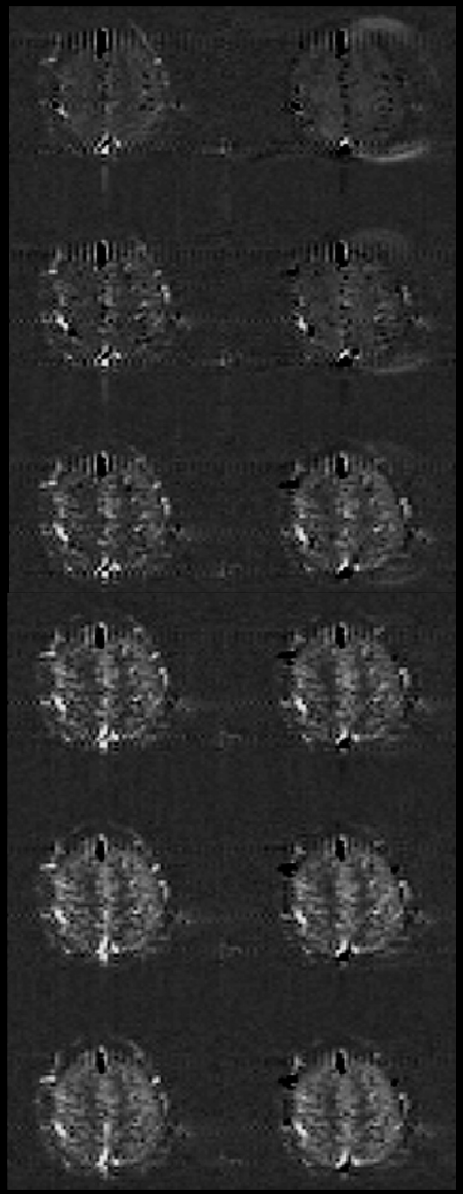
P. A. Bandettini, A. Jesmanowicz, E. C. Wong, J. S. Hyde, Processing strategies for time-course data sets in functional MRI of the human brain. *Magn. Reson. Med.* 30, 161-173 (1993).

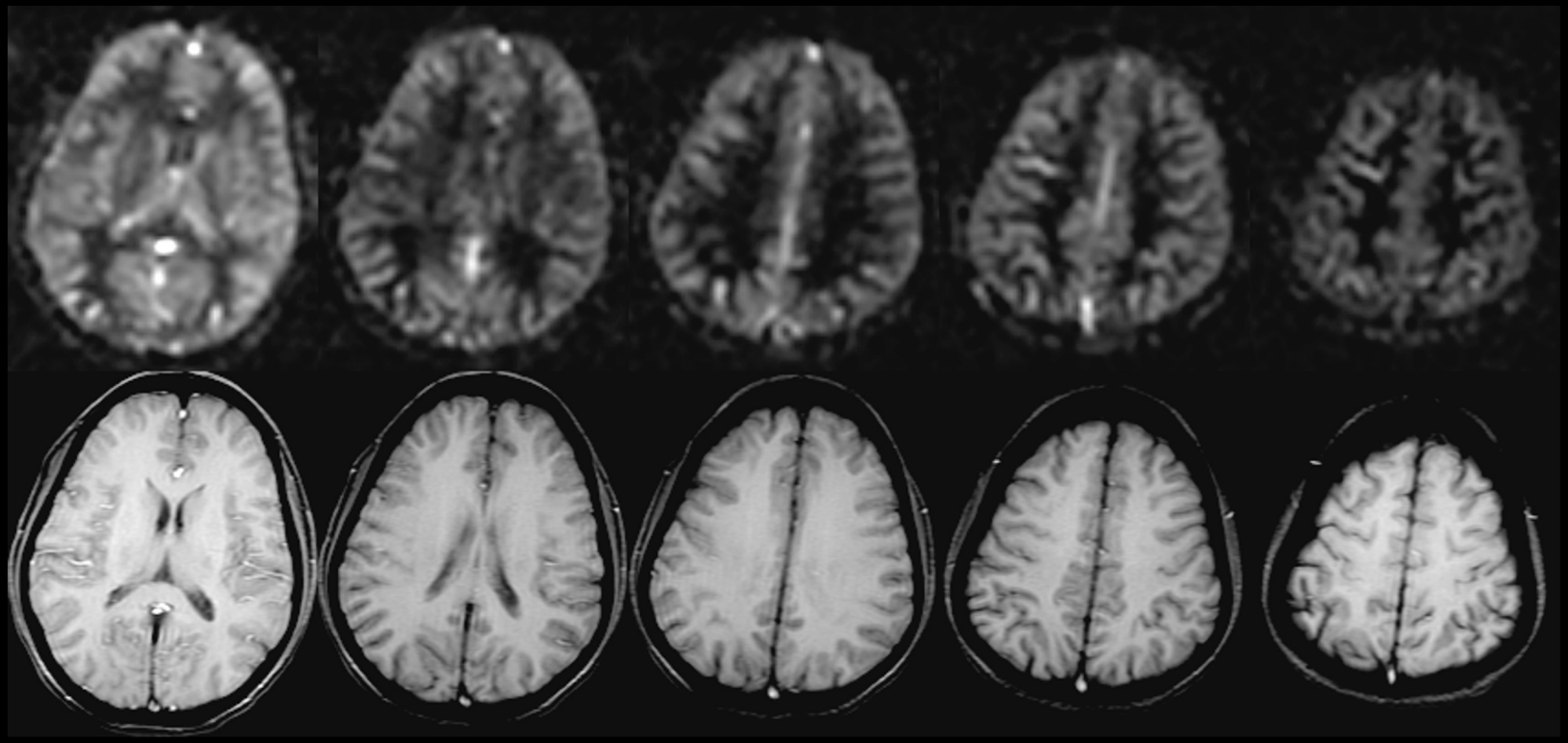
Correlation analysis, Fourier analysis, t-test, f-test...
SPM, AFNI, brain voyager, FIASCO, FSL, free surfer...

Quality of results and importance of the findings depends on type of question asked, experimental method, and analysis method...

Blood Perfusion



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



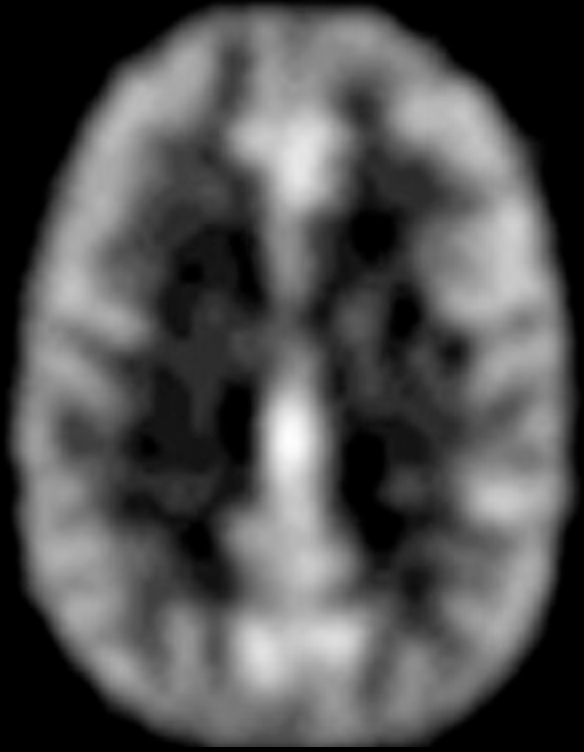
Williams, D. S., Detre, J. A., Leigh, J. S. & Koretsky, A. S. (1992) “Magnetic resonance imaging of perfusion using spin-inversion of arterial water.” Proc. Natl. Acad. Sci. USA 89, 212-216.

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.

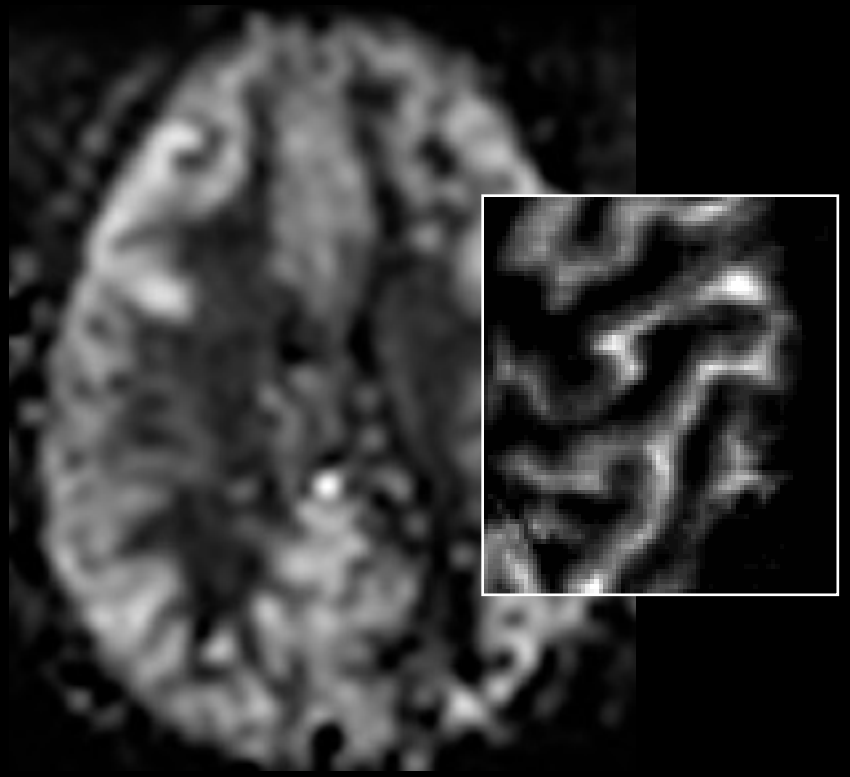
Kim, S.-G. (1995) “Quantification of relative cerebral blood flow change by flow-sensitive alternating inversion recovery (FAIR) technique: application to functional mapping.” Magn. Reson. Med. **34**, 293-301.

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

Comparison with Positron Emission Tomography



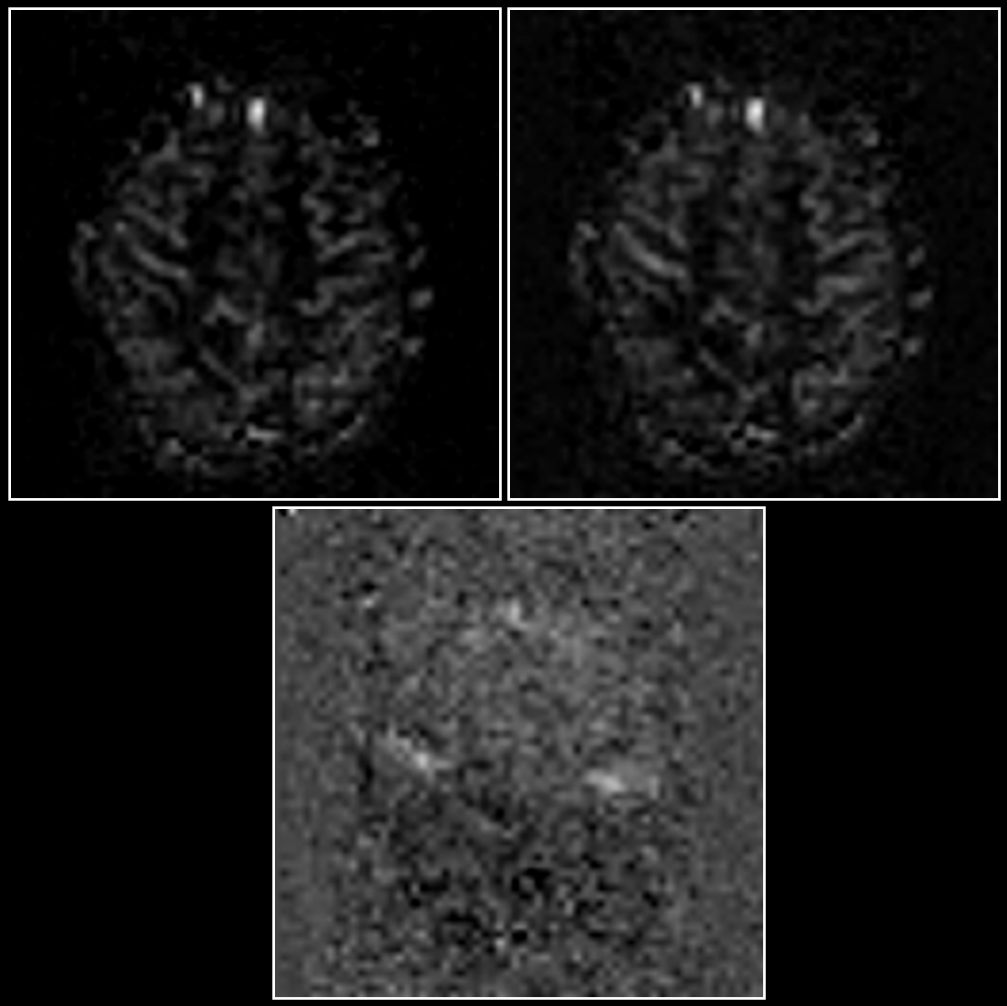
PET: $H_2{}^{15}O$



MRI: ASL

Perfusion

Rest *Activation*



	+	-
Volume	• unique information • baseline information • multislice trivial	• invasive • low C / N for func.
BOLD	• highest C / N • easy to implement • multislice trivial • non invasive • highest temp. res.	• complicated signal • no baseline info.
Perfusion	• unique information • control over ves. size • baseline information • non invasive	• multislice non trivial • lower temp. res. • low C / N

Refinements

BOLD Contrast Interpretation

Dynamics

Paradigm Design and Processing

Refinements

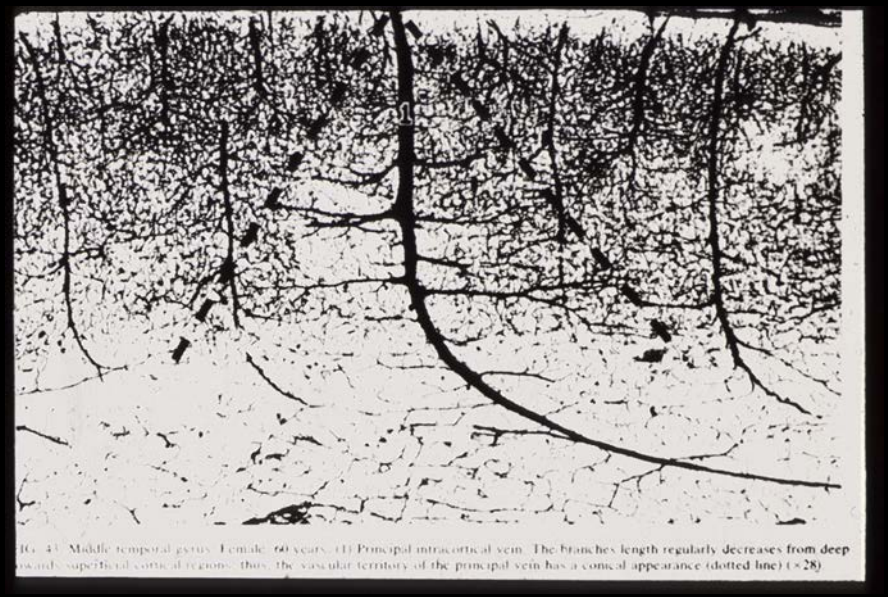
BOLD Contrast Interpretation

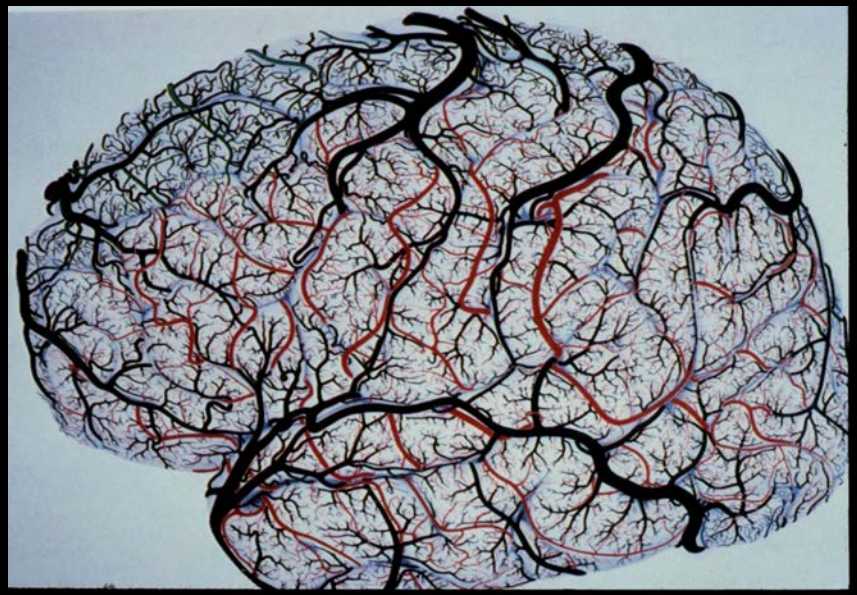
Dynamics

Paradigm Design and Processing

The Neuroscientists' Challenge:

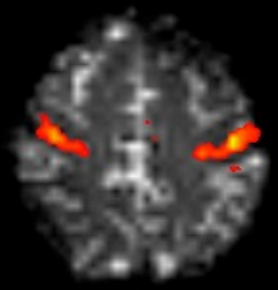
...to make progressively more precise inferences using fMRI without making too many assumptions about non-neuronal physiologic factors.

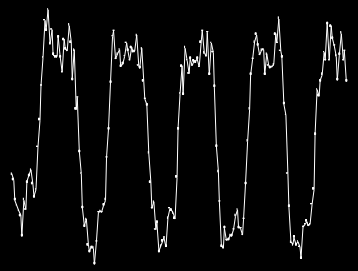




The use of fMRI for the Investigation of Brain Function and Physiology

- **Where?**
- **When?**
- **How much?**

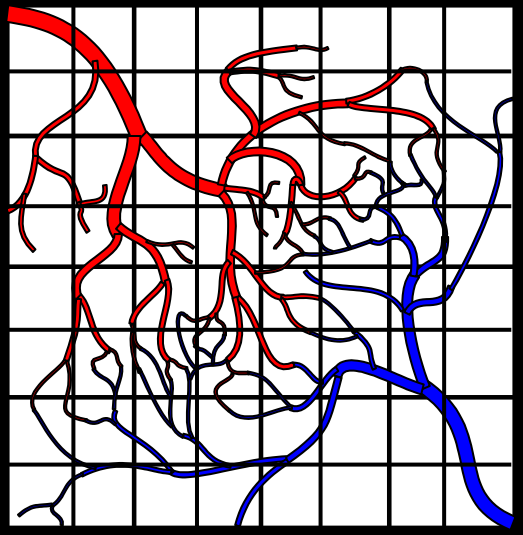




- **How to get the brain to do what we want it to do in the context of an fMRI experiment?**
  (*limitations*: limited time and signal to noise, motion, acoustic noise)

- **How much more information can we obtain?**

Neuronal Activation



Measured Signal

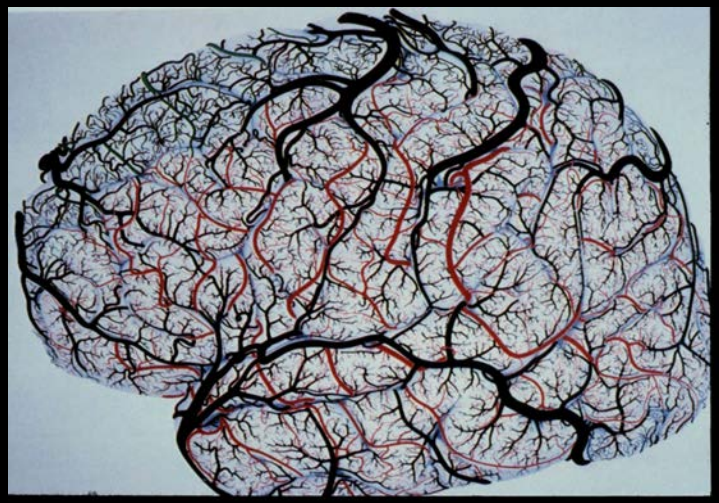
?

Hemodynamics

?

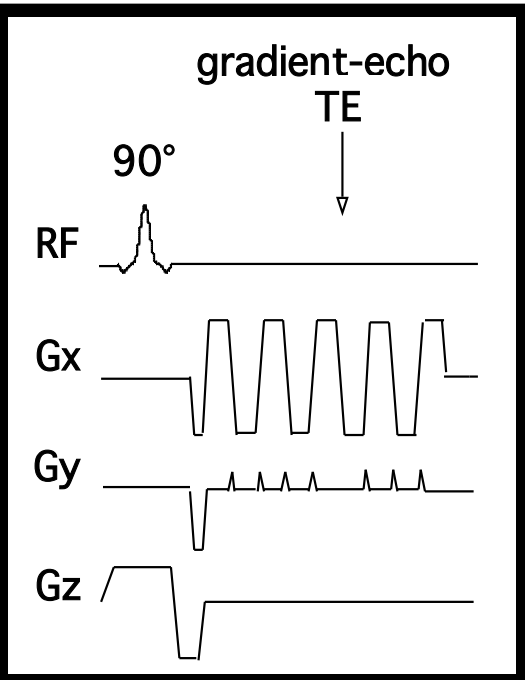
?

Noise

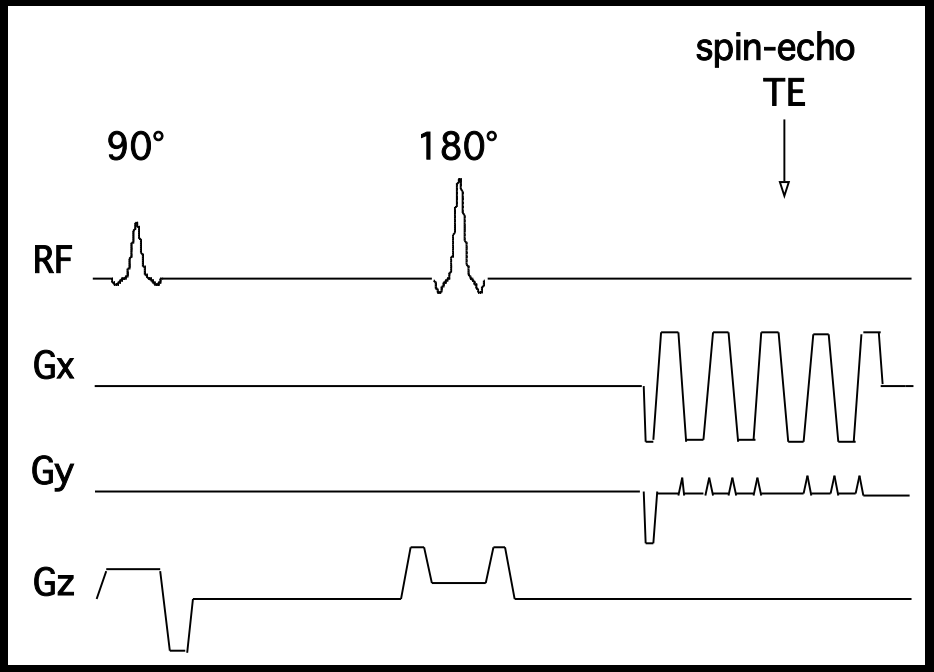


Spin-echo vs. Gradient-echo

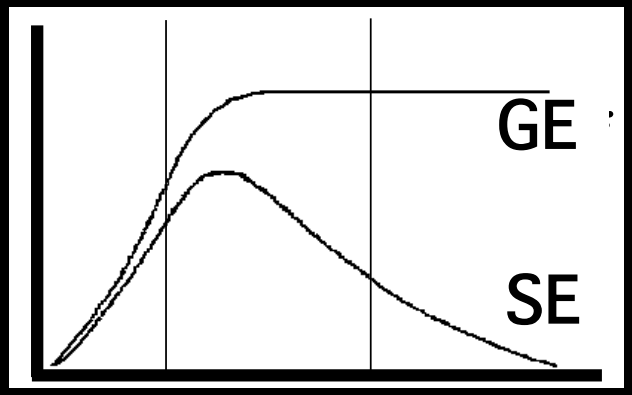
Gradient-Echo EPI



Spin-Echo EPI



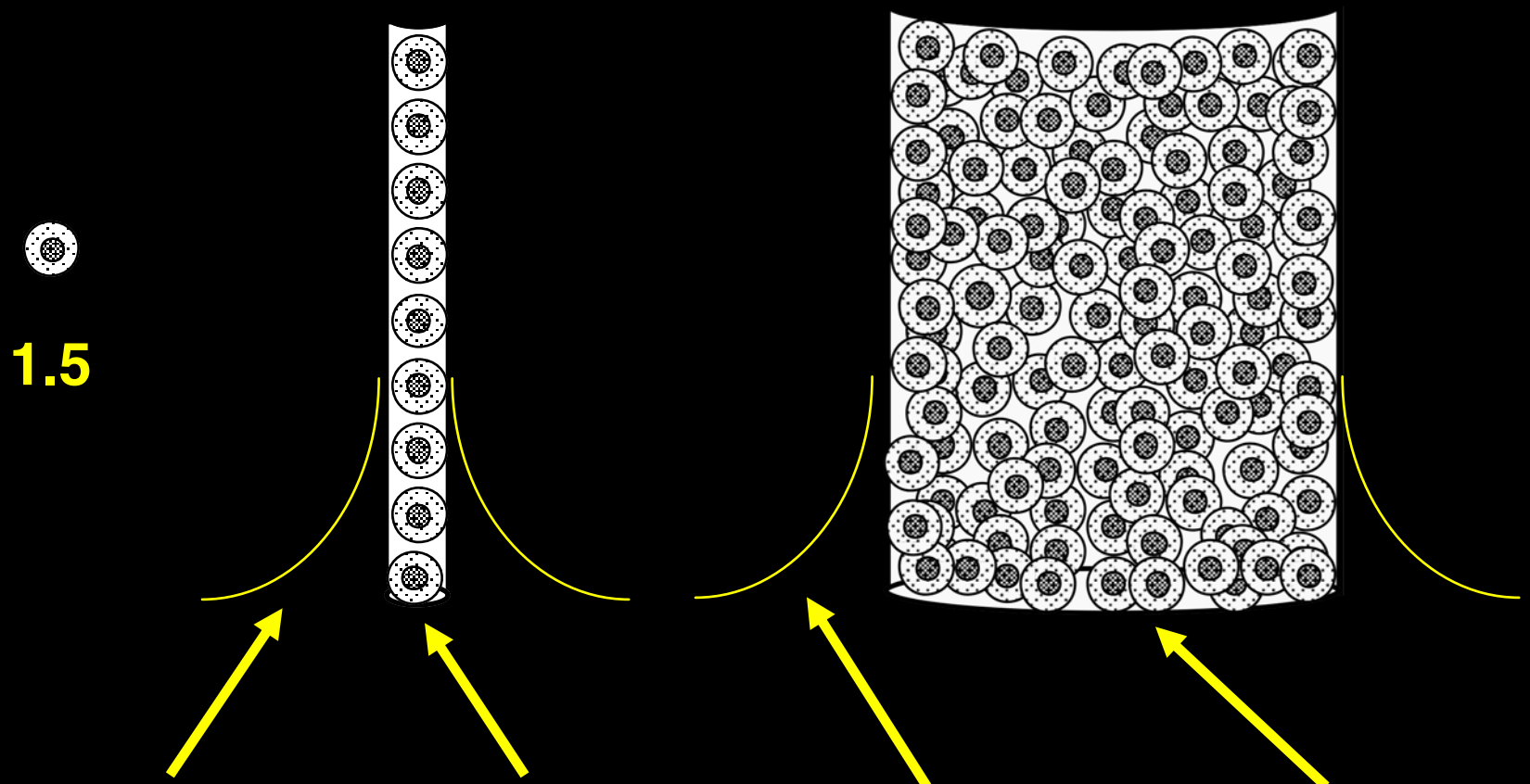
Contrast

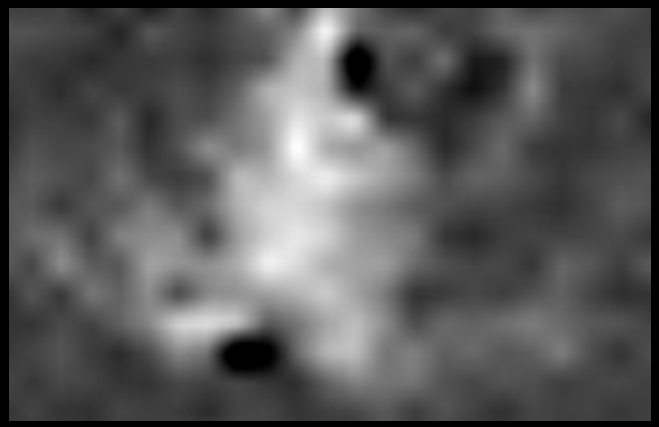


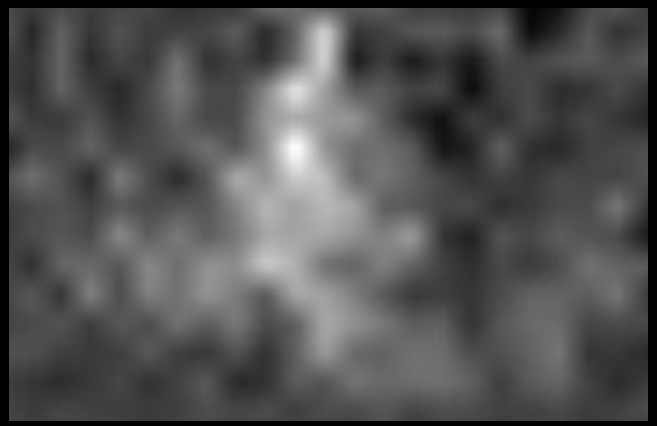
2.5 to 3 μm 3 to 15 μm 15 to ∞ μm

compartment size

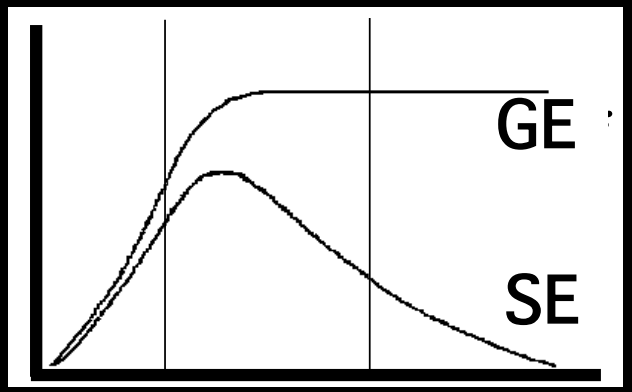
ΔR2* /ΔR2


1.5
1.5 to 3 extravascular
1.5 intravascular
3 to ∞ extravascular
1.5 intravascular





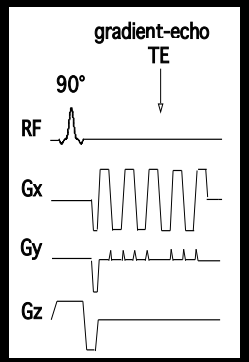
Contrast

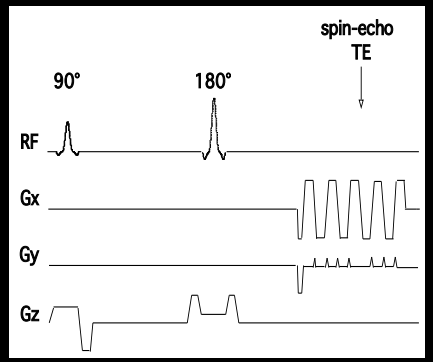


2.5 to 3 μm 3 to 15 μm 15 to ∞ μm

compartment size

Gradient - Echo

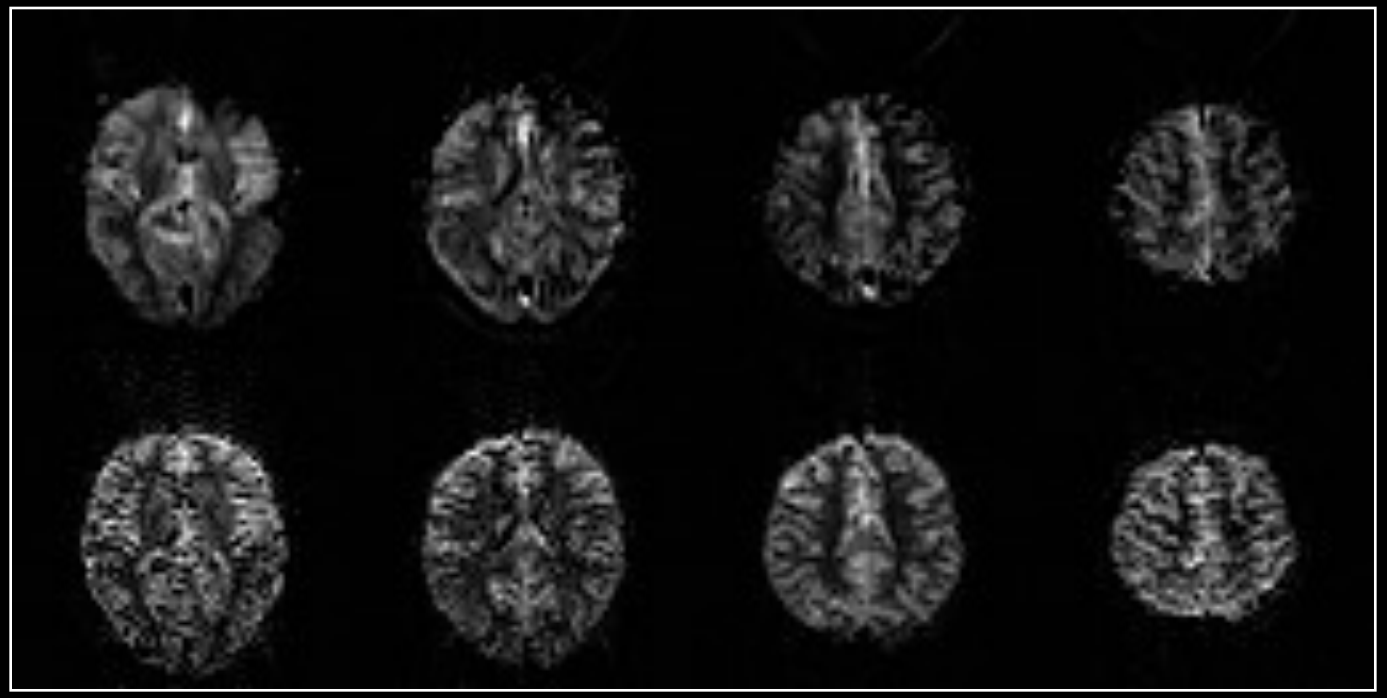


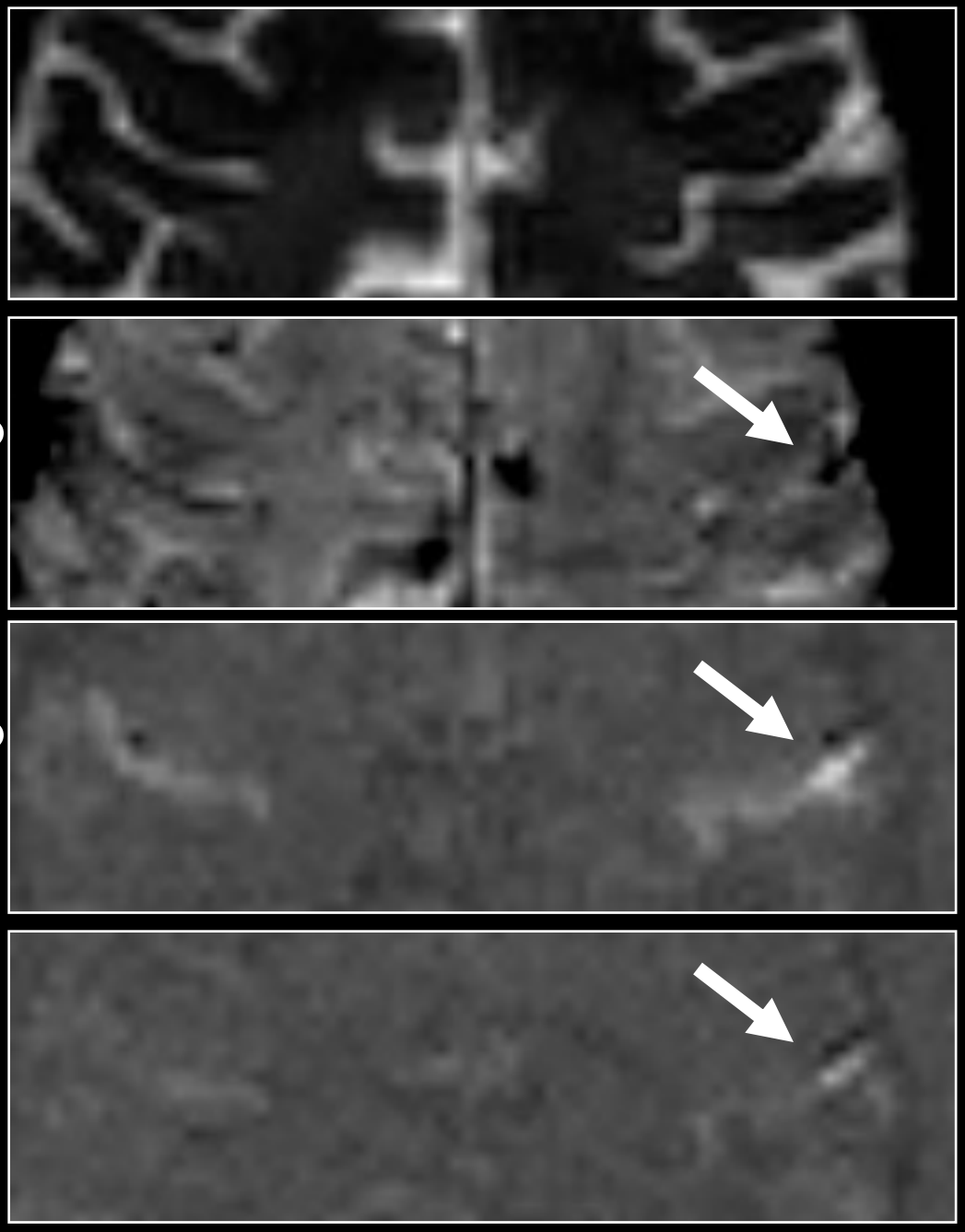


Spin - Echo

GE
TE = 30 ms

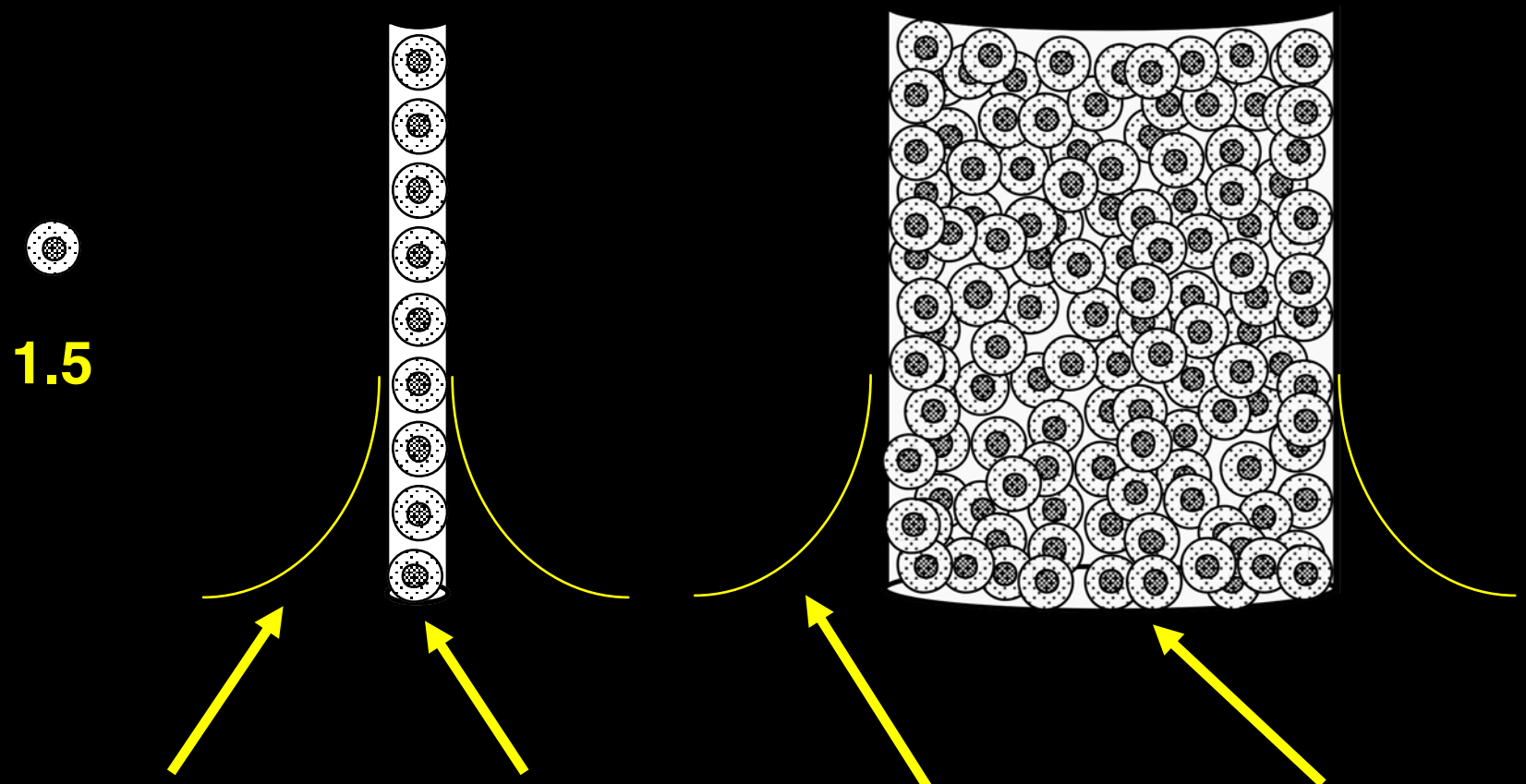
SE
TE = 110 ms




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

Effect of diffusion weighting

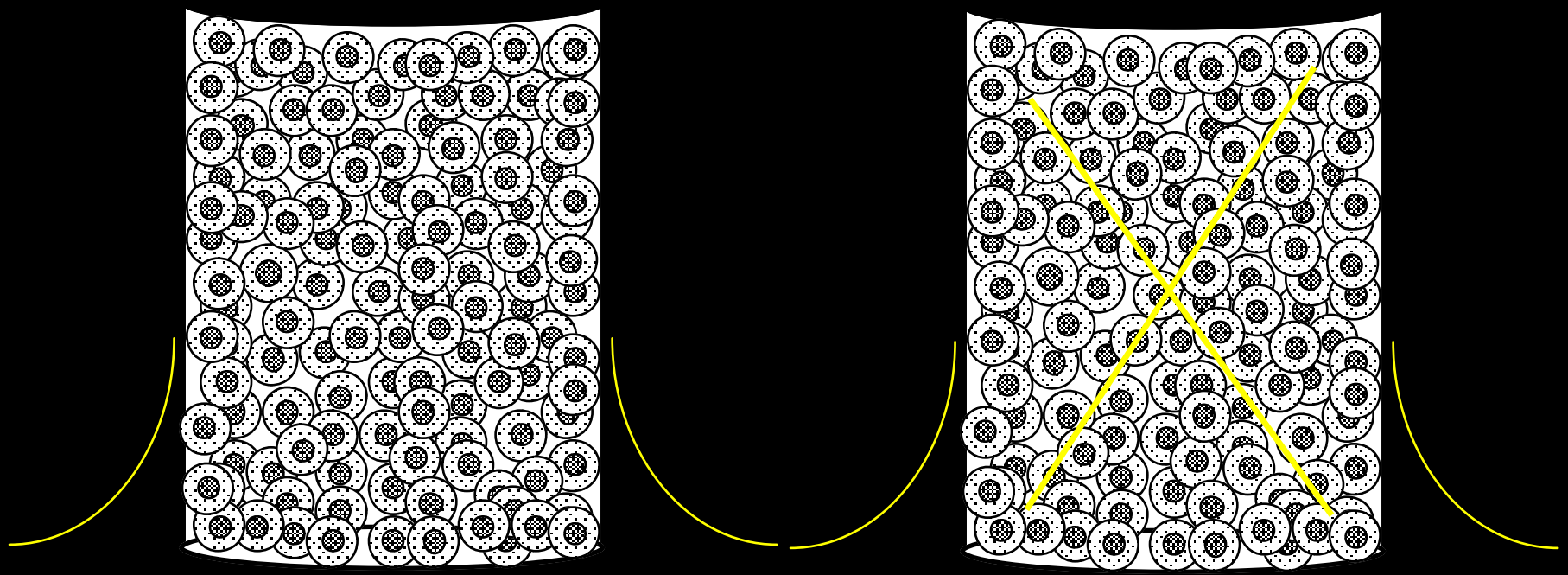
ΔR2* /ΔR2



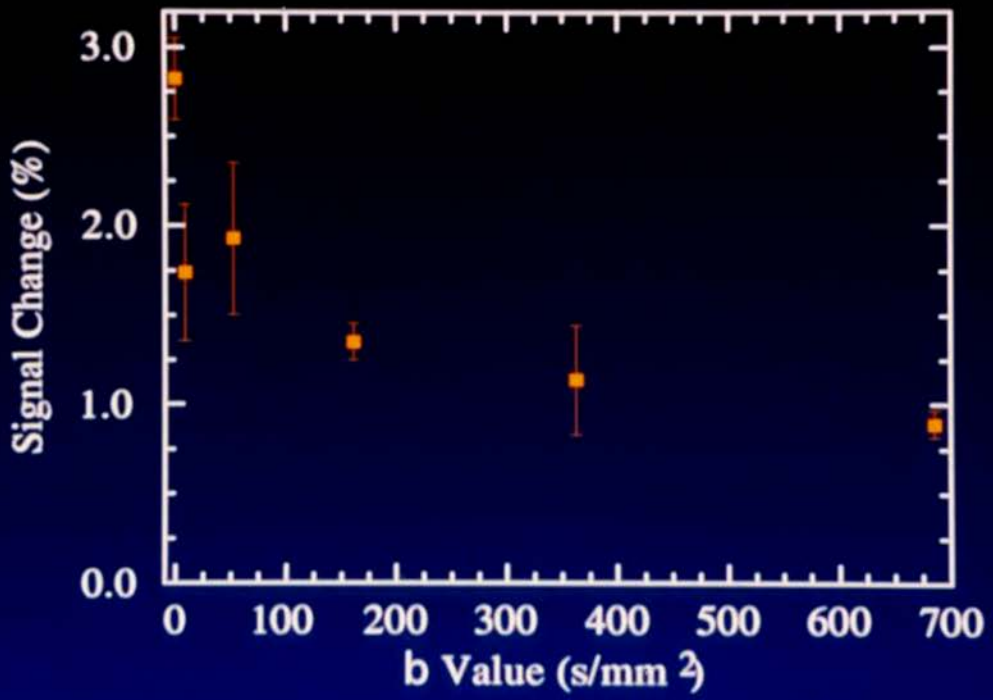
average ΔR2 / ΔR2 ≈ 3 to 4*

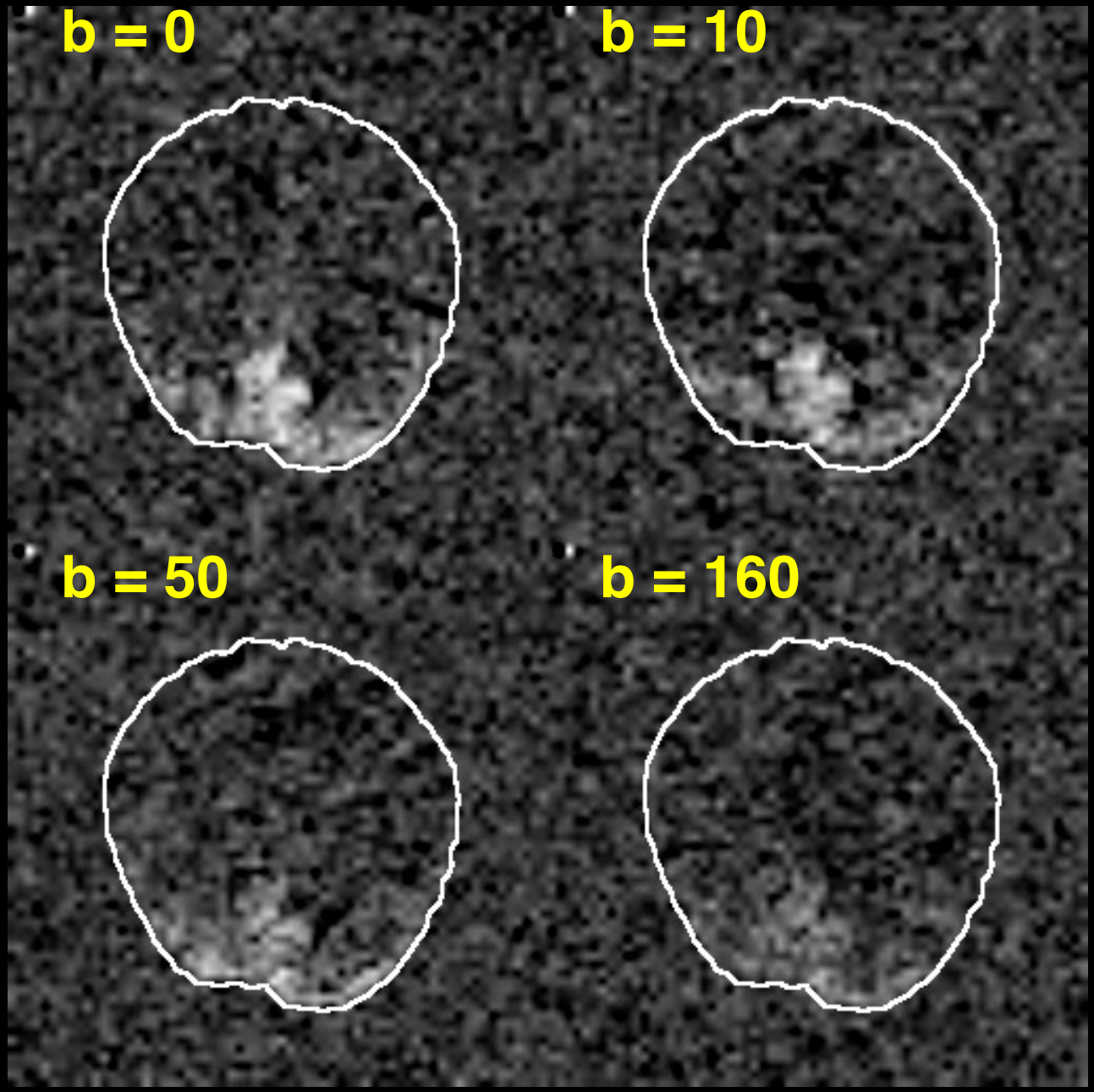
no diffusion weighting

diffusion weighting



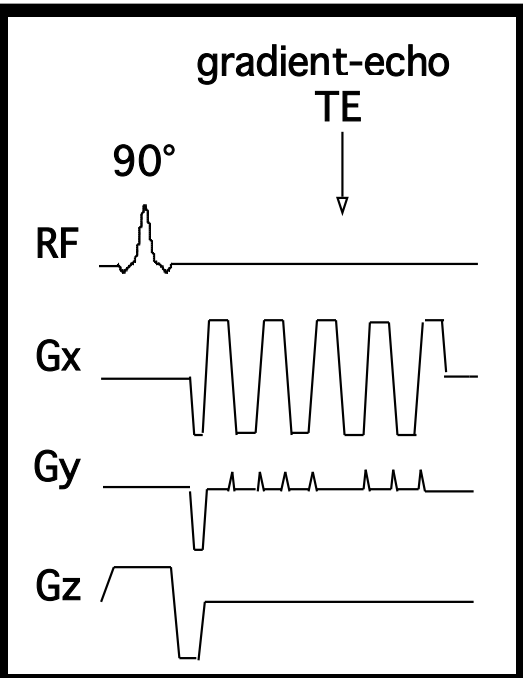
Summary of Diffusion-Weighted fMRI Data



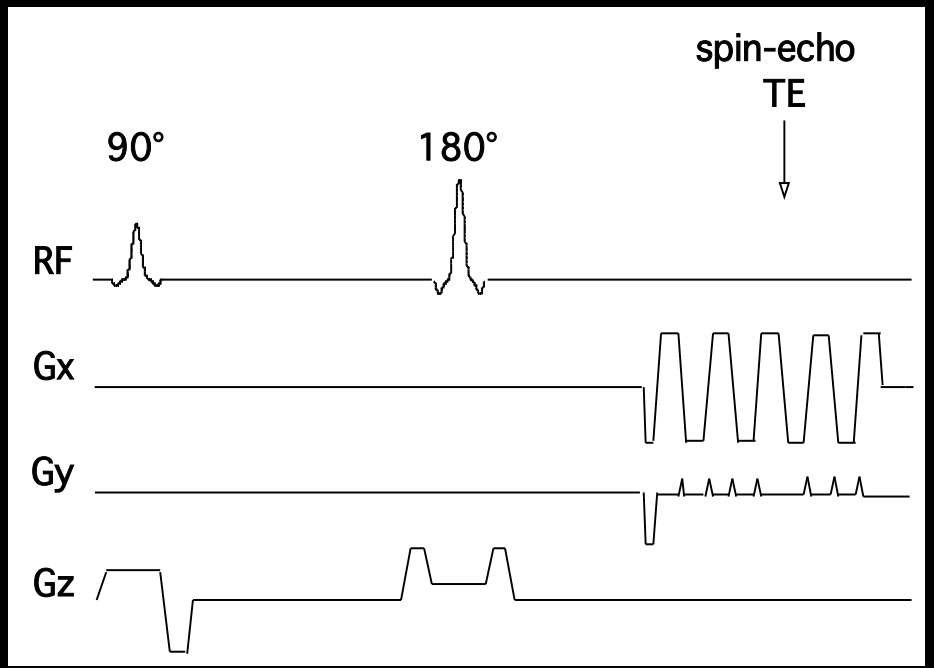

b = 0
b = 10
b = 50
b = 160

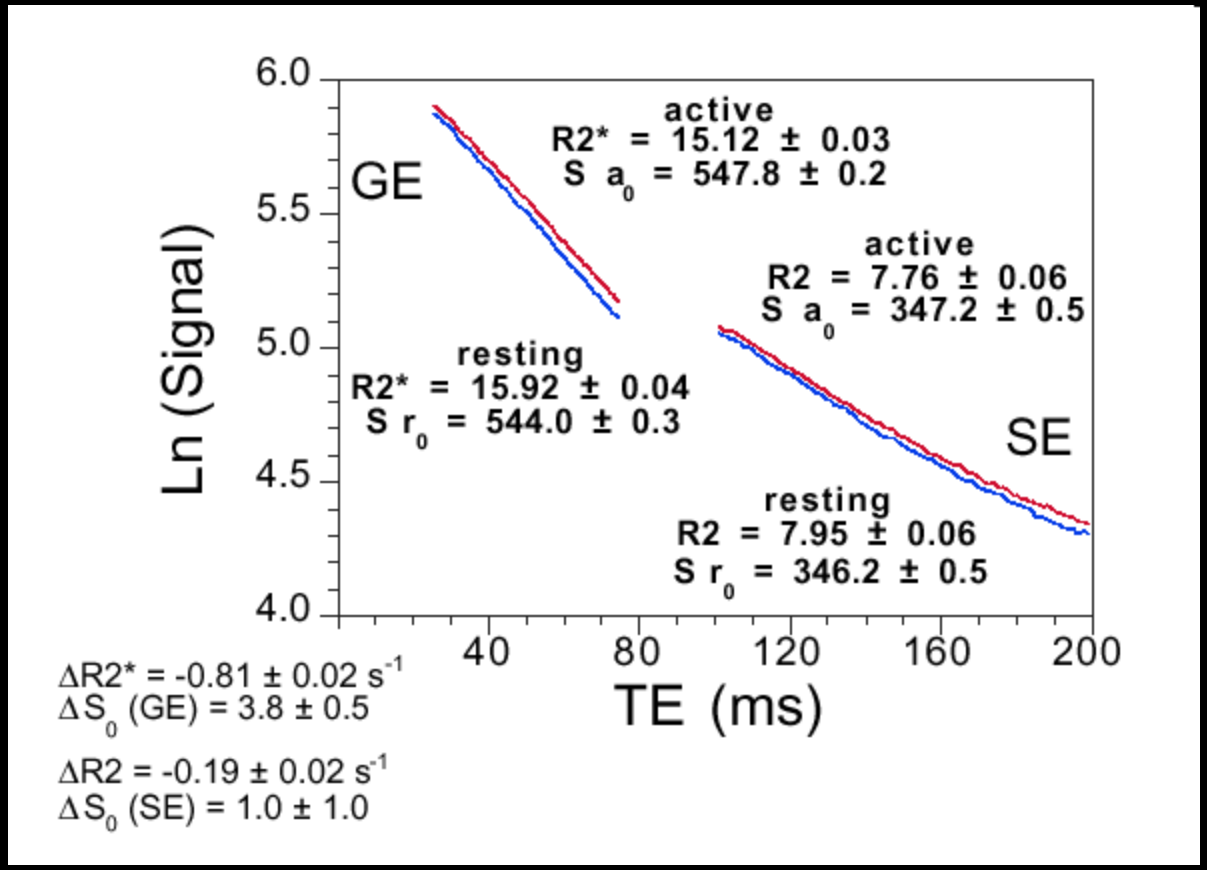
Echo time dependence

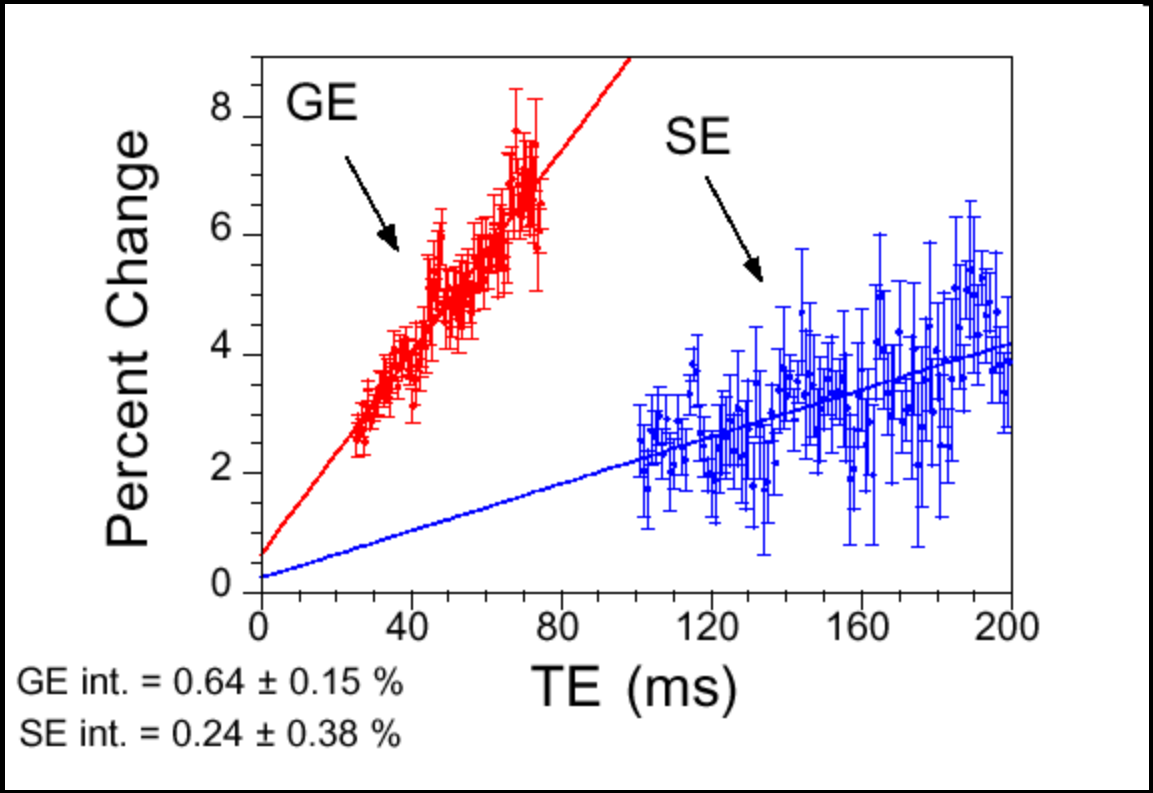
Gradient-Echo EPI

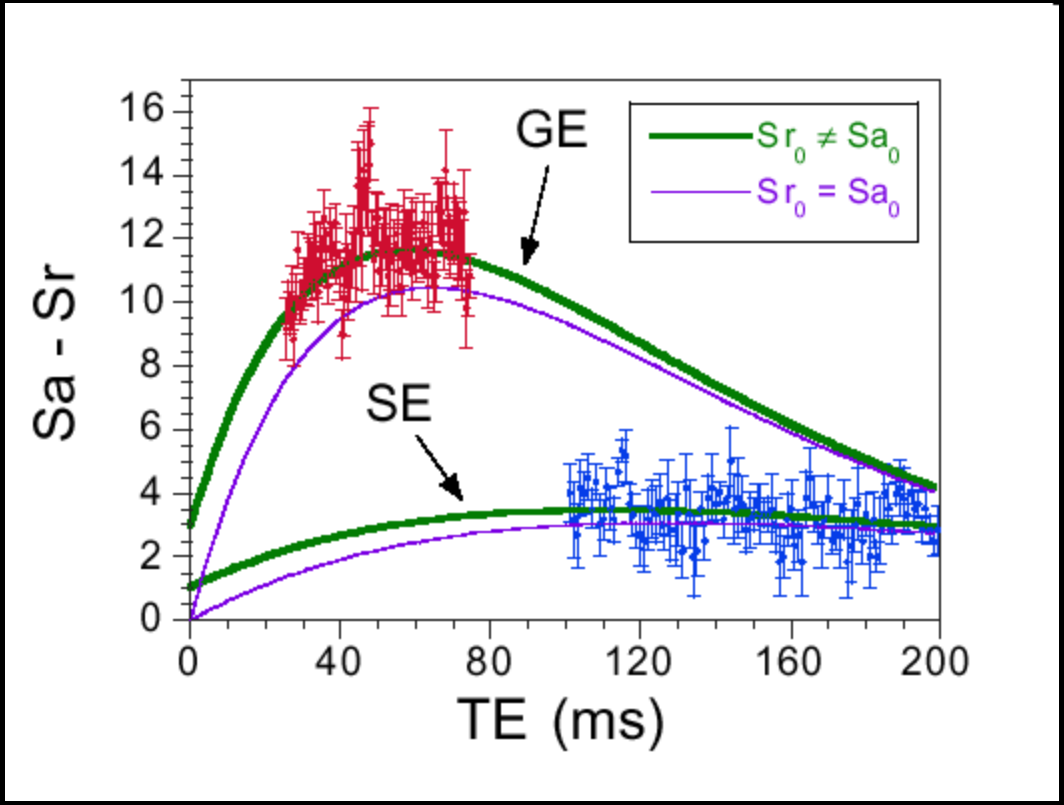


Spin-Echo EPI




6.0
5.5
5.0
4.5
4.0
Ln (Signal)
40
80
120
160
200
TE (ms)
GE
active
R2* = 15.12 ± 0.03
S a0 = 547.8 ± 0.2
resting
R2* = 15.92 ± 0.04
S r0 = 544.0 ± 0.3
SE
active
R2 = 7.76 ± 0.06
S a0 = 347.2 ± 0.5
resting
R2 = 7.95 ± 0.06
S r0 = 346.2 ± 0.5
ΔR2* = -0.81 ± 0.02 s-1
ΔS0 (GE) = 3.8 ± 0.5
ΔR2 = -0.19 ± 0.02 s-1
ΔS0 (SE) = 1.0 ± 1.0


GE
SE
Percent Change
0
2
4
6
8
0
40
80
120
160
200
TE (ms)
GE int. = 0.64 ± 0.15 %
SE int. = 0.24 ± 0.38 %


GE
SE
Sr0 ≠ Sa0
Sr0 = Sa0
Sa - Sr
TE (ms)
0
2
4
6
8
10
12
14
16
0
40
80
120
160
200

Perfusion localization vs. BOLD localization

T1 - weighted

Flow weighted

T2* weighted

BOLD weighted

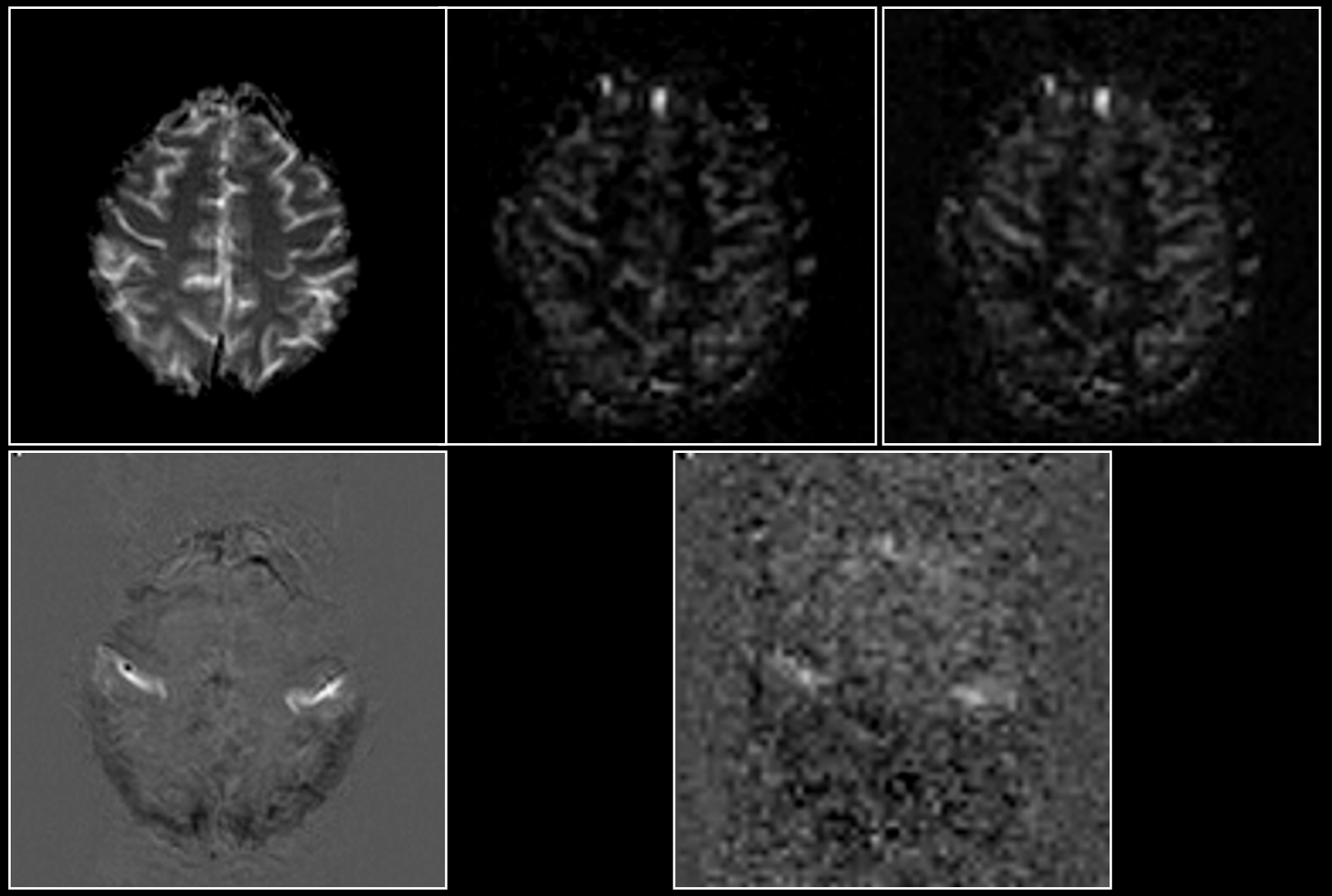
T1 and T2* weighted

Flow and BOLD weighted

P. A. Bandettini, E. C. Wong, Echo - planar magnetic resonance imaging of human brain activation, *in* "Echo Planar Imaging: Theory, Technique, and Application" (F. Schmitt, M. Stehling, R. Turner, Eds.), p.493-530, Springer - Verlag, Berlin, 1997

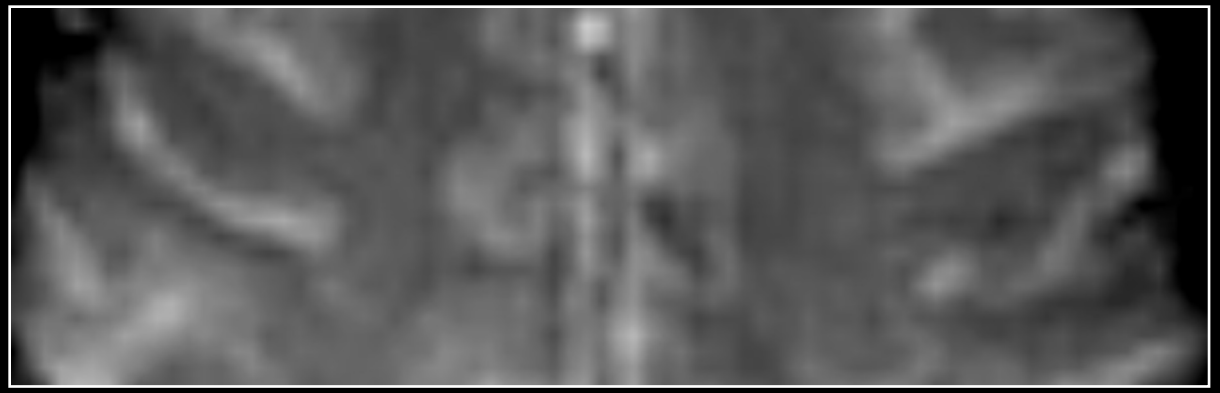
Perfusion

BOLD *Rest* *Activation*

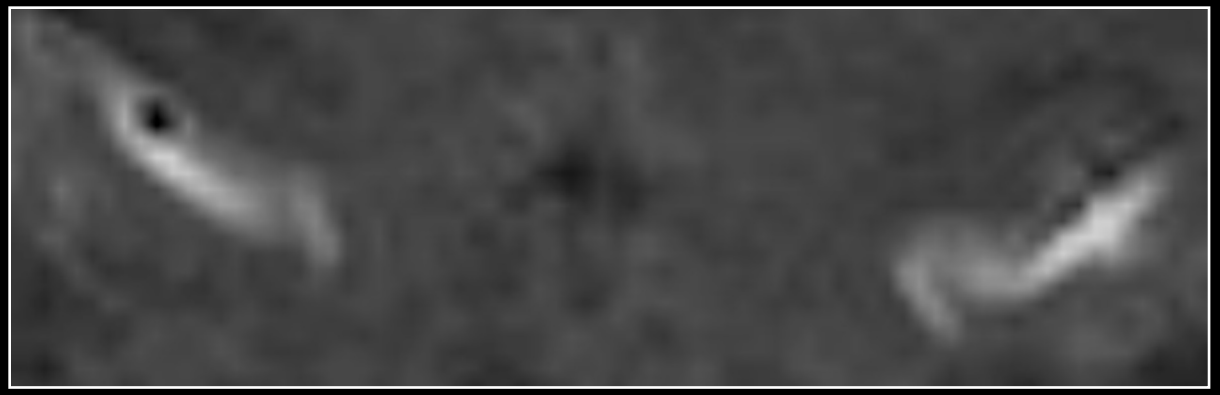


P. A. Bandettini, E. C. Wong, Magnetic resonance imaging of human brain function: principles, practicalities, and possibilities, *in* "Neurosurgery Clinics of North America: Functional Imaging" (M. Haglund, Ed.), p.345-371, W. B. Saunders Co., 1997.

Anatomy



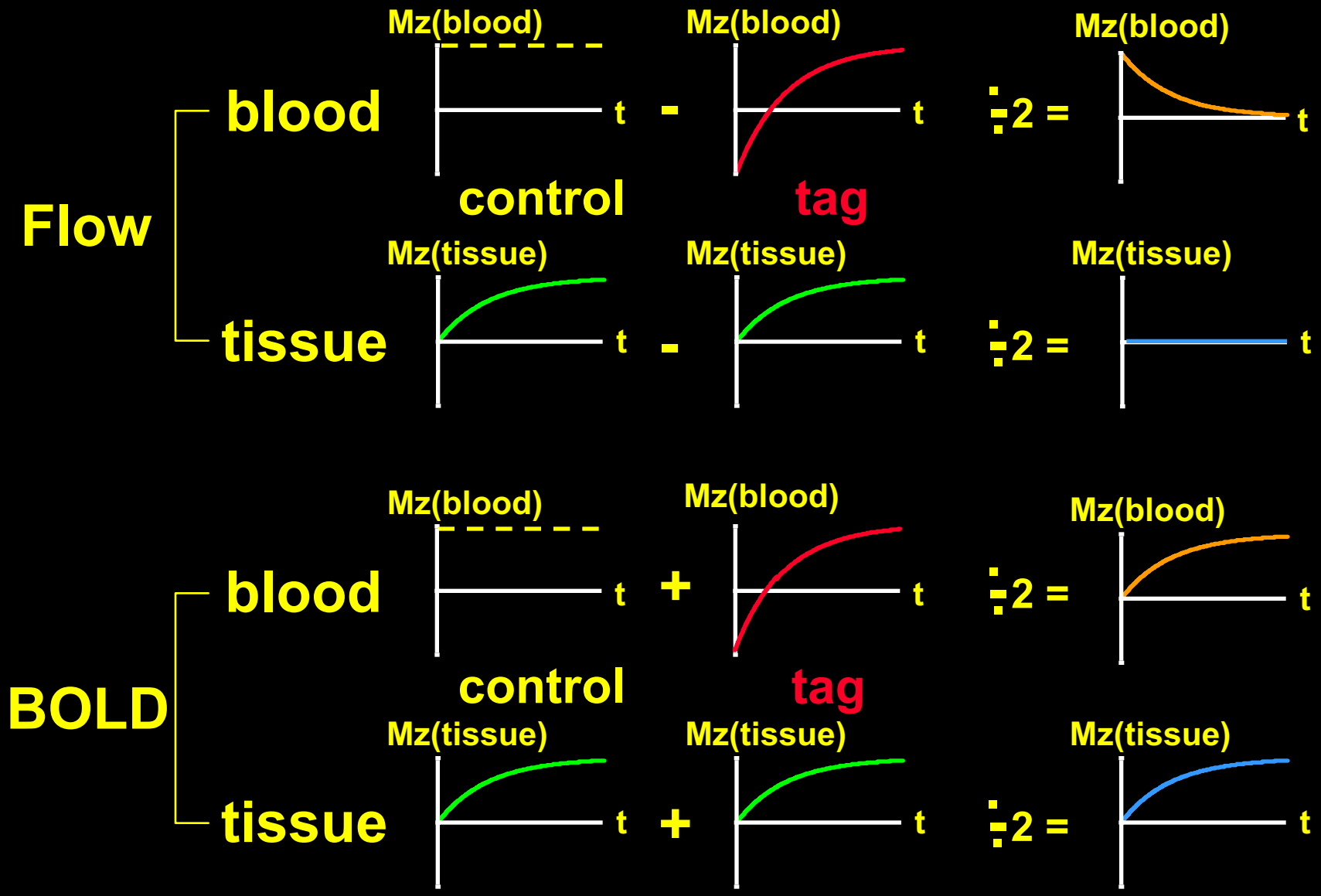
BOLD



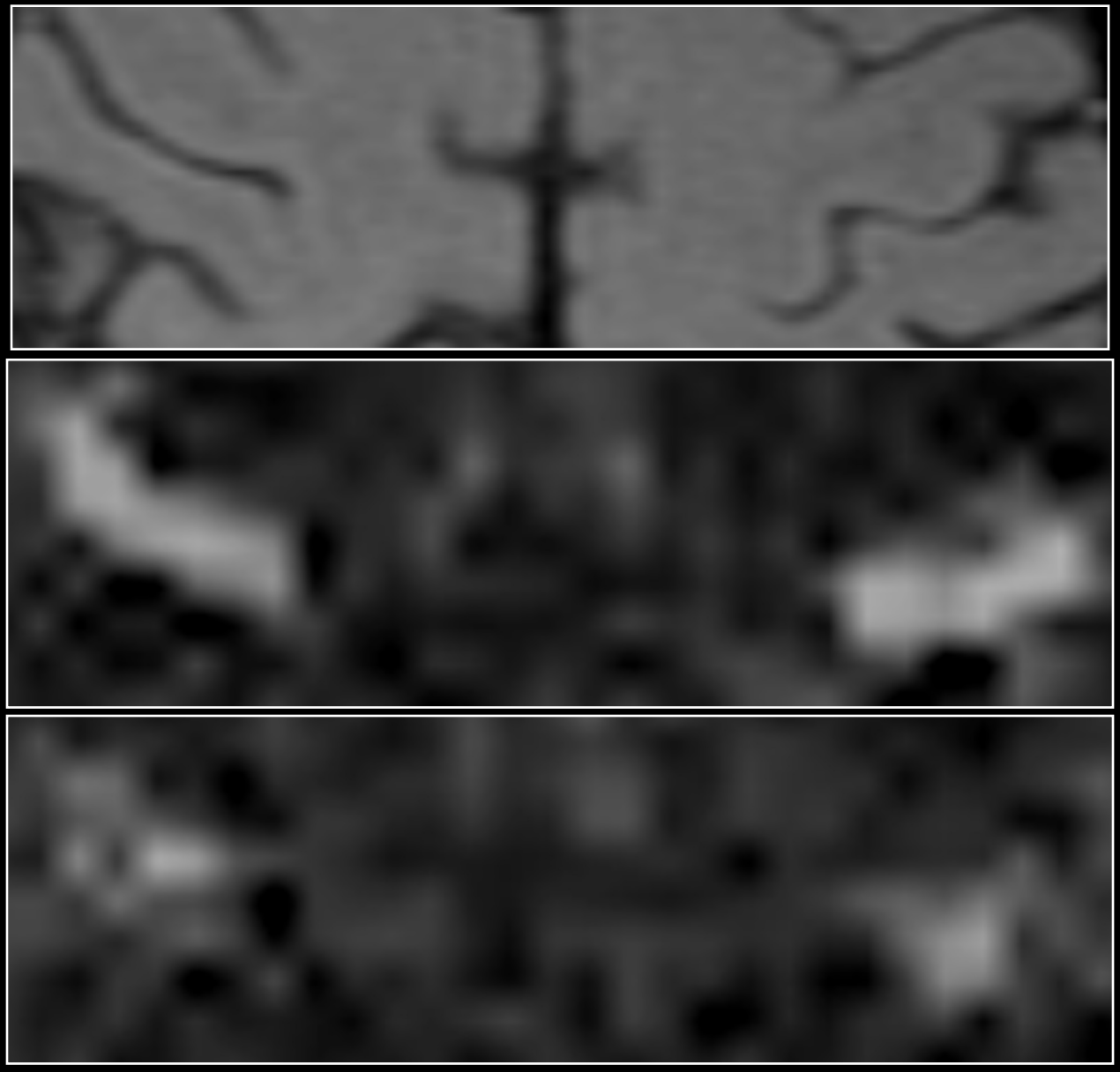
Perfusion

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.

Simultaneous Flow and BOLD



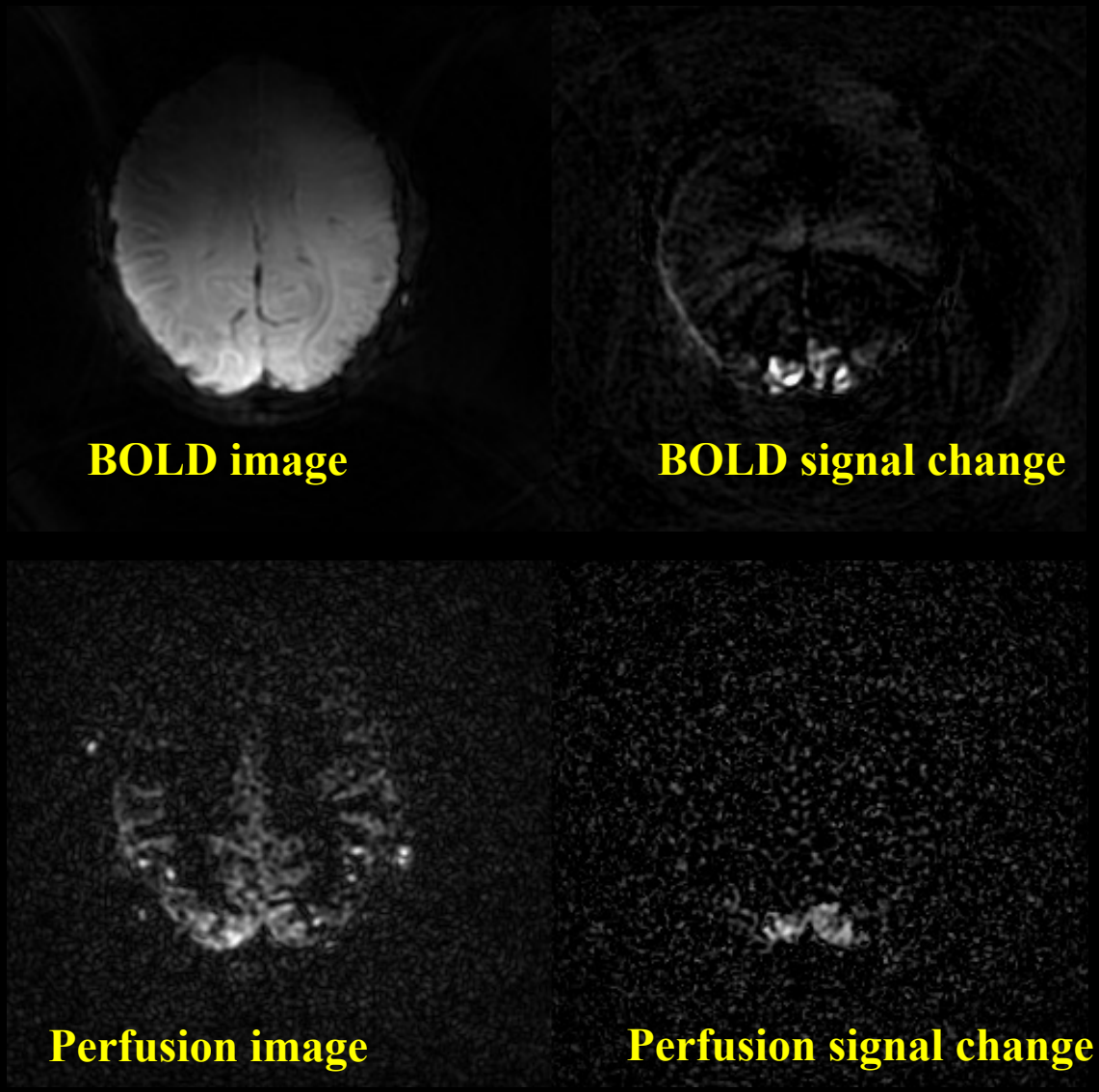
Simultaneous BOLD and Perfusion



BOLD

Perfusion

Simultaneous perfusion and BOLD imaging (10 min, 1.5x1.5x4mm^3)

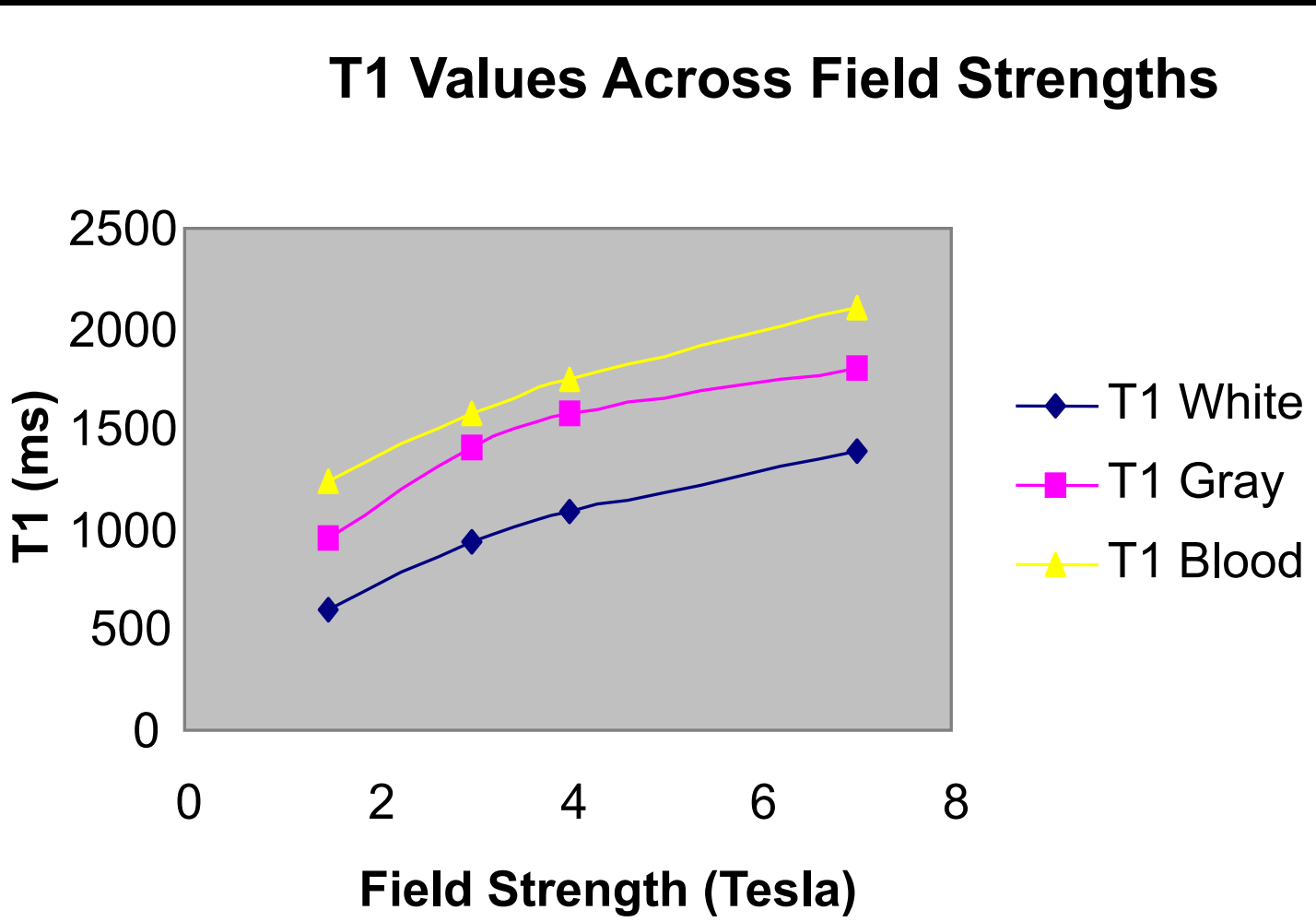


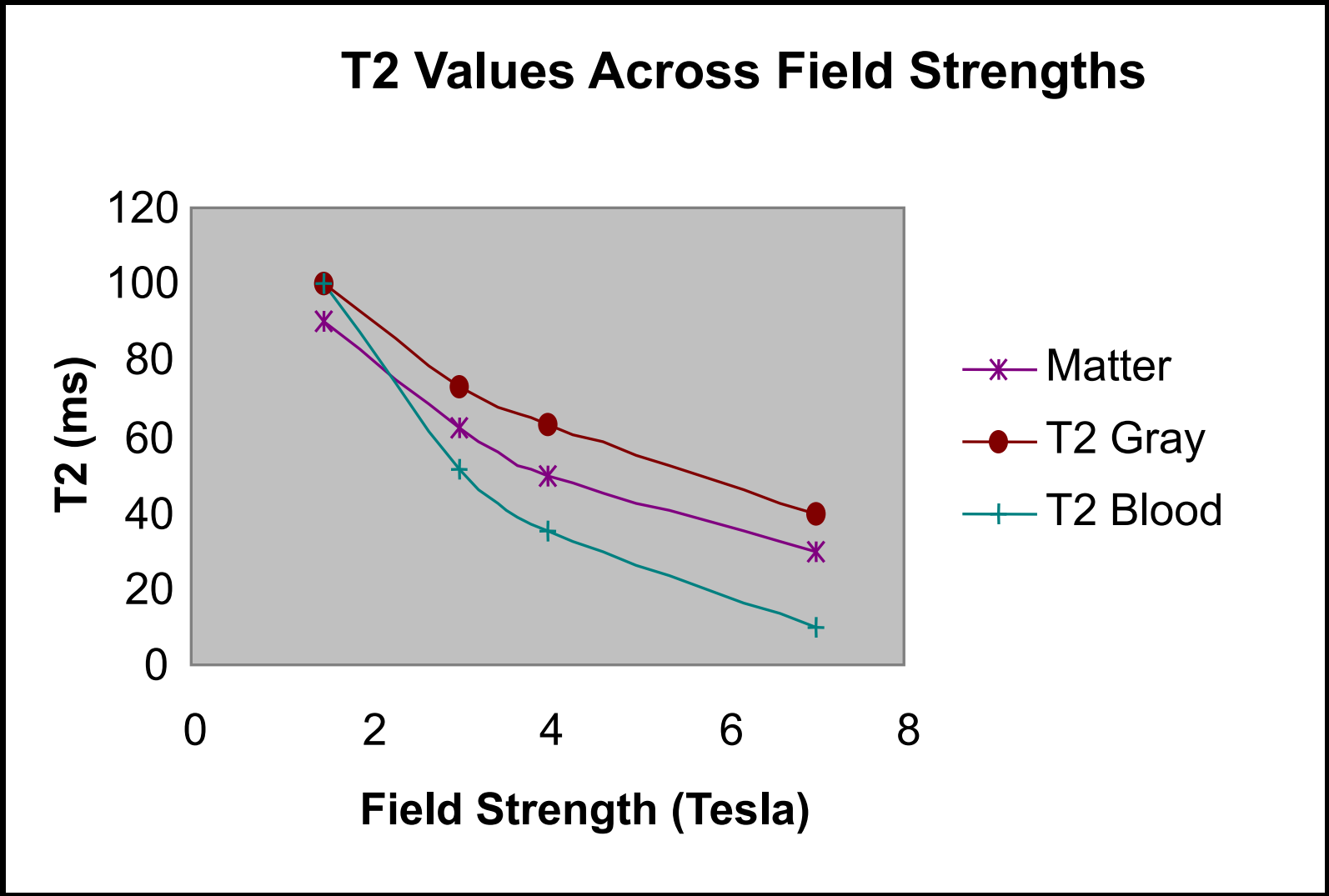
Frank Ye, et al.

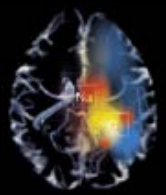
What Changes with Field Strength?

Tissue Relaxation Characteristics
Functional Contrast
Signal to Noise Ratio
Bo Inhomogeneity Effects

RF Power Deposition
Mechanical Force on Gradient Coil

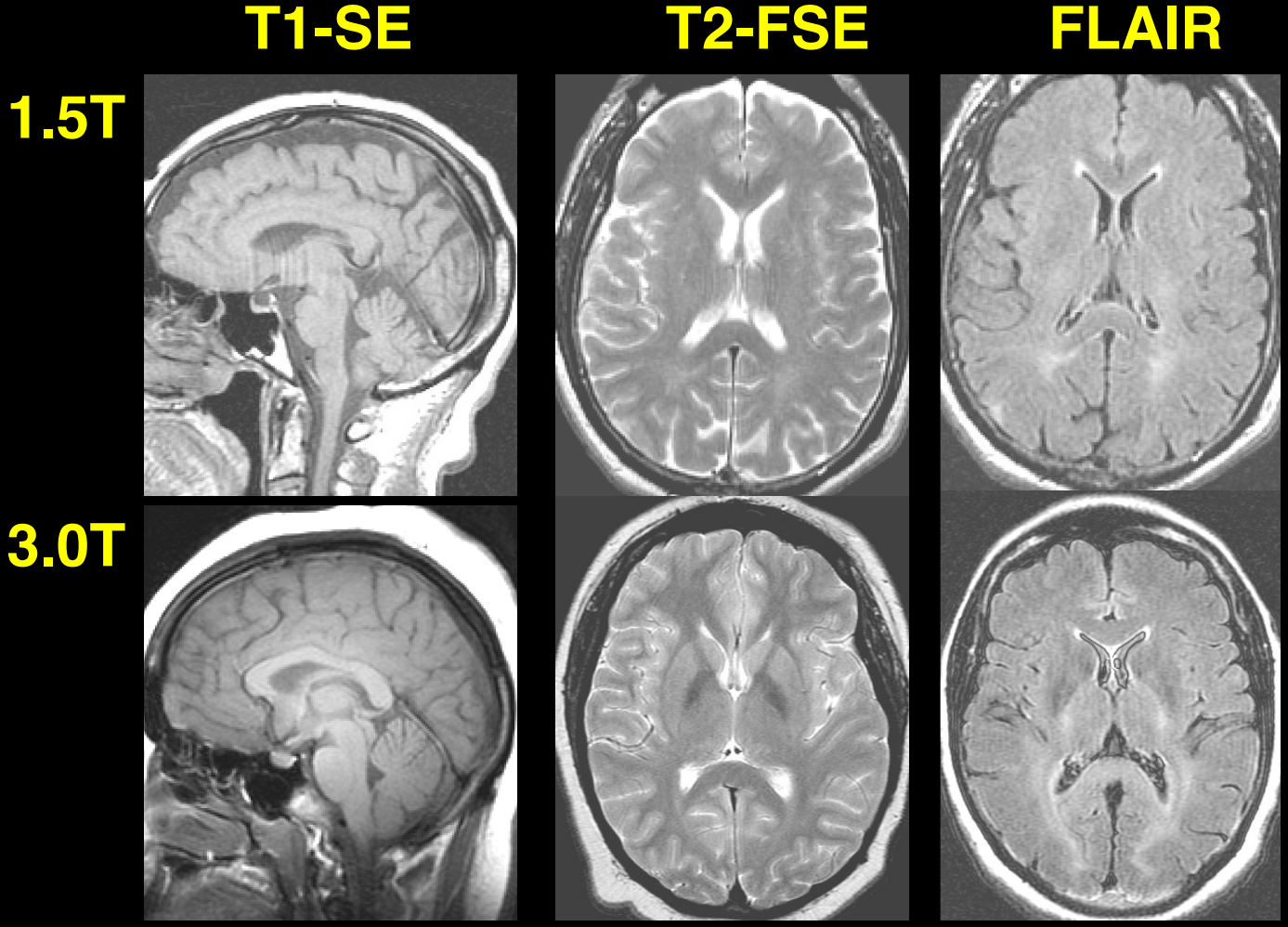

T1 Values Across Field Strengths
2500
2000
1500
1000
500
0
T1 (ms)
0
2
4
6
8
Field Strength (Tesla)
T1 White
T1 Gray
T1 Blood

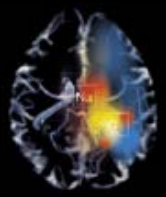

T2 Values Across Field Strengths
120
100
80
60
40
20
0
T2 (ms)
0
2
4
6
8
Field Strength (Tesla)
Matter
T2 Gray
T2 Blood



UIC
Thulborn

Whole Brain Anatomy





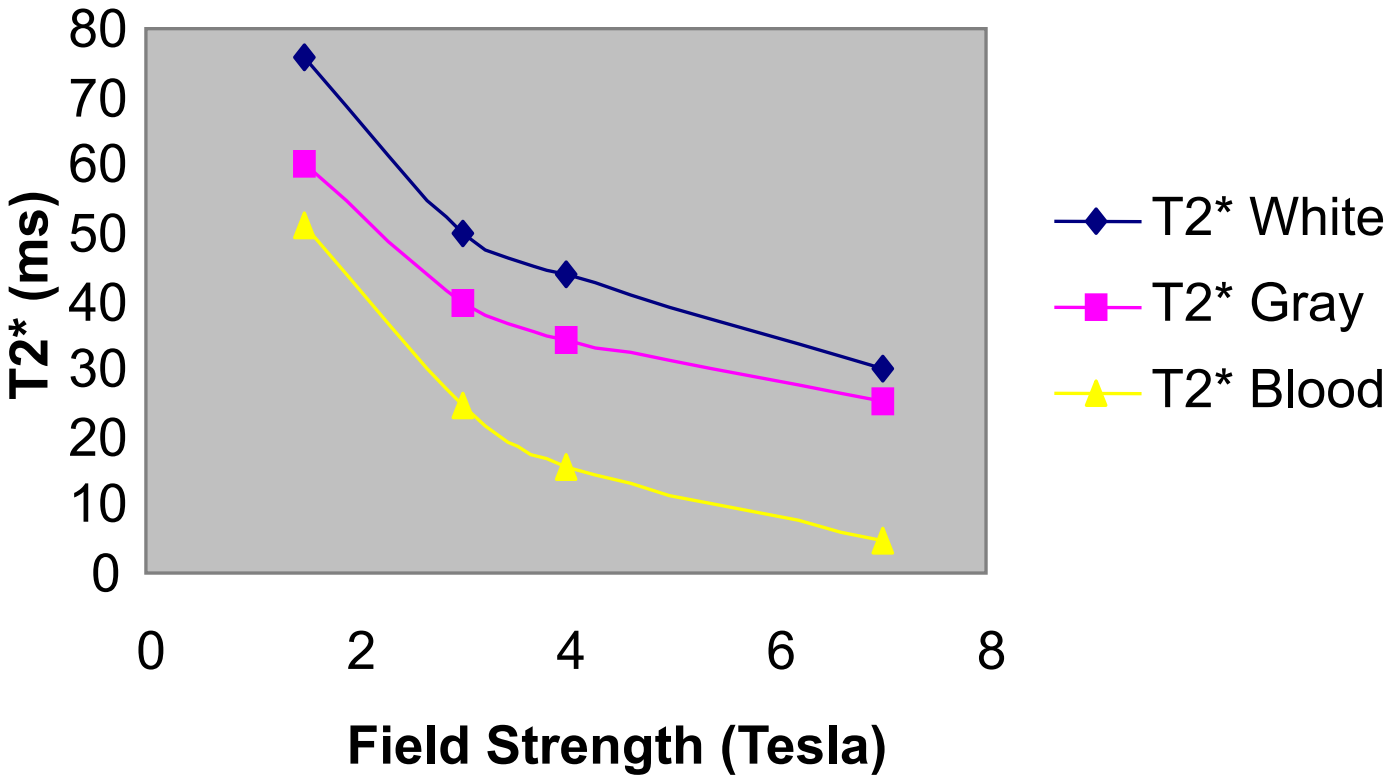
UIC
Thulborn

3.0T: 3D TOF MRA

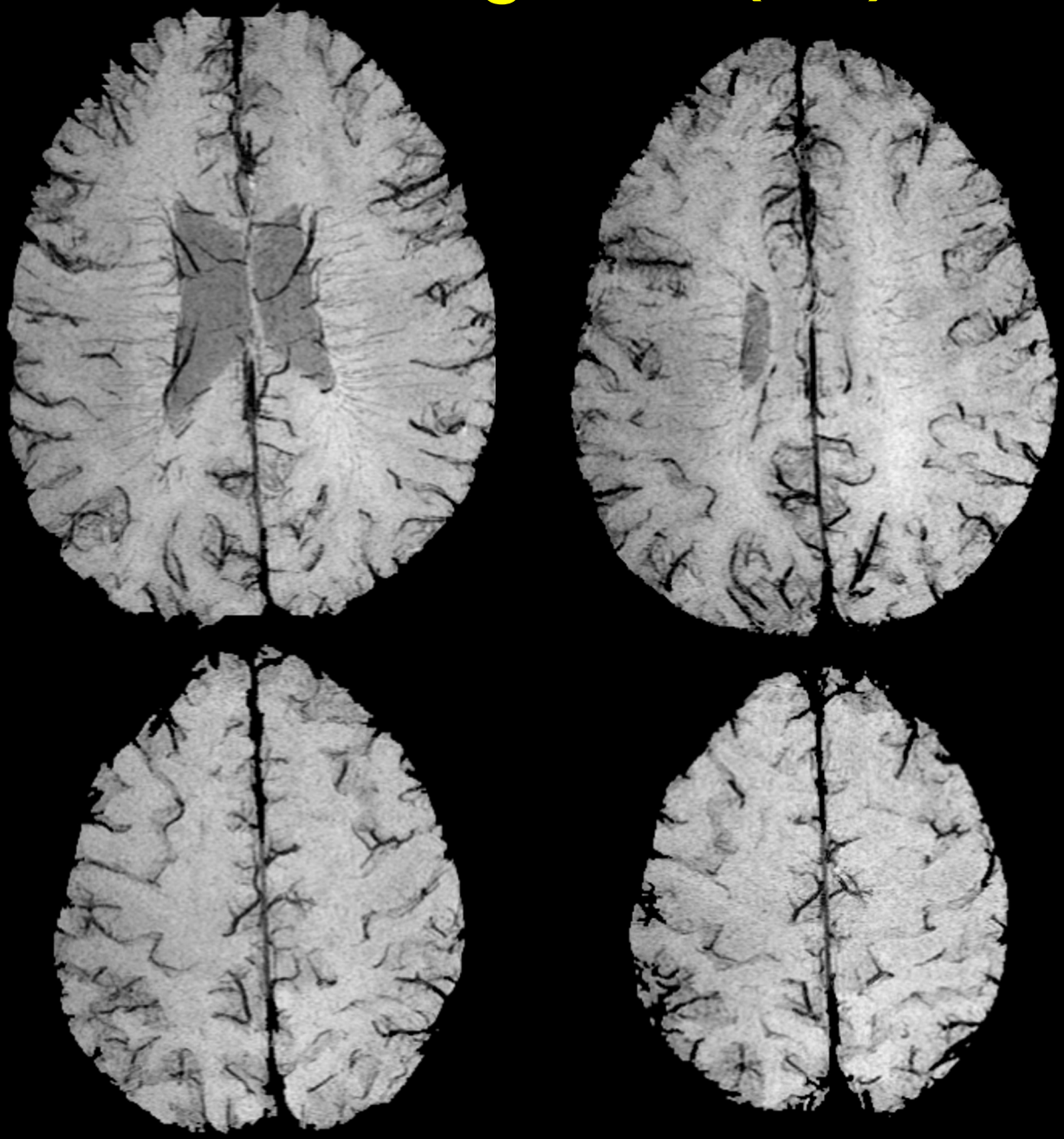
Longer T1 at 3.0T enhances flow effects and improves background suppression as well as allows higher spatial resolution

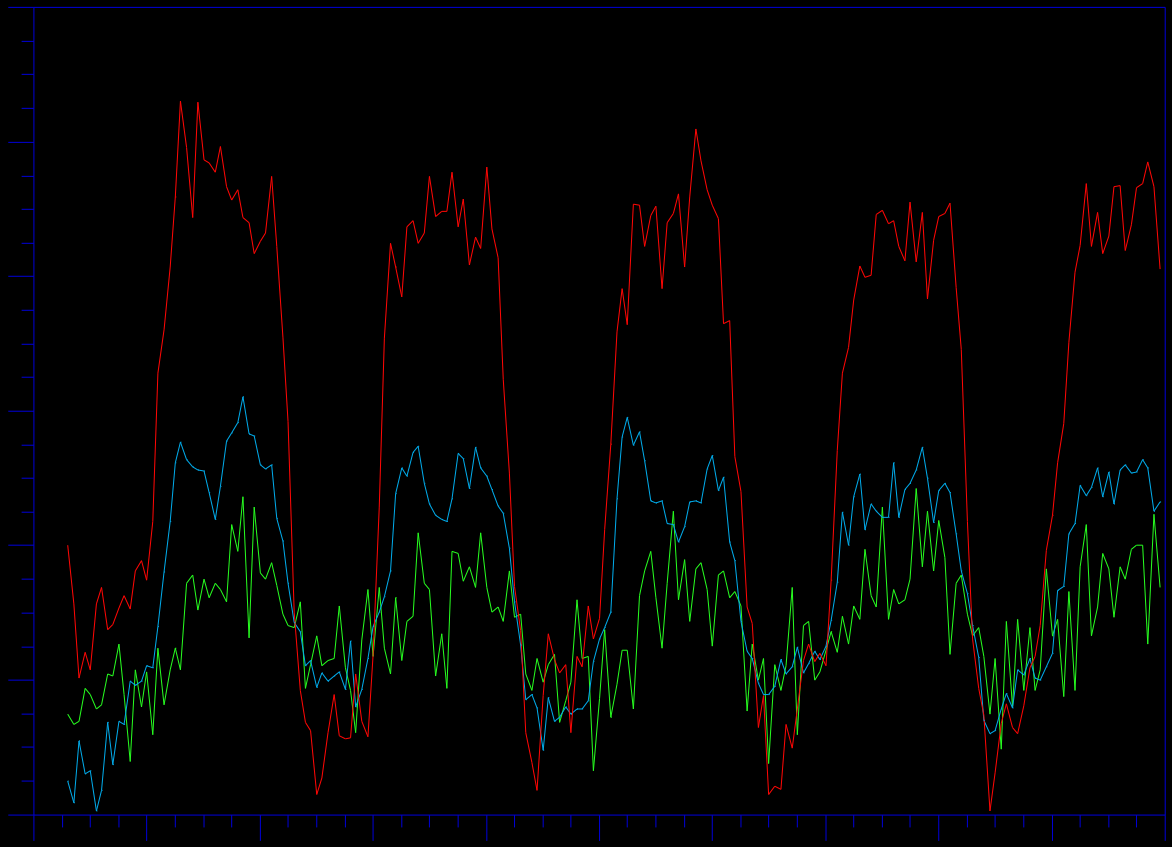
15 y.o. female patient

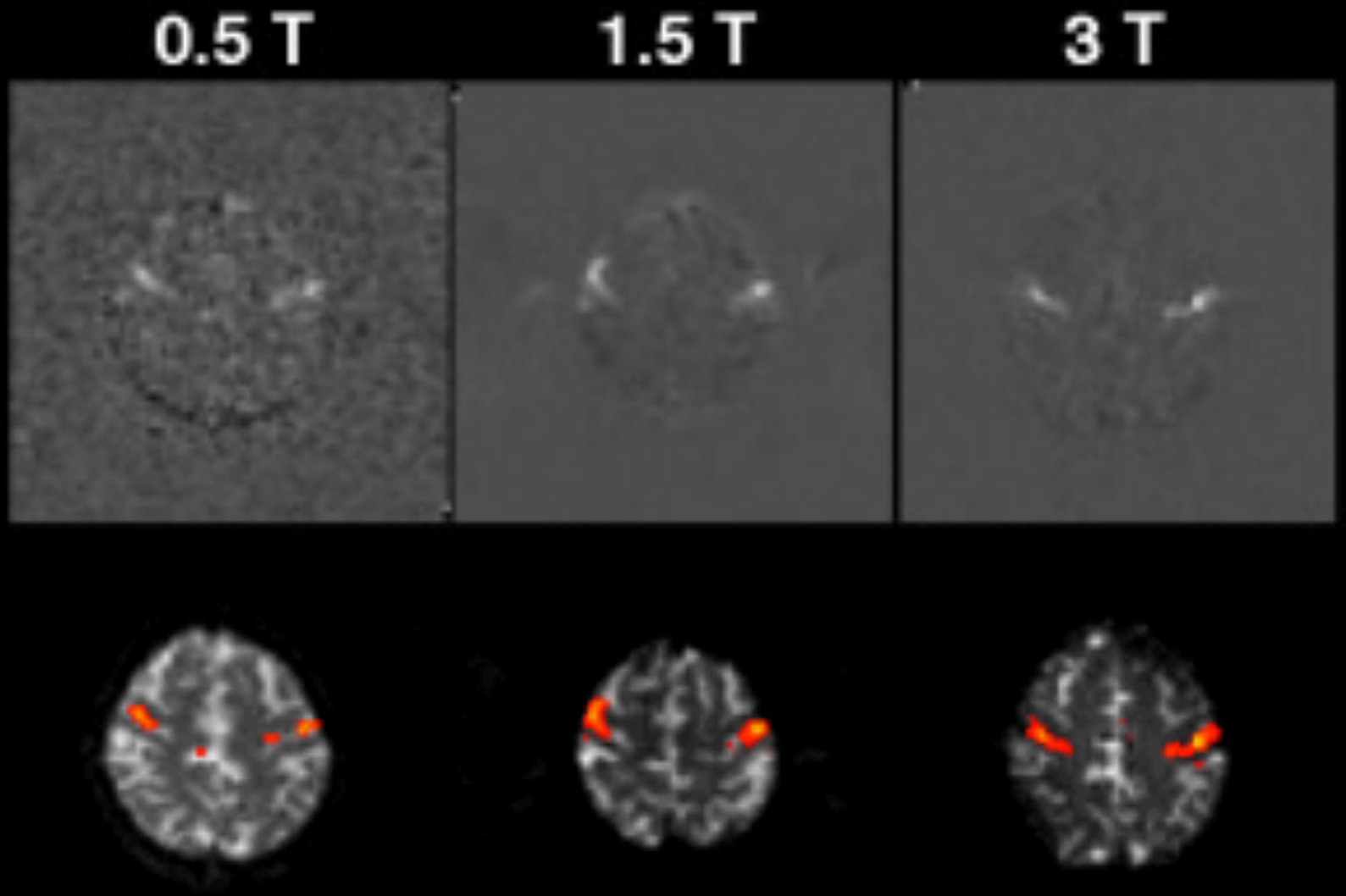
57 y.o. male patient


T2* Values Across Field Strengths
T2* (ms)
80
70
60
50
40
30
20
10
0
0
2
4
6
8
Field Strength (Tesla)
T2* White
T2* Gray
T2* Blood

Venograms (3T)






0.5 T
1.5 T
3 T

Magnetic Resonance in Medicine 45:595–604 (2001)

Neuroimaging at 1.5 T and 3.0 T: Comparison of Oxygenation-Sensitive Magnetic Resonance Imaging

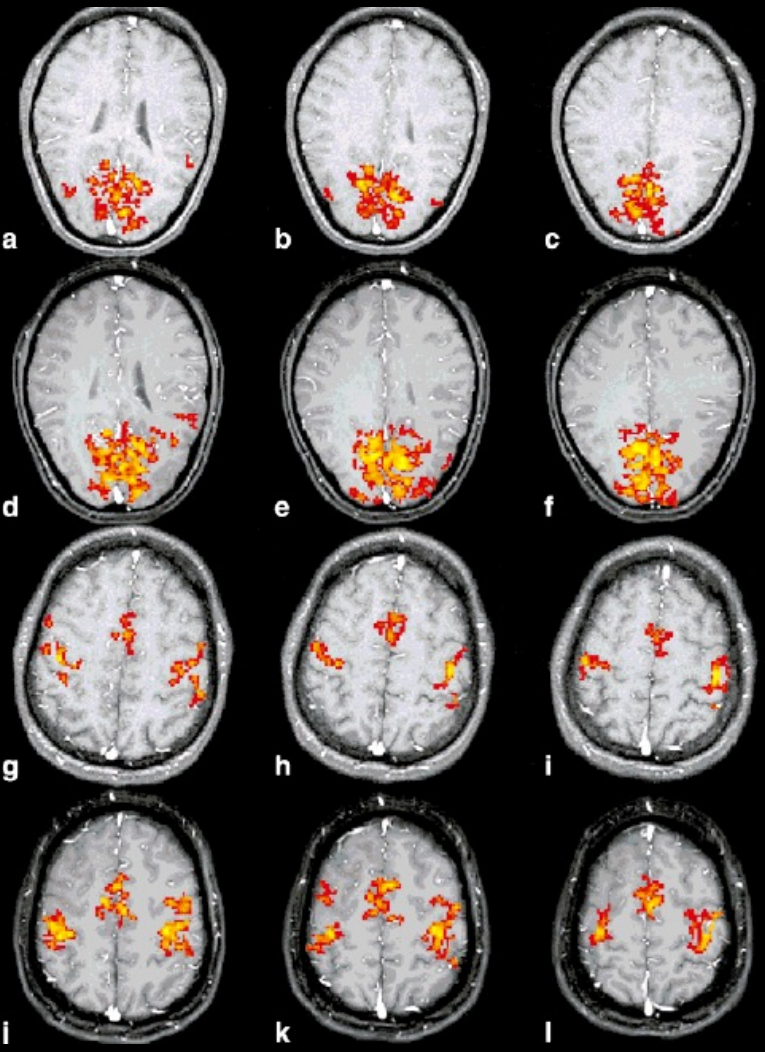
Gunnar Krüger,* Andreas Kastrup, and Gary H. Glover

1.5T

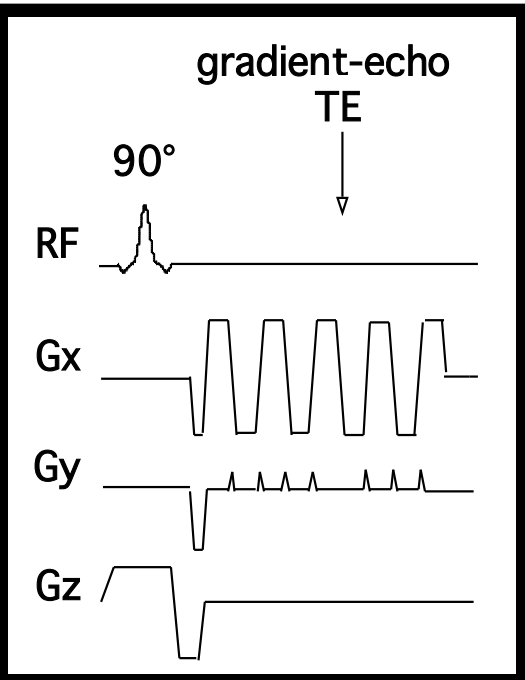
3T

1.5T

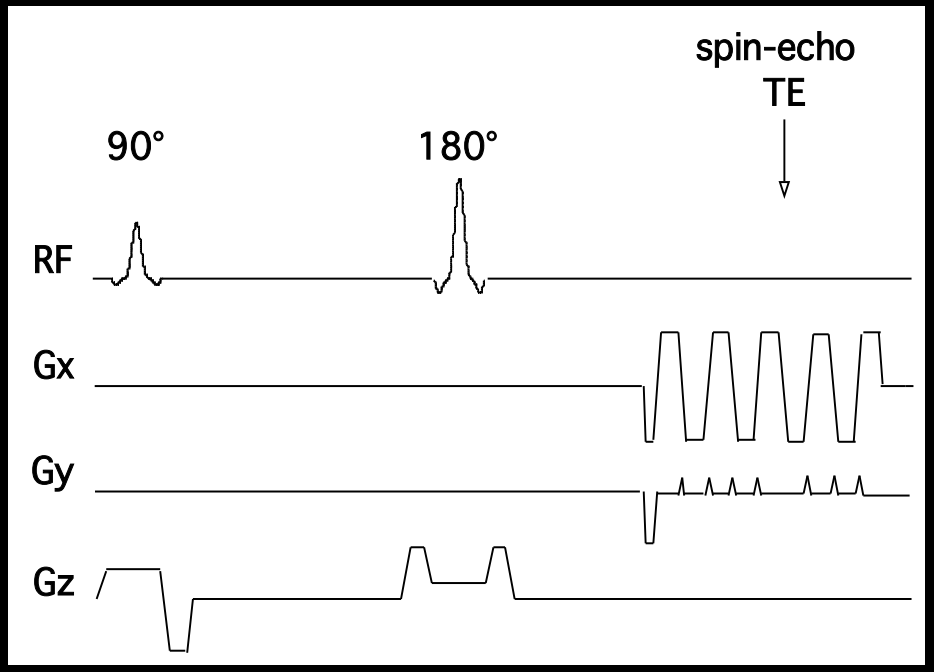
3T



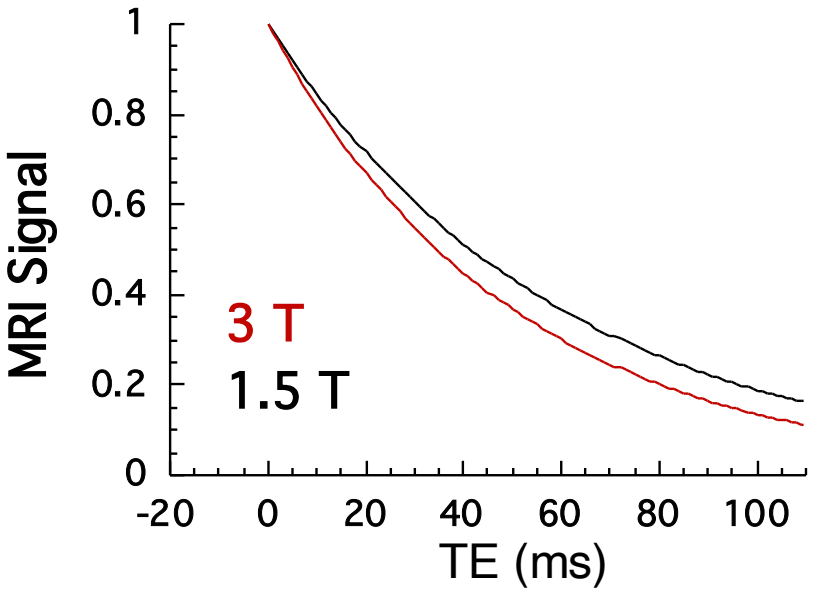
Gradient-Echo EPI



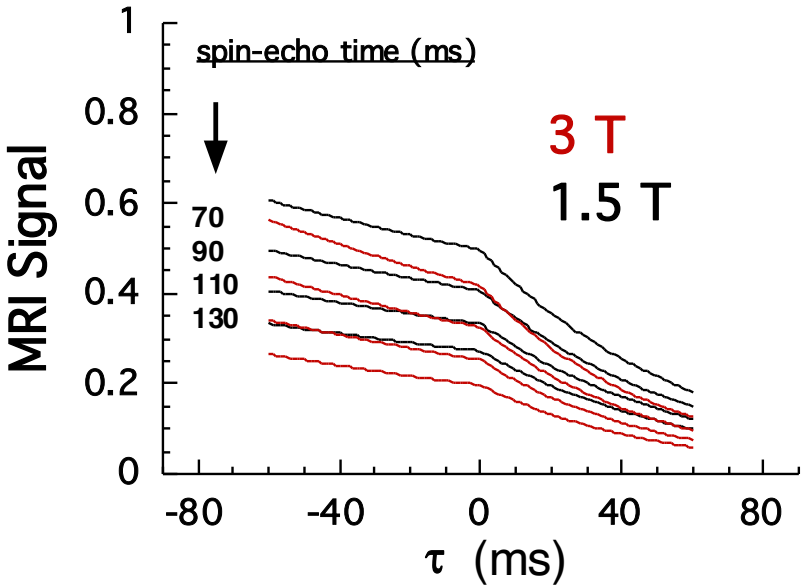
Spin-Echo EPI



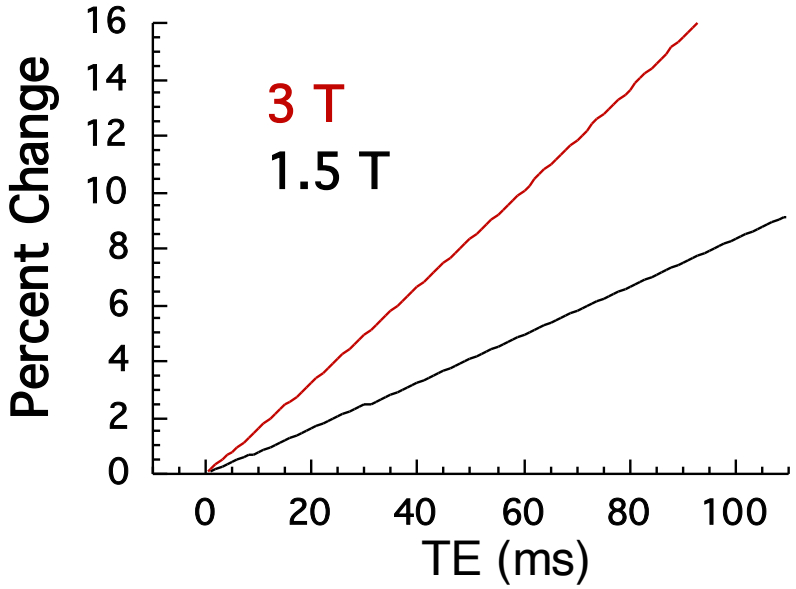
Gradient - Echo



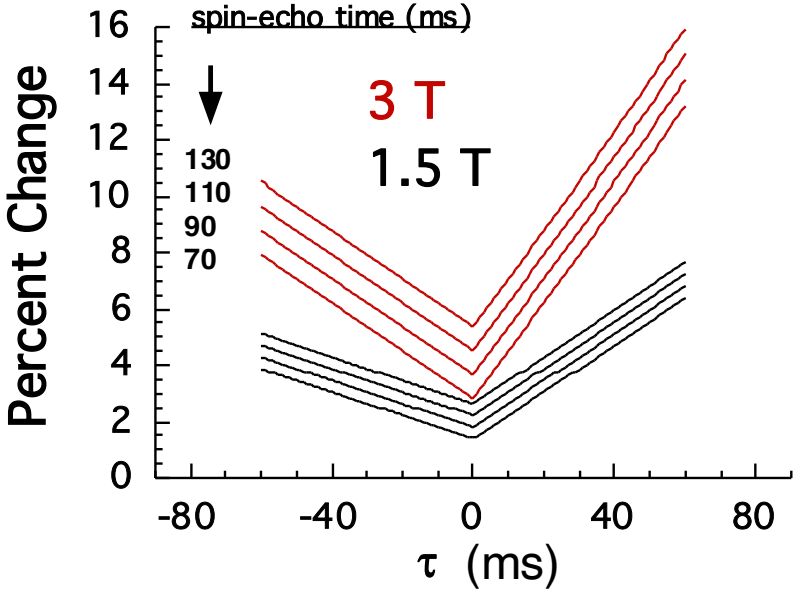
Asymmetric Spin - Echo



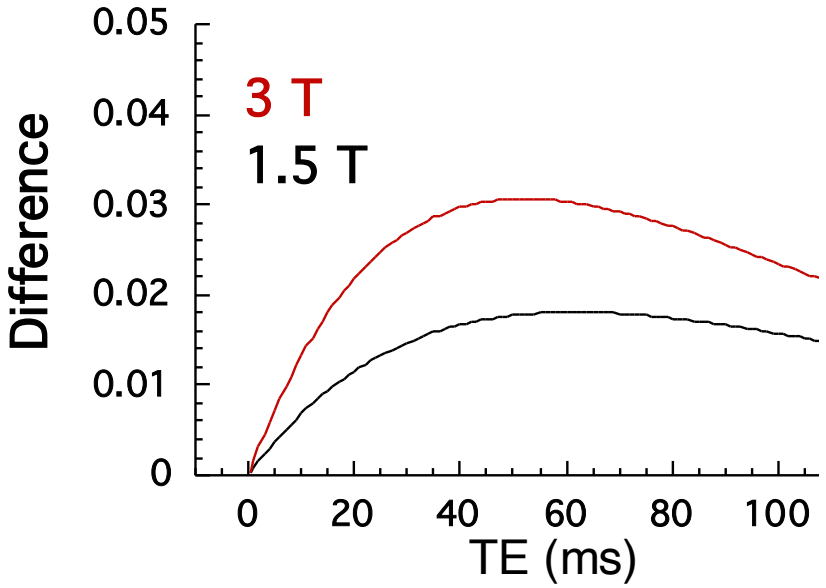
Gradient - Echo



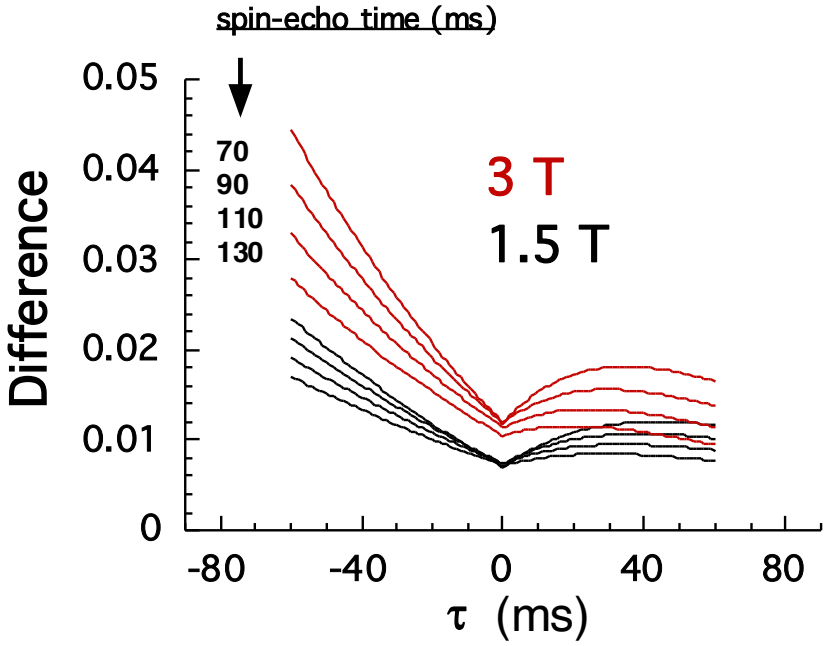
Asymmetric Spin - Echo



Gradient - Echo



Asymmetric Spin - Echo



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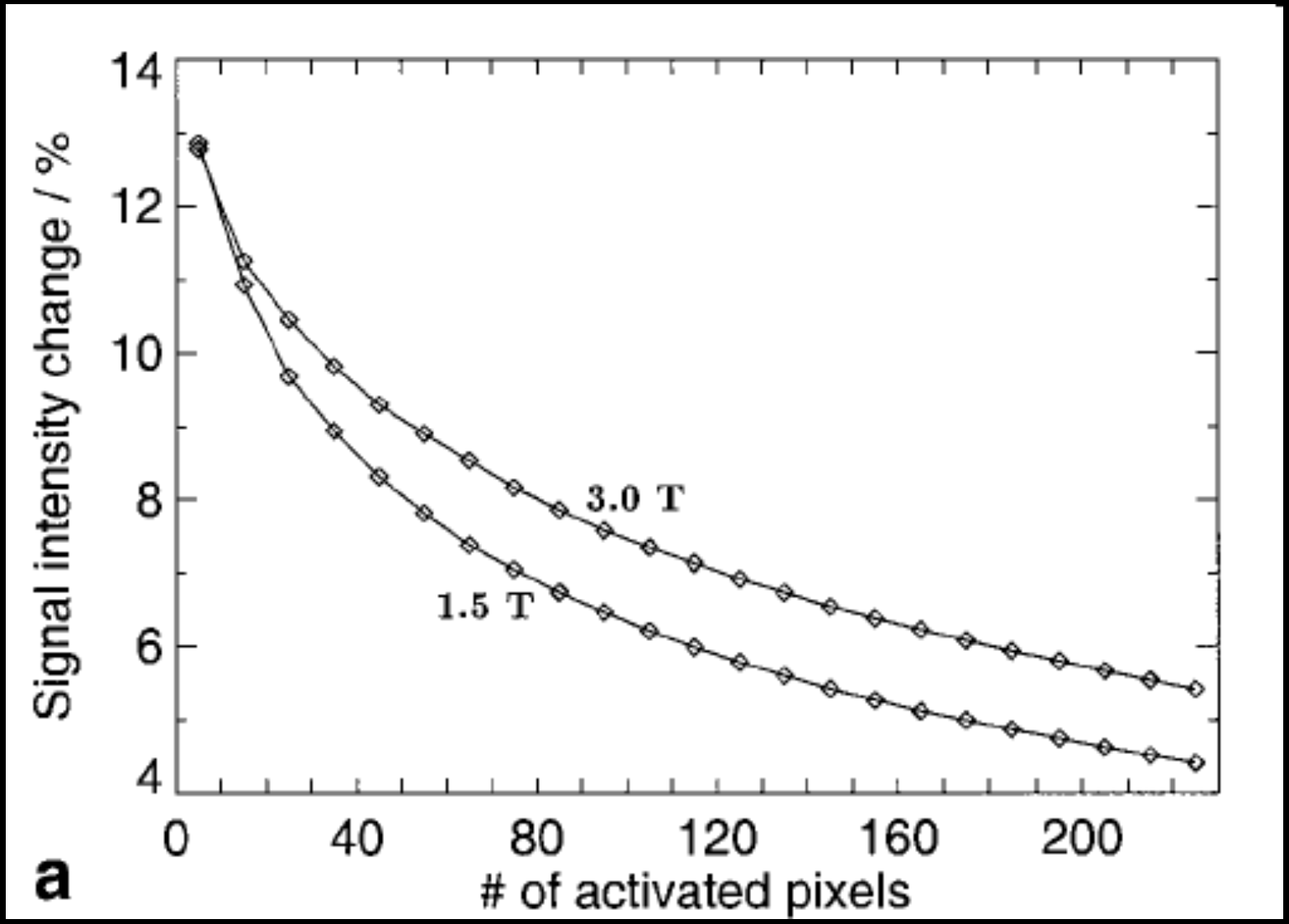

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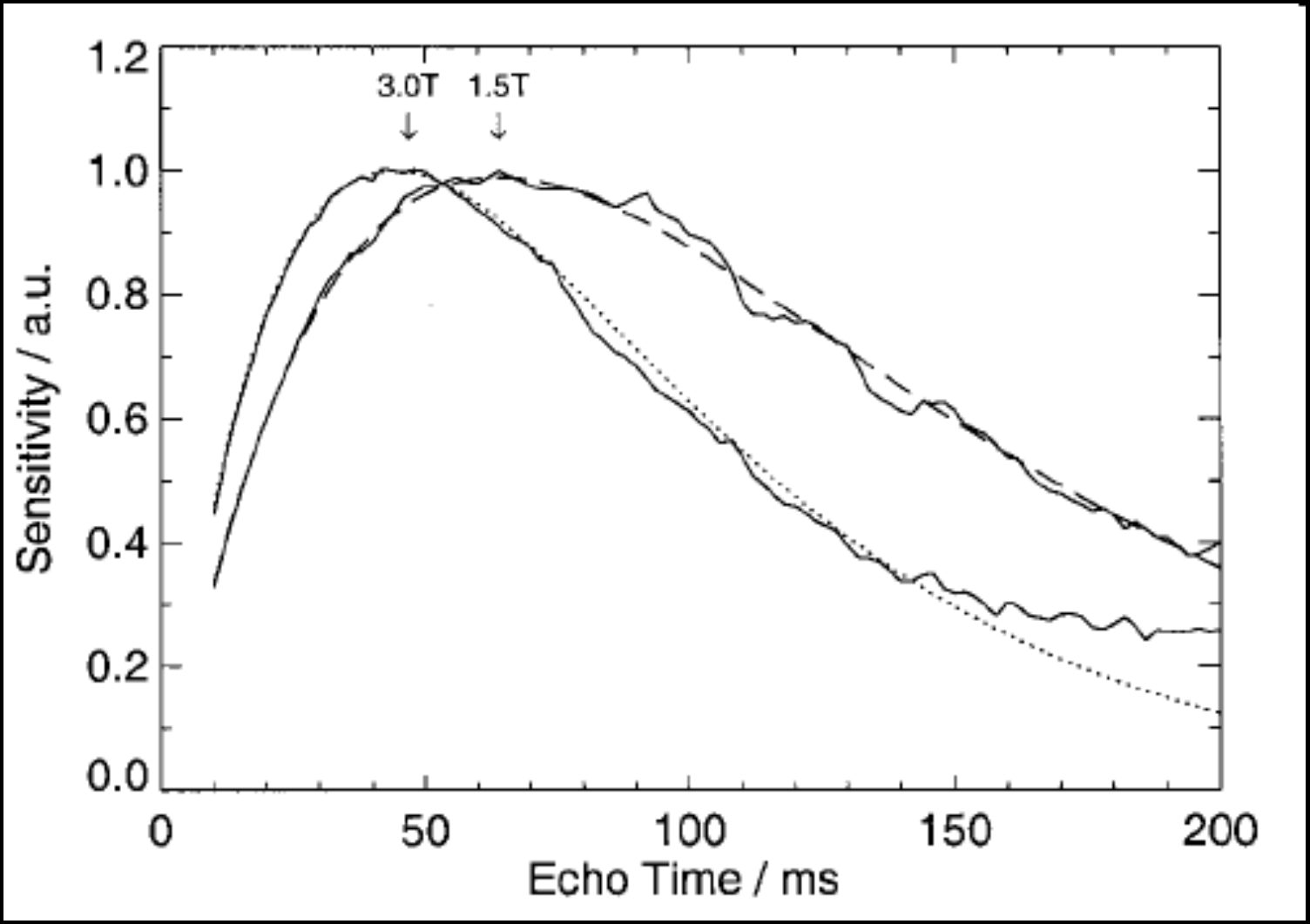
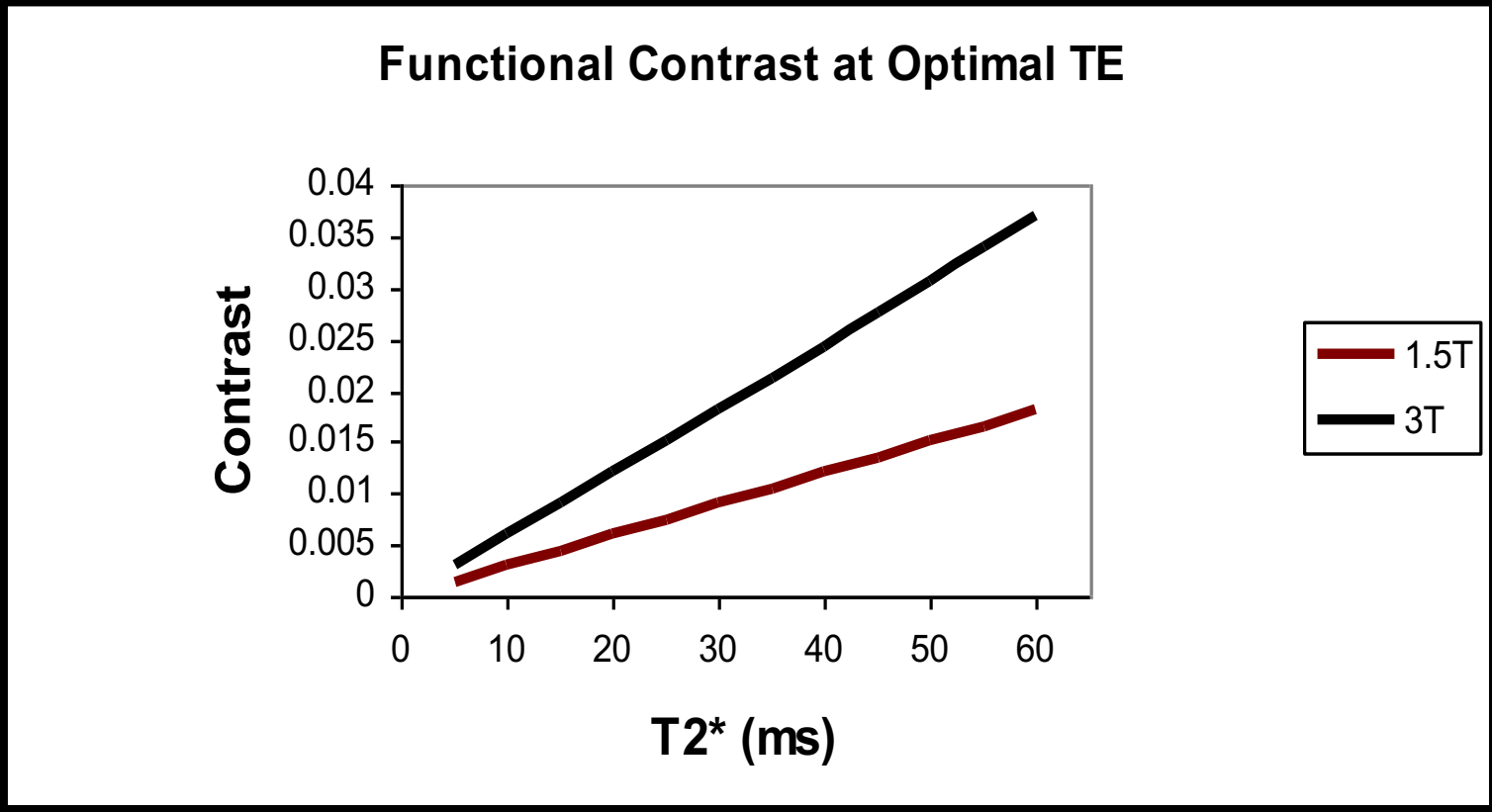
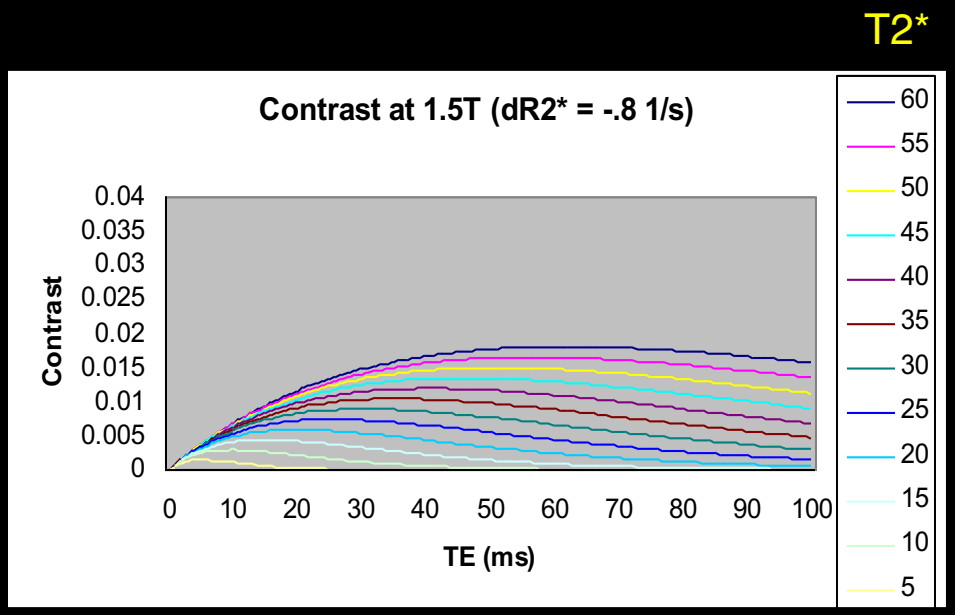
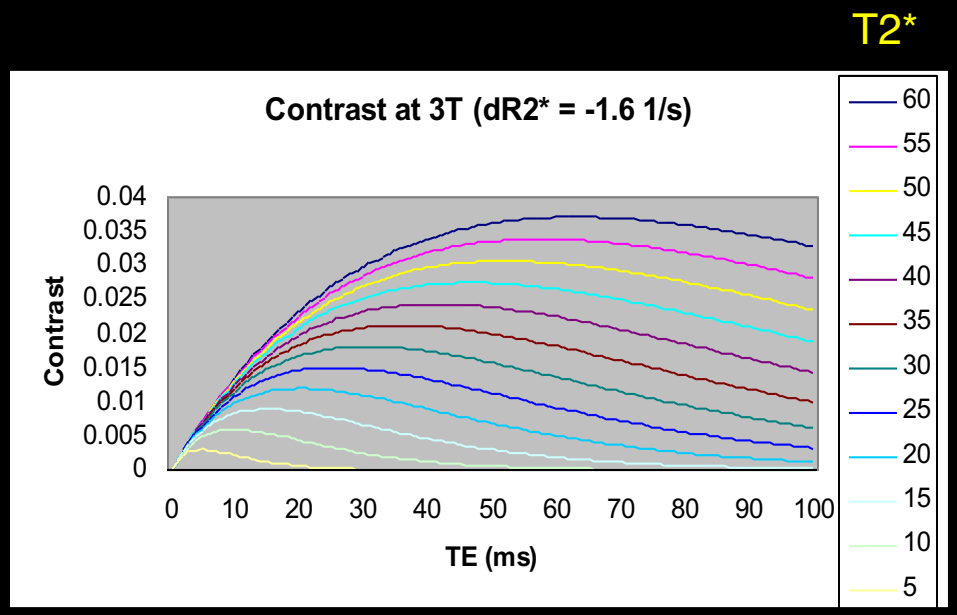
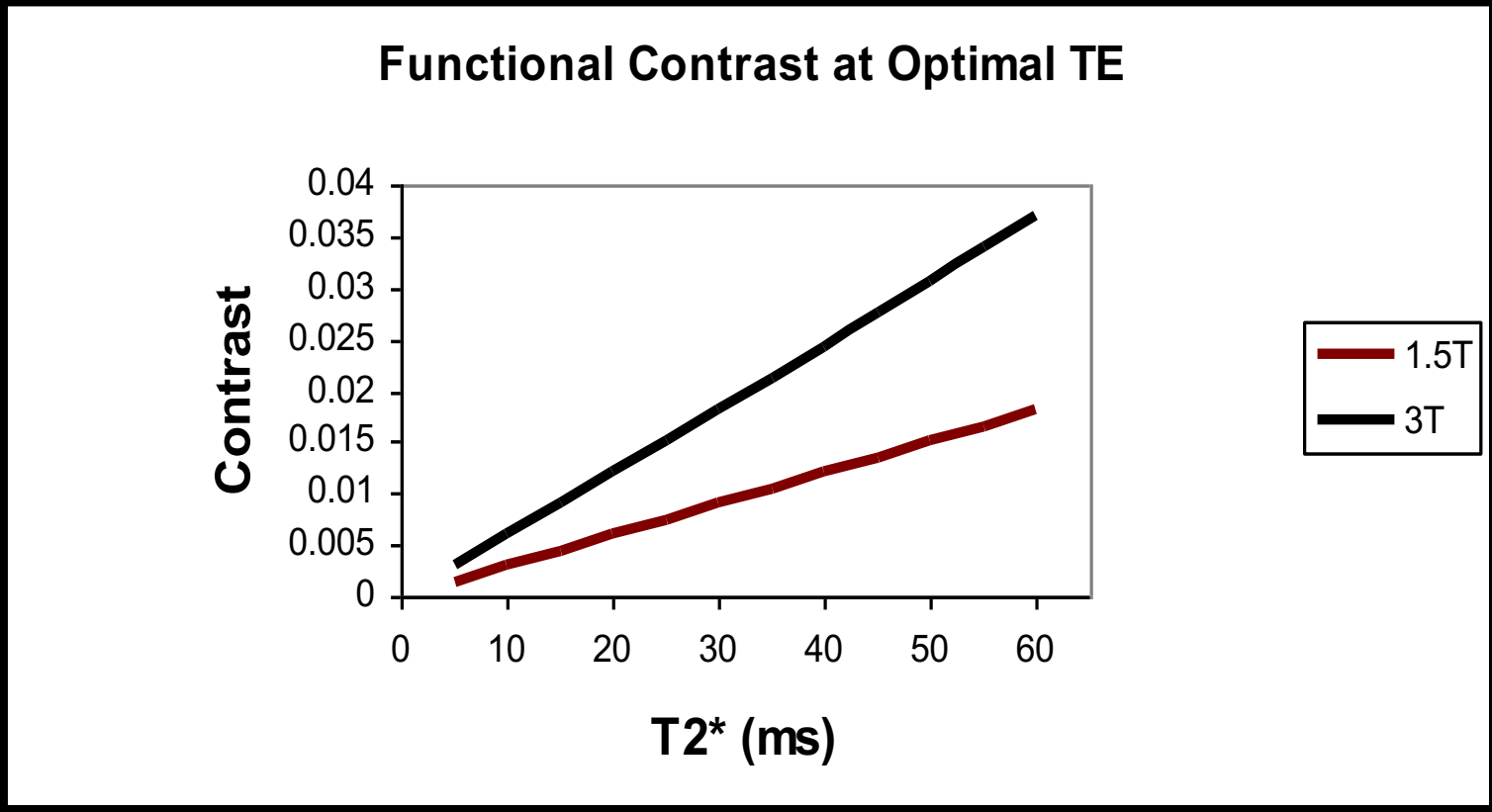



Functional Contrast at Optimal TE
Contrast
0.04
0.035
0.03
0.025
0.02
0.015
0.01
0.005
0
0
10
20
30
40
50
60
T2* (ms)
1.5T
3T

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

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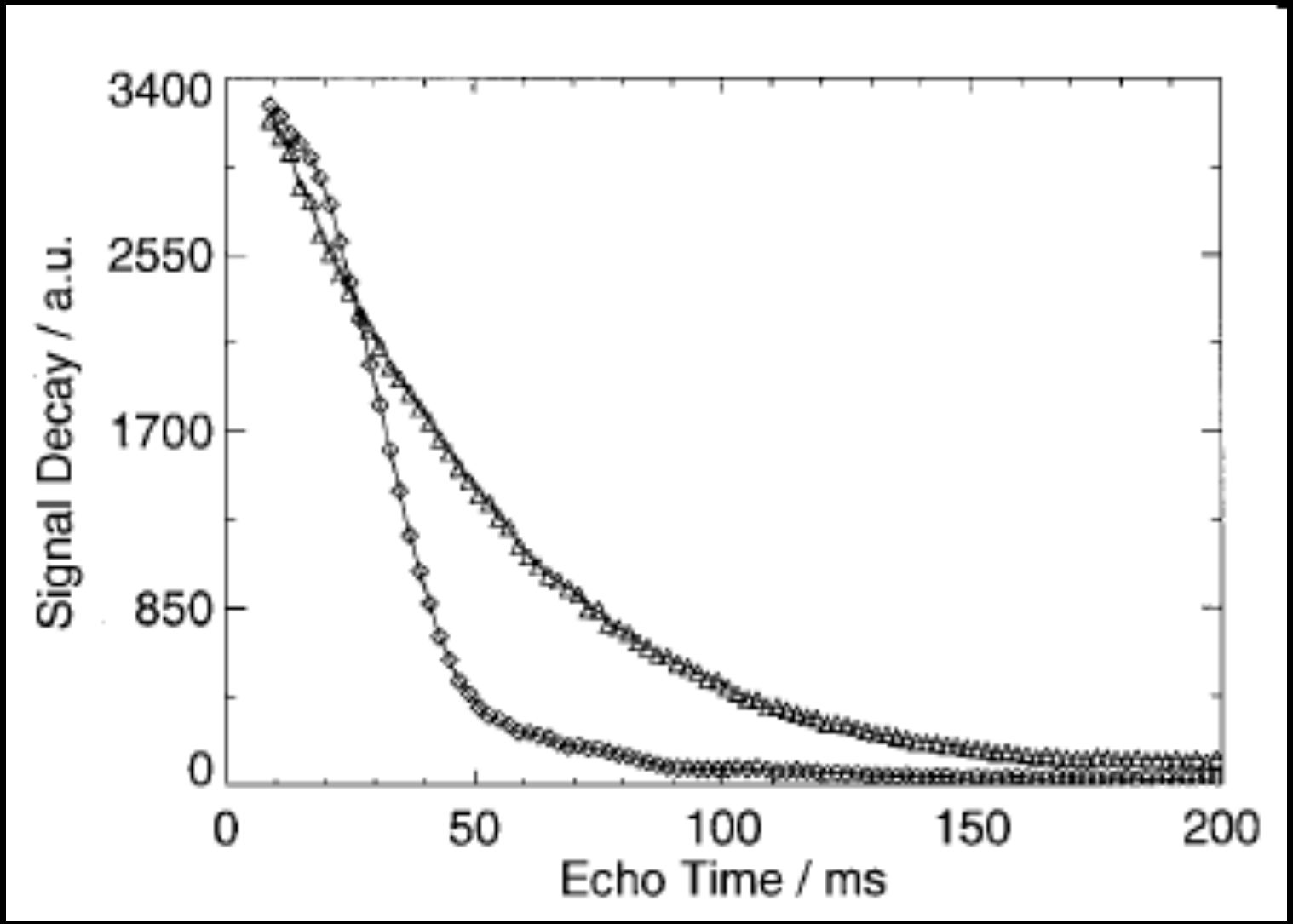
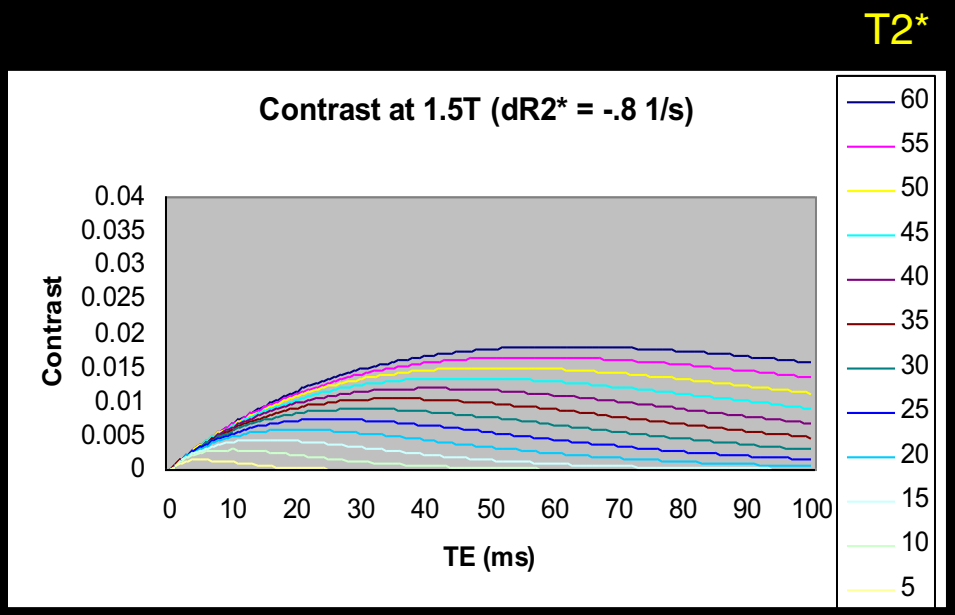
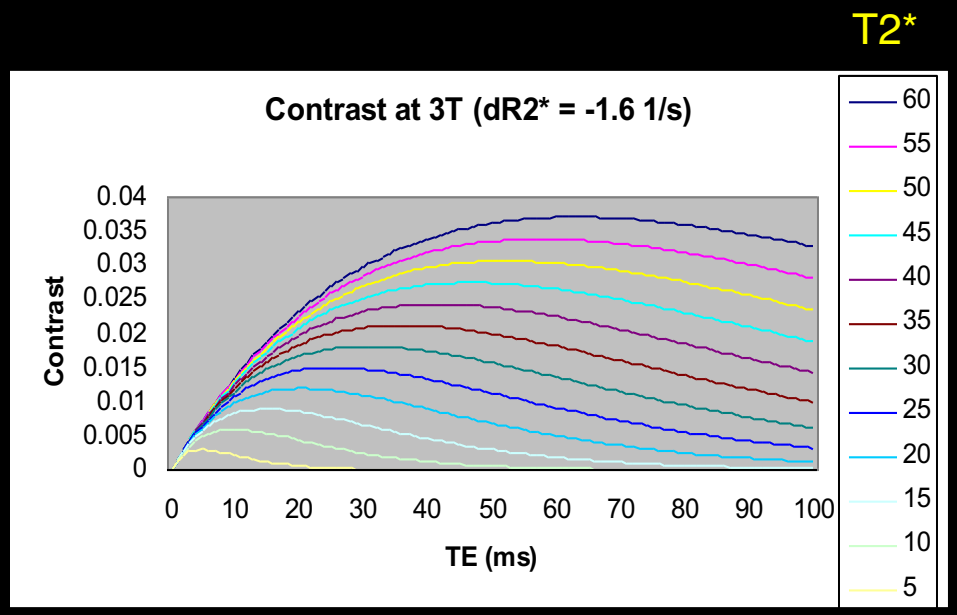
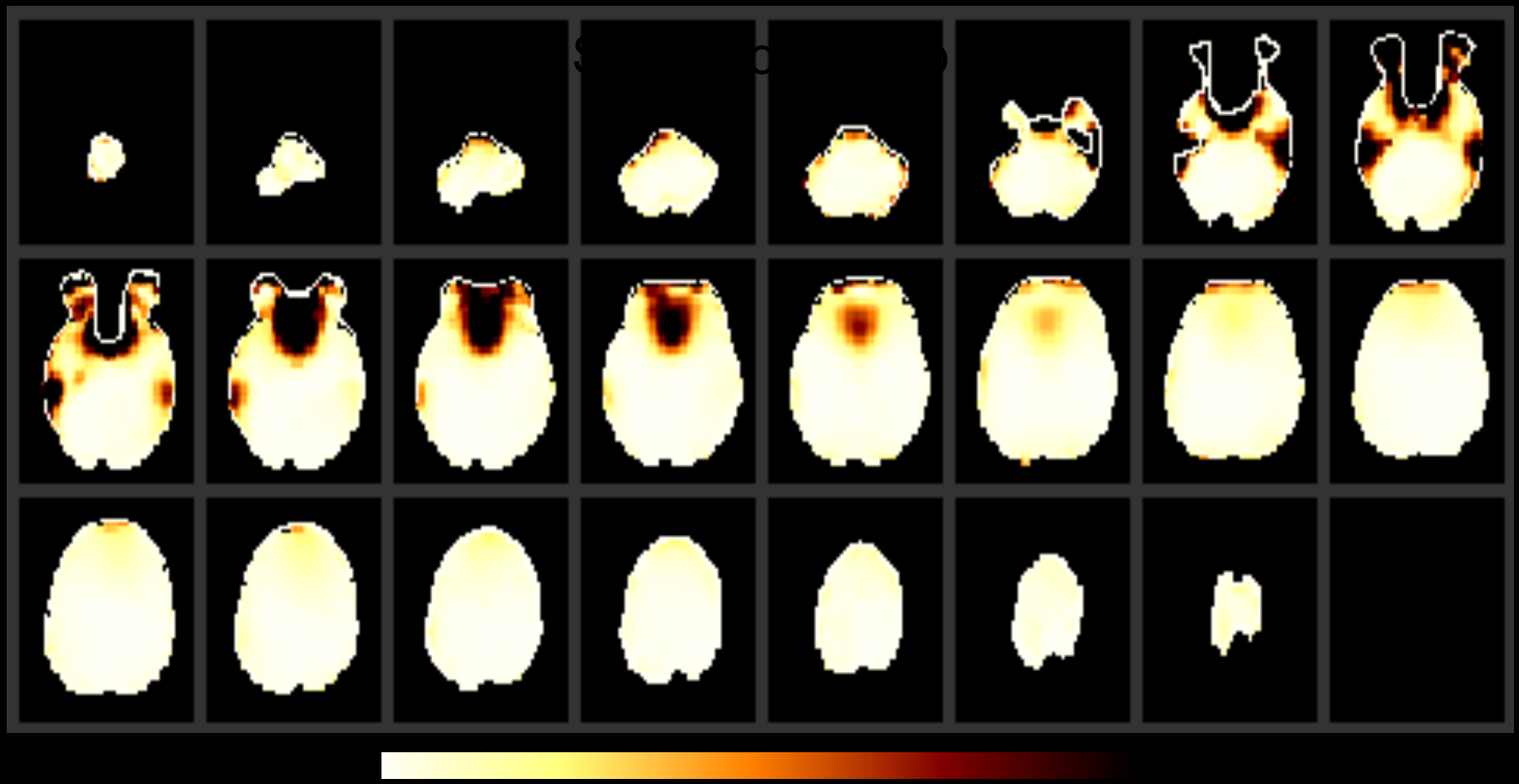


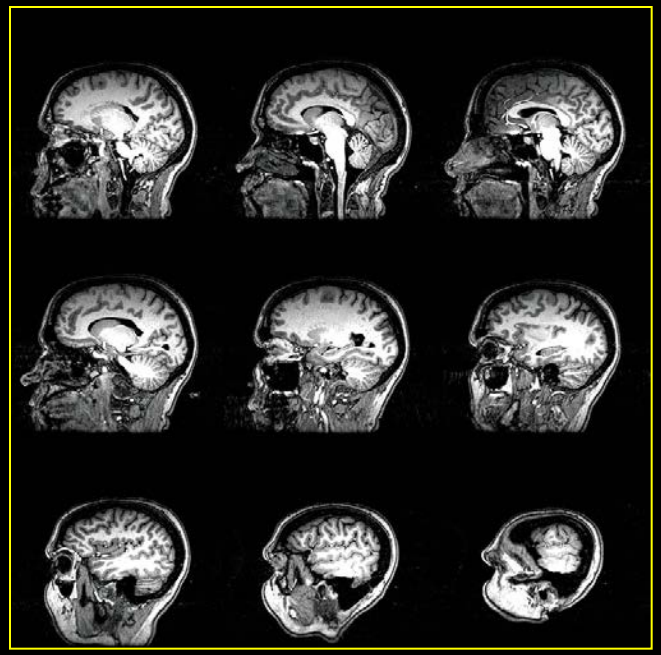
Contrast depends on:
activation-induced changes in T2* *and* resting T2*

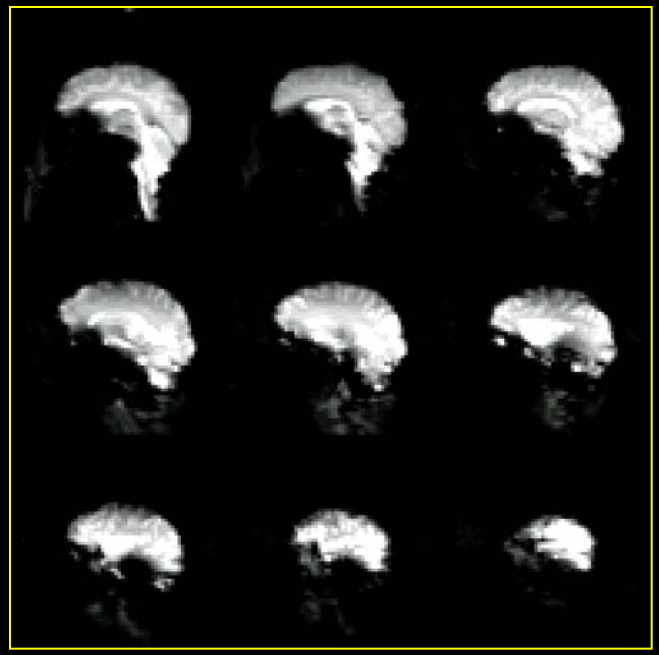


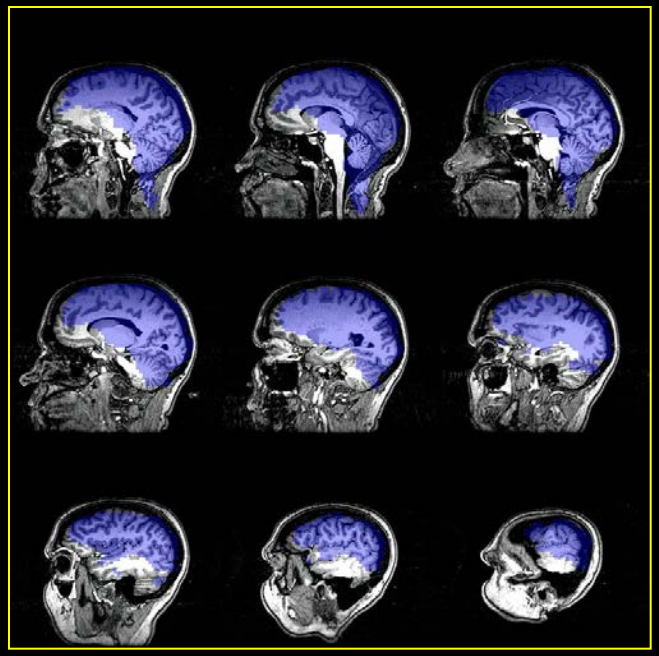


Gradient echo Signal Loss





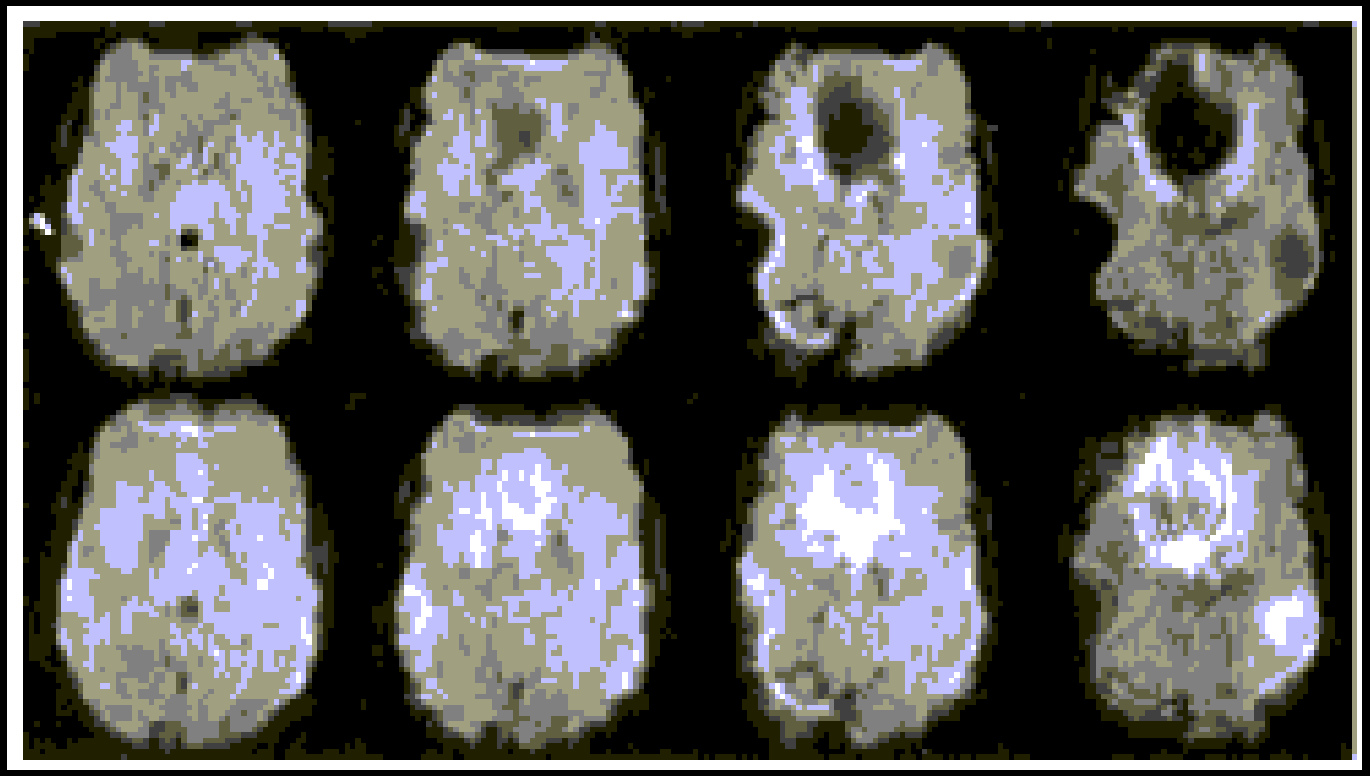


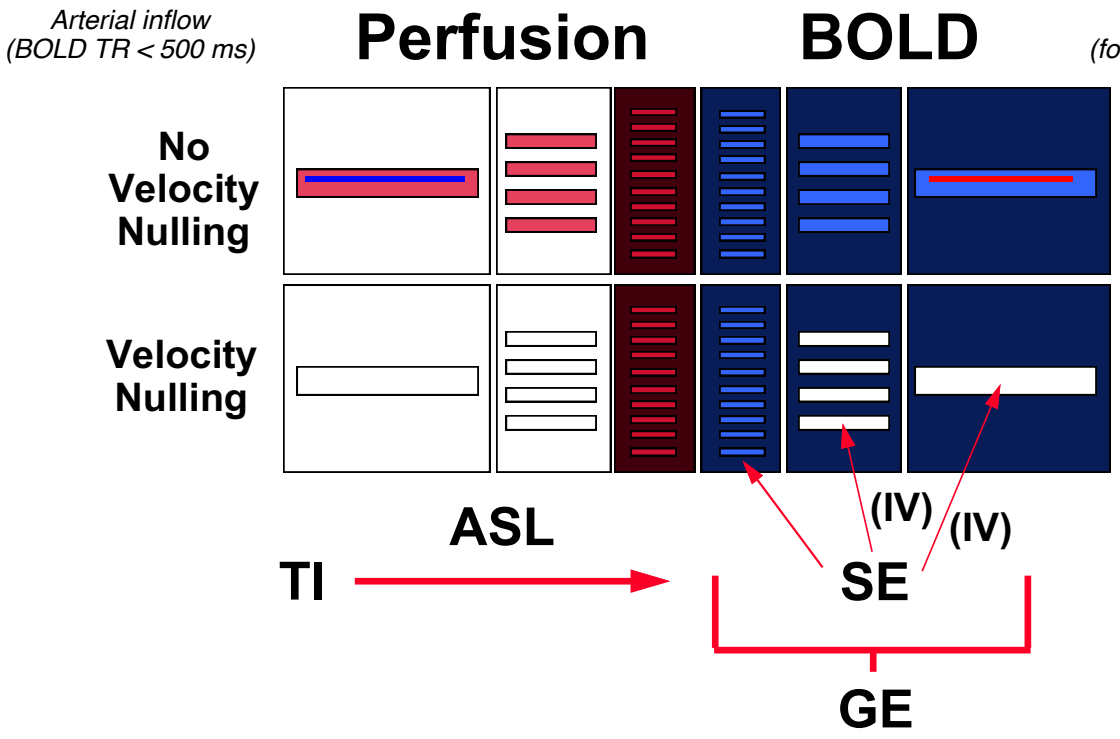


Magnetic Resonance in Medicine 42:290–299 (1999)

3D z-Shim Method for Reduction of Susceptibility Effects in BOLD fMRI

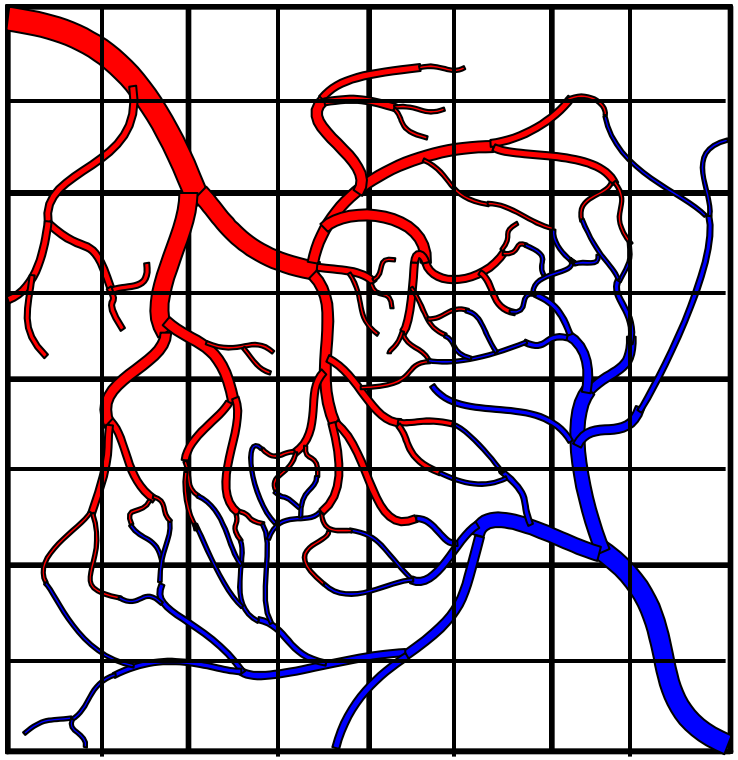
Gary H. Glover*





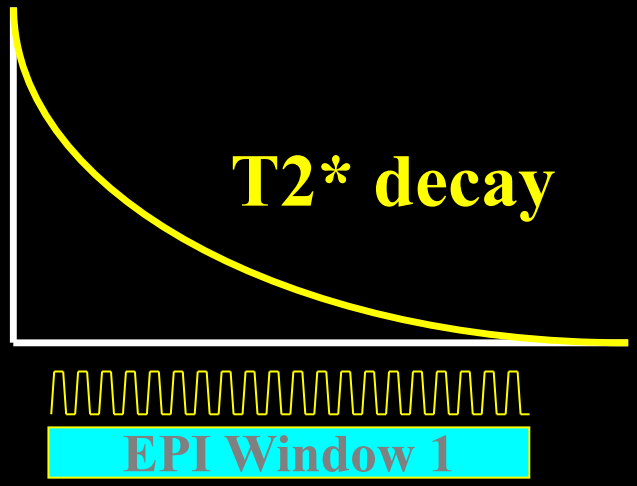
Pulse Sequence Sensitivity

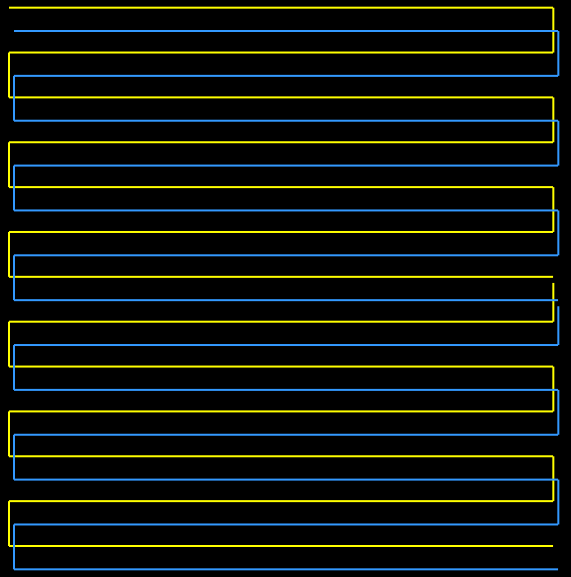
Spatial Heterogeneity

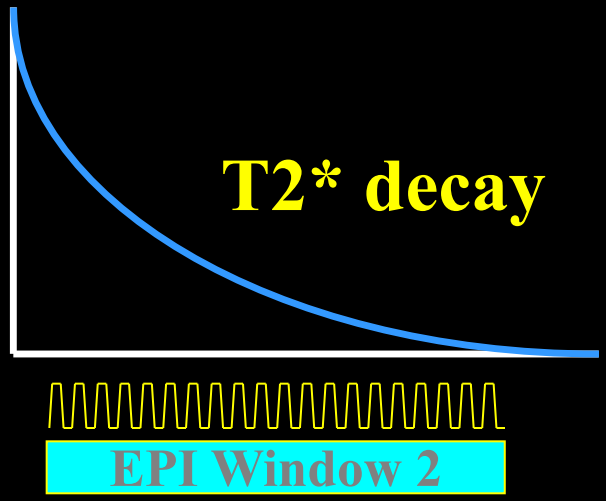


A few slides about Image Resolution and Noise...

Multishot Imaging

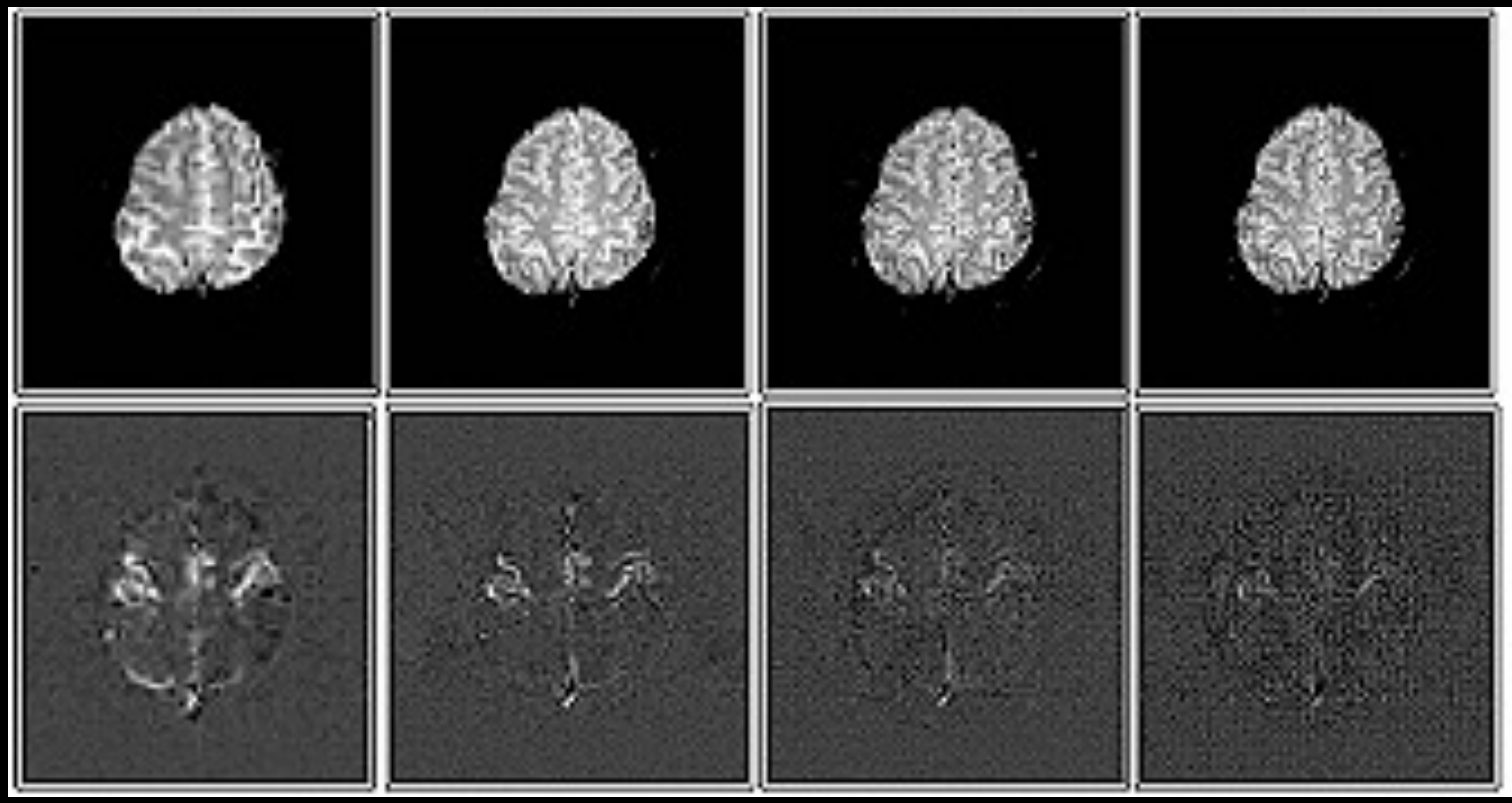




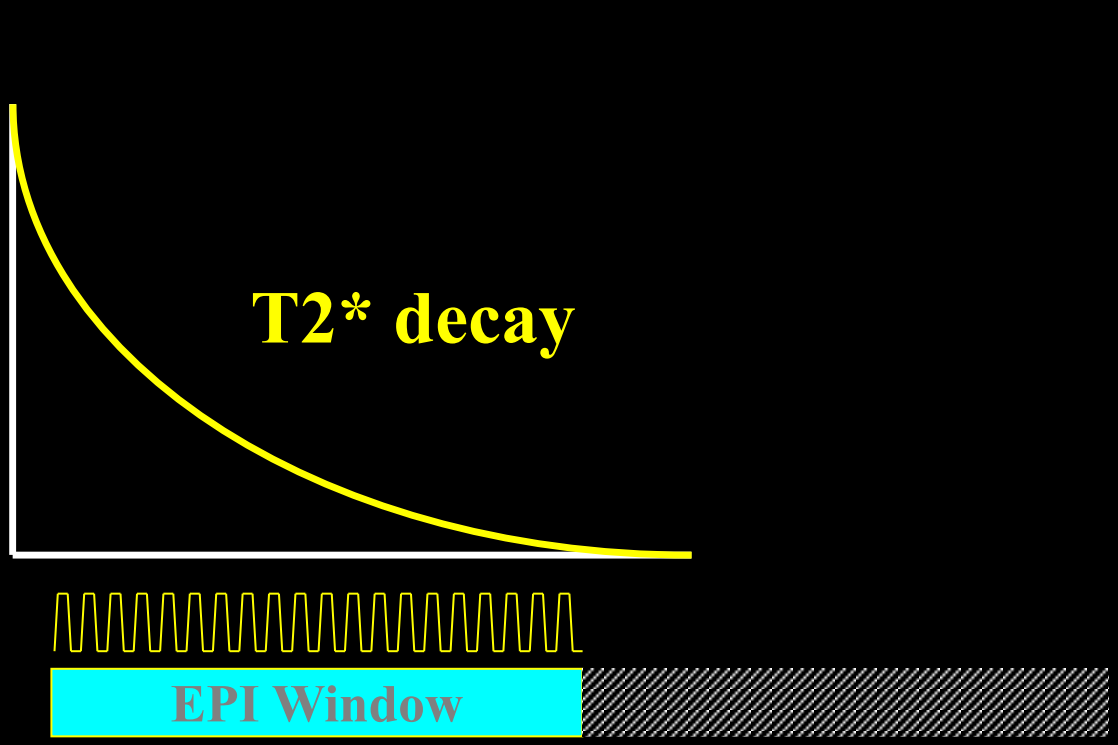


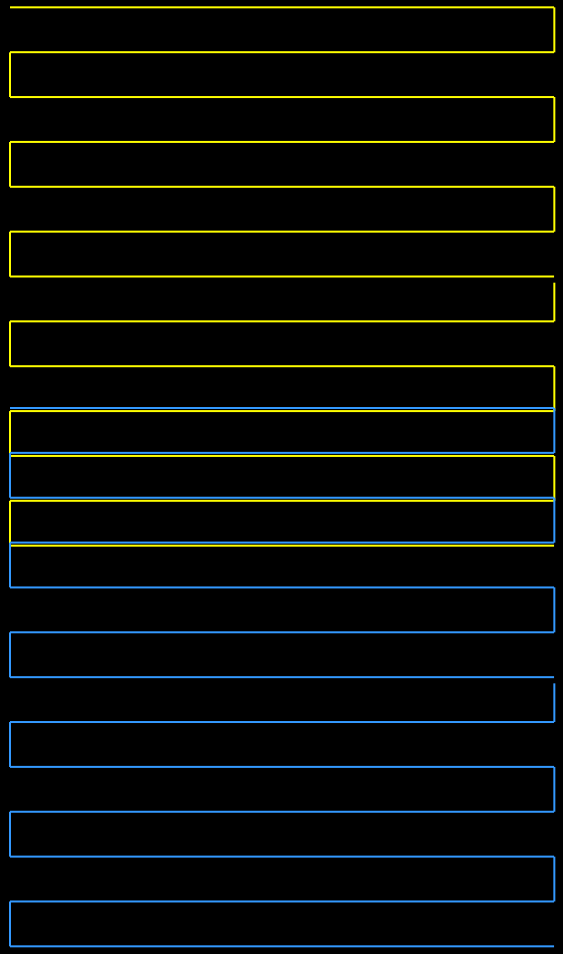
Multi Shot EPI

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

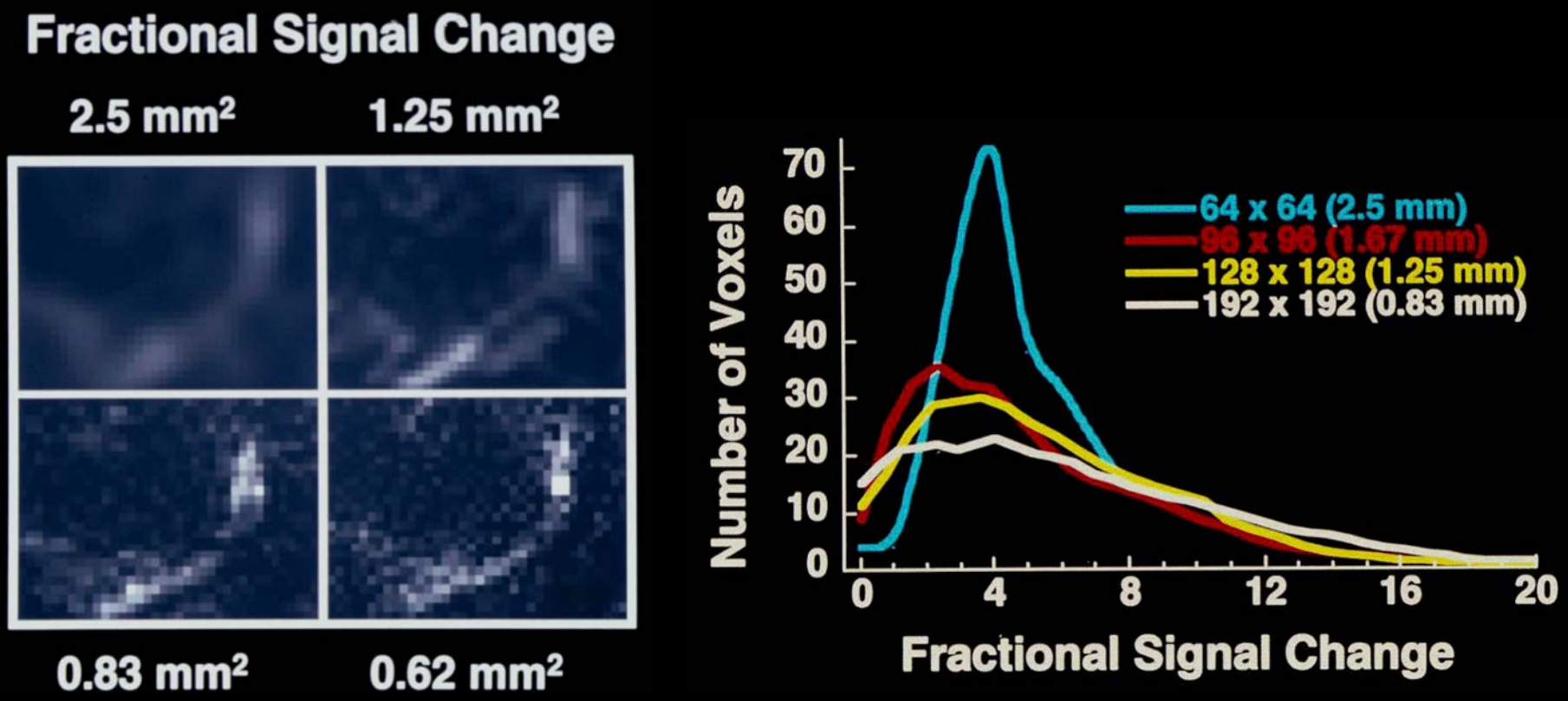


Partial k-space imaging



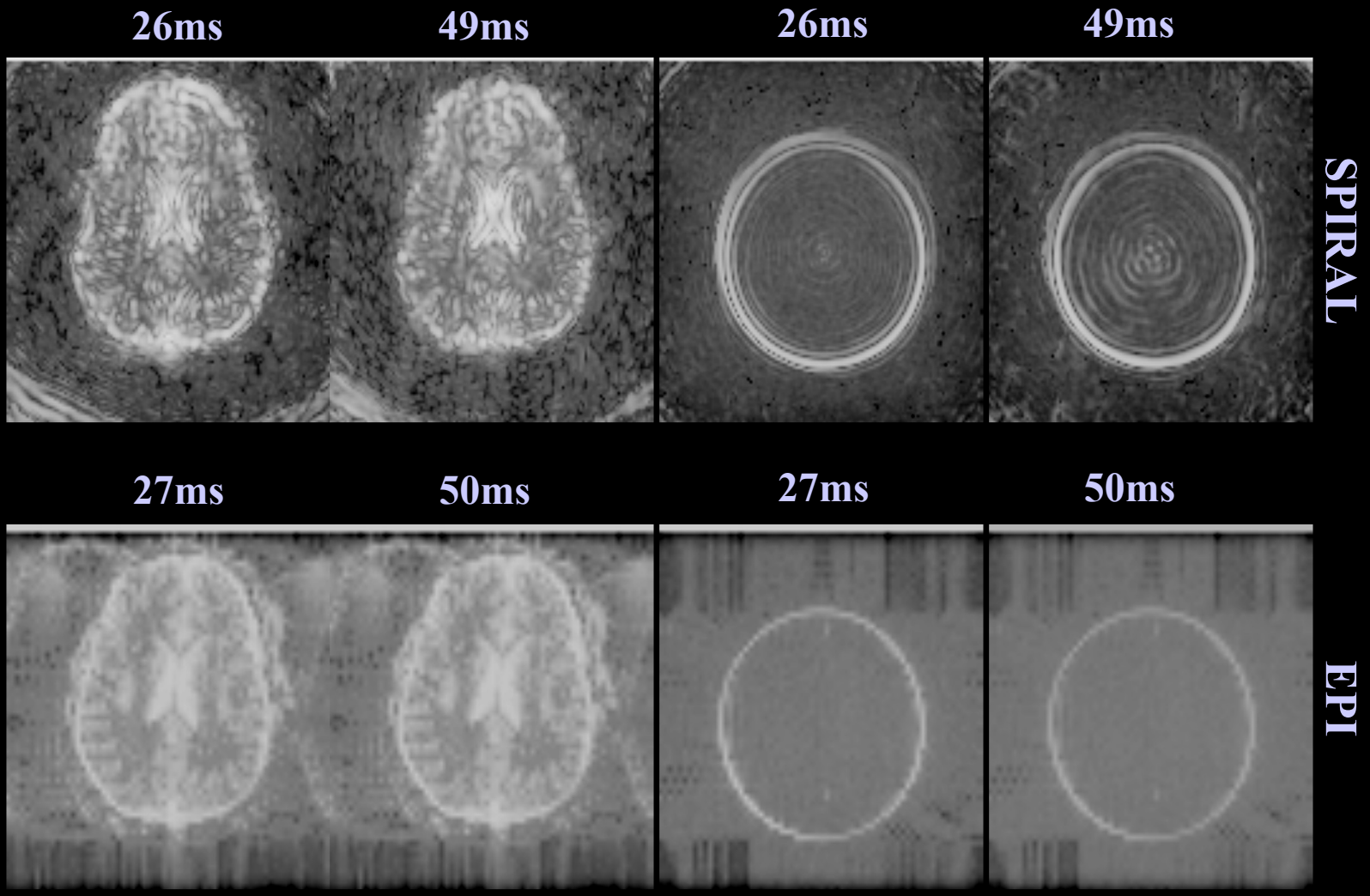


Partial k-space imaging

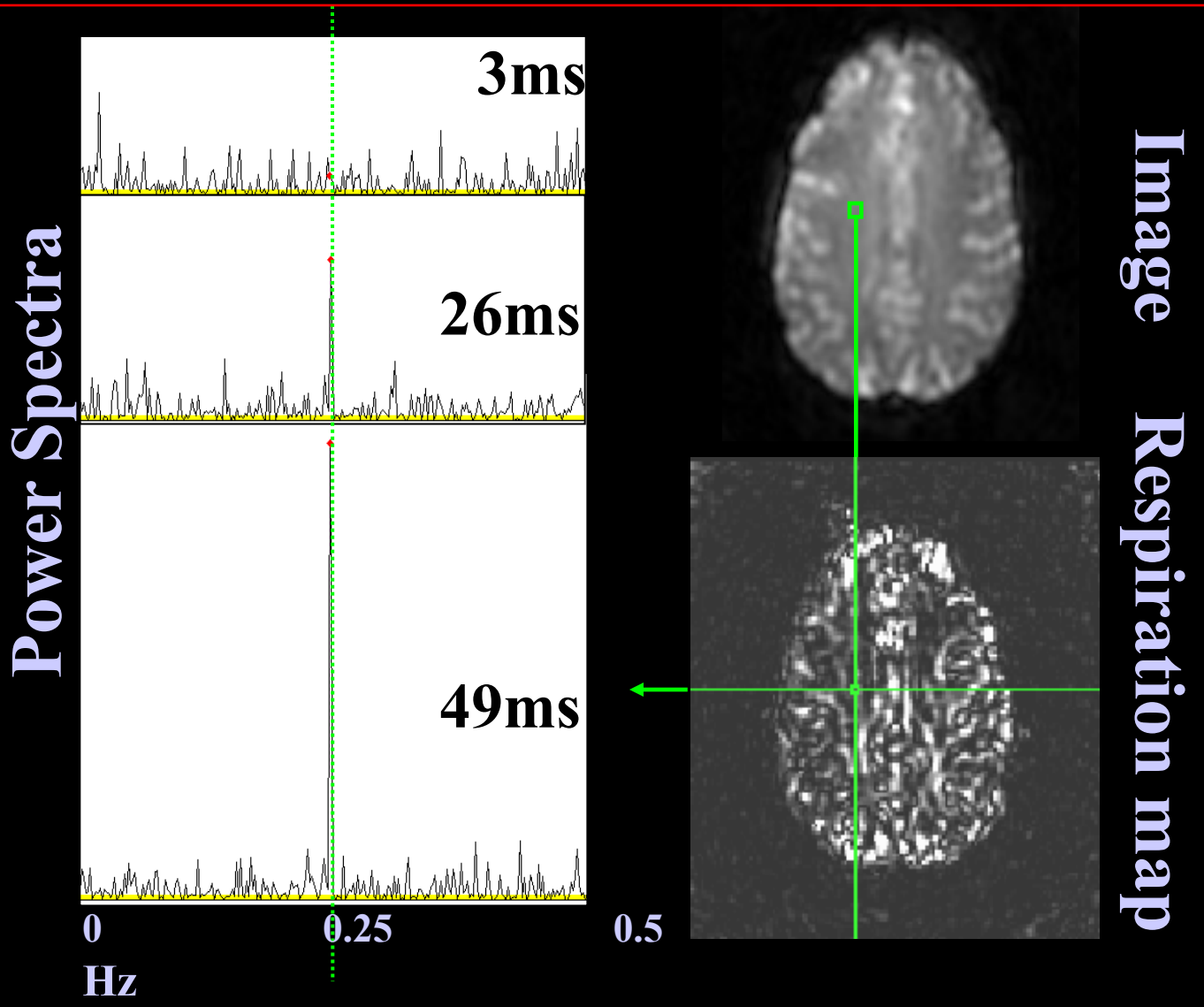


Jesmanowicz, P. A. Bandettini, J. S. Hyde, (1998) "Single shot half k-space high resolution EPI for fMRI at 3T." *Magn. Reson. Med.* 40, 754-762.

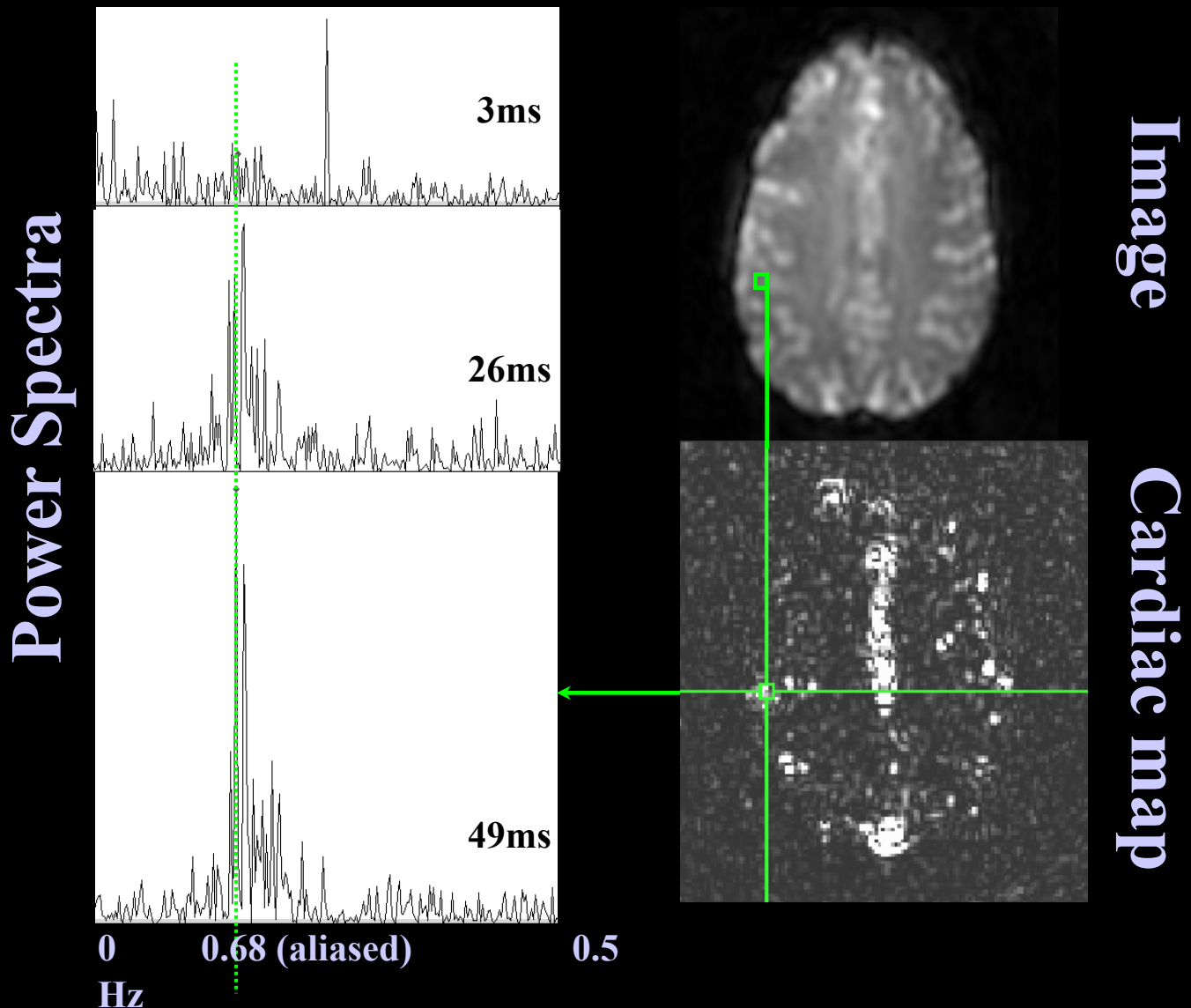
Temporal vs. Spatial SNR- 3T



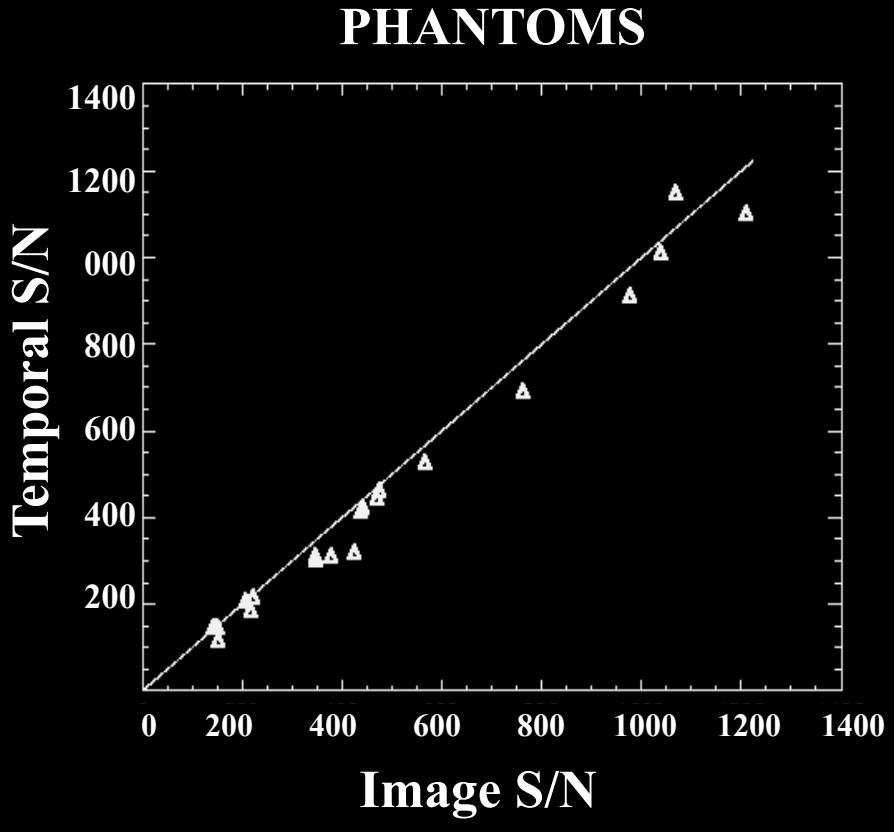
0.25 Hz Breathing at 3T

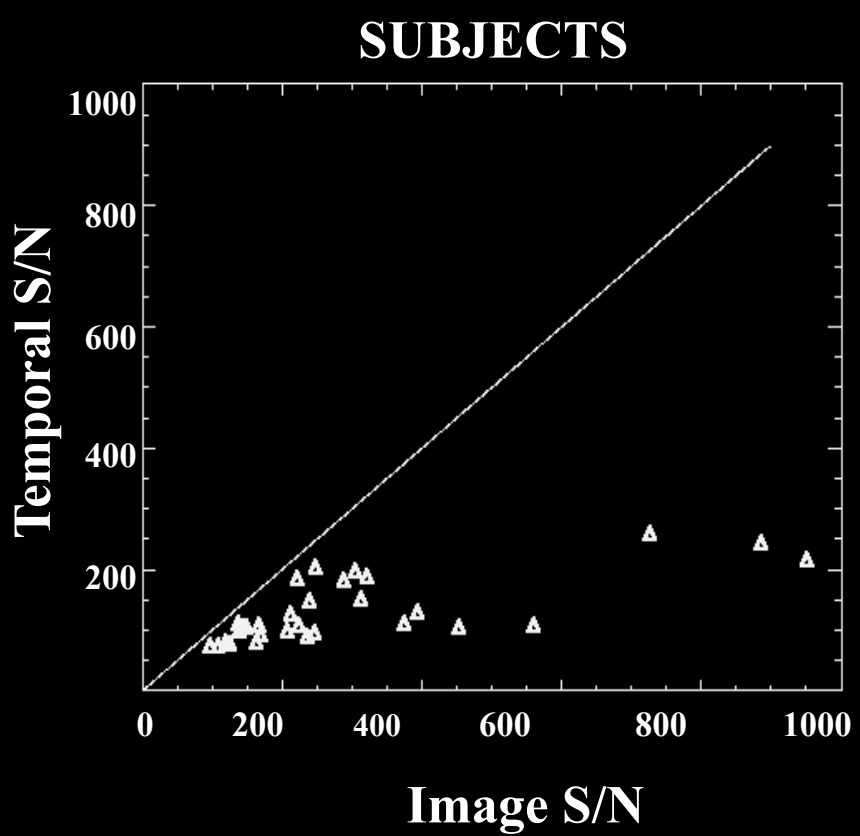


0.68 Hz Cardiac rate at 3T



Temporal S/N vs. Image S/N



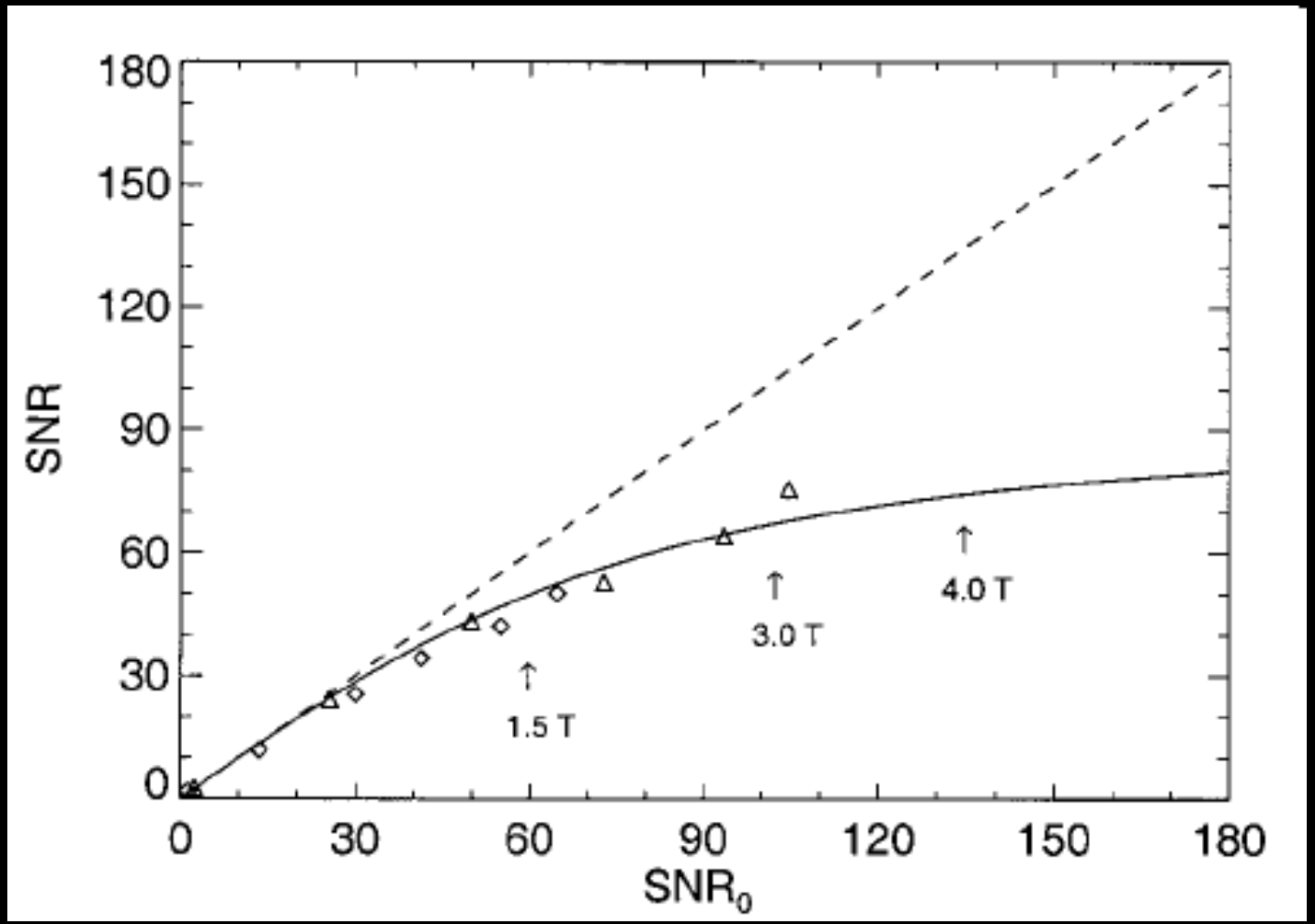


N. Petridou

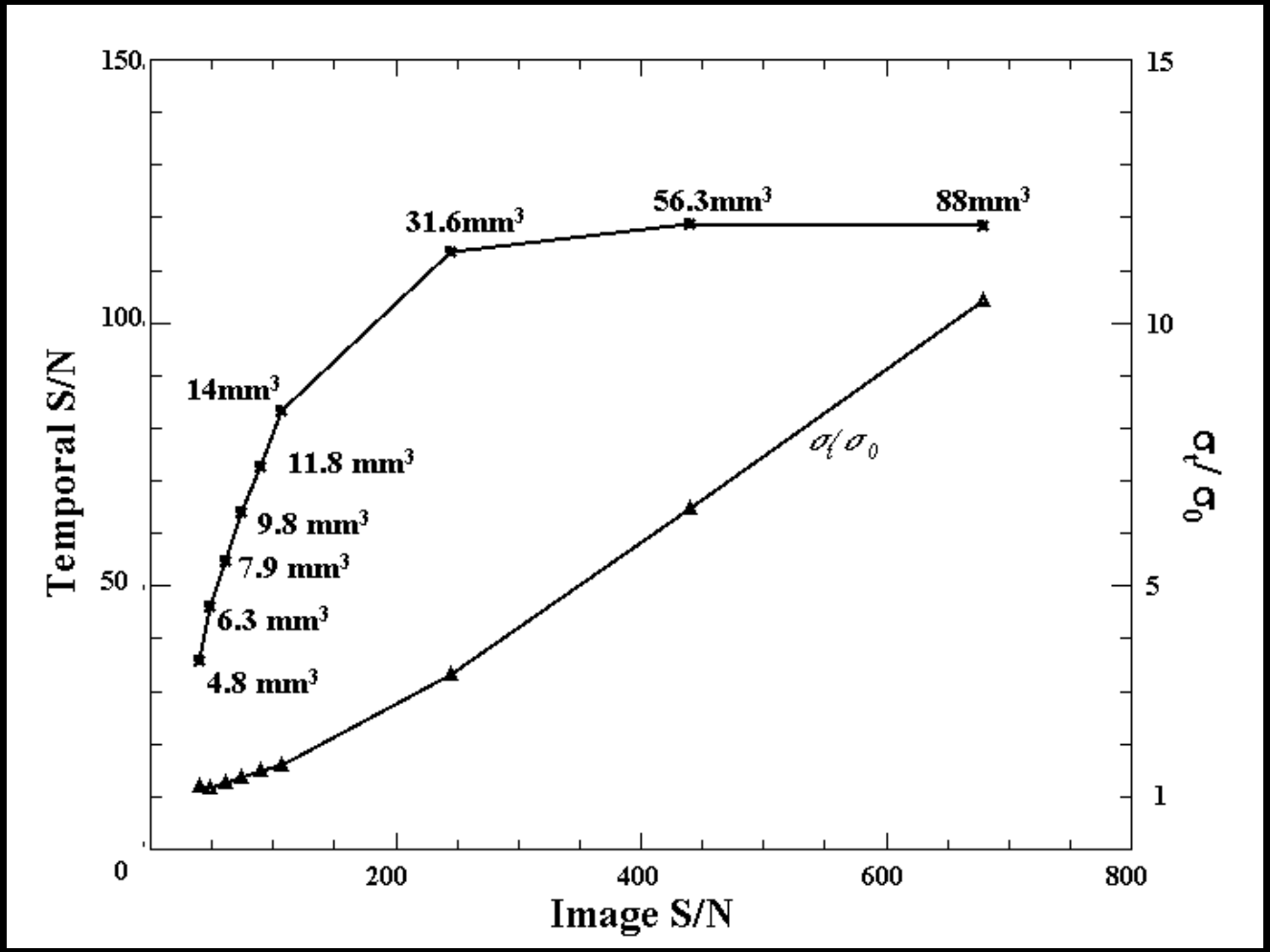
Magnetic Resonance in Medicine 45:595–604 (2001)

Neuroimaging at 1.5 T and 3.0 T: Comparison of Oxygenation-Sensitive Magnetic Resonance Imaging

Gunnar Krüger,* Andreas Kastrup, and Gary H. Glover



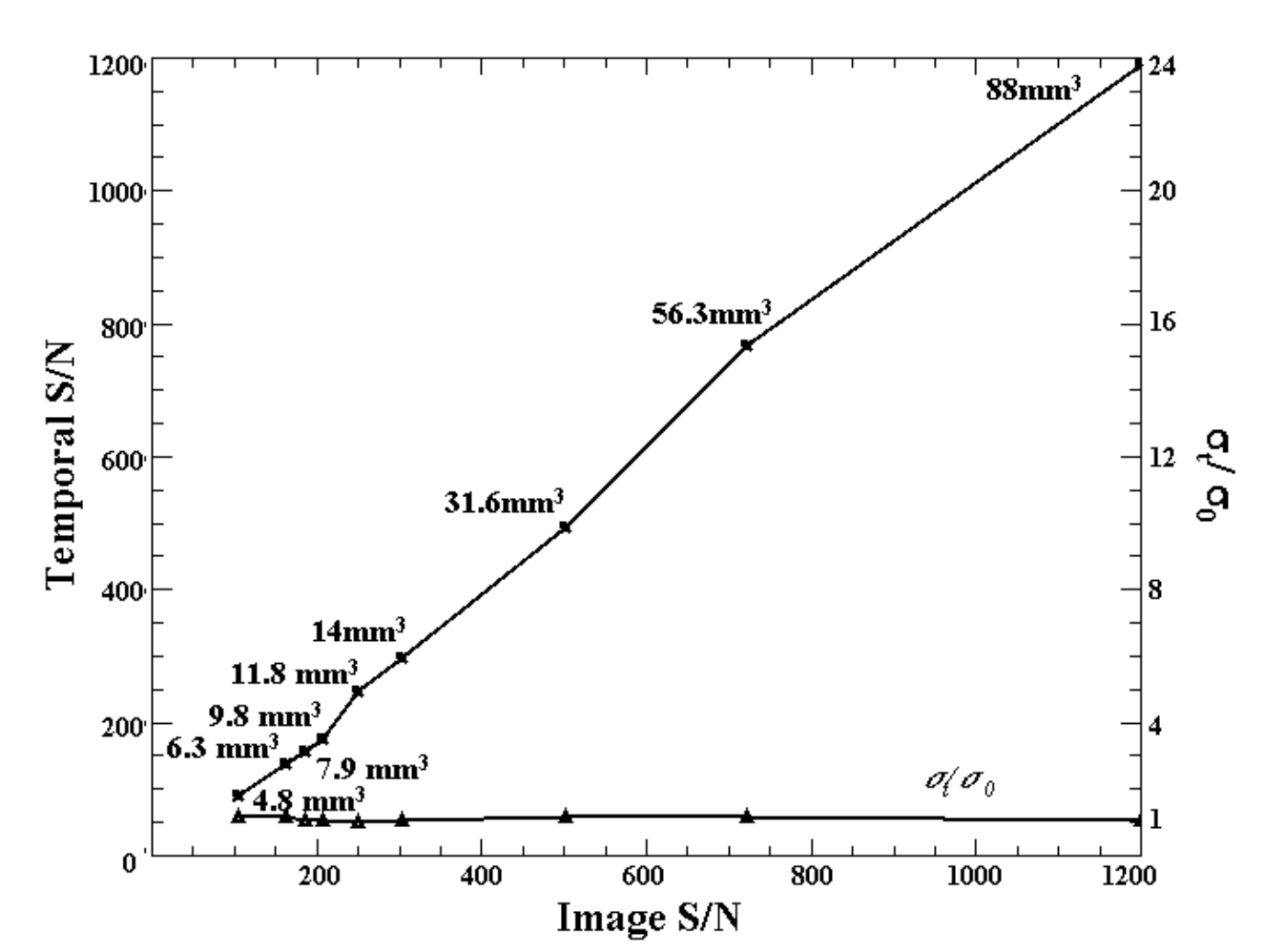
Temporal vs. Image S/N
Optimal Resolution Study



Human data

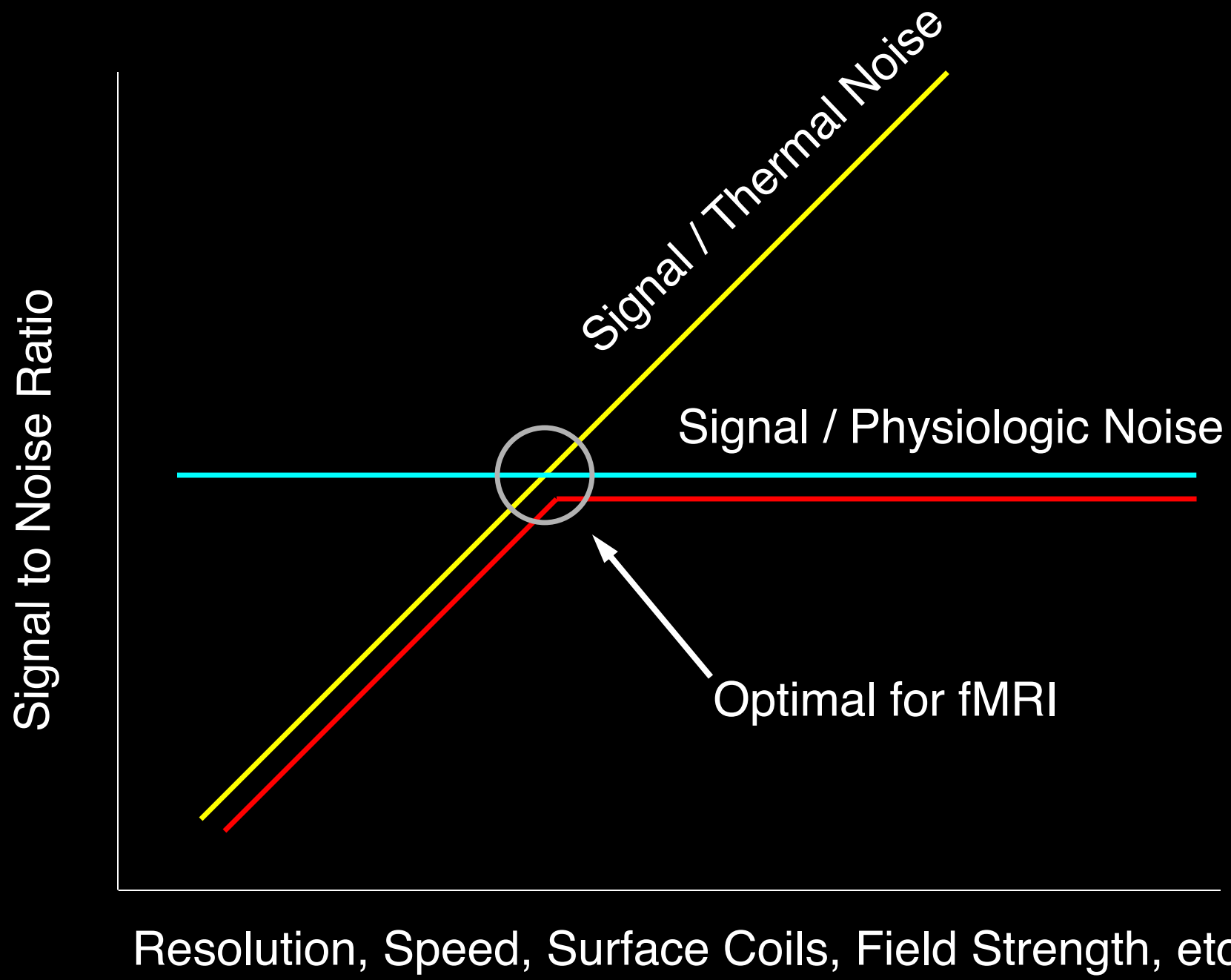
Petridou et al

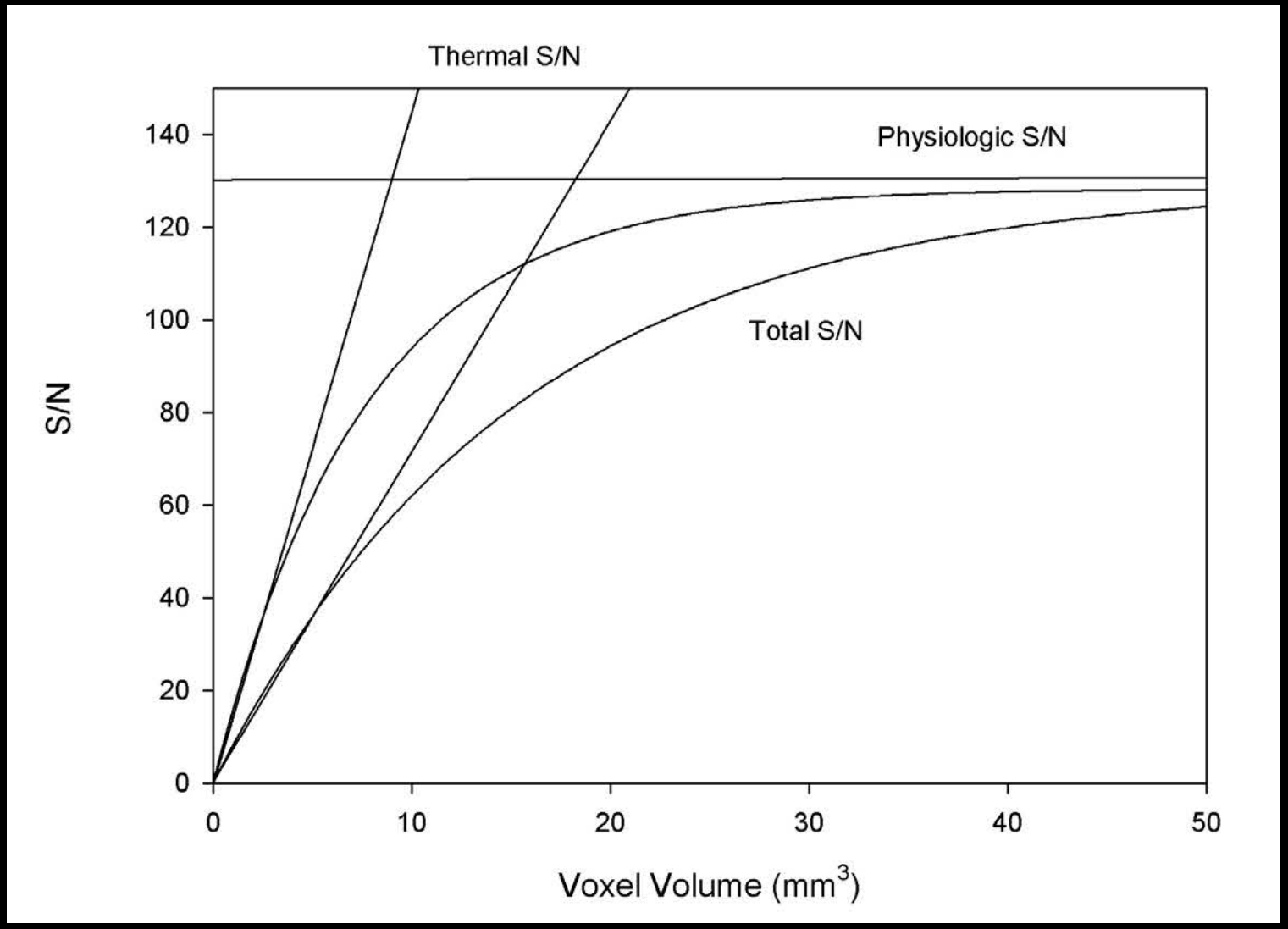
Temporal vs. Image S/N
Optimal Resolution Study



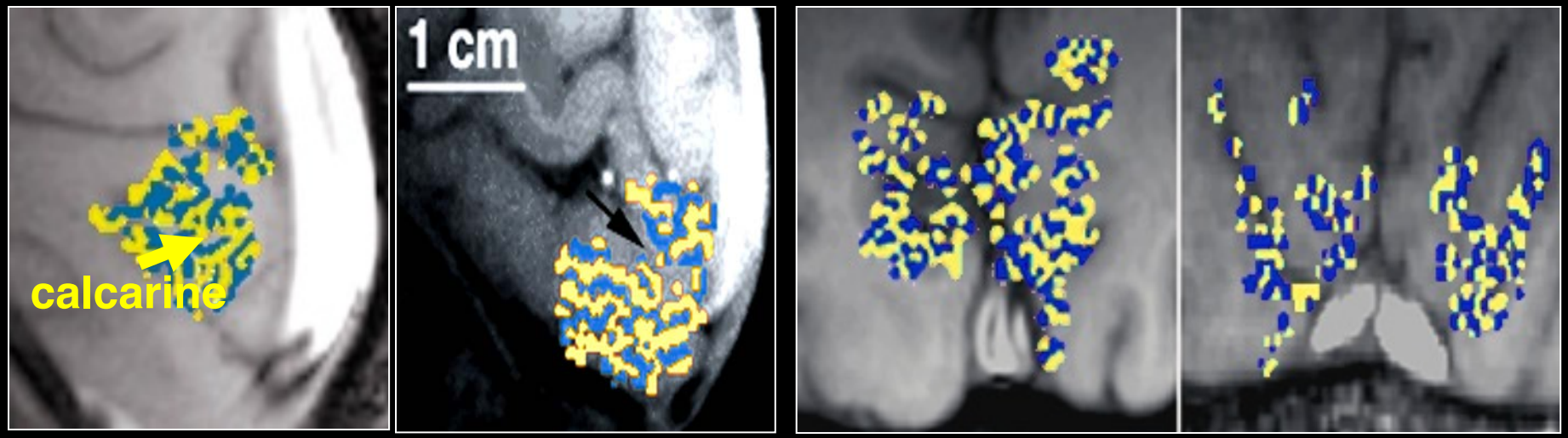
Phantom data

Petridou et al

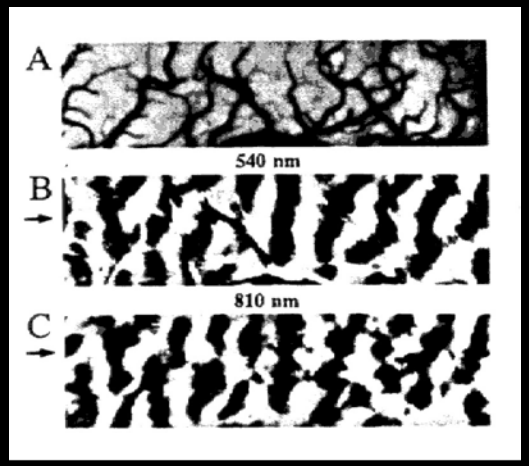

Signal / Thermal Noise
Signal / Physiologic Noise
Optimal for fMRI
Signal to Noise Ratio
Resolution, Speed, Surface Coils, Field Strength, etc..


Thermal S/N
Physiologic S/N
Total S/N
S/N
0
20
40
60
80
100
120
140
0
10
20
30
40
50
Voxel Volume (mm3)

Ocular Dominance Column Mapping using fMRI



Menon, R. S., S. Ogawa, et al. (1997). "Ocular dominance in human V1 demonstrated by functional magnetic resonance imaging." J Neurophysiol 77(5): 2780-7.



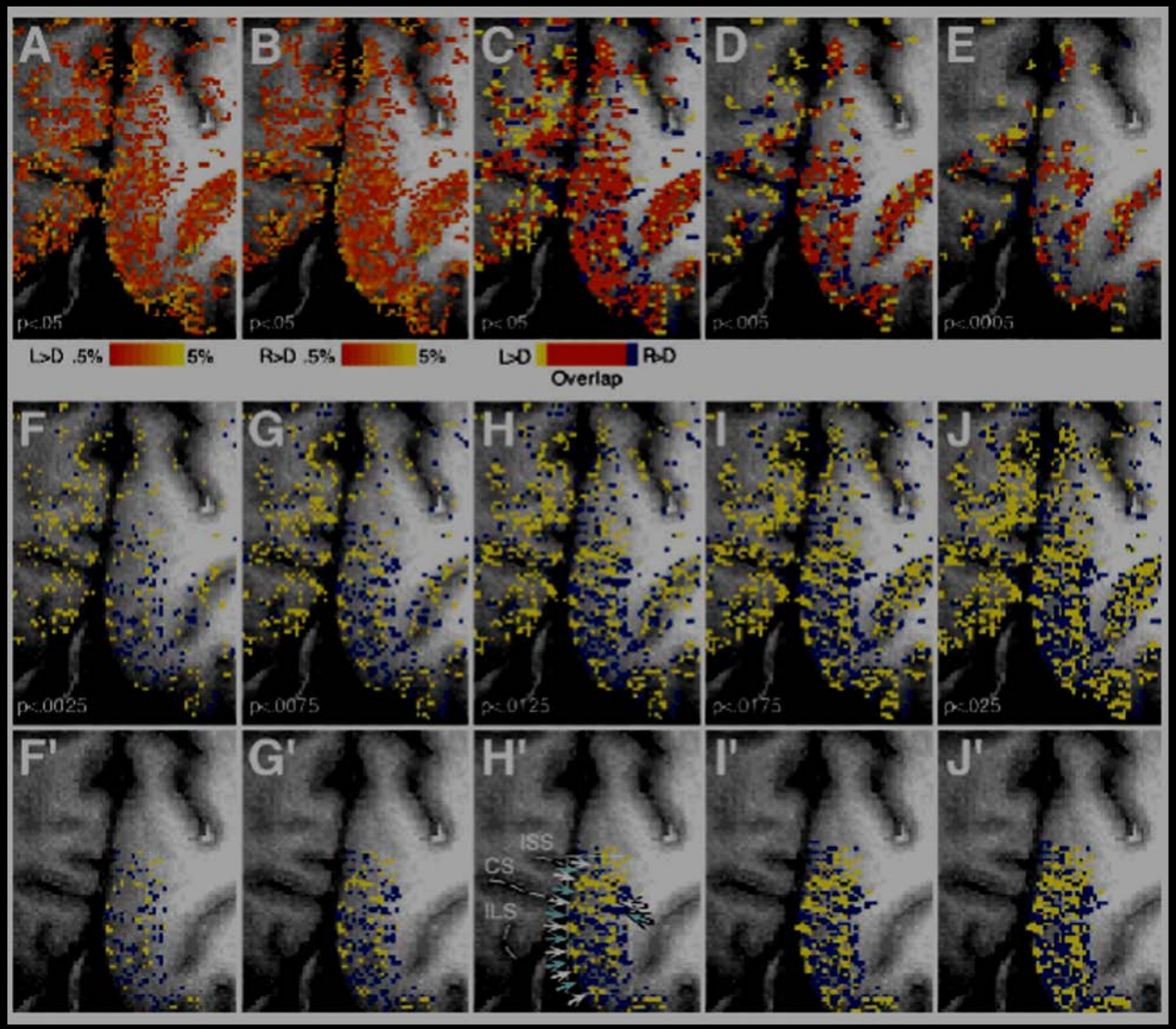
Optical Imaging

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

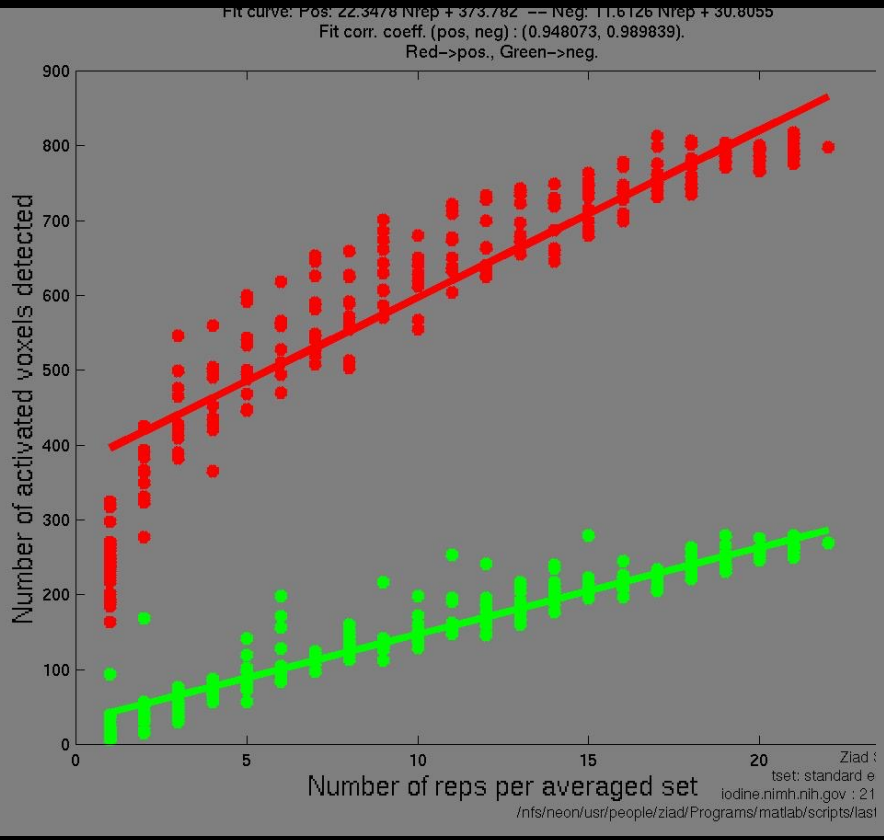
Neuron, Vol. 32, 359–374, October 25, 2001, Copyright ©2001 by Cell Press

Human Ocular Dominance Columns as Revealed by High-Field Functional Magnetic Resonance Imaging

Kang Cheng,[1] R. Allen Waggoner, and Keiji Tanaka
Laboratory for Cognitive Brain Mapping
RIKEN Brain Science Institute and
CREST
Japan Science and Technology Corporation
2-1 Hirosawa
Wako, Saitama 351-0198
Japan

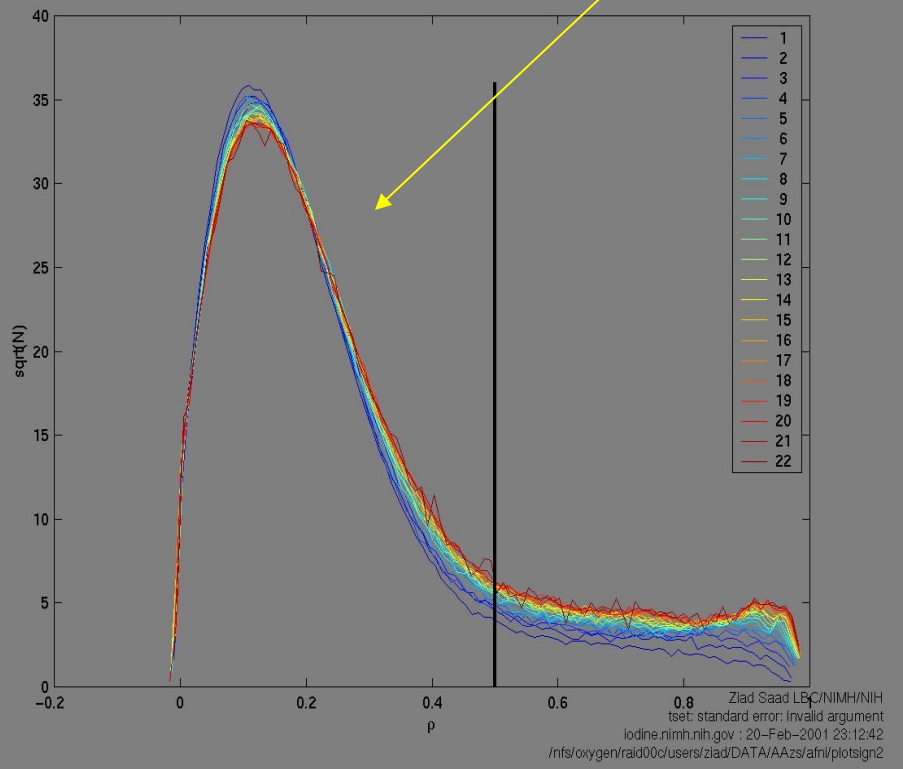


Continuously Growing Activation Area



CC Histogram

Inflection Point



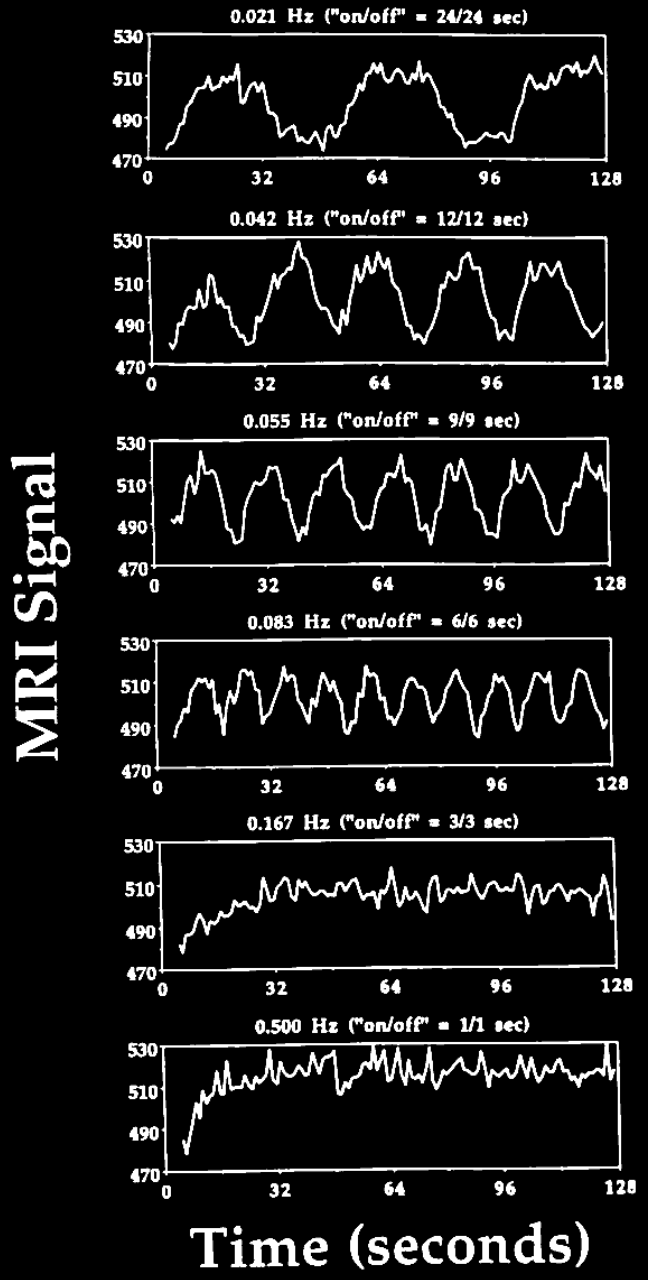
Ziad Saad, et al (Submitted)

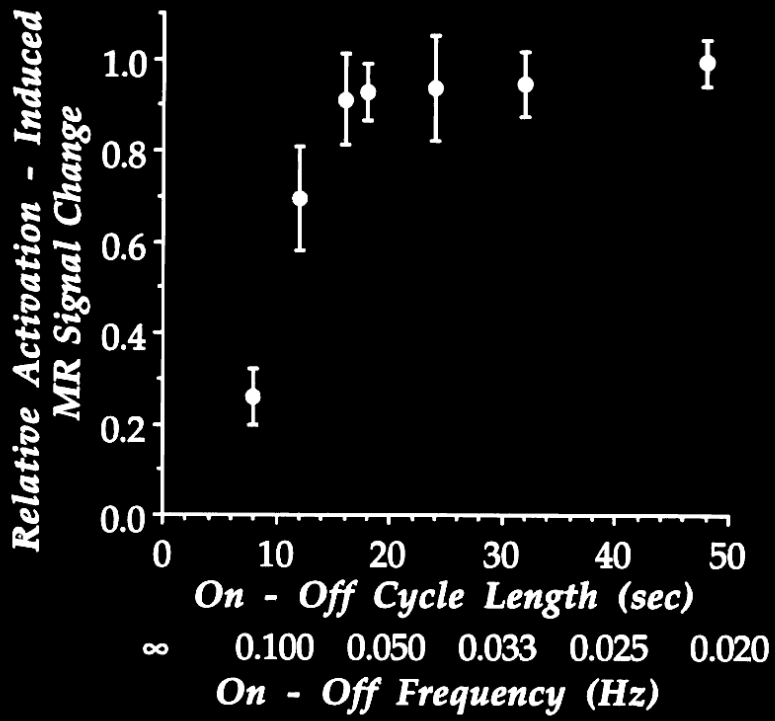
Refinements

BOLD Contrast Interpretation

Dynamics

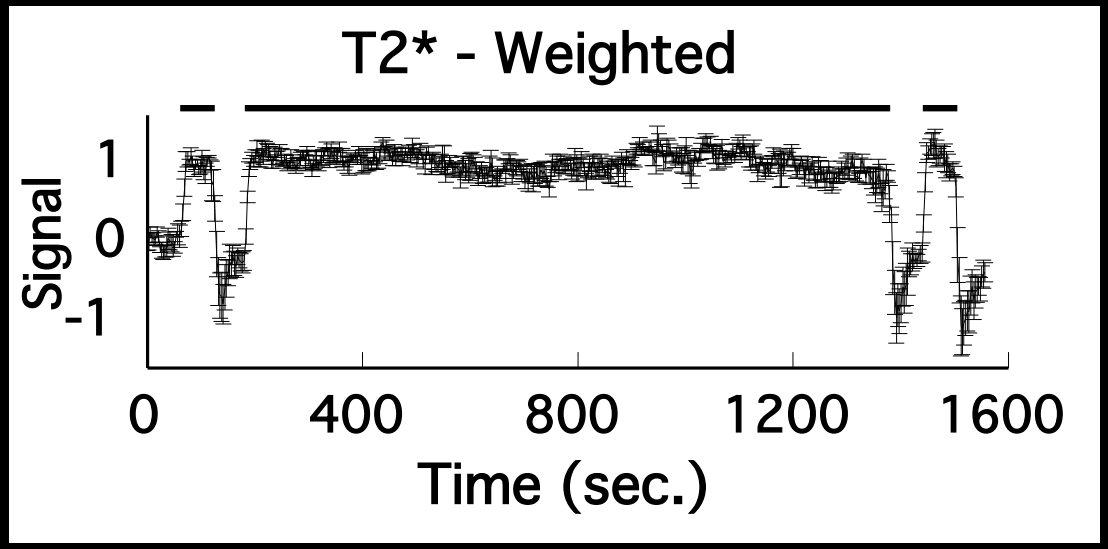
Paradigm Design and Processing



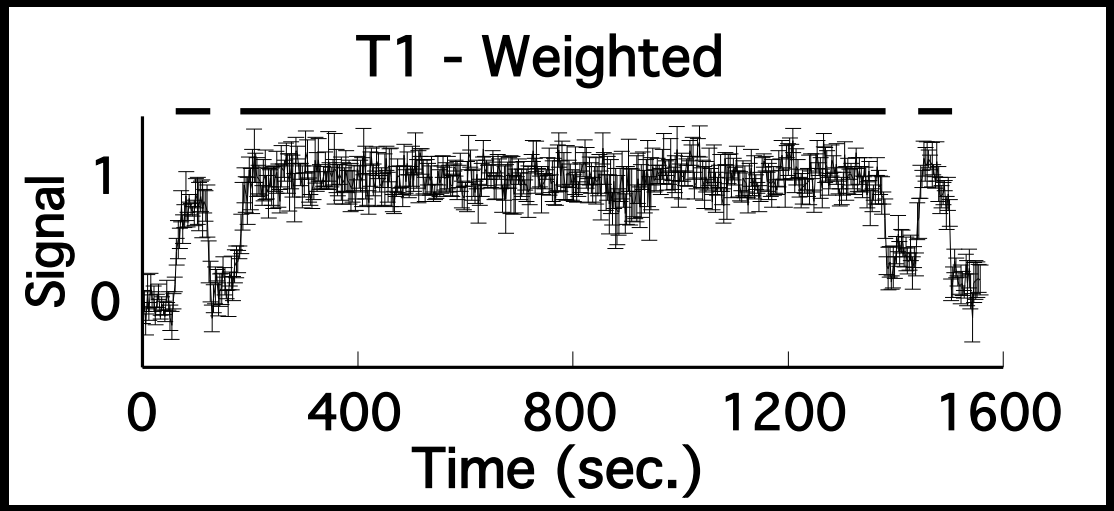


P. A. Bandettini, Functional MRI temporal resolution *in* "Functional MRI" (C. Moonen, and P. Bandettini., Eds.), p. 205-220, Springer - Verlag,. 1999.

BOLD

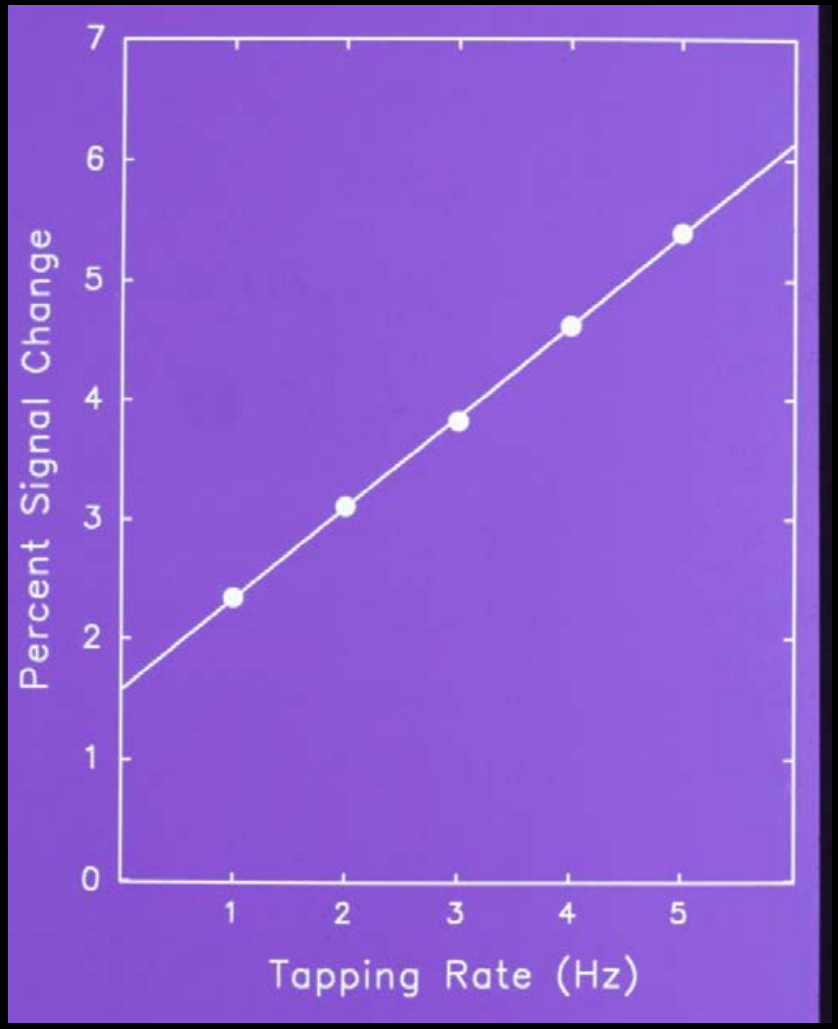


Flow



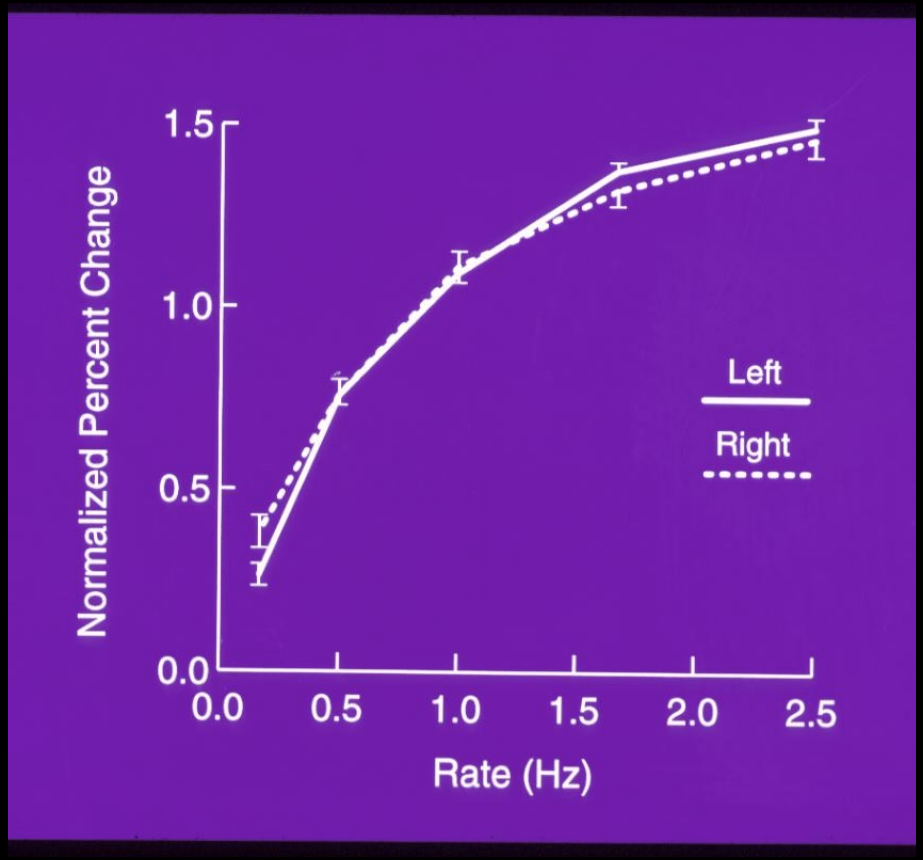
P. A. Bandettini, K. K. Kwong, T. L. Davis, R. B. H. Tootell, E. C. Wong, P. T. Fox, J. W. Belliveau, R. M. Weisskoff, B. R. Rosen, (1997). "Characterization of cerebral blood oxygenation and flow changes during prolonged brain activation." *Human Brain Mapping* 5, 93-109.

Motor Cortex

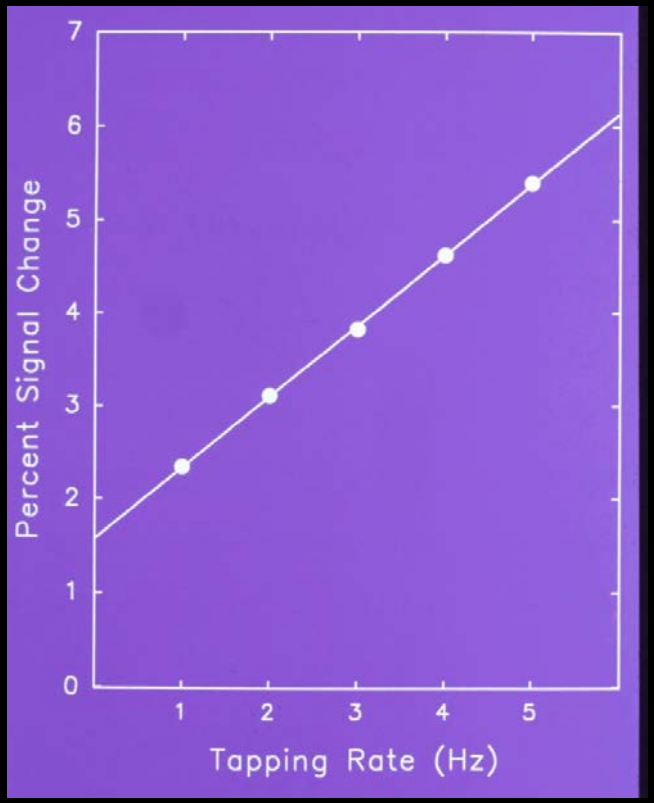


S. M. Rao et al, (1996) "Relationship between finger movement rate and functional magnetic resonance signal change in human primary motor cortex." *J. Cereb. Blood Flow and Met.* 16, 1250-1254.

Auditory Cortex

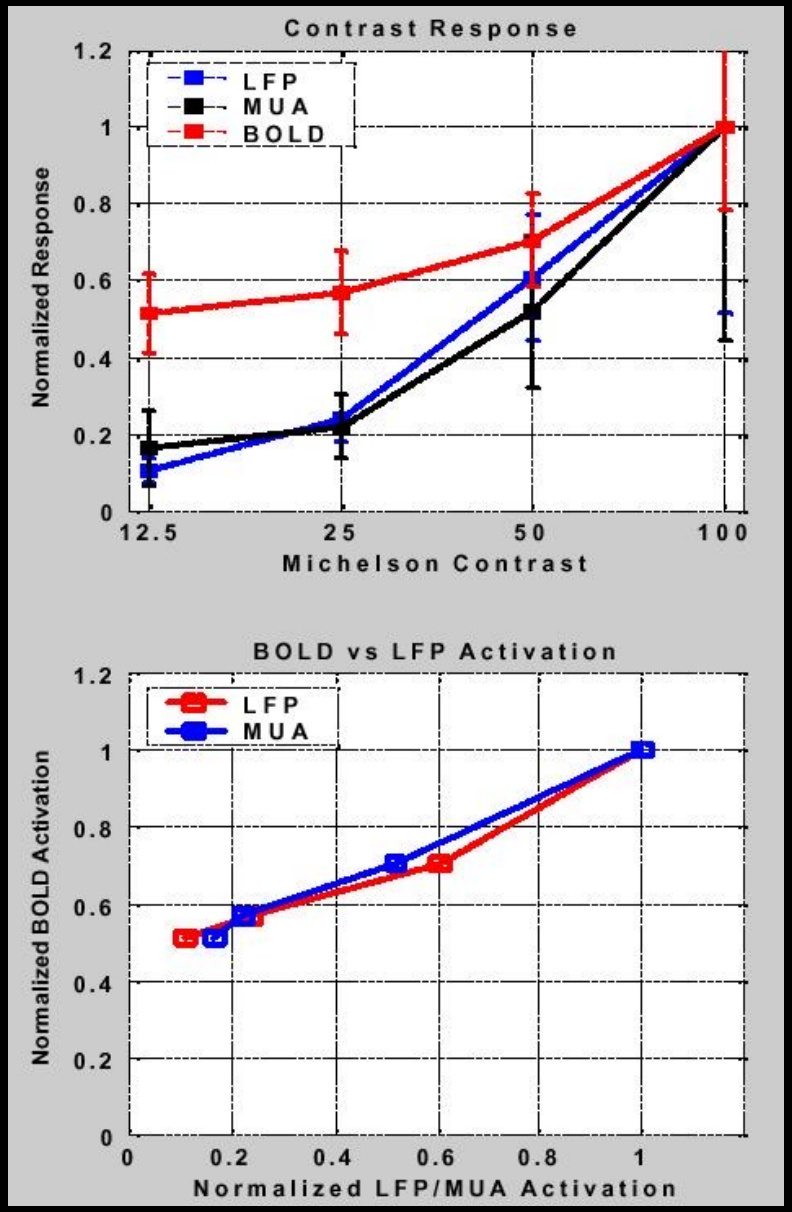


J. R. Binder, et al, (1994). "Effects of stimulus rate on signal response during functional magnetic resonance imaging of auditory cortex." *Cogn. Brain Res.* 2, 31-38

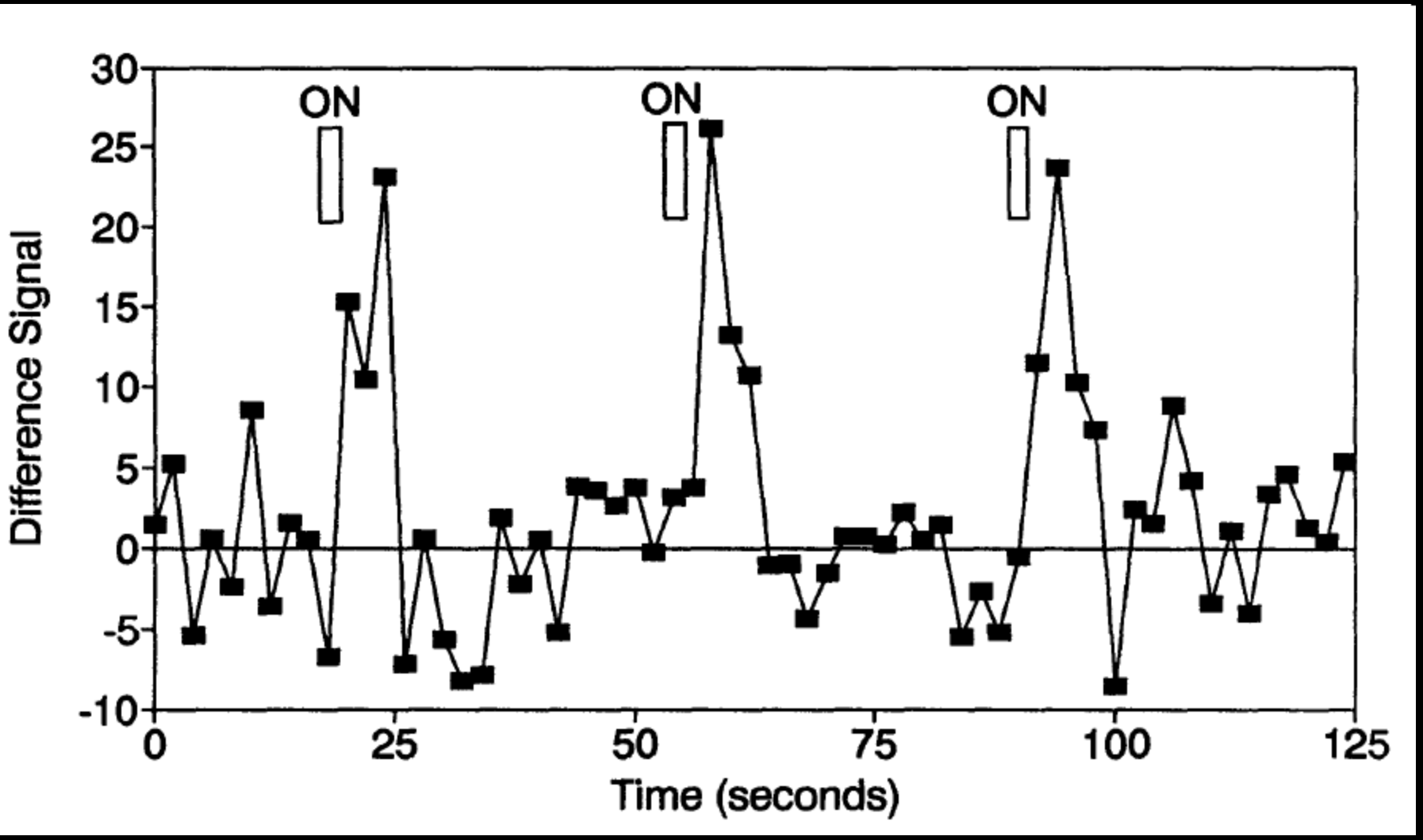


S. M. Rao et al, (1996) "Relationship between finger movement rate and functional magnetic resonance signal change in human primary motor cortex." *J. Cereb. Blood Flow and Met.* 16, 1250-1254.

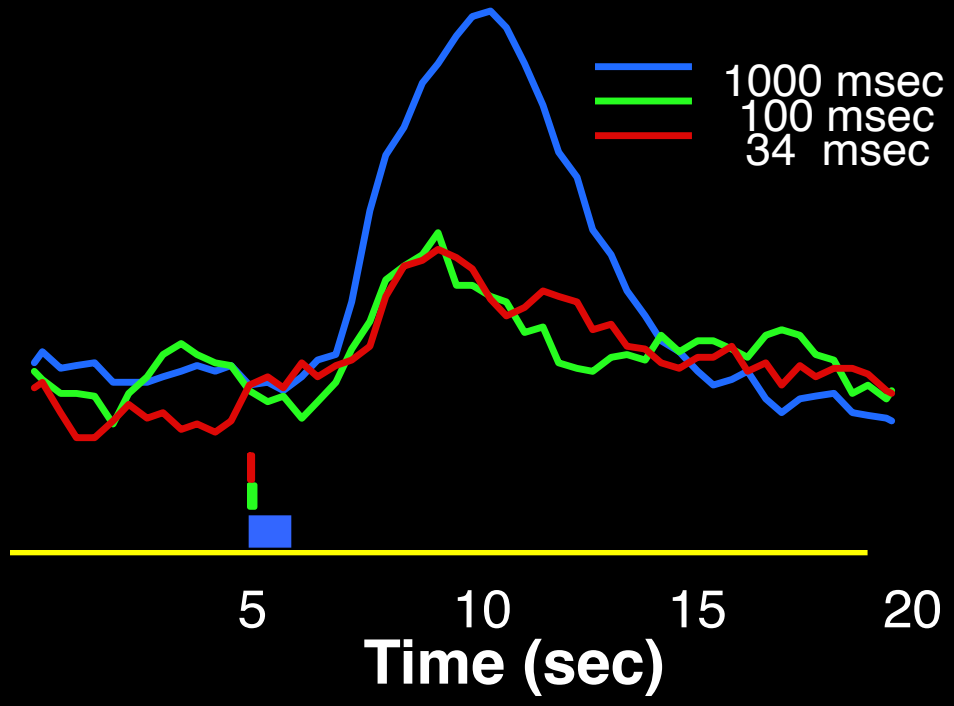
Logothetis et al. (2001) "Neurophysiological investigation of the basis of the fMRI signal" Nature, 412, 150-157



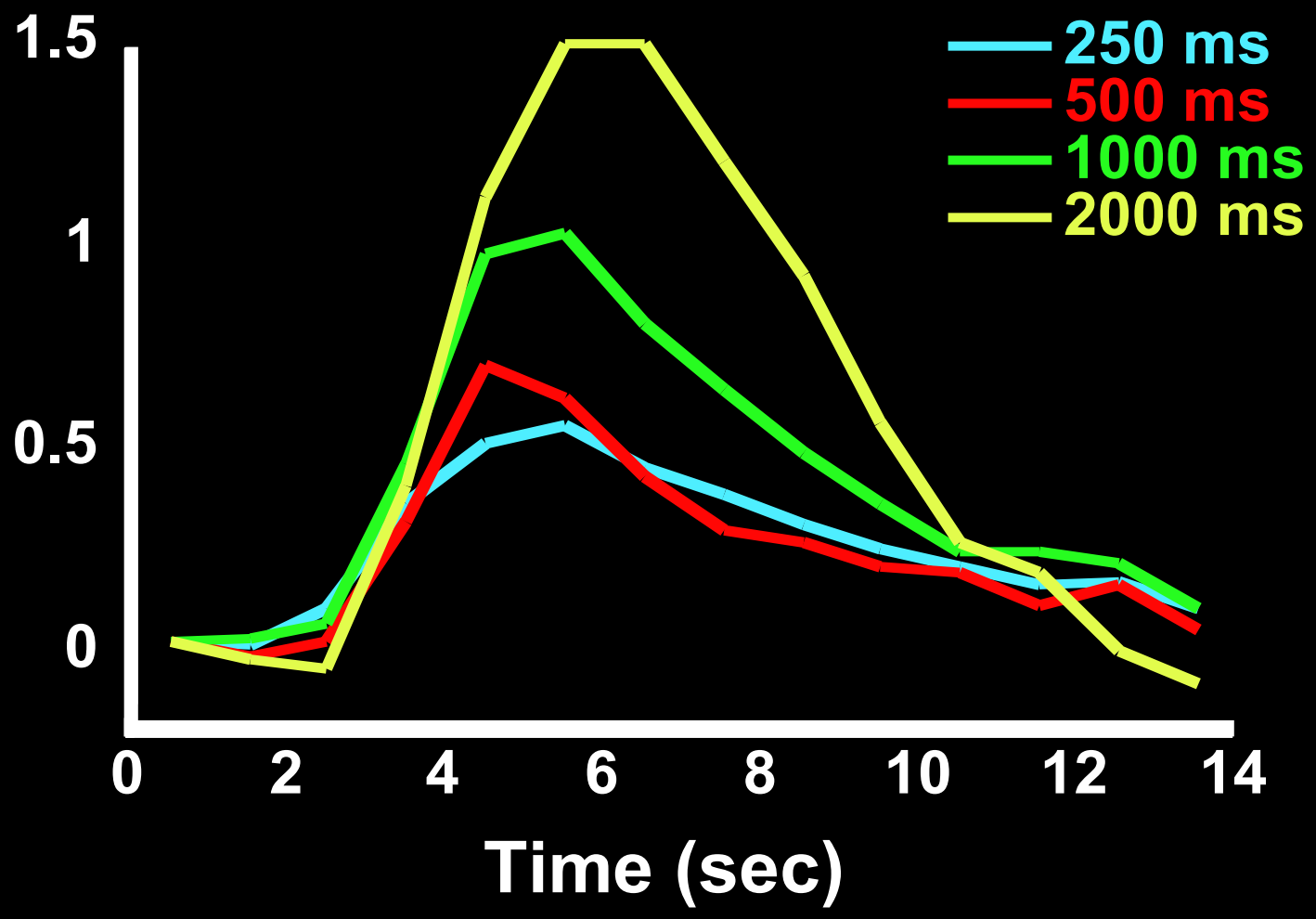
First Event-related fMRI Results



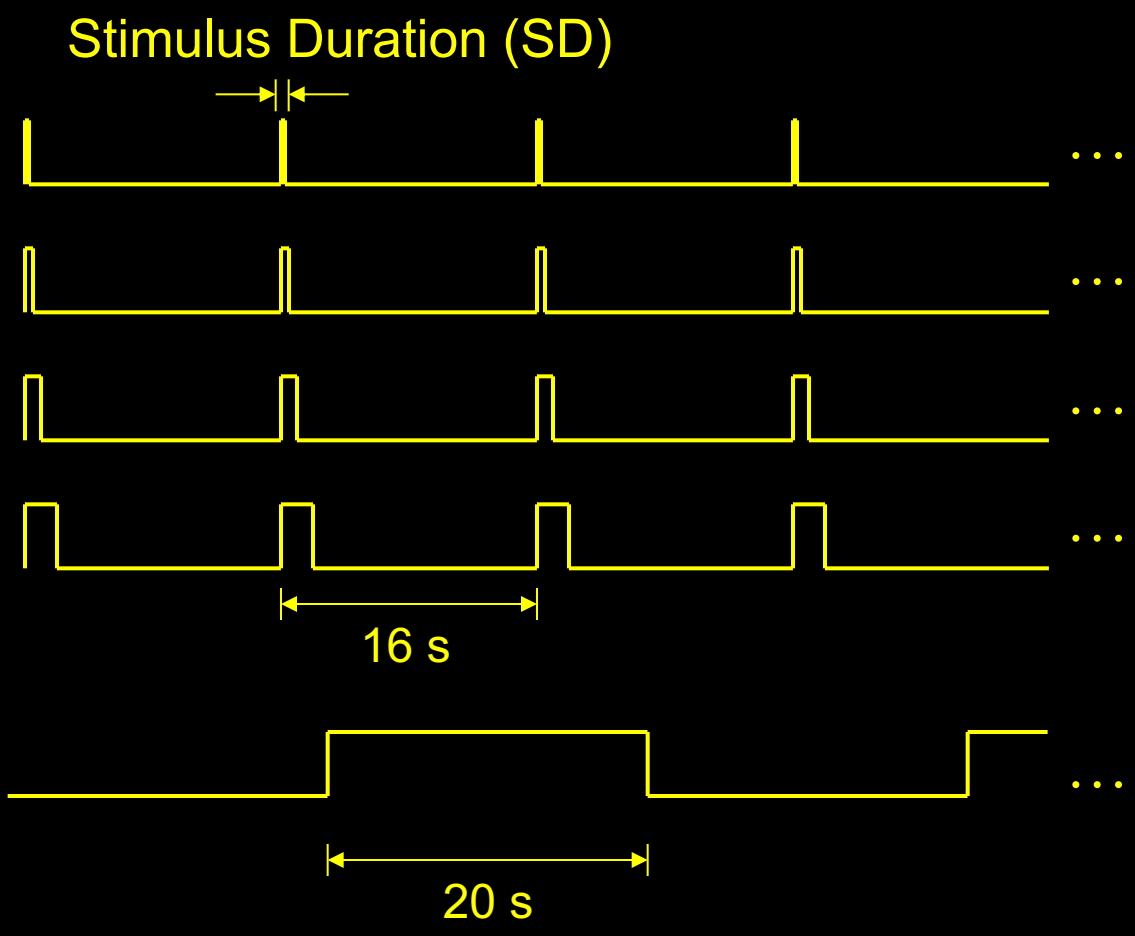
Blamire, A. M., et al. (1992). "Dynamic mapping of the human visual cortex by high-speed magnetic resonance imaging." Proc. Natl. Acad. Sci. USA 89: 11069-11073.



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 [oral], 3'rd Proc. Soc. Magn. Reson., Nice, p. 450. (1995).


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

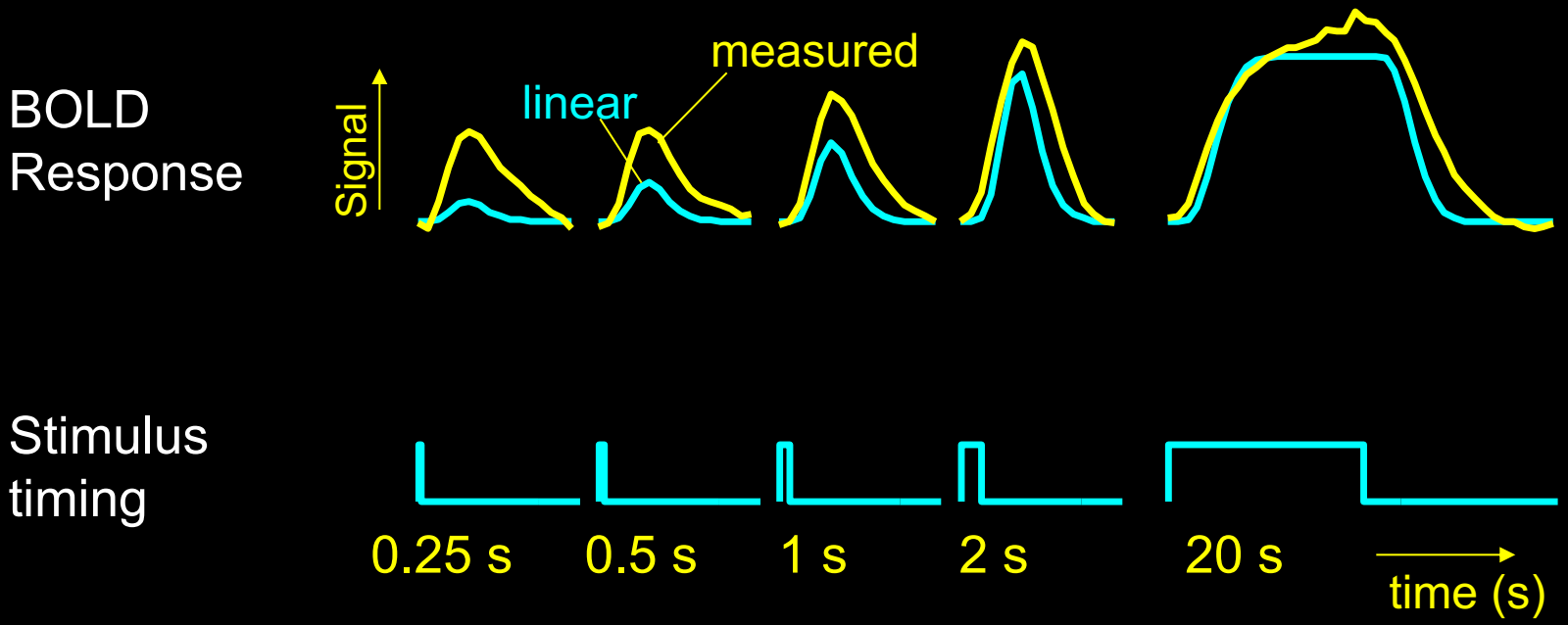
Methods



	Visual	*Motor*
···	SD = 250 ms	SD = 500 ms
···	SD = 500 ms	SD = 1000 ms
···	SD = 1000 ms	SD = 2000 ms
···	SD = 2000 ms	SD = 4000 ms
···	Blocked Trial	

Dynamic Nonlinearity Assessment

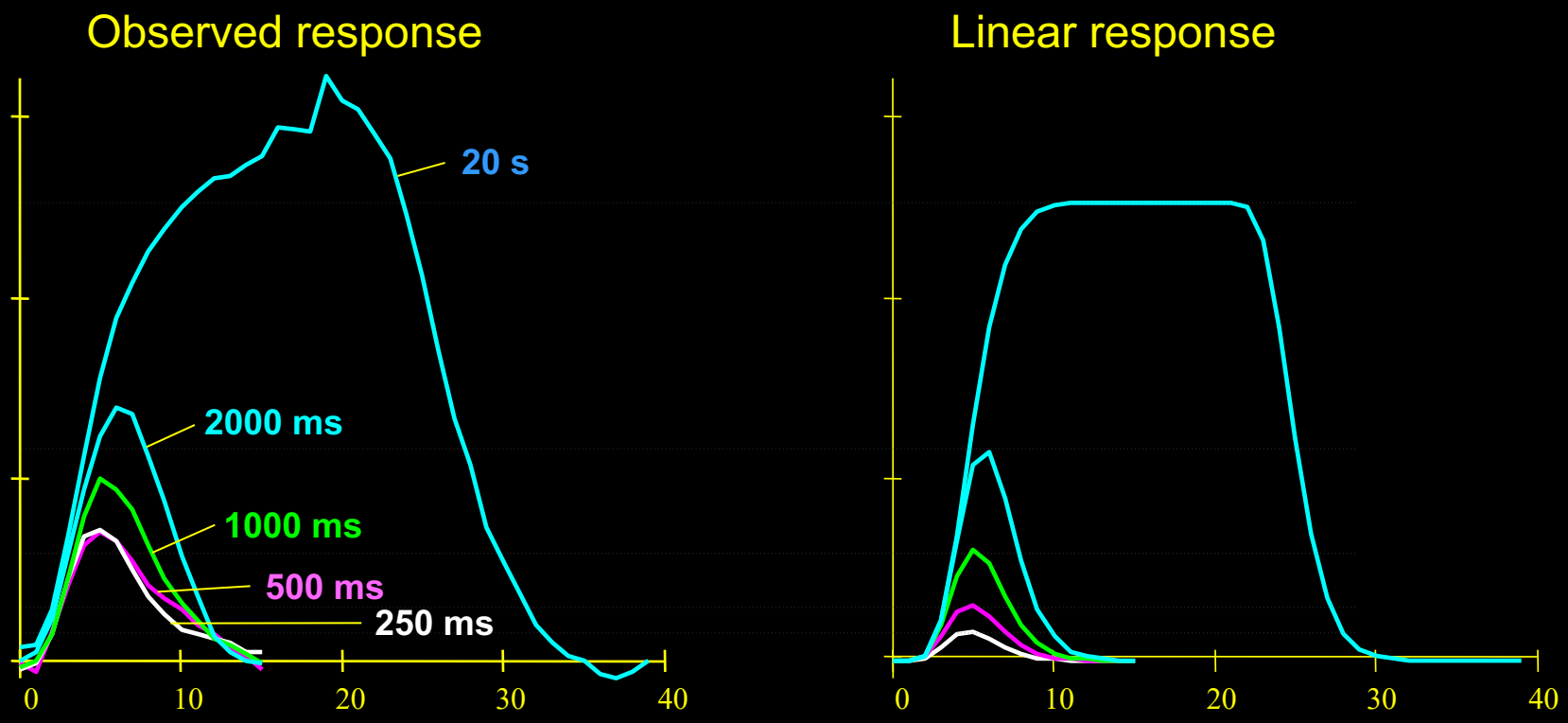
Different stimulus "ON" periods



Brief stimuli produce larger responses than expected

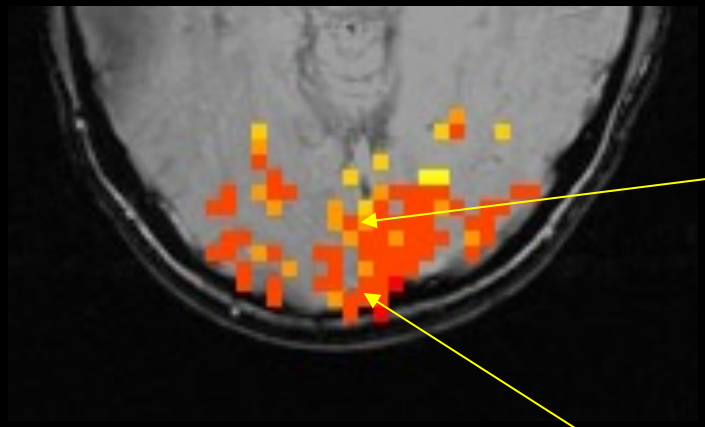
R. M. Birn, Z. Saad, P. A. Bandettini, (2001) "Spatial heterogeneity of the nonlinear dynamics in the fMRI BOLD response." *NeuroImage*, 14: 817-826.

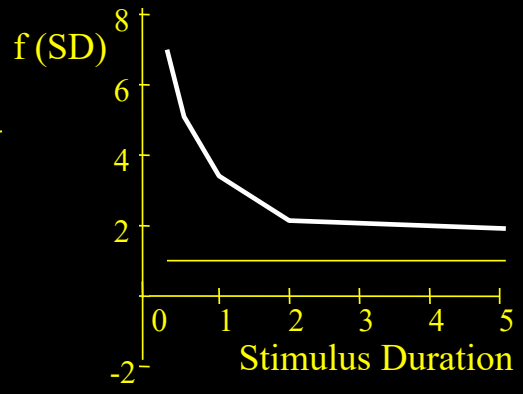
BOLD response is nonlinear

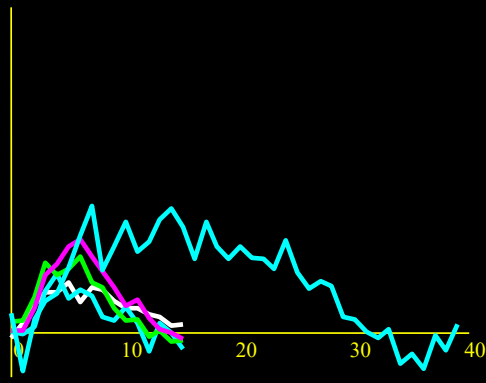


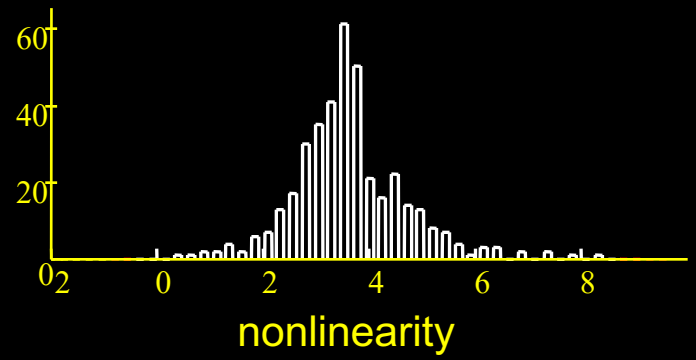
Short duration stimuli produce larger responses than expected

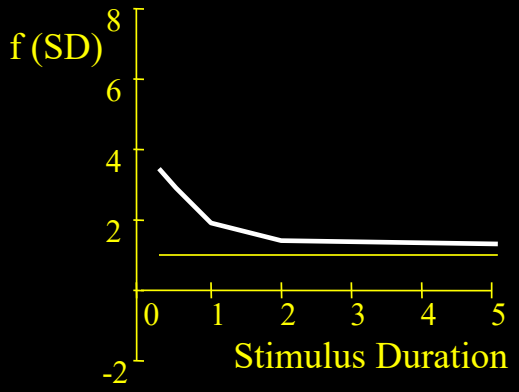
Spatial Heterogeneity of BOLD Nonlinearity

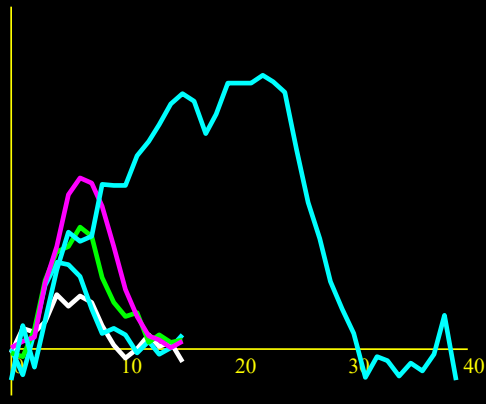












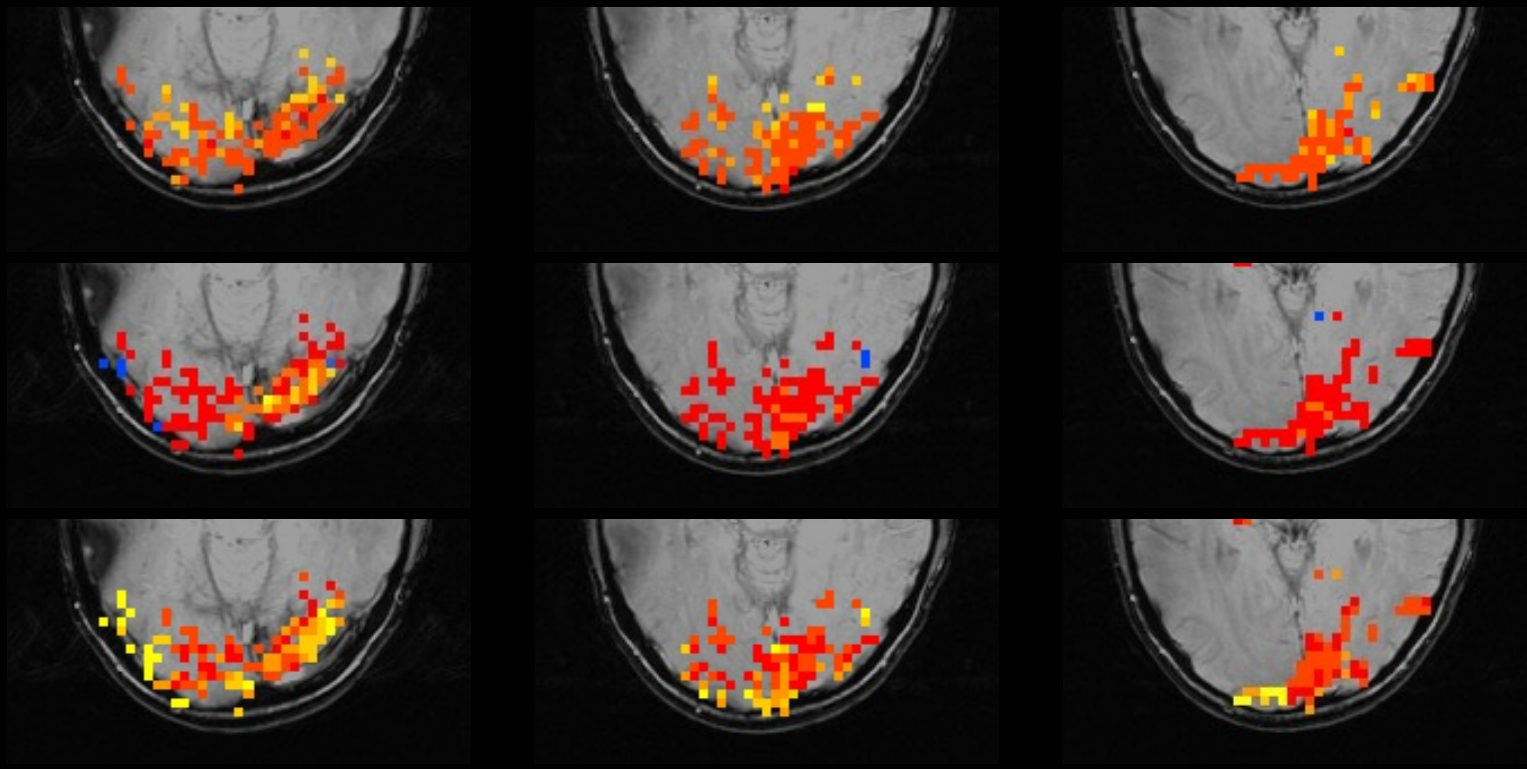
R. M. Birn, Z. Saad, P. A. Bandettini, (2001) "Spatial heterogeneity of the nonlinear dynamics in the fMRI BOLD response." *NeuroImage*, 14: 817-826.

Results – visual task

Nonlinearity

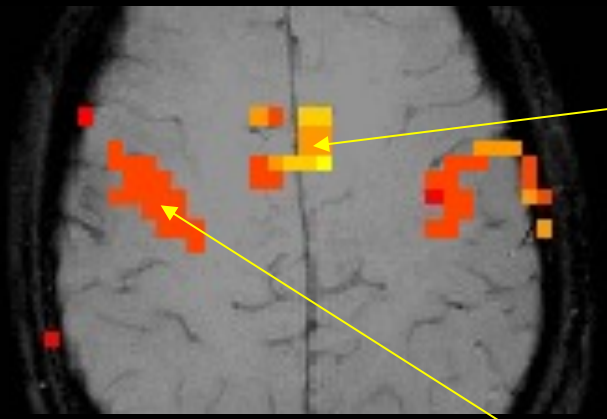
Magnitude

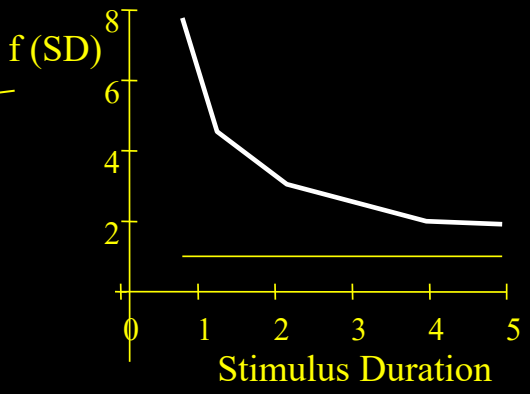
Latency

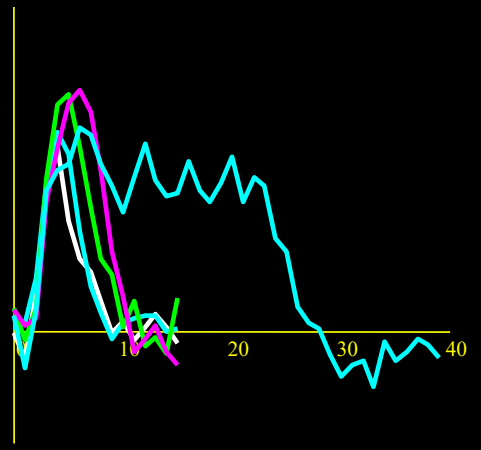


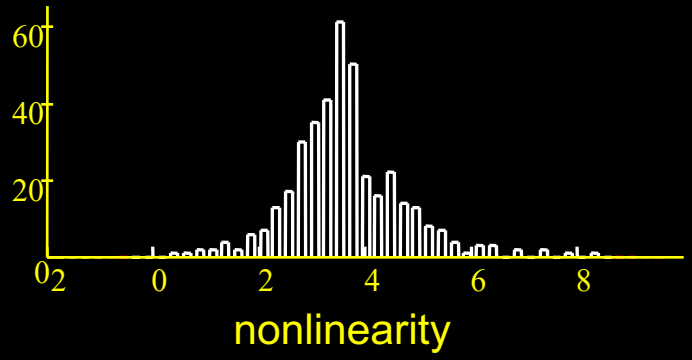
R. M. Birn, Z. Saad, P. A. Bandettini, (2001) "Spatial heterogeneity of the nonlinear dynamics in the fMRI BOLD response." *NeuroImage*, 14: 817-826.

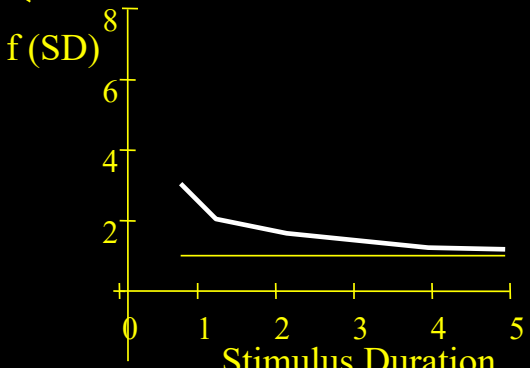
Results – motor task

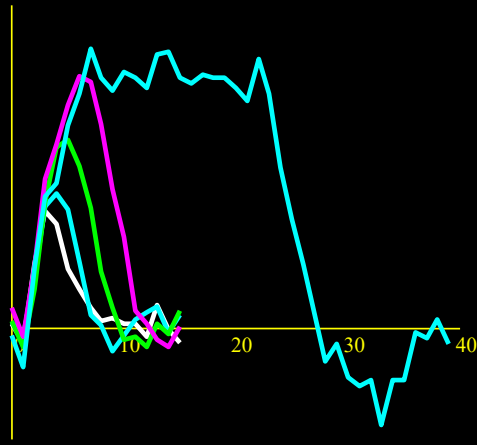










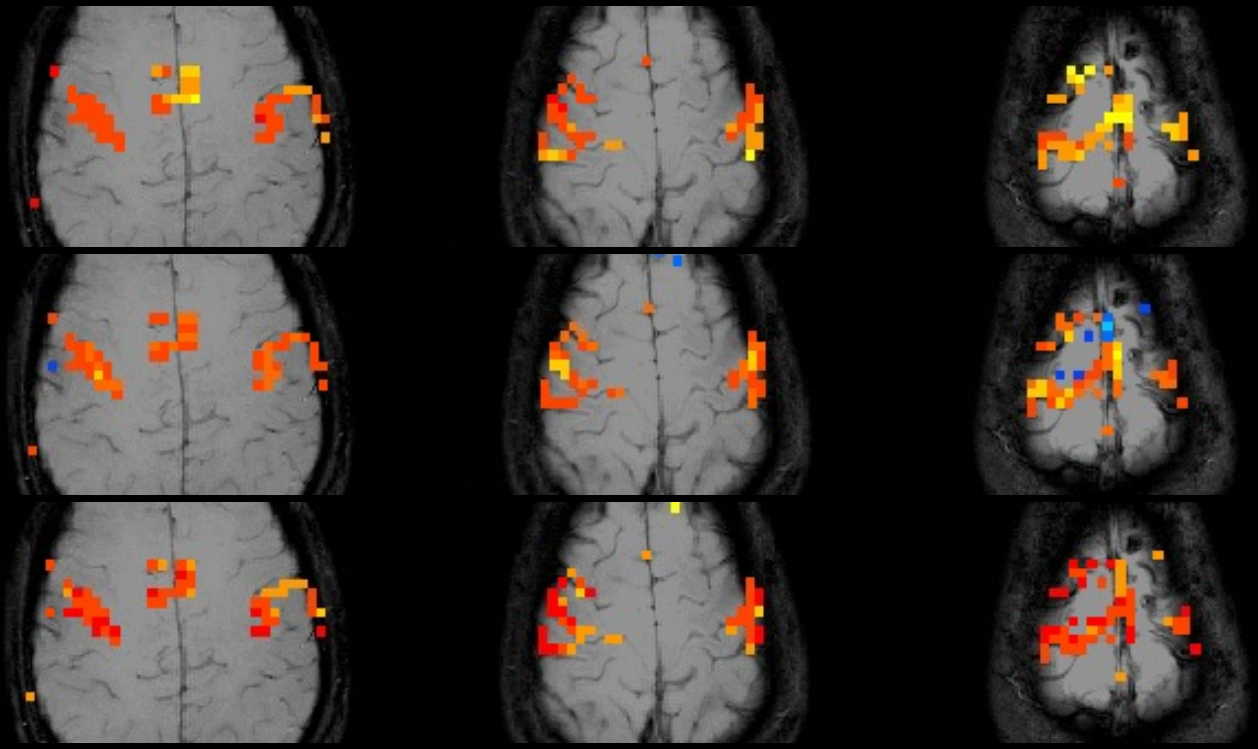


Results – motor task

Nonlinearity

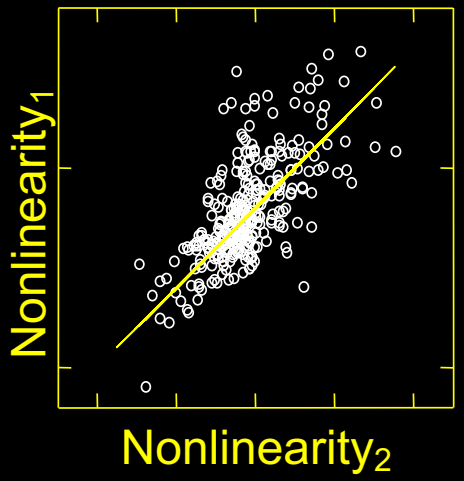
Magnitude

Latency

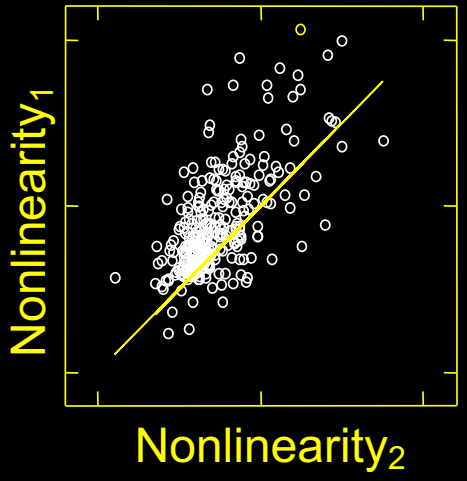


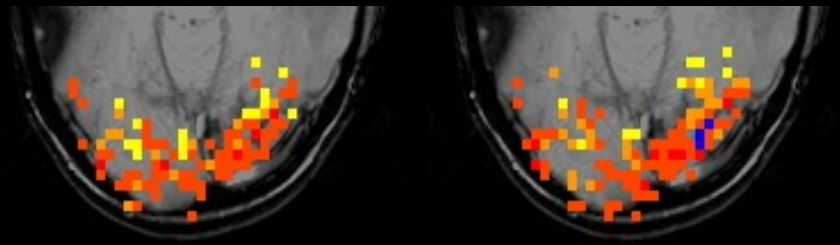
Reproducibility

Visual task

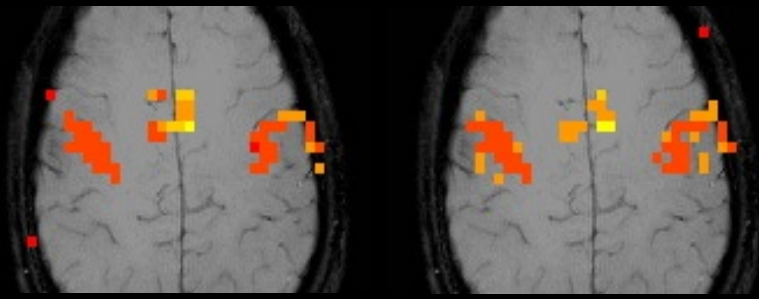


Motor task



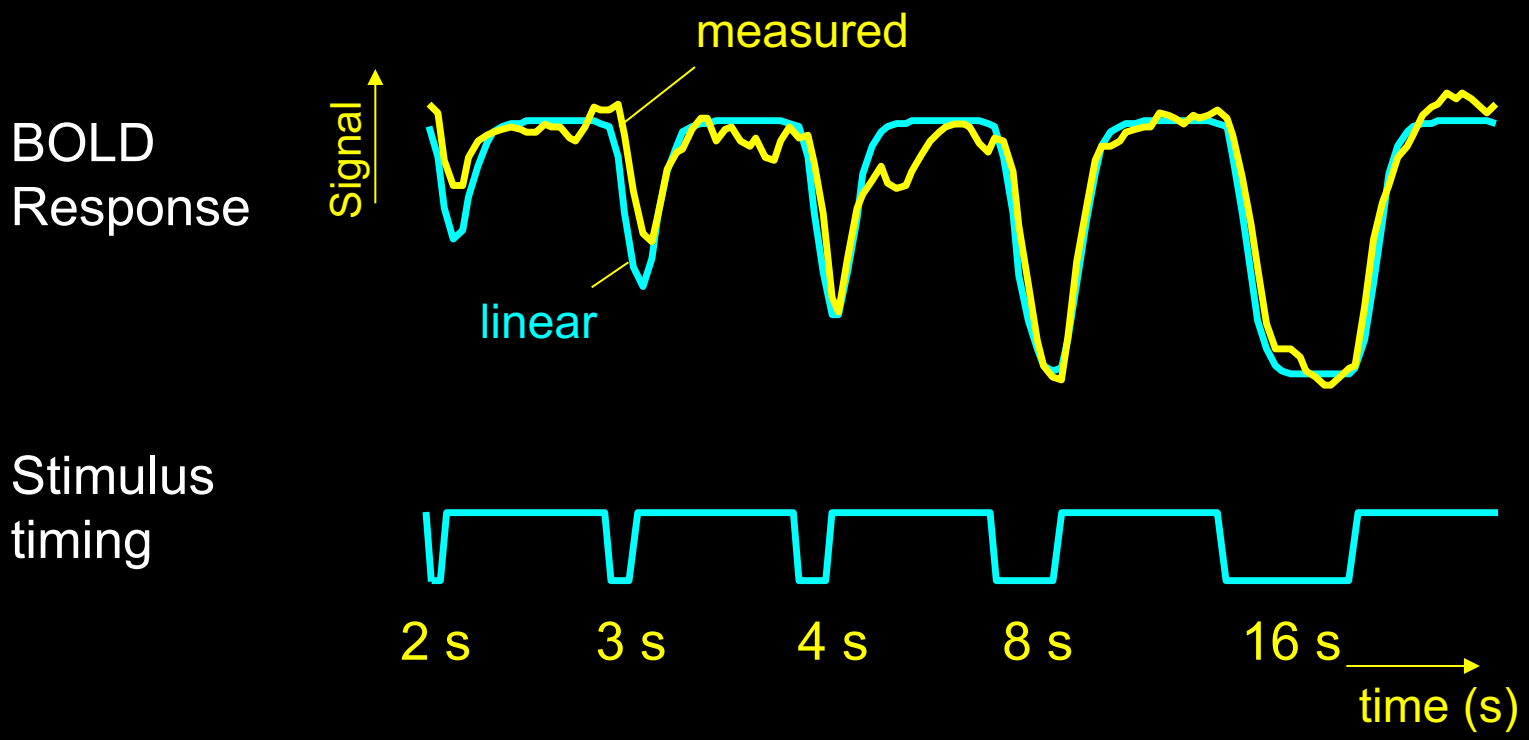


Experiment 1 Experiment 2



Experiment 1 Experiment 2

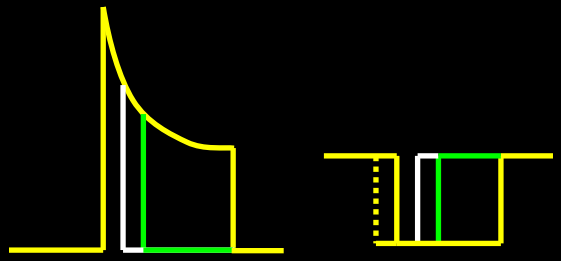
Different stimulus “ON” periods



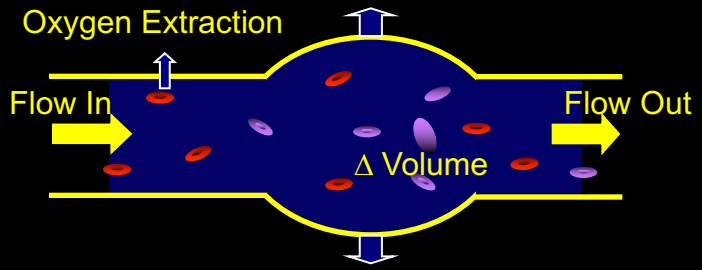
Brief stimulus OFF periods produce smaller decreases than expecte

Sources of this Nonlinearity

- Neuronal

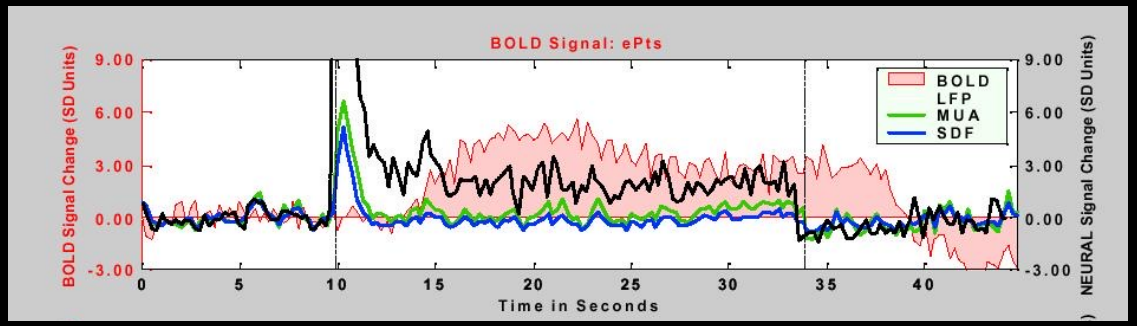


- Hemodynamic
  - Oxygen extraction
  - Blood volume dynamics

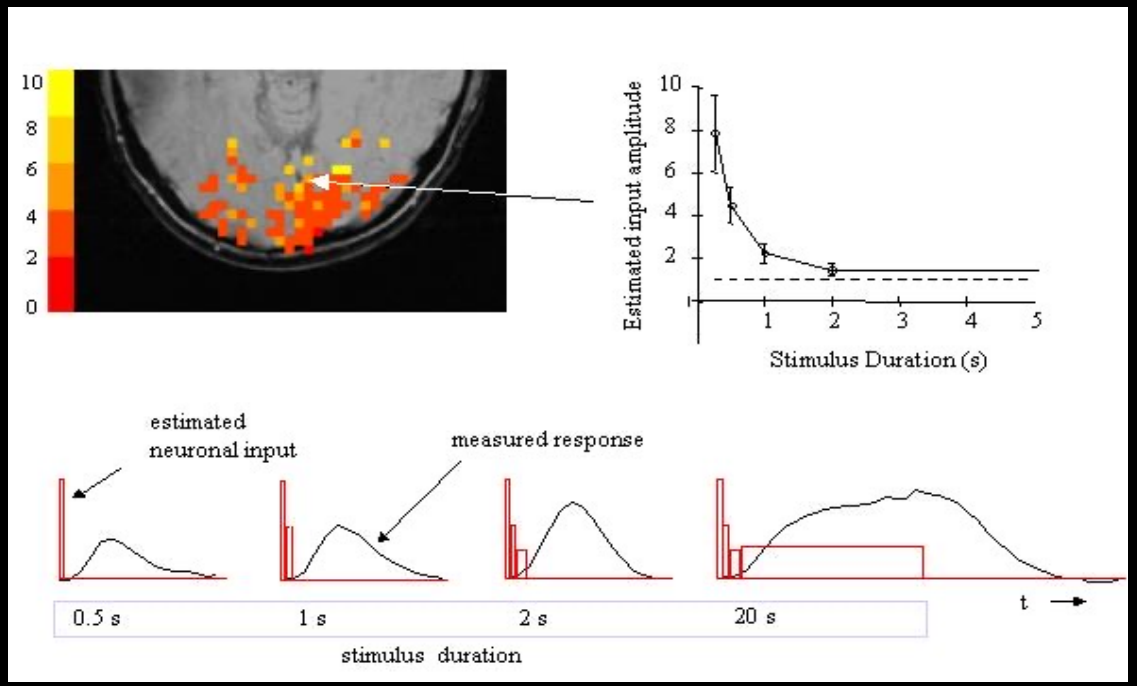


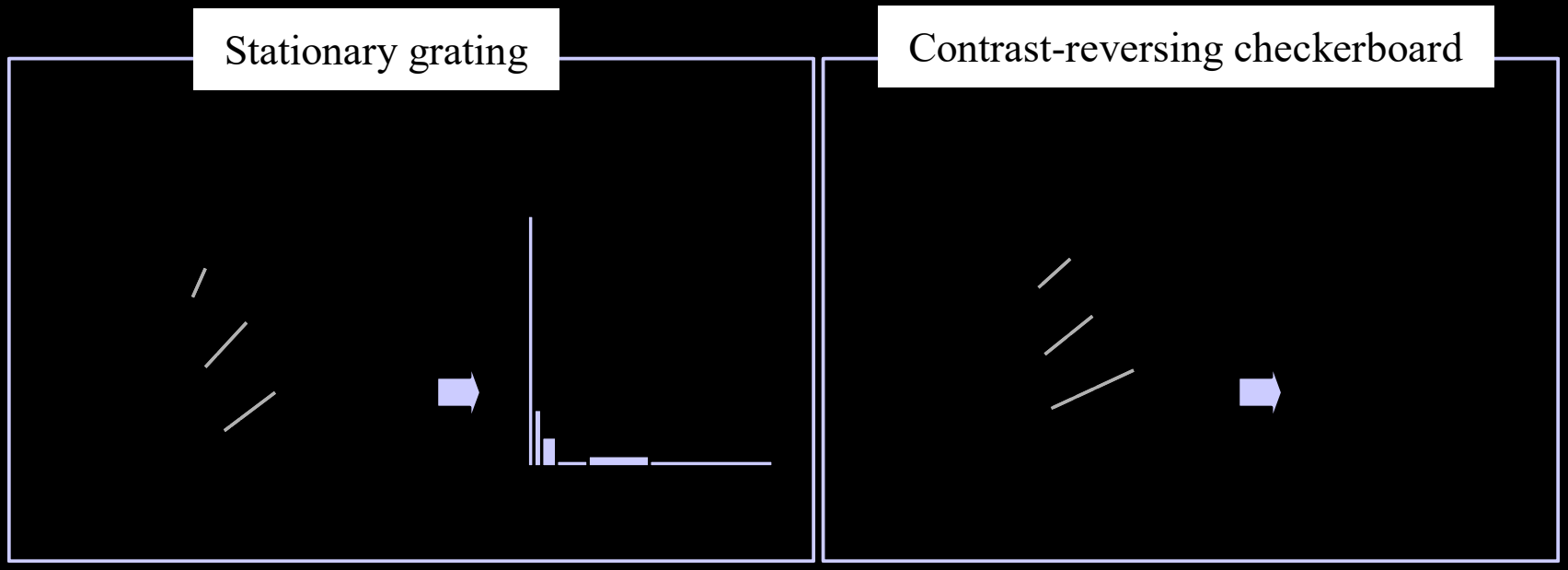
BOLD Correlation with Neuronal Activity

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



P. A. Bandettini and L. G. Ungerleider, (2001) "From neuron to BOLD: new connections." Nature Neuroscience, 4: 864-866.




Stationary grating
Contrast-reversing checkerboard

Refinements

BOLD Contrast Interpretation

Dynamics

Paradigm Design and Processing

Neuronal Activation Input Strategies

1. Block Design
2. Parametric Design
3. Frequency Encoding
4. Phase Encoding
5. Event Related
6. Orthogonal Design
7. Free Behavior Design

Neuronal Activation Input Strategies

1. Block Design
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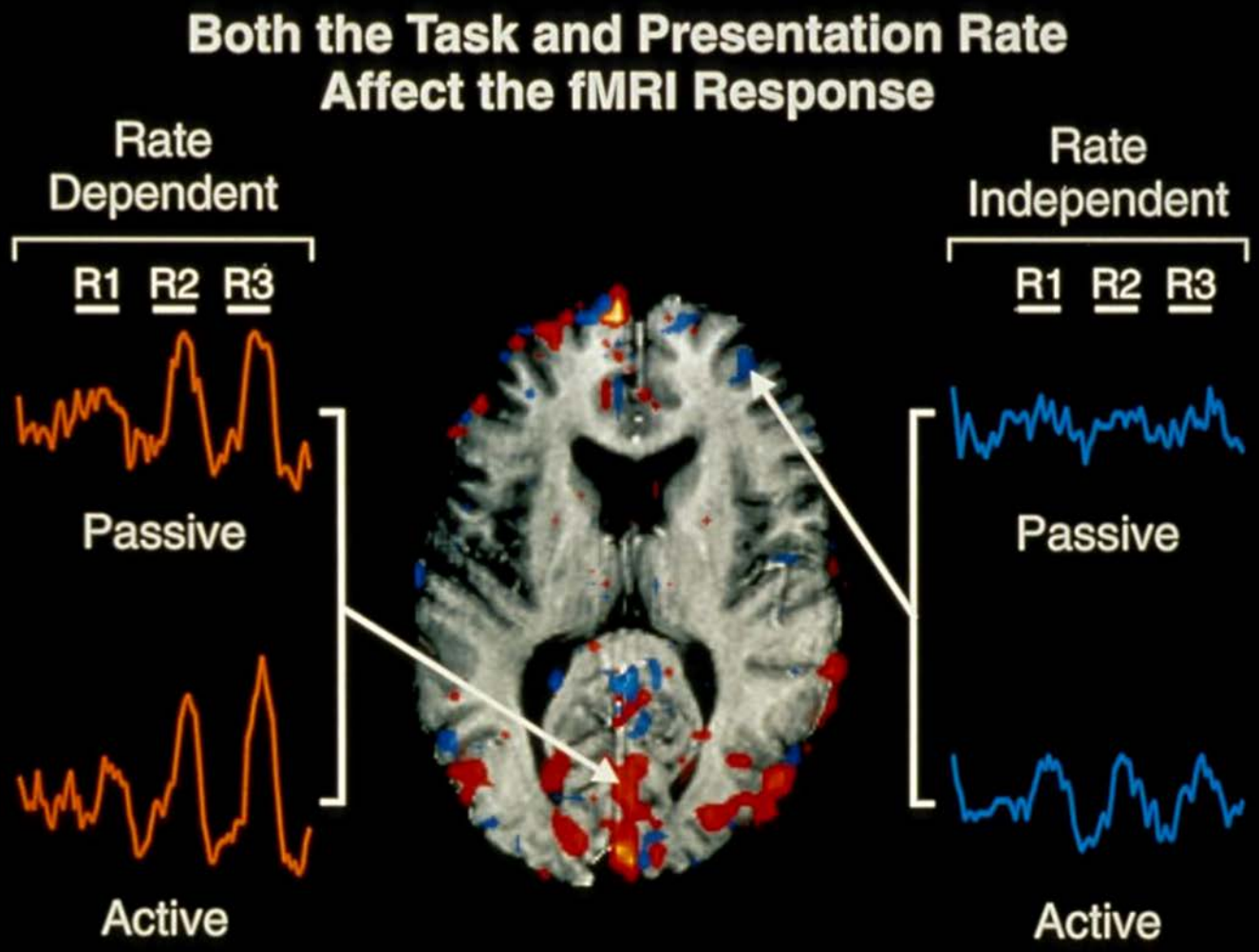

E. A. DeYoe, P. A. Bandettini, J. Nietz, D. Miller, P. Winas, Methods for functional magnetic resonance imaging (FMRI). *J. Neuroscience Methods* 54, 171-187 (1994).

Neuronal Activation Input Strategies

1. Block Design
2. Parametric Design
3. **Frequency Encoding**
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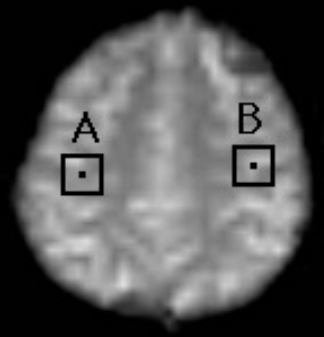
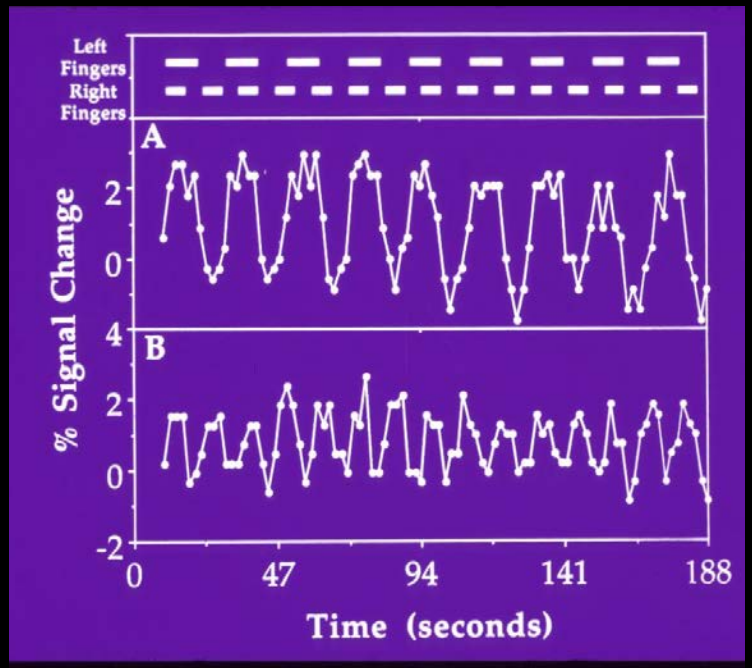
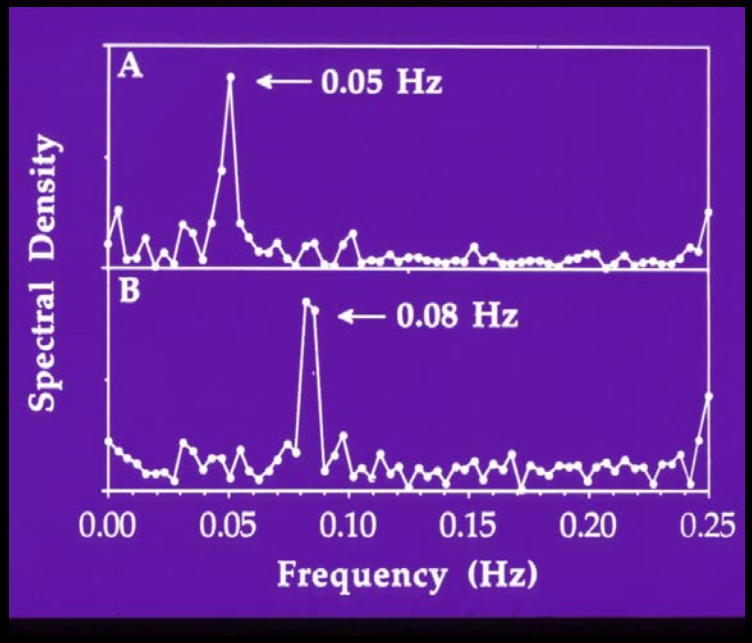
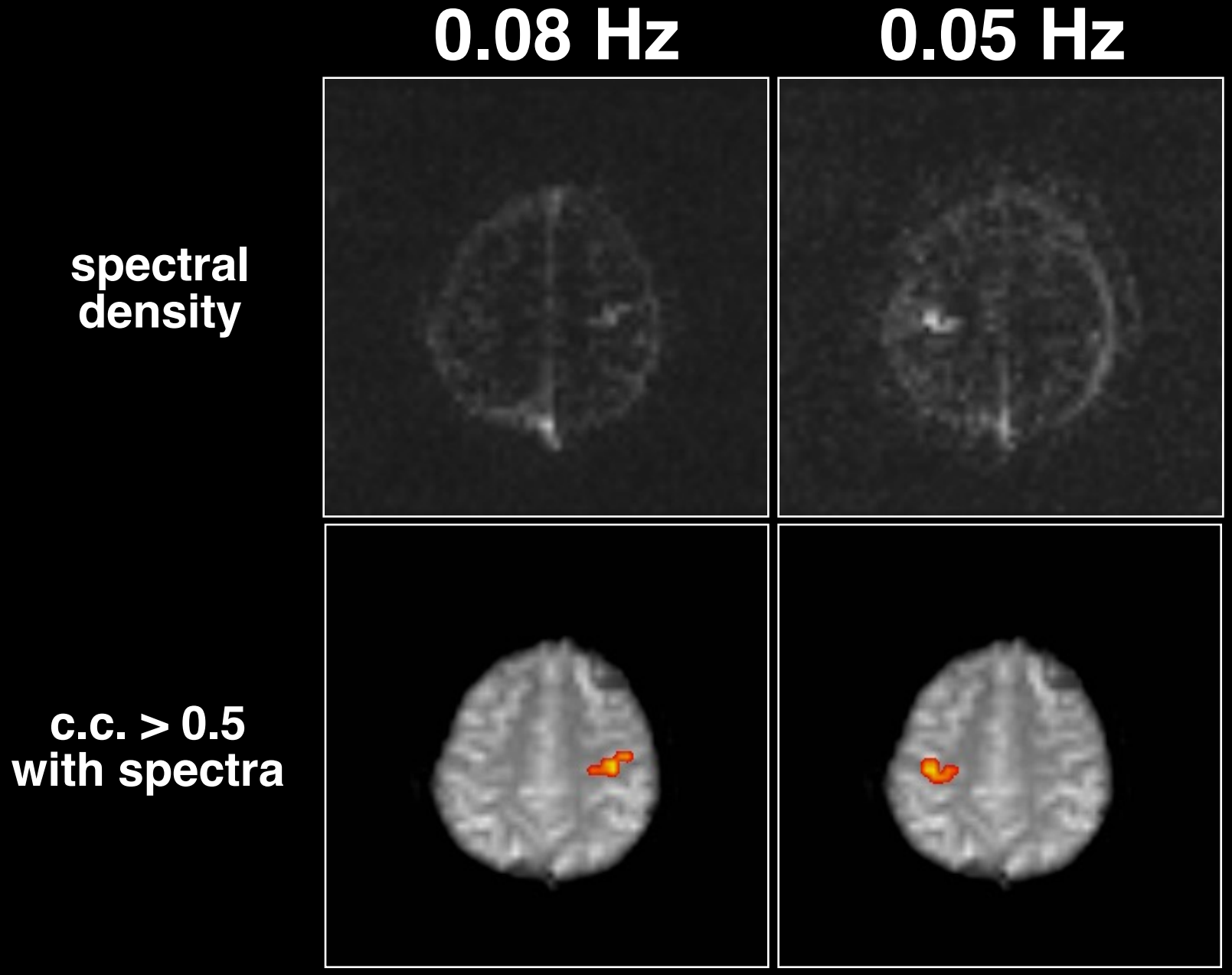
5. Event Related
6. Orthogonal Design
7. Free Behavior Design







P. A. Bandettini, A. Jesmanowicz, E. C. Wong, J. S. Hyde, Processing strategies for time-course data sets in functional MRI of the human brain. *Magn. Reson. Med.* 30, 161-173 (1993).



P. A. Bandettini, A. Jesmanowicz, E. C. Wong, J. S. Hyde, Processing strategies for time-course data sets in functional MRI of the human brain. *Magn. Reson. Med.* 30, 161-173 (1993).

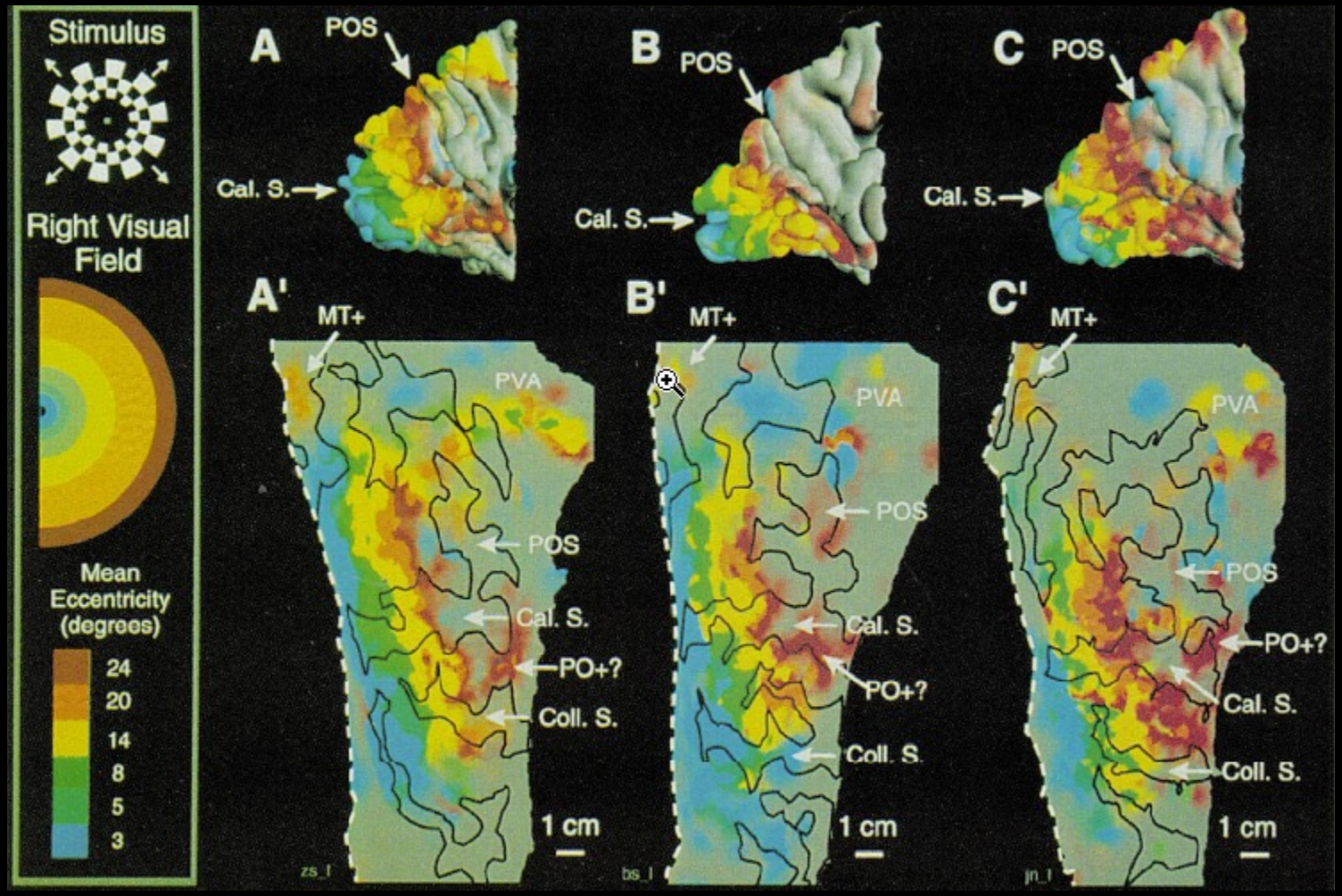
Neuronal Activation Input Strategies

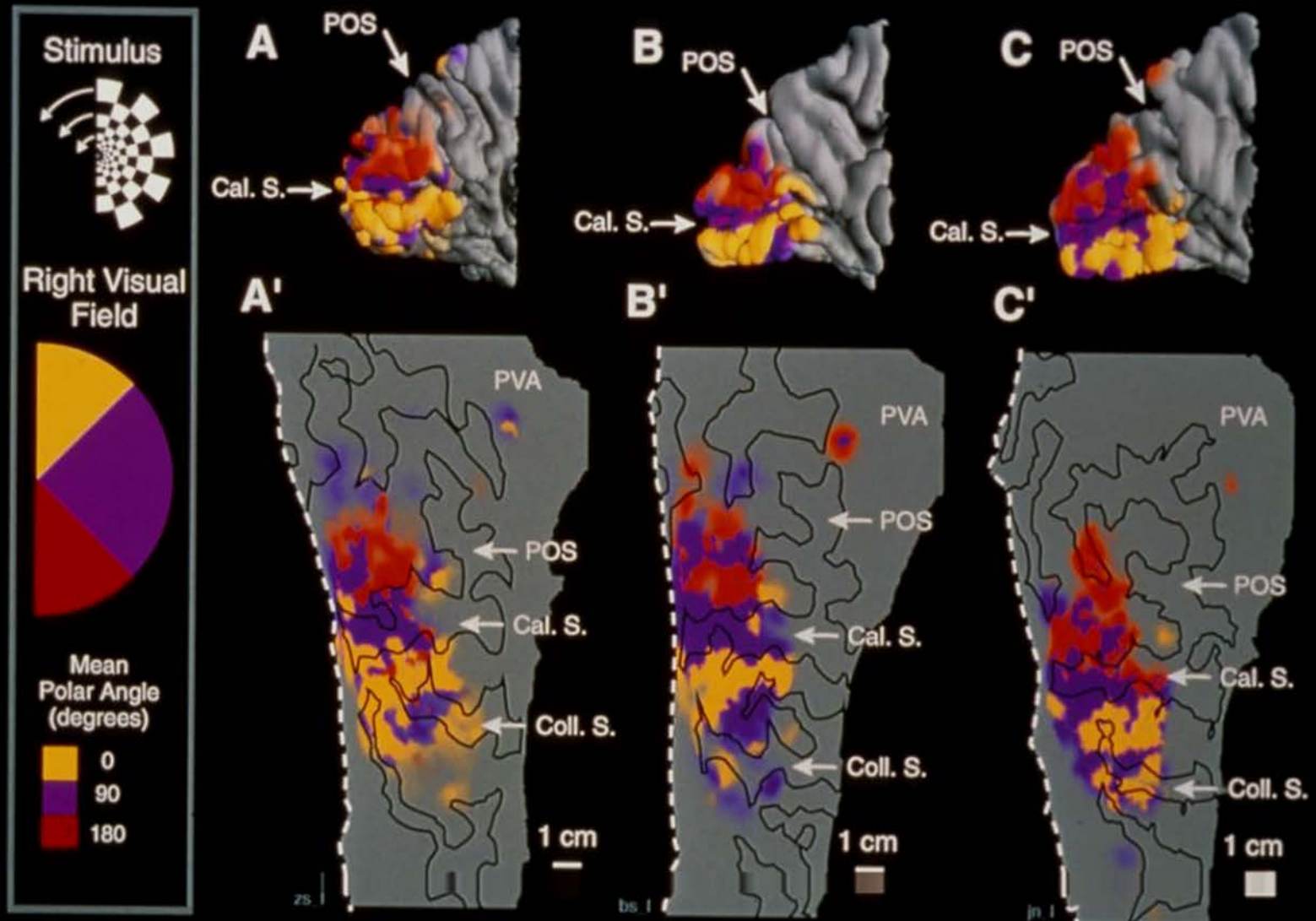
1. Block Design
2. Parametric Design
3. Frequency Encoding
4. **Phase Encoding**
5. Event Related
6. Orthogonal Design
7. Free Behavior Design

Proc. Natl. Acad. Sci. USA
Vol. 93, pp. 2382–2386, March 1996
Neurobiology

Mapping striate and extrastriate visual areas in human cerebral cortex

EDGAR A. DEYOE*, GEORGE J. CARMAN†, PETER BANDETTINI‡, SETH GLICKMAN*, JON WIESER*, ROBERT COX§, DAVID MILLER¶, AND JAY NEITZ*

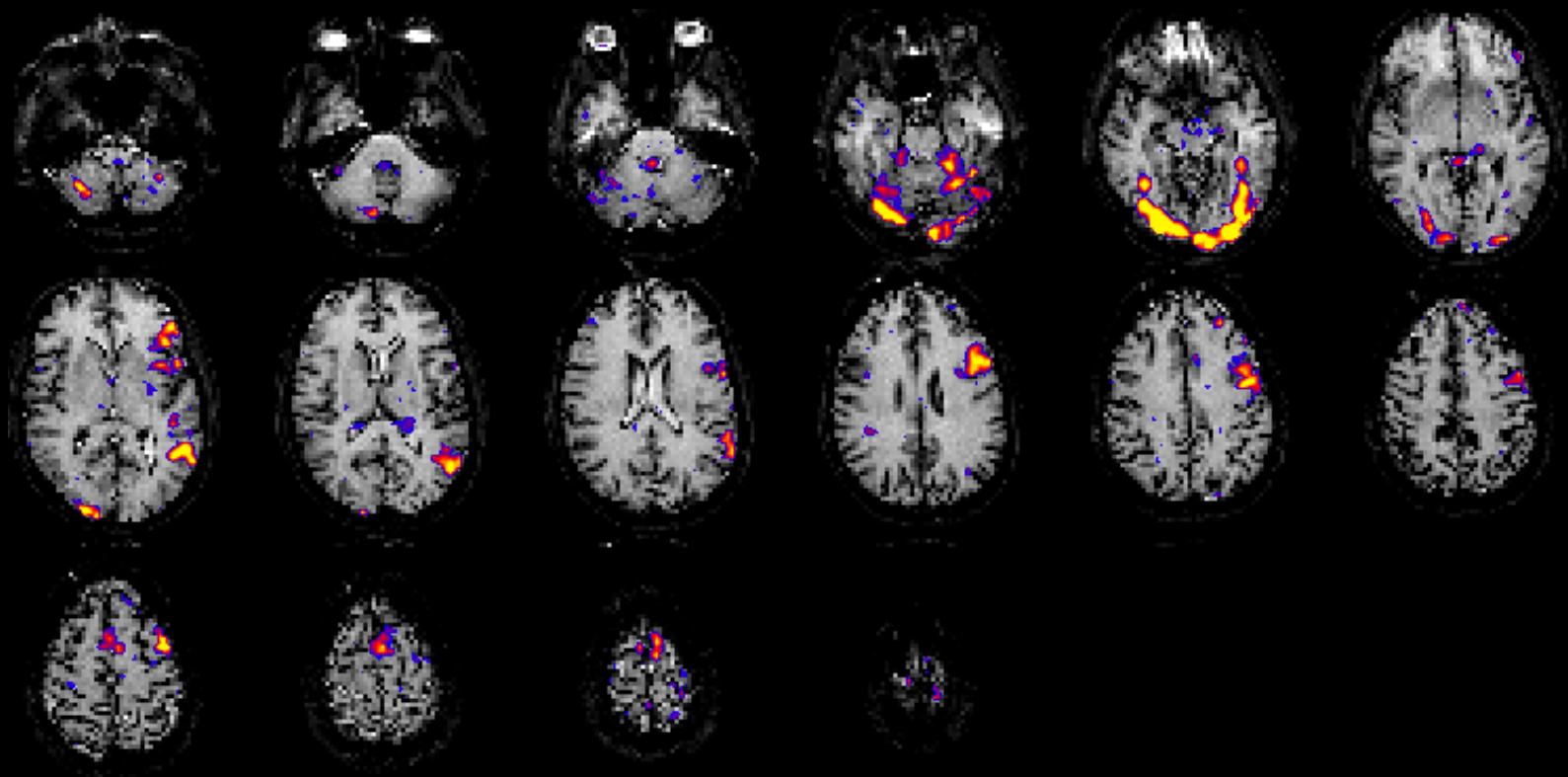



Stimulus
Right Visual Field
Mean Polar Angle (degrees)
0
90
180
A
POS
Cal. S.
B
POS
Cal. S.
C
POS
Cal. S.
A'
PVA
POS
Cal. S.
Coll. S.
1 cm
zs
B'
PVA
POS
Cal. S.
Coll. S.
1 cm
bs
C'
PVA
POS
Cal. S.
Coll. S.
1 cm
jn

Neuronal Activation Input Strategies

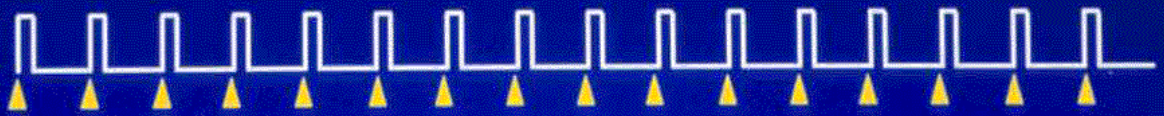
1. Block Design
2. Parametric Design
3. Frequency Encoding
4. Phase Encoding
5. **Event Related**
6. Orthogonal Design
7. Free Behavior Design

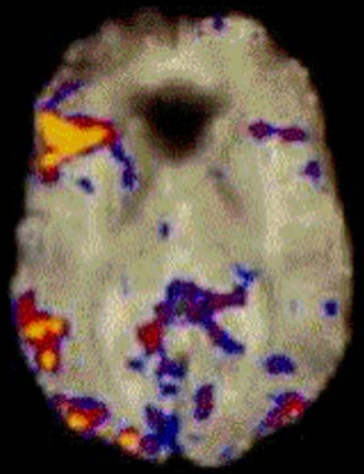
Word stem completion

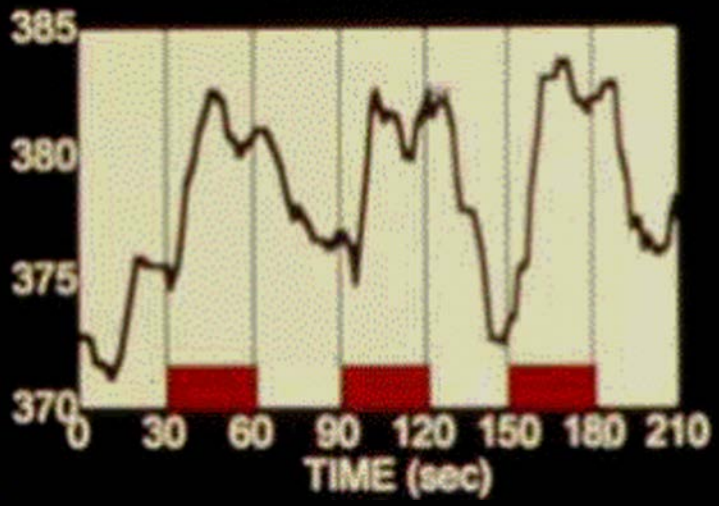


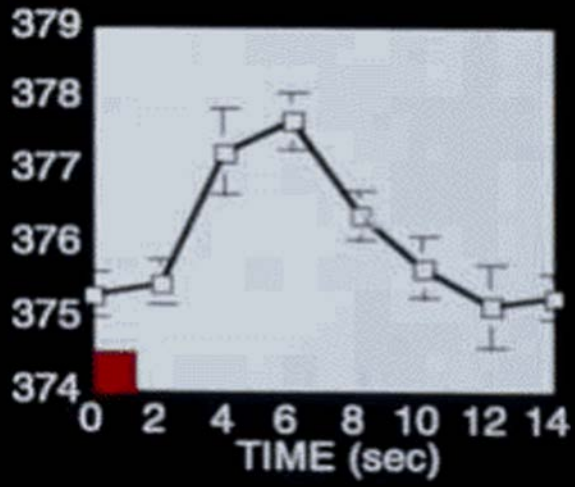
BLOCKED:

SINGLE TRIAL:

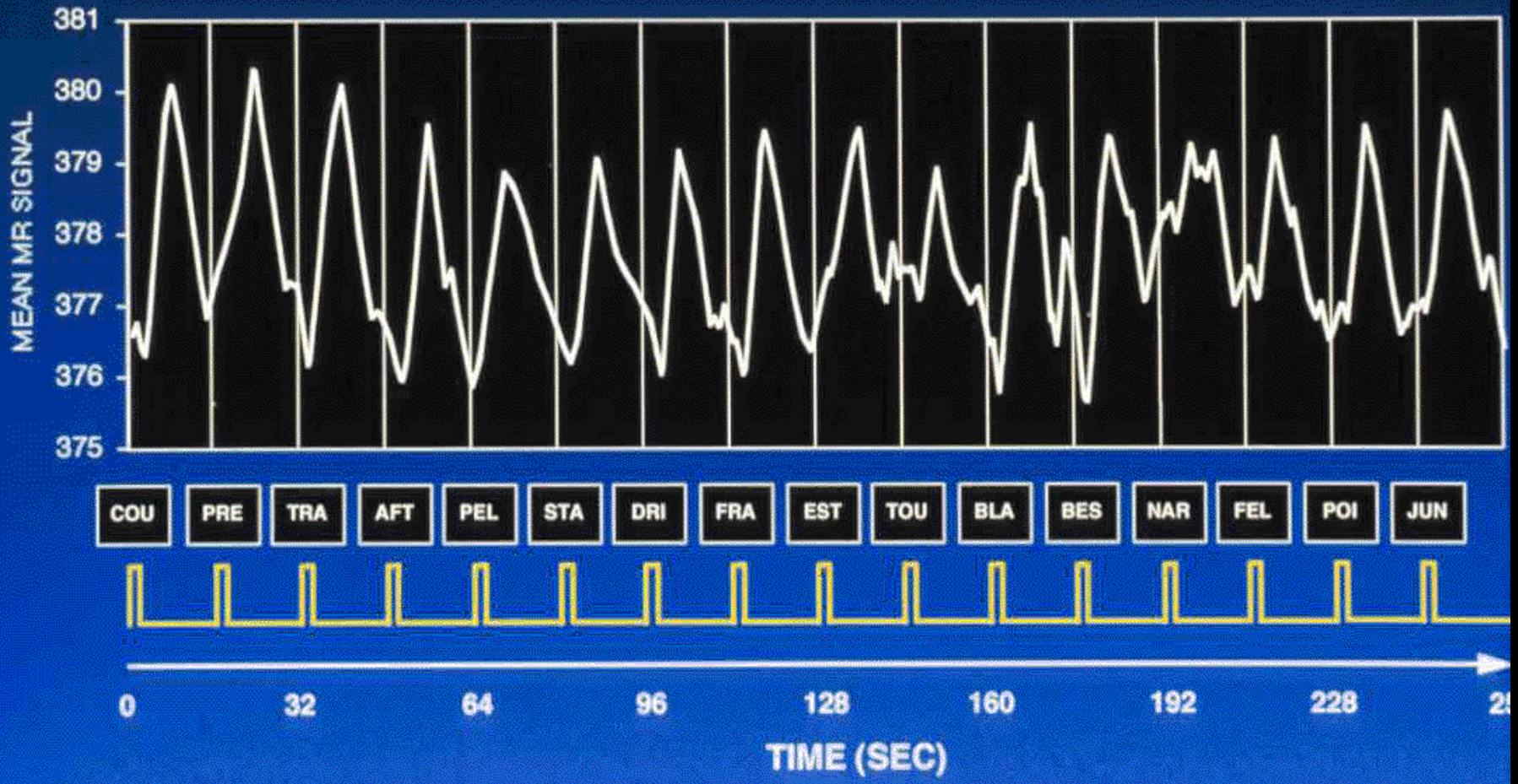








"Single-Trial" Response Across an Averaged Data Set

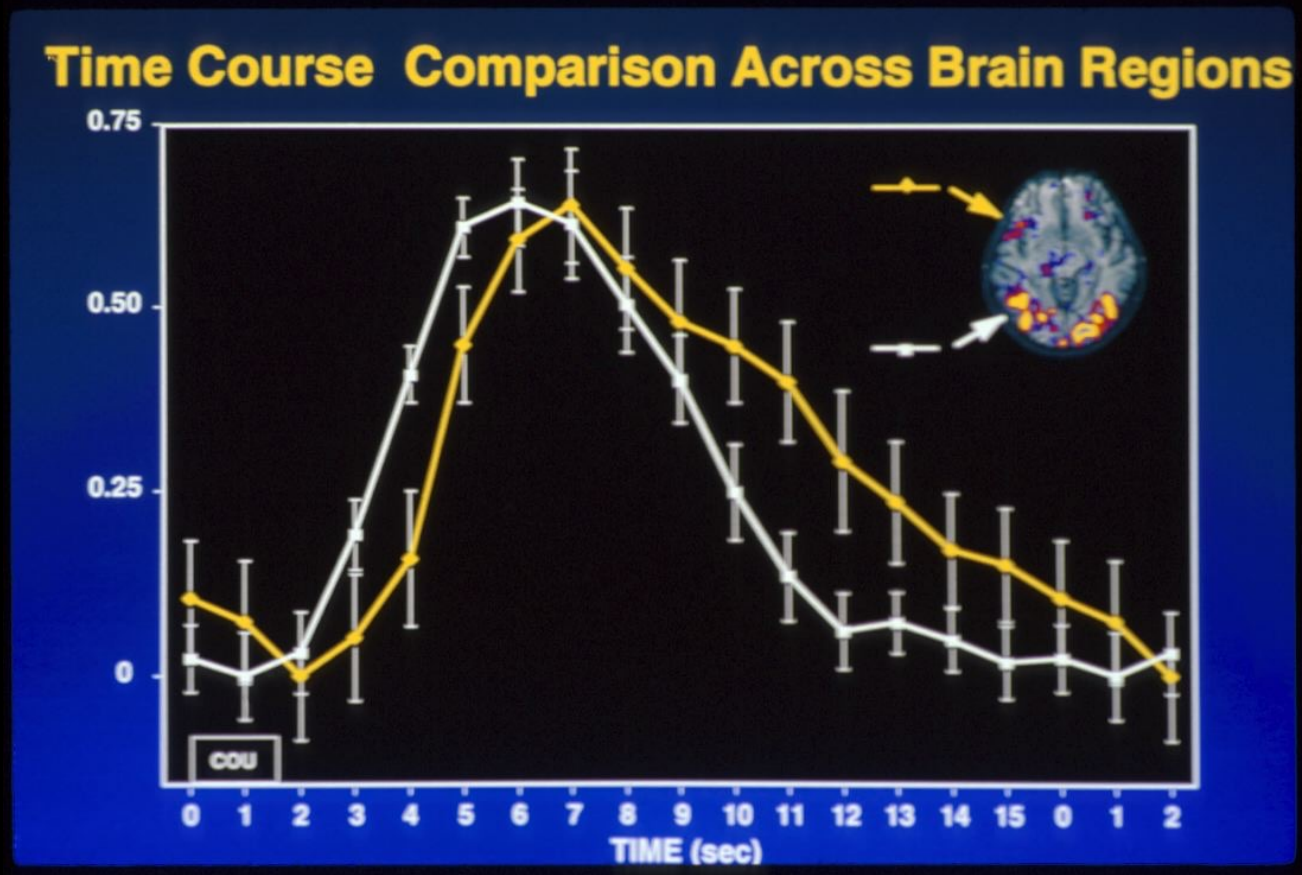


Proc. Natl. Acad. Sci. USA
Vol. 93, pp. 14878–14883, December 1996
Neurobiology

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

(neuroimaging/single trial/language/prefrontal)

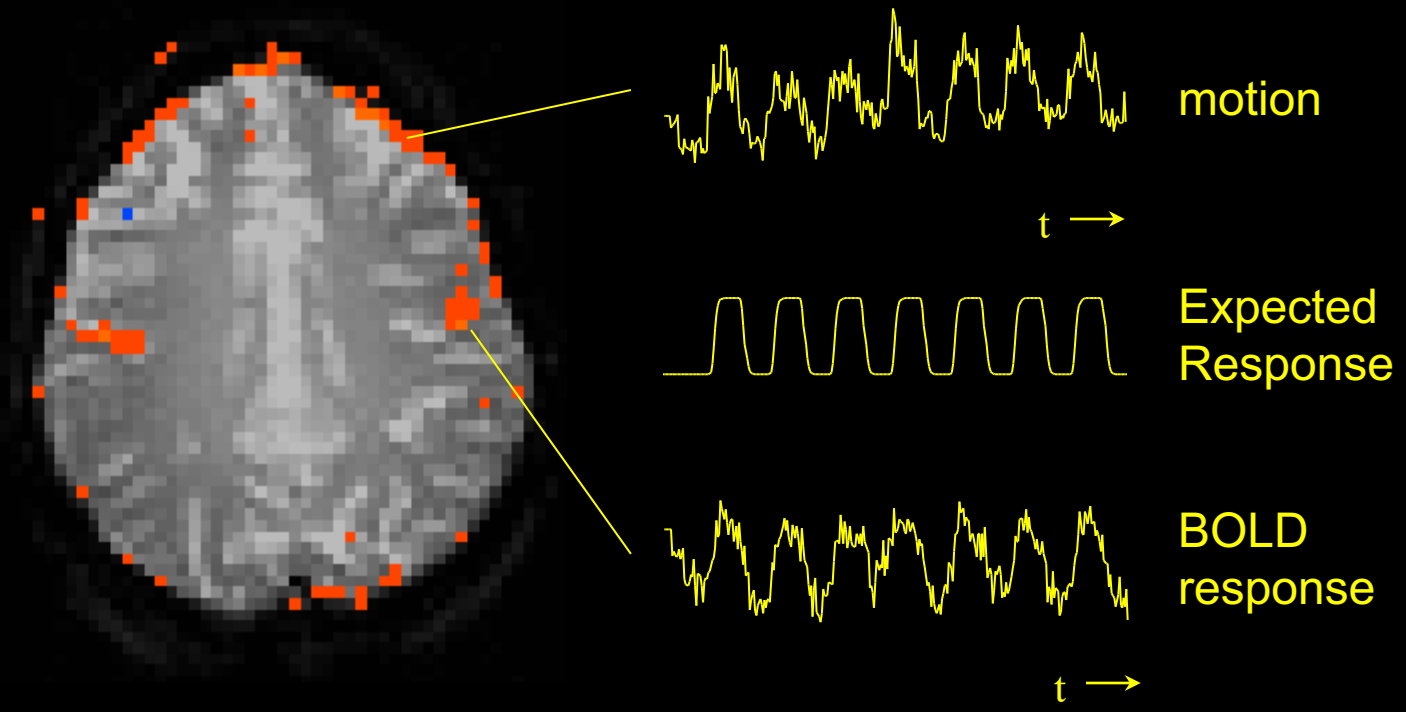
RANDY L. BUCKNER[†‡§¶], PETER A. BANDETTINI[†‡], KATHLEEN M. O'CRAVEN[†‖], ROBERT L. SAVOY[†‖], STEVEN E. PETERSEN[*††], MARCUS E. RAICHLE[§*†††], AND BRUCE R. ROSEN[†‡]



Event Related Advantages

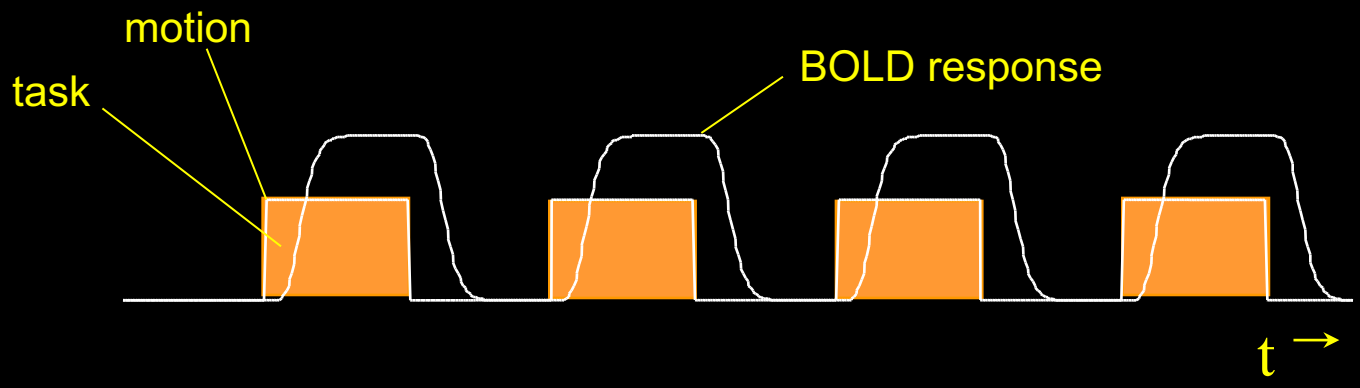
- Task Randomization
- Post acquisition, Performance-based, data binning
- Natural presentation
- Reduction of habituation effects
- Overt responses
- Reduction of scanner noise effects
- More precise estimation of hemodynamic respons

Speaking - Blocked Trial

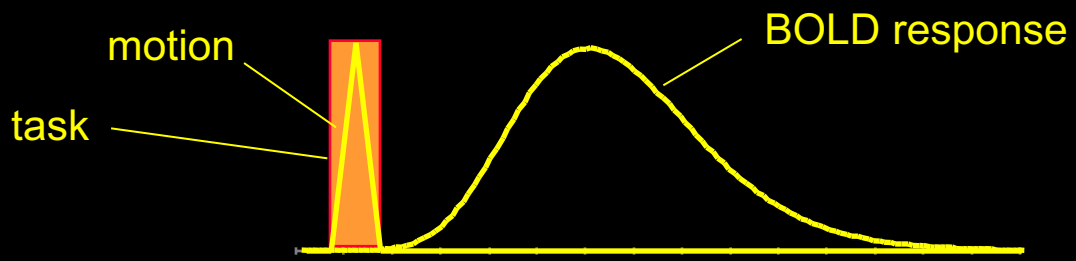


fMRI during tasks that involve brief motion

Blocked Design

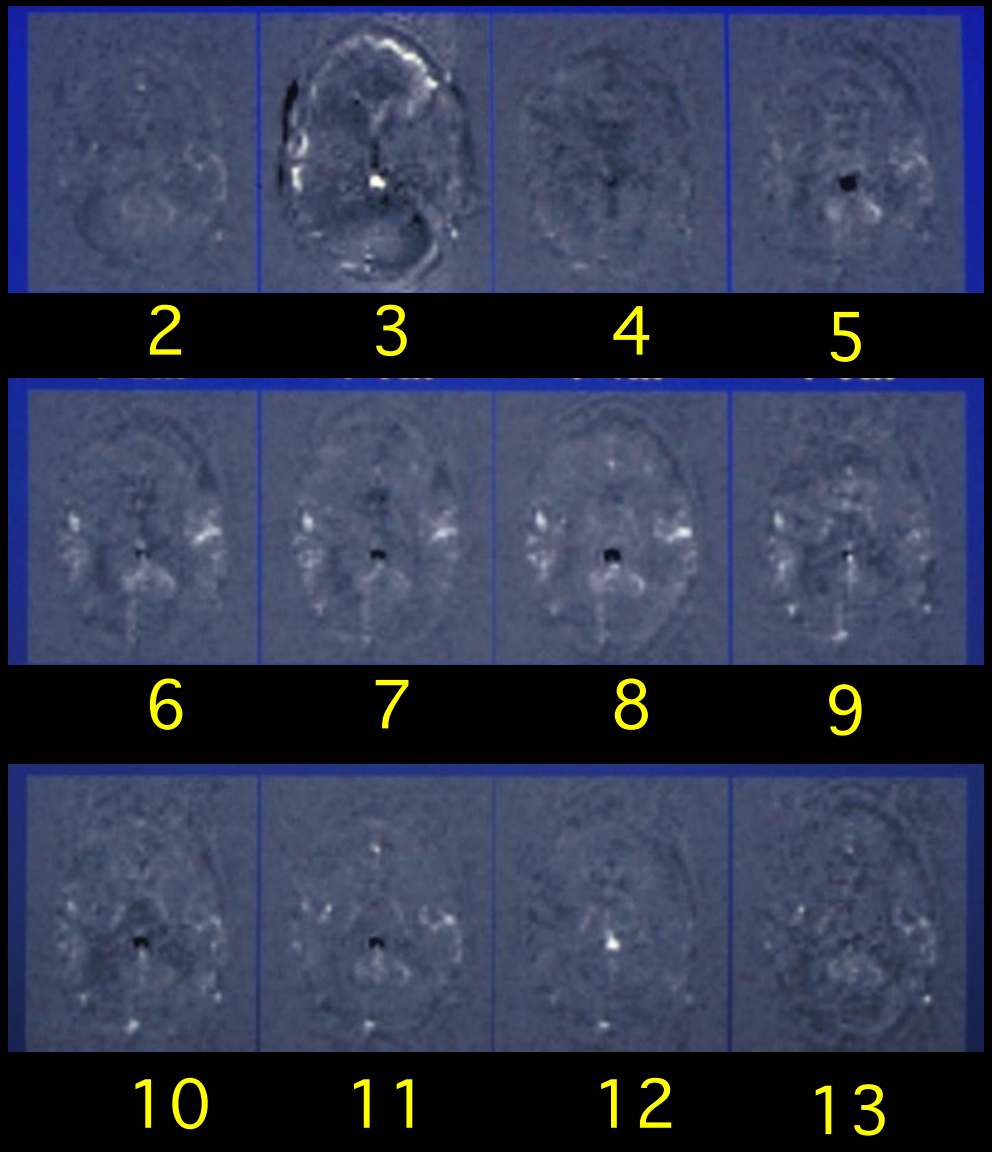


Event-Related Design



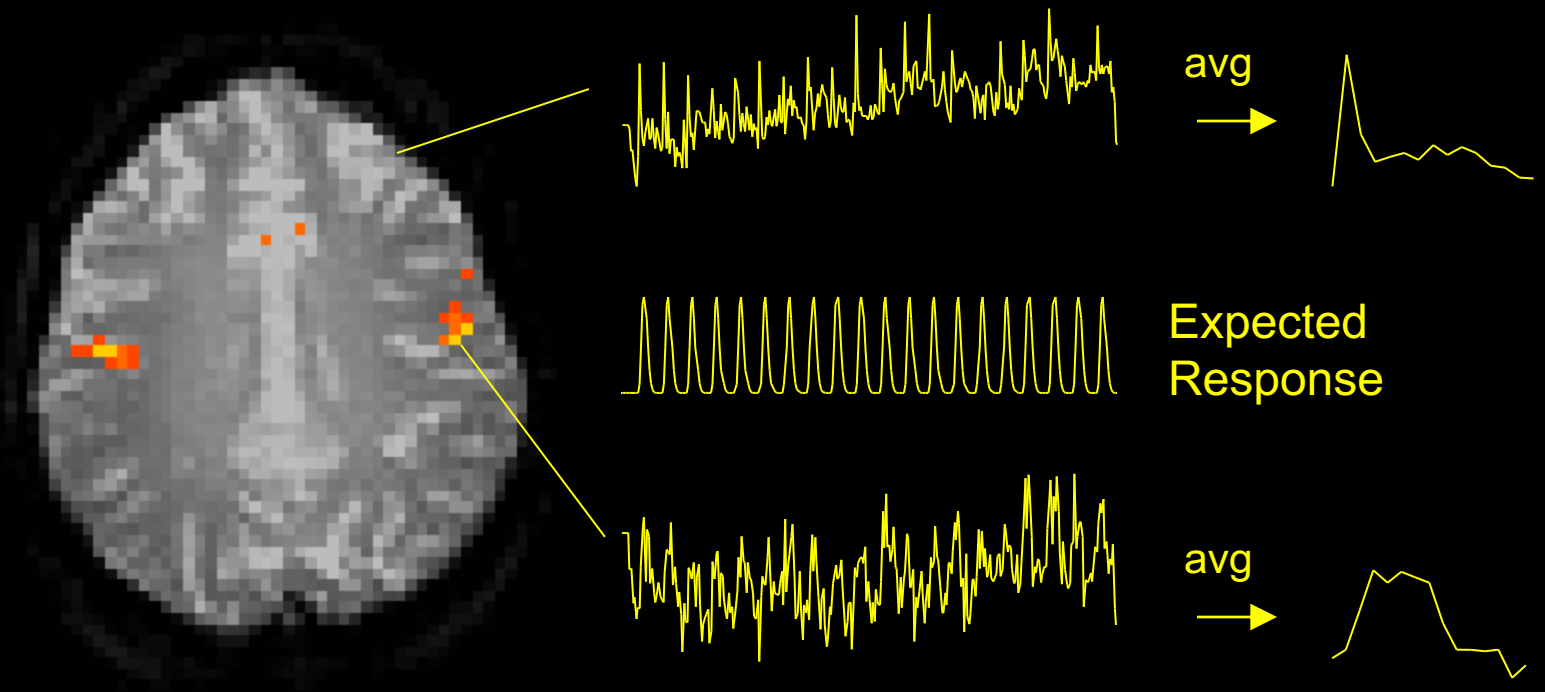
R. M. Birn, P. A. Bandettini, R. W. Cox, R. Shaker, Event - related fMRI of tasks involving brief motion. *Human Brain Mapping* 7: 106-114 (1999).

Overt Word Production



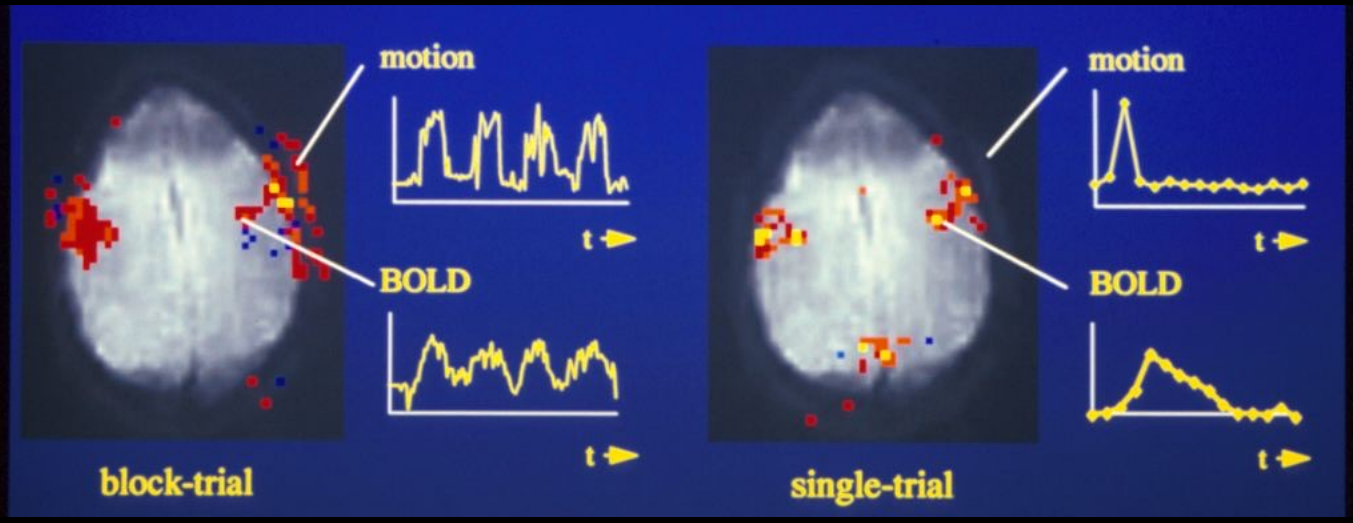
R. M. Birn, P. A. Bandettini, R. W. Cox, R. Shaker, Event - related fMRI of tasks involving brief motion. *Human Brain Mapping* 7: 106-114 (1999).

Speaking - ER-fMRI

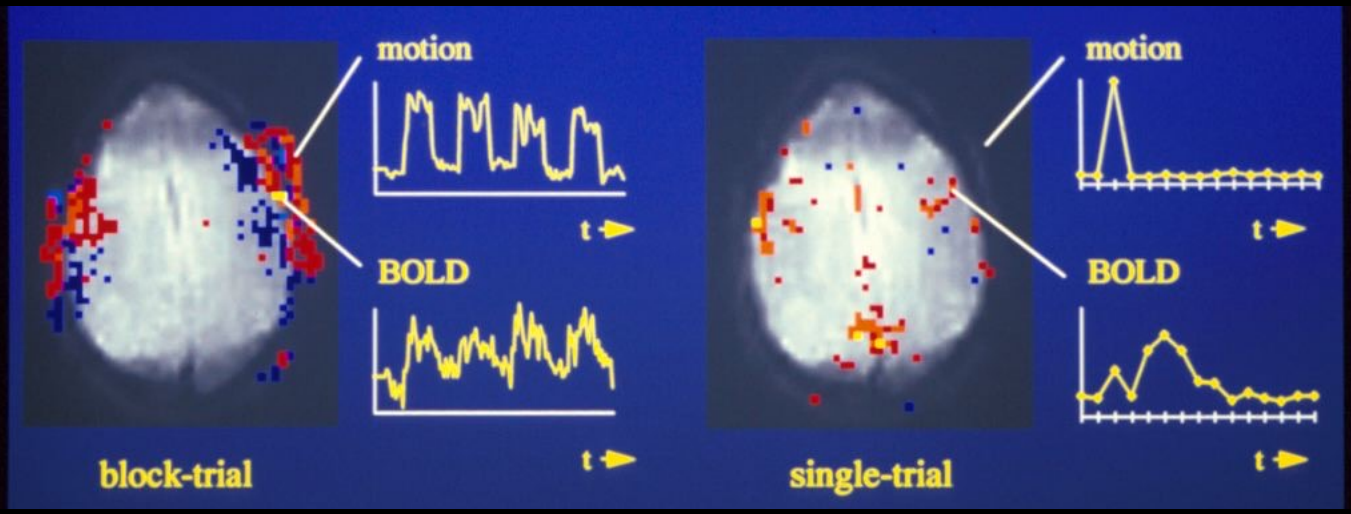


R. M. Birn, P. A. Bandettini, R. W. Cox, R. Shaker, Event - related fMRI of tasks involving brief motion. *Human Brain Mapping* 7: 106-114 (1999).

Tongue Movement



Jaw Clenching



Motion

Recognize?
- Edge effects
- Shorter signal change latencies
- Unusually high signal changes
- External measuring devices

Correct?
- Image registration algorithms
- Orthogonalize to motion-related function *(cardiac, respiration, movement)*
- Navigator echo for k-space alignment *(for multishot techniques)*
- Re-do scan

Bypass?
- Paradigm timing strategies..
- Gating (with T1-correction)

Suppress?
- Flatten image contrast
- Physical restraint
- Averaging, smoothing

Visual Cortex

ISI, SD

20, 20

12, 2

10, 2

ISI, SD

8, 2

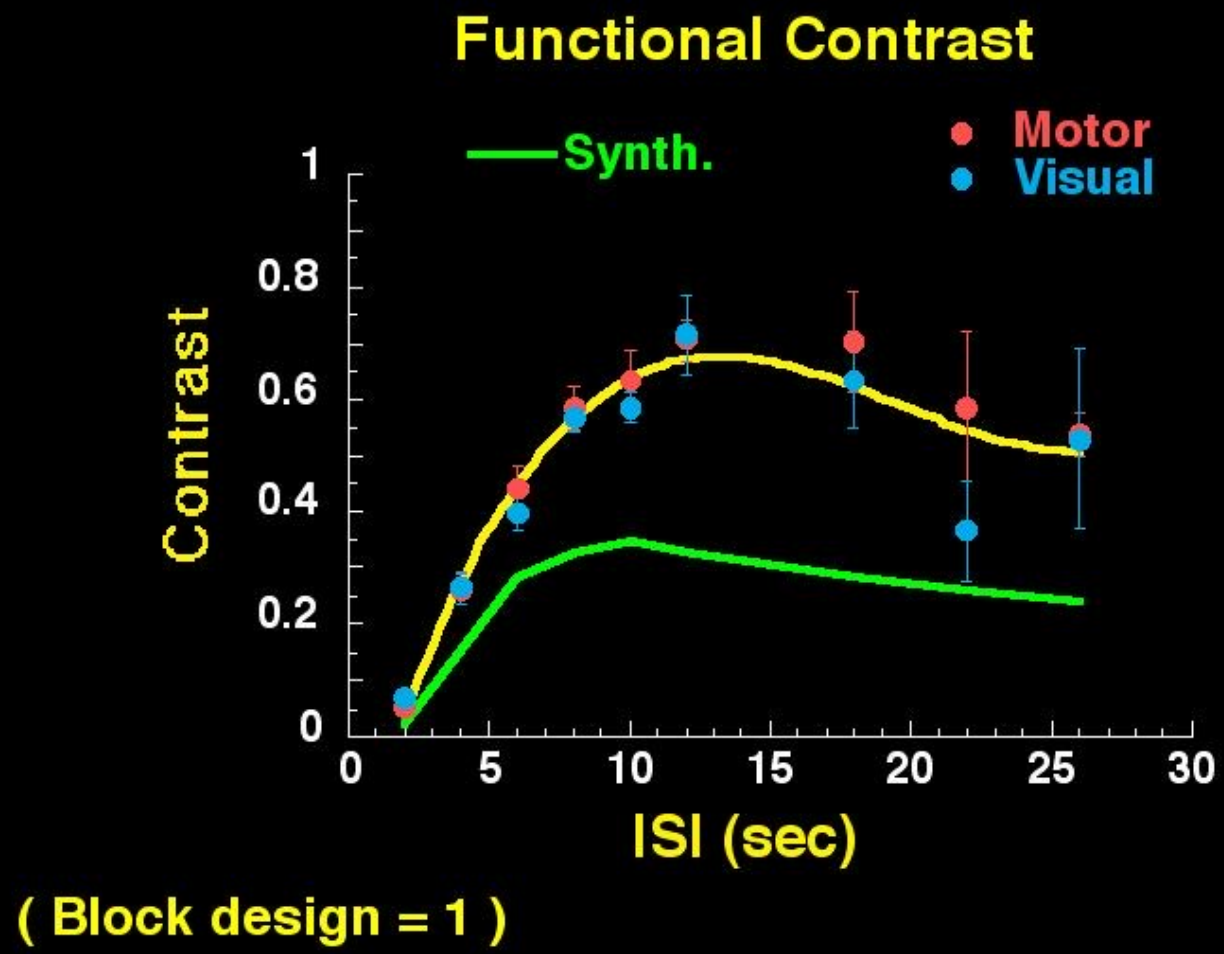
6, 2

4, 2

2, 2

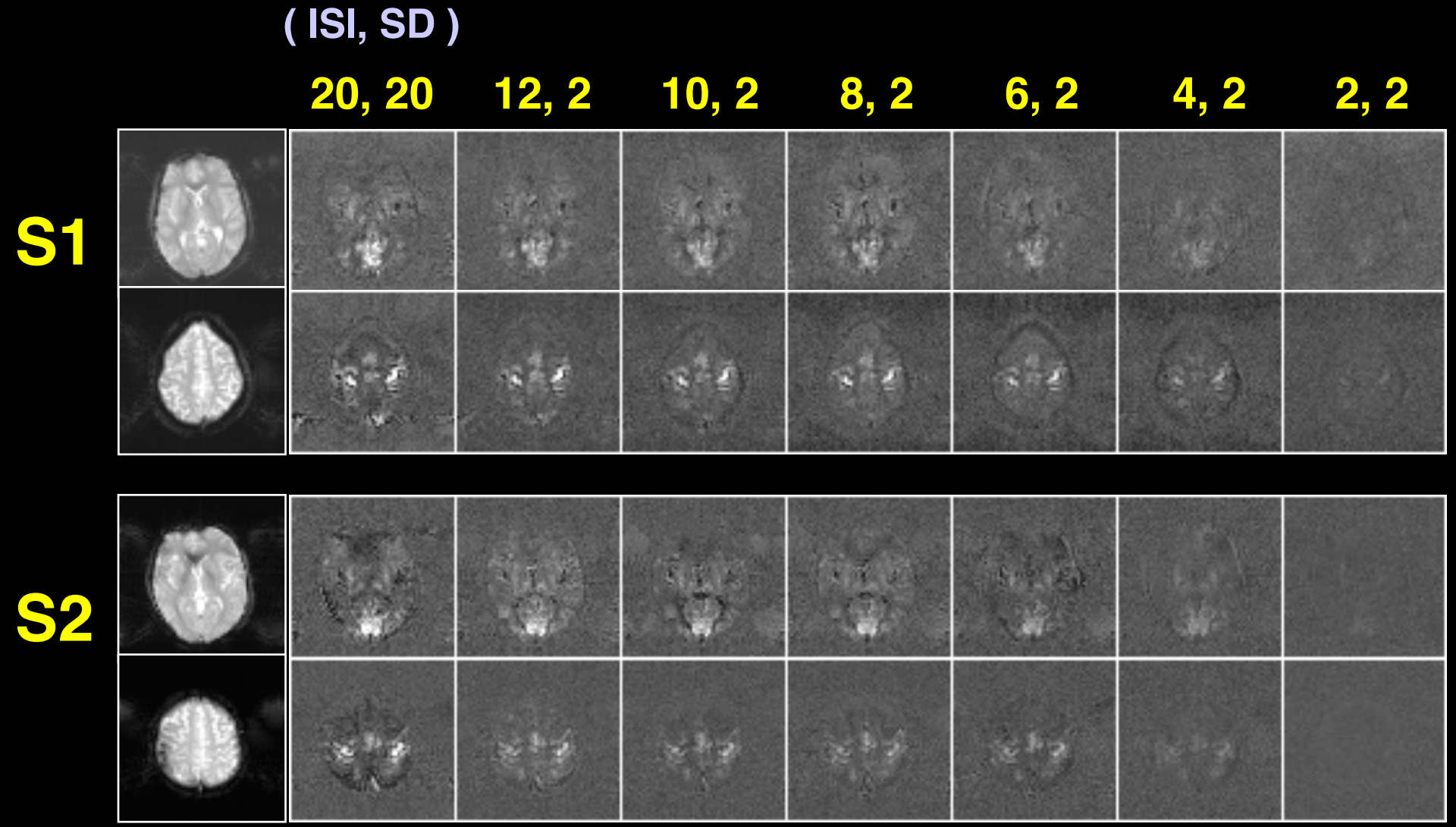
Motor Cortex

ISI, SD	ISI, SD
20, 20	8, 2
12, 2	6, 2
10, 2	4, 2
	2, 2



P. A. Bandettini, R. W. Cox. Functional contrast in constant interstimulus interval event - related fMRI: theory and experiment. *Magn. Reson. Med.* 43: 540-548 (2000).

Contrast to Noise Images



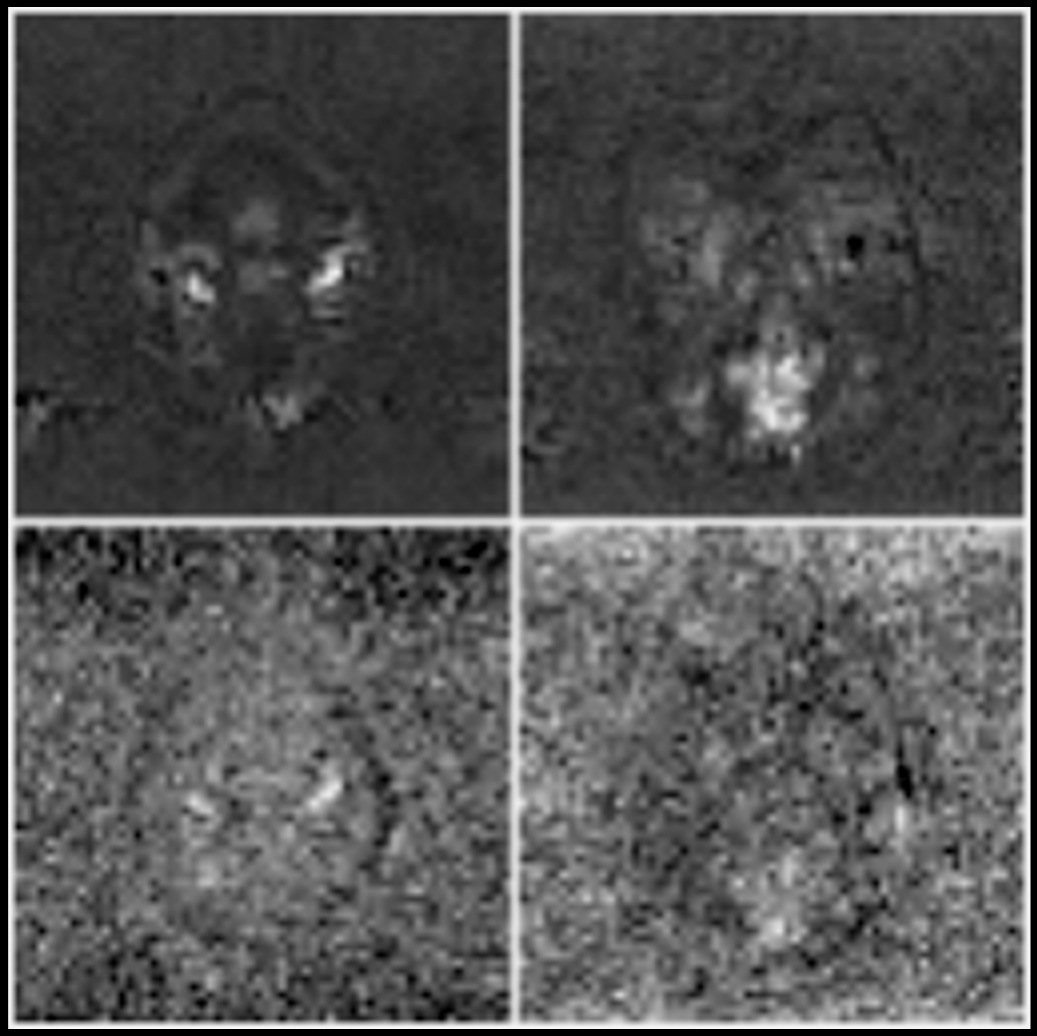
P. A. Bandettini, R. W. Cox. Functional contrast in constant interstimulus interval event - related fMRI: theory and experiment. *Magn. Reson. Med.* 43: 540-548 (2000).

Motor Visual

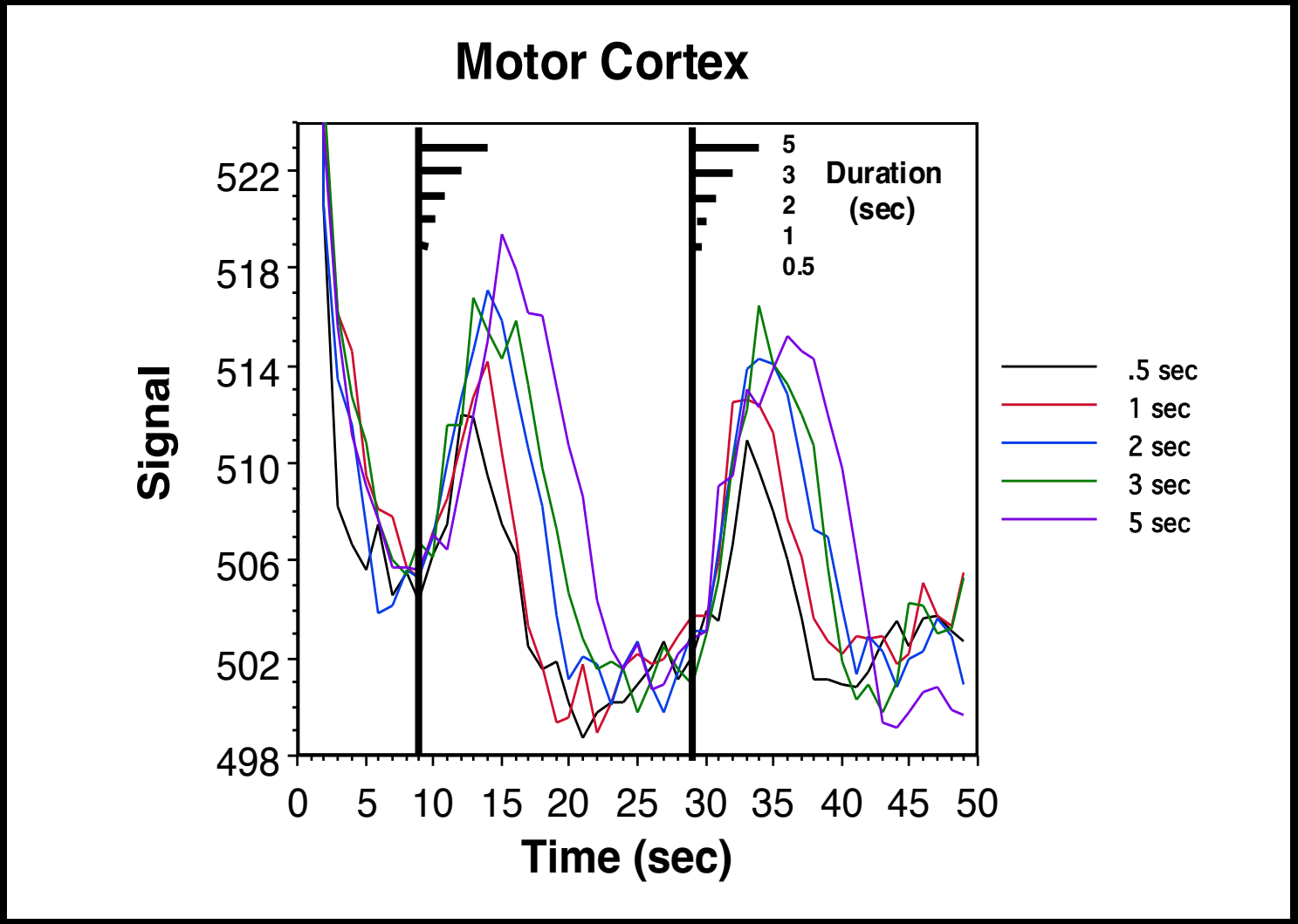
(ISI, SD)

20, 20

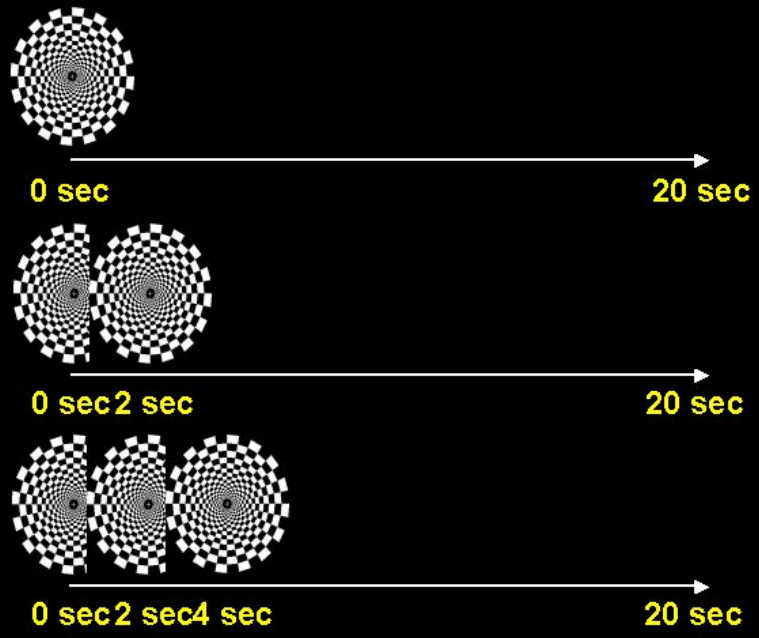
2, 2



Relative differences in activation intensities may reflect spatial differences in hemodynamic responsivity. (draining veins vs. capillaries).



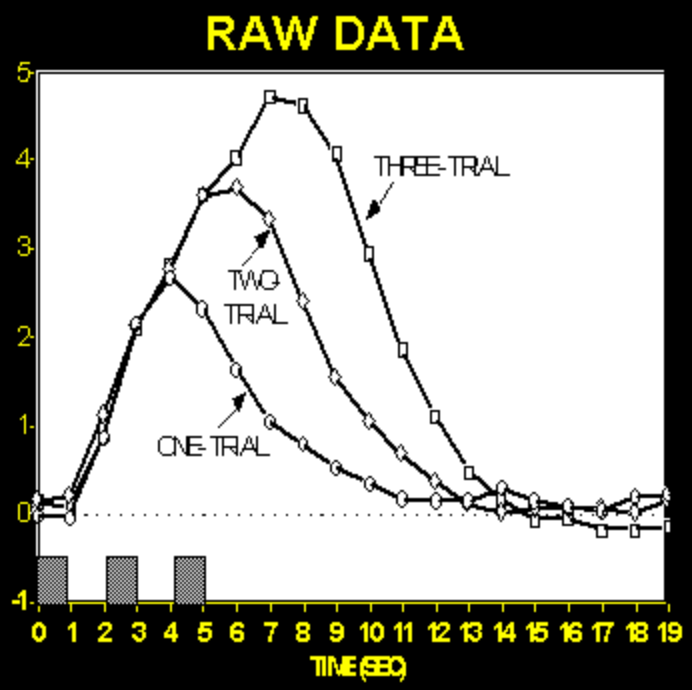
Bandettini, et al., The functional dynamics of blood oxygenation level contrast in the motor cortex, 12'th Proc. Soc. Magn. Reson. Med., New York, p. 1382. (1993).

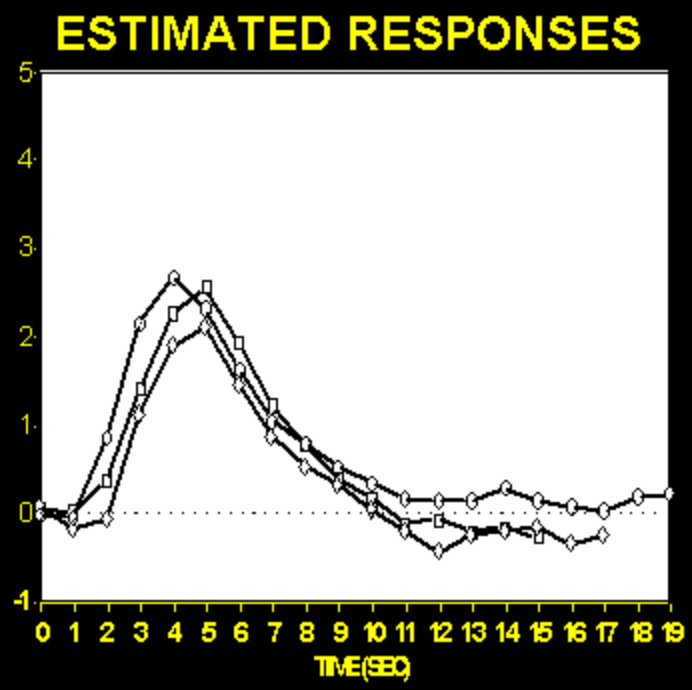


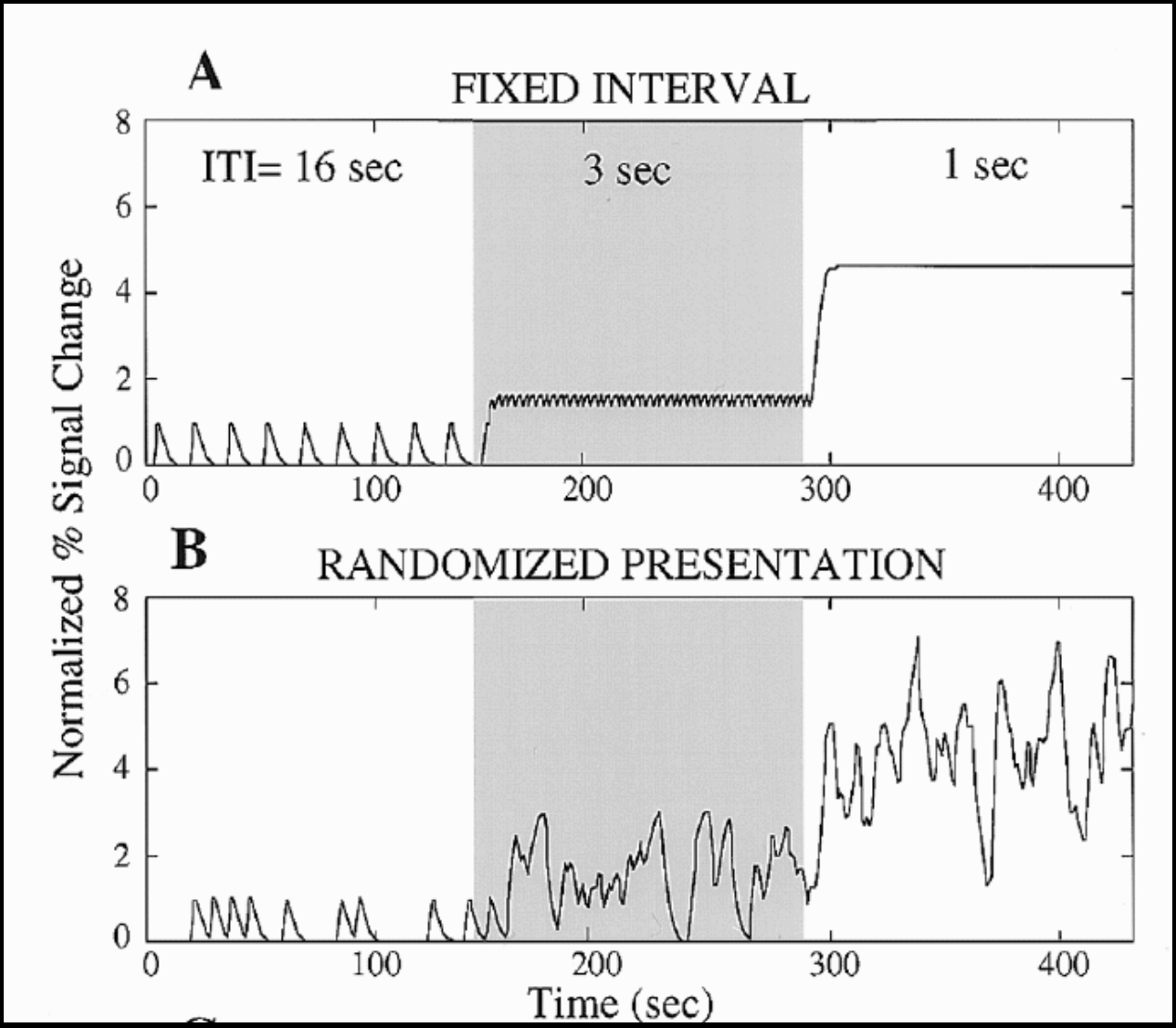
Human Brain Mapping 5:329–340(1997)

Selective Averaging of Rapidly Presented Individual Trials Using fMRI

Anders M. Dale* and Randy L. Buckner





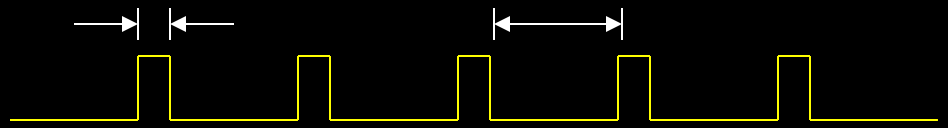


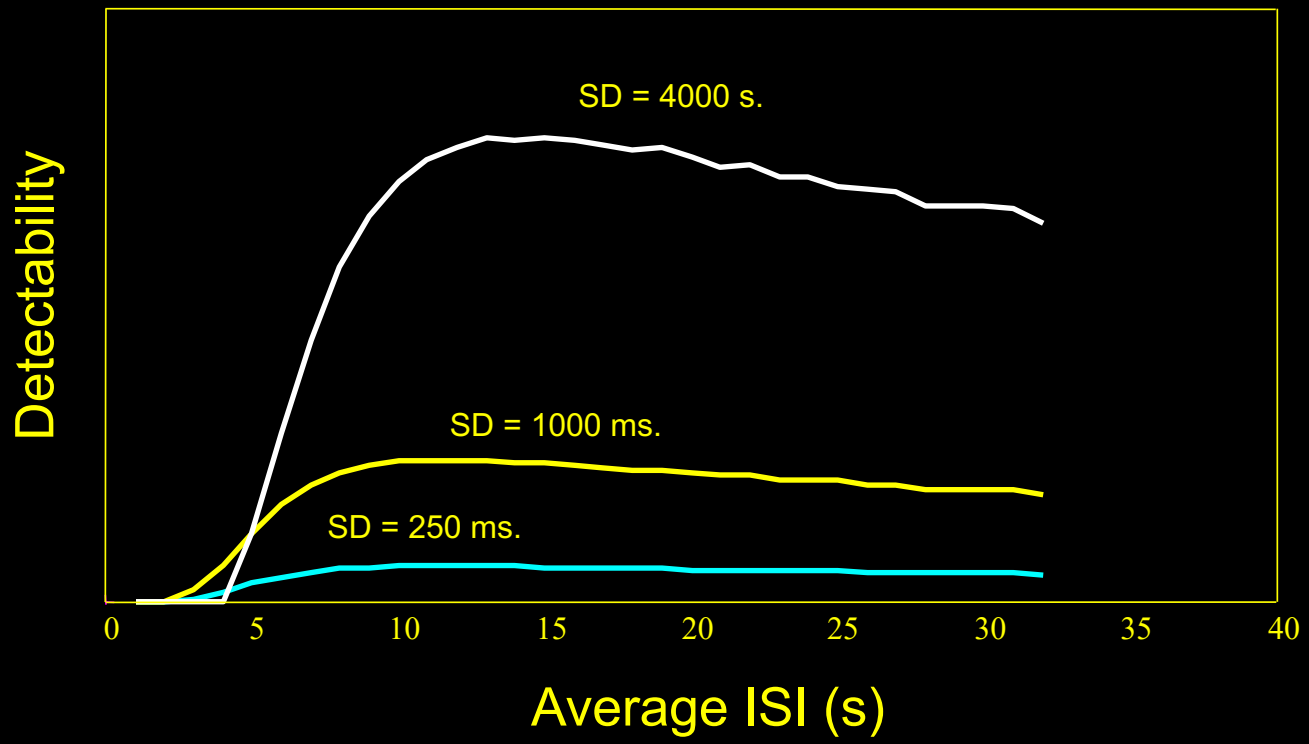
M.A. Burock et al. *NeuroReport*, 9, 3735-9 (1998)

Detectability – constant ISI

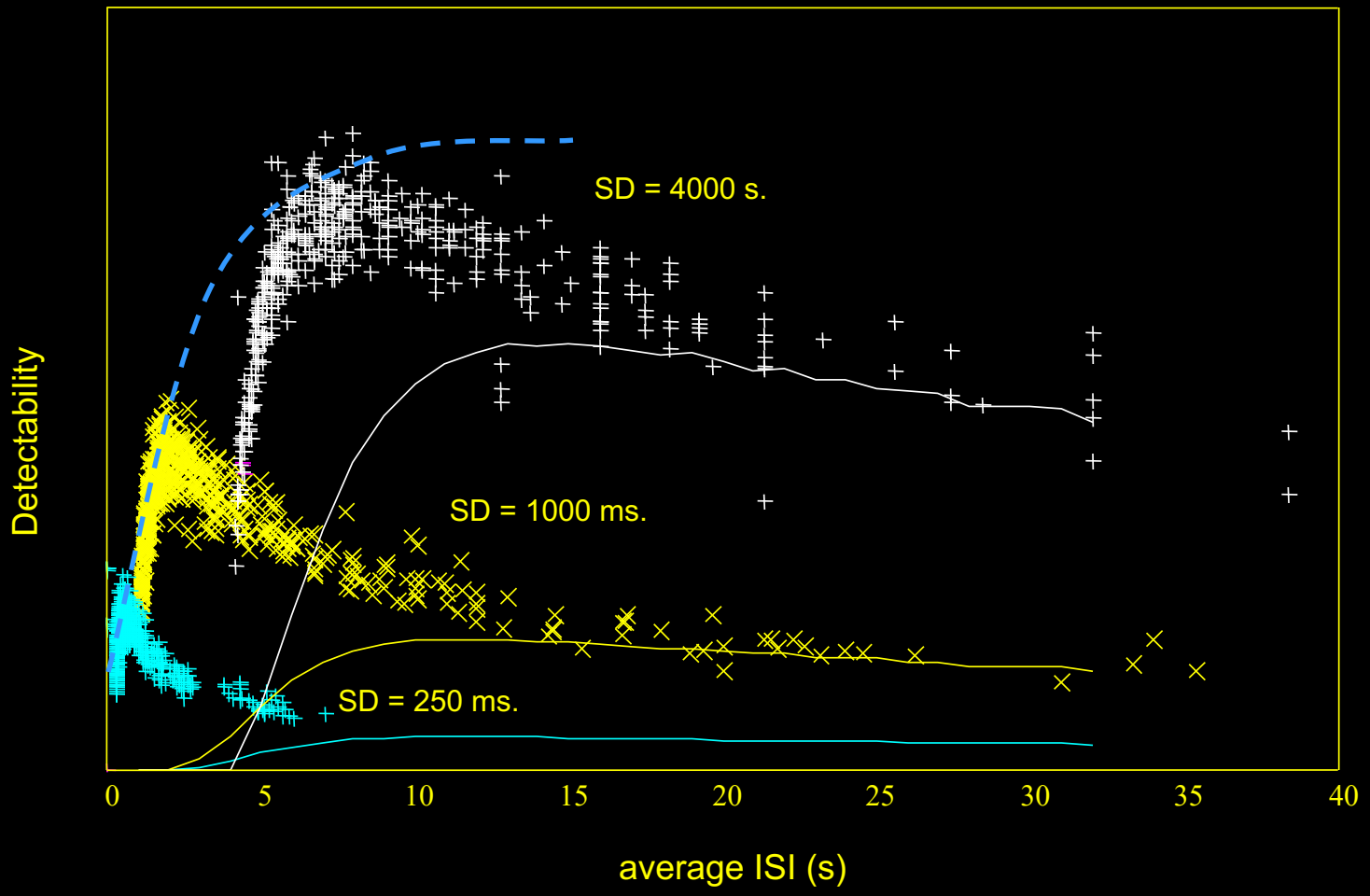
SD – stimulus duration

ISI – inter-stimulus interval



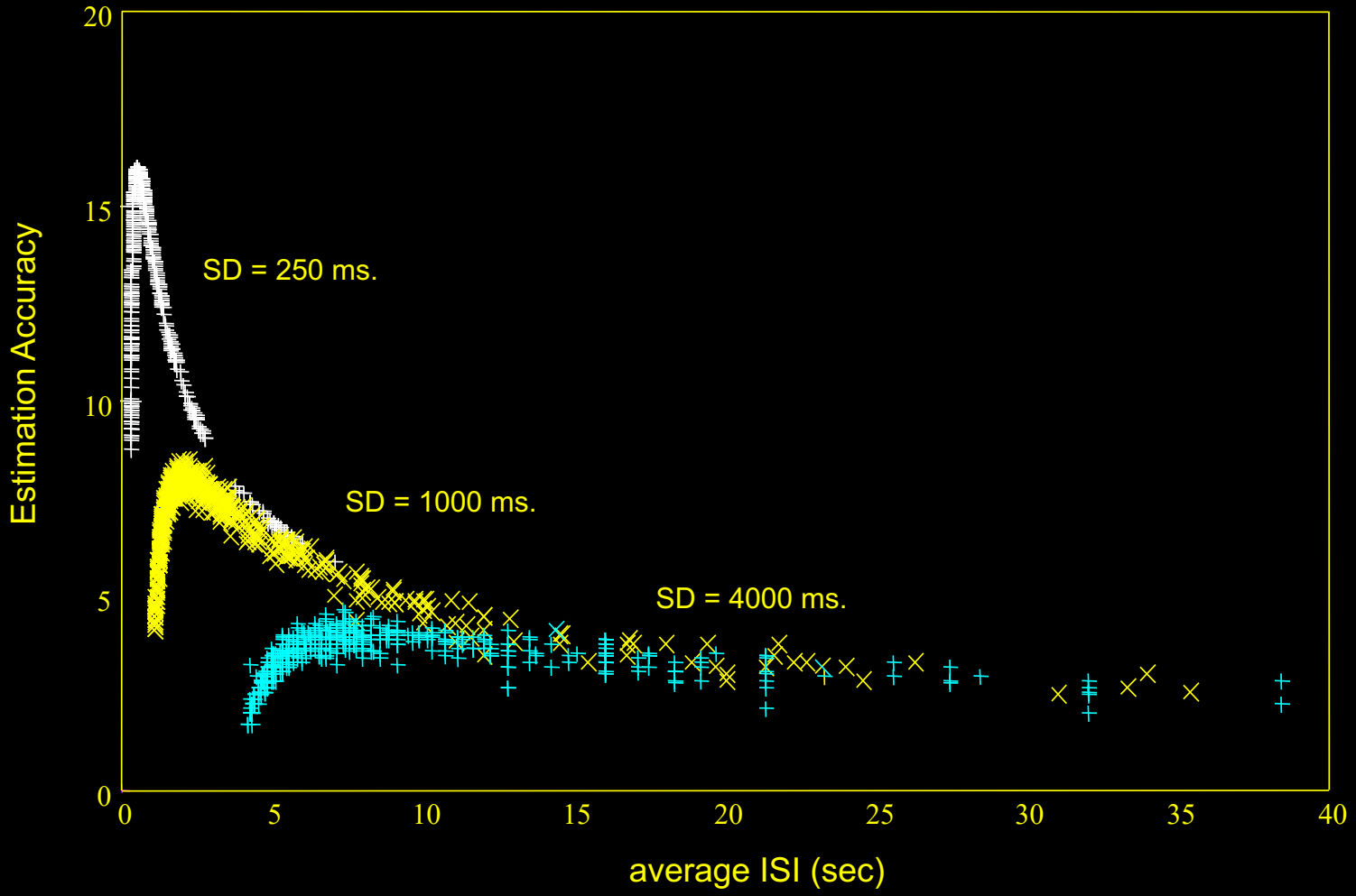


Detectability vs. Average ISI



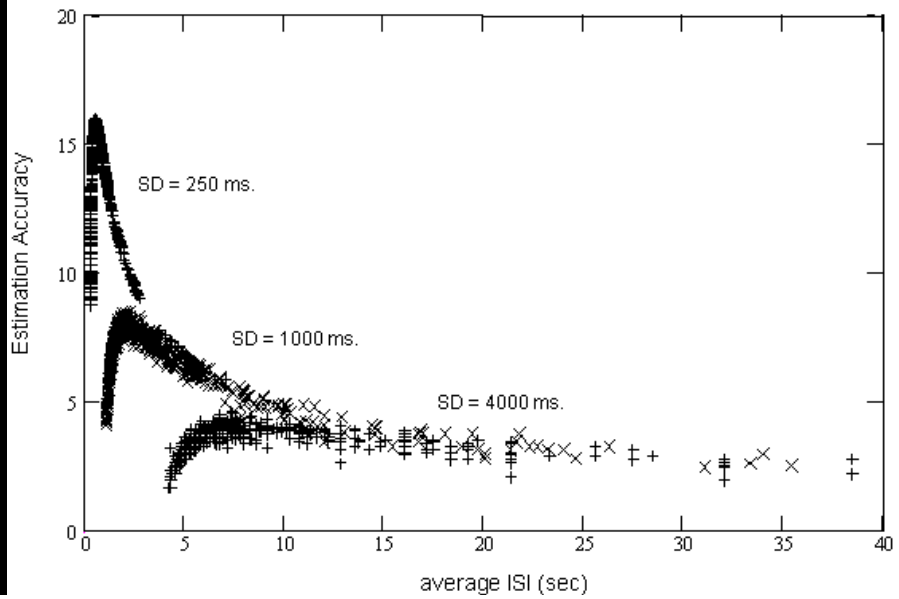
R. M. Birn, R. W. Cox, P. A. Bandettini, Detection versus estimation in Event-Related fMRI: choosing the optimal stimulus timing. *NeuroImage* 15: 262-264, (2002).

Estimation accuracy vs. average ISI

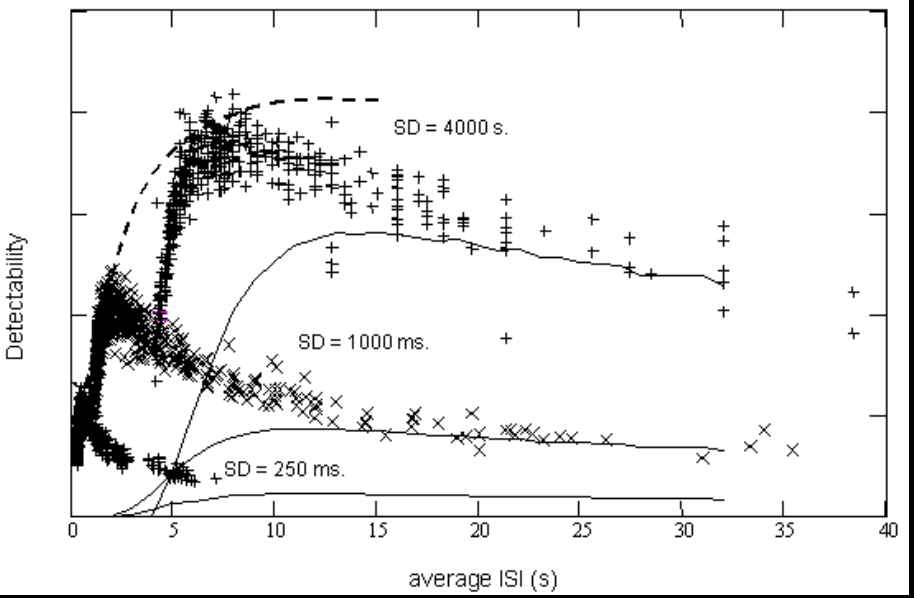


R. M. Birn, R. W. Cox, P. A. Bandettini, Detection versus estimation in Event-Related fMRI: choosing the optimal stimulus timing. *NeuroImage* 15: 262-264, (2002).

Estimation accuracy vs. average ISI

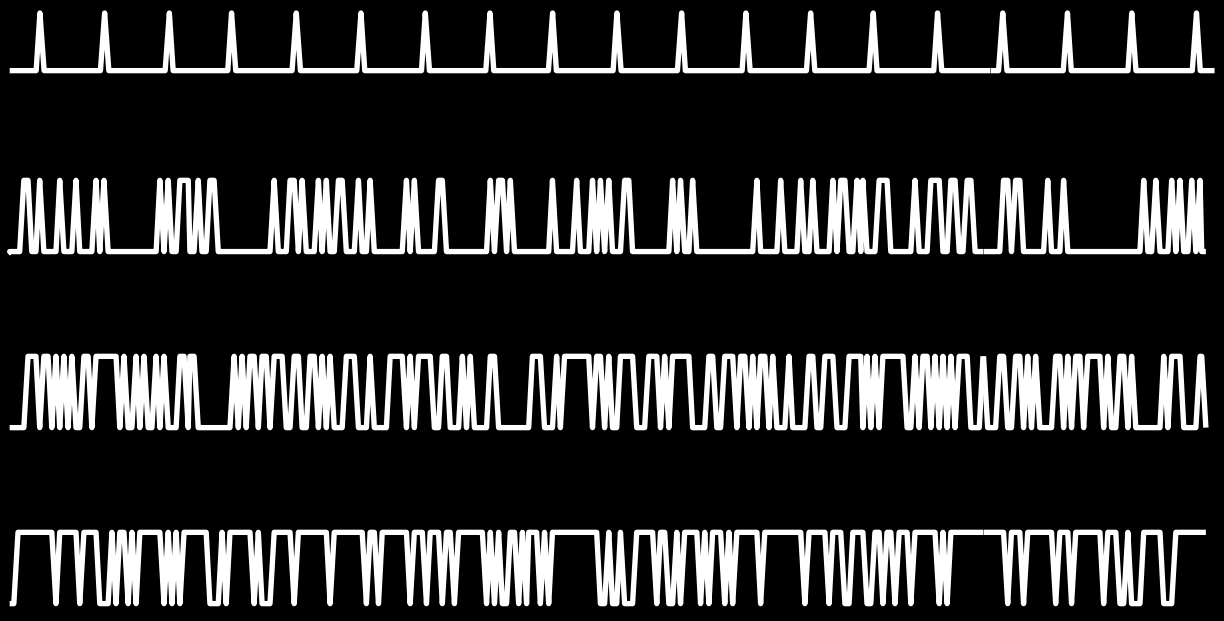


Detectability vs. Average ISI



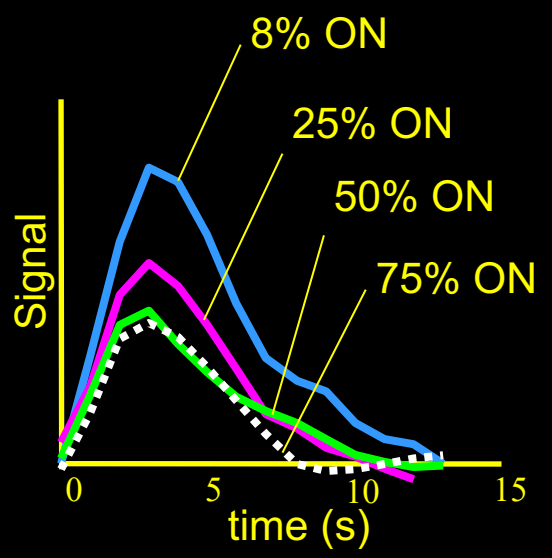
Varying “ON” and “OFF” periods

- *Rapid event-related design with varying ISI*

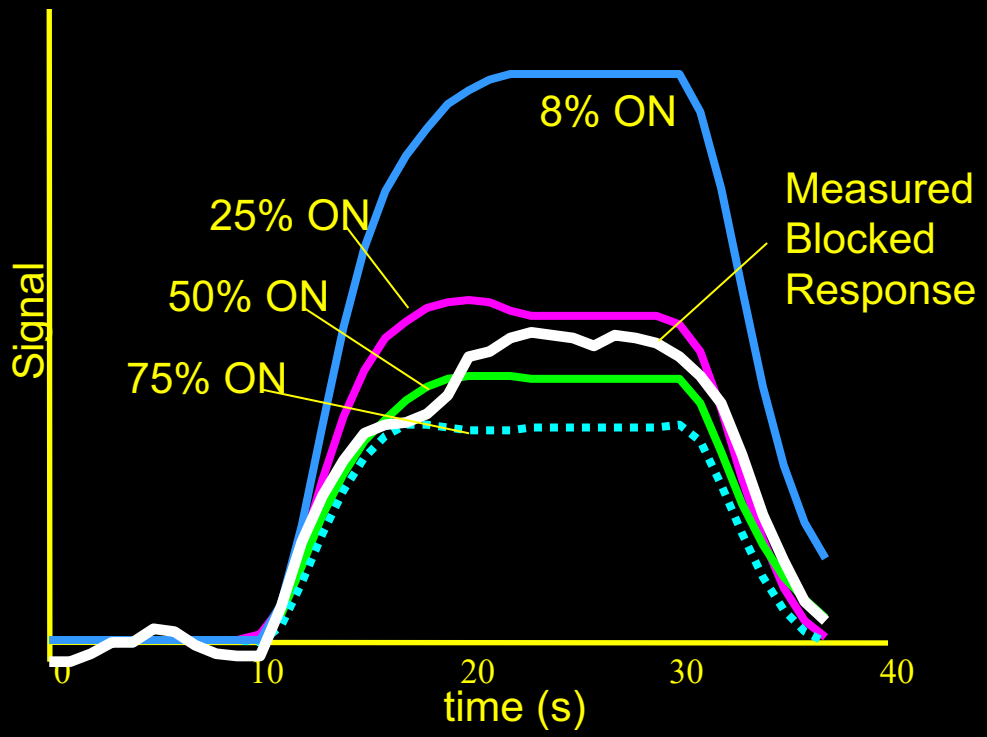


Varying “ON” and “OFF” periods

Estimated Impulse Response



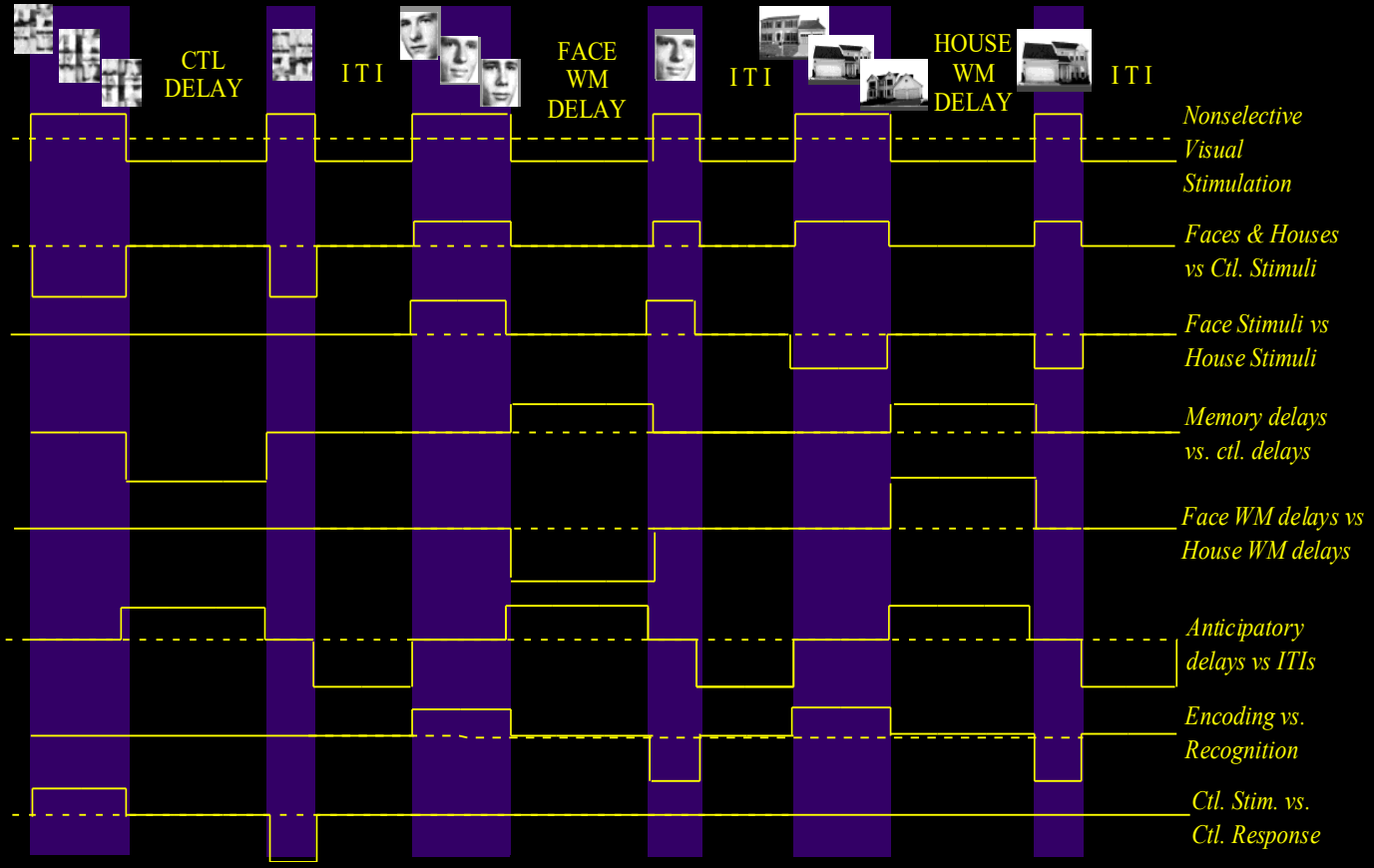
Predicted Responses to 20 s stimulation



Neuronal Activation Input Strategies

1. Block Design
2. Parametric Design
3. Frequency Encoding
4. Phase Encoding
5. Event Related
6. Orthogonal Design
7. Free Behavior Design

Example of a Set of Orthogonal Contrasts for Multiple Regression



Courtney, S. M., L. G. Ungerleider, et al. (1997). "Transient and sustained activity in a distributed neural system for human working memory." Nature 386(6625): 608-11.

Neuronal Activation Input Strategies

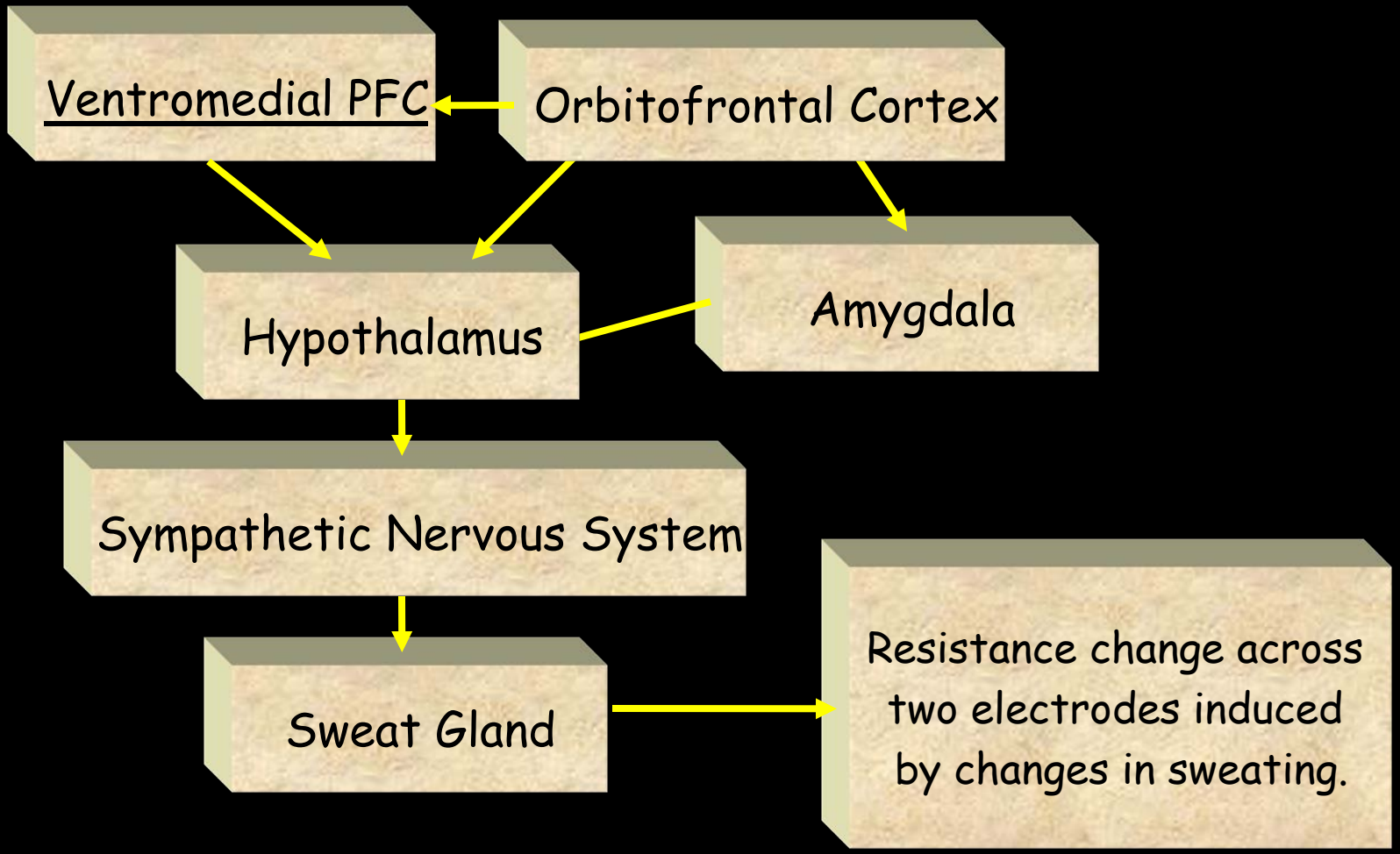
1. Block Design
2. Parametric Design
3. Frequency Encoding
4. Phase Encoding
5. Event Related
6. Orthogonal Design
7. Free Behavior Design

Free Behavior Design

Use a continuous measure as a reference function:

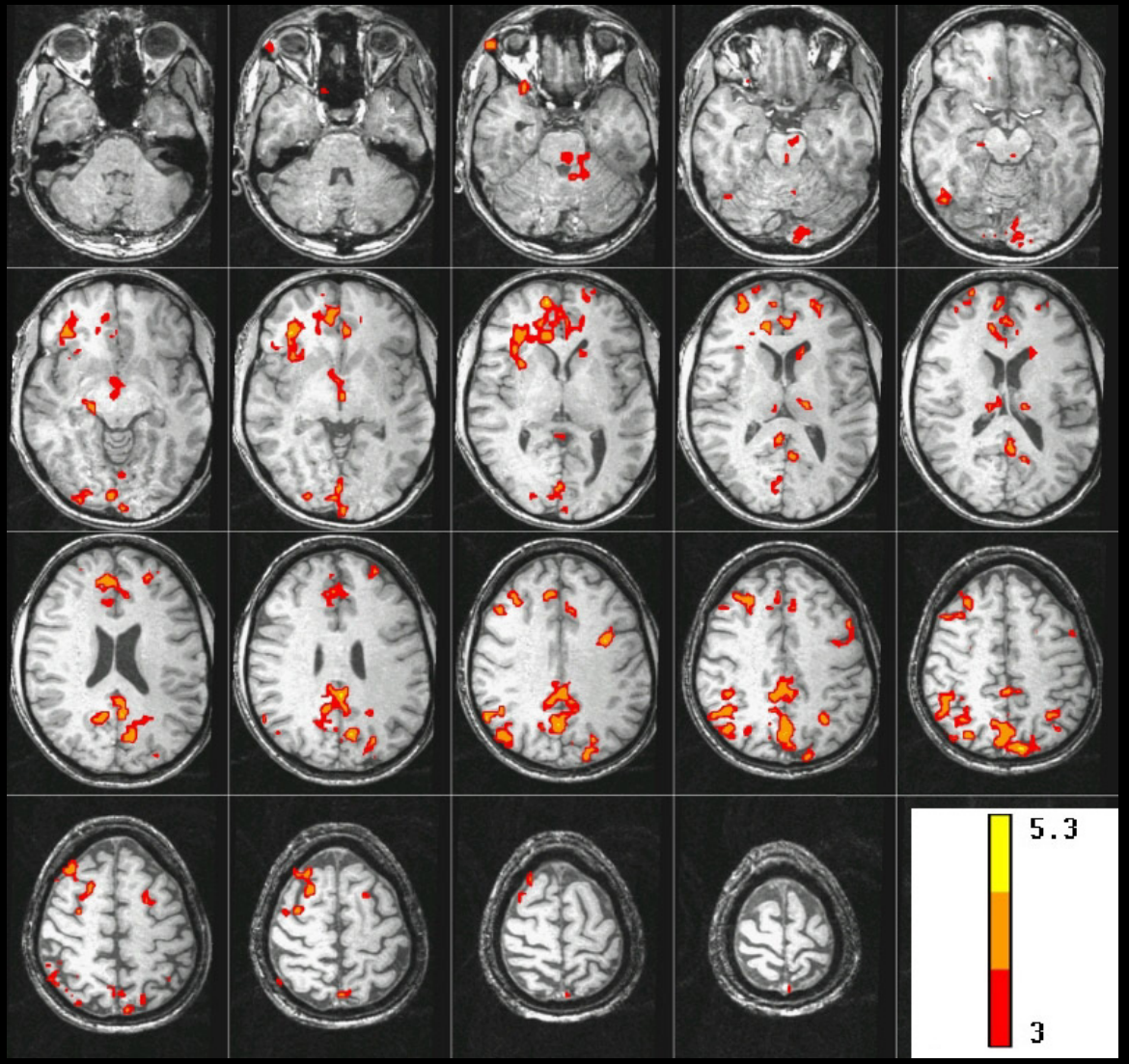
- Task performance
- Skin Conductance
- Heart, respiration rate..
- Eye position
- EEG

The Skin Conductance Response (SCR)



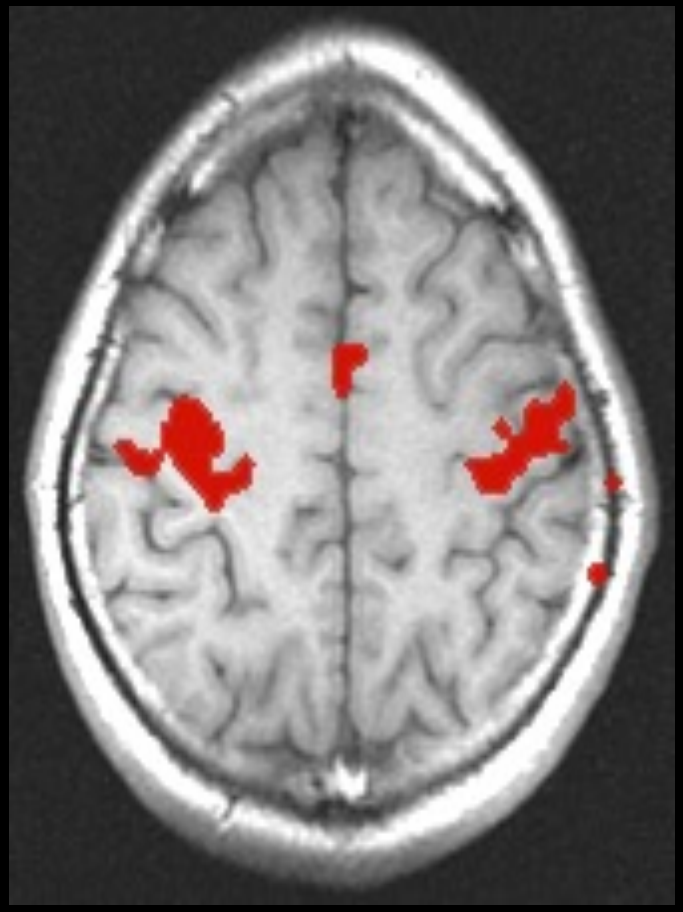
Patterson et al. (submitted)

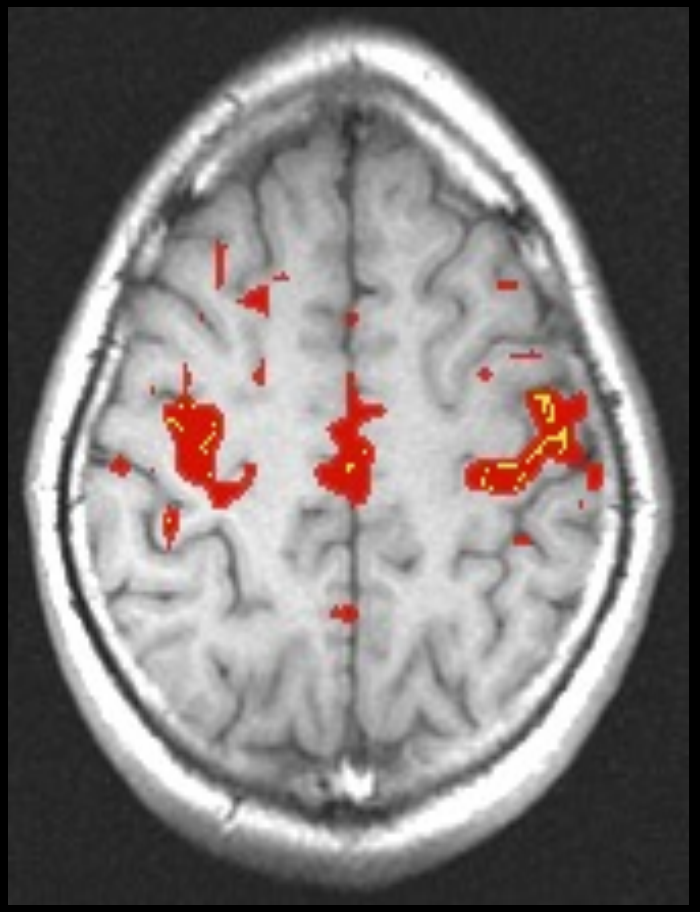
Brain activity correlated with SCR during "Rest"



Patterson et al. (submitted)

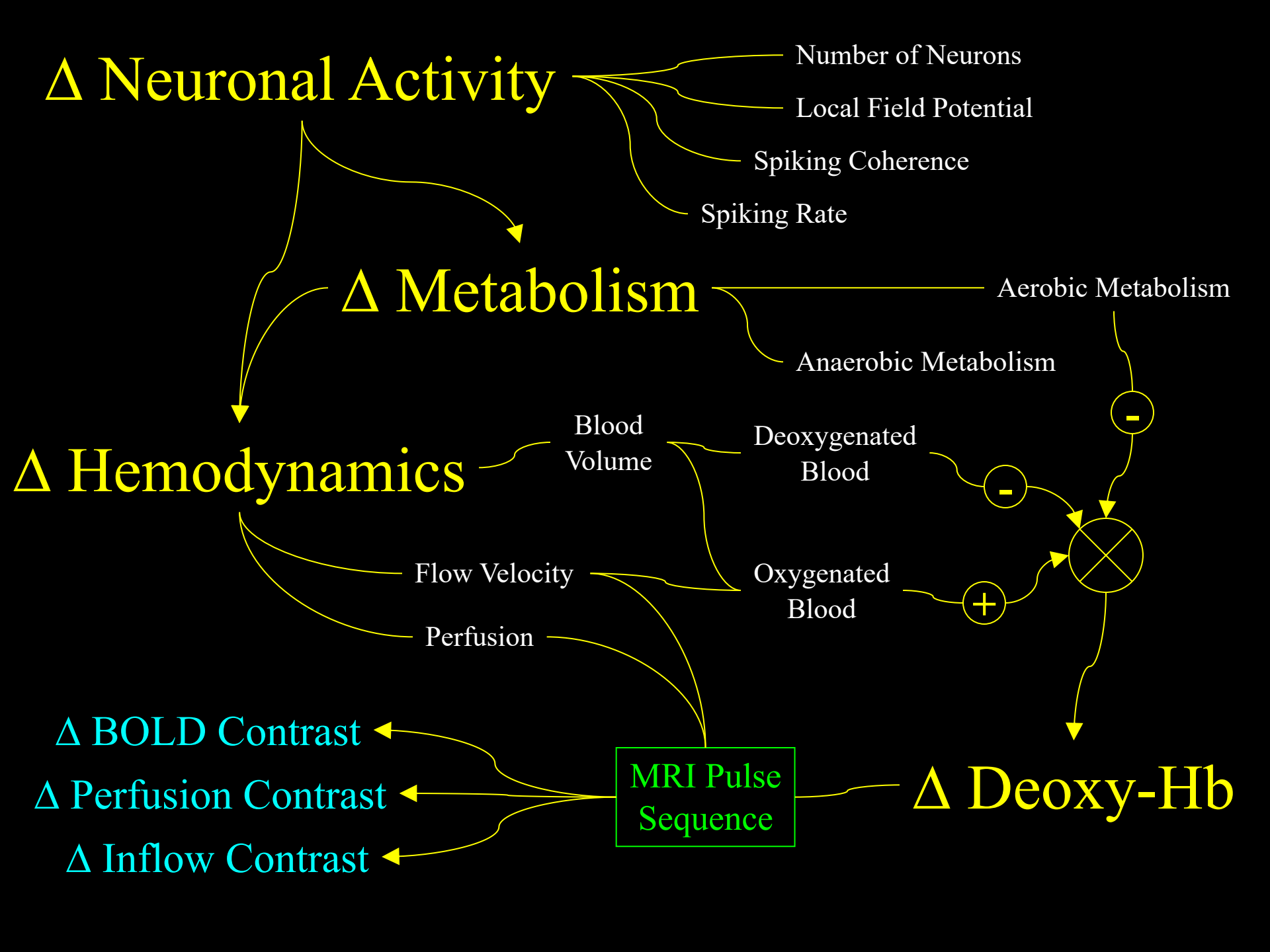
Resting Hemodynamic Autocorrelations





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

Calibration methods for Temporal Resolution and Interpretation...

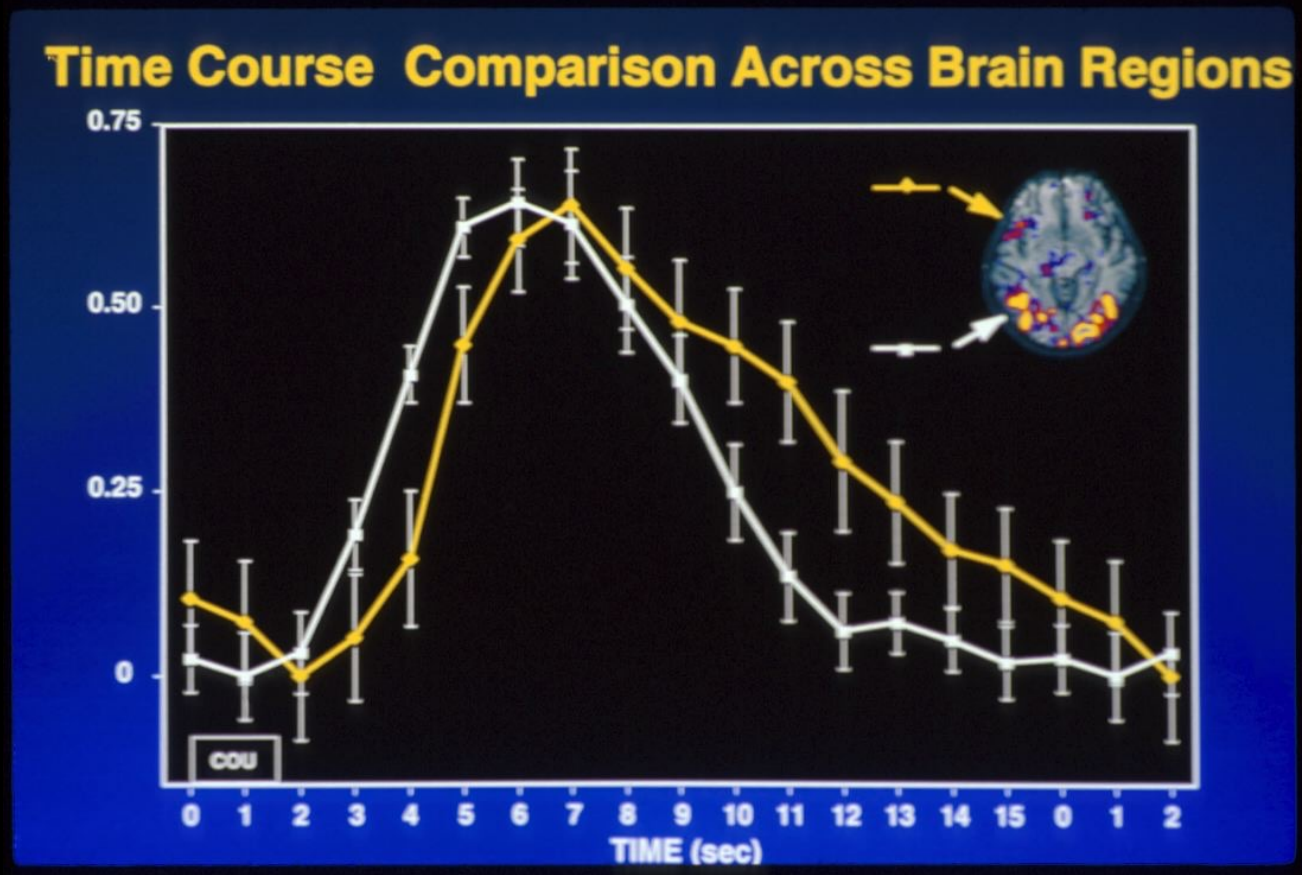

Δ Neuronal Activity
Number of Neurons
Local Field Potential
Spiking Coherence
Spiking Rate
Δ Metabolism
Aerobic Metabolism
Anaerobic Metabolism
Δ Hemodynamics
Blood Volume
Deoxygenated Blood
Flow Velocity
Oxygenated Blood
Perfusion
-
-
+
Δ BOLD Contrast
Δ Perfusion Contrast
Δ Inflow Contrast
MRI Pulse Sequence
Δ Deoxy-Hb

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

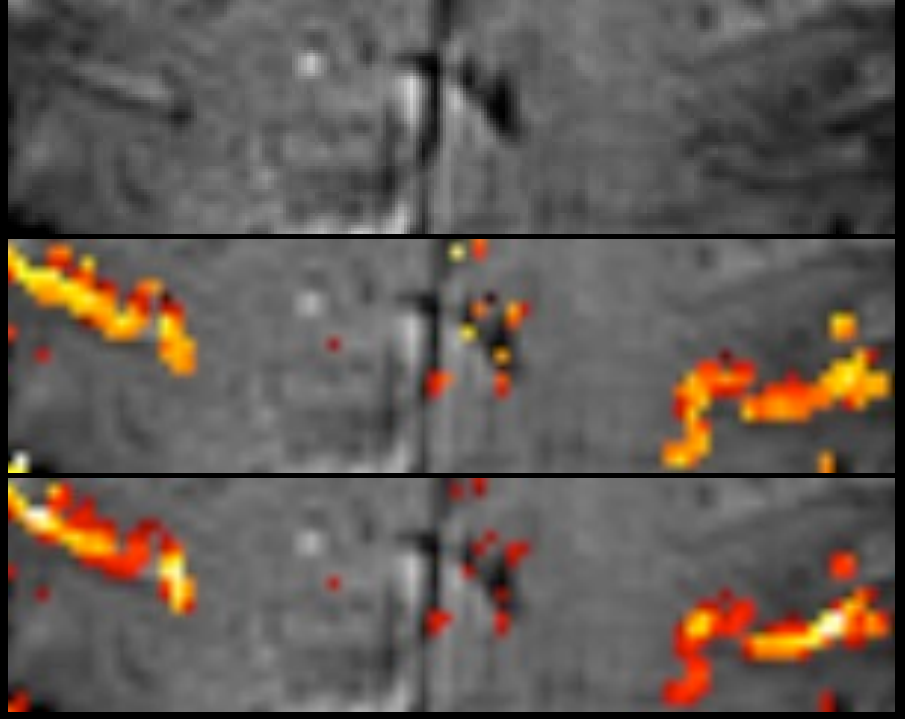
(neuroimaging/single trial/language/prefrontal)

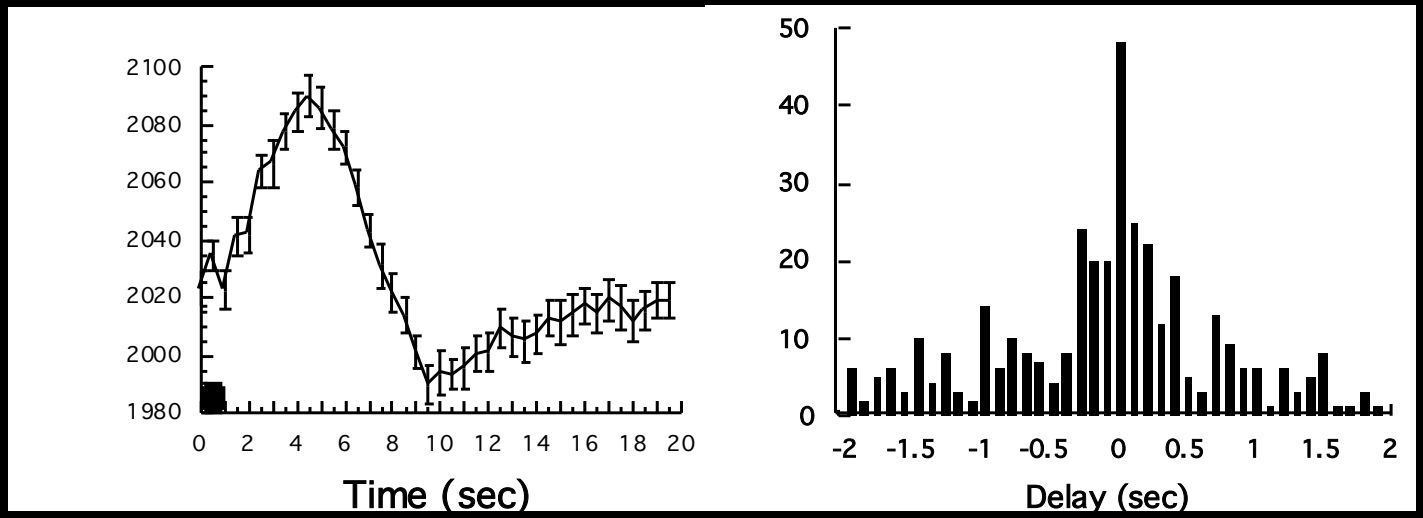
RANDY L. BUCKNER[†‡§¶], PETER A. BANDETTINI[†‡], KATHLEEN M. O'CRAVEN[†‖], ROBERT L. SAVOY[†‖], STEVEN E. PETERSEN[*††], MARCUS E. RAICHLE[§*†††], AND BRUCE R. ROSEN[†‡]



Latency

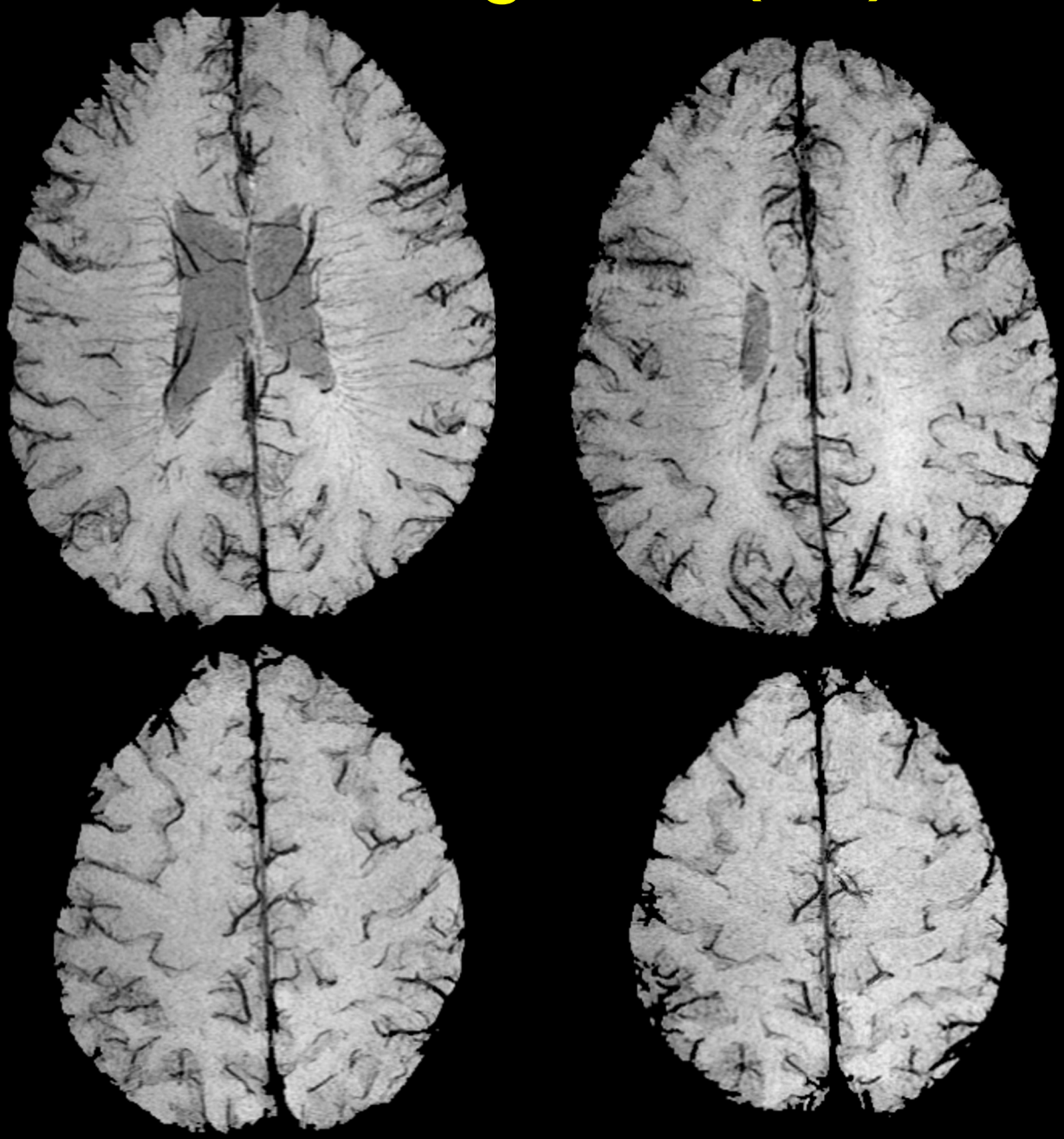
Magnitude

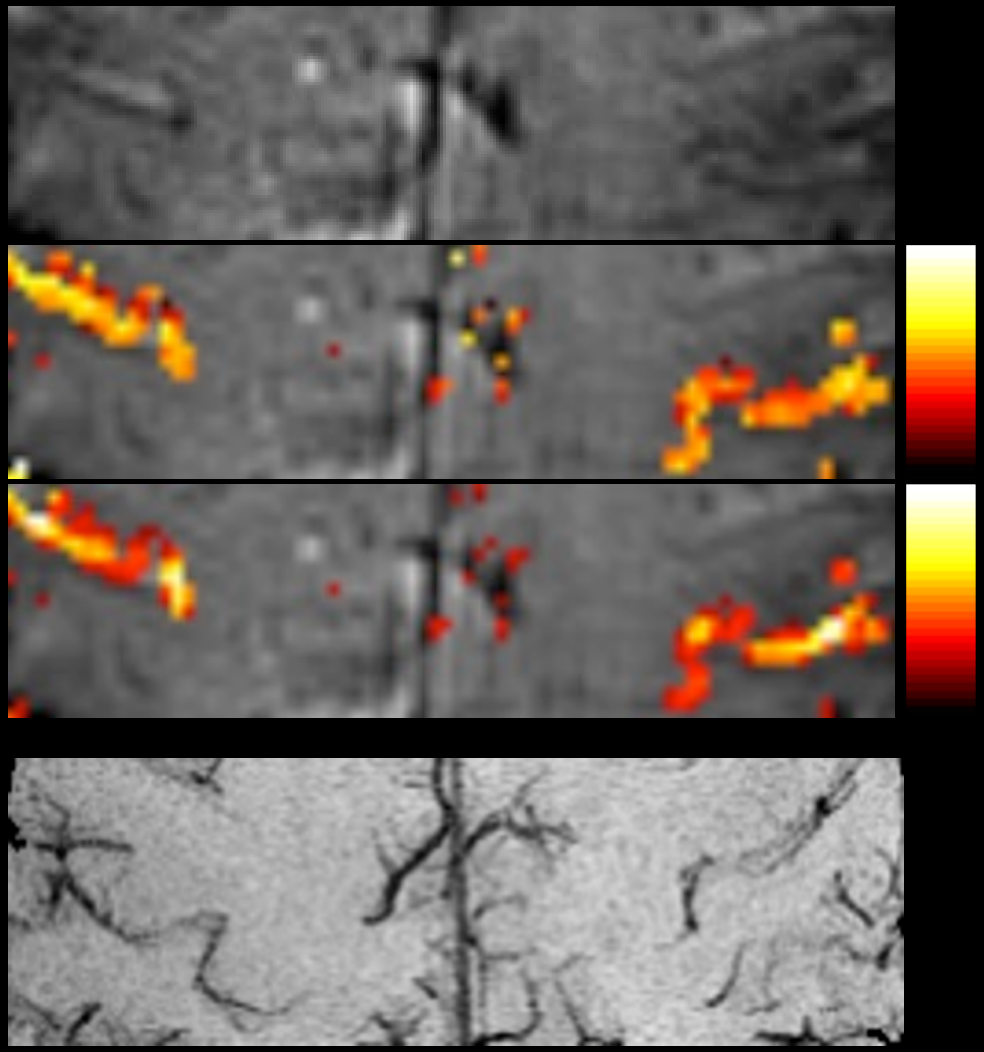




P. A. Bandettini, The temporal resolution of Functional MRI *in* "Functional MRI" (C. Moonen, and P. Bandettini., Eds.), p. 205-220, Springer - Verlag,. 1999.

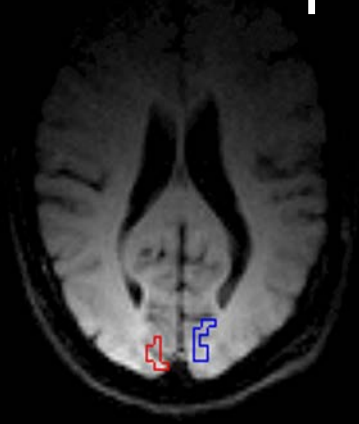
Venograms (3T)



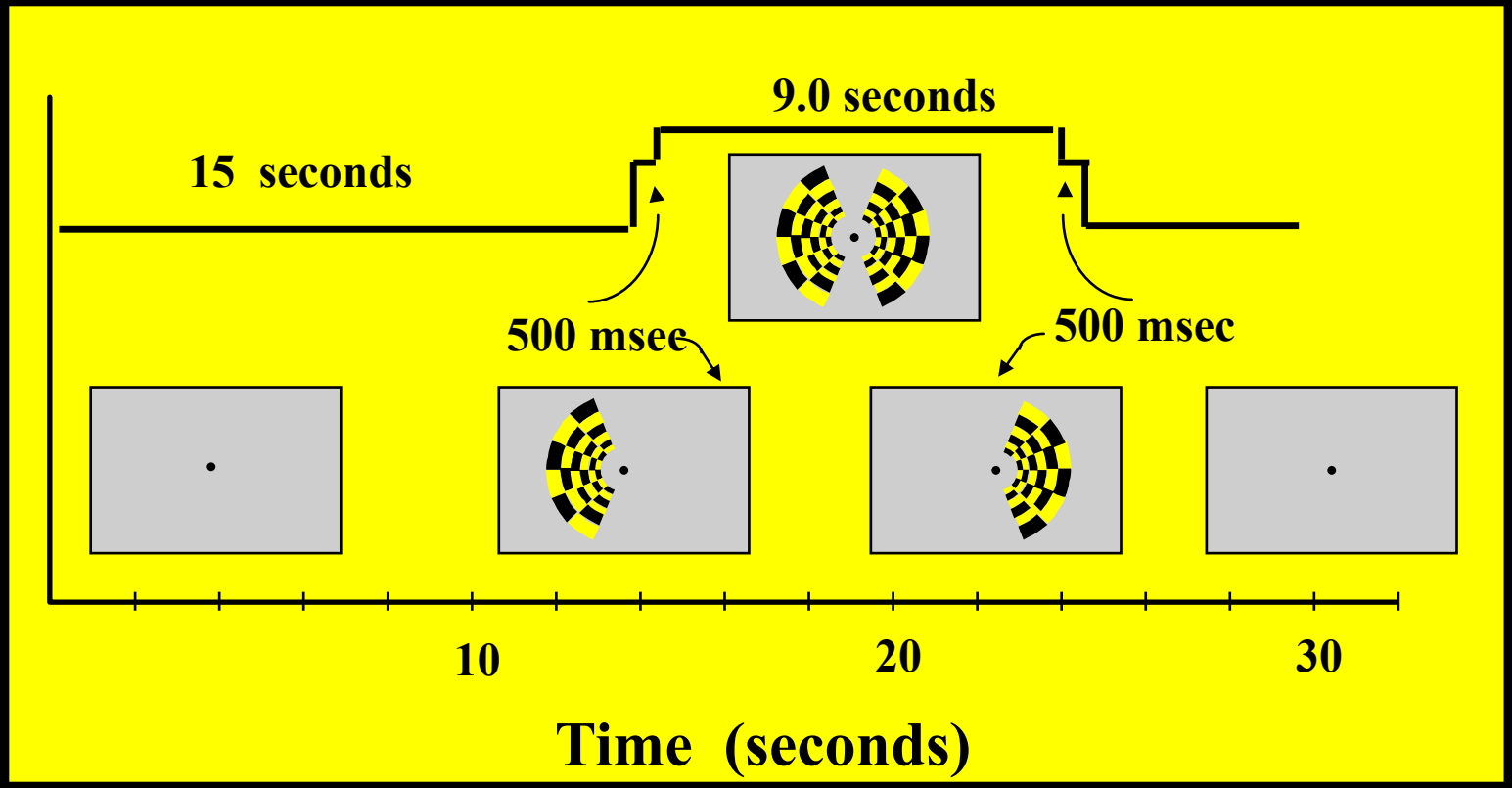


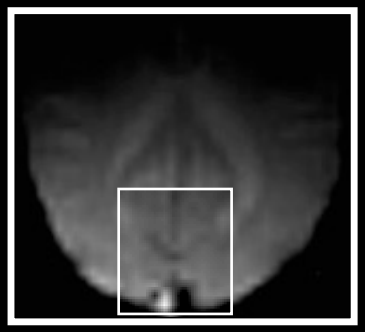
Hemi-Field Experiment

Left Hemisphere



Right Hemisphere



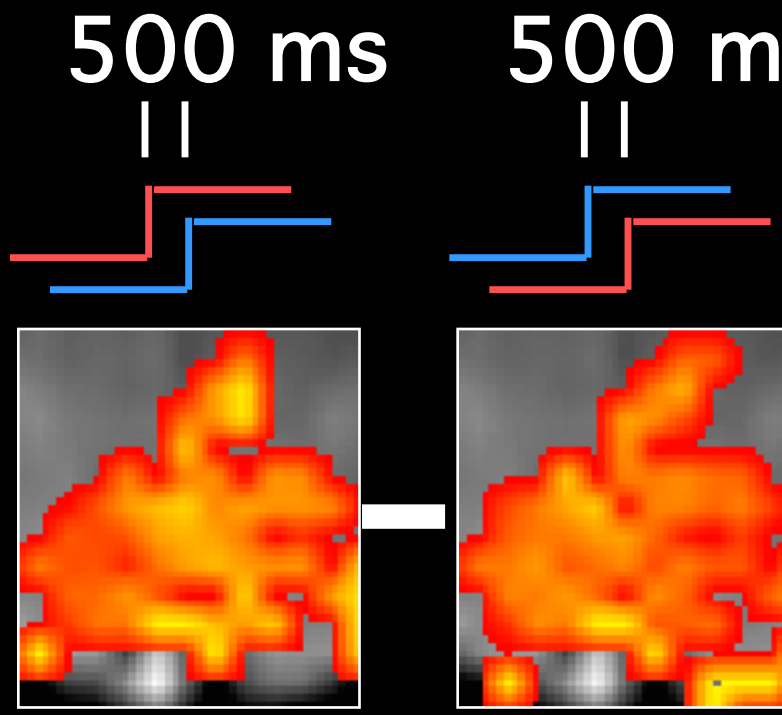


Calibration Techniques.....

500 ms 500 ms

Right Hemifield

Left Hemifield

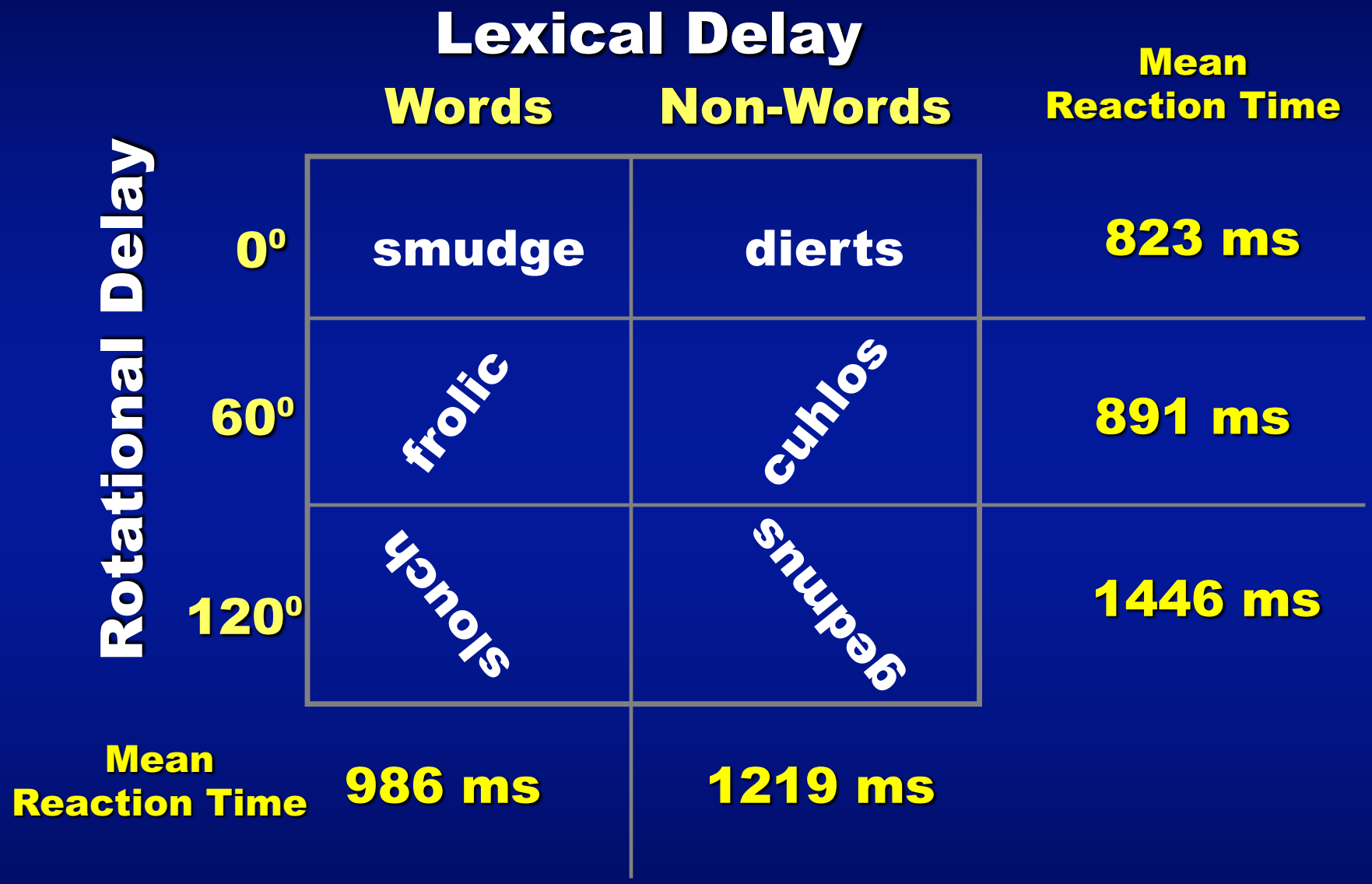


+ 2.5 s

0 s

- 2.5 s

P. A. Bandettini, The temporal resolution of Functional MRI *in* "Functional MRI" (C. Moonen, and P. Bandettini., Eds.), p. 205-220, Springer - Verlag,. 1999.


Lexical Delay
Words
Non-Words
Mean Reaction Time
Rotational Delay
0⁰
smudge
dierts
823 ms
60⁰
frolic
cuhlos
891 ms
120⁰
slouch
geamus
1446 ms
Mean Reaction Time
986 ms
1219 ms

PURPOSE / METHODS

Imaging Method: Scanner – 3T TR - 1000 ms TE - 30 ms

Behavioral Method:

Stimuli – Six-letter english words and pronounceable non-words.
Each word or non-word was rotated either 0, 60,or 120 degrees

Task – Lexical Decision (word / non-word).

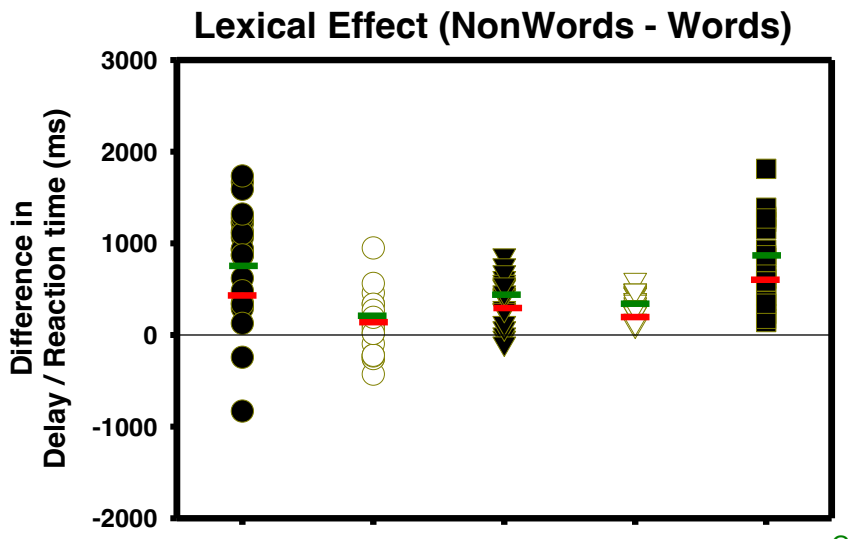
Dependent Measures – Percent Correct and Reaction Time.

Hypotheses :

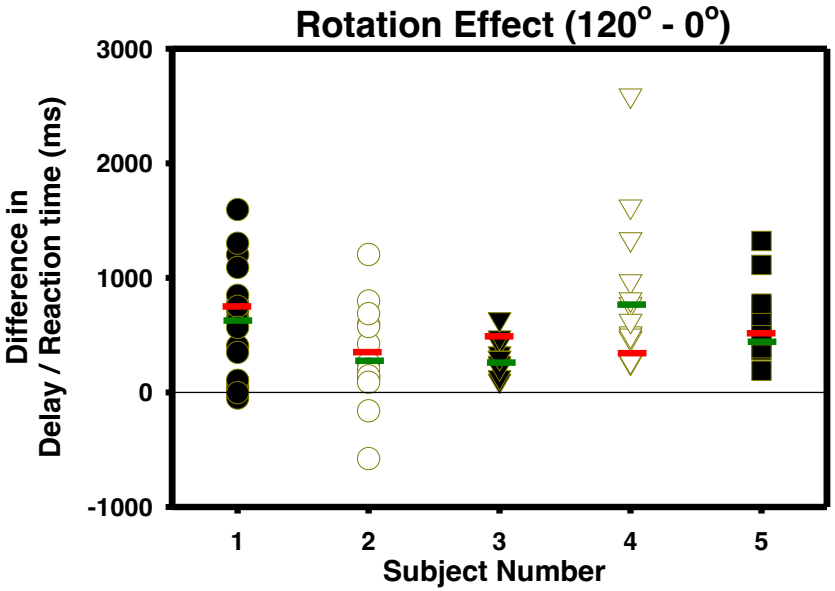
1) Stimulus rotation of 120 degrees will result in:
   a) Longer Reaction Times
   b) Wider IRF in Parietal Lobe
   c) Delayed IRF onset in Left Inferior Frontal cortex

2) Lexical discrimination will result in :
   a) Longer Reaction Times for non-words
   b) Wider IRF in Inferior Frontal cortex for non-words
   c) Delayed IRF onset in Left Middle Frontal Cortex

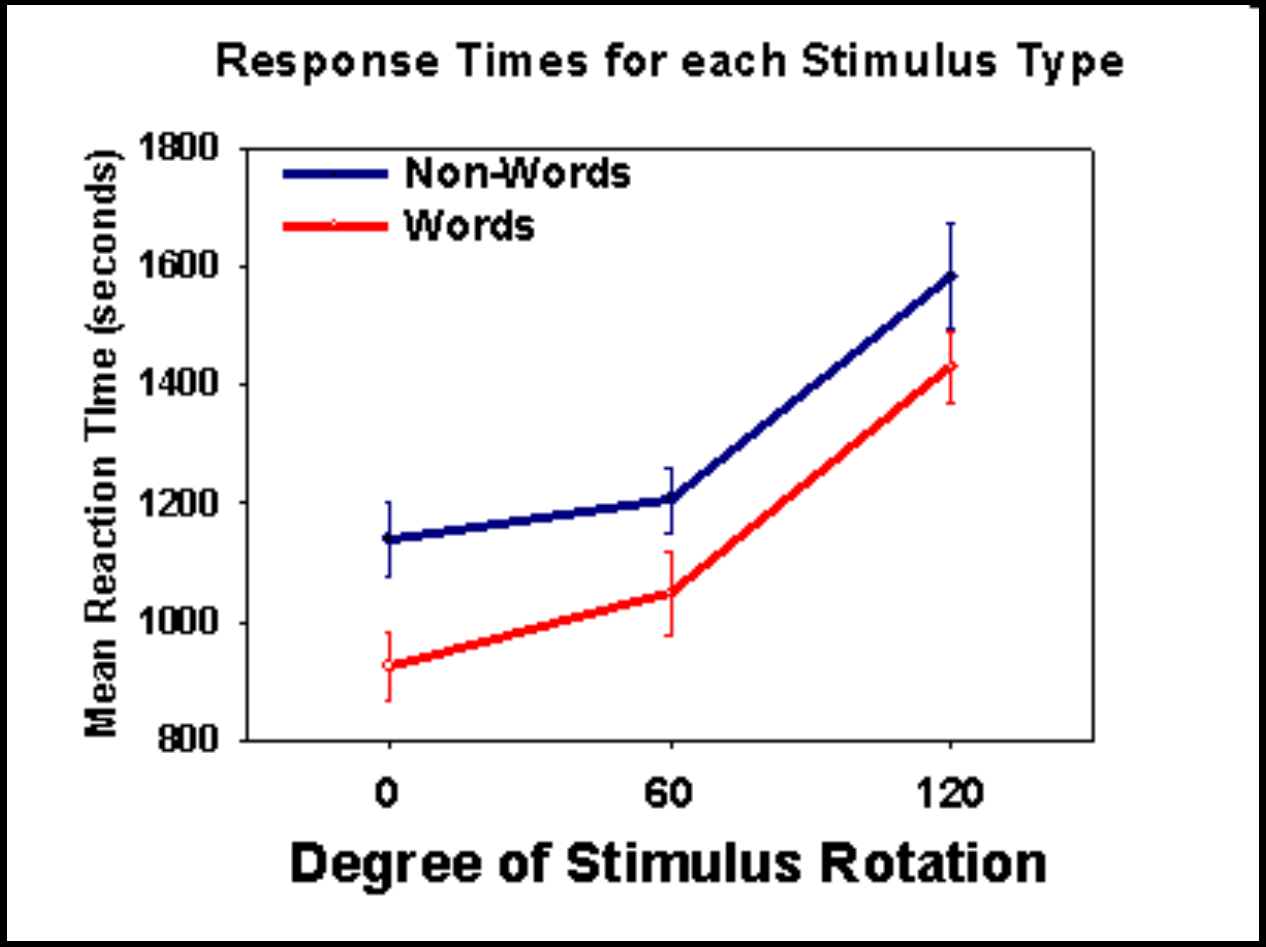
Delay Differences from Indivdual Voxels within the Above ROI's



Green lines depict the median Voxel Delay estimate



Red lines depict the mean RT difference


Response Times for each Stimulus Type
Mean Reaction Time (seconds)
1800
1600
1400
1200
1000
800
Non-Words
Words
0
60
120
Degree of Stimulus Rotation

Lexical effect maps

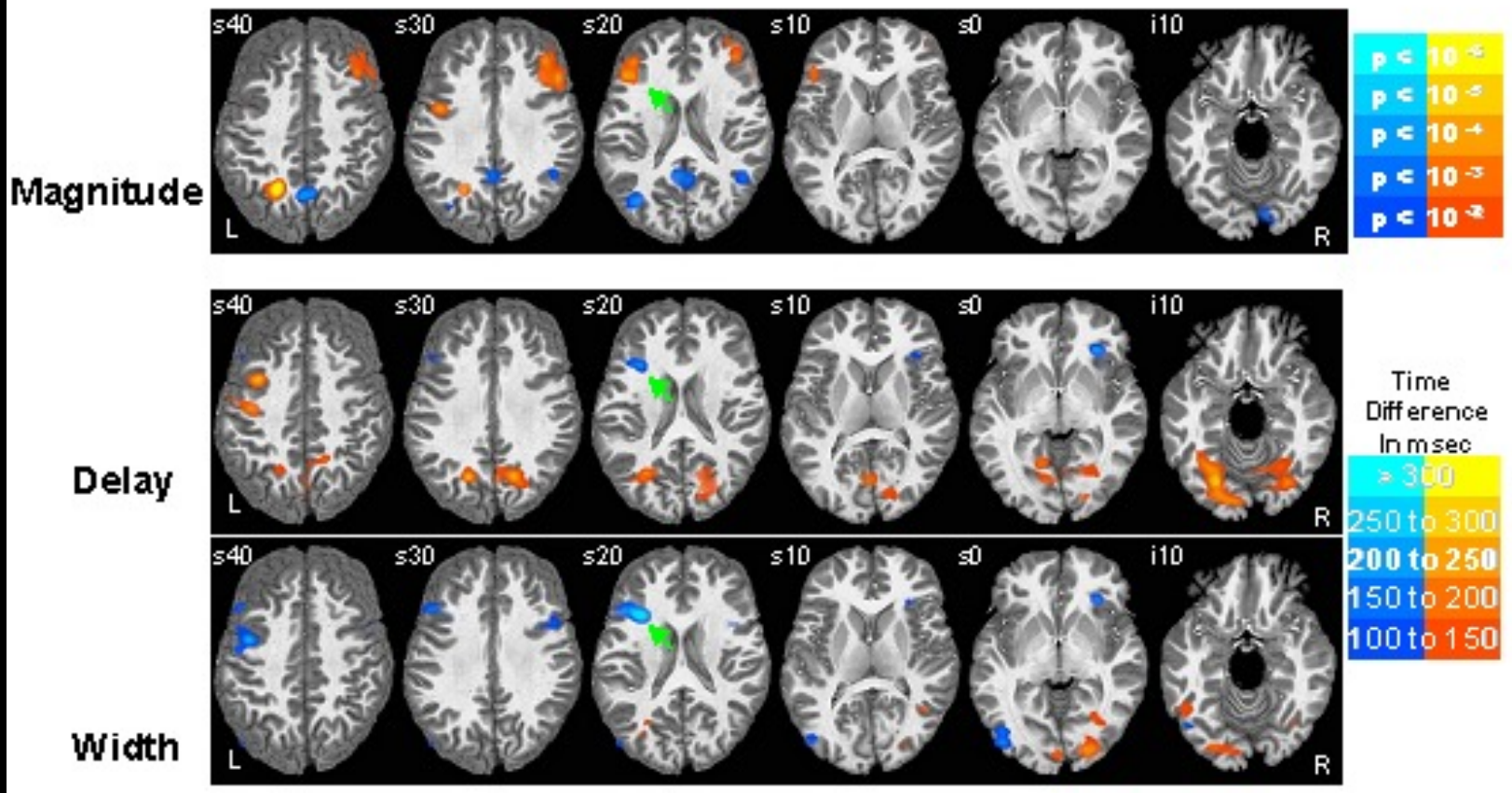
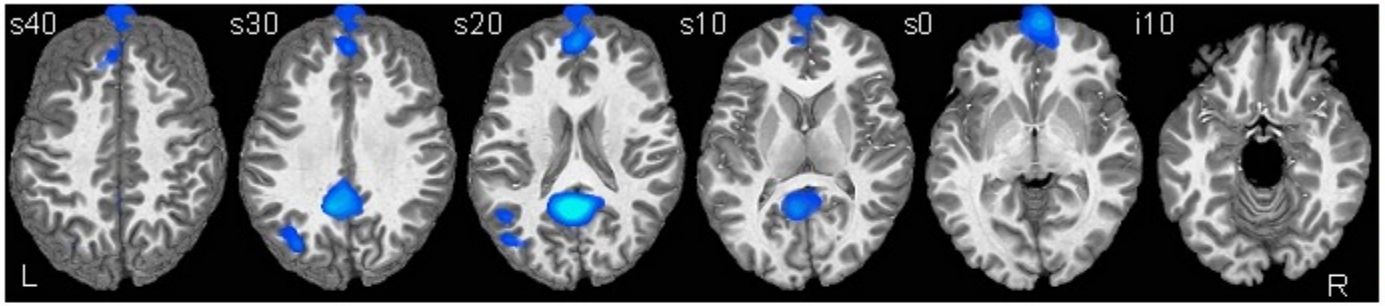
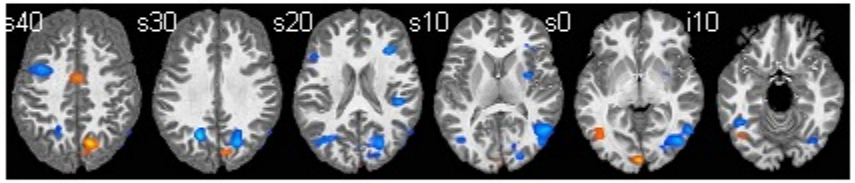


Figure 2. Warm colors are areas where Words > Non-words. Cool colors (blues) are areas Where Non-words > words. The Left hemisphere is toward the left margin. The green arrows Highlight the inferior frontal gyrus.

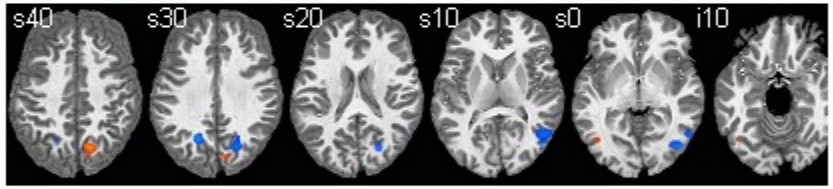
Rotational effect maps



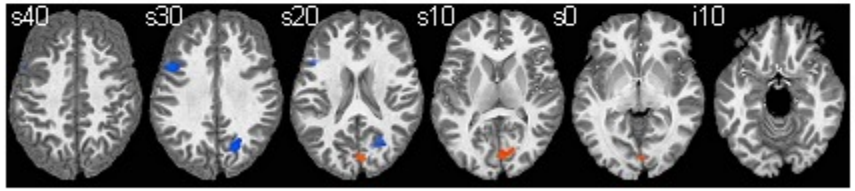
Non-rotated vs. 120° rotated



Delay



Non-rotated vs. 60° rotated



Width

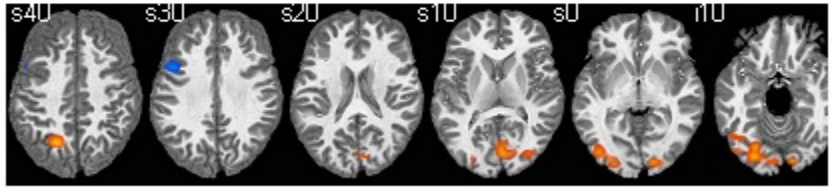


Figure 3. Warm colors are areas where Non-rotated stimuli > rotated. Cool colors (blues) are areas where Rotated stimuli > Non-rotated. The Left hemisphere is toward the left margin.

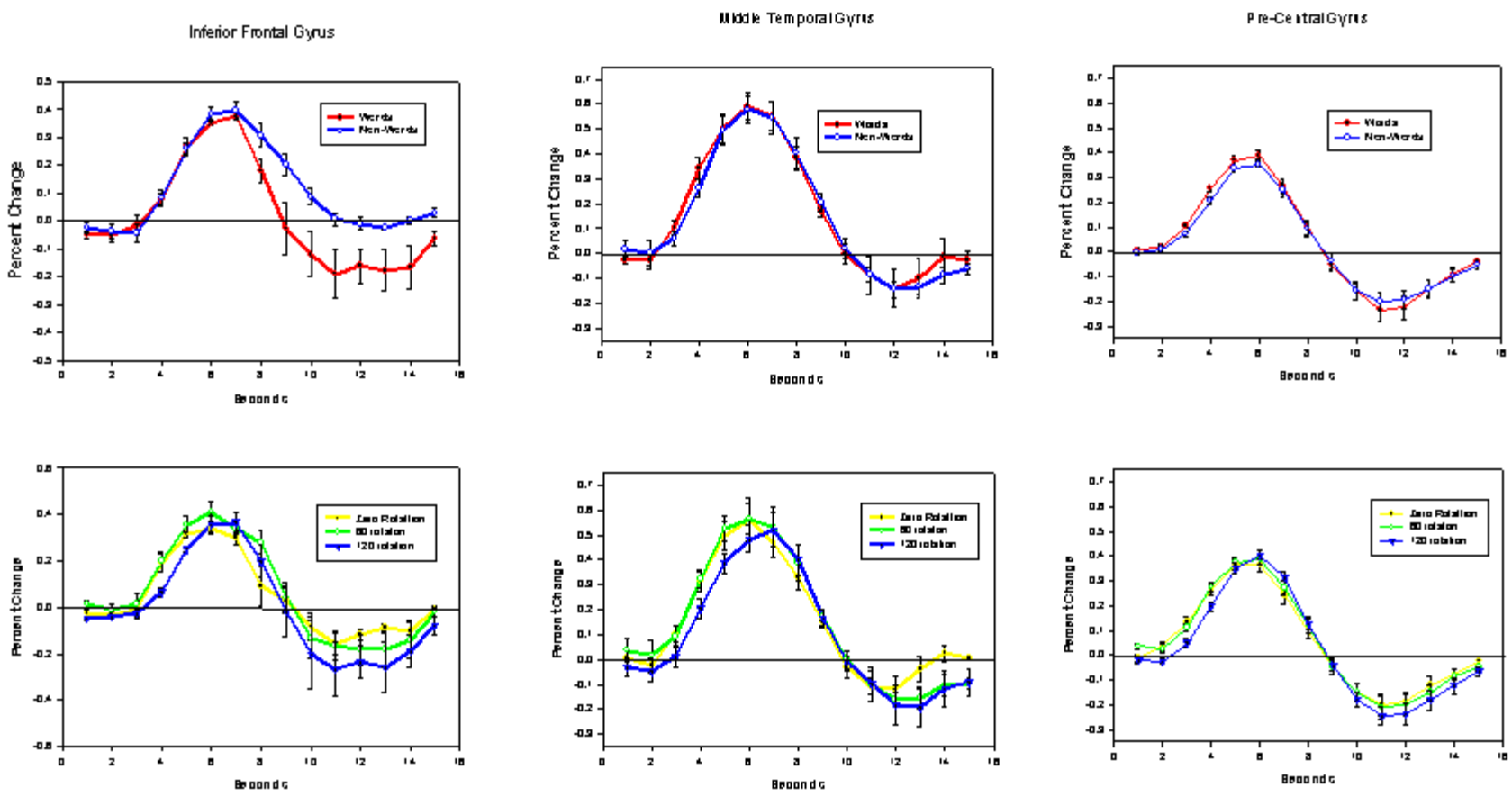
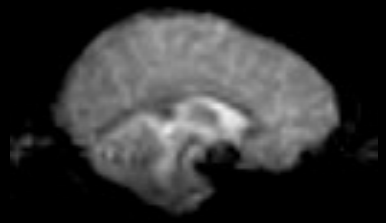
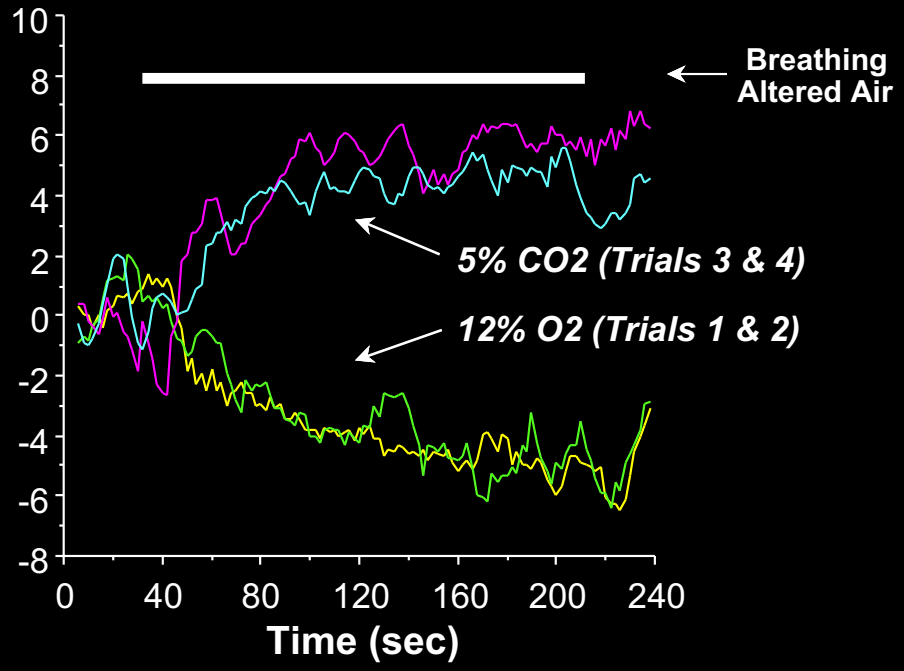
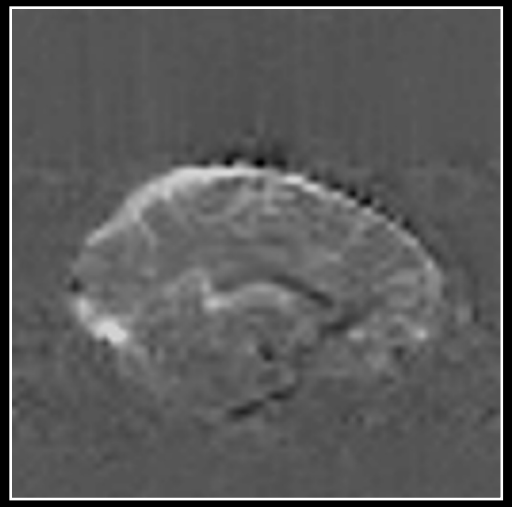


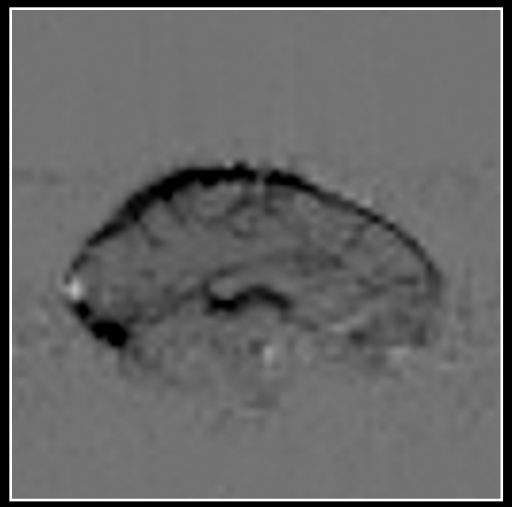
Figure 4. Graphs depicting the estimated Impulse Response Functions calculated by collapsing across all conditions. Error bars represent the standard error of the mean.




10
8
6
4
2
0
-2
-4
-6
-8
0
40
80
120
160
200
240
Time (sec)
Breathing
Altered Air
5% CO2 (Trials 3 & 4)
12% O2 (Trials 1 & 2)

5% CO2





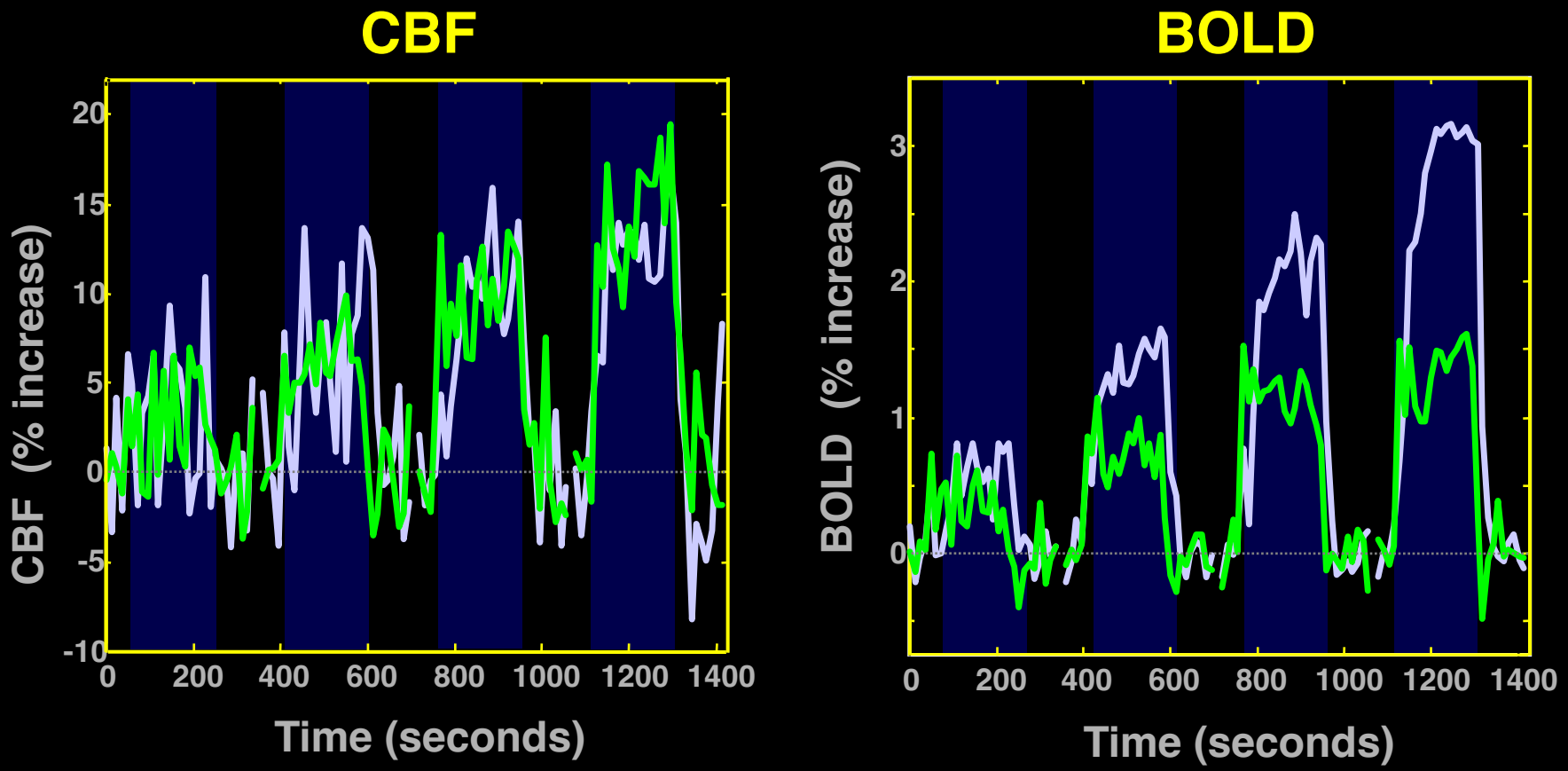
12% O2

Proc. Natl. Acad. Sci. USA
Vol. 96, pp. 9403–9408, August 1999
Neurobiology

Linear coupling between cerebral blood flow and oxygen consumption in activated human cortex

RICHARD D. HOGE*†, JEFF ATKINSON*, BRAD GILL*, GÉRARD R. CRELIER*, SEAN MARRETT‡, AND G. BRUCE PIKE*

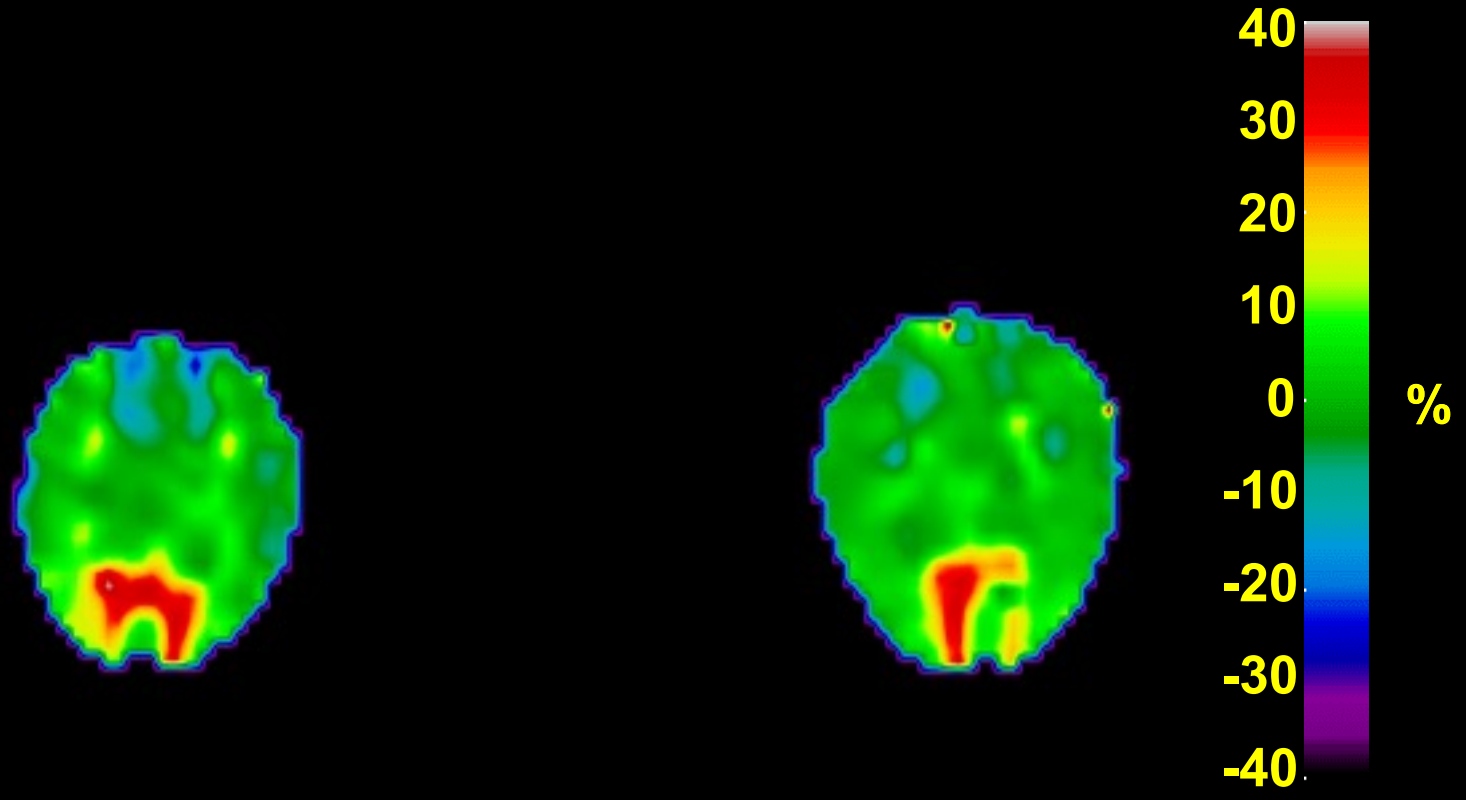
*Room WB325, McConnell Brain Imaging Centre, Montreal Neurological Institute, Quebec, Canada H3A 2B4; and ‡Nuclear Magnetic Resonance Center, Massachusetts General Hospital, Building 149, 13th Street, Charlestown, MA 02129



Simultaneous Perfusion and BOLD imaging during graded visual activation and hypercapnia

N=12

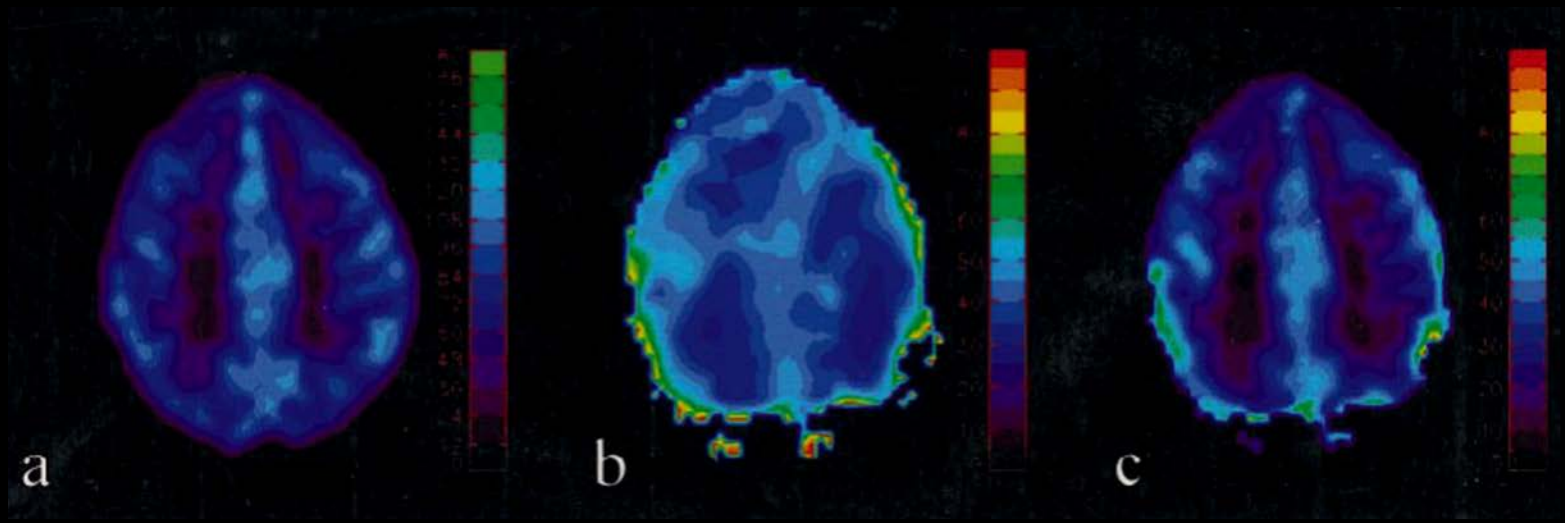
Computed $CMRO_2$ Changes



NMR IN BIOMEDICINE
NMR Biomed. 2001;**14**:441–447
DOI:10.1002/nbm.717

Quantitative measurements of cerebral metabolic rate of oxygen utilization using MRI: a volunteer study

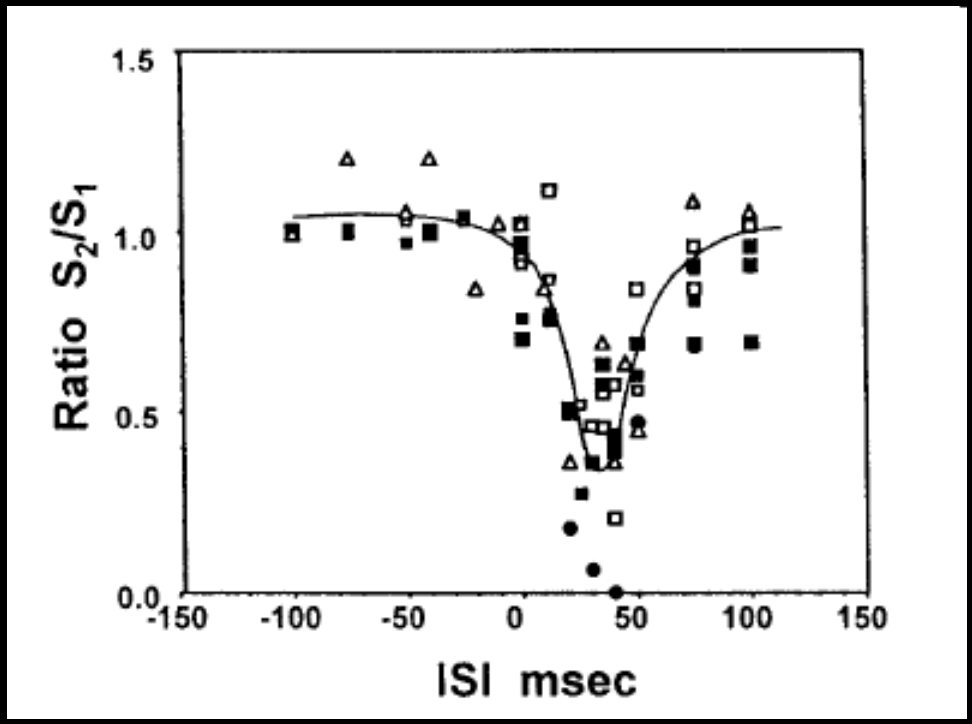
Hongyu An,[1] Weili Lin,[2]* Azim Celik[3] and Yueh Z. Lee[2]



CBF OEF $CMRO_2$

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

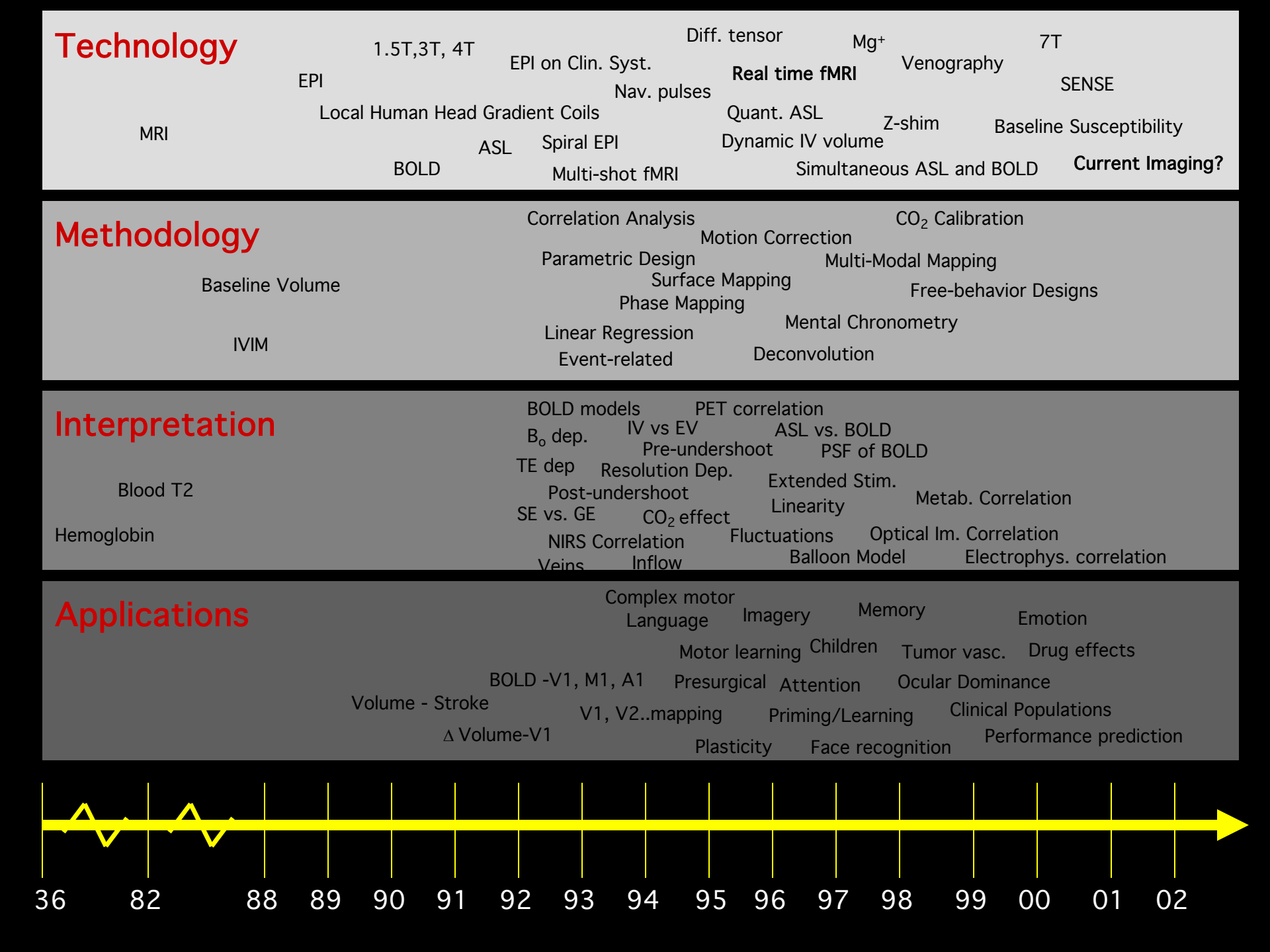
Seiji Ogawa[†‡], Tso-Ming Lee[†], Ray Stepnoski[†], Wei Chen[§], Xiao-Hong Zhu[§], and Kamil Ugurbil[§]



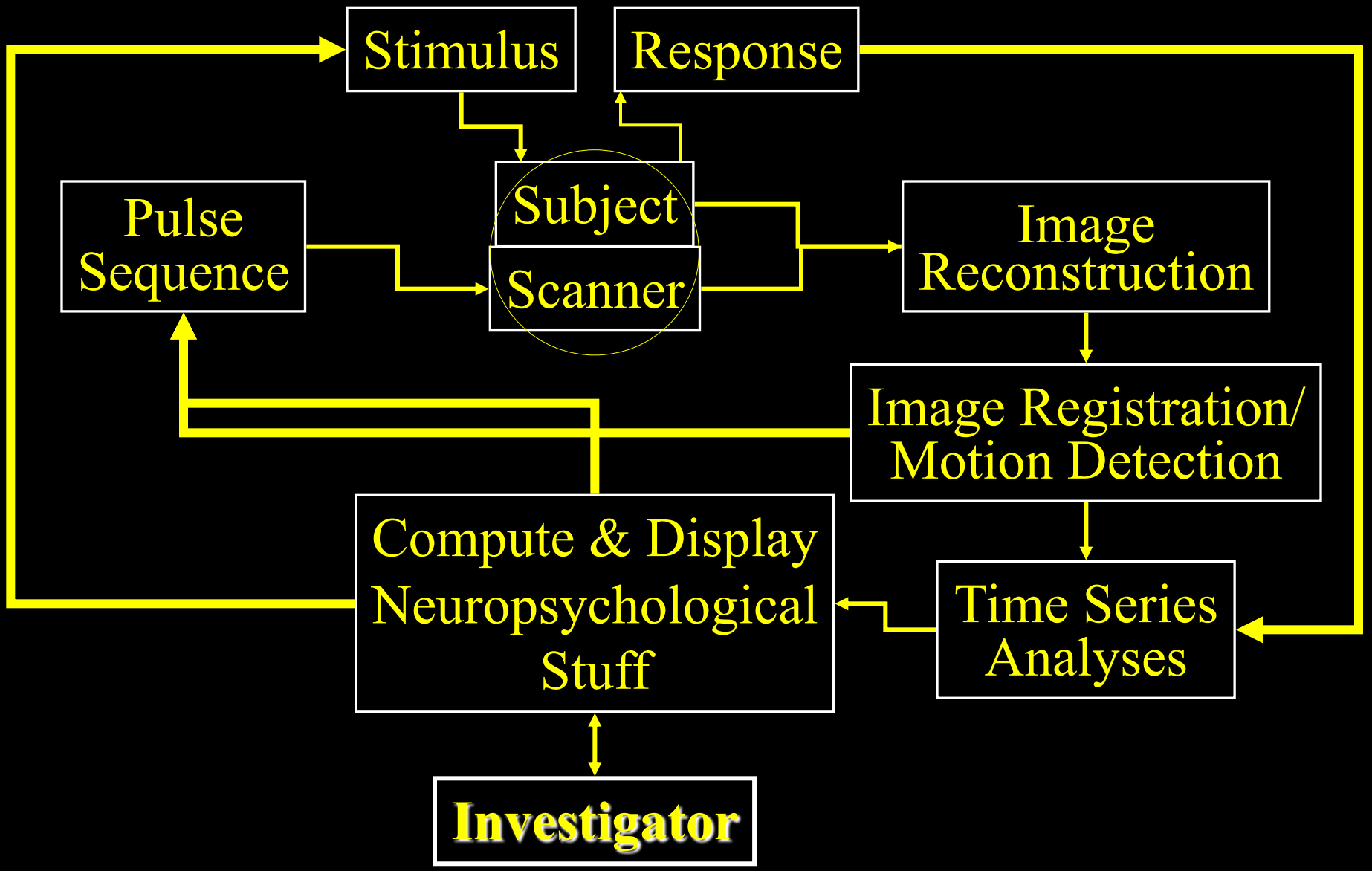
11026–11031 PNAS **September 26, 2000** vol. 97 no. 20

Future....

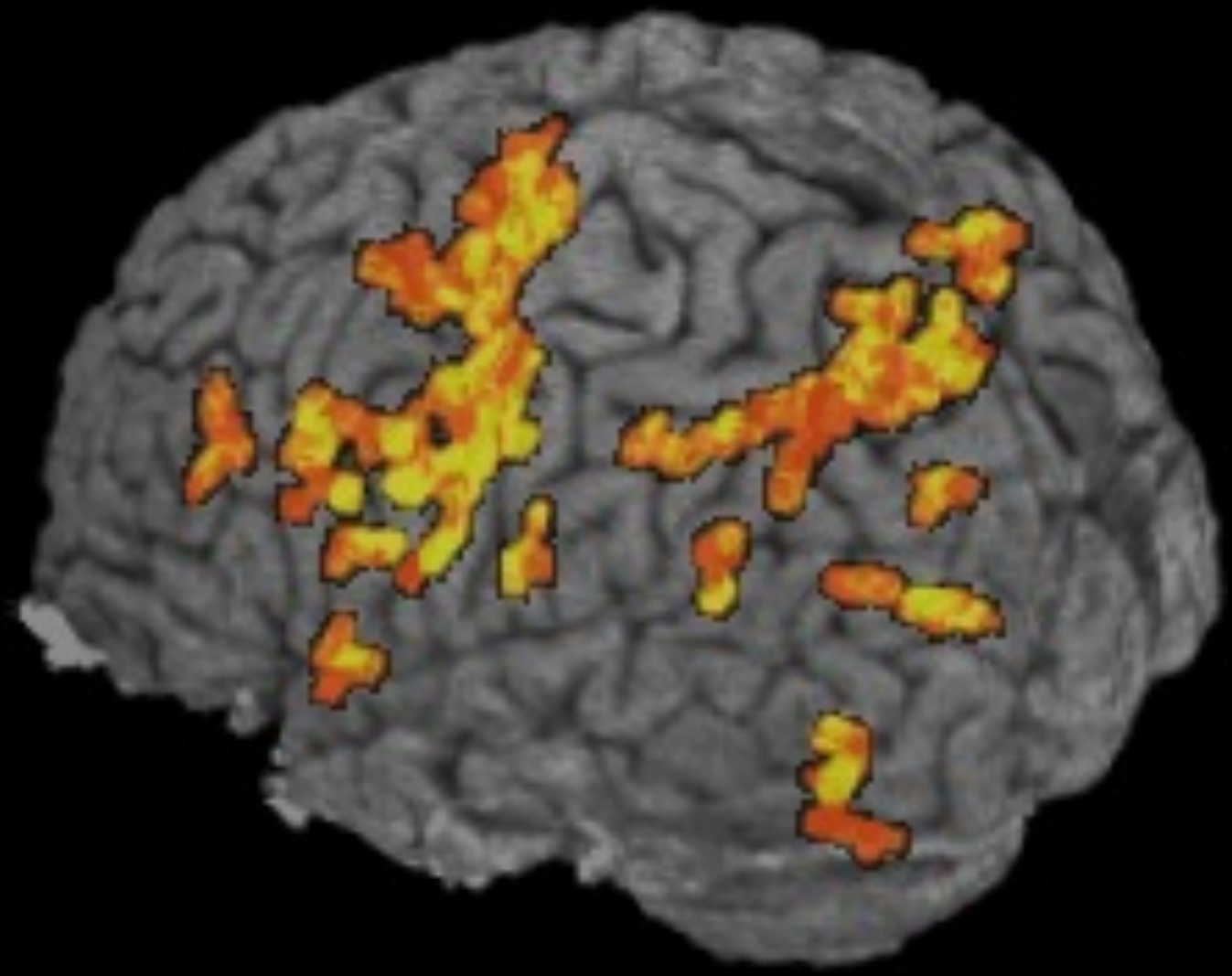
- Shimming
- Acoustic Noise
- Multishot Techniques
- Increased Gradient Performance
- Higher Field Strengths
- Surface Coil Arrays
- Calibration / Quantification
- Embedded Functional Contrast
- Noise / Fluctuations
- Direct Neuronal Current Imaging
- Clinical Populations
- Neuronal,Vascular, and Metabolic Informatic


Technology
1.5T,3T, 4T
Diff. tensor
Mg+
7T
EPI on Clin. Syst.
Venography
EPI
Real time fMRI
SENSE
Nav. pulses
Local Human Head Gradient Coils
Quant. ASL
Z-shim
MRI
Baseline Susceptibility
ASL
Spiral EPI
Dynamic IV volume
BOLD
Multi-shot fMRI
Simultaneous ASL and BOLD
Current Imaging?
Methodology
Correlation Analysis
CO2 Calibration
Motion Correction
Parametric Design
Multi-Modal Mapping
Baseline Volume
Surface Mapping
Free-behavior Designs
Phase Mapping
Mental Chronometry
Linear Regression
IVIM
Deconvolution
Event-related
Interpretation
BOLD models
PET correlation
IV vs EV
B0 dep.
ASL vs. BOLD
Pre-undershoot
PSF of BOLD
TE dep
Resolution Dep.
Extended Stim.
Blood T2
Post-undershoot
Metab. Correlation
Linearity
SE vs. GE
CO2 effect
Hemoglobin
Fluctuations
Optical Im. Correlation
NIRS Correlation
Balloon Model
Electrophys. correlation
Veins
Inflow
Applications
Complex motor
Language
Imagery
Memory
Emotion
Motor learning
Children
Tumor vasc.
Drug effects
BOLD -V1, M1, A1
Presurgical
Attention
Ocular Dominance
Volume - Stroke
V1, V2..mapping
Priming/Learning
Clinical Populations
Δ Volume-V1
Plasticity
Face recognition
Performance prediction
36
82
88
89
90
91
92
93
94
95
96
97
98
99
00
01
02

Processing Stream with Real Time fMRI



End of Acquisition



< 1 s to render

Blocked trials:
20 s on/20 s off
8 blocks

Blocks: 12345678

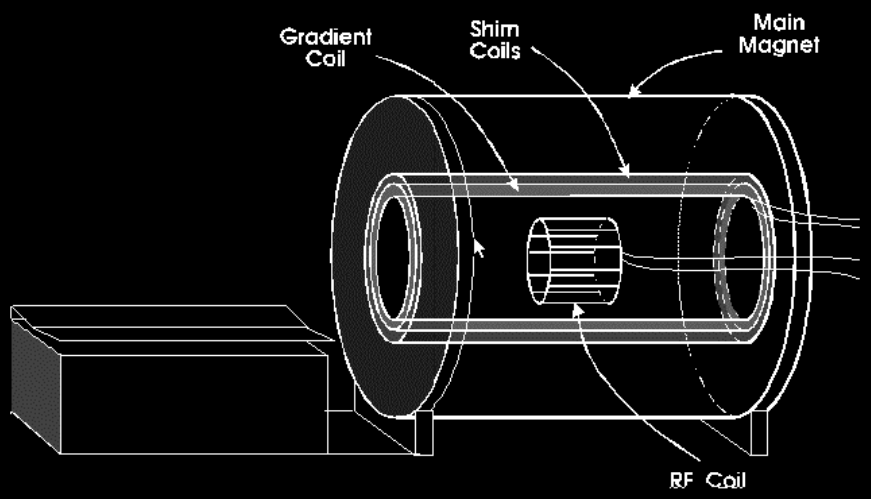
Color shows through brain

Correlation > 0.45

The End

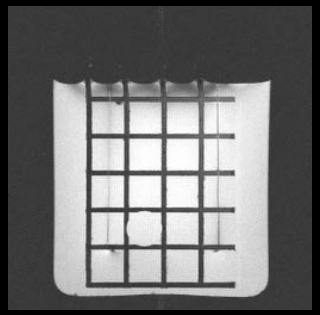
2 G/cm, 350 T/m/s

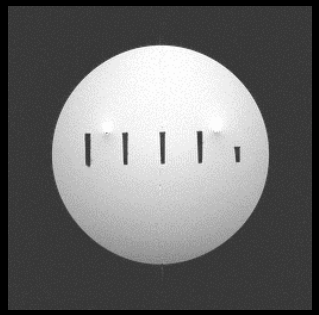
4 G/cm, 150 T/m/s



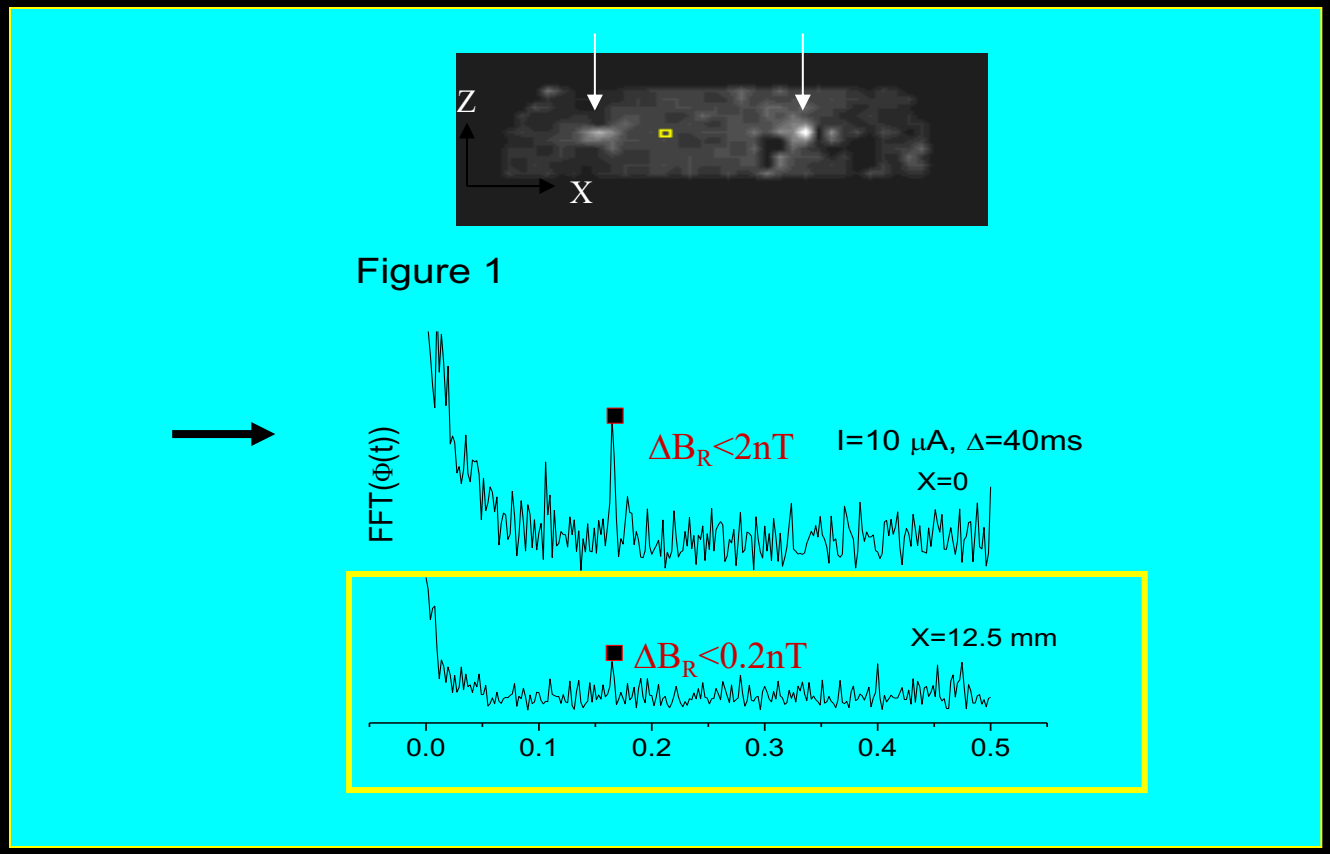
10 G/cm, 1000 T/m/s

Diffusion imaging
Faster imaging
Higher resolution





Neuronal Current Imaging



J. Bodurka, P. A. Bandettini. Toward direct mapping of neuronal activity: MRI detection of ultra weak transient magnetic field changes, *Magn. Reson. Med* 47: 1052-1058, (2002)

FIM Unit & FMRI Core Facility

Director:

Peter Bandettini

Staff Scientists:

Sean Marrett

Jerzy Bodurka

Frank Ye

Wen-Ming Luh

Computer Specialist:

Adam Thomas

Post Docs:

Rasmus Birn

Hauke Heekeren

David Knight

Patrick Bellgowan

Ziad Saad

Graduate Student:

Natalia Petridou

Post-Back. IRTA Students:

Elisa Kapler

August Tuan

Dan Kelley

Visiting Fellows:

Sergio Casciaro

Marta Maieron

Guosheng Ding

Clinical Fellow:

James Patterson

Psychologist:

Julie Frost

Summer Students:

Hannah Chang

Courtney Kemps

Douglass Ruff

Carla Wettig

Kang-Xing Jin

Program Assistant:

Kay Kuhns

Scanning Technologists:

Karen Bove-Bettis

Paula Rowser