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

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&
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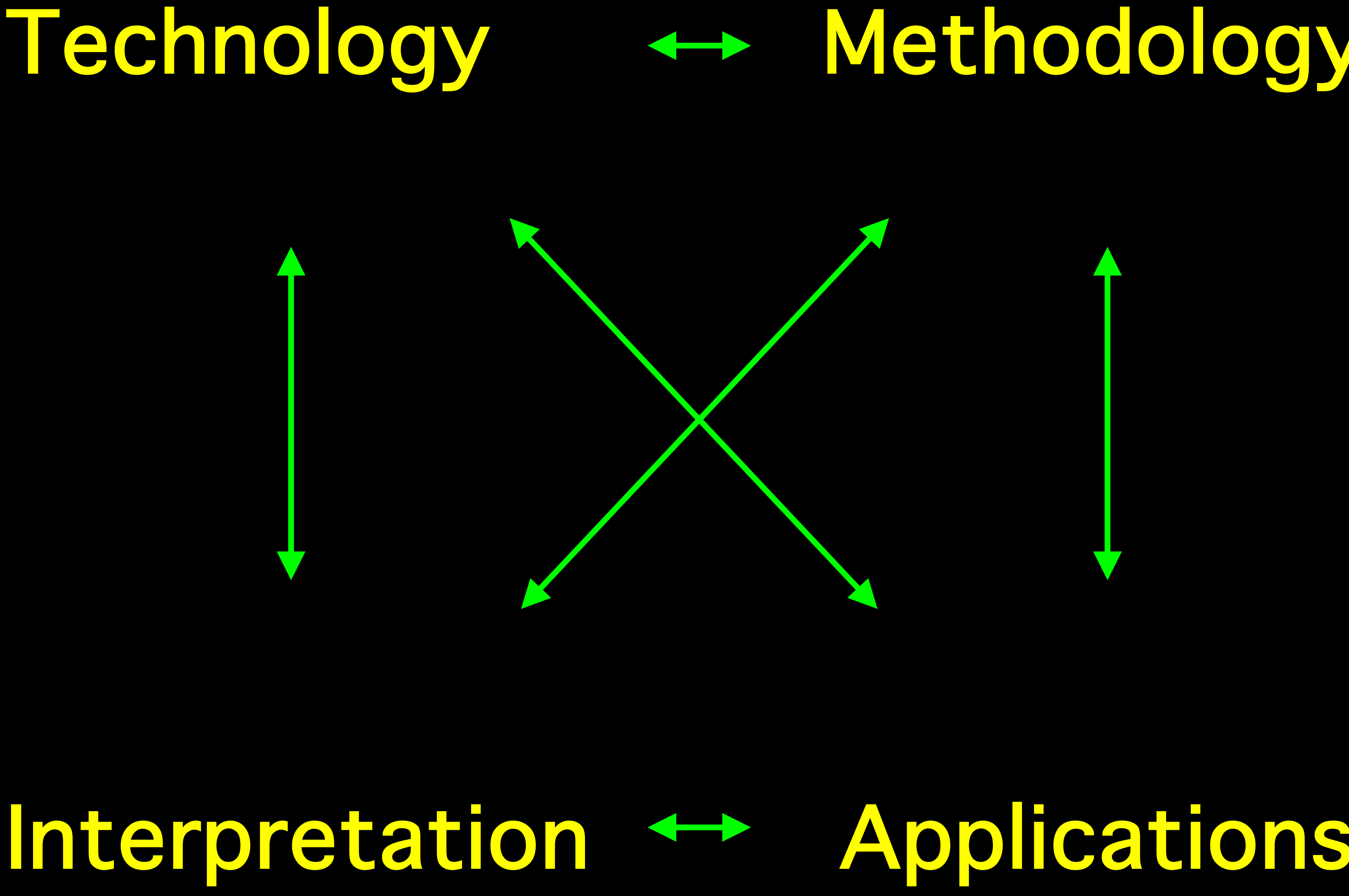
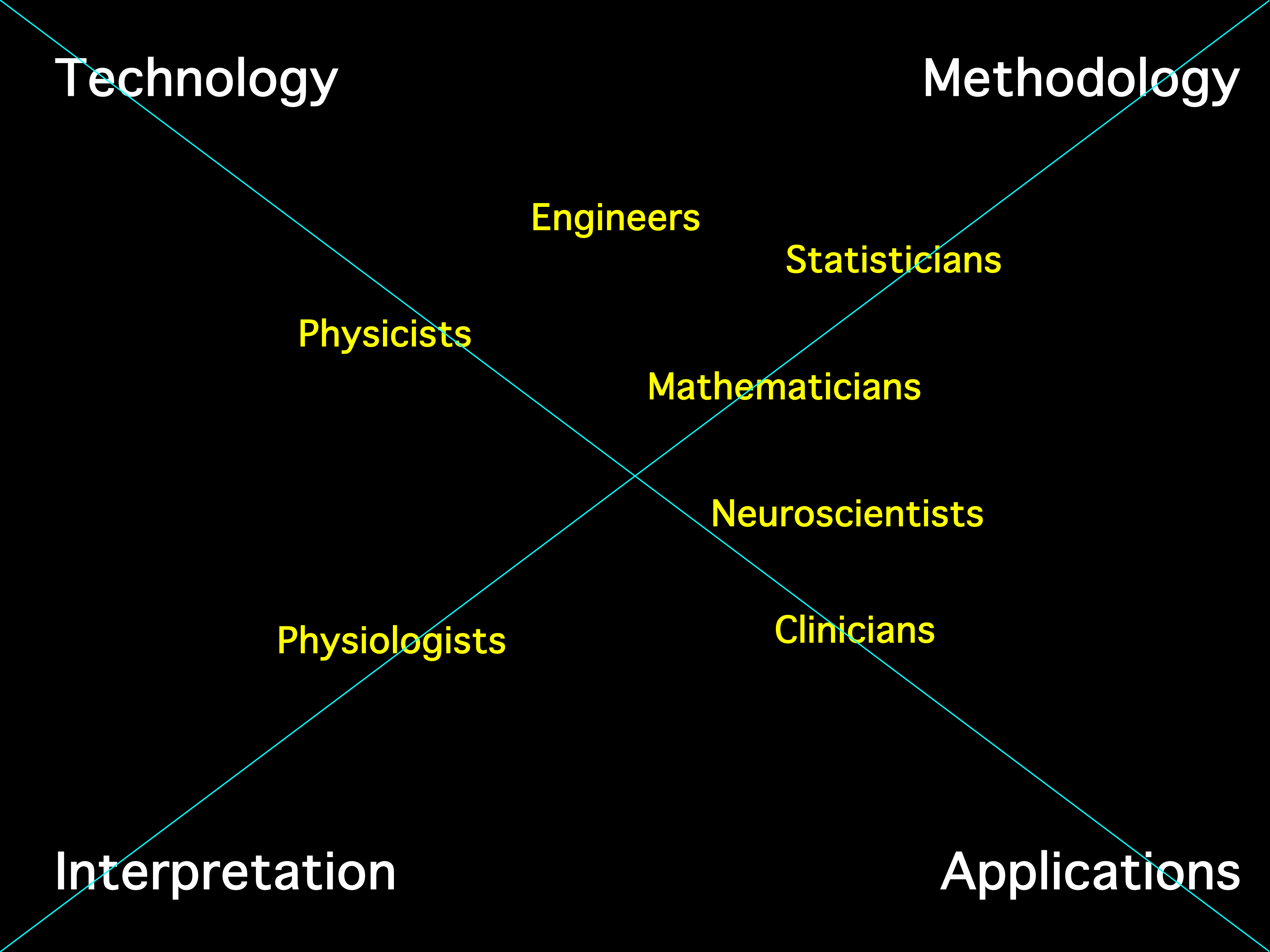
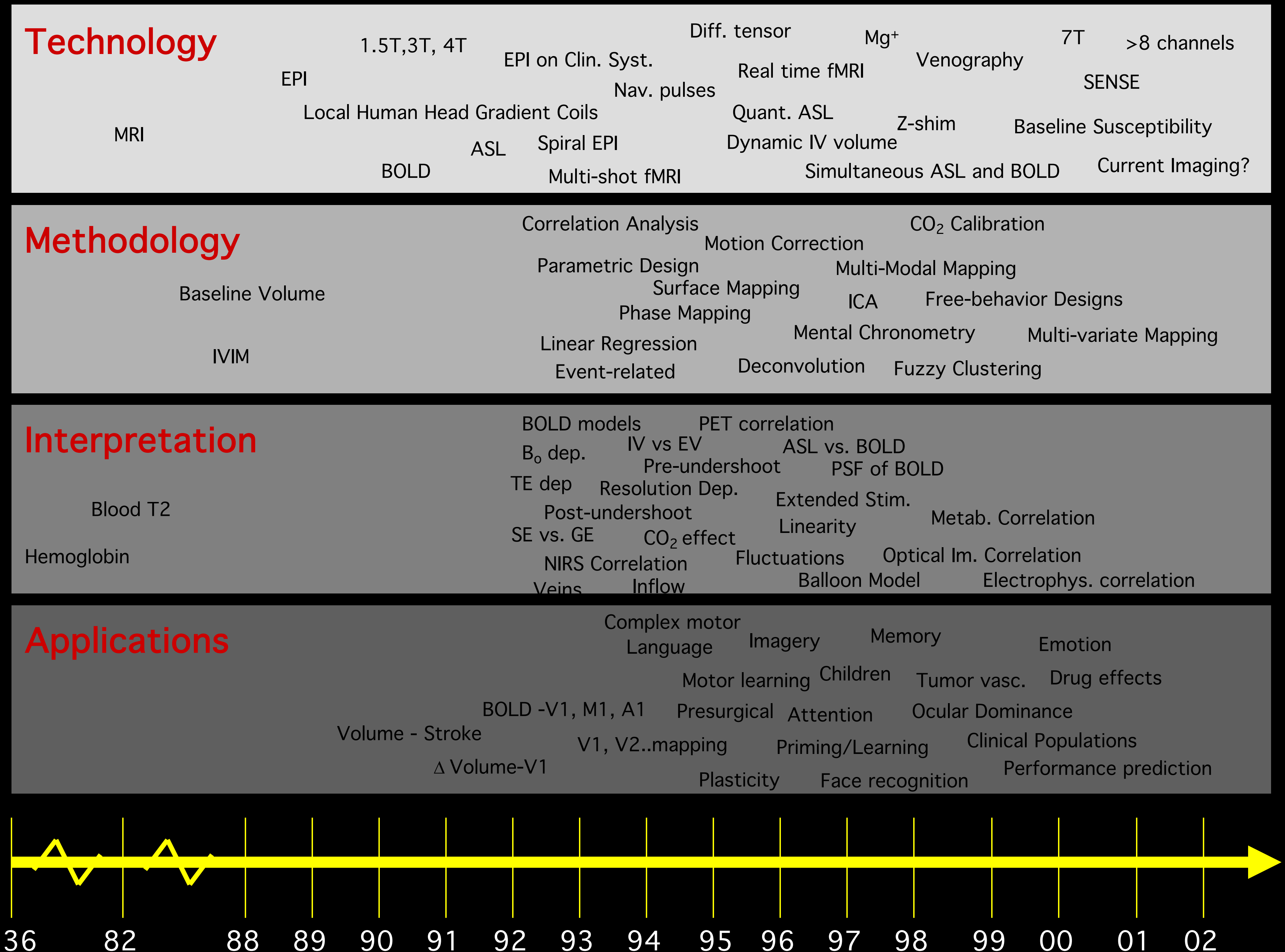
Laboratory of Brain and Cognition
National Institute of Mental Health


Technology
Methodology
Interpretation
Applications


Technology
Methodology
Engineers
Statisticians
Physicists
Mathematicians
Neuroscientists
Physiologists
Clinicians
Interpretation
Applications


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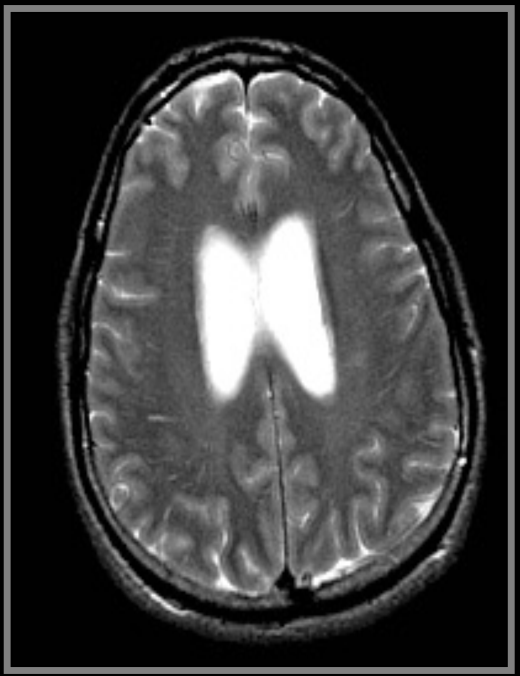
L. Pauling, C. D. Coryell, (1936) “The magnetic properties and structure of hemoglobin, oxyhemoglobin, and carbonmonoxyhemoglobin.” Proc.Natl. Acad. Sci. USA 22, 210-216.

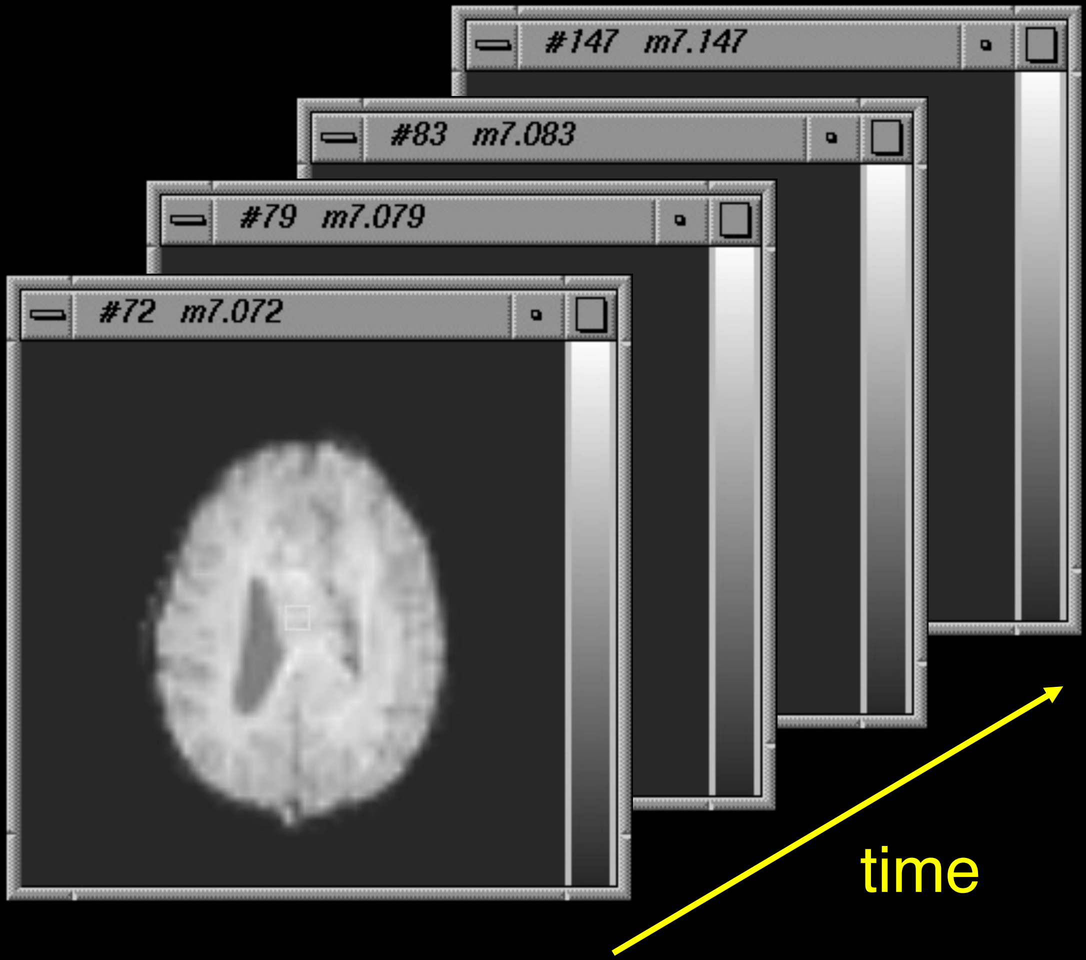
Thulborn, K. R., J. C. Waterton, et al. (1982).“Oxygenation dependence of the transverse relaxation time of water protons in whole blood at high field.” Biochim. Biophys. Acta. 714: 265-270.

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.

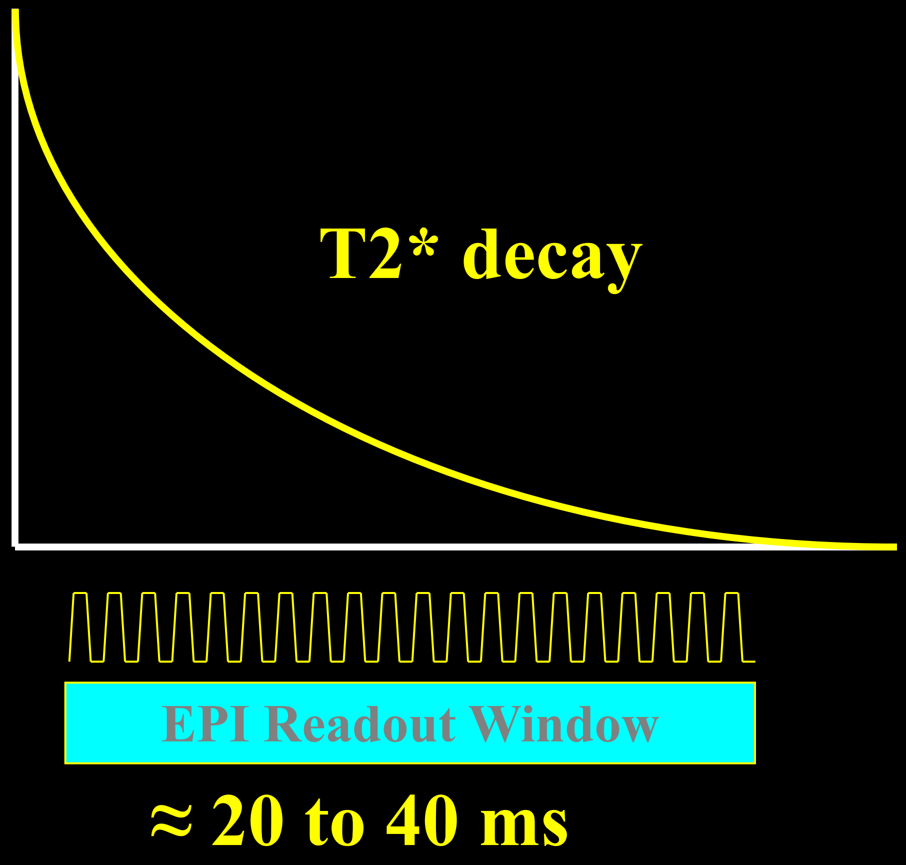


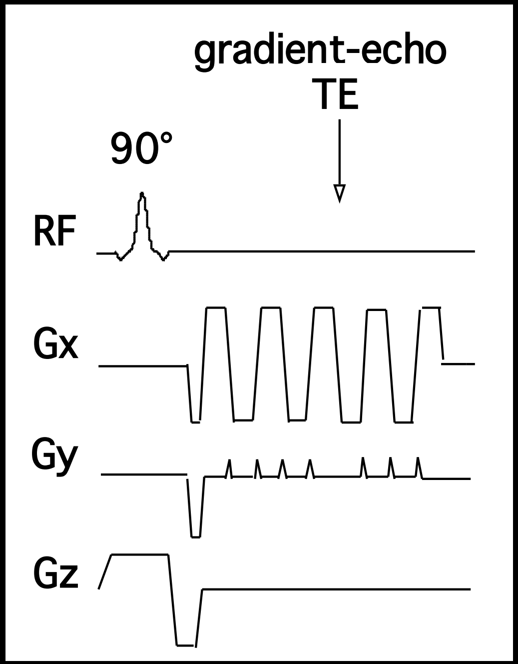
Anatomic

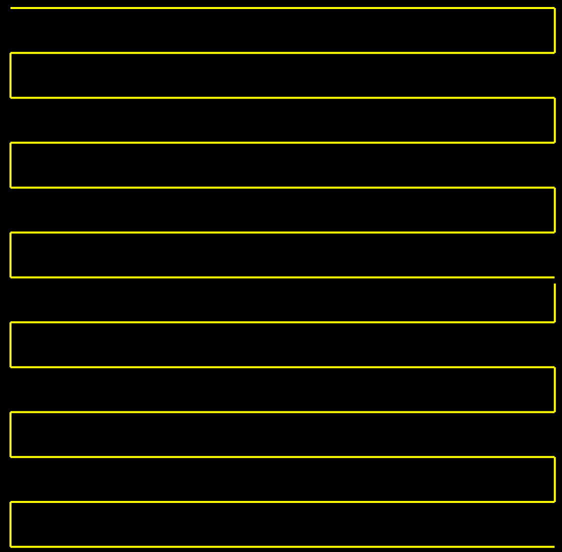


Functional

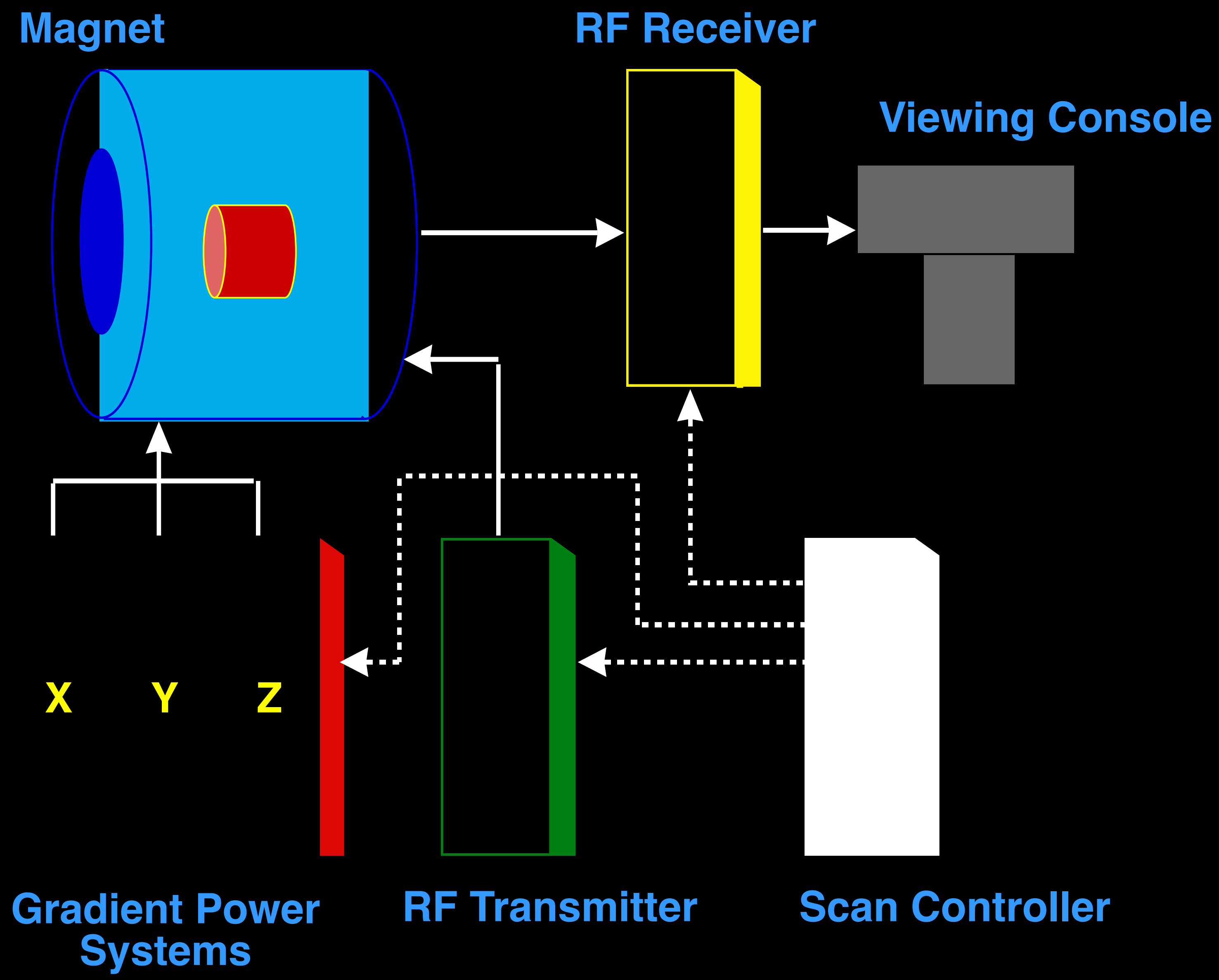
Single Shot EPI



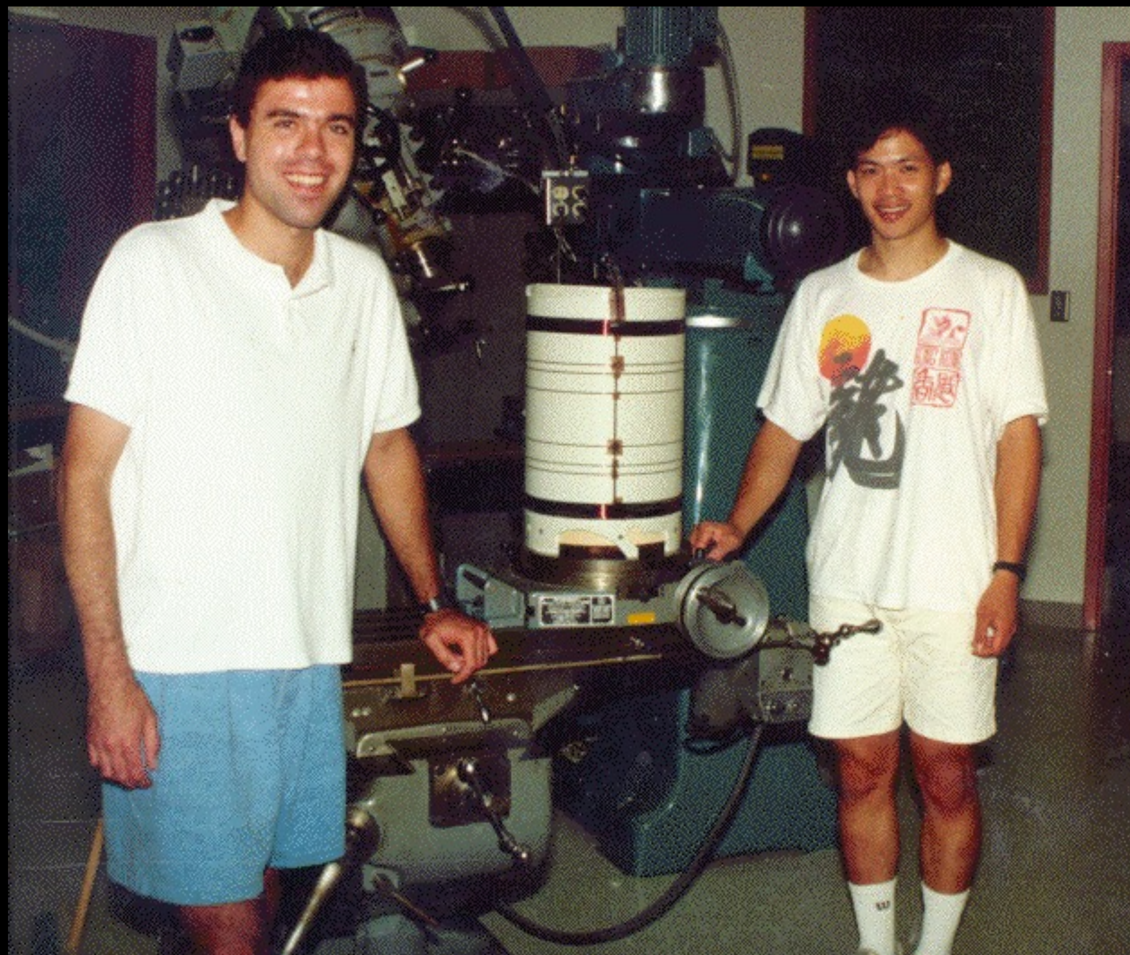




Imaging System Components



Local gradients solved the problem

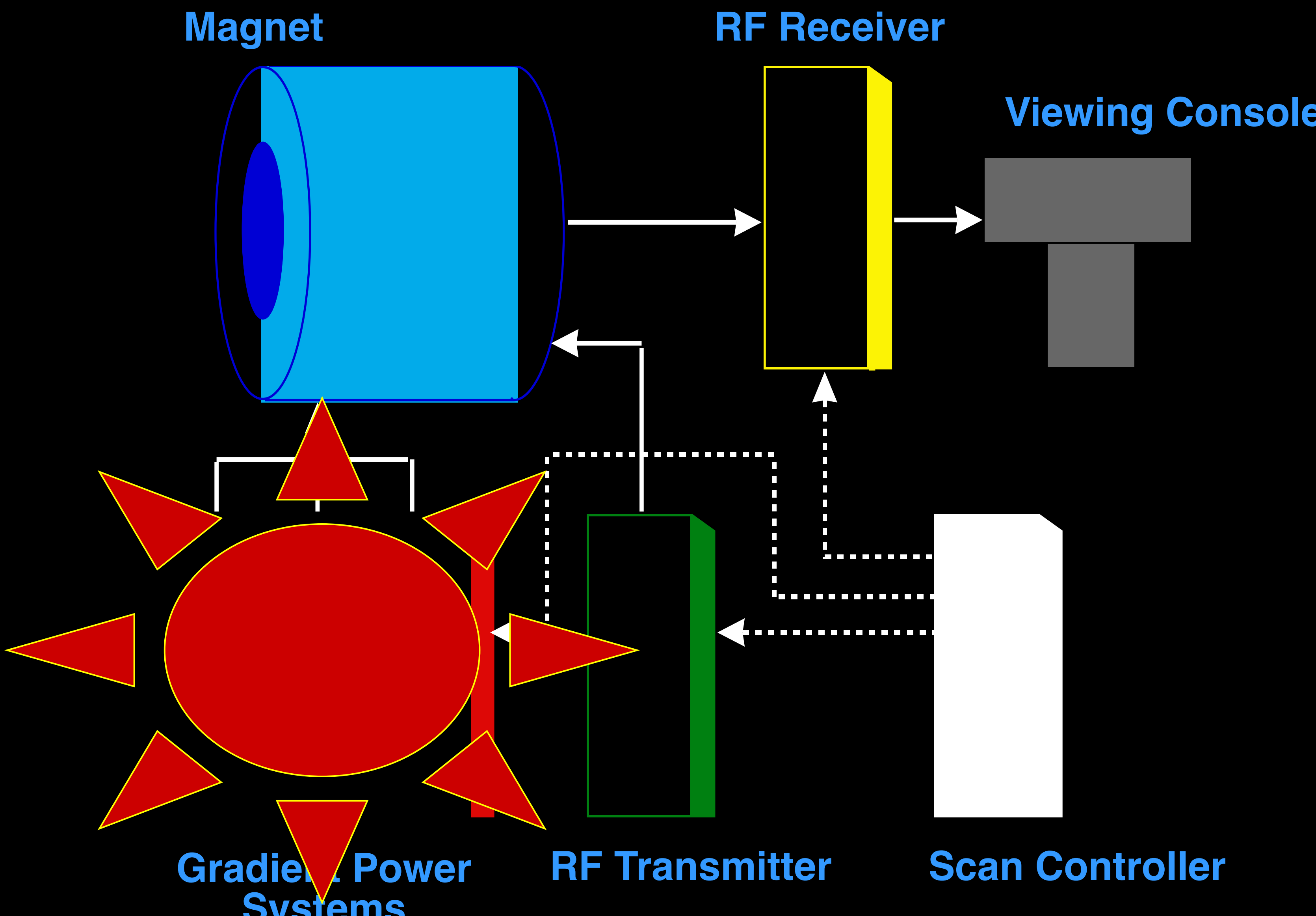


August, 1991

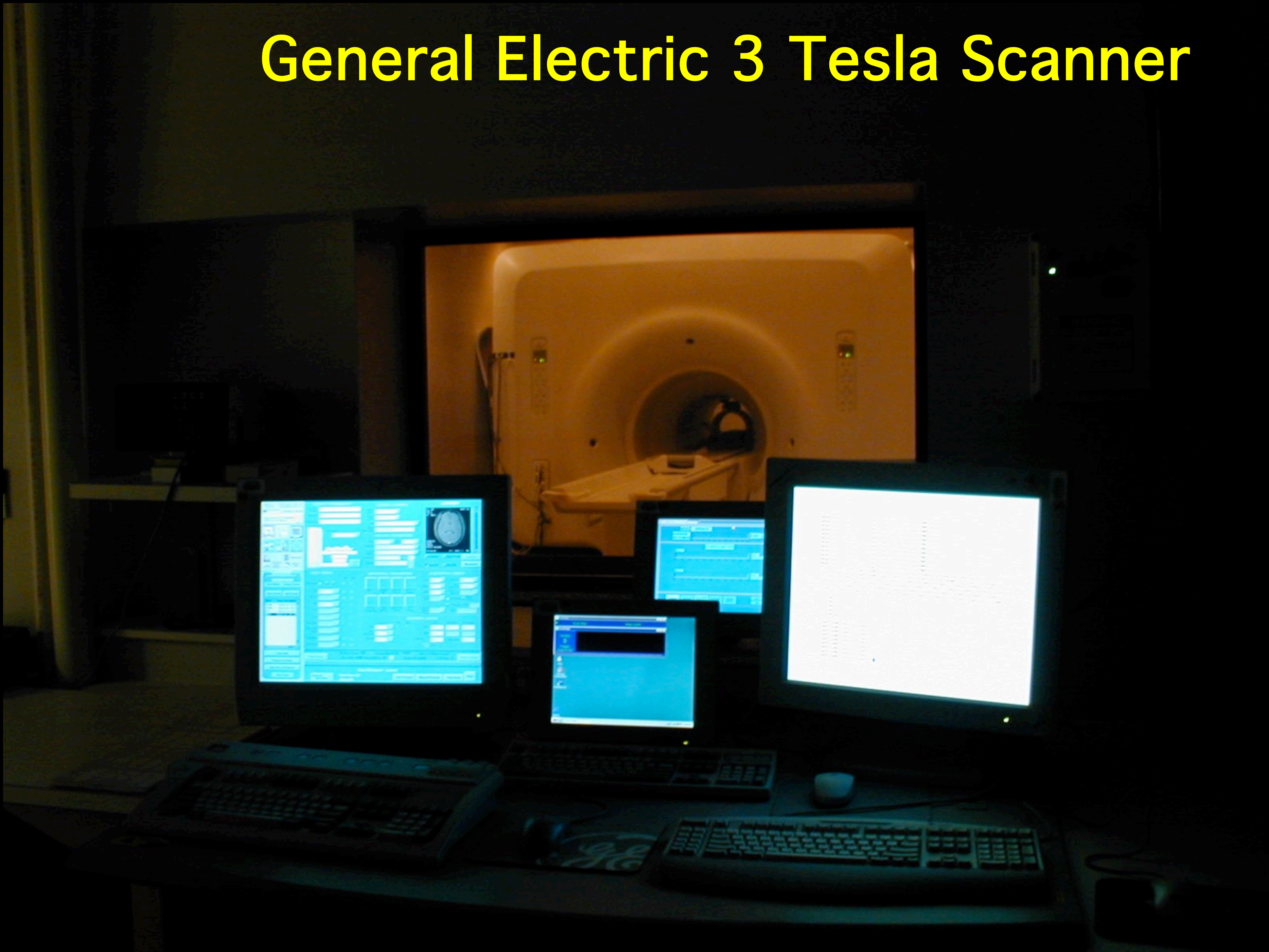
1991-1992

1992-1999

Imaging System Components



General Electric 3 Tesla Scanner



Functional MRI Methods

Blood Volume Imaging

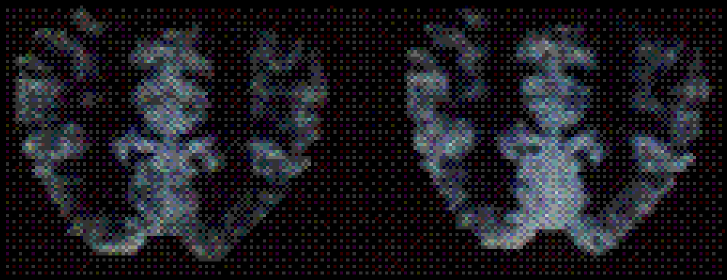
BOLD Contrast

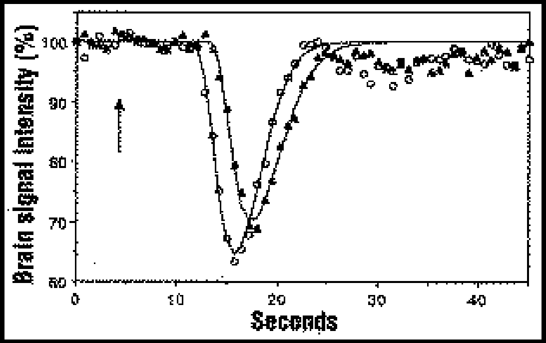
Arterial Spin Labeling

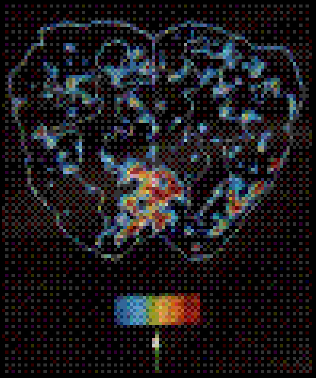
Blood Volume Imaging

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

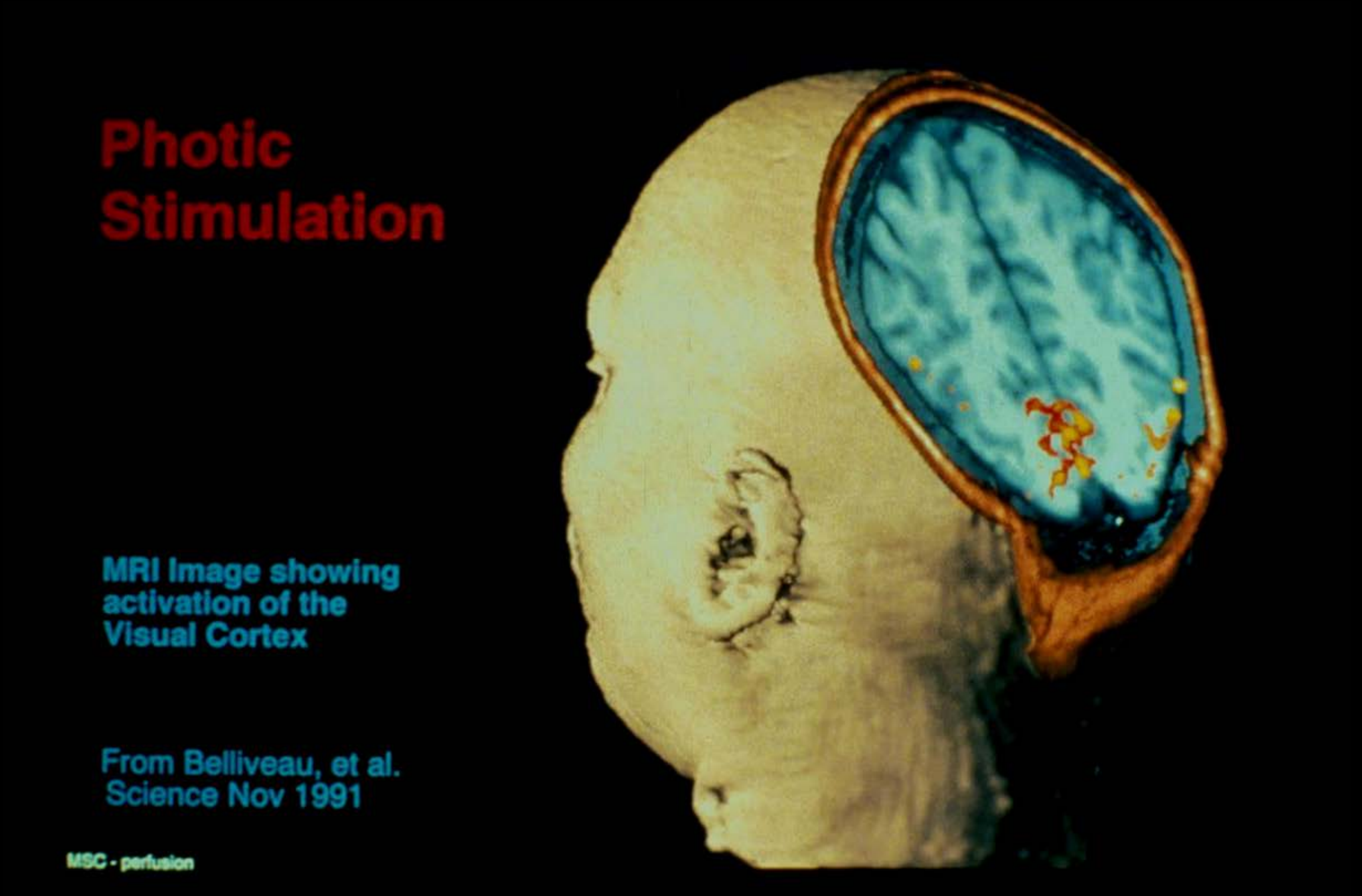
Resting **Active**





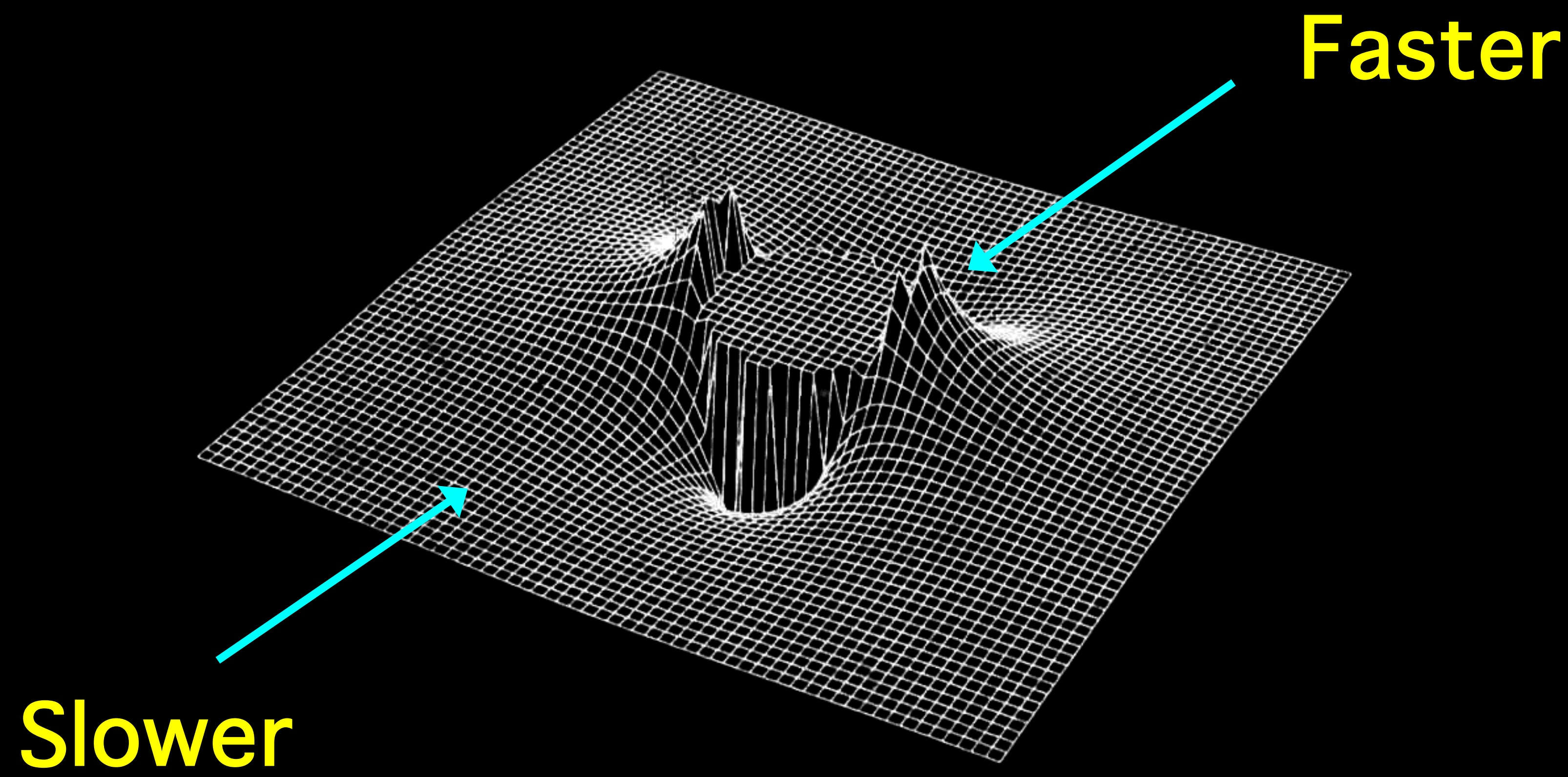


Blood Volume



Susceptibility Contrast

Susceptibility-Induced Field Distortion in the Vicinity of a Microvessel ⊥ 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

↓

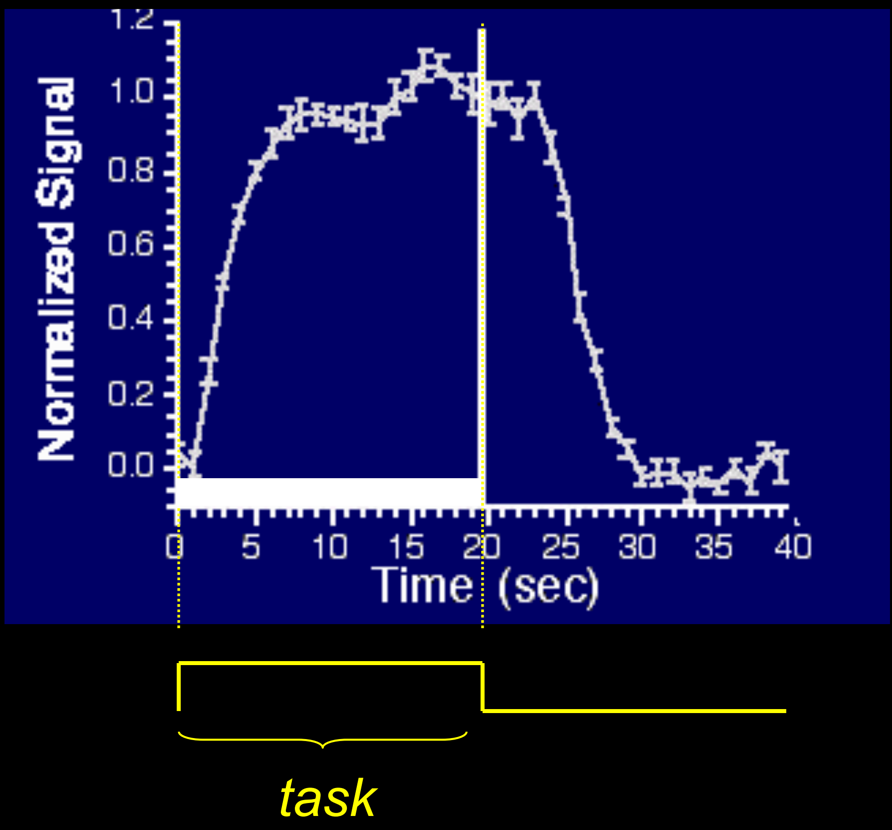
Decrease in susceptibility-related intravoxel dephasing → Increase in T2 and T2*

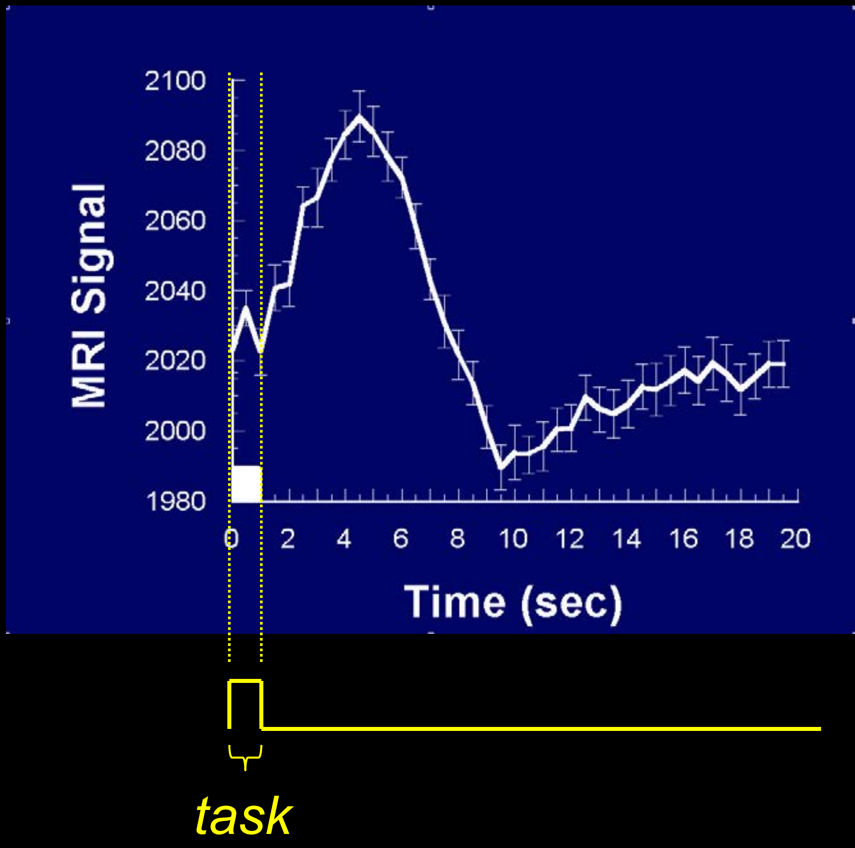
↓

Local Signal Increase in T2 and T2* - weighted sequences

The BOLD Signal

Blood Oxygenation Level Dependent (BOLD) signal changes





Alternating Left and Right Finger Tapping

~ 1992

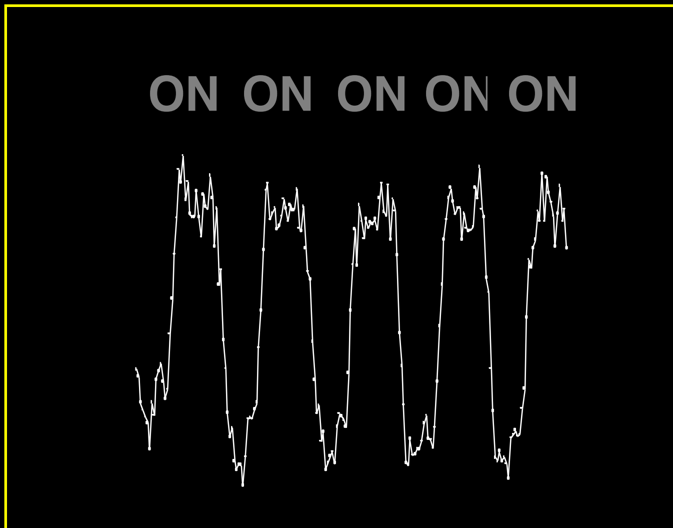
K. K. Kwong, et al, (1992) "Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation." Proc. Natl. Acad. Sci. USA. 89, 5675-5679.

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.

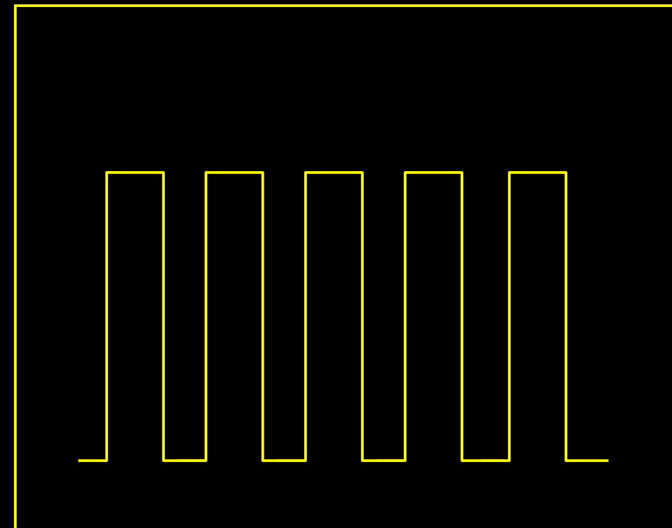
Blamire, A. M., et al. (1992). "Dynamic mapping of the human visual cortex by high-speed magnetic resonance imaging." Proc. Natl. Acad. Sci. USA 89: 11069-11073.

Creating a Functional Image



Signal Time Course

X

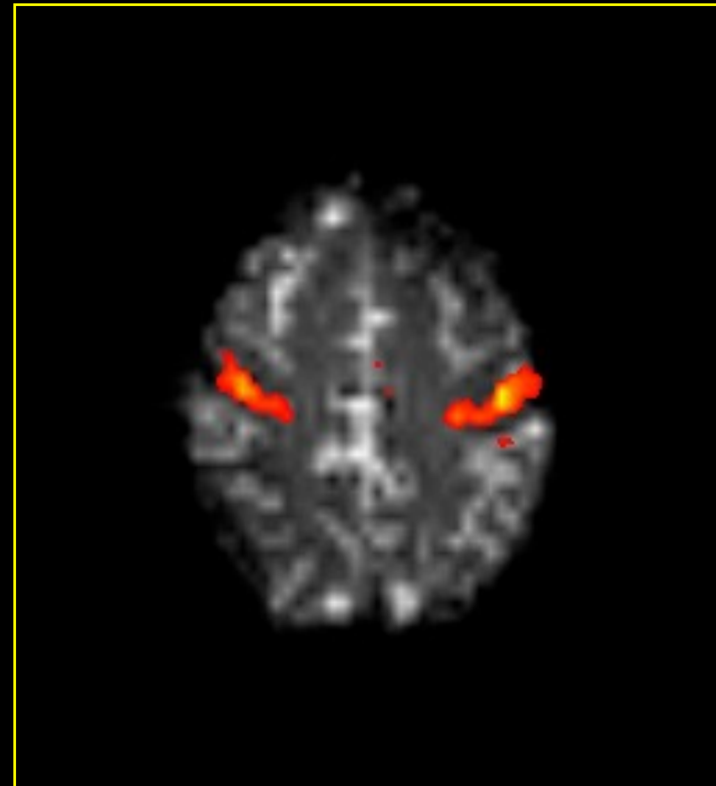


Reference Function

=

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



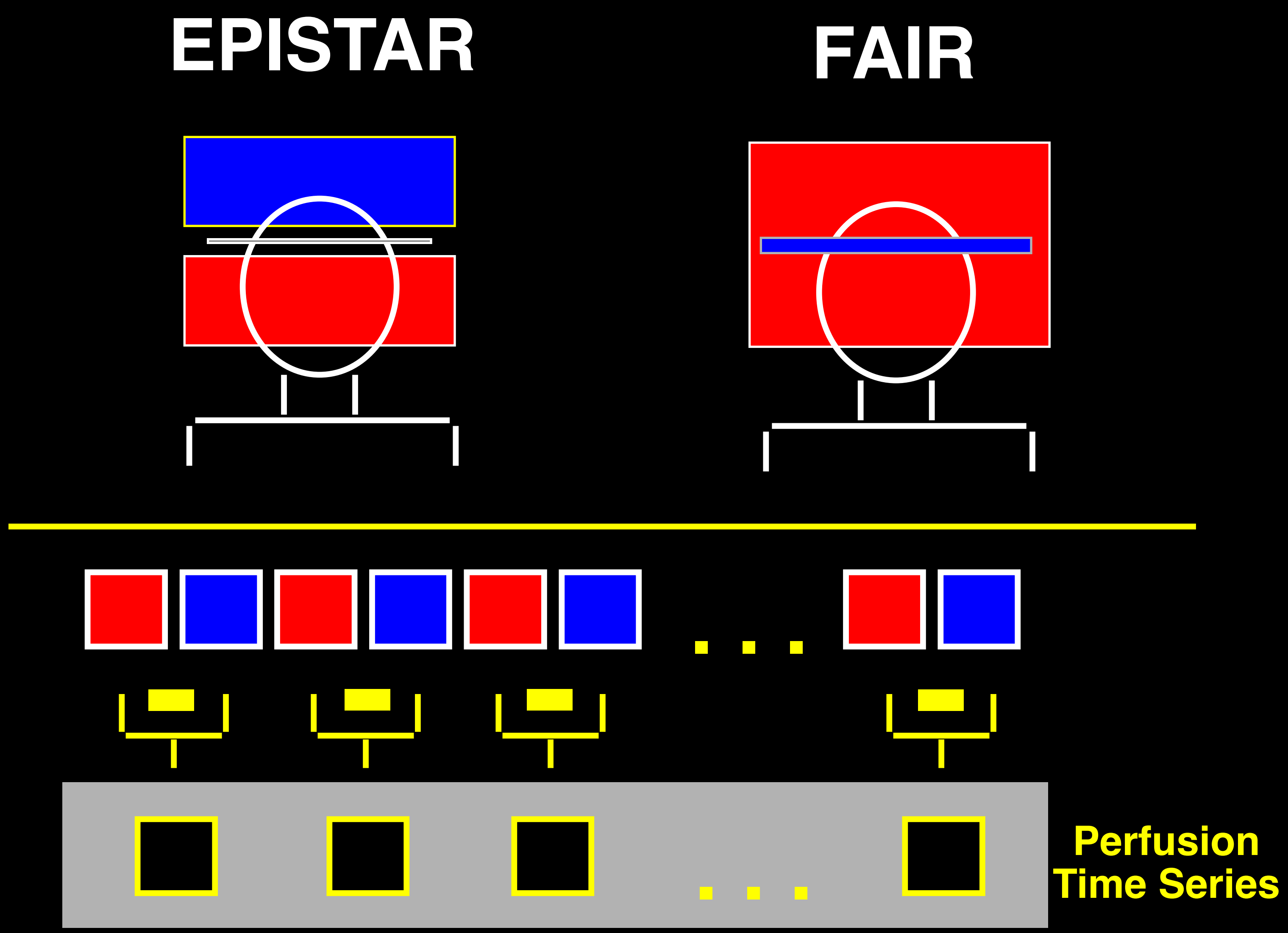
Cross Correlation Image
Anatomical Image

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

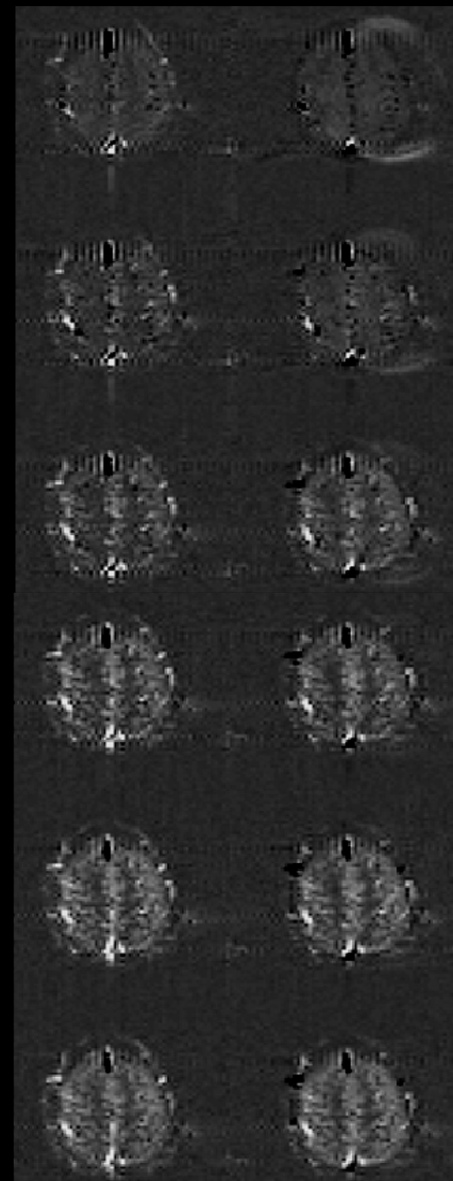
400

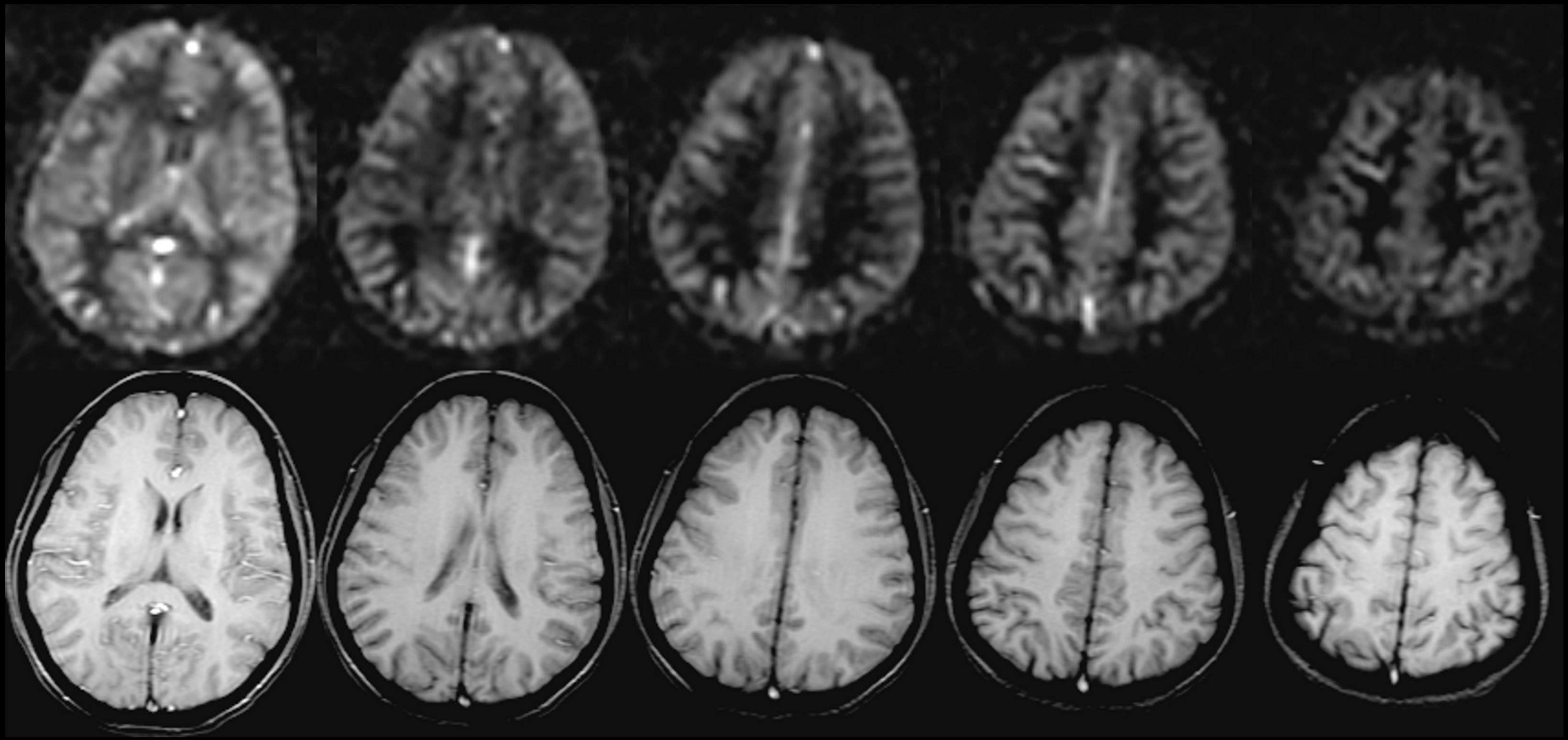
600

800

1000

1200





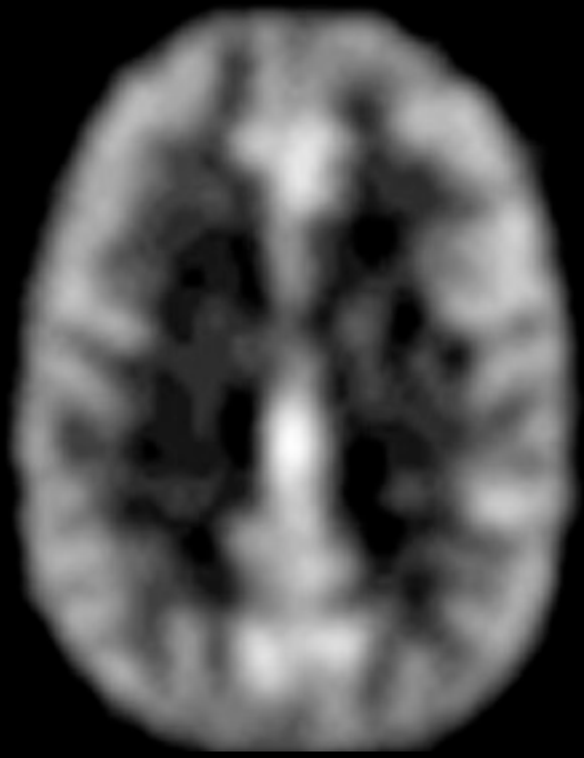
Williams, D. S., Detre, J. A., Leigh, J. S. & Koretsky, A. S. (1992) “Magnetic resonance imaging of perfusion using spin-inversion of arterial water.” Proc. Natl. Acad. Sci. USA 89, 212-216.

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.

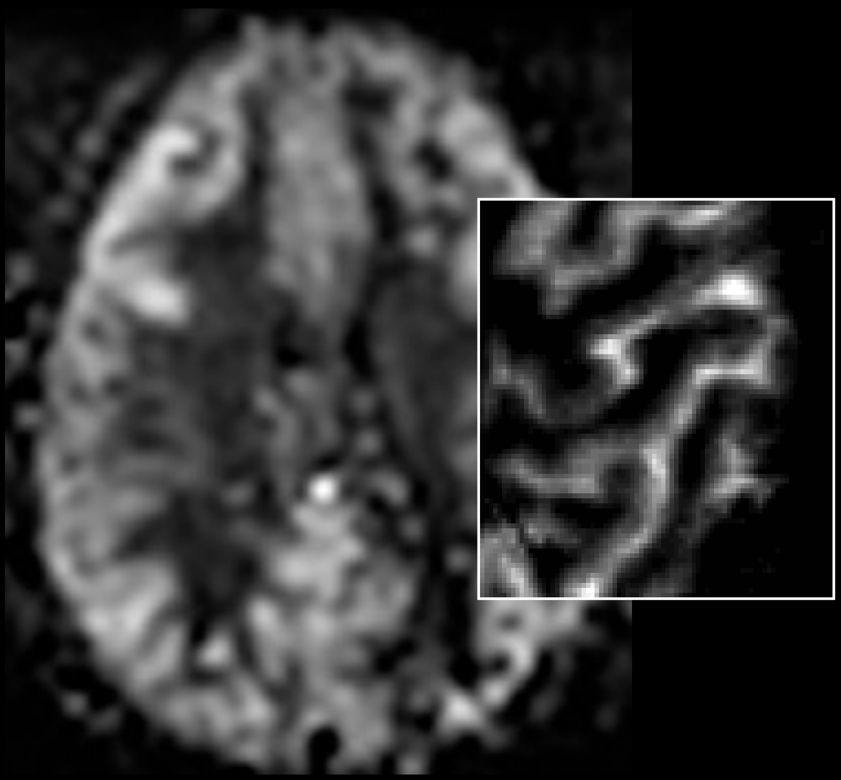
Kim, S.-G. (1995) “Quantification of relative cerebral blood flow change by flow-sensitive alternating inversion recovery (FAIR) technique: application to functional mapping.” Magn. Reson. Med. **34**, 293-301.

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



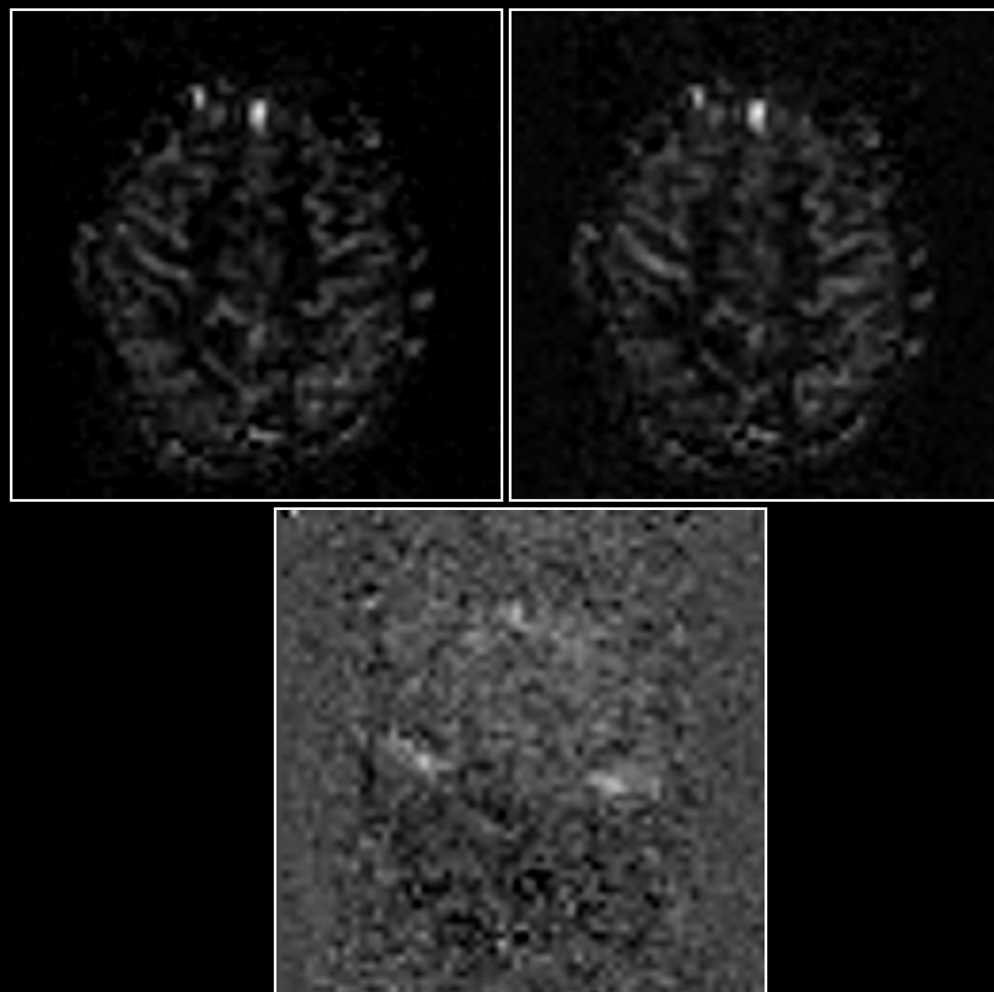
PET: $H_2{}^{15}O$



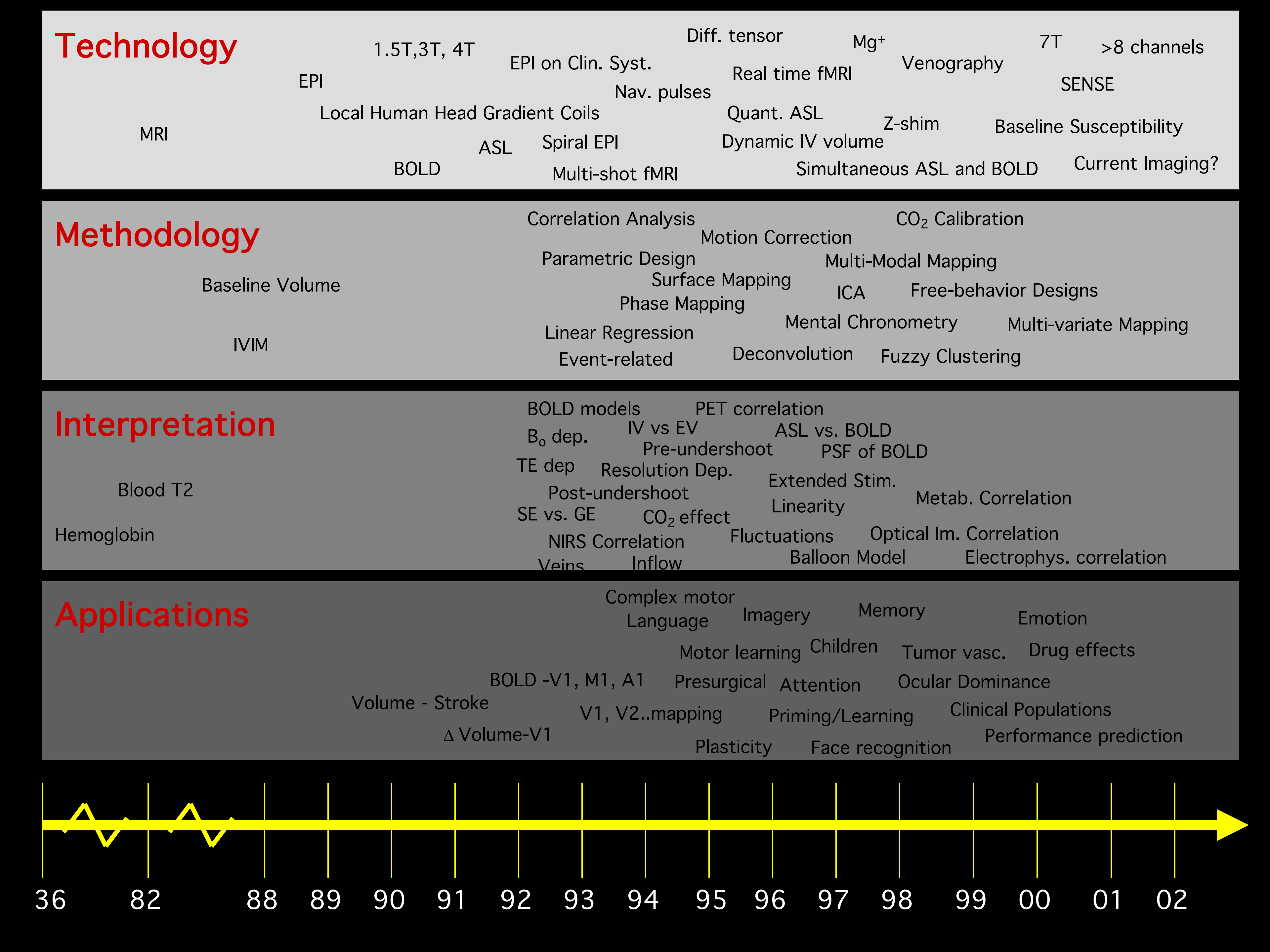
MRI: ASL

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



Technology
1.5T,3T, 4T
Diff. tensor
Mg+
7T
>8 channels
EPI on Clin. Syst.
Venography
Real time fMRI
EPI
SENSE
Nav. pulses
Local Human Head Gradient Coils
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Refinements

BOLD Contrast Interpretation

Dynamics

Paradigm Design and Processing

Refinements

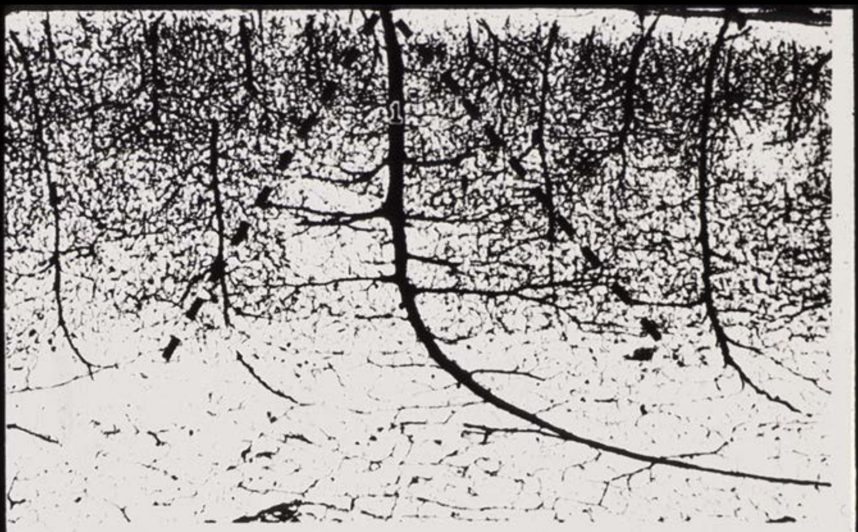
BOLD Contrast Interpretation

Dynamics

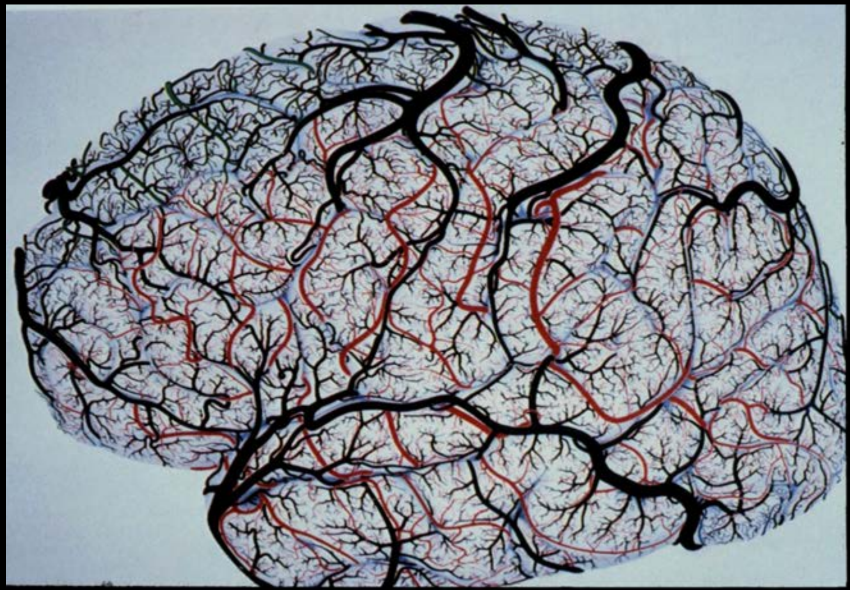
Paradigm Design and Processing

The Neuroscientists' Challenge:

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

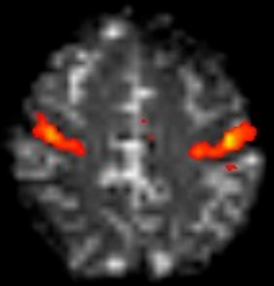


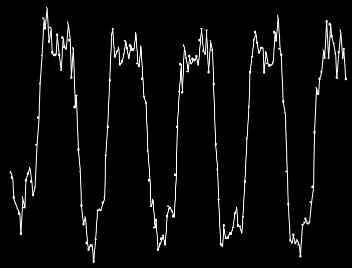
IG. 43. Middle temporal gyrus. Female, 60 years. (1) Principal intracortical vein. The branches length regularly decreases from deep wards superficial cortical regions; thus, the vascular territory of the principal vein has a conical appearance (dotted line) (×28)



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

- **Where?**
- **When?**

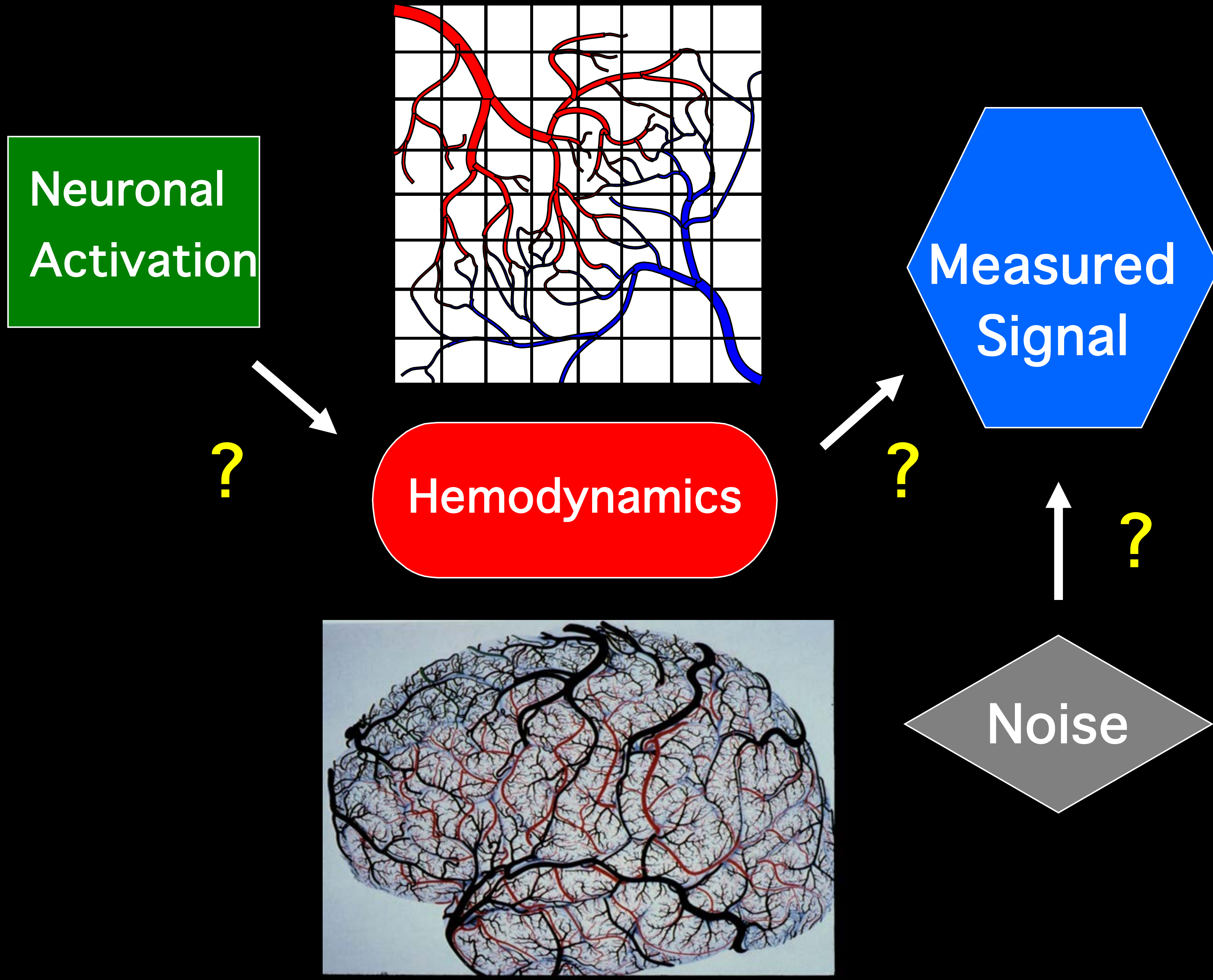




- **How much?**

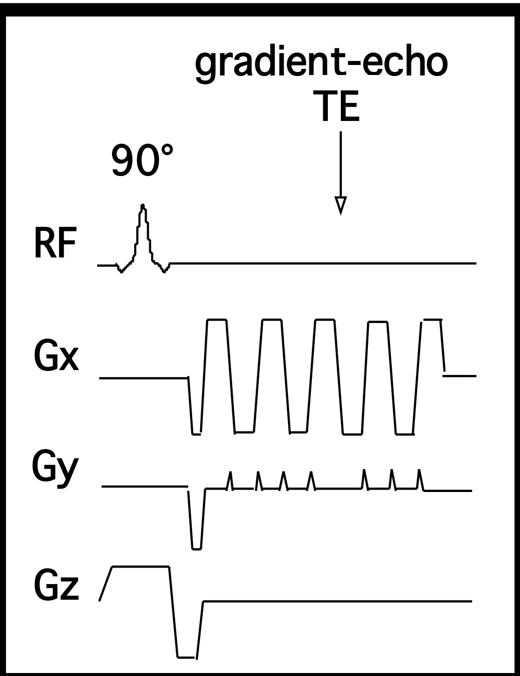
- **How to get the brain to do what we want it to do in the context of an fMRI experiment?**
(*limitations*: limited time and signal to noise, motion, acoustic noise)

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

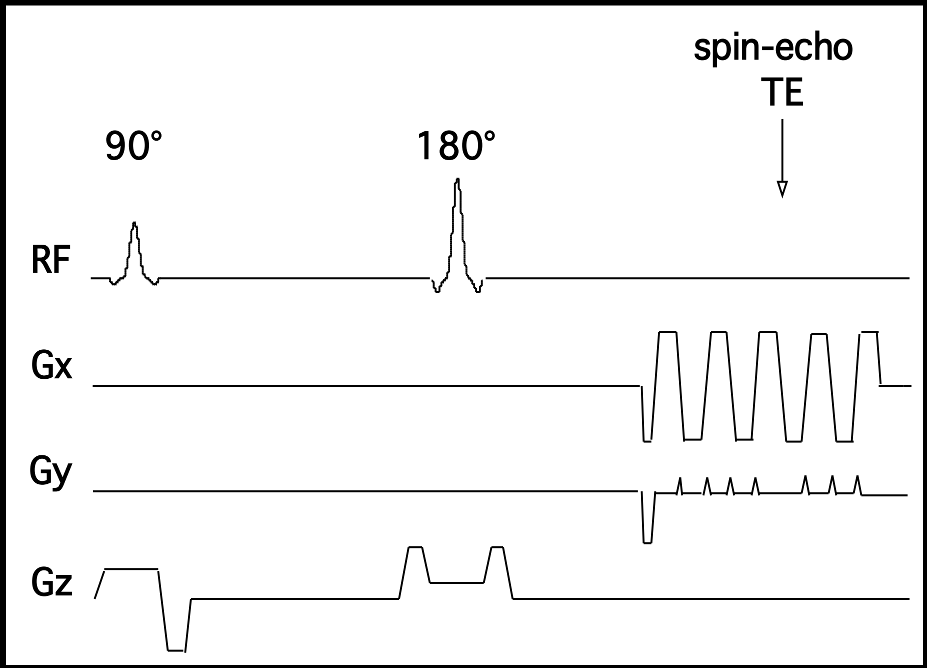

Neuronal Activation
?
Hemodynamics
?
Measured Signal
?
Noise

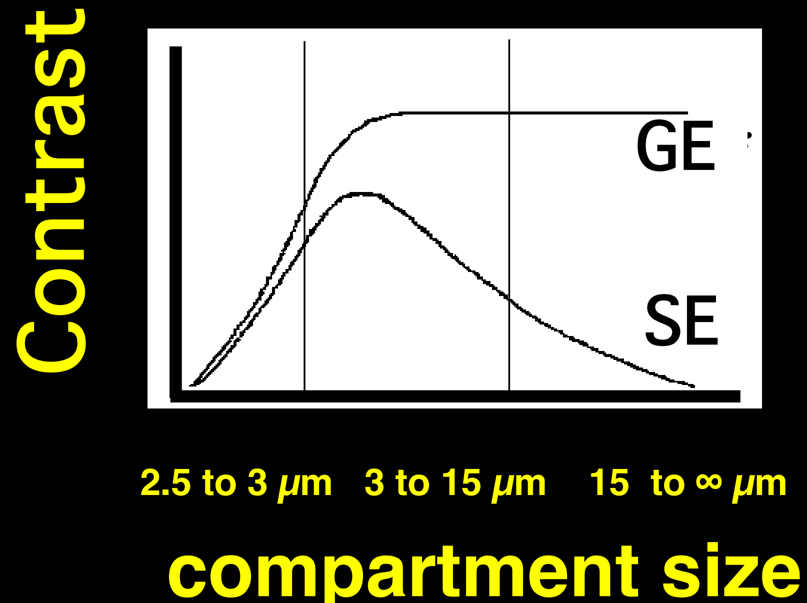
Spin-echo vs. Gradient-echo

Gradient-Echo EPI

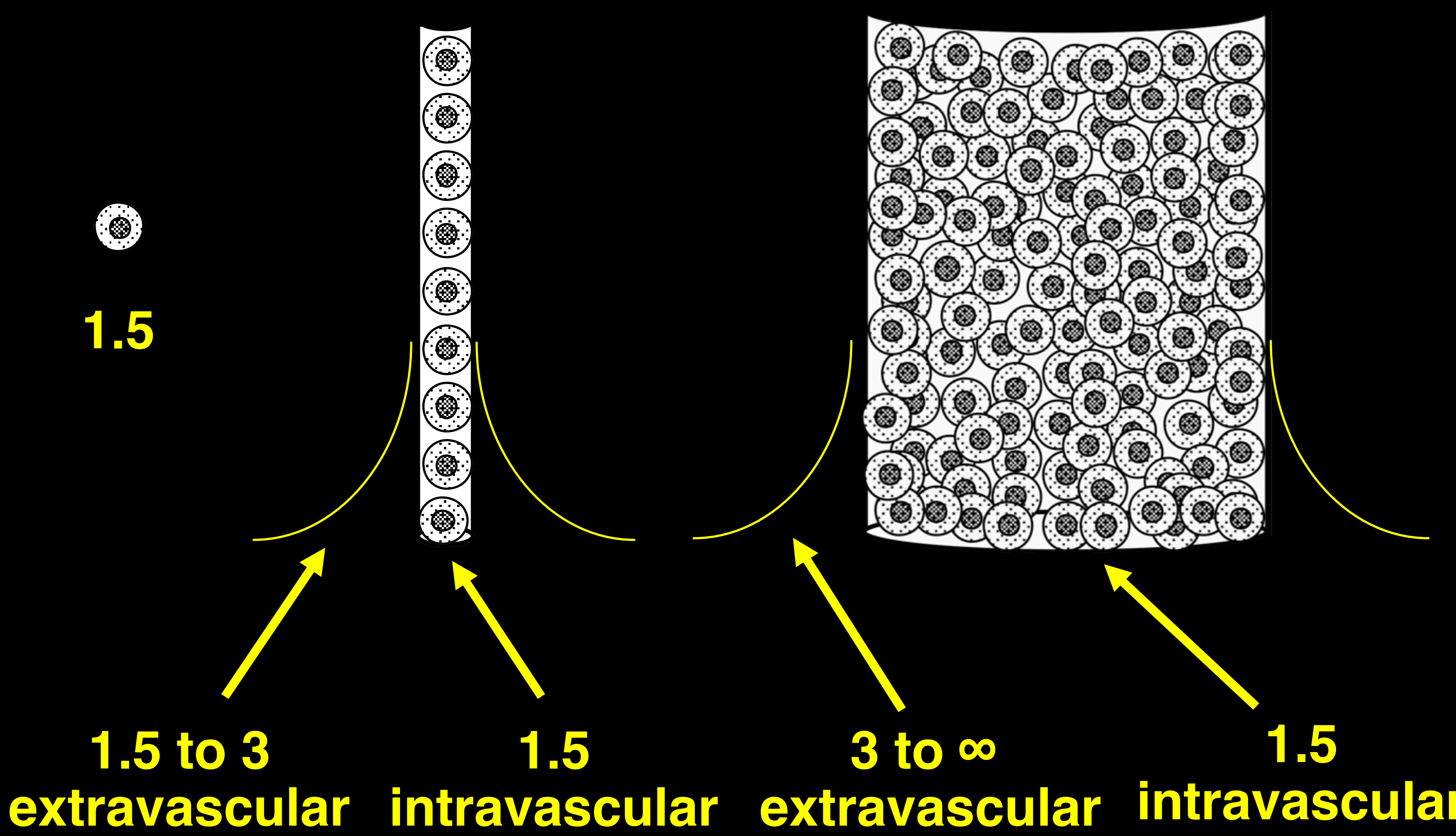


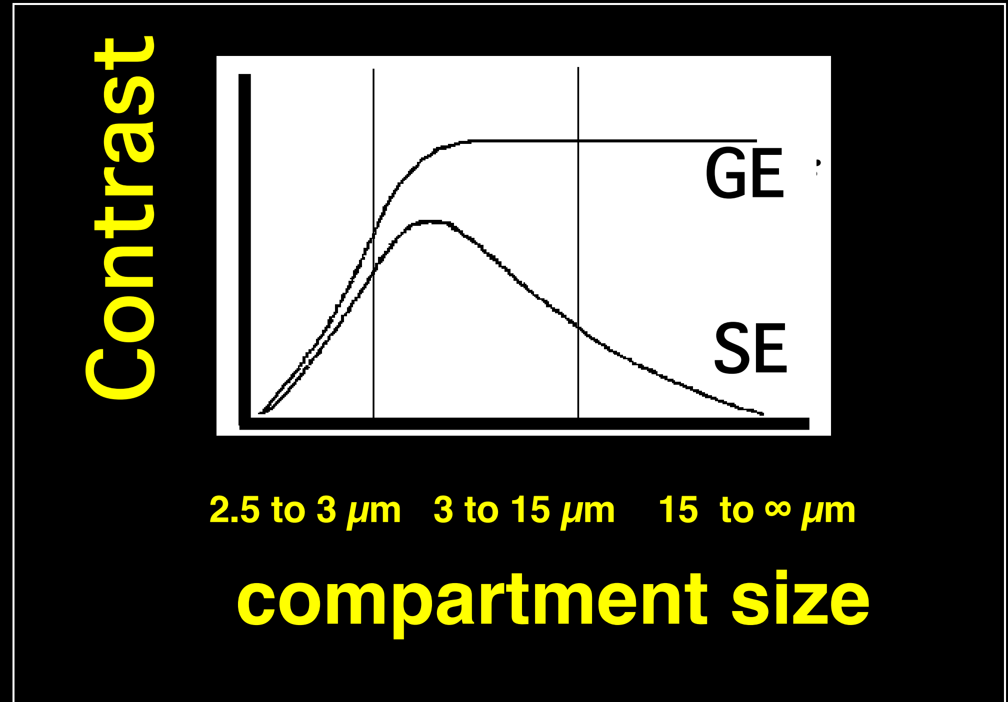
Spin-Echo EPI

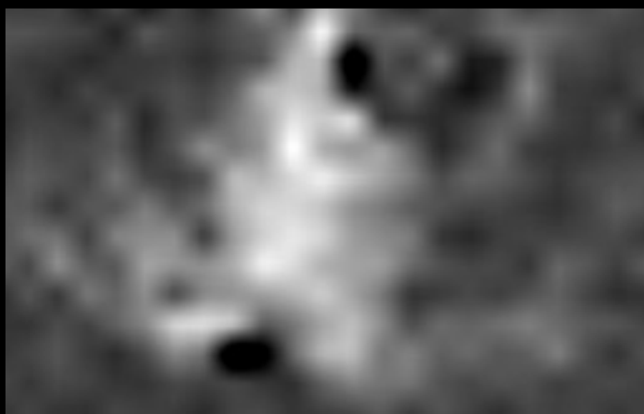




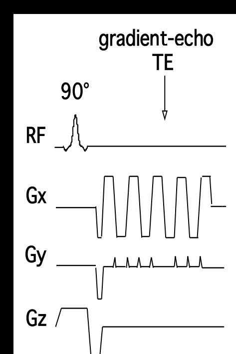
ΔR2* /ΔR2

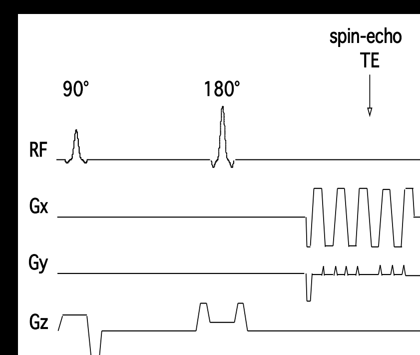

1.5
1.5 to 3
extravascular
1.5
intravascular
3 to ∞
extravascular
1.5
intravascular





Gradient - Echo

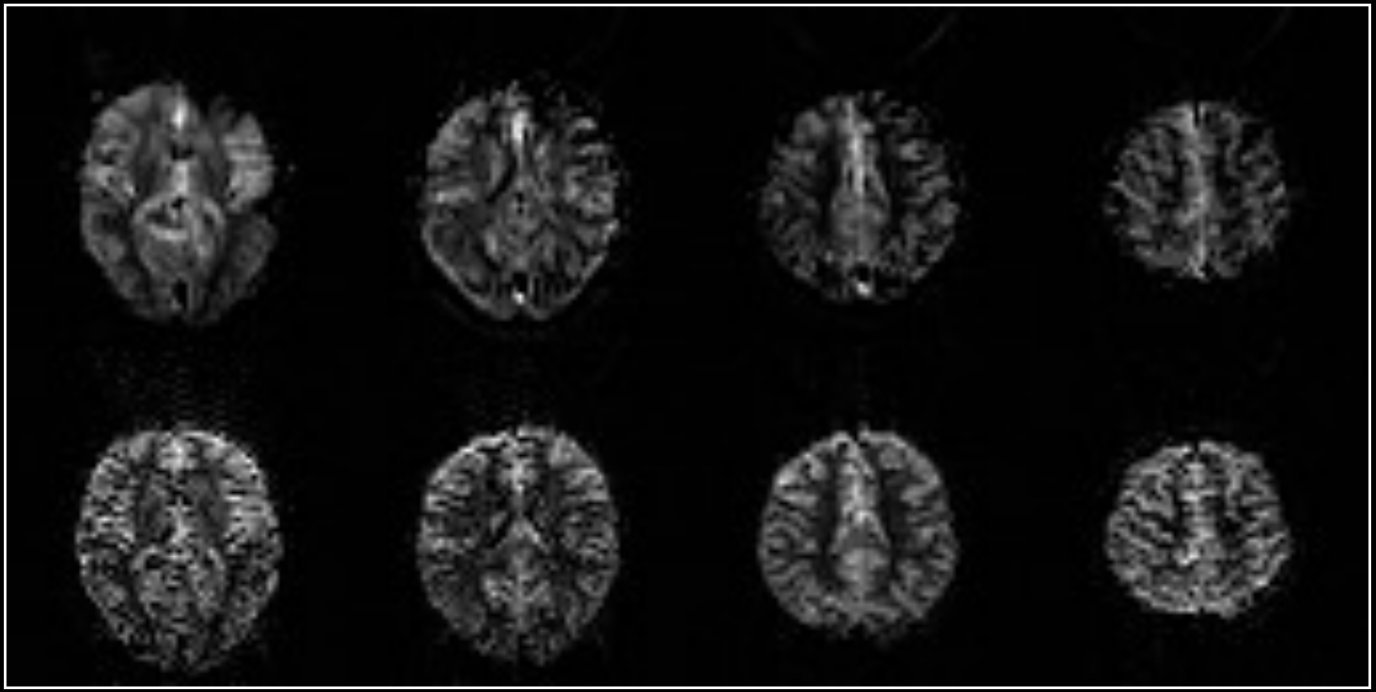




Spin - Echo

GE
TE = 30 ms

SE
TE = 110 ms



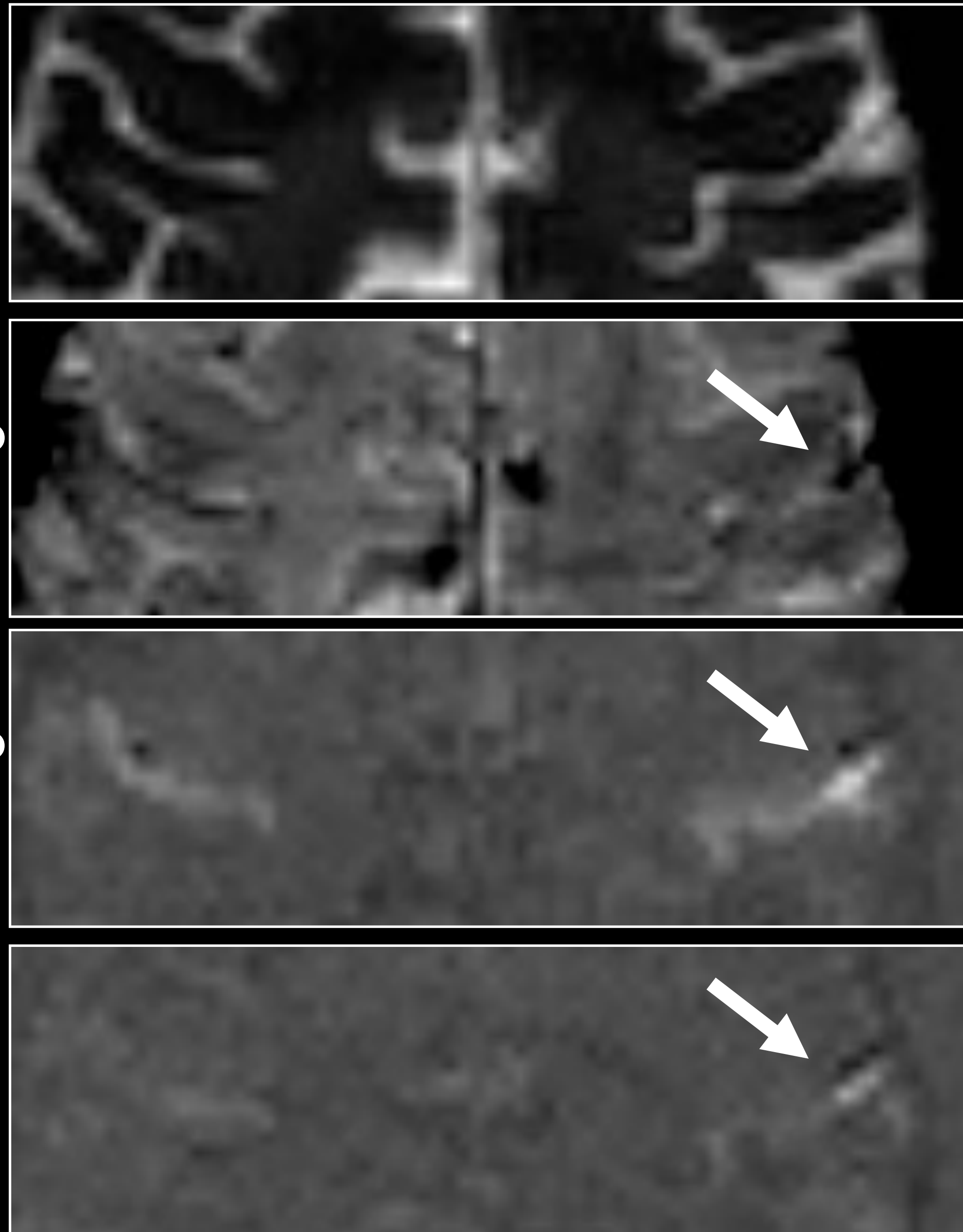
3T

Spin-Echo
TE = 105 ms
TR = ∞

Gradient-Echo
TE = 50 ms

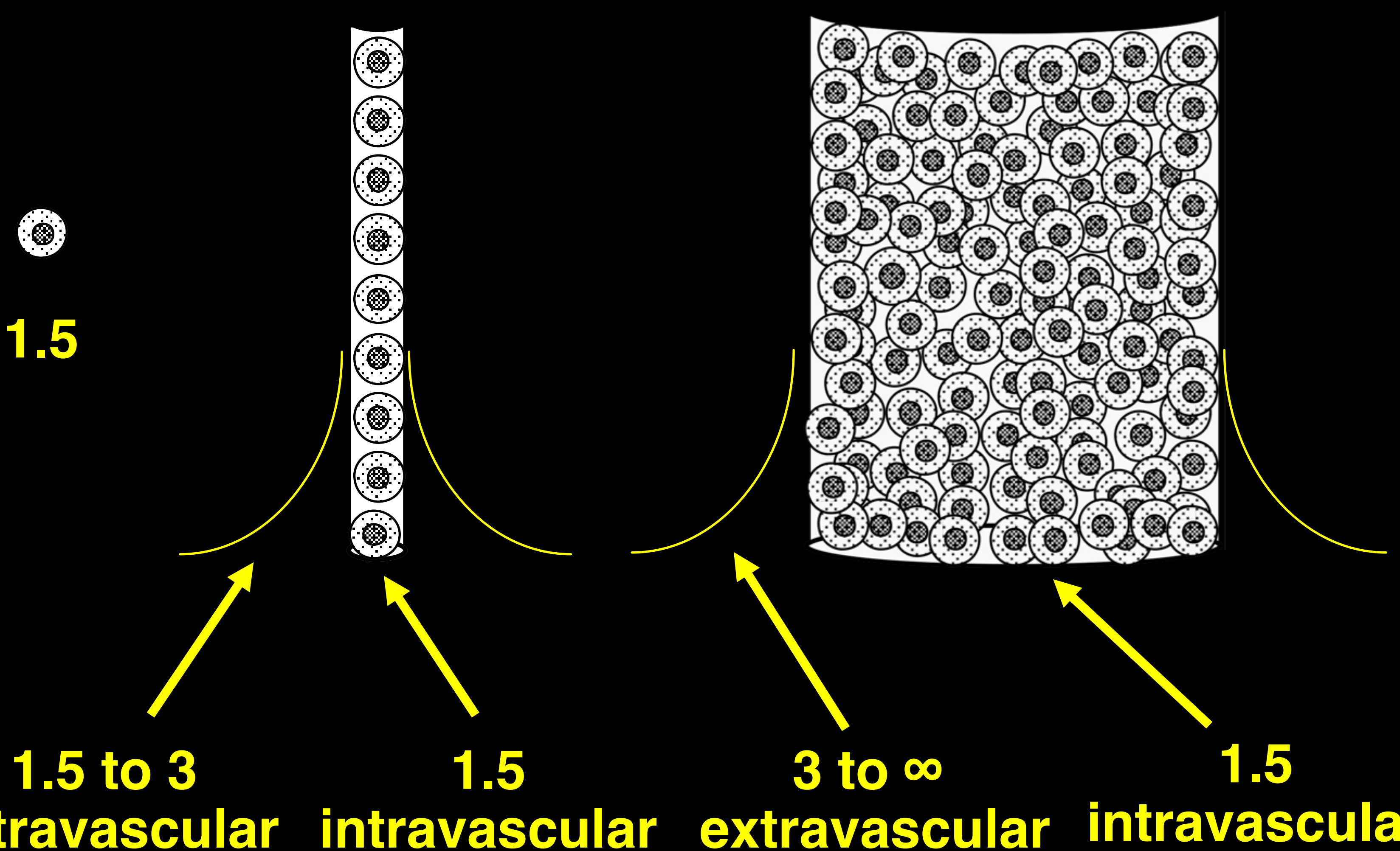
Gradient-Echo
functional
TE = 50 ms

Spin-Echo
functional
TE = 105 ms



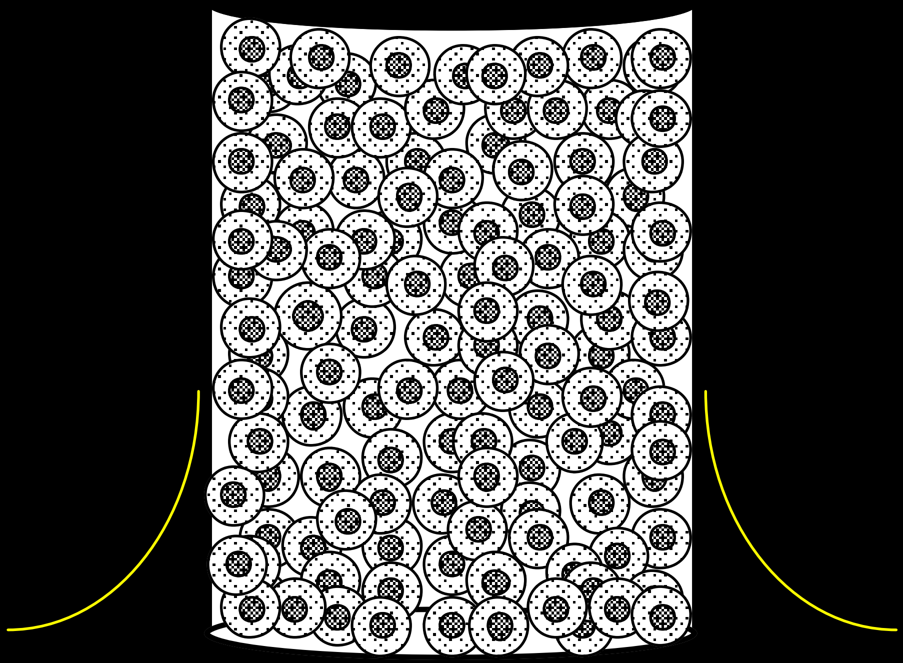
Effect of diffusion weighting

ΔR2* /ΔR2

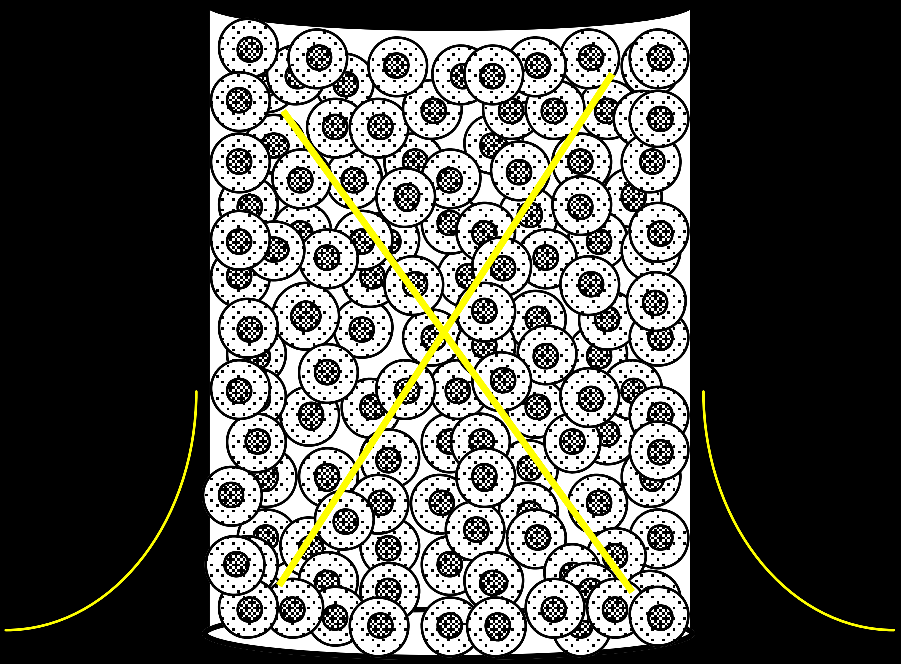


average ΔR2 / ΔR2 ≈ 3 to 4*

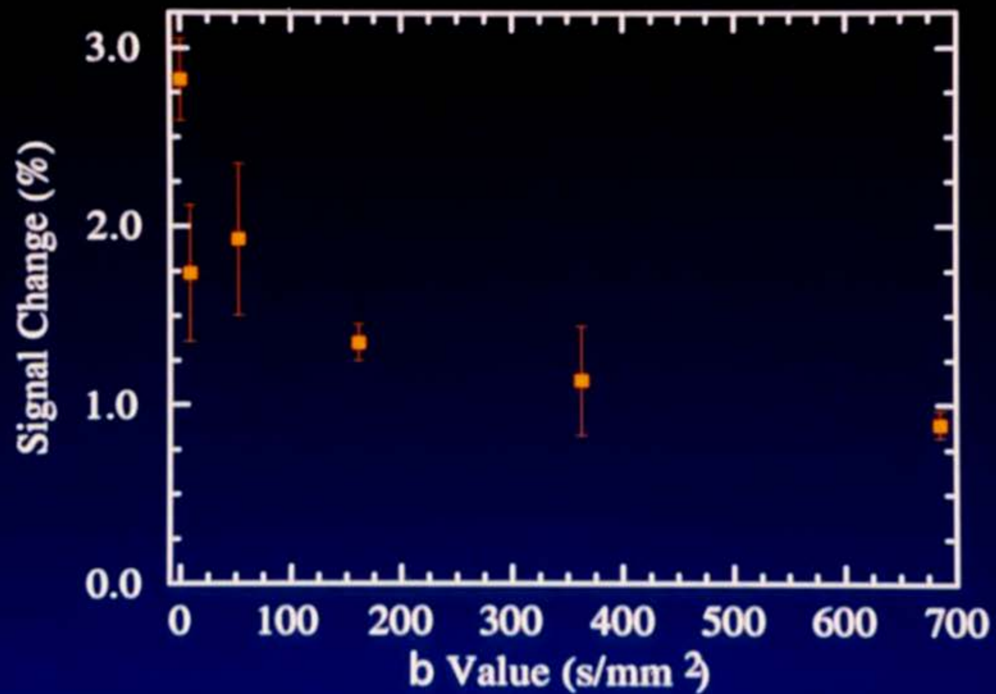
no diffusion weighting

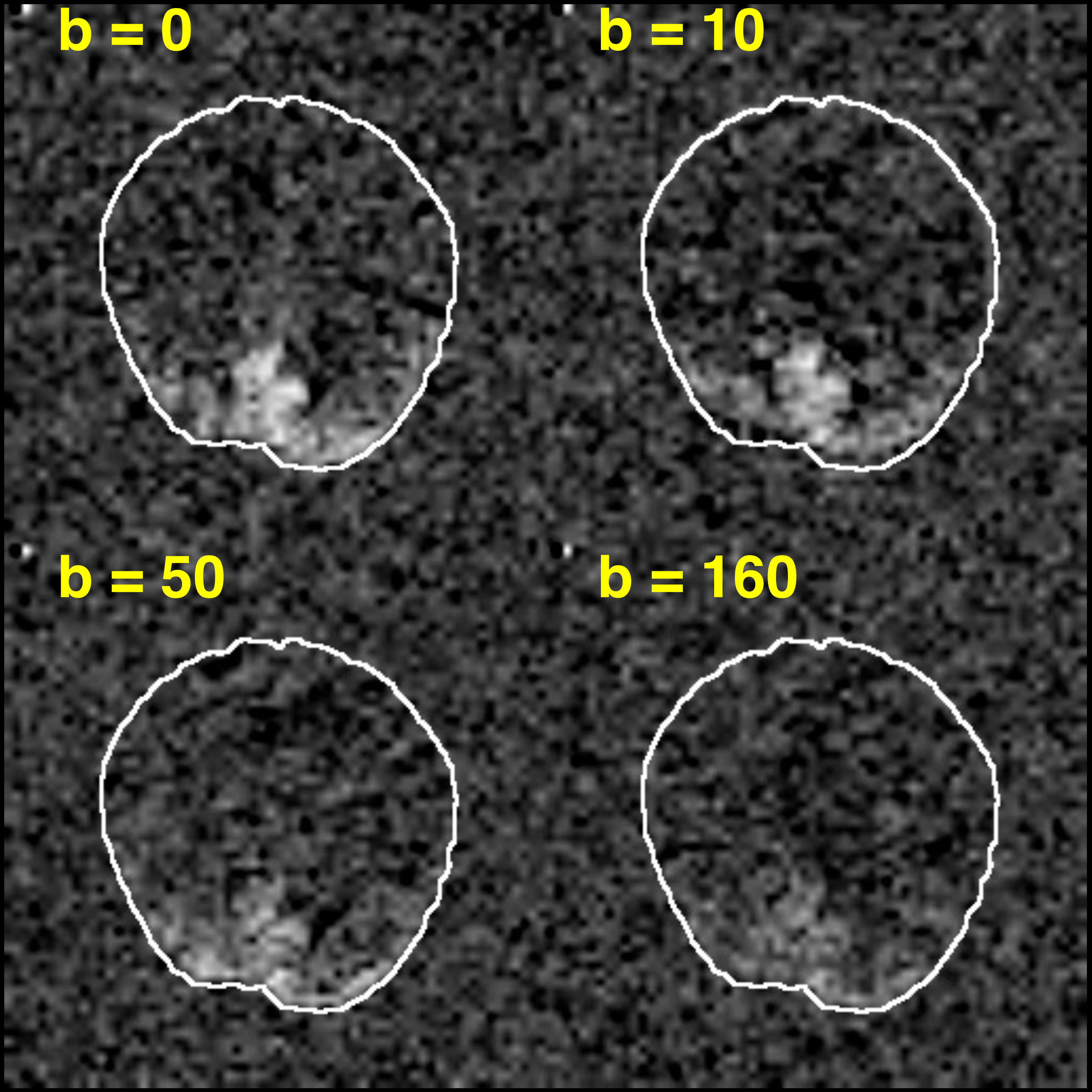


diffusion weighting



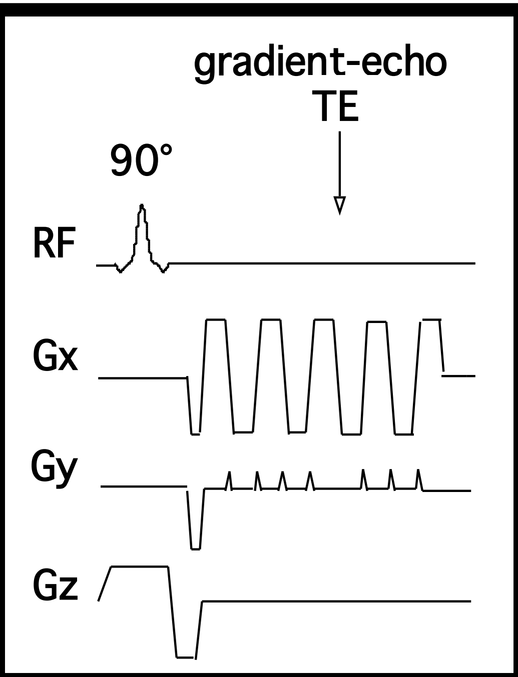
Summary of Diffusion-Weighted fMRI Data



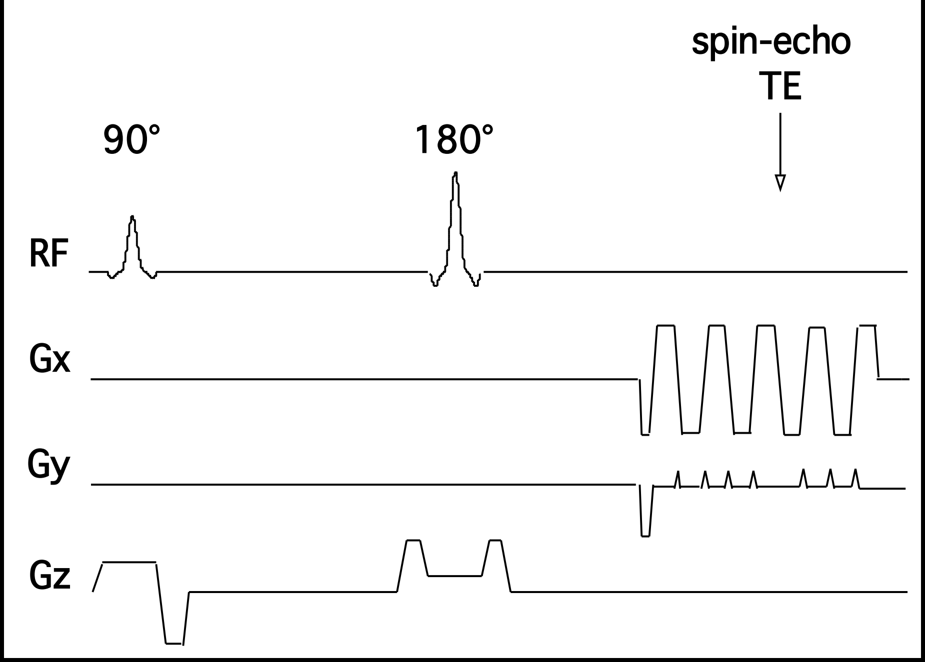

b = 0
b = 10
b = 50
b = 160

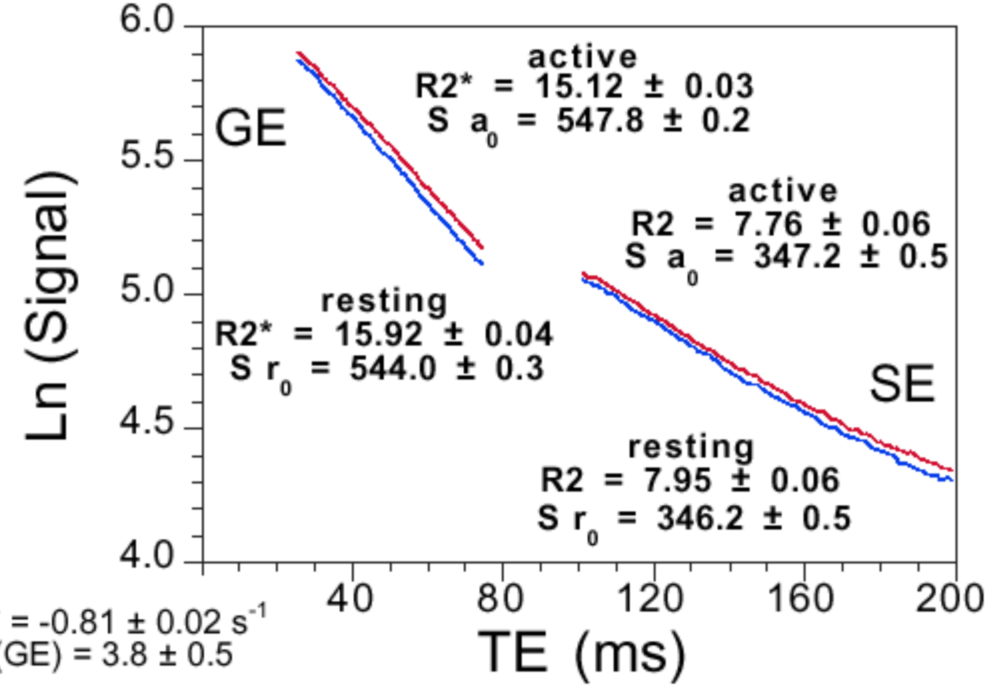
Echo time dependence

Gradient-Echo EPI



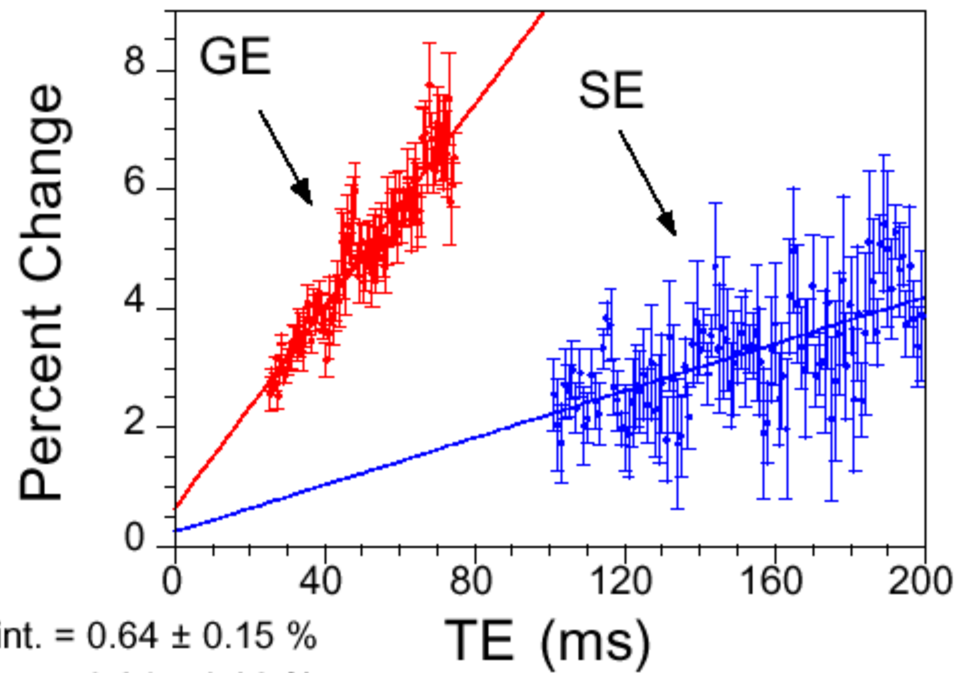
Spin-Echo EPI





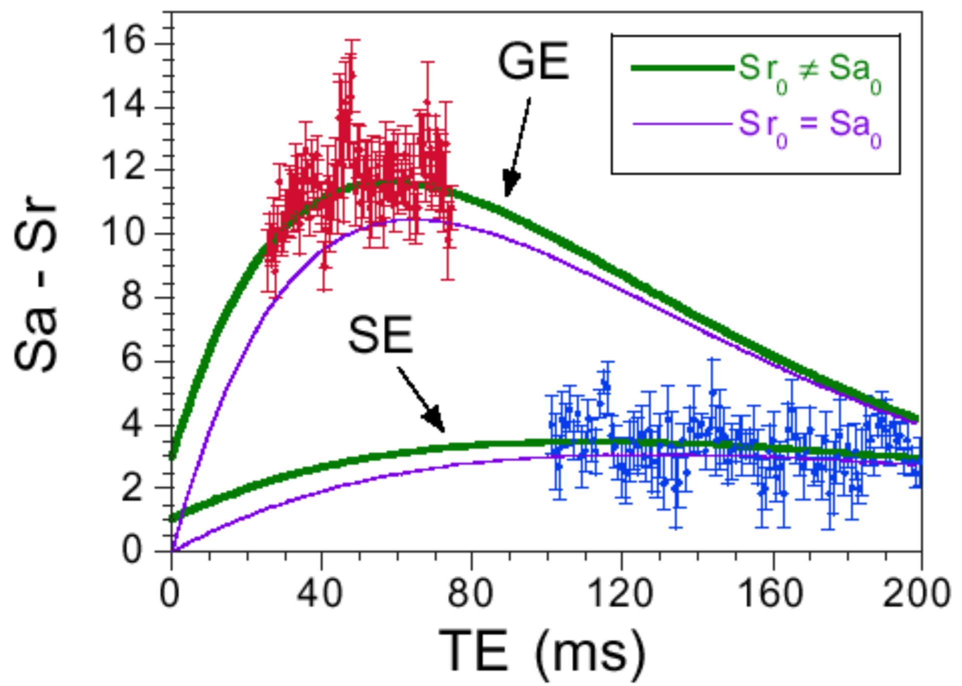
$\Delta R2^* = -0.81 \pm 0.02\ s^{-1}$
ΔS_0 (GE) = 3.8 ± 0.5

$\Delta R2 = -0.19 \pm 0.02\ s^{-1}$
ΔS_0 (SE) = 1.0 ± 1.0



GE int. = 0.64 ± 0.15 %

SE int. = 0.24 ± 0.38 %



Sa - Sr
TE (ms)
GE
SE
$Sr_0 \neq Sa_0$
$Sr_0 = Sa_0$
0
2
4
6
8
10
12
14
16
0
40
80
120
160
200

Perfusion localization vs. BOLD localization

T1 - weighted

Flow weighted

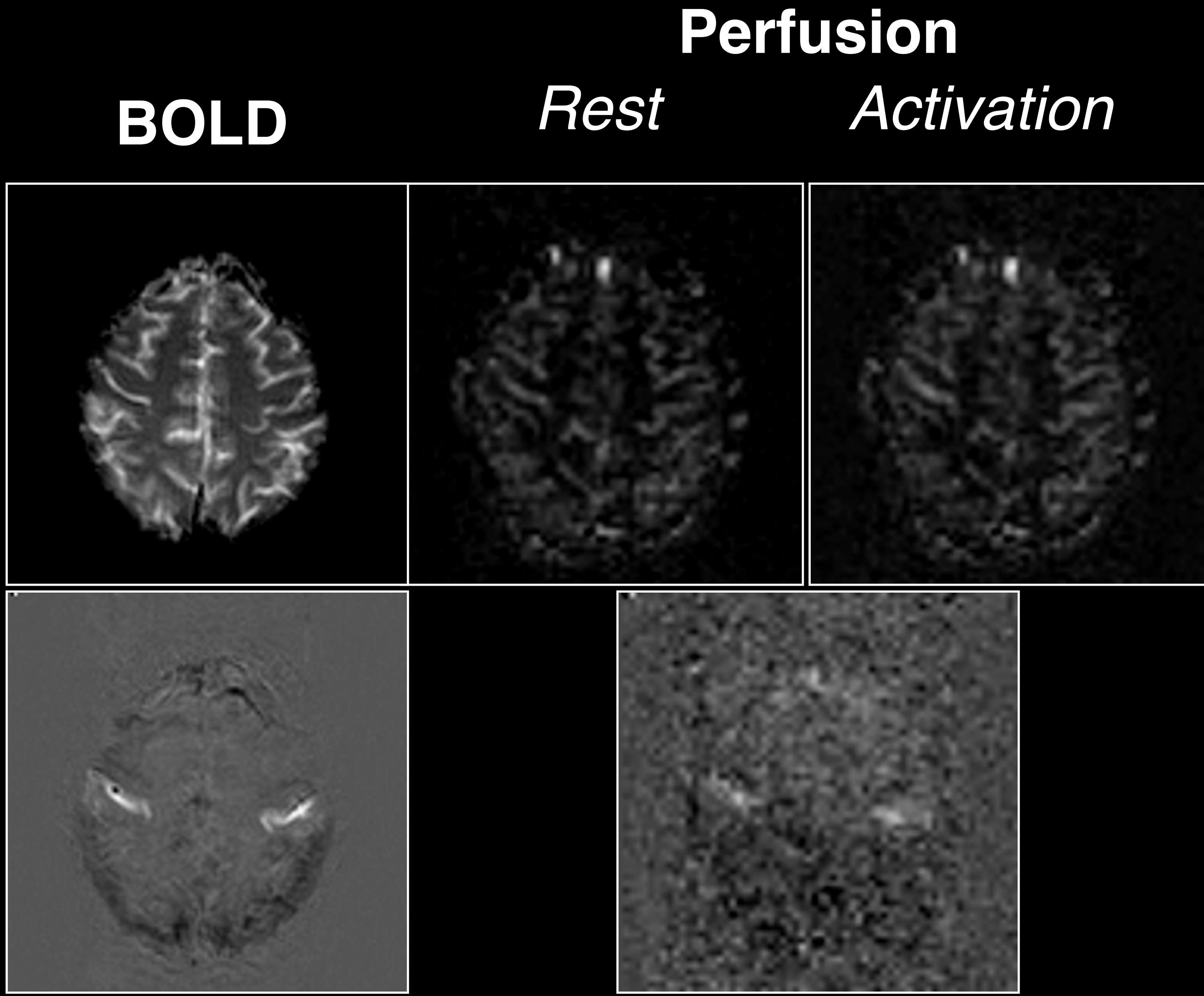
T2* weighted

BOLD weighted

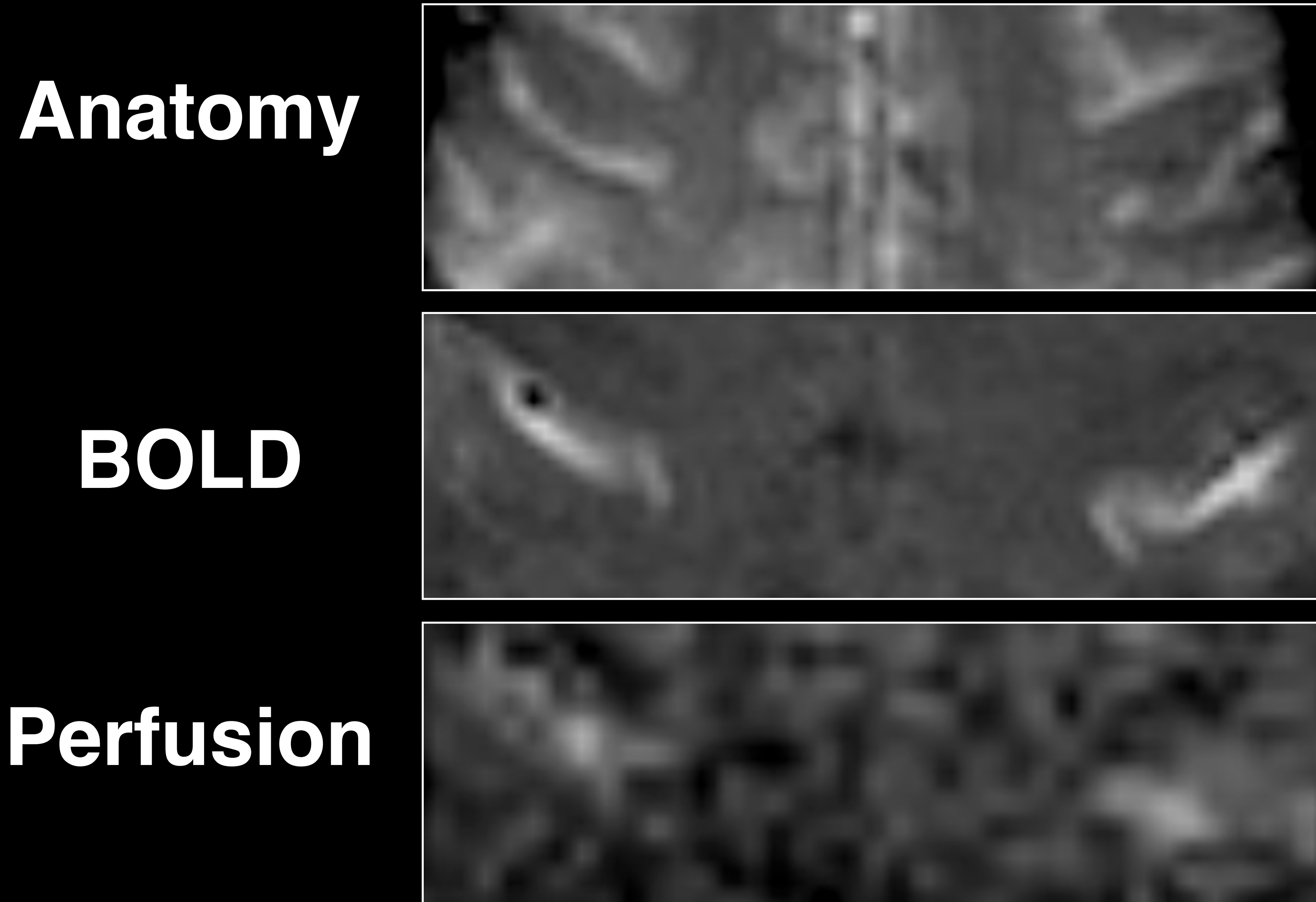
T1 and T2* weighted

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

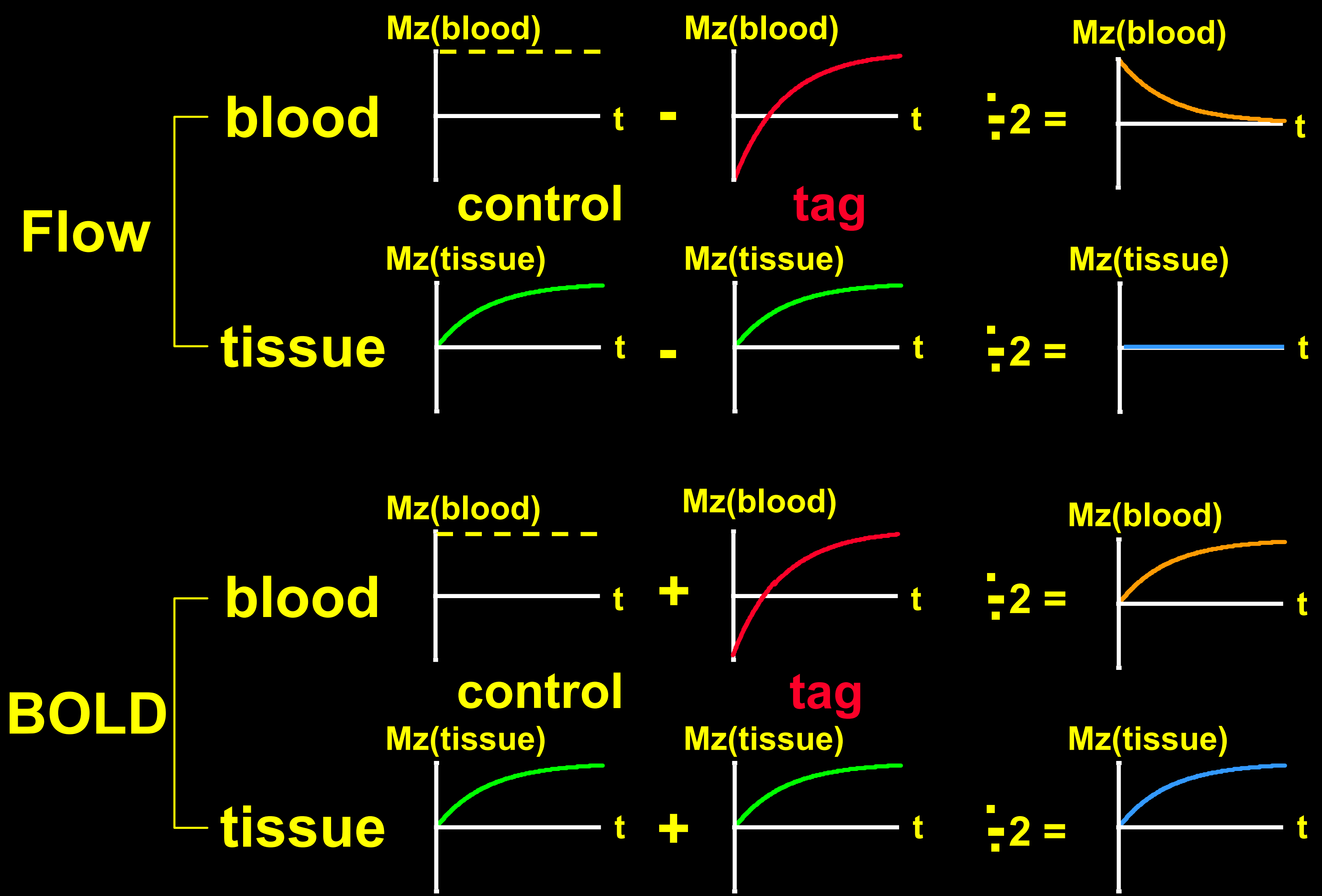


P. A. Bandettini, E. C. Wong, Magnetic resonance imaging of human brain function: principles, practicalities, and possibilities, *in* "Neurosurgery Clinics of North America: Functional Imaging" (M. Haglund, Ed.), p.345-371, W. B. Saunders Co., 1997.



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.

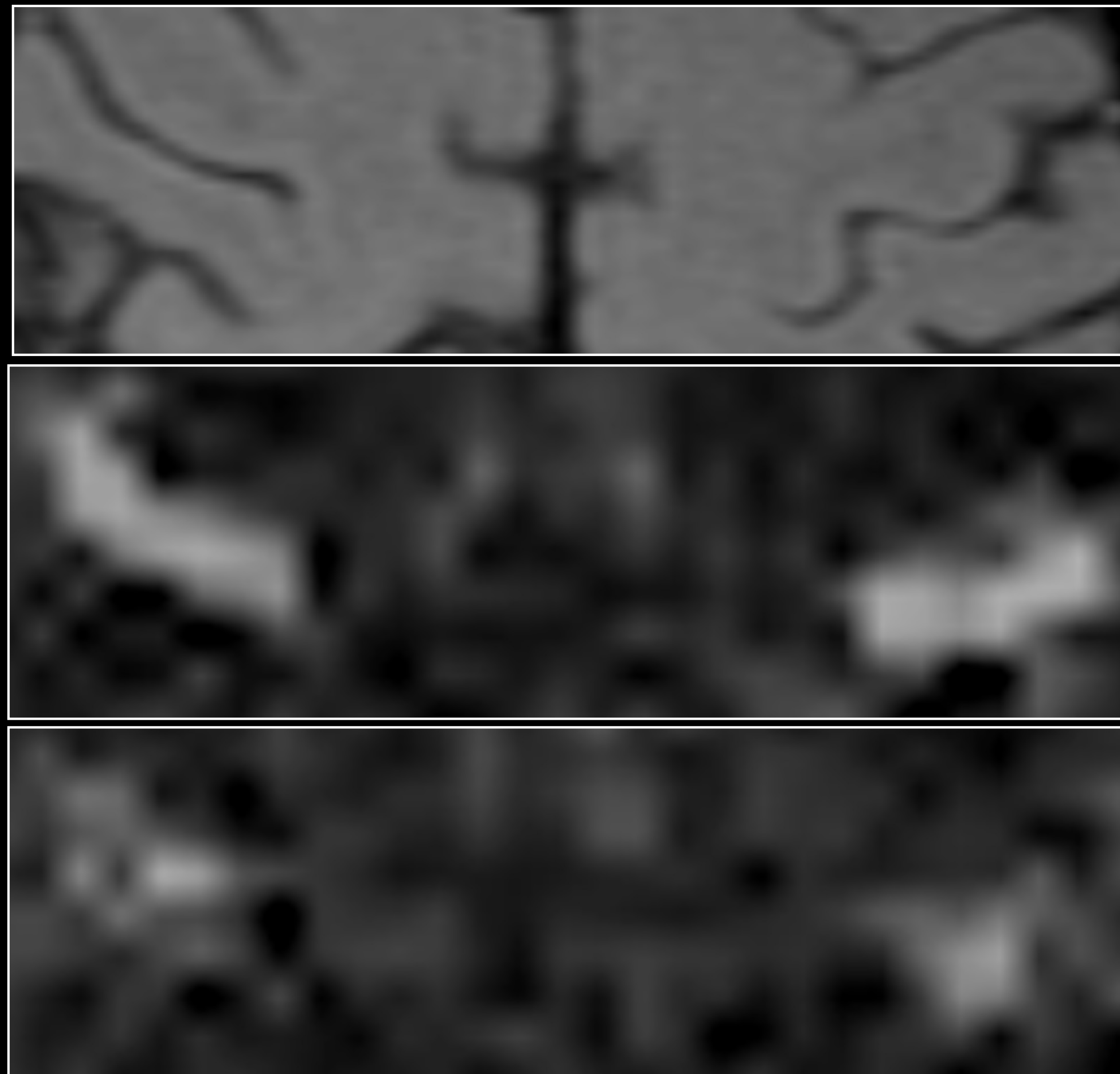
Simultaneous Flow and BOLD



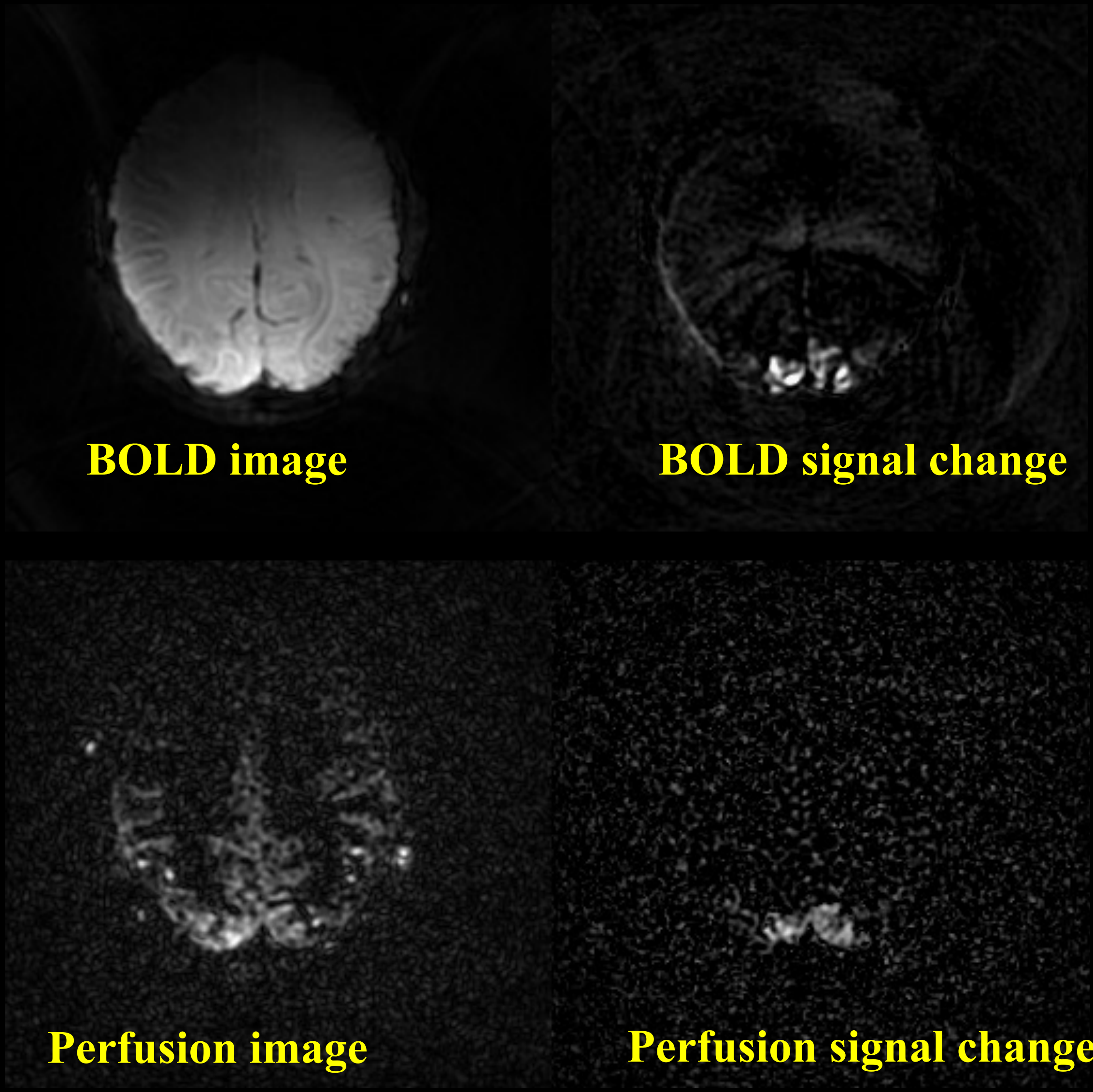
Simultaneous BOLD and Perfusion

BOLD

Perfusion



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

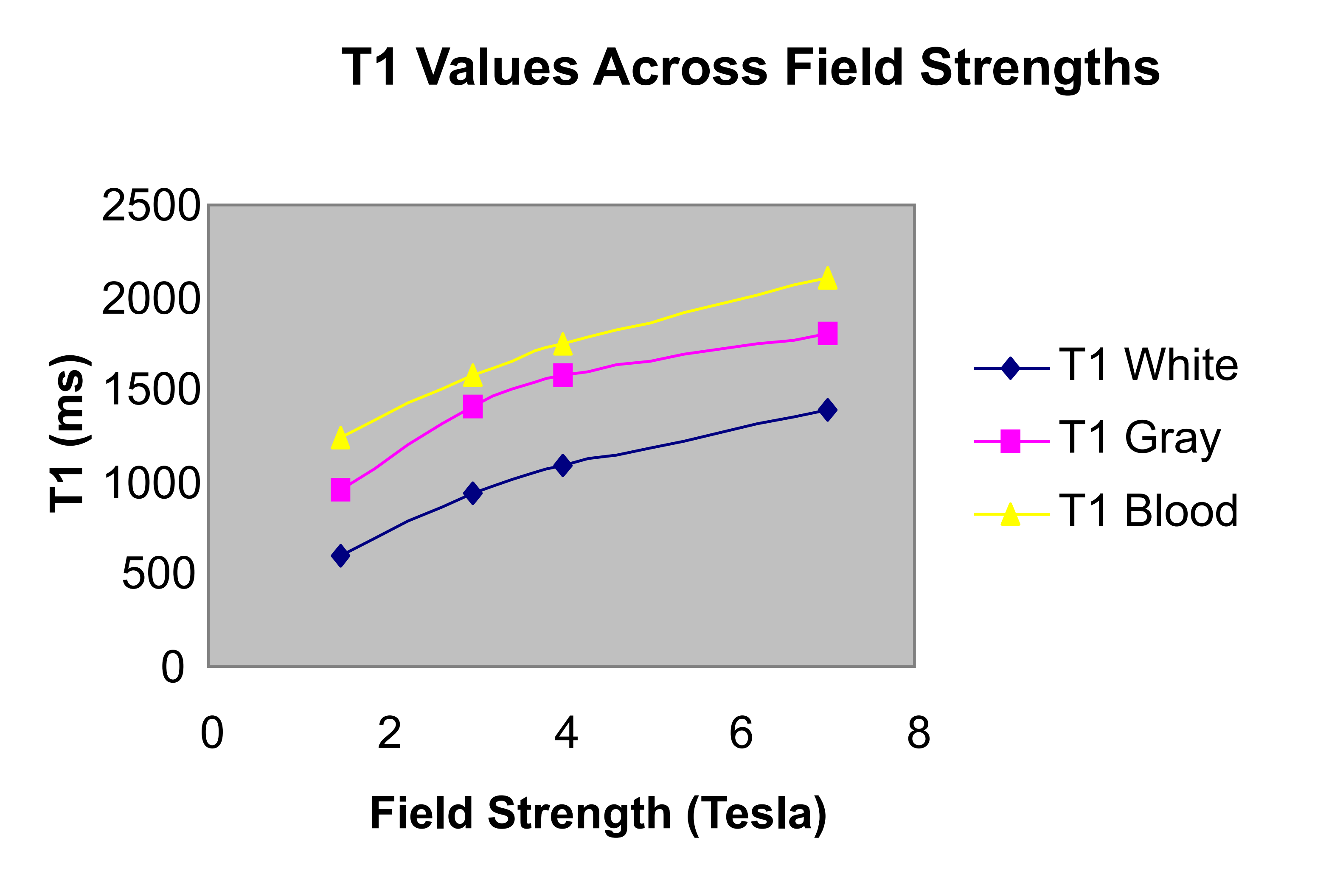


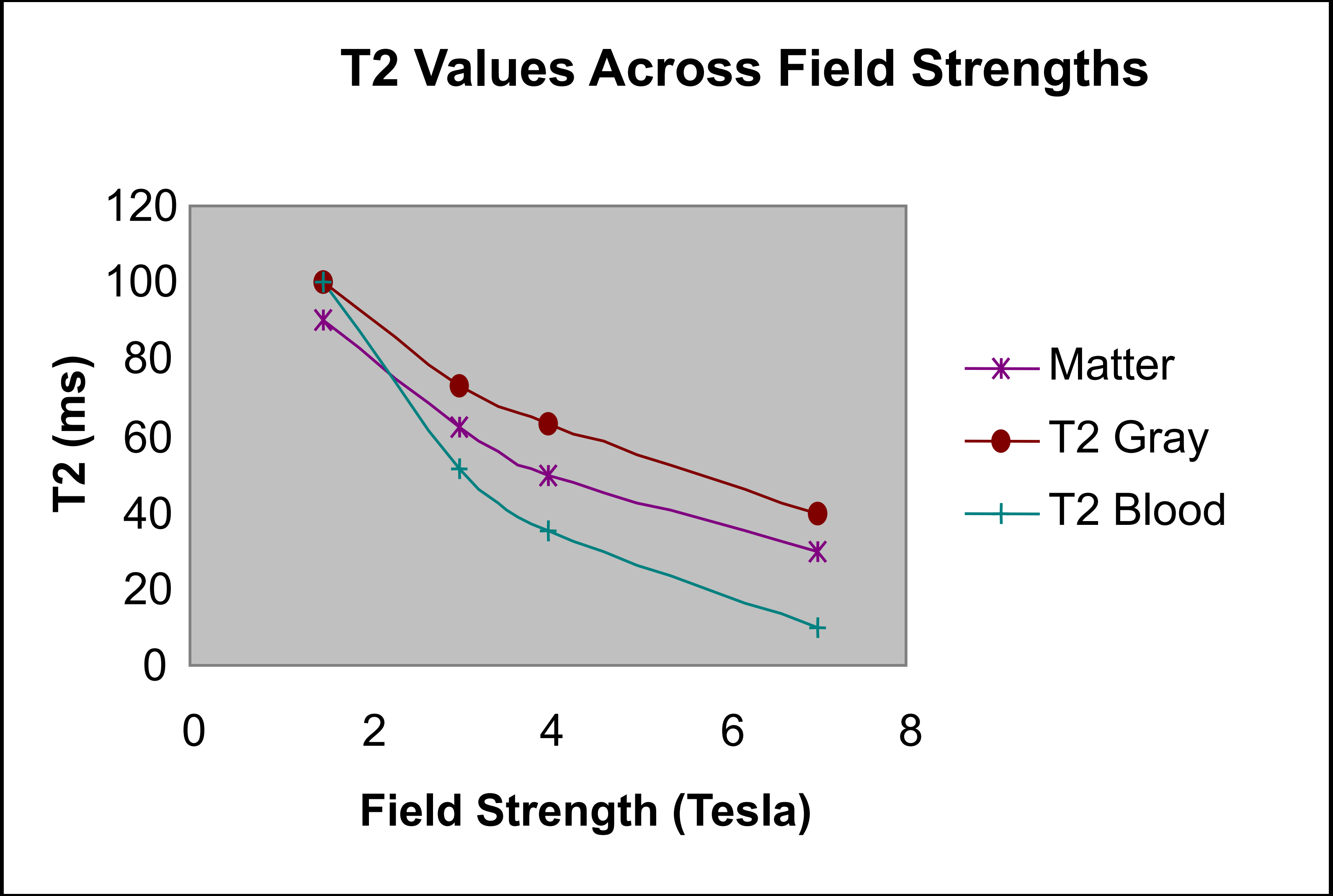
Frank Ye, et al.

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

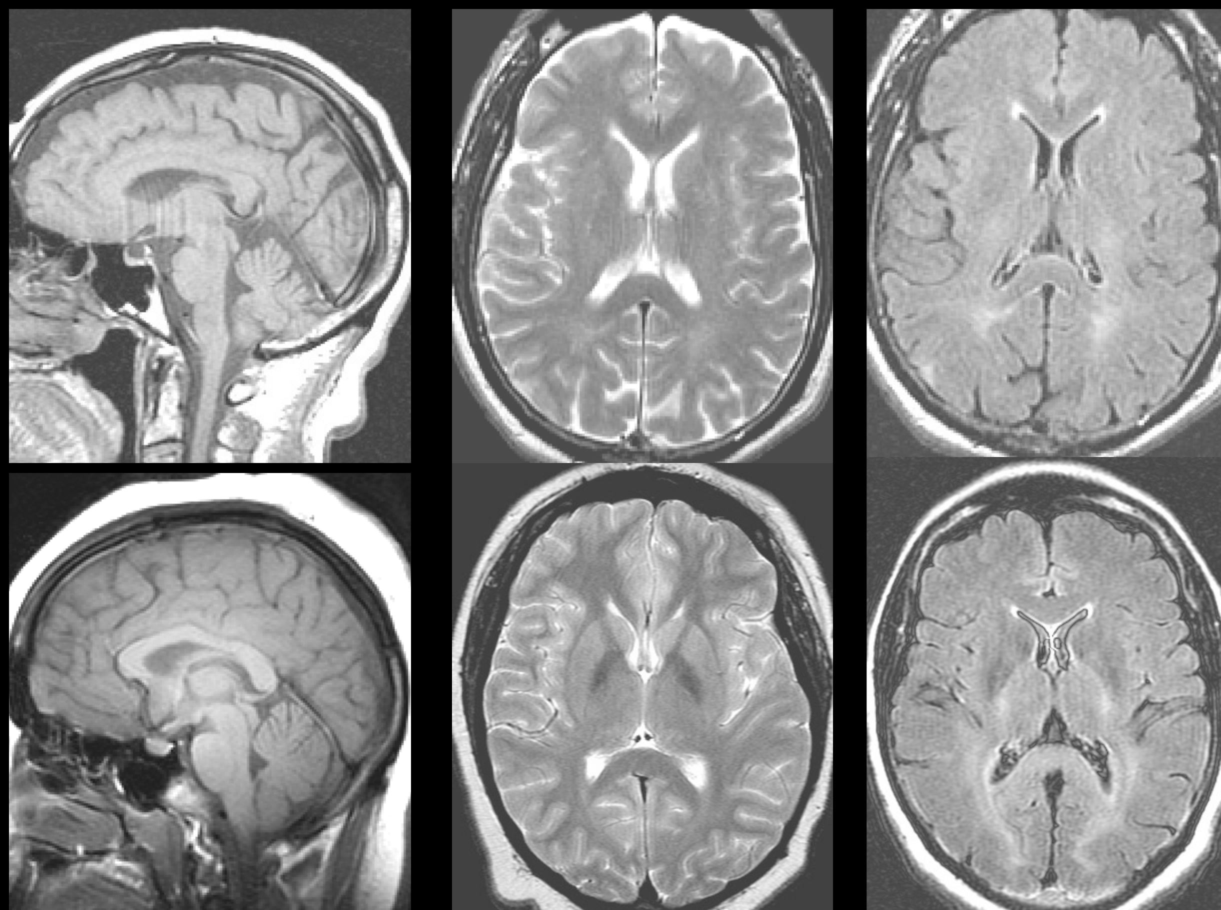
UIC
Thulborn

Whole Brain Anatomy

T1-SE T2-FSE FLAIR

1.5T

3.0T



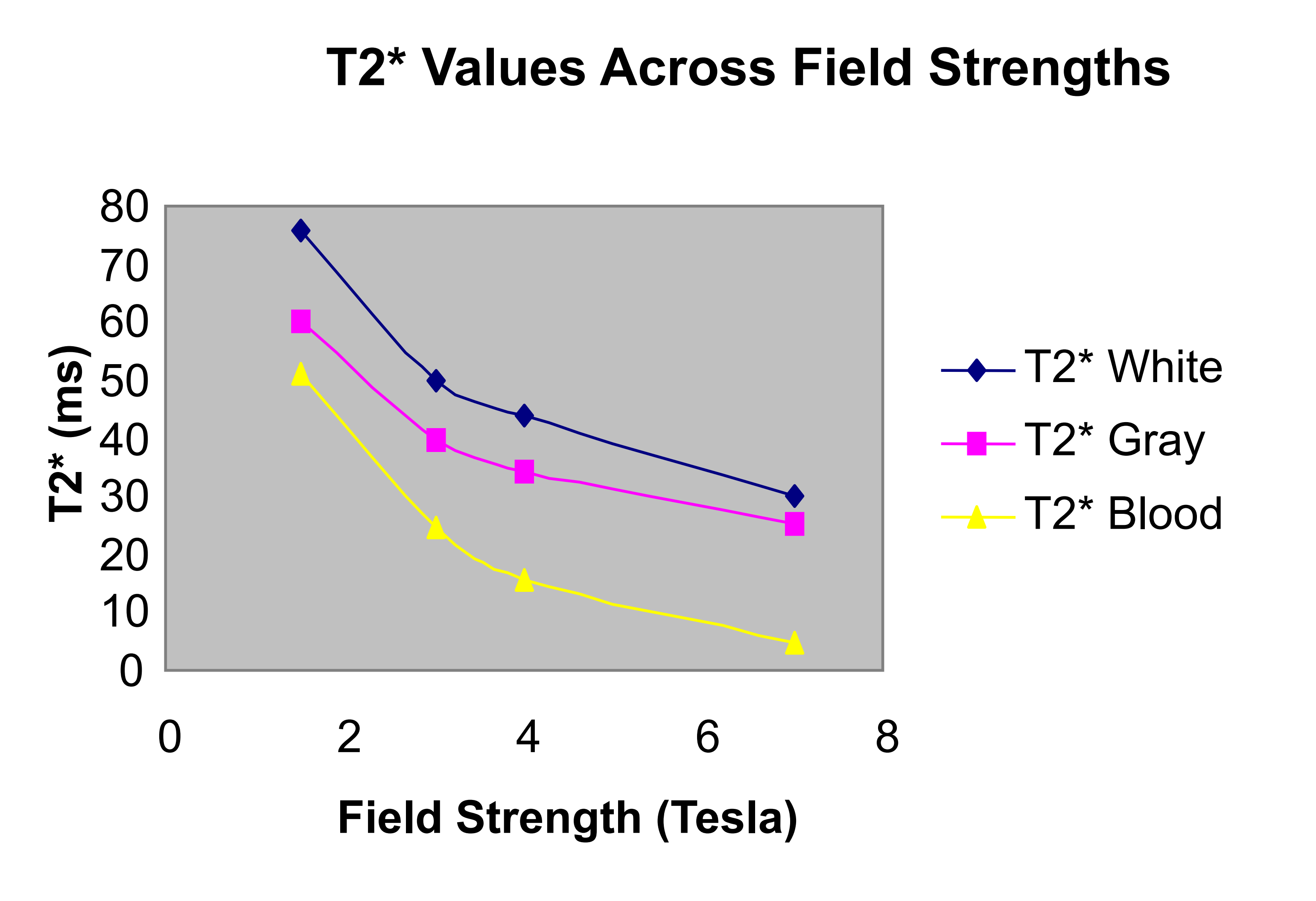
UIC
Thulborn

3.0T: 3D TOF MRA

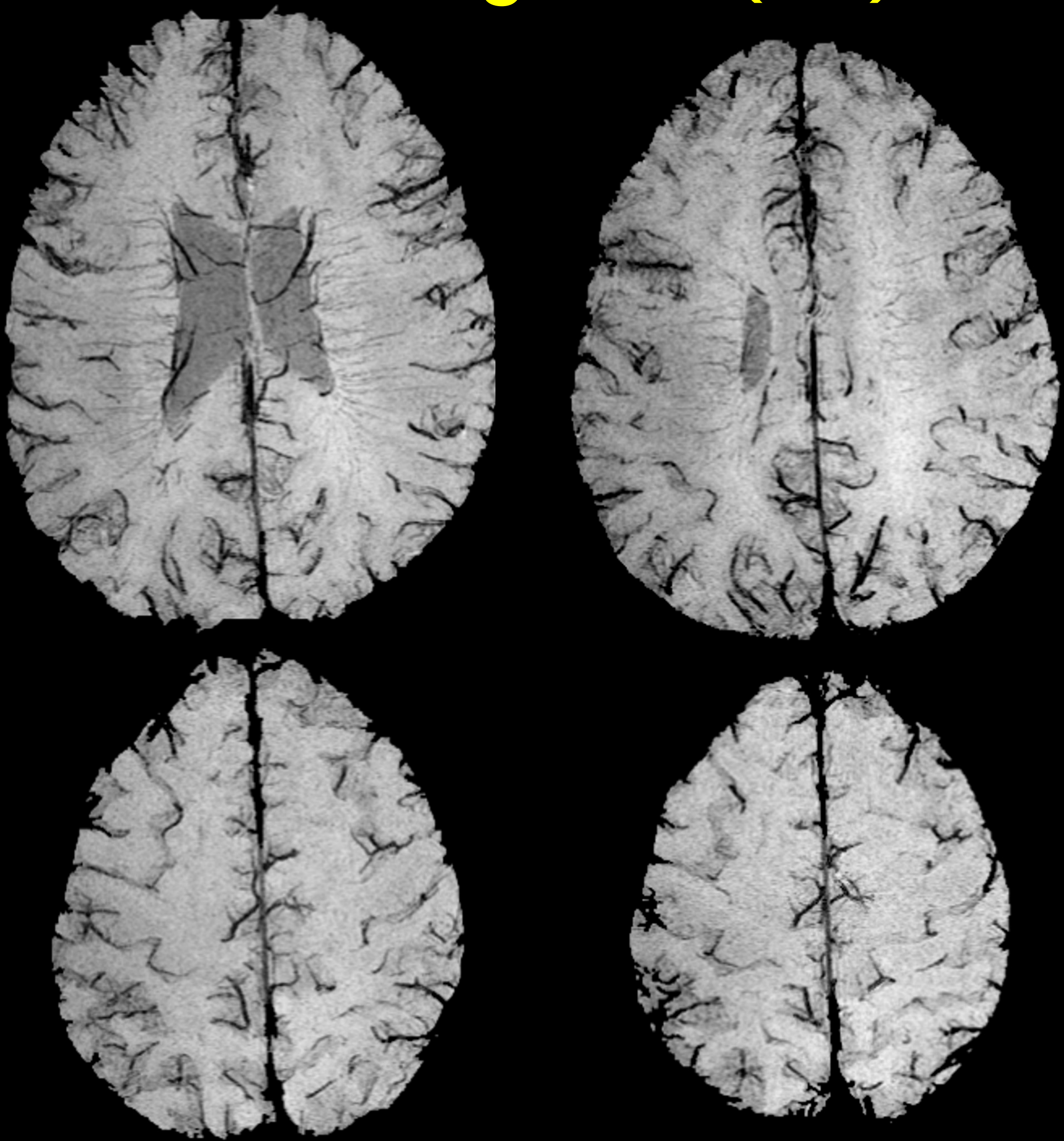
Longer T1 at 3.0T enhances flow effects and improves background suppression as well as allows higher spatial resolution

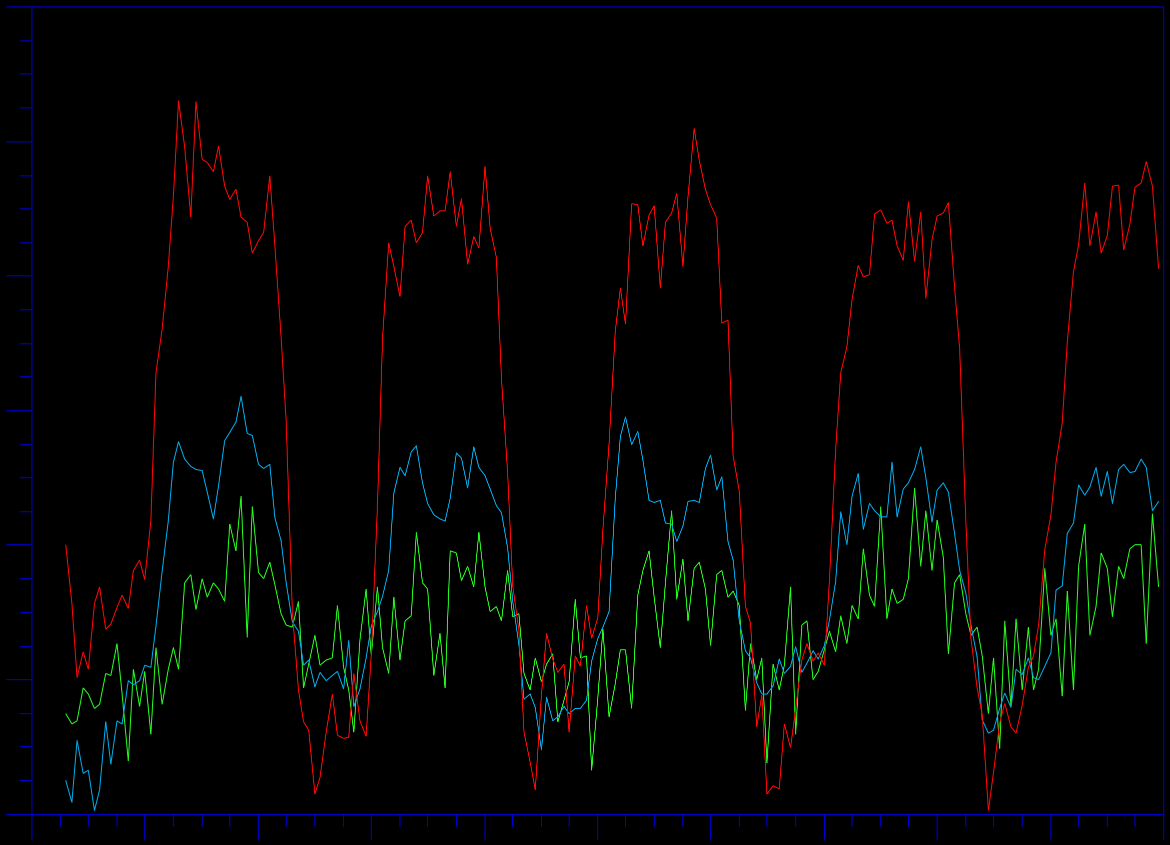
15 y.o. female patient

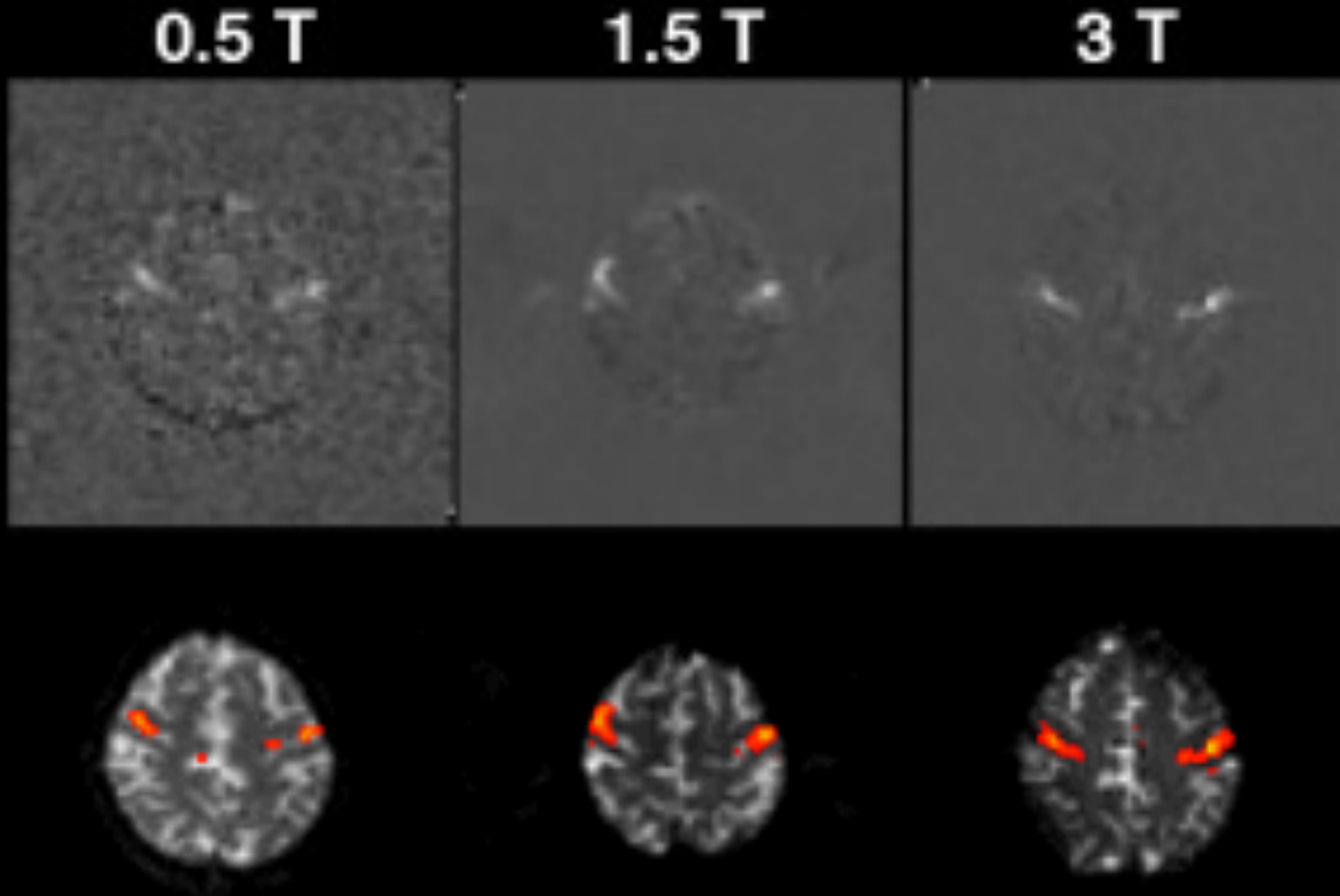
57 y.o. male patient


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

Venograms (3T)



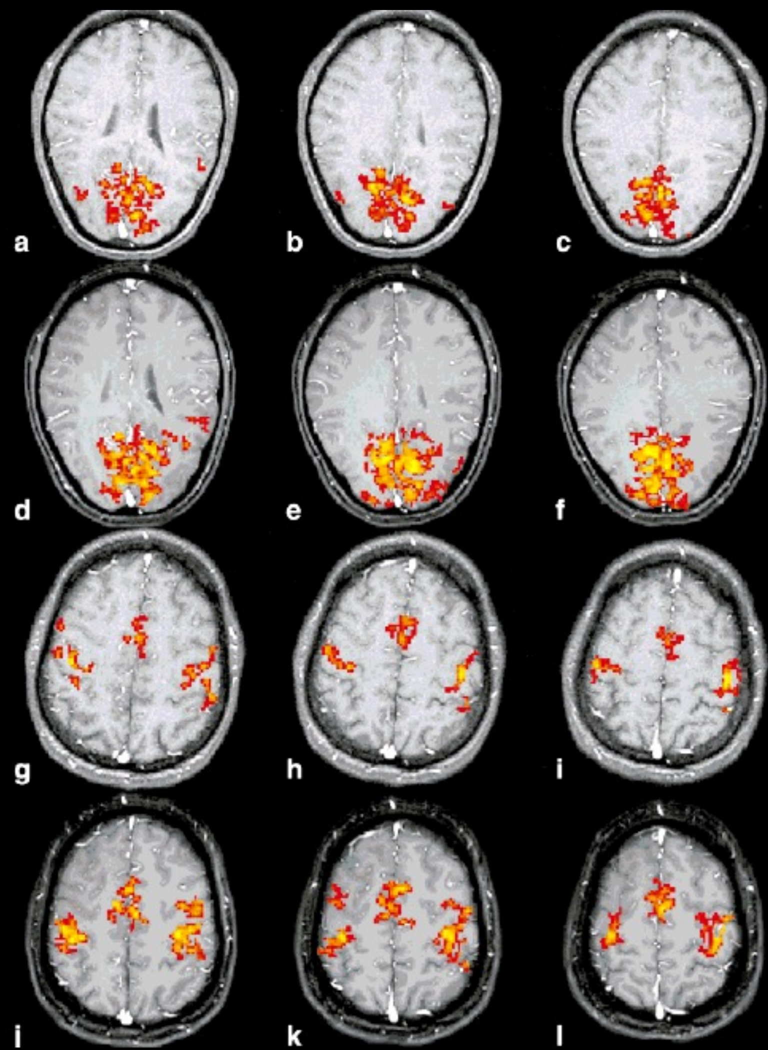



0.5 T
1.5 T
3 T

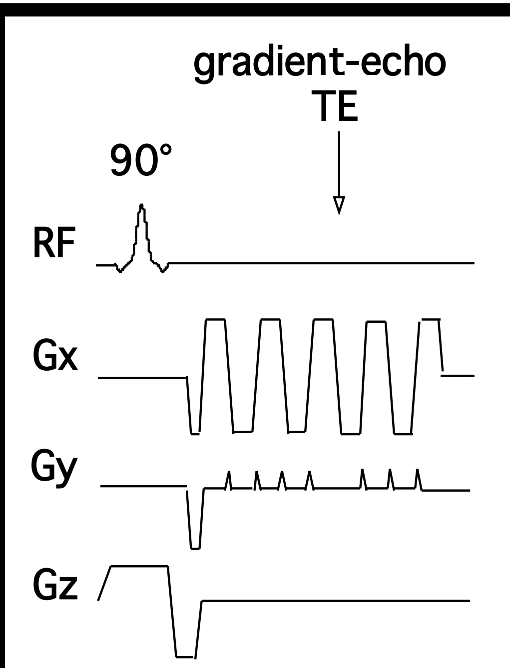
Magnetic Resonance in Medicine 45:595–604 (2001)

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

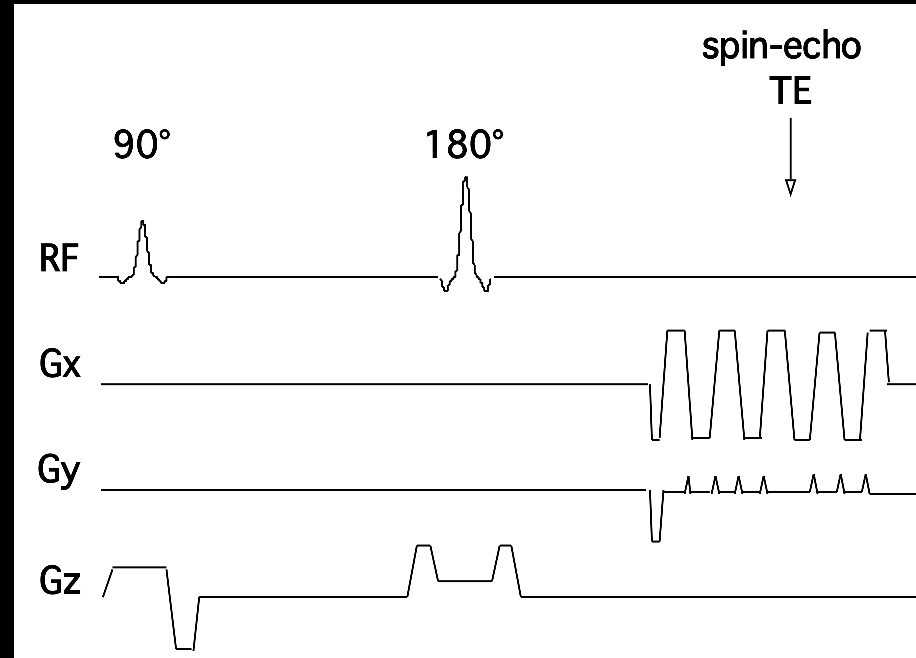
Gunnar Krüger,* Andreas Kastrup, and Gary H. Glover



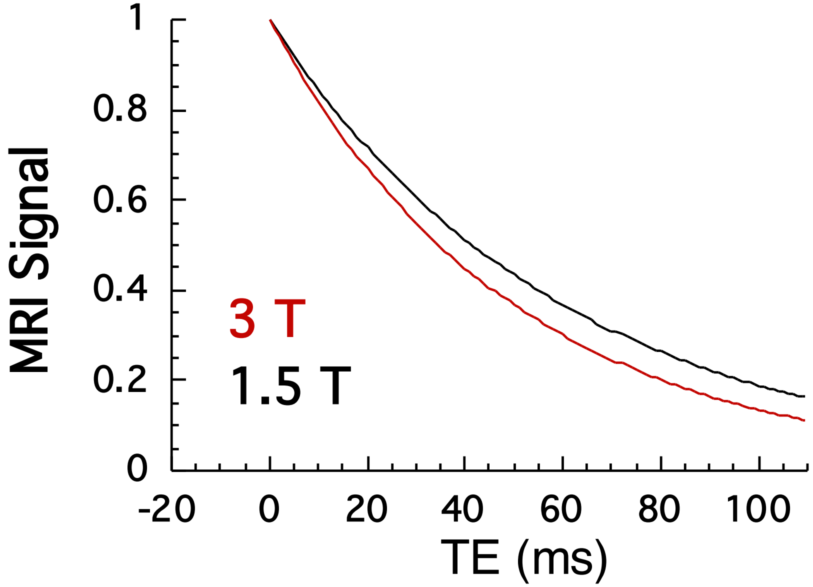
Gradient-Echo EPI



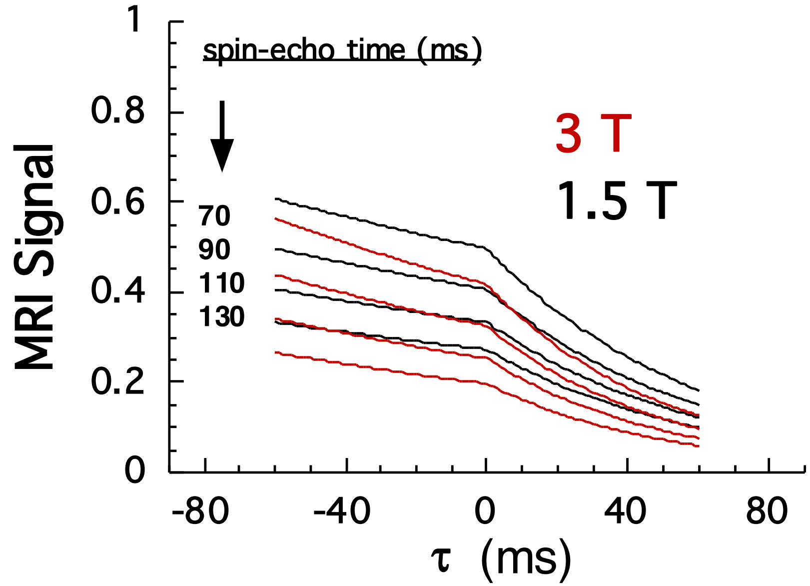
Spin-Echo EPI



Gradient - Echo

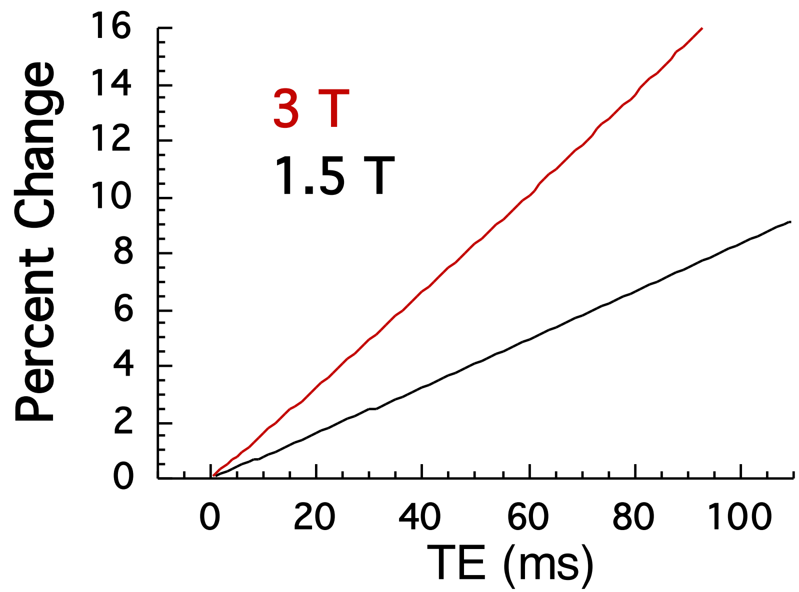


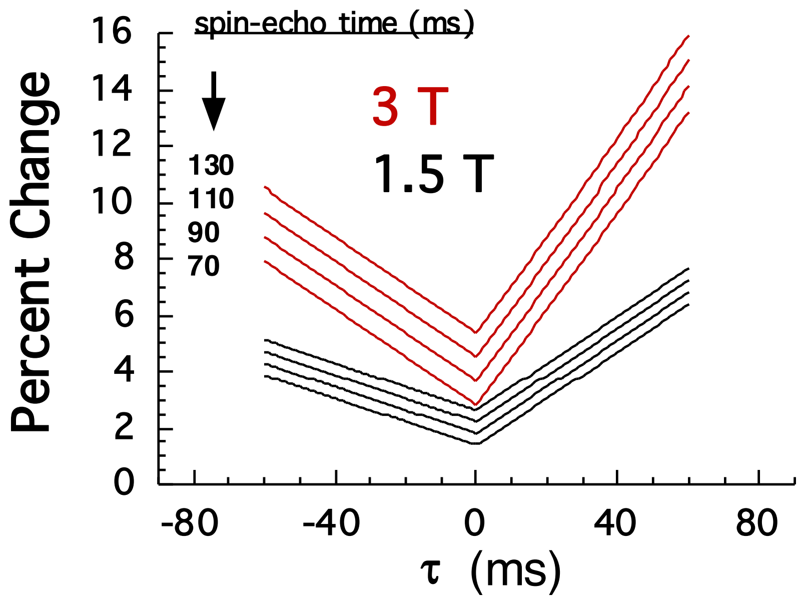
Asymmetric Spin - Echo



Gradient - Echo

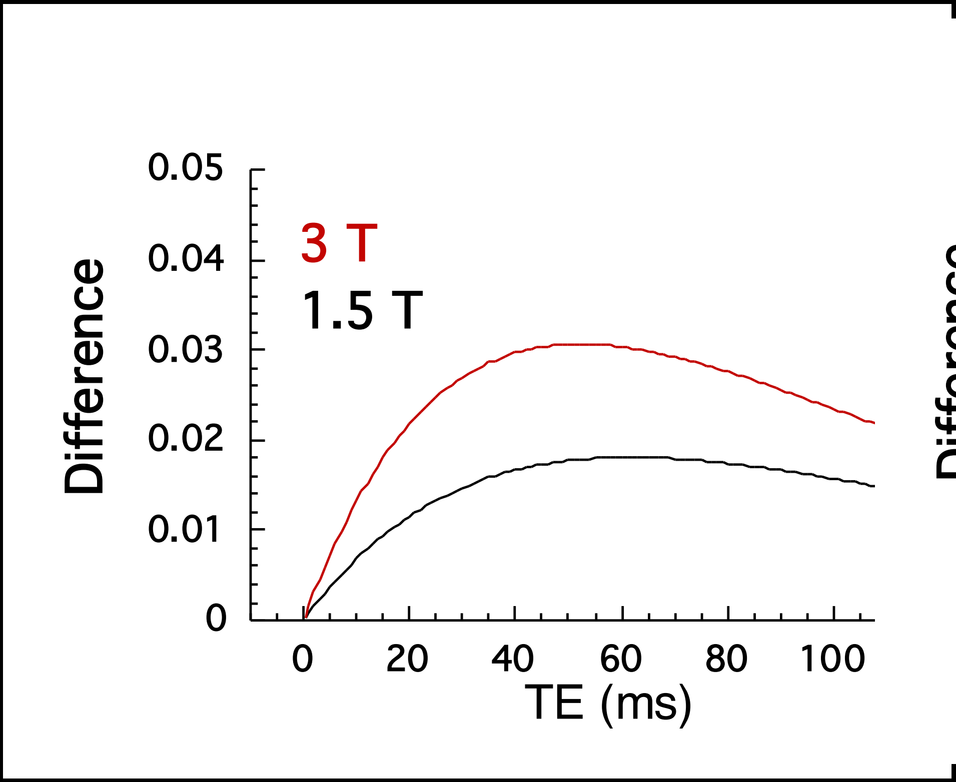
Asymmetric Spin - Echo

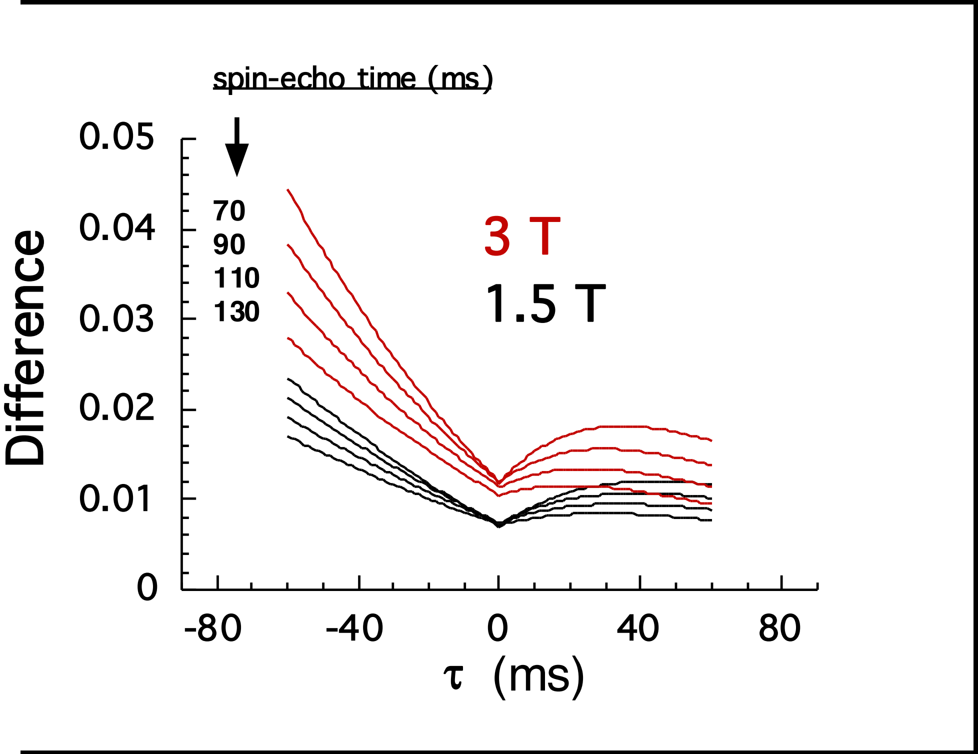




Gradient - Echo

Asymmetric Spin - Echo





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

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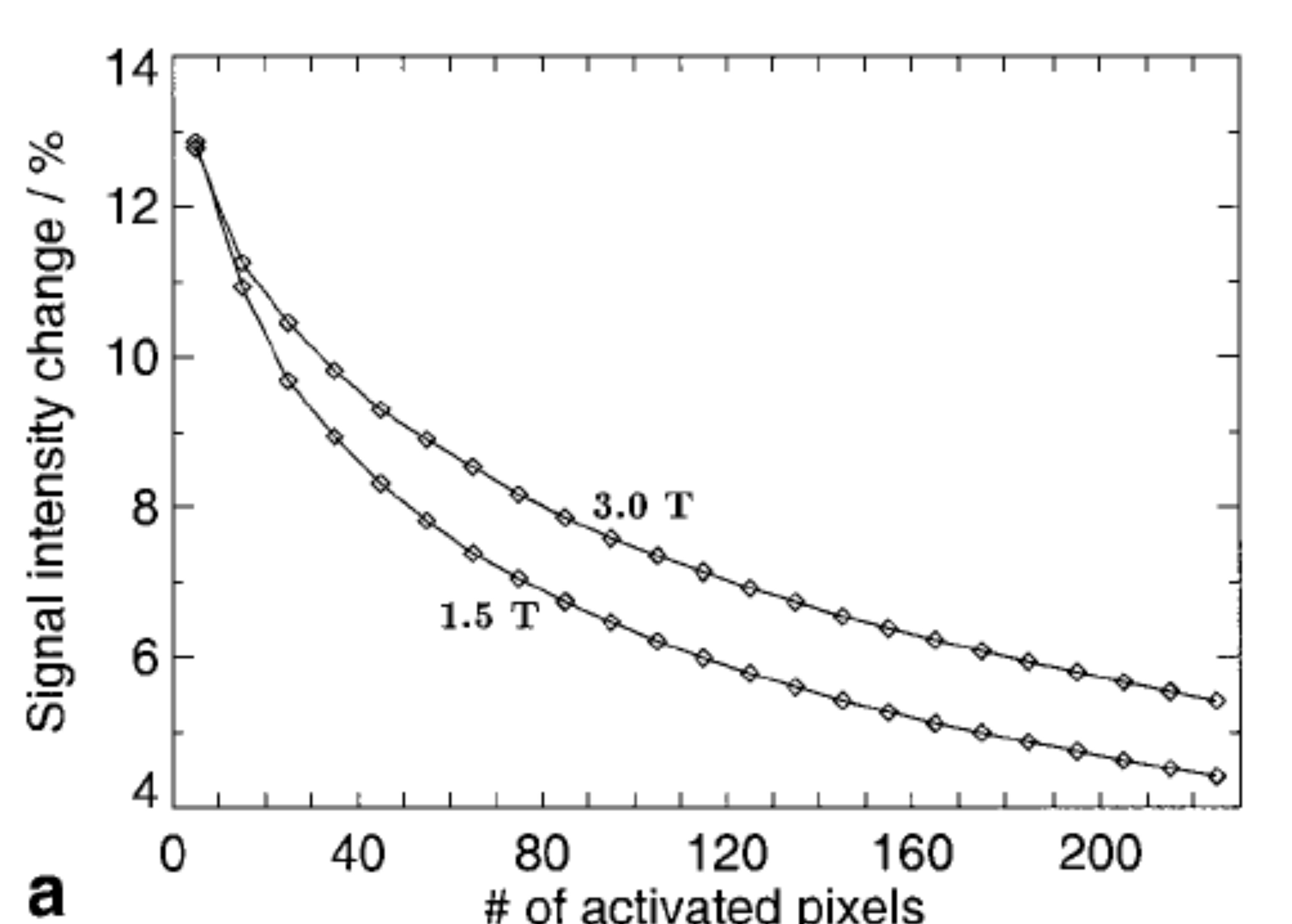
Gunnar Krüger,* Andreas Kastrup, and Gary H. Glover



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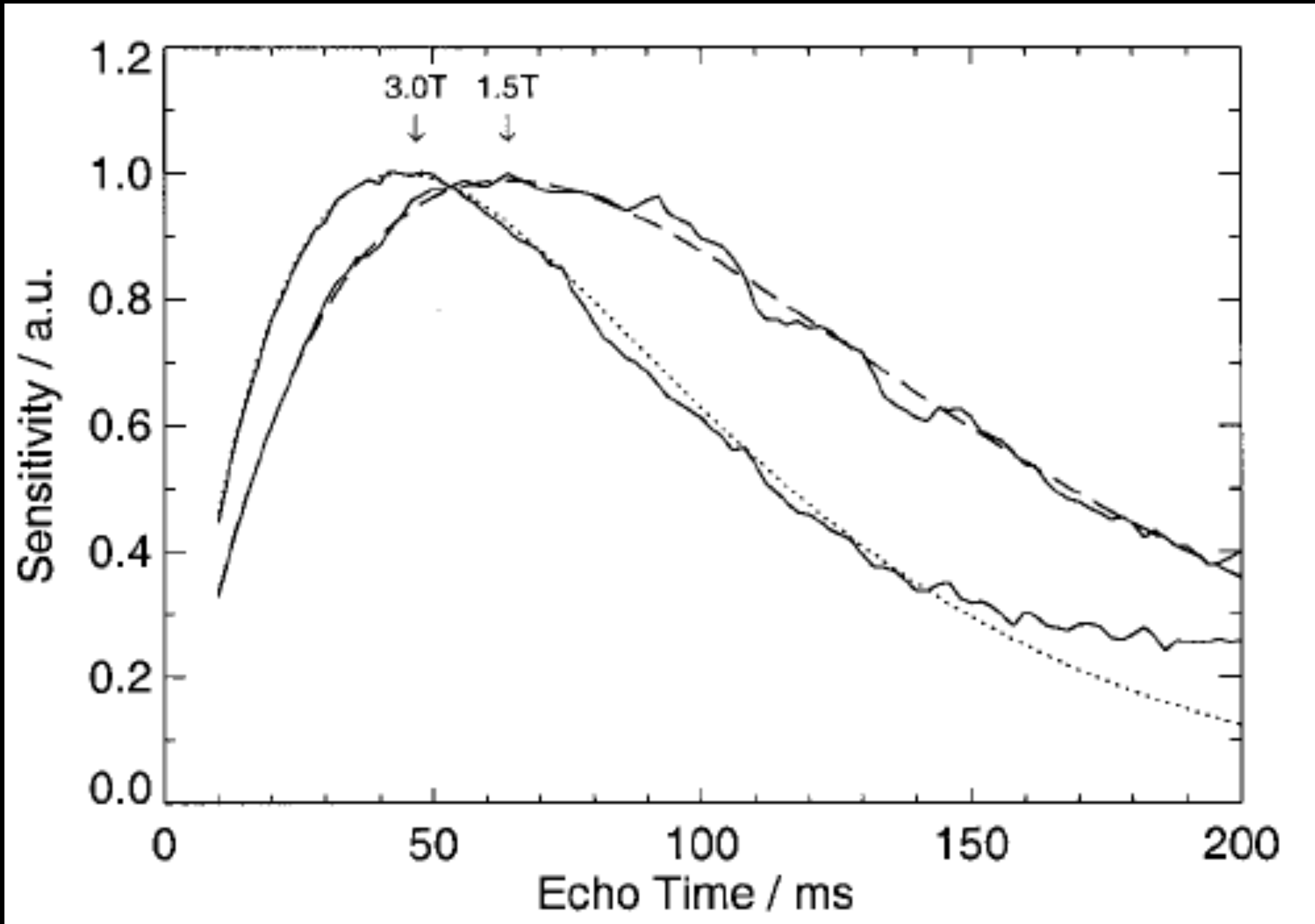
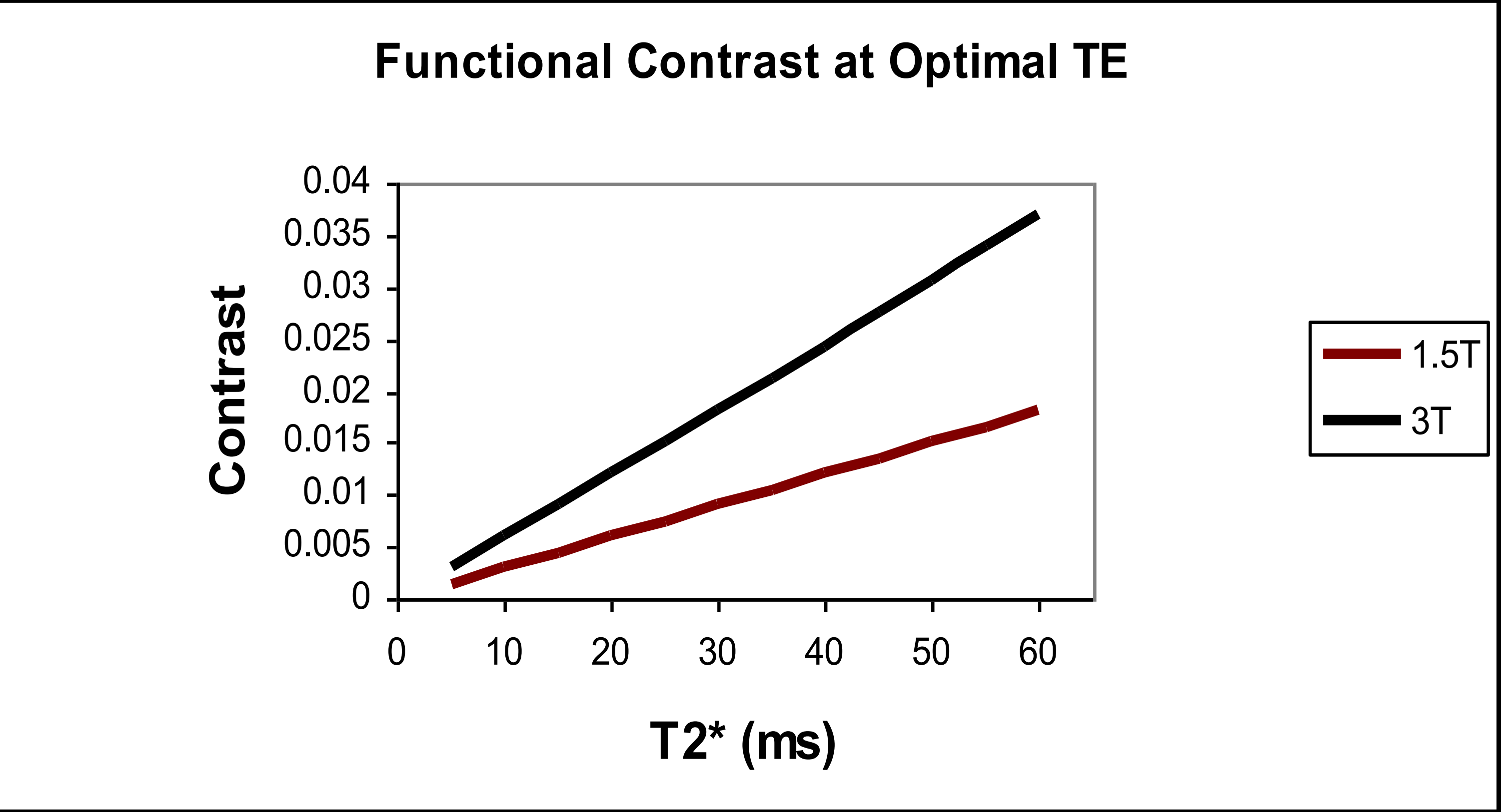
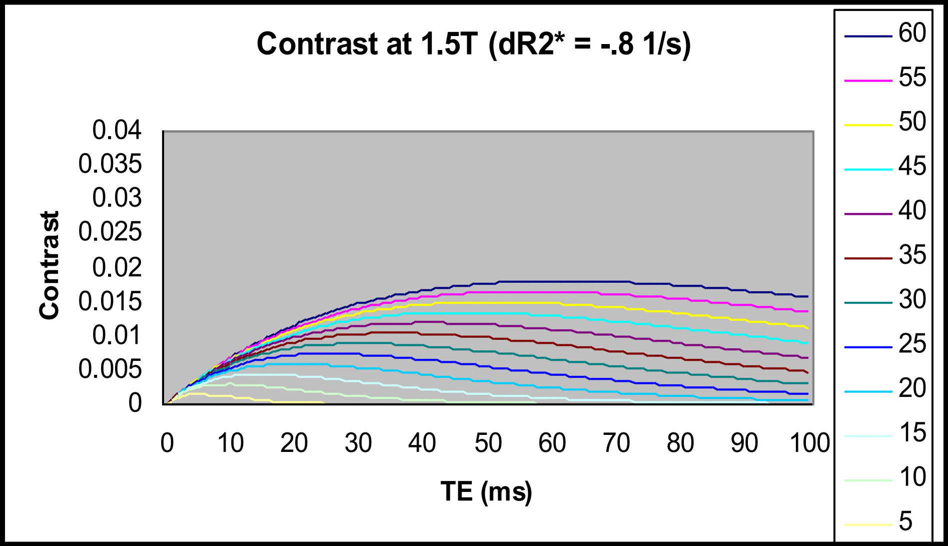


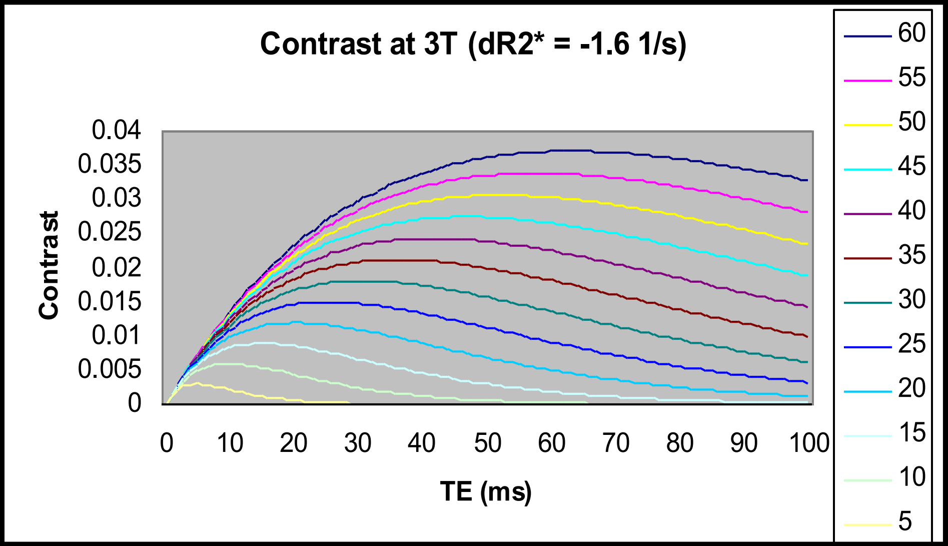

Functional Contrast at Optimal TE
Contrast
0.04
0.035
0.03
0.025
0.02
0.015
0.01
0.005
0
0
10
20
30
40
50
60
T2* (ms)
1.5T
3T

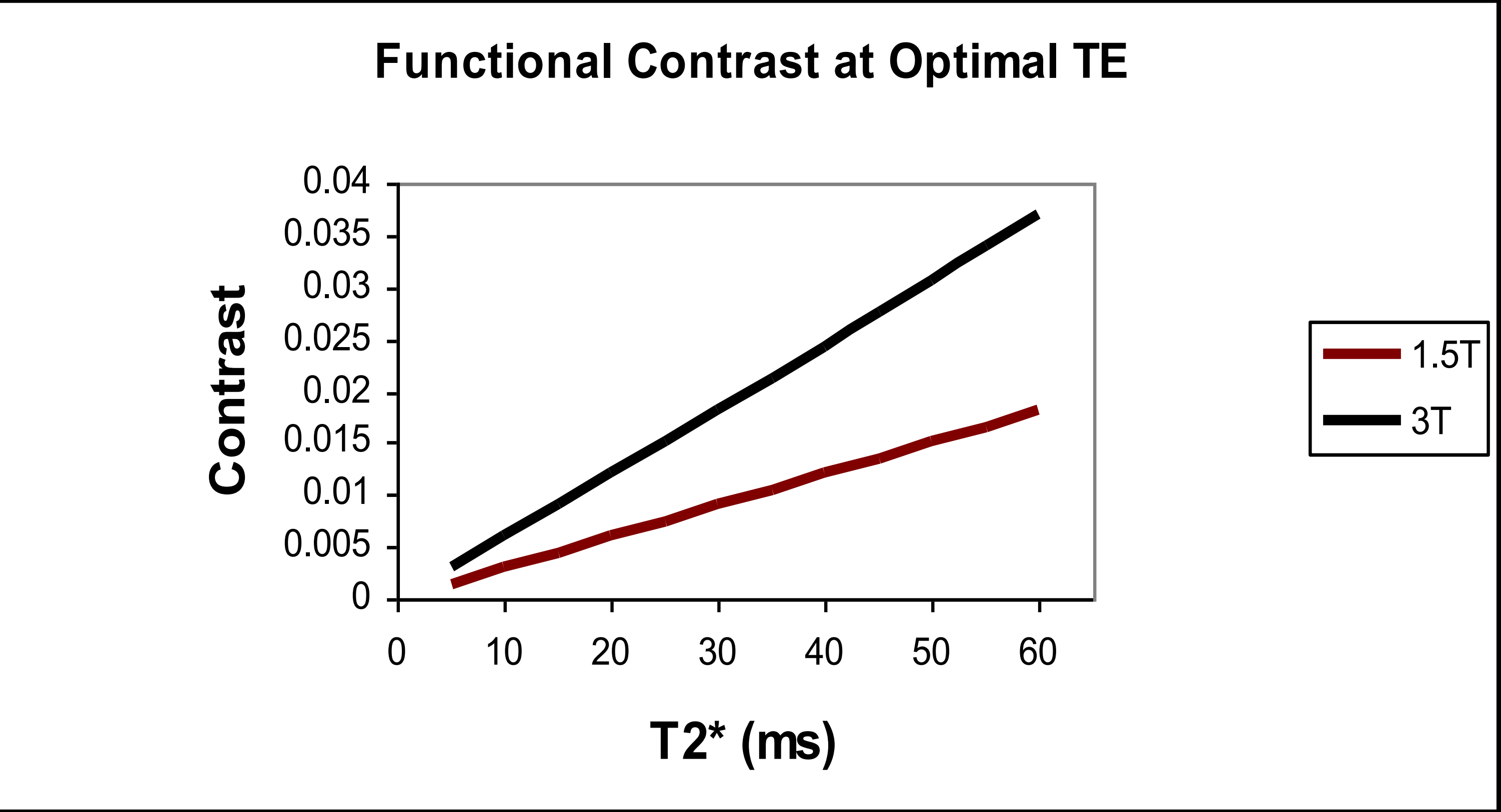
Contrast depends on:
activation-induced changes in T2* *and* resting T2*

T2*



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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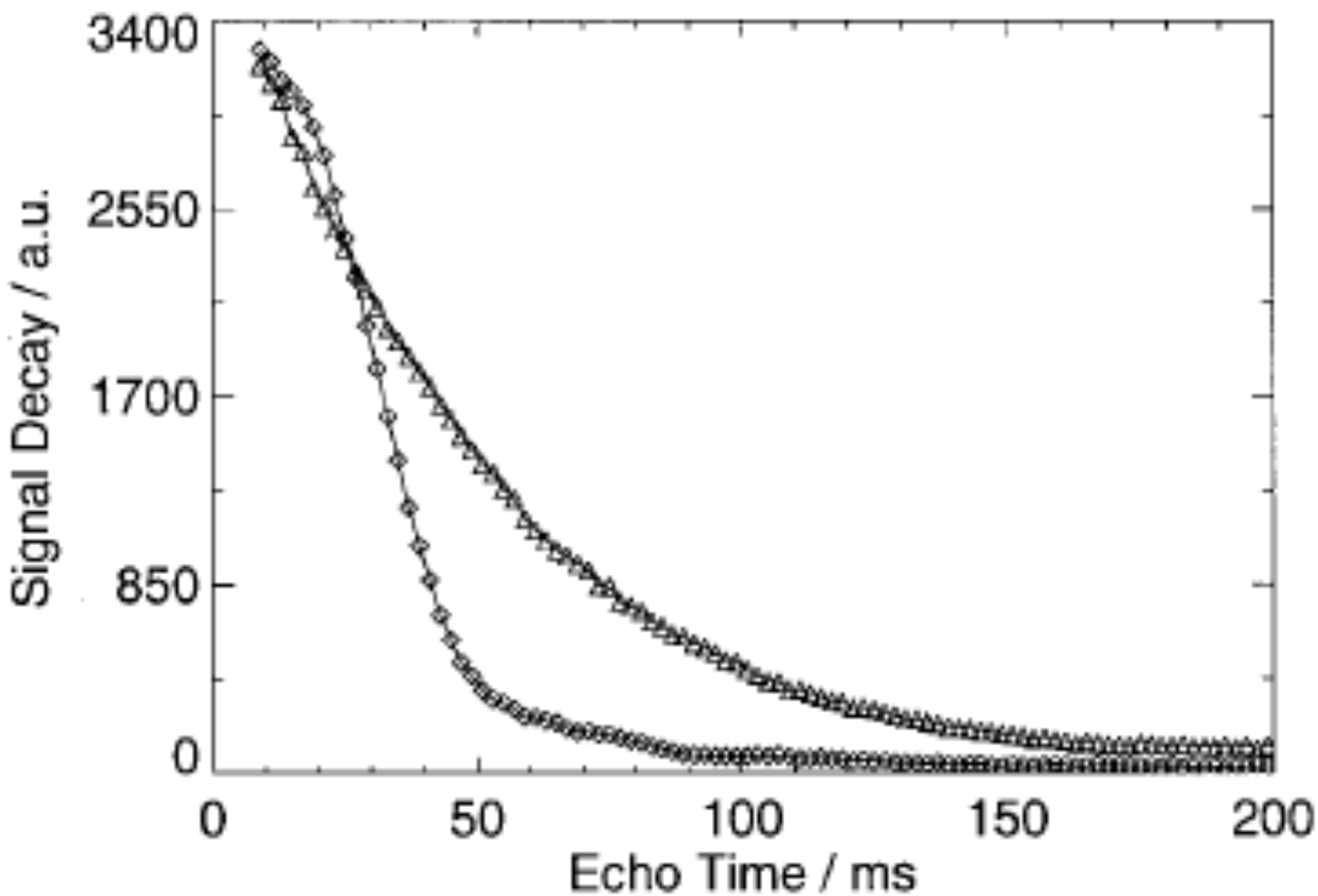
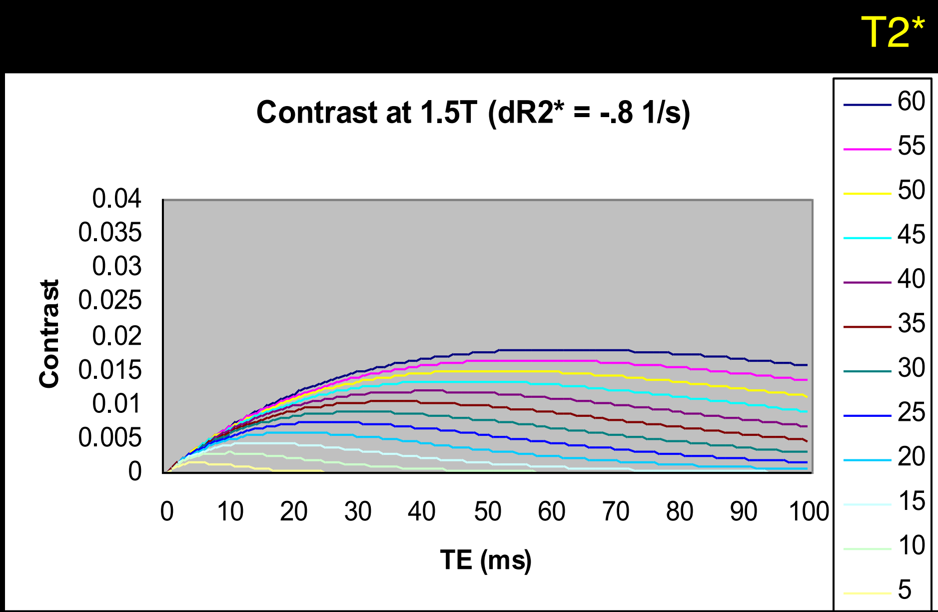
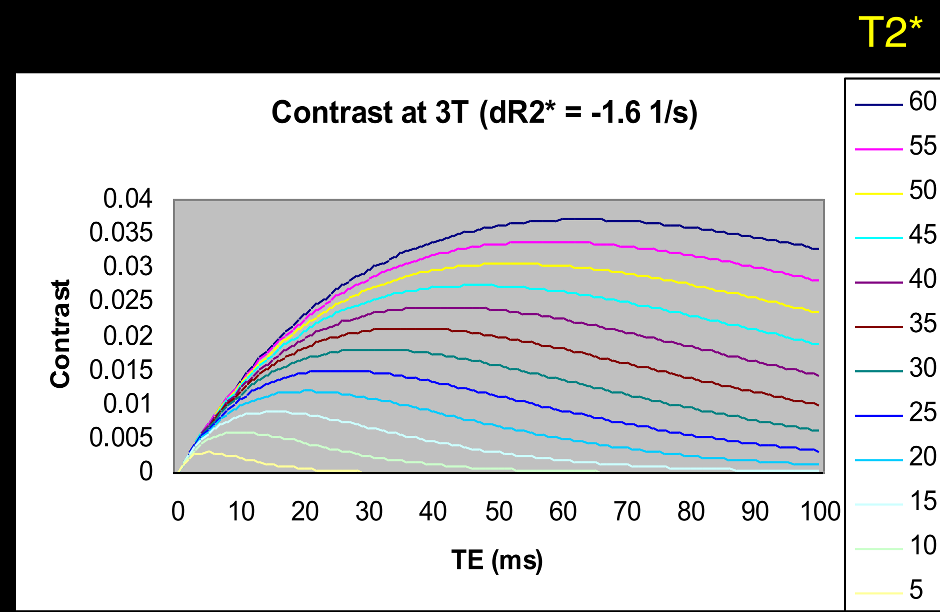
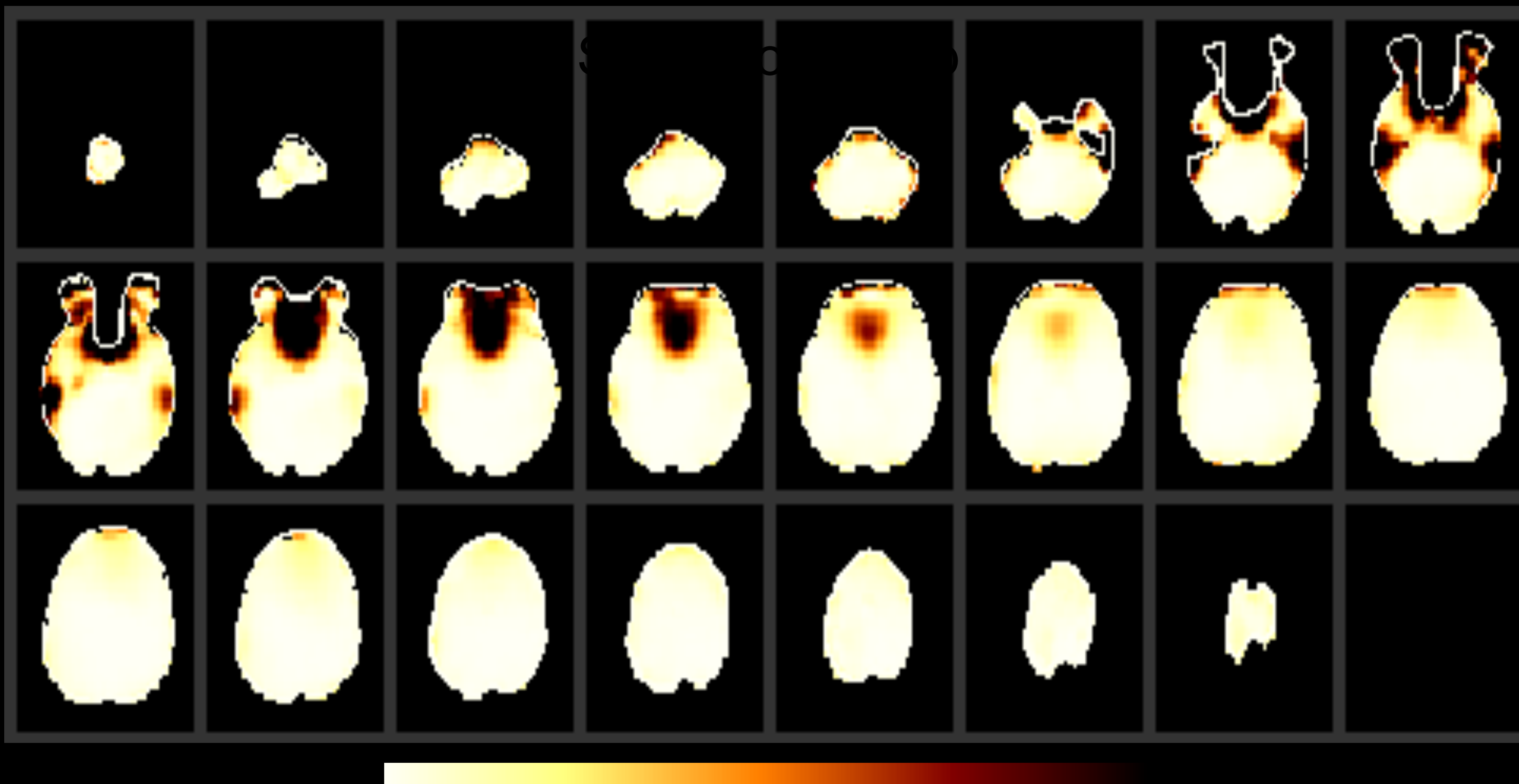


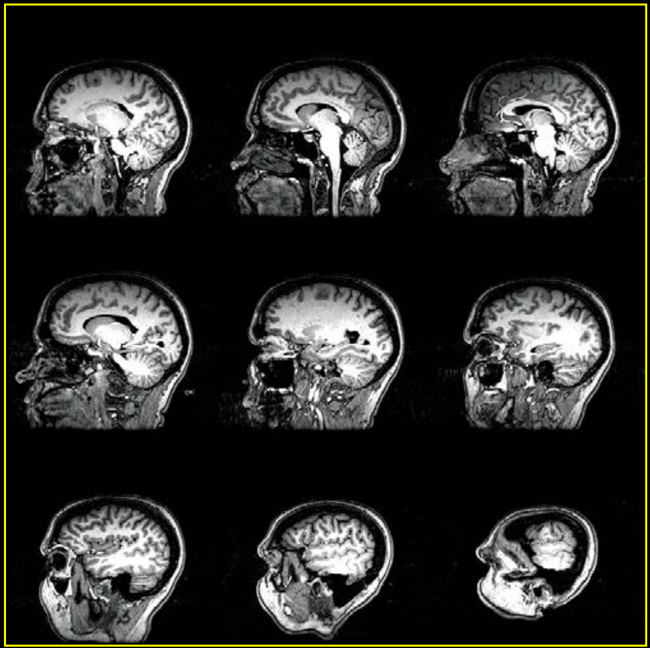
Contrast depends on:
activation-induced changes in T2* *and* resting T2*

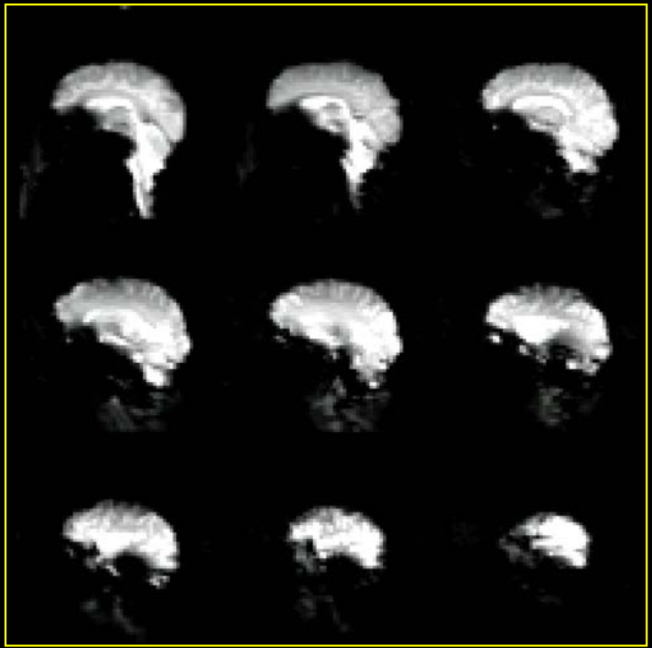


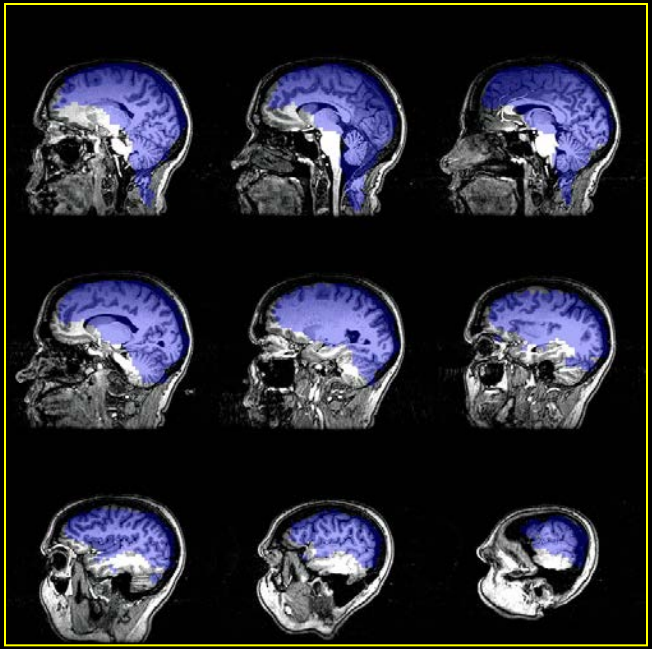


Gradient echo Signal Loss





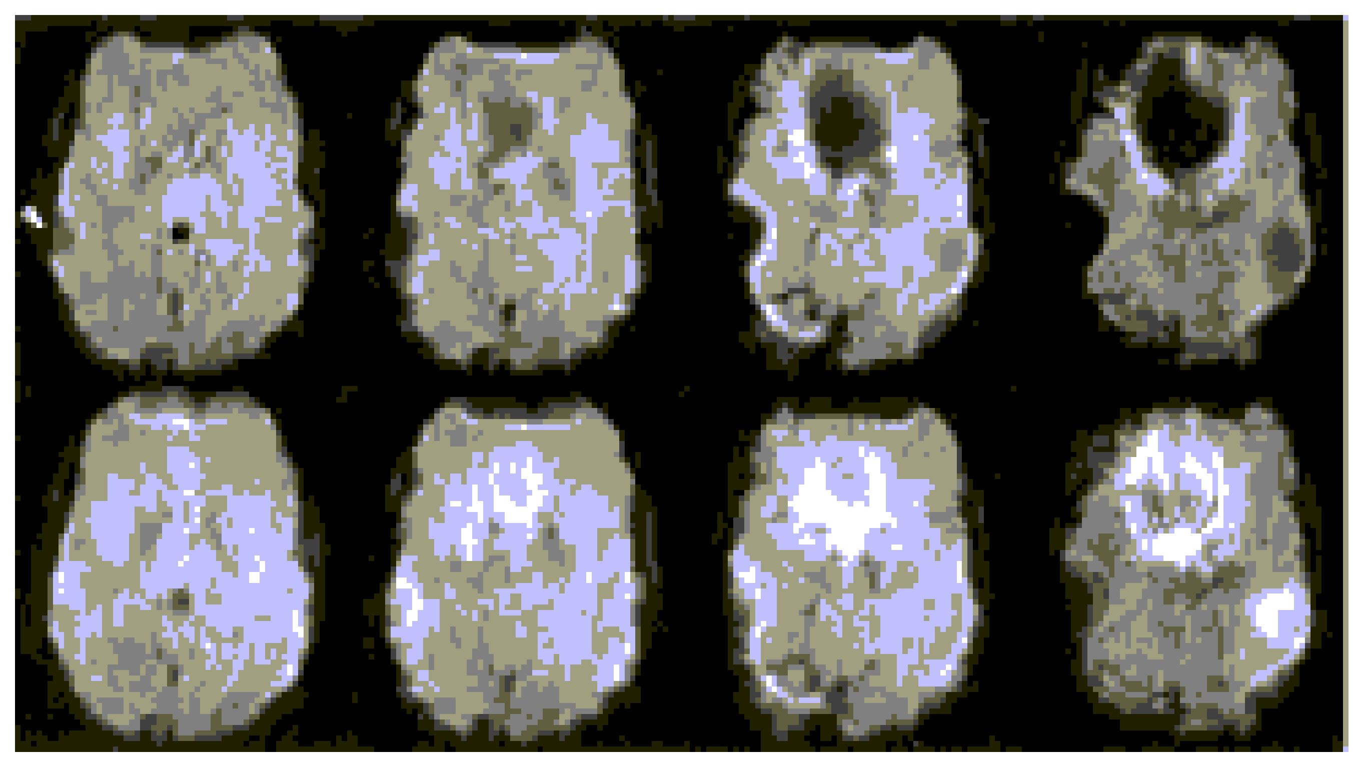


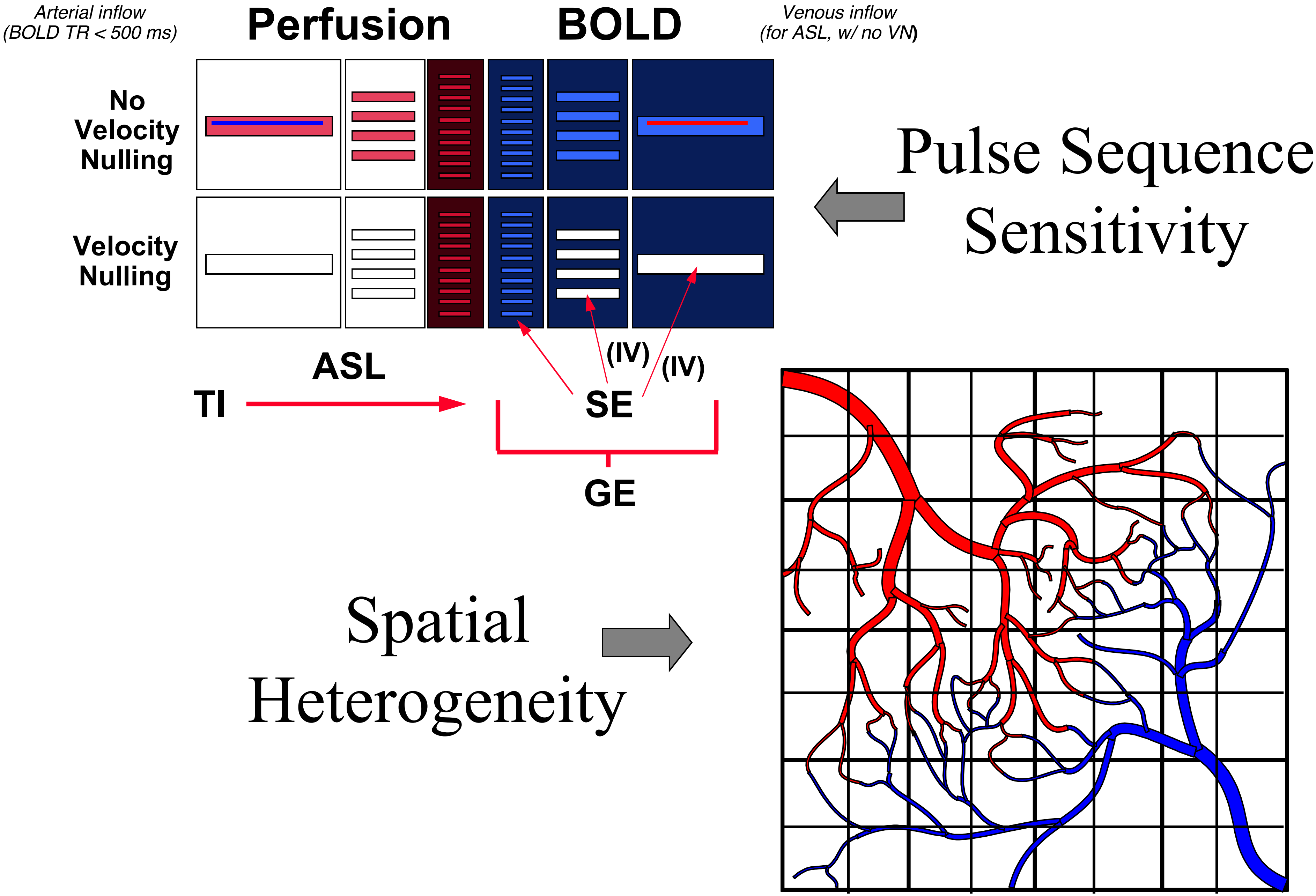


Magnetic Resonance in Medicine 42:290–299 (1999)

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

Gary H. Glover*

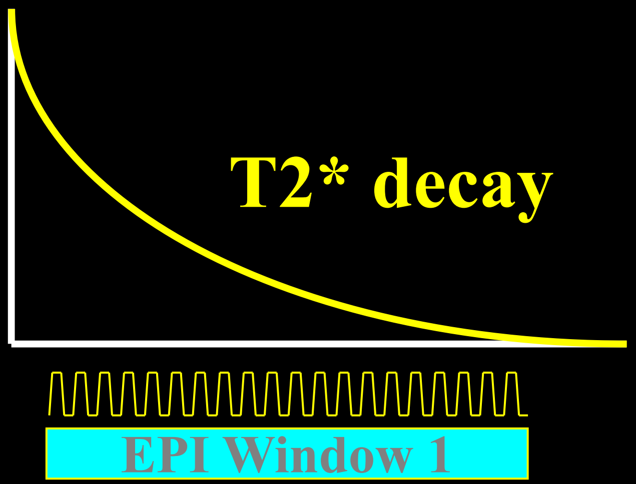


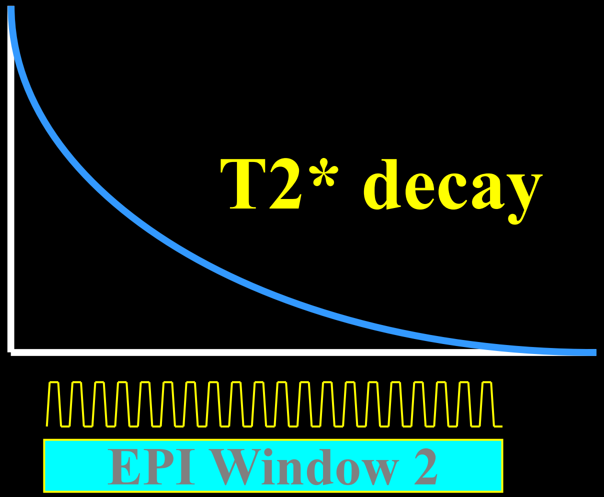


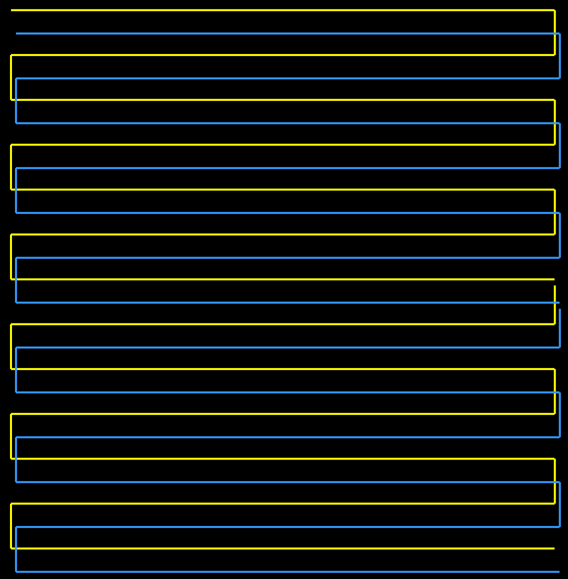
Arterial inflow
(BOLD TR < 500 ms)
Perfusion
BOLD
Venous inflow
(for ASL, w/ no VN)
No Velocity Nulling
Velocity Nulling
Pulse Sequence Sensitivity
ASL
TI
(IV)
(IV)
SE
GE
Spatial Heterogeneity

A few slides about Image Resolution and Noise...

Multishot Imaging

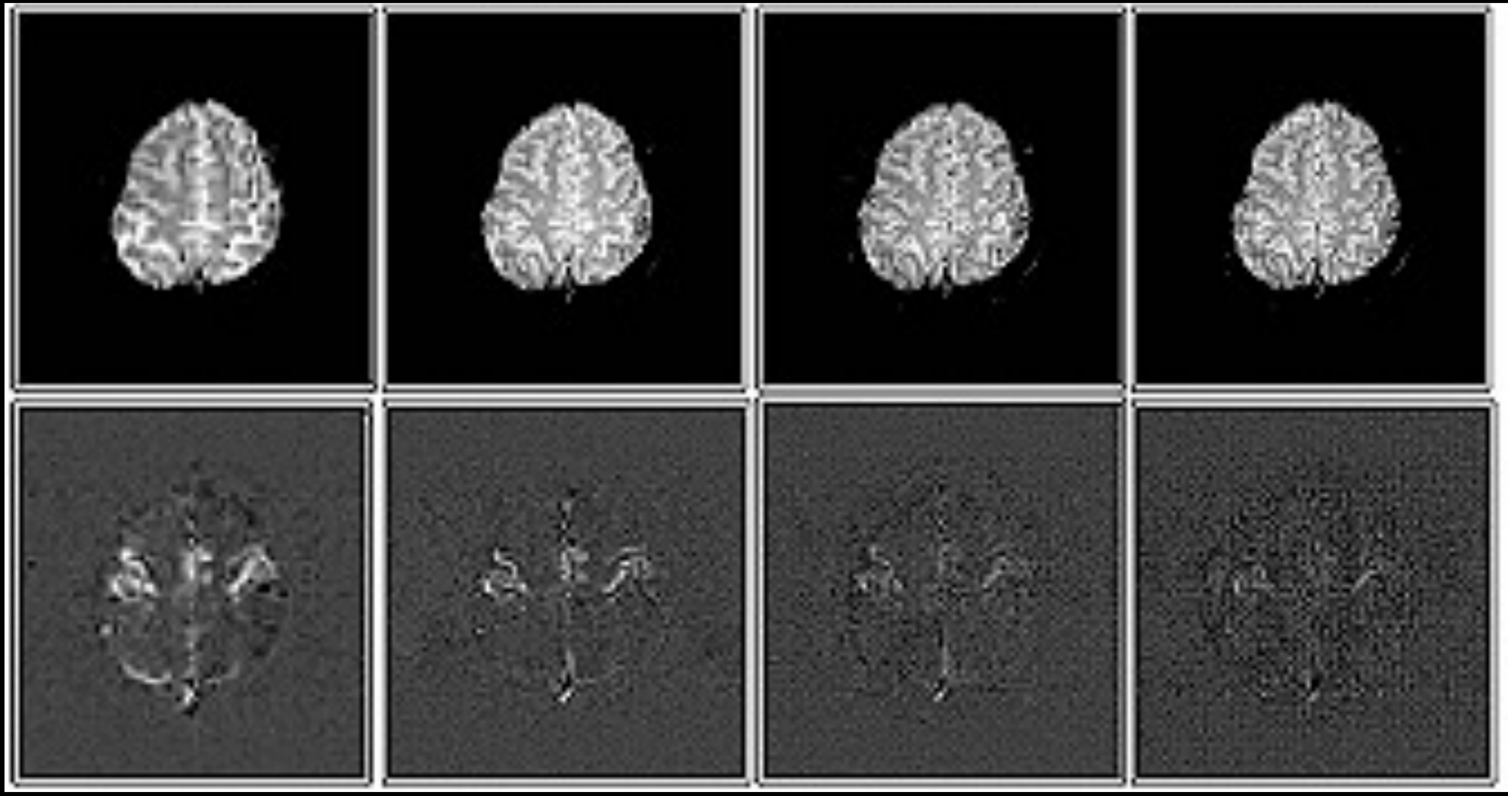




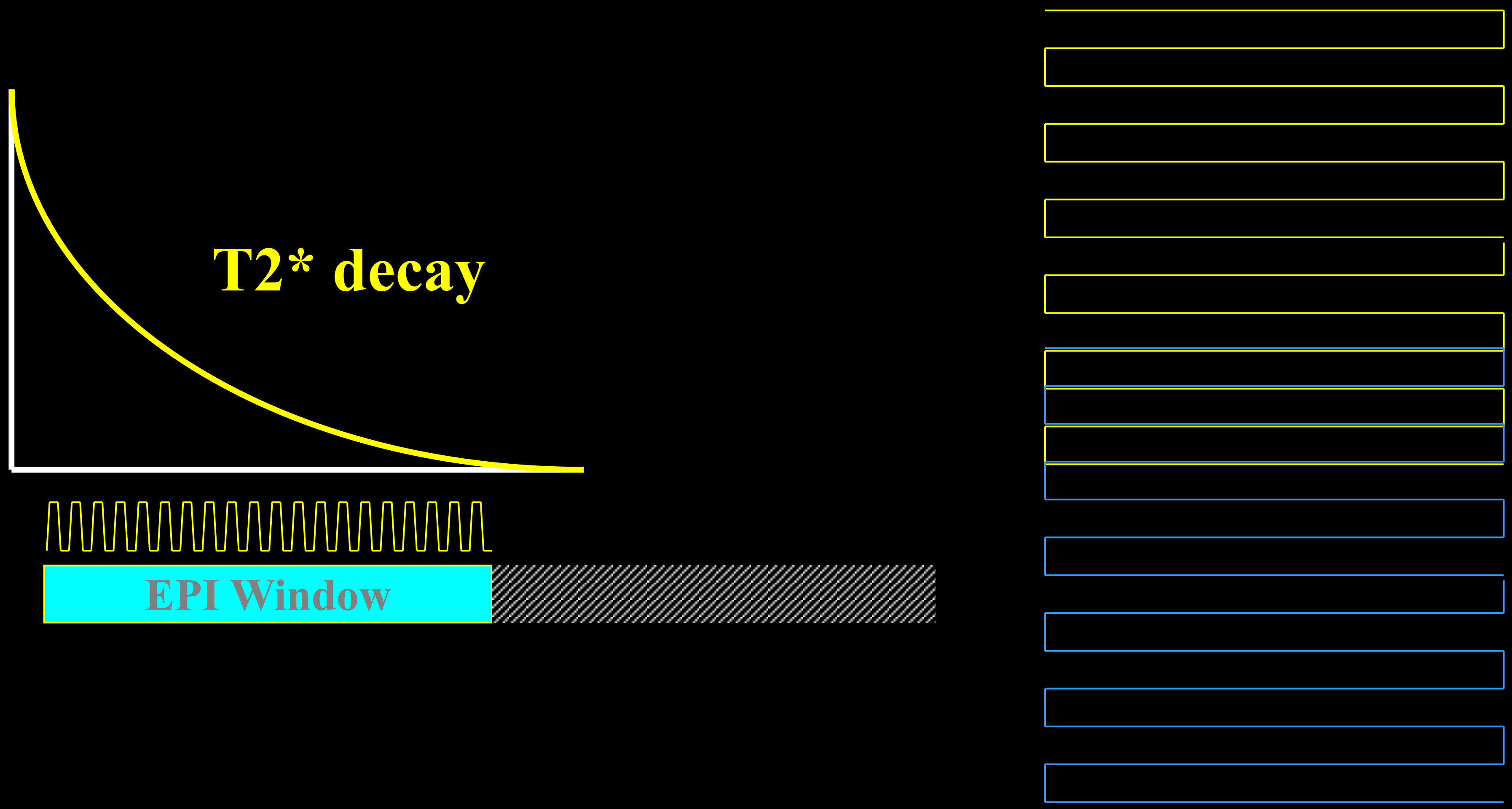


Multi Shot EPI

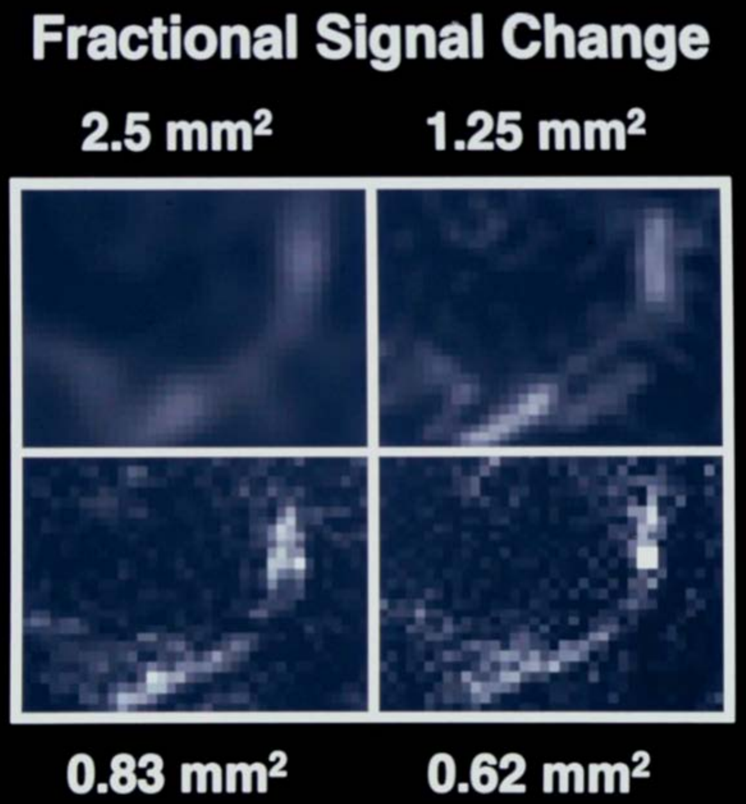
Excitations	1	2	4	8
Matrix Size	64 x 64	128 x 128	256 x 128	256 x 256

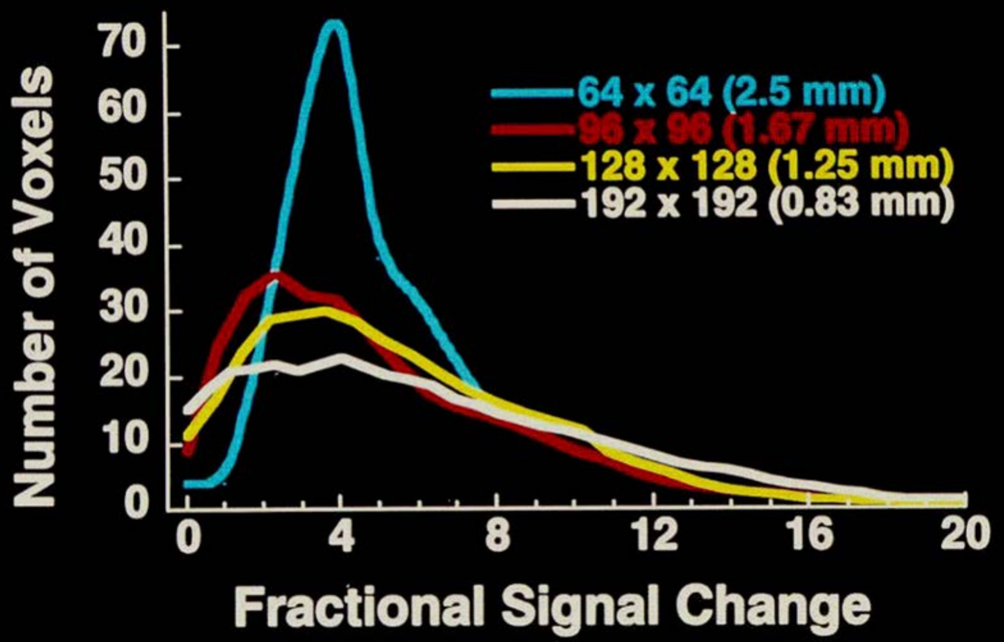


Partial k-space imaging



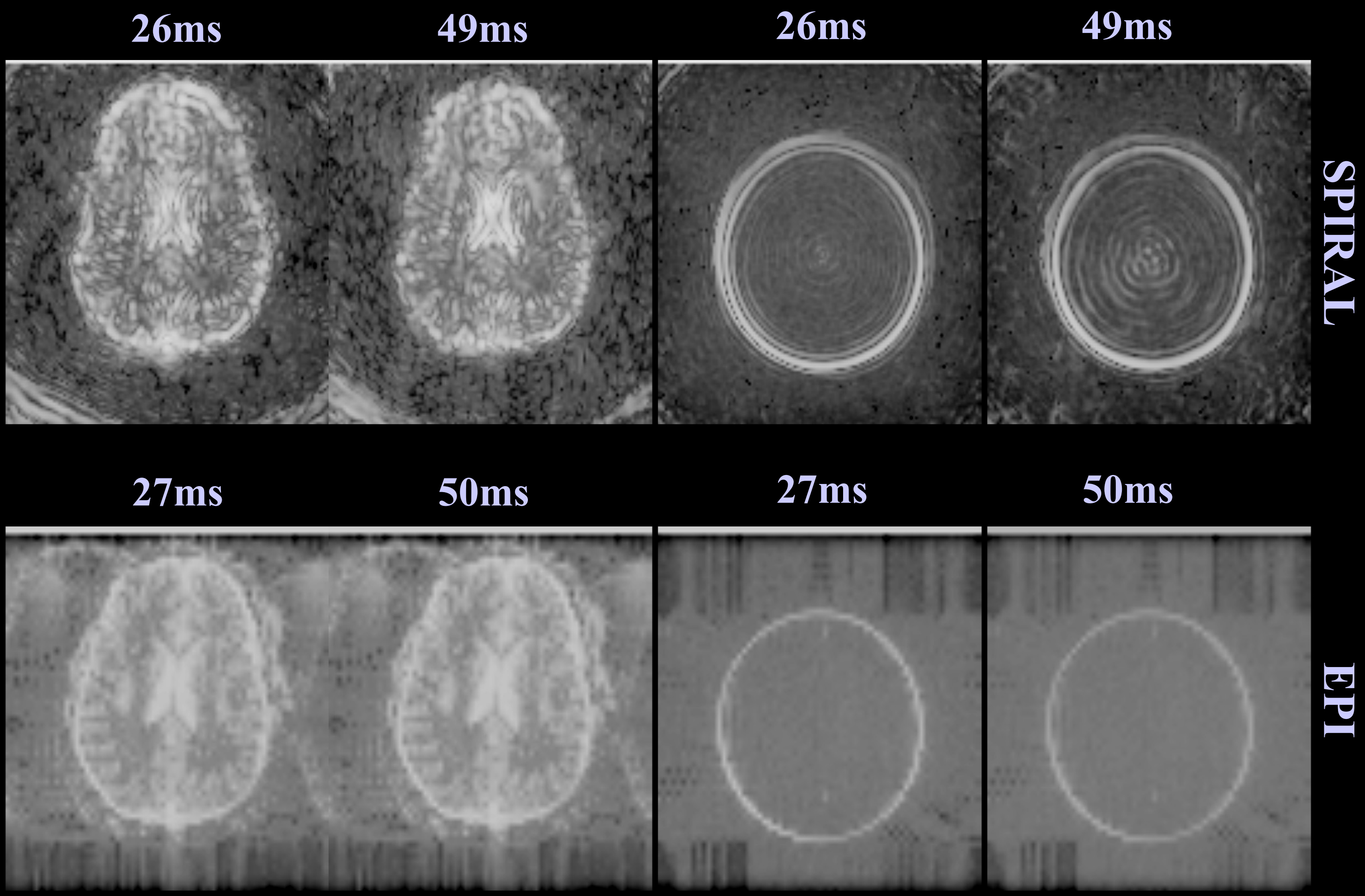
Partial k-space imaging



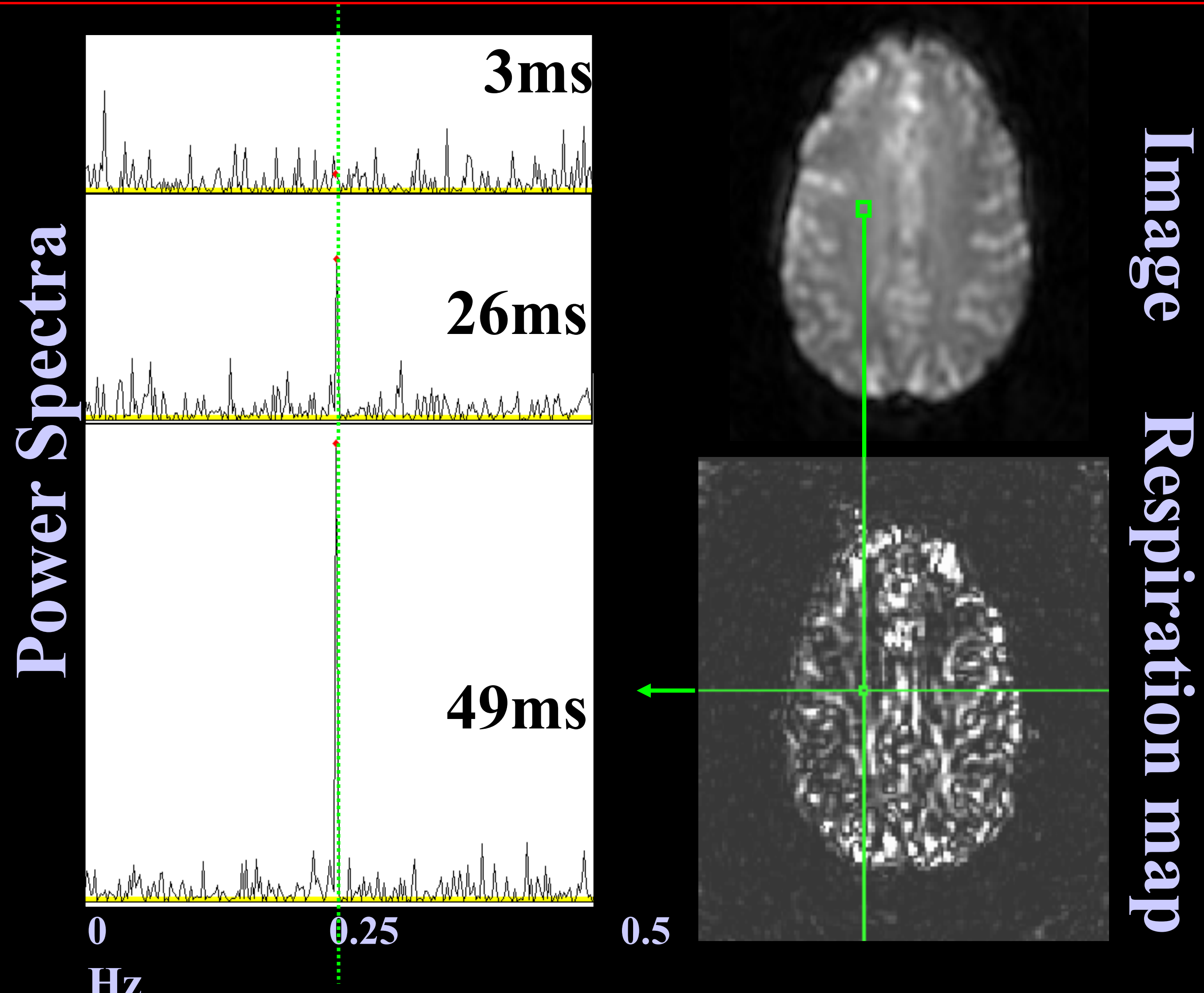


Jesmanowicz, P. A. Bandettini, J. S. Hyde, (1998) "Single shot half k-space high resolution EPI for fMRI at 3T." *Magn. Reson. Med.* 40, 754-762.

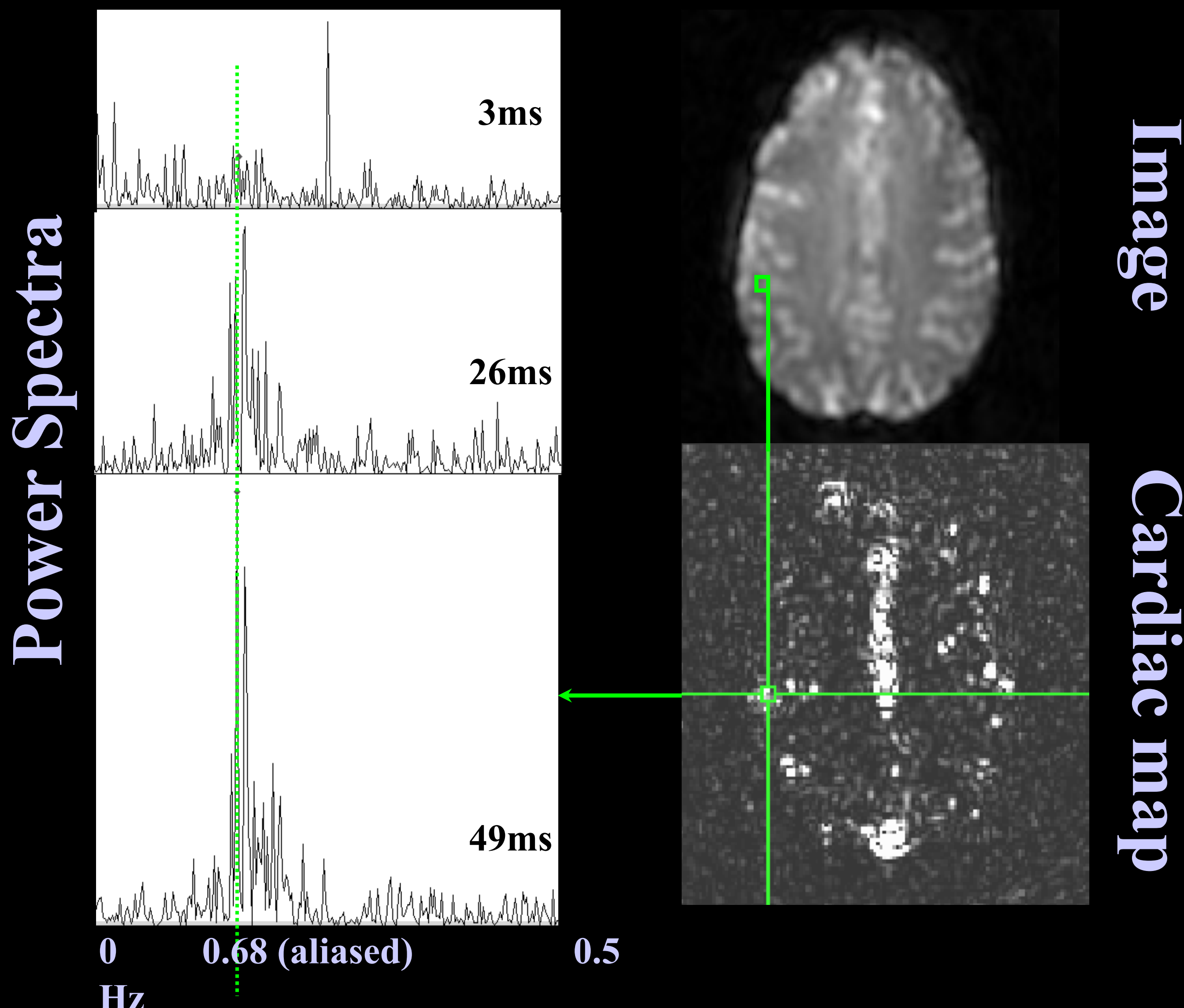
Temporal vs. Spatial SNR- 3T



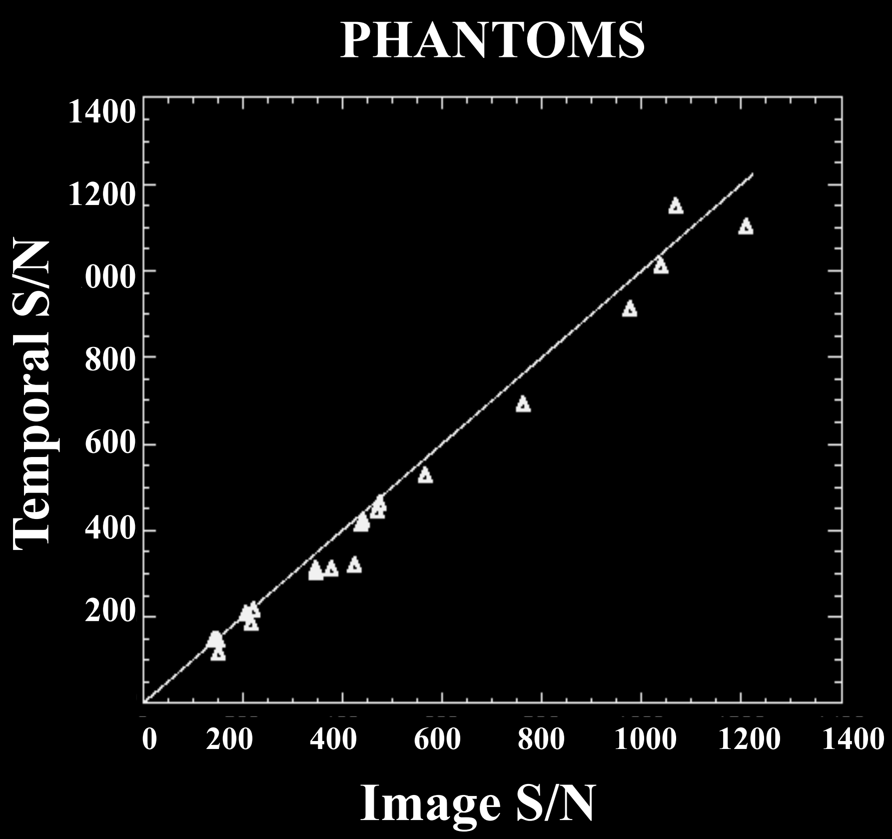
0.25 Hz Breathing at 3T

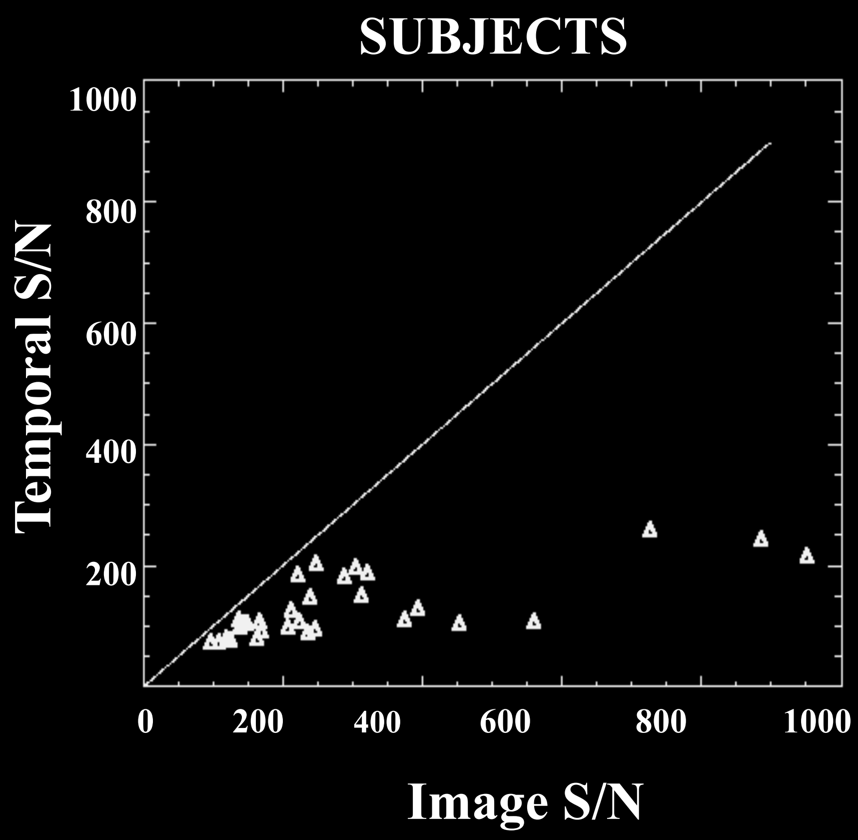


0.68 Hz Cardiac rate at 3T



Temporal S/N vs. Image S/N





N. Petridou

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

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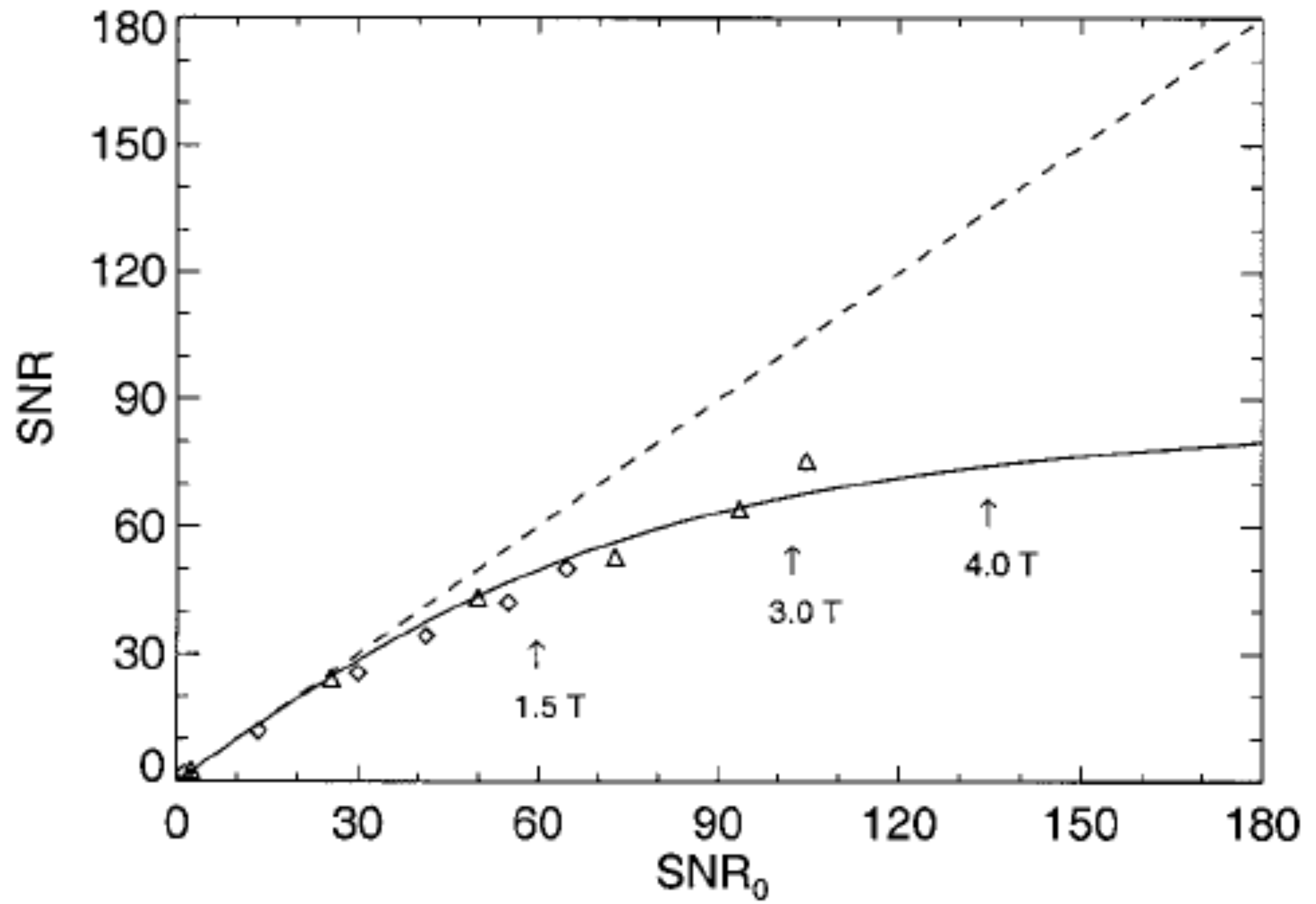
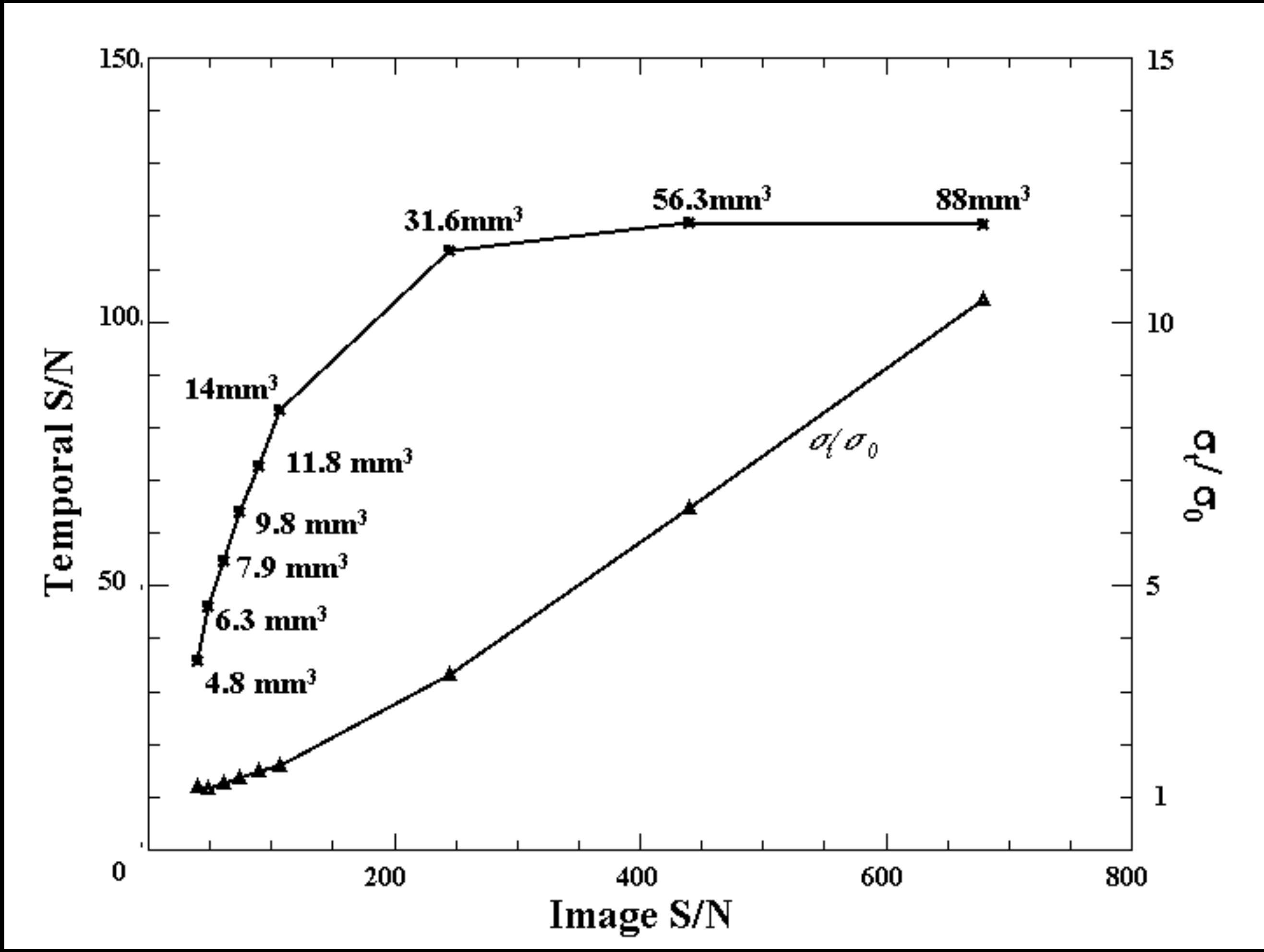


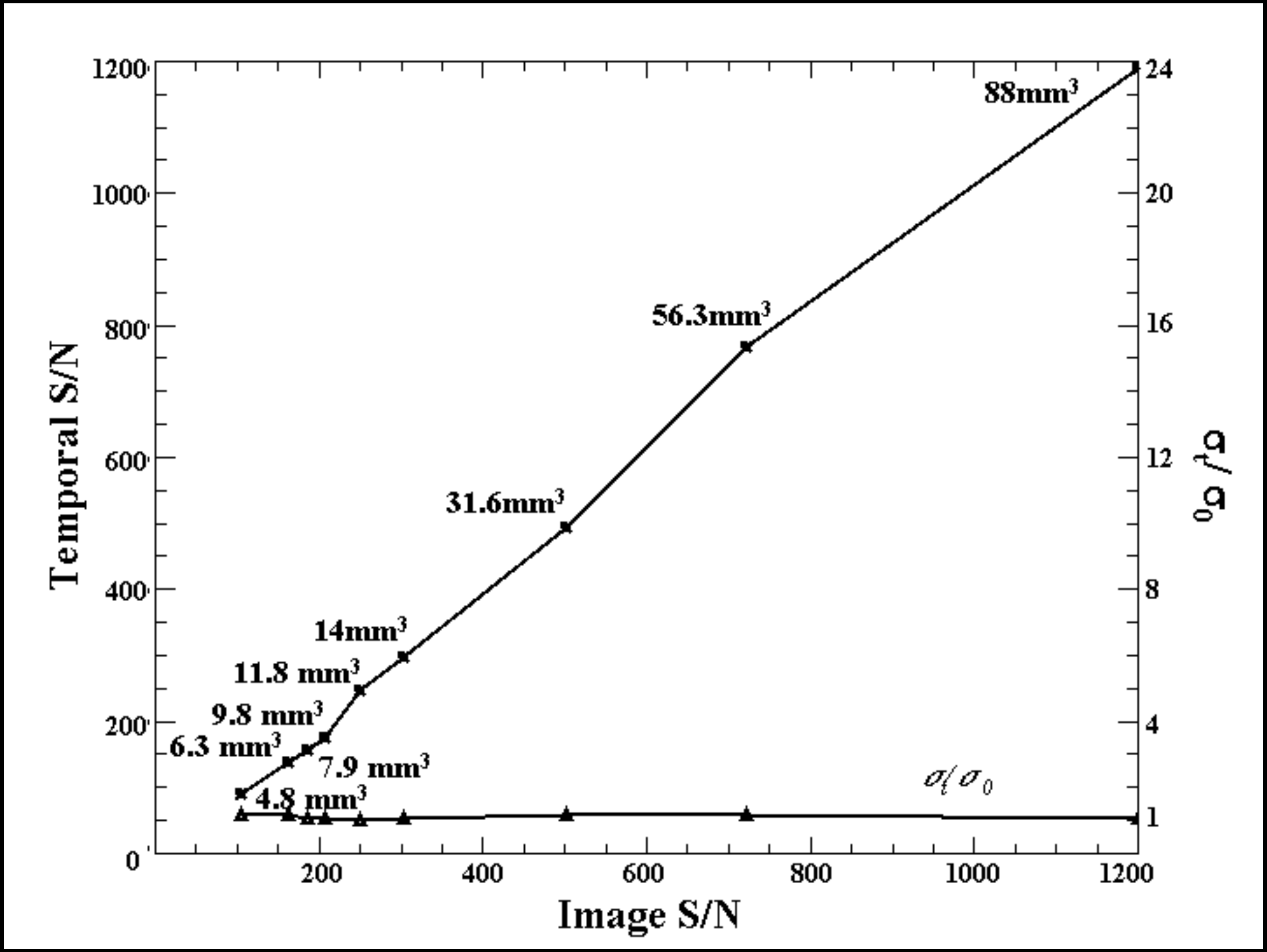
Temporal vs. Image S/N Optimal Resolution Study



Human data

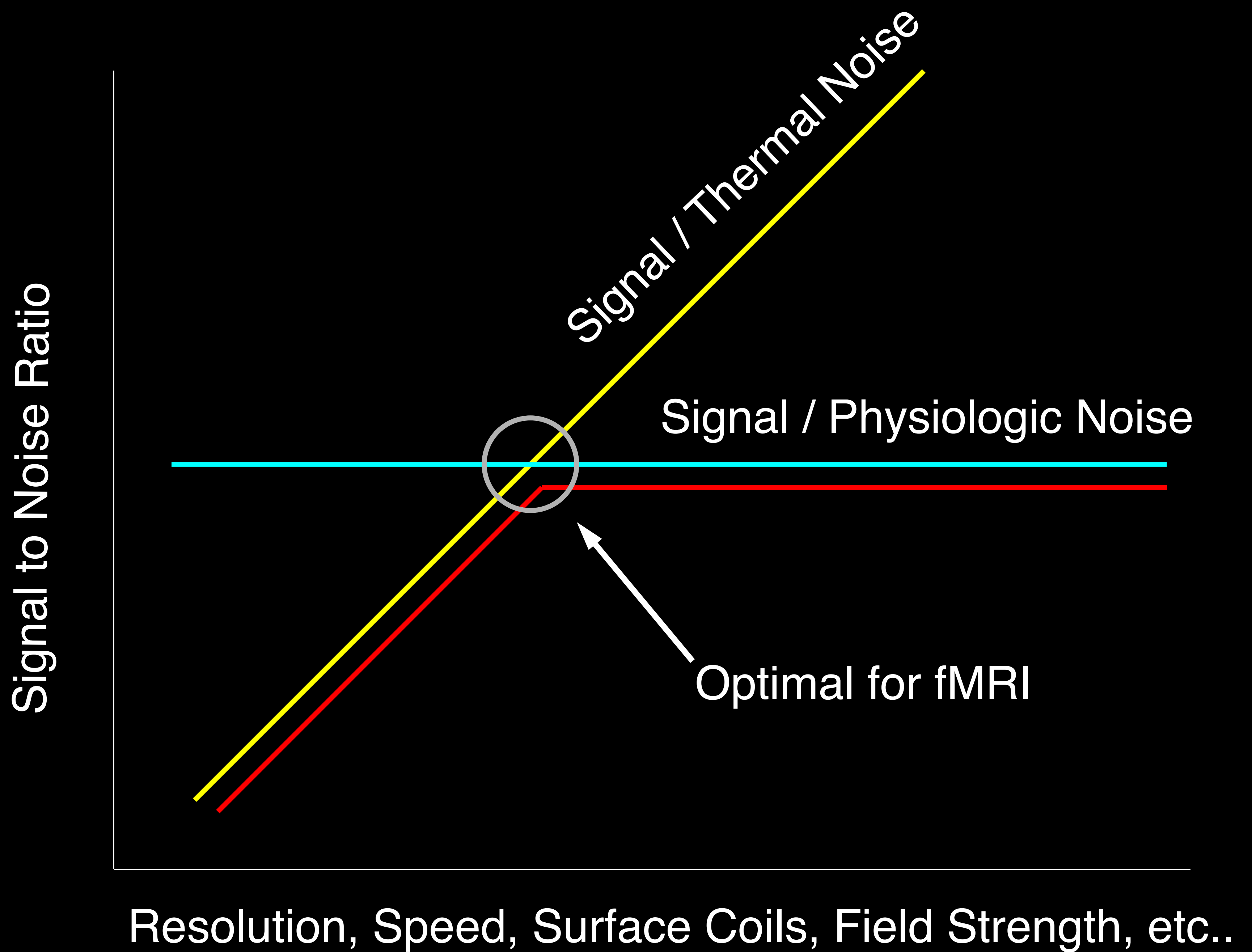
Petridou et al

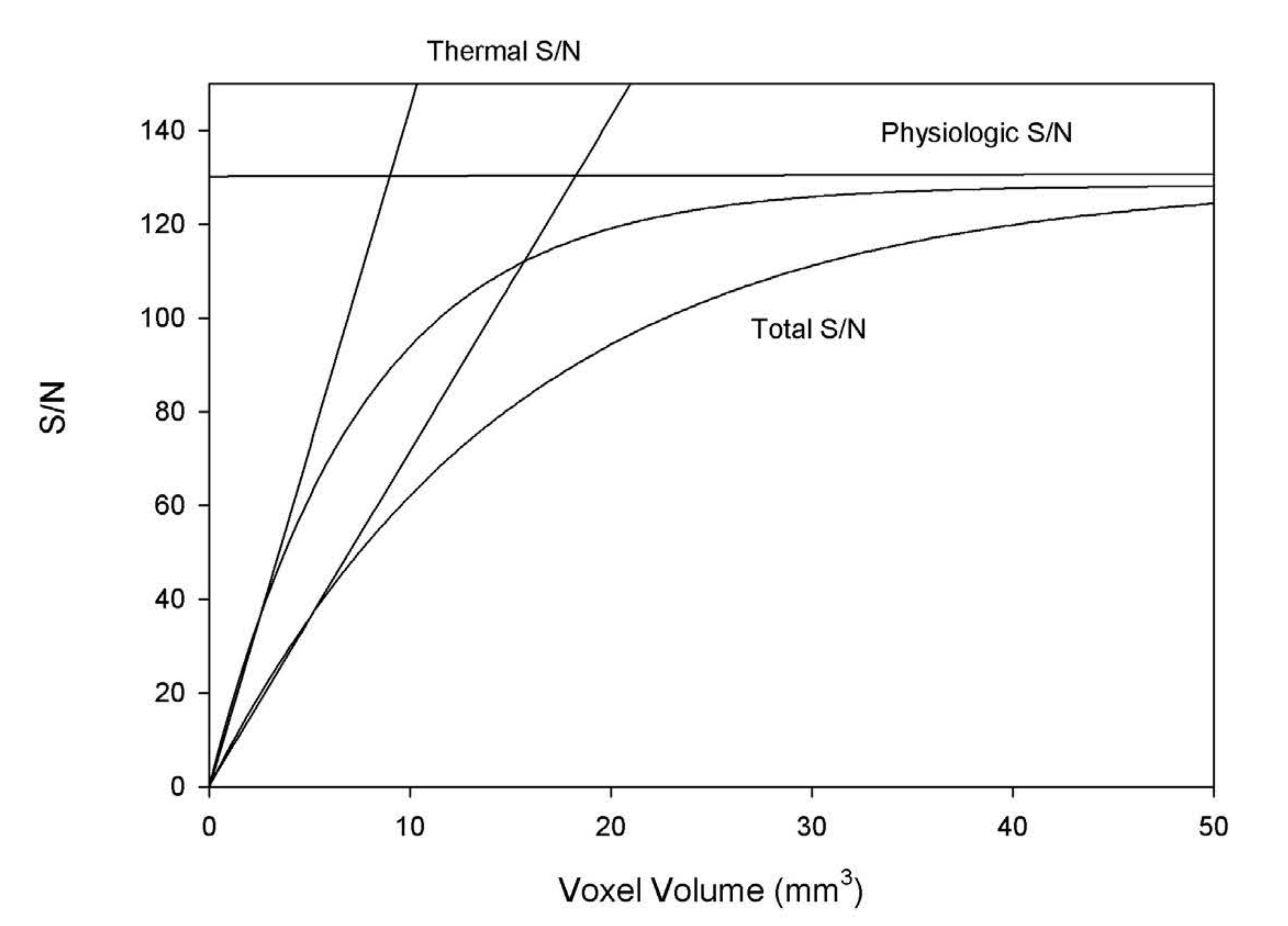
Temporal vs. Image S/N Optimal Resolution Study



Phantom data

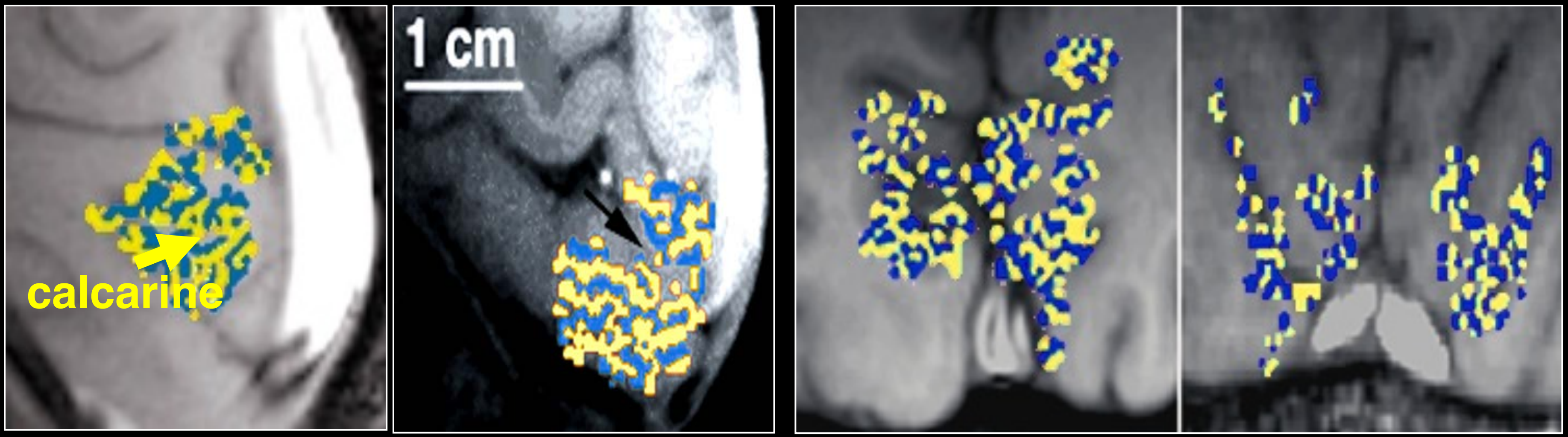
Petridou et al


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

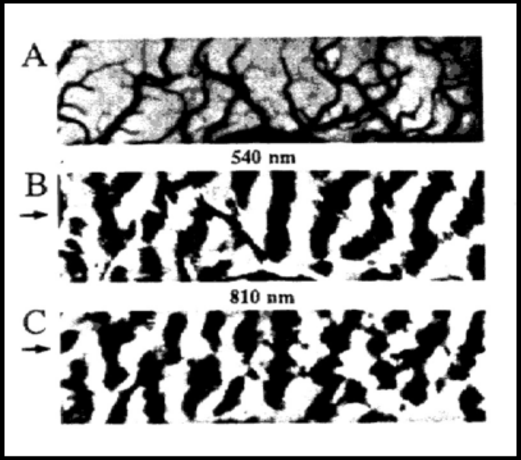


Thermal S/N
Physiologic S/N
Total S/N
S/N
140
120
100
80
60
40
20
0
0
10
20
30
40
50
Voxel Volume (mm³)

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.



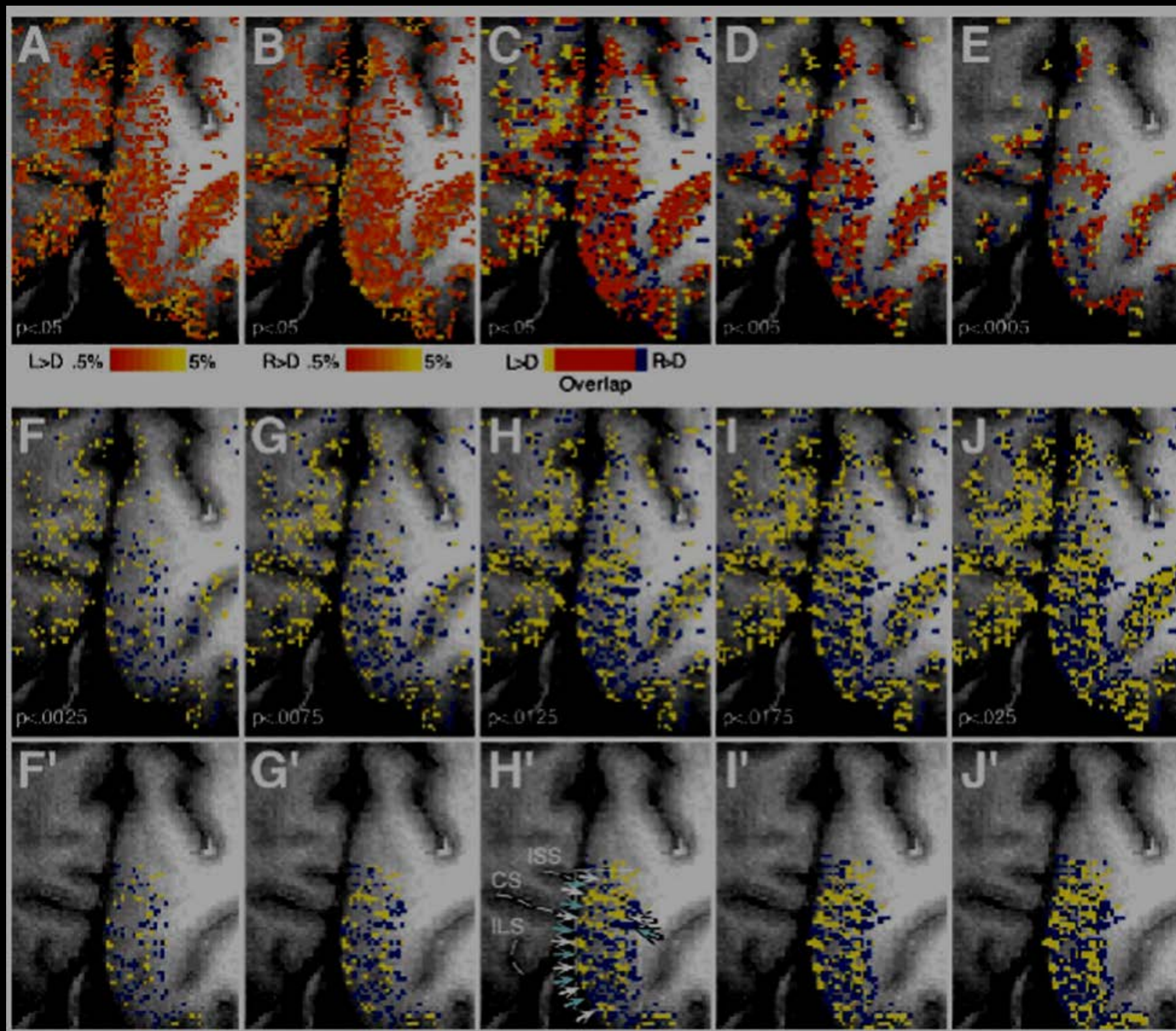
Optical Imaging

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

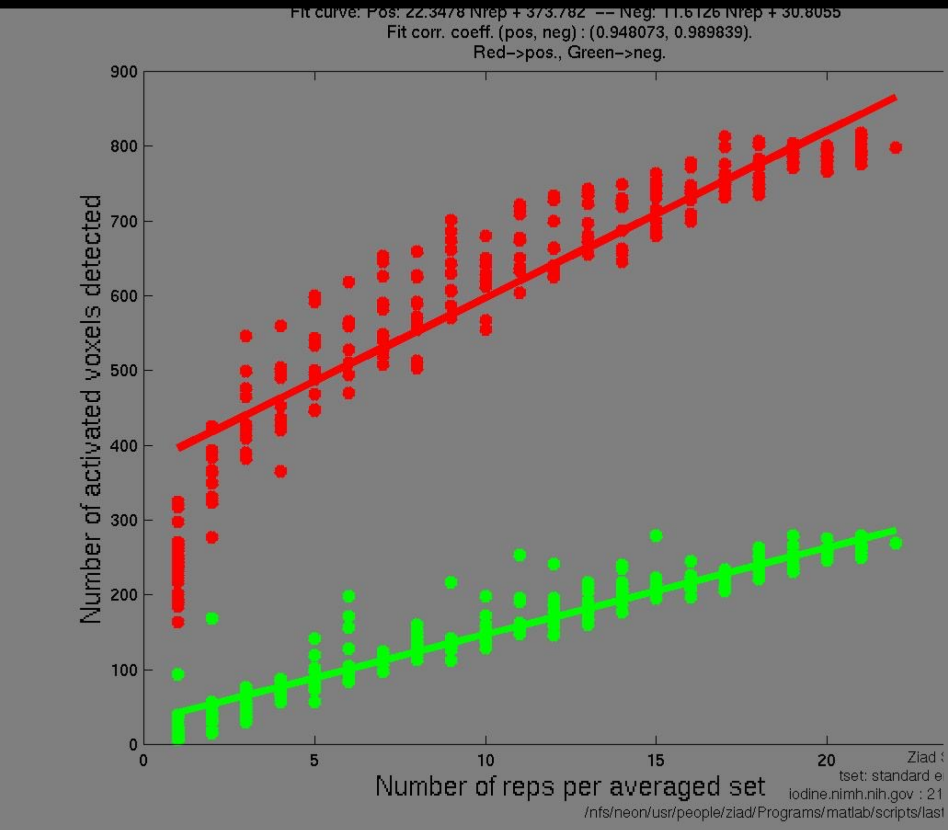
Neuron, Vol. 32, 359–374, October 25, 2001, Copyright ©2001 by Cell Press

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

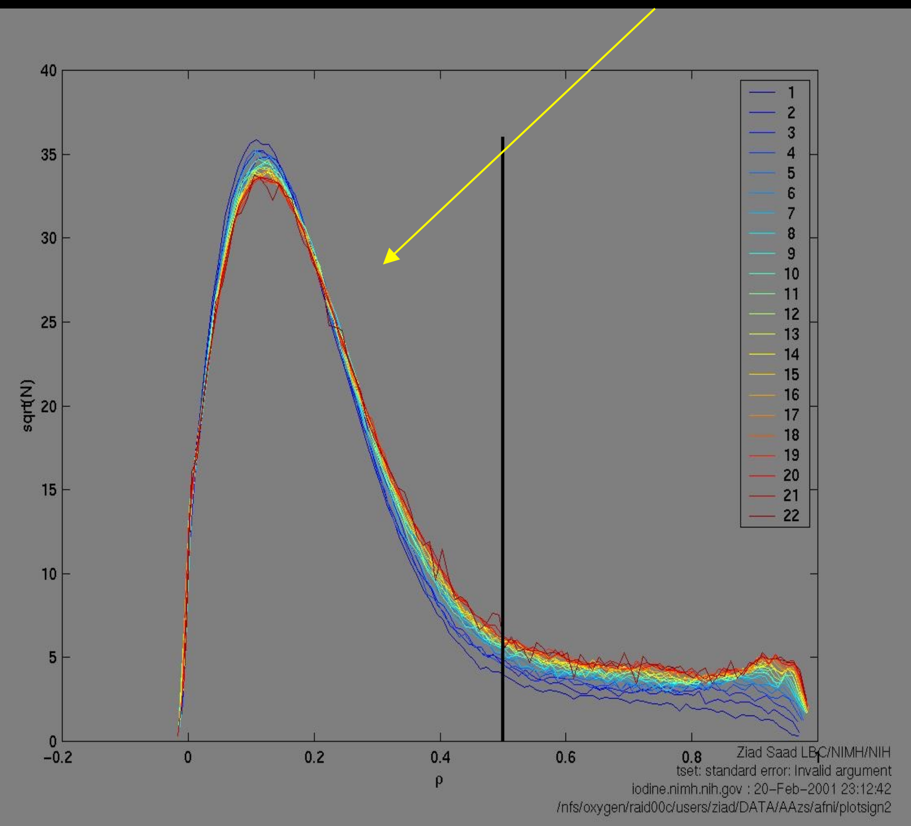


Continuously Growing Activation Area



CC Histogram

Inflection Point



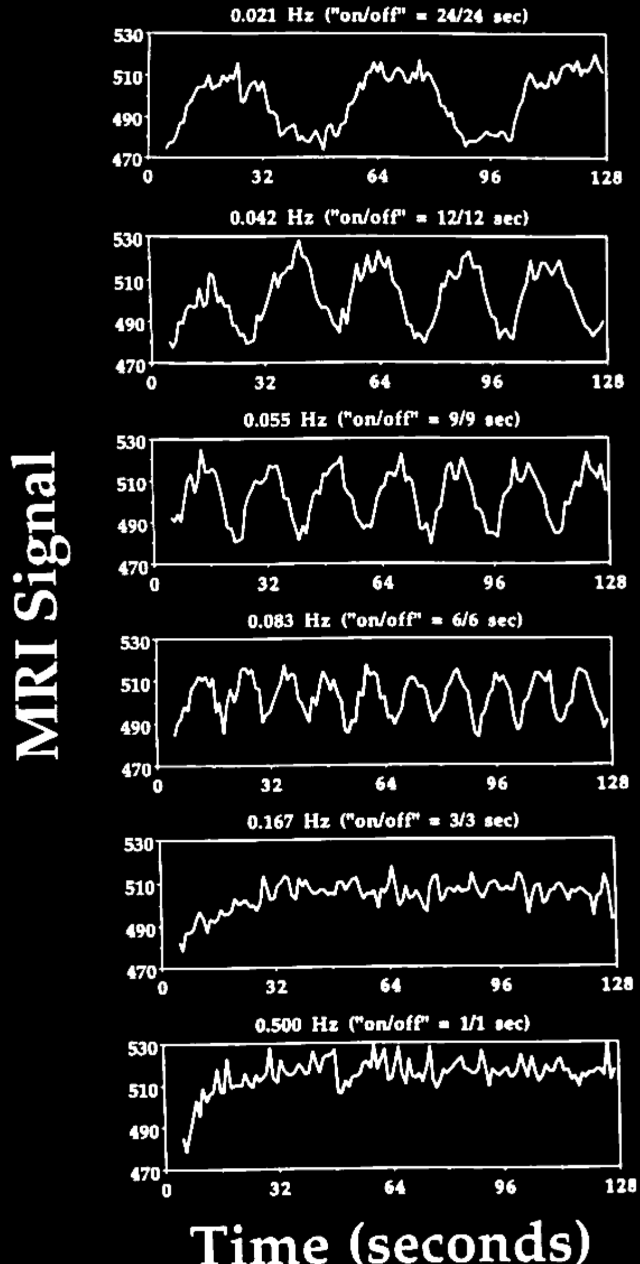
Ziad Saad, et al (Submitted)

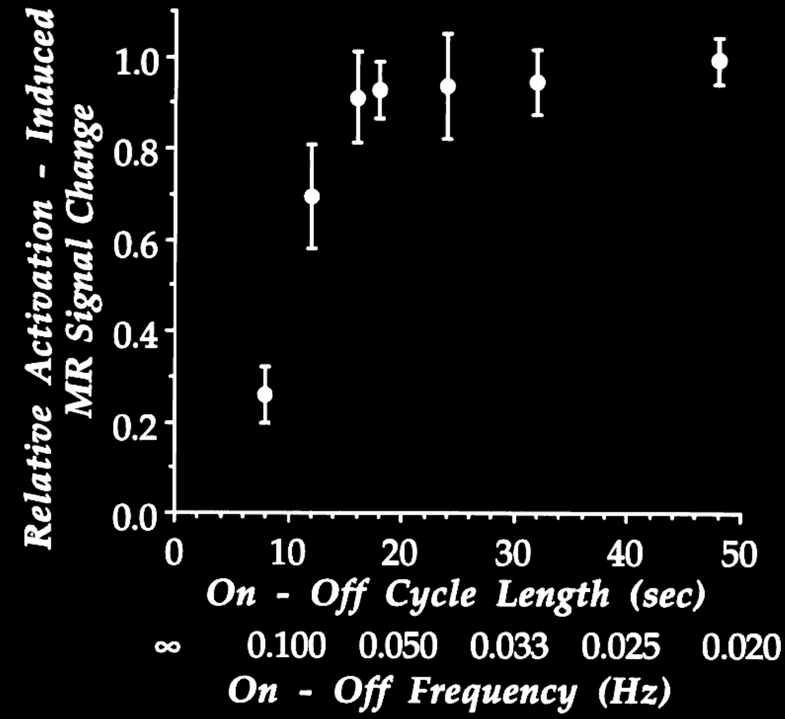
Refinements

BOLD Contrast Interpretation

Dynamics

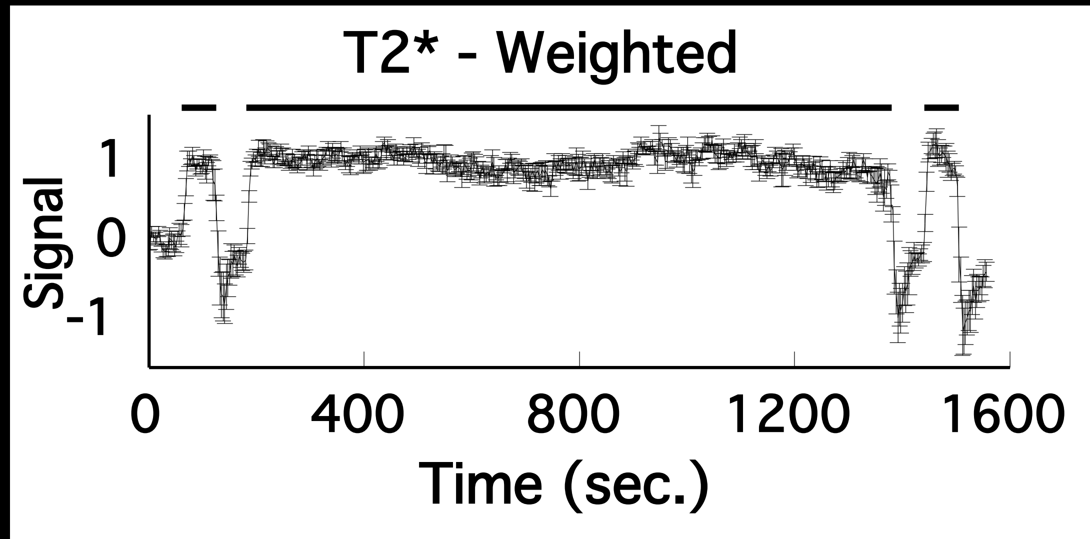
Paradigm Design and Processing



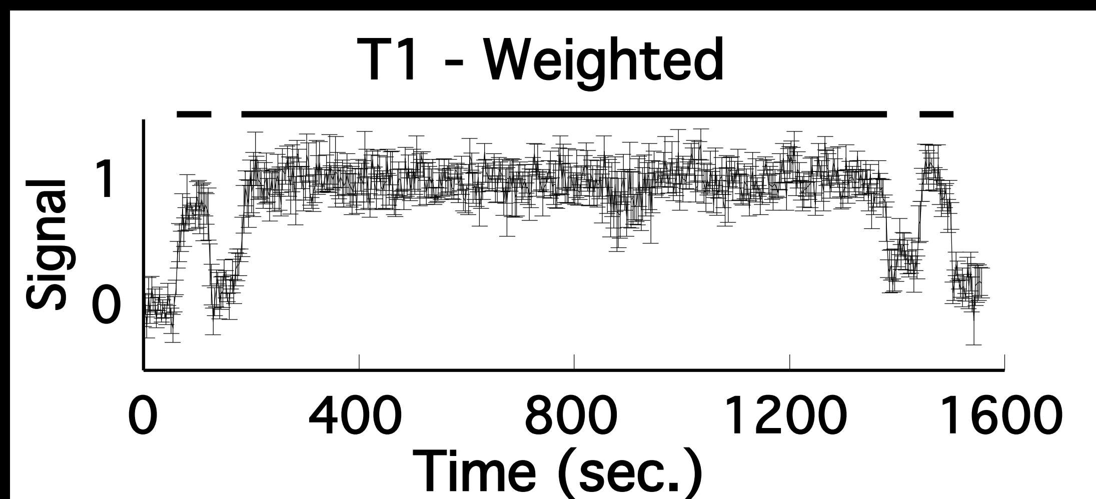


P. A. Bandettini, Functional MRI temporal resolution *in* "Functional MRI" (C. Moonen, and P. Bandettini., Eds.), p. 205-220, Springer - Verlag,. 1999.

BOLD

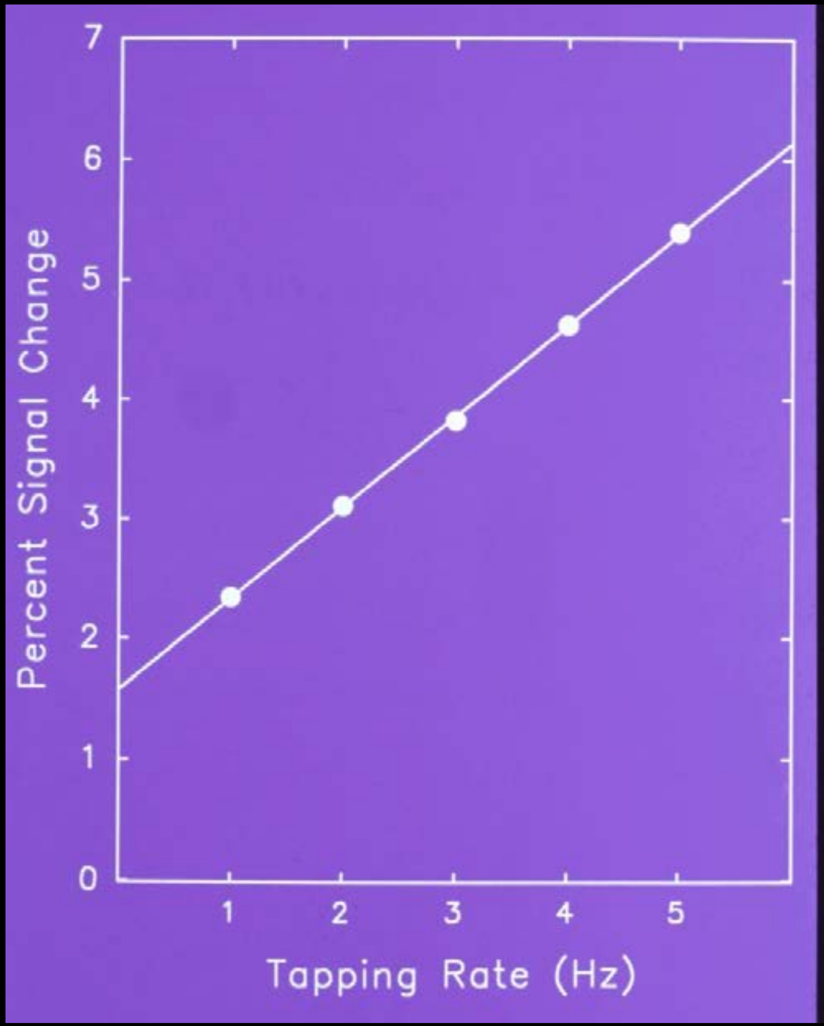


Flow



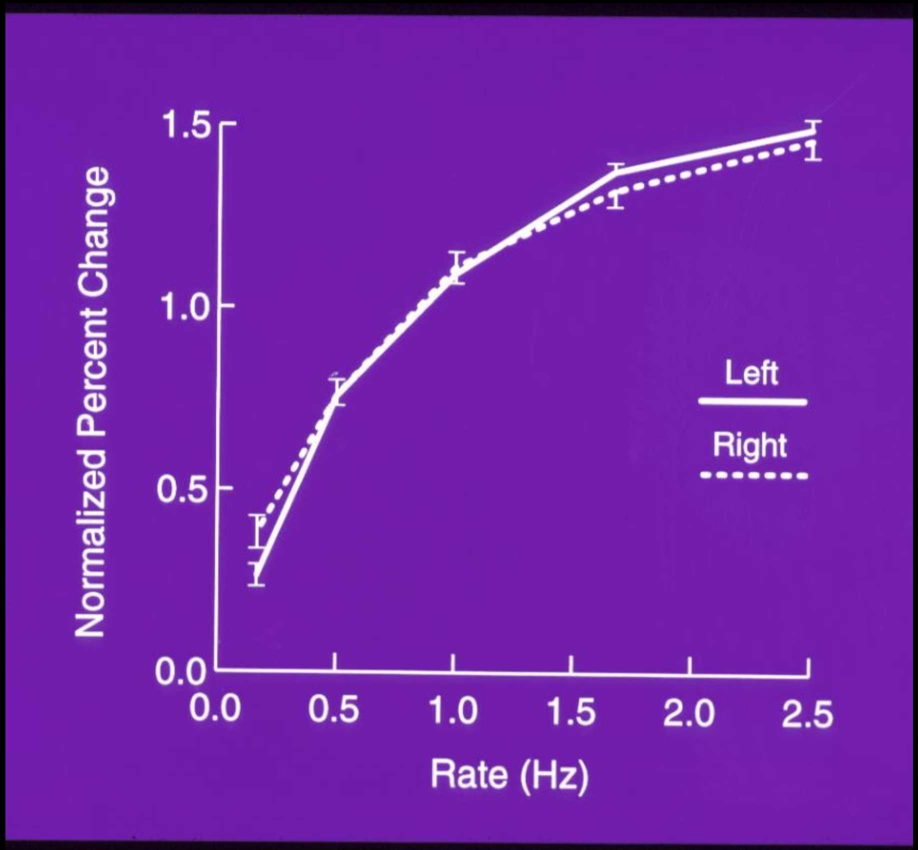
P. A. Bandettini, K. K. Kwong, T. L. Davis, R. B. H. Tootell, E. C. Wong, P. T. Fox, J. W. Belliveau, R. M. Weisskoff, B. R. Rosen, (1997). "Characterization of cerebral blood oxygenation and flow changes during prolonged brain activation." *Human Brain Mapping* 5, 93-109.

Motor Cortex



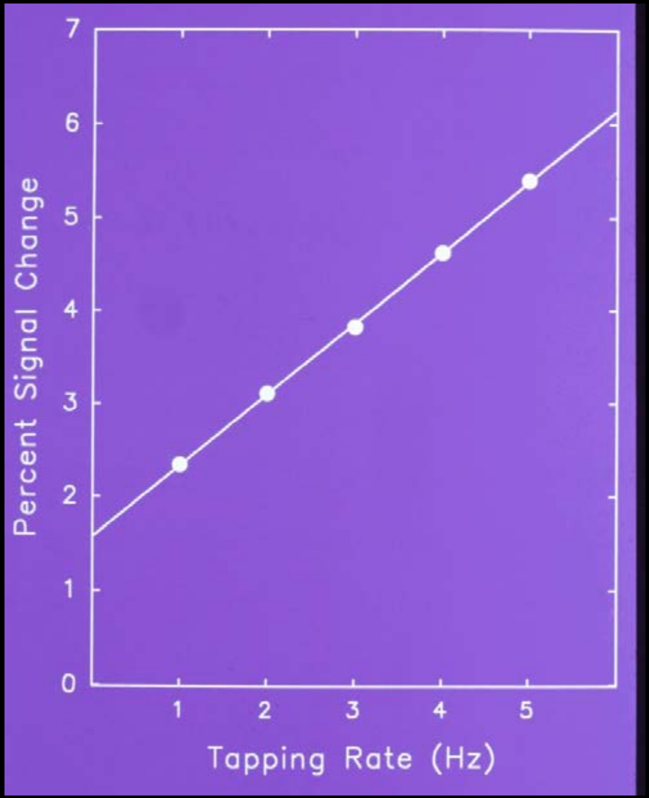
S. M. Rao et al, (1996) "Relationship between finger movement rate and functional magnetic resonance signal change in human primary motor cortex." *J. Cereb. Blood Flow and Met.* 16, 1250-1254.

Auditory Cortex

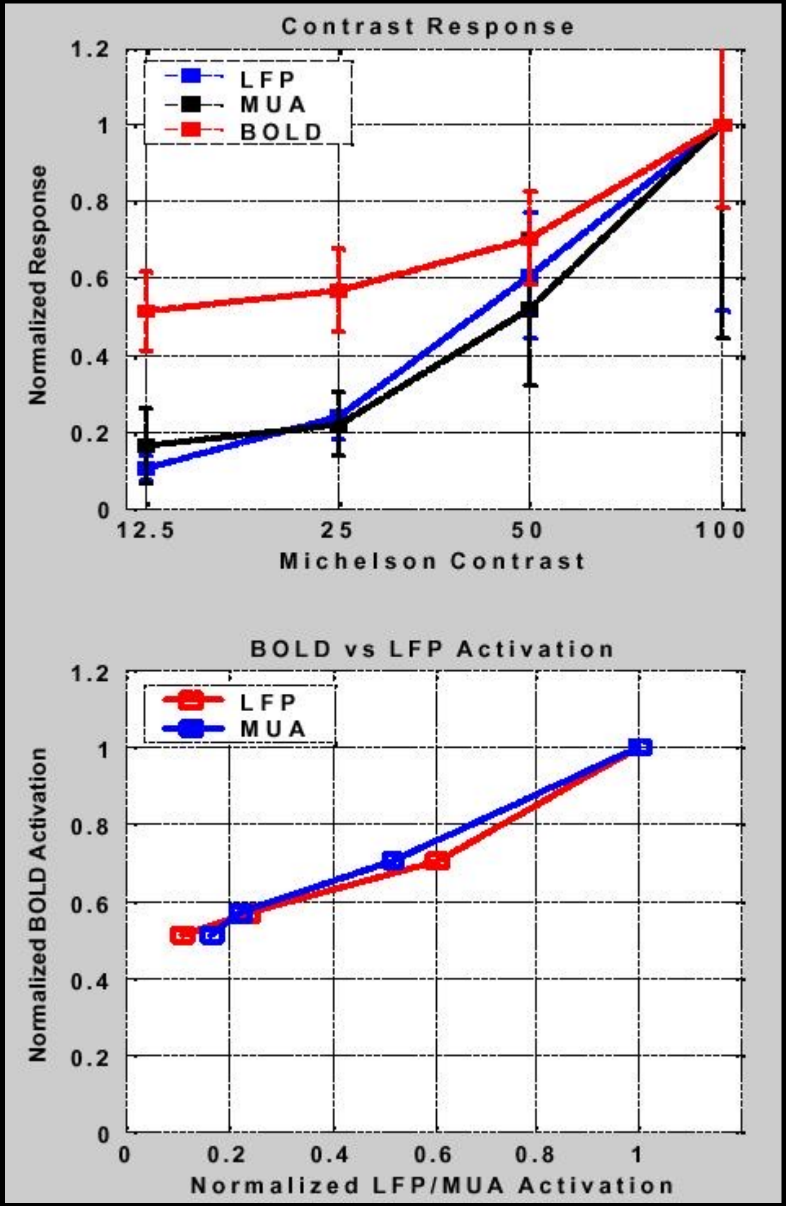


J. R. Binder, et al, (1994). "Effects of stimulus rate on signal response during functional magnetic resonance imaging of auditory cortex." *Cogn. Brain Res.* 2, 31-38

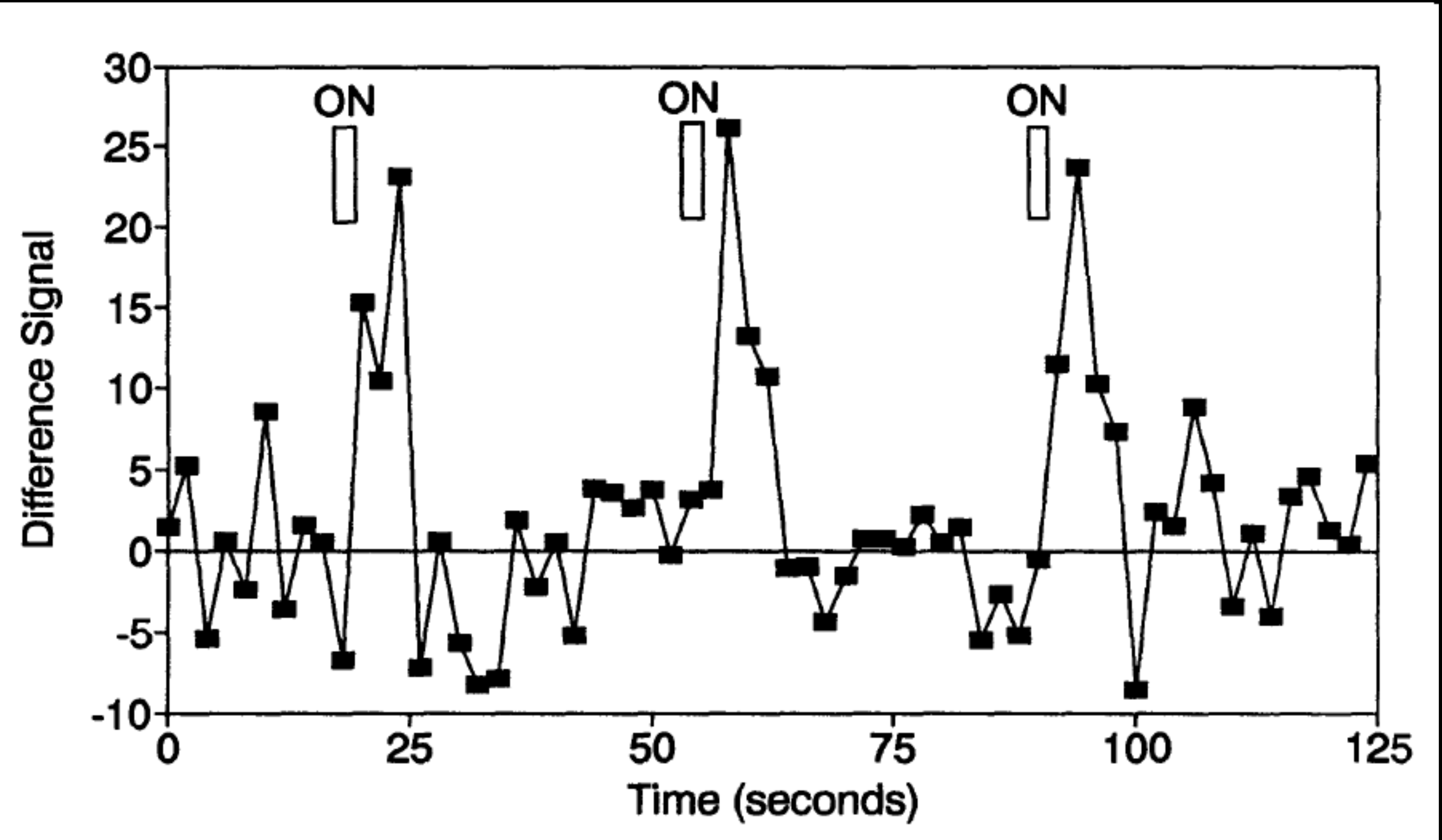
Logothetis et al. (2001) "Neurophysiological investigation of the basis of the fMRI signal" Nature, 412, 150-157



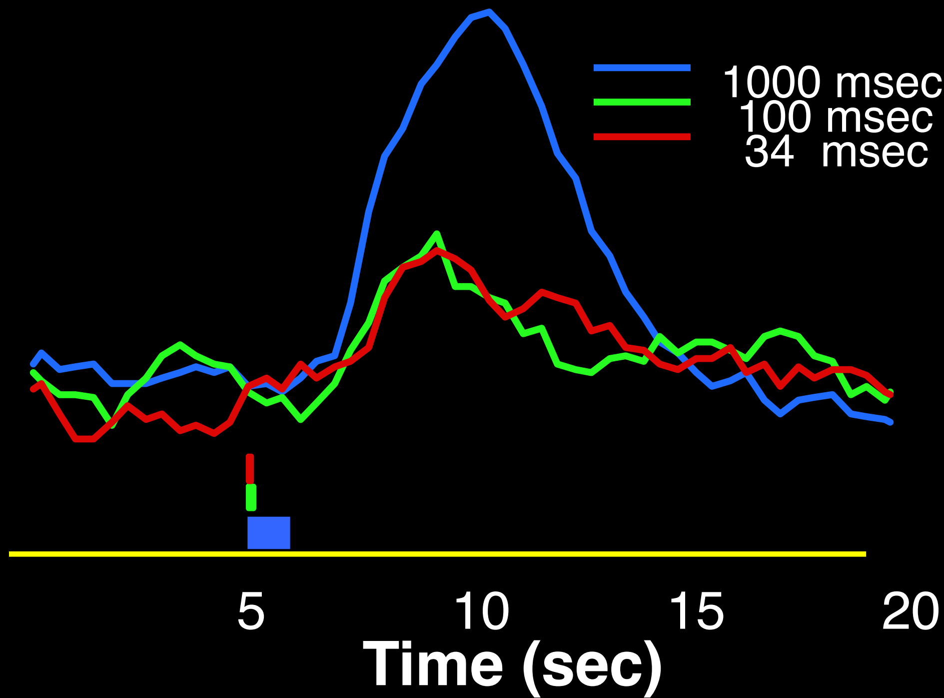
S. M. Rao et al, (1996) "Relationship between finger movement rate and functional magnetic resonance signal change in human primary motor cortex." *J. Cereb. Blood Flow and Met.* 16, 1250-1254.



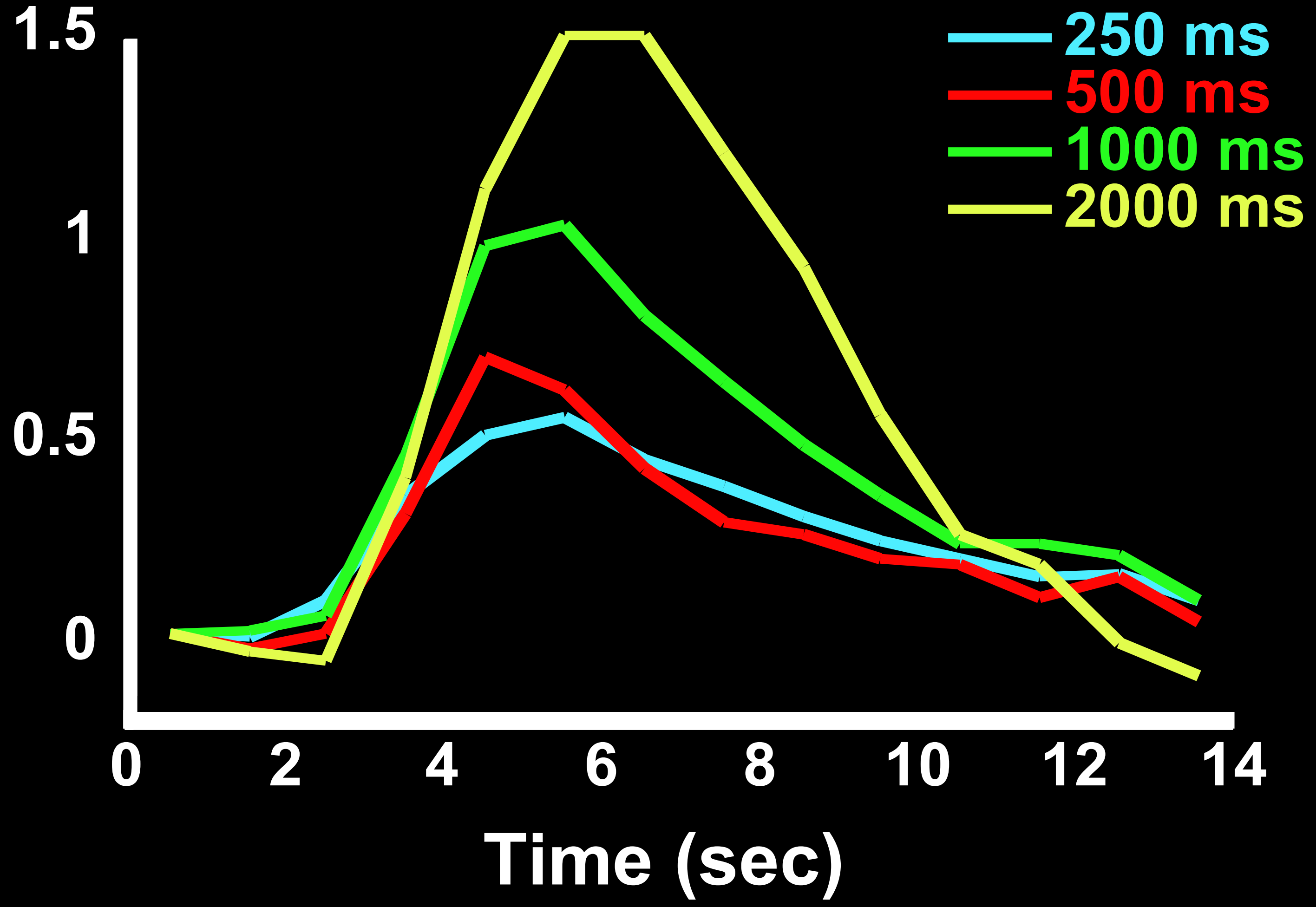
First Event-related fMRI Results



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.

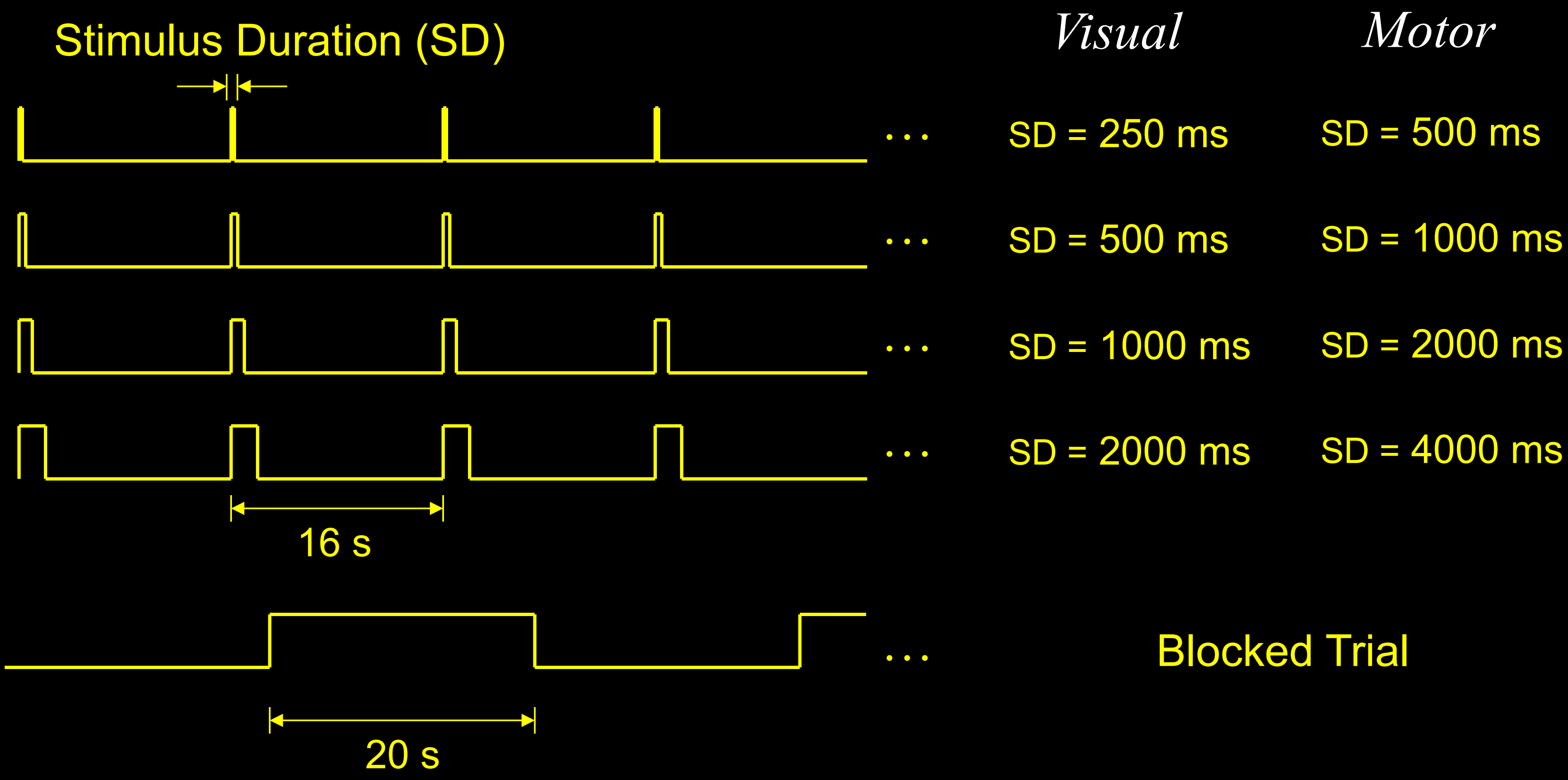


R. L. Savoy, et al., Pushing the temporal resolution of fMRI: studies of very brief visual stimuli, onset variability and asynchrony, and stimulus-correlated changes in noise [oral], 3'rd Proc. Soc. Magn. Reson., Nice, p. 450. (1995).



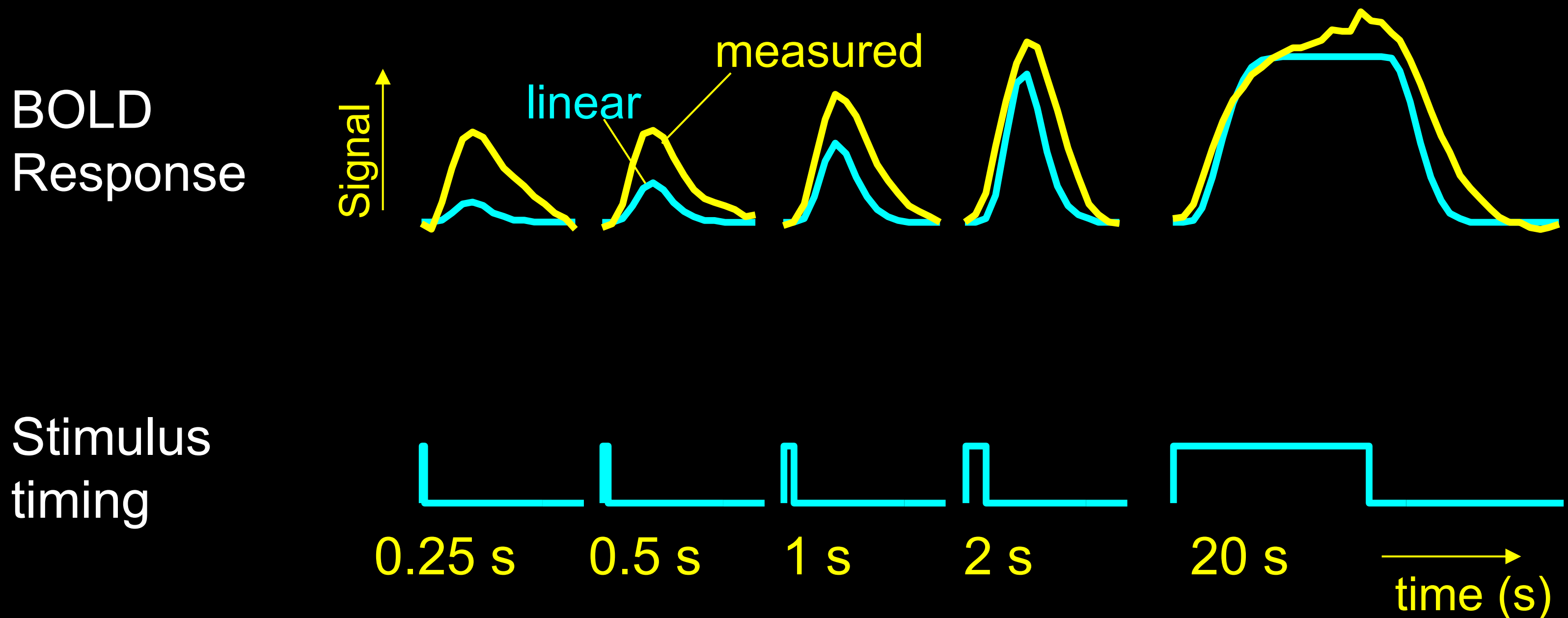
250 ms
500 ms
1000 ms
2000 ms
1.5
1
0.5
0
0
2
4
6
8
10
12
14
Time (sec)

Methods


Stimulus Duration (SD)
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
16 s
Blocked Trial
20 s

Dynamic Nonlinearity Assessment

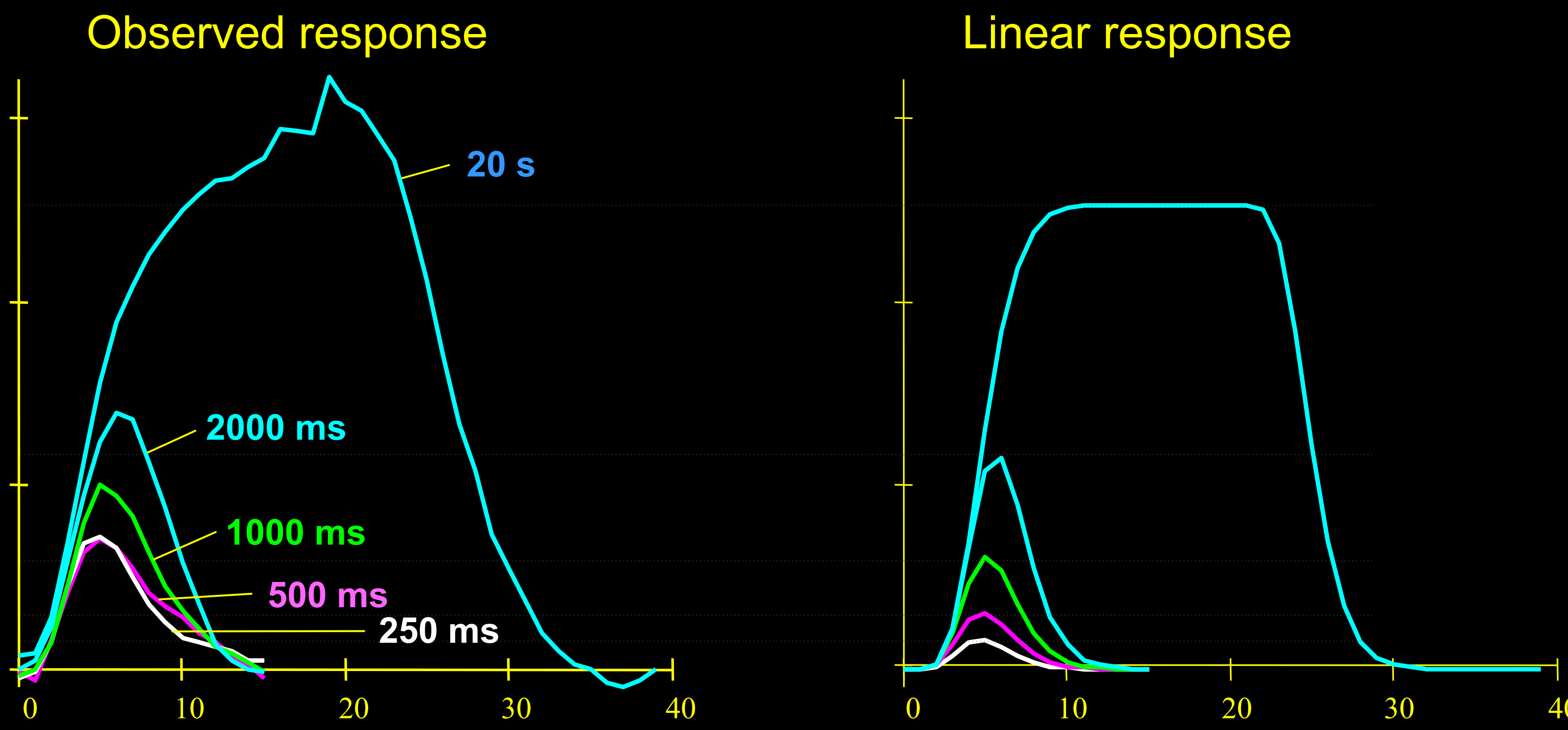
Different stimulus "ON" periods



Brief stimuli produce larger responses than expected

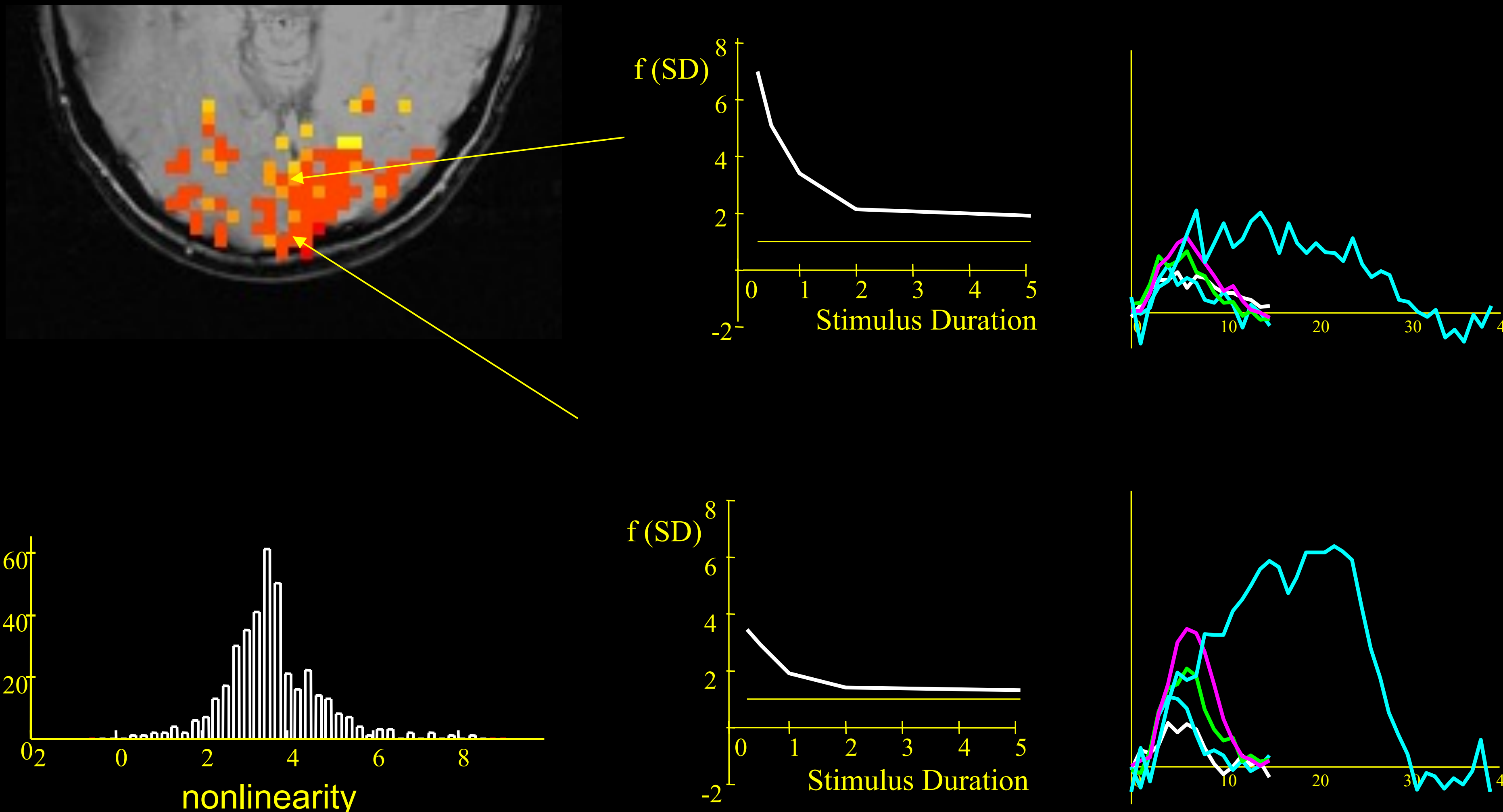
R. M. Birn, Z. Saad, P. A. Bandettini, (2001) "Spatial heterogeneity of the nonlinear dynamics in the fMRI BOLD response." ***NeuroImage*****, 14: 817-826.**

BOLD response is nonlinear



Short duration stimuli produce larger responses than expected

Spatial Heterogeneity of BOLD Nonlinearity



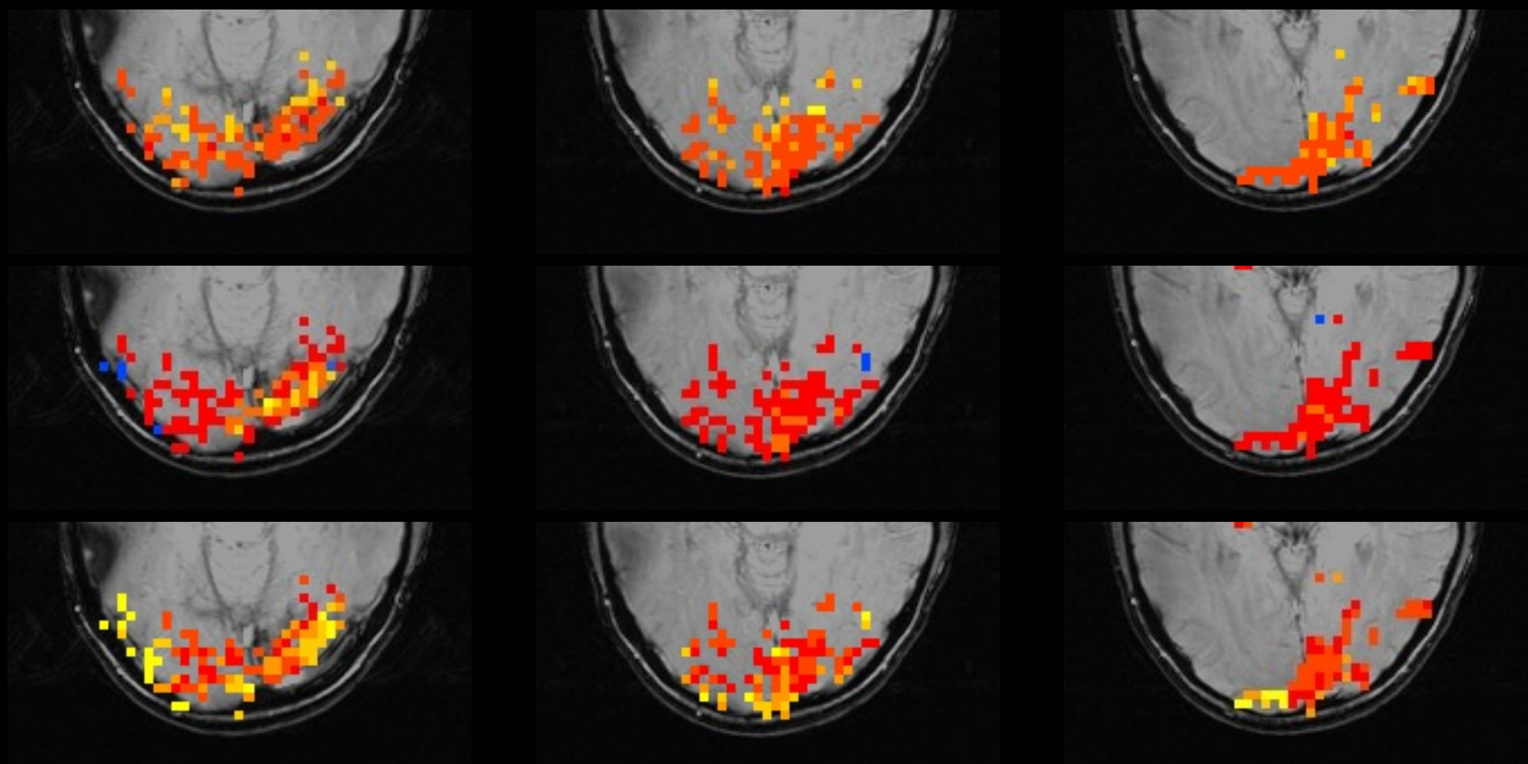
R. M. Birn, Z. Saad, P. A. Bandettini, (2001) "Spatial heterogeneity of the nonlinear dynamics in the fMRI BOLD response." *NeuroImage*, 14: 817-826.

Results – visual task

Nonlinearity

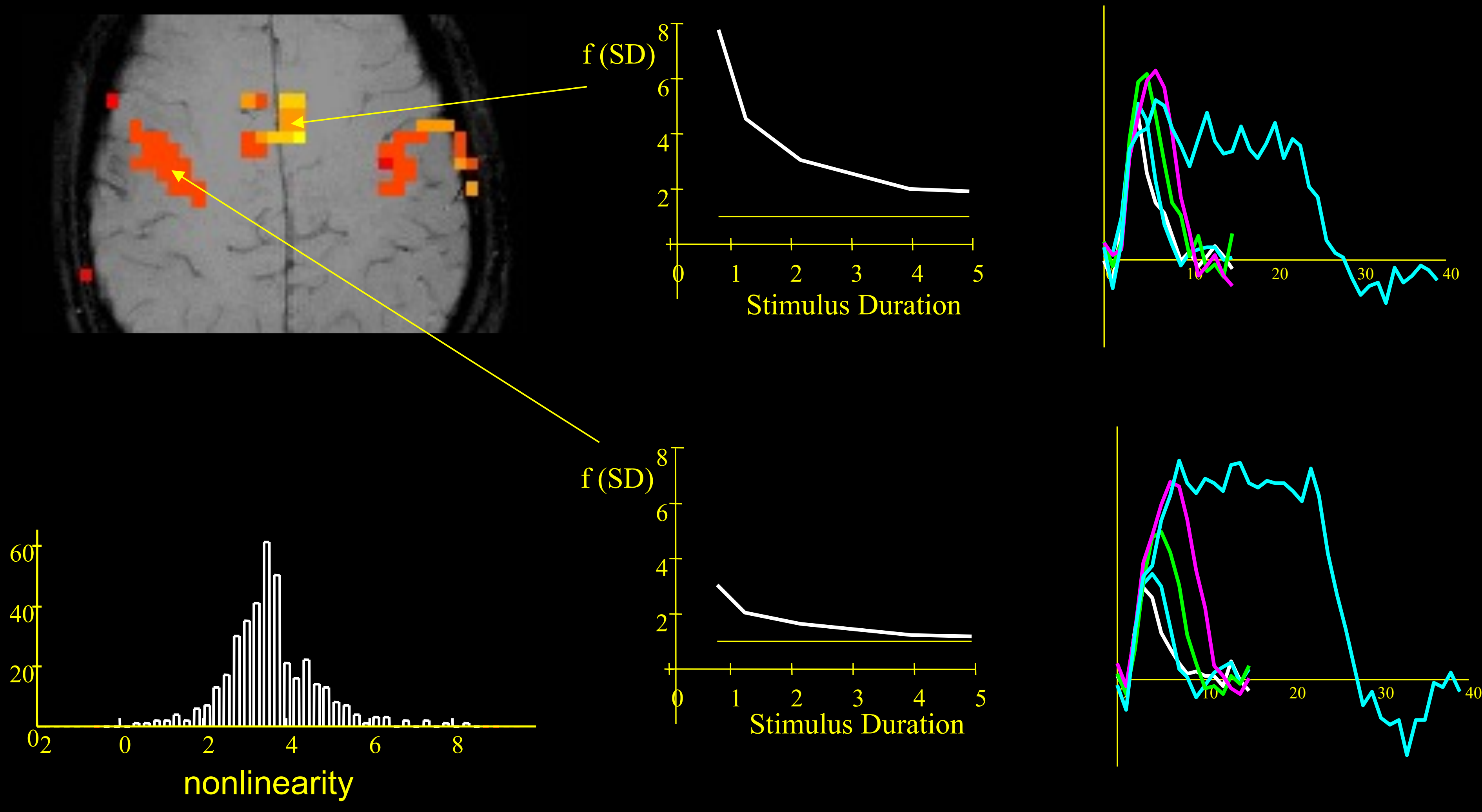
Magnitude

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

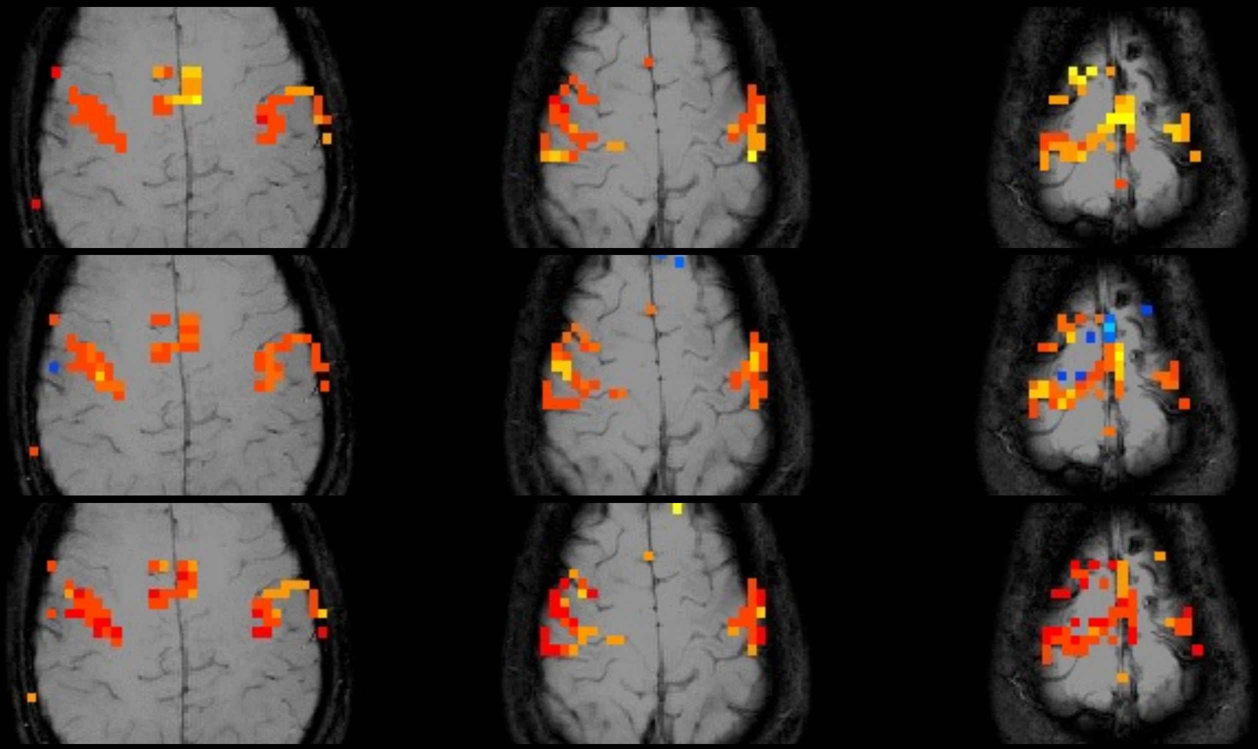


Results – motor task

Nonlinearity

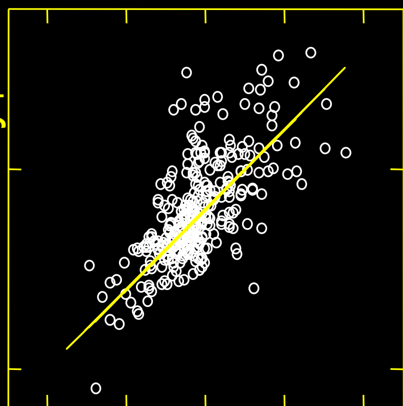
Magnitude

Latency



Reproducibility

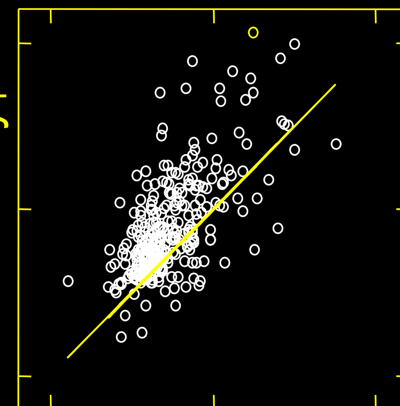
Visual task



Nonlinearity$_1$

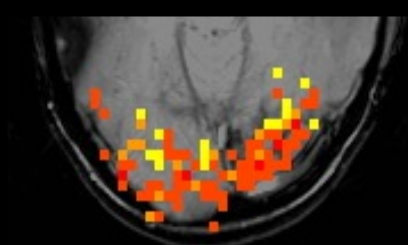
Nonlinearity$_2$

Motor task

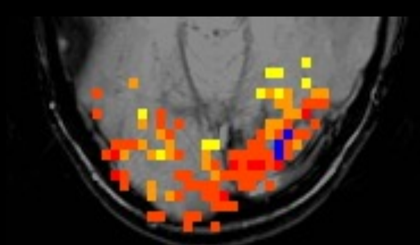


Nonlinearity$_1$

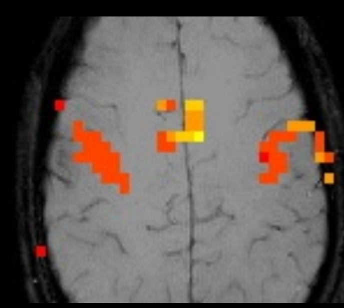
Nonlinearity$_2$



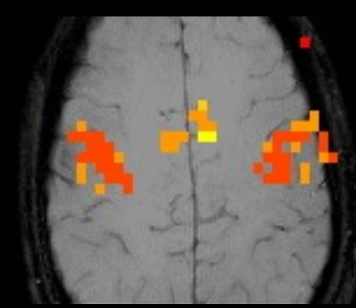
Experiment 1



Experiment 2

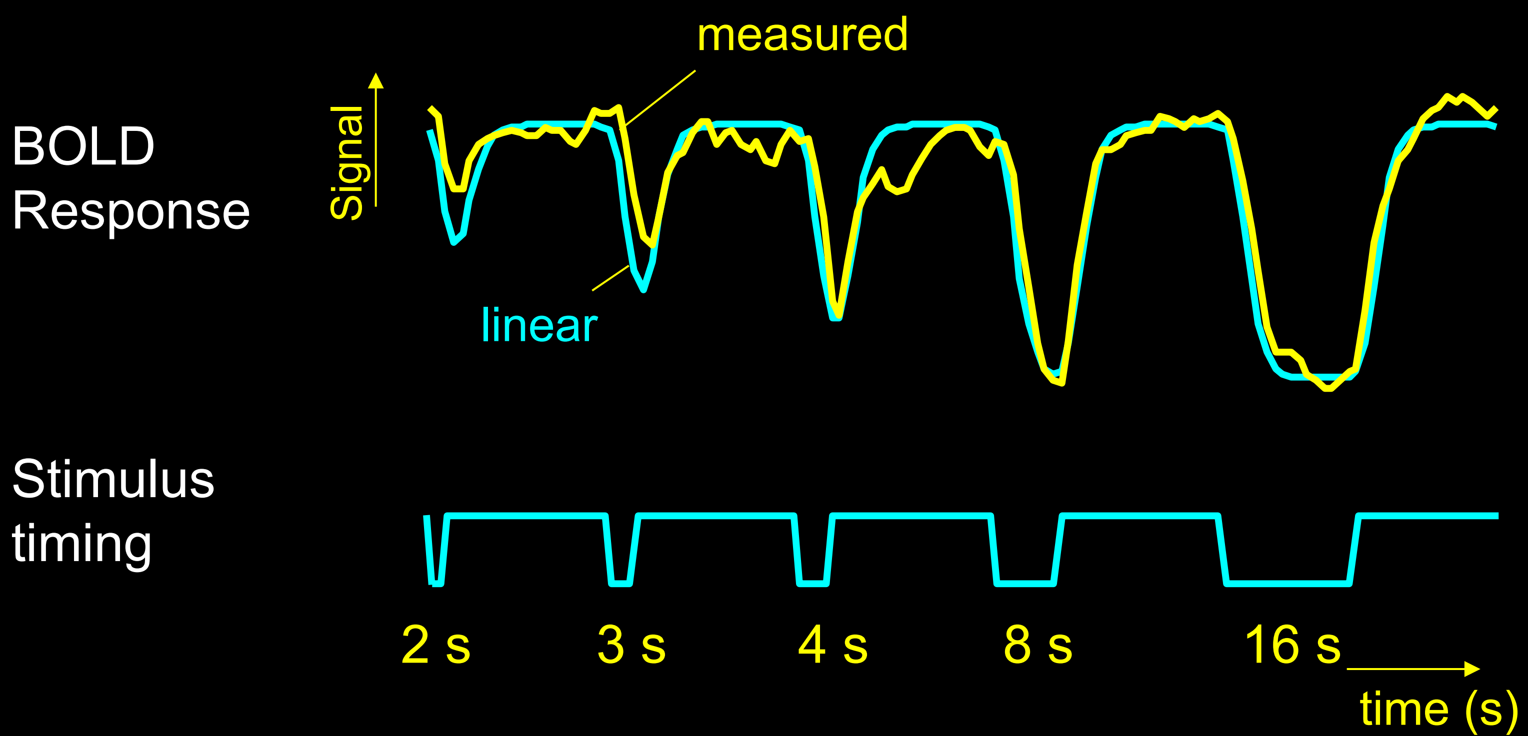


Experiment 1



Experiment 2

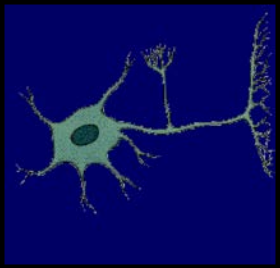
Different stimulus “ON” periods

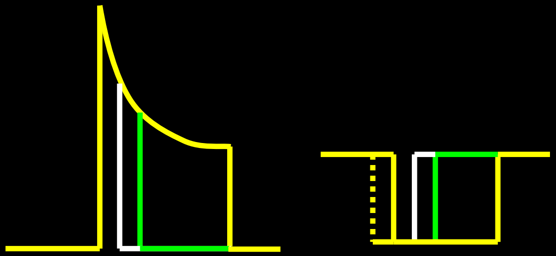


Brief stimulus OFF periods produce smaller decreases than expecte

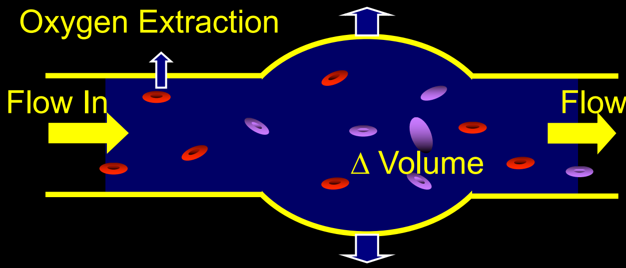
Sources of this Nonlinearity

- Neuronal



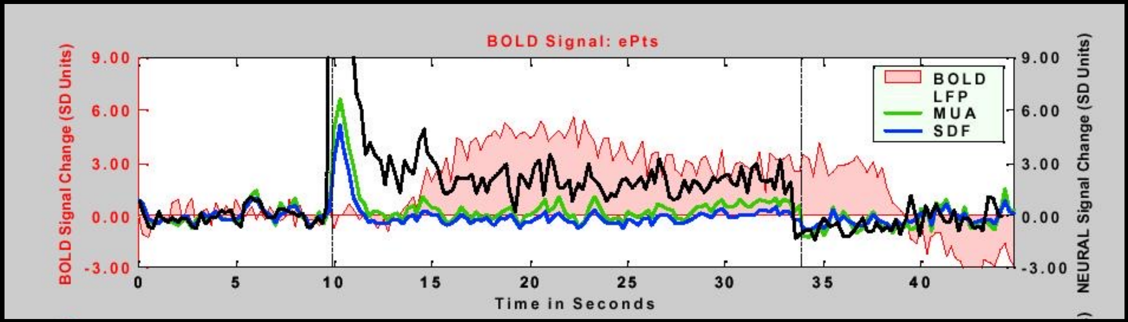


- Hemodynamic
  - Oxygen extraction
  - Blood volume dynamics

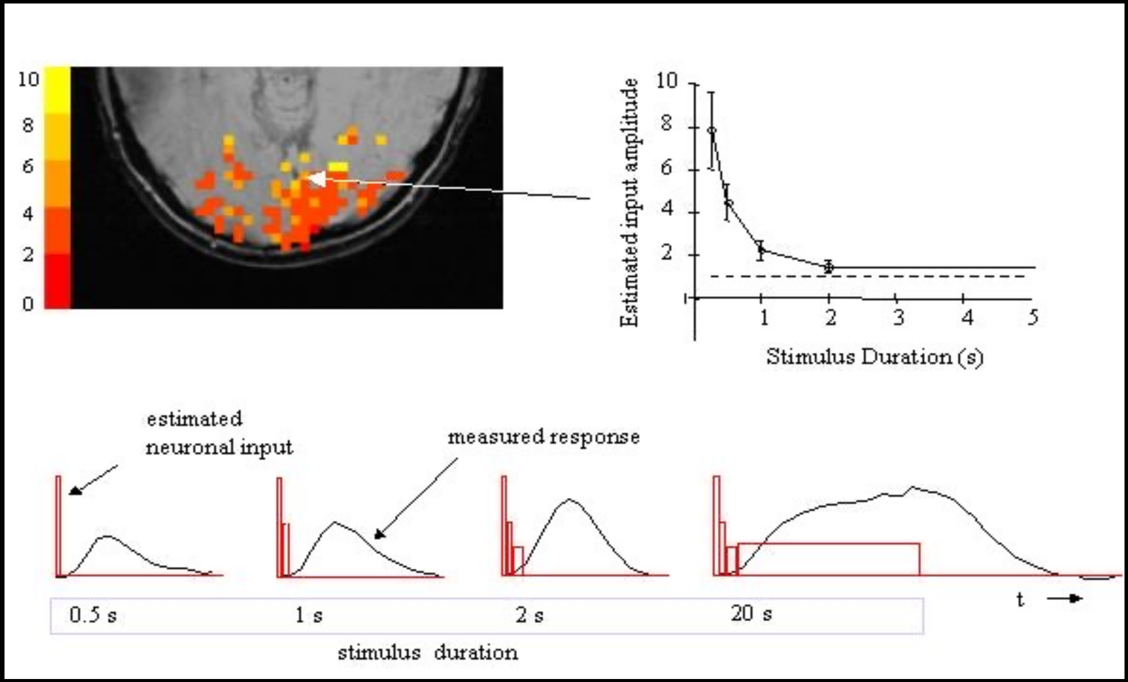


BOLD Correlation with Neuronal Activity

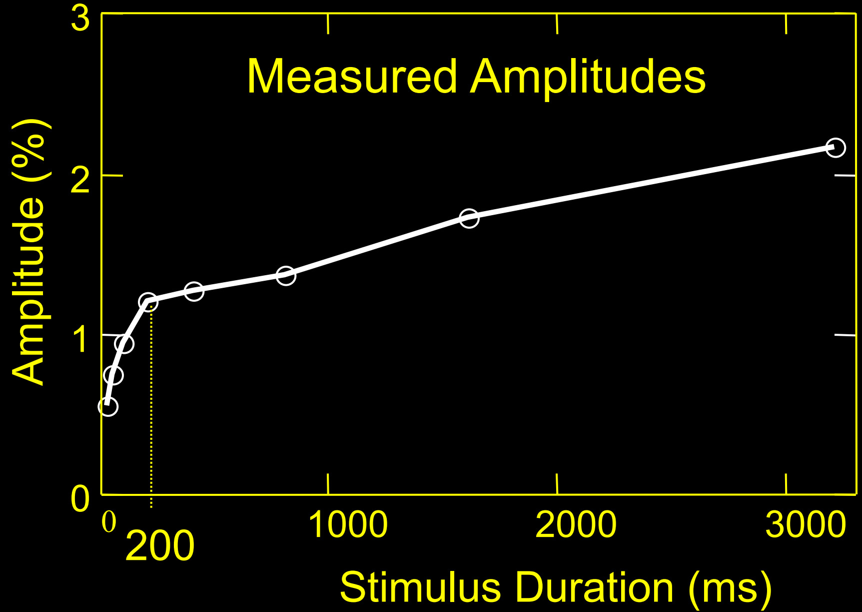
Logothetis et al. (2001) "Neurophysiological investigation of the basis of the fMRI signal" Nature, 412, 150-157.

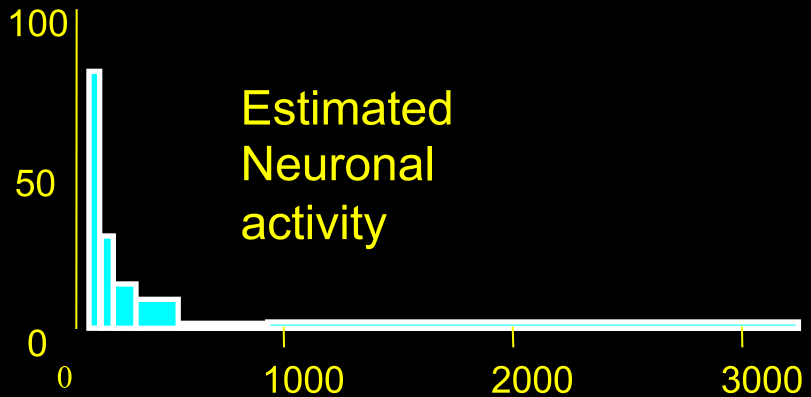


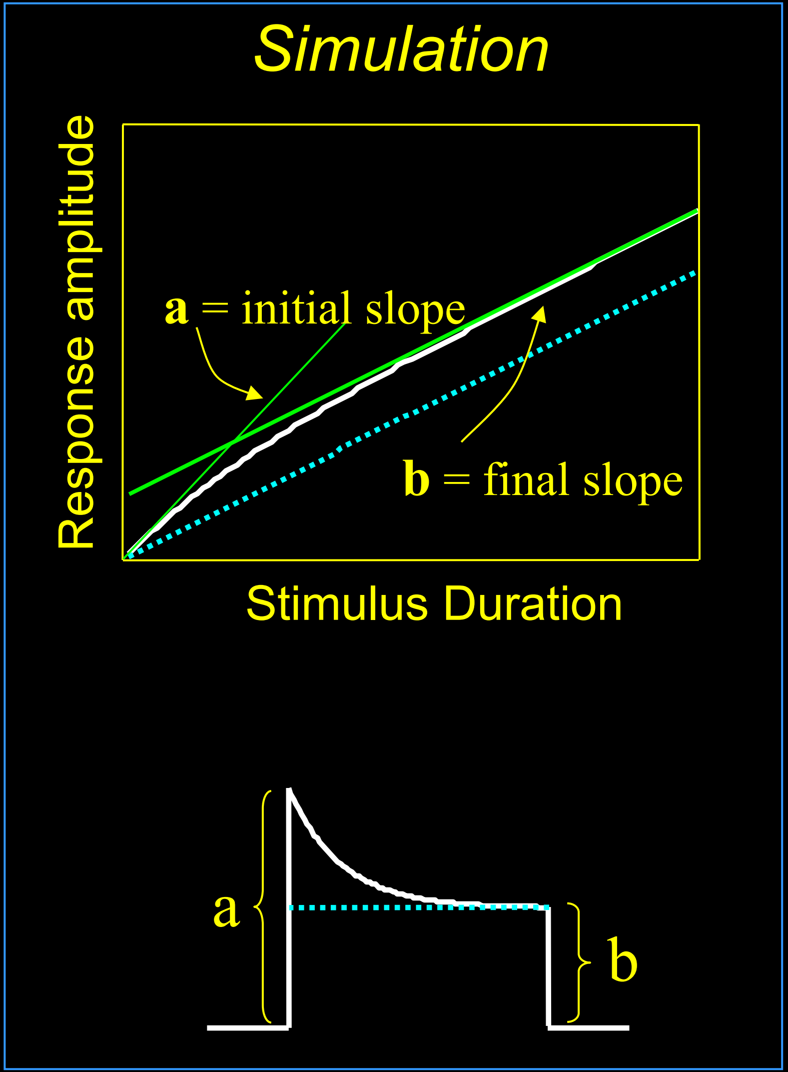
P. A. Bandettini and L. G. Ungerleider, (2001) "From neuron to BOLD: new connections." Nature Neuroscience, 4: 864-866.

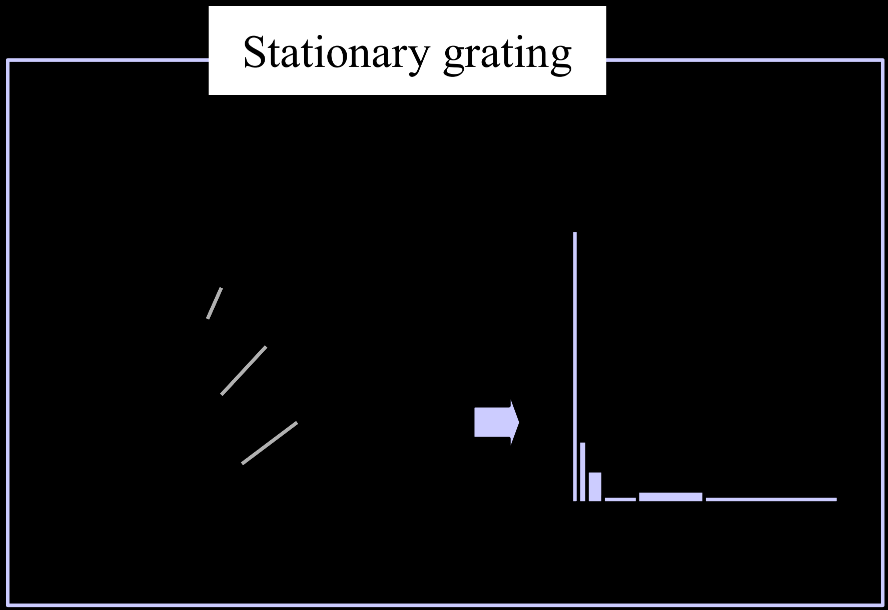


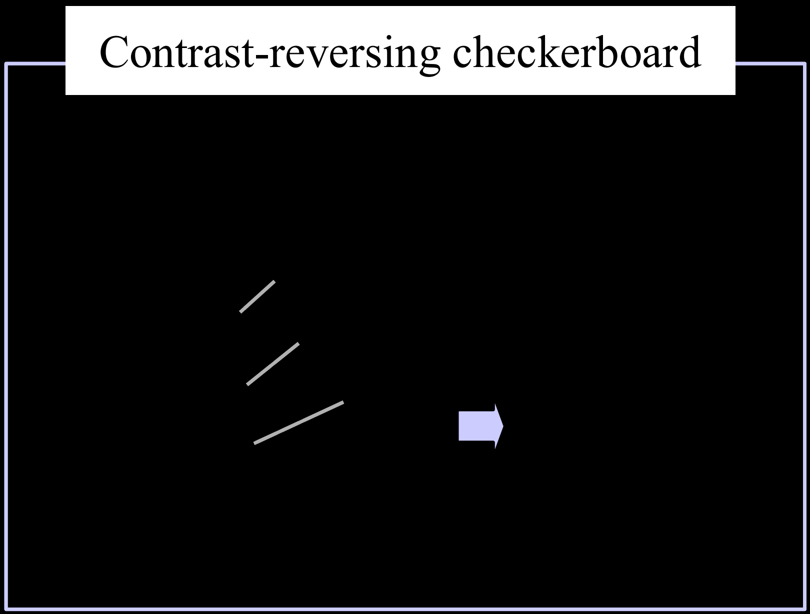
Results – constant gratings








Stationary grating


Contrast-reversing checkerboard

Refinements

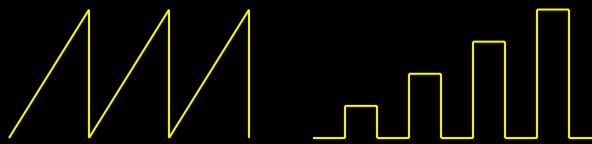
BOLD Contrast Interpretation

Dynamics

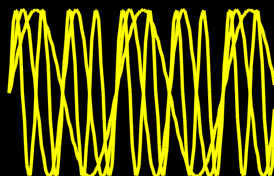
Paradigm Design and Processing

Neuronal Activation Input Strategies

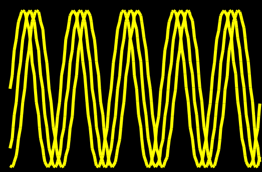
1. Block Design
2. Parametric Design



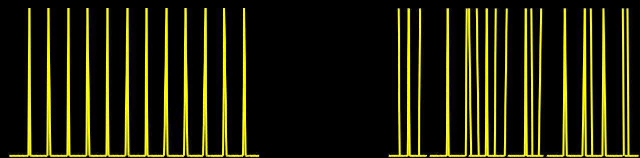
3. Frequency Encoding



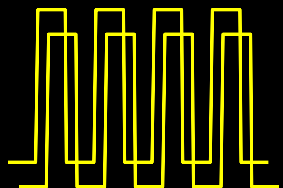
4. Phase Encoding



5. Event Related



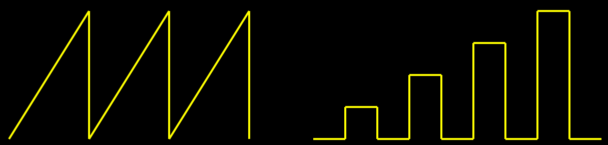
6. Orthogonal Design



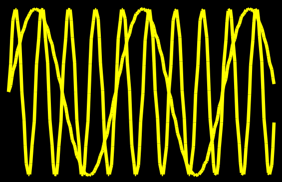
7. Free Behavior Design

Neuronal Activation Input Strategies

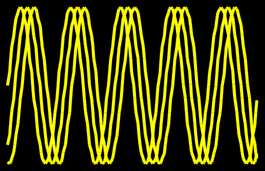
1. Block Design
2. **Parametric Design**



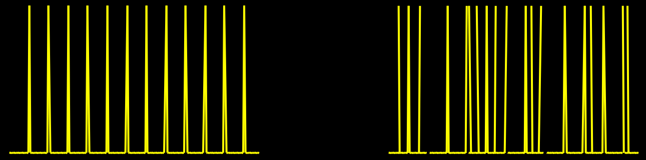
3. Frequency Encoding



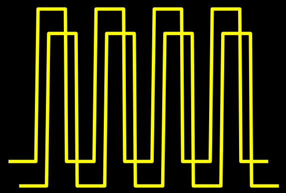
4. Phase Encoding



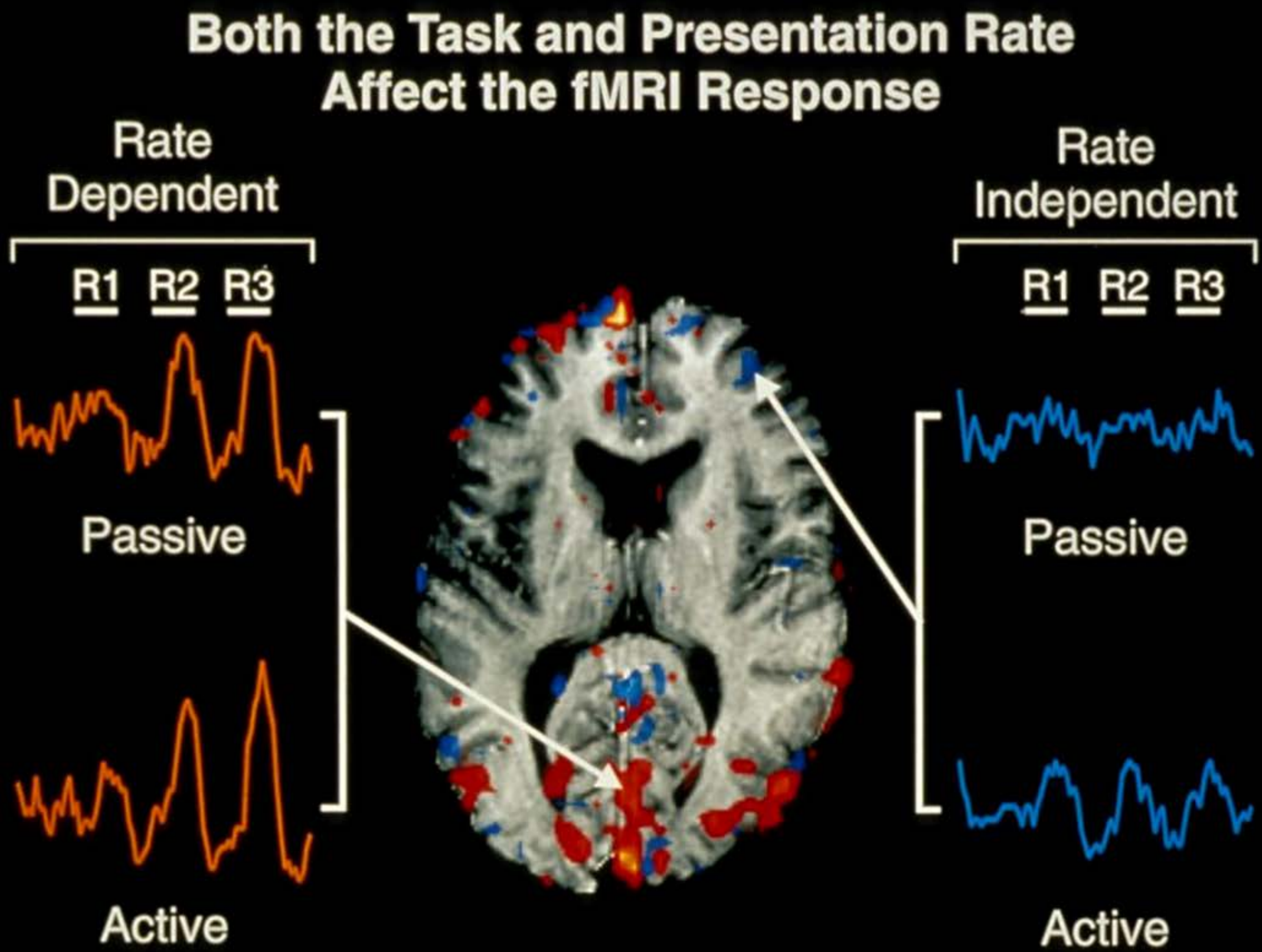
5. Event Related



6. Orthogonal Design



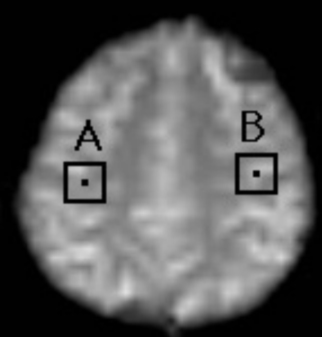
7. Free Behavior Design

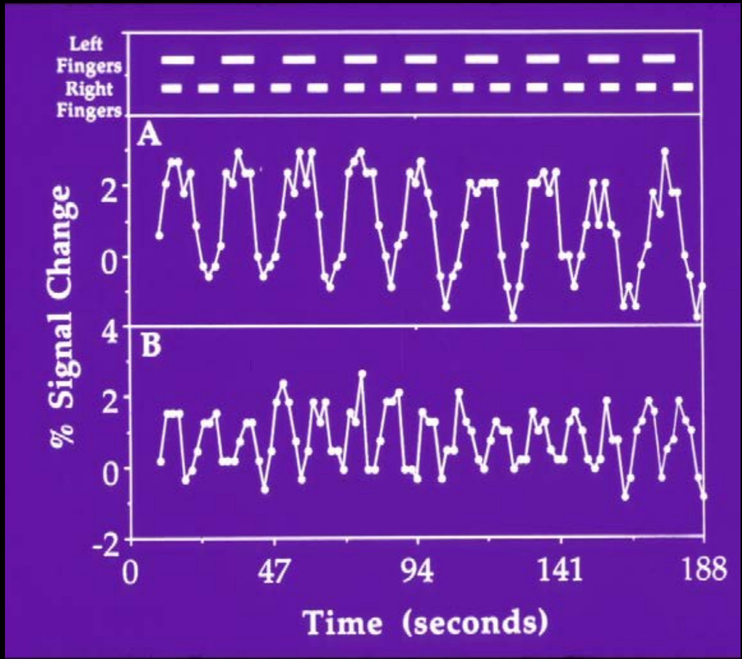


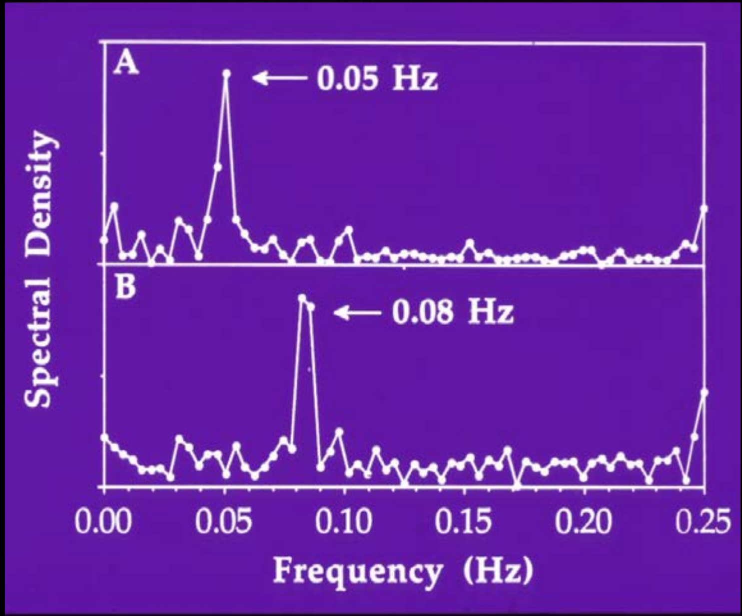
E. A. DeYoe, P. A. Bandettini, J. Nietz, D. Miller, P. Winas, Methods for functional magnetic resonance imaging (FMRI). *J. Neuroscience Methods* 54, 171-187 (1994).

Neuronal Activation Input Strategies

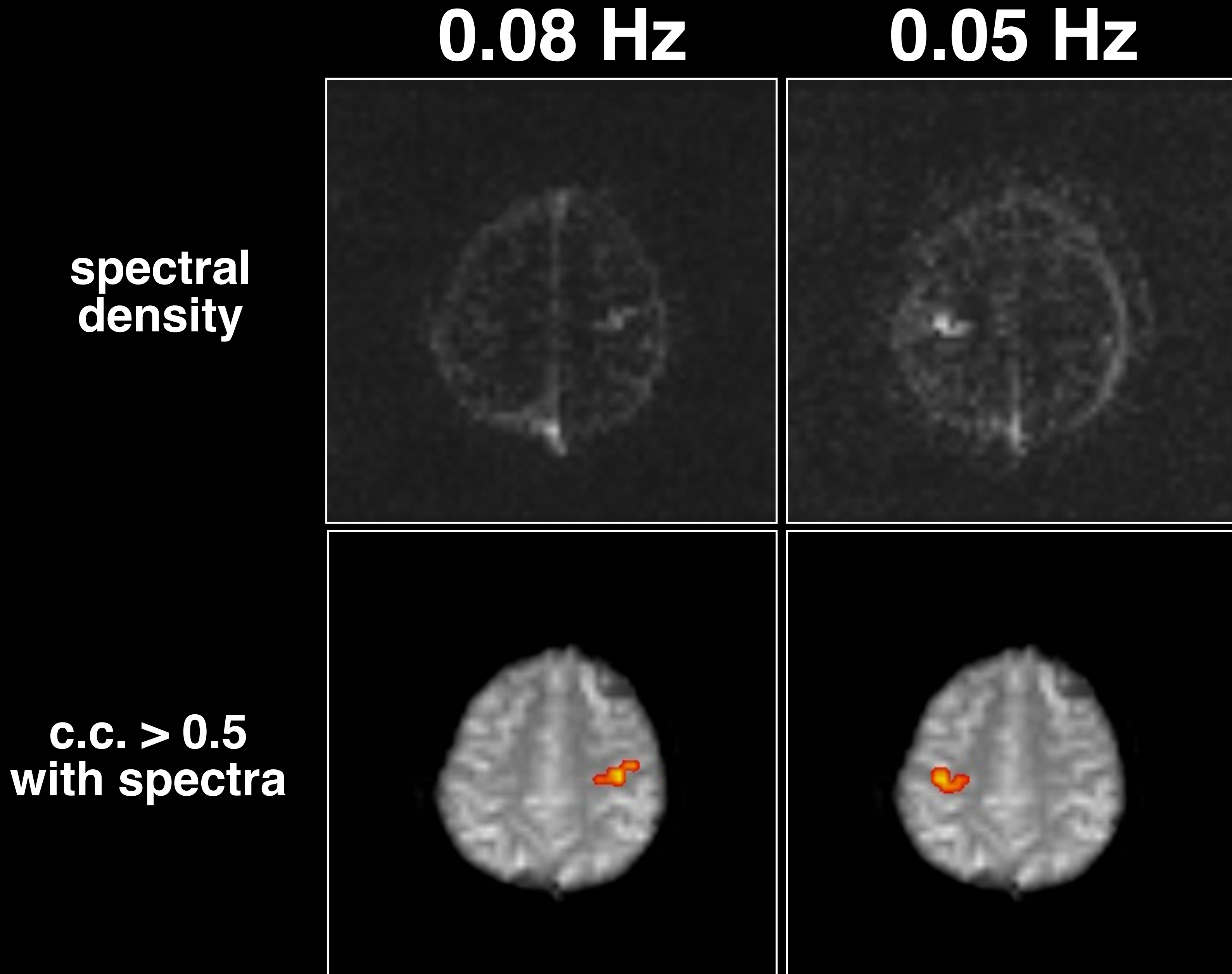
1. Block Design
2. Parametric Design
3. **Frequency Encoding**
4. Phase Encoding
5. Event Related
6. Orthogonal Design
7. Free Behavior Design







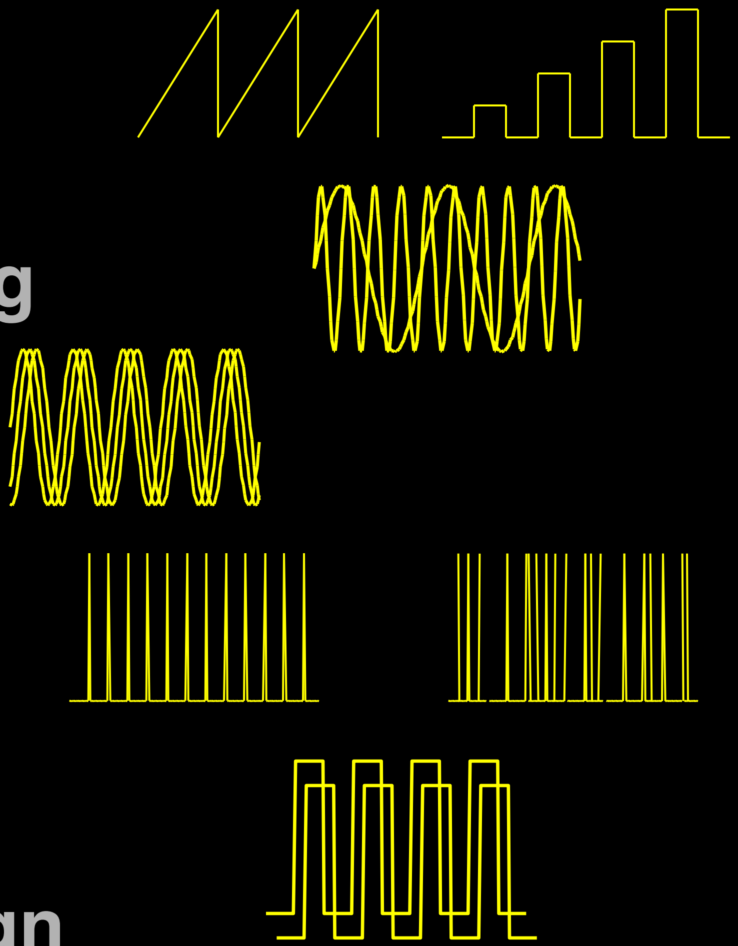
P. A. Bandettini, A. Jesmanowicz, E. C. Wong, J. S. Hyde, Processing strategies for time-course data sets in functional MRI of the human brain. *Magn. Reson. Med.* 30, 161-173 (1993).



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

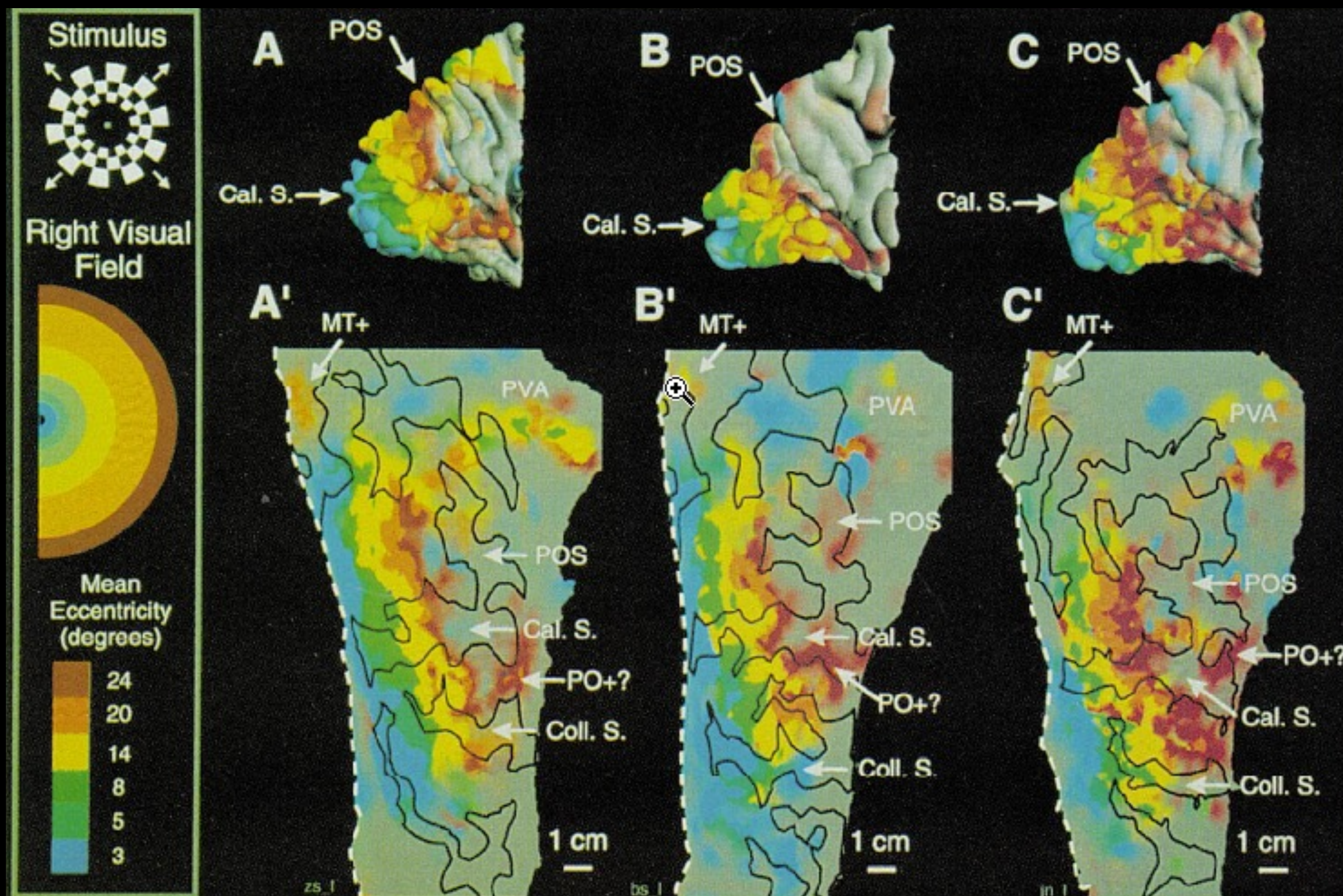
1. Block Design
2. Parametric Design
3. Frequency Encoding
4. **Phase Encoding**
5. Event Related
6. Orthogonal Design
7. Free Behavior Design

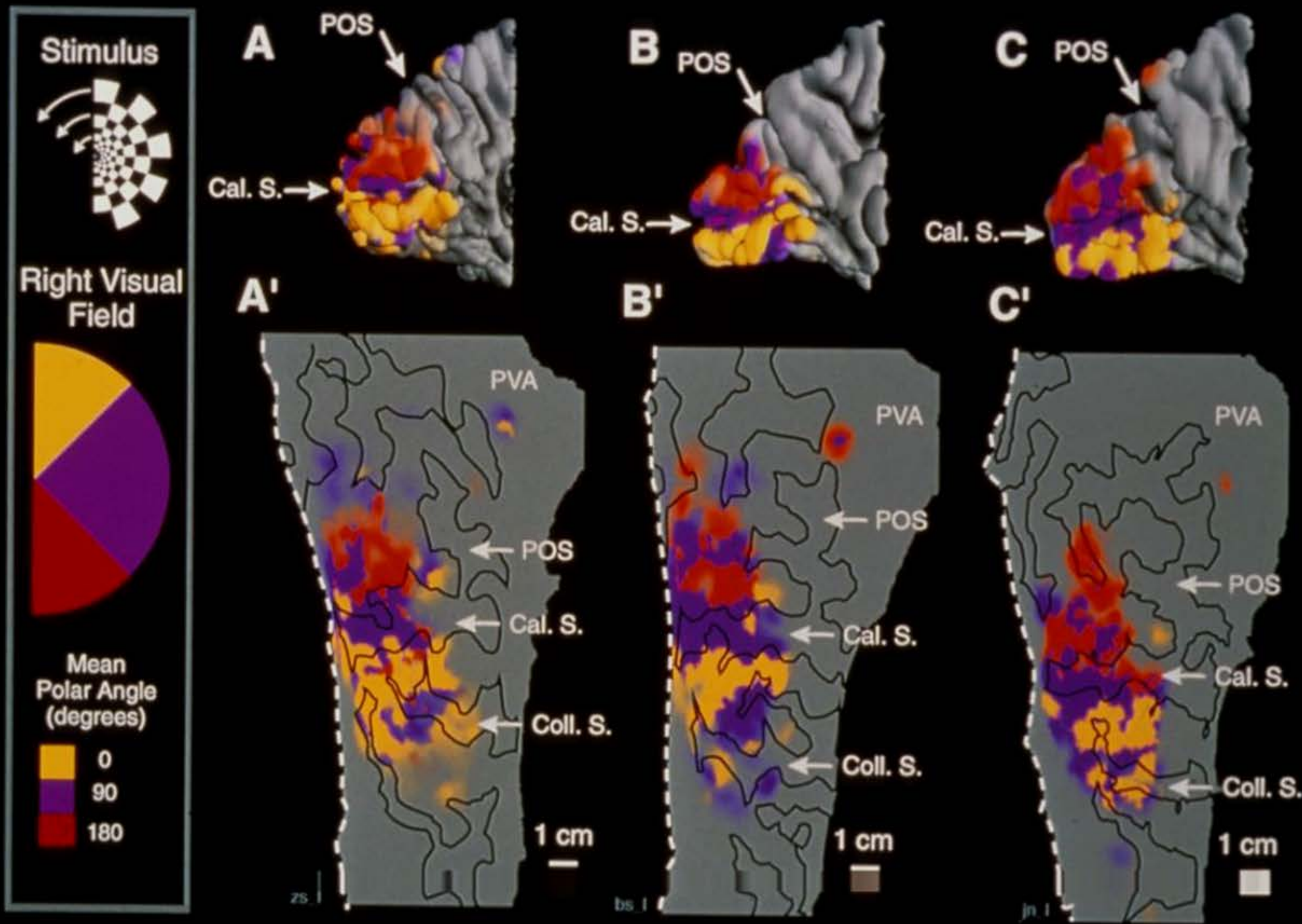


Proc. Natl. Acad. Sci. USA
Vol. 93, pp. 2382–2386, March 1996
Neurobiology

Mapping striate and extrastriate visual areas in human cerebral cortex

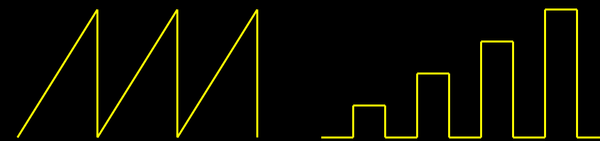
EDGAR A. DEYOE*, GEORGE J. CARMAN†, PETER BANDETTINI‡, SETH GLICKMAN*, JON WIESER*, ROBERT COX§, DAVID MILLER¶, AND JAY NEITZ*



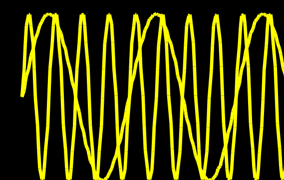

Stimulus
Right Visual Field
Mean Polar Angle (degrees)
0
90
180
A
POS
Cal. S.
B
POS
Cal. S.
C
POS
Cal. S.
A'
PVA
POS
Cal. S.
Coll. S.
1 cm
B'
PVA
POS
Cal. S.
Coll. S.
1 cm
C'
PVA
POS
Cal. S.
Coll. S.
1 cm

Neuronal Activation Input Strategies

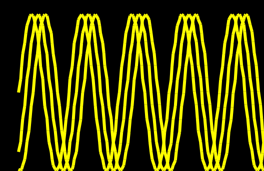
1. Block Design
2. Parametric Design



3. Frequency Encoding

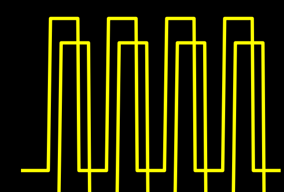


4. Phase Encoding



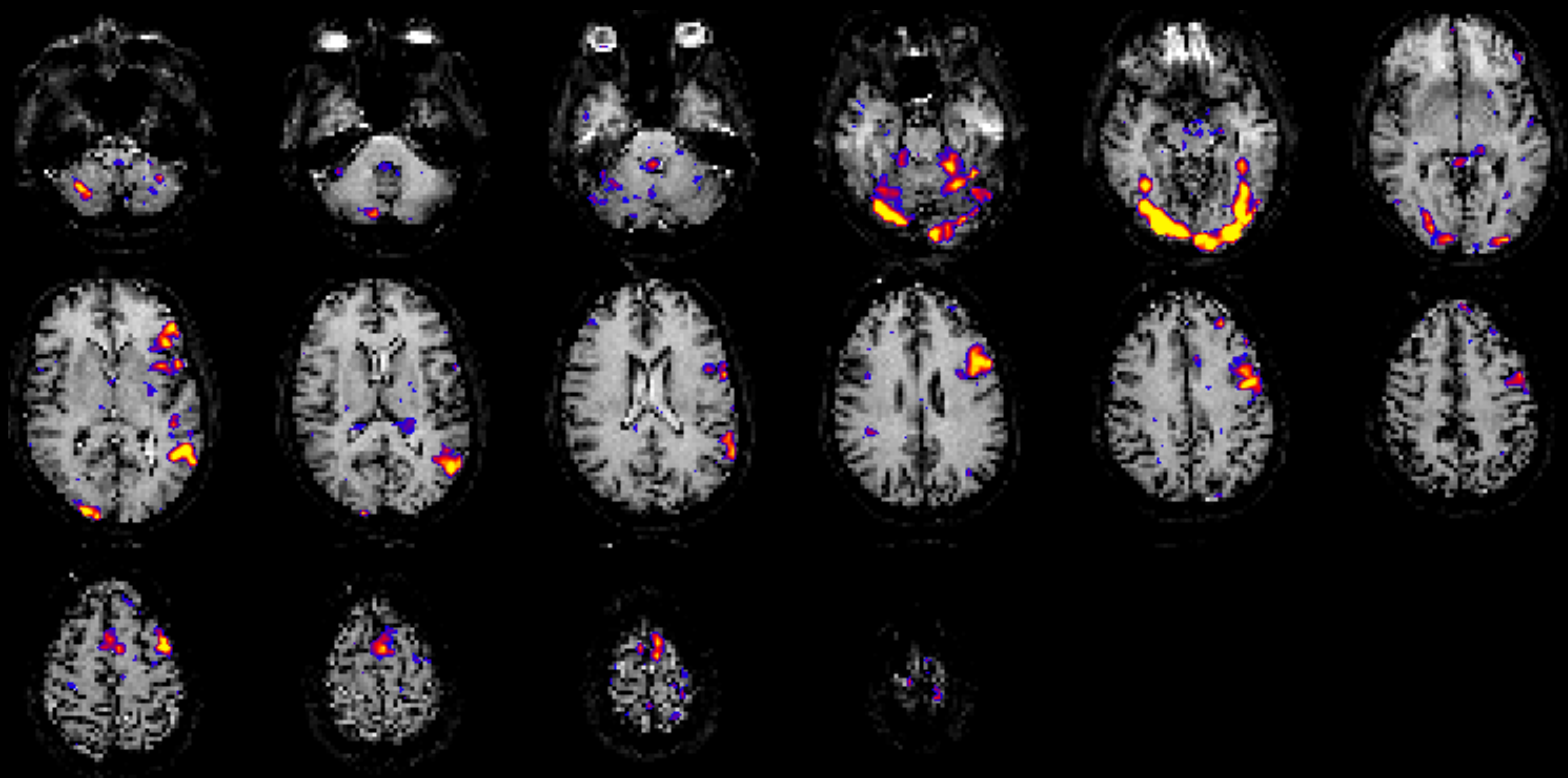
5. **Event Related**

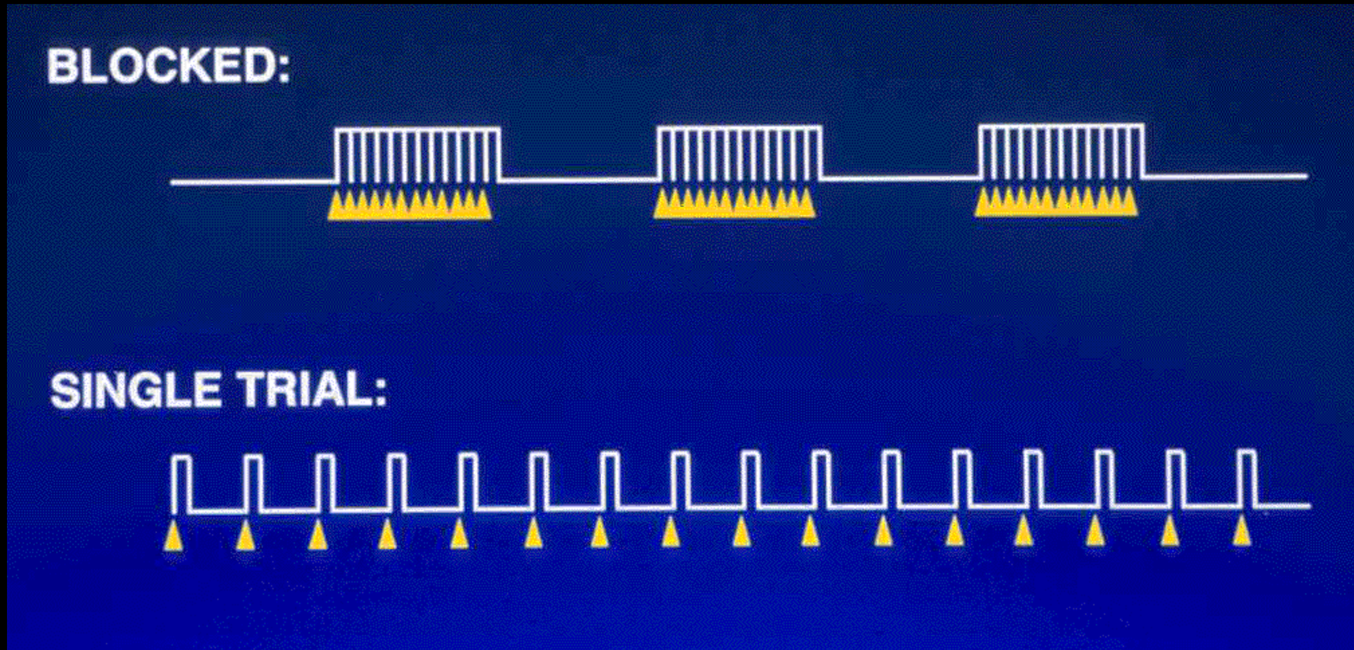
6. Orthogonal Design

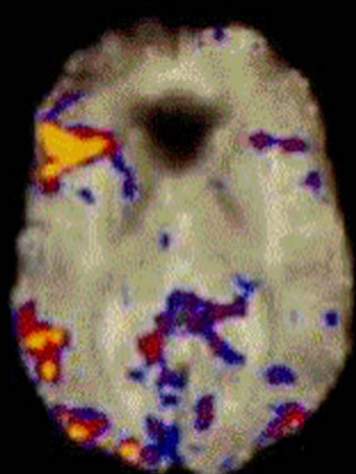


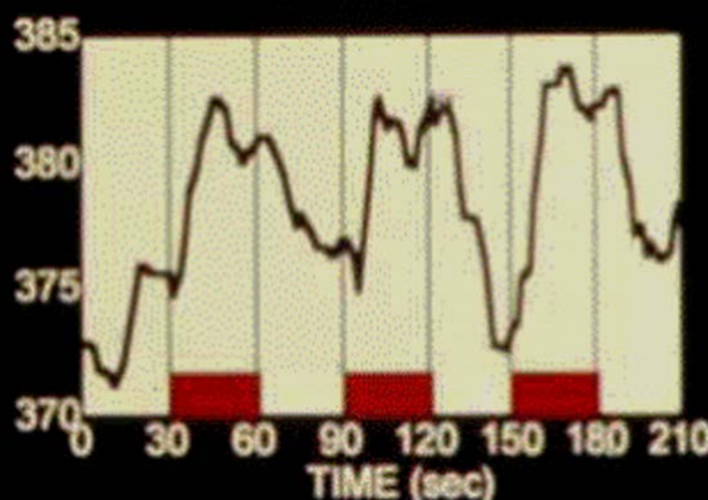
7. Free Behavior Design

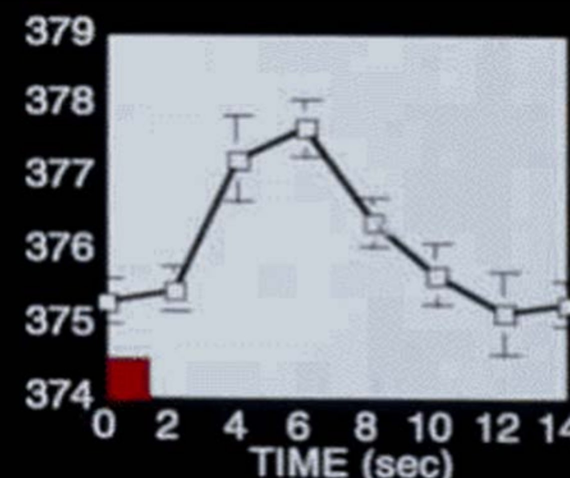
Word stem completion



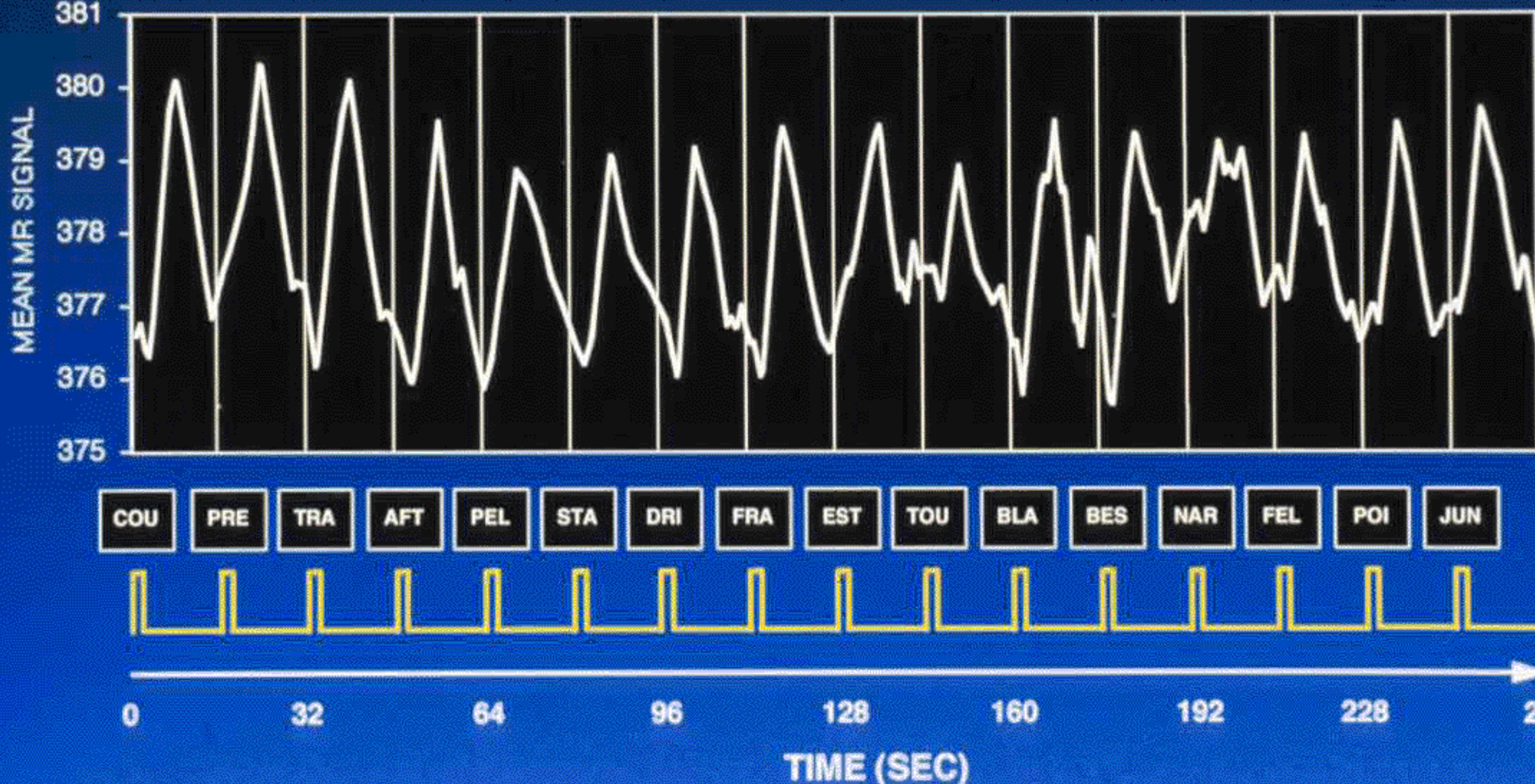

BLOCKED:
SINGLE TRIAL:




385
380
375
370
0
30
60
90
120
150
180
210
TIME (sec)


379
378
377
376
375
374
0
2
4
6
8
10
12
14
TIME (sec)

“Single-Trial” Response Across an Averaged Data Set

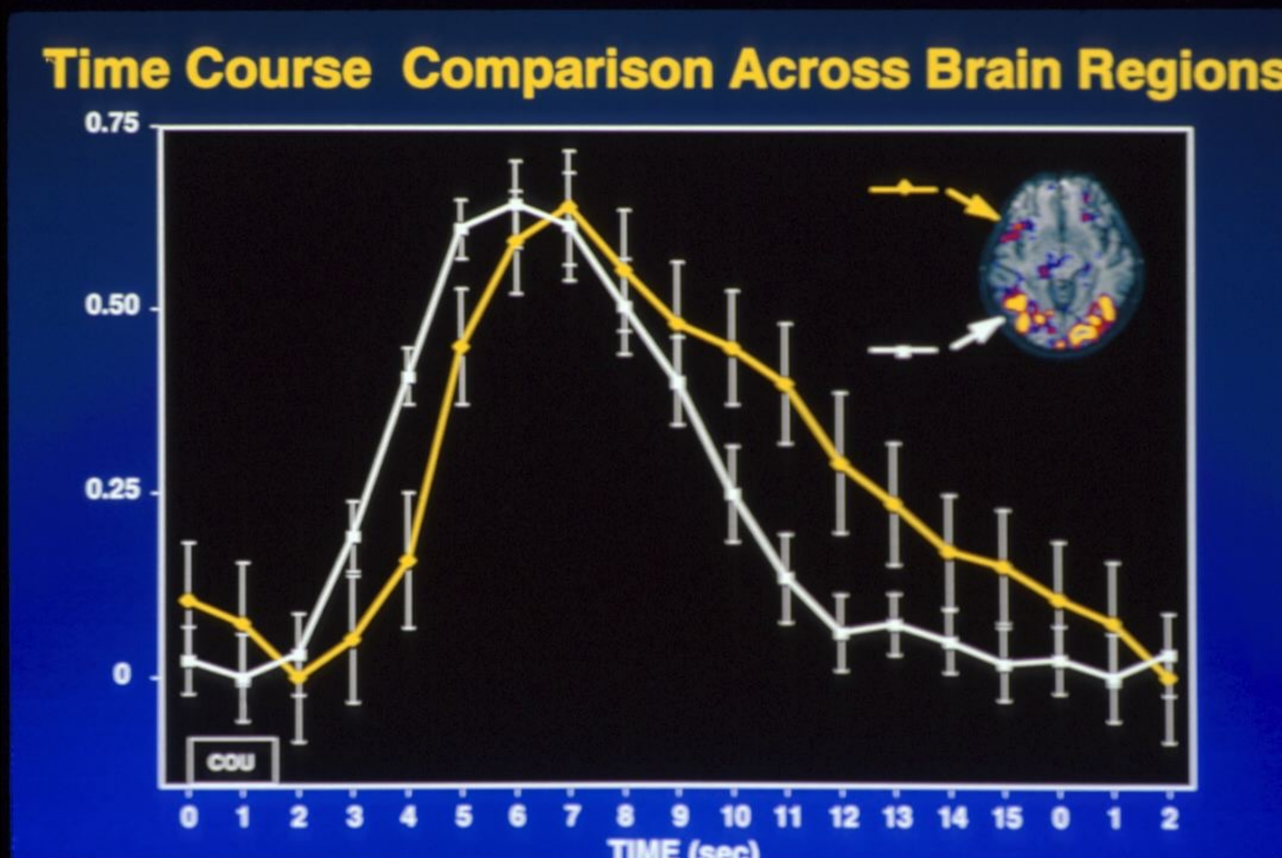


Proc. Natl. Acad. Sci. USA
Vol. 93, pp. 14878–14883, December 1996
Neurobiology

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

(neuroimaging/single trial/language/prefrontal)

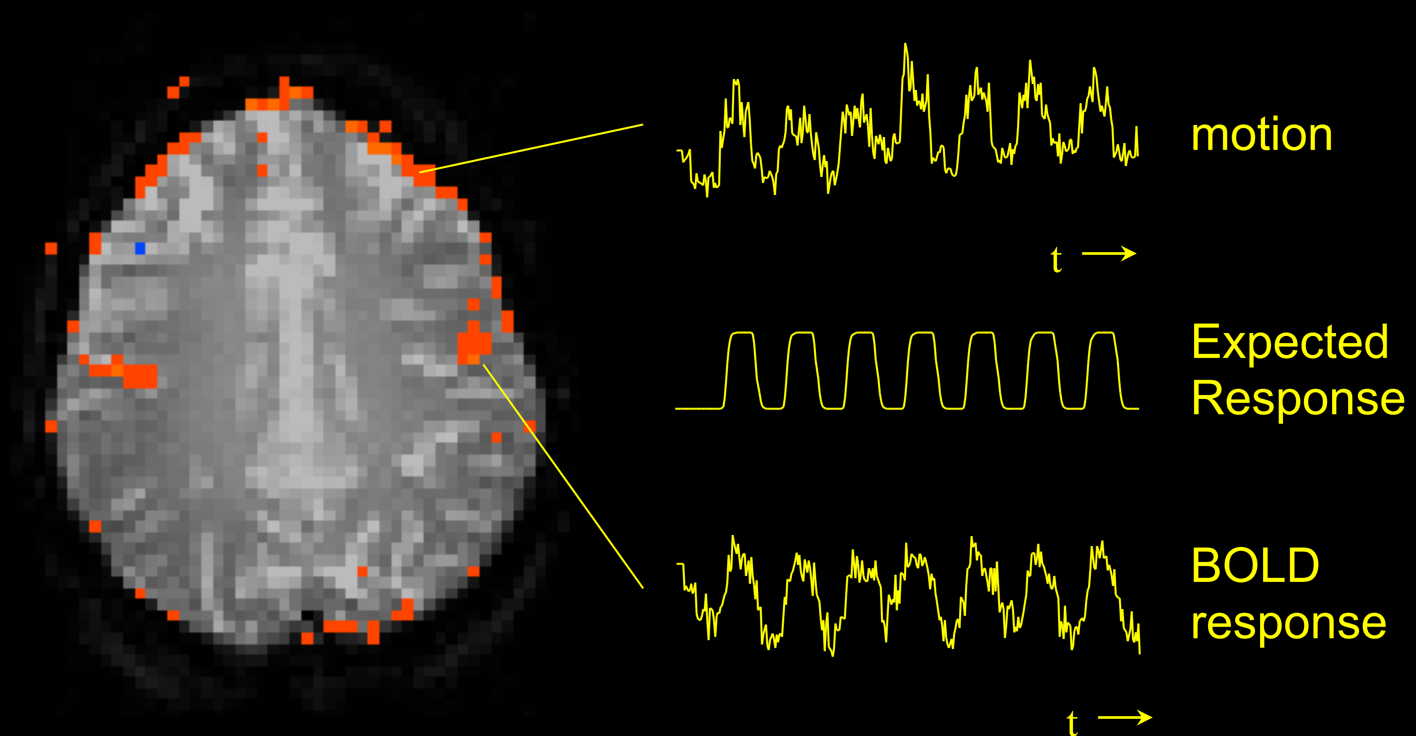
RANDY L. BUCKNER[†‡§¶], PETER A. BANDETTINI[†‡], KATHLEEN M. O'CRAVEN[†‖], ROBERT L. SAVOY[†‖],
STEVEN E. PETERSEN[**††], MARCUS E. RAICHLE[§**††], AND BRUCE R. ROSEN[†‡]



Event Related Advantages

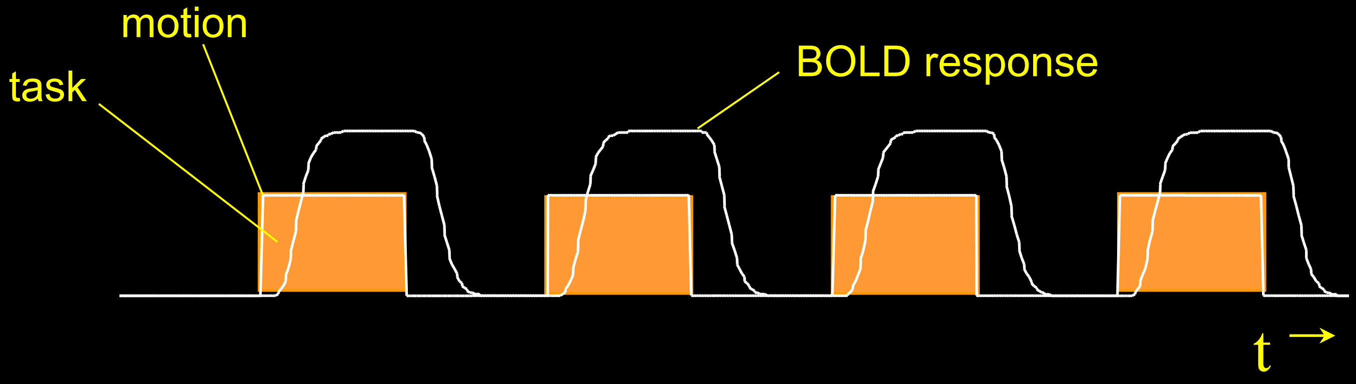
- Task Randomization
- Post acquisition, Performance-based, data binning
- Natural presentation
- Reduction of habituation effects
- Overt responses
- Reduction of scanner noise effects
- More precise estimation of hemodynamic respons

Speaking - Blocked Trial

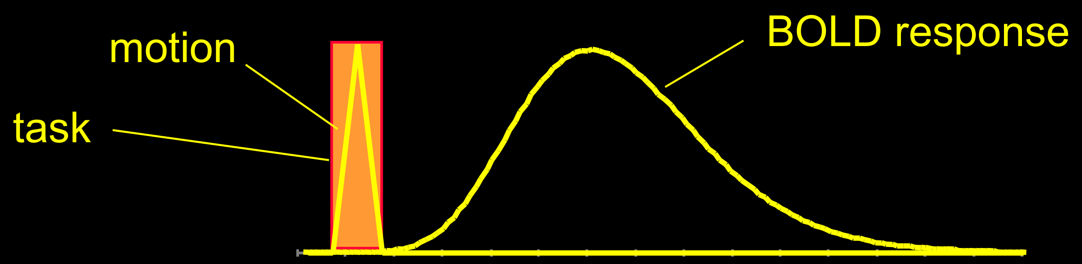


fMRI during tasks that involve brief motion

Blocked Design

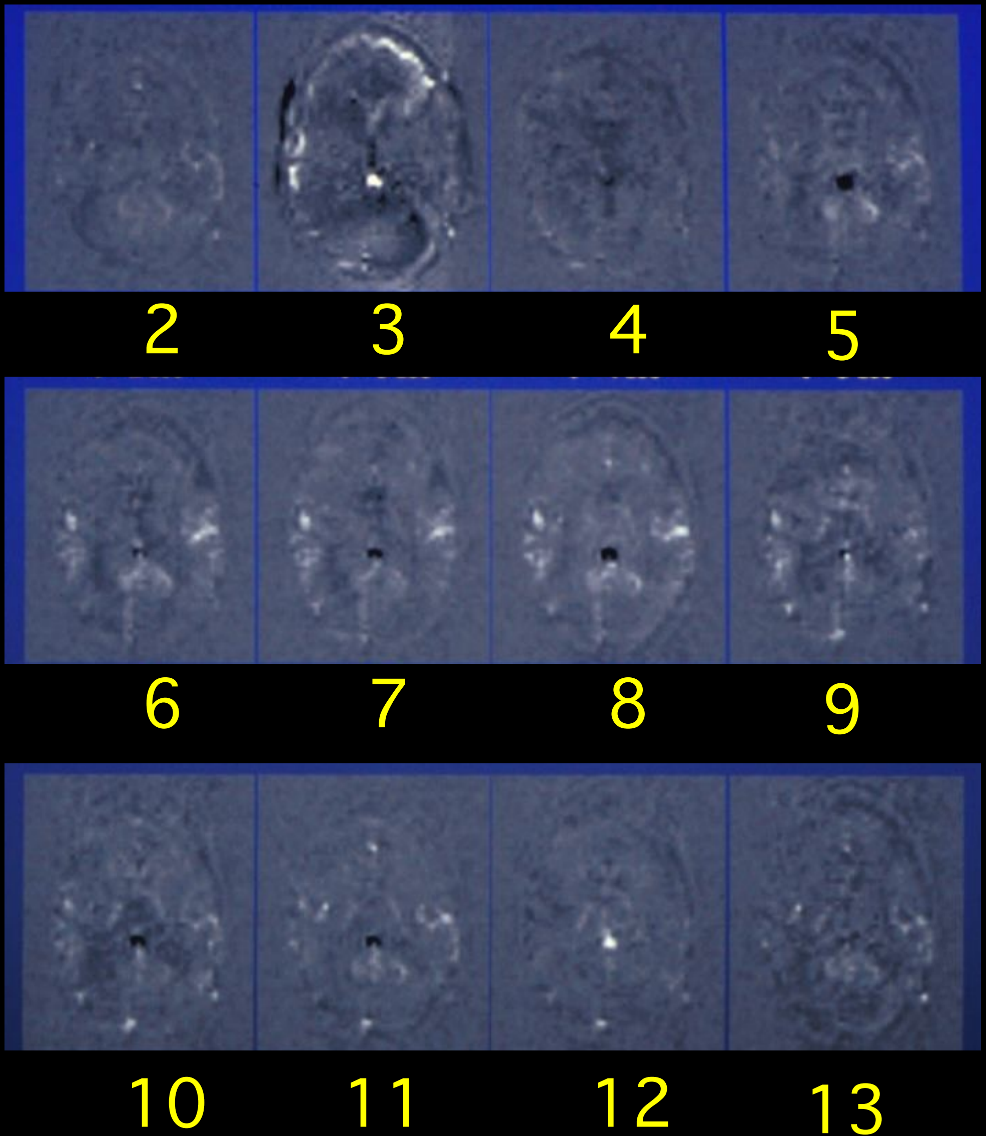


Event-Related Design



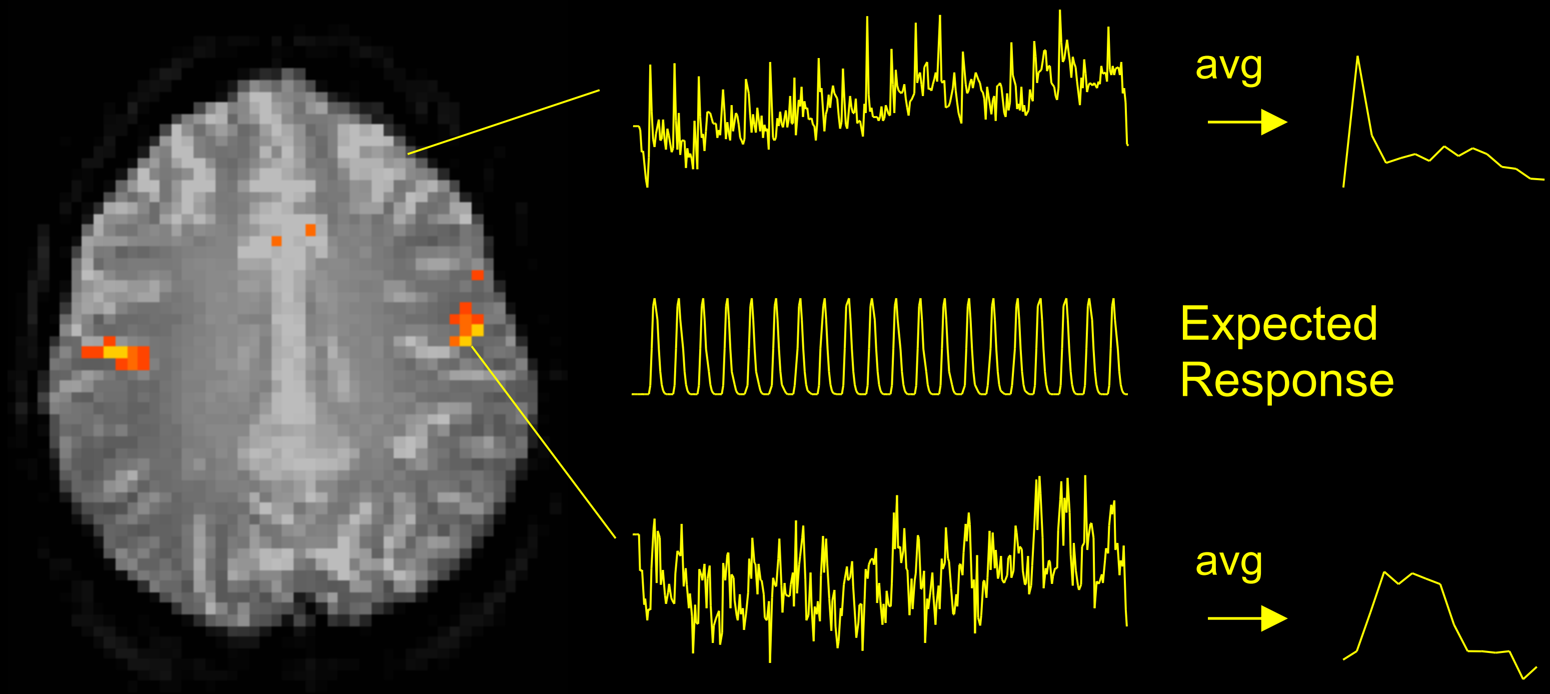
R. M. Birn, P. A. Bandettini, R. W. Cox, R. Shaker, Event - related fMRI of tasks involving brief motion. *Human Brain Mapping* 7: 106-114 (1999).

Overt Word Production



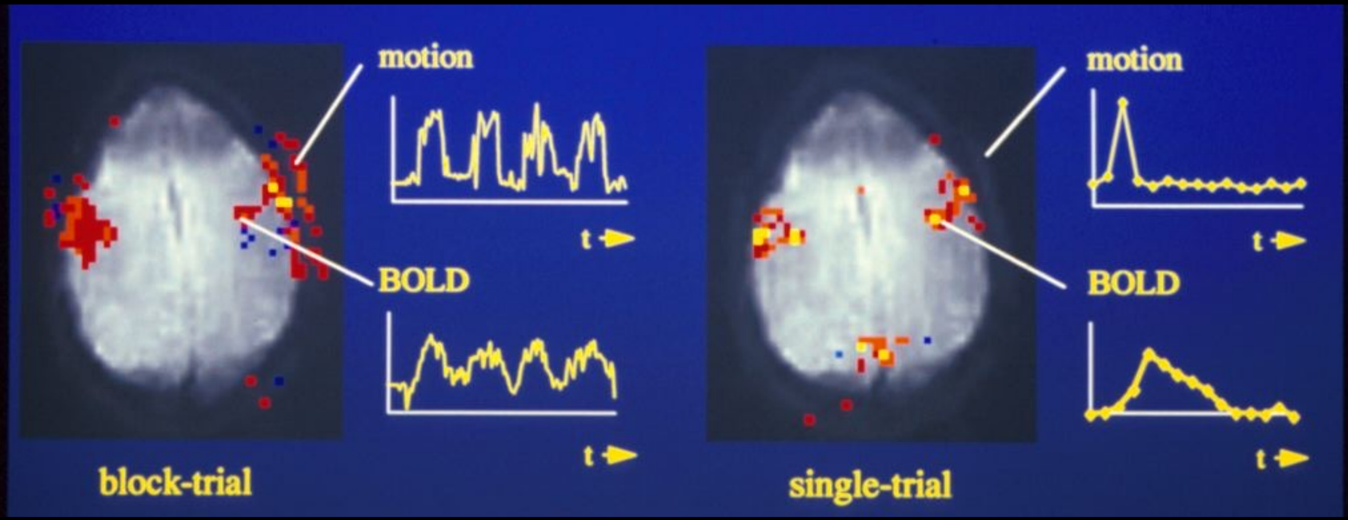
R. M. Birn, P. A. Bandettini, R. W. Cox, R. Shaker, Event - related fMRI of tasks involving brief motion. *Human Brain Mapping* 7: 106-114 (1999).

Speaking - ER-fMRI

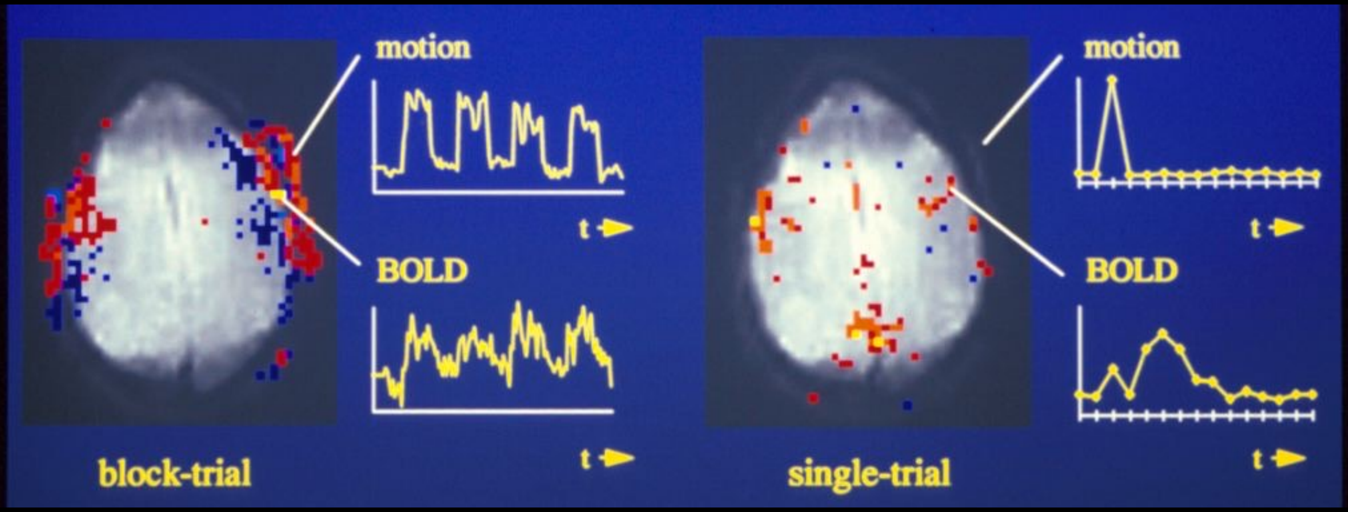


R. M. Birn, P. A. Bandettini, R. W. Cox, R. Shaker, Event - related fMRI of tasks involving brief motion. *Human Brain Mapping* 7: 106-114 (1999).

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)

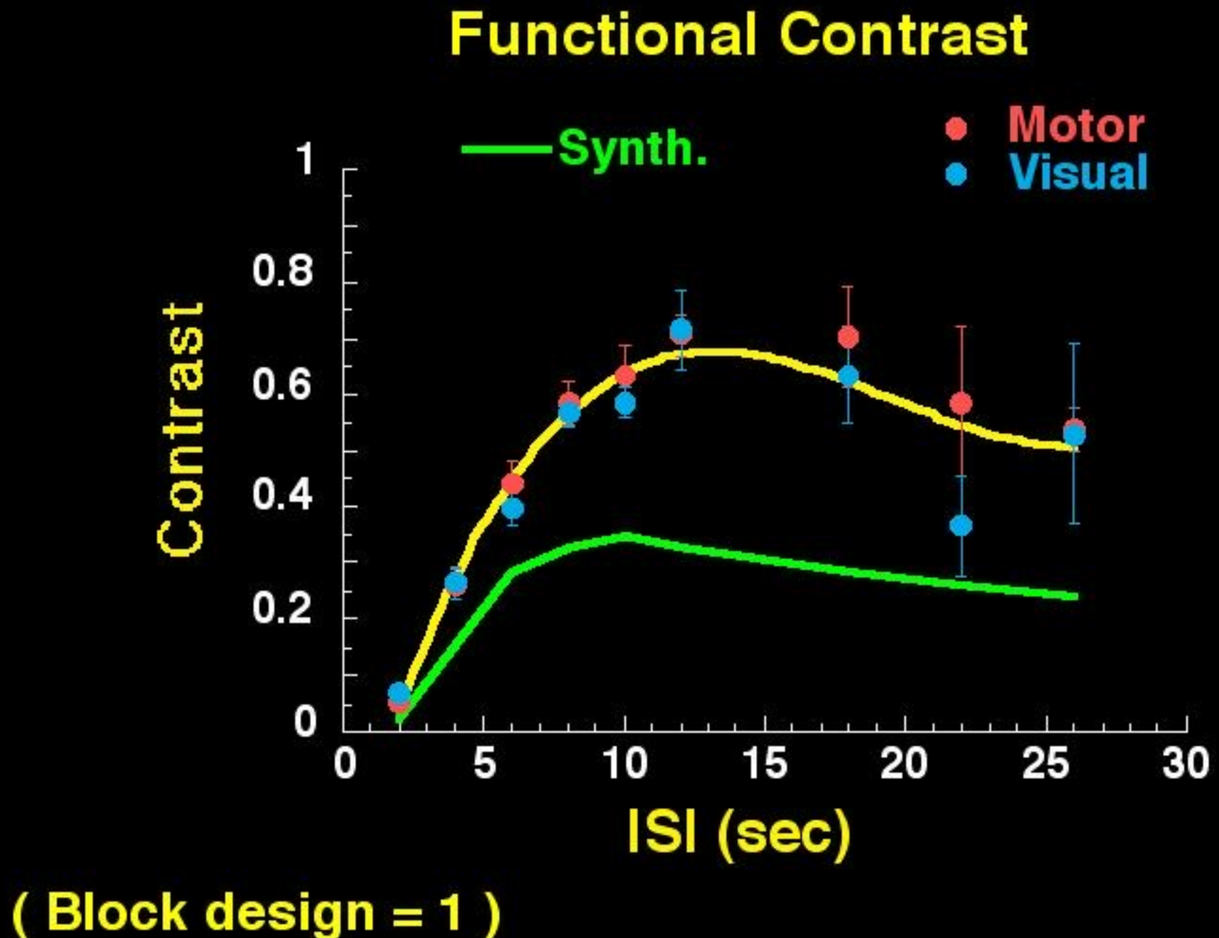
Suppress?
- Flatten image contrast
- Physical restraint
- Averaging, smoothing

Visual Cortex

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

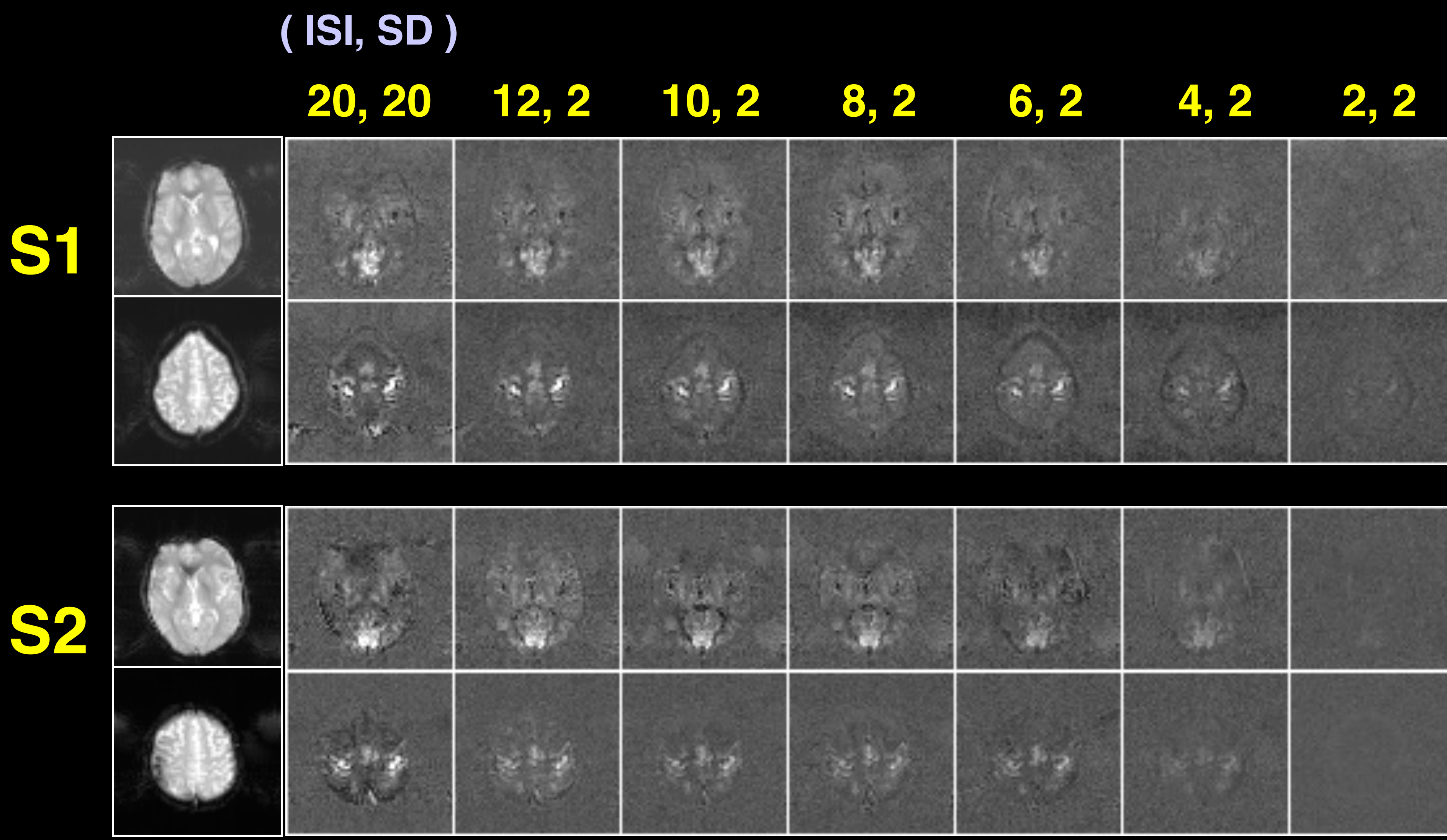
Motor Cortex

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



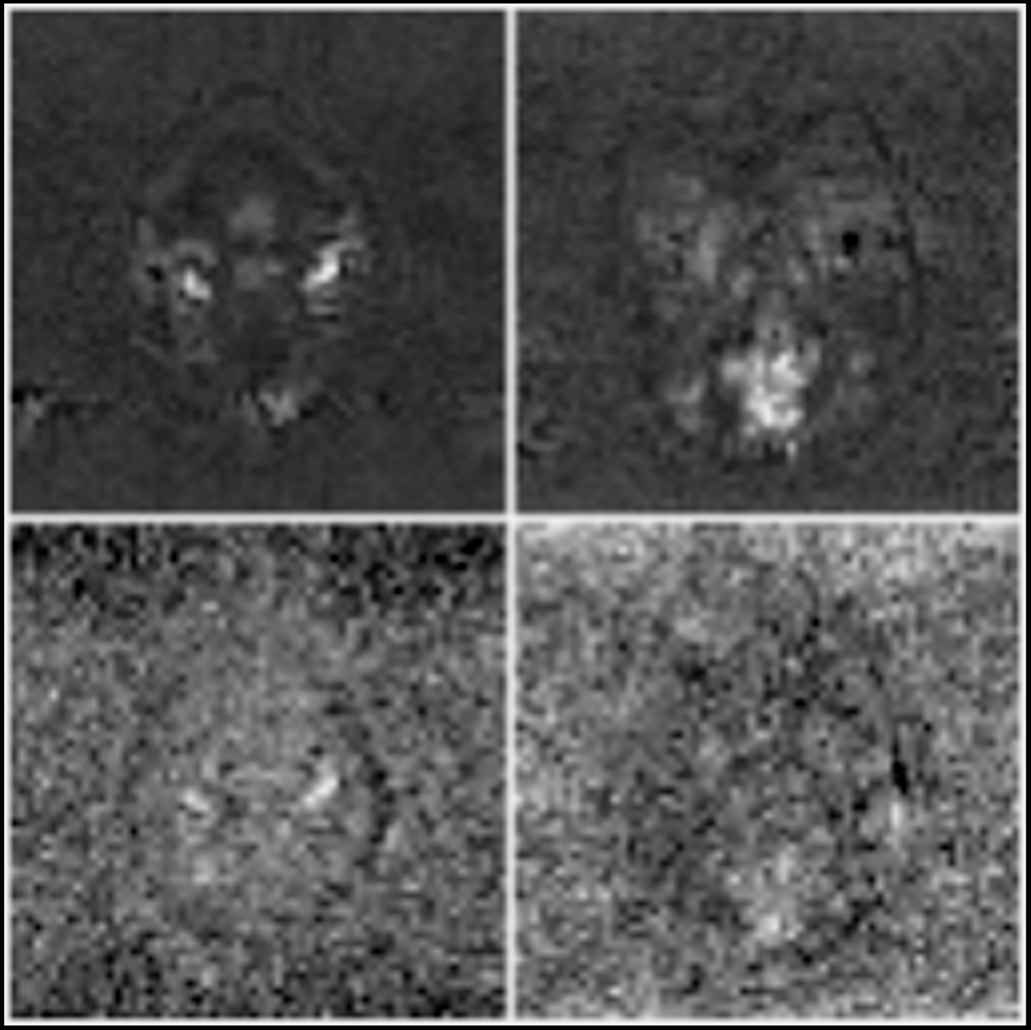
P. A. Bandettini, R. W. Cox. Functional contrast in constant interstimulus interval event - related fMRI: theory and experiment. *Magn. Reson. Med.* 43: 540-548 (2000).

Motor Visual

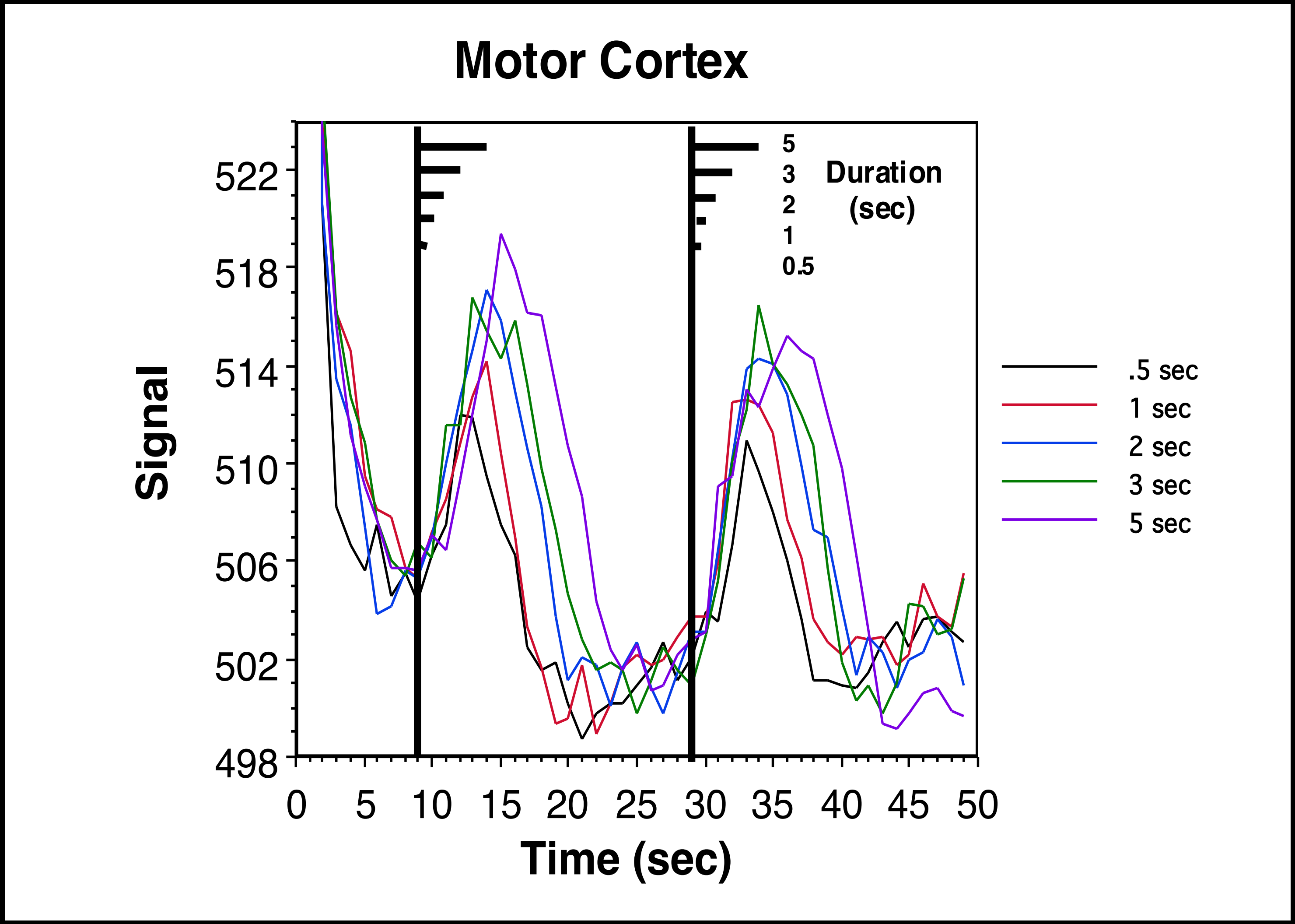
(ISI, SD)

20, 20

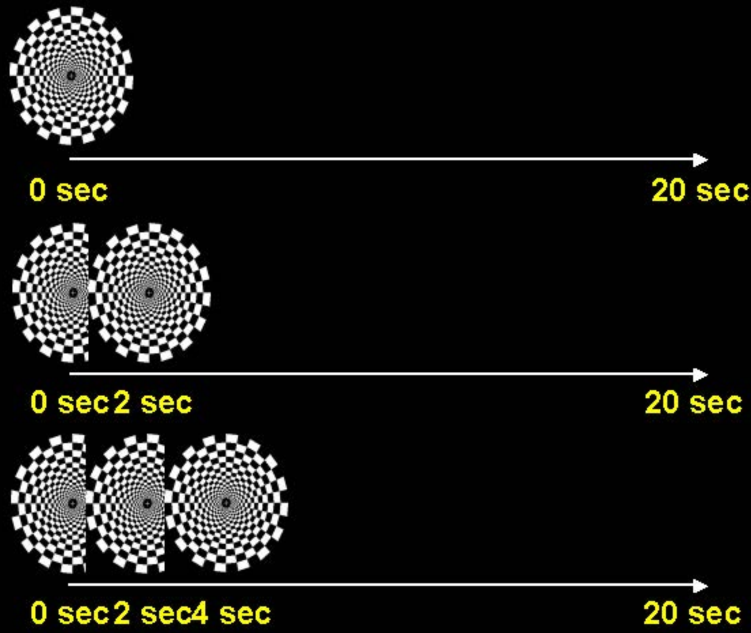
2, 2



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).

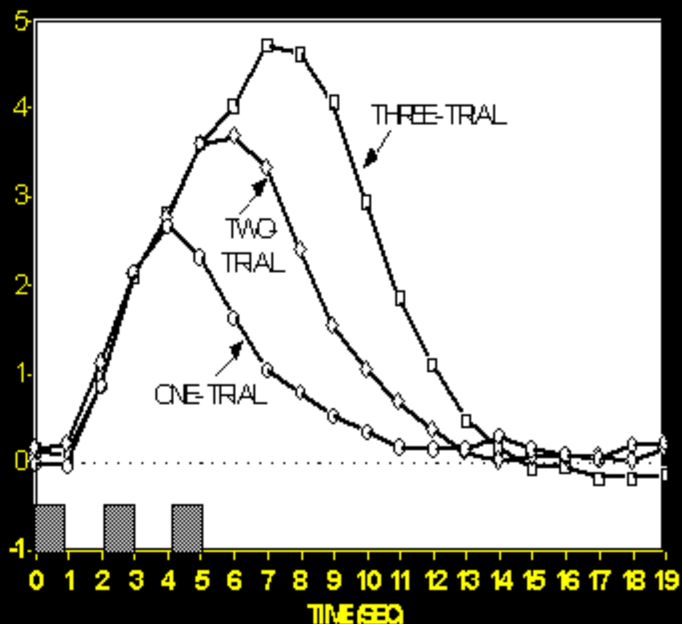



• Human Brain Mapping 5:329–340(1997) •

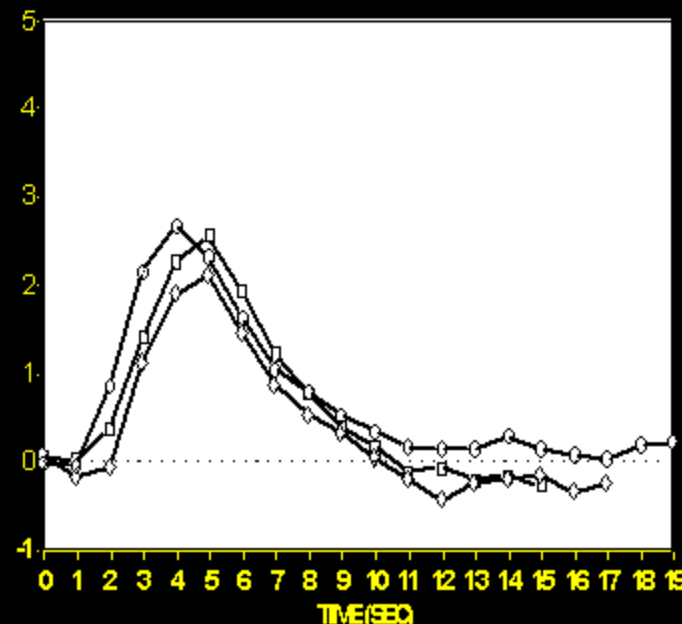
Selective Averaging of Rapidly Presented Individual Trials Using fMRI

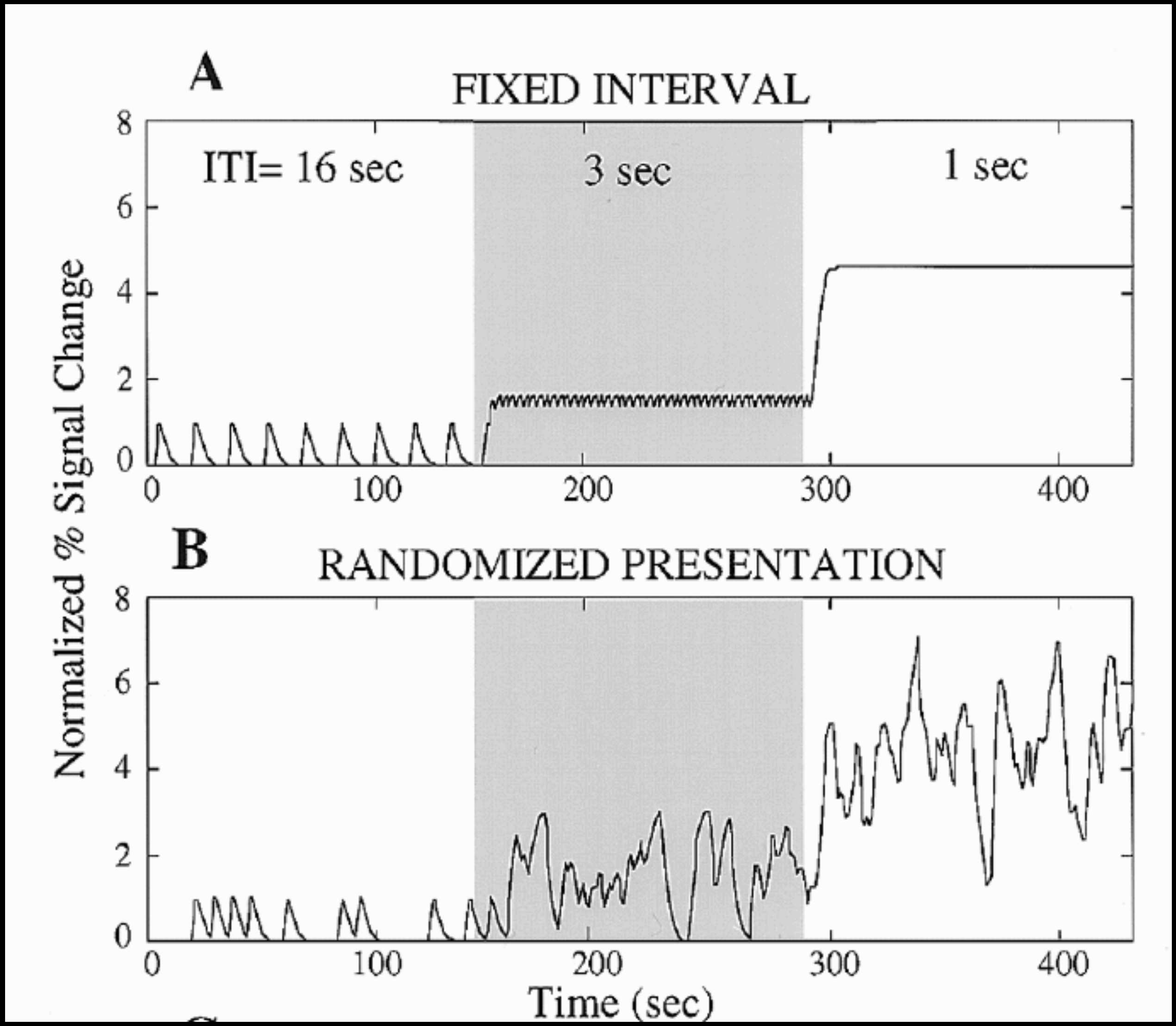
Anders M. Dale* and Randy L. Buckner

RAW DATA



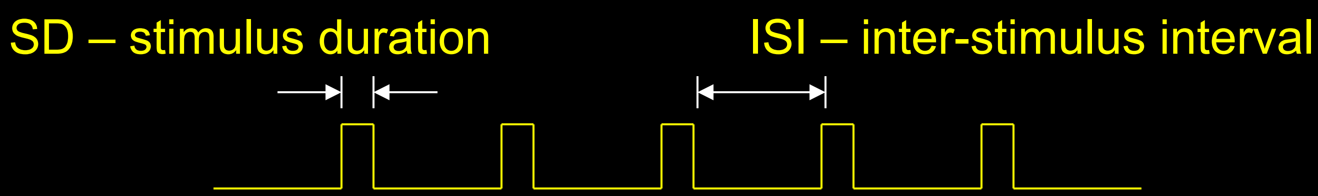
ESTIMATED RESPONSES

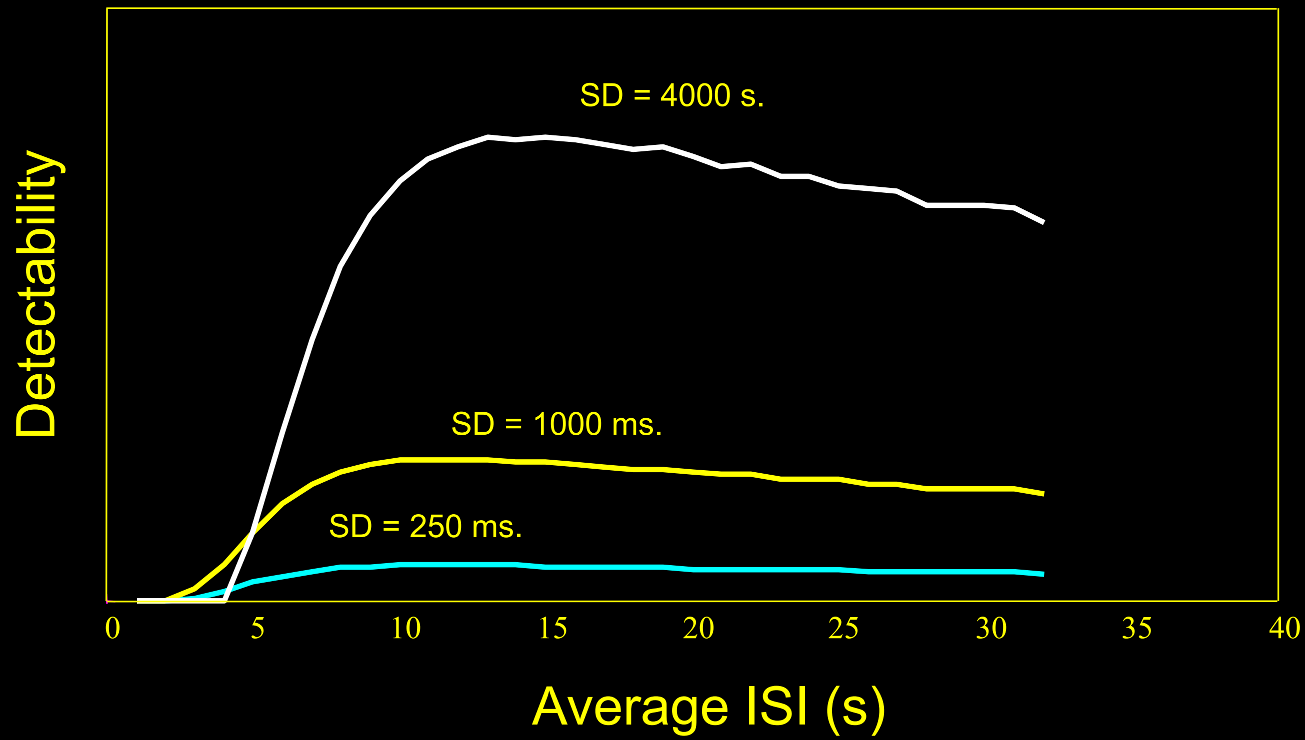




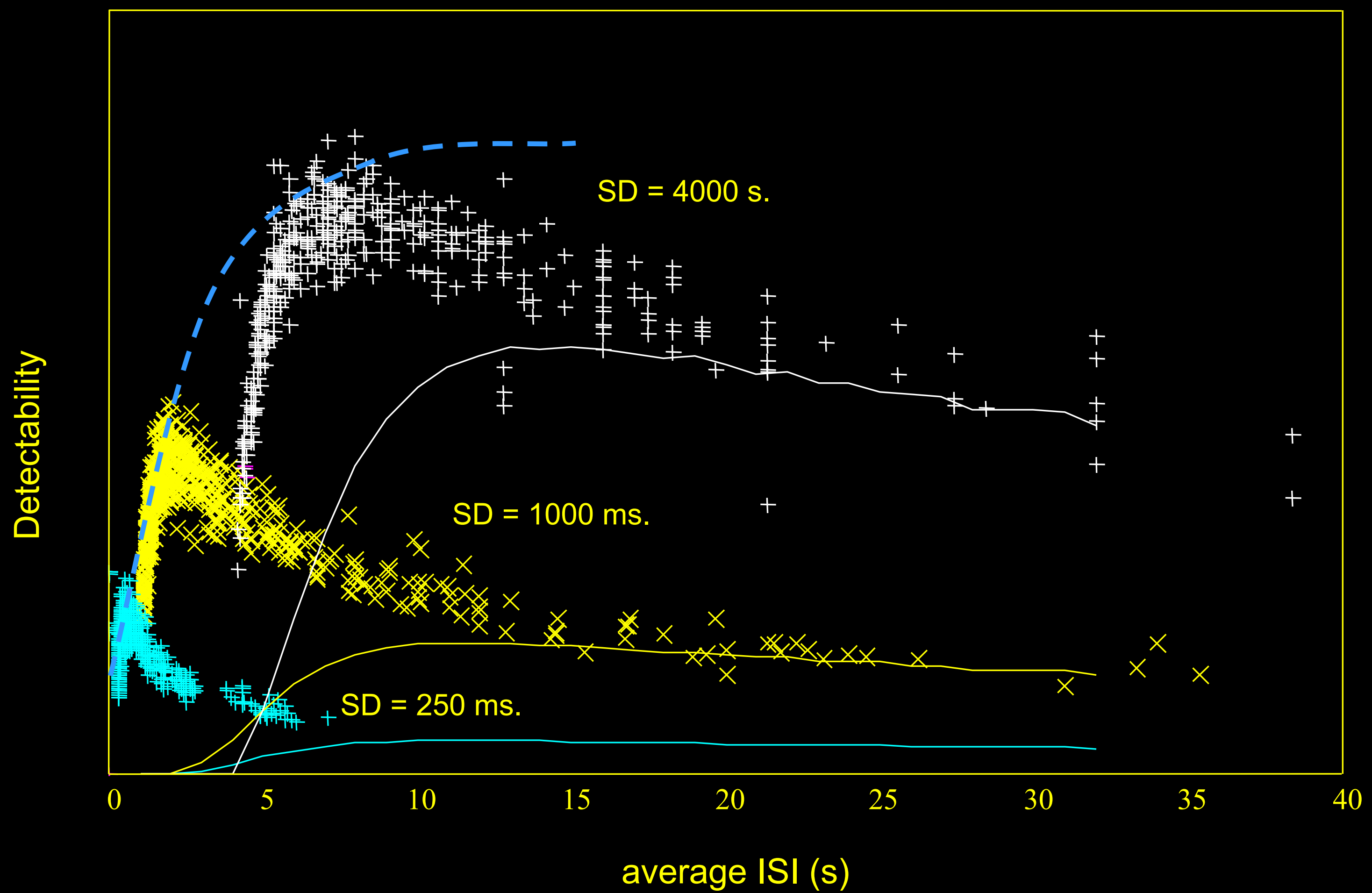
M.A. Burock et al. *NeuroReport*, 9, 3735-9 (1998)

Detectability – constant ISI



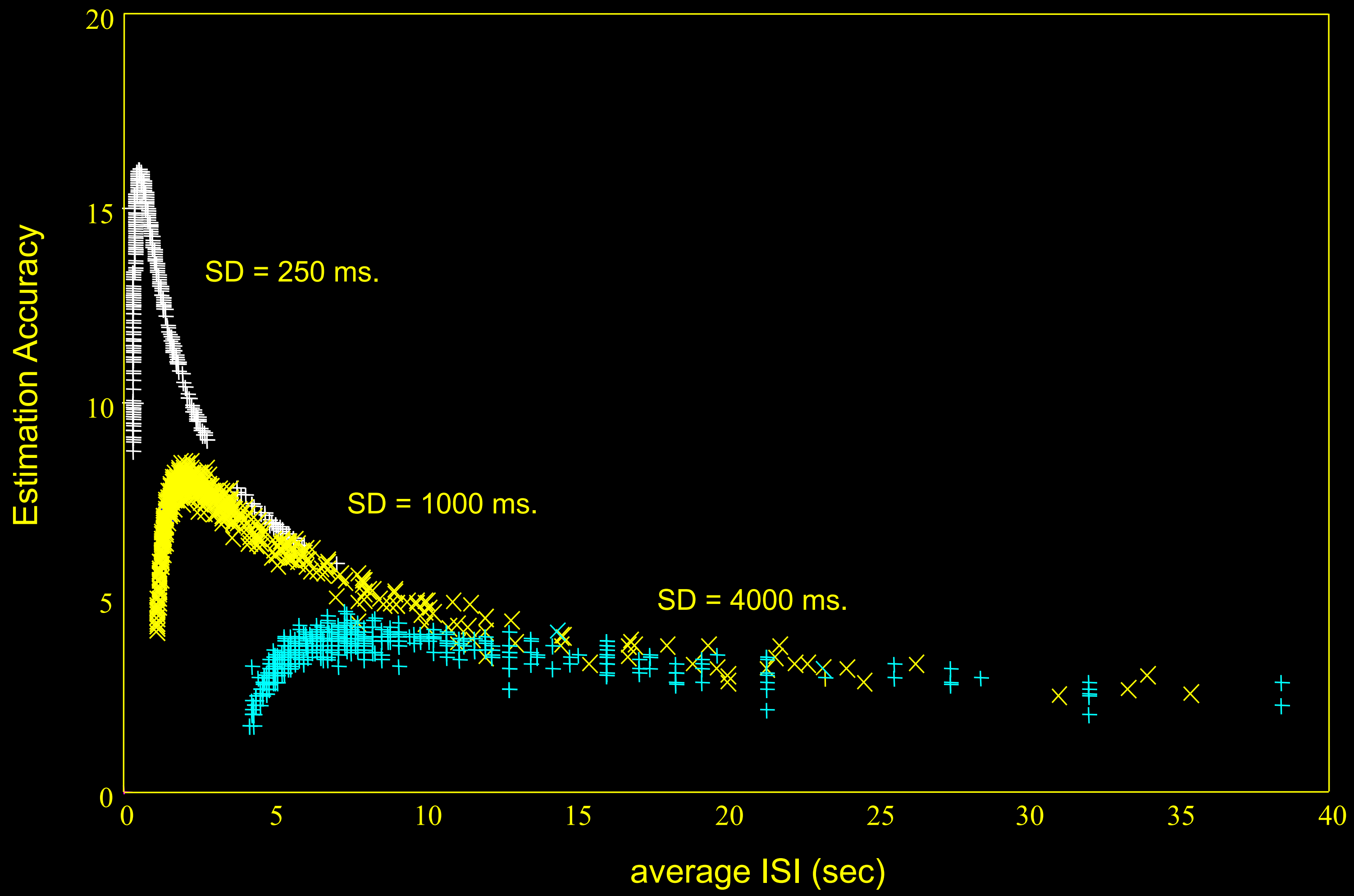


Detectability vs. Average ISI



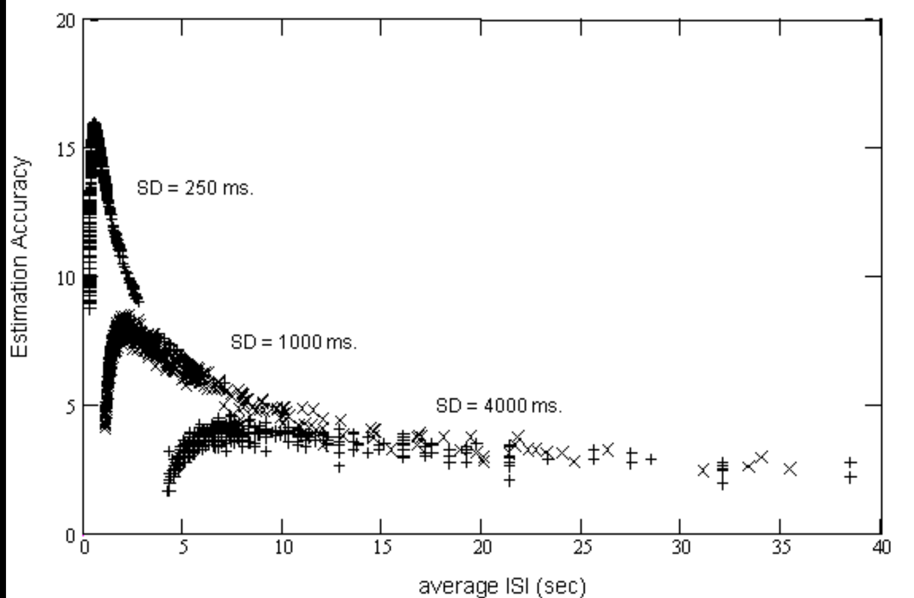
R. M. Birn, R. W. Cox, P. A. Bandettini, Detection versus estimation in Event-Related fMRI: choosing the optimal stimulus timing. *NeuroImage* 15: 262-264, (2002).

Estimation accuracy vs. average ISI

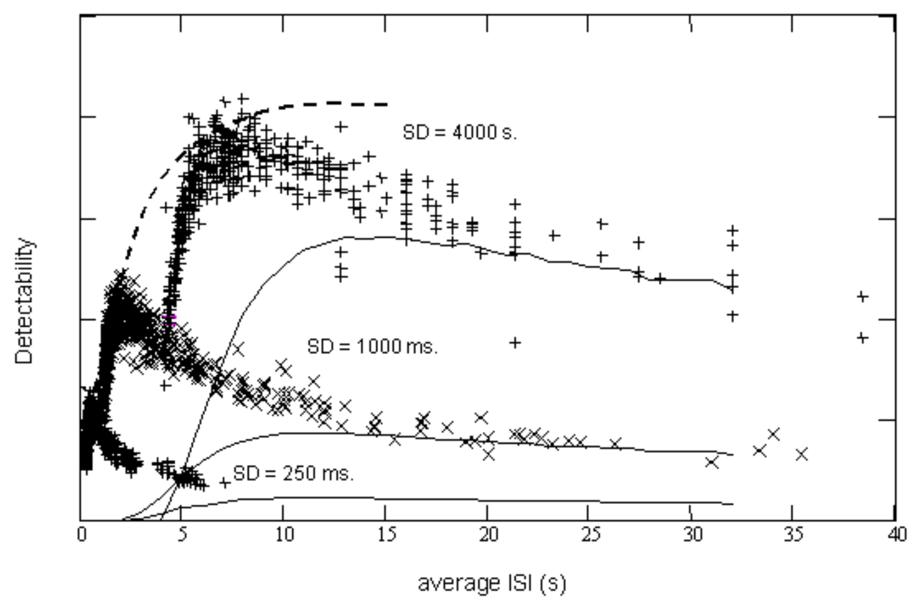


R. M. Birn, R. W. Cox, P. A. Bandettini, Detection versus estimation in Event-Related fMRI: choosing the optimal stimulus timing. *NeuroImage* 15: 262-264, (2002).

Estimation accuracy vs. average ISI

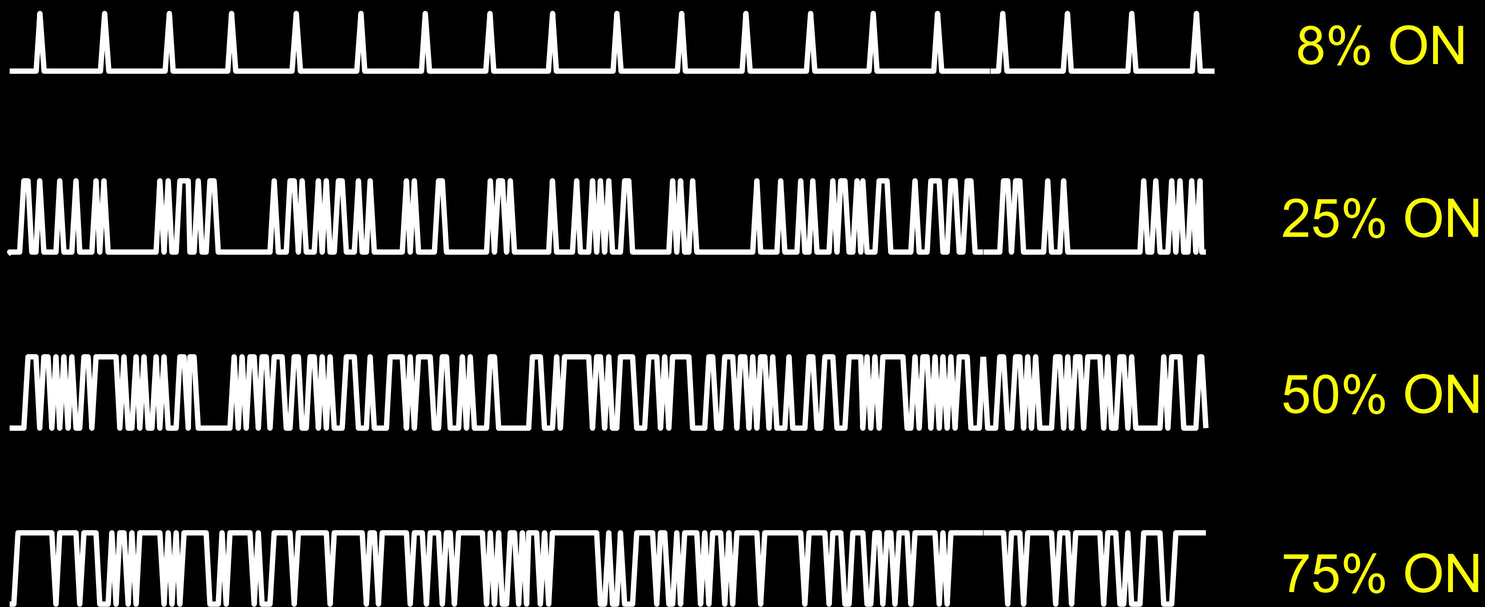


Detectability vs. Average ISI

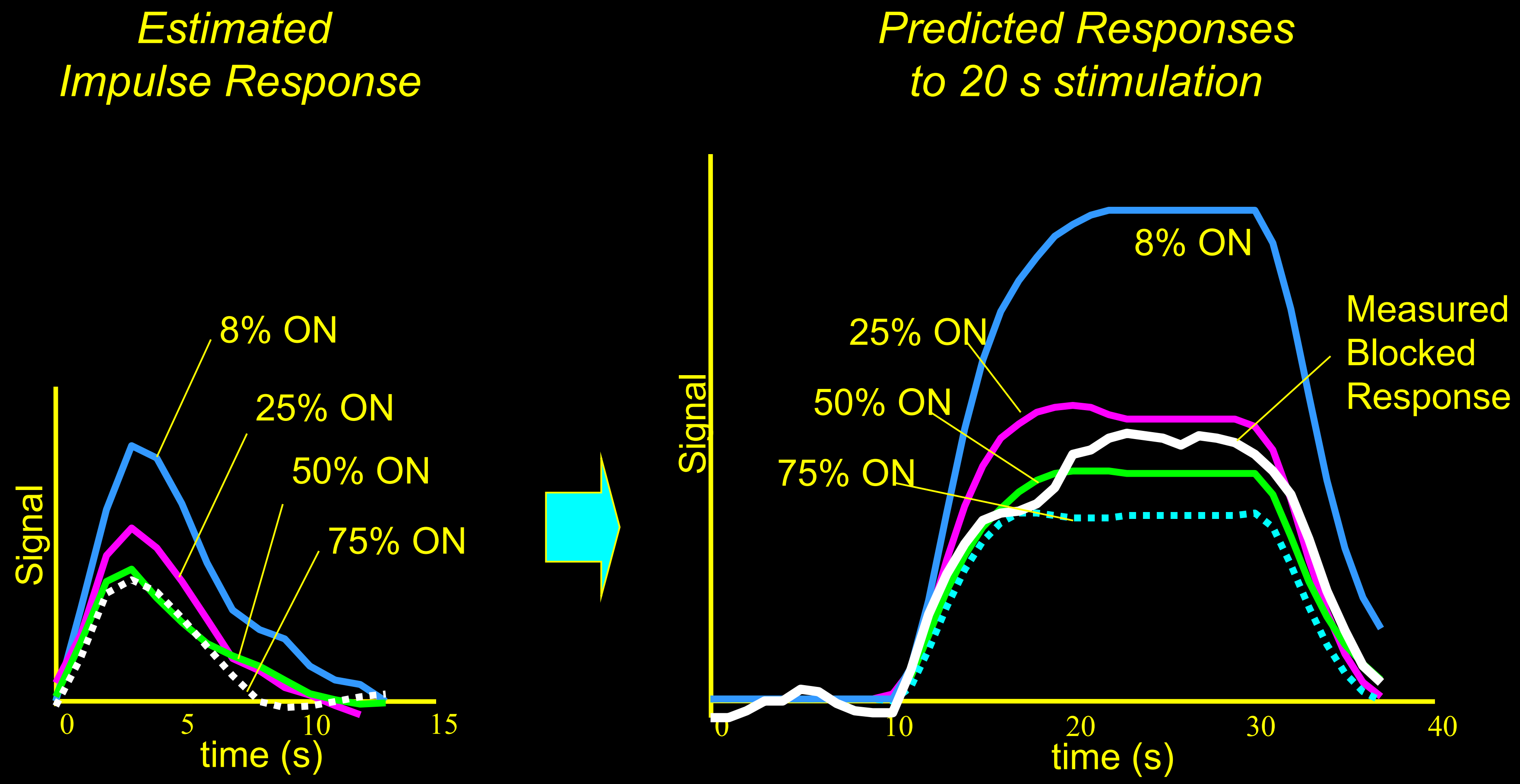


Varying "ON" and "OFF" periods

- *Rapid event-related design with varying ISI*

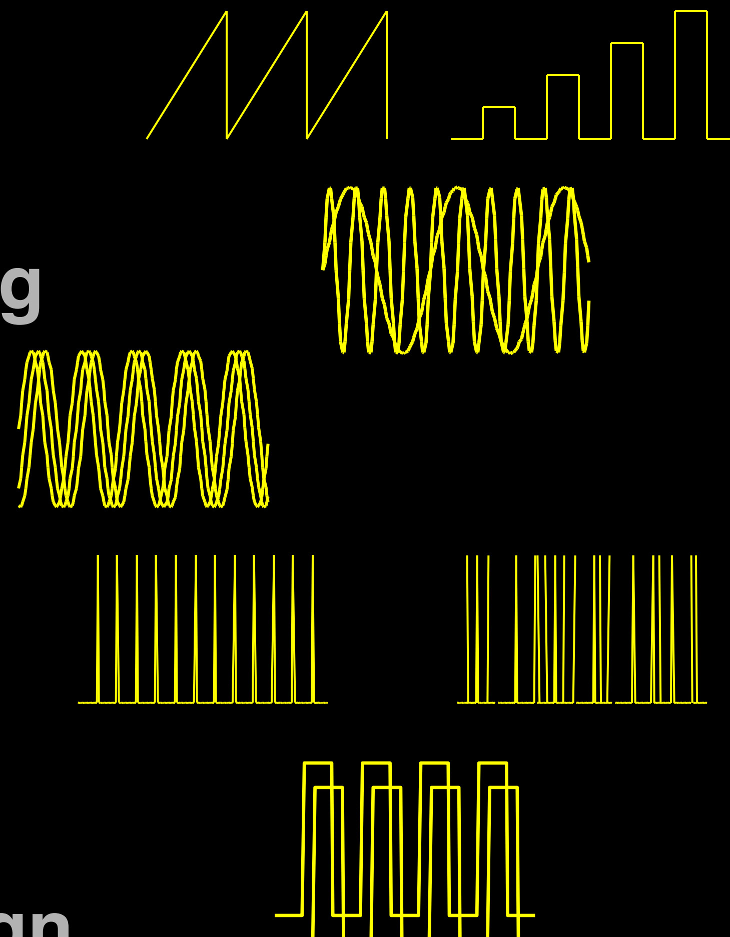


Varying "ON" and "OFF" periods

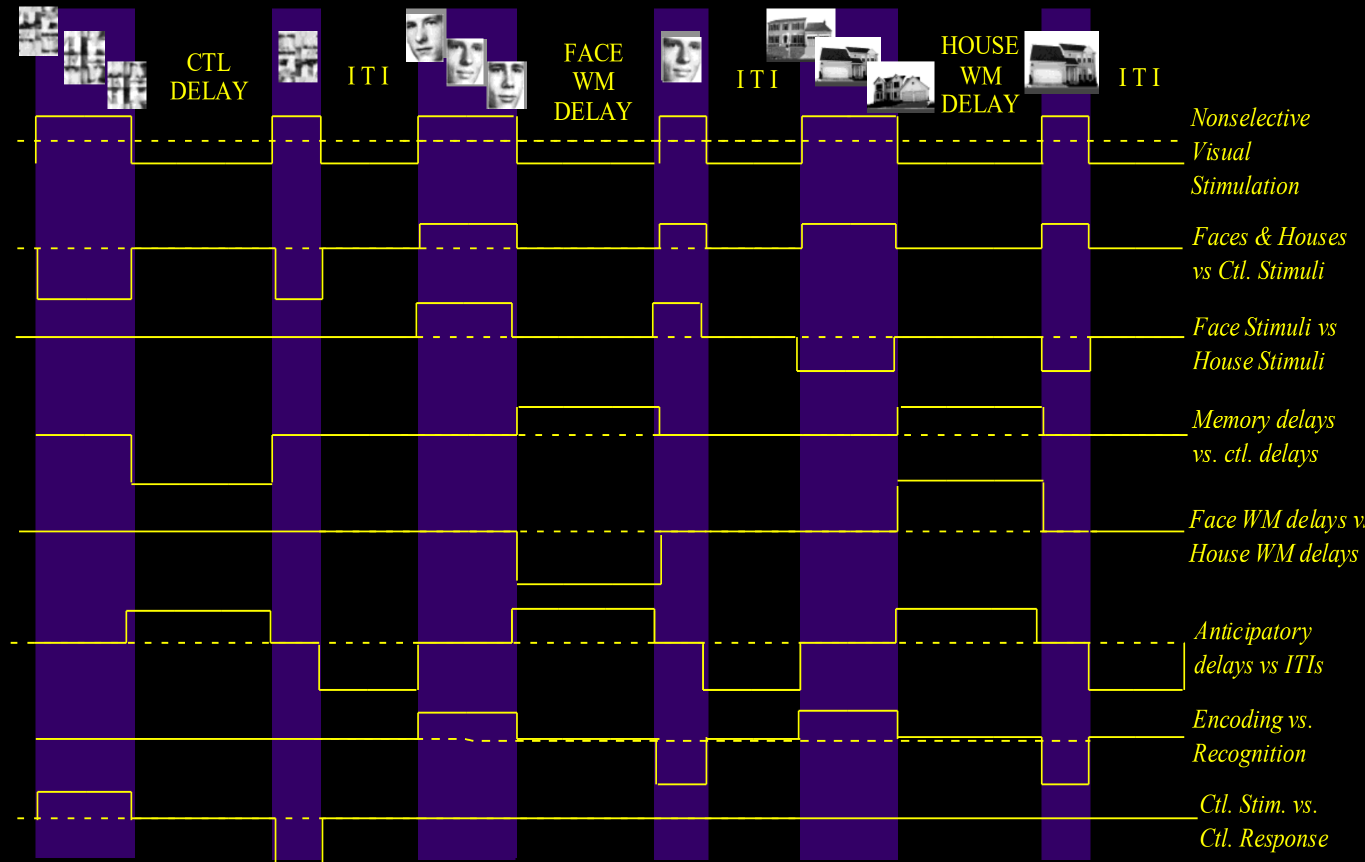


Neuronal Activation Input Strategies

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

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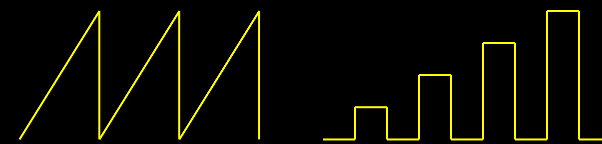
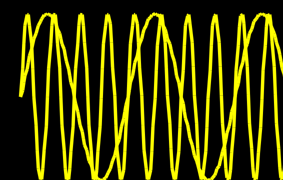
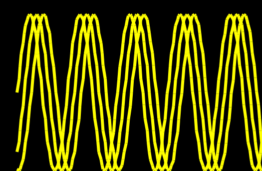
2. Parametric Design



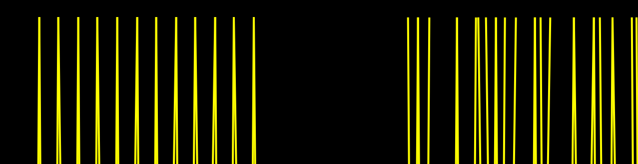
3. Frequency Encoding



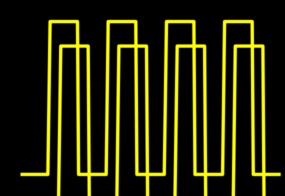
4. Phase Encoding



5. Event Related



6. Orthogonal Design



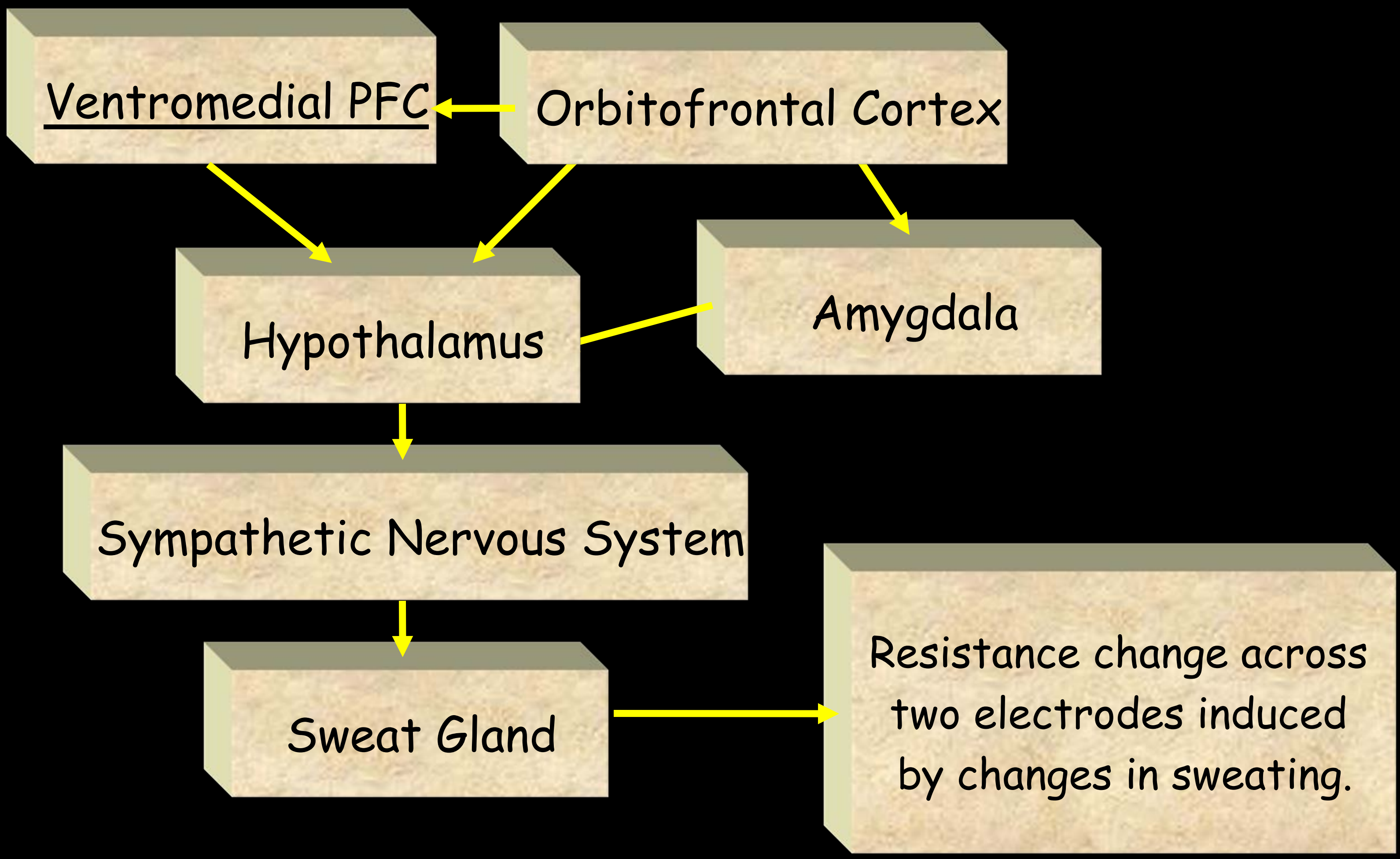
7. Free Behavior Design

Free Behavior Design

Use a continuous measure as a reference function:

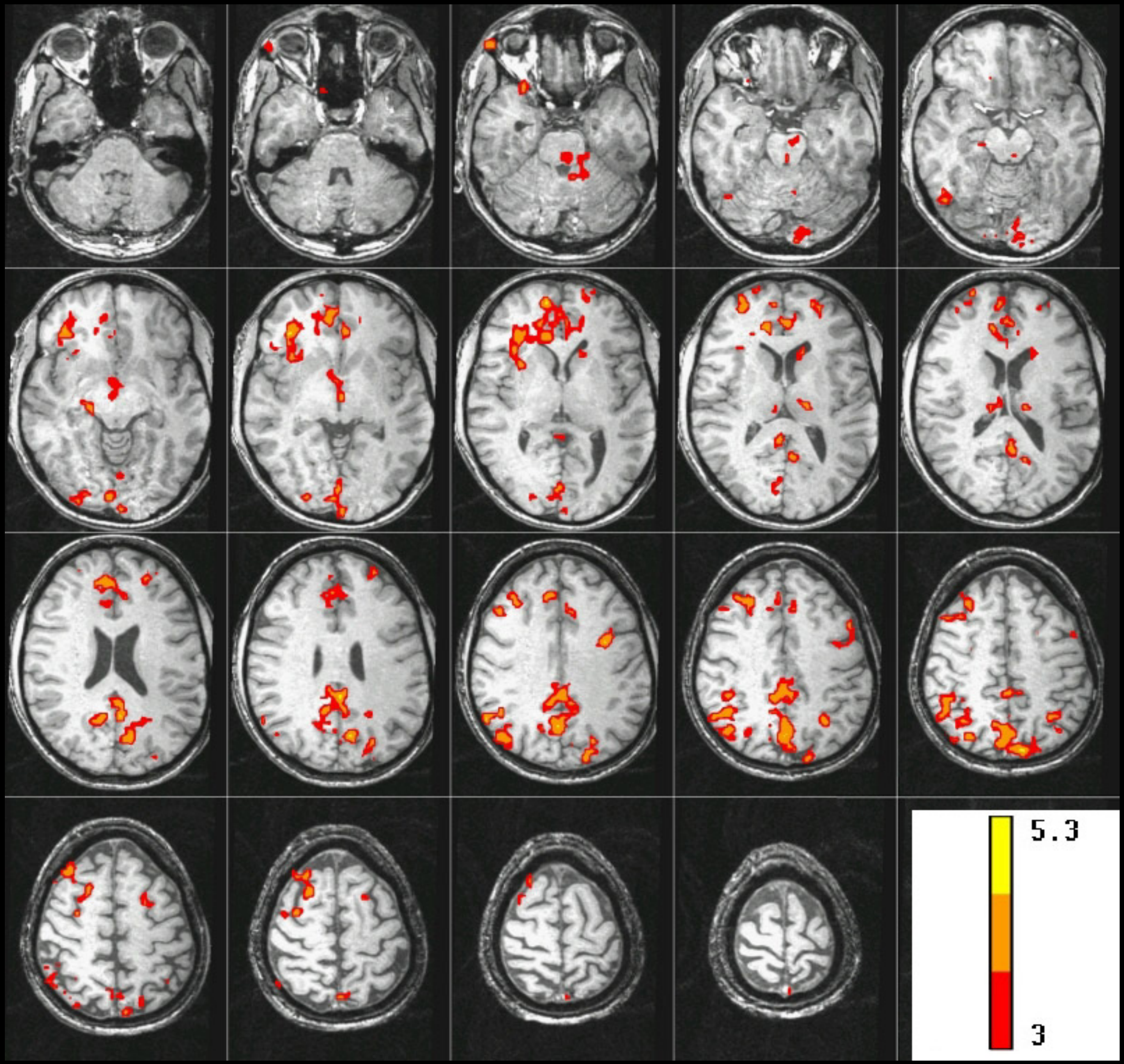
- Task performance
- Skin Conductance
- Heart, respiration rate..
- Eye position
- EEG

The Skin Conductance Response (SCR)



Patterson et al. (submitted)

Brain activity correlated with SCR during "Rest"



Patterson et al. (submitted)

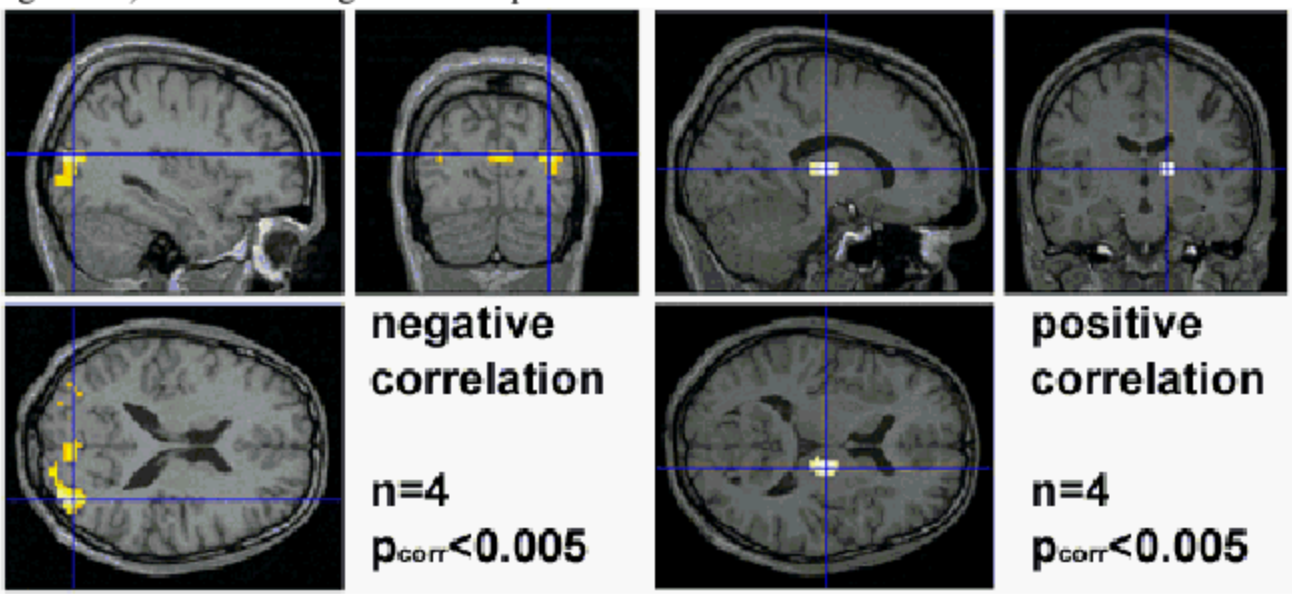
Order to appear: 20

OHBM 200

Correlates of Alpha Rhythm in BOLD-fMRI

Matthias Moosmann, Petra Ritter, Andrea Brink, Ina Krastel, Sebastian Thees, Felix Blankenburg, Birol Taskin, Jan Ruben, Arno Villringer

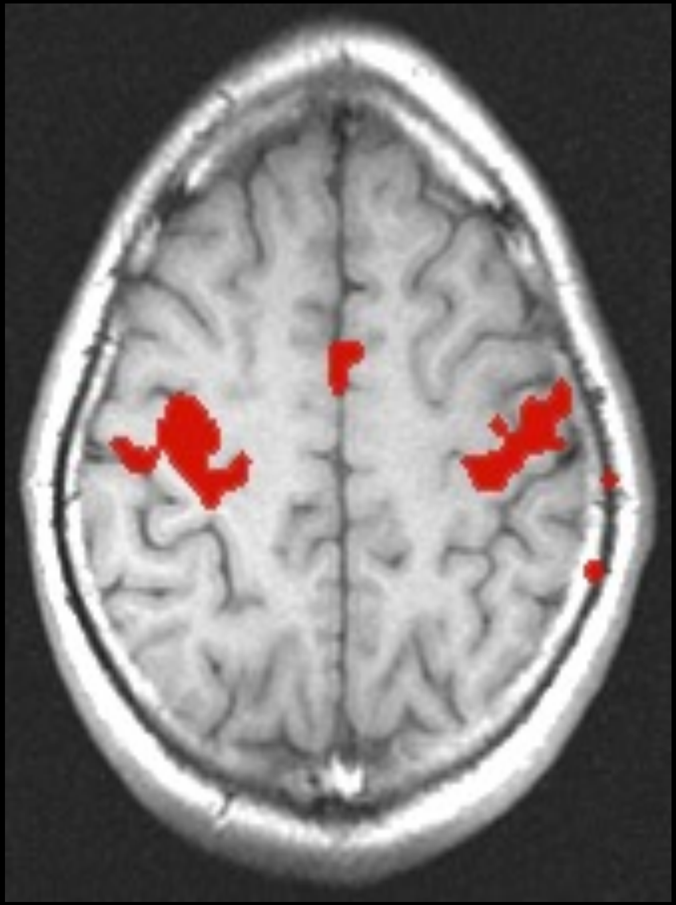
The group analysis based on four volunteers showed a negative correlation between alpha-power and fMRI signal in the occipital cortex (figure, left side) and a positive correlation in the thalamus (figure, right side). These findings were not present for the beta band.

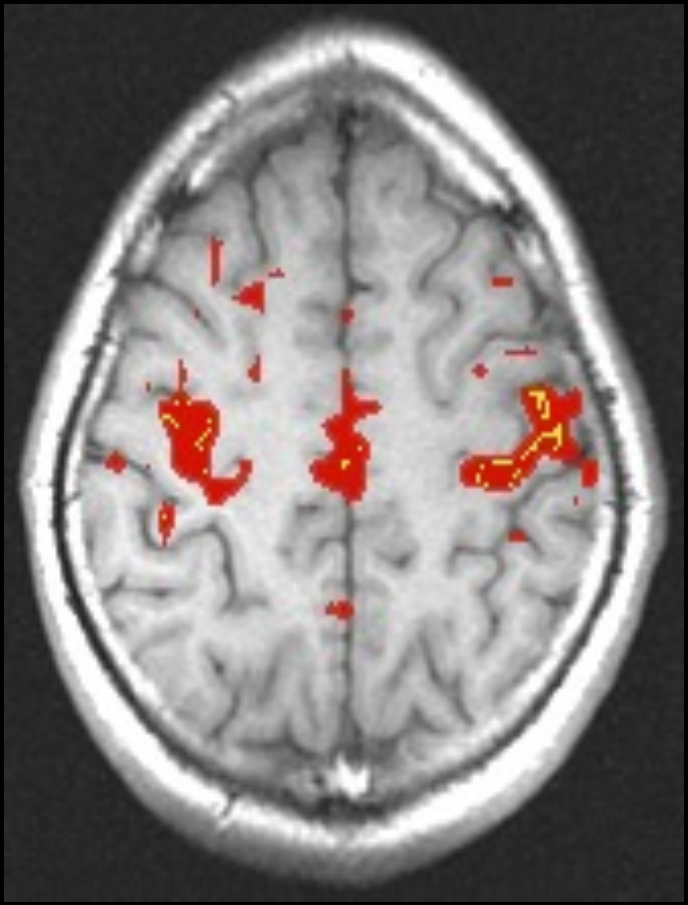


Discussion:

Localization of alpha activity in the occipital lobe agrees with previous electrophysiological findings. The negative correlations of fMRI signal and alpha suggests less energy consumption with higher degrees of synchronization. Positive correlations in the thalamus suggest the thalamus to be an active energy consuming generator of alpha synchronization. Our results are in concordance with findings recently reported by other groups, showing deactivations in the occipital pole and activations in the thalamus or in the brain stem using PET (Sadato et al. 1998) and fMRI (Goldman et al. 2001).

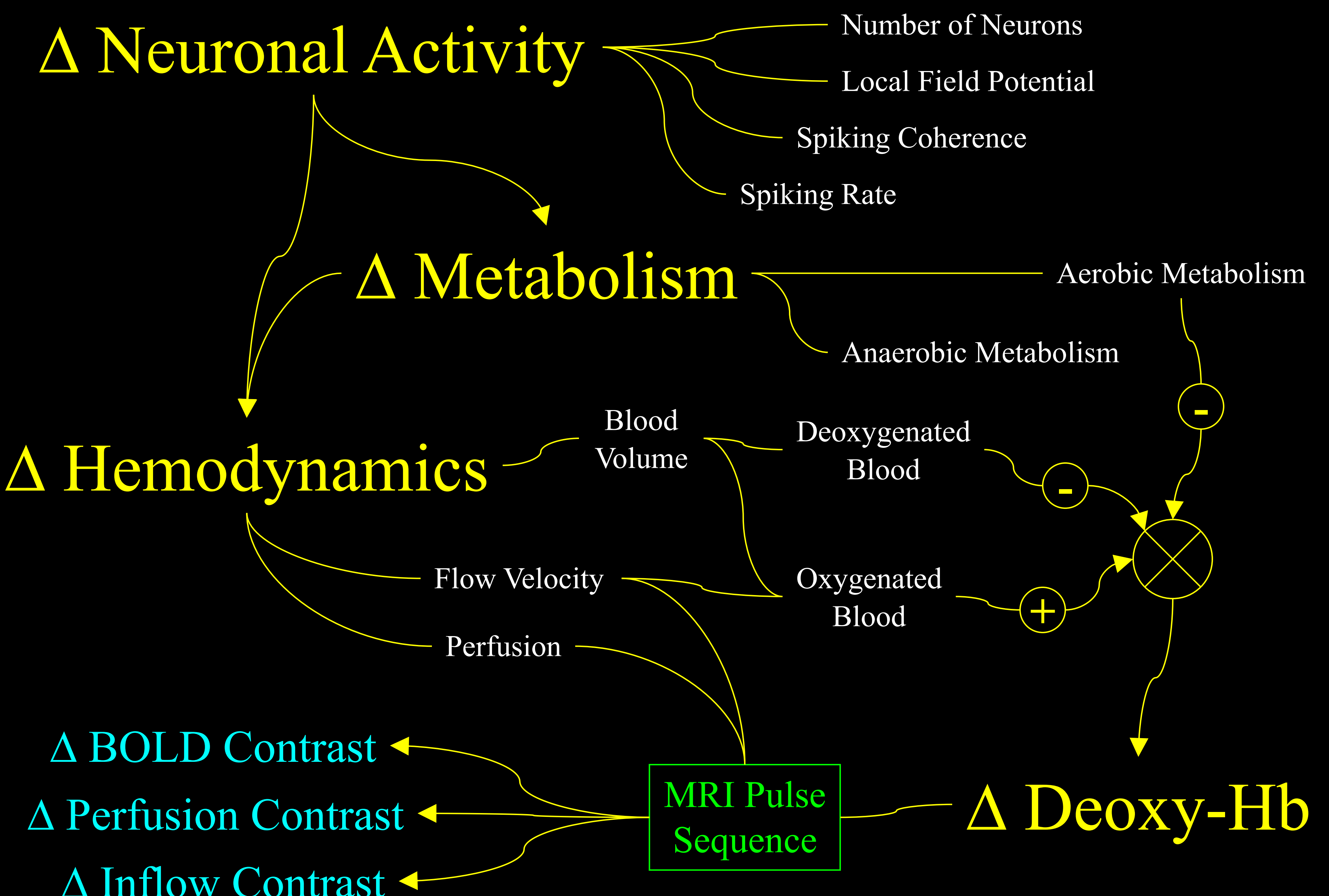
Resting Hemodynamic Autocorrelations





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

Calibration methods for Temporal Resolution and Interpretation...



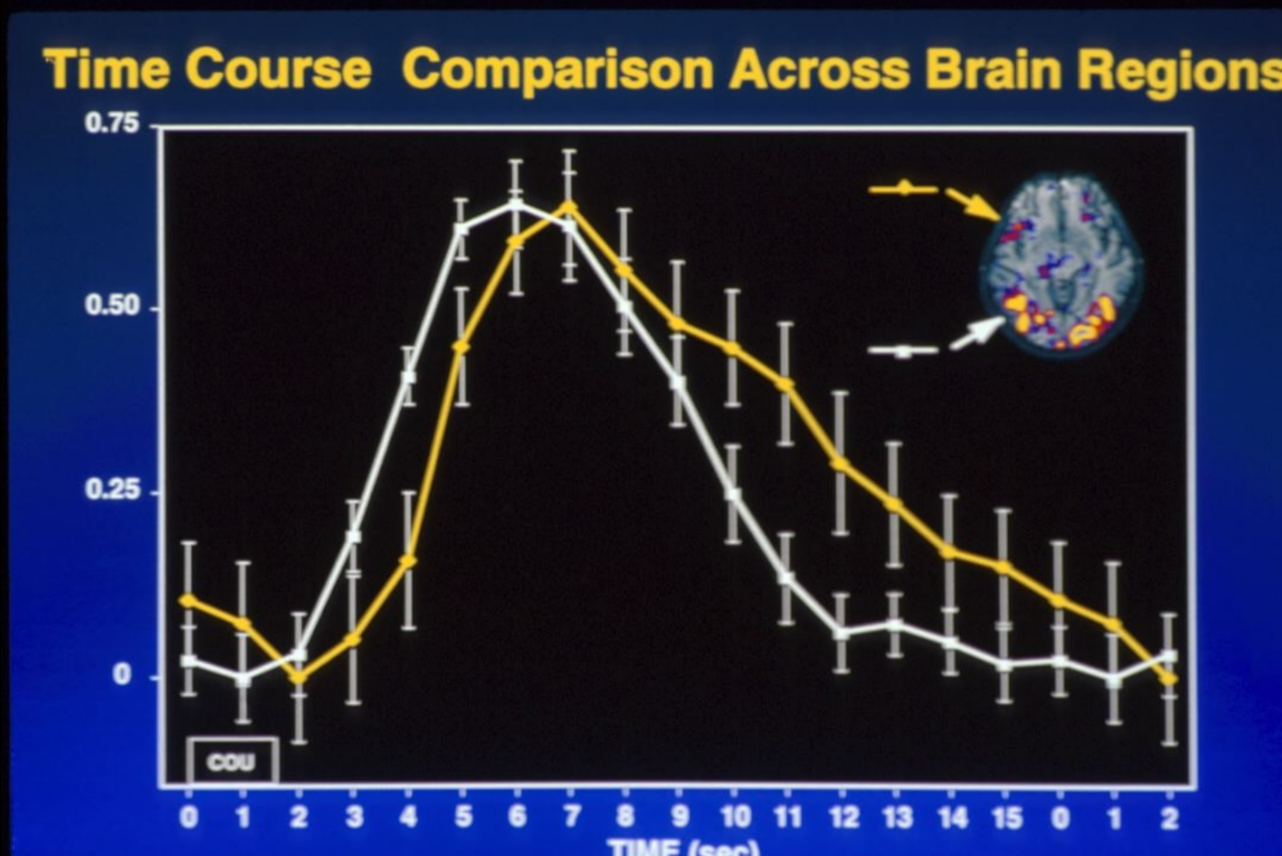
Δ Neuronal Activity
Number of Neurons
Local Field Potential
Spiking Coherence
Spiking Rate
Δ Metabolism
Aerobic Metabolism
Anaerobic Metabolism
Δ Hemodynamics
Blood Volume
Deoxygenated Blood
Oxygenated Blood
Flow Velocity
Perfusion
-
-
+
Δ BOLD Contrast
Δ Perfusion Contrast
Δ Inflow Contrast
MRI Pulse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

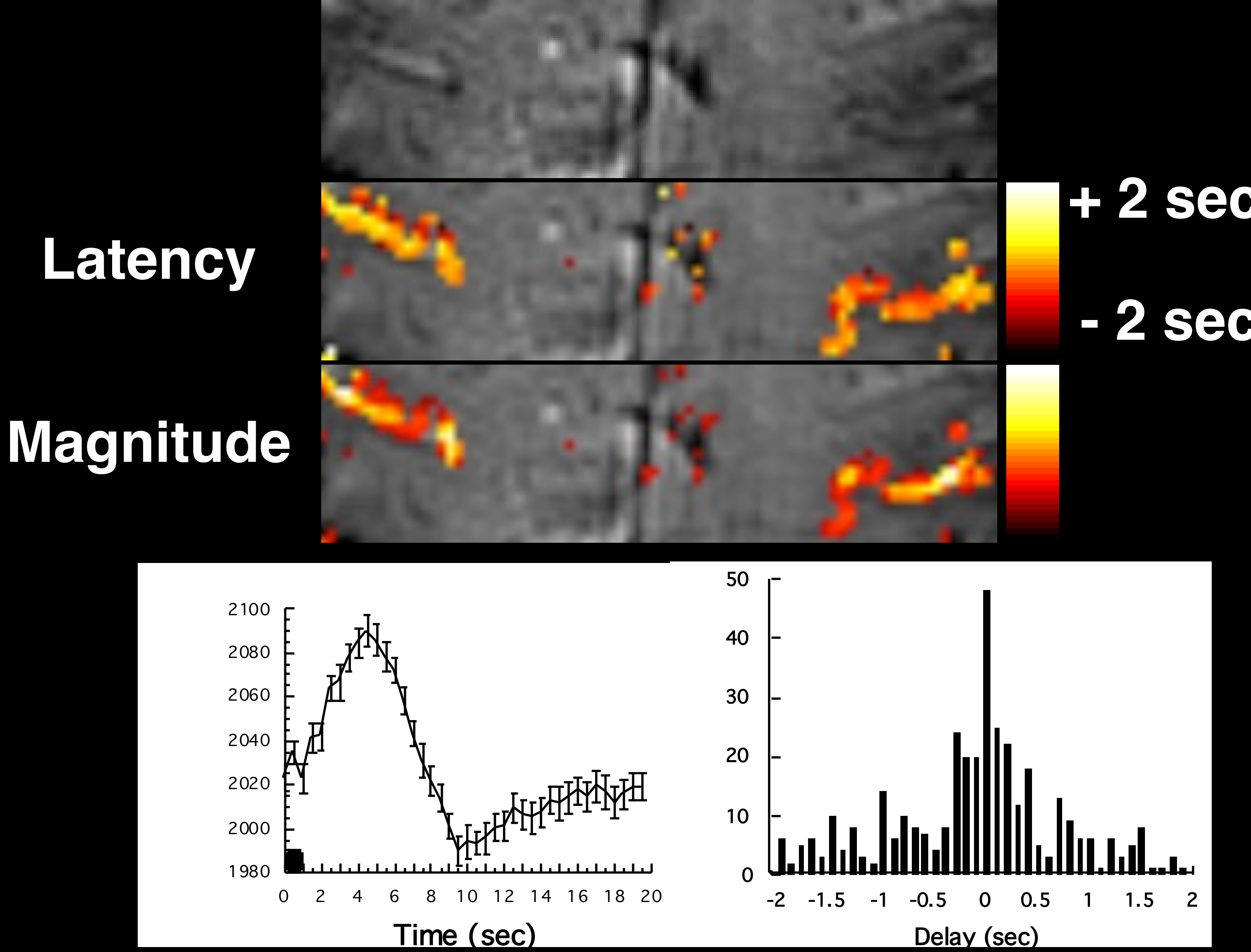
Proc. Natl. Acad. Sci. USA
Vol. 93, pp. 14878–14883, December 1996
Neurobiology

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

(neuroimaging/single trial/language/prefrontal)

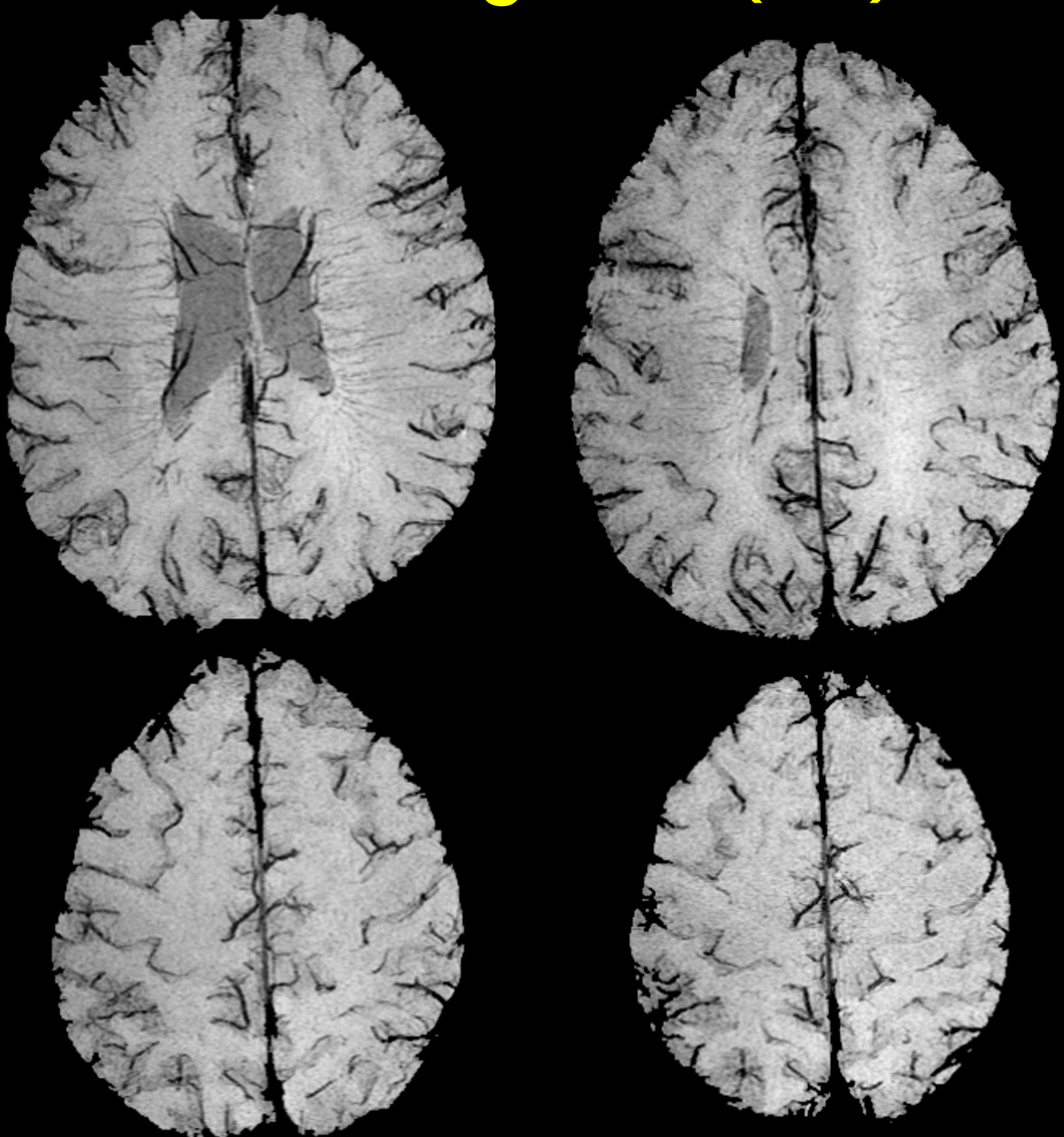
RANDY L. BUCKNER[†‡§¶], PETER A. BANDETTINI[†‡], KATHLEEN M. O'CRAVEN[†‖], ROBERT L. SAVOY[†‖], STEVEN E. PETERSEN[**††], MARCUS E. RAICHLE[§**††], AND BRUCE R. ROSEN[†‡]

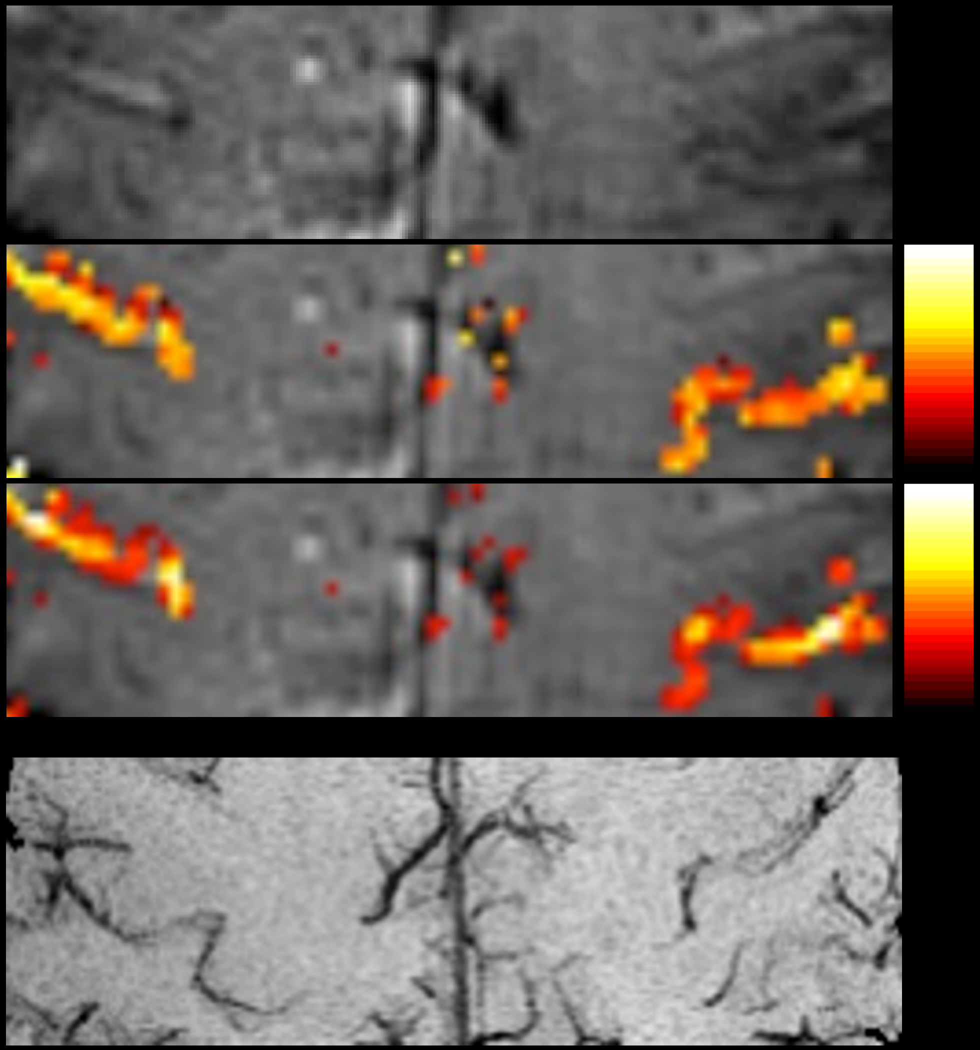




P. A. Bandettini, The temporal resolution of Functional MRI *in* "Functional MRI" (C. Moonen, and P. Bandettini., Eds.), p. 205-220, Springer - Verlag,. 1999.

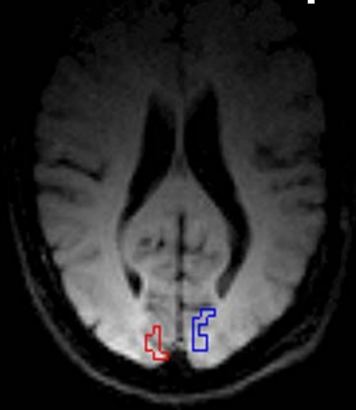
Venograms (3T)



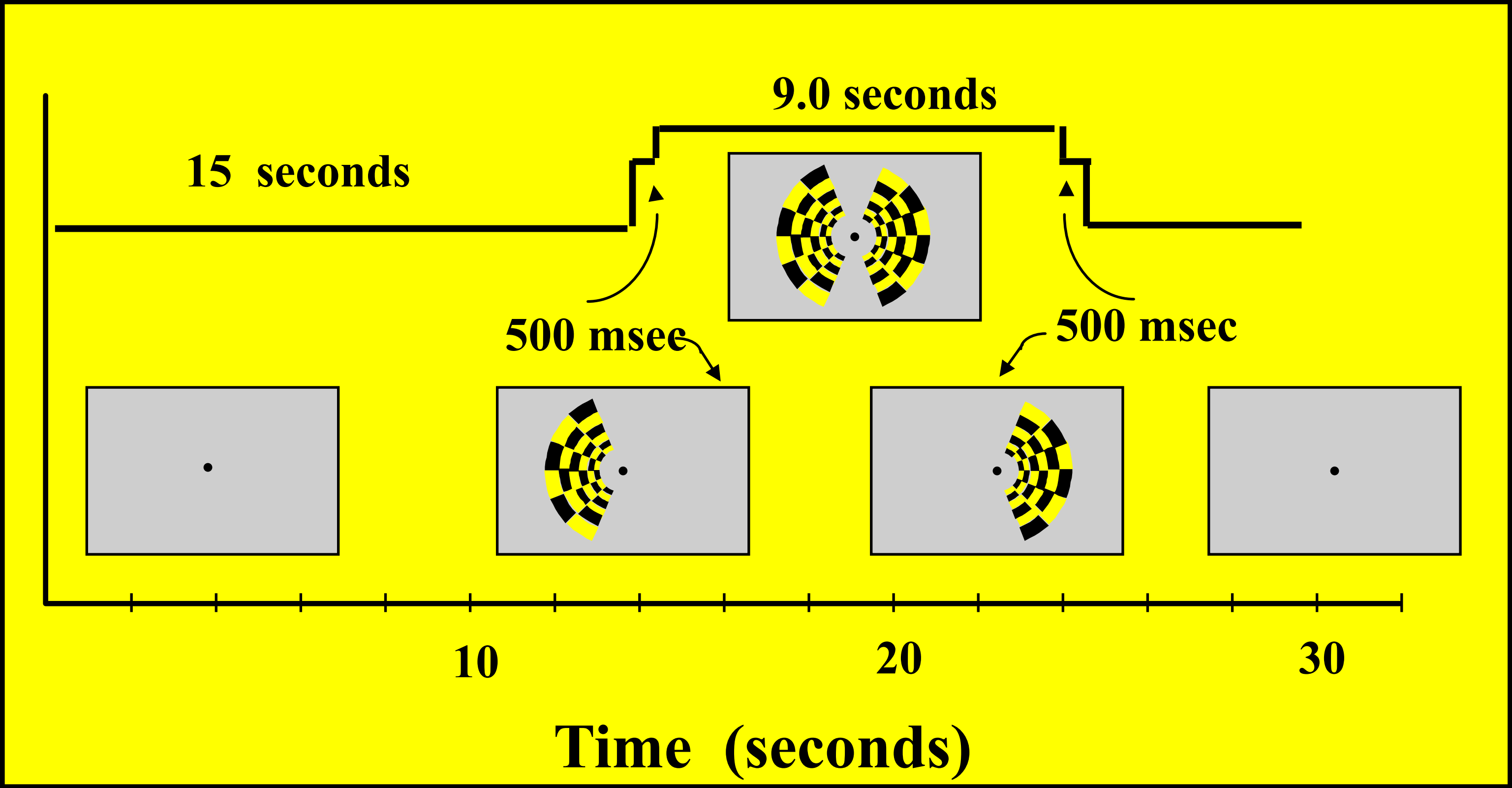


Hemi-Field Experiment

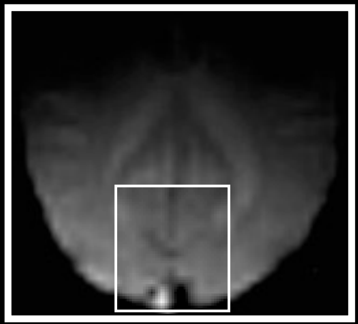
Left Hemisphere

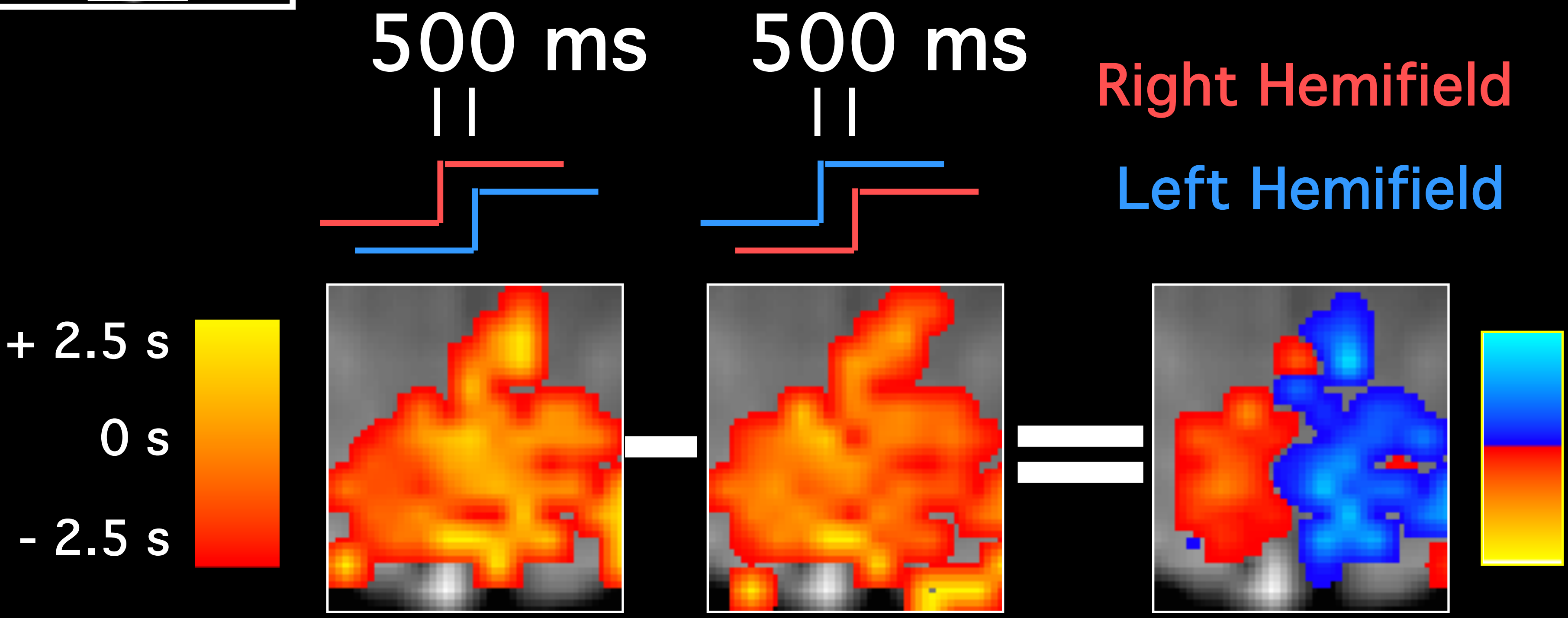


Right Hemisphere



Calibration Techniques.....

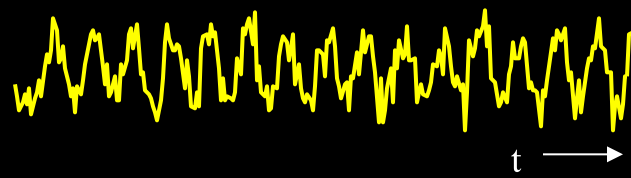


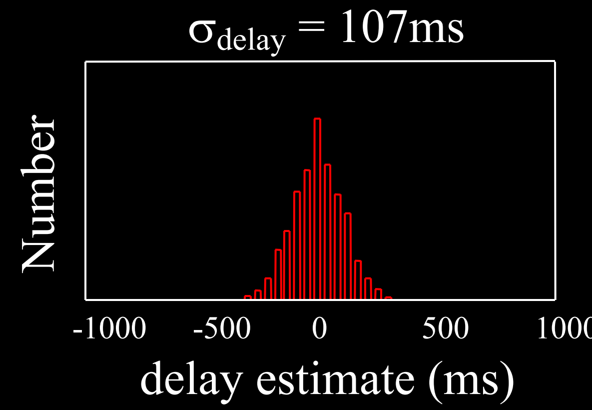


P. A. Bandettini, The temporal resolution of Functional MRI *in* "Functional MRI" (C. Moonen, and P. Bandettini., Eds.), p. 205-220, Springer - Verlag,. 1999.

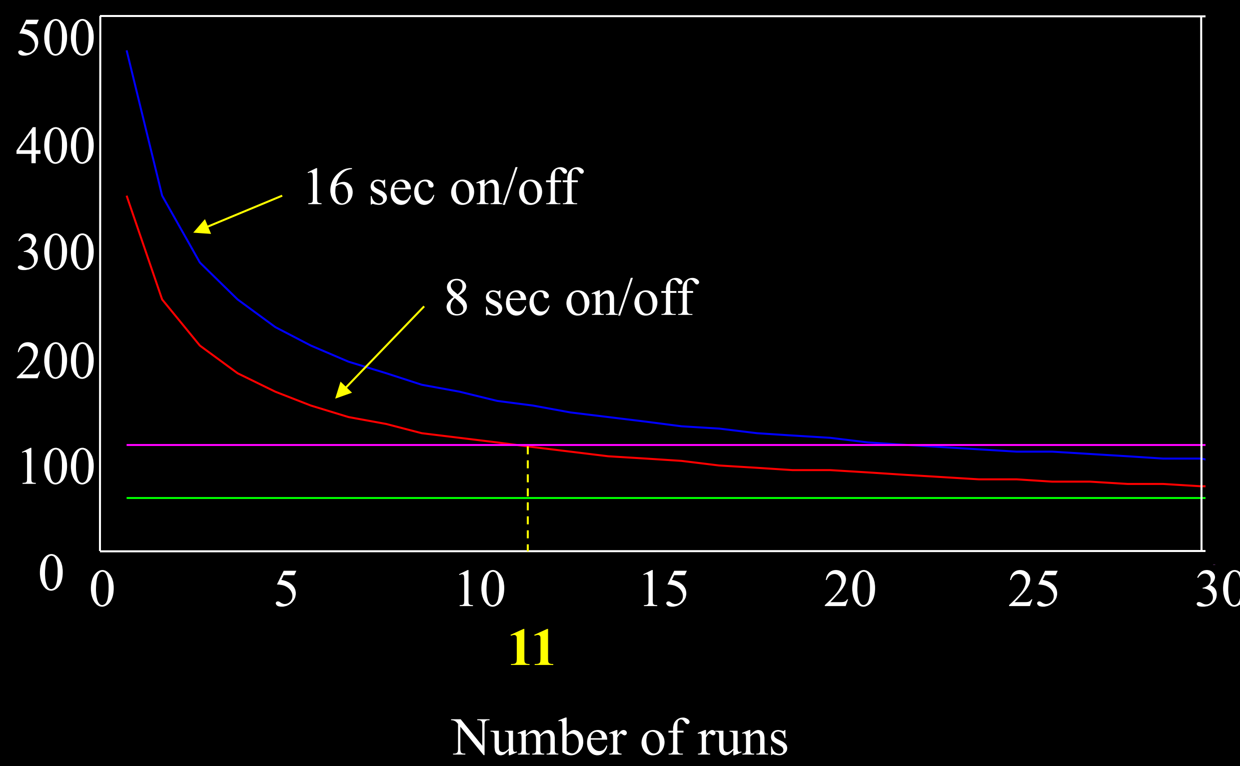
1 run:

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

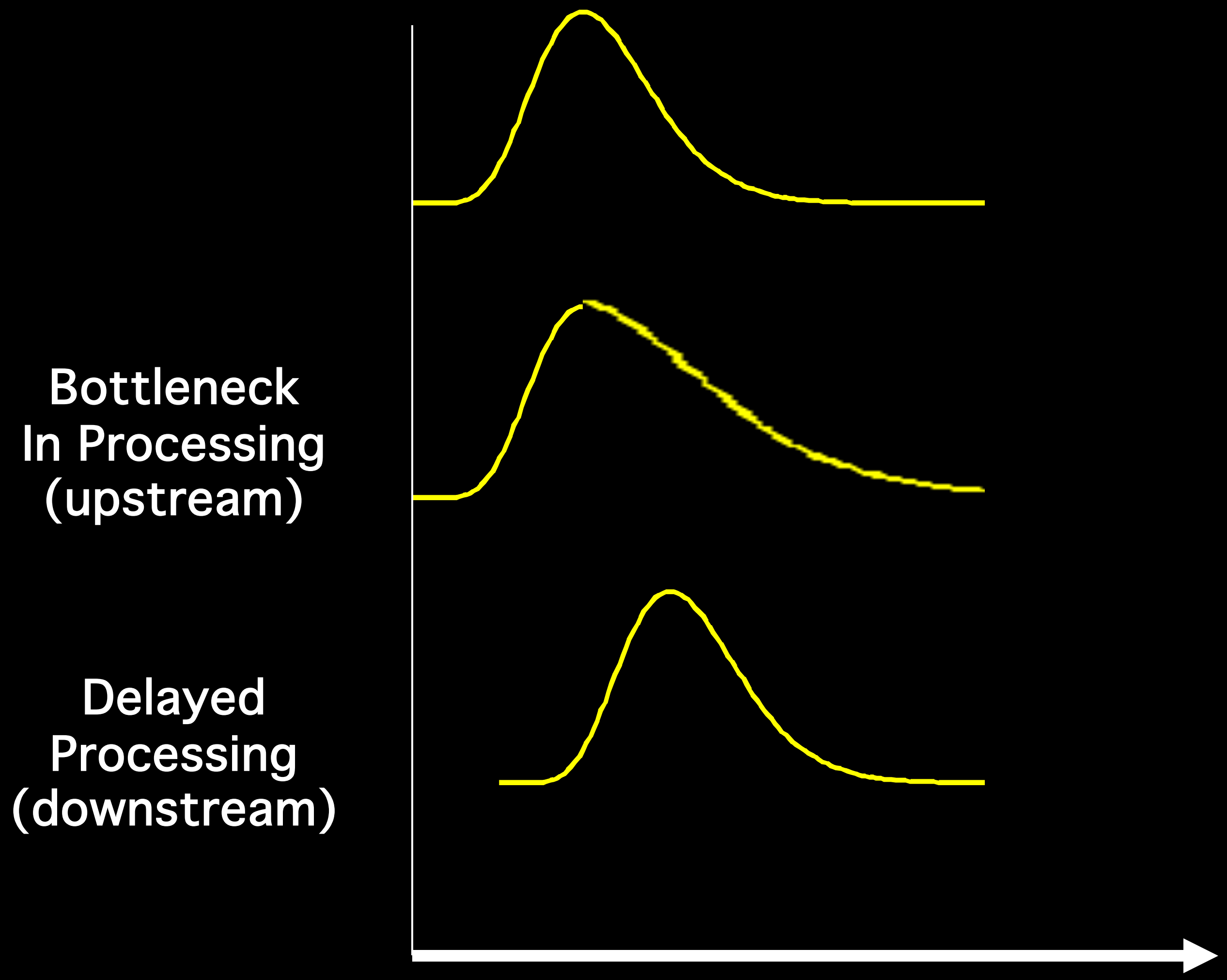




Smallest latency Variation Detectable (ms) ($p < 0.001$)



Hemodynamic Response Modulation



Use of Task Timing Modulation to Extract Processing Streams

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) Stimulus rotation demands a change in perceptual perspective prior to linguistic processing. This will result in a delayed IRF onset in areas involved in Lexical and Pre-Lexical processing.

2**) Lexical discrimination will result in :**

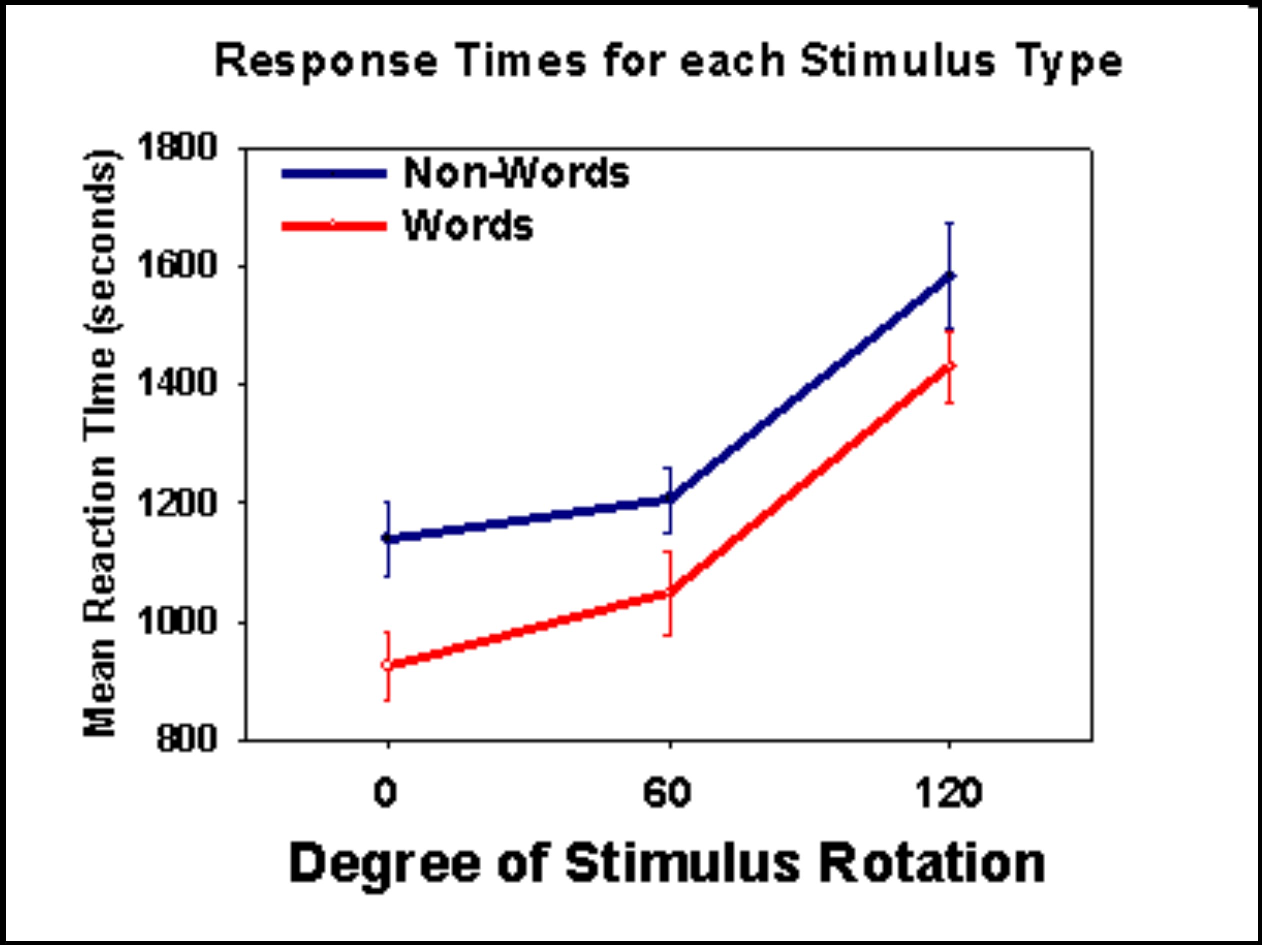
a) Longer Reaction Times for non-words due to increased Pre-Lexical processing demands.

b) Wider IRF in Inferior Frontal cortex for non-words

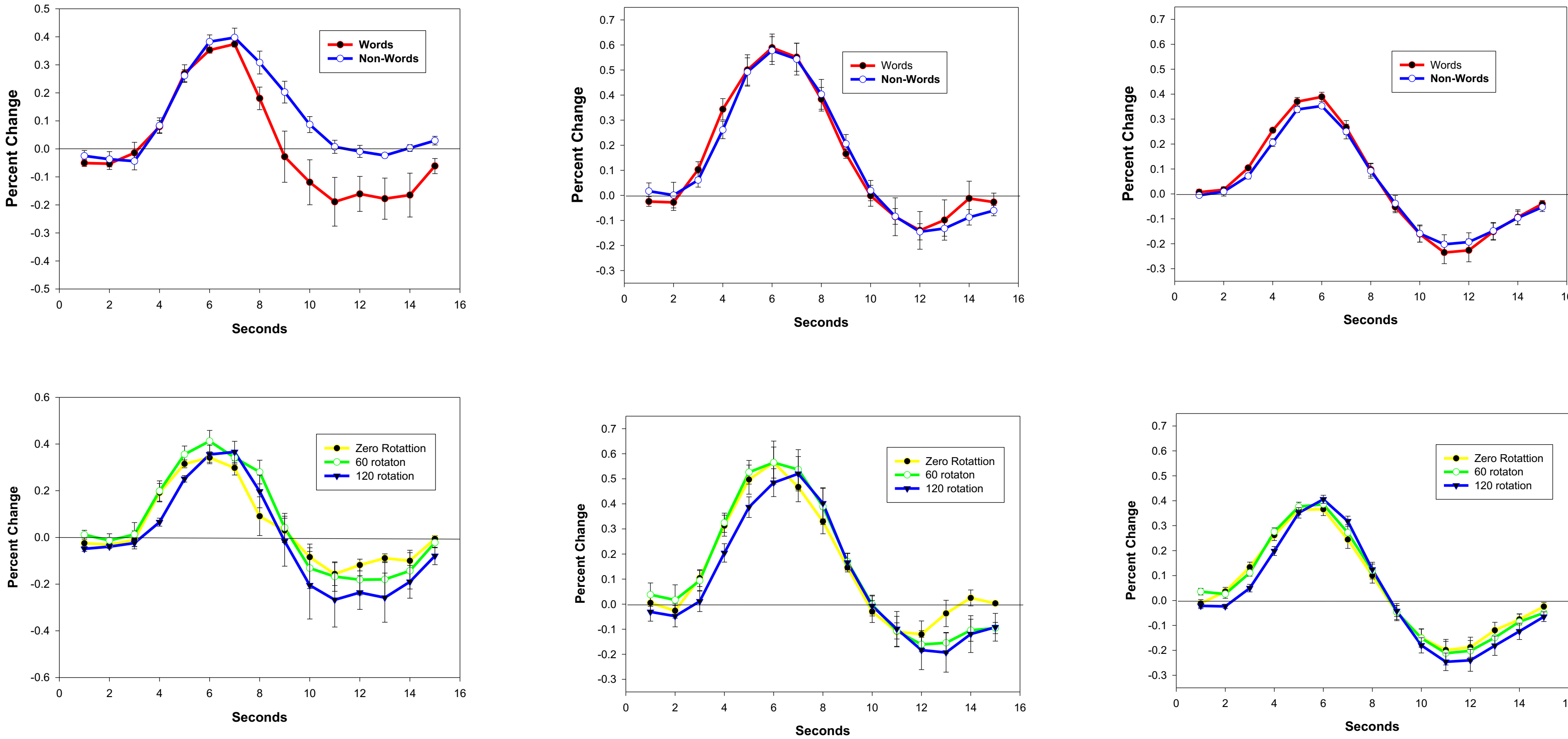
c) Delayed IRF onset in Left Middle Frontal Cortex

Lexical Delay

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

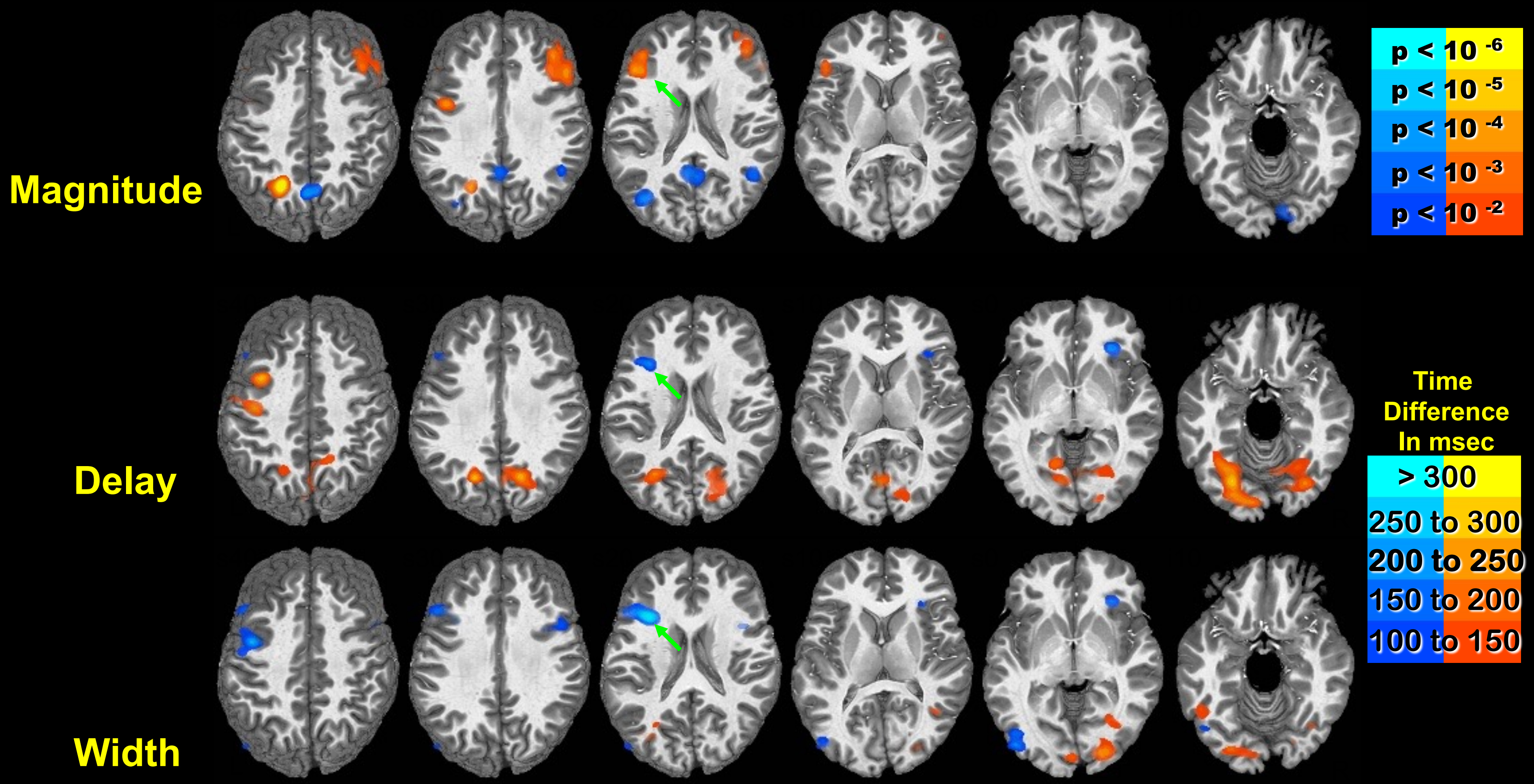

Response Times for each Stimulus Type
Non-Words
Words
Mean Reaction TIme (seconds)
1800
1600
1400
1200
1000
800
0
60
120
Degree of Stimulus Rotation

Inferior Frontal Gyrus   Middle Temporal Gyrus   Pre-Central Gyrus



Graphs depicting the estimated Impulse Response Functions.

Lexical effect maps



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.

Laminar Specificity of fMRI Onset Times During Somatosensory Stimulation in Rat

Afonso C. Silva and Alan P. Koretsky

Laboratory of Functional and Molecular Imaging

National Institute of Neurological Disorders and Stroke

Bethesda, Maryland, USA

Can fMRI be used to distinguish neuronal signaling within laminar sub-regions of the brain?

fMRI Methods

- 11.7T/31cm magnet (Magnex Scientific, Ltd.)
- AVANCE electronics (Bruker-Biospin, Inc.)
- Conventional gradient-echo images
- FOV = 1.28 x 1.28 x 0.2 cm^3
- TE = 10 ms, TR = 40 ms, tip-angle ≈ 11°
- Matrix size:
  - 64 x 64 (200 x 200 x 2000 μm^3), 2.5 s/frame
  - 128 x 128 (100 x 100 x 2000 μm^3, 5.0 s/frame
  - 256 x 256 (50 x 50 x 2000 μm^3), 10 s/frame
- CBV: 20 mg/kg of AMI-227 (Advanced Magnetics, MA)

Somatosensory Stimulation

- Electrical stimulation of the forepaw:
  - Two needle electrodes inserted subcutaneously
  - Stimulation parameters: 2.0 mA; 3 Hz; 0.3 ms
  - Paradigm:
    1. Single stimulation **off – on – off** epoch

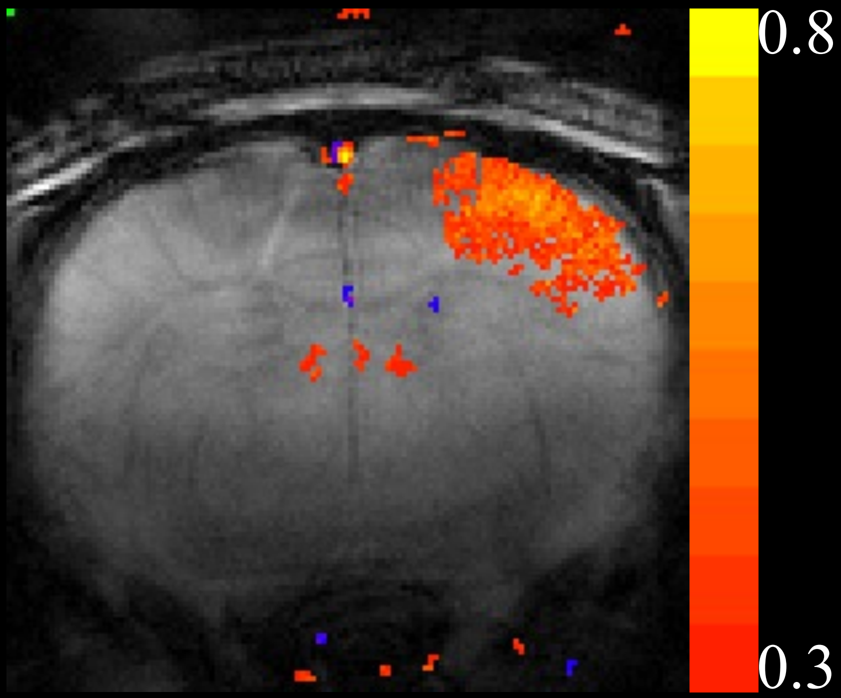
off	on	off		
24	12	24	images	
60	30	60	seconds,	200 x 200 μm^2
240	120	240	seconds,	50 x 50 μm^2

    2. Multiple stimuli block design

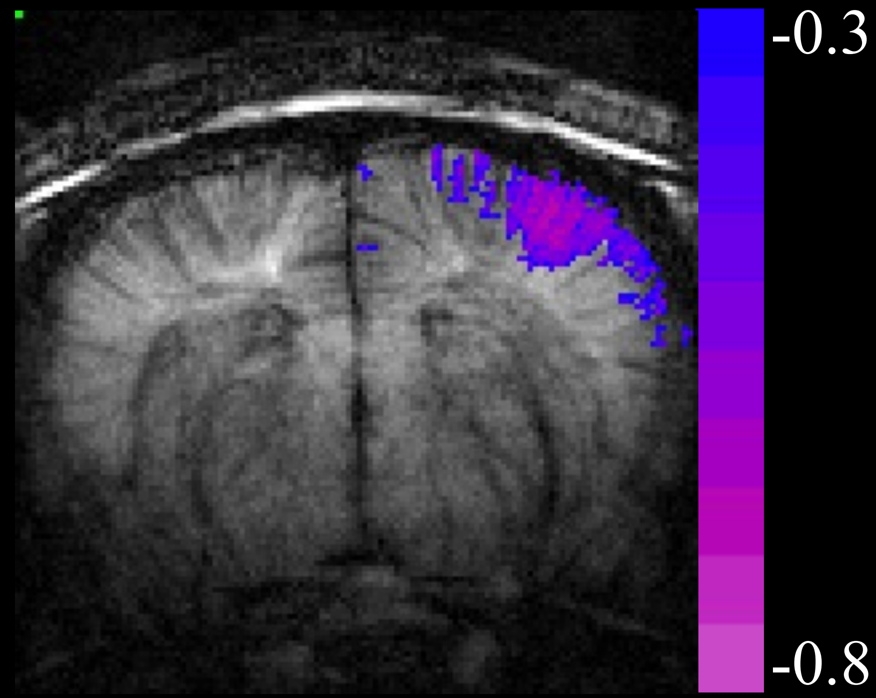
off	on	off		
325	100	325	images	200 x 200 μm^2
13	4	13	seconds,	repeated 64 times

MRI of Functional Hemodynamics

BOLD



rCBV



Gradient-Echo Sequence

Resolution = 100x100x2000 μm^3

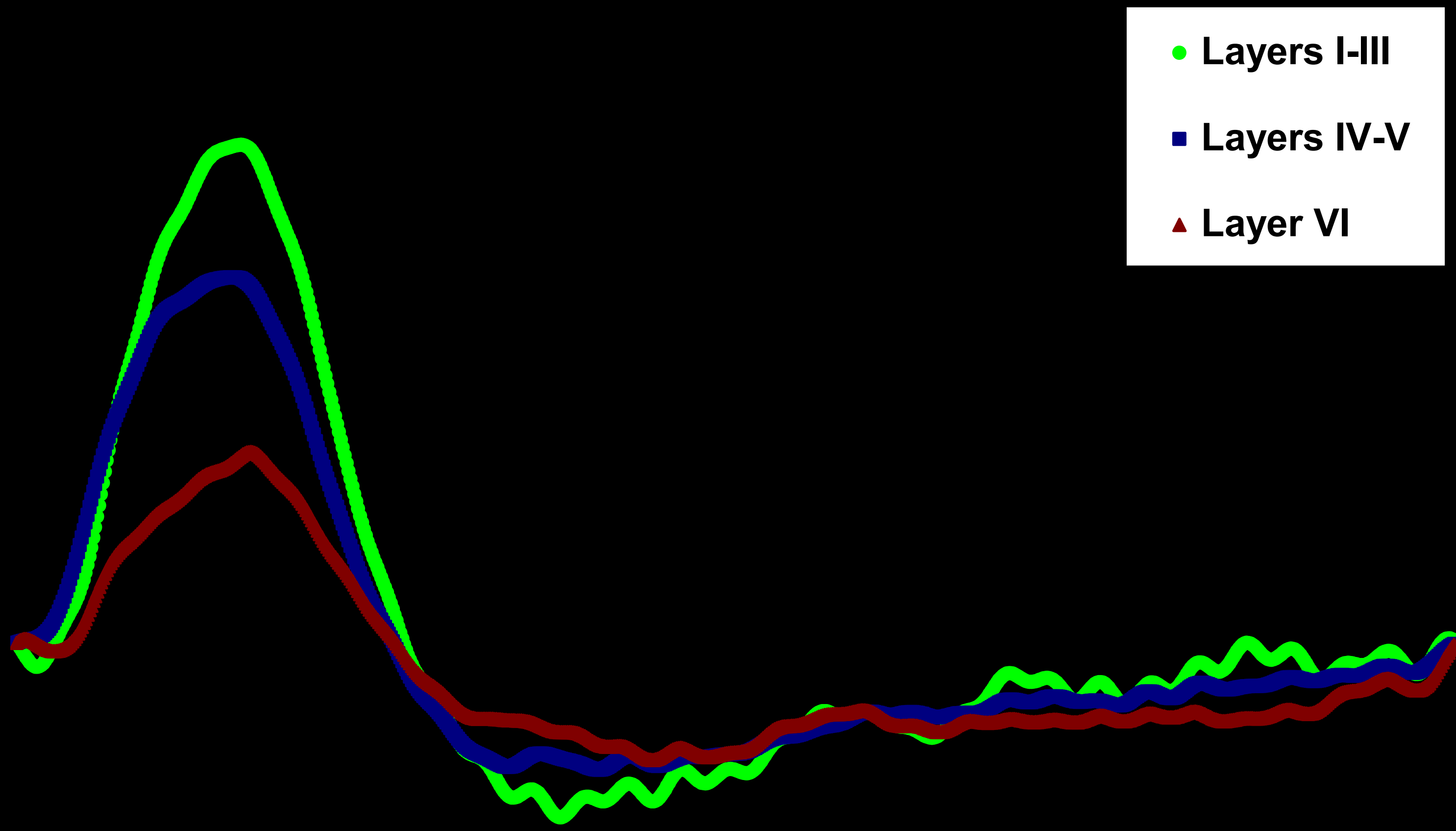
Iron Oxide Contrast Agent

Resolution = 100x100x2000 μm^3

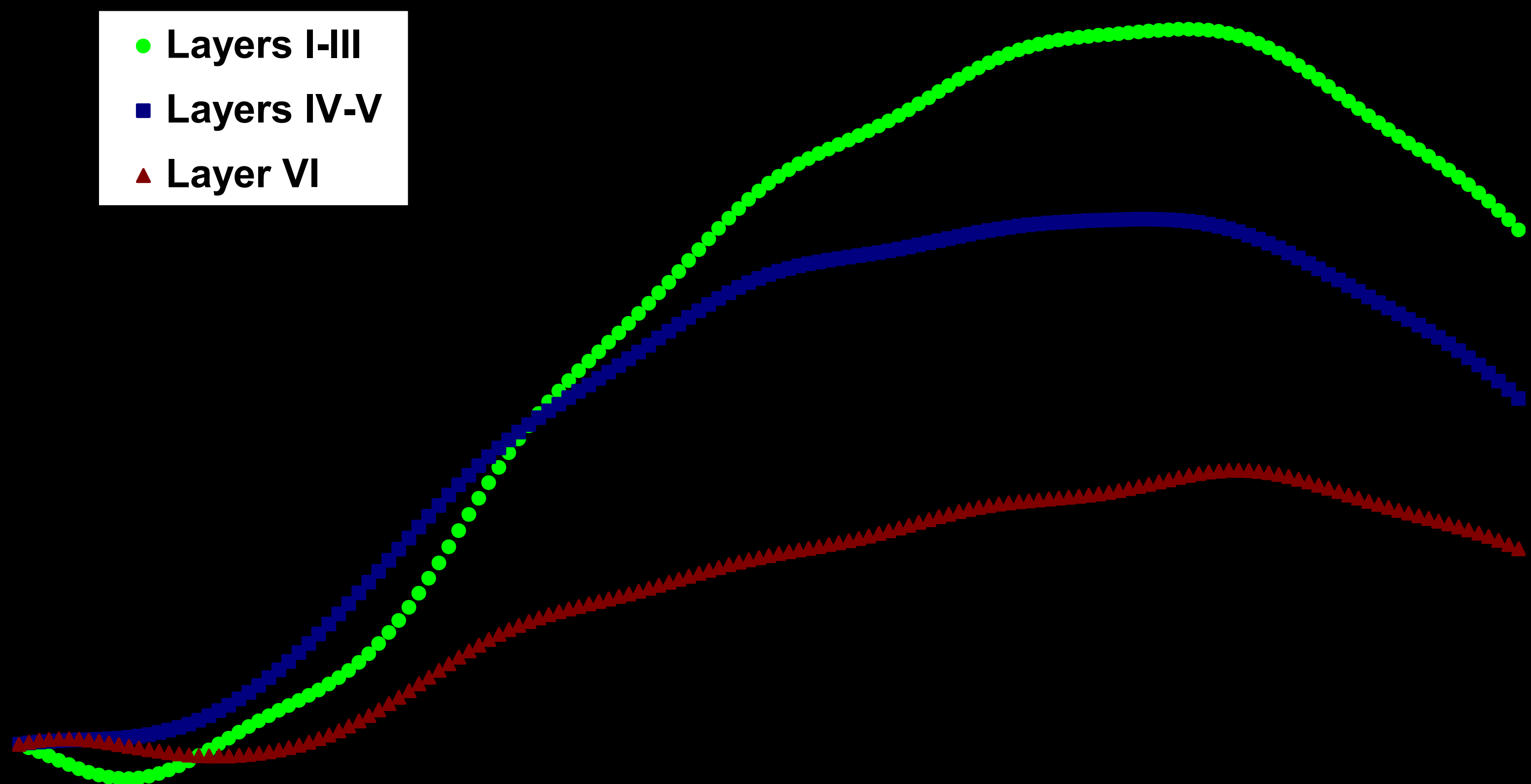
Mapping Onset Times of fMRI Response

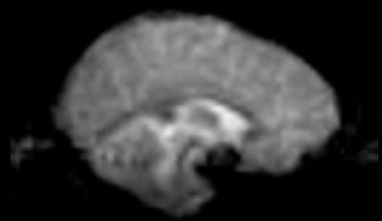
- Hemodynamic response is stable if duty-cycle of repeated stimuli is low enough
- *Strategy*: to acquire multiple high-resolution images using conventional GRE-MRI, swapping phase-encode loop with image repetition loop to obtain one k-space line for all images per stimulus epoch
- Spatial in-plane resolution: 200 x 200 μm^2
- Temporal resolution: 40 ms

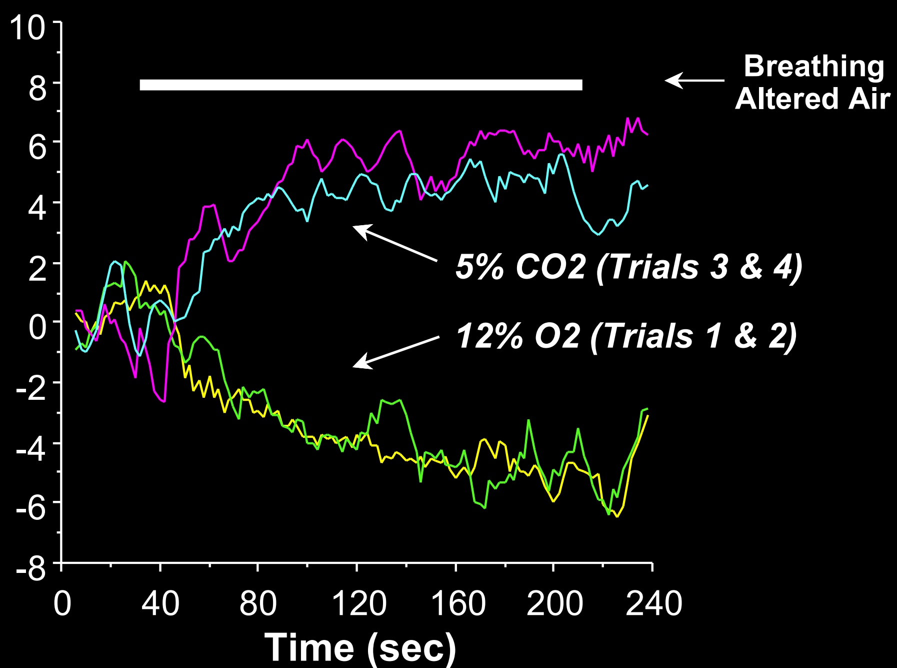
Averaged BOLD Time-Courses



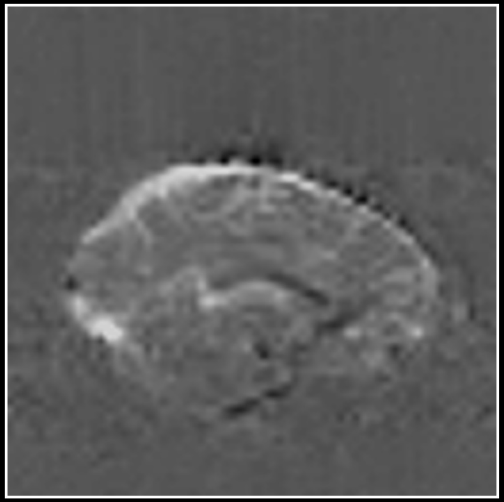
Onset Time Detail

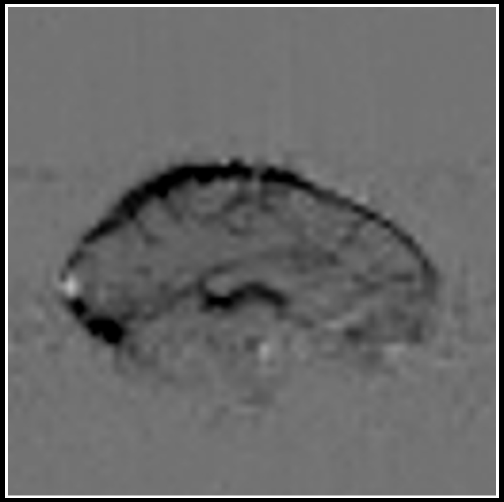





10
8
6
4
2
0
-2
-4
-6
-8
0
40
80
120
160
200
240
Time (sec)
Breathing
Altered Air
5% CO2 (Trials 3 & 4)
12% O2 (Trials 1 & 2)

5% CO2





12% O2

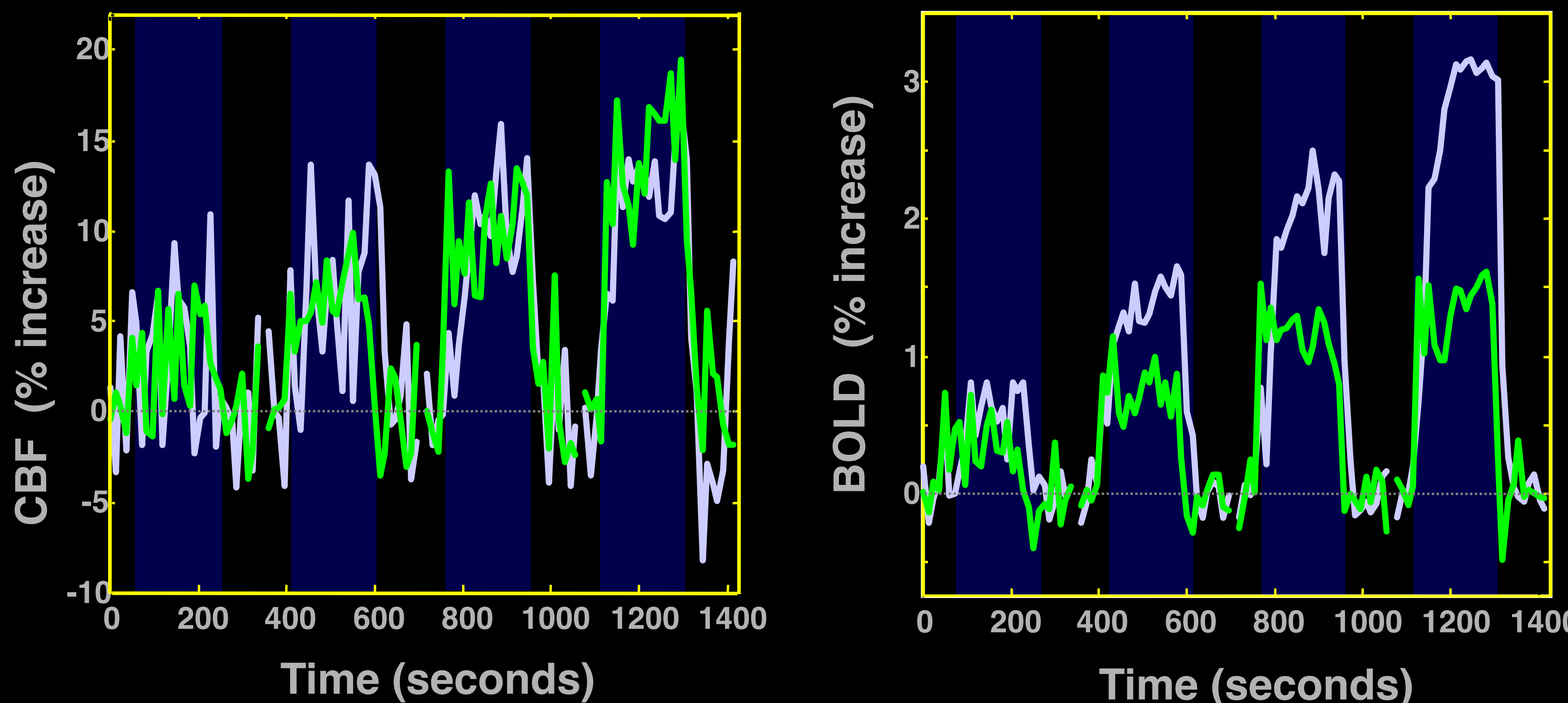
Proc. Natl. Acad. Sci. USA
Vol. 96, pp. 9403–9408, August 1999
Neurobiology

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

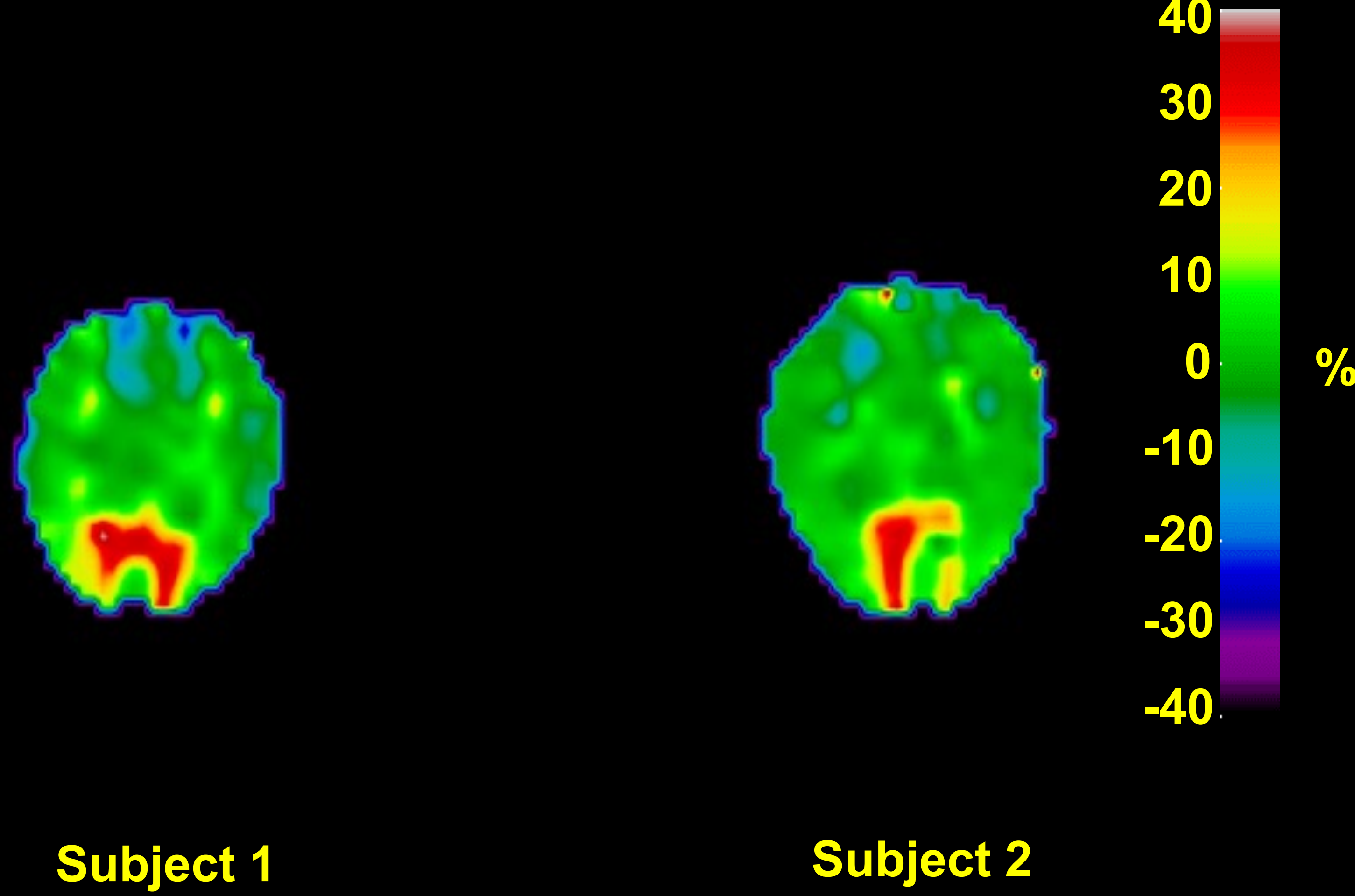
CBF BOLD



Simultaneous Perfusion and BOLD imaging during graded visual activation and hypercapnia

N=12

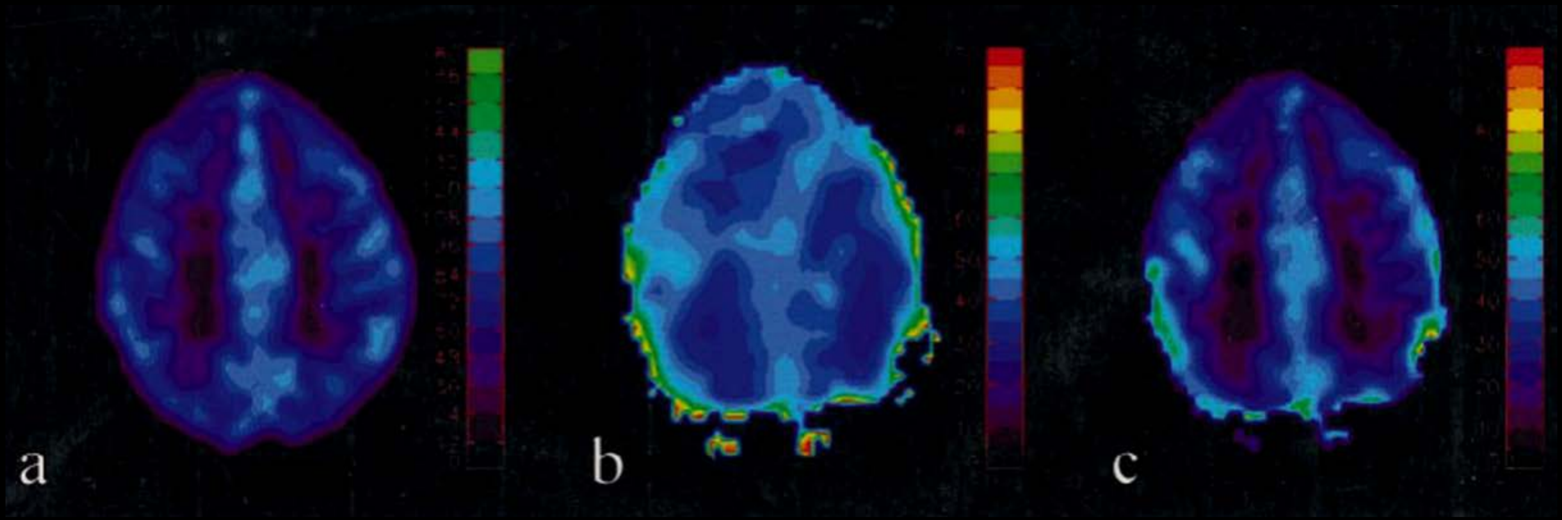
Computed $CMRO_2$ Changes



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

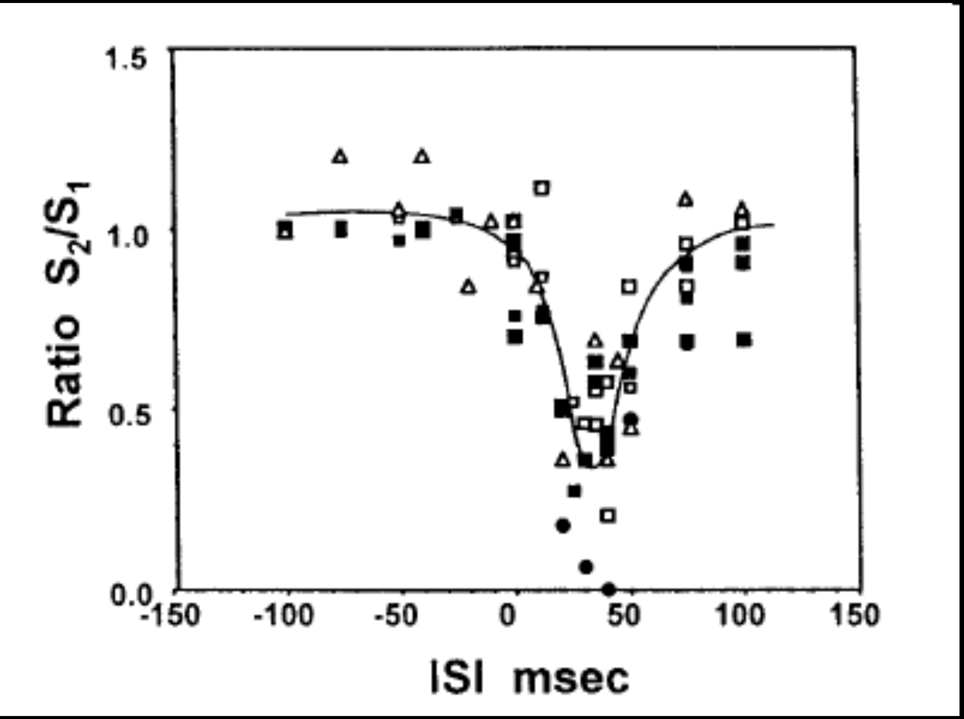
Hongyu An,[1] Weili Lin,[2]* Azim Celik[3] and Yueh Z. Lee[2]



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[§]

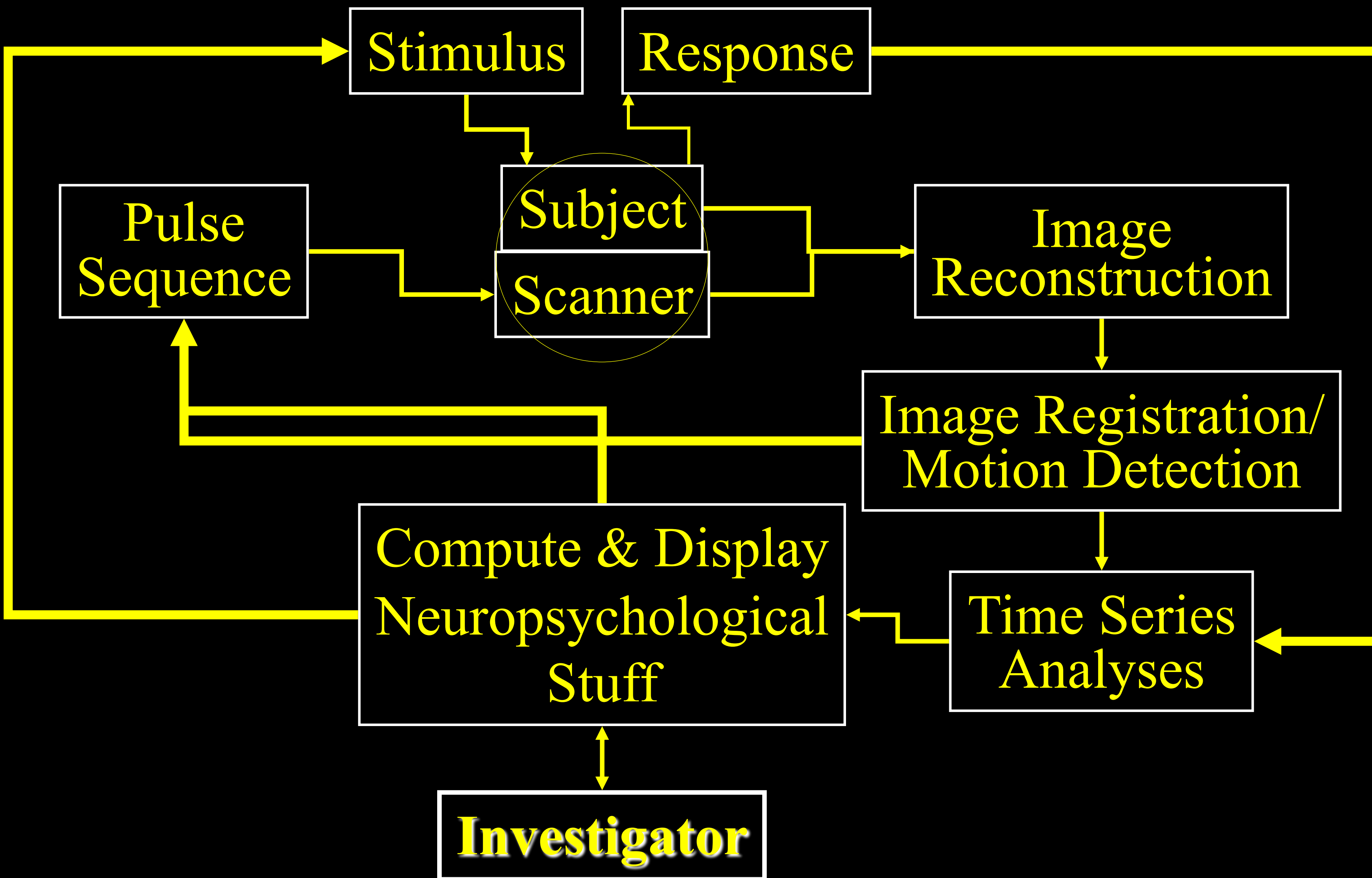


11026–11031 PNAS **September 26, 2000** vol. 97 no. 20

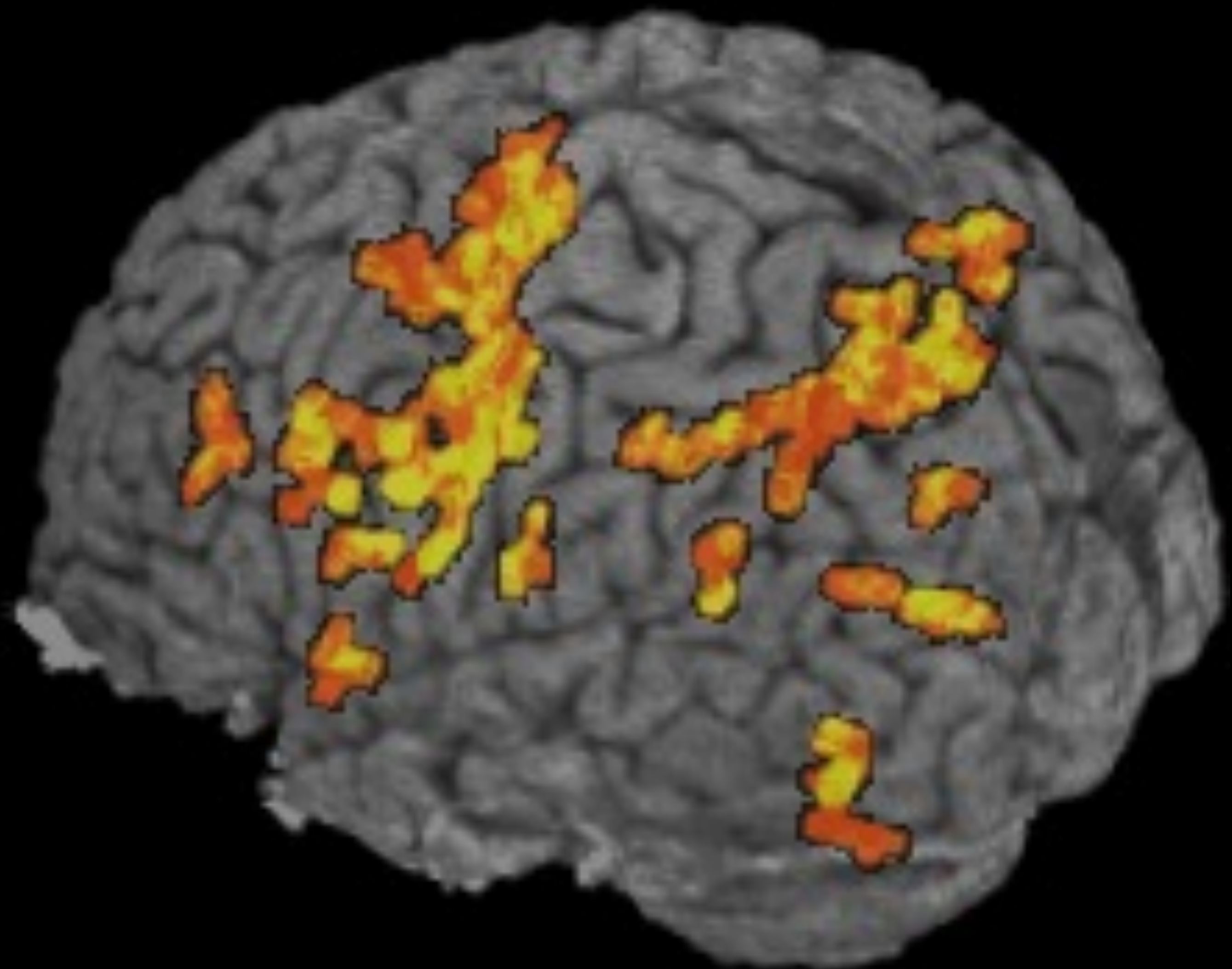
Future....

- 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 Informatio

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

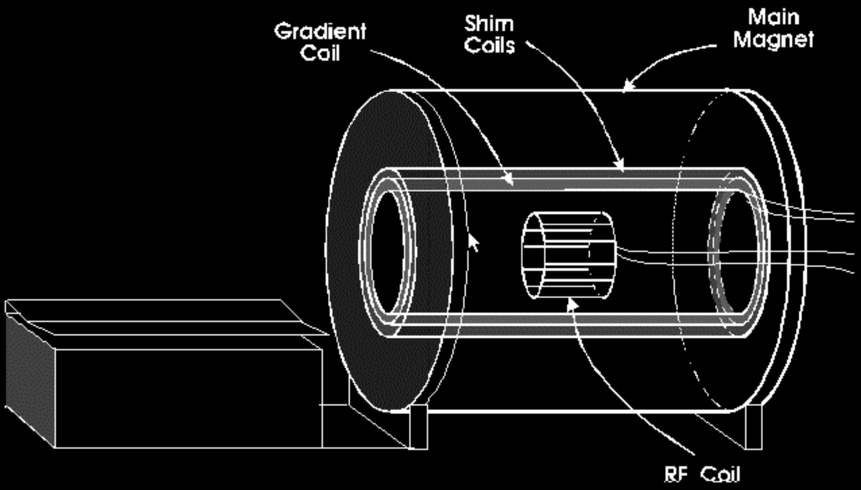
Color shows
through brain

Correlation > 0.45

The End

2 G/cm, 350 T/m/s

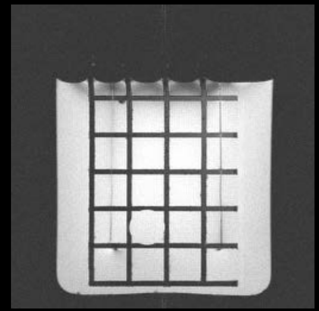
4 G/cm, 150 T/m/s

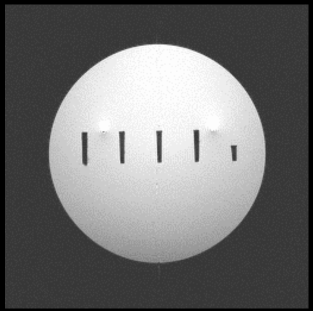


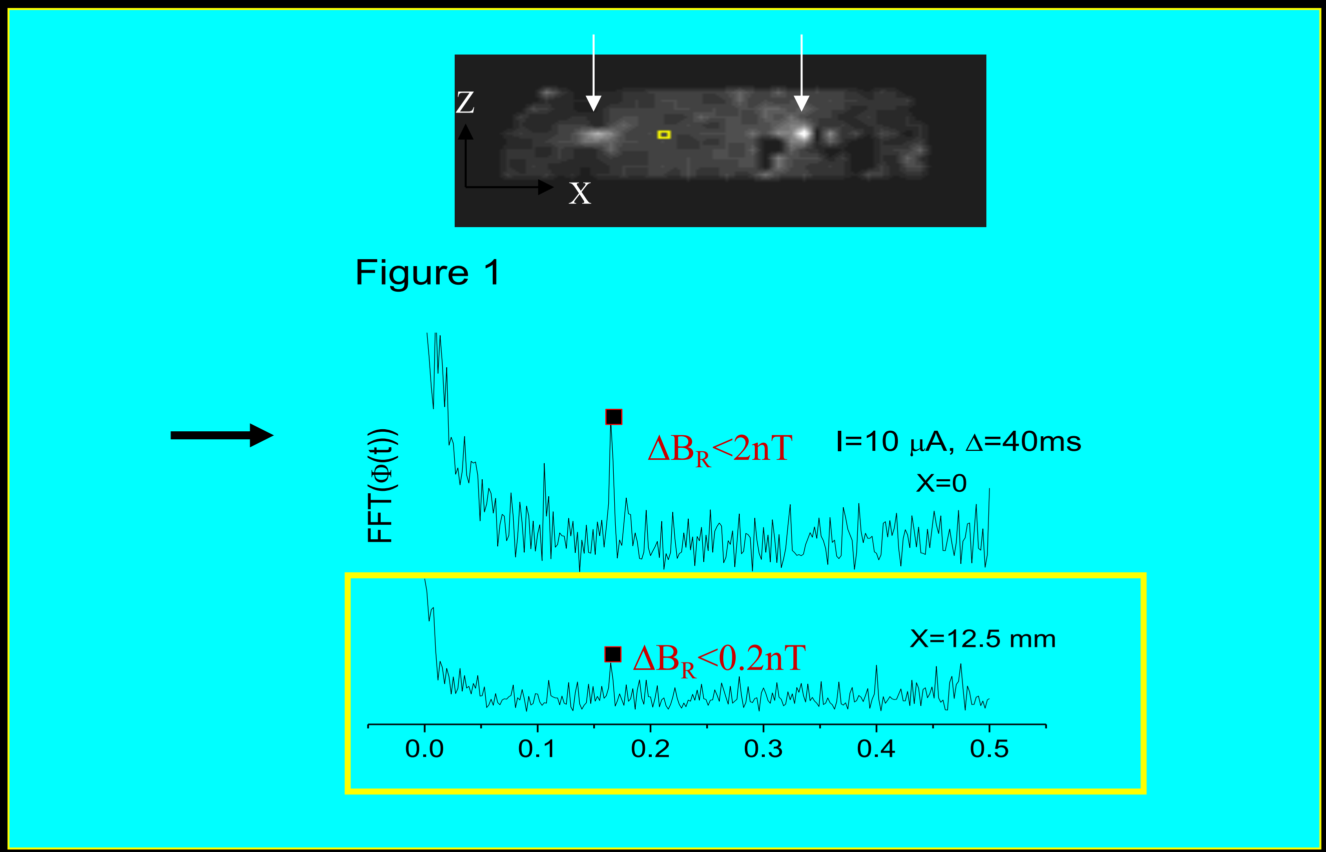
10 G/cm, 1000 T/m/s

➡ Diffusion imaging
Faster imaging
Higher resolution

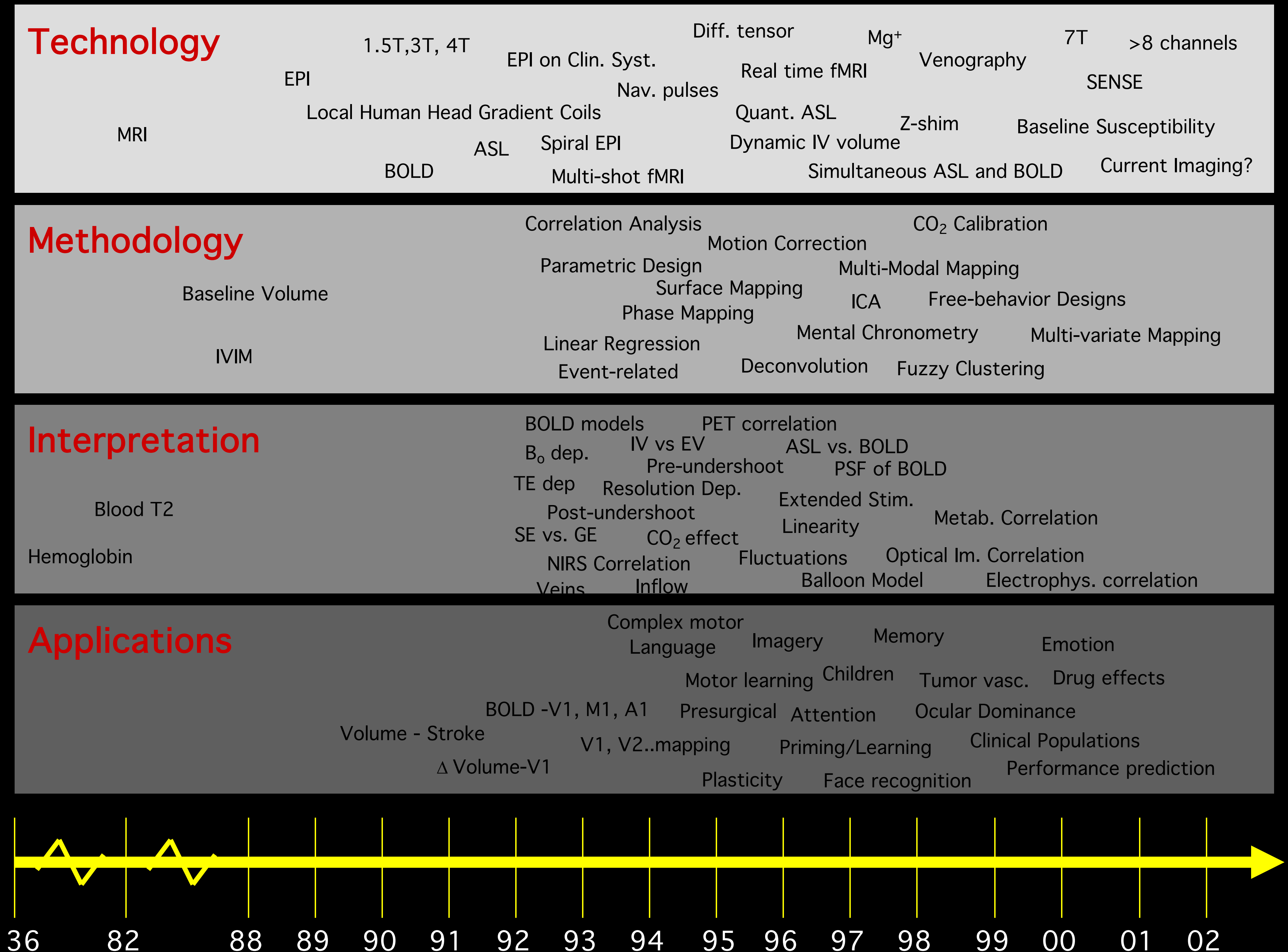
Neuronal Current Imaging







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)


Technology
MRI
EPI
1.5T,3T, 4T
Local Human Head Gradient Coils
BOLD
ASL
EPI on Clin. Syst.
Spiral EPI
Multi-shot fMRI
Nav. pulses
Diff. tensor
Real time fMRI
Quant. ASL
Dynamic IV volume
Mg+
Z-shim
Simultaneous ASL and BOLD
Venography
7T
SENSE
Baseline Susceptibility
>8 channels
Current Imaging?
Methodology
Baseline Volume
IVIM
Correlation Analysis
Parametric Design
Linear Regression
Event-related
Surface Mapping
Phase Mapping
Motion Correction
Deconvolution
Mental Chronometry
Multi-Modal Mapping
ICA
CO2 Calibration
Free-behavior Designs
Fuzzy Clustering
Multi-variate Mapping
Interpretation
Blood T2
Hemoglobin
BOLD models
Bo dep.
TE dep
SE vs. GE
Post-undershoot
NIRS Correlation
Veins
IV vs EV
Resolution Dep.
Pre-undershoot
CO2 effect
Inflow
PET correlation
ASL vs. BOLD
Extended Stim.
Linearity
Fluctuations
Balloon Model
PSF of BOLD
Metab. Correlation
Optical Im. Correlation
Electrophys. correlation
Applications
Volume - Stroke
Δ Volume-V1
BOLD -V1, M1, A1
V1, V2..mapping
Complex motor
Language
Motor learning
Presurgical
Plasticity
Imagery
Children
Attention
Priming/Learning
Face recognition
Memory
Tumor vasc.
Ocular Dominance
Emotion
Drug effects
Clinical Populations
Performance prediction
36
82
88
89
90
91
92
93
94
95
96
97
98
99
00
01
02

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