Latest Developments in fMRI

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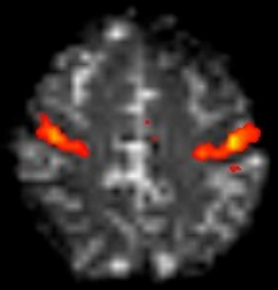
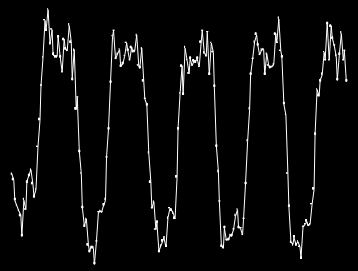
Laboratory of Brain and Cognition
National Institute of Mental Health

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

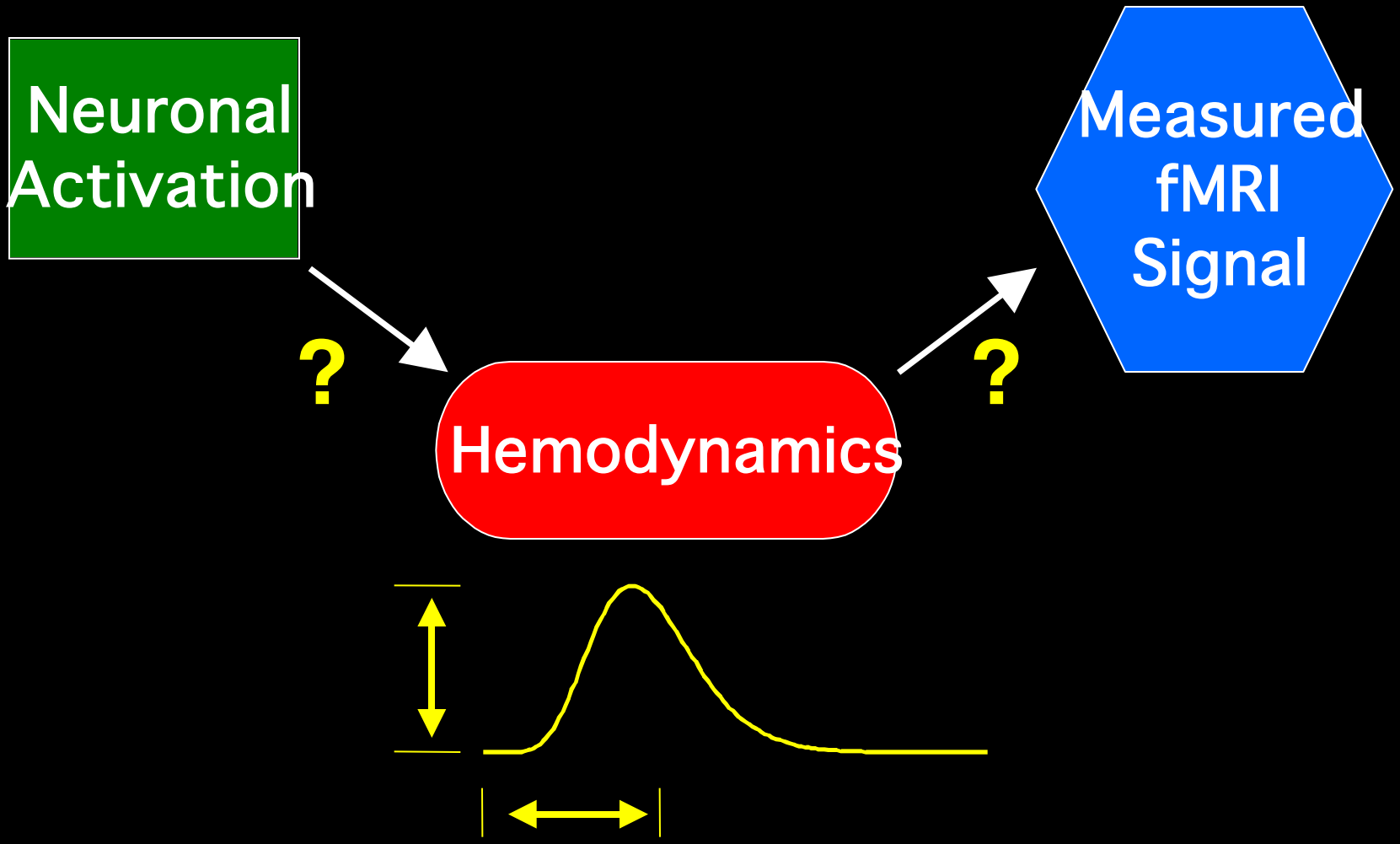
- **Where?**
- **When?**
- **How much?**





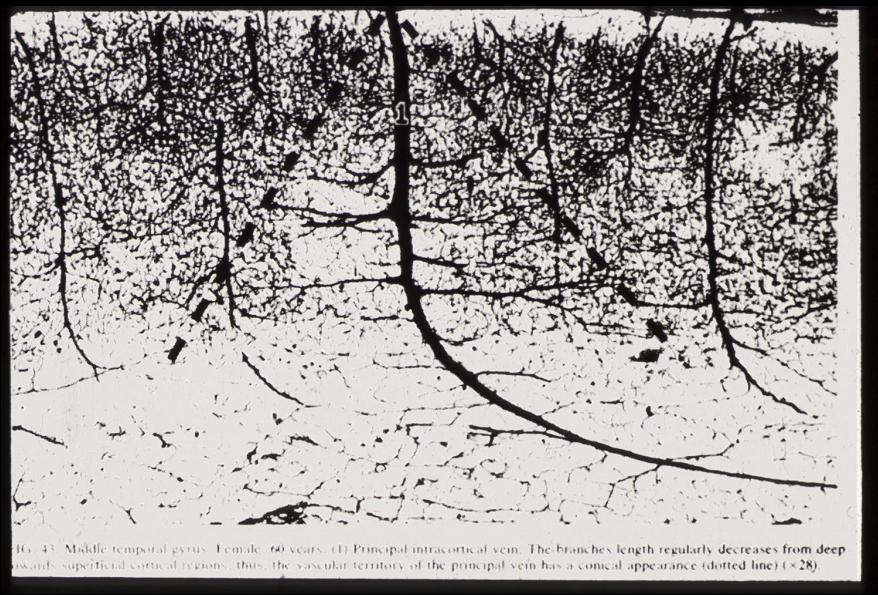
- **How to get the brain to do what we want it to do in the context of an fMRI experiment?**
  (*limitations*: limited time and signal to noise, motion, acoustic noise)

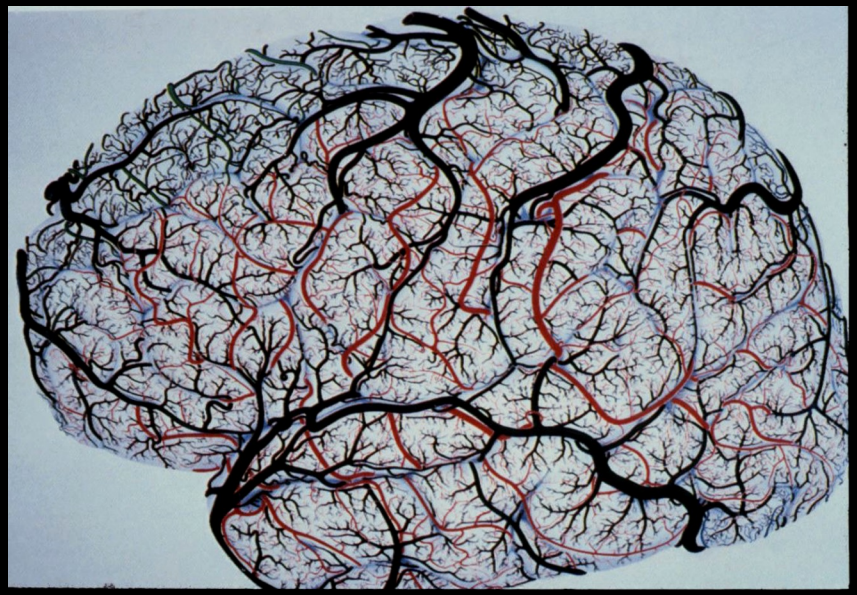
- **How much more information can we obtain?**


Neuronal Activation
?
Hemodynamics
?
Measured fMRI Signal
Physiologic Factors

A Primary Challenge for Observing Brain Activation:

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

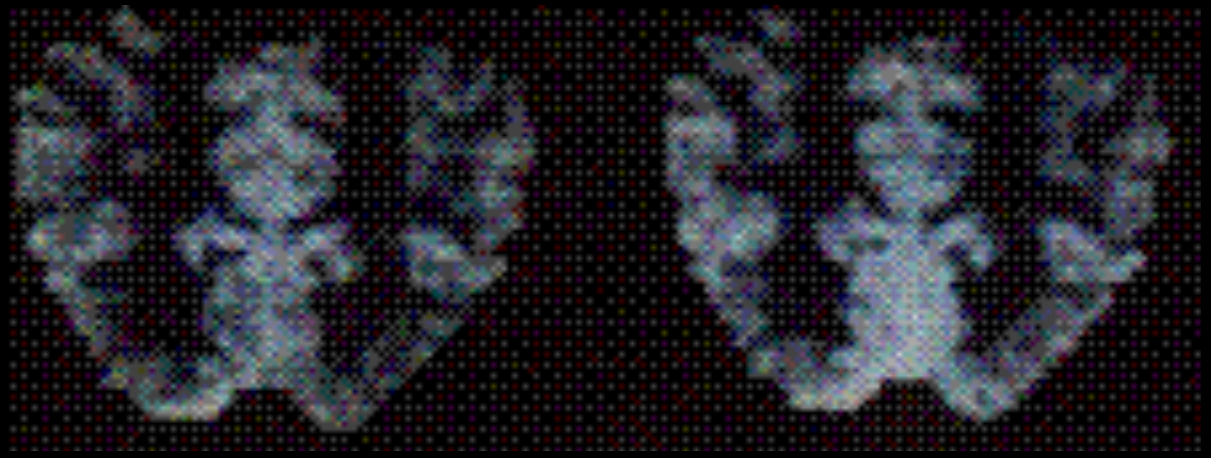


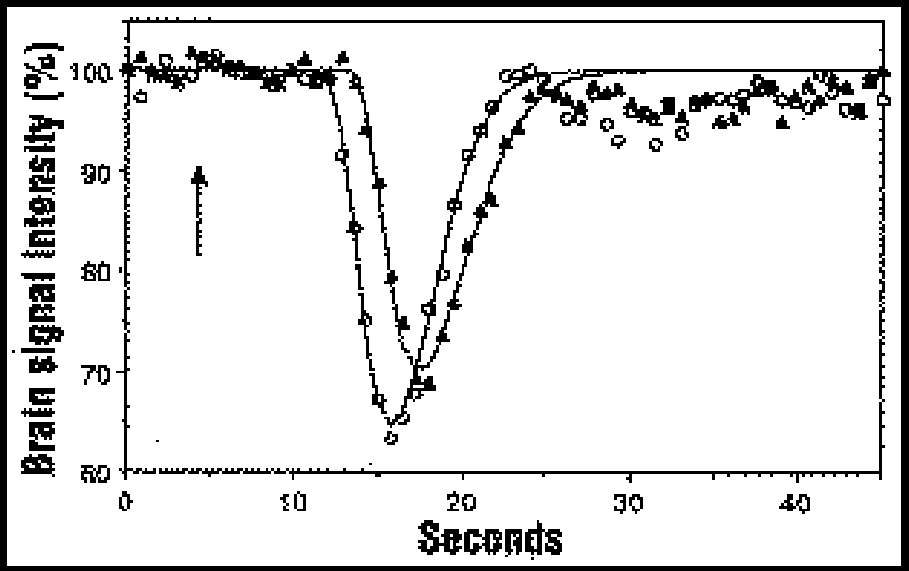


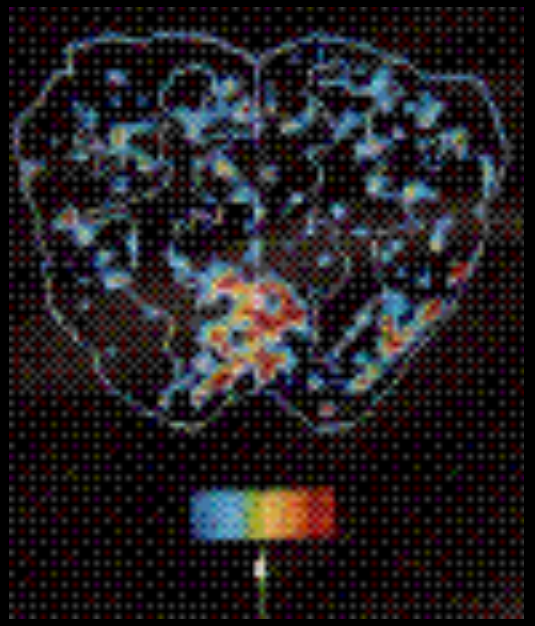
Contrast in Functional MRI

- **Blood Volume**
  - Contrast agent injection and time series collection of T2* or T2 - weighted images
- **BOLD**
  - Time series collection of T2* or T2 - weighted images
- **Perfusion**
  - T1 weighting
  - Arterial spin labeling

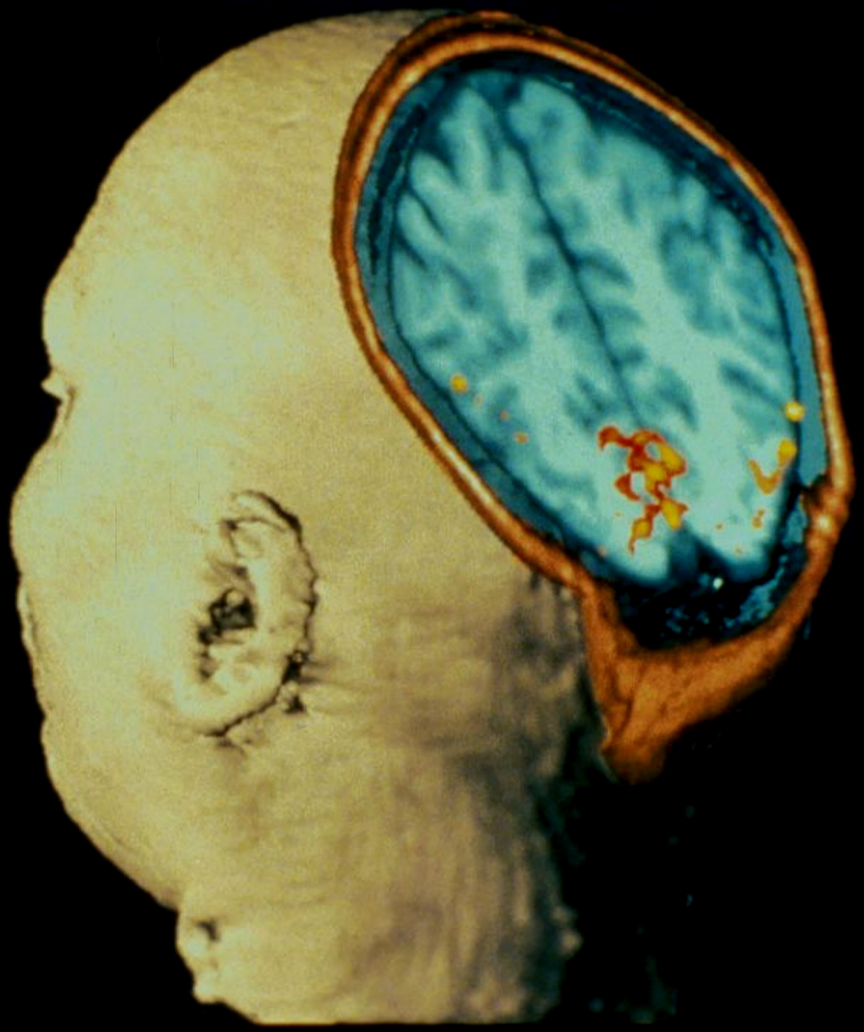
Resting Active







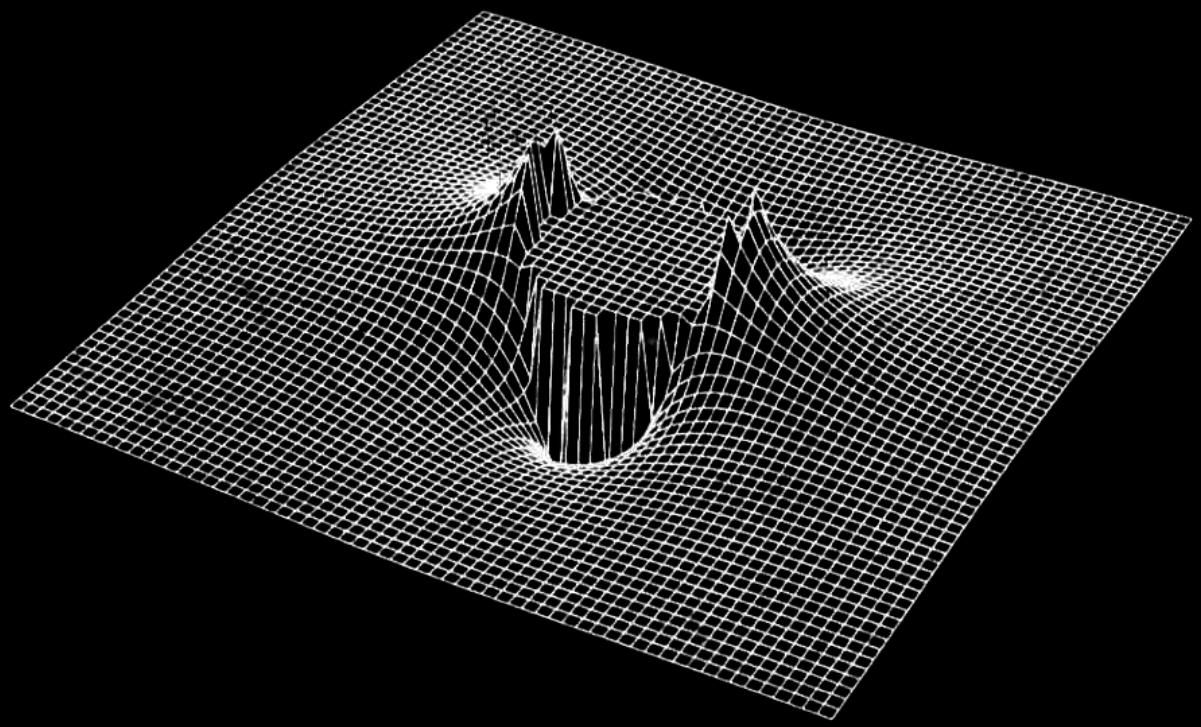
Photic Stimulation



MRI Image showing activation of the Visual Cortex

From Belliveau, et al. Science Nov 1991

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

↓

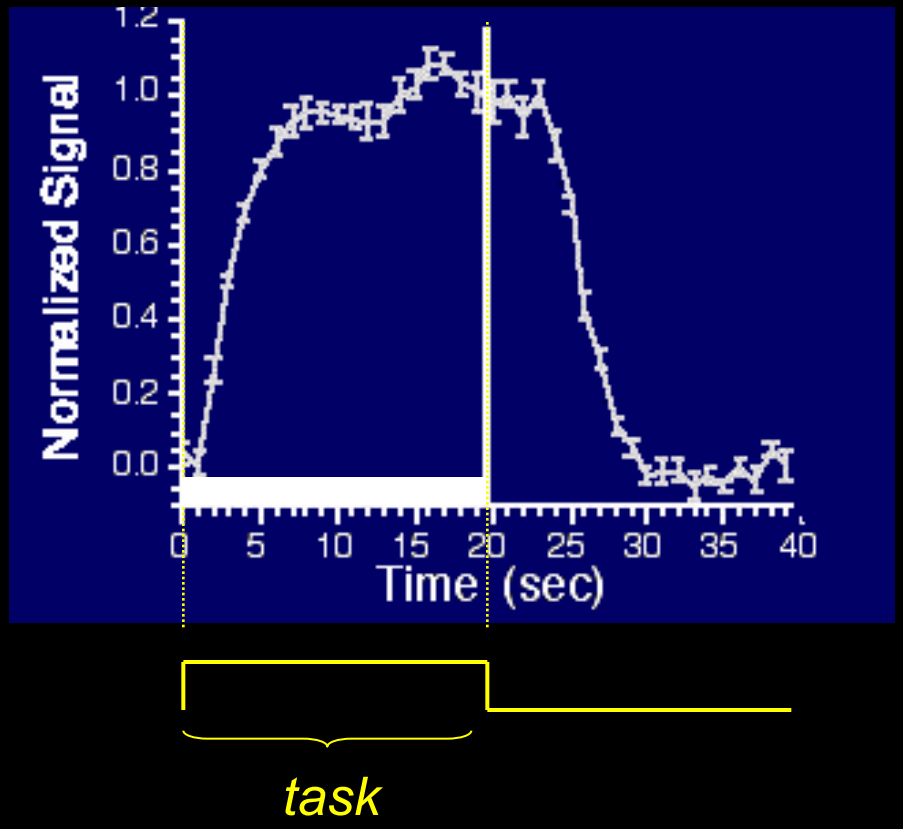
Decrease in susceptibility-related intravoxel dephasing → Increase in T2 and T2*

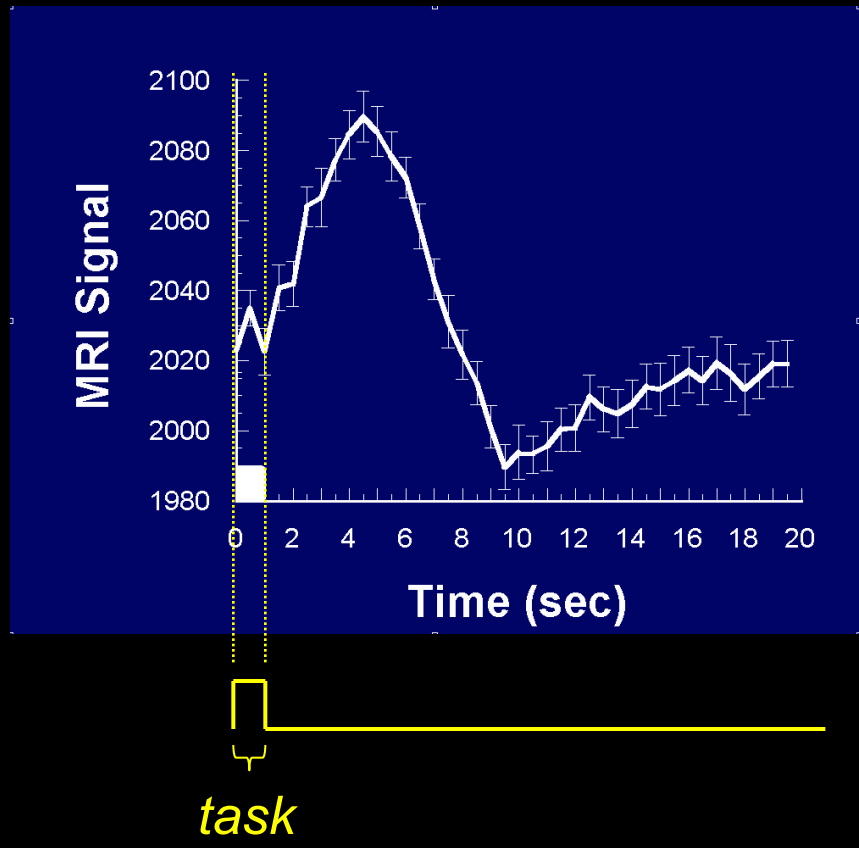
↓

Local Signal Increase in T2 and T2* - weighted sequences

The BOLD Signal

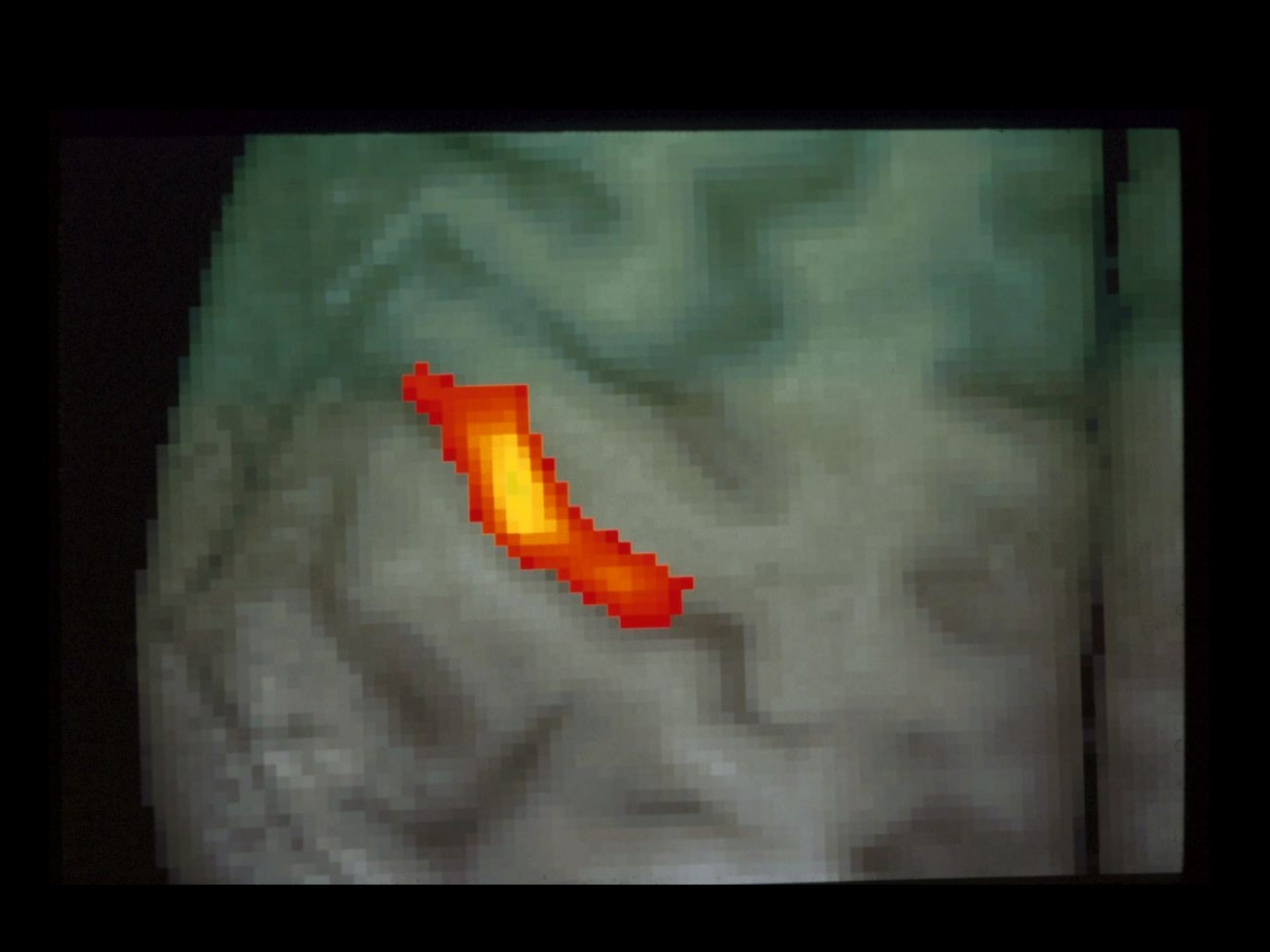
Blood Oxygenation Level Dependent (BOLD) signal changes





Alternating Left and Right Finger Tapping

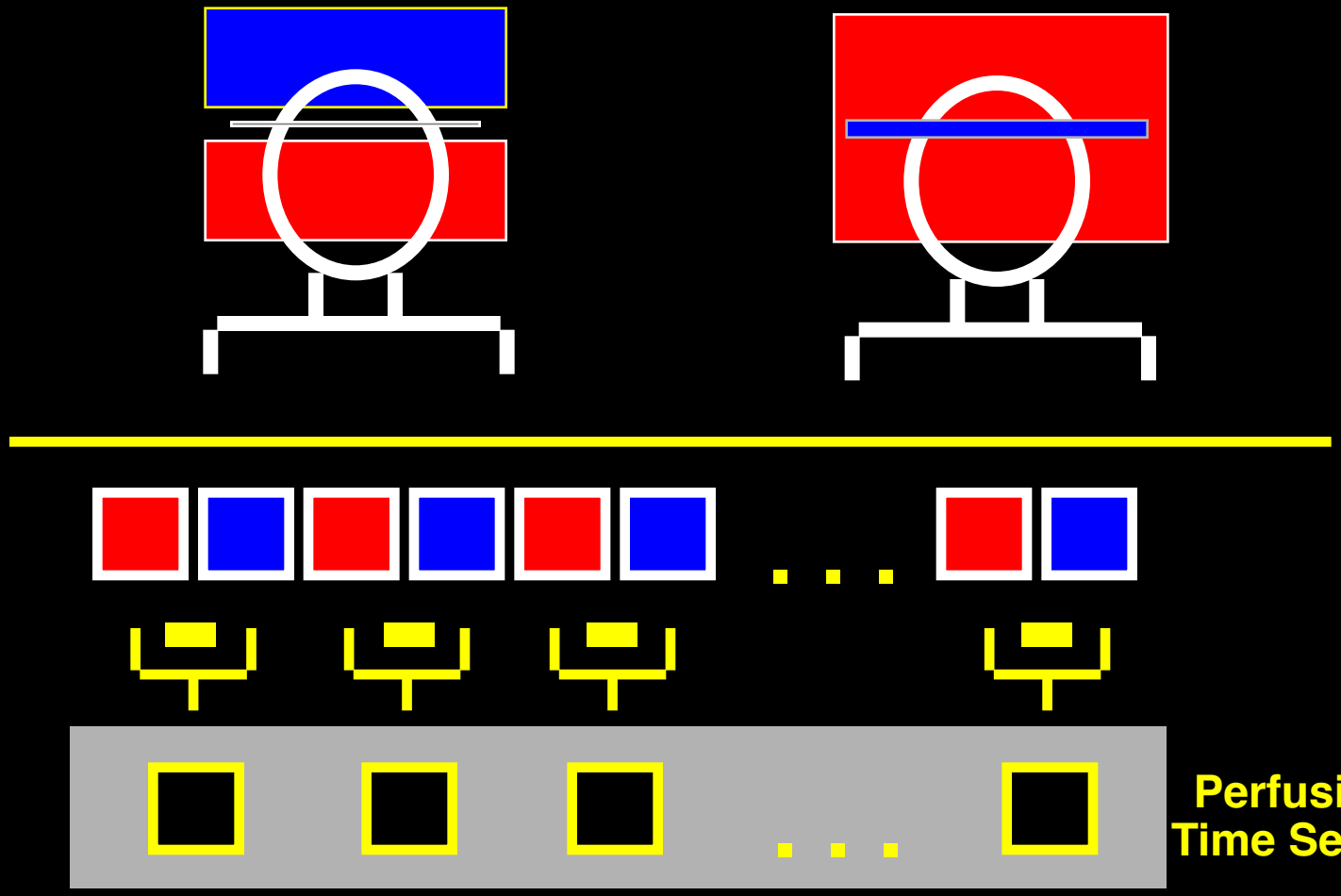
~ 1992

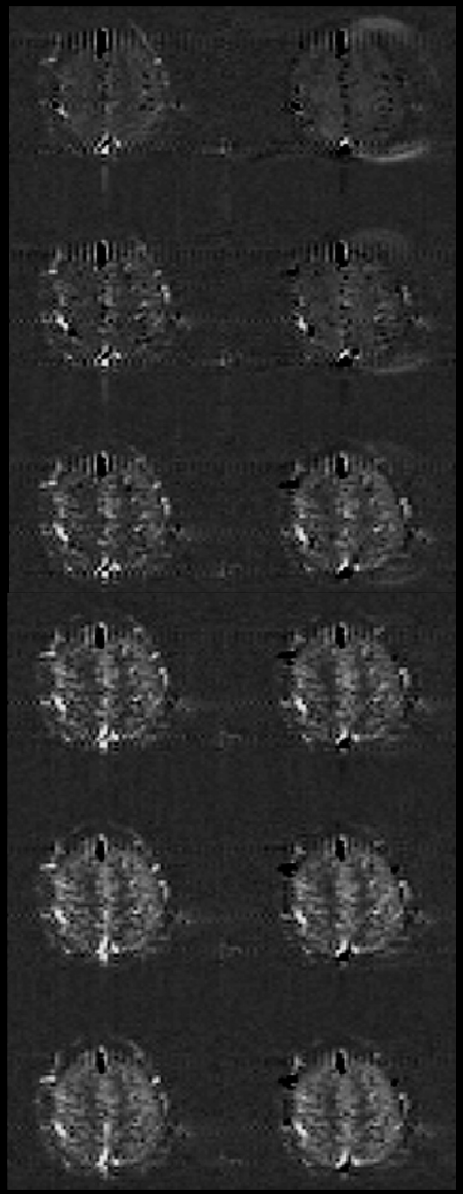


Perfusion / Flow Imaging

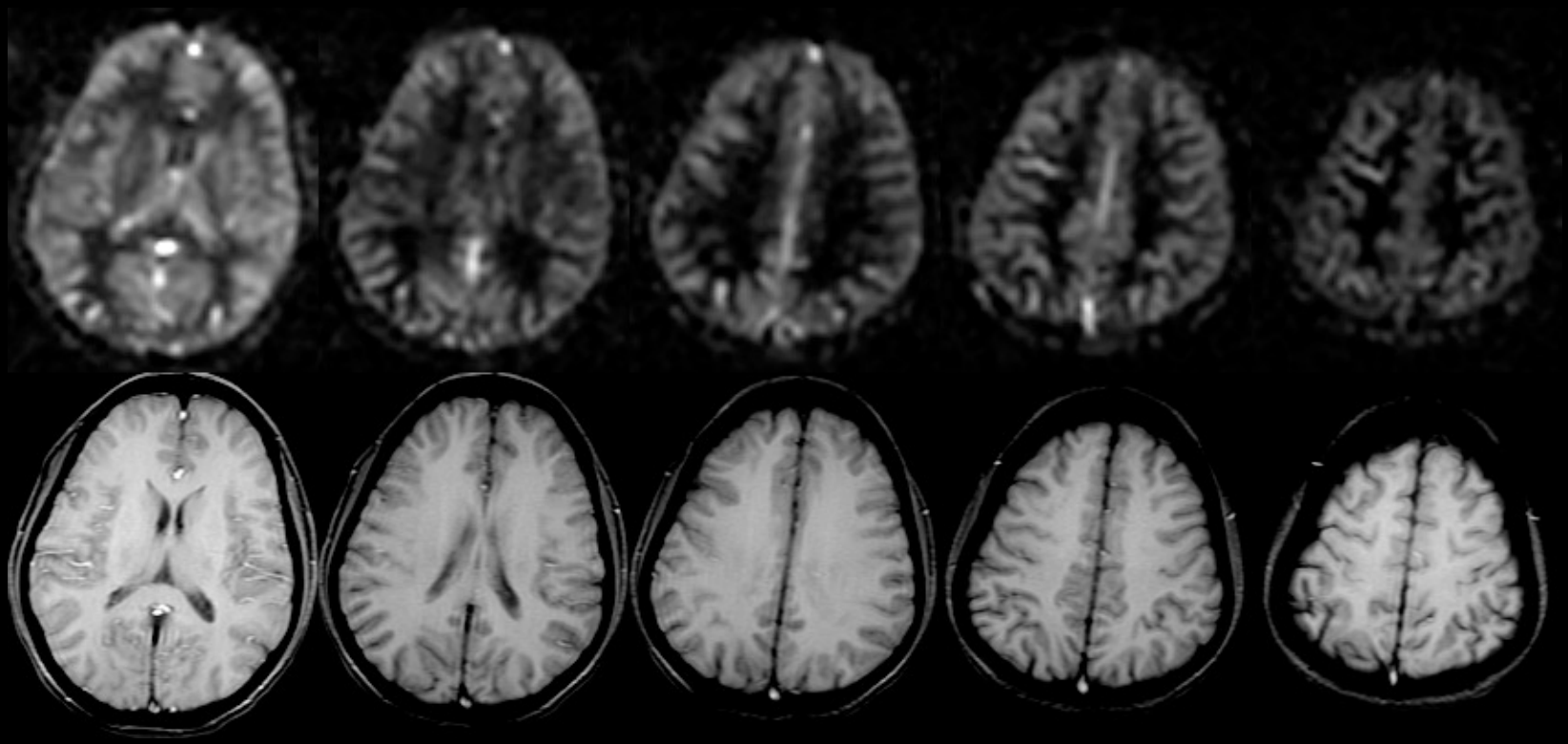
EPISTAR

FAIR

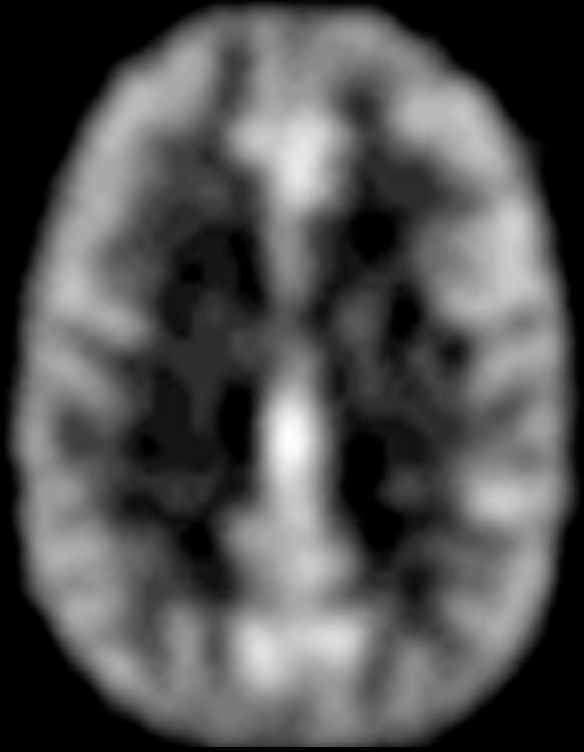


TI (ms)	FAIR	EPISTAR
200		
400		
600		
800		
1000		
1200		

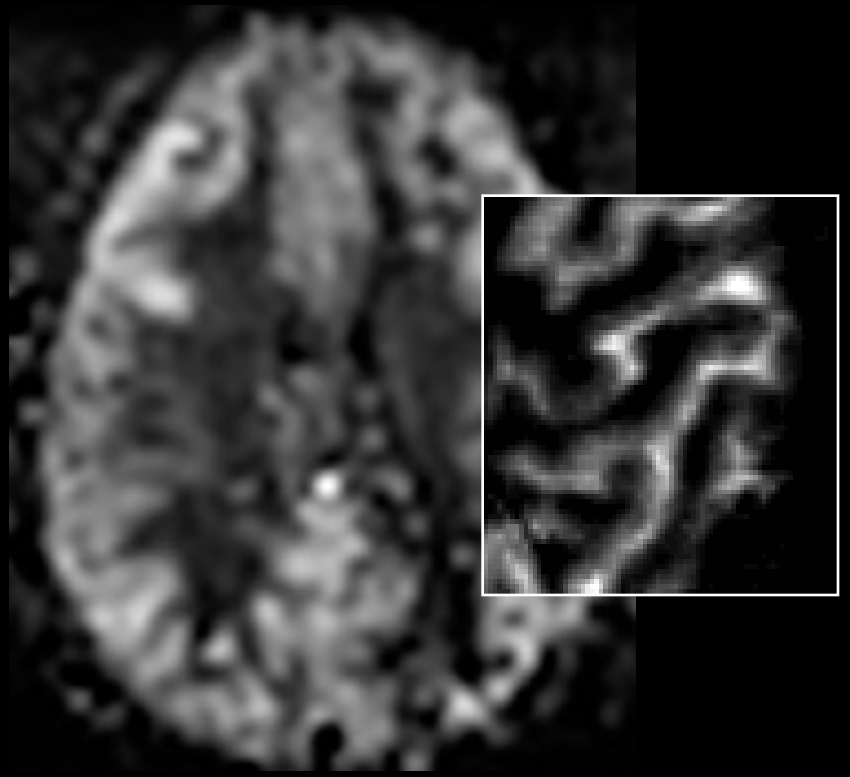
Resting ASL Signal



Comparison with Positron Emission Tomography



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



MRI: ASL

Pushing the Envelope...

1. Temporal Resolution
2. Spatial Resolution
3. Sensitivity and Noise
4. Information Content
5. Implementation

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1. Temporal Resolution
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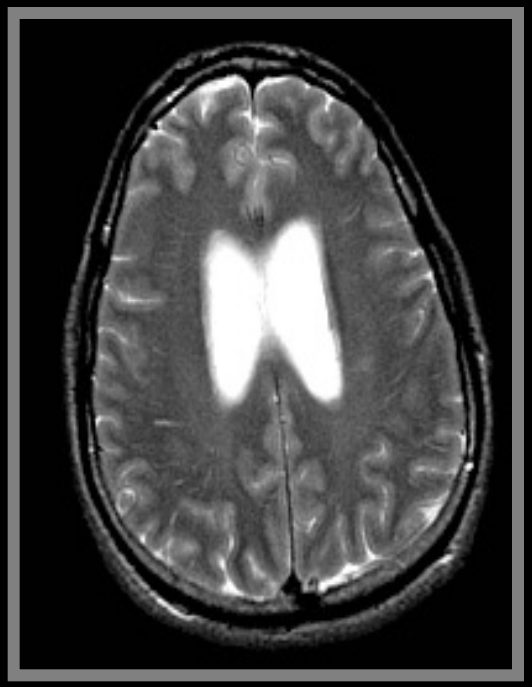
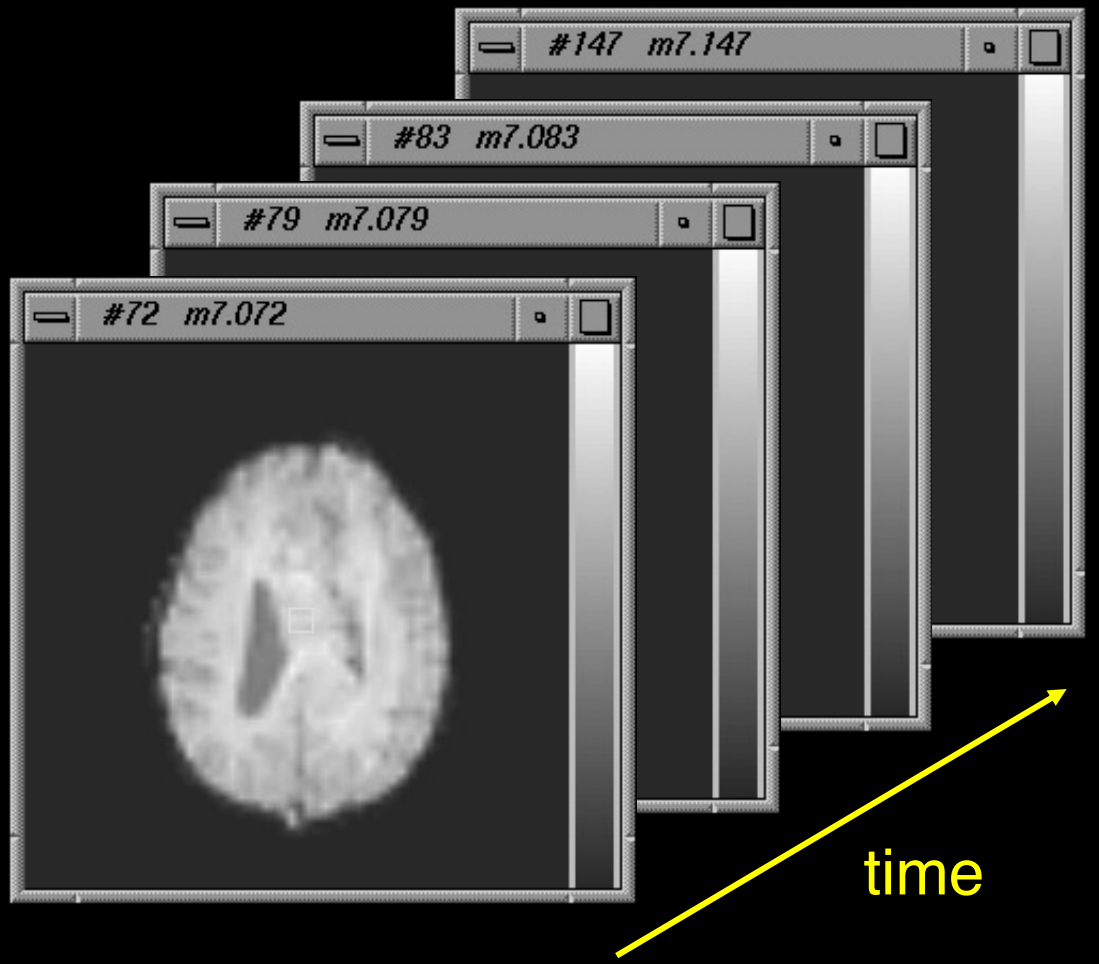
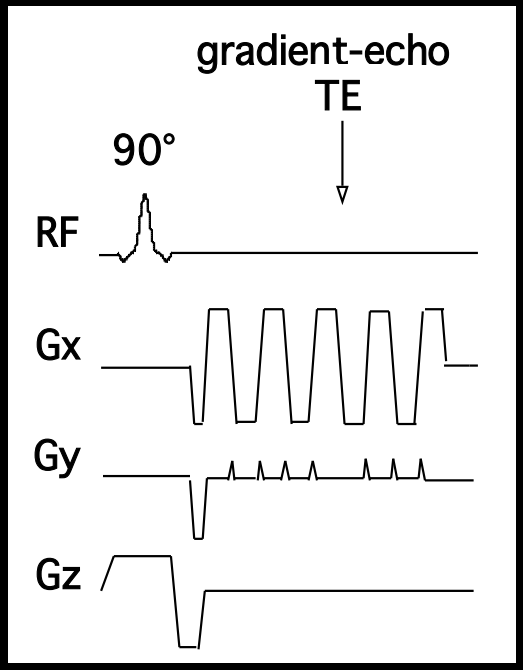


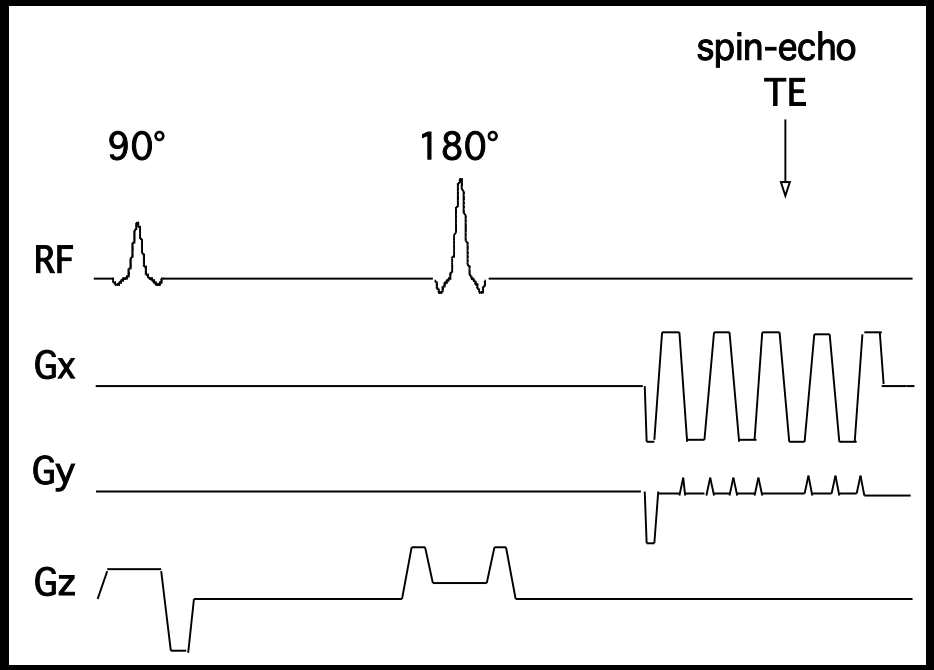


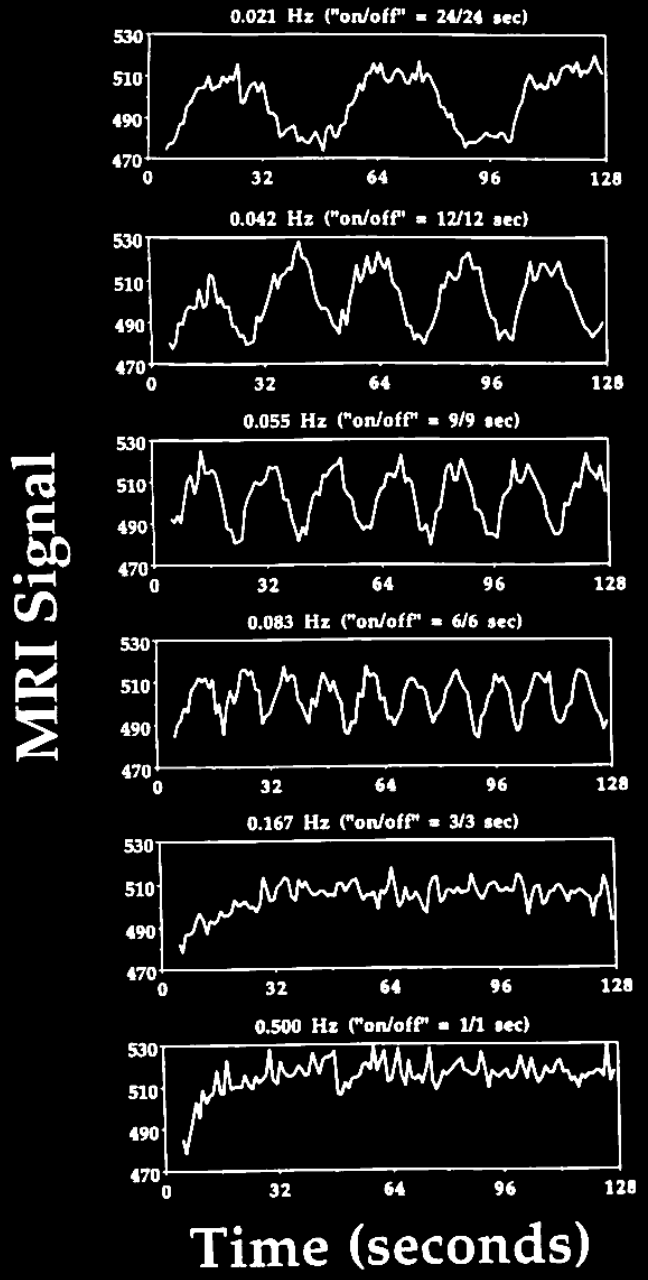
Anatomic

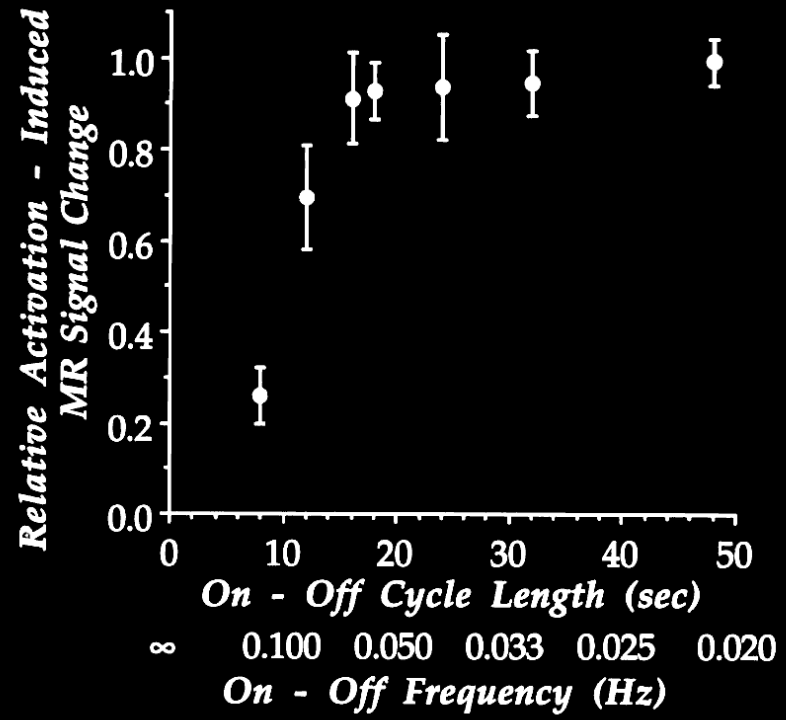
Functional

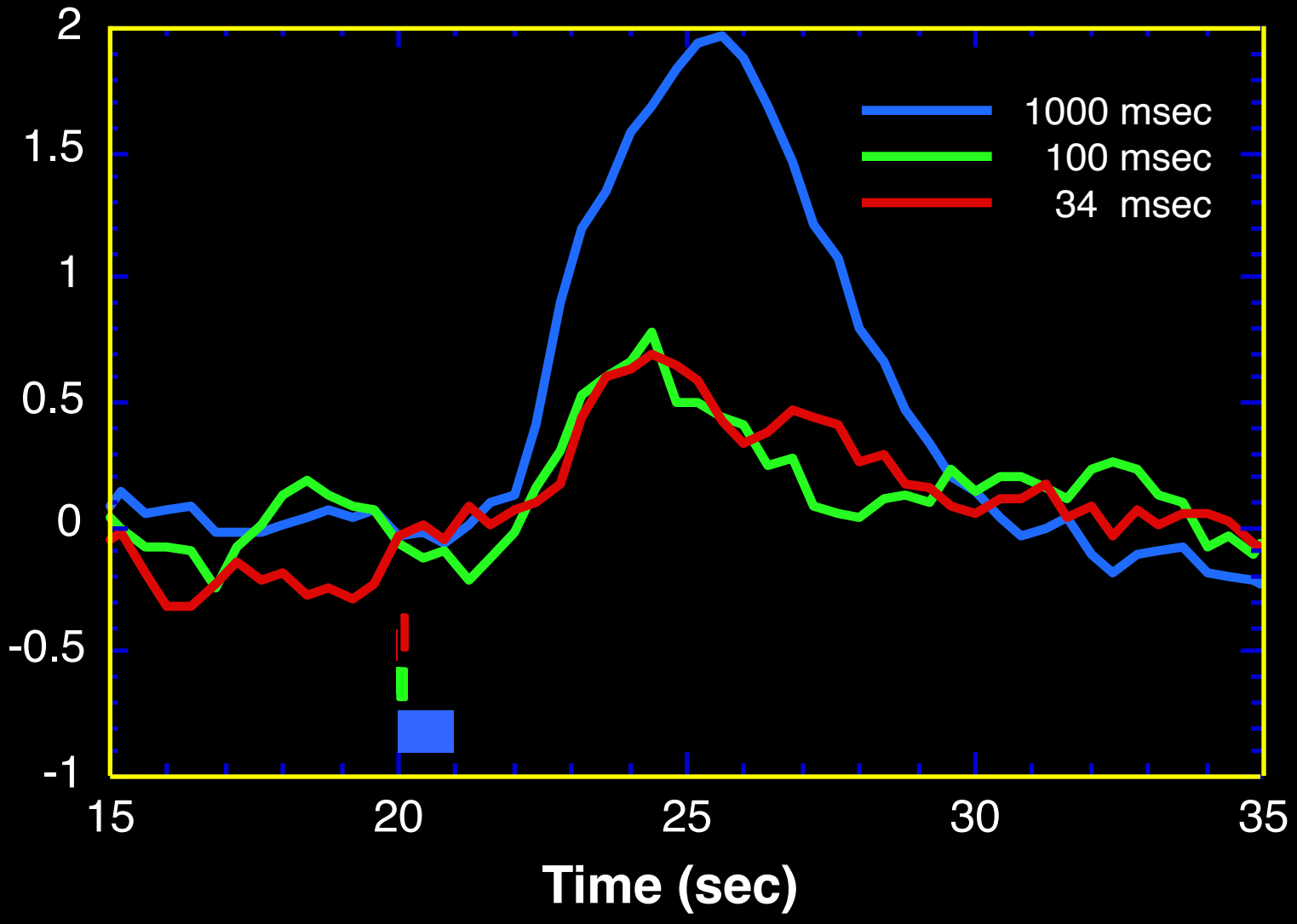
Echo-Planar Imaging

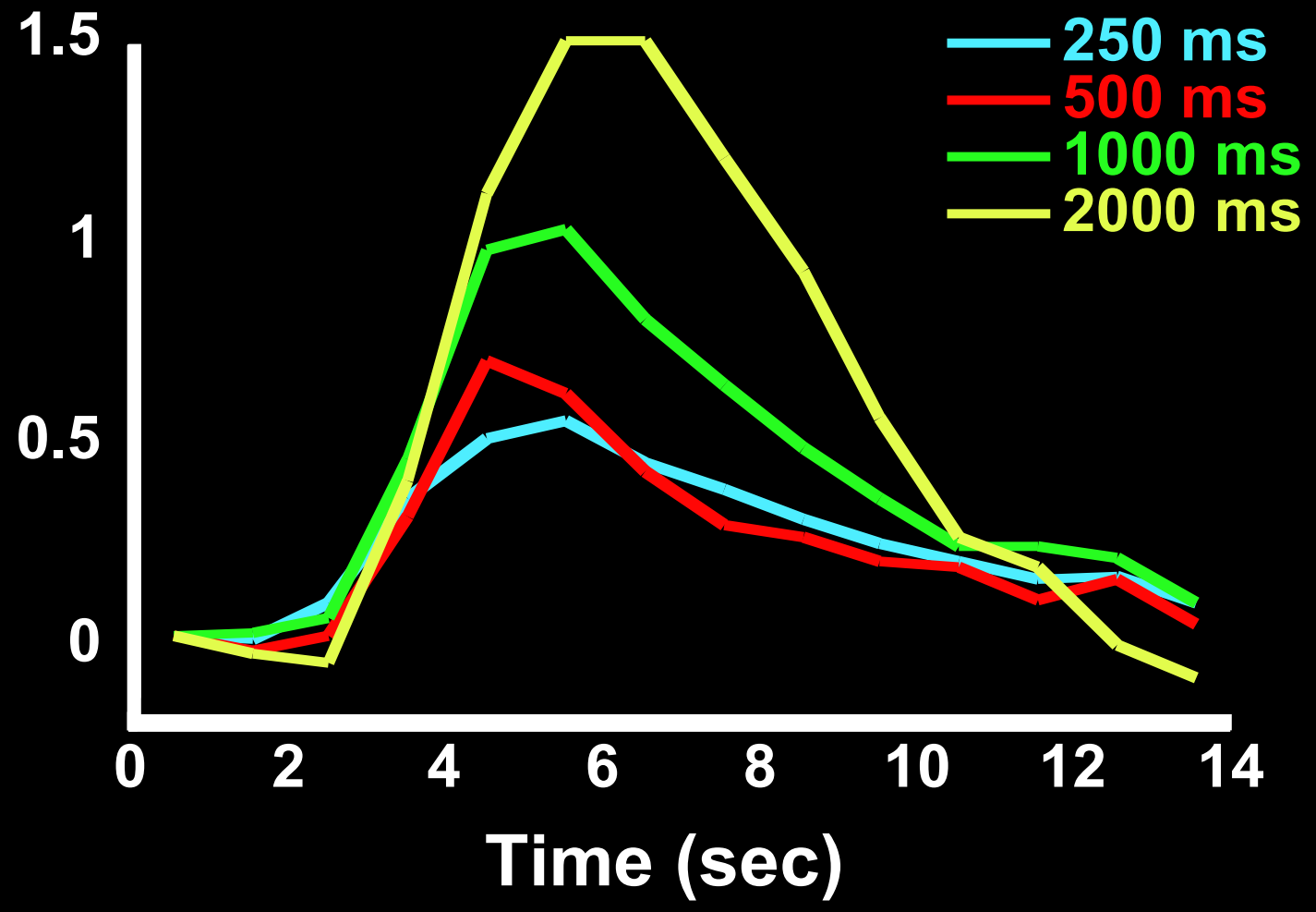




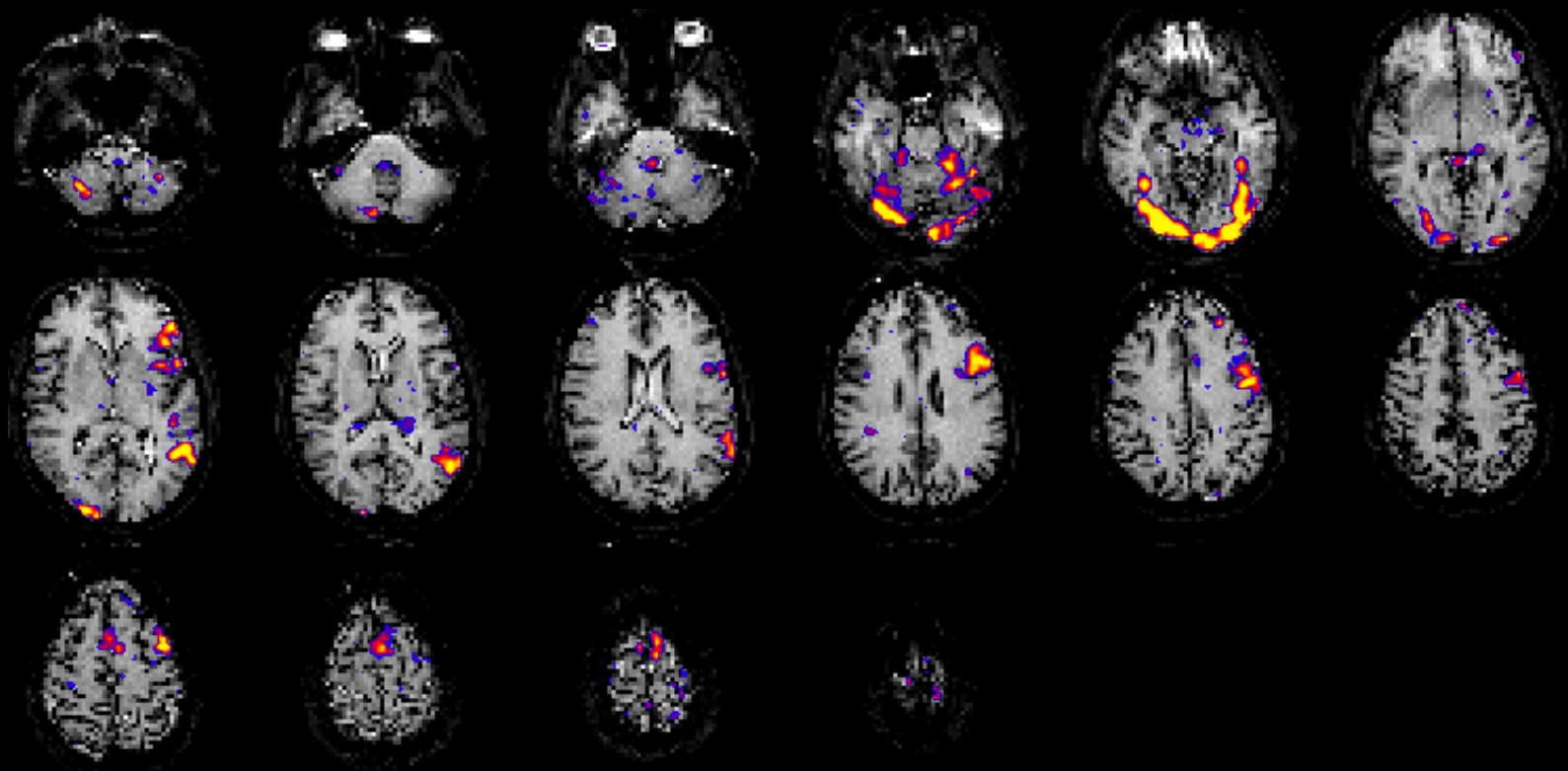

0.021 Hz ("on/off" = 24/24 sec)
0.042 Hz ("on/off" = 12/12 sec)
0.055 Hz ("on/off" = 9/9 sec)
0.083 Hz ("on/off" = 6/6 sec)
0.167 Hz ("on/off" = 3/3 sec)
0.500 Hz ("on/off" = 1/1 sec)
530
510
490
470
0
32
64
96
128
MRI Signal
Time (seconds)


Relative Activation - Induced MR Signal Change
1.0
0.8
0.6
0.4
0.2
0.0
0
10
20
30
40
50
On - Off Cycle Length (sec)
∞
0.100
0.050
0.033
0.025
0.020
On - Off Frequency (Hz)

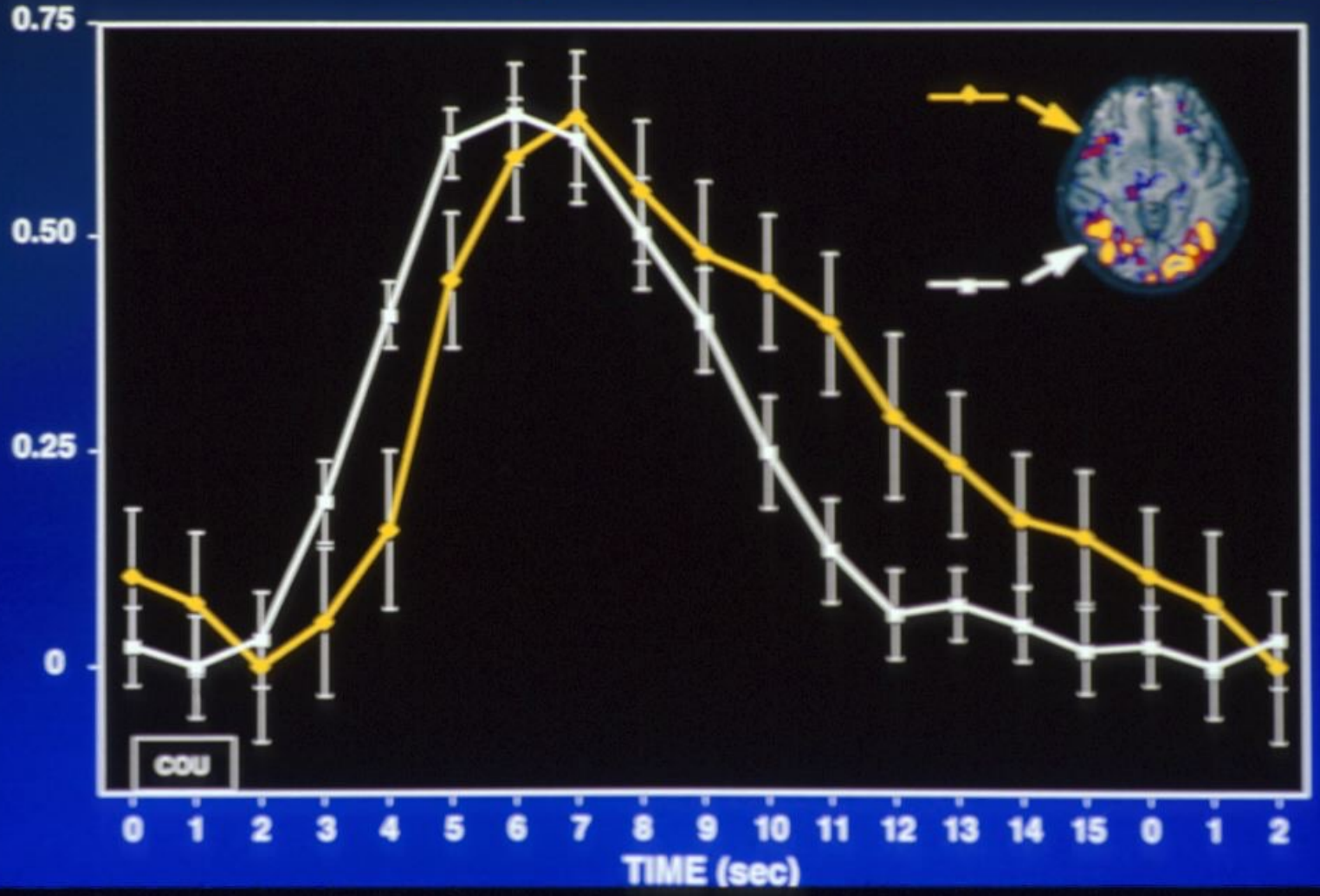

2
1.5
1
0.5
0
-0.5
-1
15
20
25
30
35
1000 msec
100 msec
34 msec
Time (sec)


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

Word stem completion

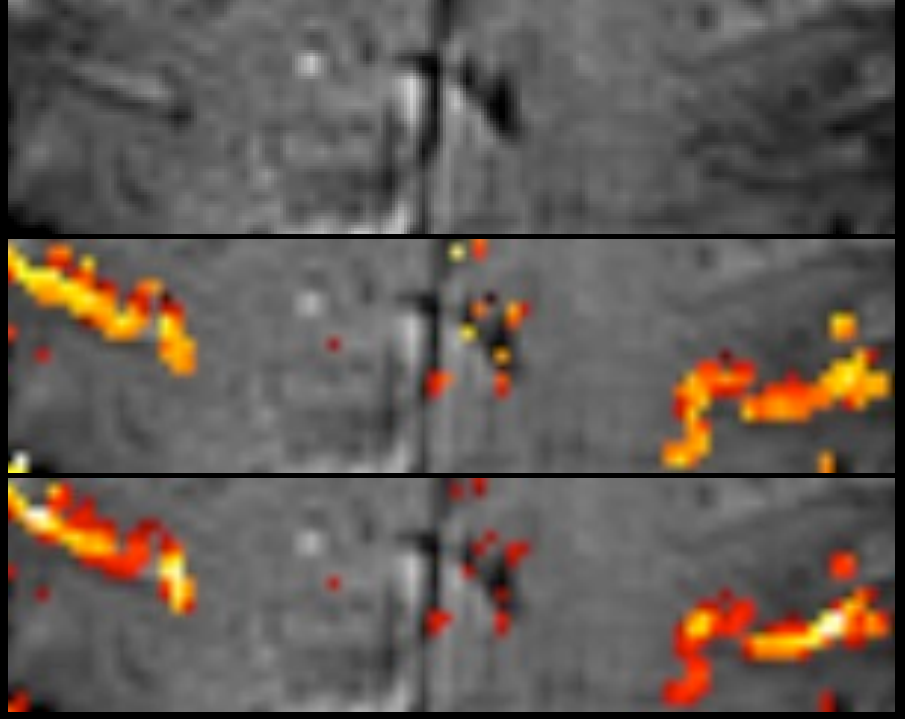


Time Course Comparison Across Brain Regions



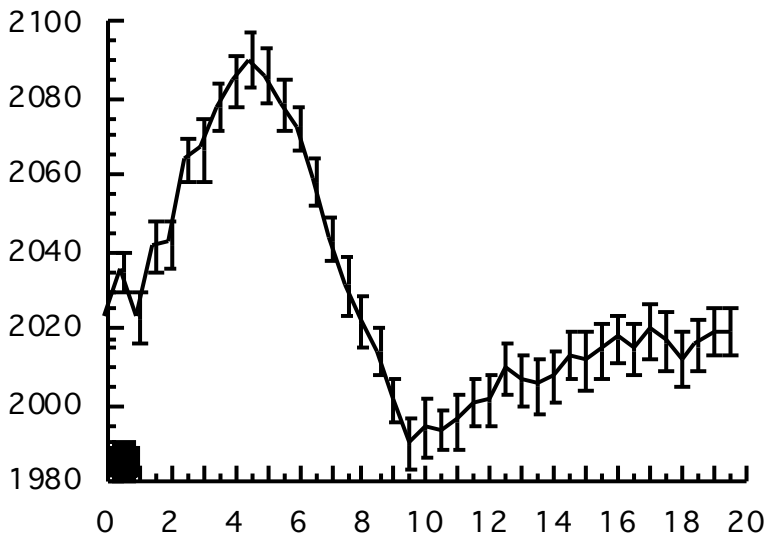
Latency

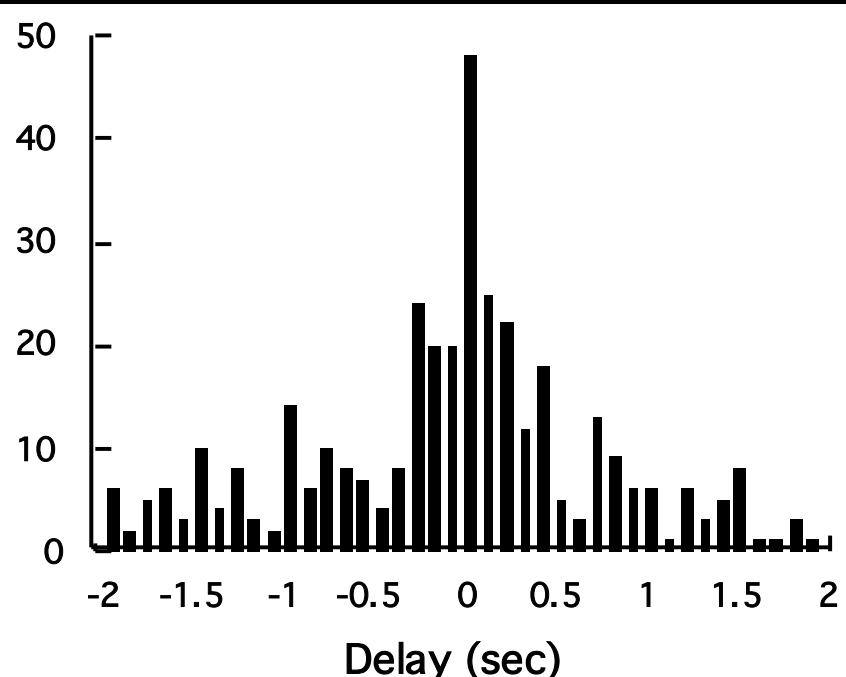
Magnitude



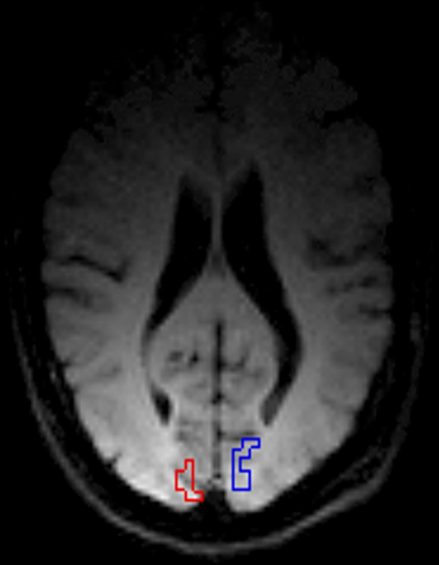
+ 2 sec

- 2 sec



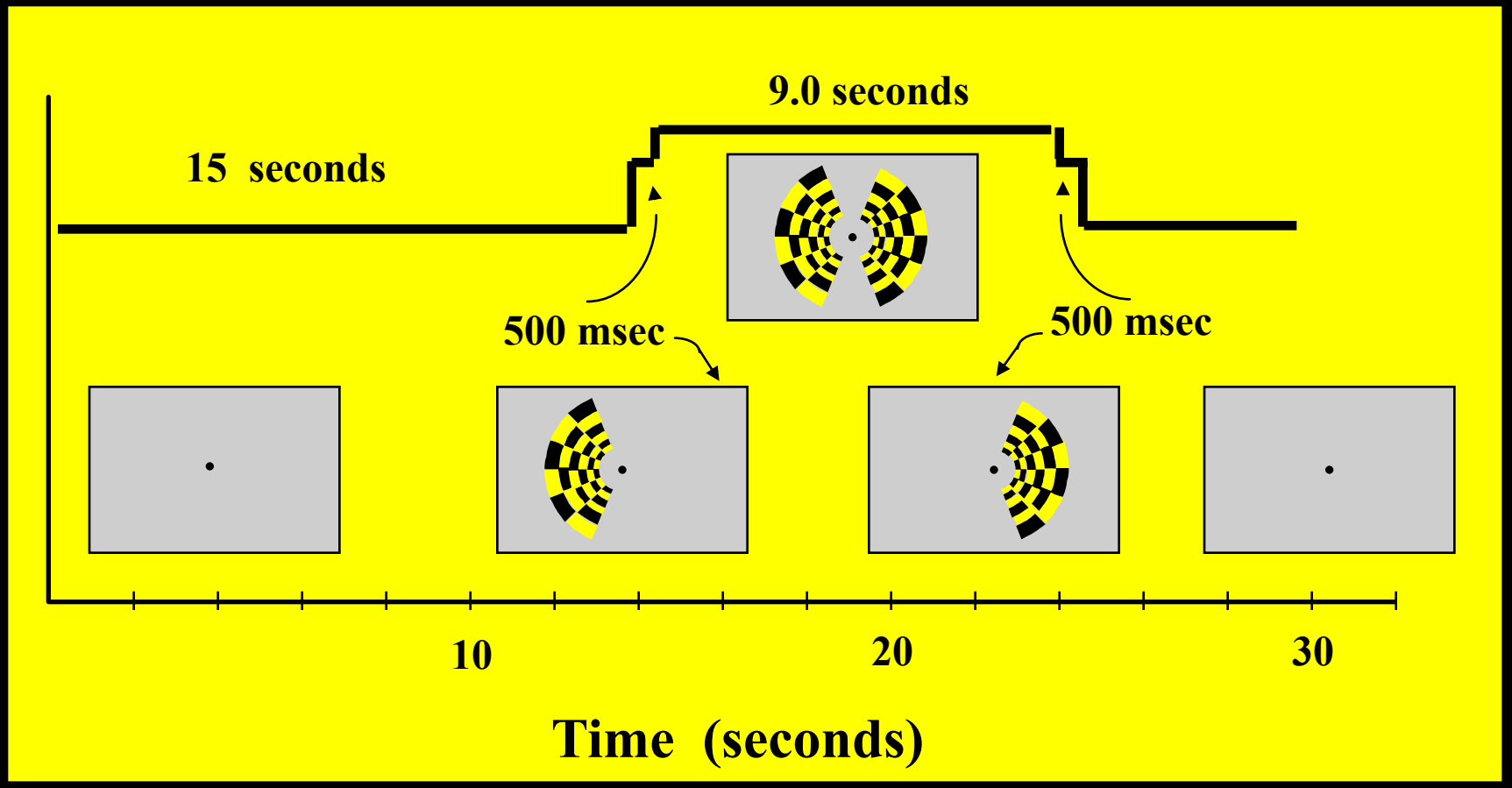


Regions of Interest Used for Hemi-Field Experiment

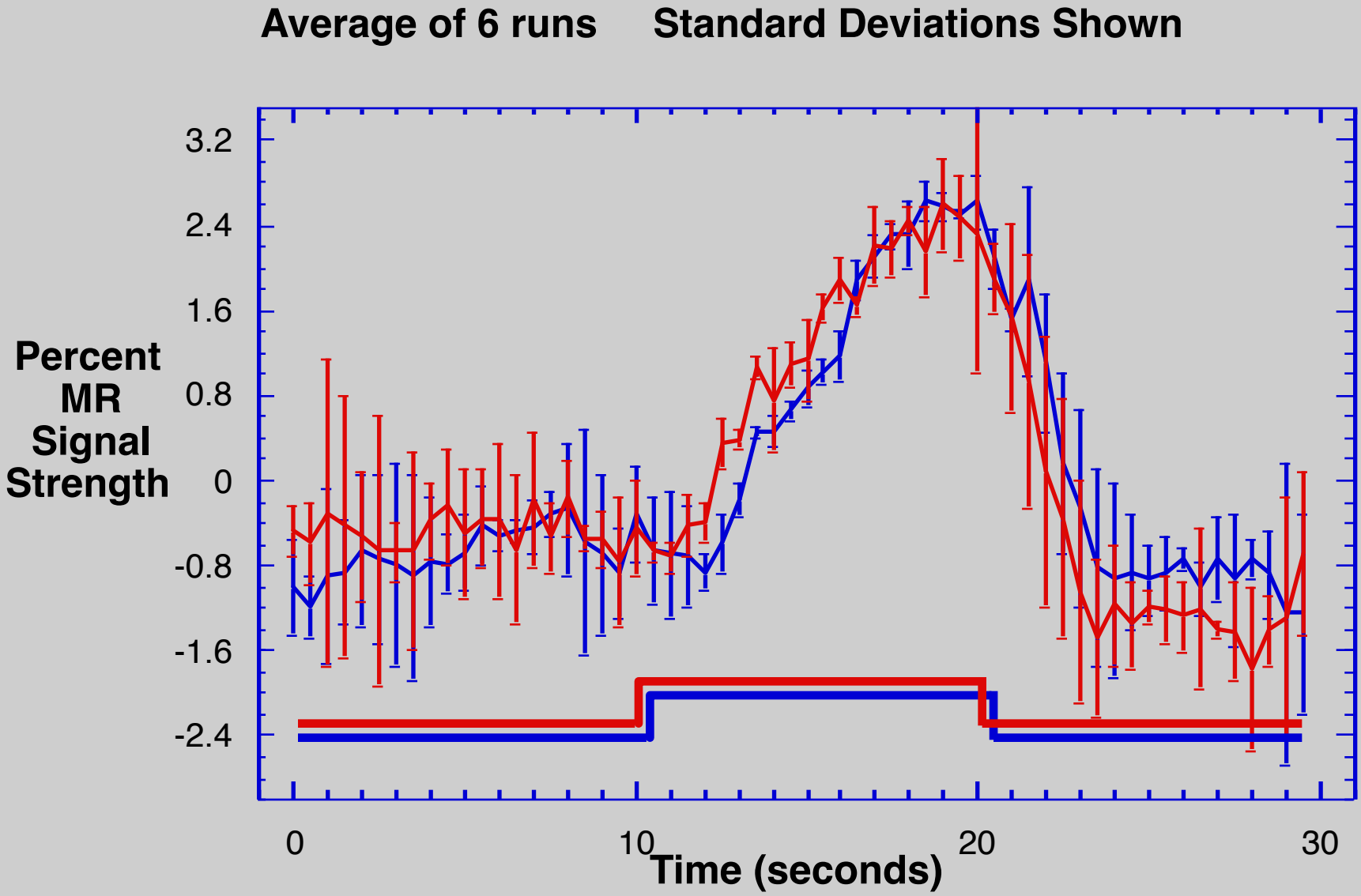


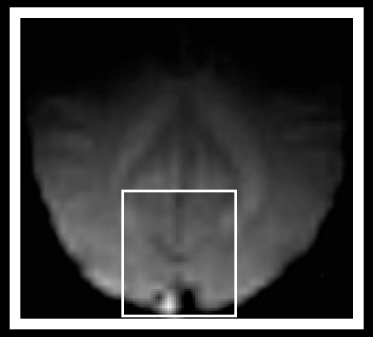
Right Hemisphere

Left Hemisphere


9.0 seconds
15 seconds
500 msec
500 msec
10
20
30
Time (seconds)

Hemi-field with 500 msec asynchrony

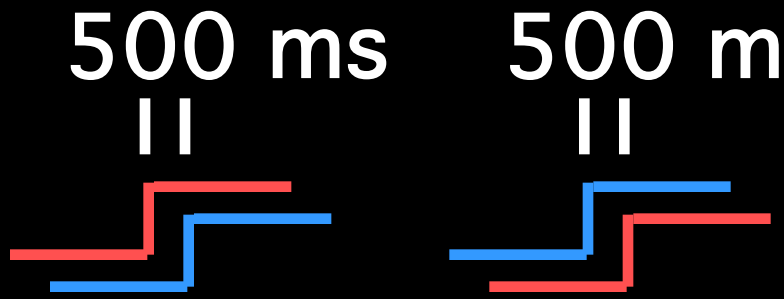




500 ms 500 ms

Right Hemifield

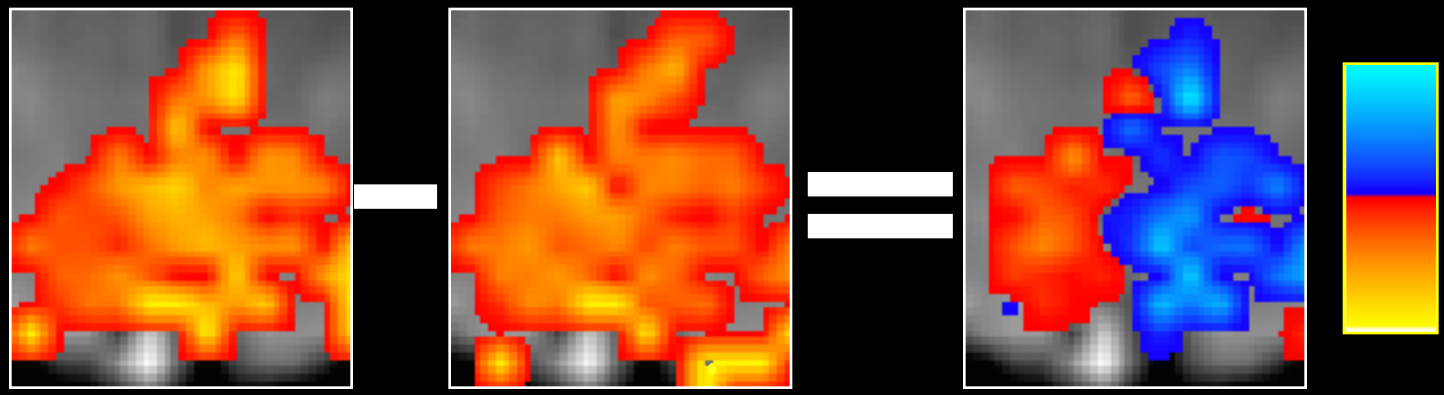
Left Hemifield



+ 2.5 s

0 s

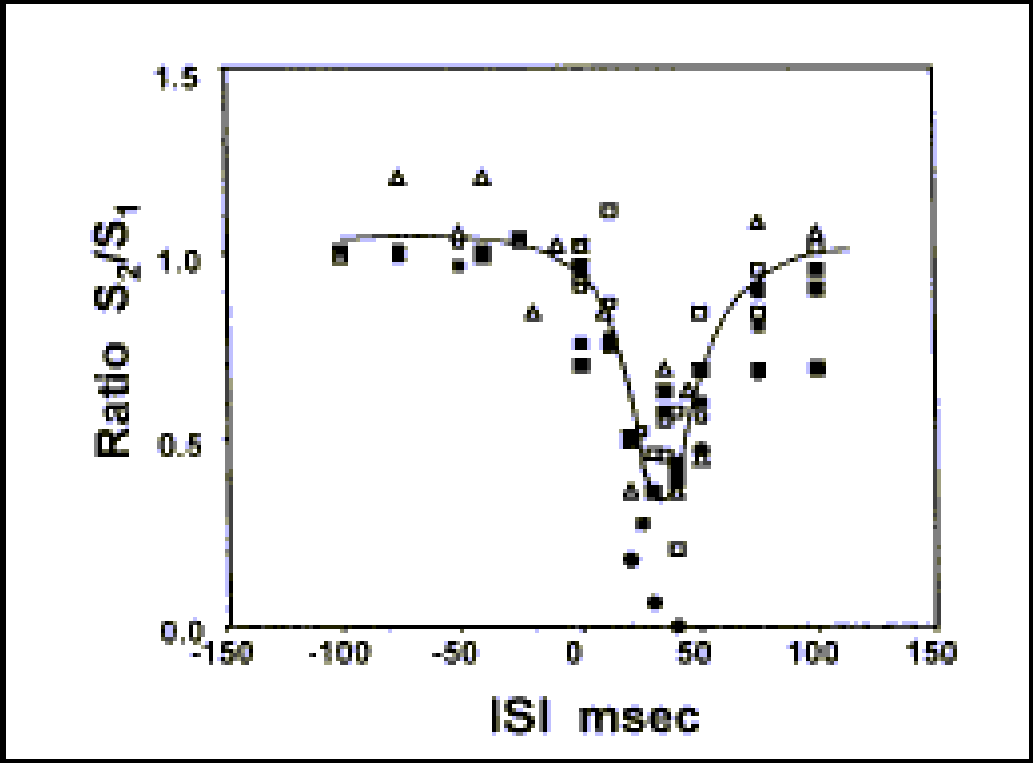
- 2.5 s



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[§]

[†]Bell Laboratories, Lucent Technologies, Murray Hill, NJ 07974; and [§]Center for Magnetic Resonance Research, University of Minnesota Medical School, Minneapolis, MN 55455



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Pushing the Envelope...

1. Temporal Resolution
2. Spatial Resolution
3. Sensitivity and Noise
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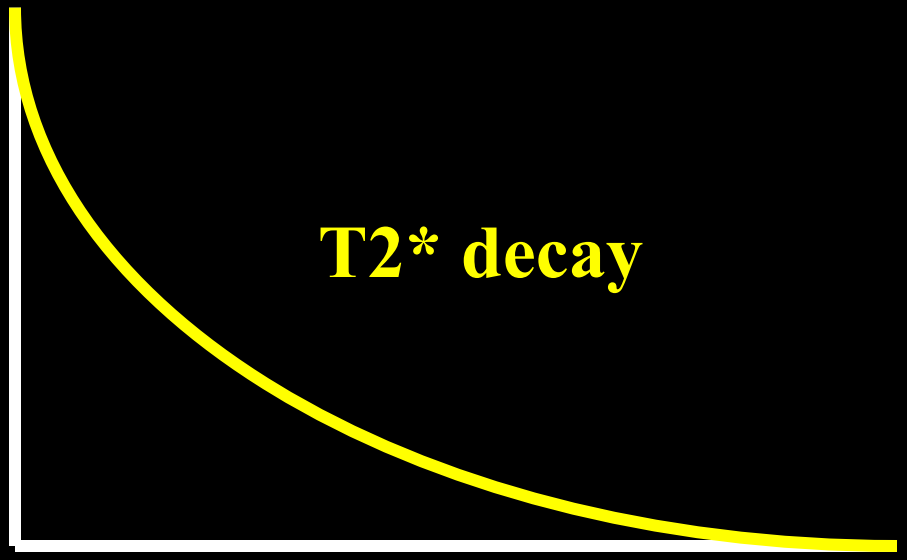
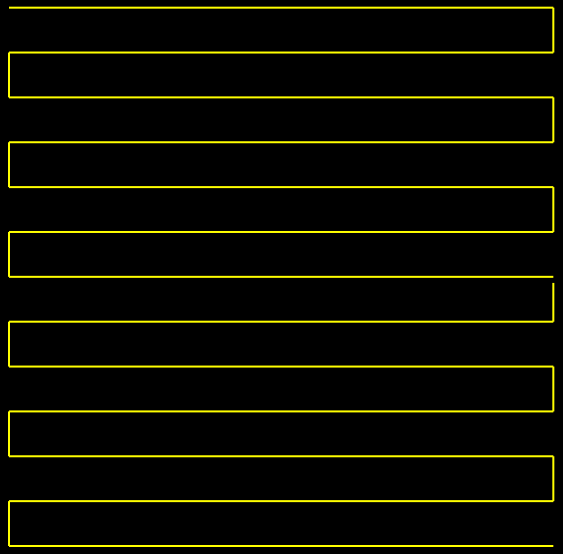
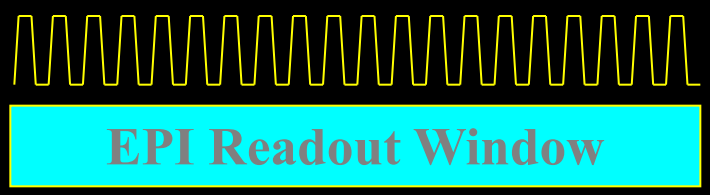
5. Implementation

Single Shot Imaging

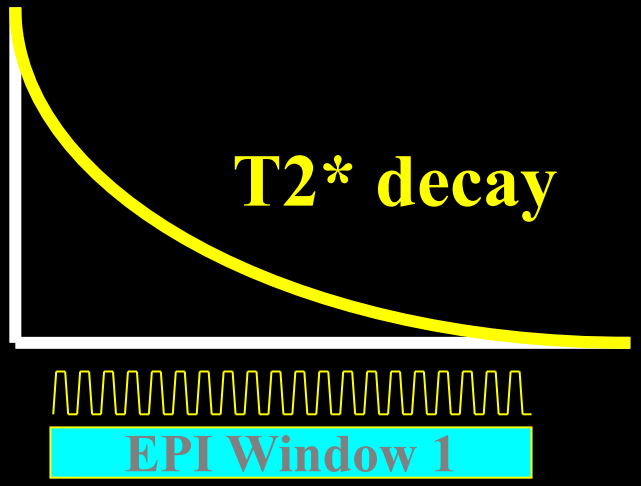


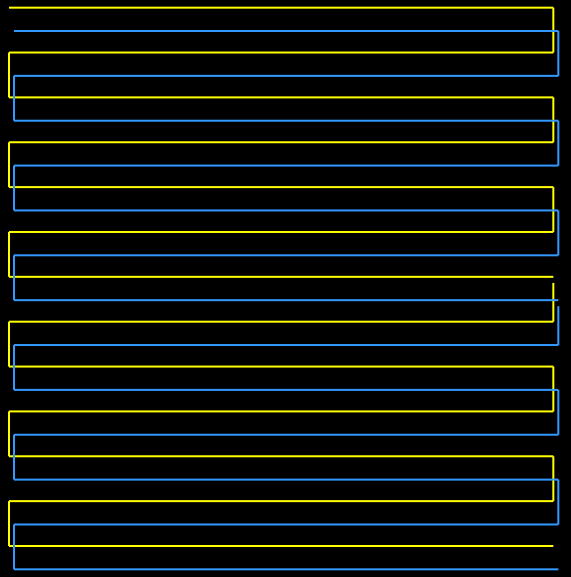


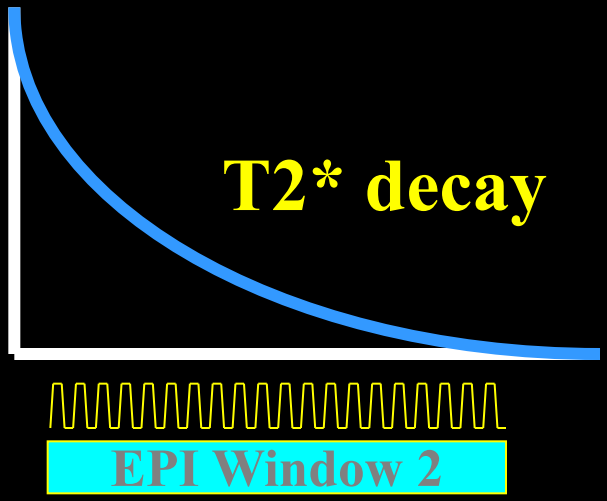


≈ 20 to 40 ms

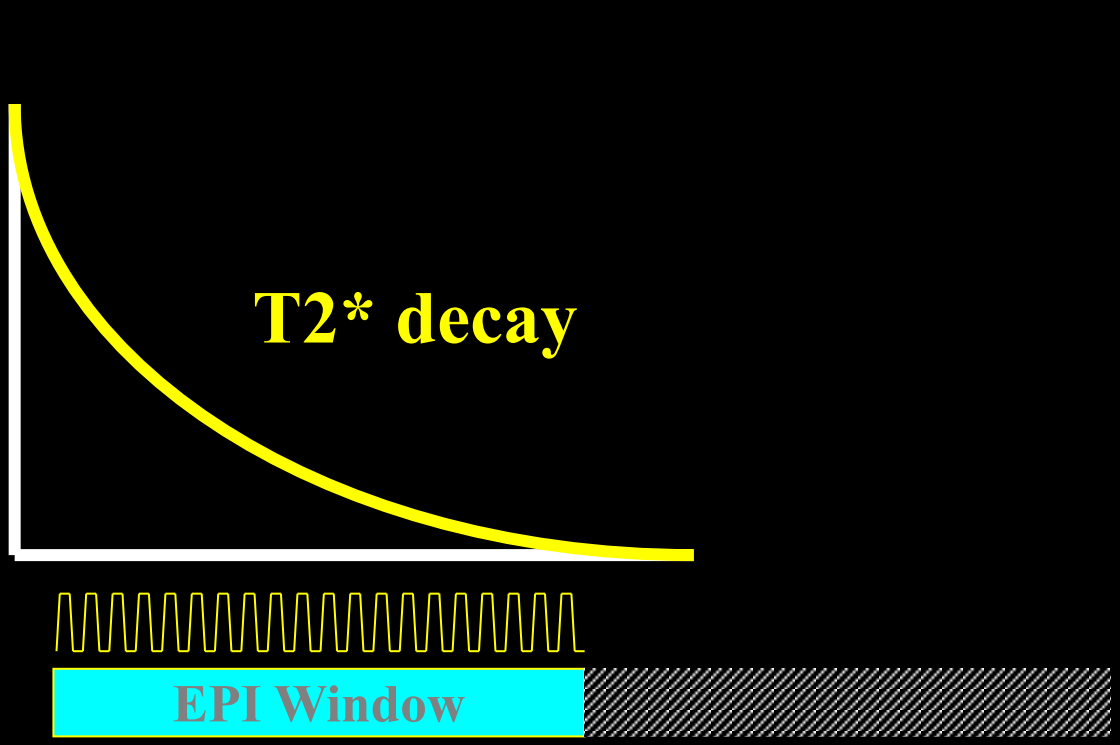
Multishot Imaging

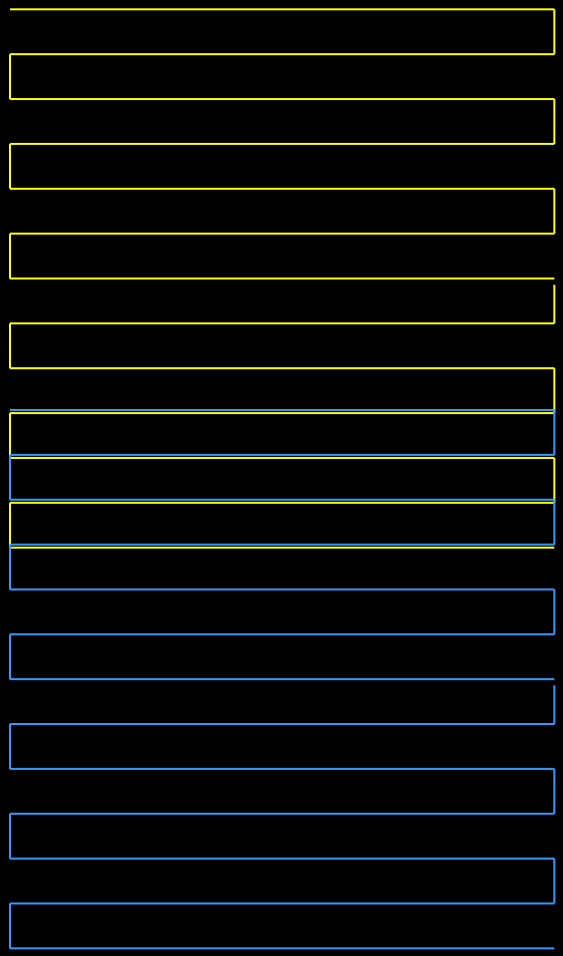






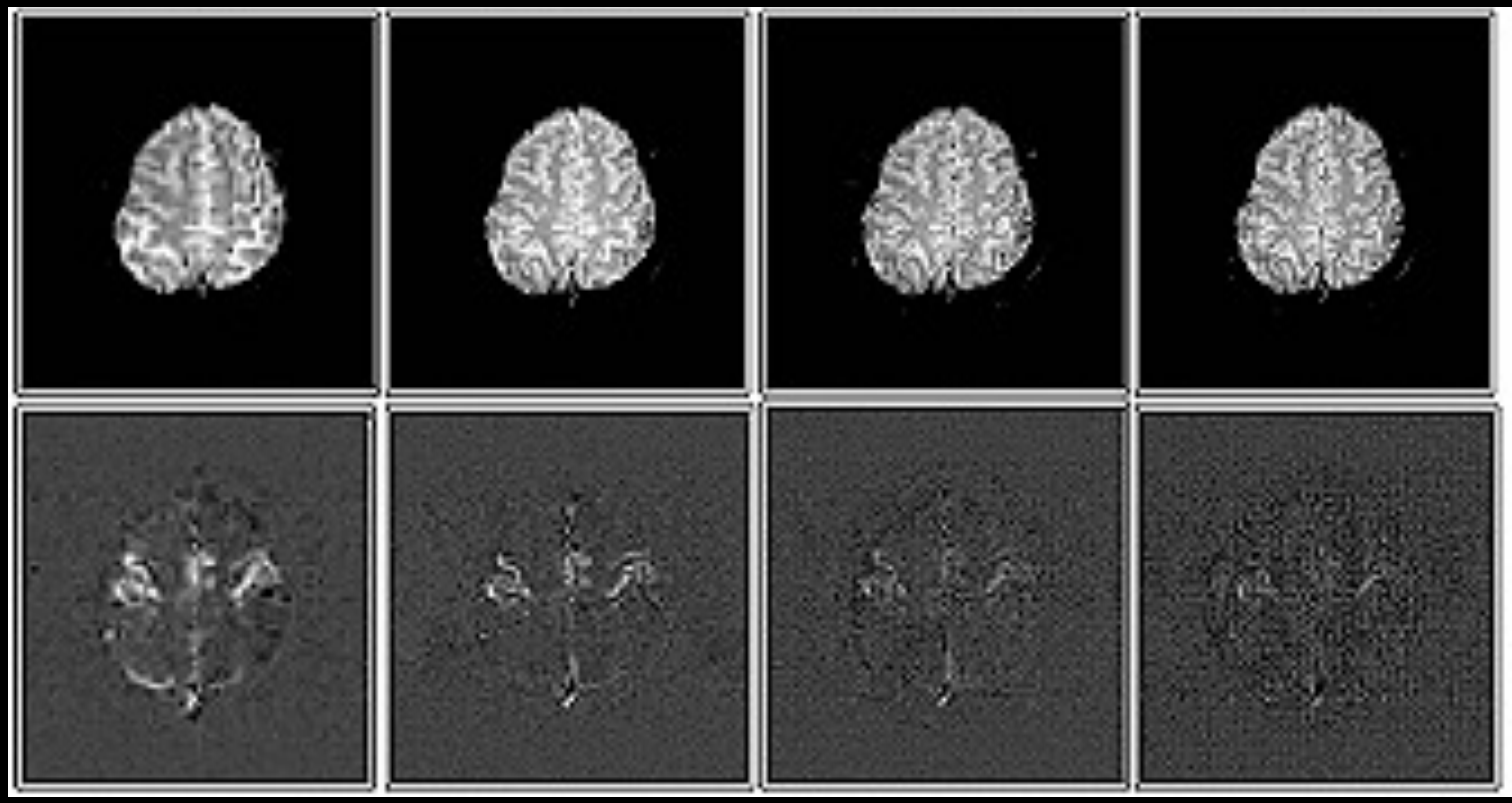
Partial k-space imaging



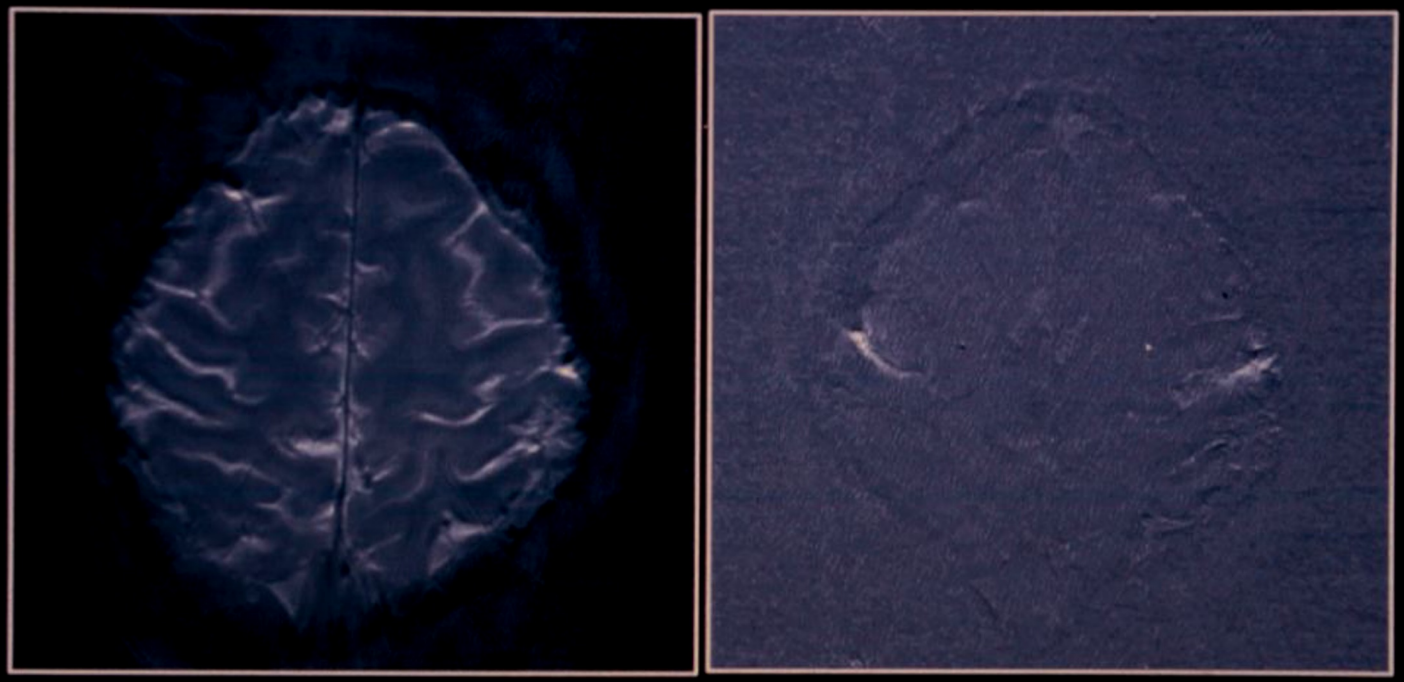


Multi Shot EPI

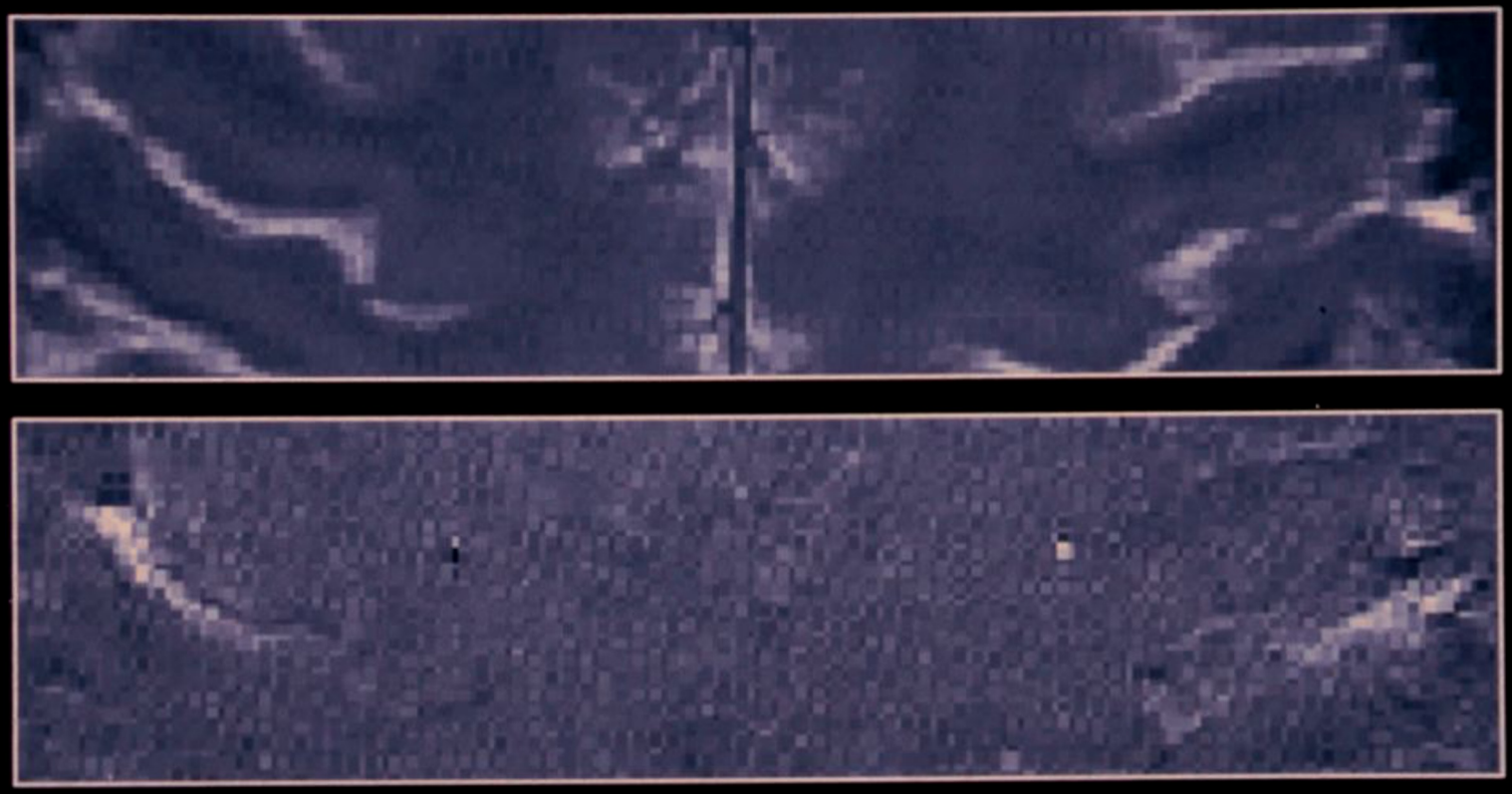
Excitations	1	2	4	8	
Matrix Size	64 x 64		128 x 128	256 x 128	256

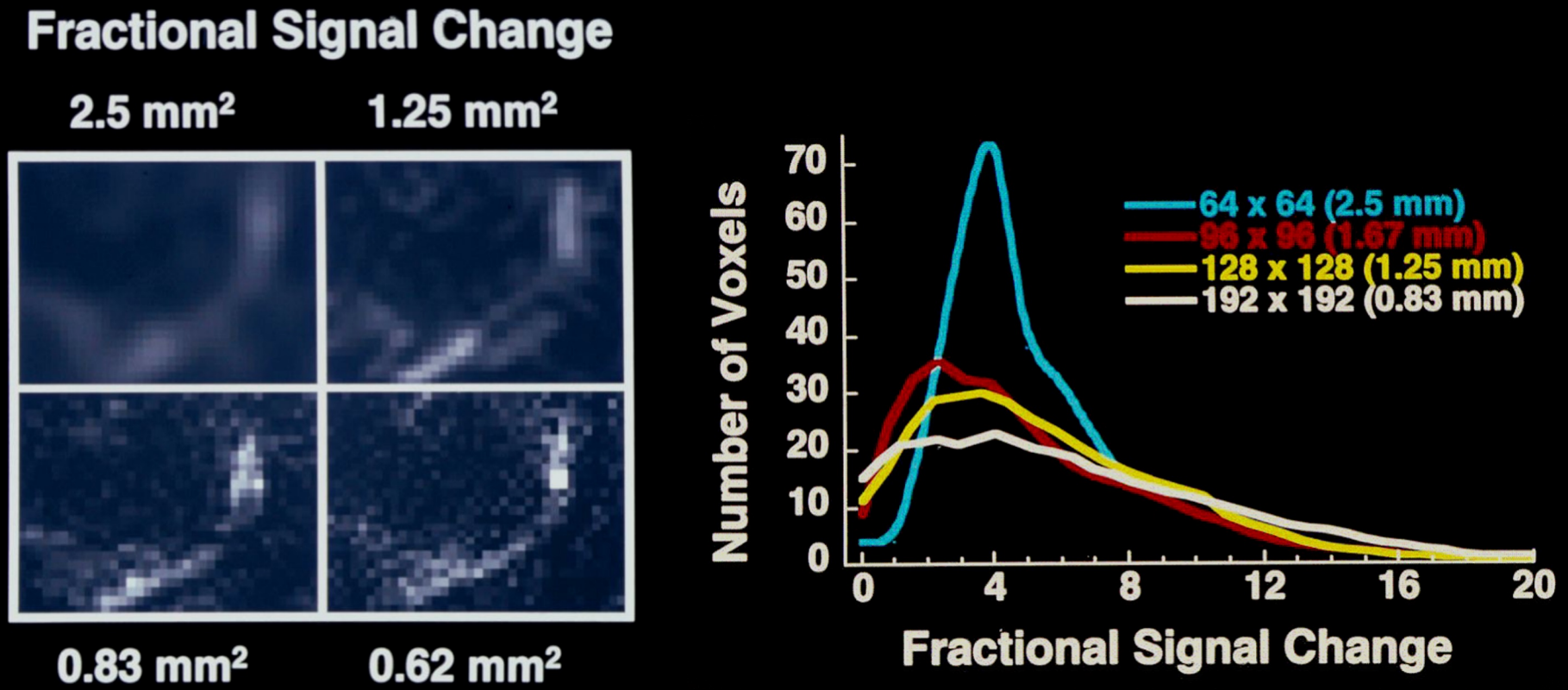


Single - Shot EPI at 3T:
Half NEX, 256 x 256, 16 cm FOV



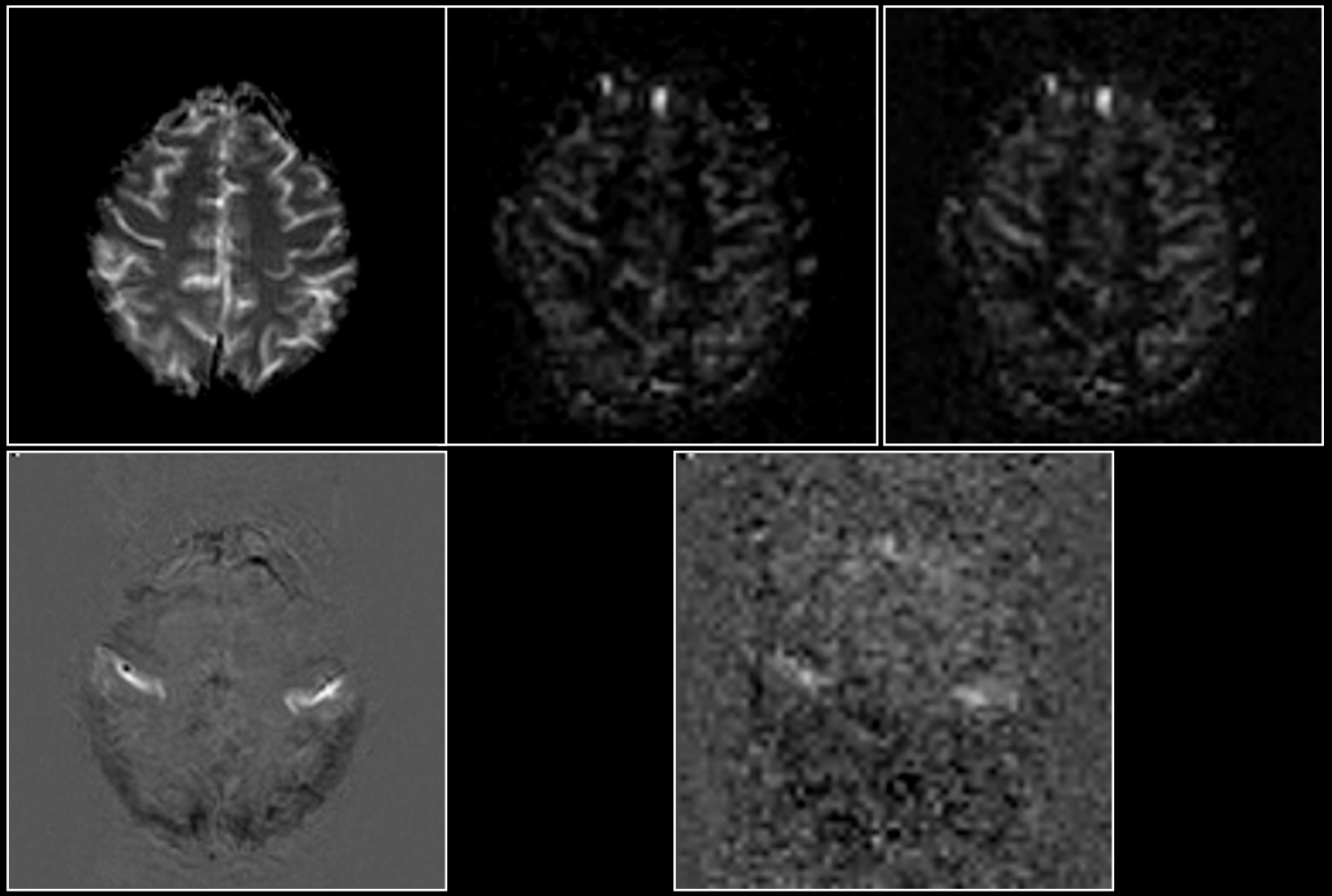
Single - Shot EPI at 3T:
Half NEX 256 x 256, 16 cm FOV



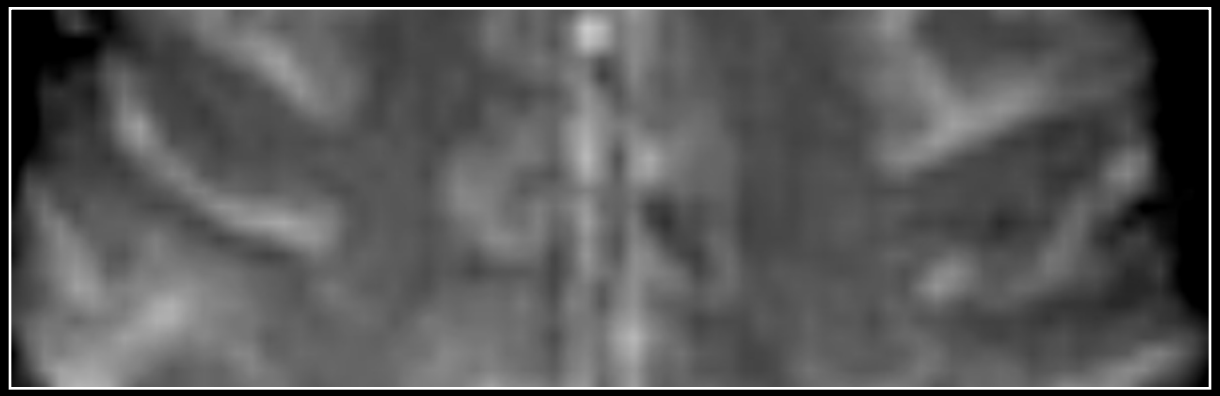

Fractional Signal Change
2.5 mm²
1.25 mm²
0.83 mm²
0.62 mm²
Number of Voxels
0
10
20
30
40
50
60
70
0
4
8
12
16
20
Fractional Signal Change
64 x 64 (2.5 mm)
96 x 96 (1.67 mm)
128 x 128 (1.25 mm)
192 x 192 (0.83 mm)

Perfusion

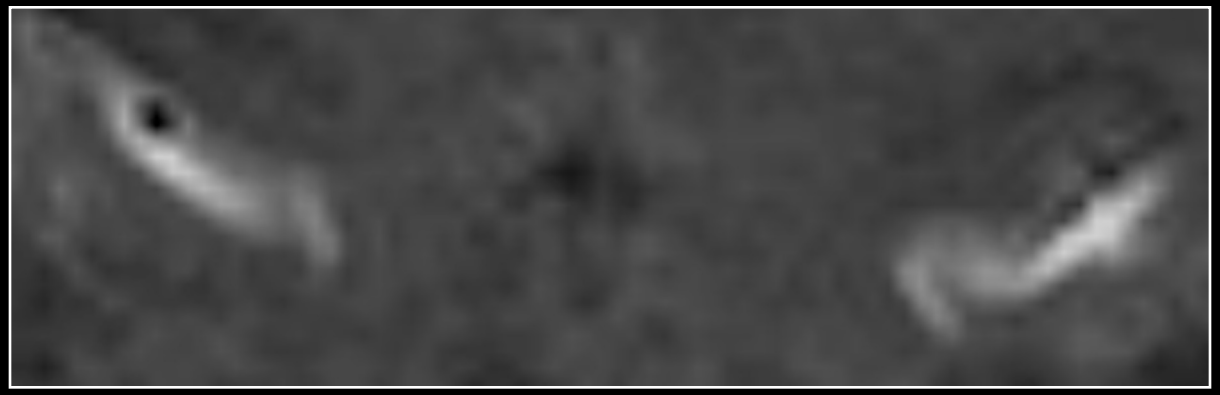
BOLD *Rest* *Activation*



Anatomy

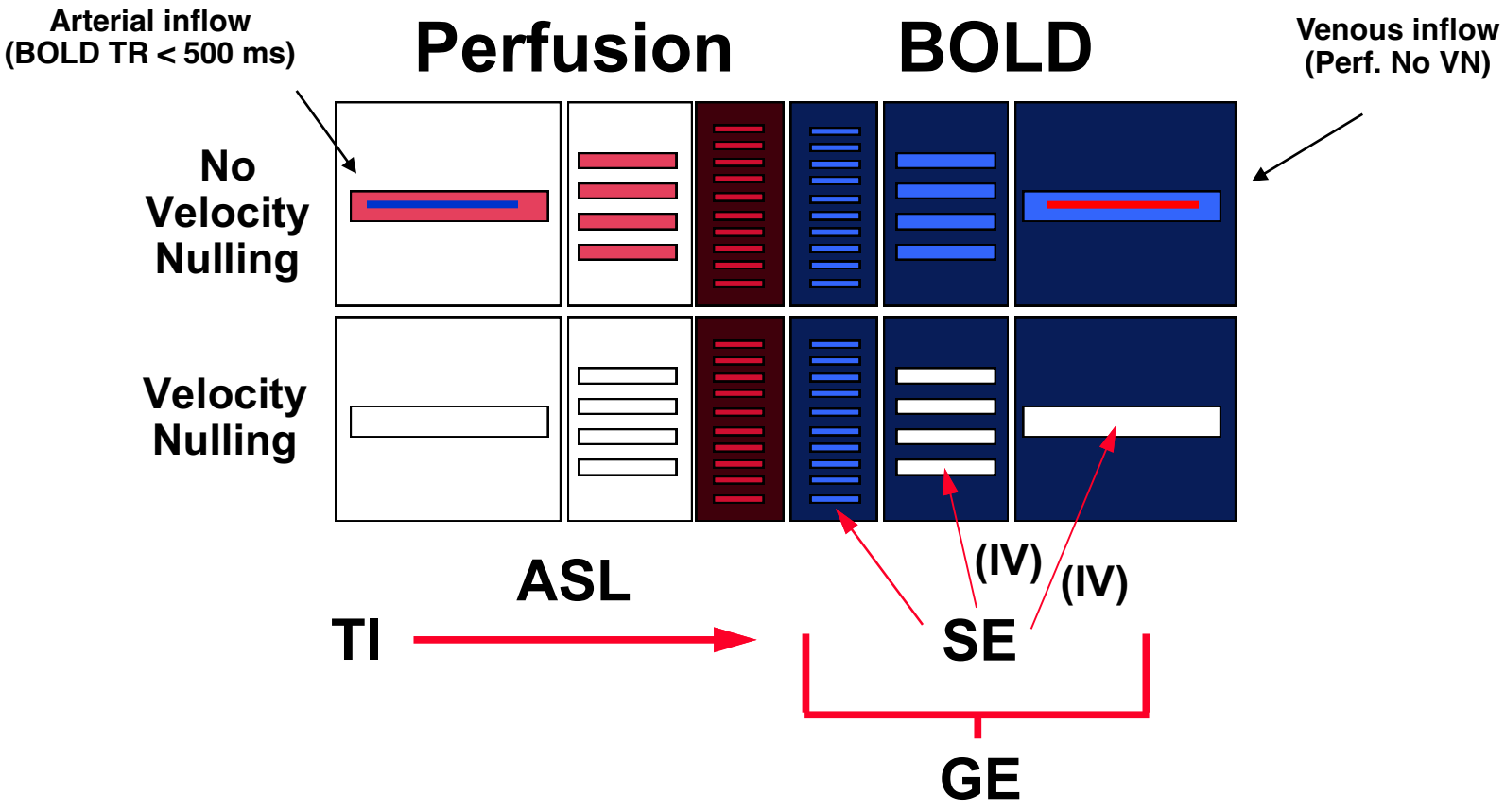


BOLD

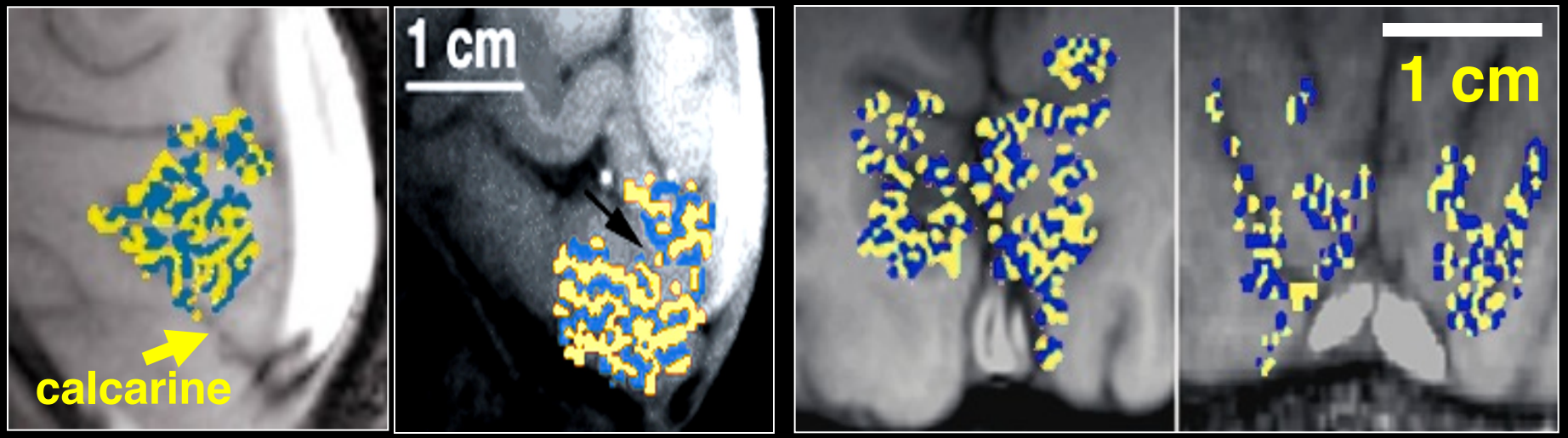


Perfusion

Hemodynamic Specificity



ODC Maps using fMRI

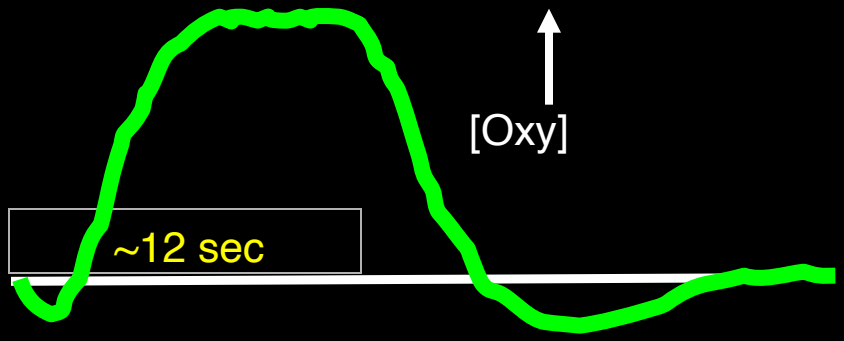


- Identical in size, orientation, and appearance to those obtained by optical imaging[1] and histology[3,4].

[1]Malonek D, Grinvald A. *Science* 272, 551-4 (1996).
[3]Horton JC, Hocking DR. *J Neurosci* 16, 7228-39 (1996).
[4]Horton JC, et al. *Arch Ophthalmol* 108, 1025-31 (1990).

Why short is better than long

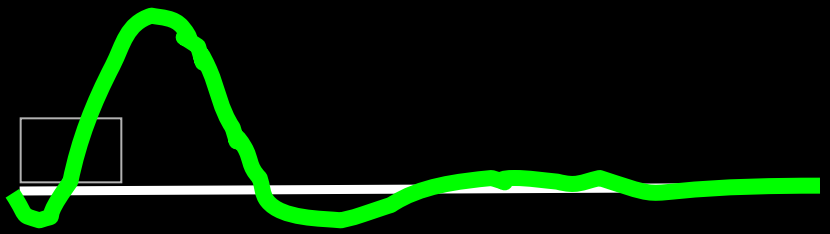
The vascular response to prolonged neural stimulation



It is argued that fMRI cannot achieve submillimeter functional resolution because a saturated hyperoxic vascular response to neural activity spreads over many millimeters[1,2].

However, optical imaging has demonstrated that the hyperoxic response can yield well-localized maps when using short duration stimuli (<5 sec)[1].

The vascular response to brief neural stimulation

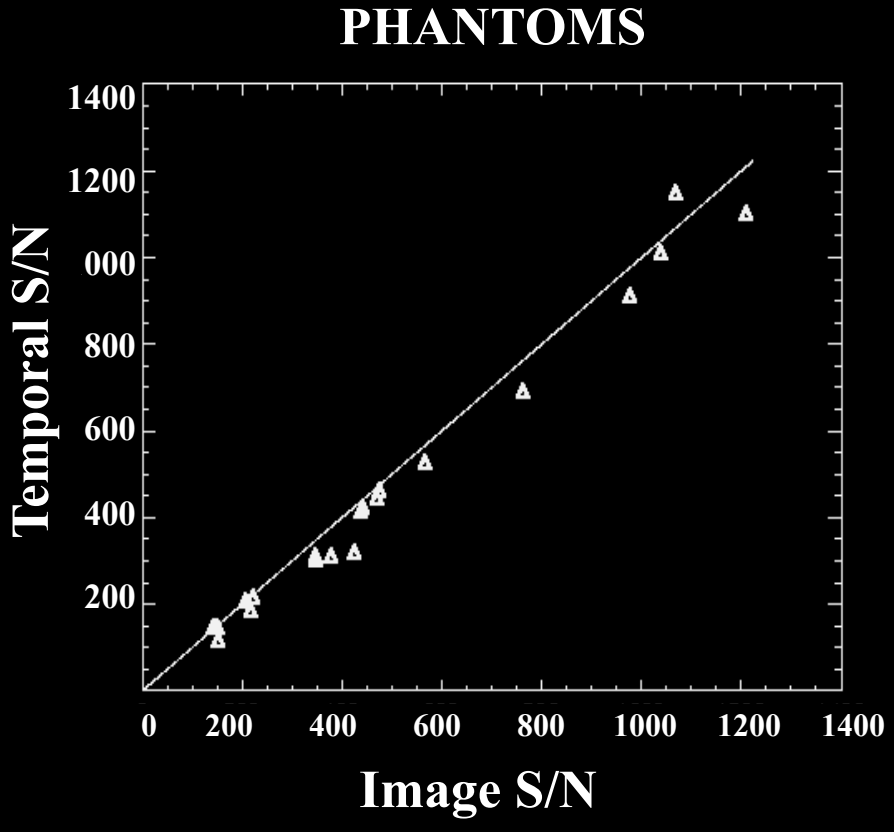


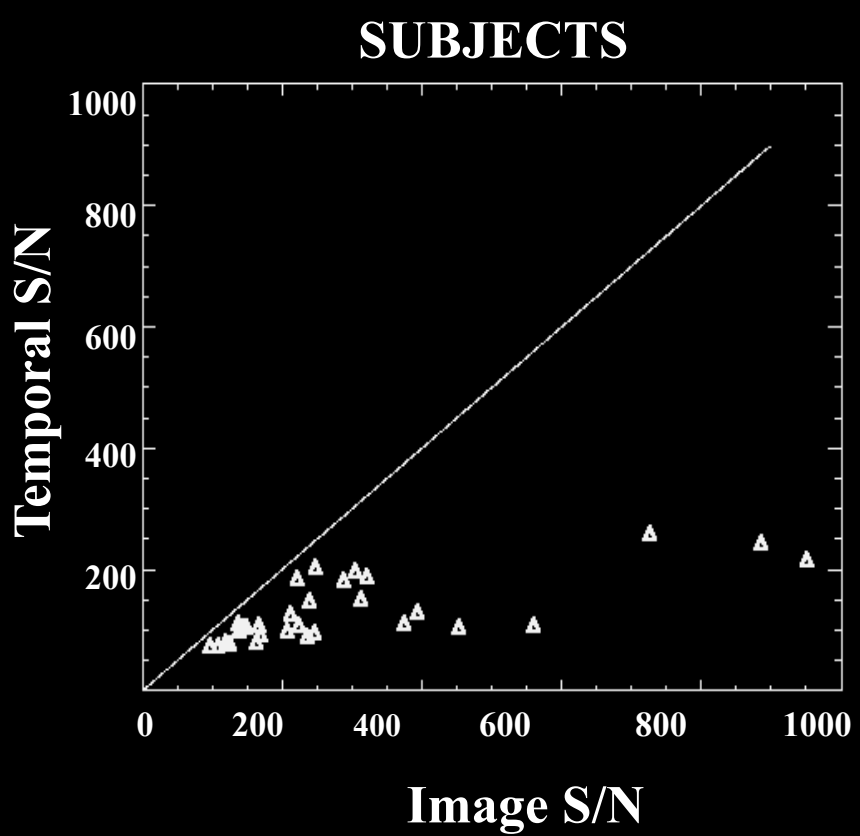
[1]Malonek D, Grinvald A. Science 272, 551-4 (1996).
[2]Kim D-S, Duong T, Kim S-G. Nat Neurosci 3, 164-9 (2000).

Pushing the Envelope...

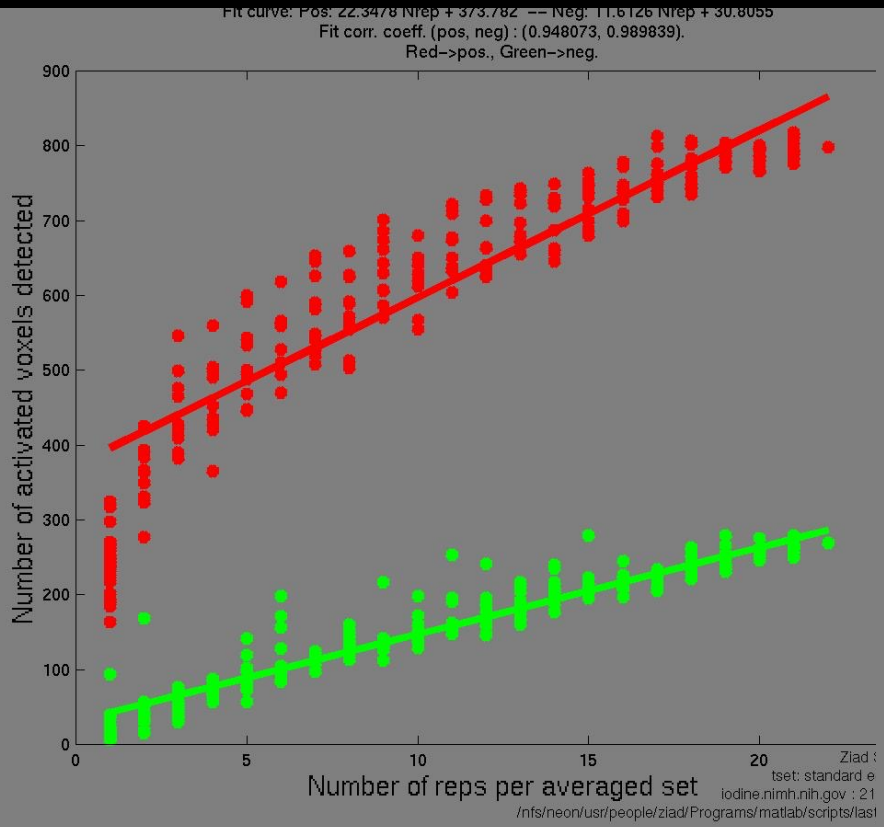
1. Temporal Resolution
2. Spatial Resolution
3. Sensitivity and Noise
4. Information Content
5. Implementation

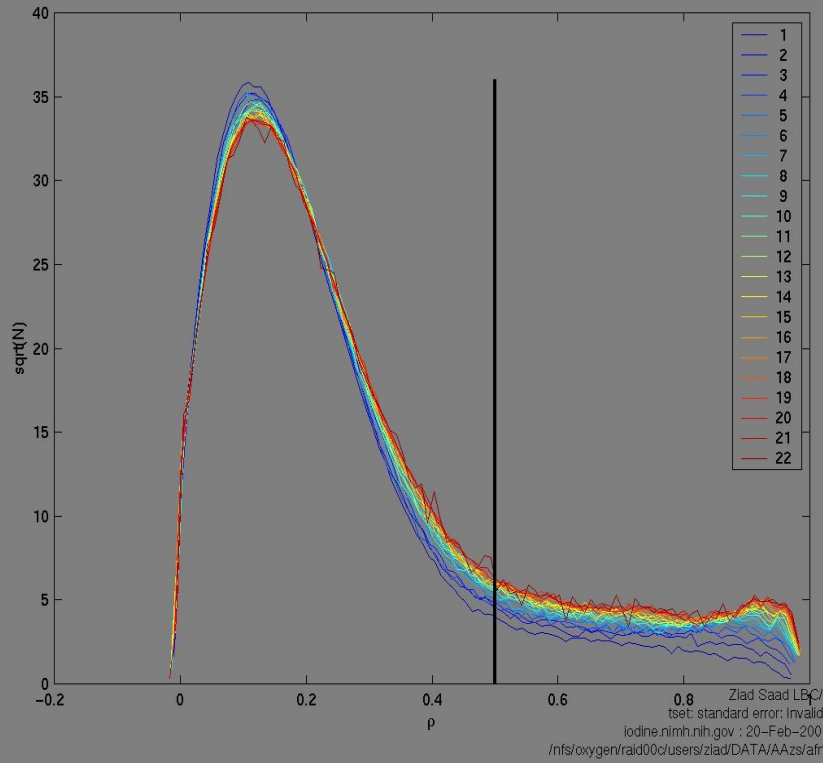
Temporal S/N vs. Image S/N





N. Petridou

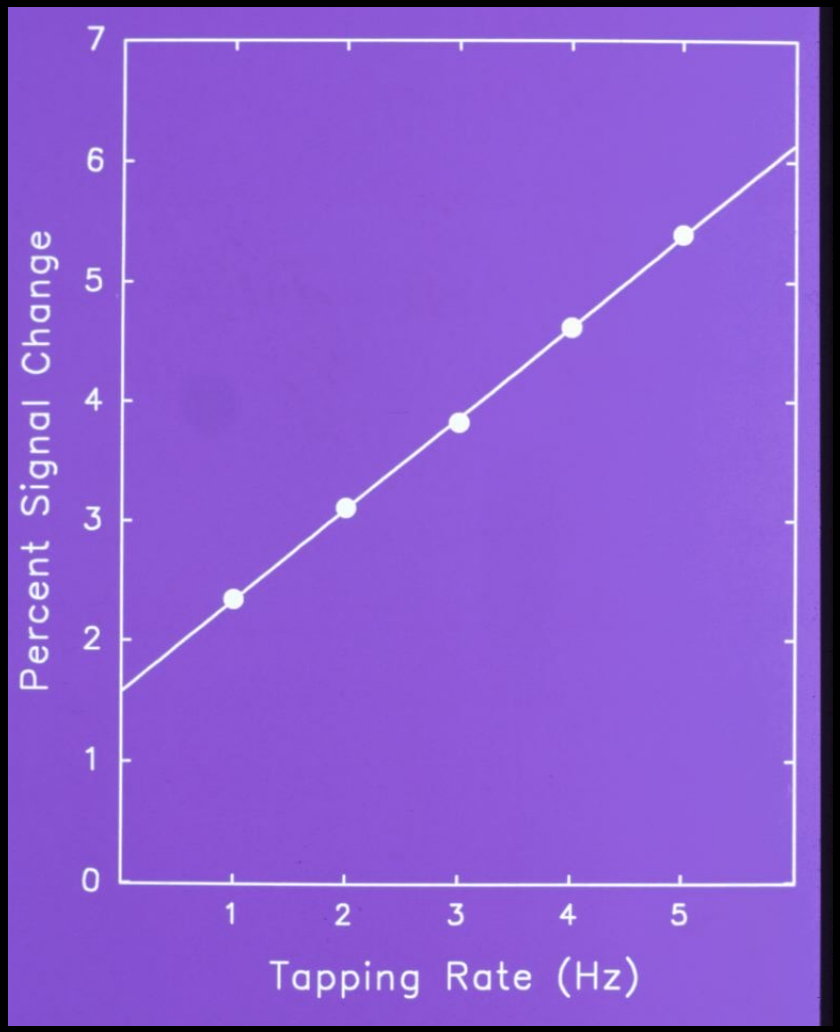

Fit curve: Pos: 22.3478 Nrep + 373.782 -- Neg: 11.6126 Nrep + 30.8055
Fit corr. coeff. (pos, neg) : (0.948073, 0.989839).
Red->pos., Green->neg.
Number of activated voxels detected
Number of reps per averaged set
0
100
200
300
400
500
600
700
800
900
0
5
10
15
20
Ziad
tset: standard e
iodine.nimh.nih.gov : 21
/nfs/neon/usr/people/ziad/Programs/matlab/scripts/las


sqrt(N)
ρ
0
5
10
15
20
25
30
35
40
−0.2
0
0.2
0.4
0.6
0.8
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
Ziad Saad LBC/NIMH/NIH
tset: standard error: Invalid argument
iodine.nimh.nih.gov : 20−Feb−2001 23:12:42
/nfs/oxygen/raid00c/users/ziad/DATA/AAzs/afni/plotsign2

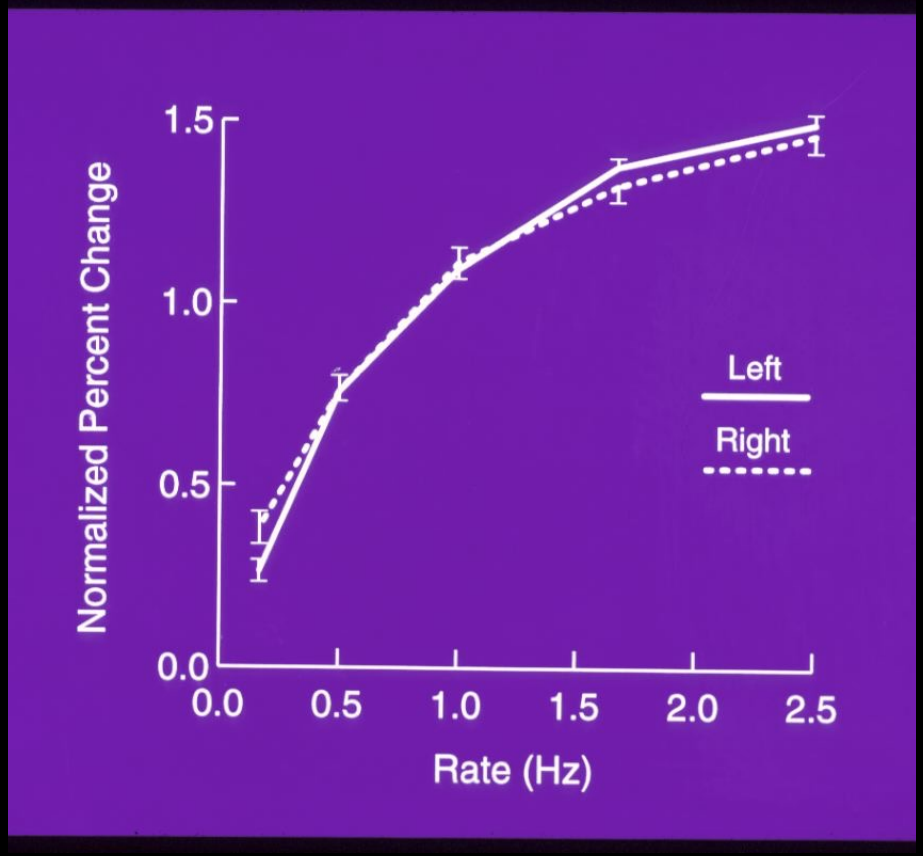
Pushing the Envelope...

1. Temporal Resolution
2. Spatial Resolution
3. Sensitivity and Noise
4. Information Content
5. Implementation

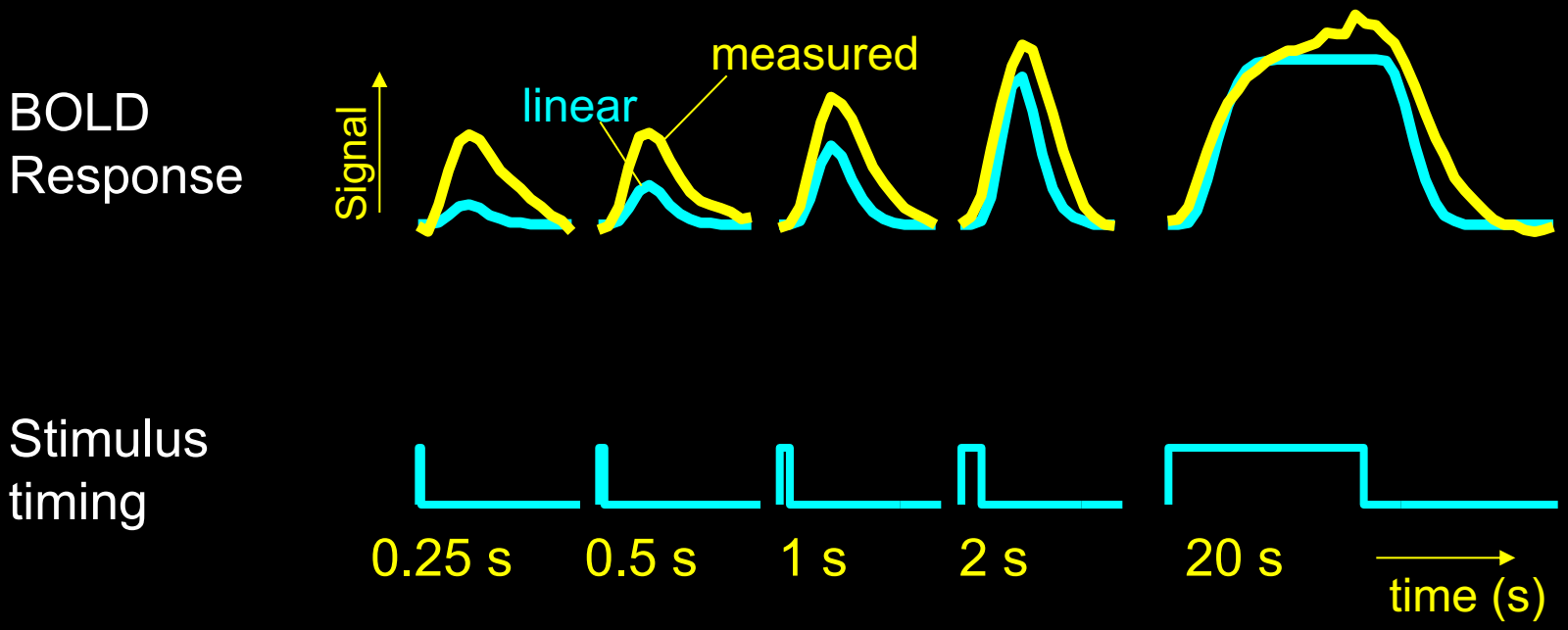
Motor Cortex



Auditory Cortex



Different stimulus “ON” periods



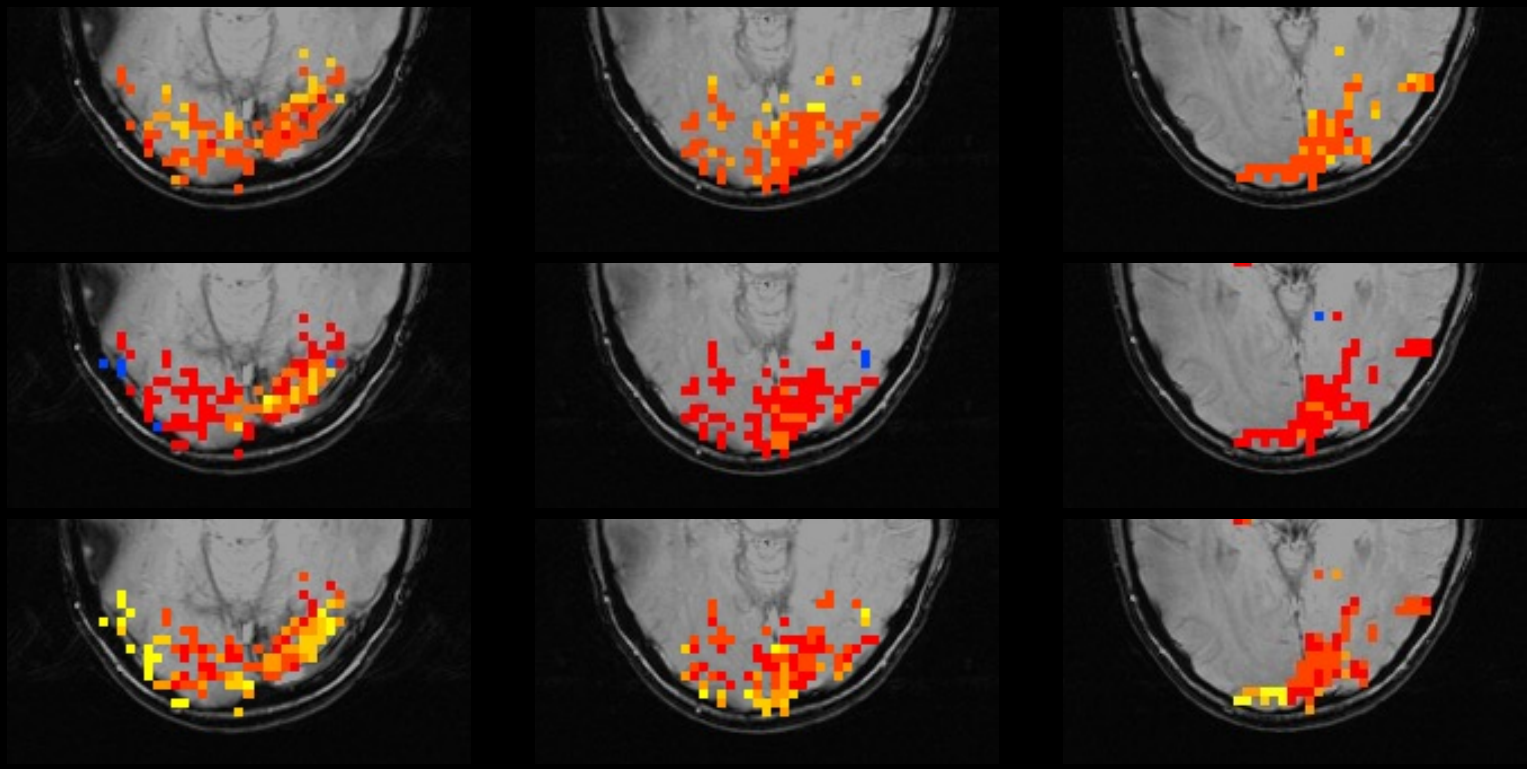
Brief stimuli produce larger responses than expected

Results – visual task

Nonlinearity

Magnitude

Latency

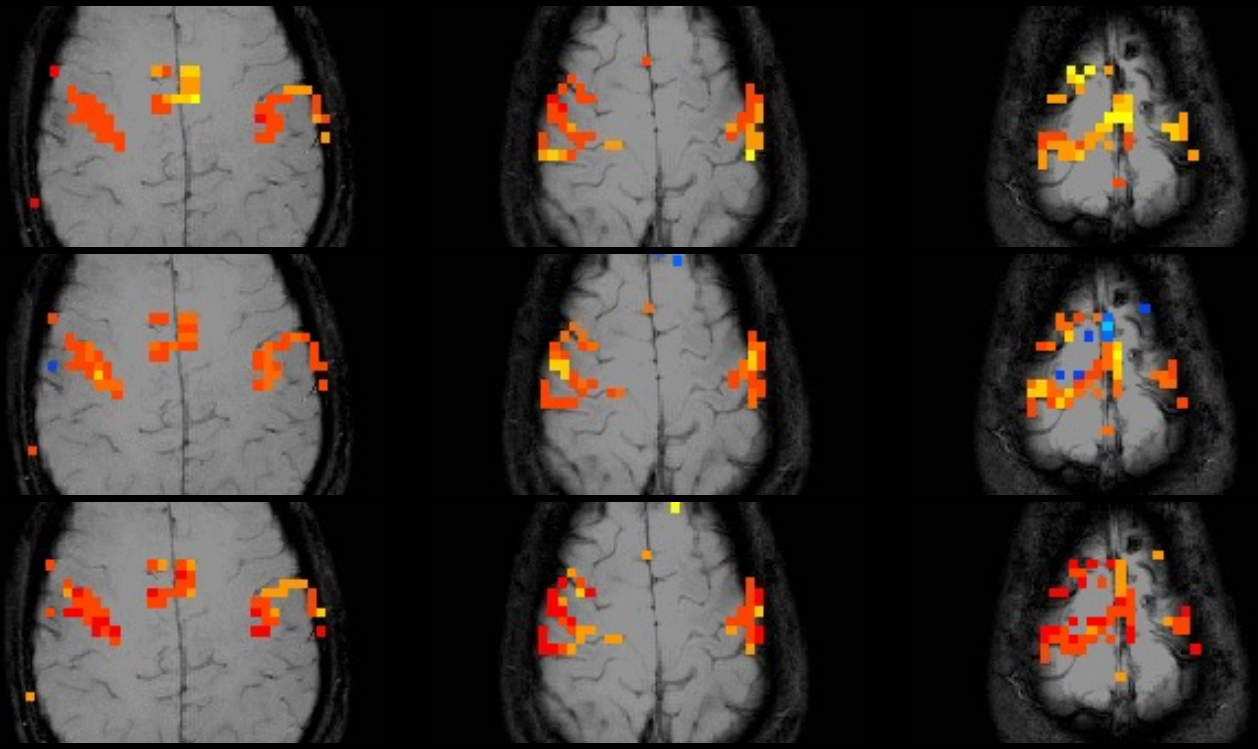


Results – motor task

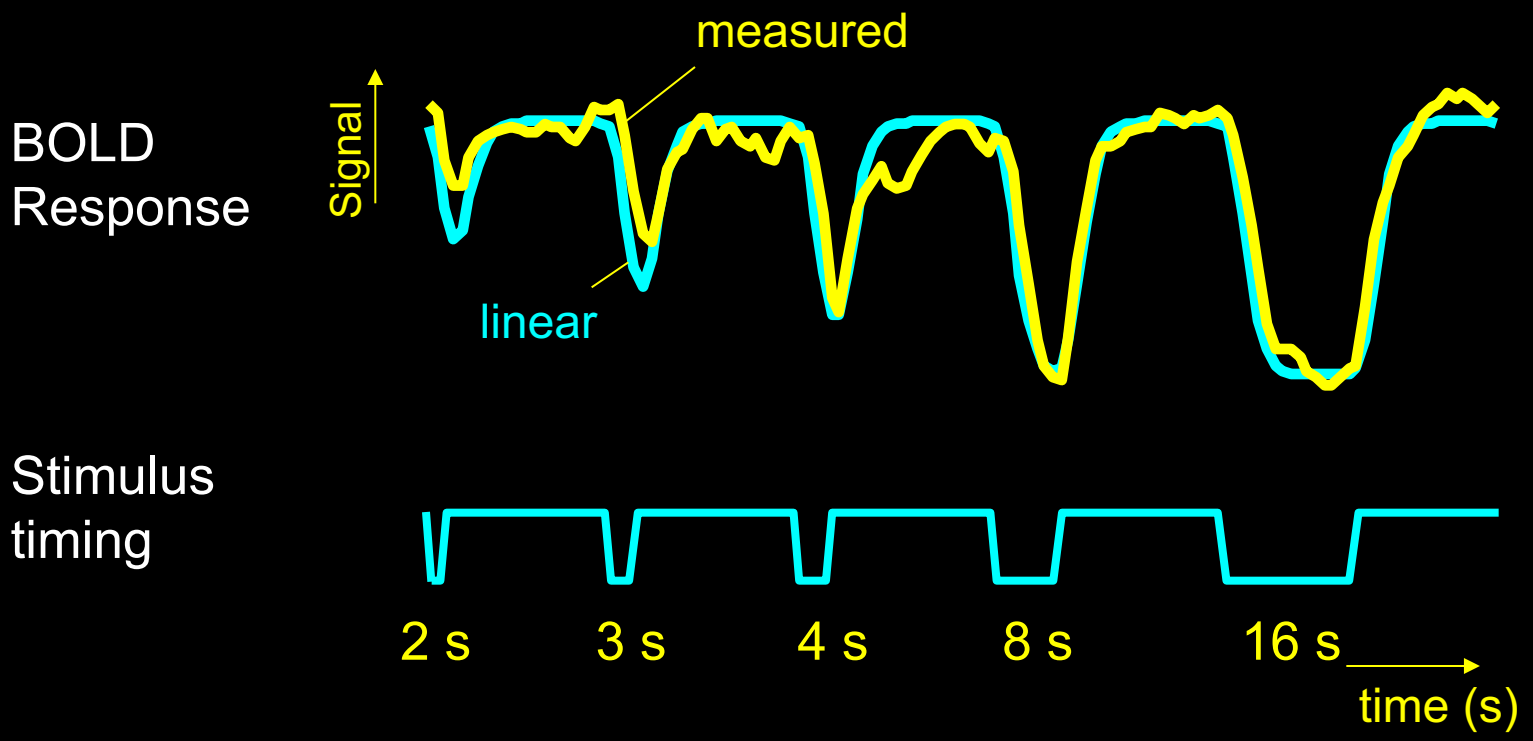
Nonlinearity

Magnitude

Latency



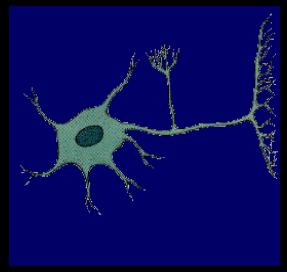
Different stimulus “OFF” periods

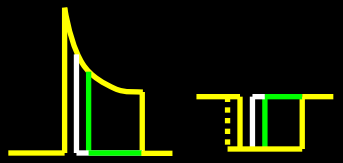


Brief stimulus OFF periods produce smaller decreases than expecte

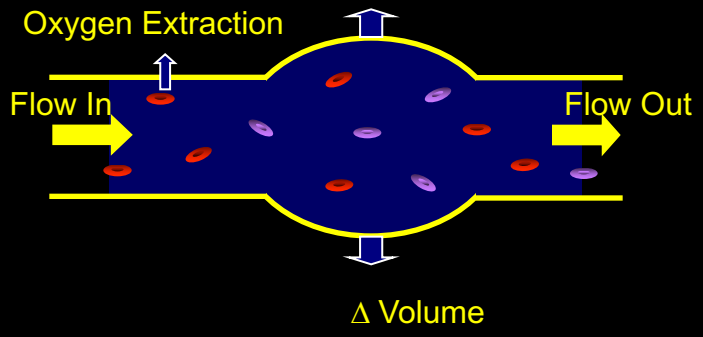
Sources of this Nonlinearity

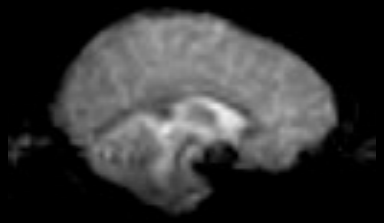
- Neuronal

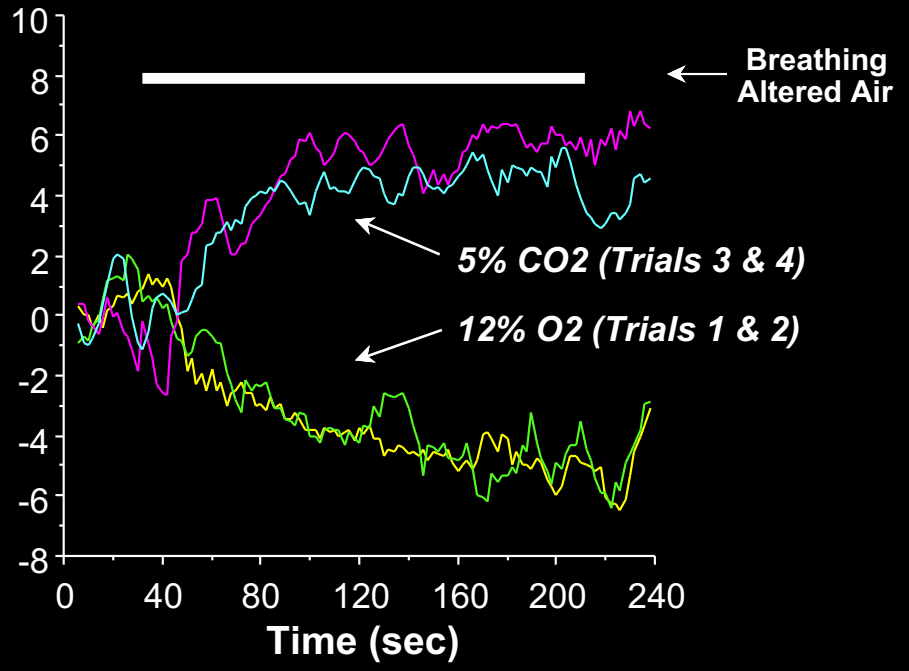




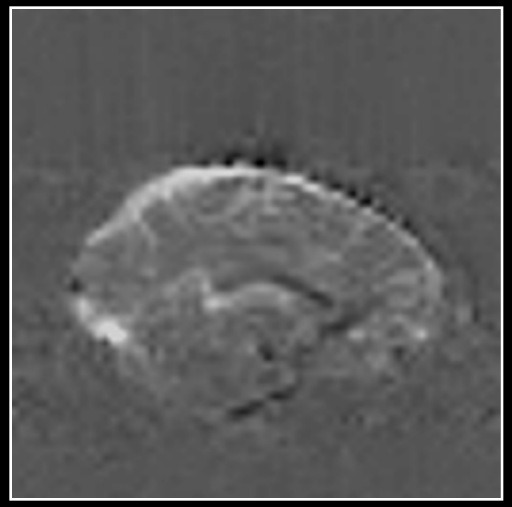
- Hemodynamic
  - Oxygen extraction
  - Blood volume dynamics

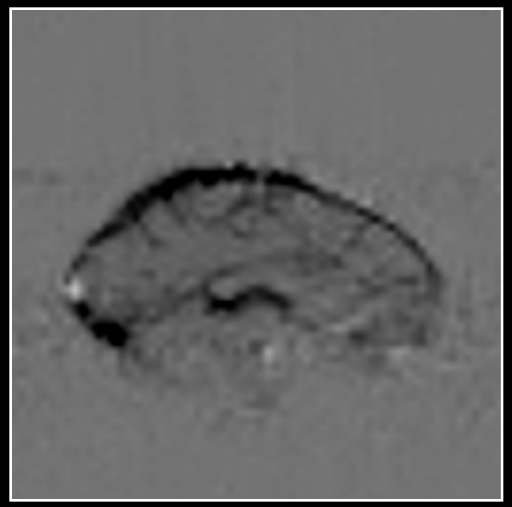





10
8
6
4
2
0
-2
-4
-6
-8
0
40
80
120
160
200
240
Time (sec)
Breathing
Altered Air
5% CO2 (Trials 3 & 4)
12% O2 (Trials 1 & 2)

5% CO2

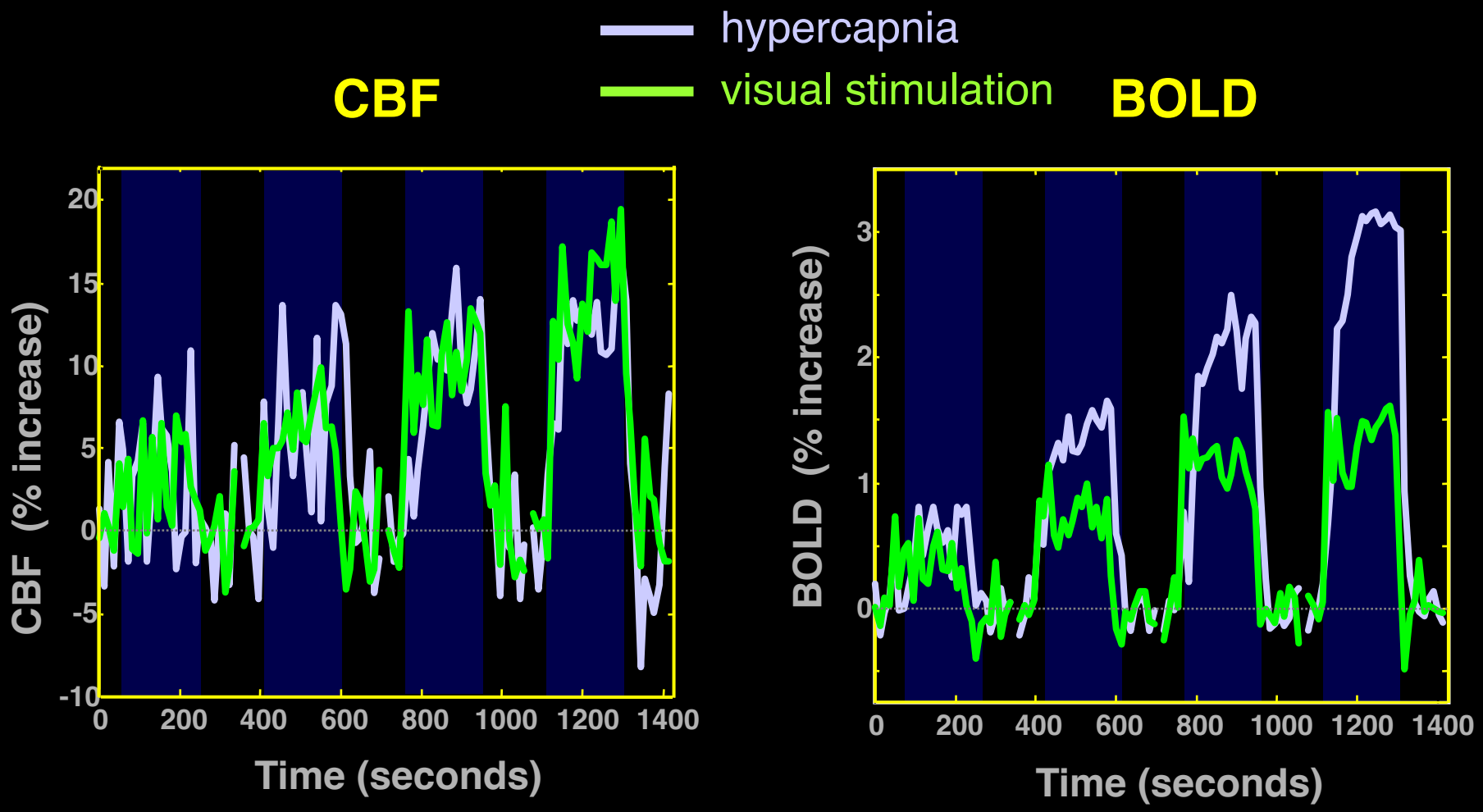




12% O2

$CMRO_2$-related BOLD signal deficit:

Hoge, et al.

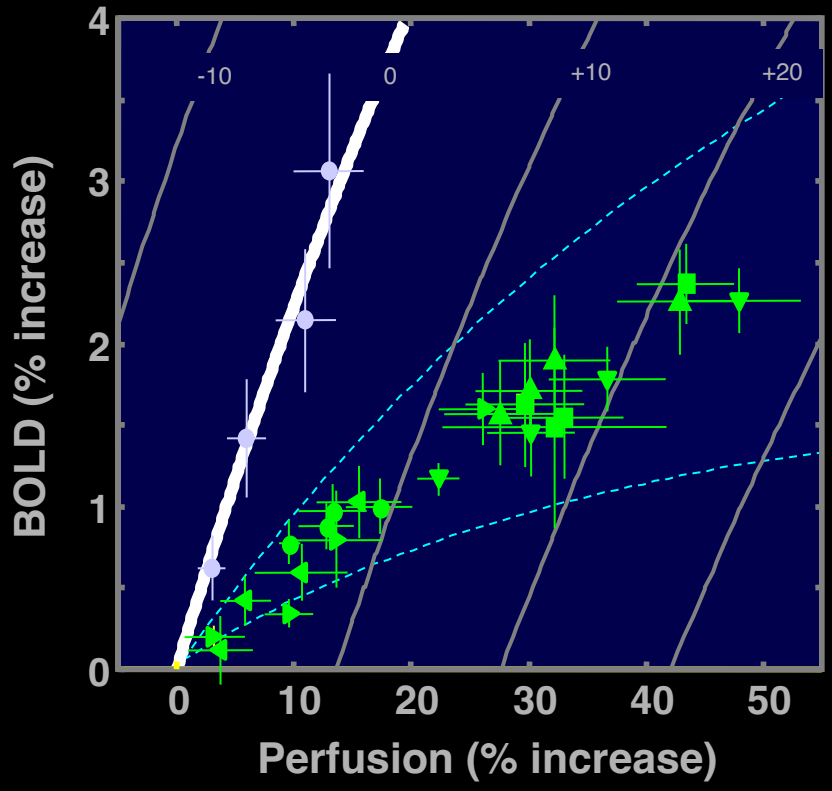


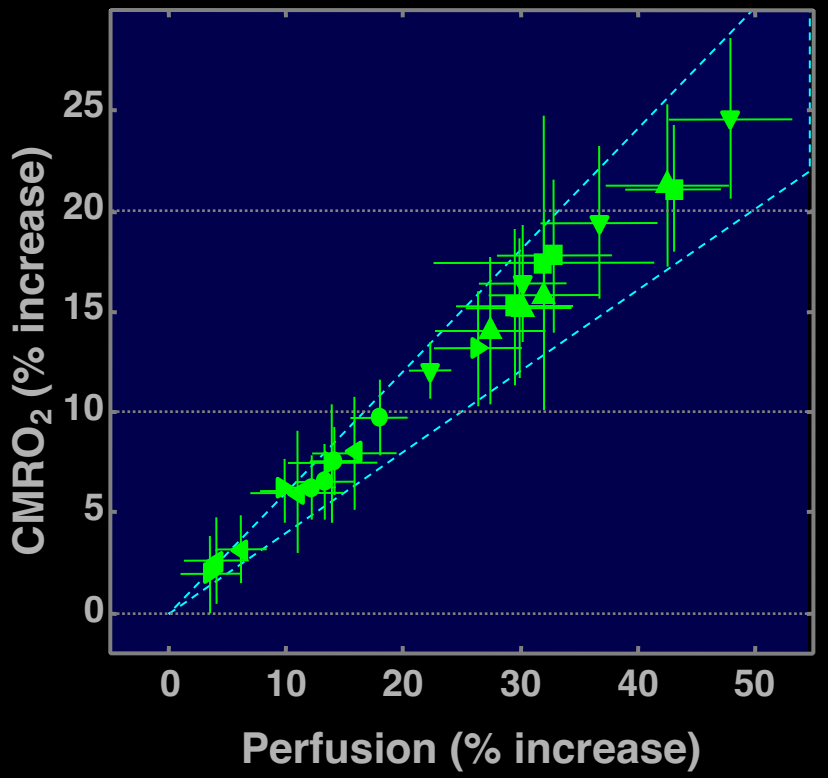
Simultaneous Perfusion and BOLD imaging during graded visual activation and hypercapnia

N=12

CBF-$CMRO_2$ coupling

Hoge, et al.

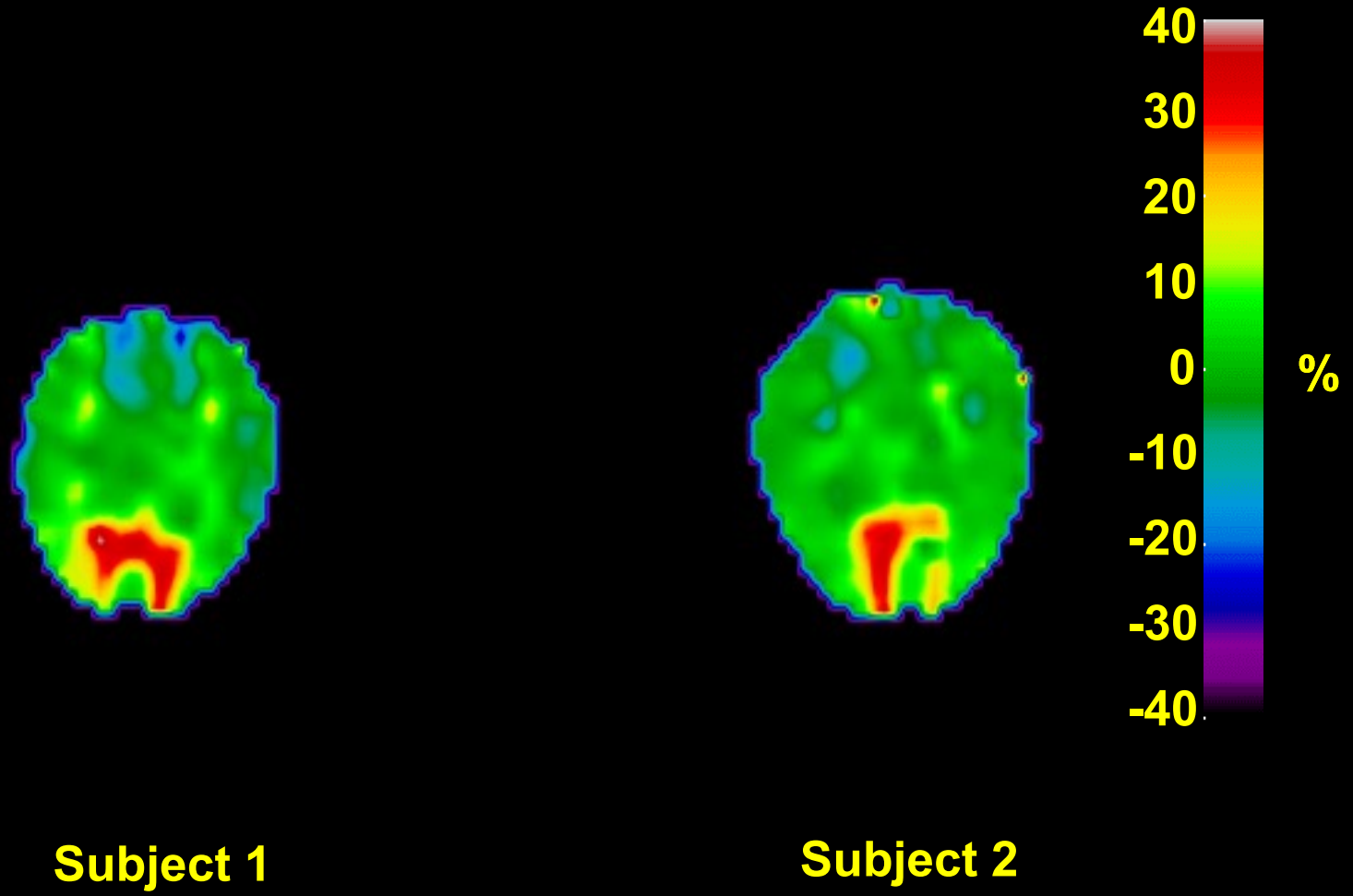




Characterizing Activation-induced $CMRO_2$ changes using calibration with hypercapnia

Hoge, et al.

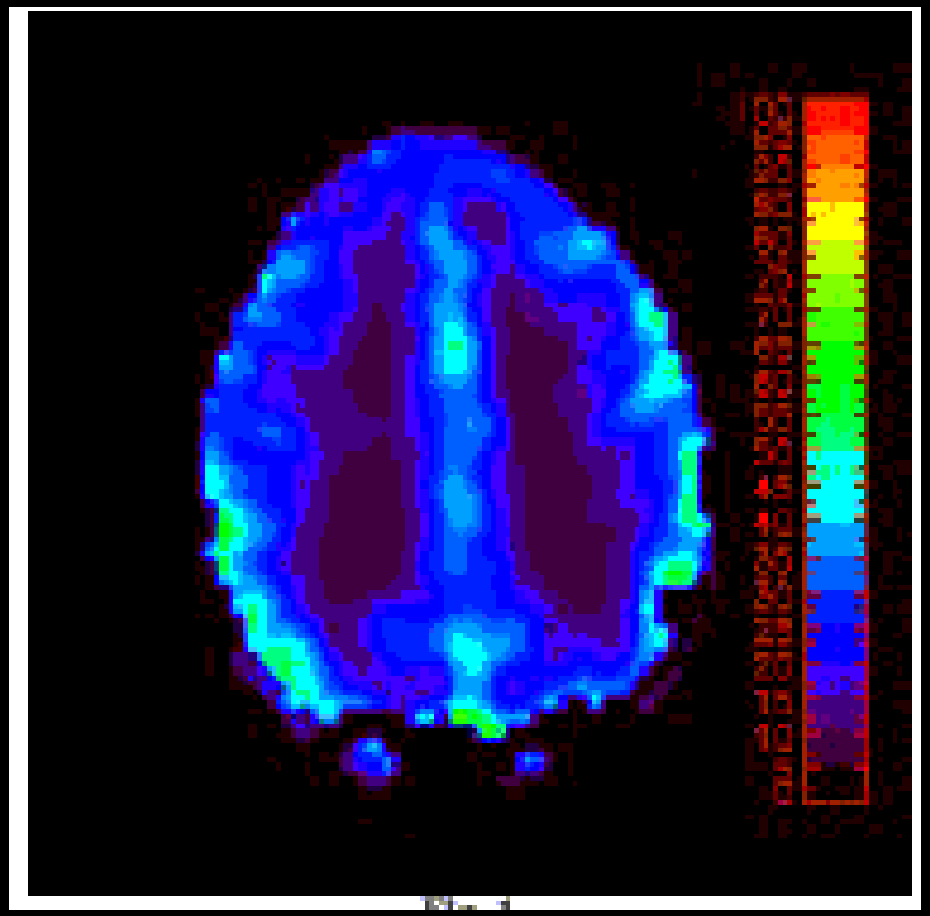
Computed $CMRO_2$ changes



Quantitative Measurements of Cerebral Metabolic Rate of Oxygen (CMRO2) Using MRI: A Volunteer Study

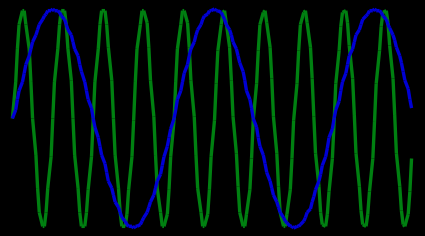
Hongyu AN[1], Weili LIN[2], Azim CELIK[3], Yueh Z. LEE[4]

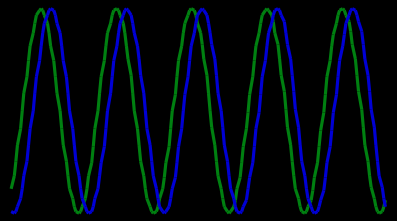
[1]Washington University, 600 Airport Road, Chapel Hill, NC USA; [2]UNC-Chapel Hill, Department of Radiology, CB#7515, Chapel Hill, NC USA; [3]GE Medical Systems, ; [4]UNC-Chapel Hill, ;

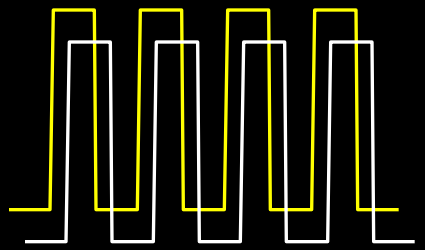


Neuronal Activation Input Strategies

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





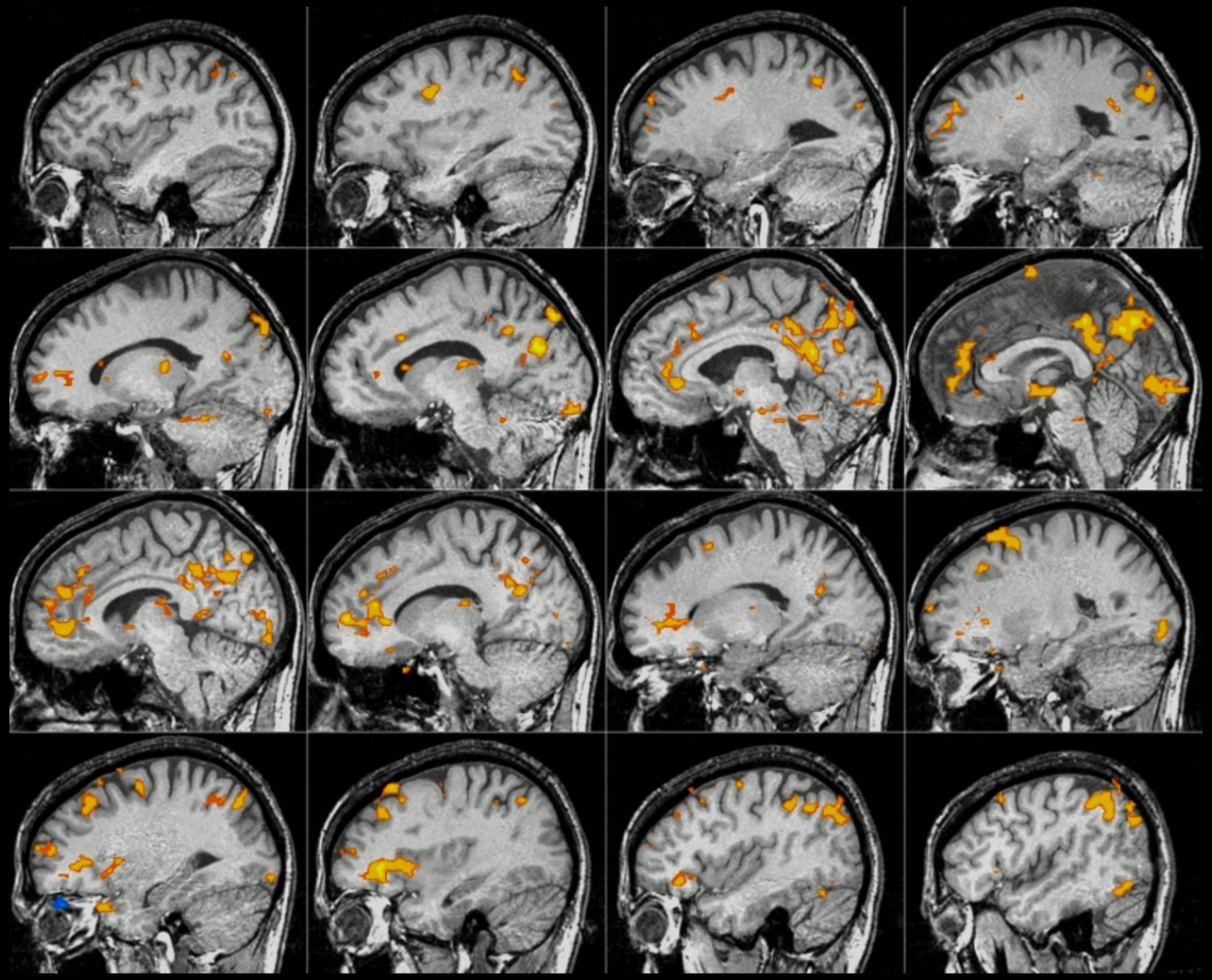


Free Behavior Design

Use a continuous measure as a reference function:

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

Brain activity correlated with SCR during “Rest”



Pushing the Envelope...

1. Temporal Resolution
2. Spatial Resolution
3. Sensitivity and Noise
4. Information Content
5. Implementation

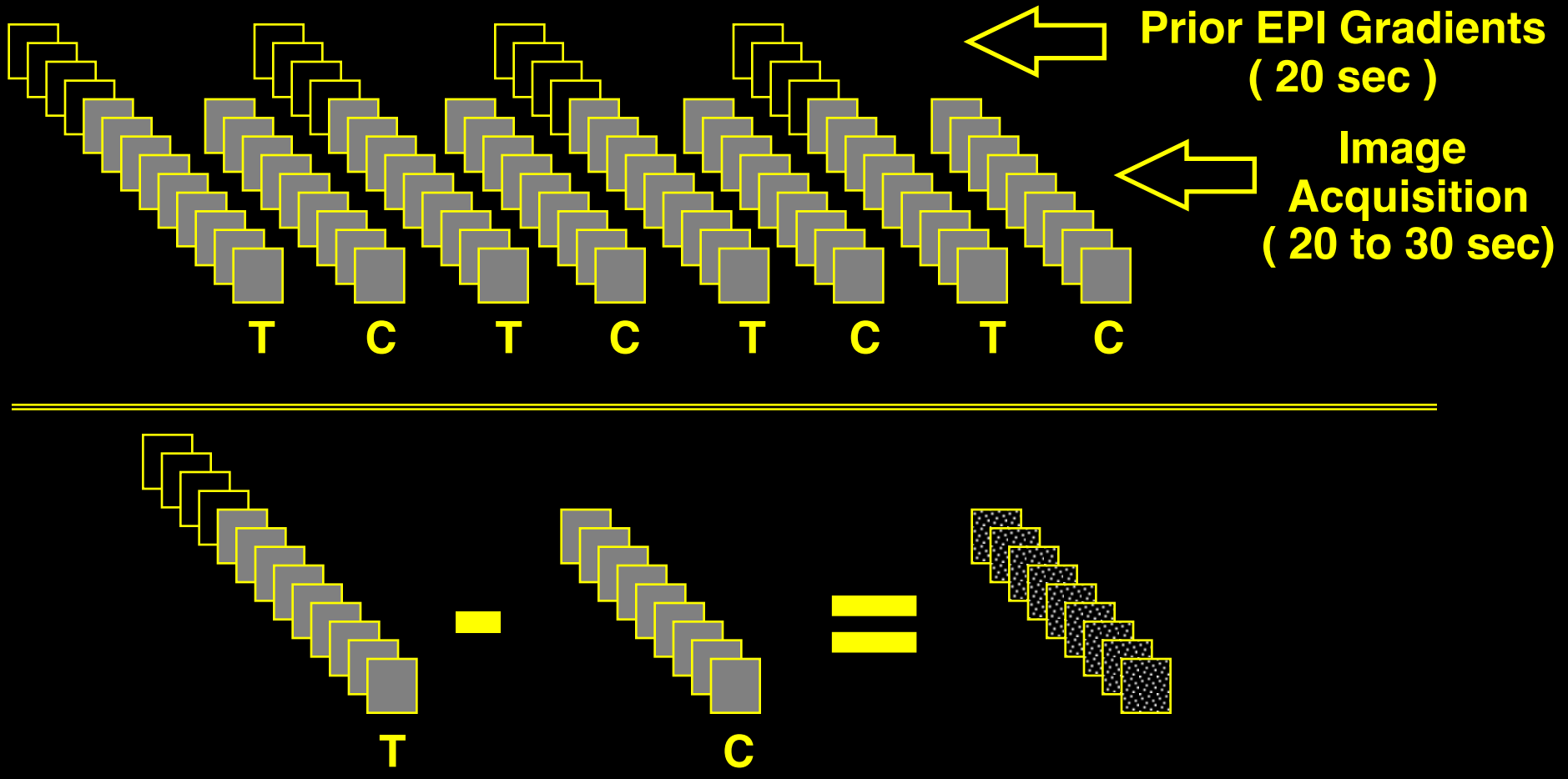
Motion

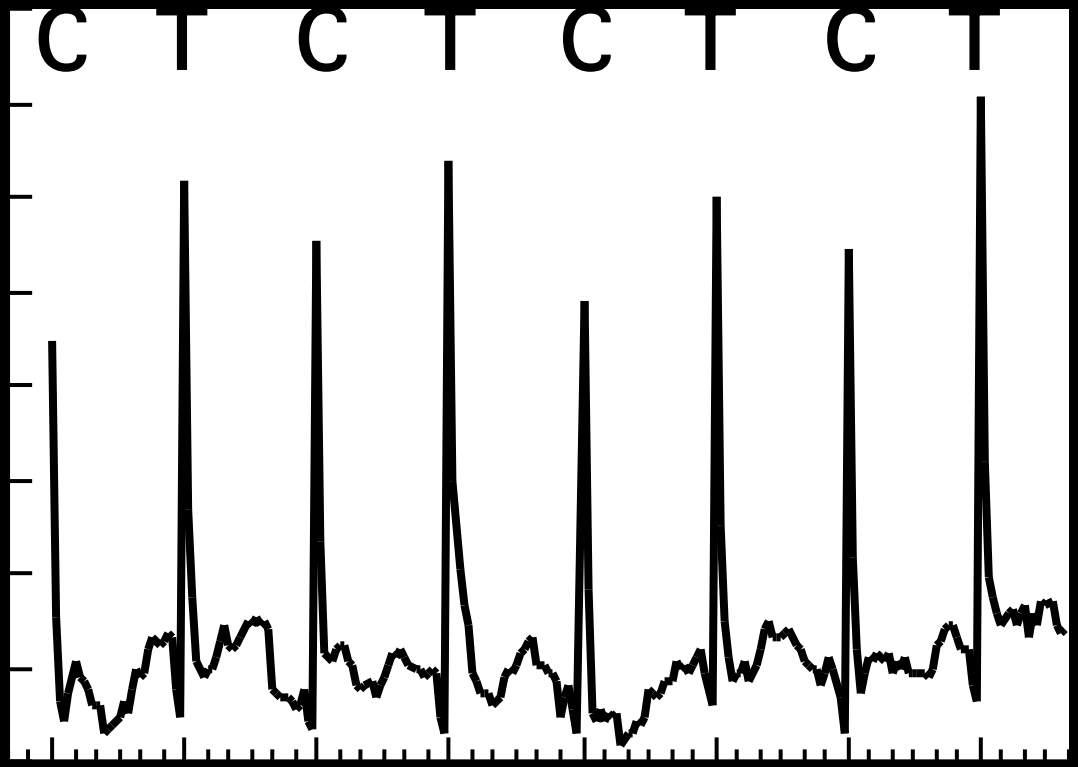
Recognize?
- Edge effects
- Shorter signal change latencies
- Unusually high signal changes
- External measuring devices

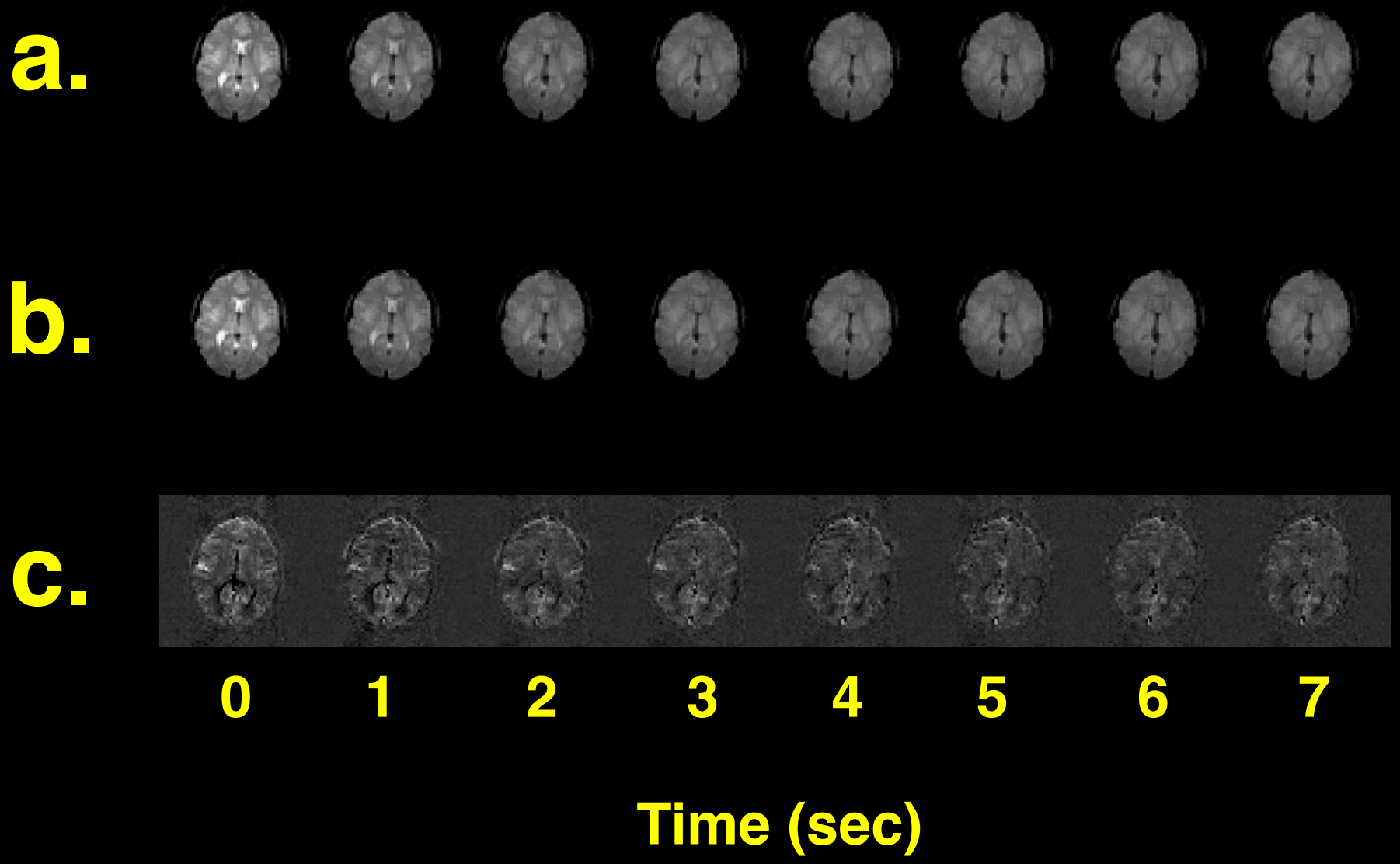
Correct?
- Image registration algorithms
- Orthogonalize to motion-related function *(cardiac, respiration, movement)*
- Navigator echo for k-space alignment *(for multishot techniques)*
- Re-do scan

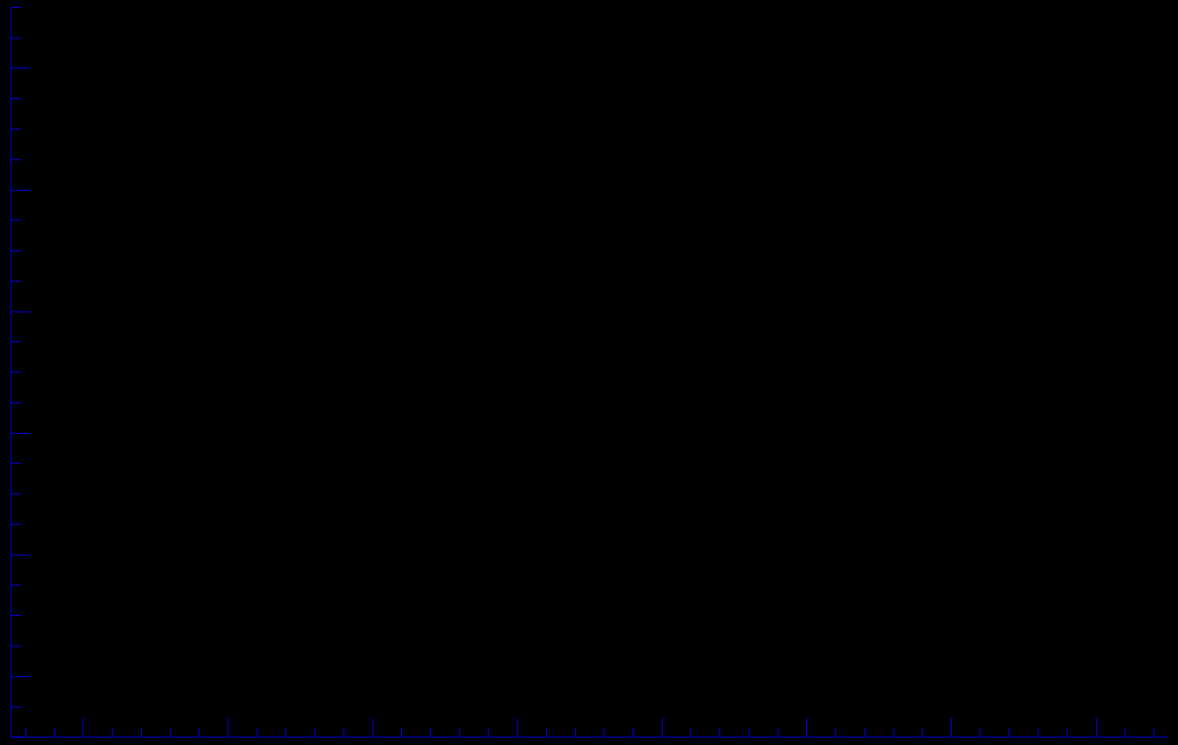
Bypass?
- Paradigm timing strategies..
- Gating (with T1-correction)

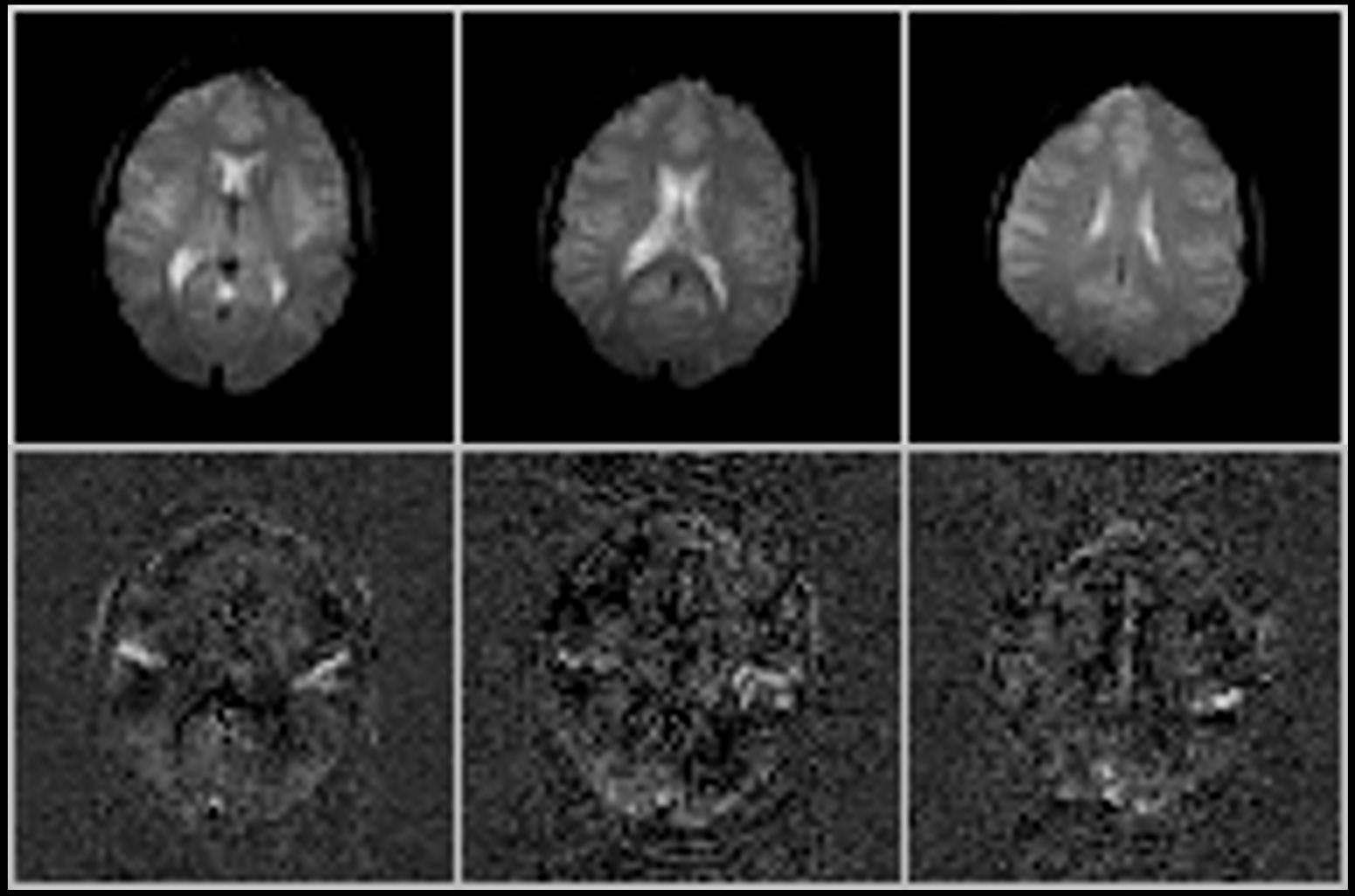
Suppress?
- Flatten image contrast
- Physical restraint
- Averaging, smoothing


Prior EPI Gradients
(20 sec)
Image
Acquisition
(20 to 30 sec)
T
C
T
C
T
C
T
C
T
C
Average Time Series
Difference Time Series


C
T
C
T
C
T
C
T


a.
b.
c.
0
1
2
3
4
5
6
7
Time (sec)





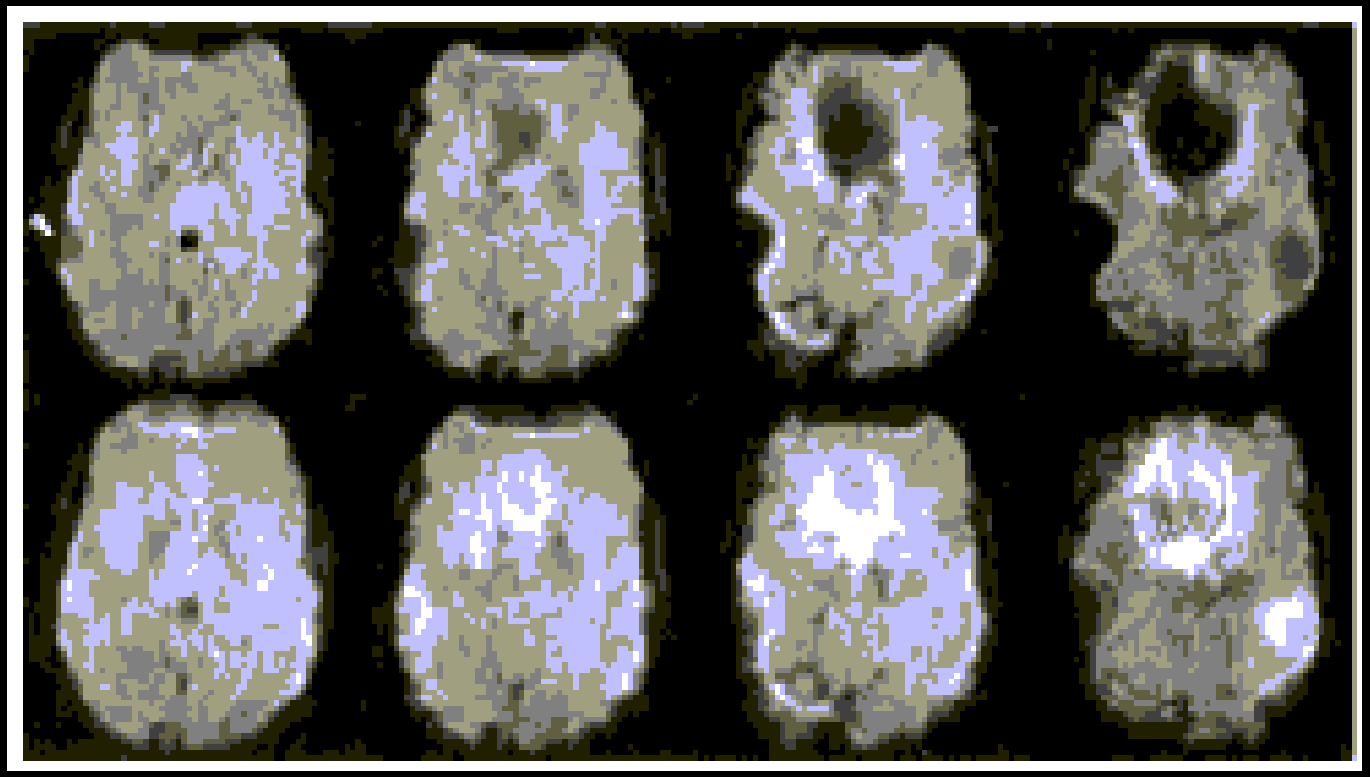
How to deal with Scanner Noise?

- Clustered volume acquisition
  Talavage et al.
- Silent sequences

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

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

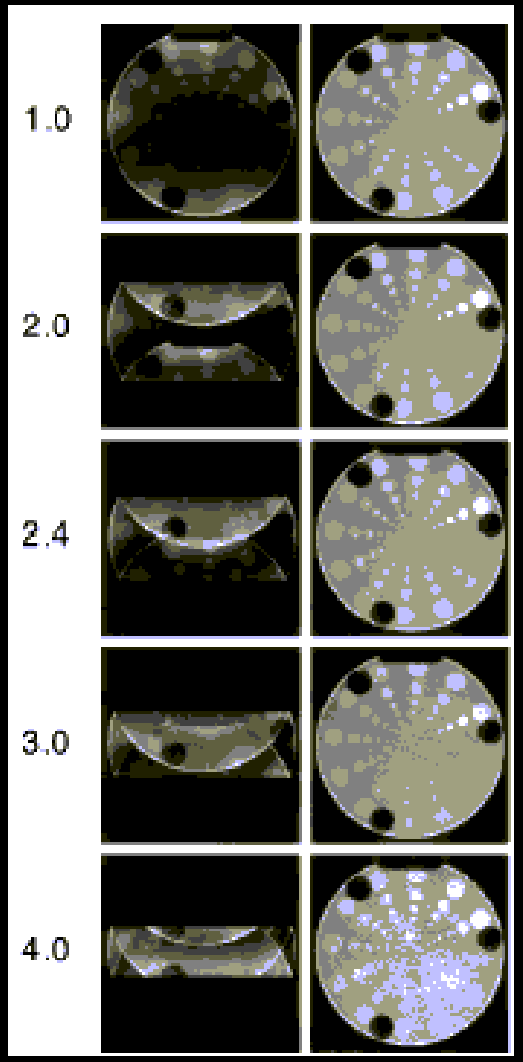
Gary H. Glover*



Magnetic Resonance in Medicine 42:952–962 (1999)

SENSE: Sensitivity Encoding for Fast MRI

Klaas P. Pruessmann, Markus Weiger, Markus B. Scheidegger, and Peter Boesiger*



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Ziad Saad

Graduate Student:

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Summer Student:

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Kay Kuhns

August, 2000