Strategies for Information Extraction and Artifact Reduction in Functional MRI

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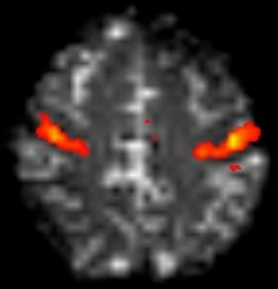
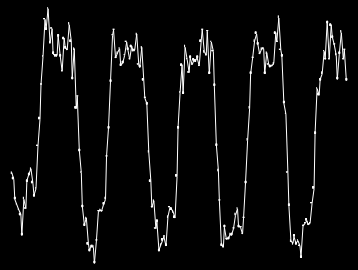
Categories of Questions Asked with fMRI

Where?



When?



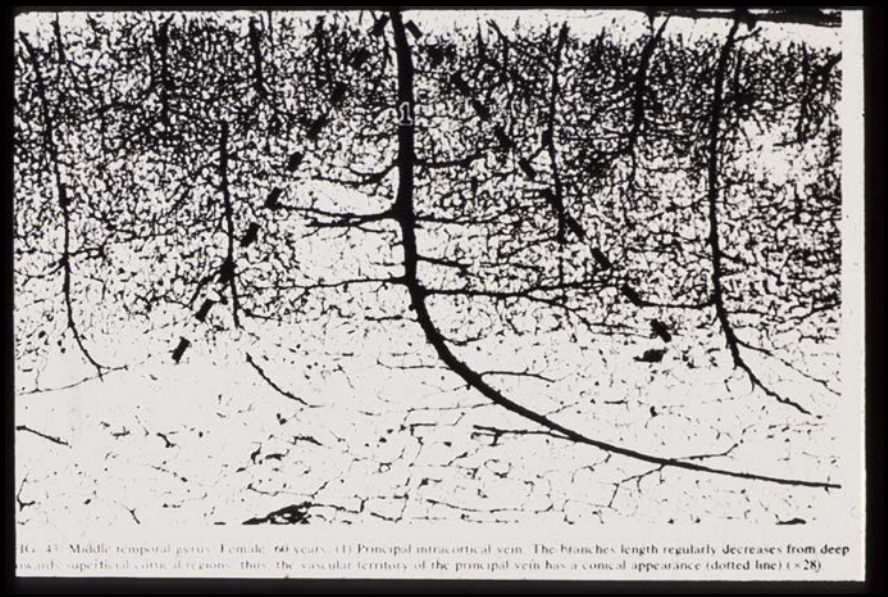
How much?

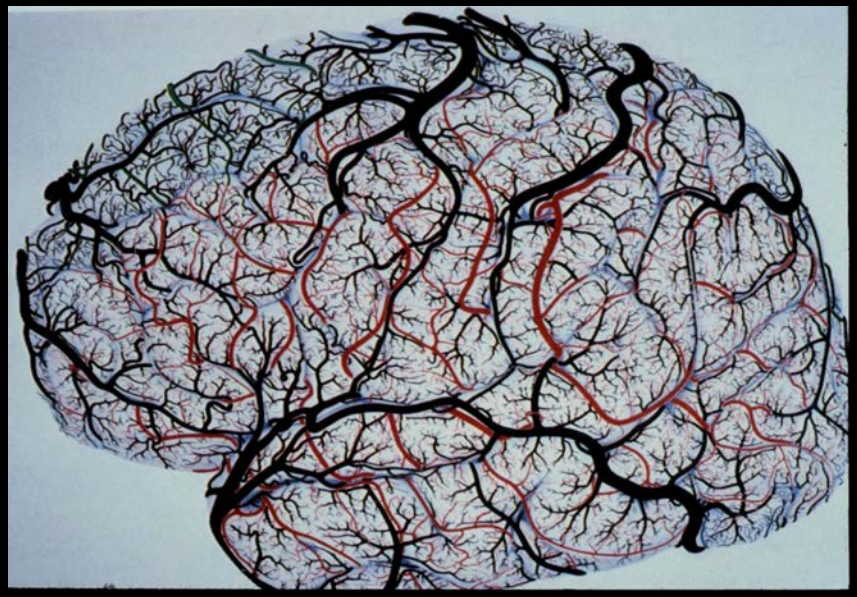
How to get the brain to do what we want it to do in the context of an fMRI experiment?

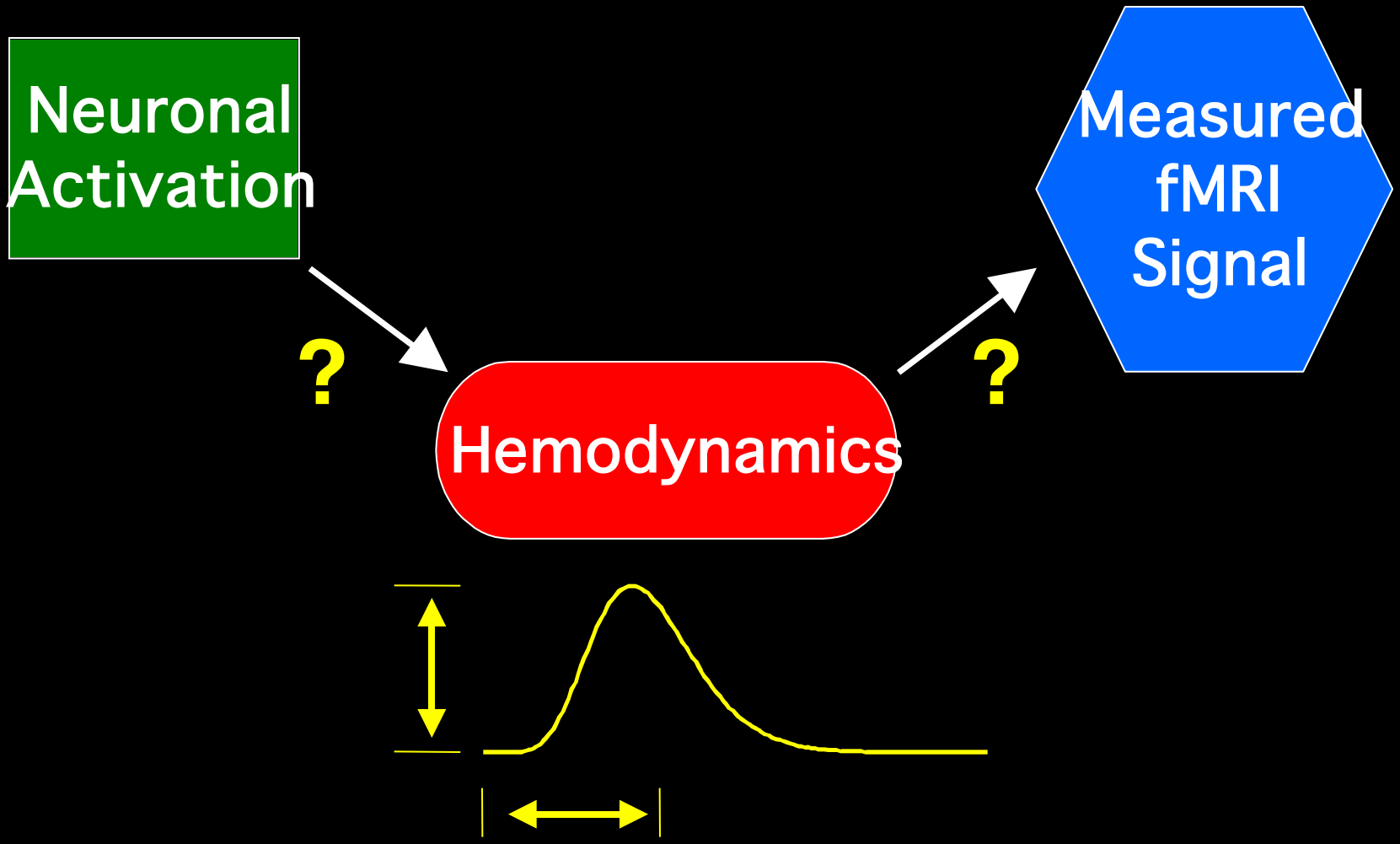
(*limitations*: limited time and signal to noise, motion, acoustic noise)

A Primary Challenge:

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



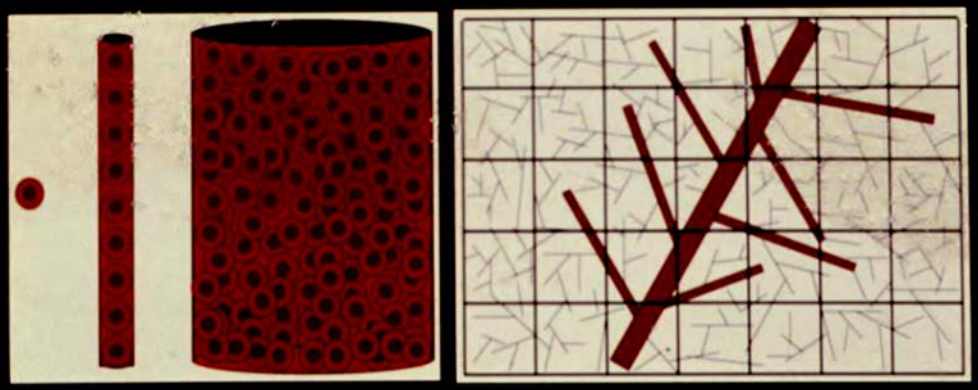



Neuronal Activation
?
Hemodynamics
?
Measured fMRI Signal
Physiologic Factors

Physiologic Factors that Influence BOLD Contrast

- Blood oxygenation
- Blood volume
- Blood pressure
- Hematocrit
- Vessel size

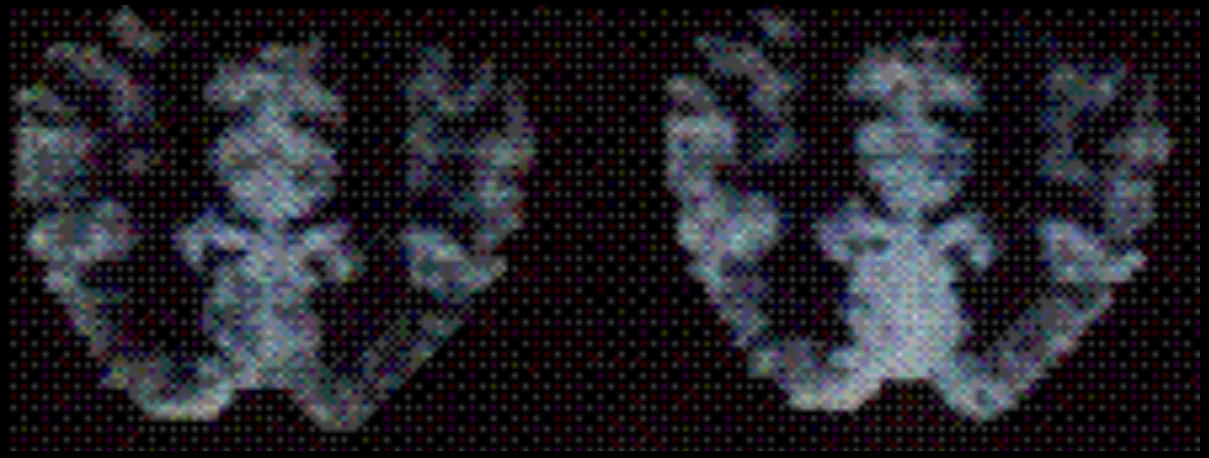
Coupling: Flow & $CMRO_2$

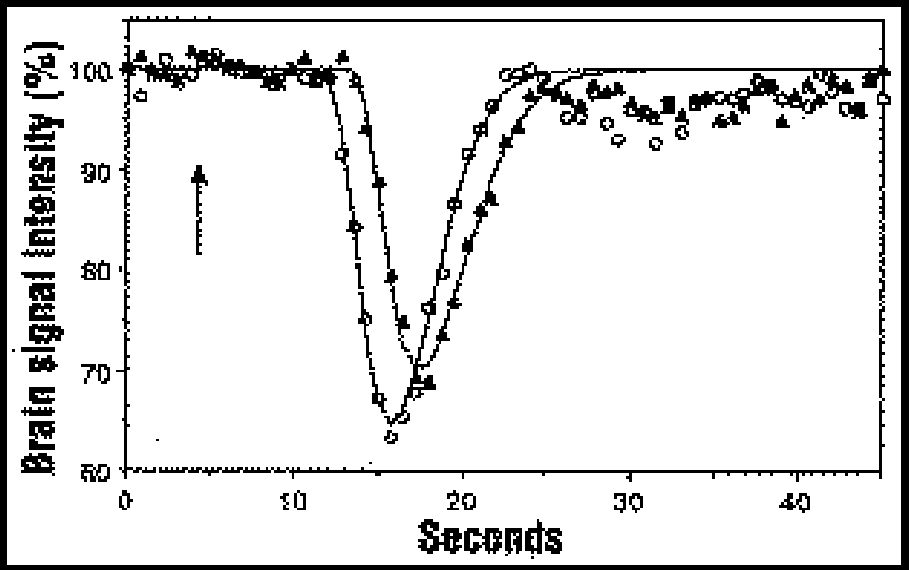


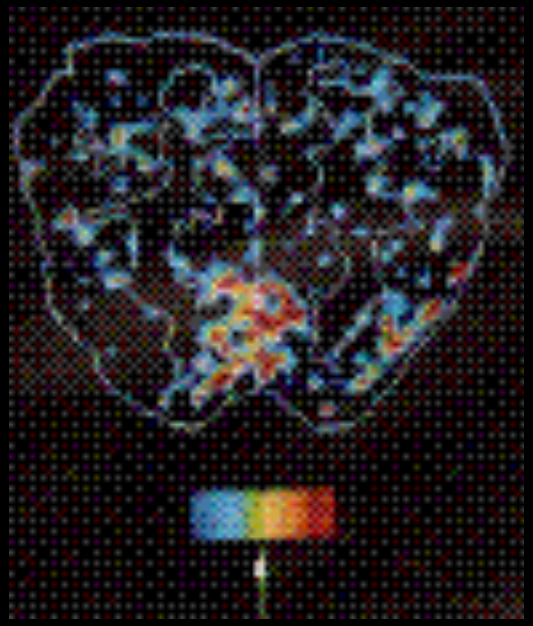
Contrast in Functional MRI

- **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

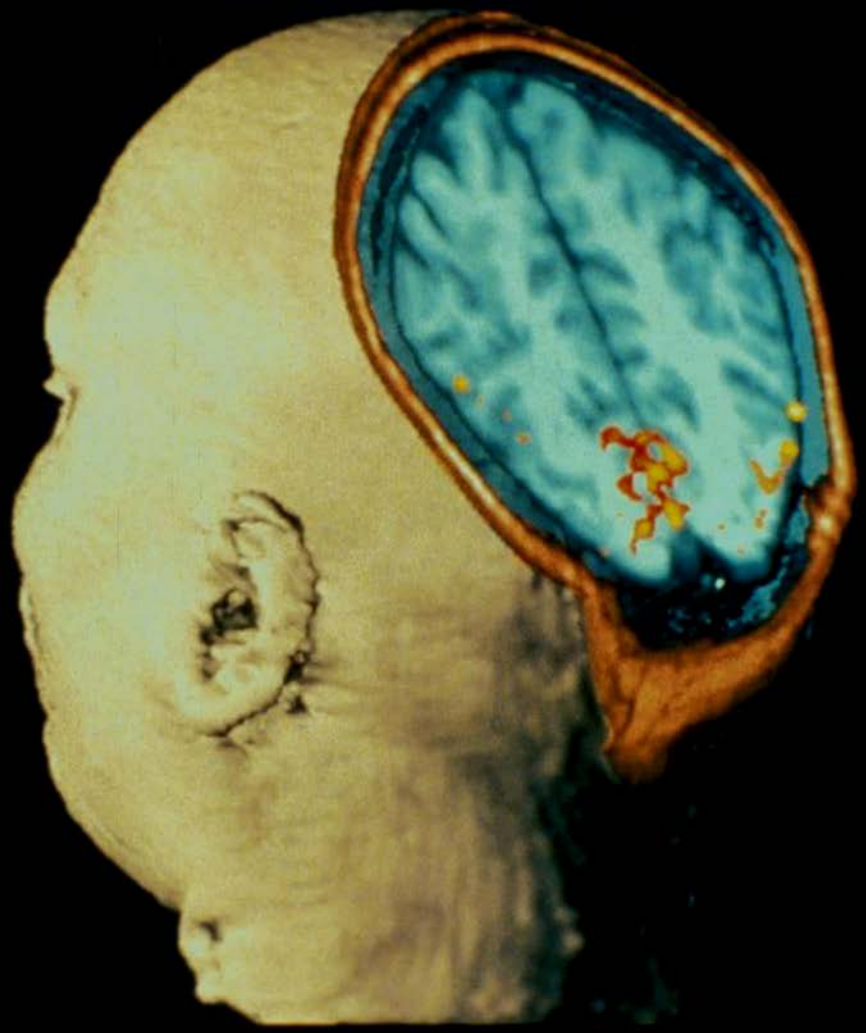
Resting Active







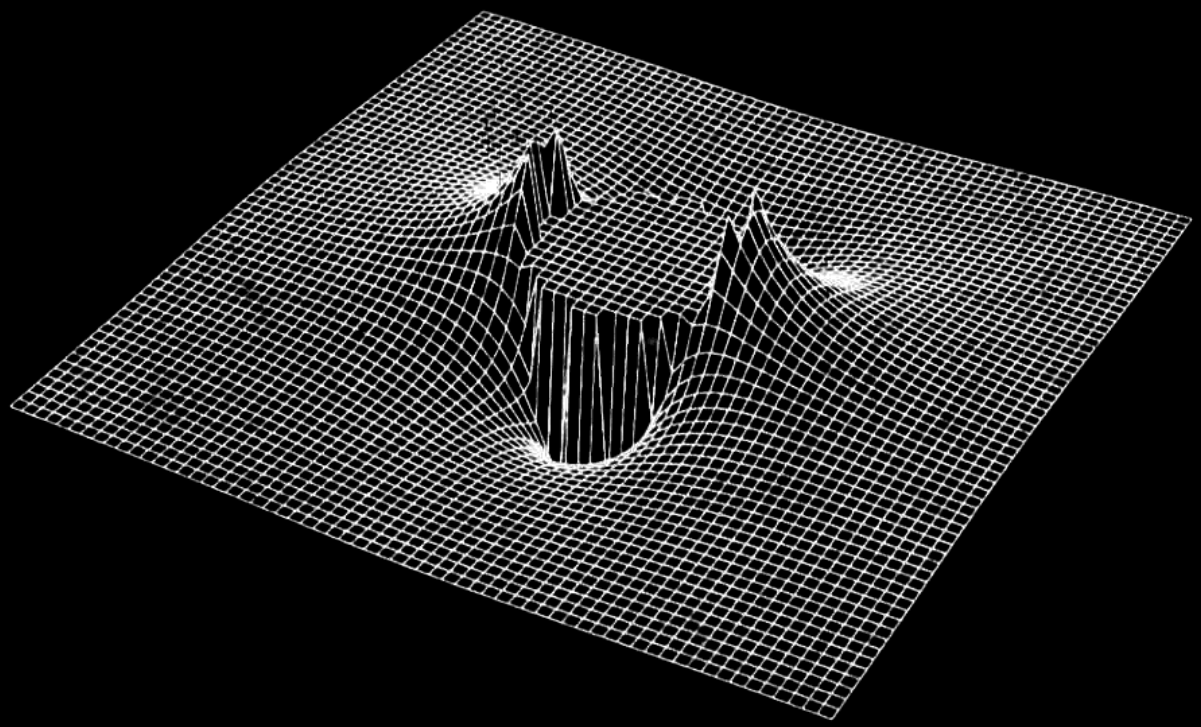
Photic Stimulation



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

↓

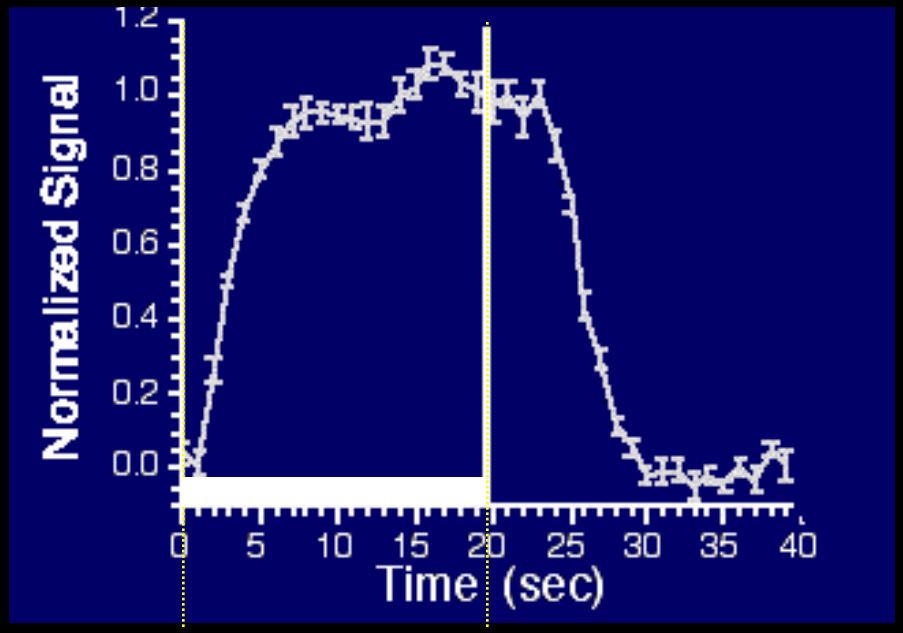
Decrease in susceptibility-related intravoxel dephasing → Increase in T2 and T2*

↓

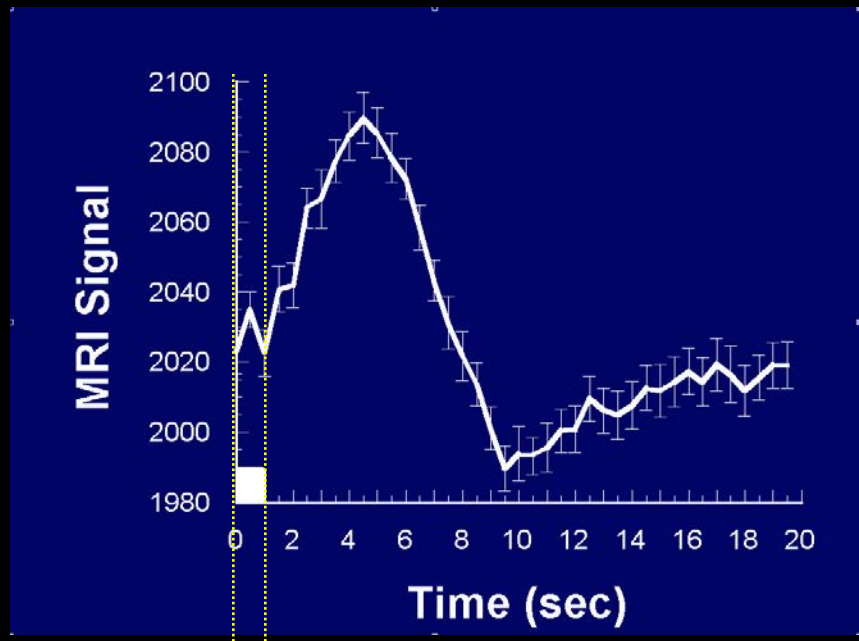
Local Signal Increase in T2 and T2* - weighted sequences

The BOLD Signal

Blood Oxygenation Level Dependent (BOLD) signal changes

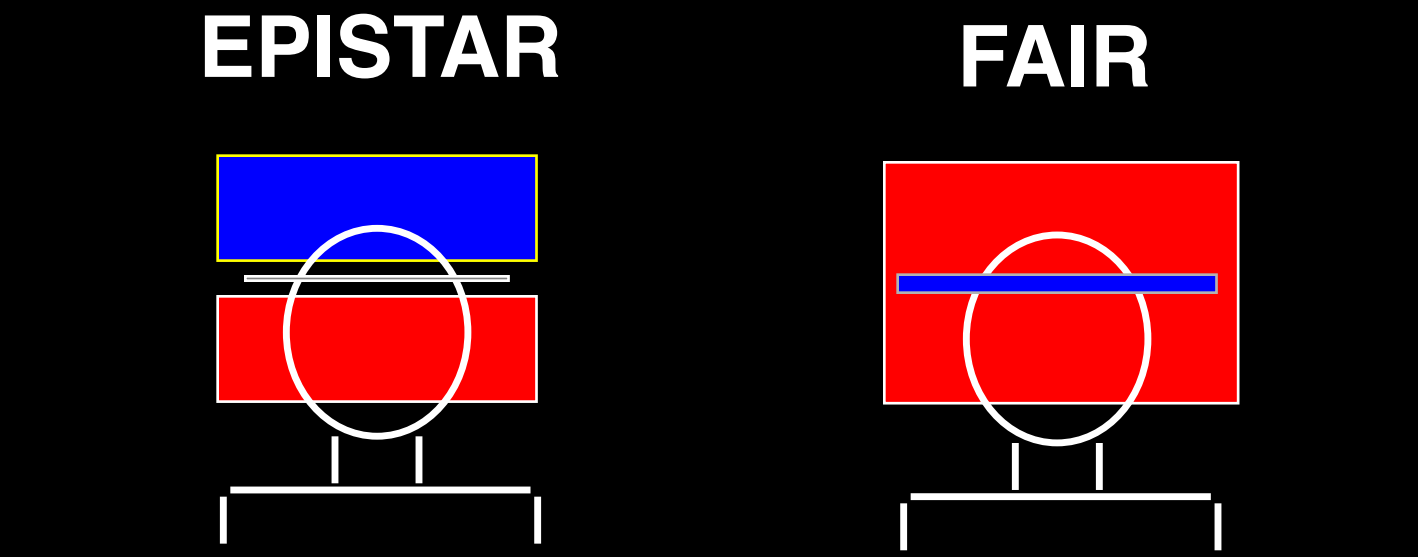


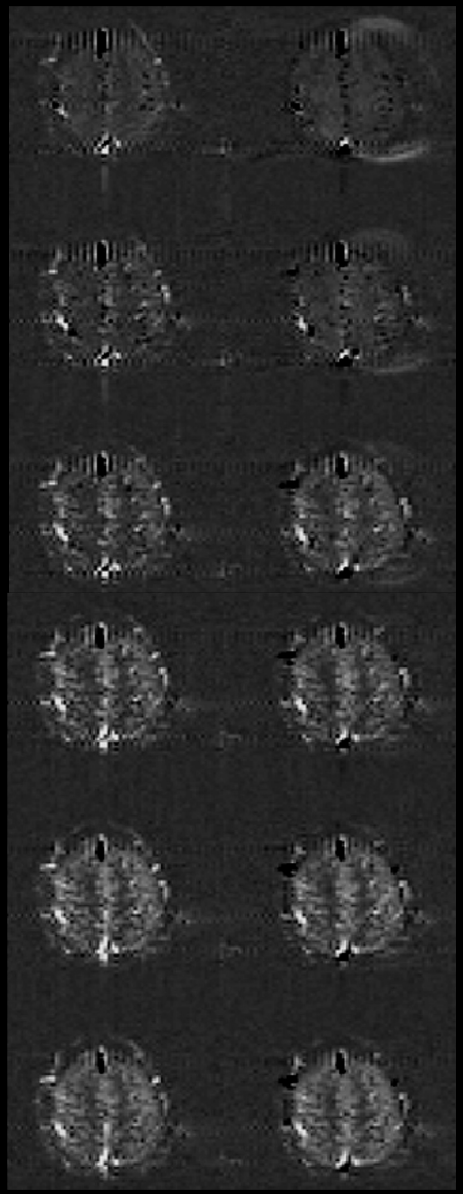
task



task

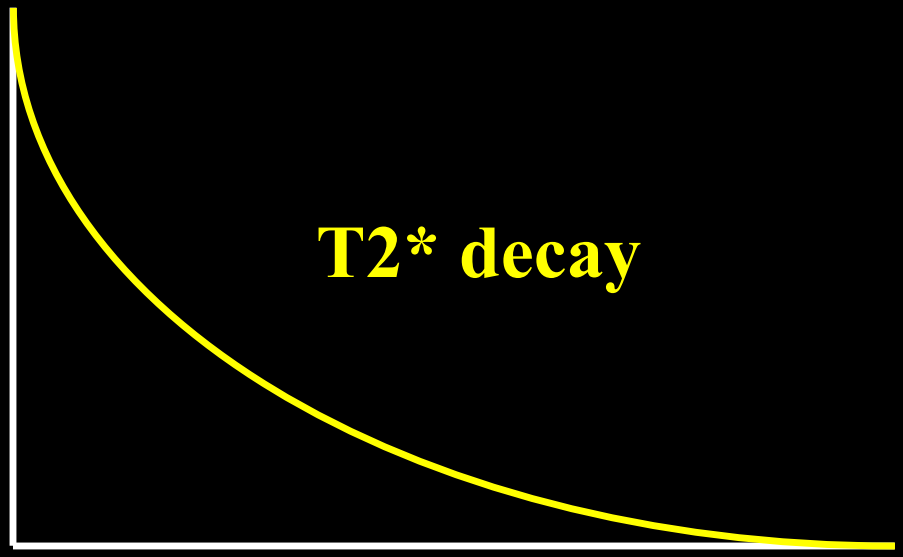
Perfusion / Flow Imaging

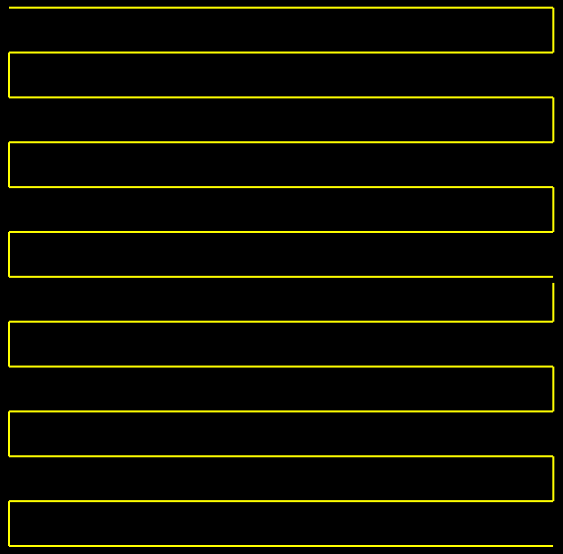


TI (ms)	FAIR	EPISTAR
200		
400		
600		
800		
1000		
1200		

Scanner and Hemodynamic Limits

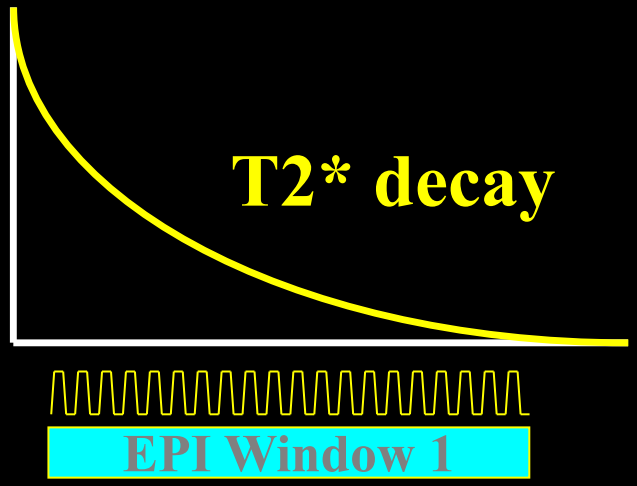
Single Shot Imaging

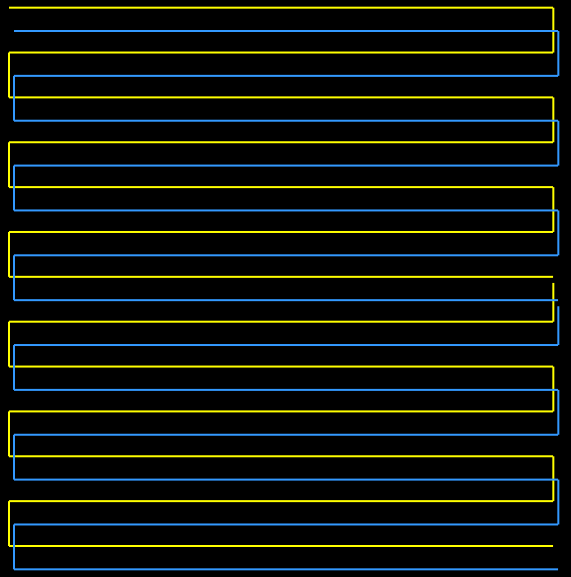


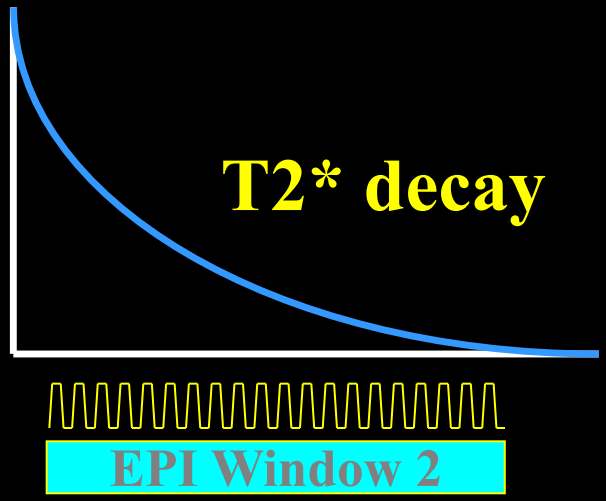


≈ 20 to 40 ms

Multishot Imaging

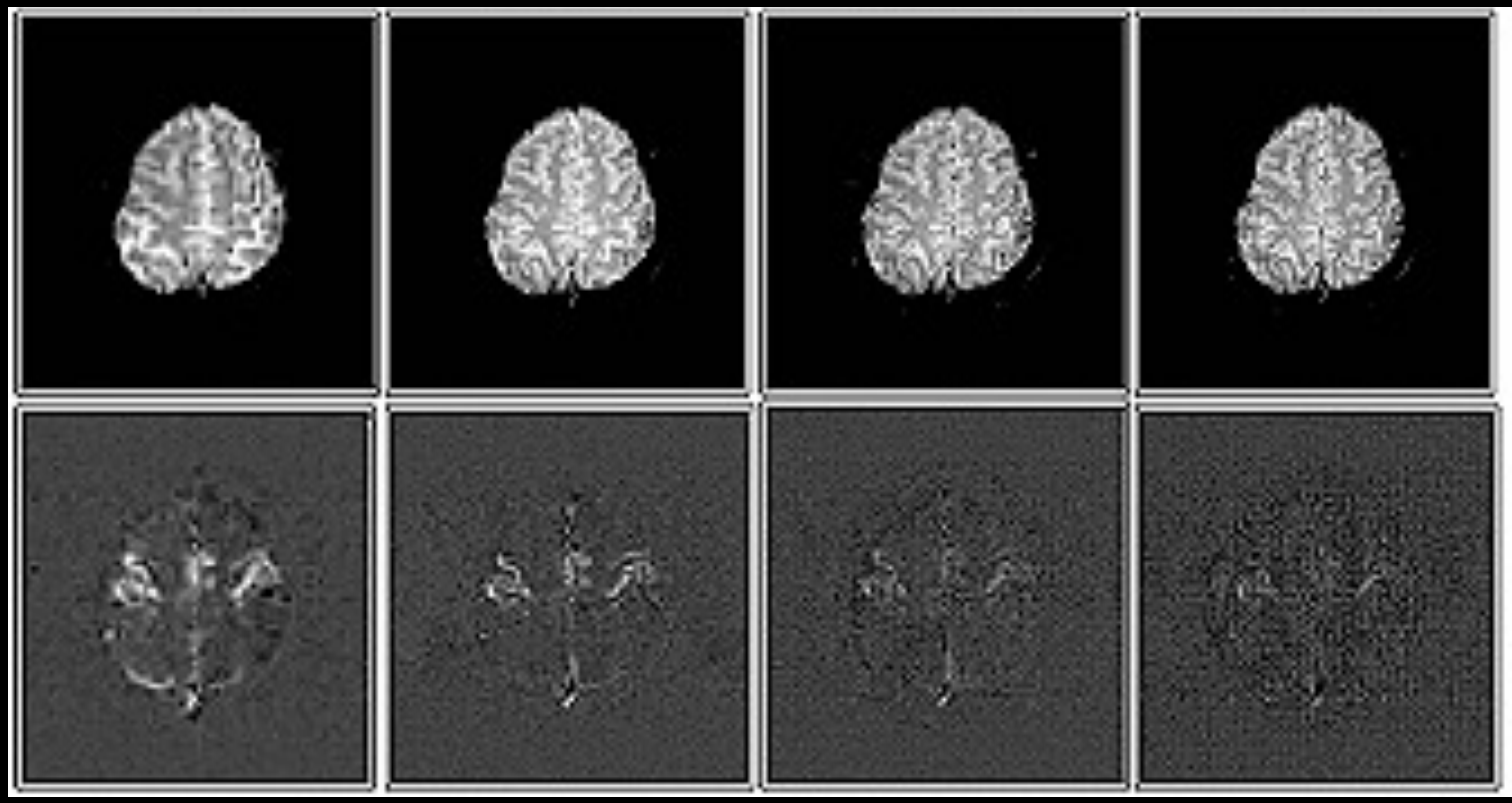




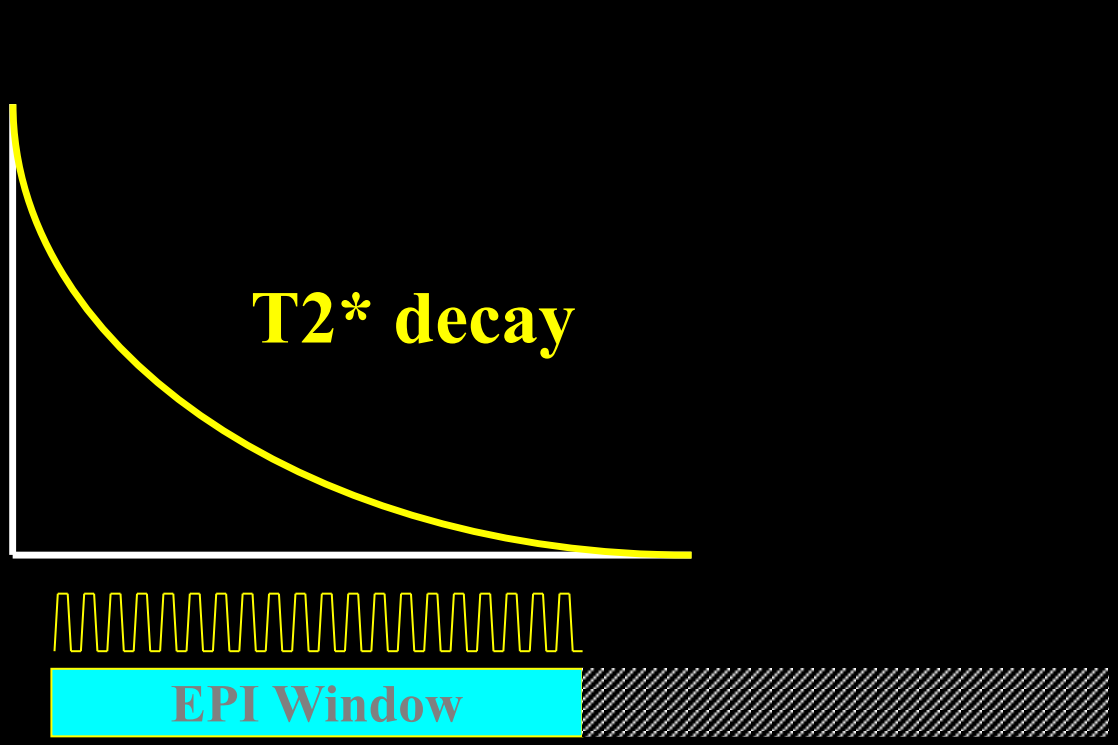


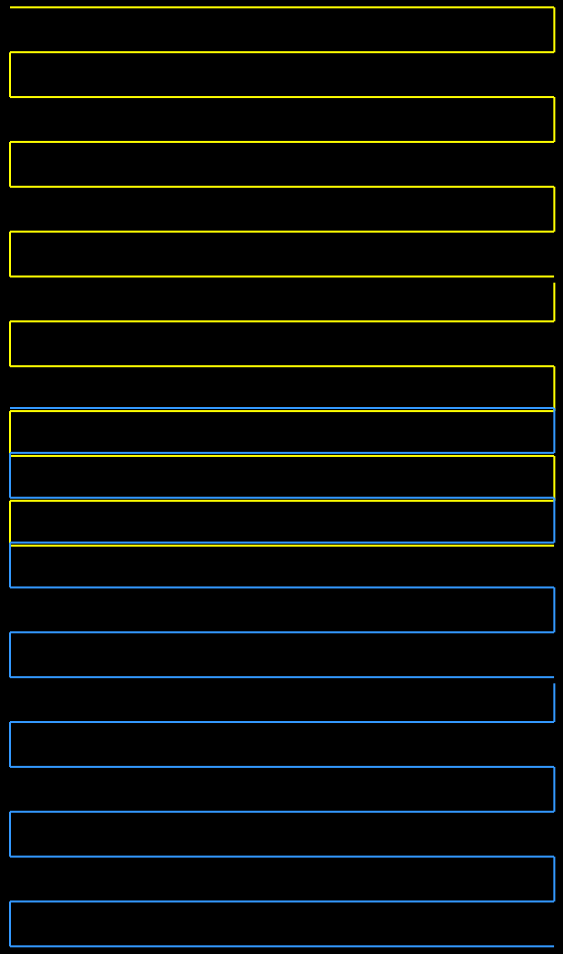
Multi Shot EPI

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

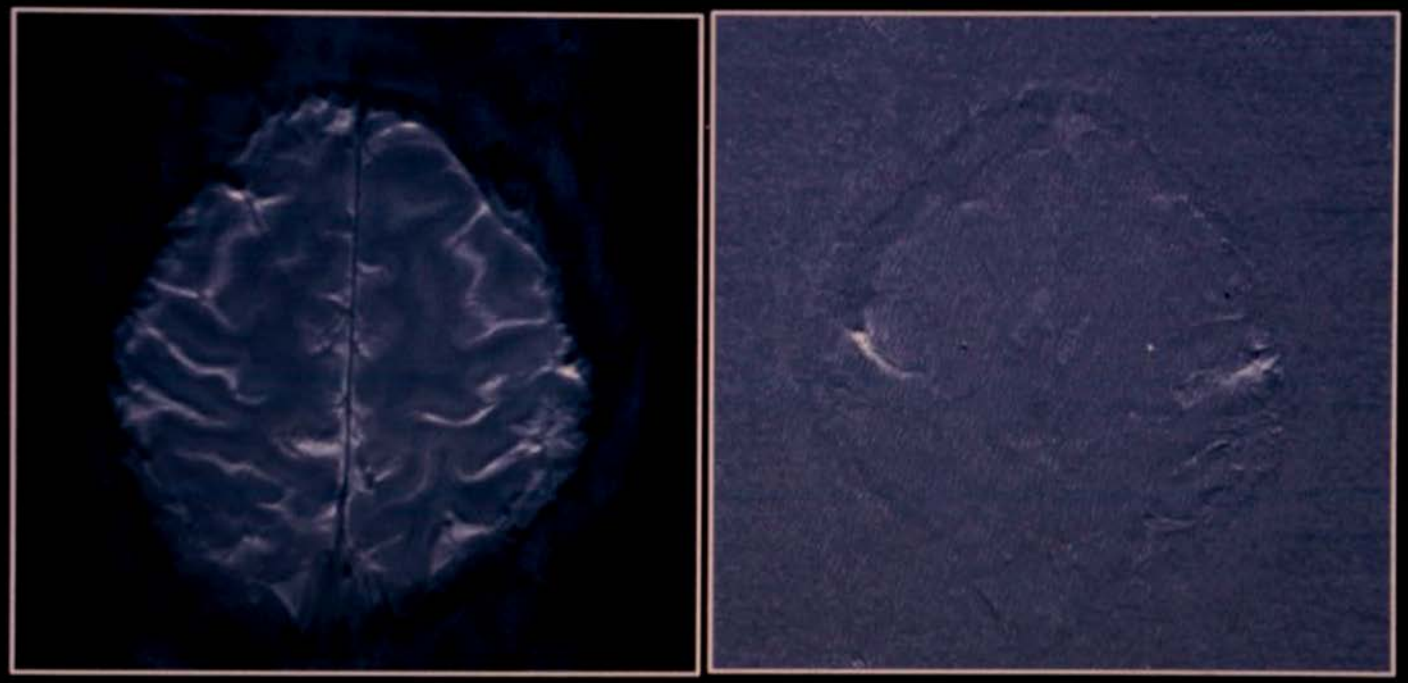


Partial k-space imaging

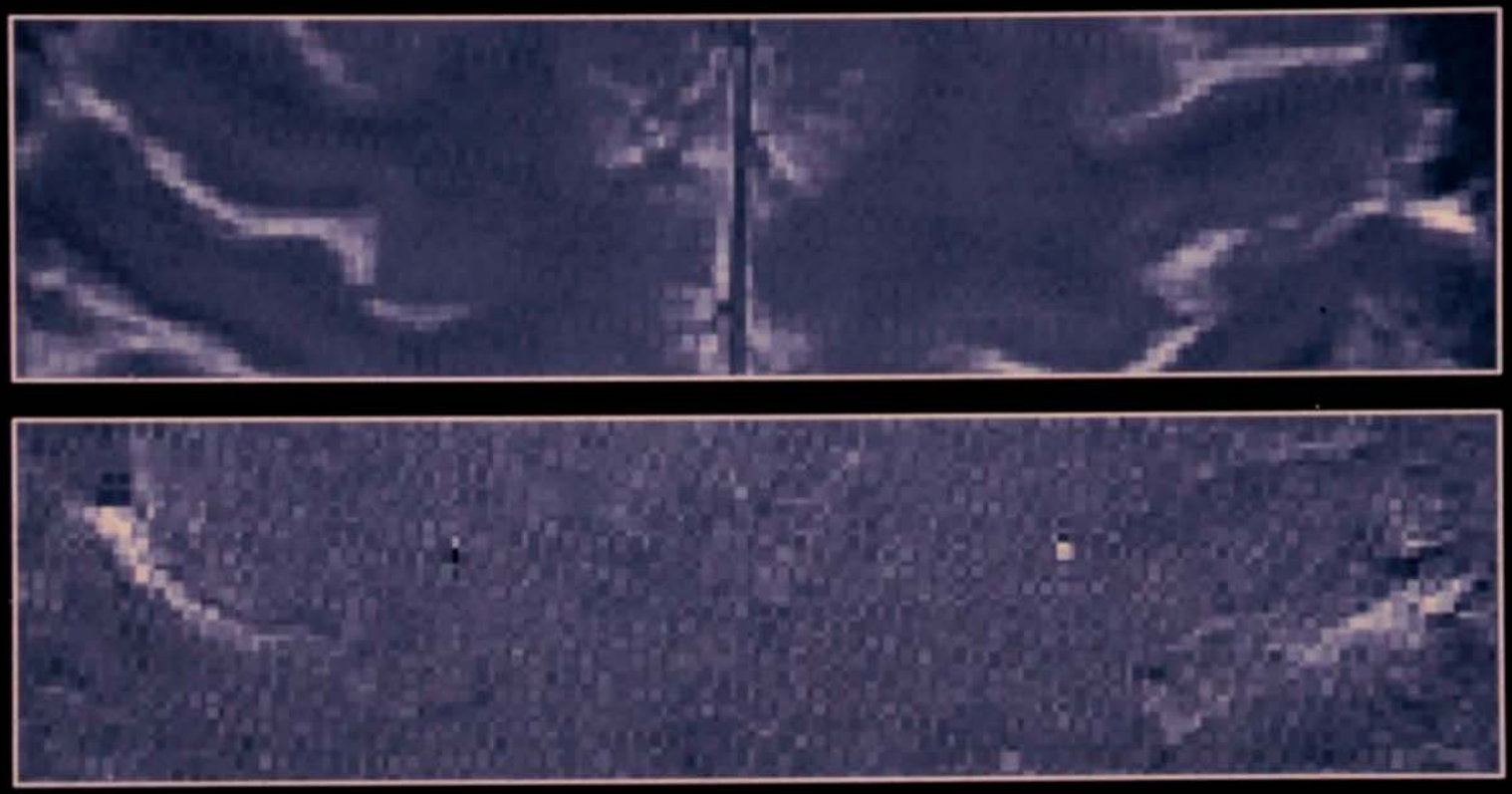


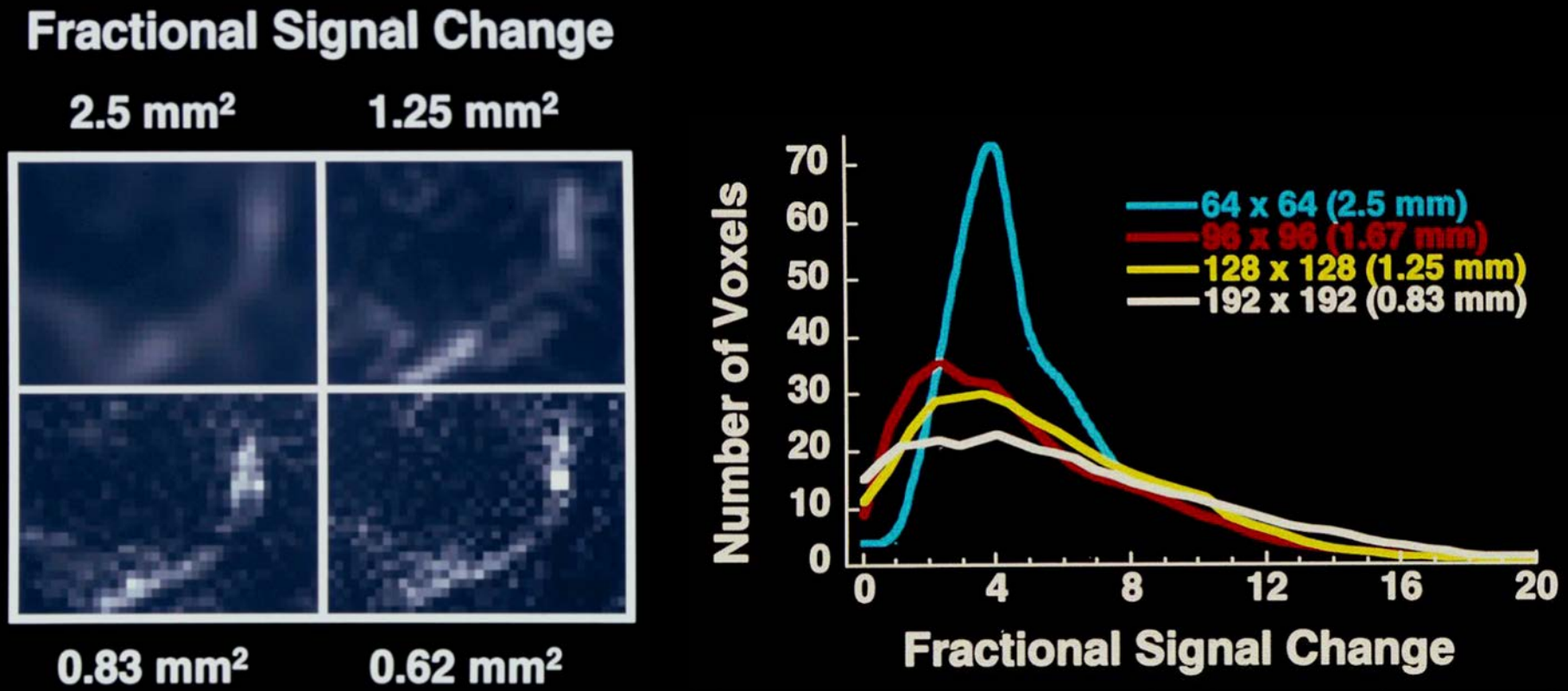


Single - Shot EPI at 3T:
Half NEX, 256 x 256, 16 cm FOV



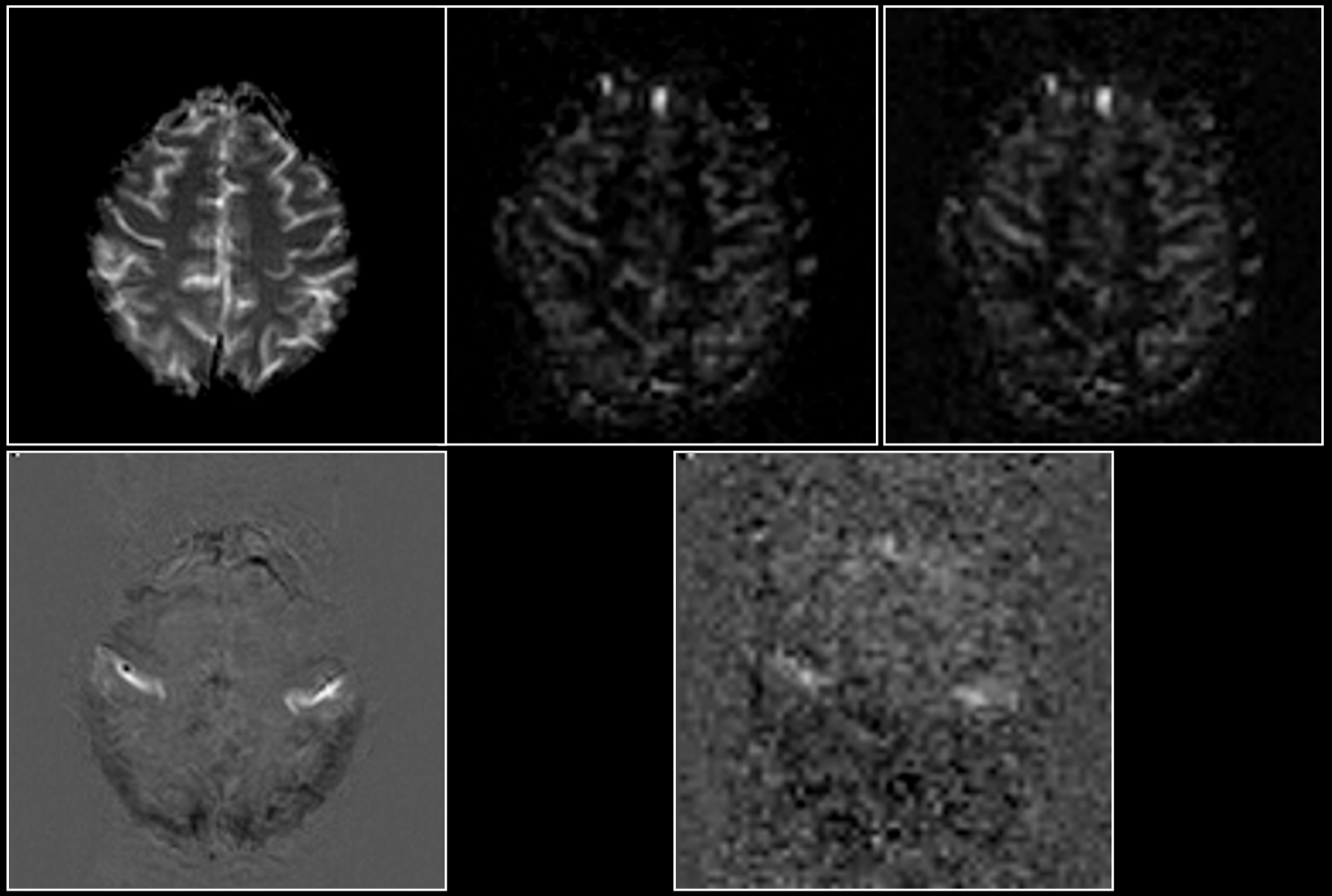
Single - Shot EPI at 3T:
Half NEX 256 x 256, 16 cm FOV




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)

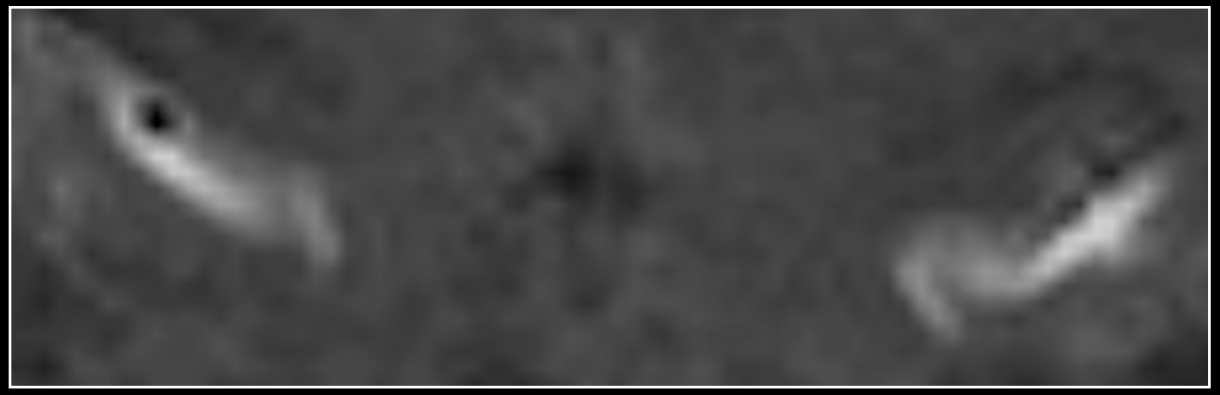
Perfusion

BOLD *Rest* *Activation*



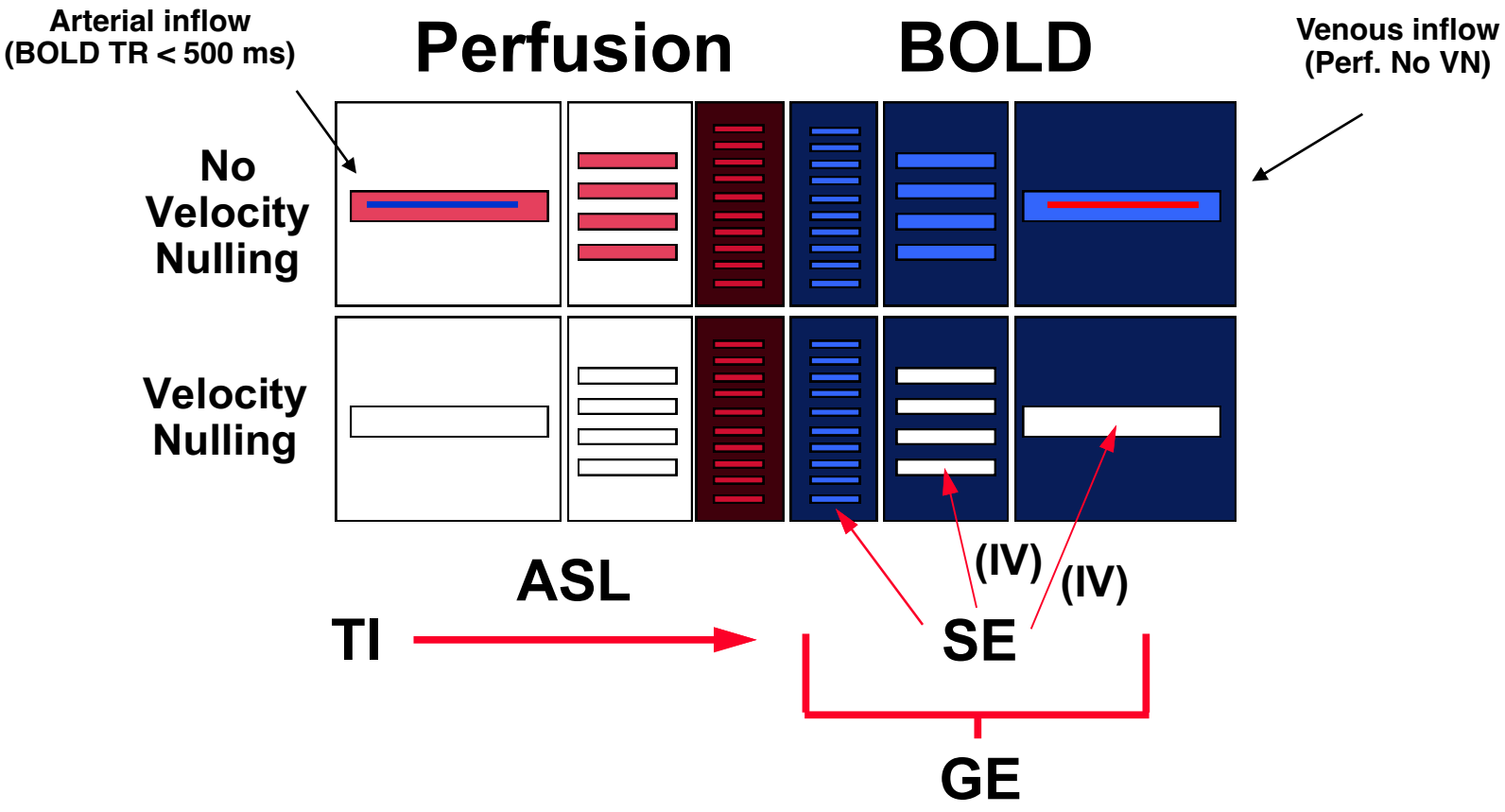
Anatomy

BOLD



Perfusion

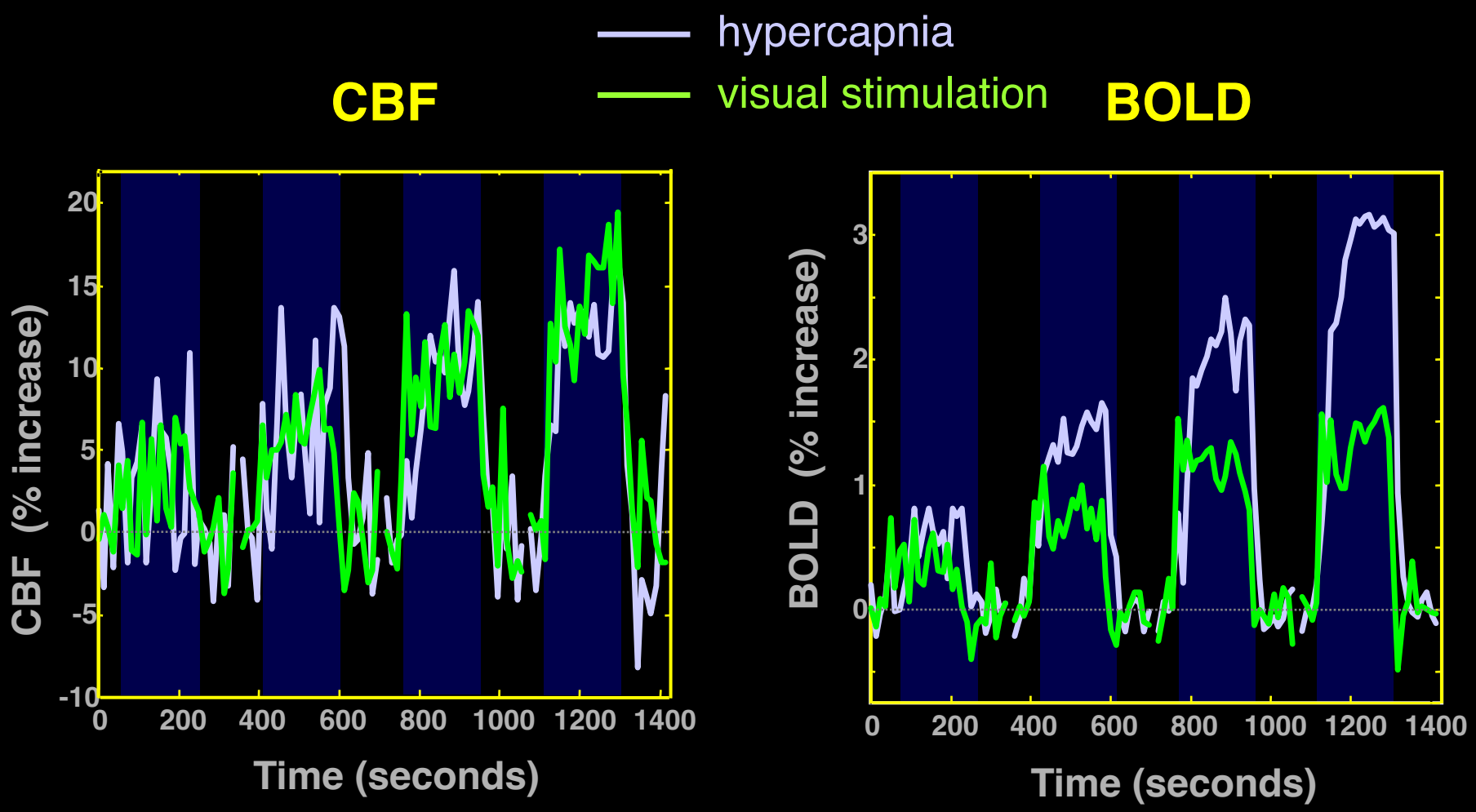
Hemodynamic Specificity



	+	-
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

$CMRO_2$-related BOLD signal deficit:

Hoge, et al.

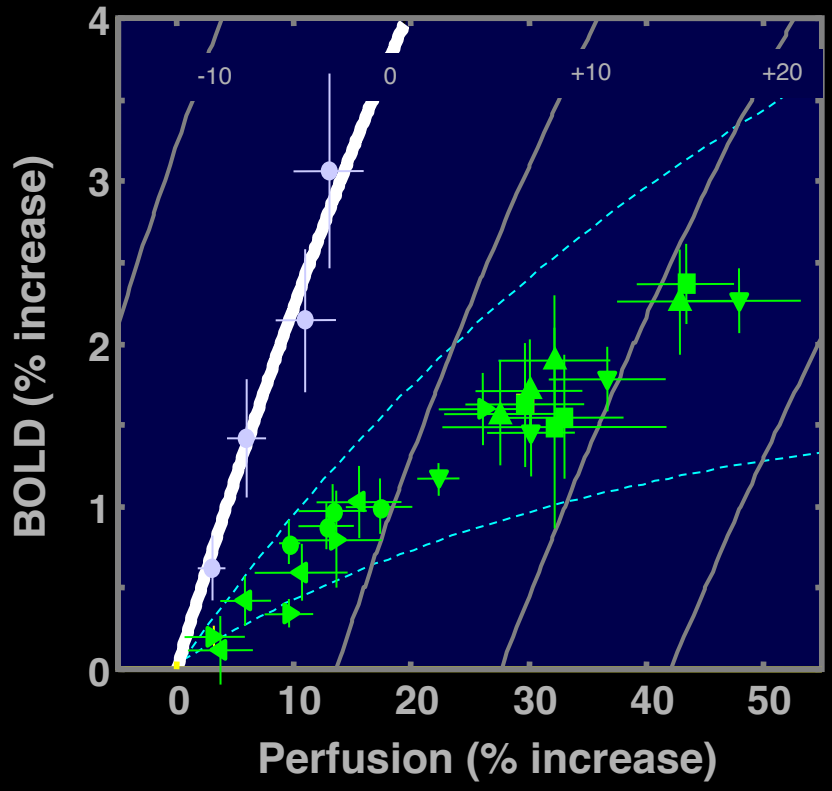


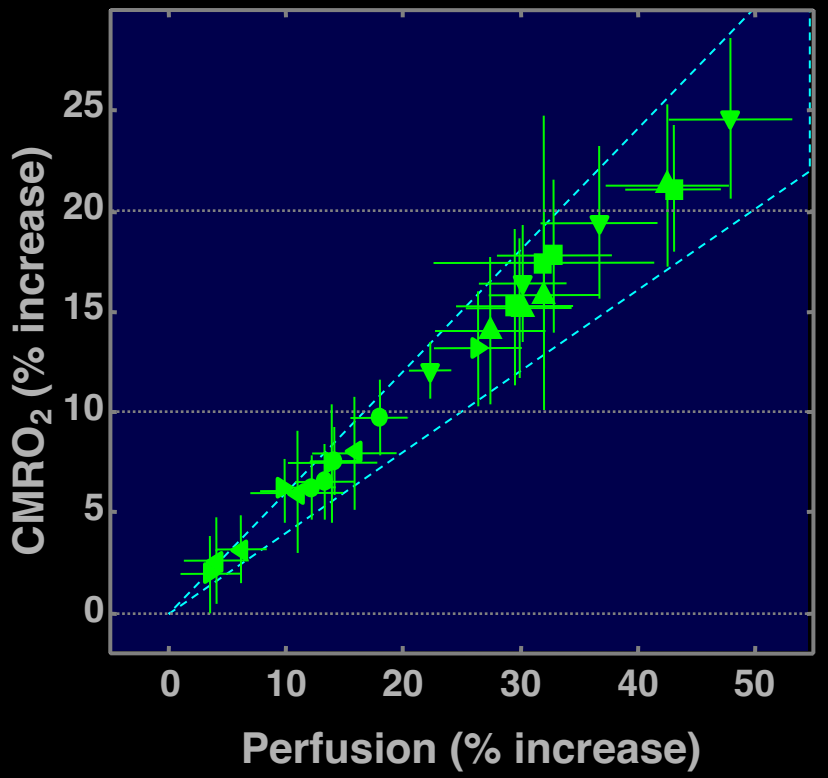
Simultaneous Perfusion and BOLD imaging during graded visual activation and hypercapnia

N=12

CBF-$CMRO_2$ coupling

Hoge, et al.

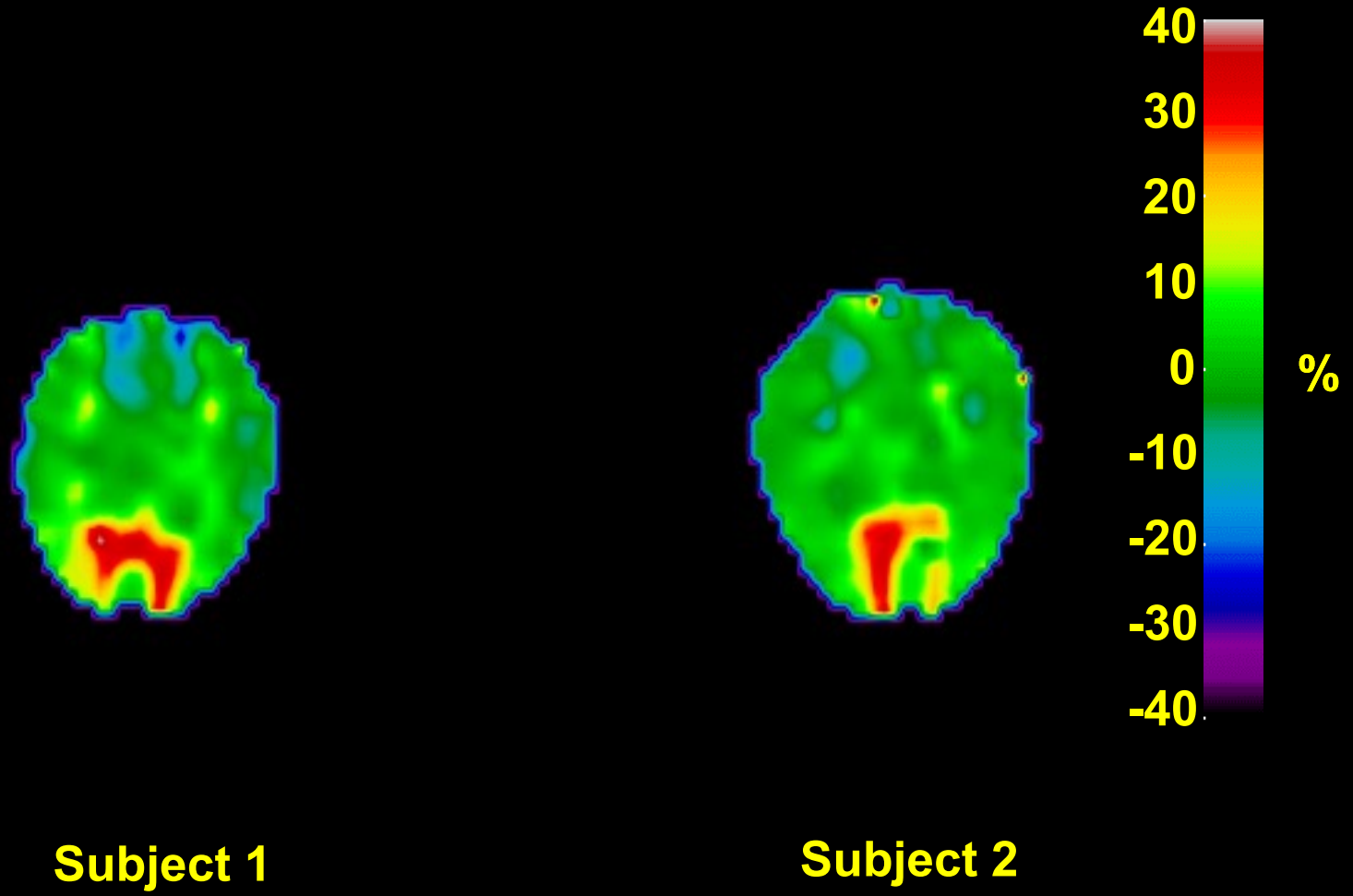




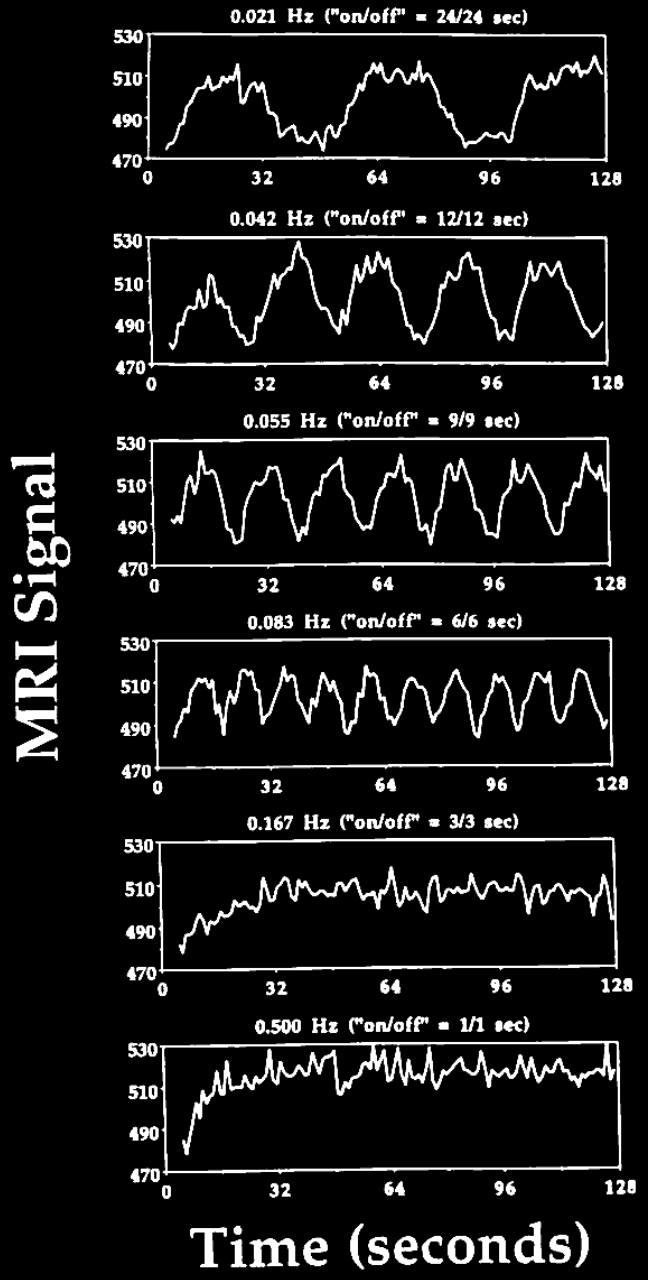
Characterizing Activation-induced $CMRO_2$ changes using calibration with hypercapnia

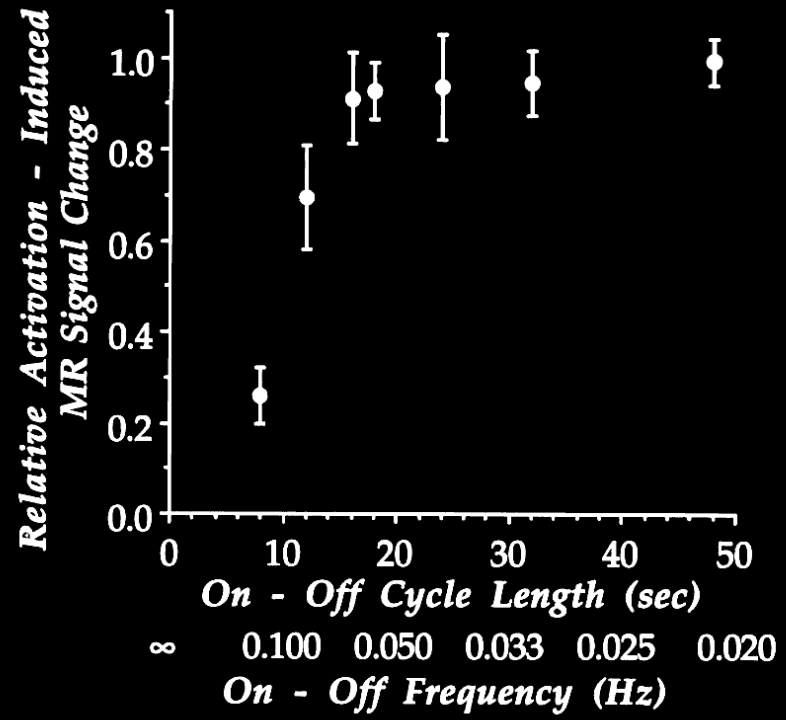
Hoge, et al.

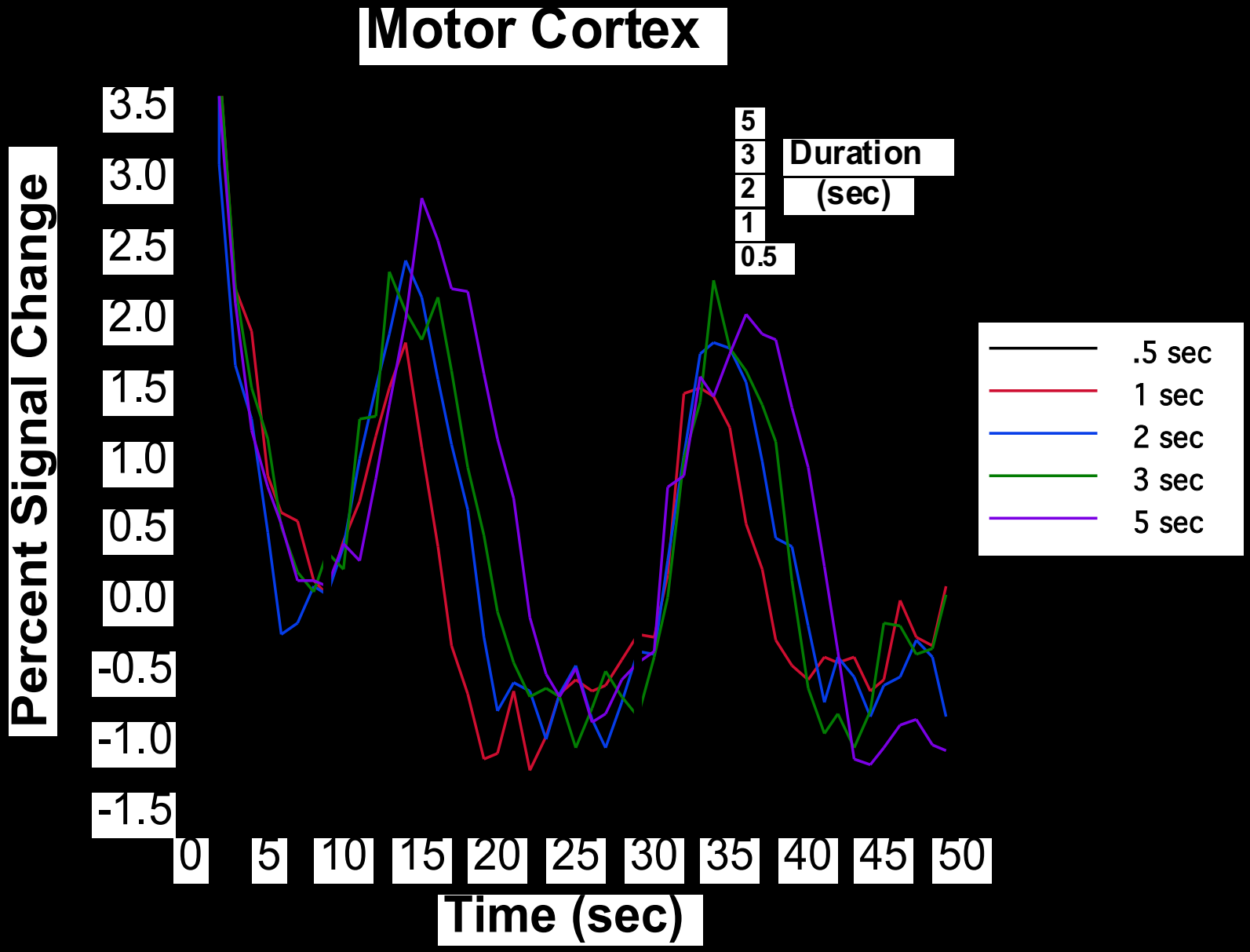
Computed $CMRO_2$ changes

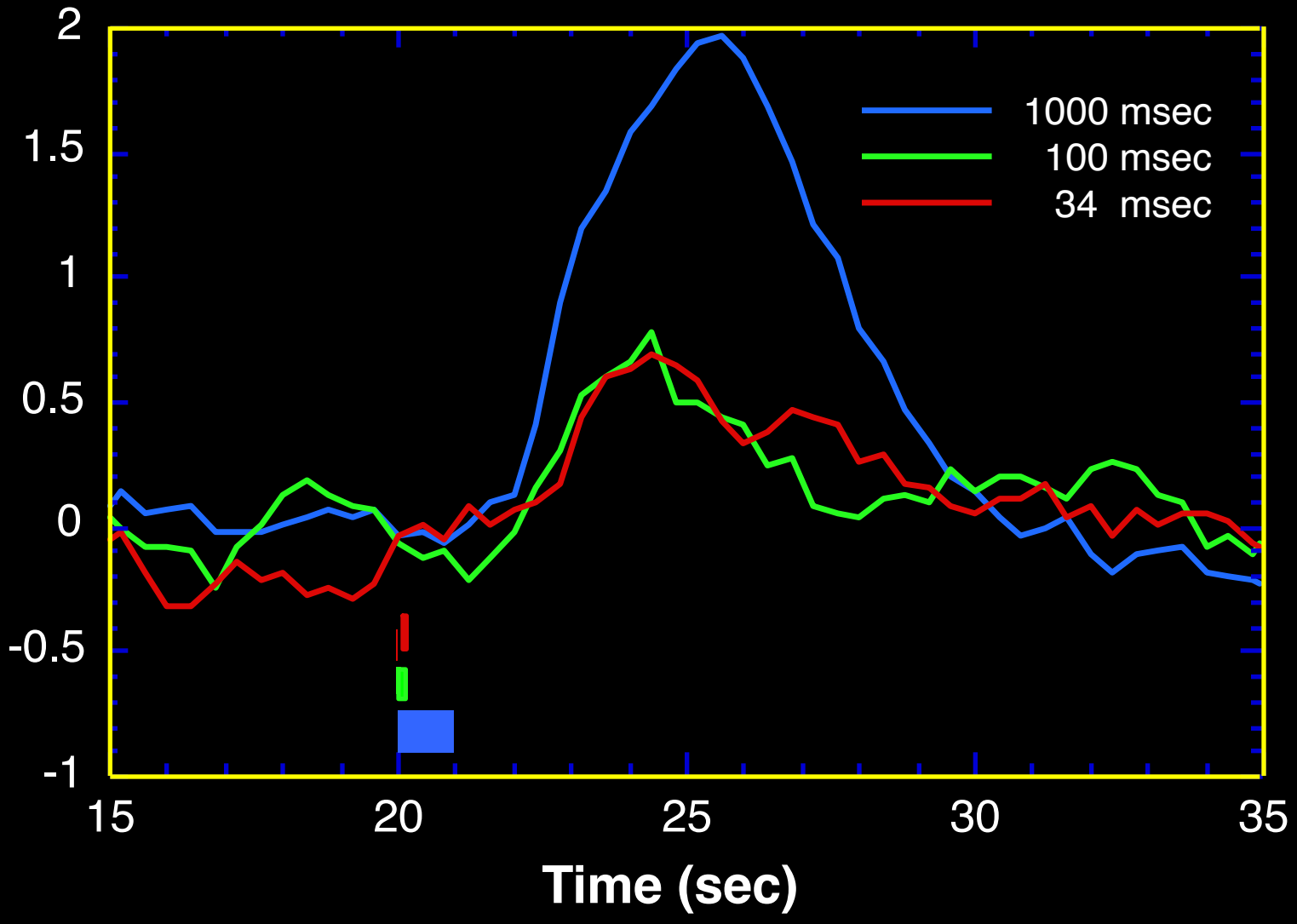


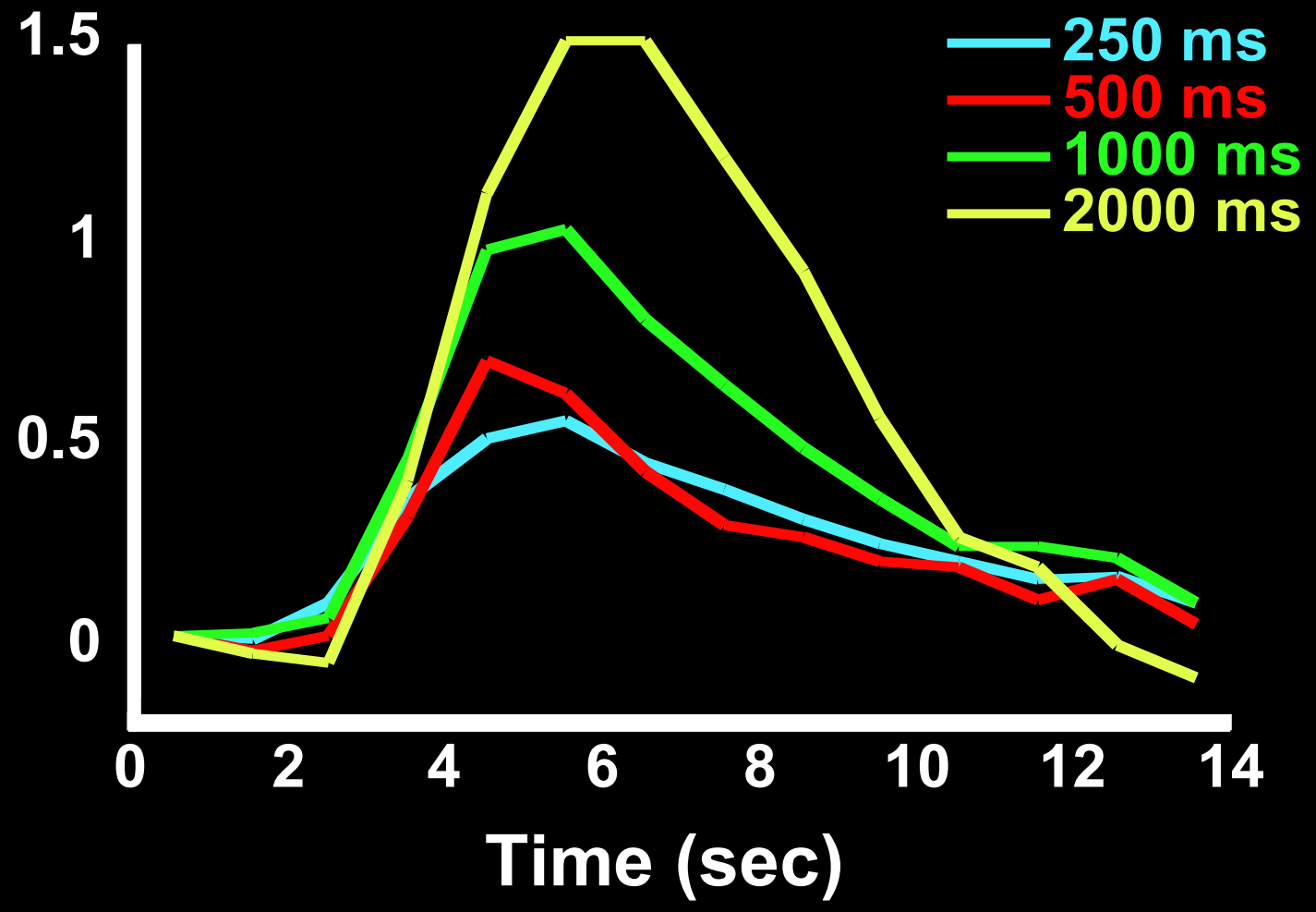
fMRI signal change dynamics...


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)

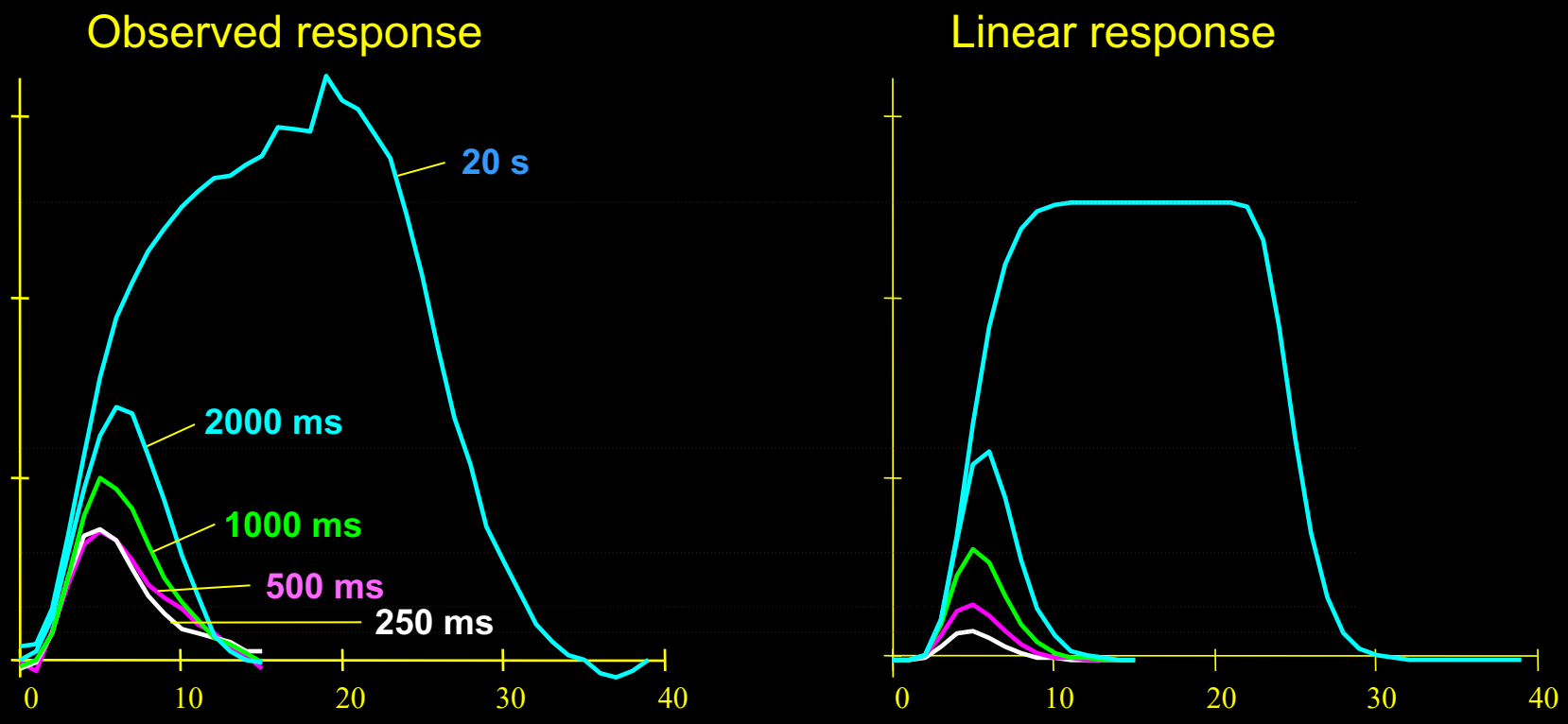

Relative Activation - Induced MR Signal Change
1.0
0.8
0.6
0.4
0.2
0.0
0
10
20
30
40
50
On - Off Cycle Length (sec)
∞
0.100
0.050
0.033
0.025
0.020
On - Off Frequency (Hz)


Motor Cortex
Percent Signal Change
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
0
5
10
15
20
25
30
35
40
45
50
Time (sec)
5
3
2
1
0.5
Duration
(sec)
.5 sec
1 sec
2 sec
3 sec
5 sec


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


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

BOLD response is nonlinear



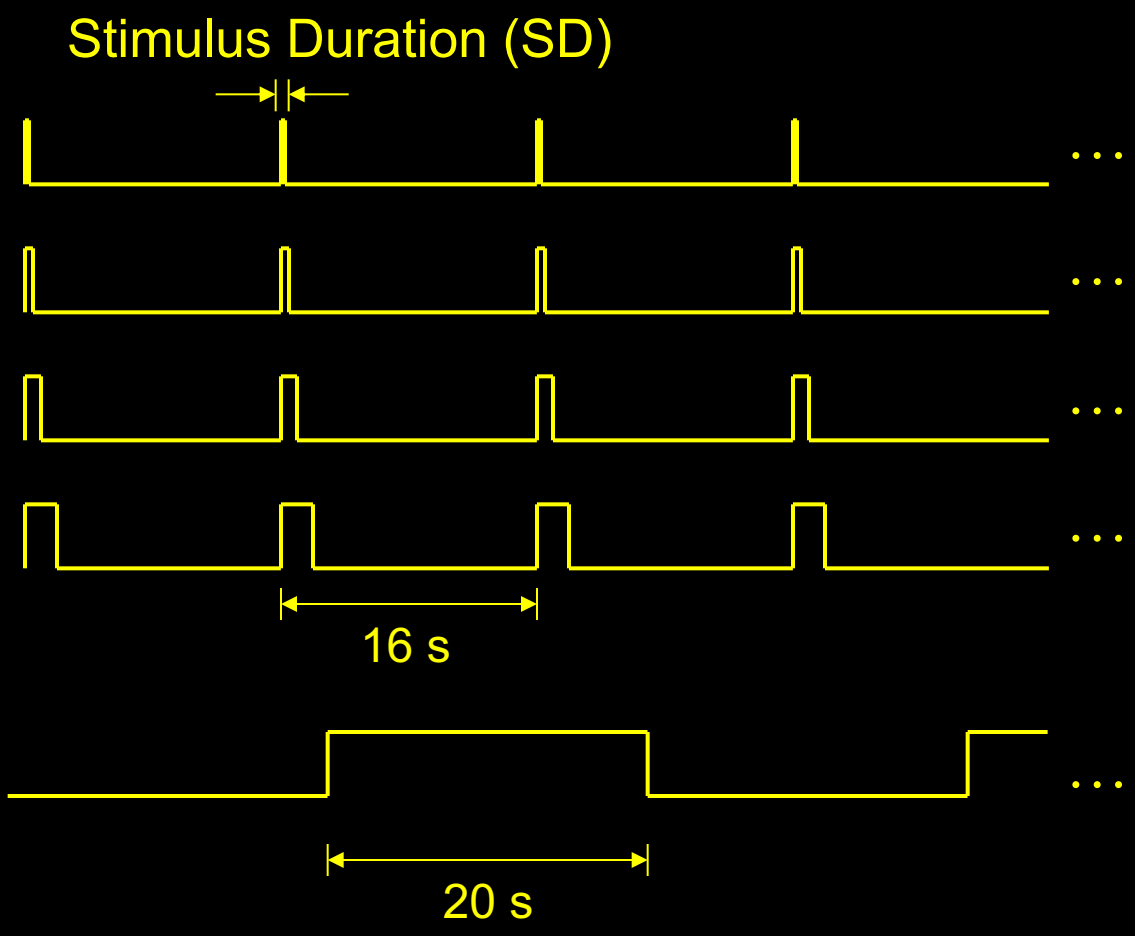
Short duration stimuli produce larger responses than expected

Source of the Nonlinearity

- Neuronal
- Hemodynamic
  - *Miller et al. 1998* – Flow is linear, BOLD is nonlinear
  - *Friston et al.* 2000 – hemodynamics can explain nonlinearity

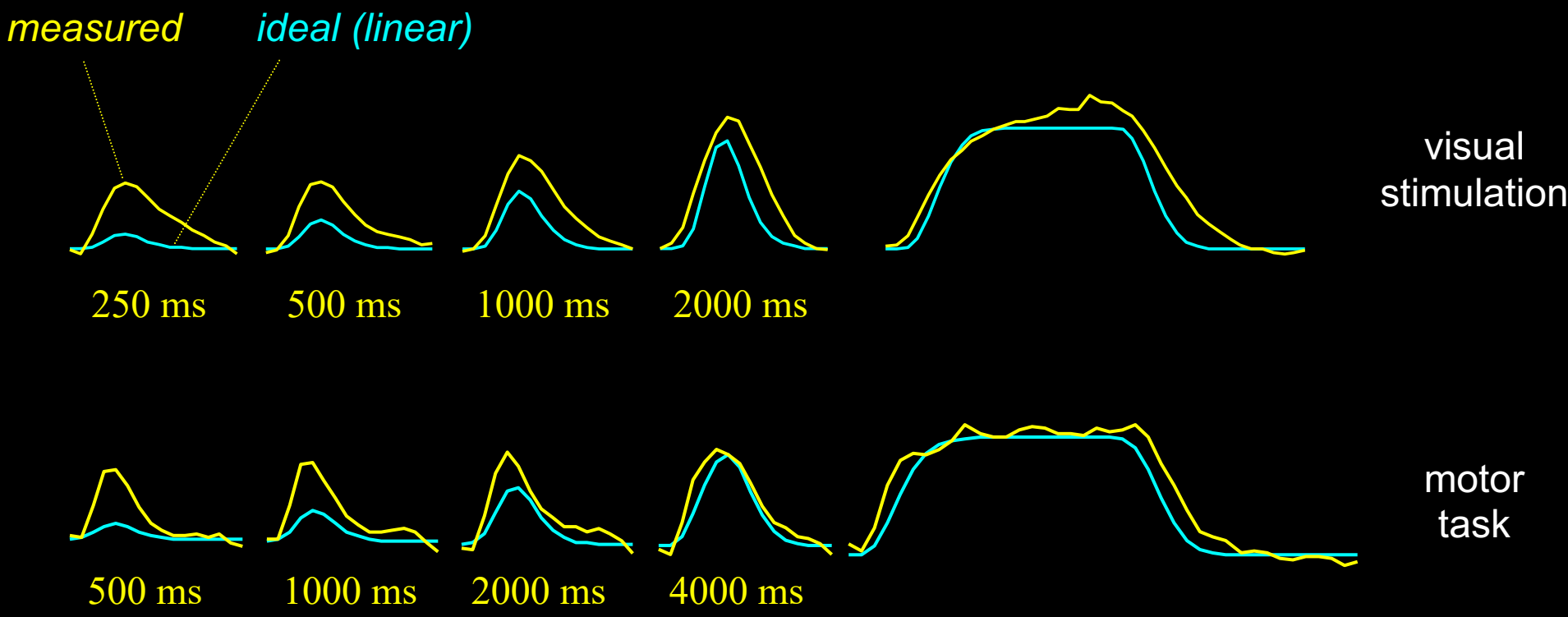
If nonlinearity is hemodynamic in origin, a measure of this nonlinearity will reflect any spatial variation of the vasculature

Methods



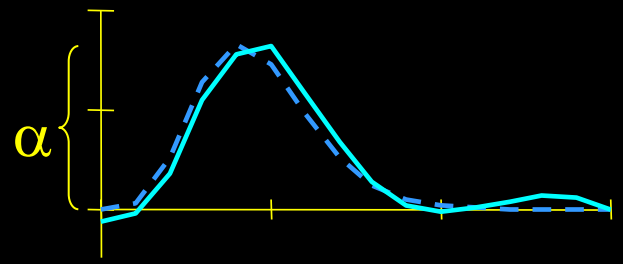
	Visual	*Motor*
···	SD = 250 ms	SD = 500 ms
···	SD = 500 ms	SD = 1000 ms
···	SD = 1000 ms	SD = 2000 ms
···	SD = 2000 ms	SD = 4000 ms
···	Blocked Trial	

Observed Responses



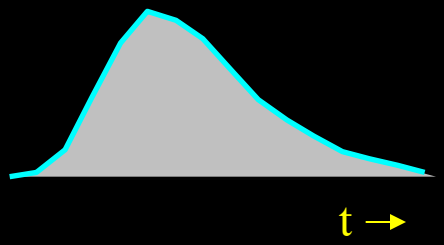
Compute nonlinearity *(for each voxel)*

- Amplitude of Response



Fit ideal (linear) to response

- Area under response / Stimulus Duration



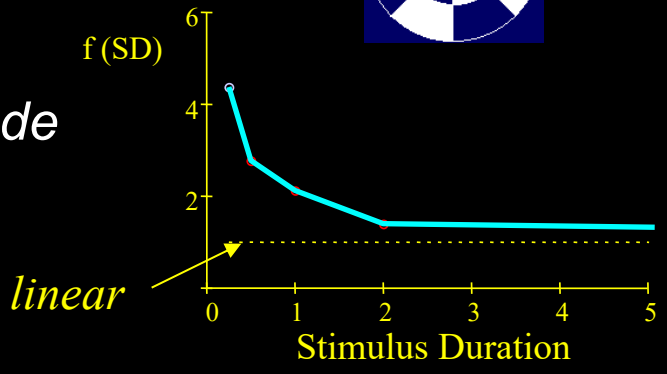
Output Area / Input Area

Nonlinearity

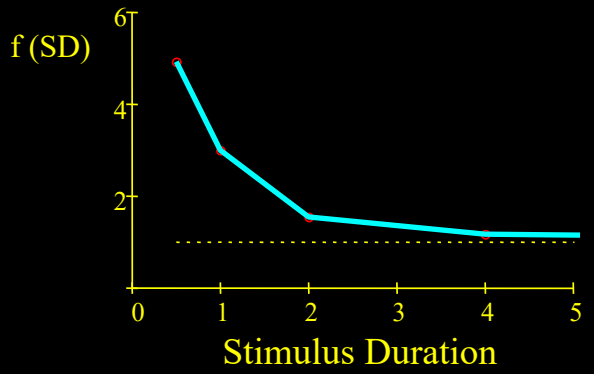
Visual

Motor

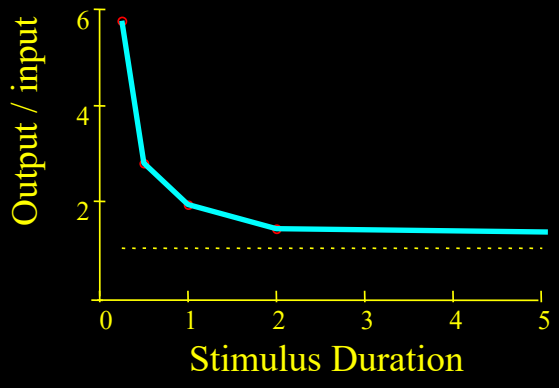
Magnitude

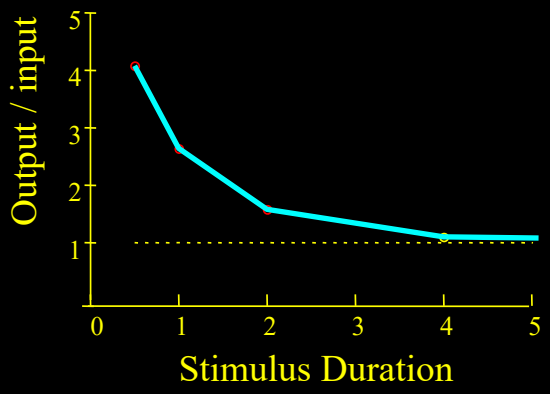


linear



Area



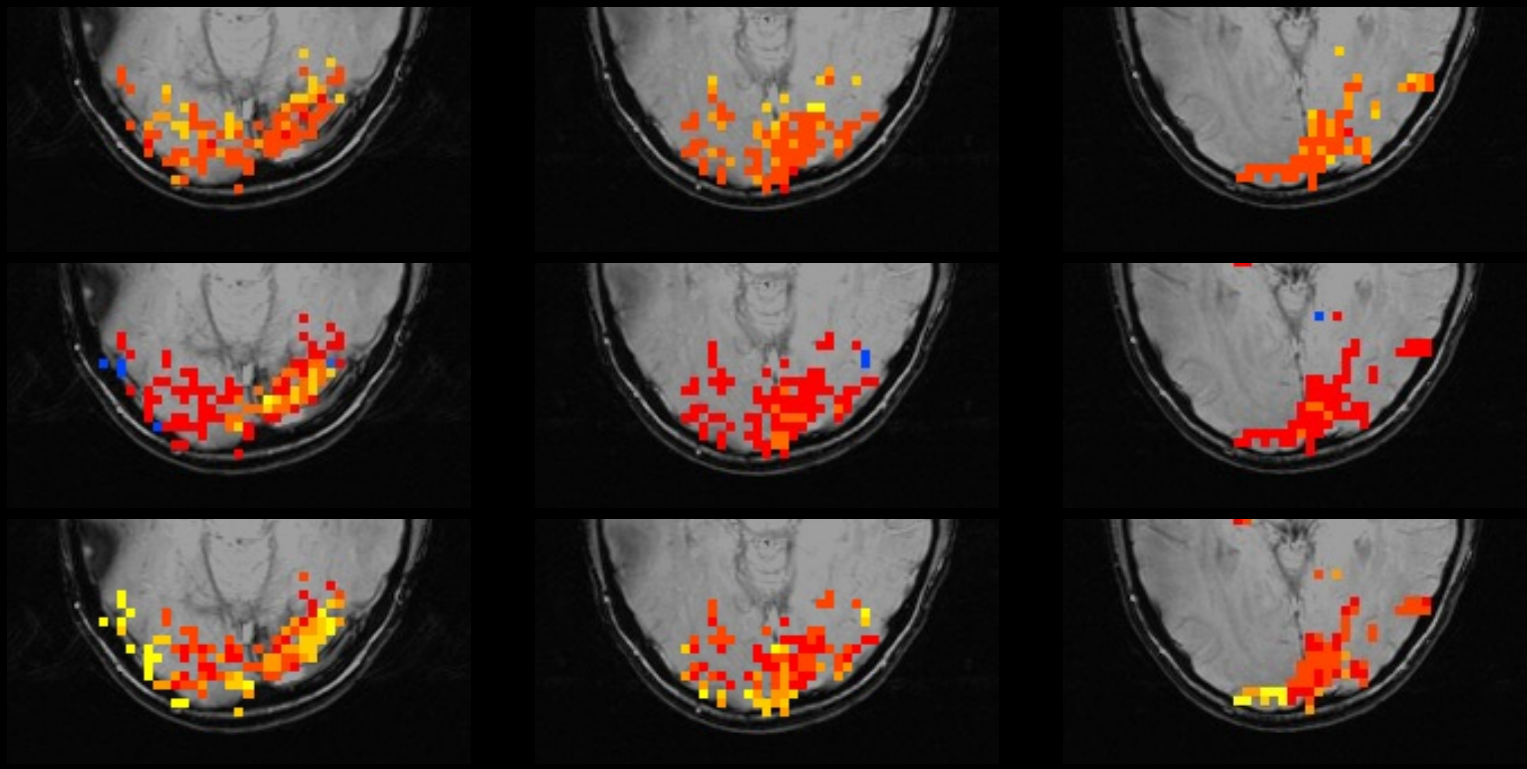


Results – visual task

Nonlinearity

Magnitude

Latency

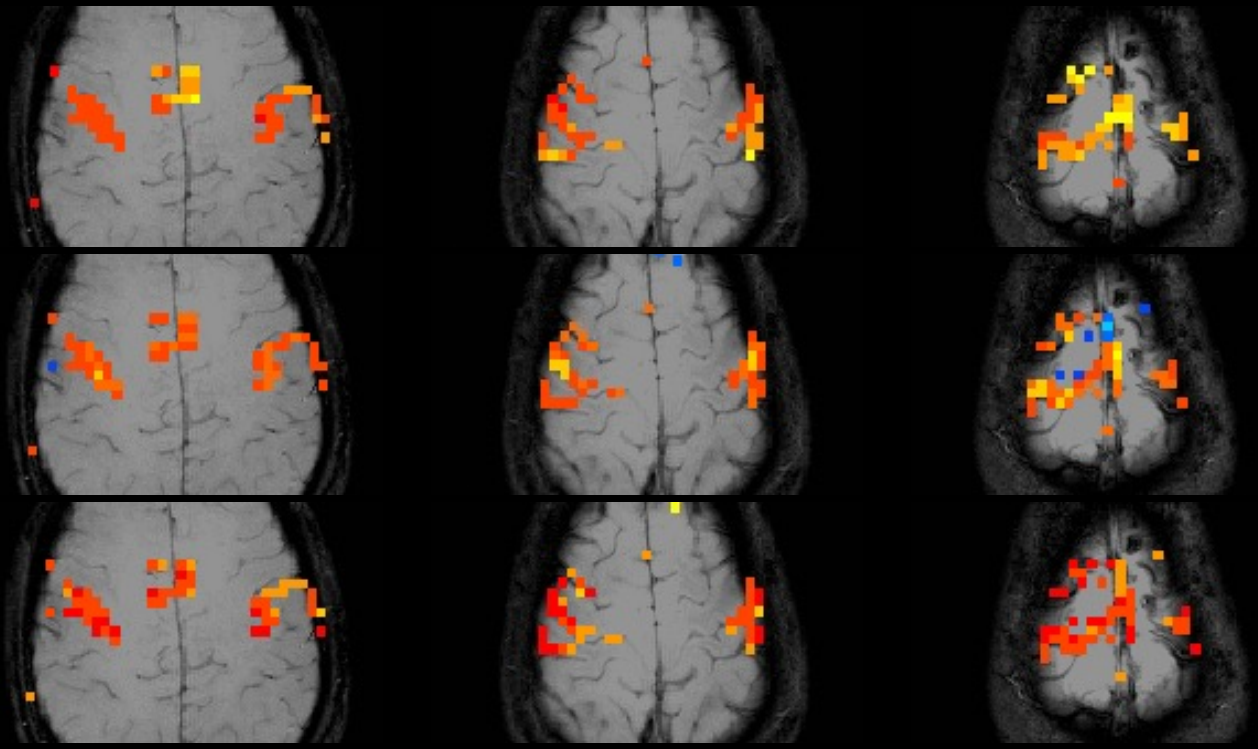


Results – motor task

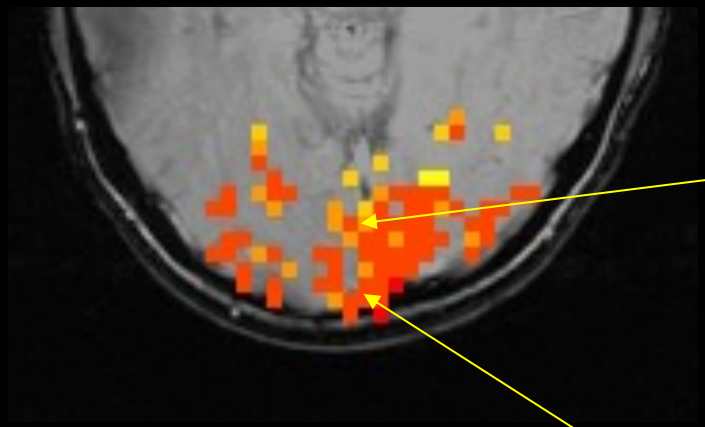
Nonlinearity

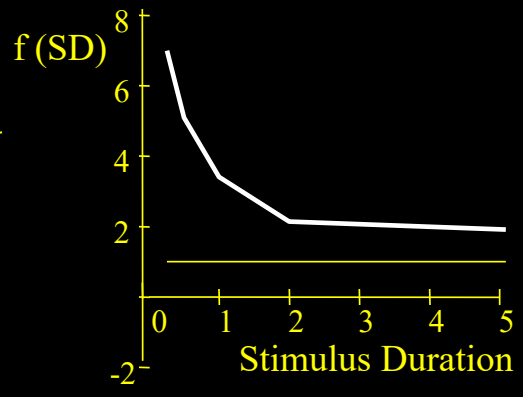
Magnitude

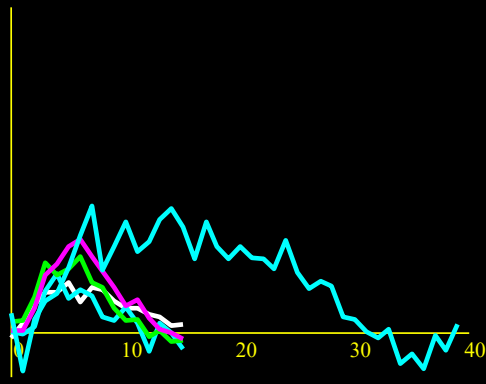
Latency

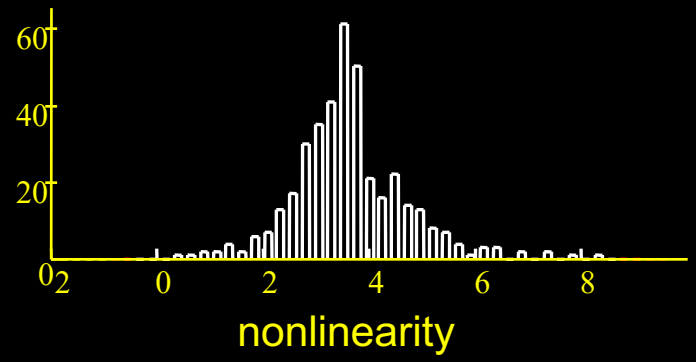


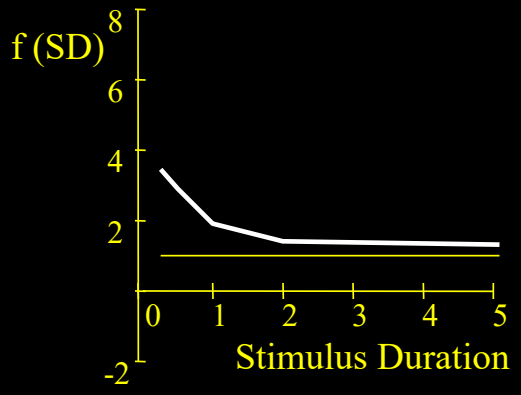
Results – visual task

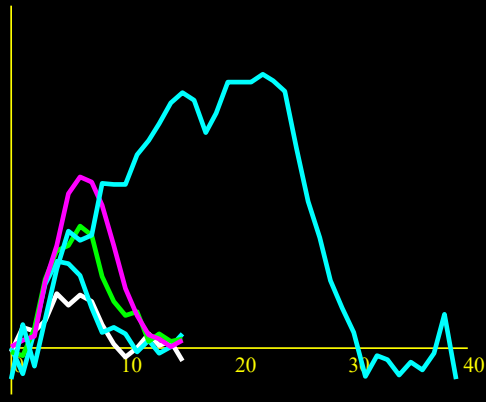




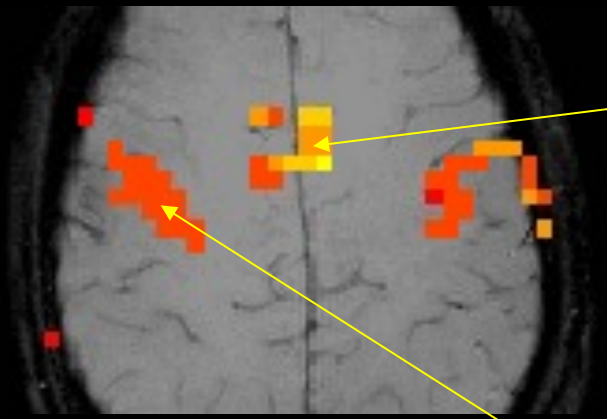


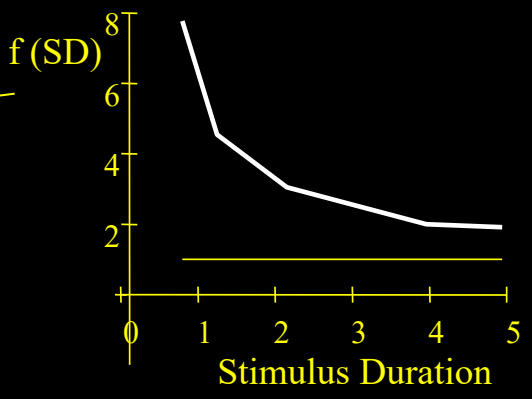


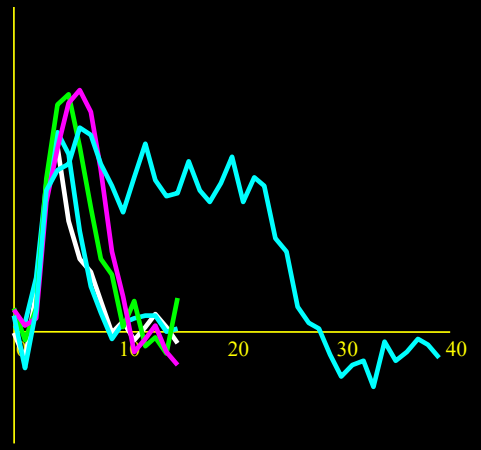


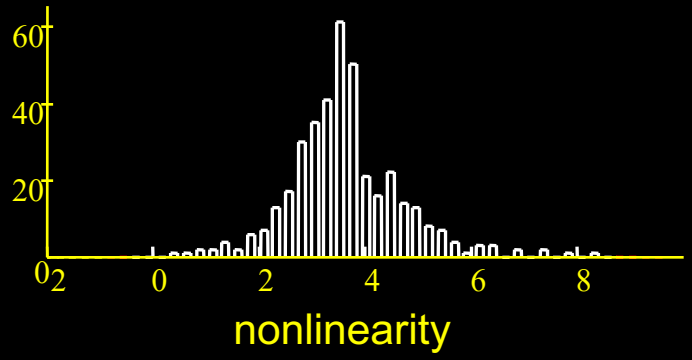


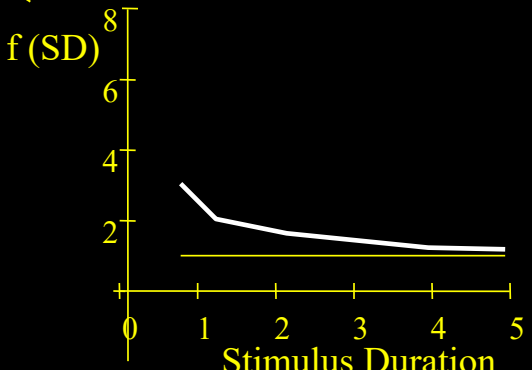
Results – motor task

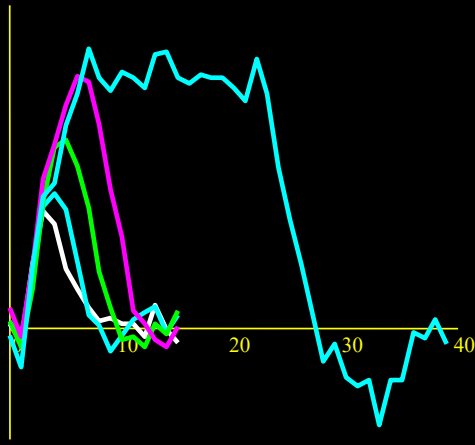






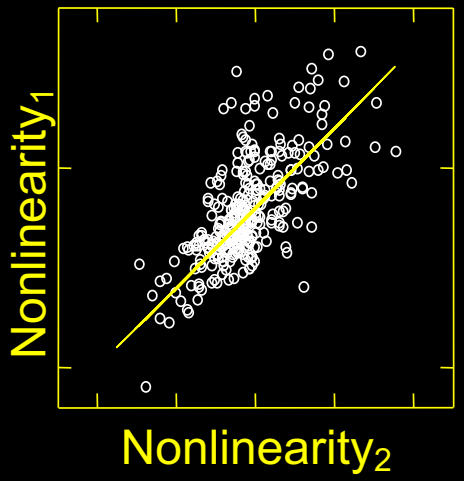




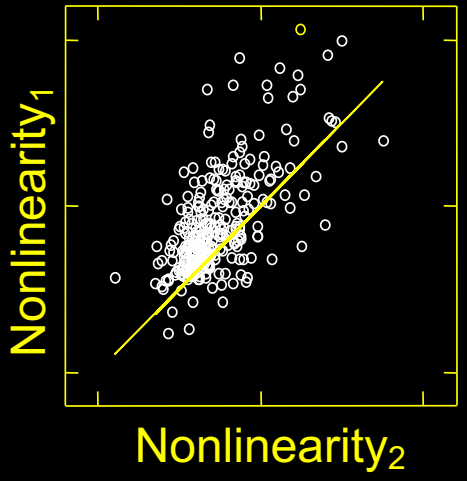


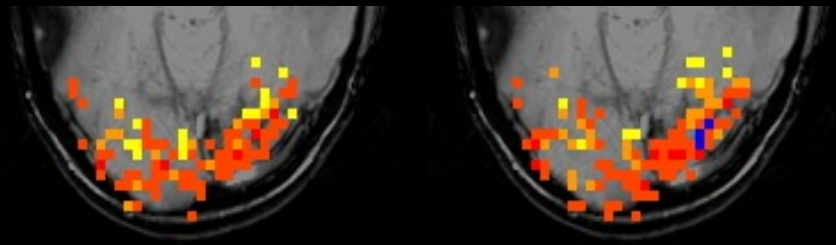
Reproducibility

Visual task

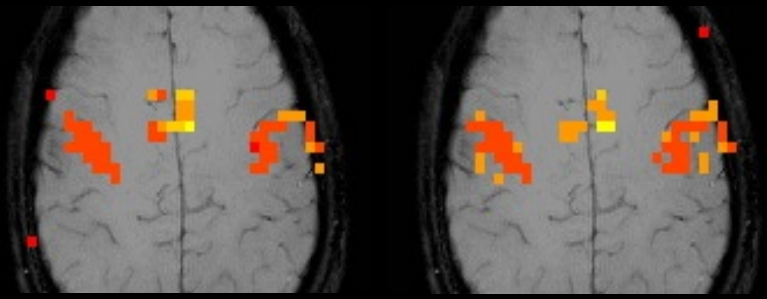


Motor task



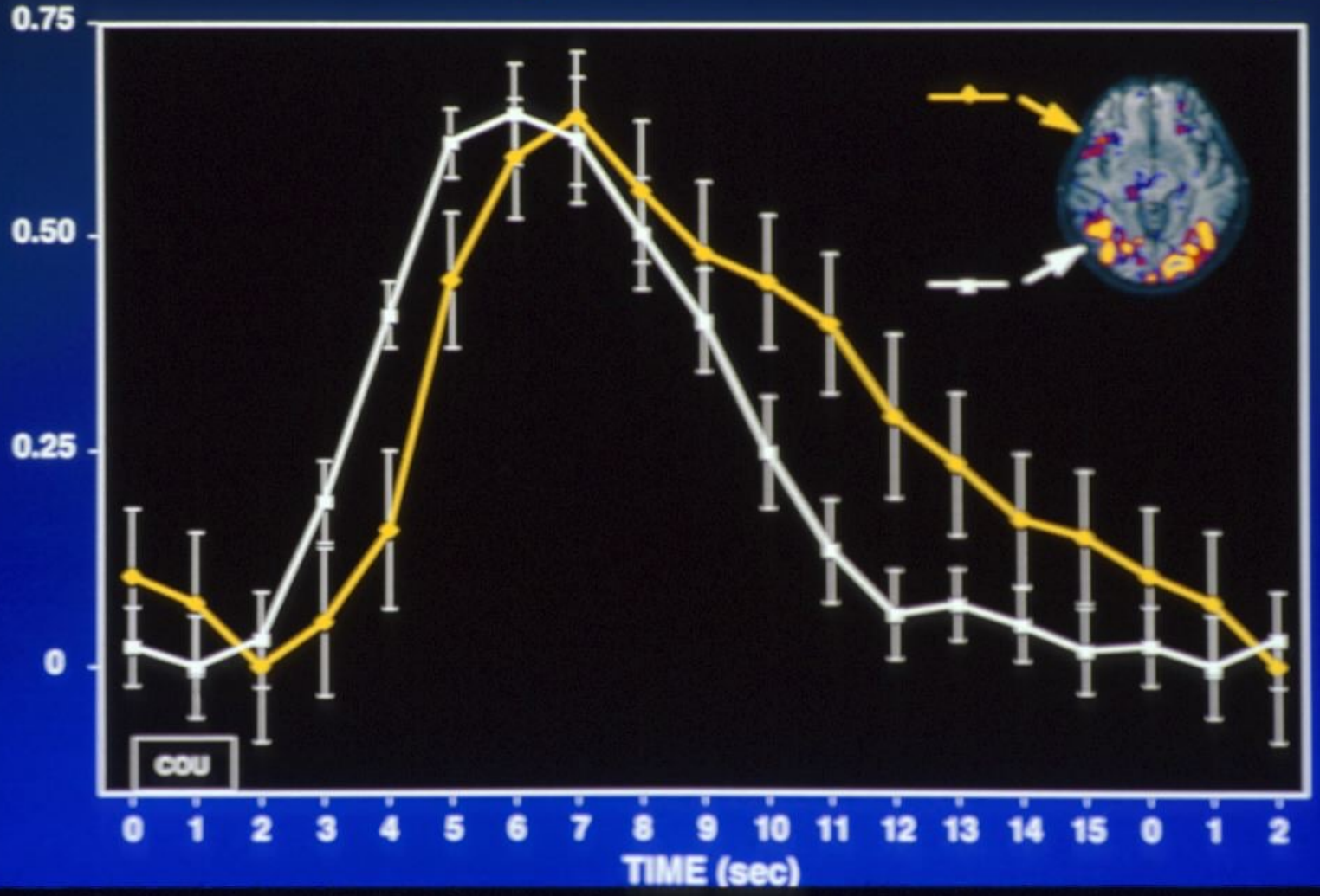


Experiment 1 Experiment 2



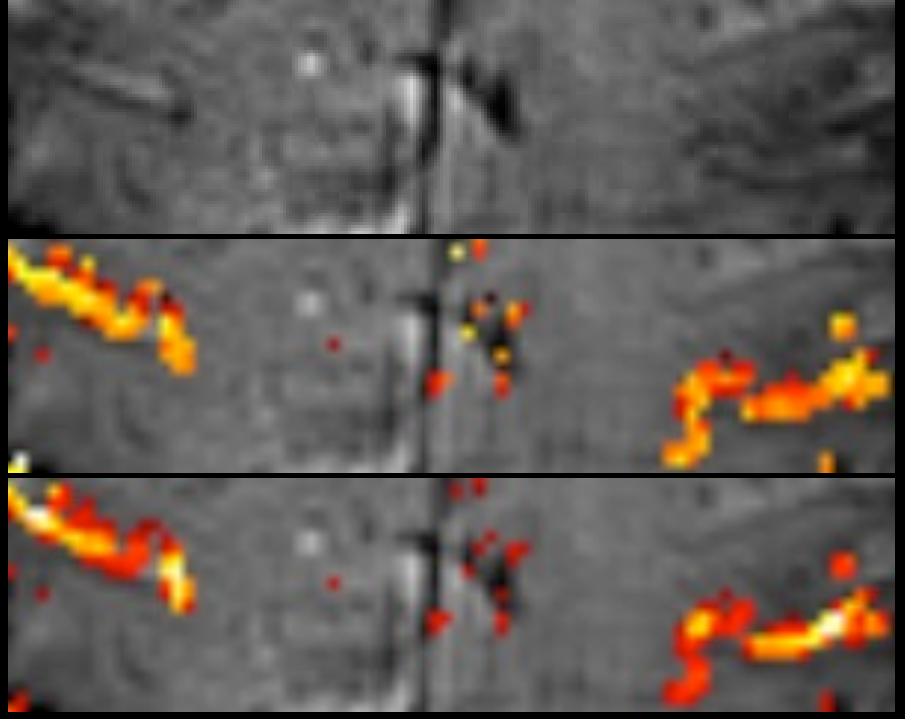
Experiment 1 Experiment 2

Time Course Comparison Across Brain Regions



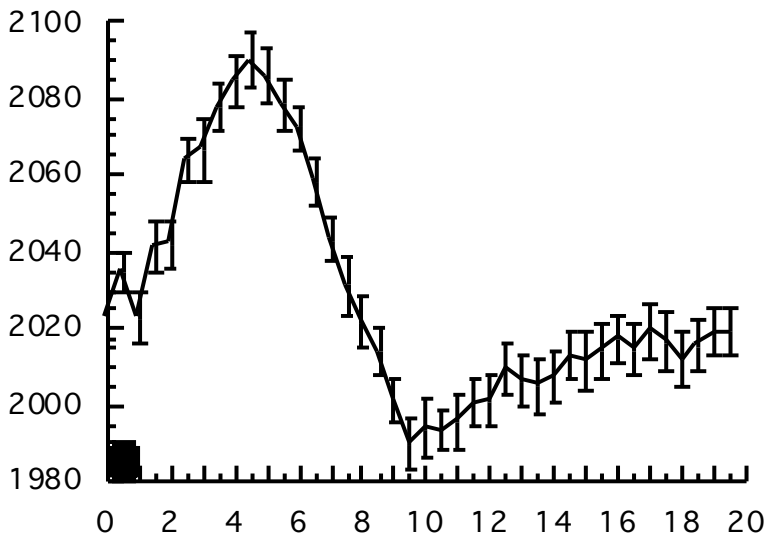
Latency

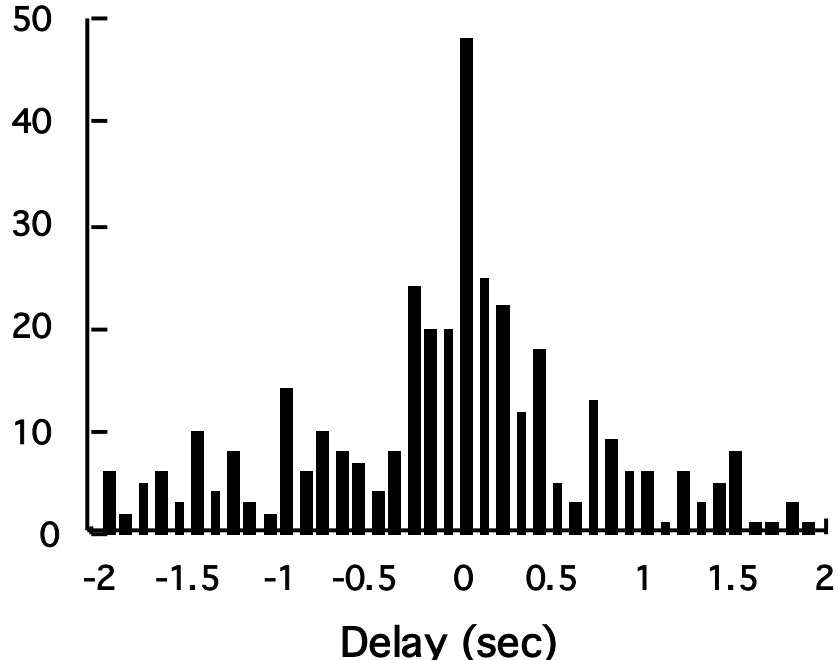
Magnitude



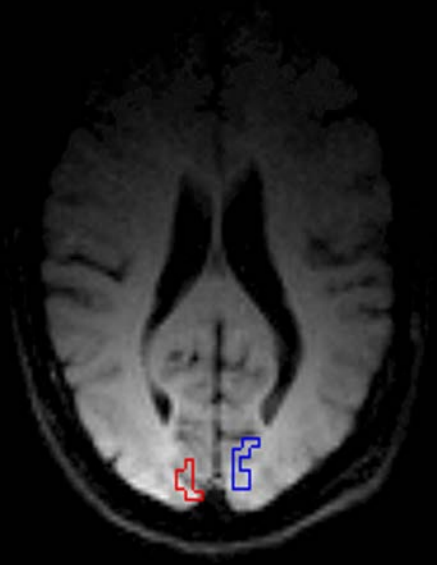
+ 2 sec

- 2 sec



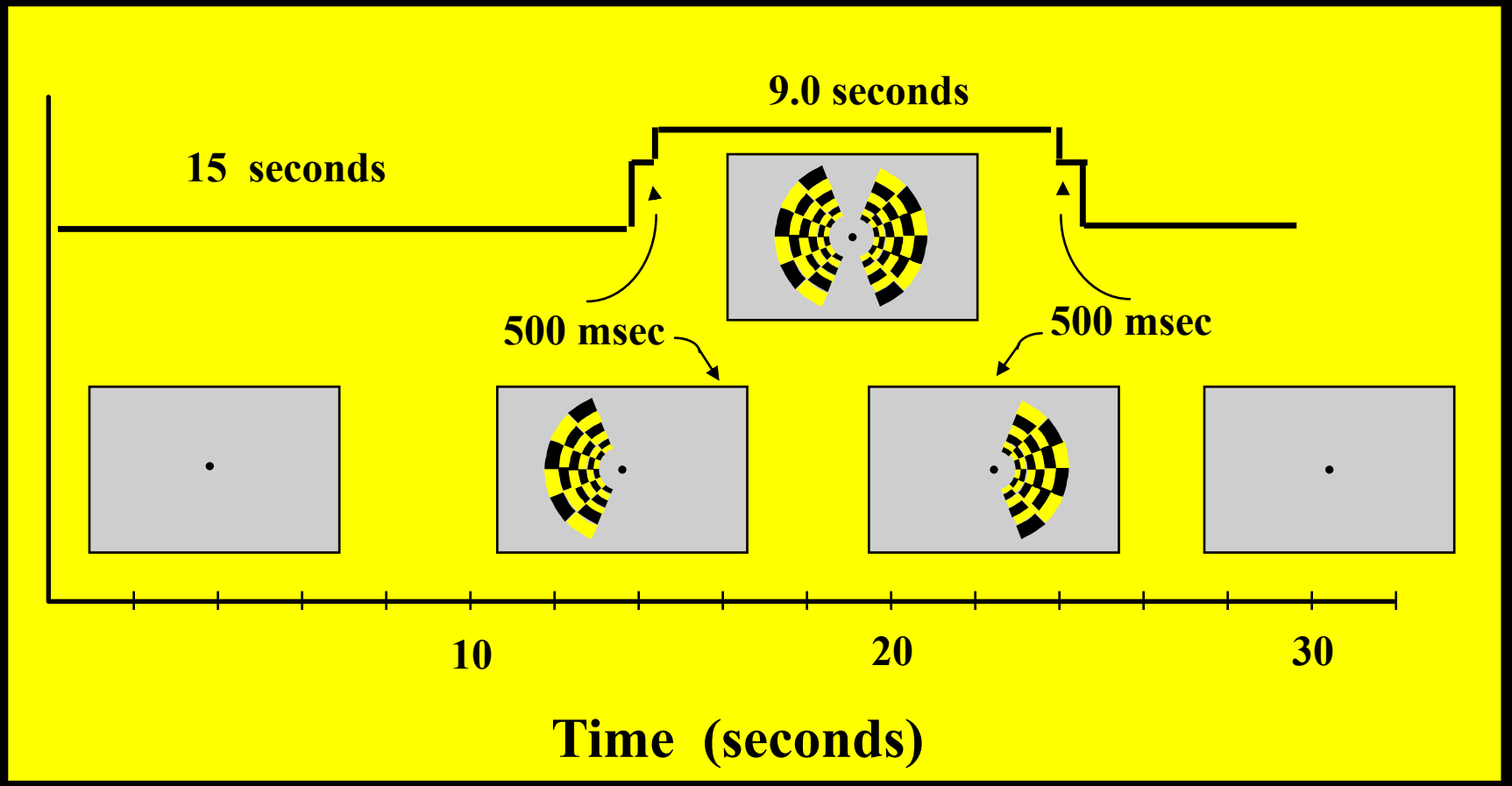


Regions of Interest Used for Hemi-Field Experiment

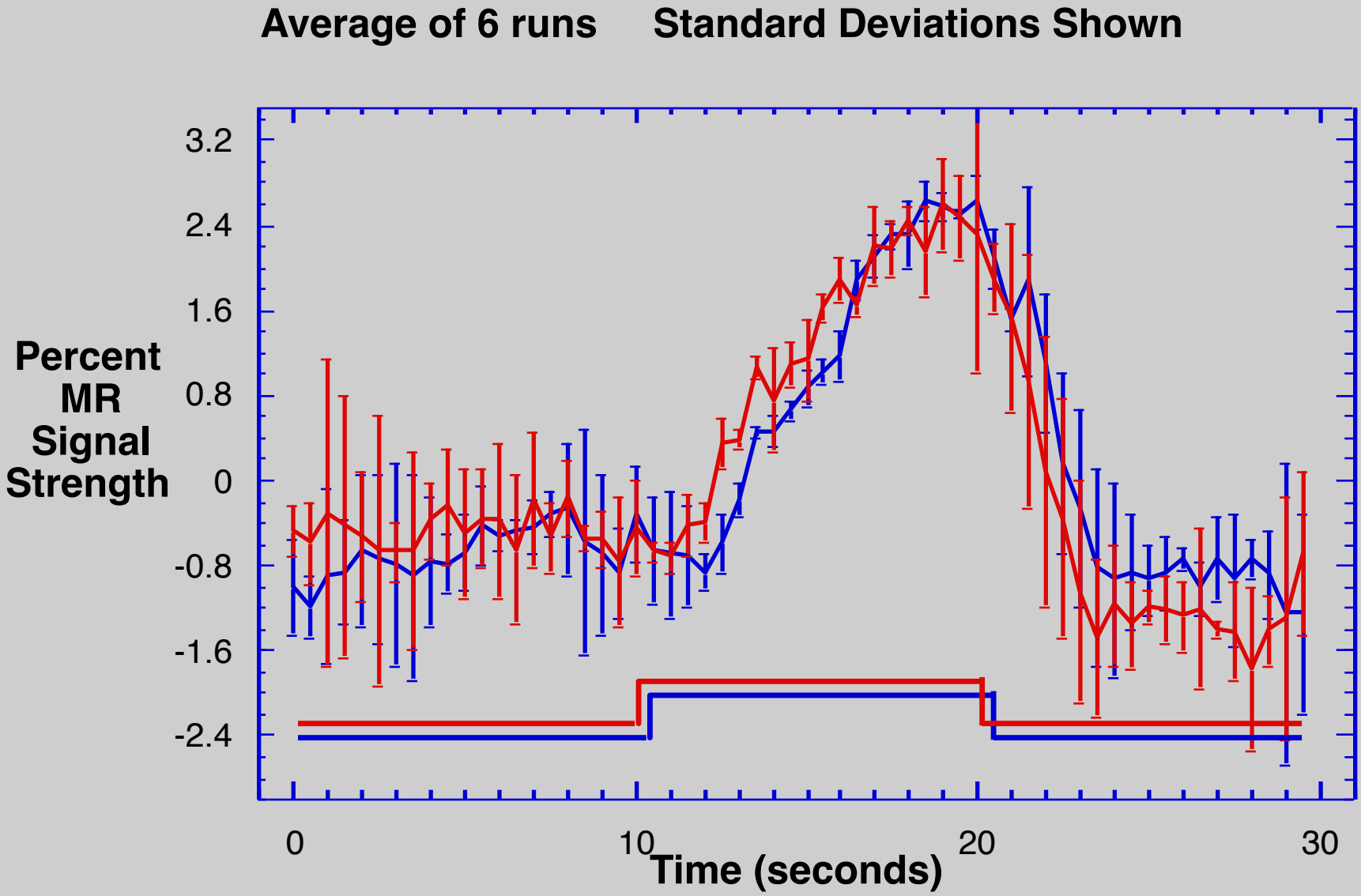


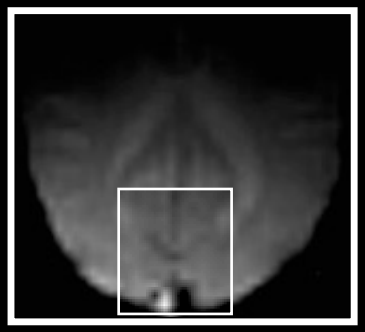
Right Hemisphere

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

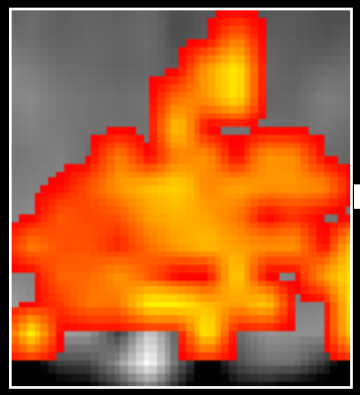
Right Hemifield

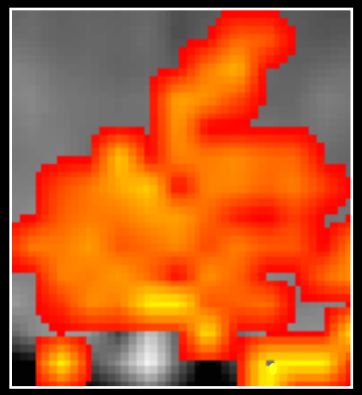
Left Hemifield

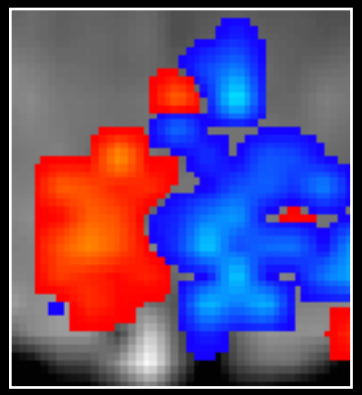
+ 2.5 s

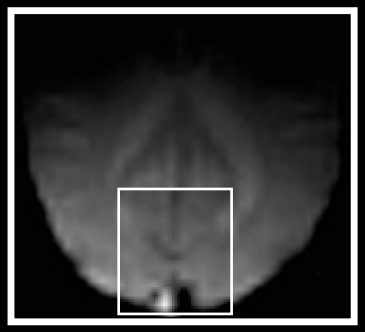
0 s

- 2.5 s





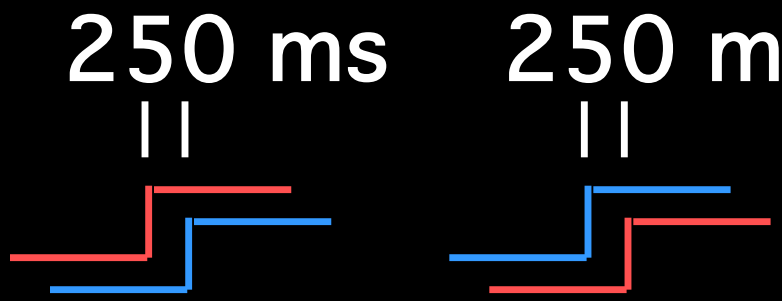




250 ms 250 ms

Right Hemifield

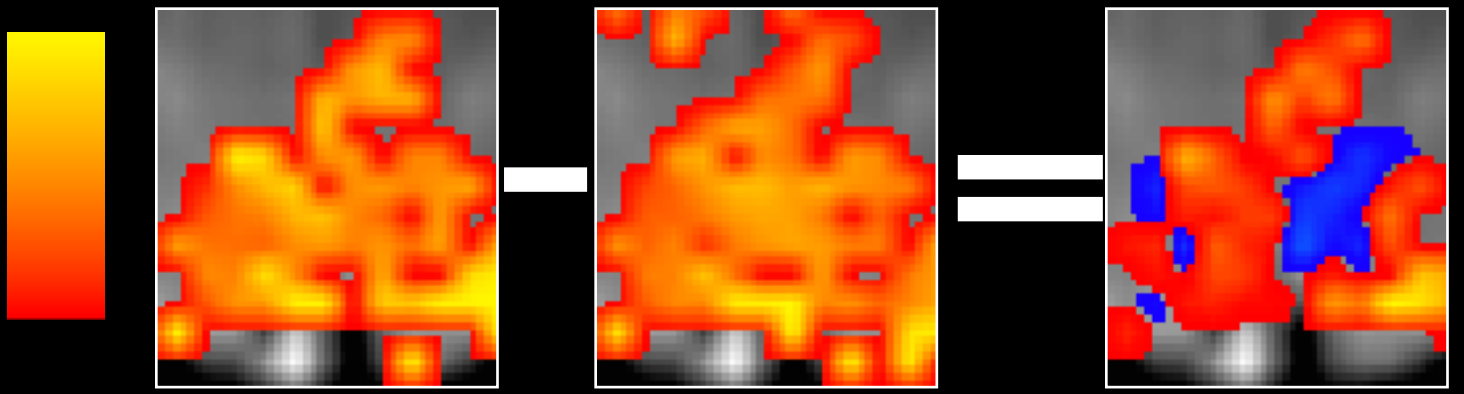
Left Hemifield



+ 2.5 s

0 s

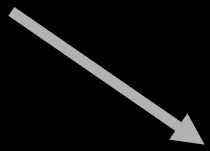
- 2.5 s



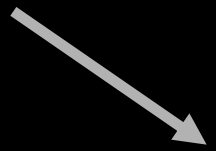
What is “in” the data?

Neuronal Activation

1. Task Related & Time Locked
2. Task Related & Not Time Locked
3. Not Task Related



Hemodynamics



Cardiac Pulsation
Respiration
Motion

MRI Signal Changes

Motion

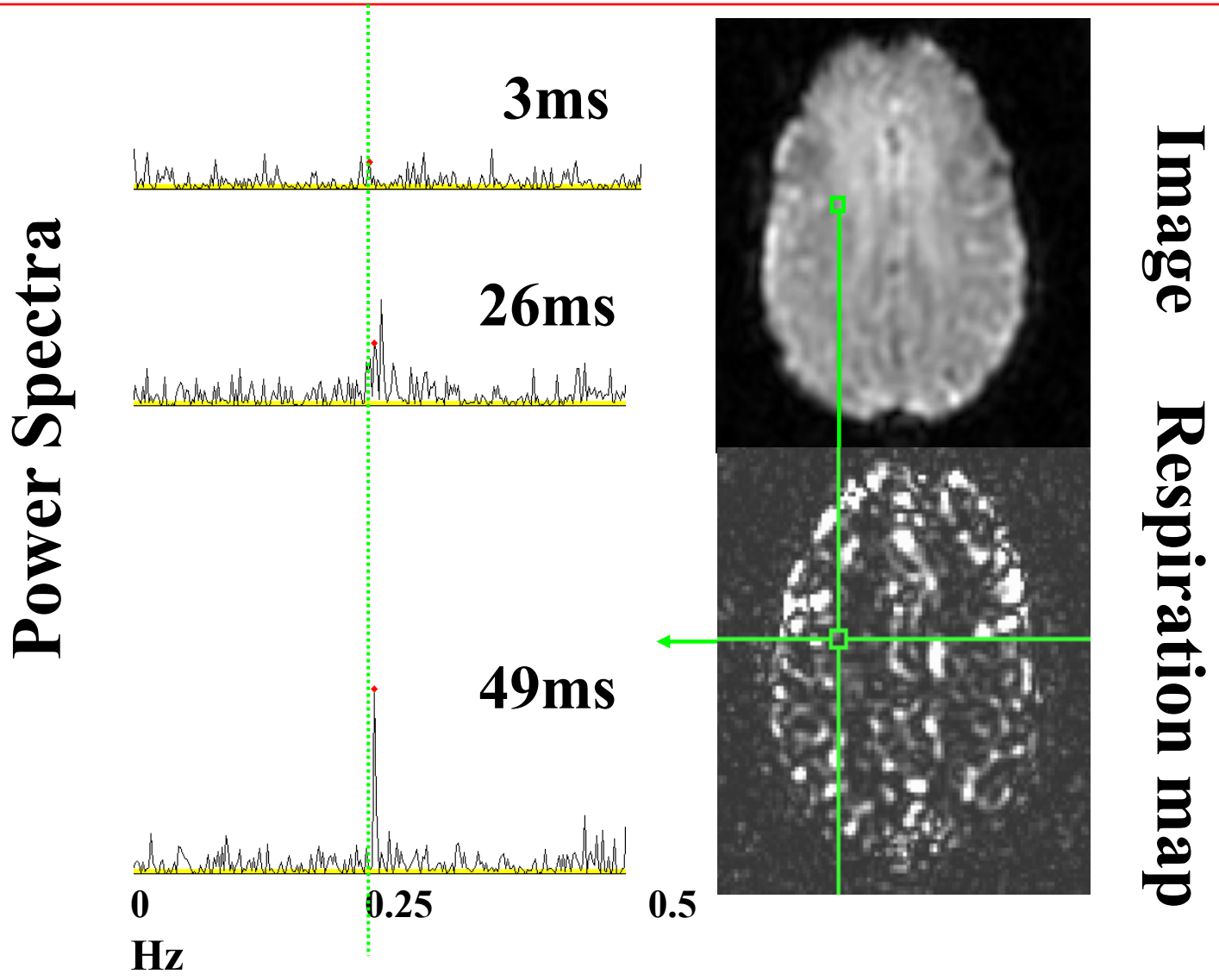
Recognize?
- Edge effects
- Shorter signal change latencies
- Unusually high signal changes
- External measuring devices

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

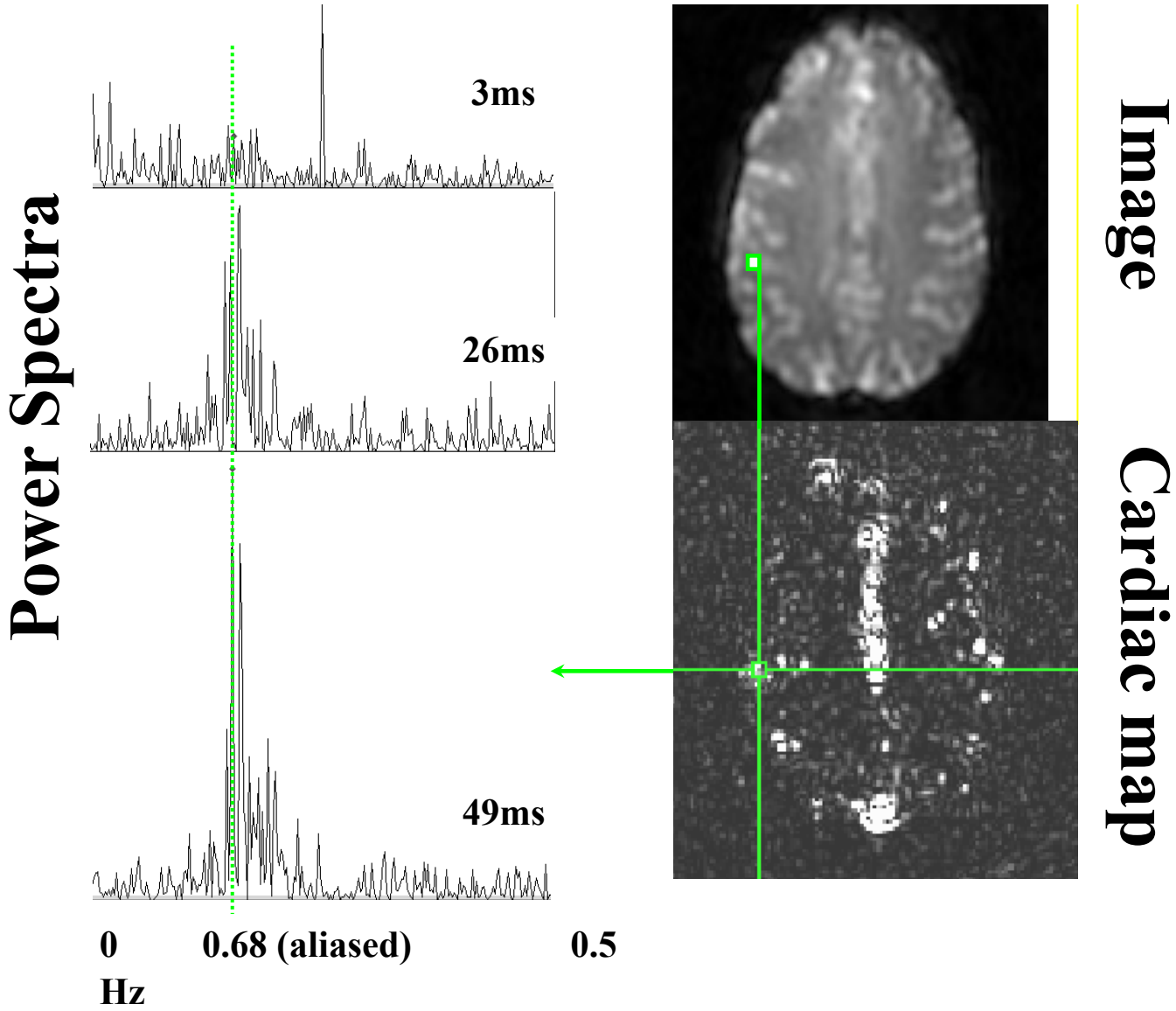
Bypass?
- Paradigm timing strategies..
- Gating (with T1-correction)

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

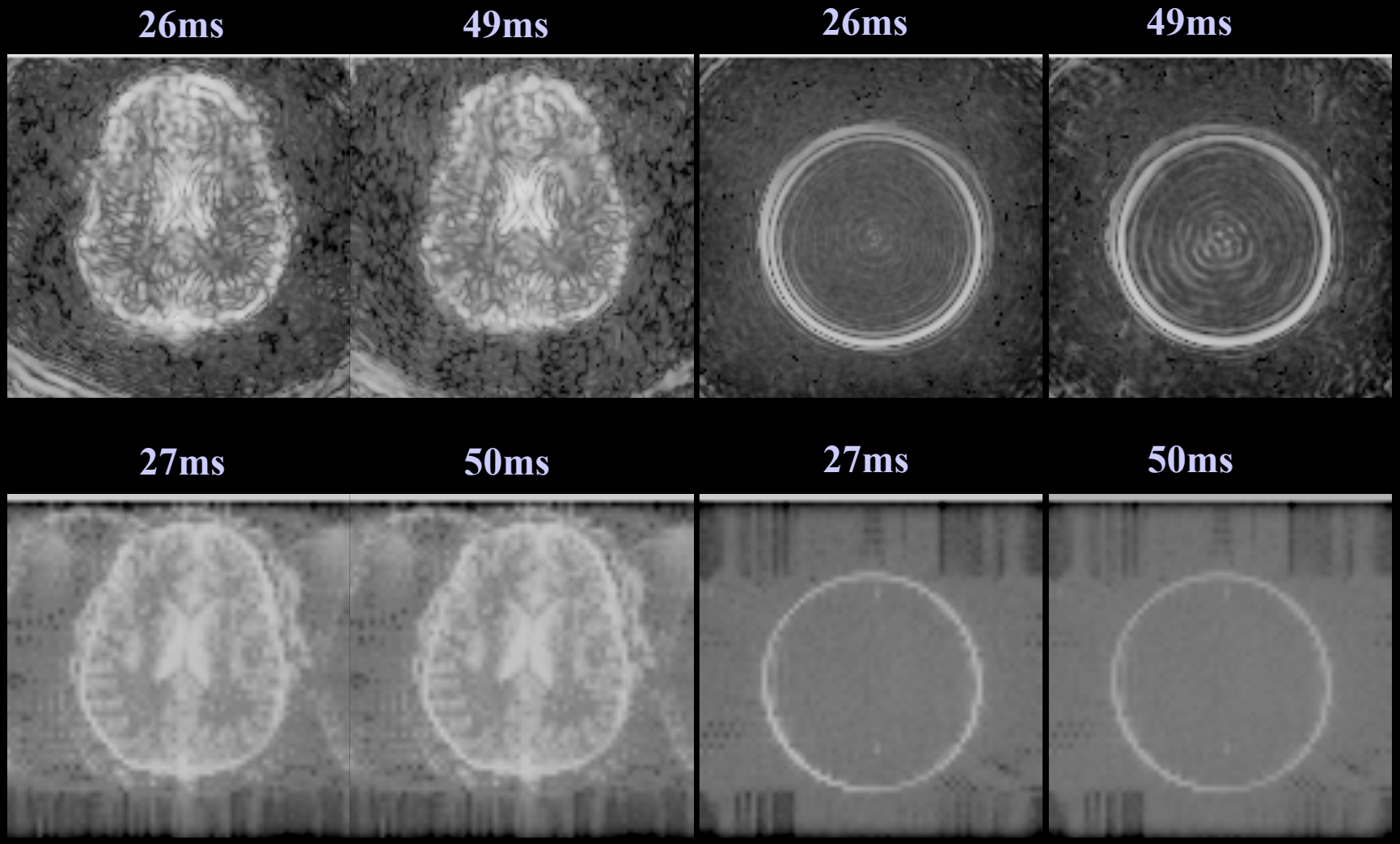
0.25 Hz Breathing at 1.5T



0.68 Hz Cardiac rate at 3T

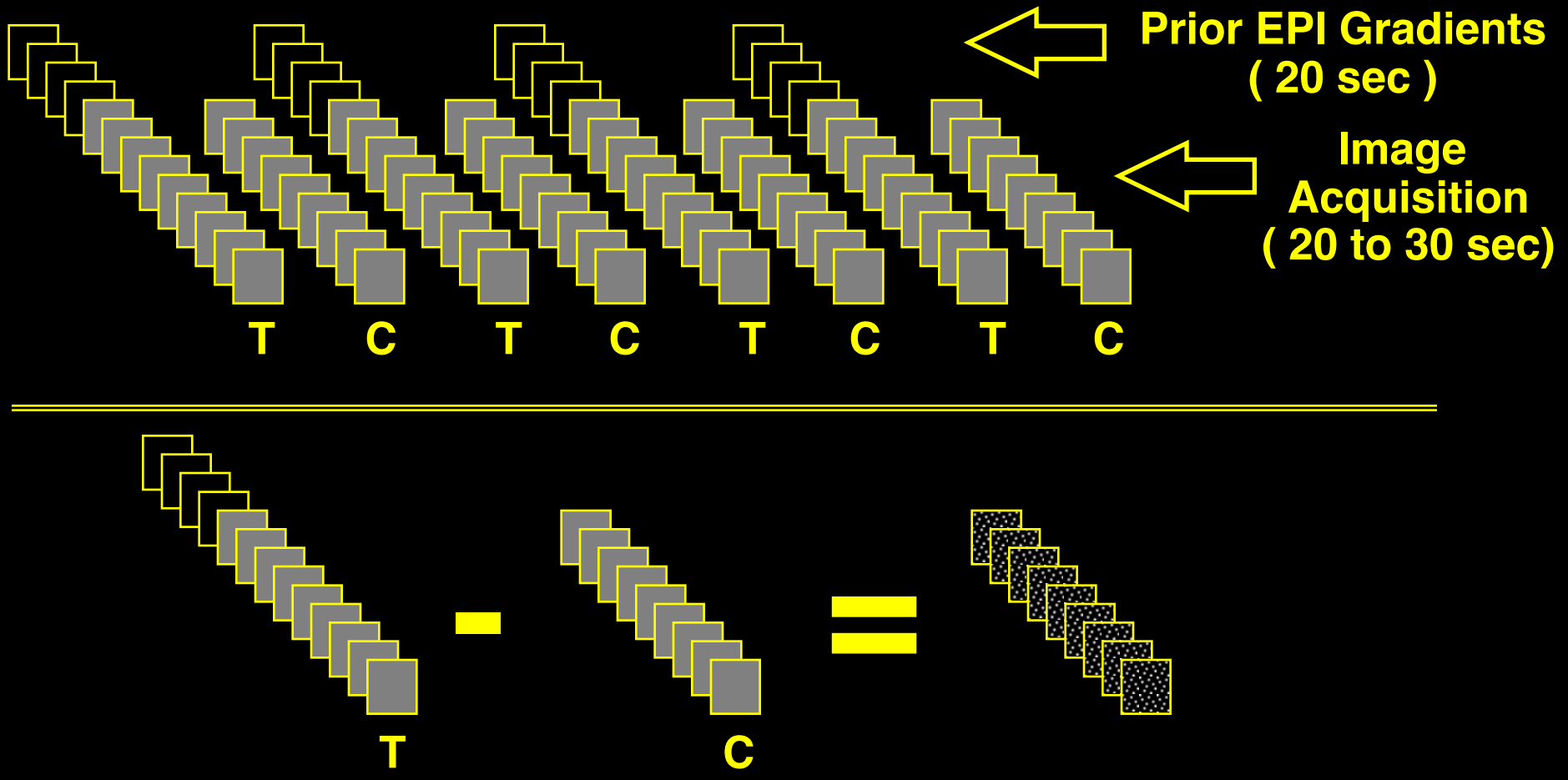


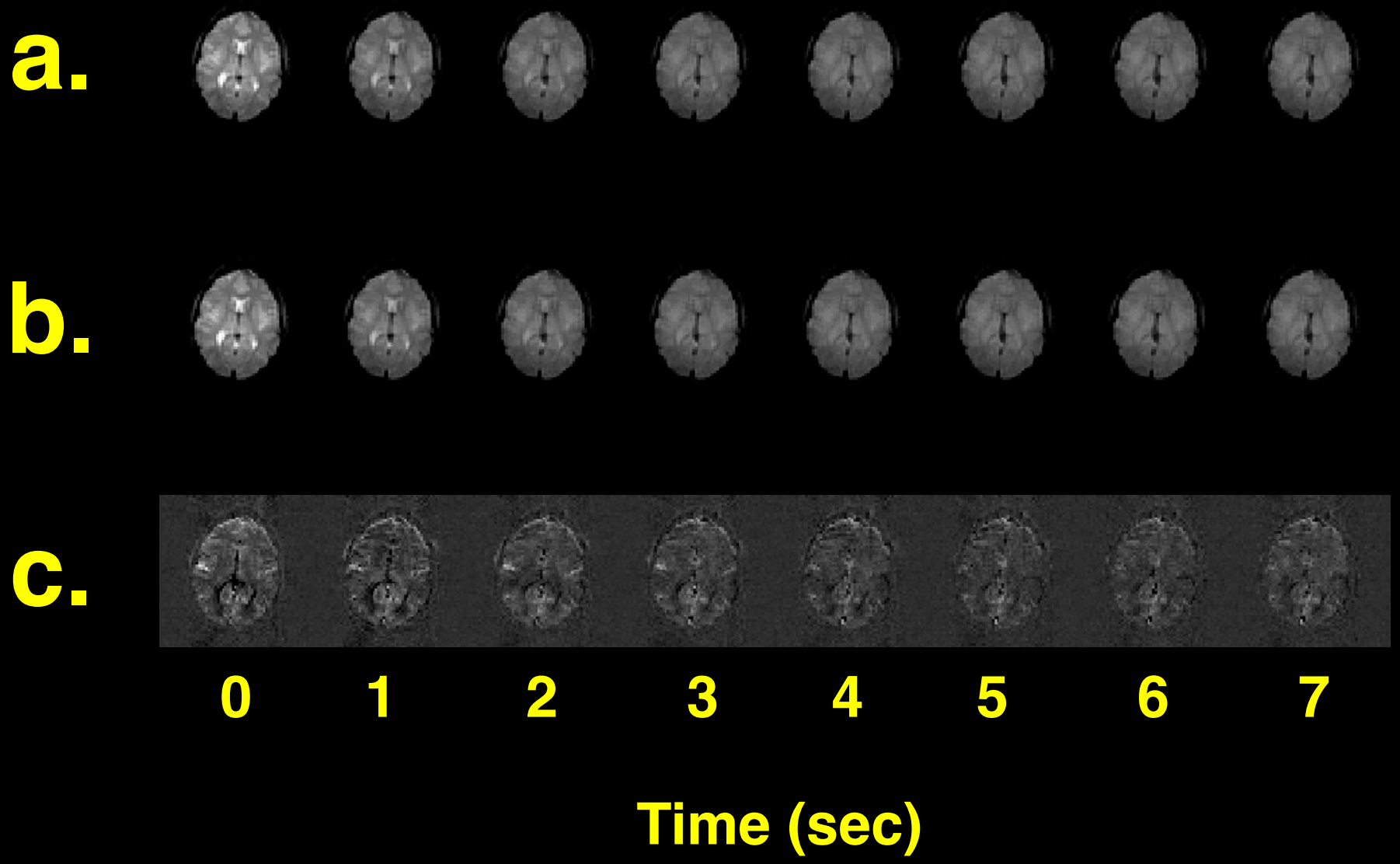
Temporal vs. Spatial SNR- 3T

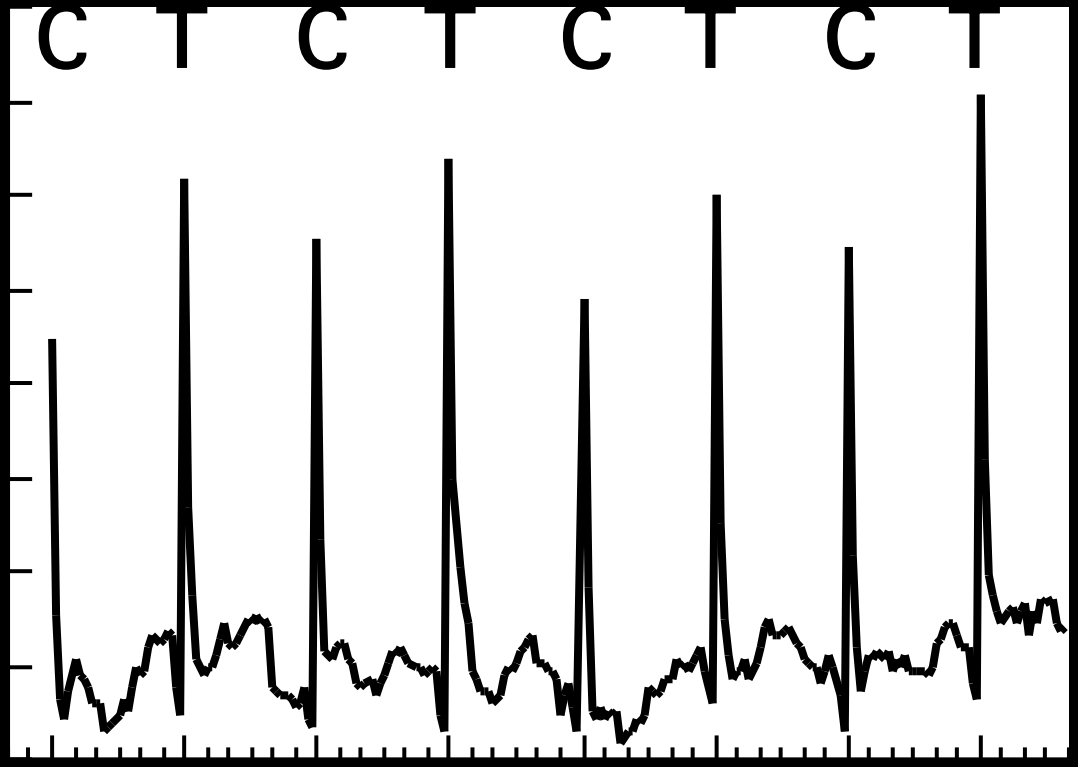


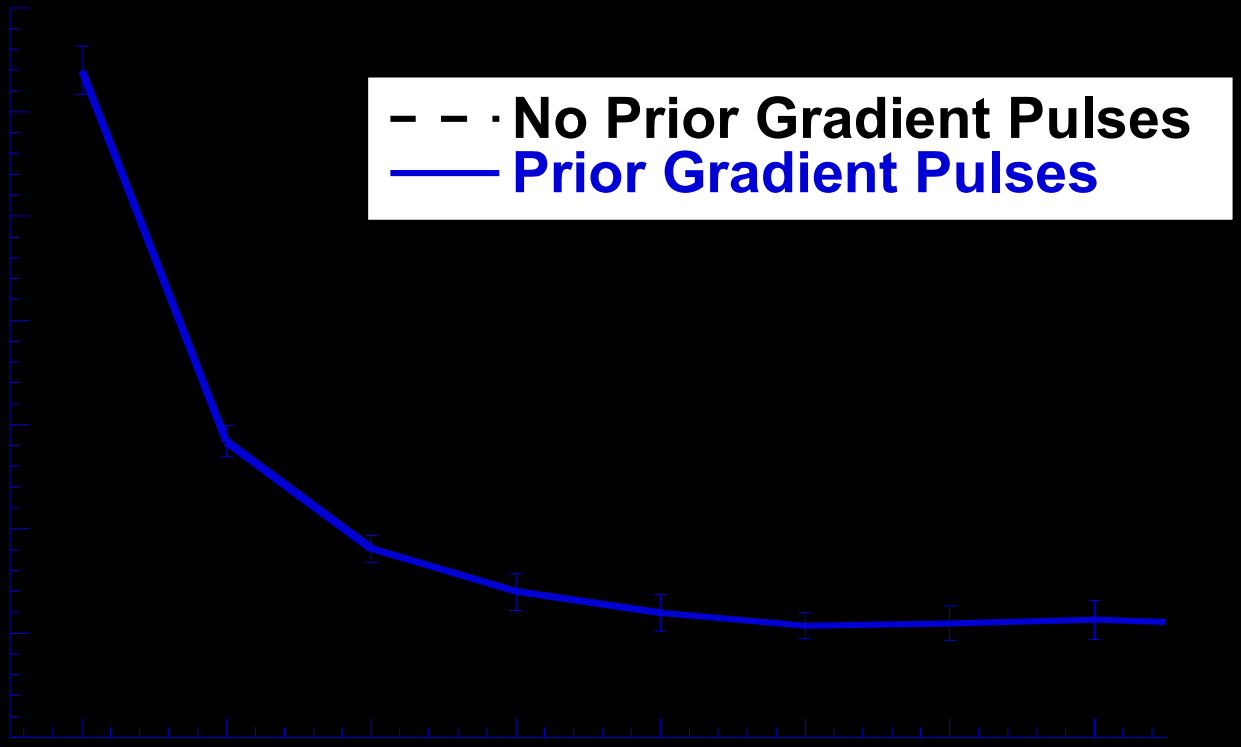
Another artifact...

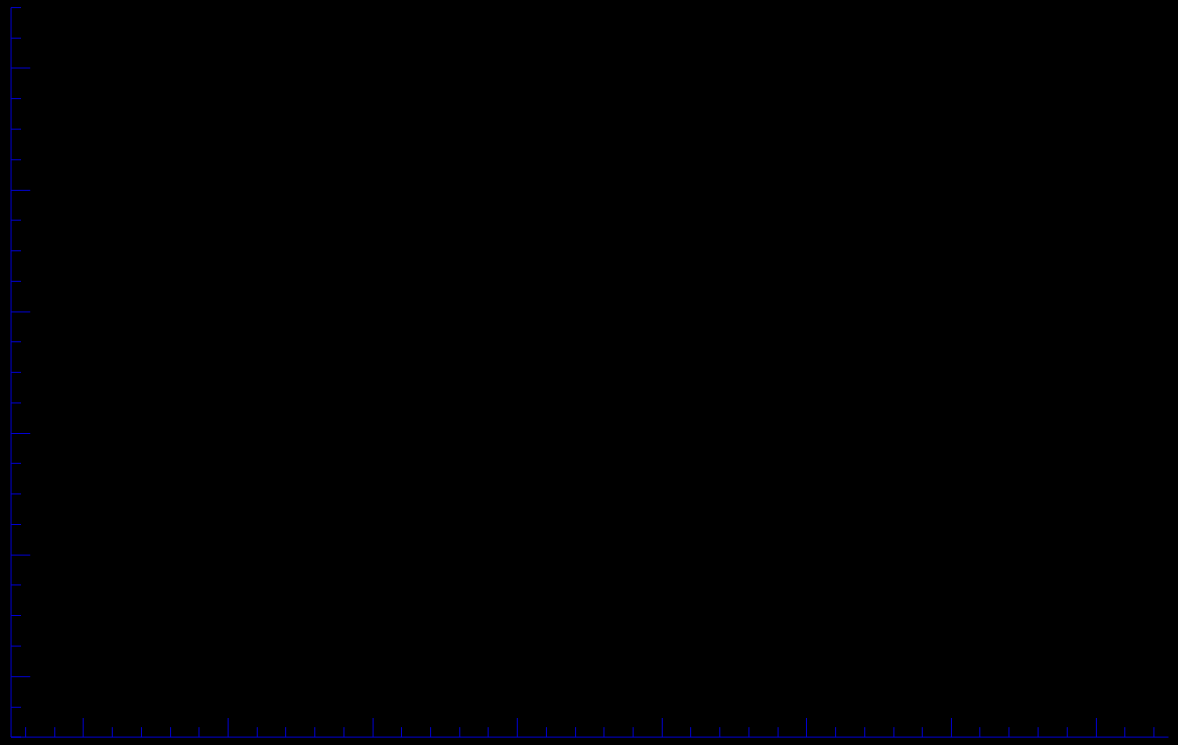
Auditory Activation by the Scanner...

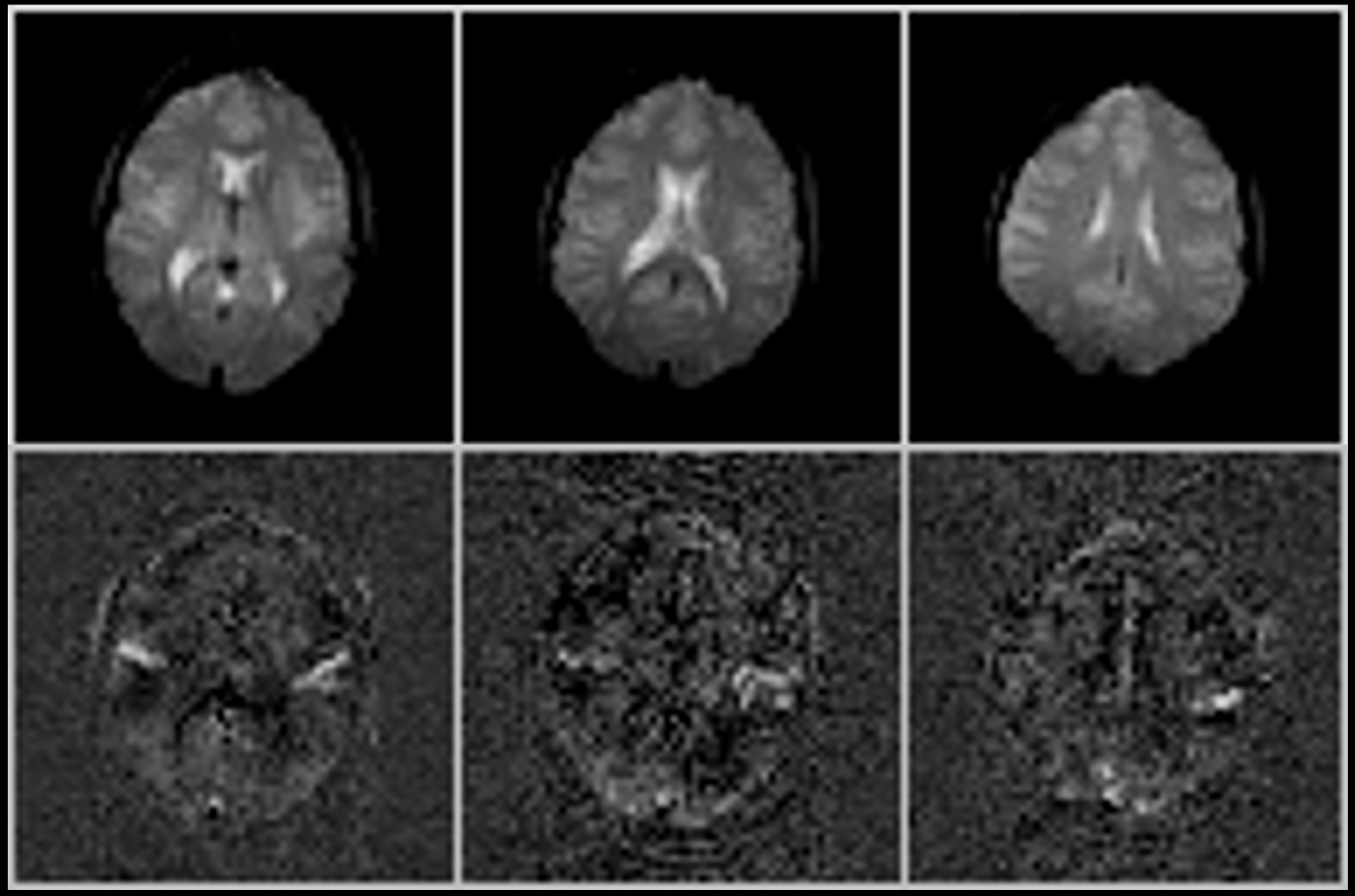

Prior EPI Gradients
(20 sec)
Image
Acquisition
(20 to 30 sec)
T
C
T
C
T
C
T
C
T
C
Average Time Series
Difference Time Series


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


C T C T C T C T


No Prior Gradient Pulses
Prior Gradient Pulses





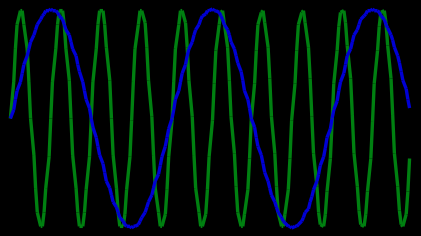
How to deal with Scanner Noise?

- Clustered volume acquisition
  Talavage et al.
- Silent sequences

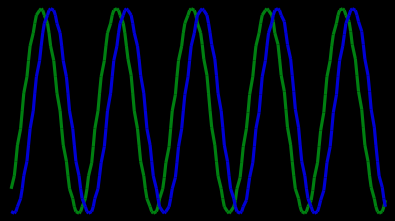
Neuronal Activation Input Strategies

1. Block Design

2. Frequency Encoding

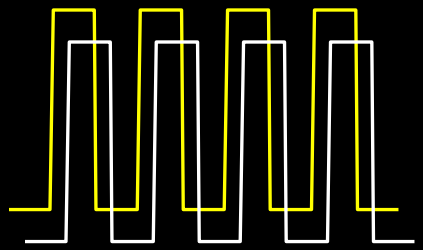


3. Phase Encoding

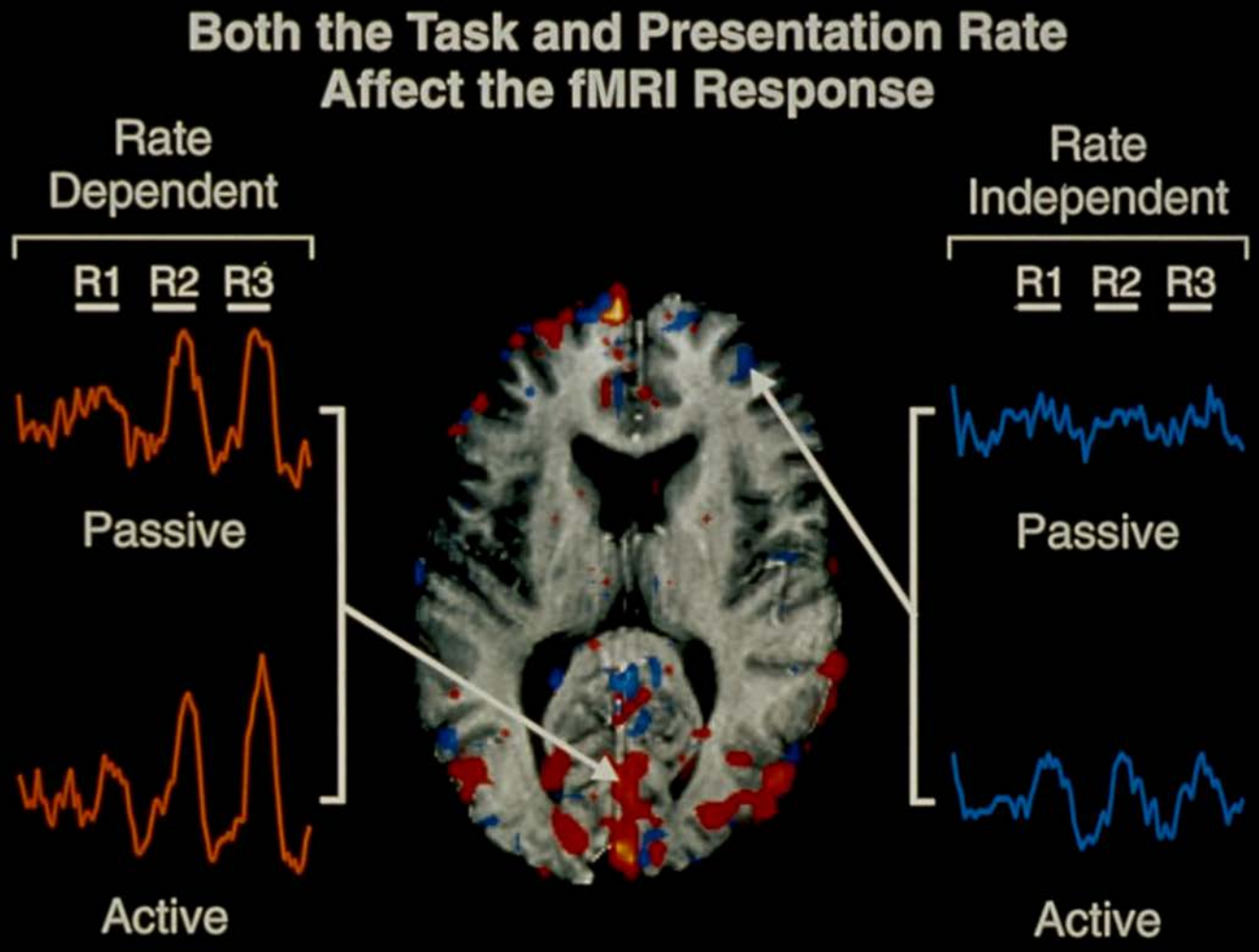


4. Single Event

5. Orthogonal Block Design



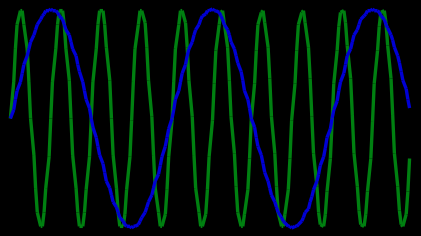
6. Free behavior Design.


Both the Task and Presentation Rate
Affect the fMRI Response
Rate
Dependent
R1 R2 R3
Passive
Active
Rate
Independent
R1 R2 R3
Passive
Active

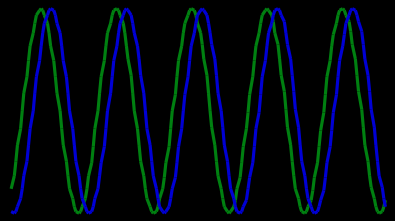
DeYoe et al.

Neuronal Activation Input Strategies

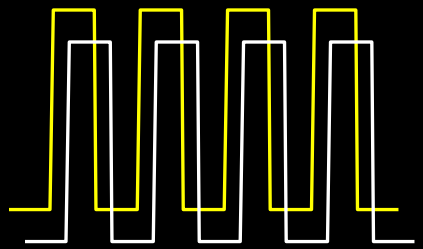
1. Block Design
2. Frequency Encoding



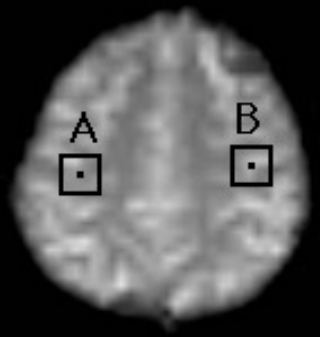
3. Phase Encoding

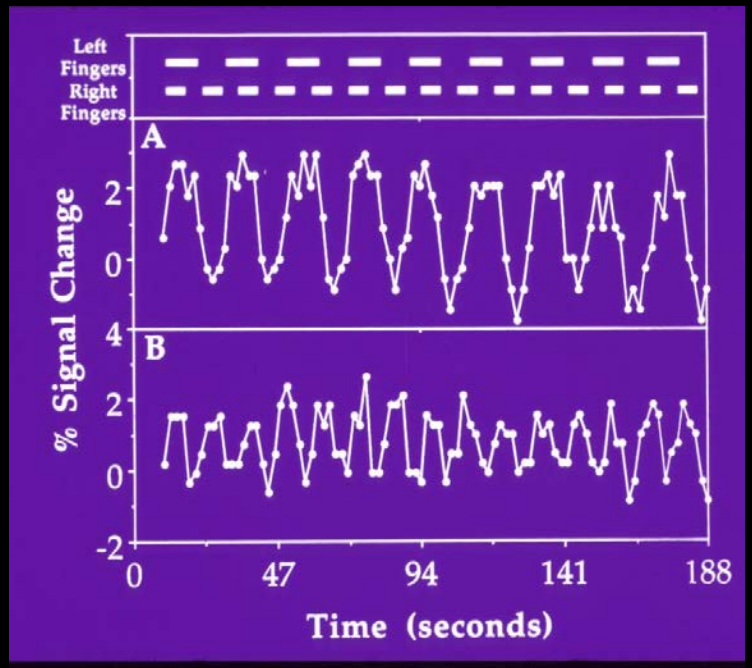


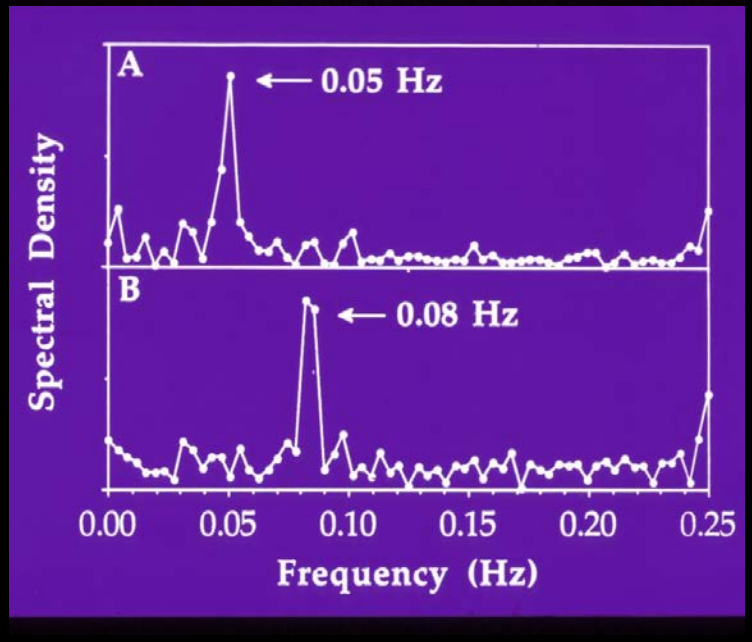
4. Single Event
5. Orthogonal Block Design

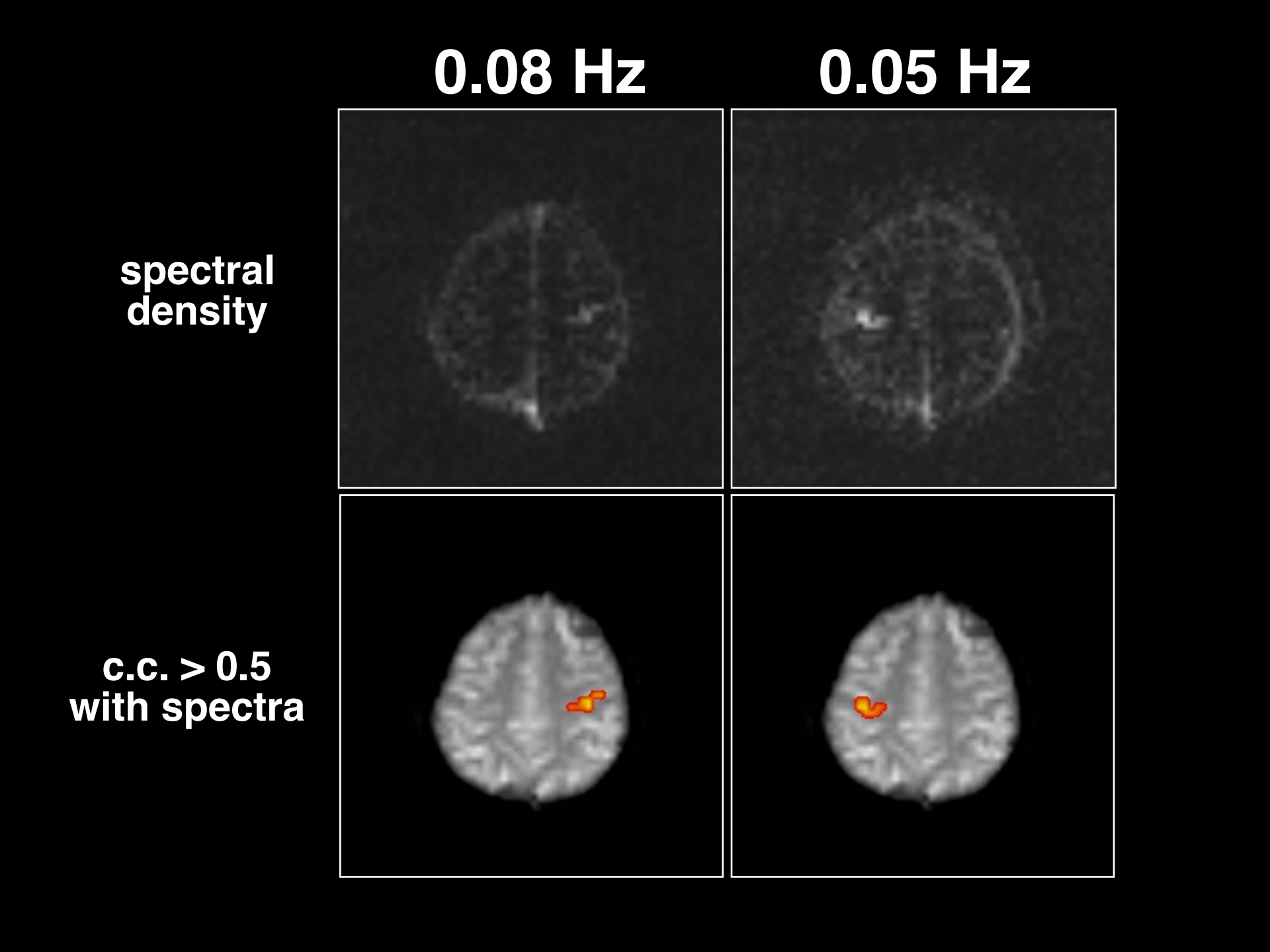


6. Free behavior Design.


A
B

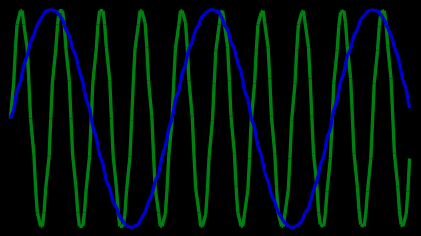

Left Fingers
Right Fingers
A
B
% Signal Change
2
0
4
2
0
-2
0
47
94
141
188
Time (seconds)


A
0.05 Hz
B
0.08 Hz
Spectral Density
0.00
0.05
0.10
0.15
0.20
0.25
Frequency (Hz)

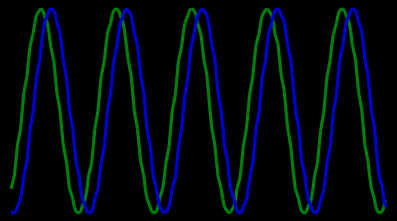

0.08 Hz
0.05 Hz
spectral density
c.c. > 0.5 with spectra

Neuronal Activation Input Strategies

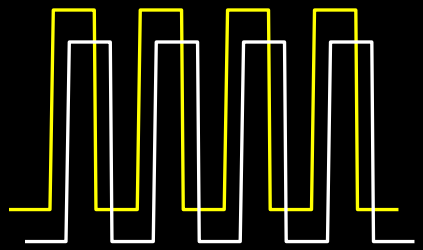
1. Block Design
2. Frequency Encoding



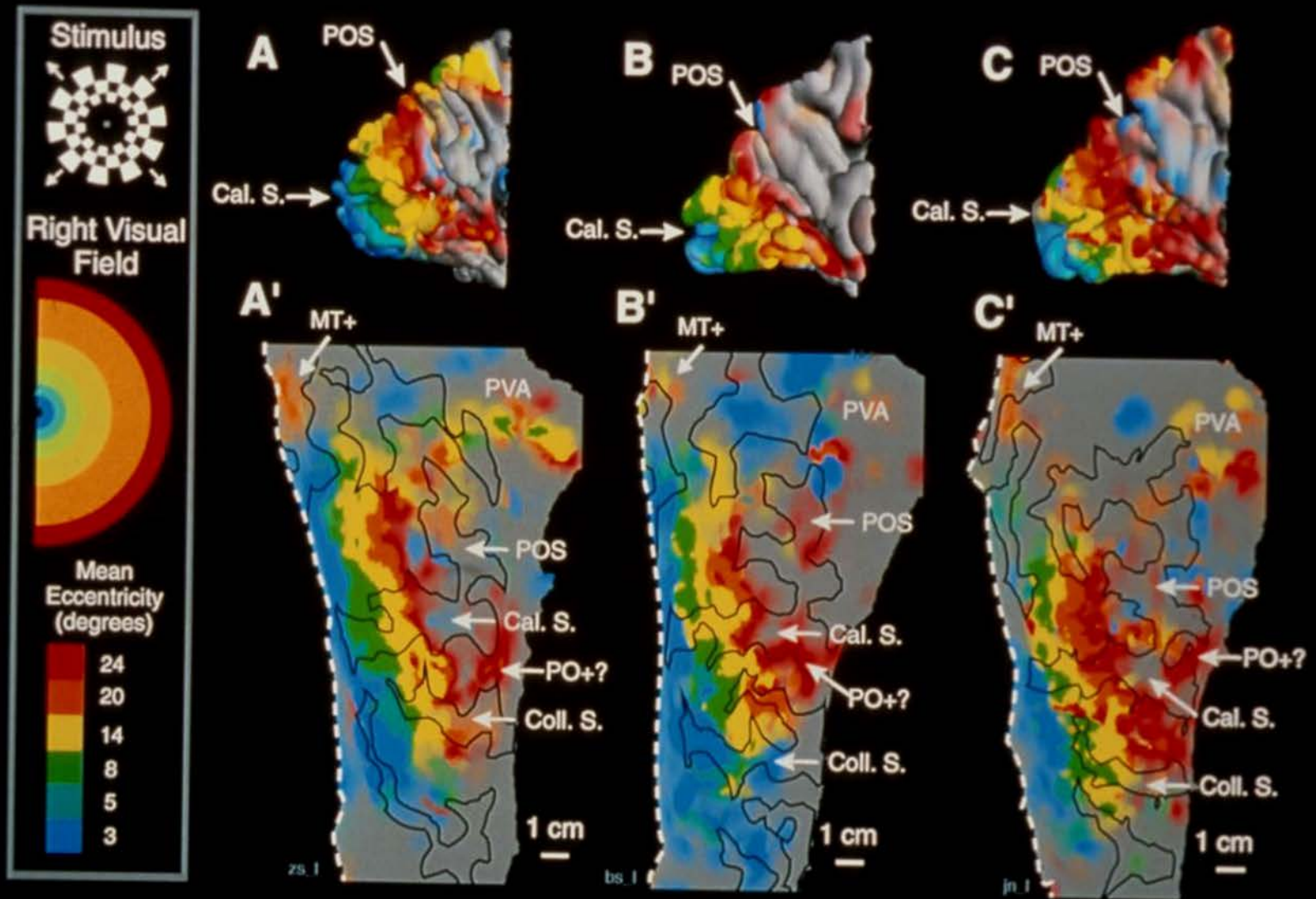
3. Phase Encoding

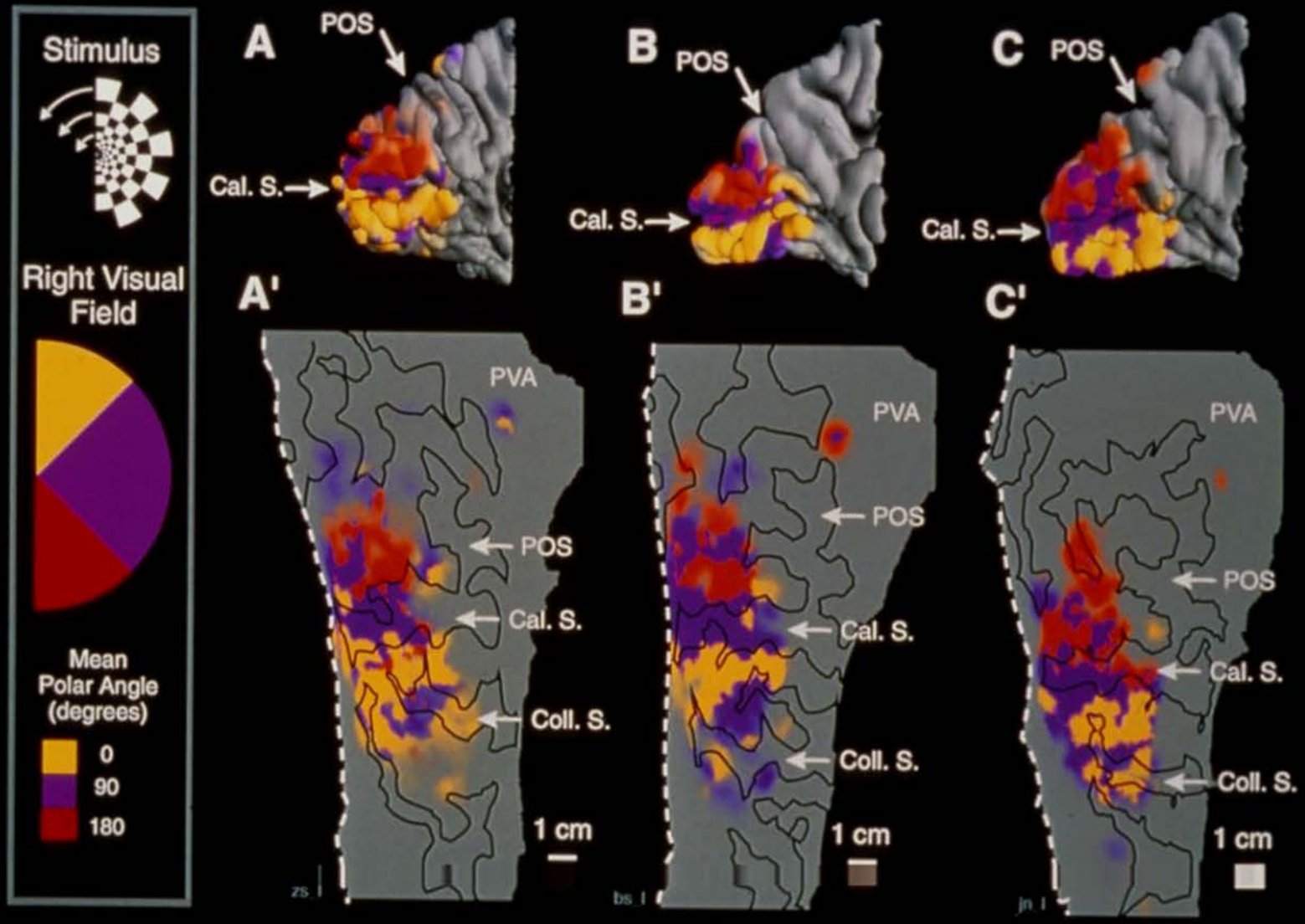


4. Single Event
5. Orthogonal Block Design



6. Free behavior Design.

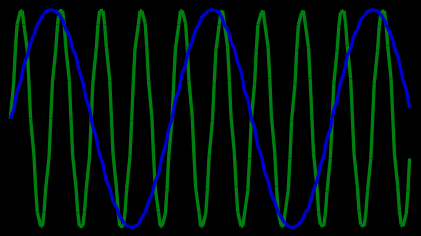

Stimulus
Right Visual Field
Mean Eccentricity (degrees)
24
20
14
8
5
3
A
POS
Cal. S.
B
POS
Cal. S.
C
POS
Cal. S.
A'
MT+
PVA
POS
Cal. S.
PO+?
Coll. S.
1 cm
zs_l
B'
MT+
PVA
POS
Cal. S.
PO+?
Coll. S.
1 cm
bs_l
C'
MT+
PVA
POS
PO+?
Cal. S.
Coll. S.
1 cm
jn_l


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

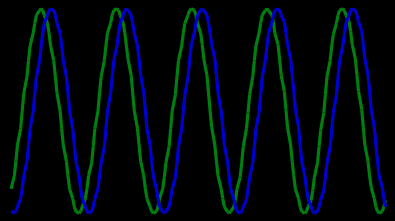
Neuronal Activation Input Strategies

1. Block Design

2. Frequency Encoding

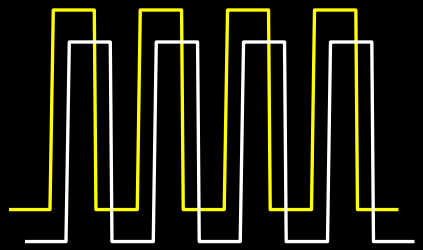


3. Phase Encoding



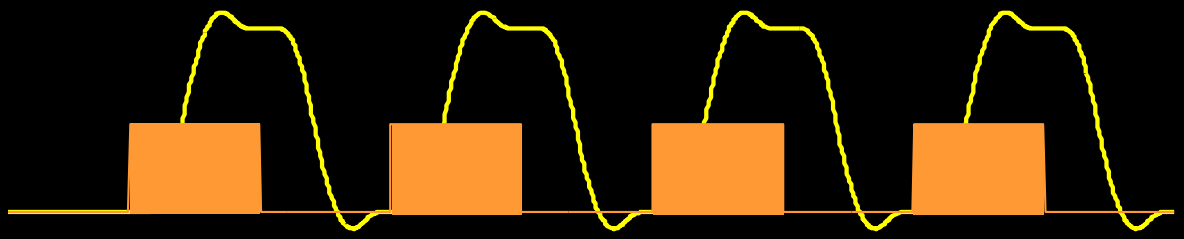
4. Single Event

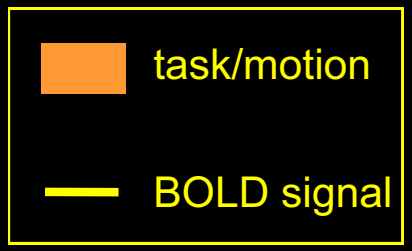
5. Orthogonal Block Design



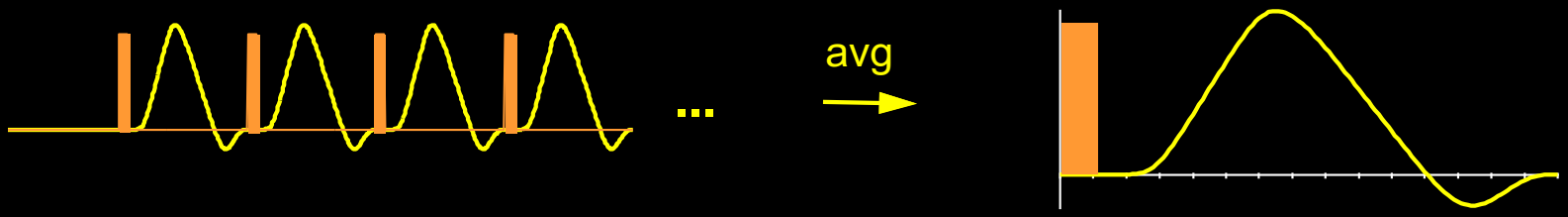
6. Free behavior Design.

Block-trial

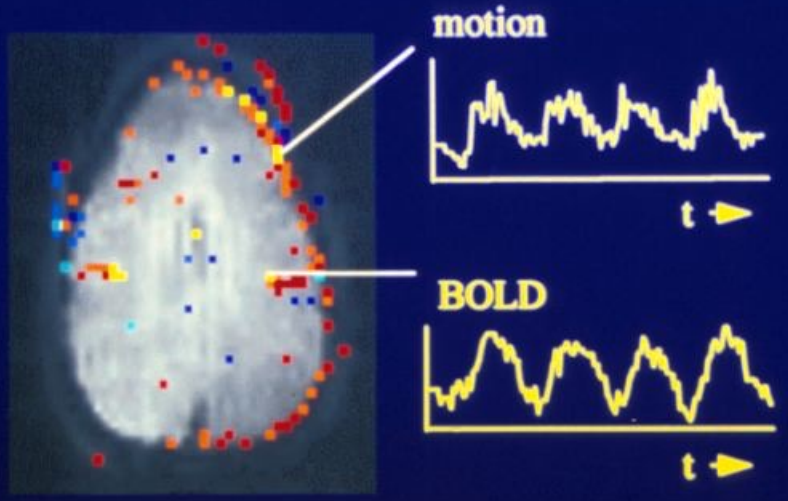


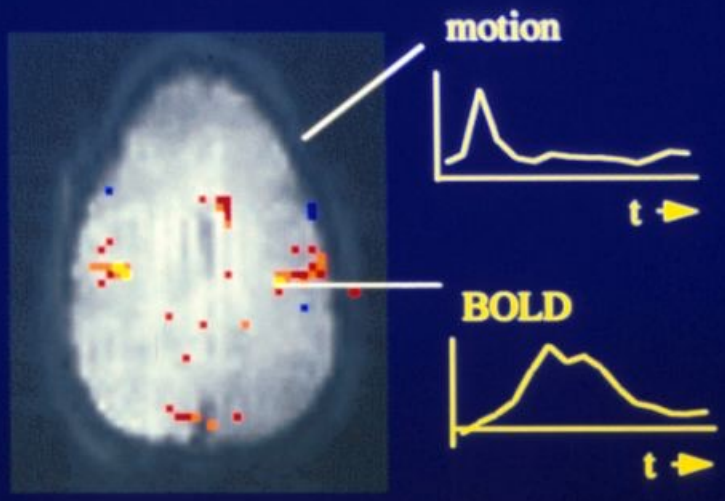


Single-trial (brief stimulus)



Motion-Decoupled fMRI:
Functional MRI during of overt word production





"block-trial" paradigm

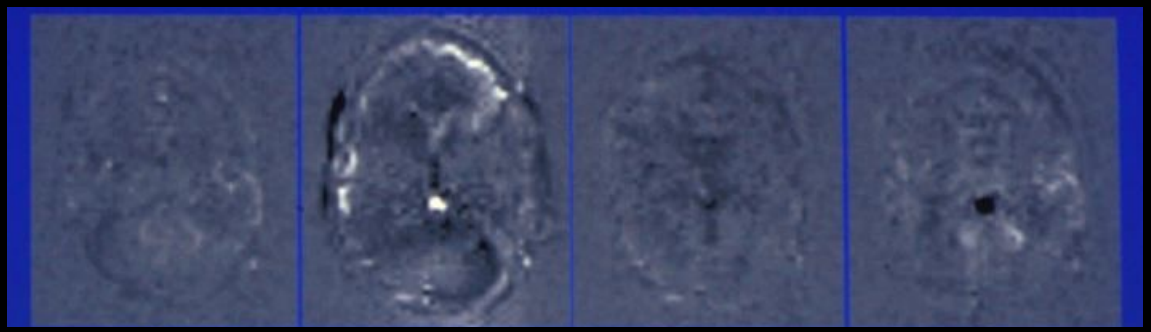
Motion induced signal changes resemble functional (BOLD) signal changes

"single-trial" paradigm

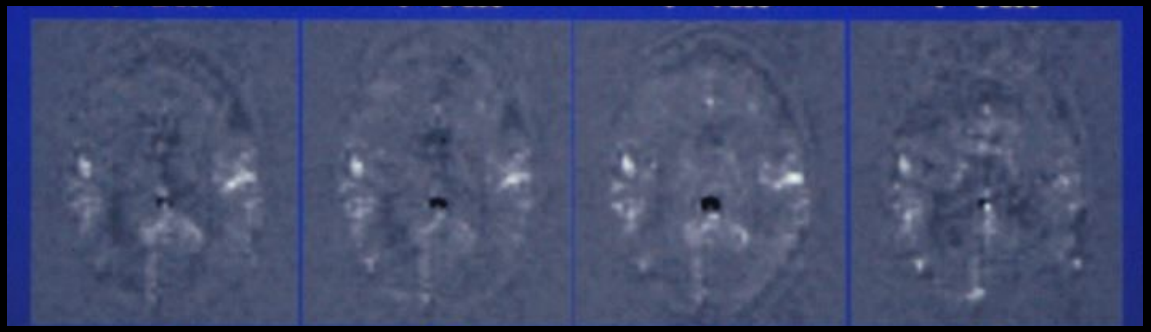
Motion induced and BOLD signal changes are separated in time

R.M. Birn, et al.

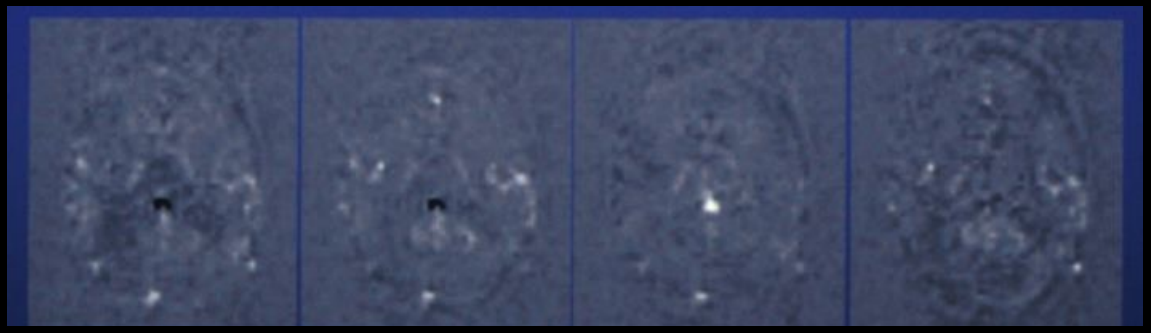
Overt Word Production



2 3 4 5

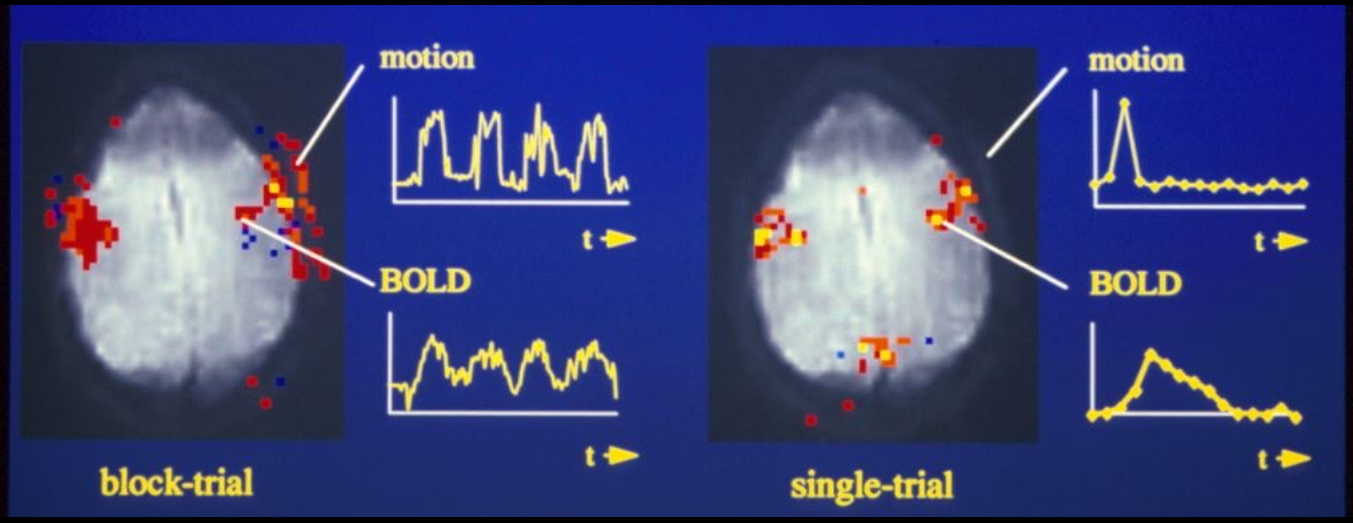


6 7 8 9

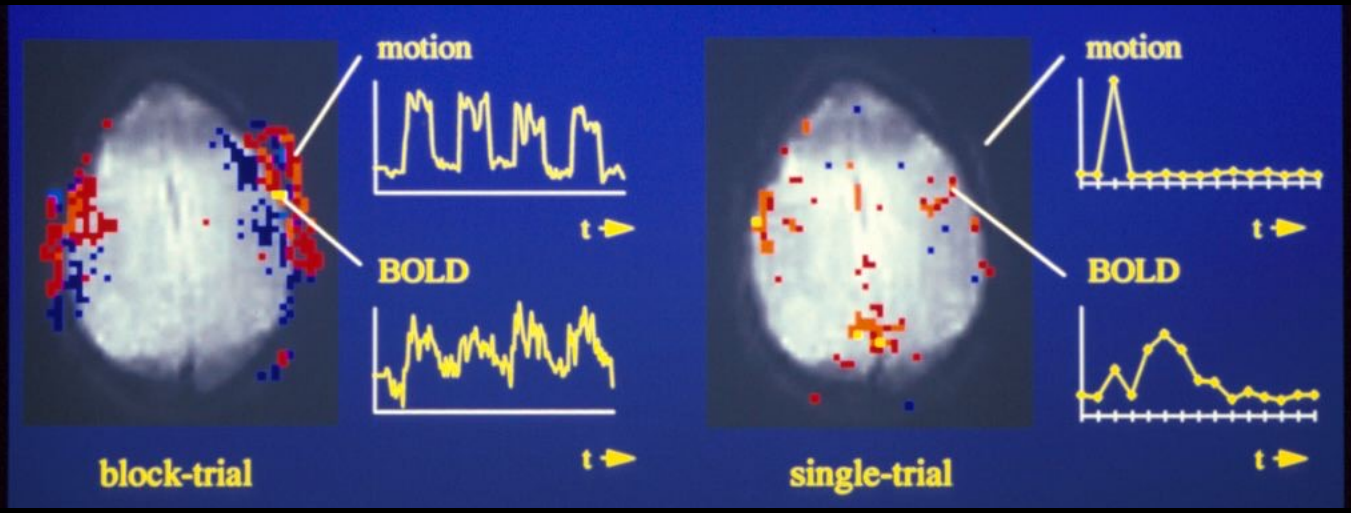


10 11 12 13

Tongue Movement

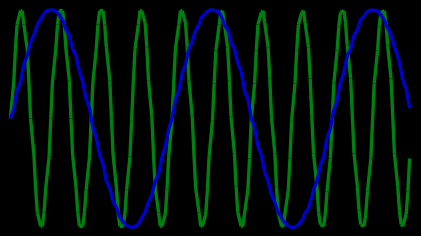


Jaw Clenching

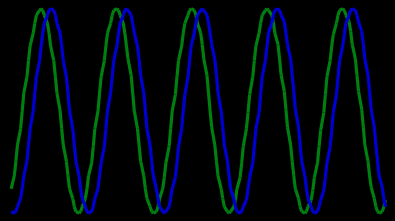


Neuronal Activation Input Strategies

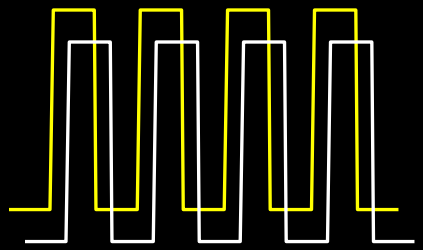
1. Block Design
2. Frequency Encoding



3. Phase Encoding

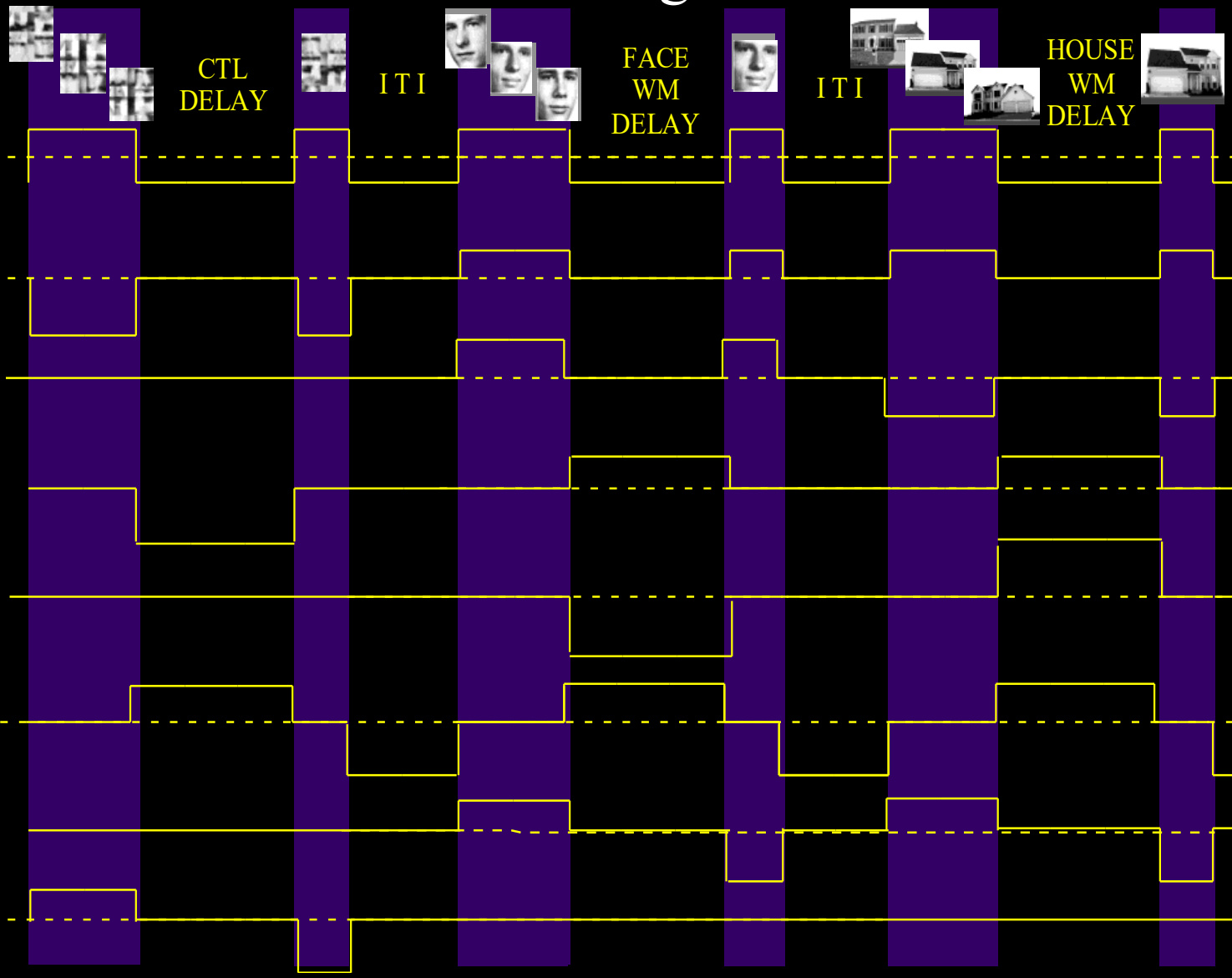


4. Single Event
5. Orthogonal Block Design



6. Free behavior Design.

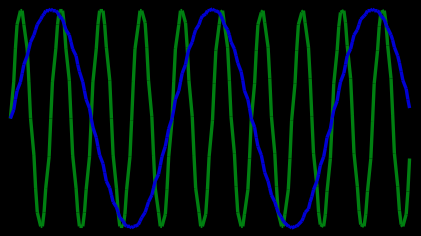
Example of a Set of Orthogonal Contrasts for Multiple Regression



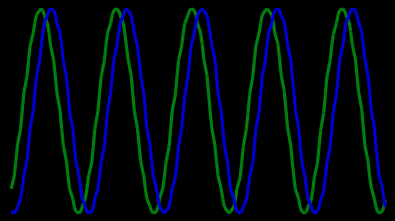
Neuronal Activation Input Strategies

1. Block Design

2. Frequency Encoding

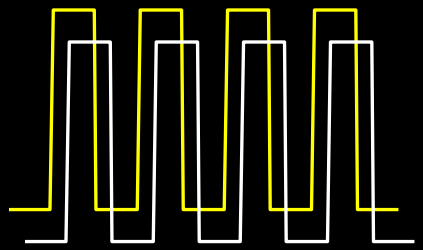


3. Phase Encoding



4. Single Event

5. Orthogonal Block Design



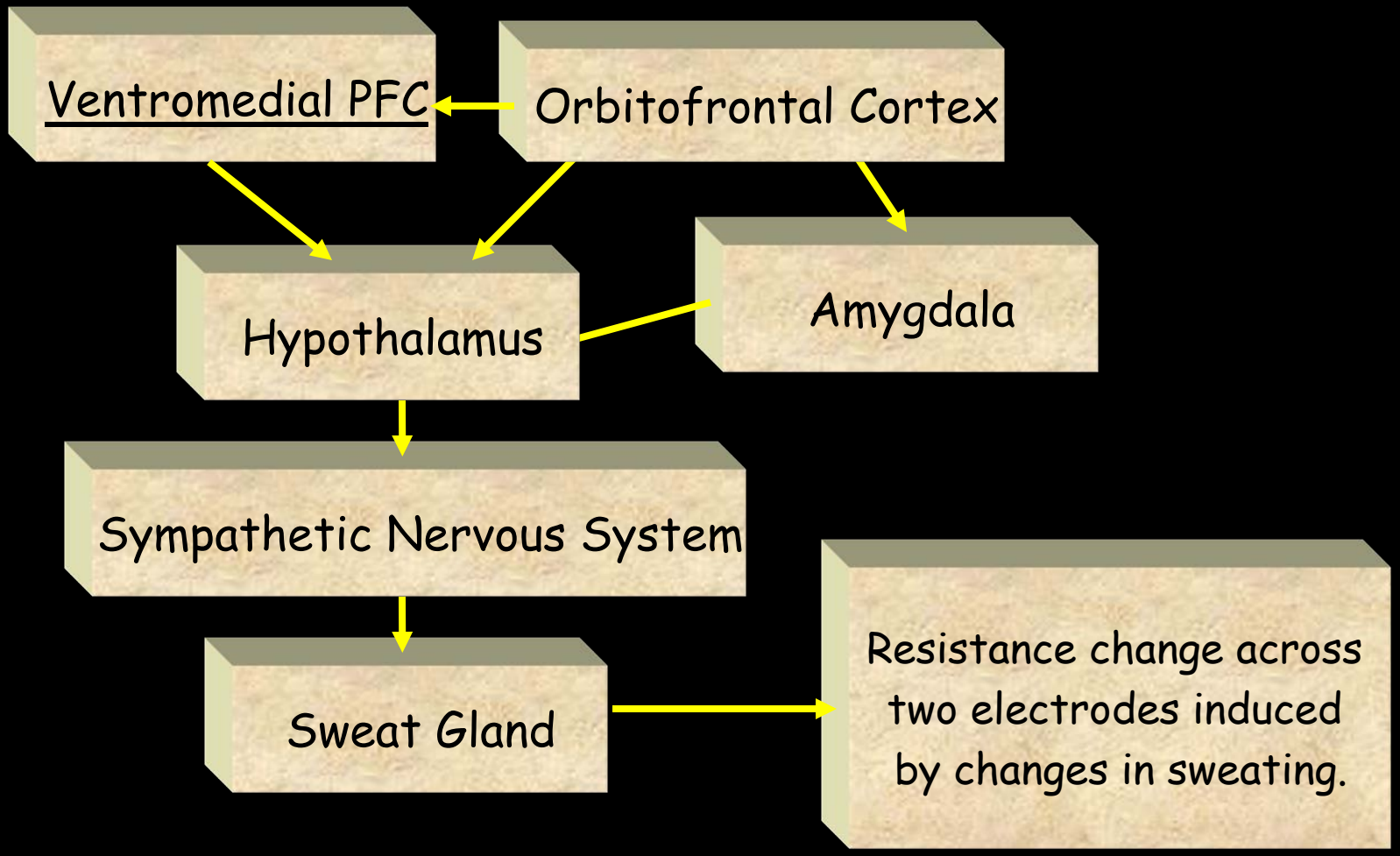
6. Free behavior Design.

Free Behavior Design

Use a continuous measure as a reference function:

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

The Skin Conductance Response (SCR)



Skin conductance data collection

- Equipment: UFI BioDerm Model 2701 Skin Conductance Meter, Slic-8000 8-channel A>D converter, Slic Software for Windows.

- Time from stim. to $T_{1/2}$:~6 to 10 s
- 4000mv range
- 0.1 μS = to 500 mV amplitude
- 0.05 μS threshold level: 250 mV
- 1 μS = 1 mmhos

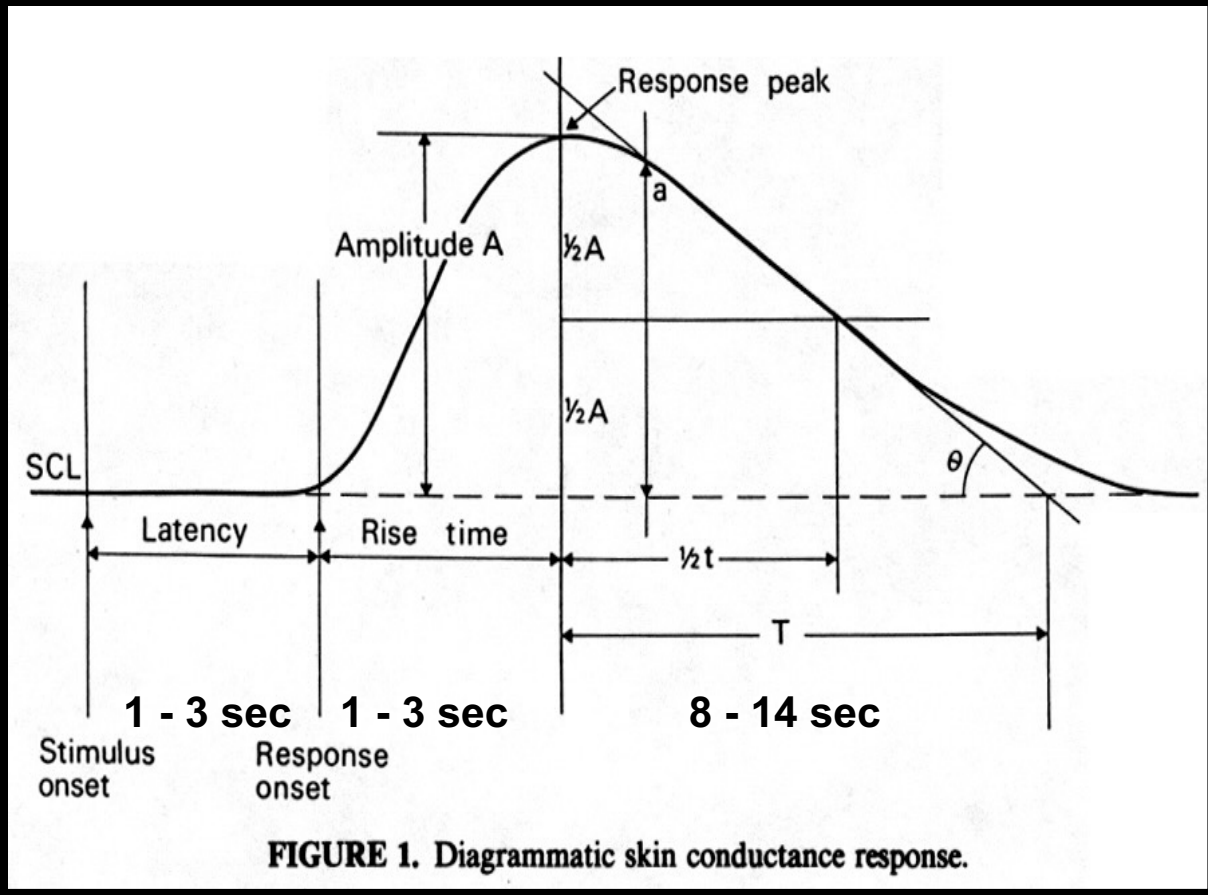
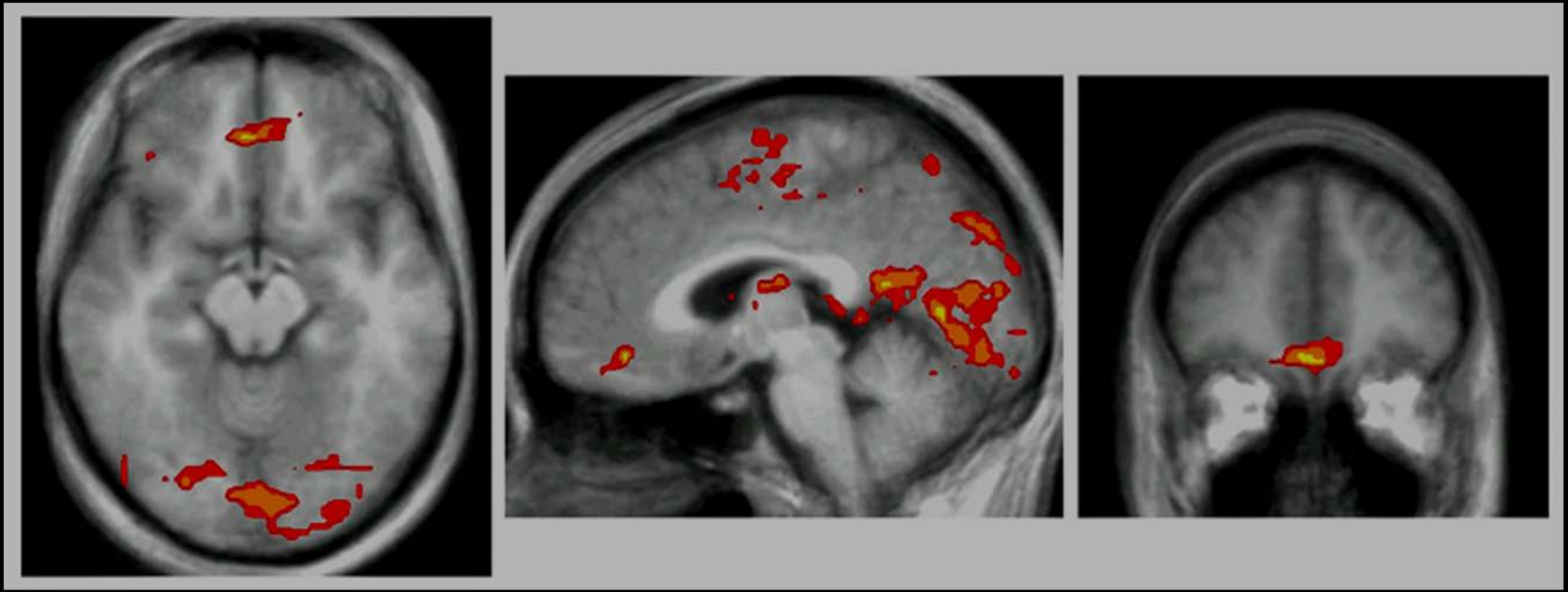


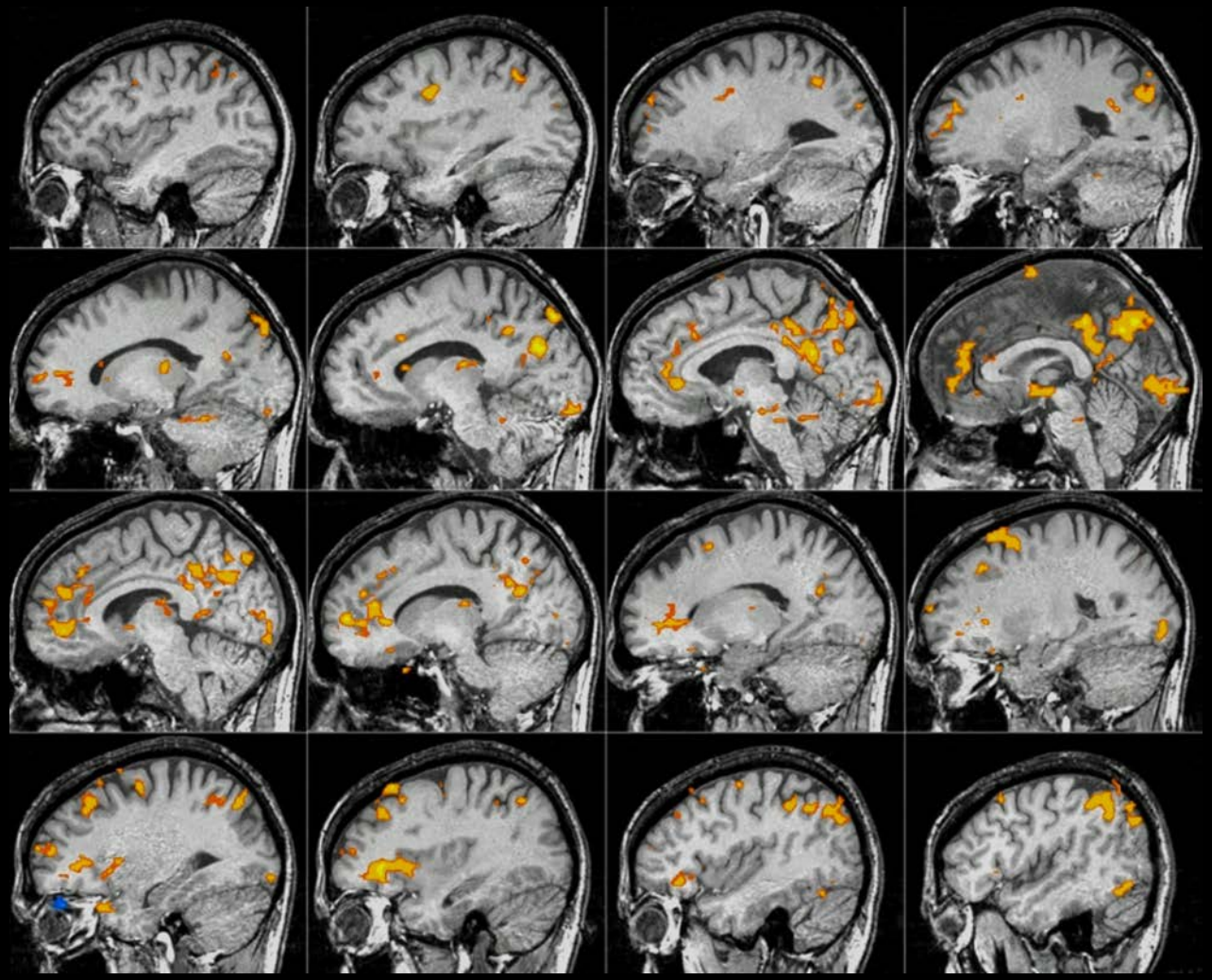
FIGURE 1. Diagrammatic skin conductance response.

- Boucsein, Wolfram (1992). Electrodermal Activity. Plenum Press, NY
- Venables, Peter, (1991). Autonomic Activity ANYAS 620:191-207.

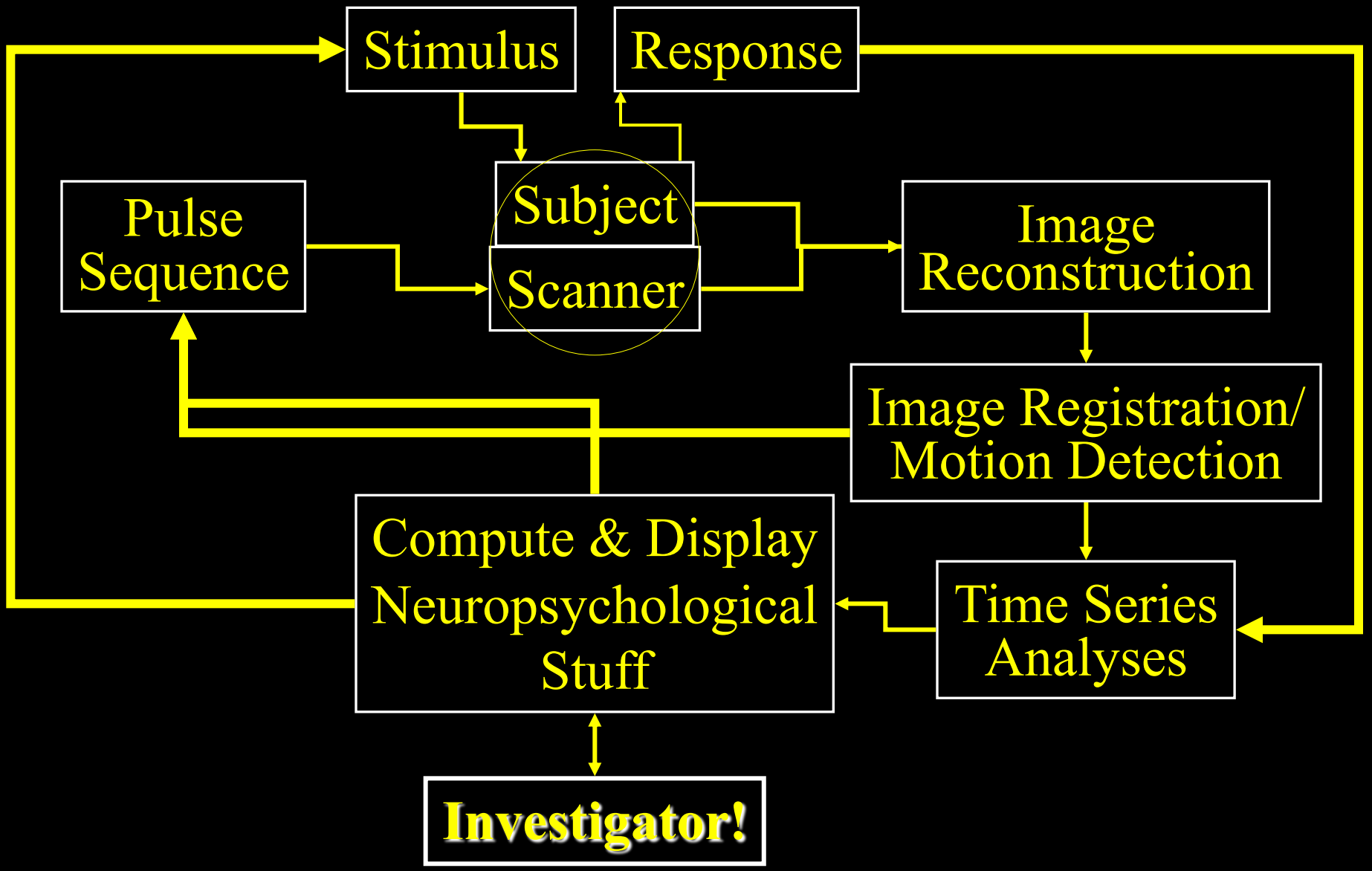
Activity correlated with SCR changes



Brain activity correlated with SCR during “Rest”



Processing Stream with Real Time fMRI

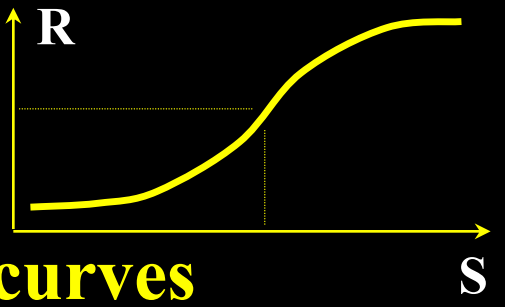


Reasons for real time fMRI

- Make sure you have good data before subject leaves the scanner
- Repeat bad imaging runs
- Provide feedback to subject (*e.g.*, "stop nodding your head!")
- Most important when dealing with patient populations
  - **when FMRI is used for pre-surgical planning**
  - **when patients in study are hard to come by**

Further Reasons..

- Adjustment of stimulus level to reach a desired response magnitude
  - **½ of peak response**
  - **mapping of voxel stimulus-response curves**



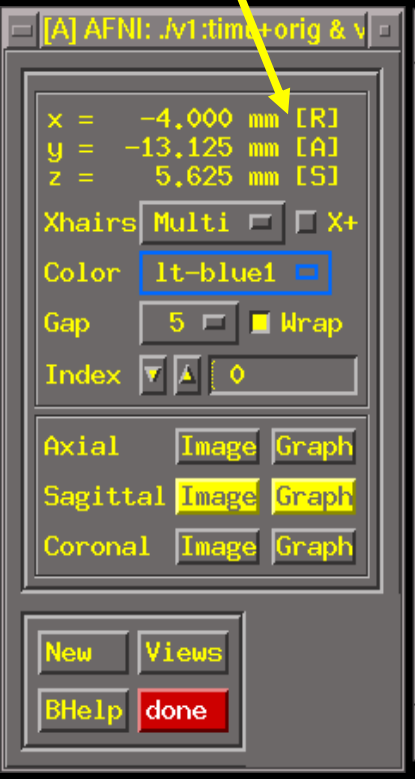
- Carrying out experiment until some statistically significant result has been reached
  - **Must pay attention to statisticians for this!**
  - ***e.g.*, do tasks until language lateralization has been established**

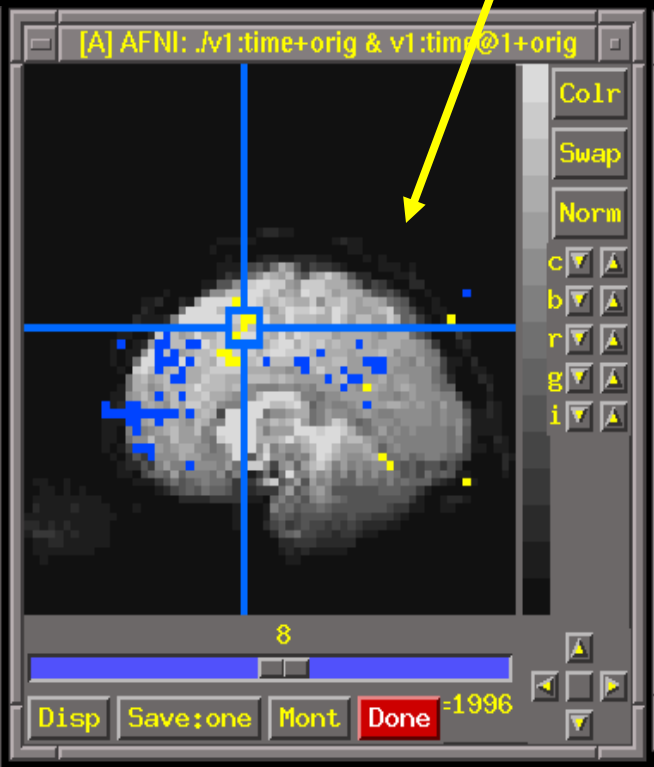
Things to Look At (*à la AFNI*)

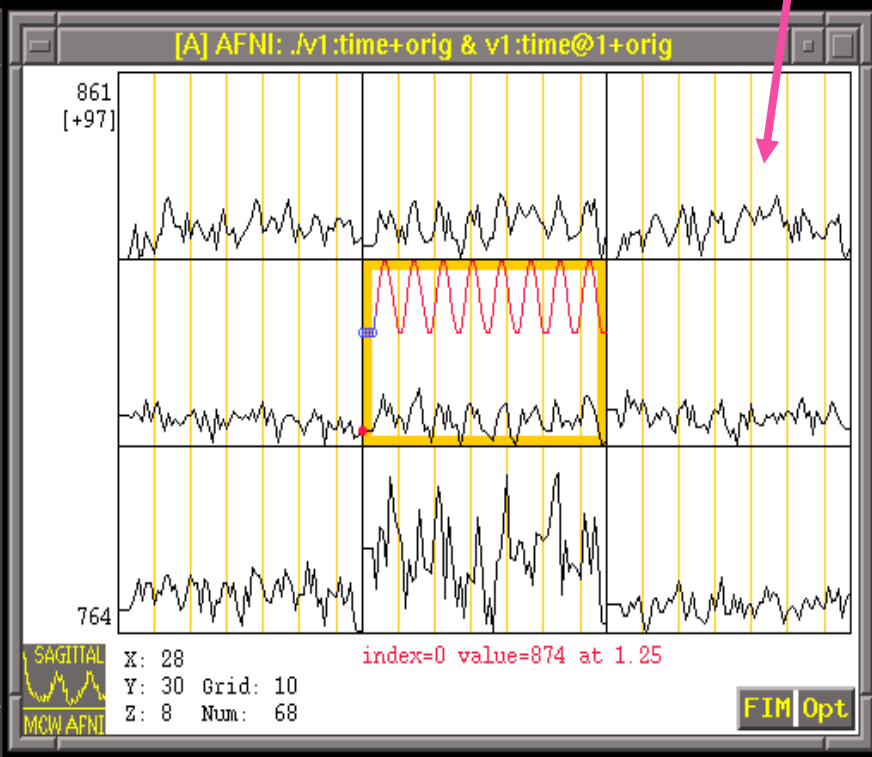
Control Panel

Displaying EP images from time series

Graphing voxel time series data

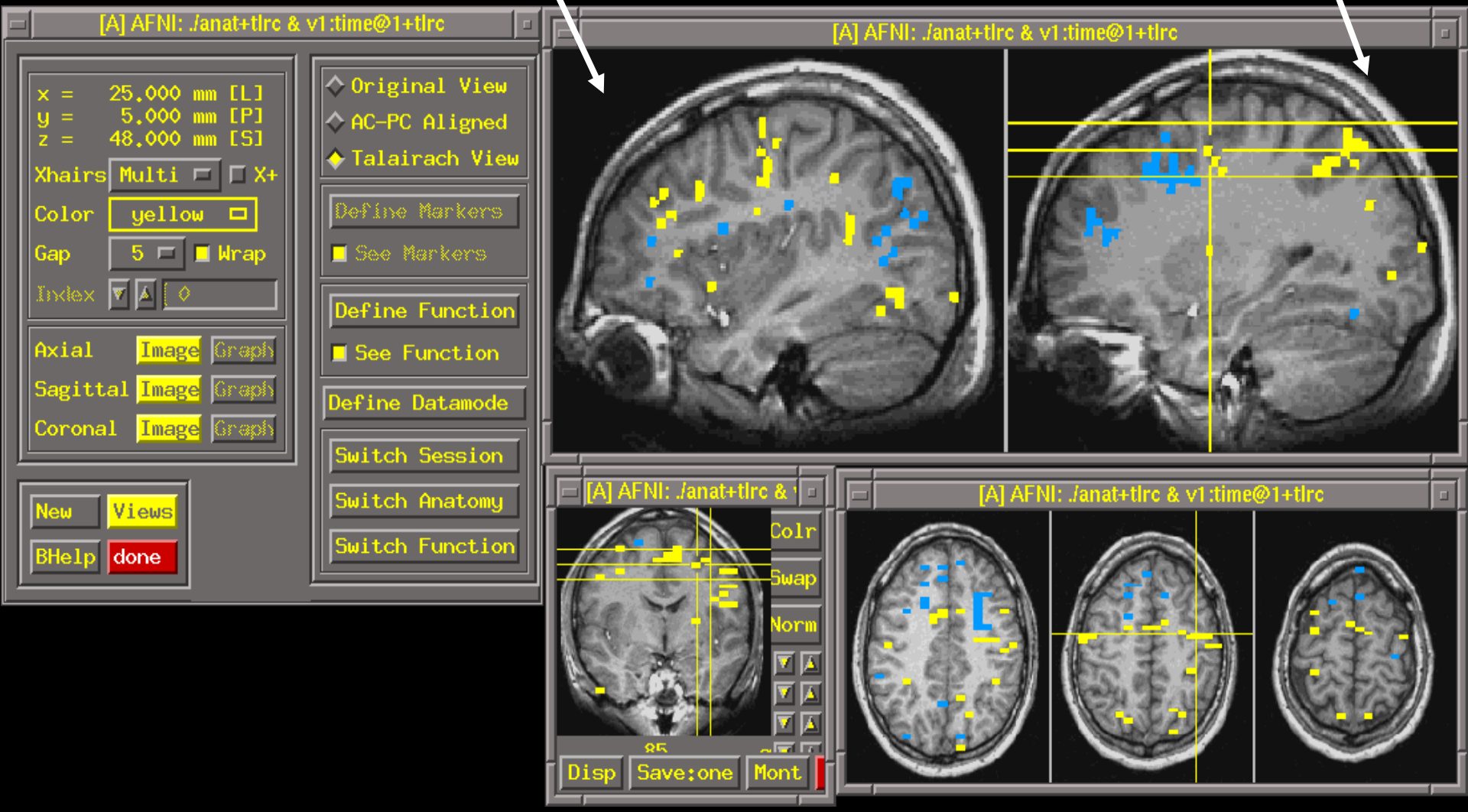


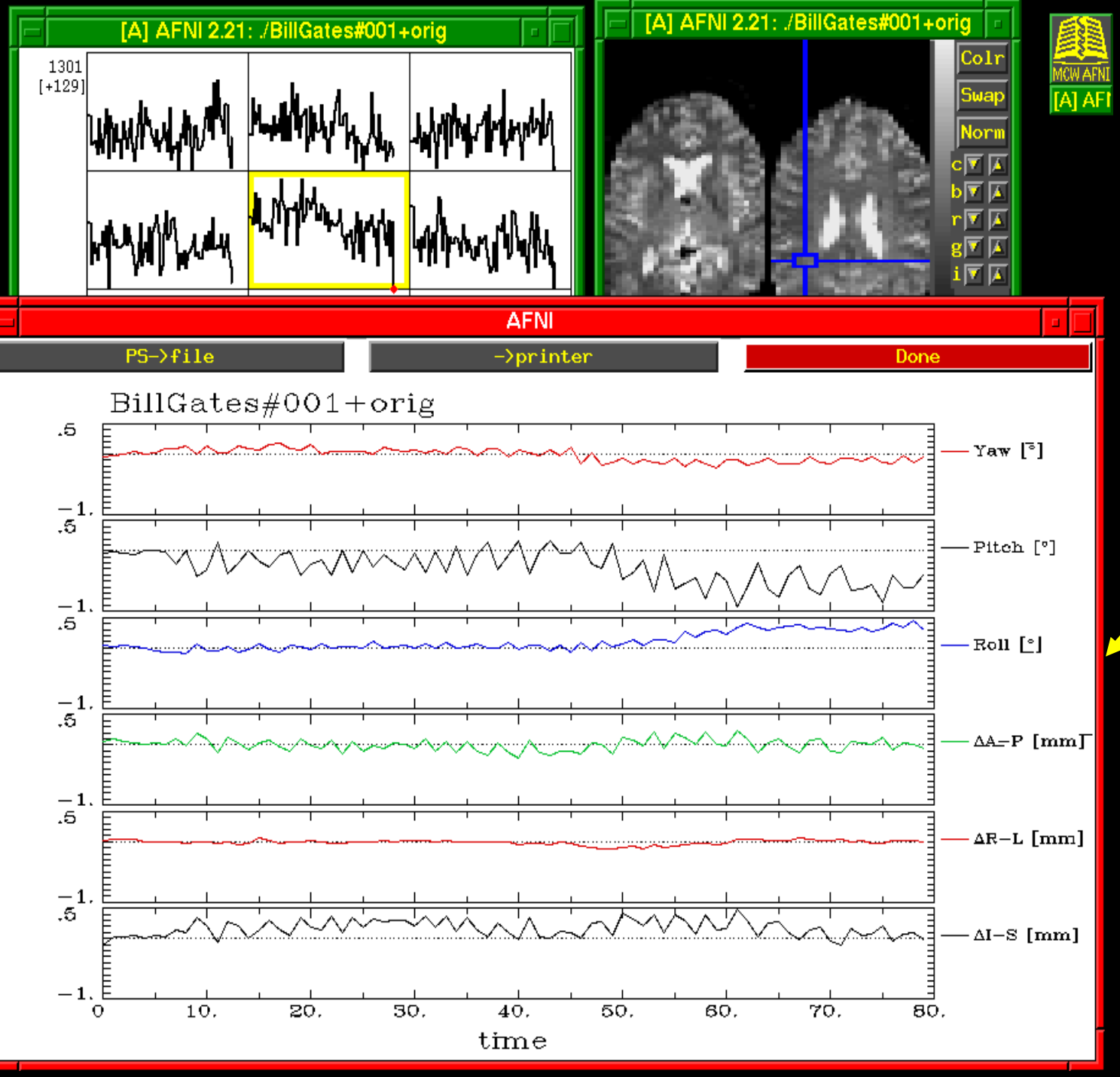




Multislice layouts

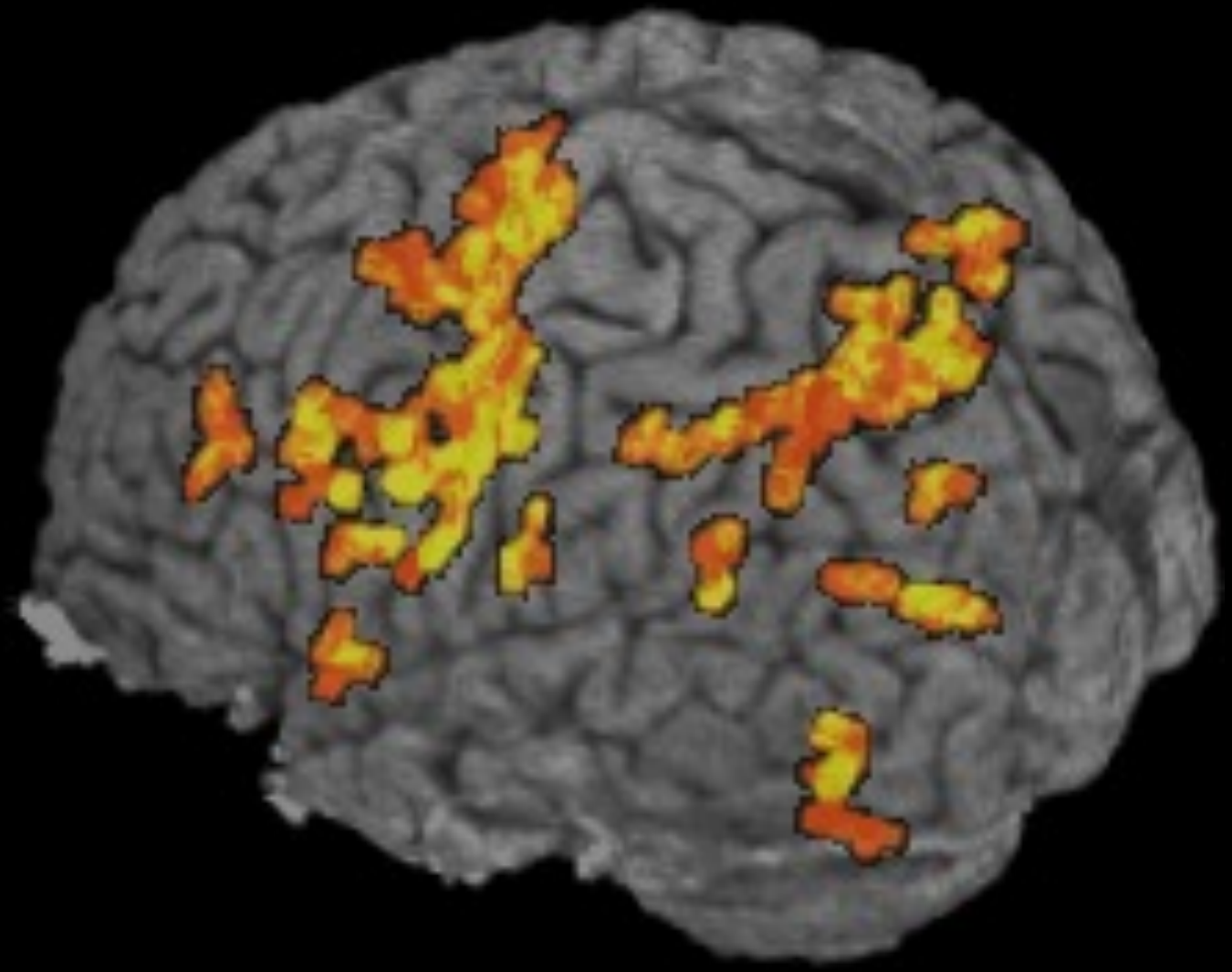
FIM overlaid on SPGR, in Talairach coords





Estimated subject movement parameters

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

Functional Imaging Methods / 3T Group

Staff Scientists:
Sean Marrett
Jerzy Bodurka

Post Docs:
Rasmus Birn
Patrick Bellgowan
Ziad Saad

Clinical Fellow:
James Patterson

Graduate Student:
Natalia Petridou

Summer Students:
Hannah Chang
Courtney Kemps

July 7, 2000