10 things you need to know to be a successful fMRI researcher

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Unit on Functional Imaging Methods
&
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Laboratory of Brain and Cognition
National Institute of Mental Health

The 10 Things

1. The Scanning Technique (MRI)
2. Necessary Technical skills and/or People
3. Imaging and Processing steps
4. Types of Functional Contrast
5. Details of Functional Contrast
6. Types of Artifacts
7. Methods to Bypass or Remove Artifacts
8. Types of Applications
9. Limits of Techniques and Applications
10. Some “rules of thumb”

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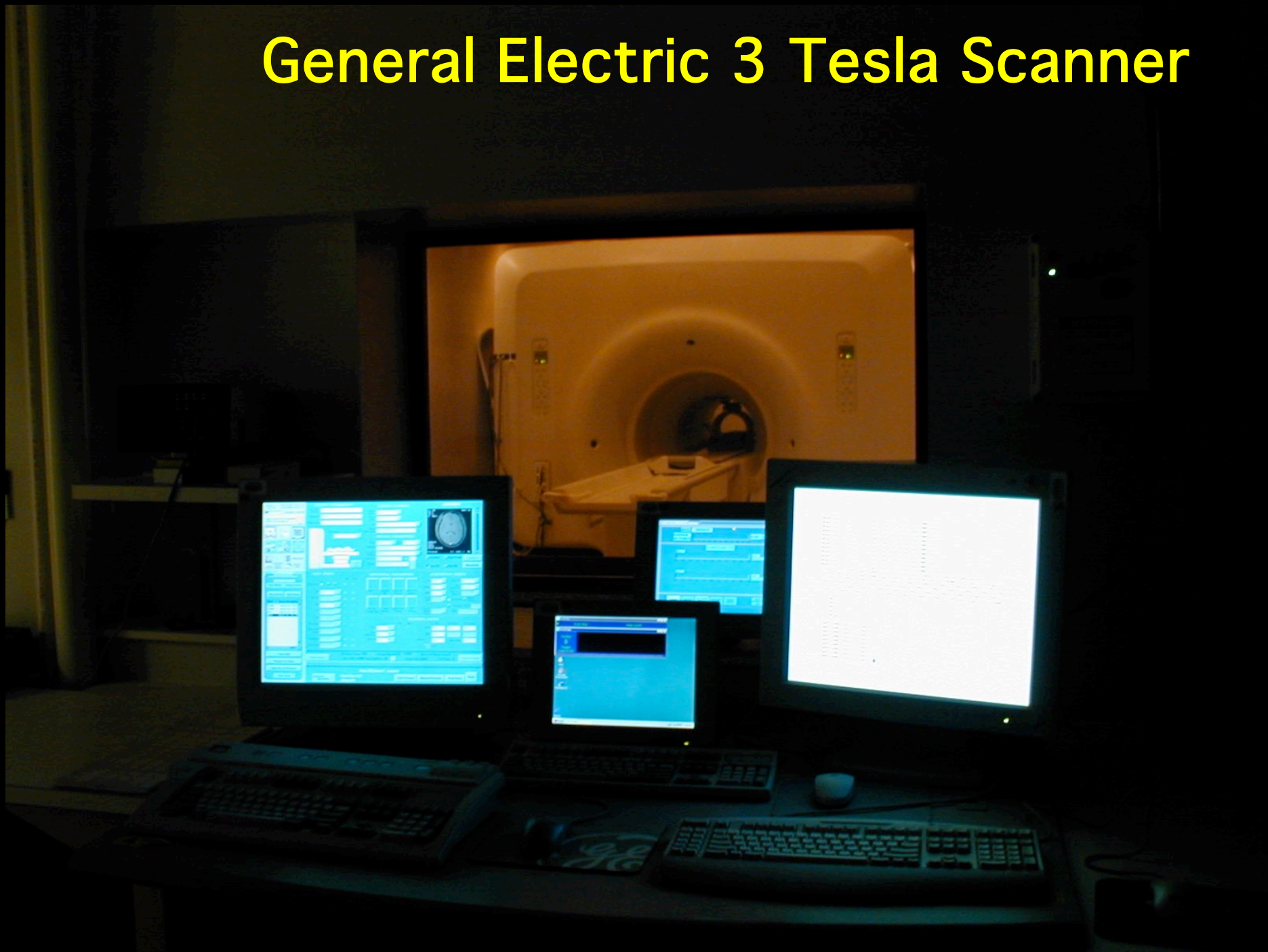
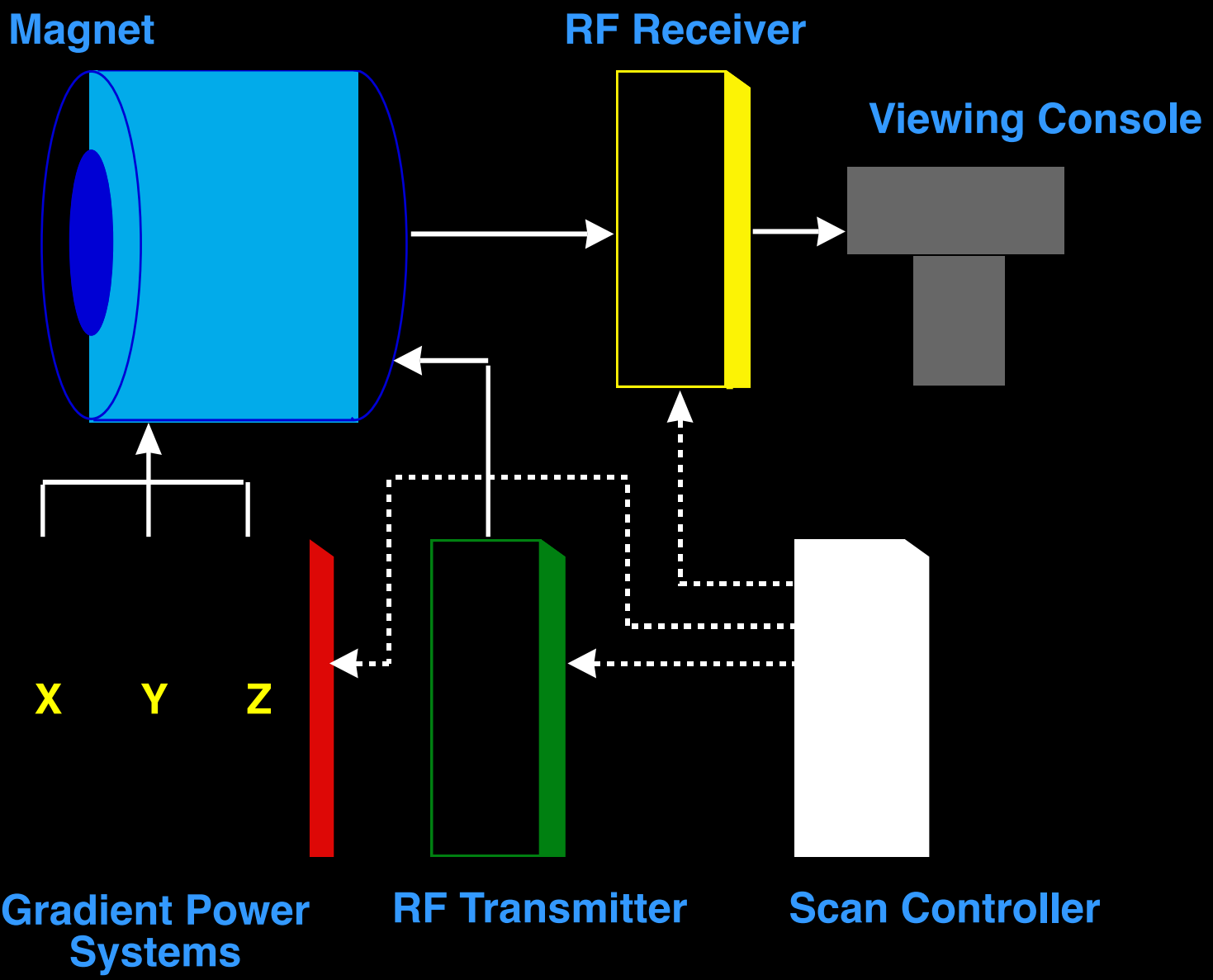
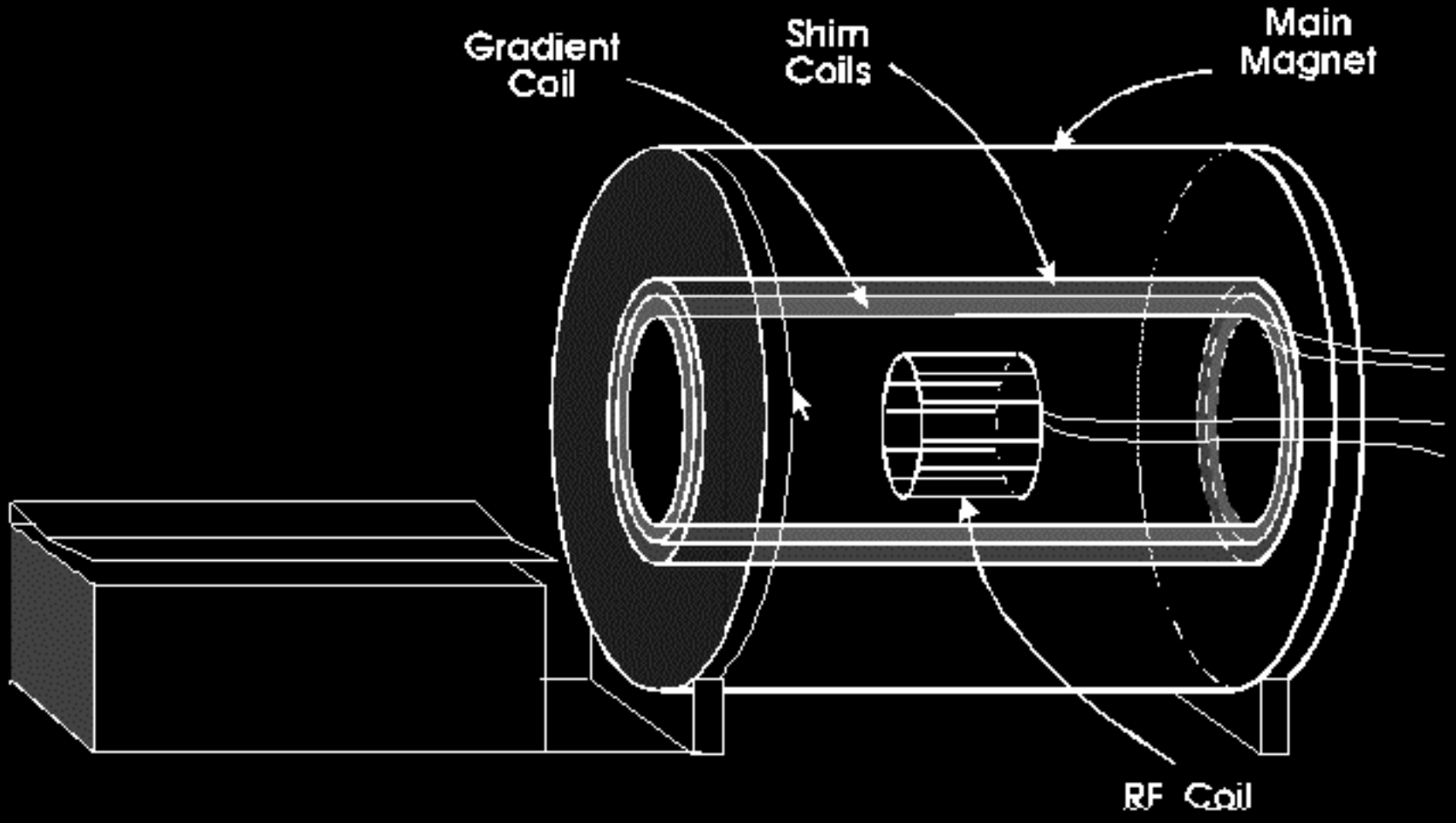
General Electric 3 Tesla Scanner

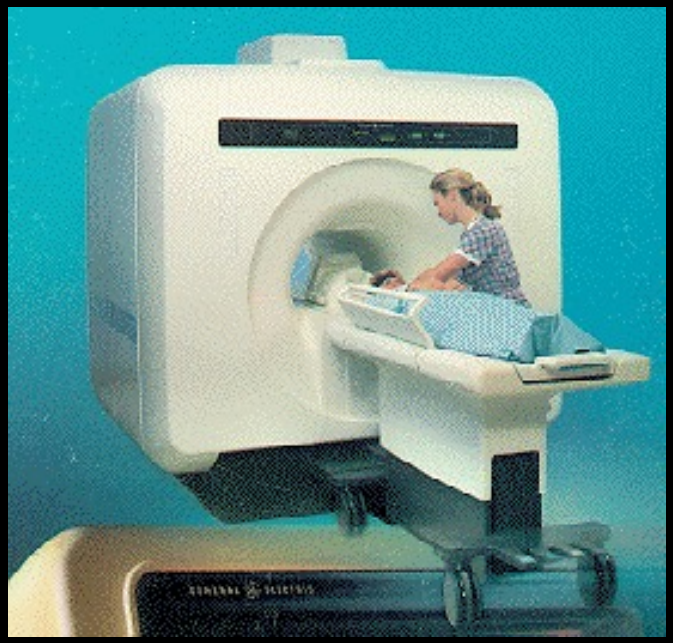


Imaging System Components




Gradient Coil
Shim Coils
Main Magnet
RF Coil

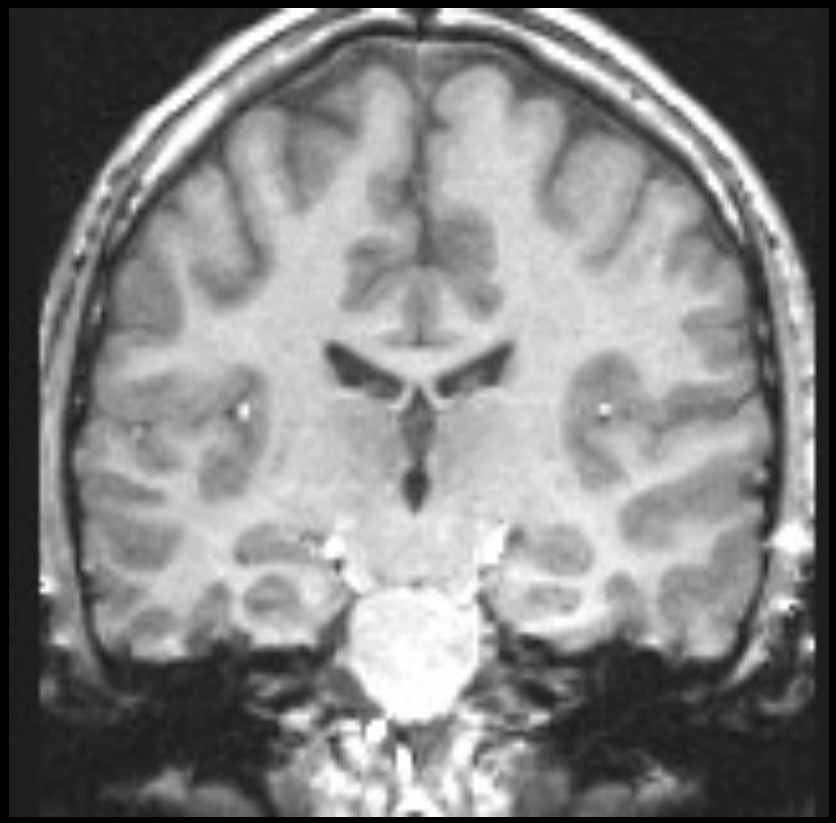
To perform an MRI Experiment:

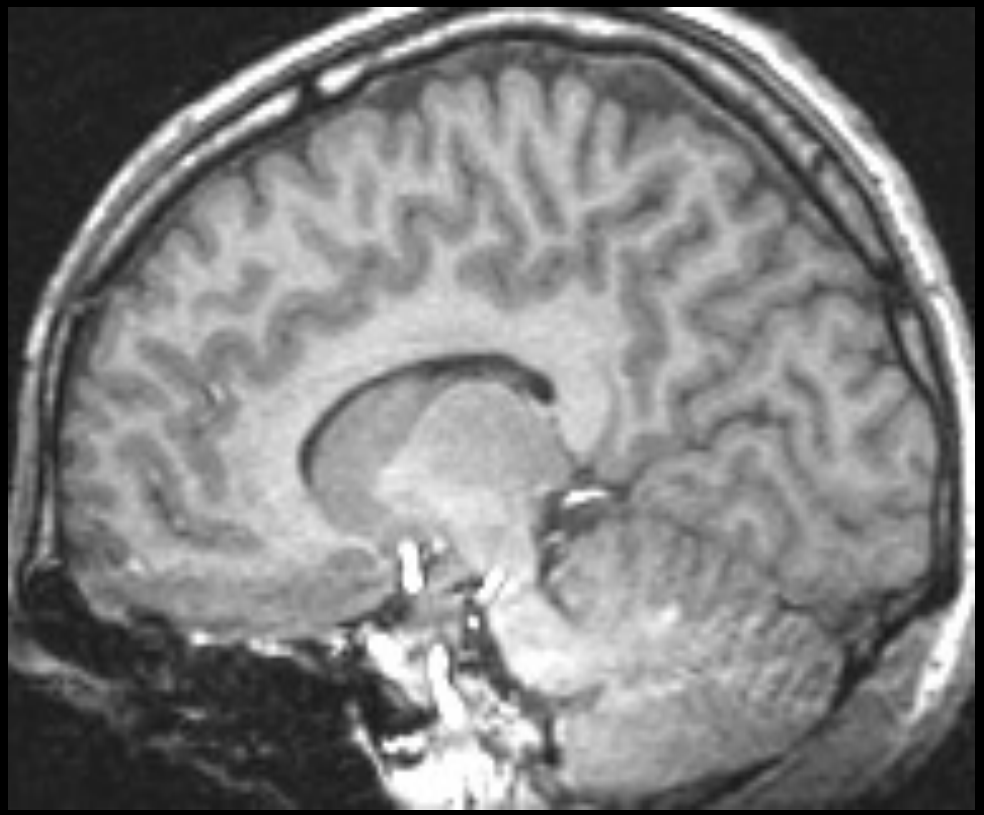


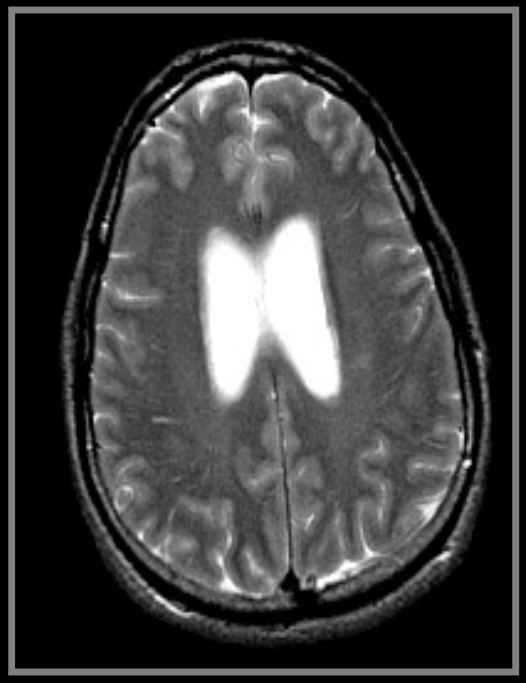
1. Place patient in magnet
2. Send in a radio frequency (RF) wave
3. Turn off the RF wave.
4. Patients emits a signal
5. Image is reconstructed

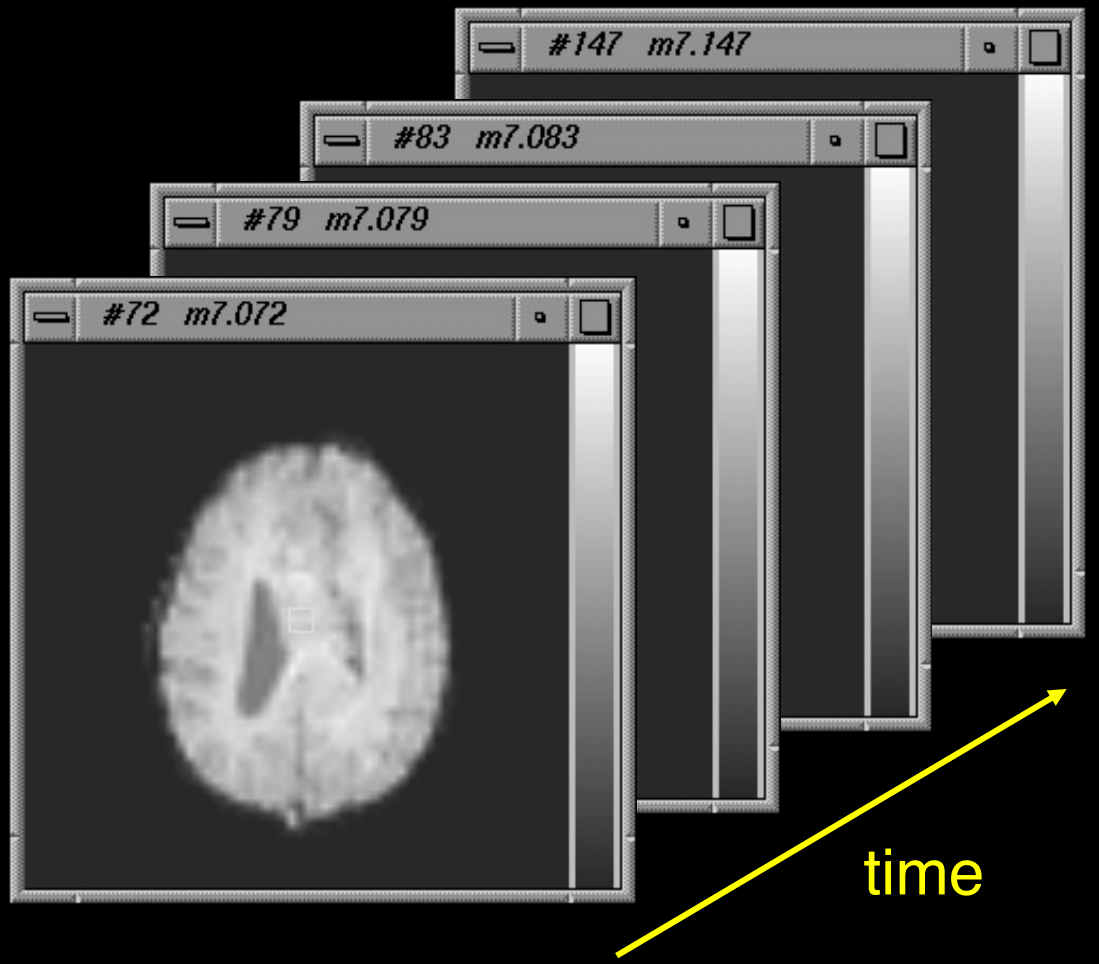
The Concept of Contrast (or Weighting)

- *Contrast* = difference in RF signals — emitted by water protons — between different tissues
- Example: gray-white contrast is possible because T1 is different between these two types of tissue





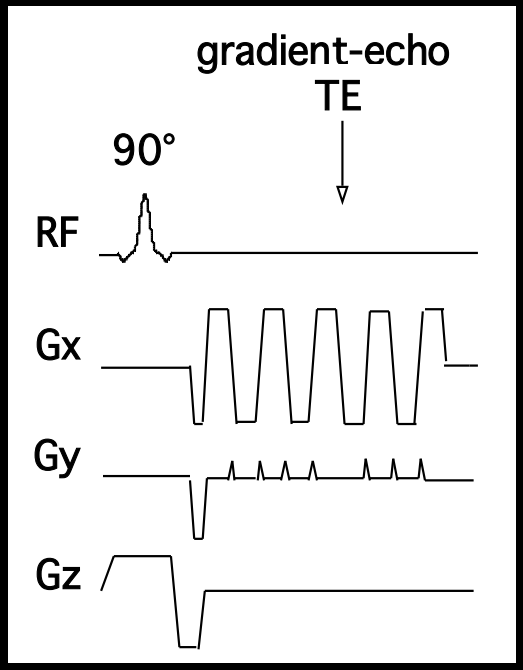


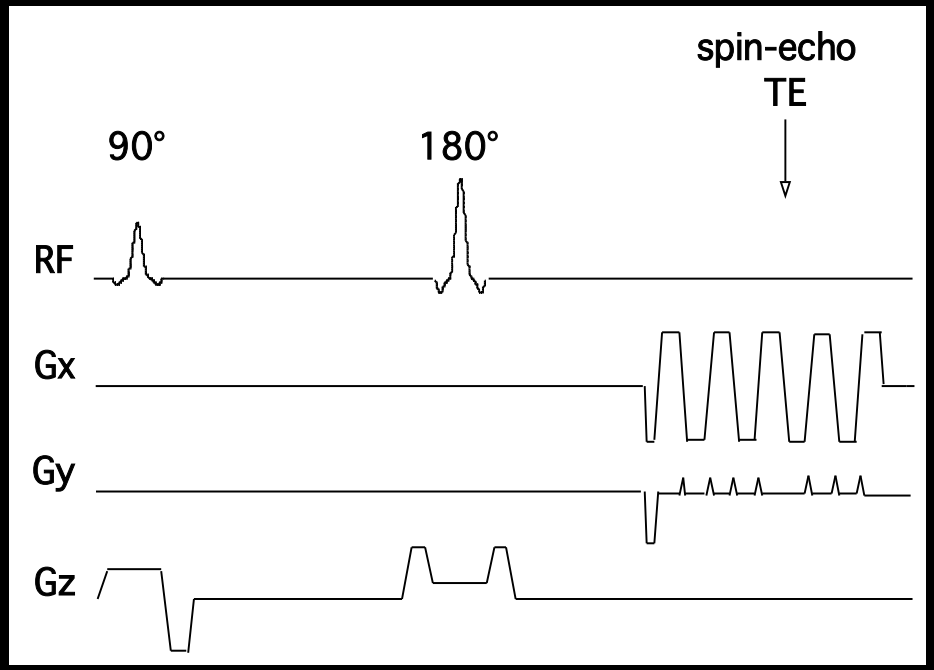


Anatomic

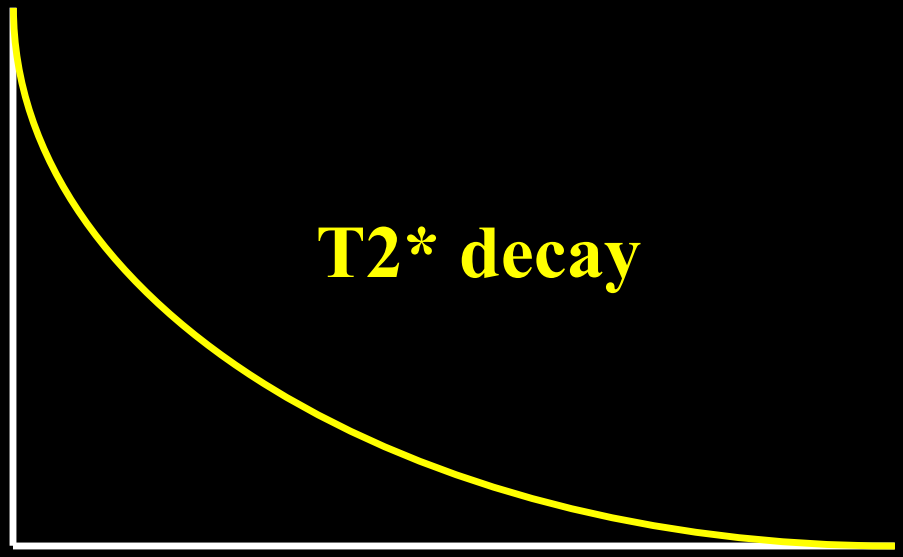
Functional

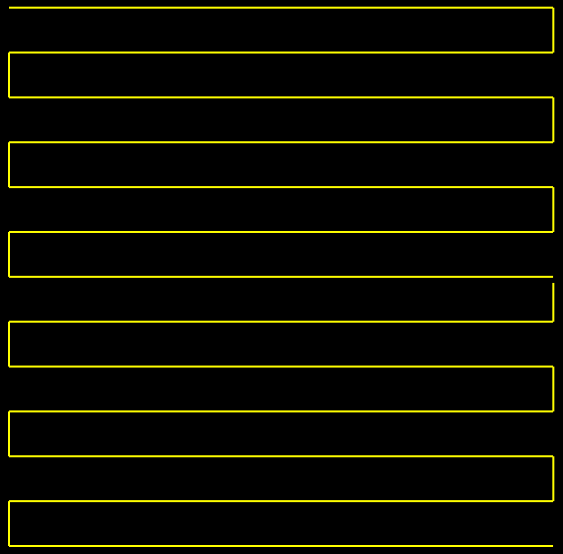
Echo-Planar Imaging





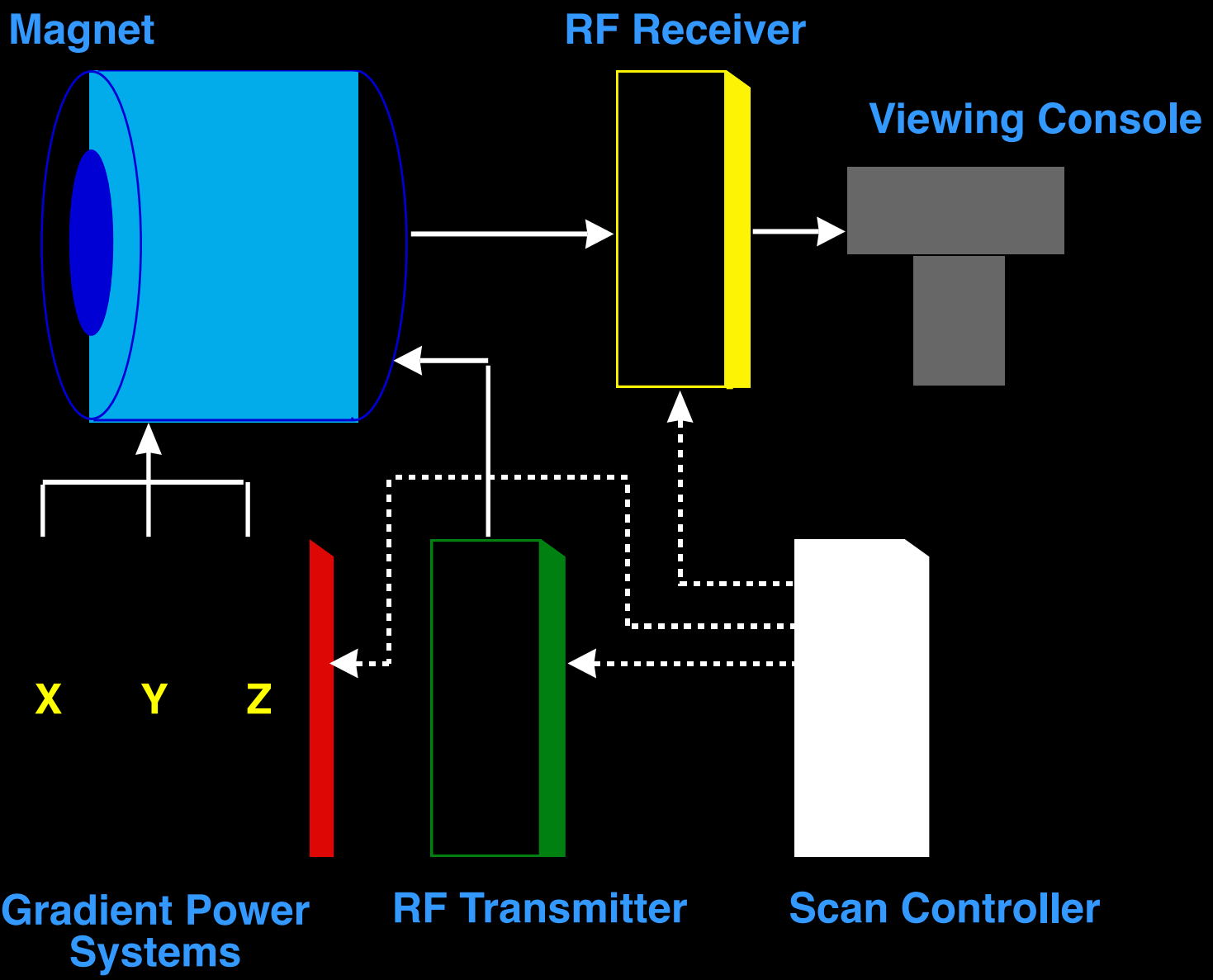
Single Shot Imaging





≈ 20 to 40 ms

Imaging System Components

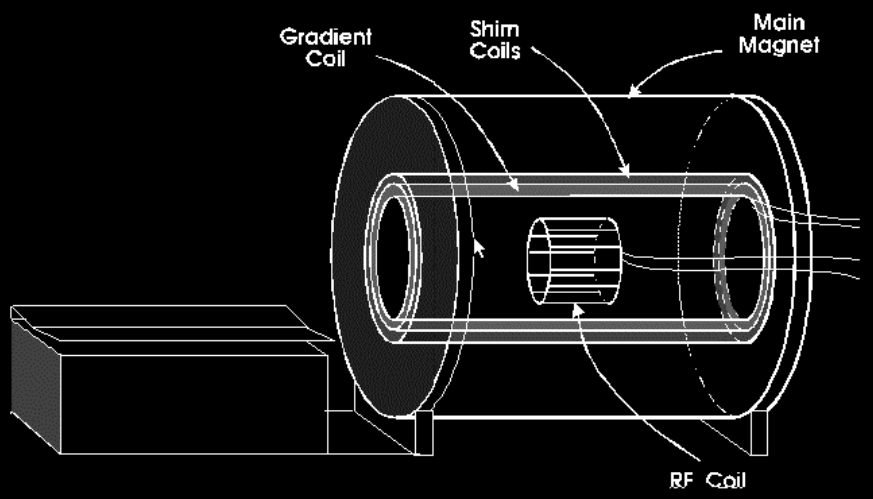


1991-1992

1992-1999

2 G/cm, 350 T/m/s

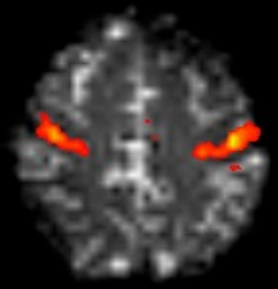
4 G/cm, 150 T/m/s



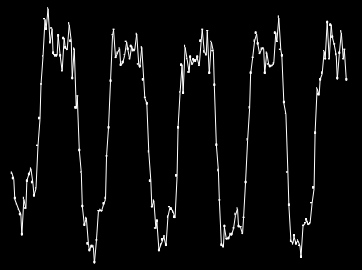
10 G/cm, 1000 T/m/s

The use of fMRI to Investigate Brain Function

Where?



When?



How much?

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

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Minimum Staff

Physicist (or Engineer)
Computer Specialist
Scanning Technologist
Researcher and team

- -paradigm design
- -paradigm construction
- -processing
- -interpretation

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Imaging and Processing Steps

- Shimming
- Localizer
- High resolution anatomical image
- Functional time series collection
- Image reconstruction
- Time series analysis
  - Registration
  - Correlation, Regression, t-test, etc..
  - Statistical threshold
  - Display
  - Image normalization
  - Multiple subject comparison
- Interpretation

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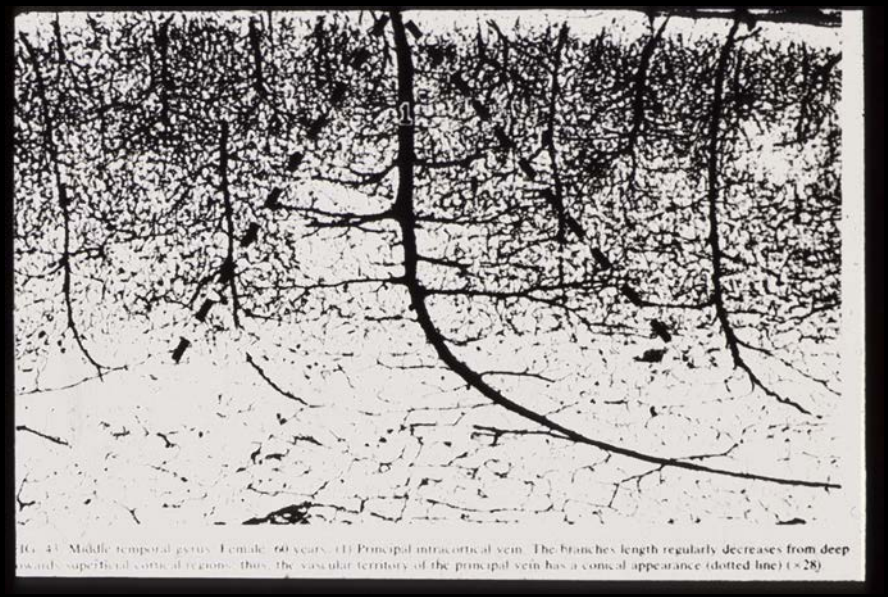
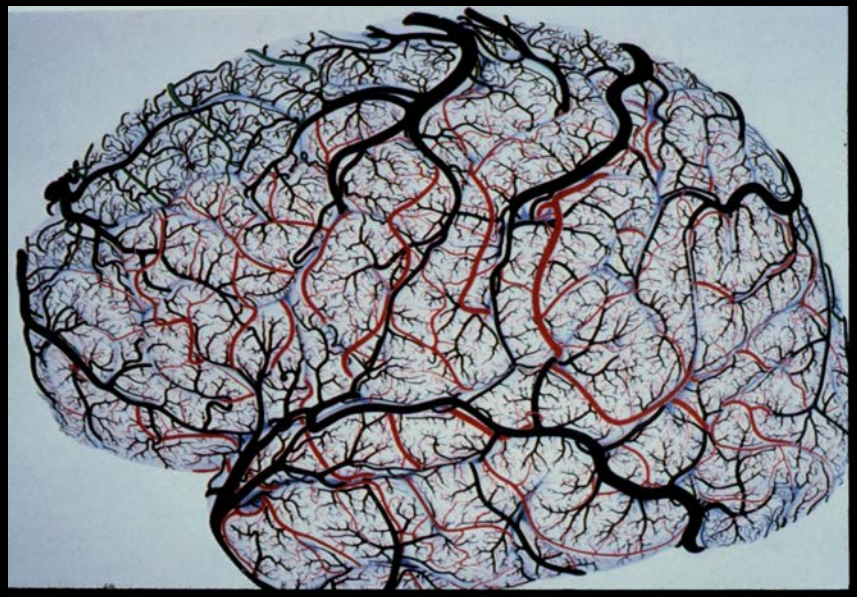
A Primary Challenge:

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



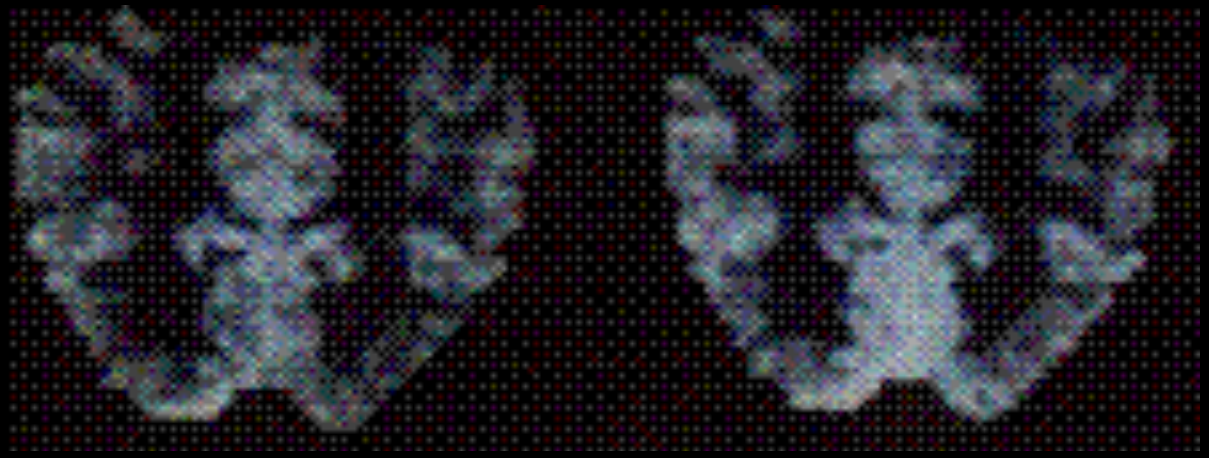


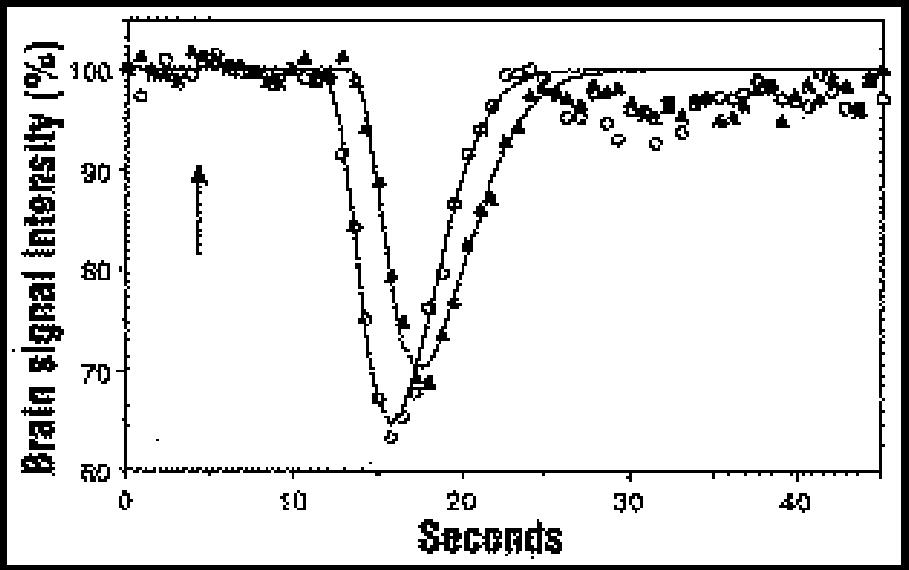
Contrast in Functional MRI

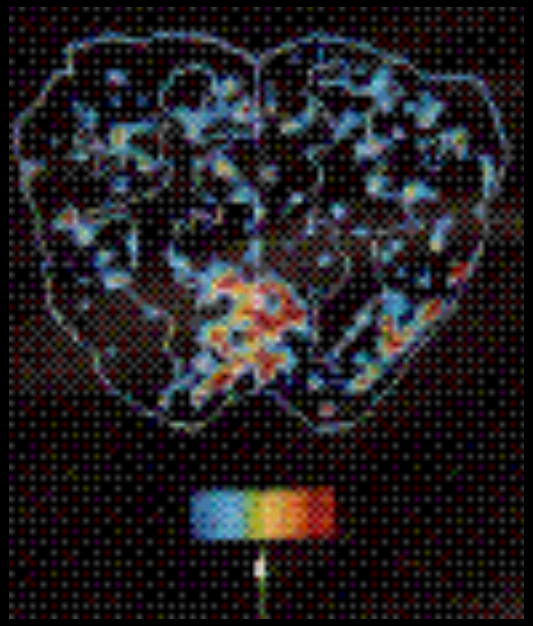
- **Blood Volume**
  - Contrast agent injection and time series collection of T2* or T2 - weighted images
- **BOLD**
  - Time series collection of T2* or T2 - weighted images
- **Perfusion**
  - T1 weighting
  - Arterial spin labeling
- **$CMRO_2$**
  - BOLD and Perfusion w/

  Normalization to Global Perfusion Change

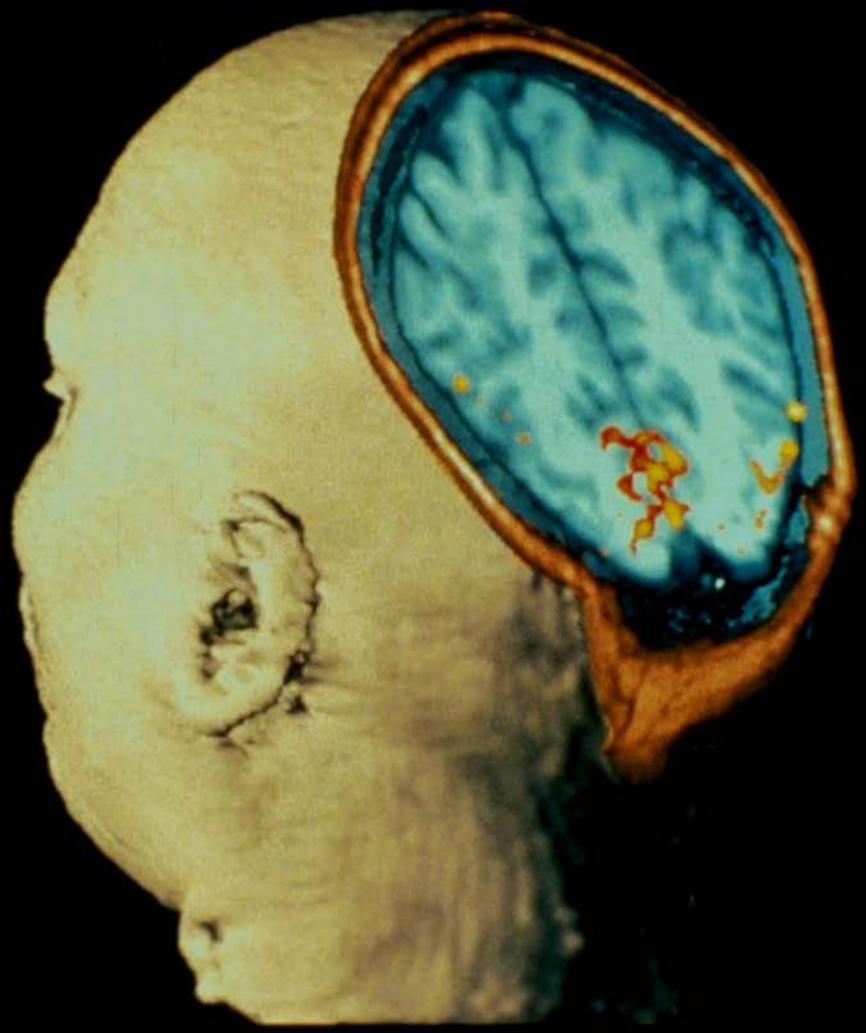
Resting Active







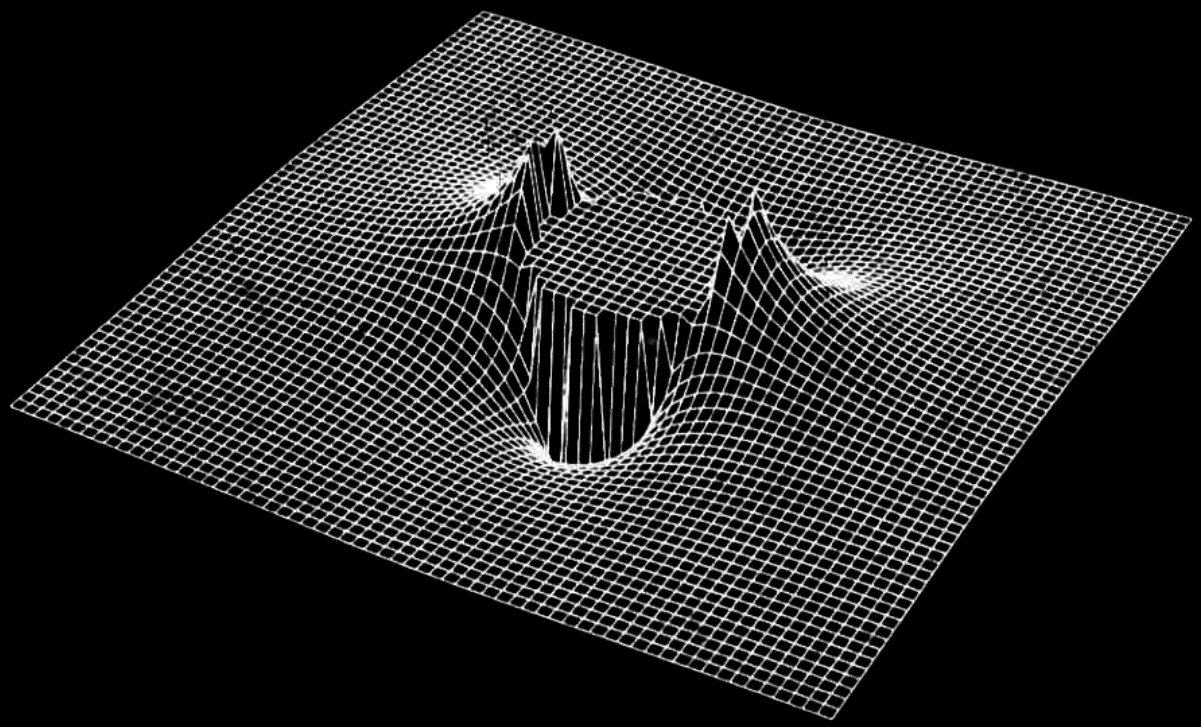
Photic Stimulation



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

↓

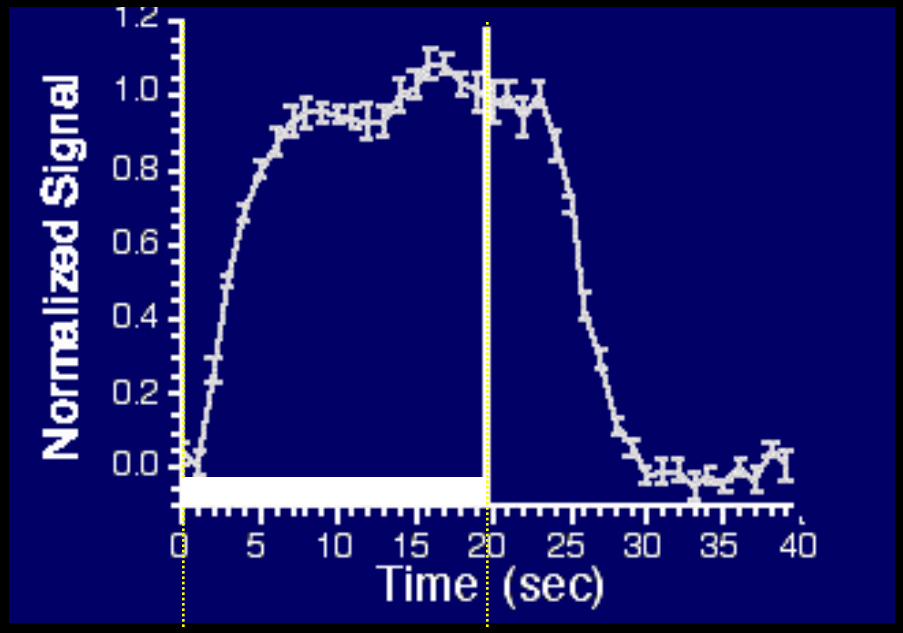
Decrease in susceptibility-related intravoxel dephasing → Increase in T2 and T2*

↓

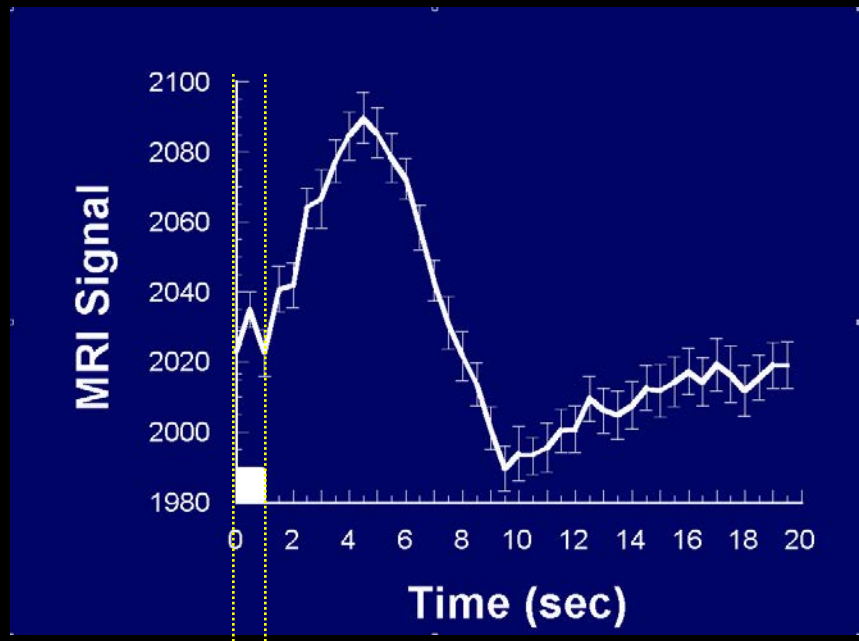
Local Signal Increase in T2 and T2* - weighted sequences

The BOLD Signal

Blood Oxygenation Level Dependent (BOLD) signal changes



task

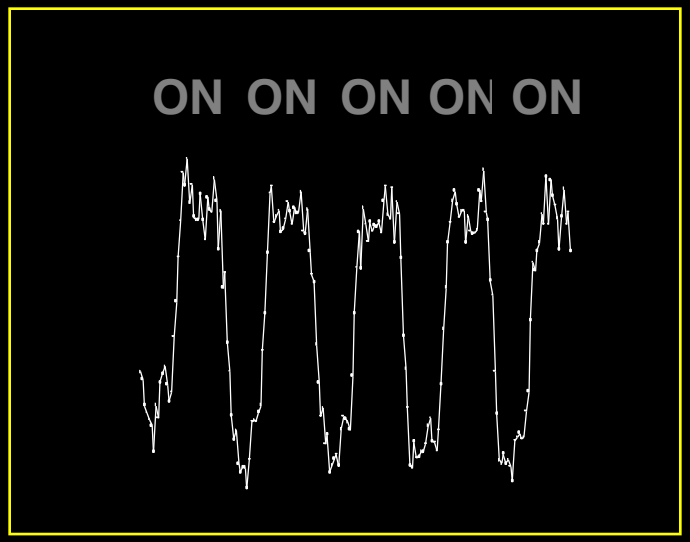


task

Alternating Left and Right Finger Tapping

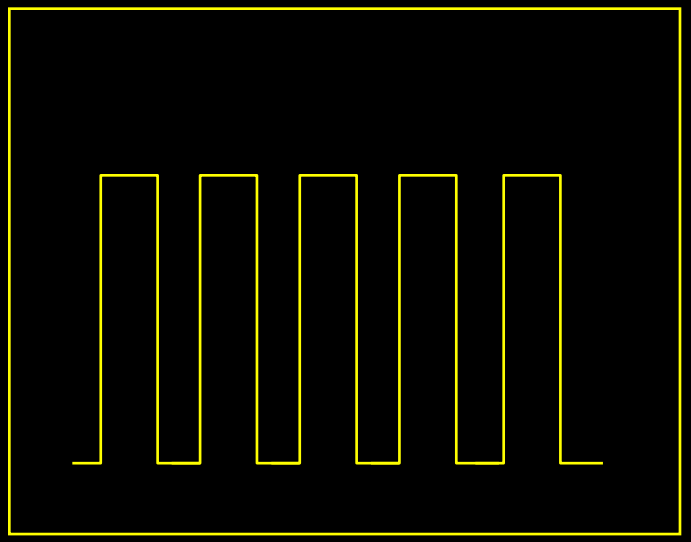
~ 1992

Creating a Functional Image



Signal Time Course

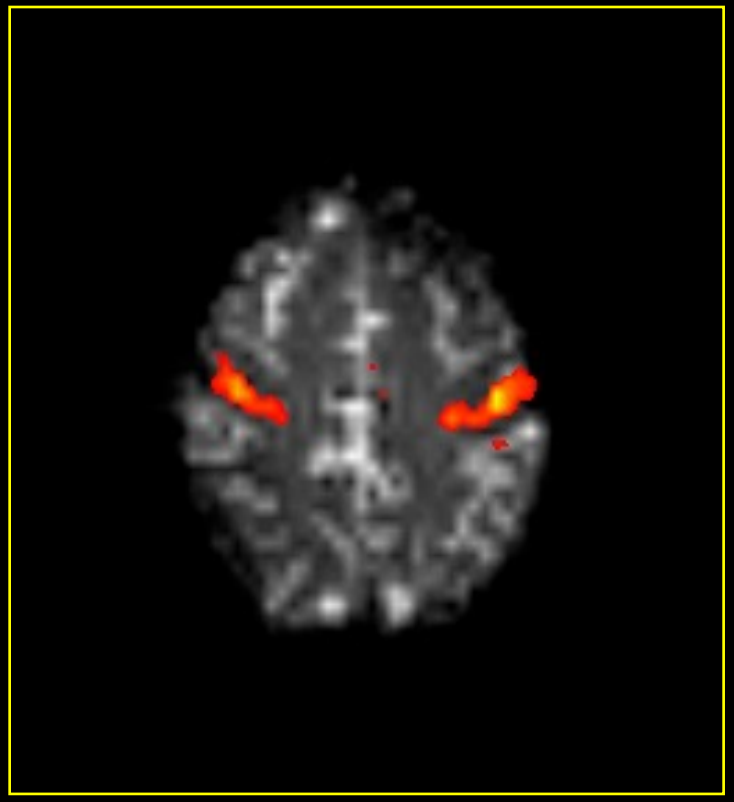
X



Reference Function

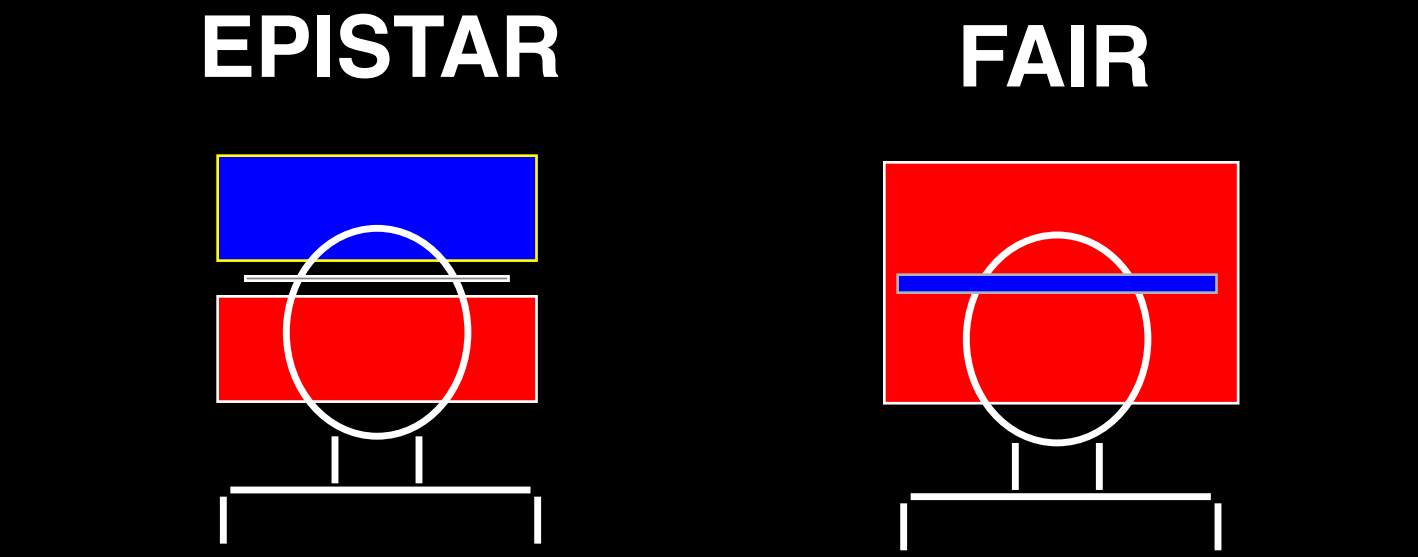
=

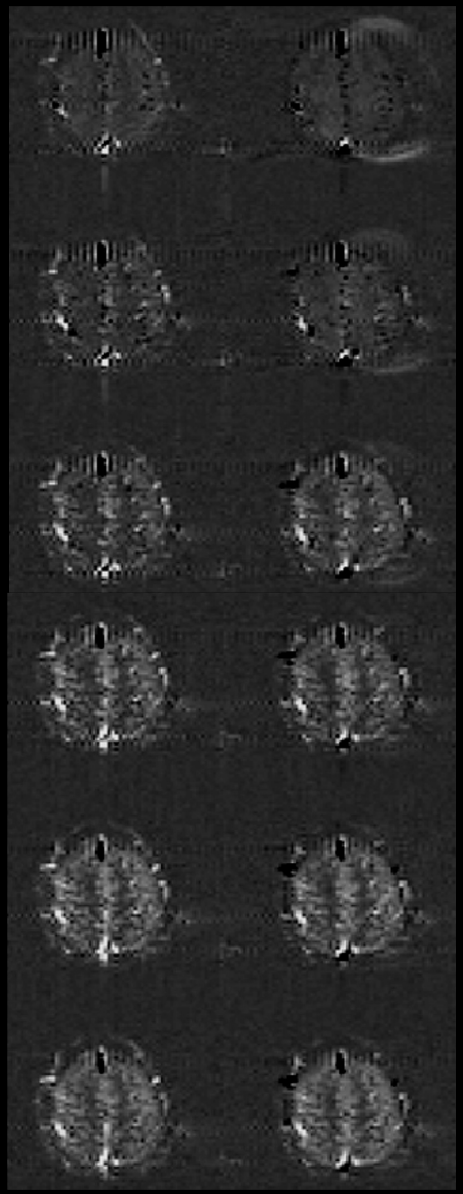
Cross Correlation Image



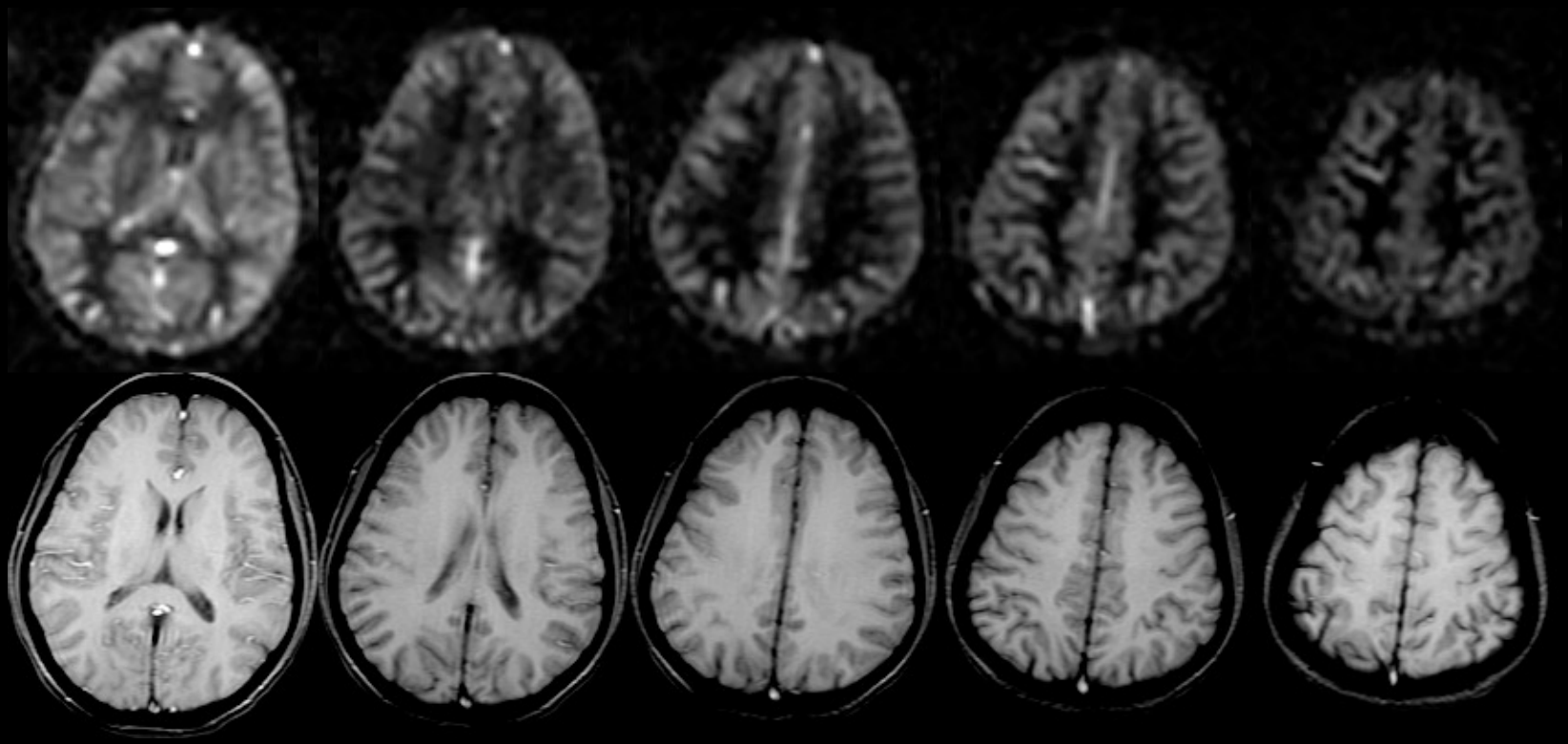
Cross Correlation Image
Anatomical Image

Perfusion / Flow Imaging

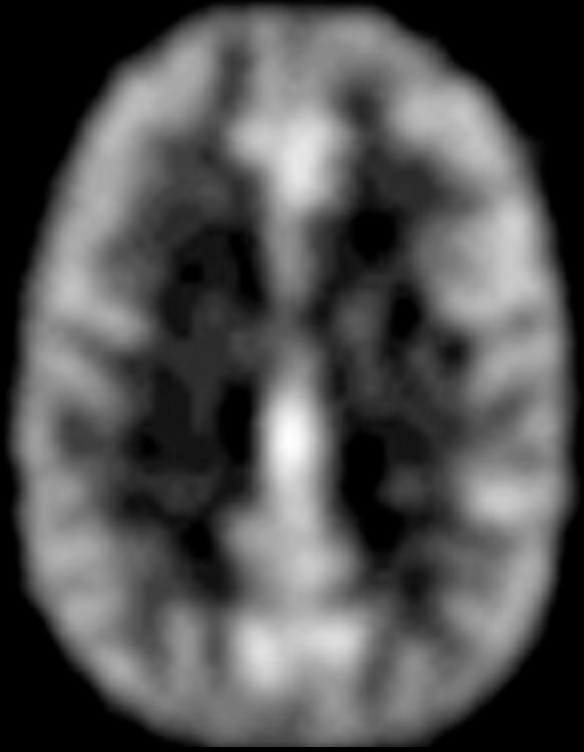


TI (ms)	FAIR	EPISTAR
200		
400		
600		
800		
1000		
1200		

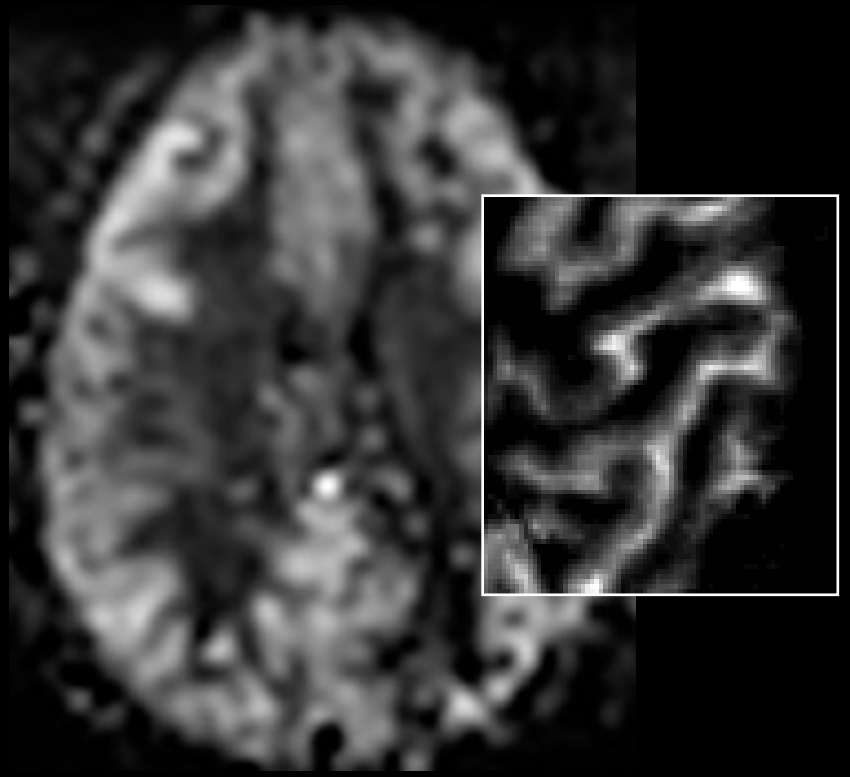
Resting ASL Signal



Comparison with Positron Emission Tomography



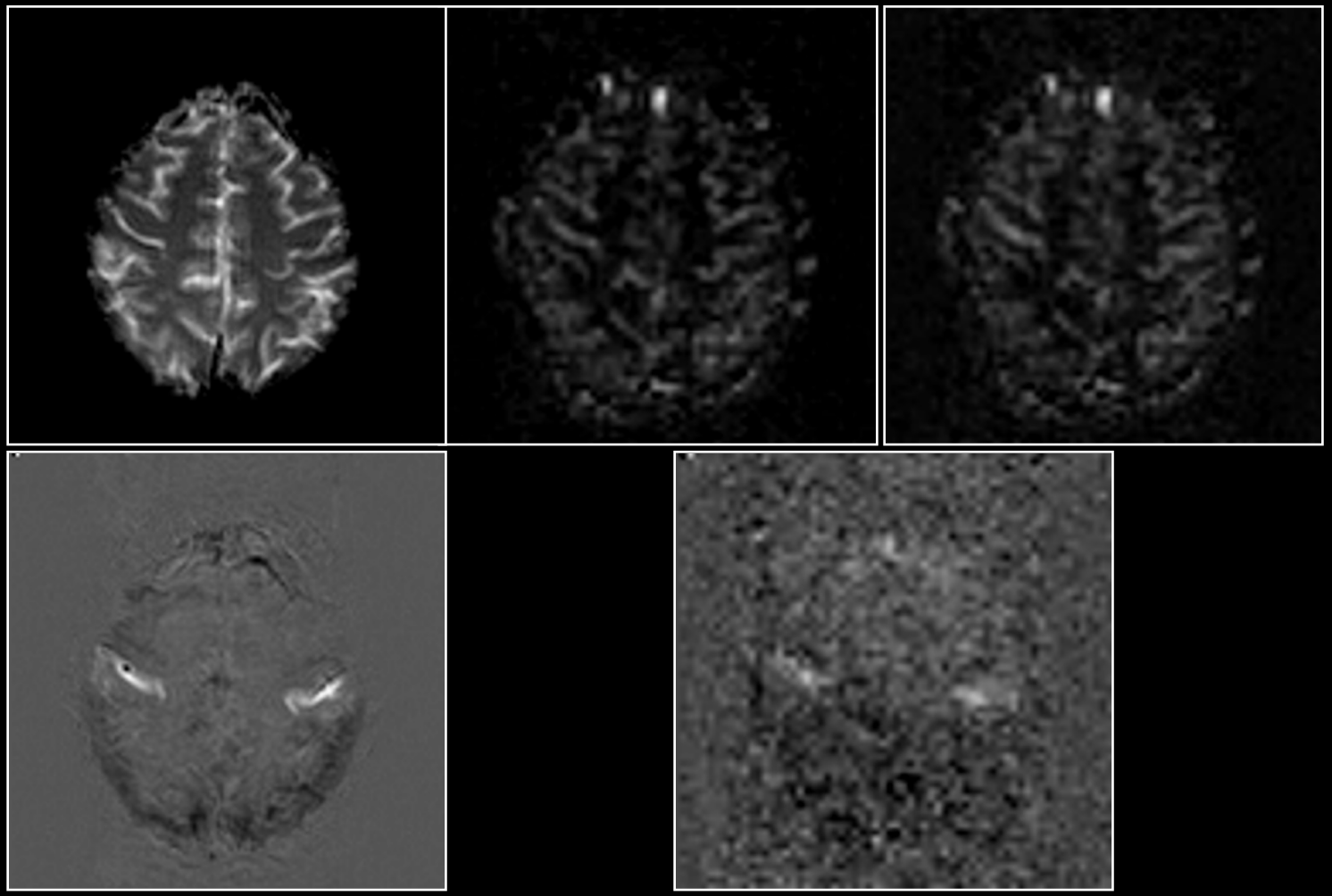
PET: $H_2{}^{15}O$



MRI: ASL

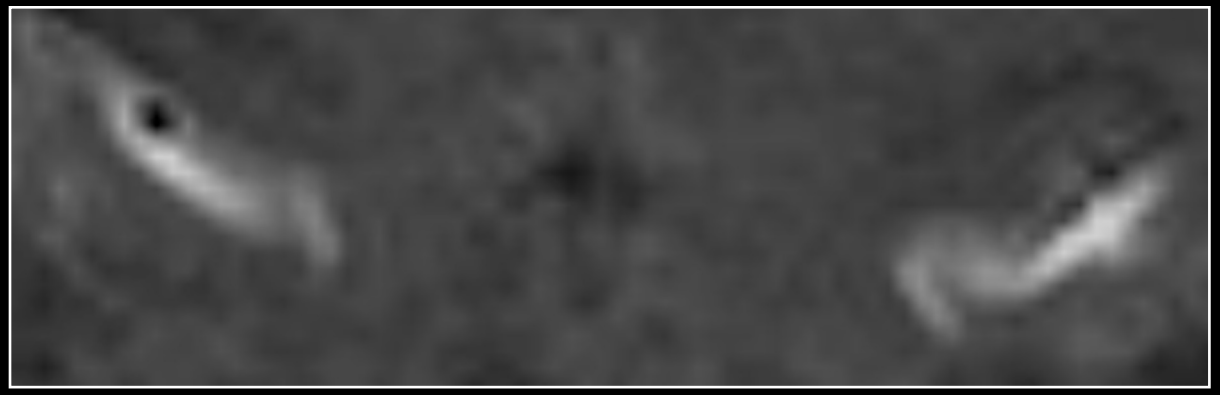
Perfusion

BOLD *Rest* *Activation*



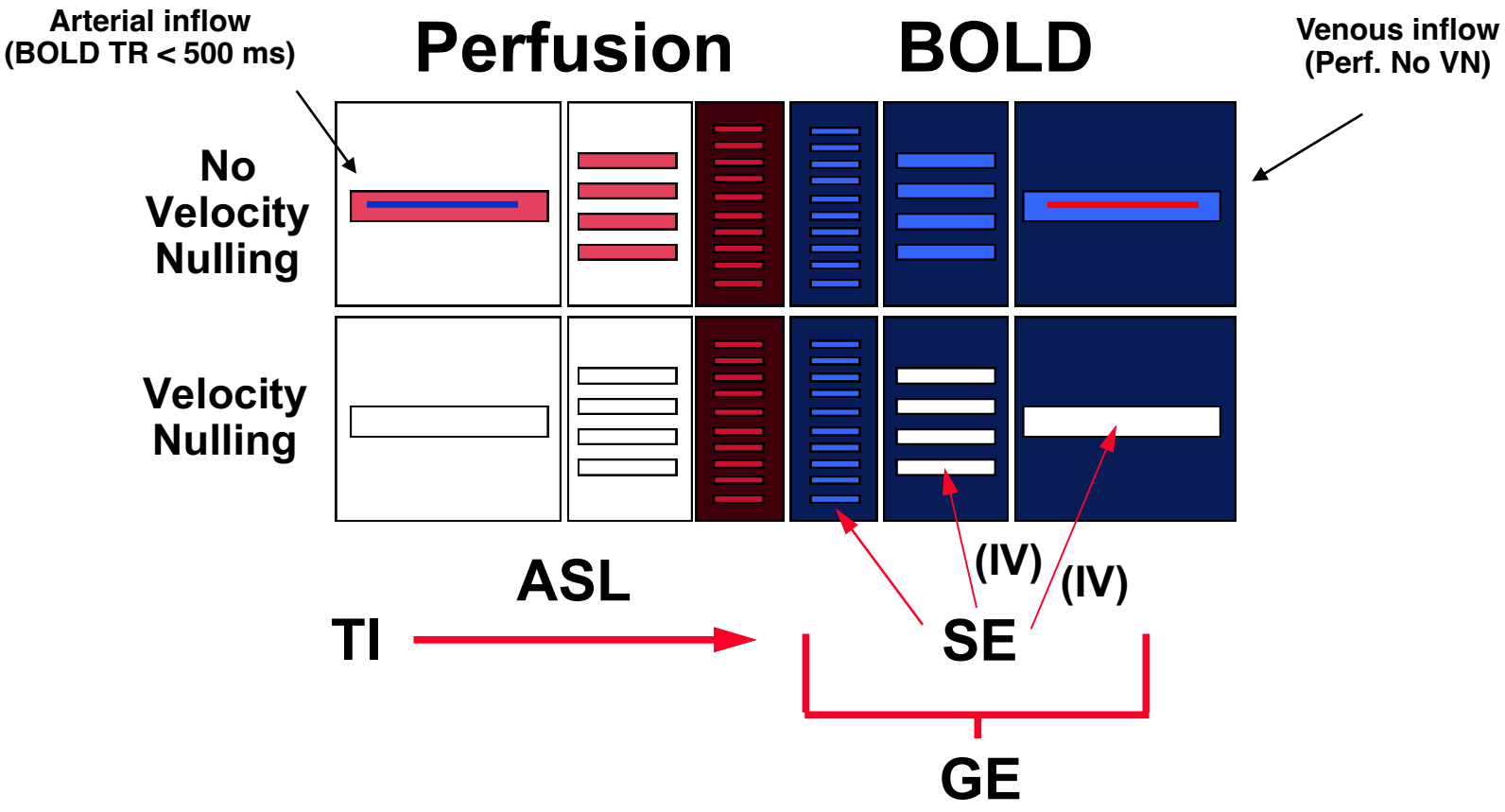
Anatomy

BOLD

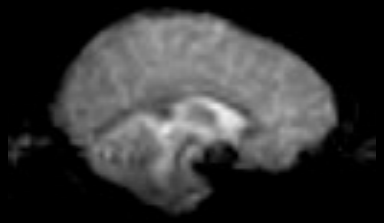


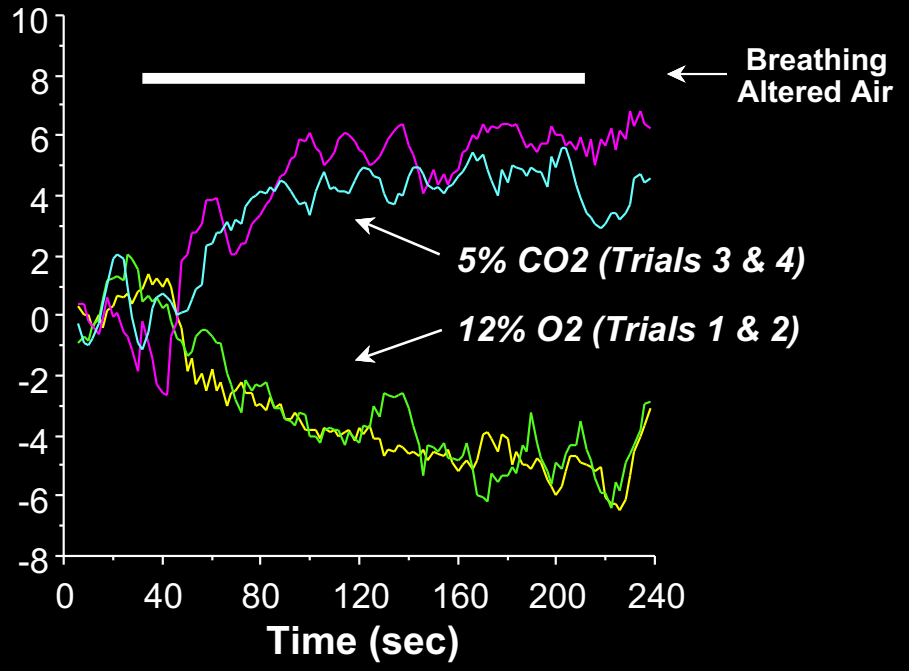
Perfusion

Hemodynamic Specificity

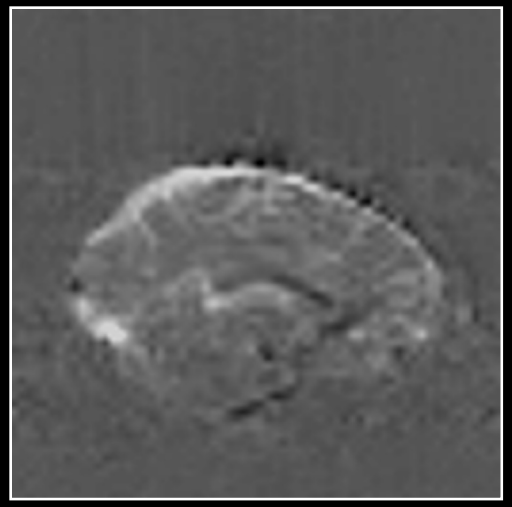


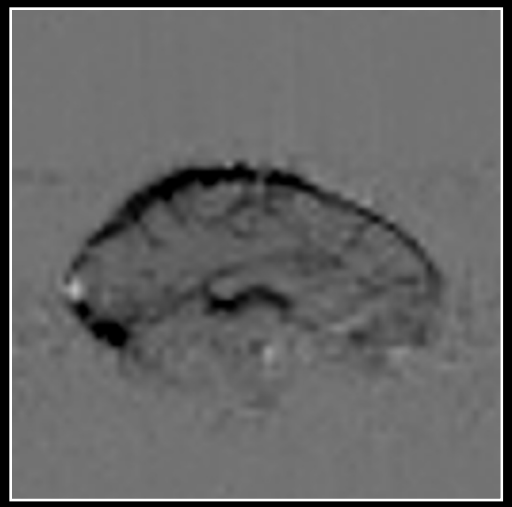
Hemdodynamic Stress Calibration





5% CO2

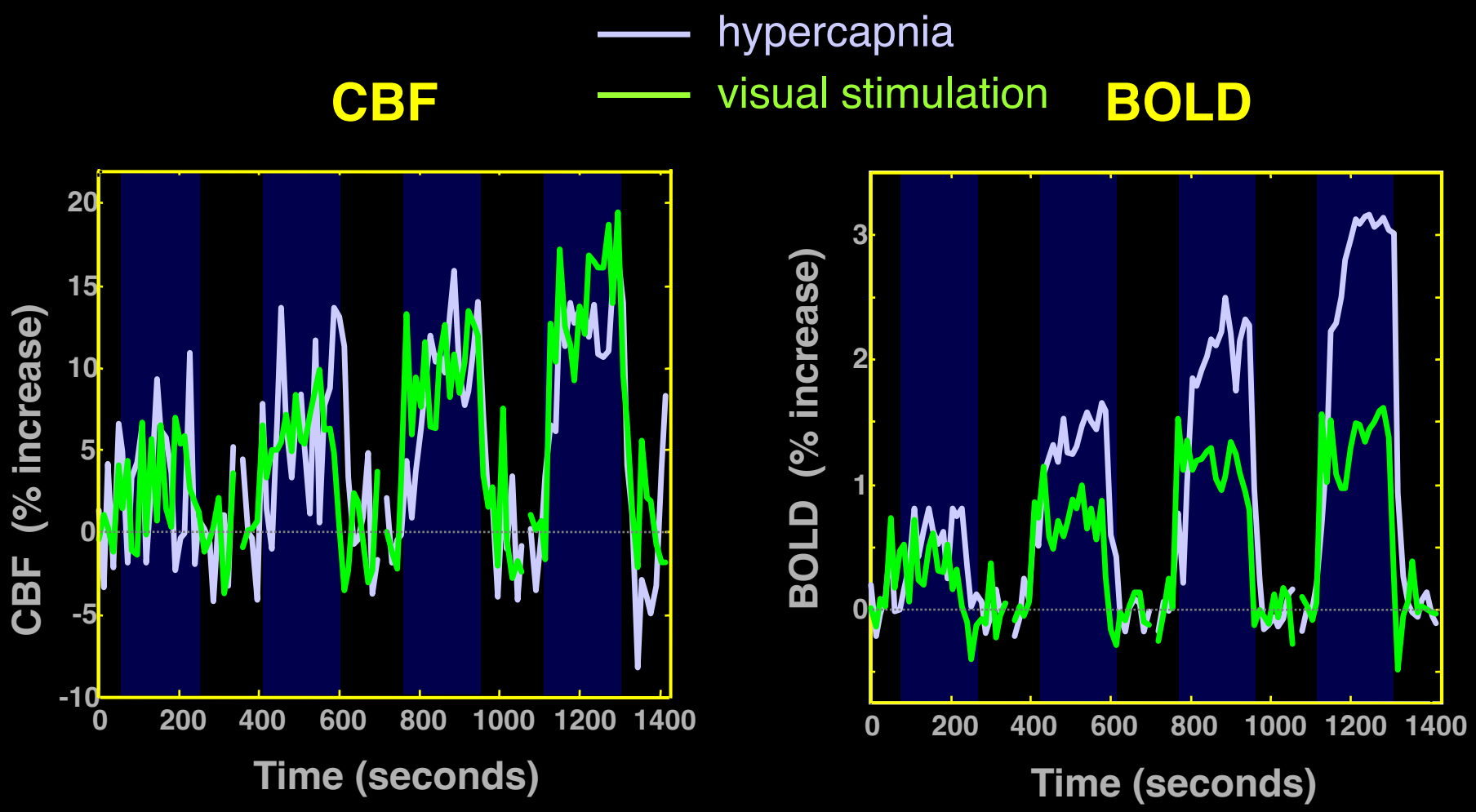




12% O2

$CMRO_2$-related BOLD signal deficit:

Hoge, et al.

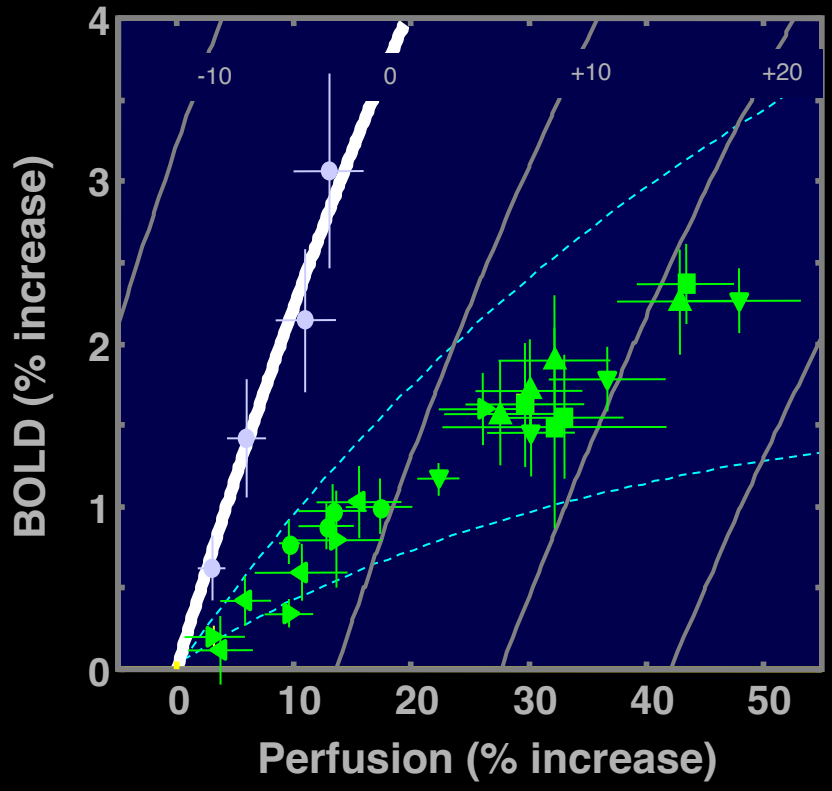


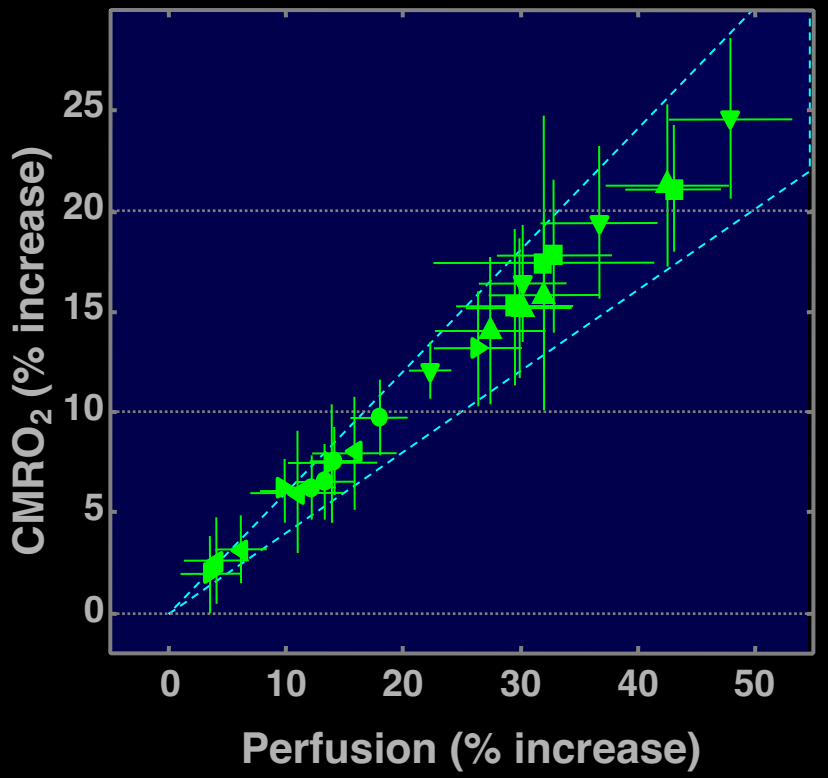
Simultaneous Perfusion and BOLD imaging during graded visual activation and hypercapnia

N=12

CBF-$CMRO_2$ coupling

Hoge, et al.

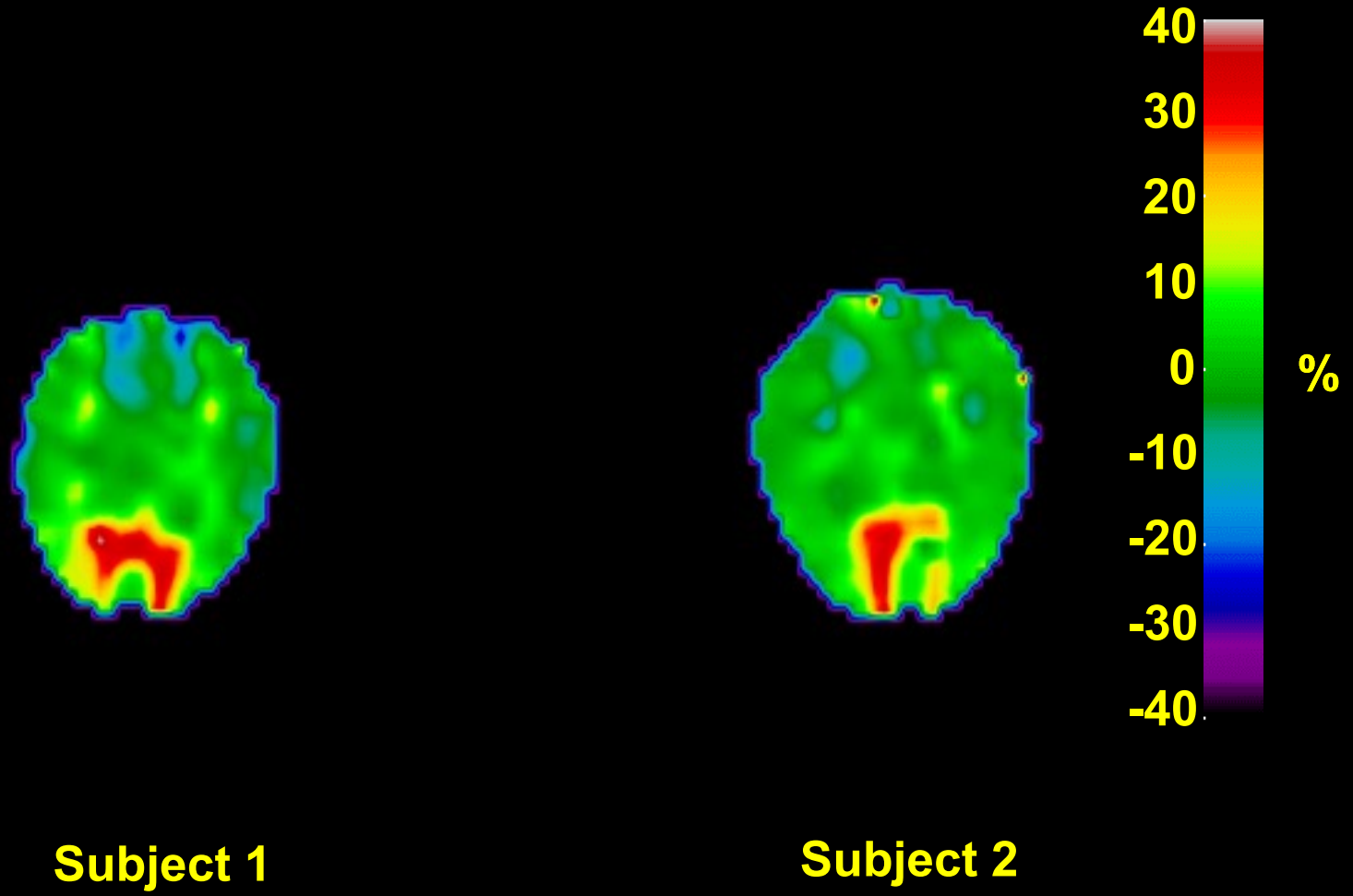




Characterizing Activation-induced $CMRO_2$ changes using calibration with hypercapnia

Hoge, et al.

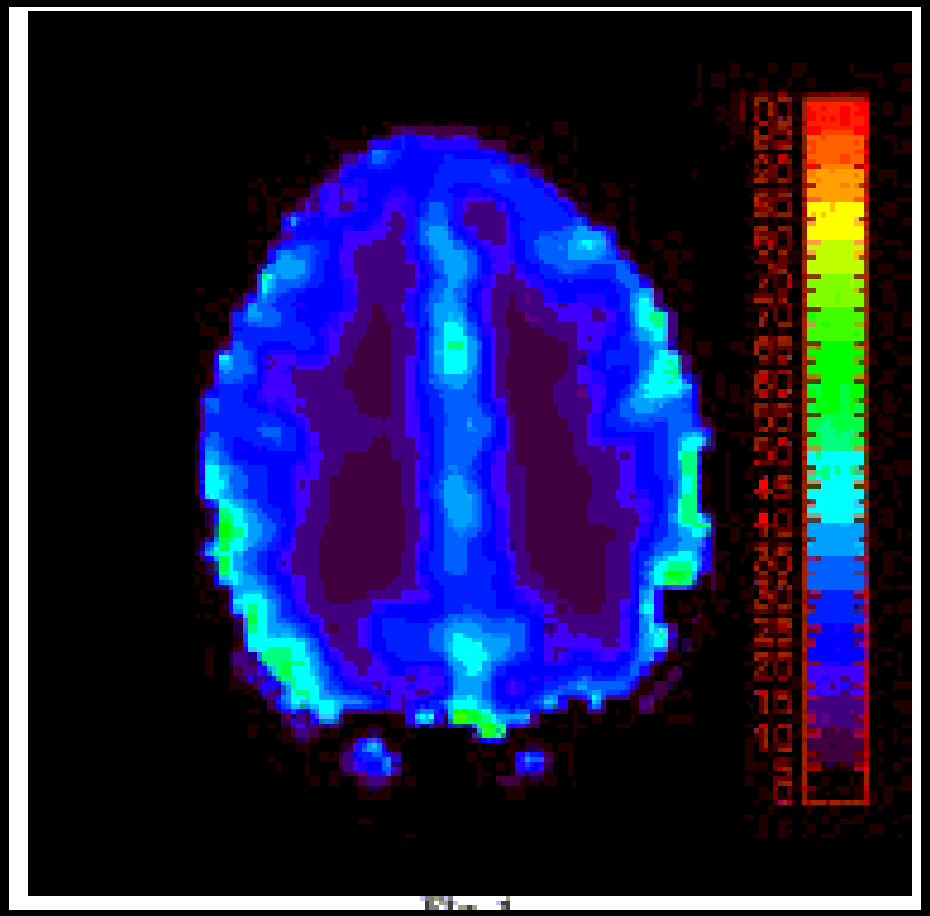
Computed $CMRO_2$ changes



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, ;



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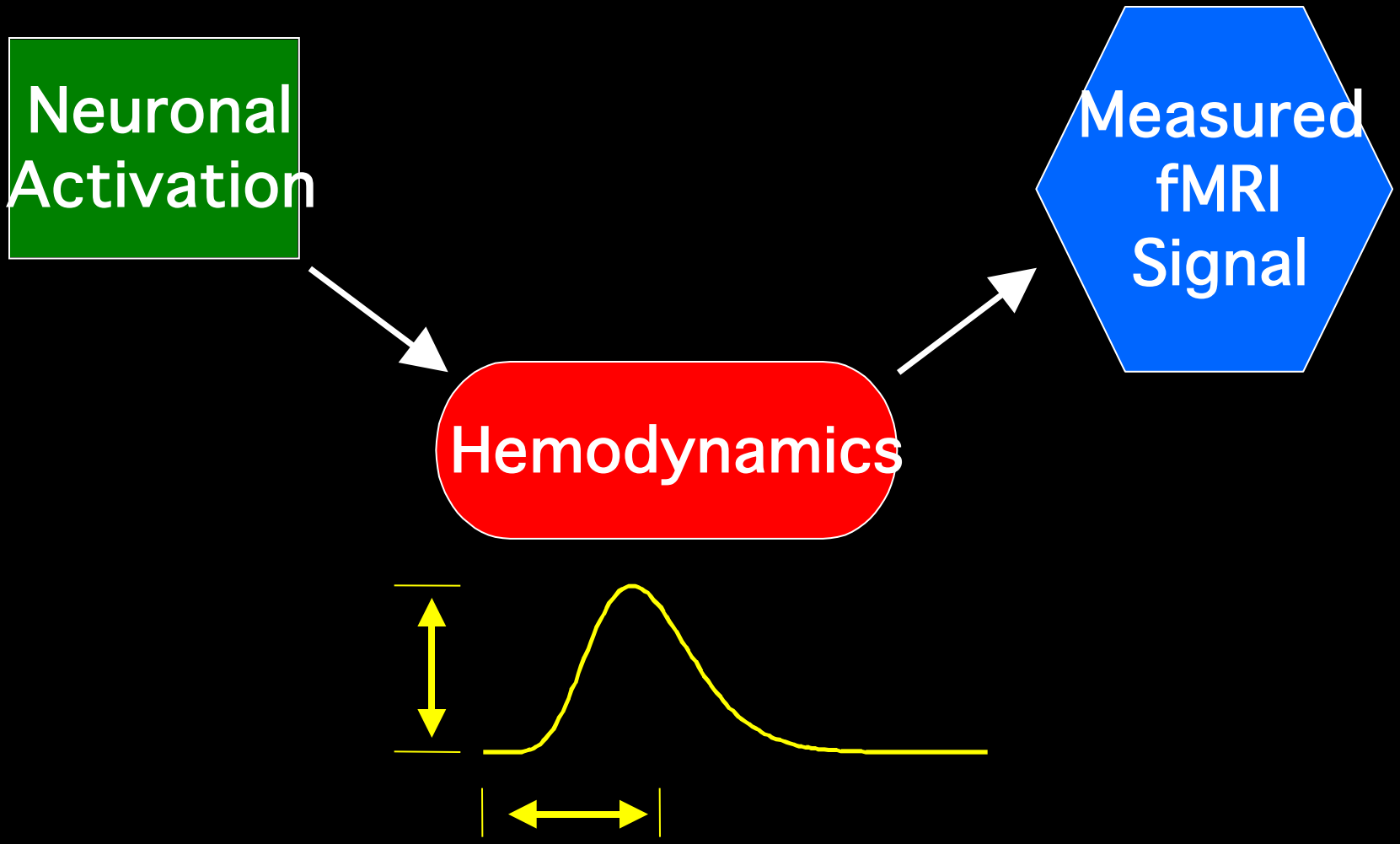
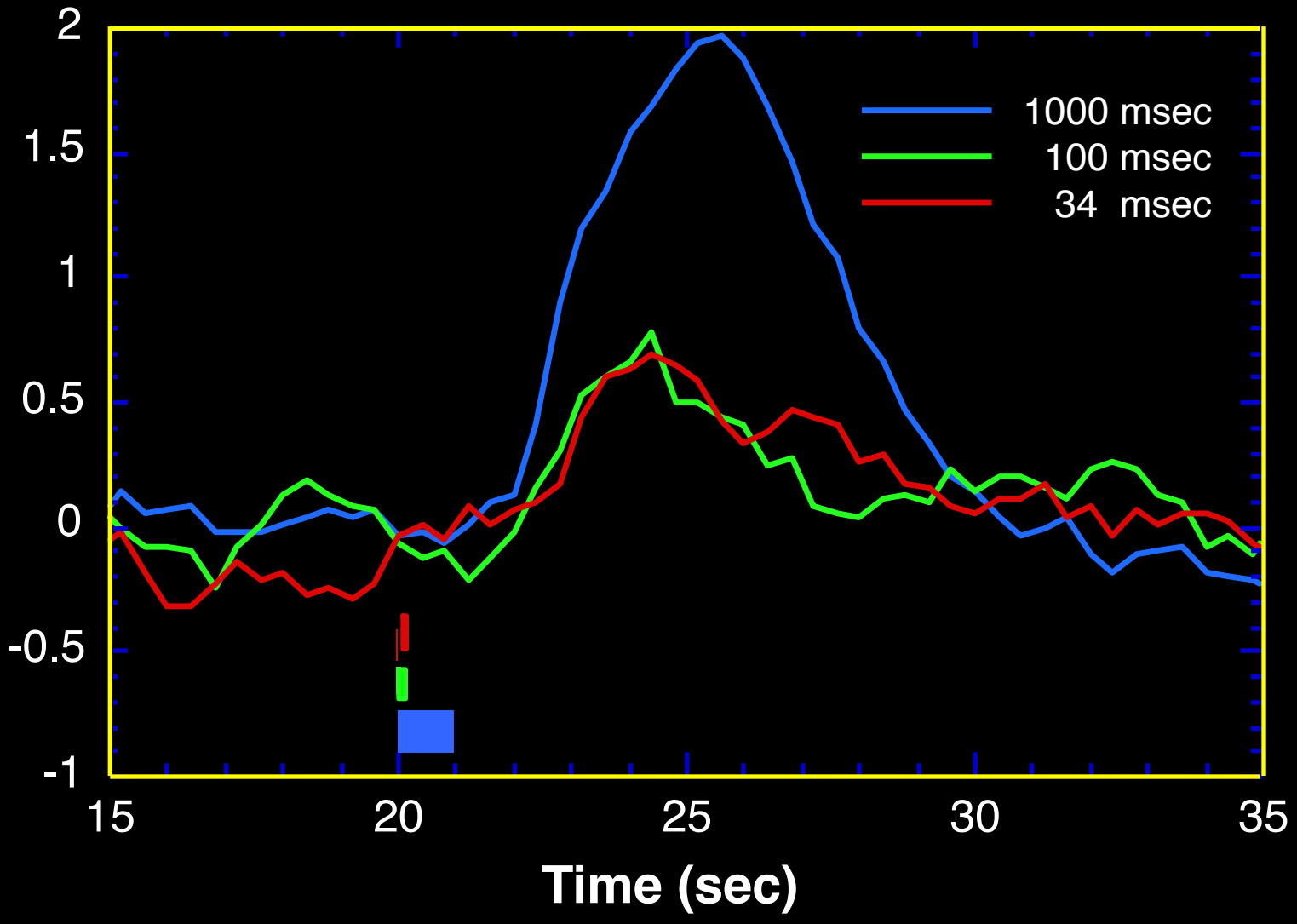
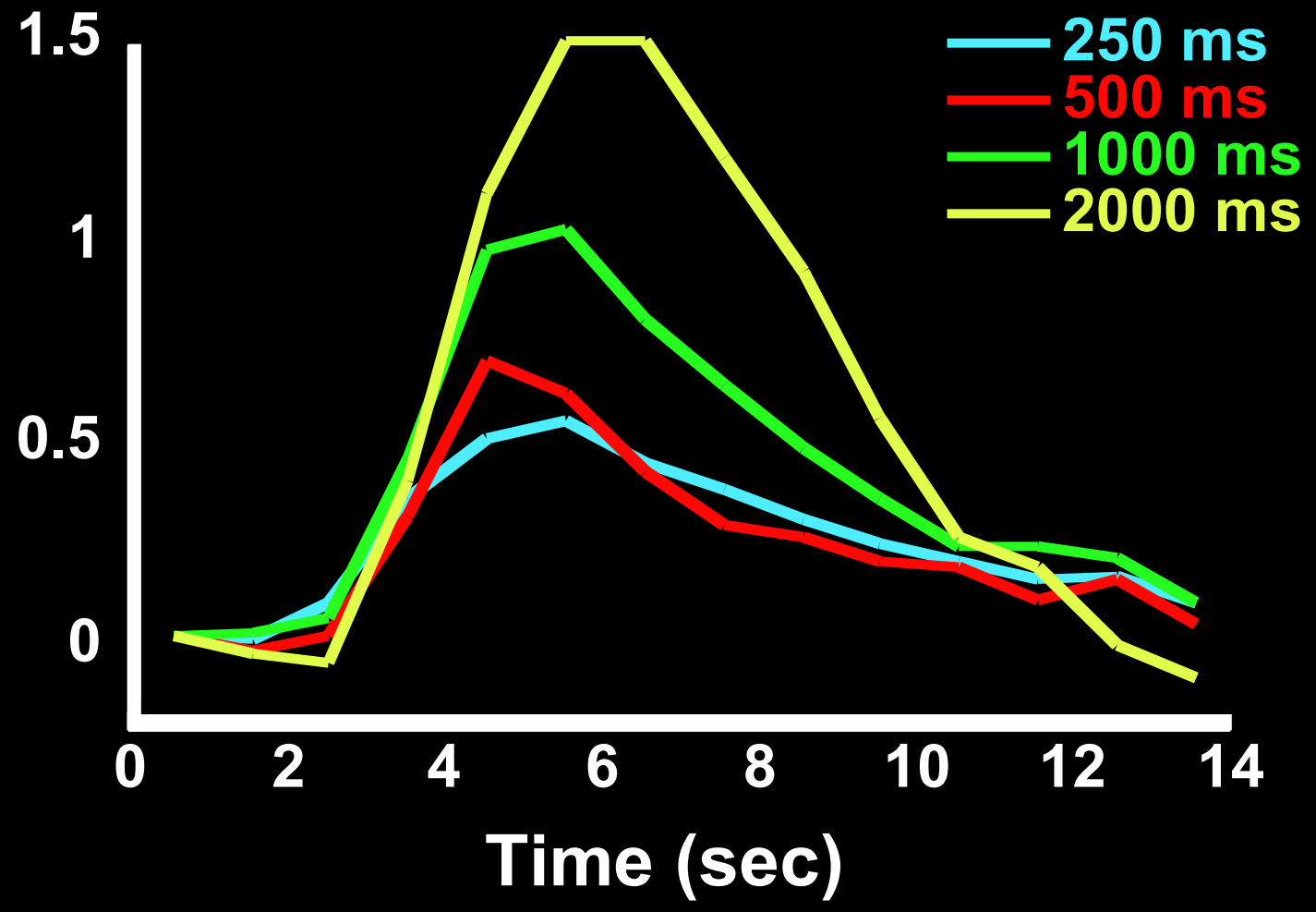
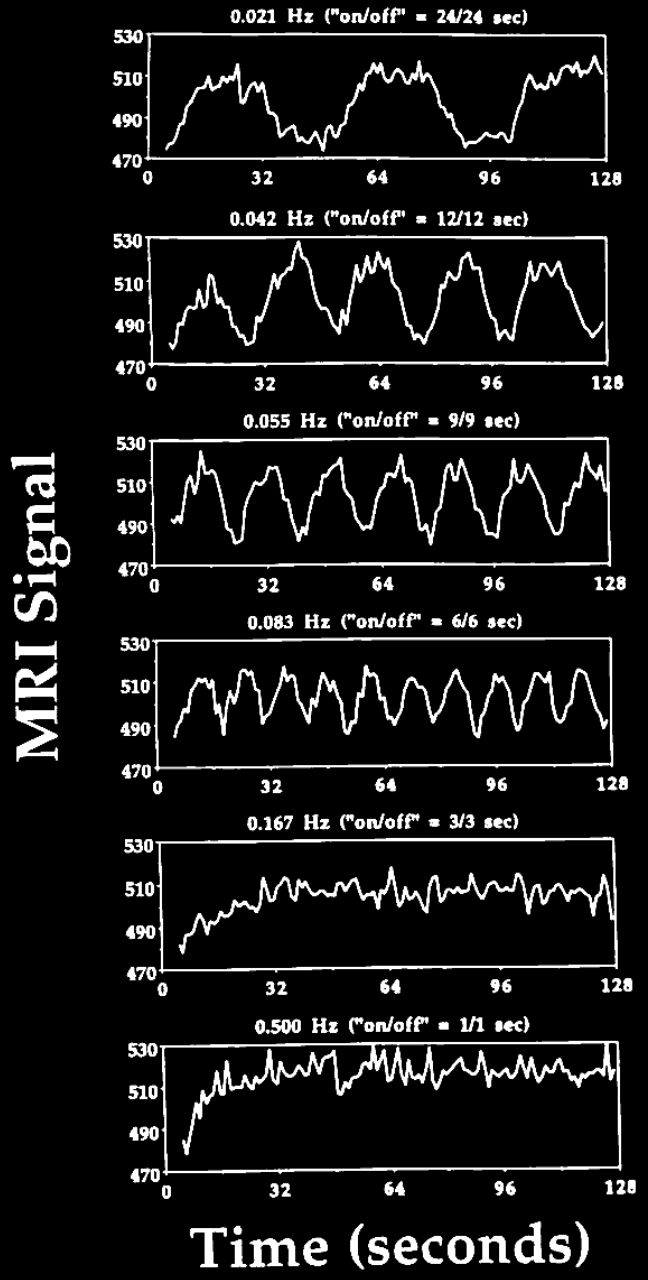
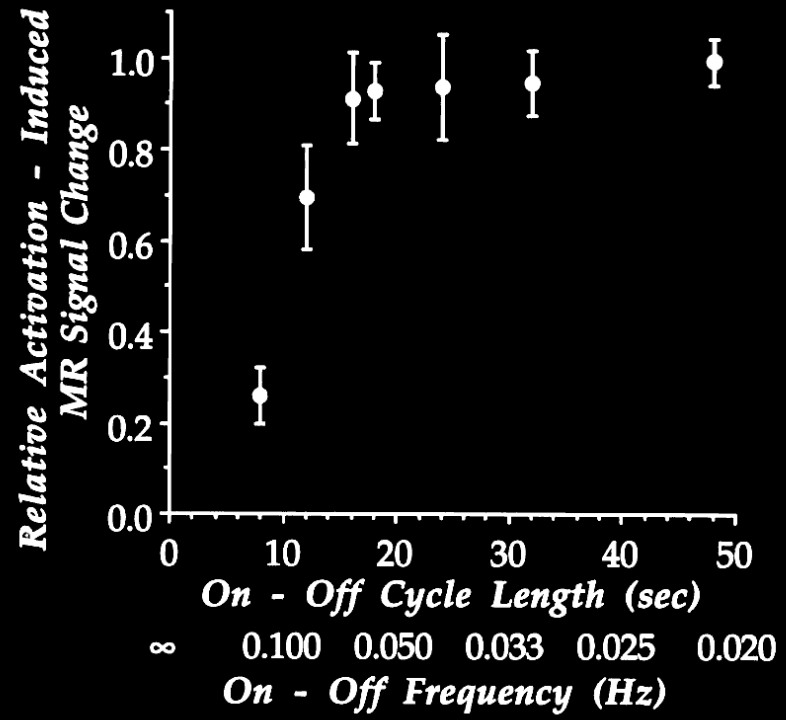
Hemodynamic Transfer Function



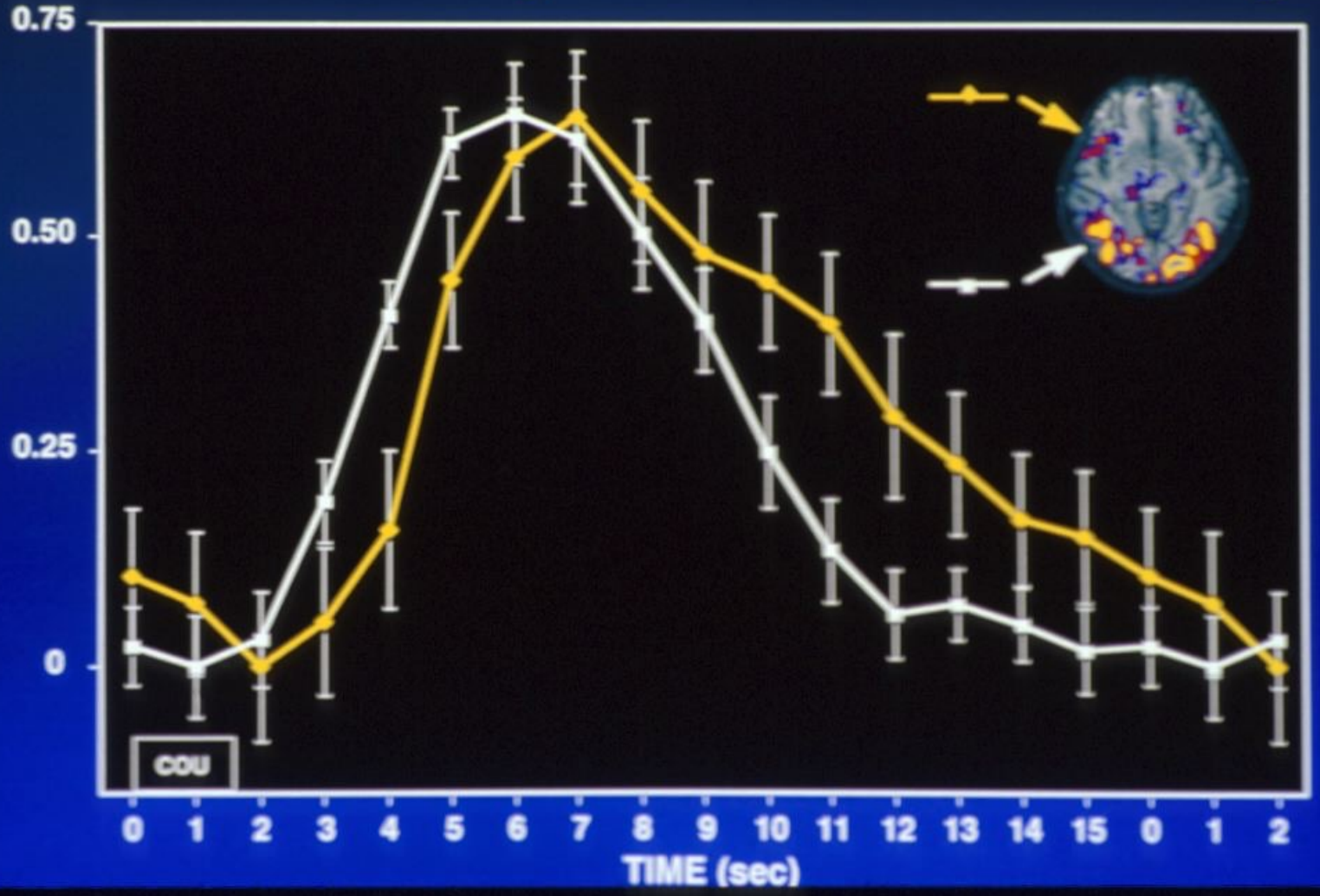

2
1.5
1
0.5
0
-0.5
-1
15
20
25
30
35
Time (sec)
1000 msec
100 msec
34 msec


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


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)

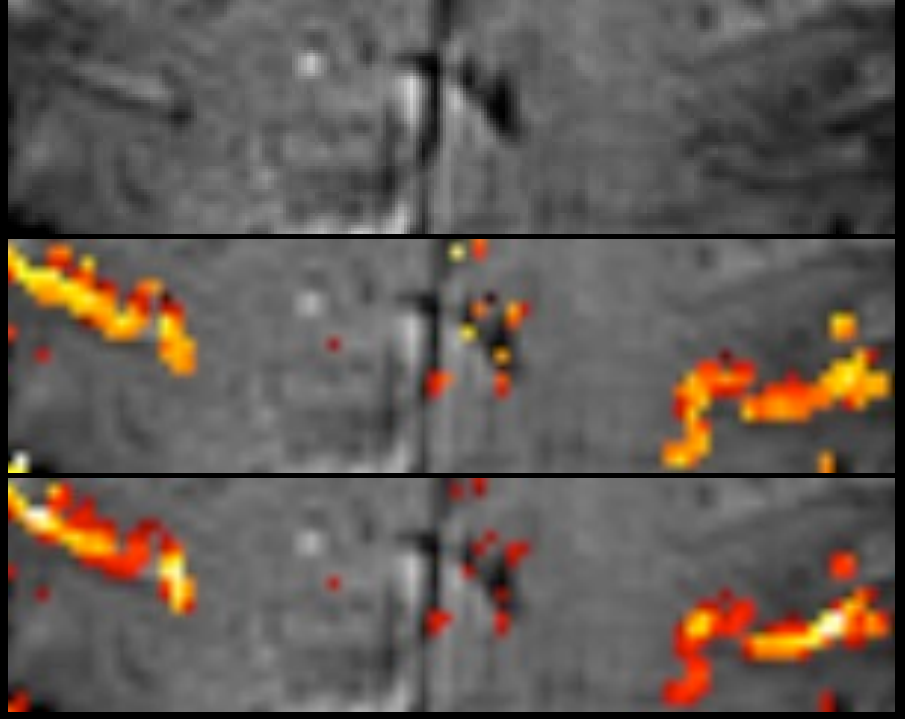

Relative Activation - Induced MR Signal Change
1.0
0.8
0.6
0.4
0.2
0.0
0
10
20
30
40
50
On - Off Cycle Length (sec)
∞
0.100
0.050
0.033
0.025
0.020
On - Off Frequency (Hz)

Time Course Comparison Across Brain Regions



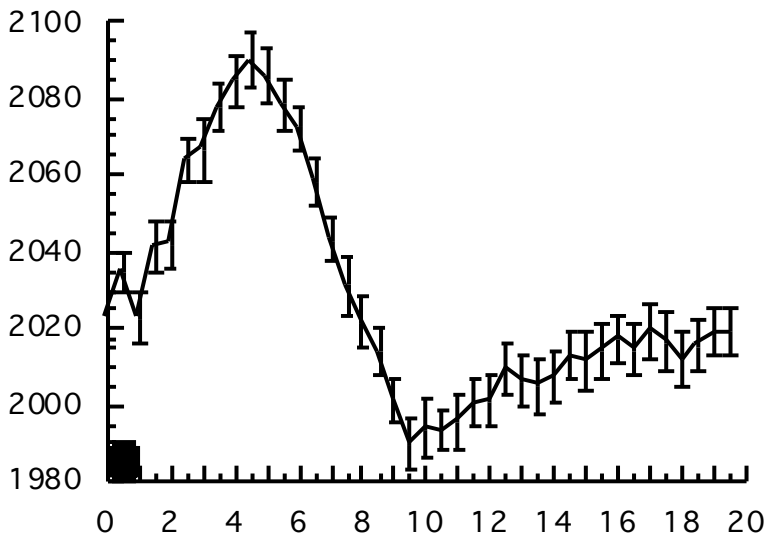
Latency

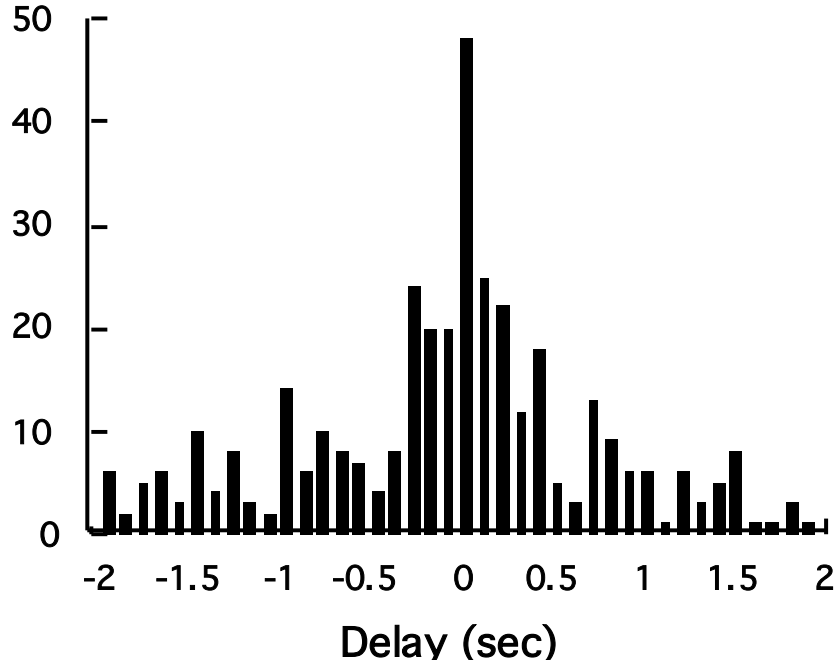
Magnitude



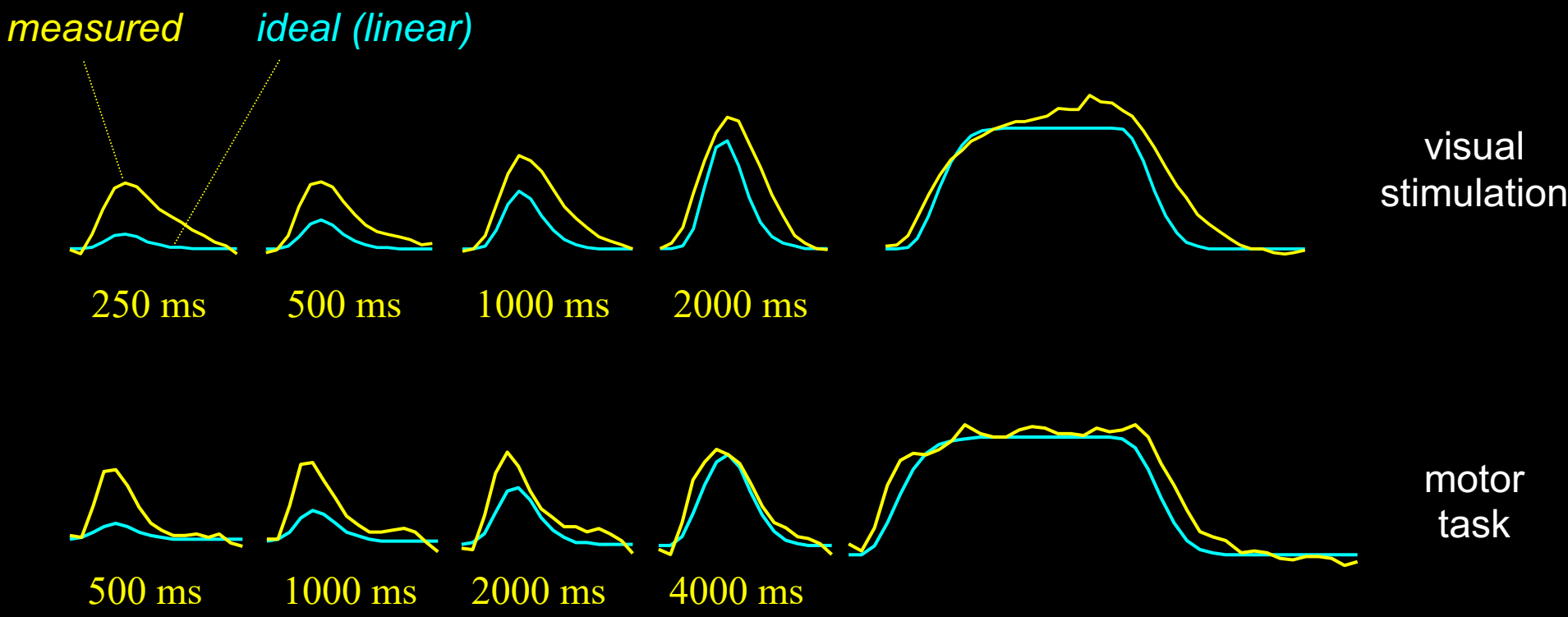
+ 2 sec

- 2 sec

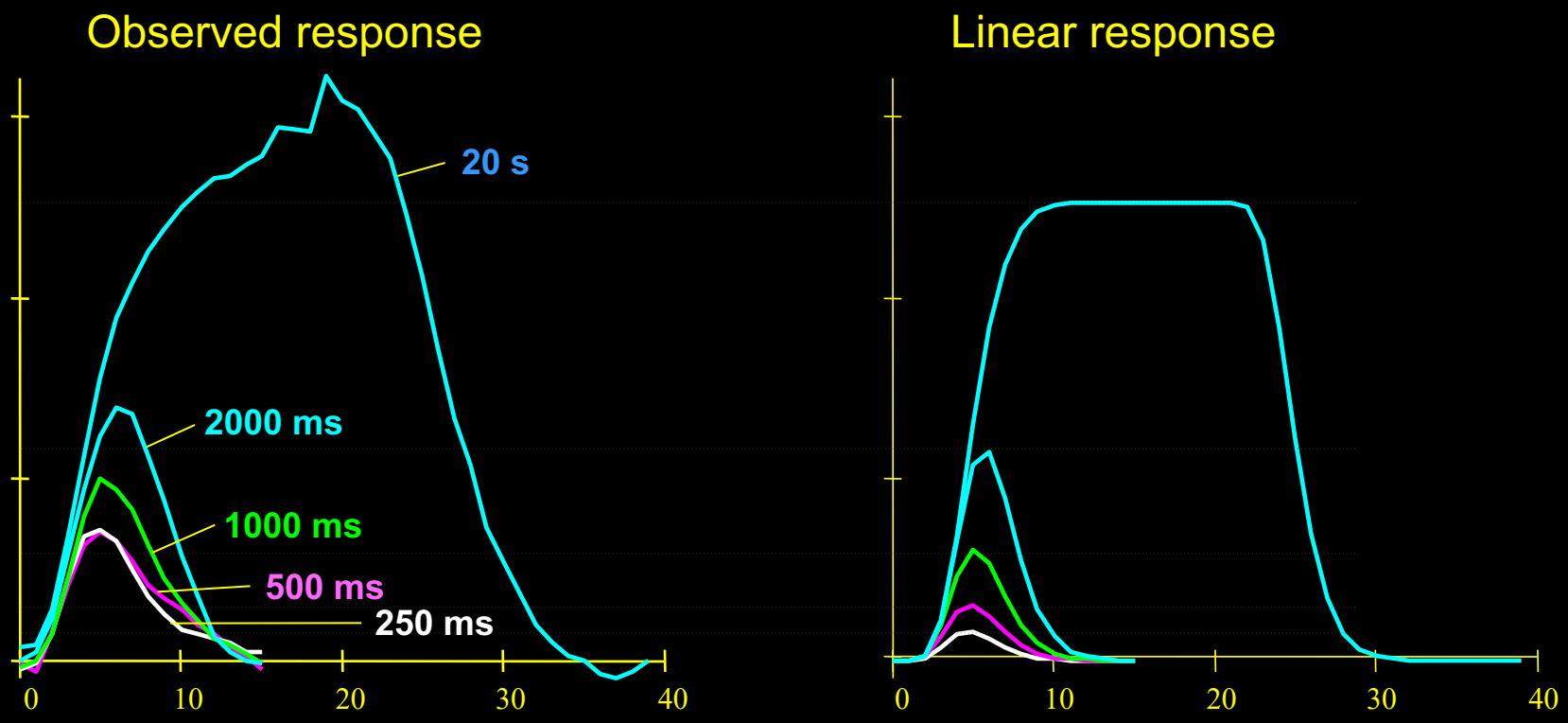




Observed Responses

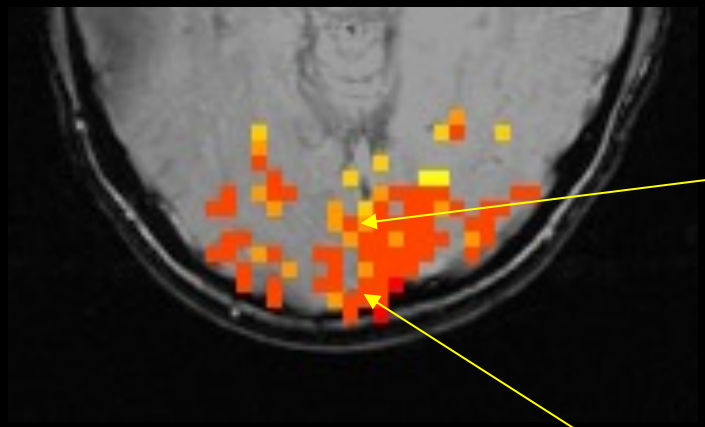


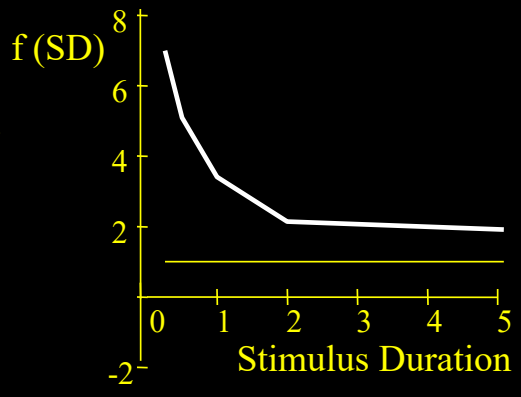
BOLD response is nonlinear

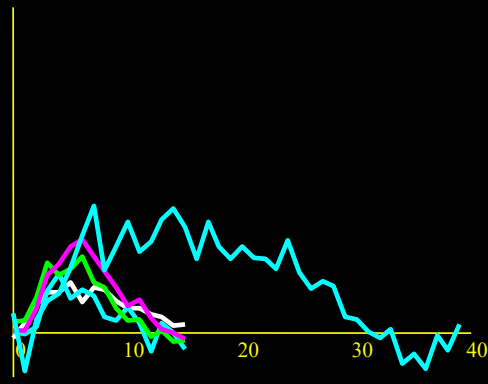


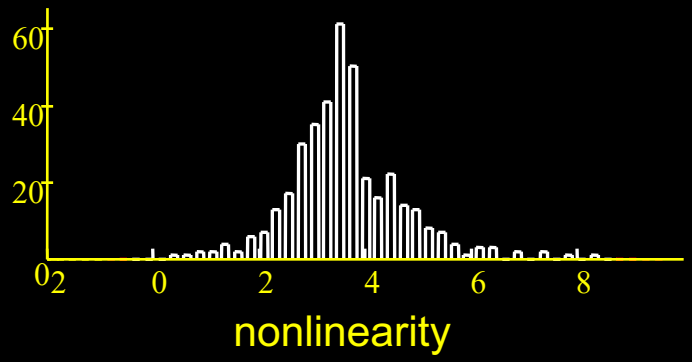
Short duration stimuli produce larger responses than expected

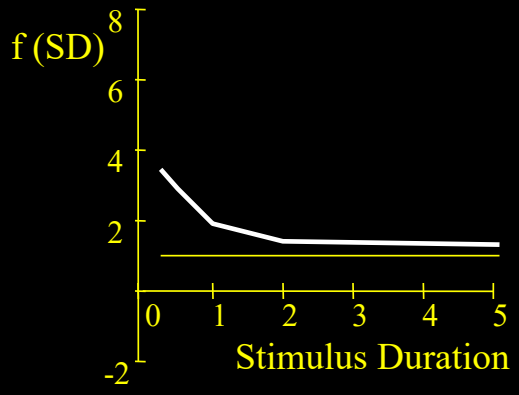
Results – visual task

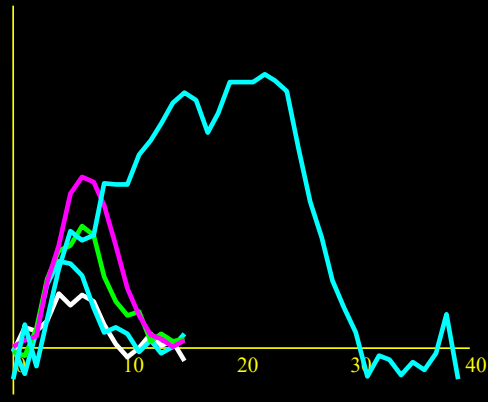






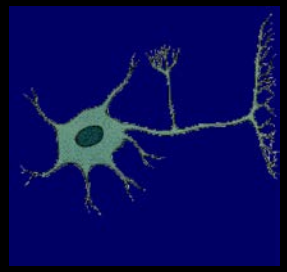


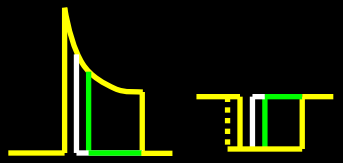




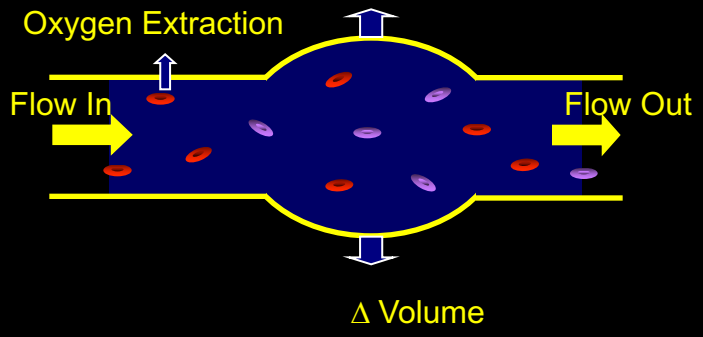
Sources of this Nonlinearity

- Neuronal

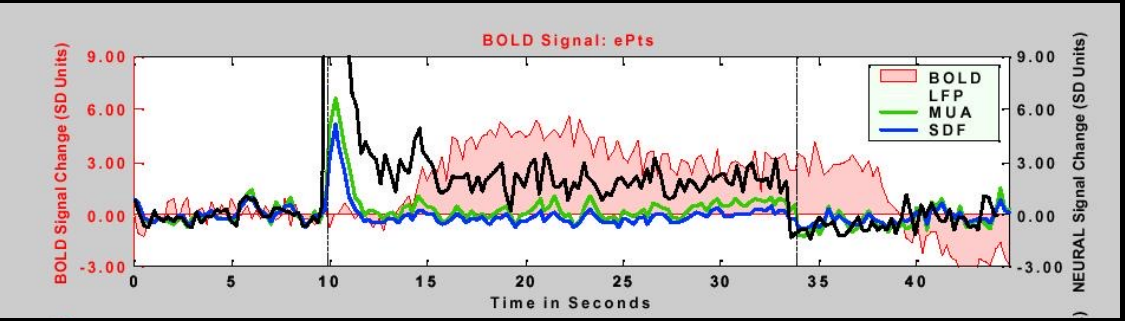




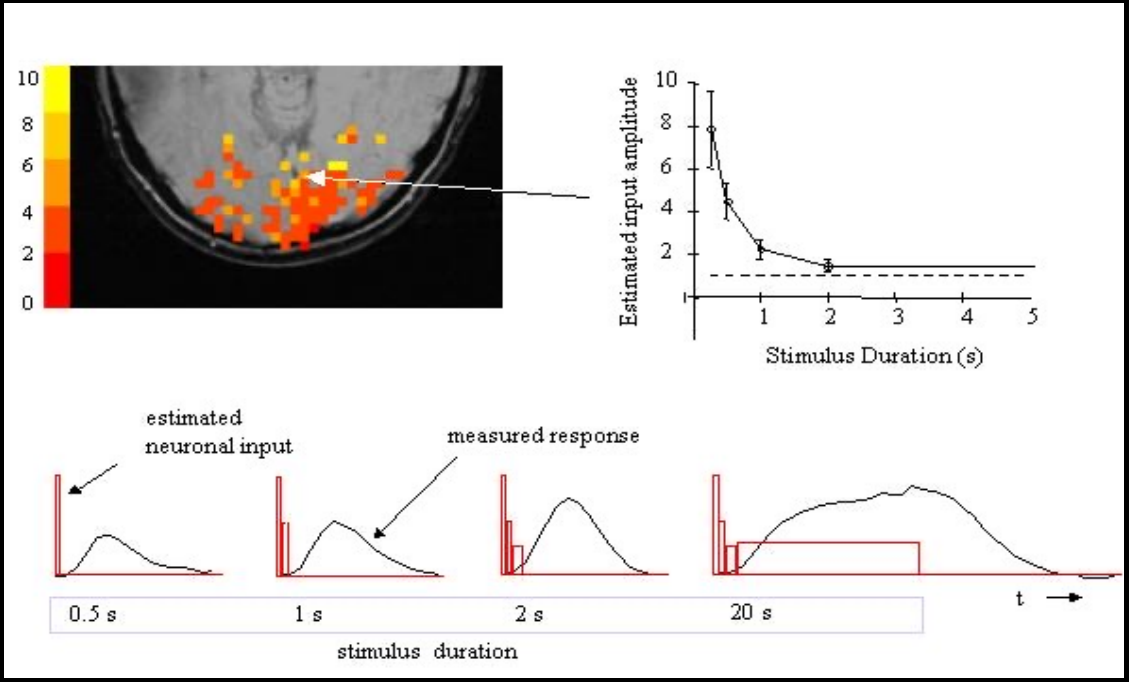
- Hemodynamic
  - Oxygen extraction
  - Blood volume dynamics



BOLD Correlation with Neuronal Activity

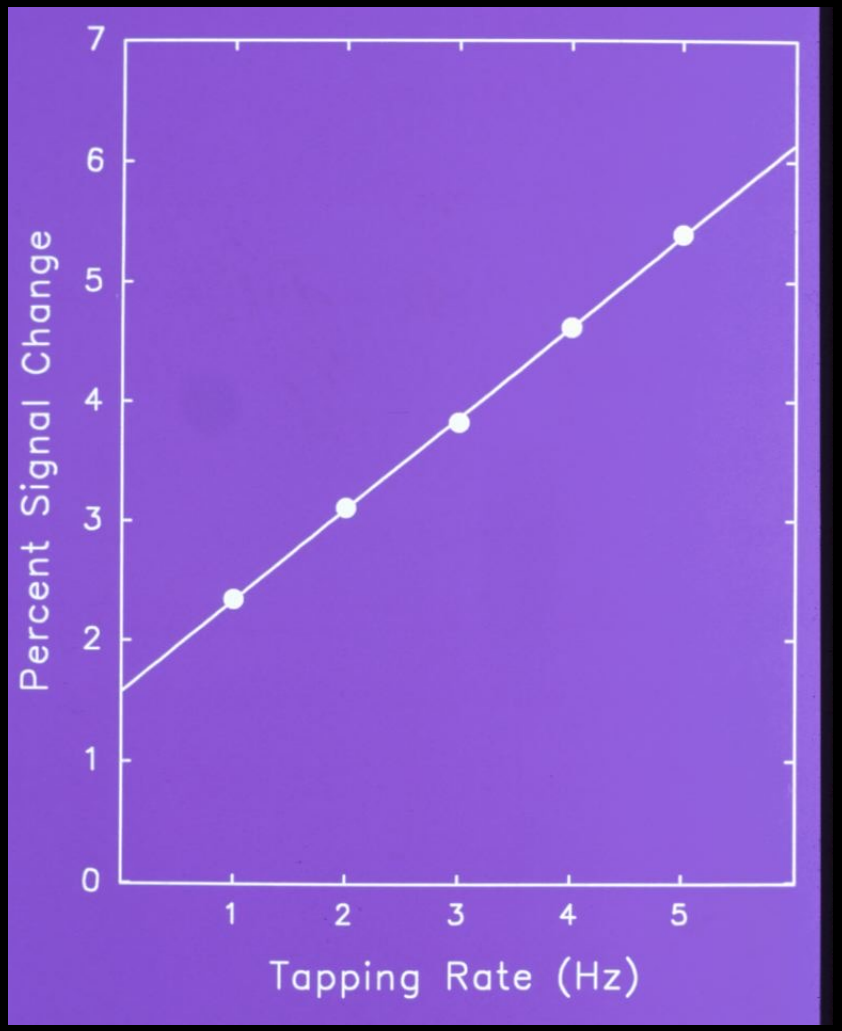


Logothetis et al. Nature, 412, 150-157

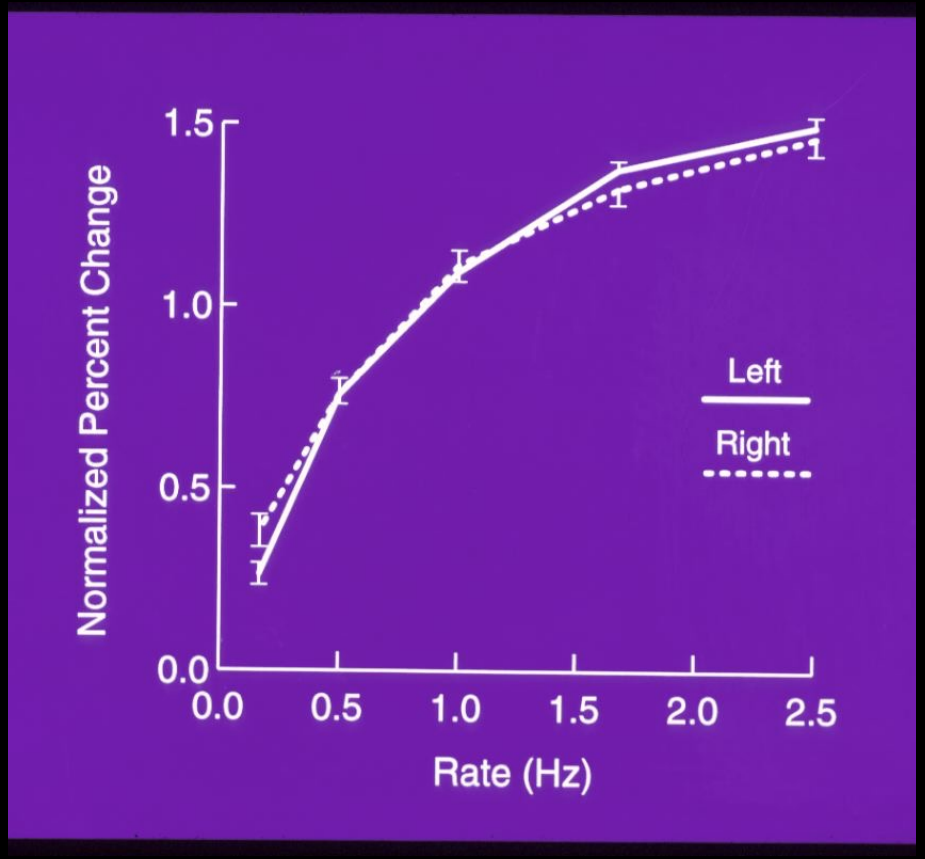


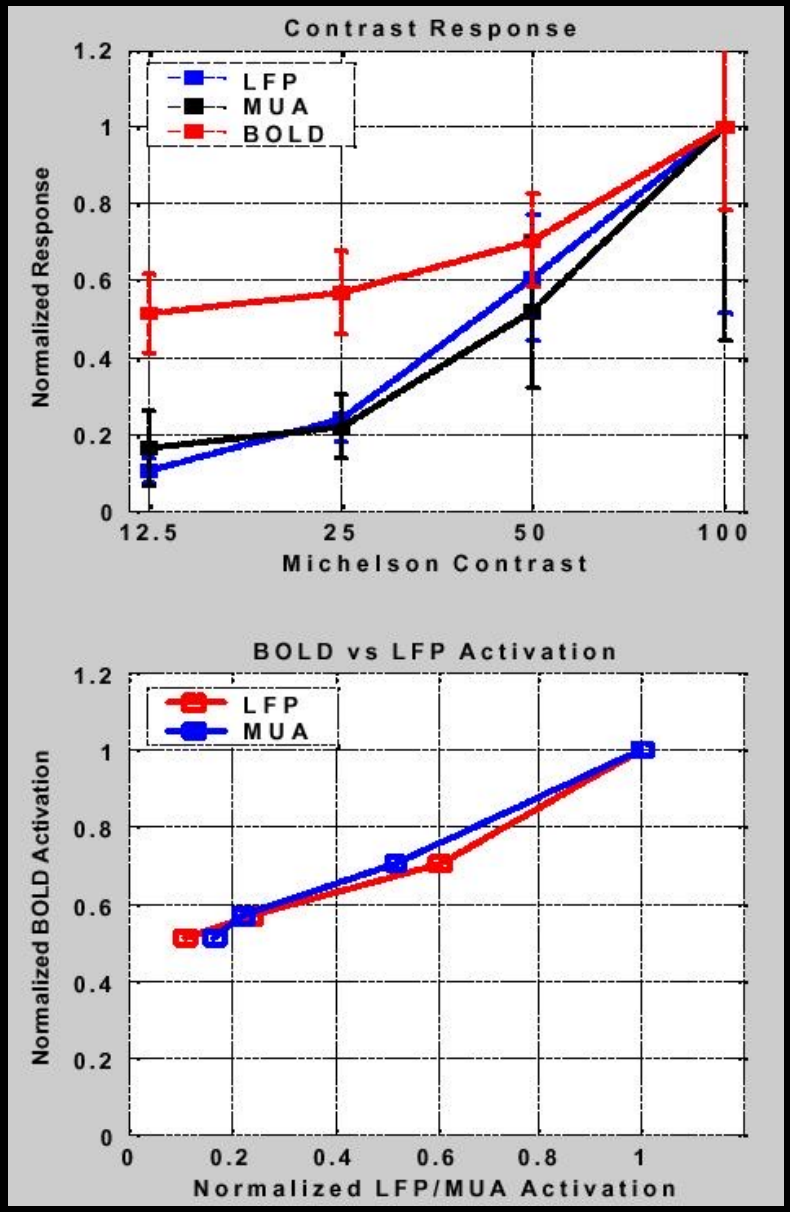
Bandettini and Ungerleider, Nature Neuroscience, 4, 864-866

Motor Cortex



Auditory Cortex





Logothetis et al. Nature, 412, 150-157

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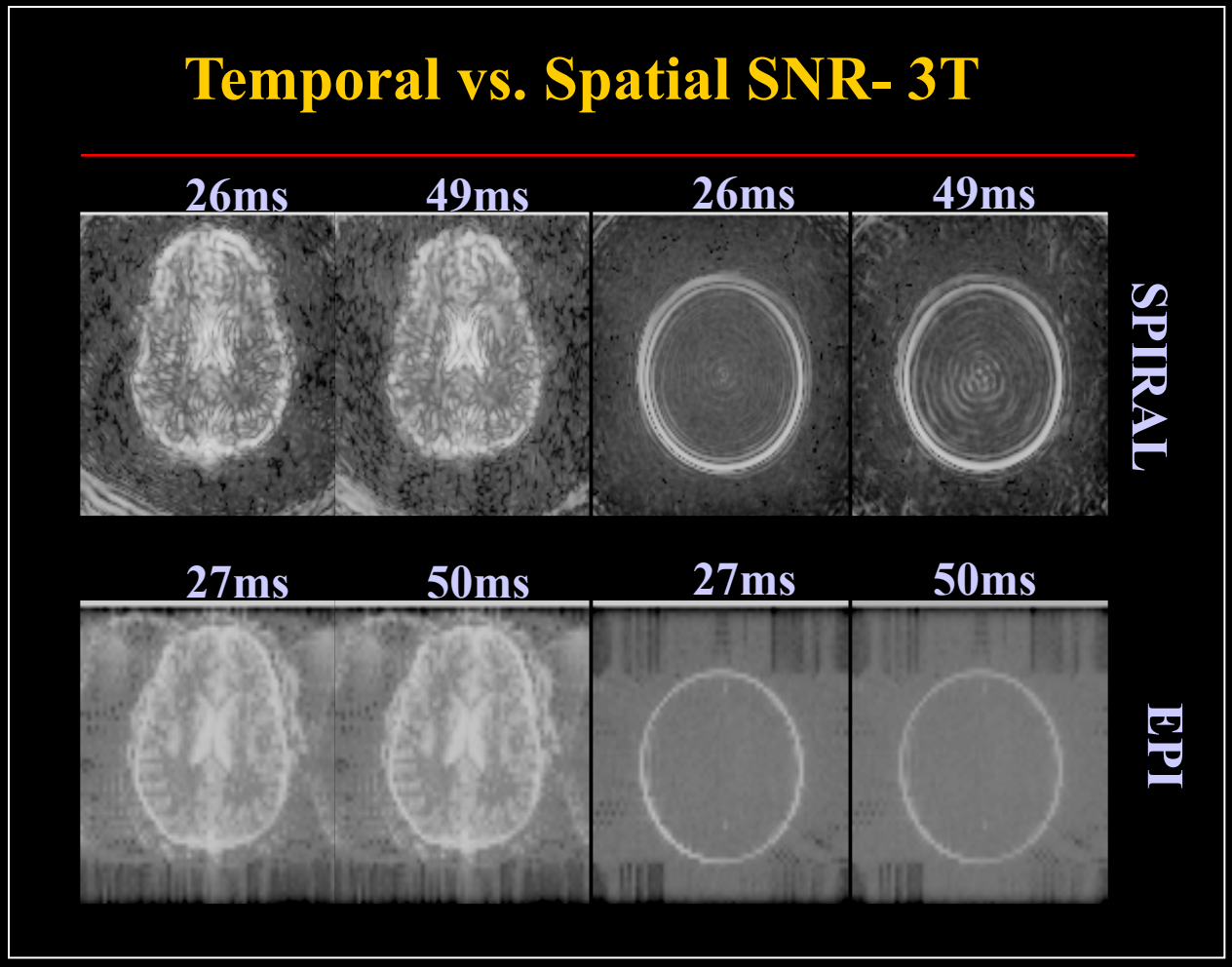
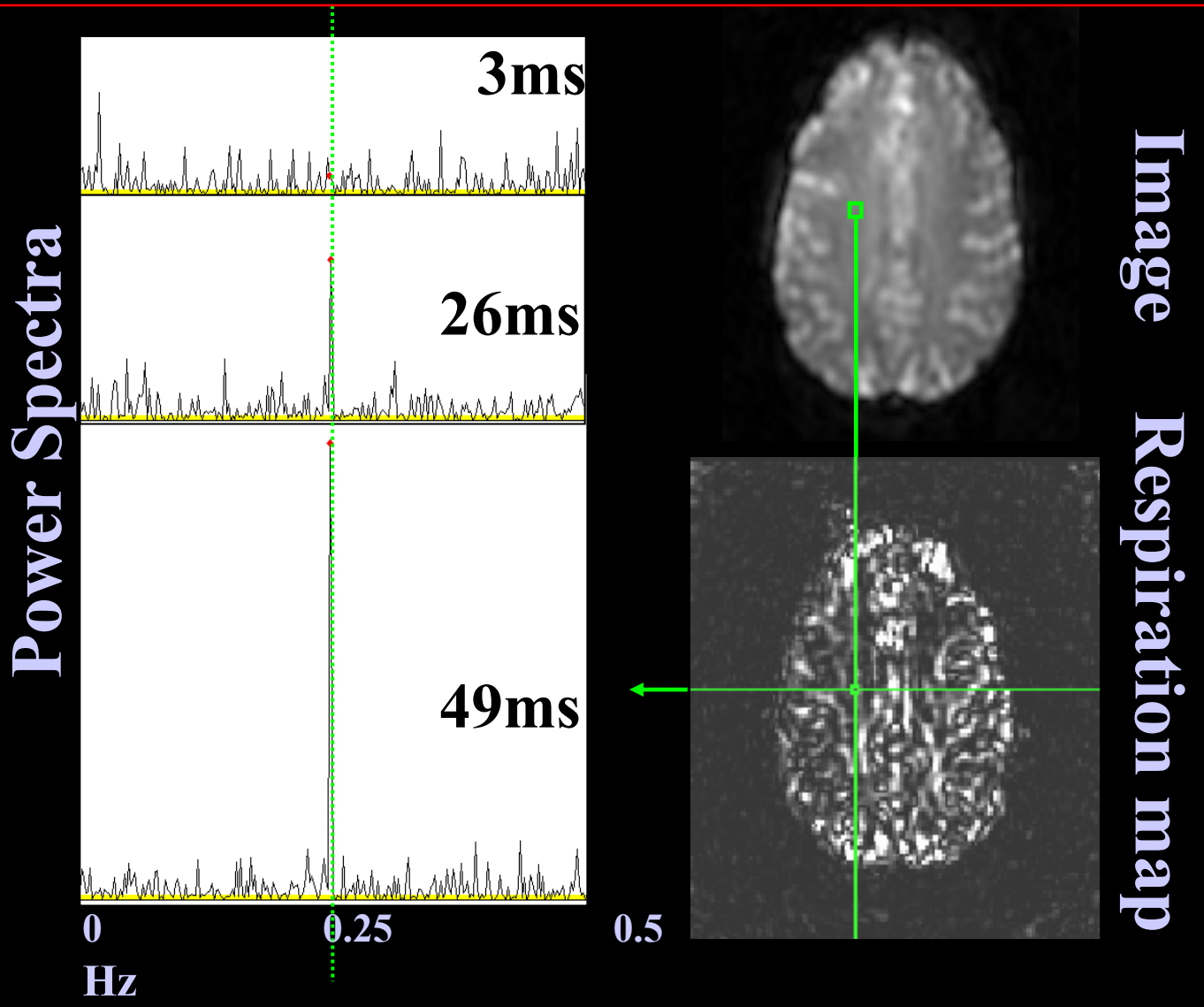
Types of Artifacts & Nature of Noise

- Drift (scanner and/or subject)
- Stimulus correlated motion
- Cardiac, respiratory motion
- Bo changes (mouth movement, etc..)
- Eye movement
- Equipment in scanner room (RF interference)
- Scanner spiking

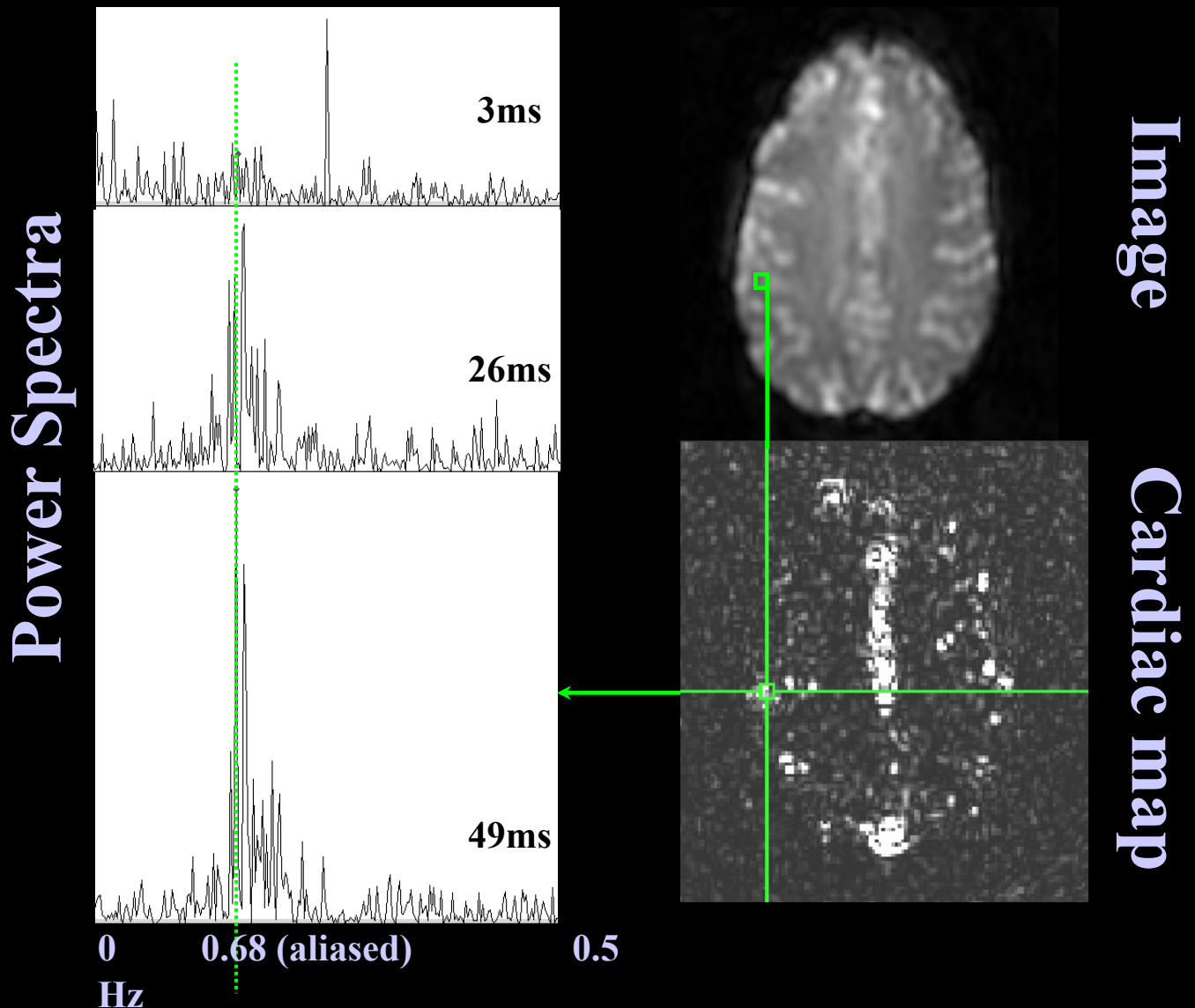
Higher Signal to Noise in a single image does not necessarily translate to higher Signal to Noise over time.



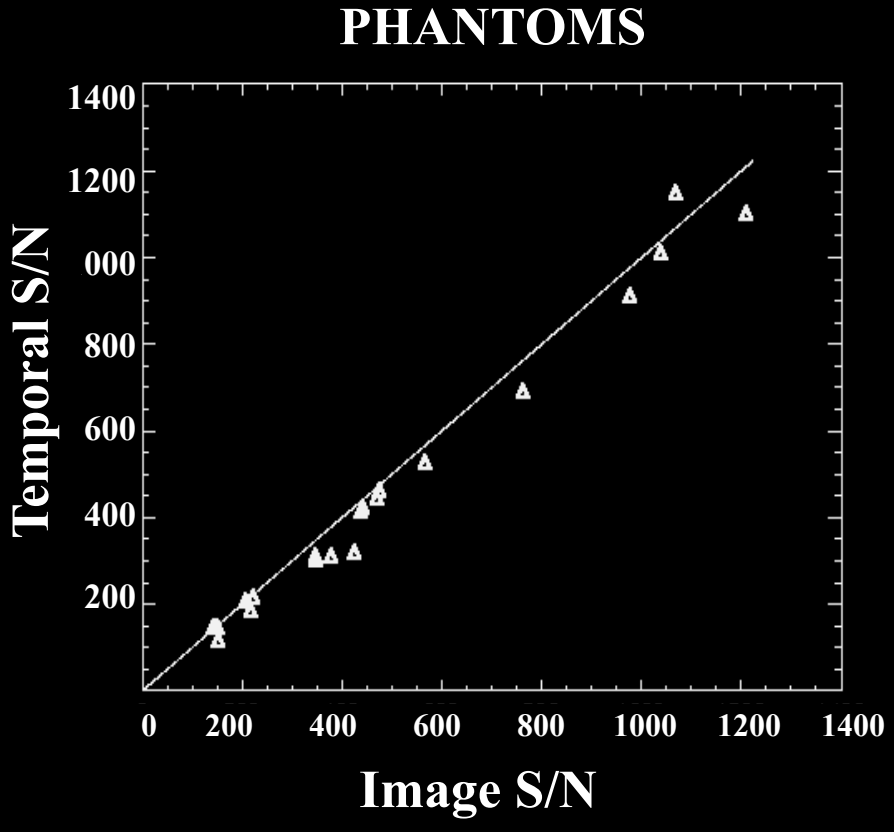
0.25 Hz Breathing at 3T

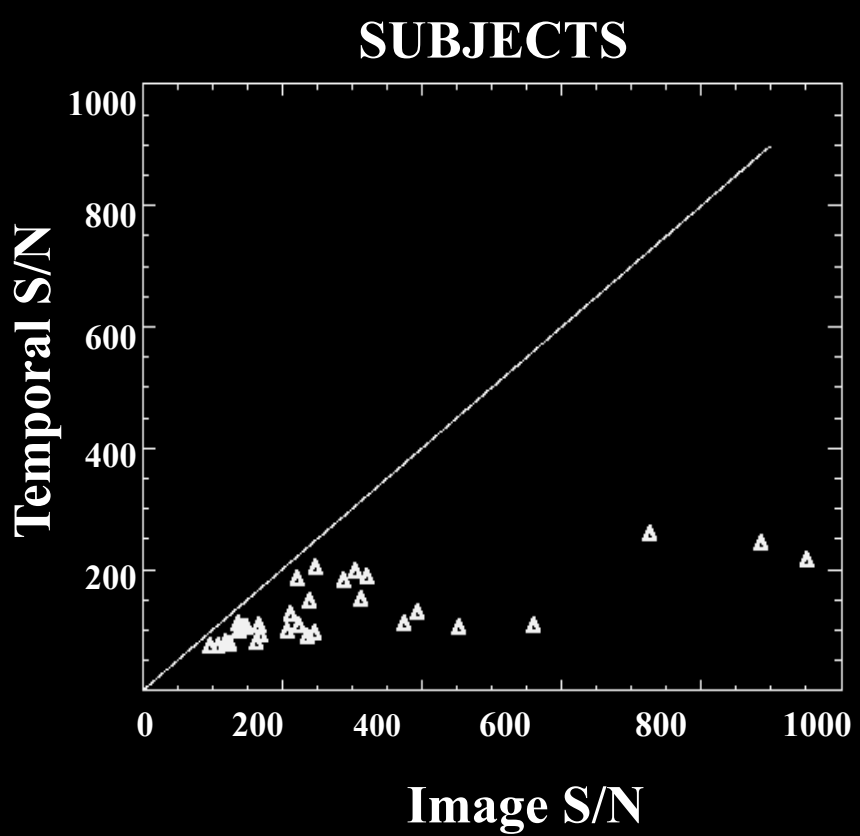


0.68 Hz Cardiac rate at 3T



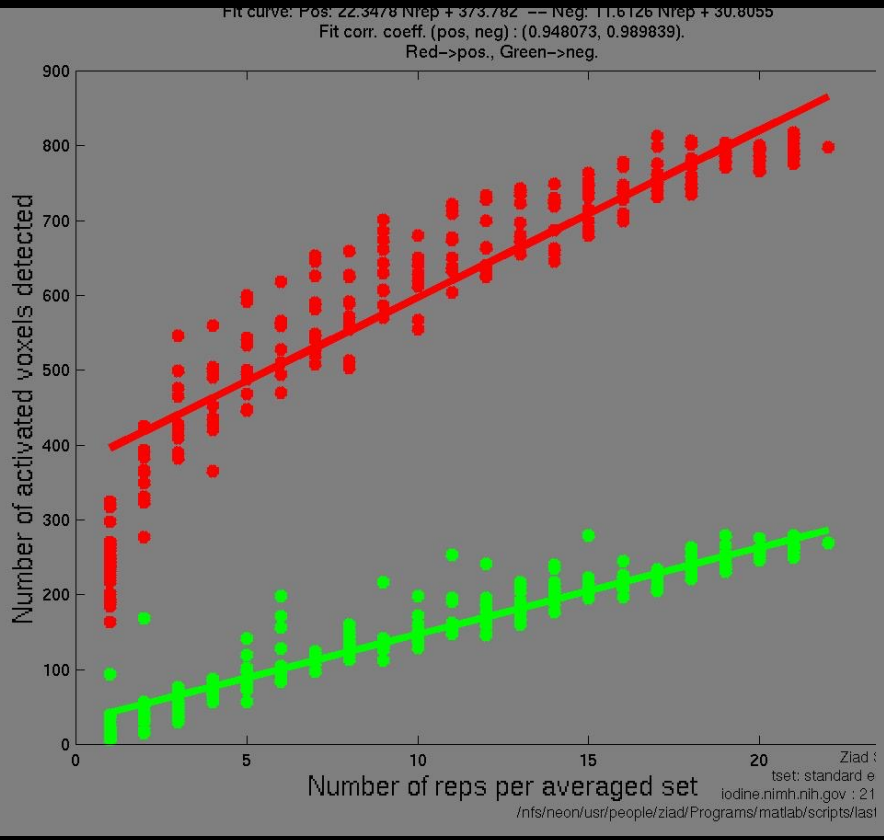
Temporal S/N vs. Image S/N





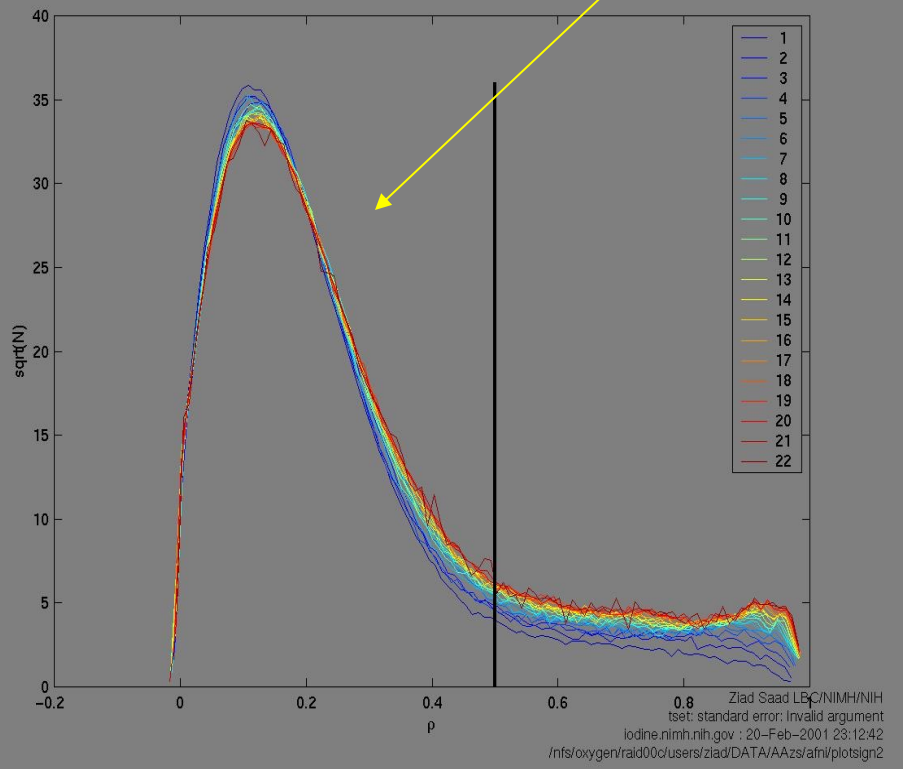
N. Petridou

Continuously Growing Activation Area



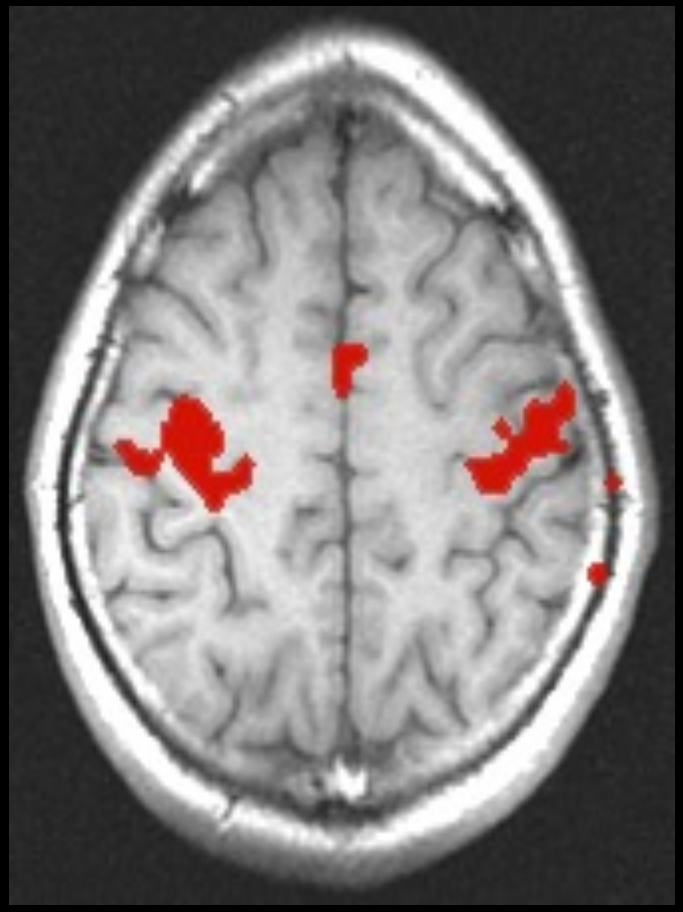
CC Histogram

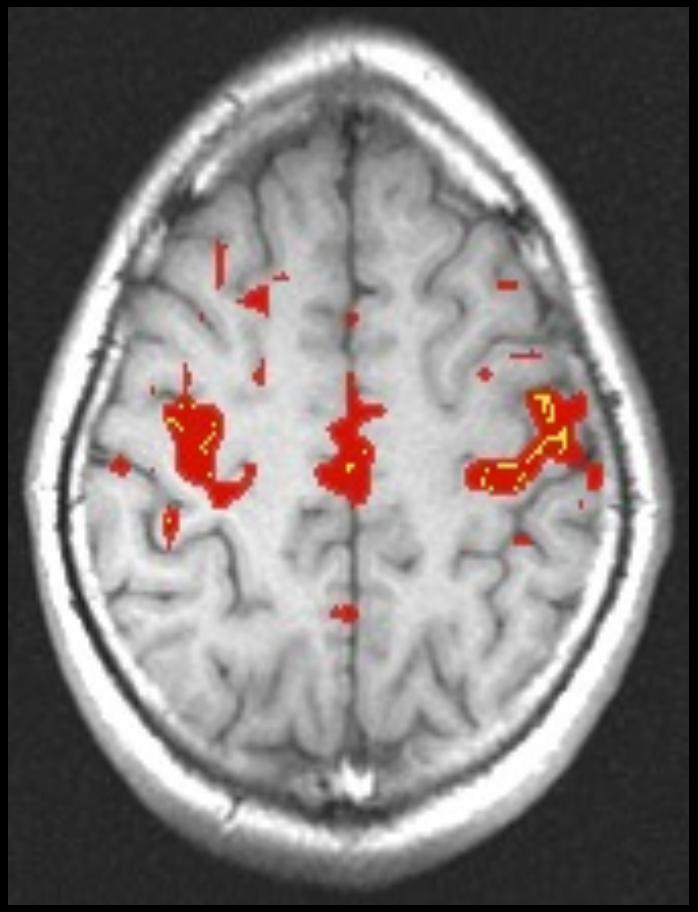
Inflection Point



Ziad Saad, et al

Resting Hemodynamic Autocorrelations





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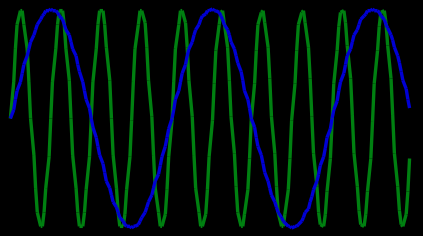
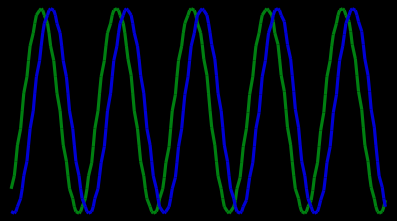
Neuronal Activation Input Strategies

1. Block Design

2. Frequency Encoding

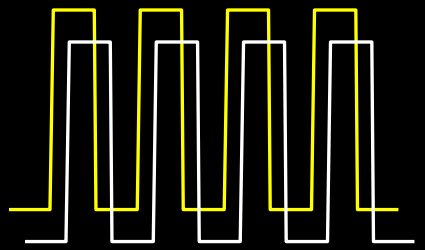


3. Phase Encoding



4. Single Event

5. Orthogonal Block Design

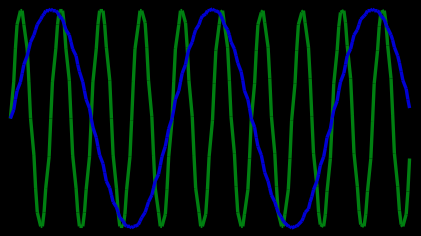


6. Free Behavior Design.

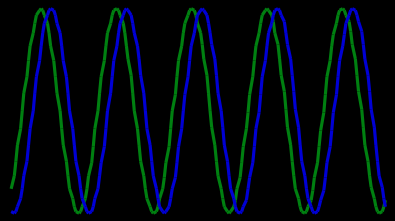
Neuronal Activation Input Strategies

1. Block Design

2. Frequency Encoding



3. Phase Encoding



4. Single Event

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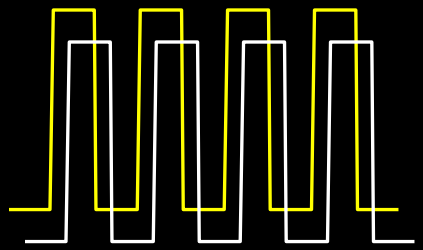
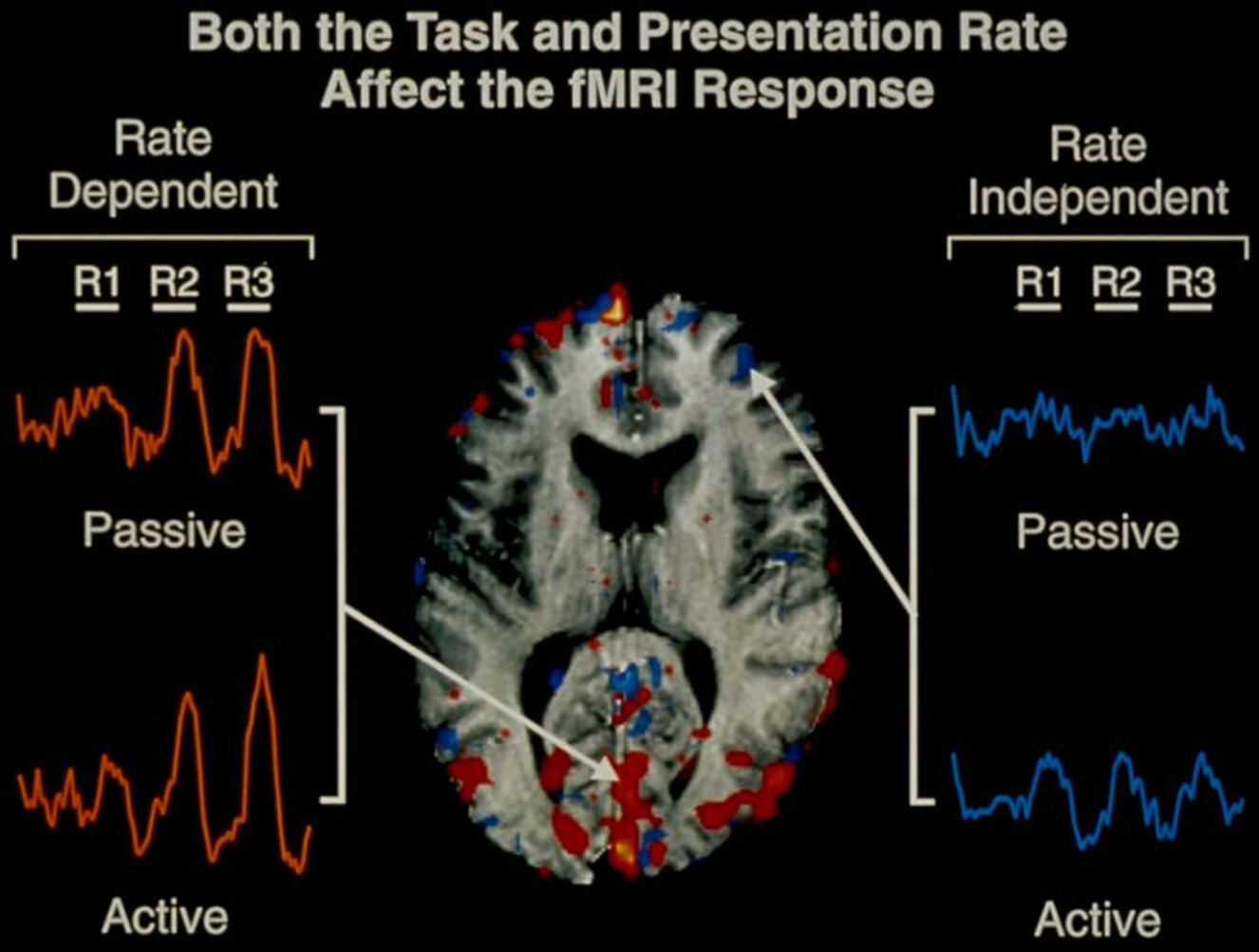


6. Free Behavior Design.


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

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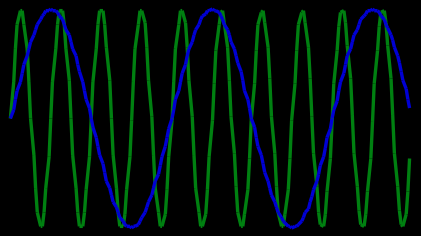
2. Frequency Encoding



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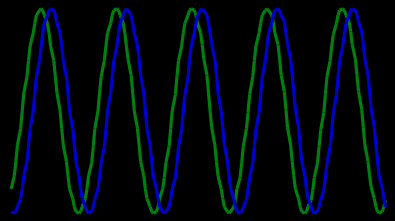

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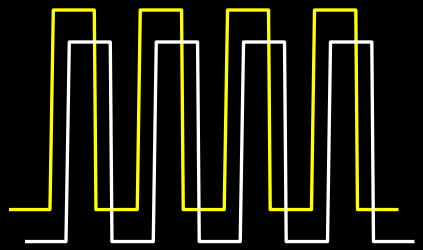

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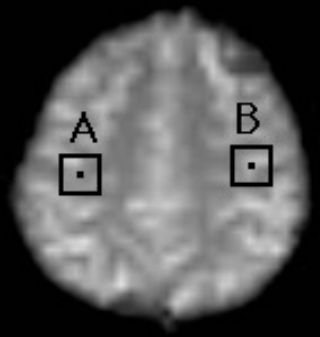
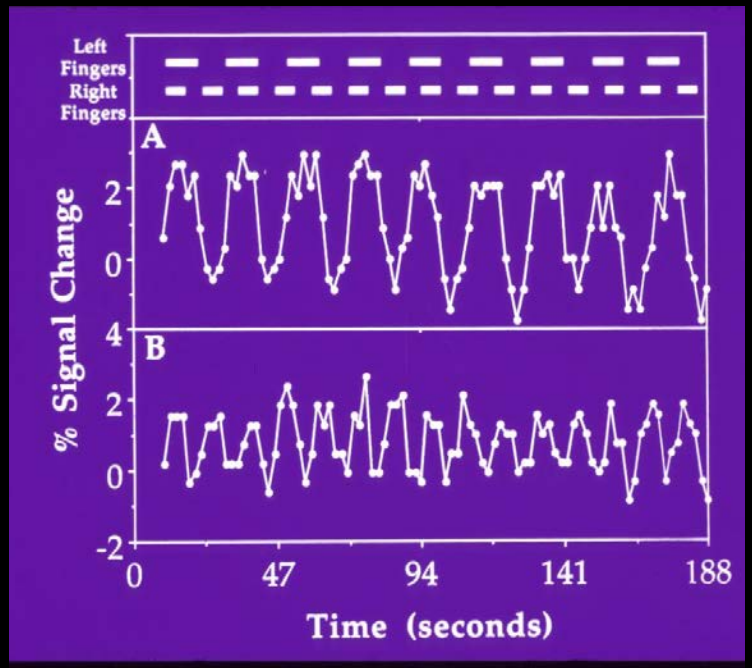
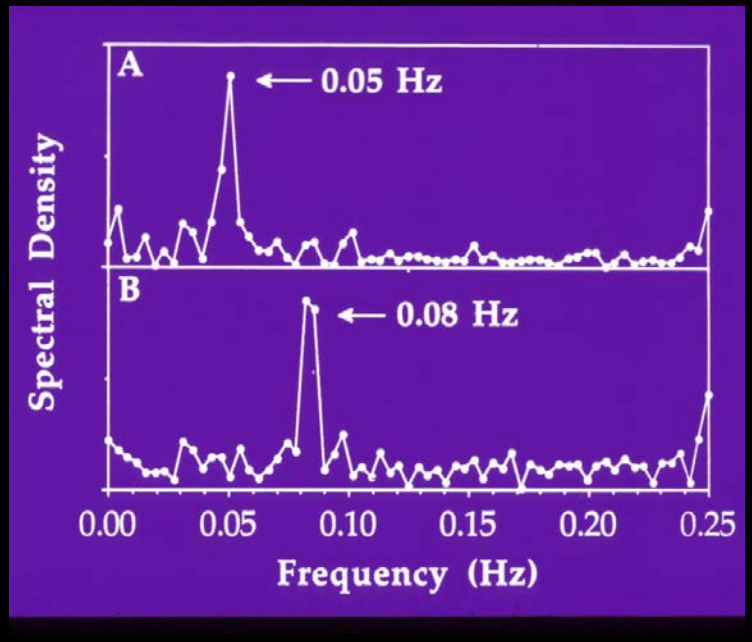
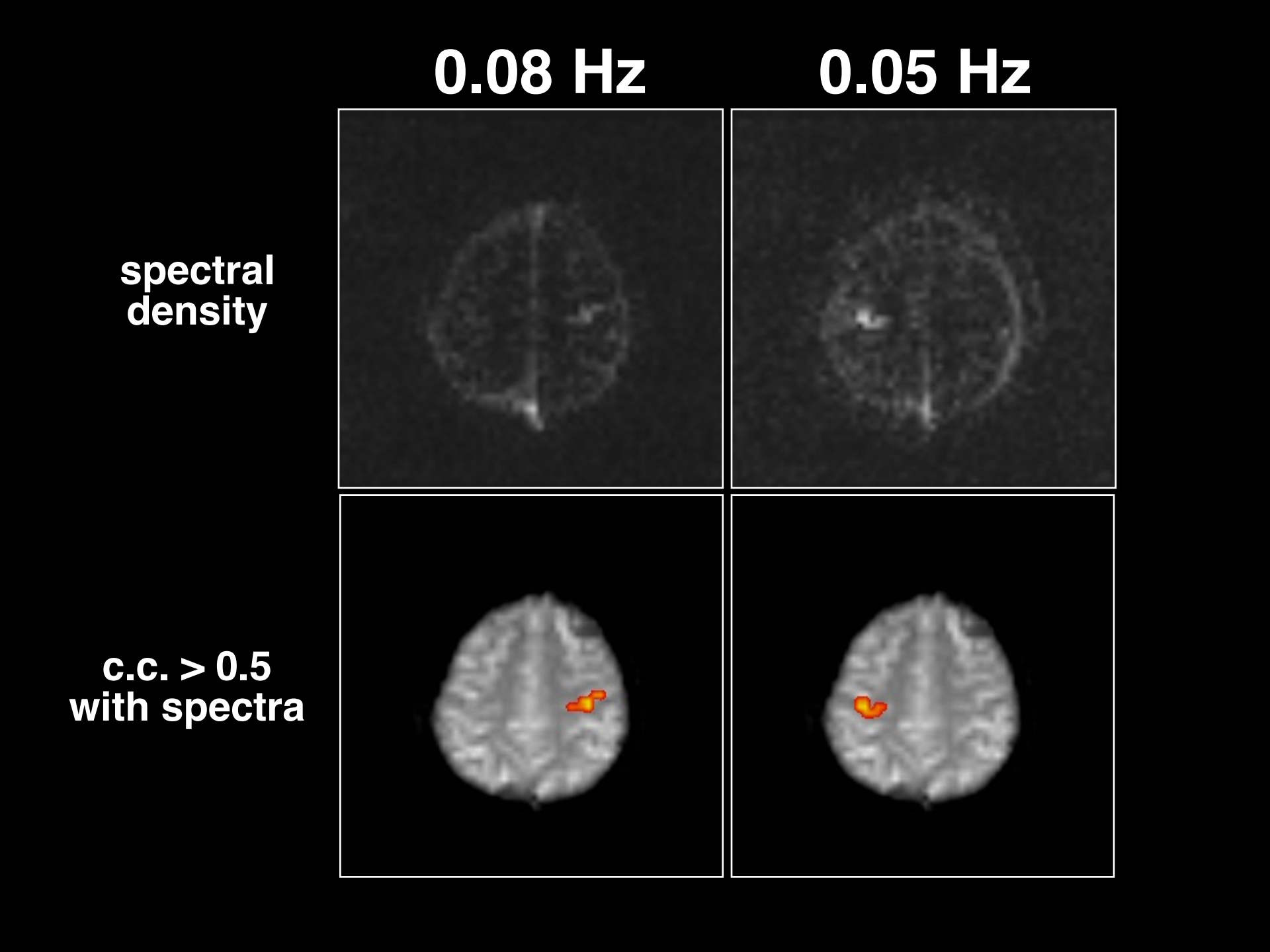

A
B

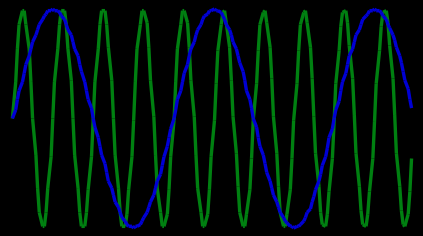

Left Fingers
Right Fingers
A
B
% Signal Change
2
0
4
2
0
-2
0
47
94
141
188
Time (seconds)

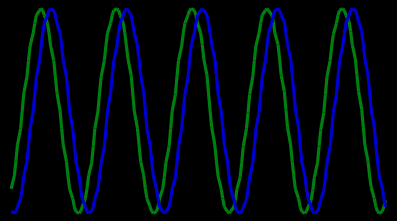

A
0.05 Hz
B
0.08 Hz
Spectral Density
0.00
0.05
0.10
0.15
0.20
0.25
Frequency (Hz)

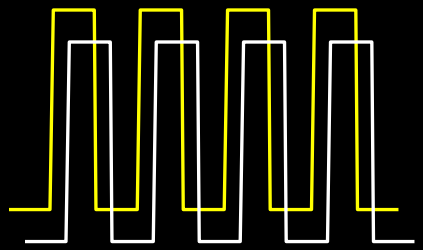

0.08 Hz
0.05 Hz
spectral density
c.c. > 0.5 with spectra

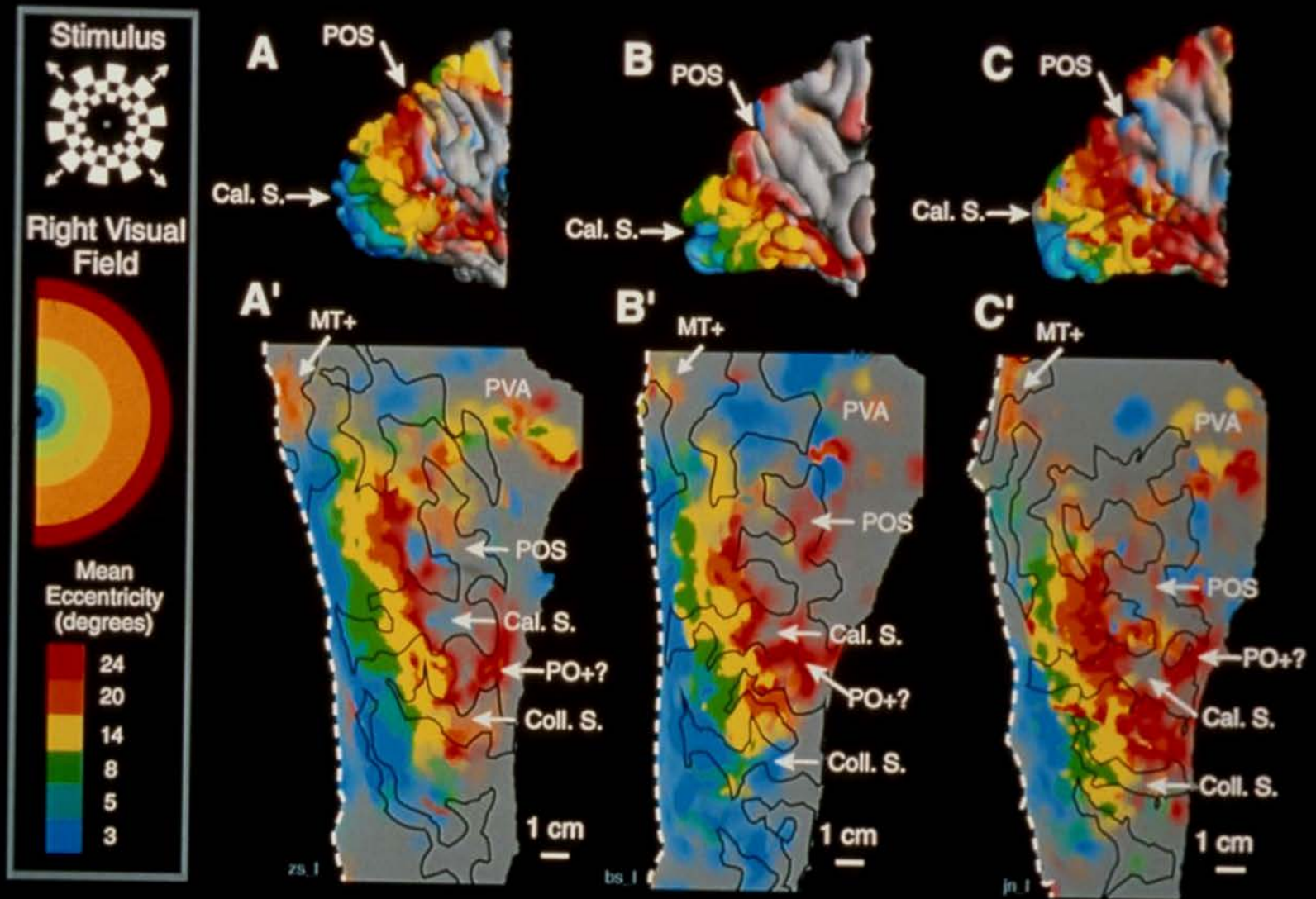
Neuronal Activation Input Strategies

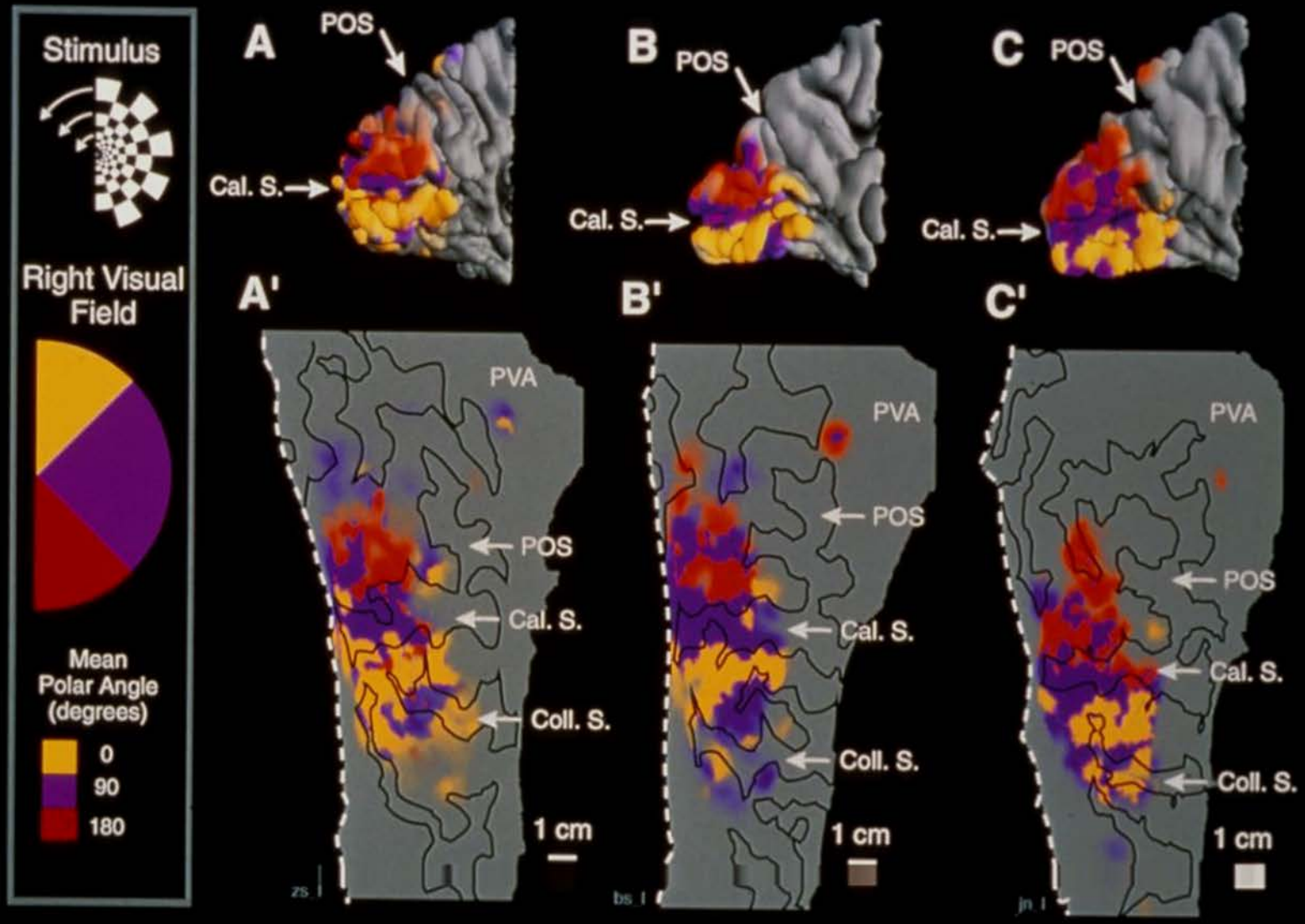
1. Block Design
2. Frequency Encoding
3. Phase Encoding
4. Single Event
5. Orthogonal Block Design
6. Free Behavior Design.







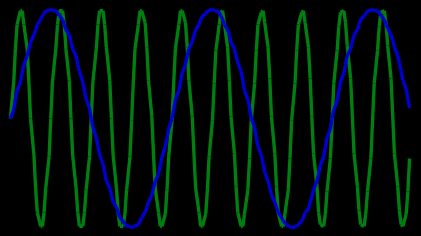

Stimulus
Right Visual Field
Mean Eccentricity (degrees)
24
20
14
8
5
3
A
POS
Cal. S.
B
POS
Cal. S.
C
POS
Cal. S.
A'
MT+
PVA
POS
Cal. S.
PO+?
Coll. S.
1 cm
zs_l
B'
MT+
PVA
POS
Cal. S.
PO+?
Coll. S.
1 cm
bs_l
C'
MT+
PVA
POS
PO+?
Cal. S.
Coll. S.
1 cm
jn_l


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

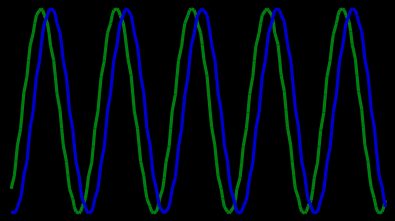
Neuronal Activation Input Strategies

1. Block Design

2. Frequency Encoding

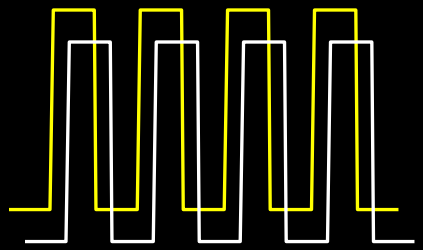


3. Phase Encoding



4. Single Event

5. Orthogonal Block Design

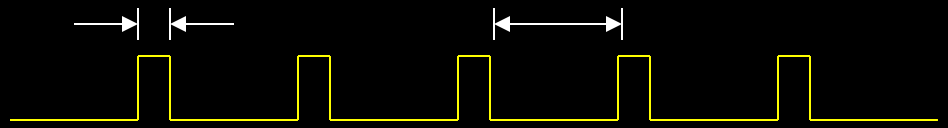


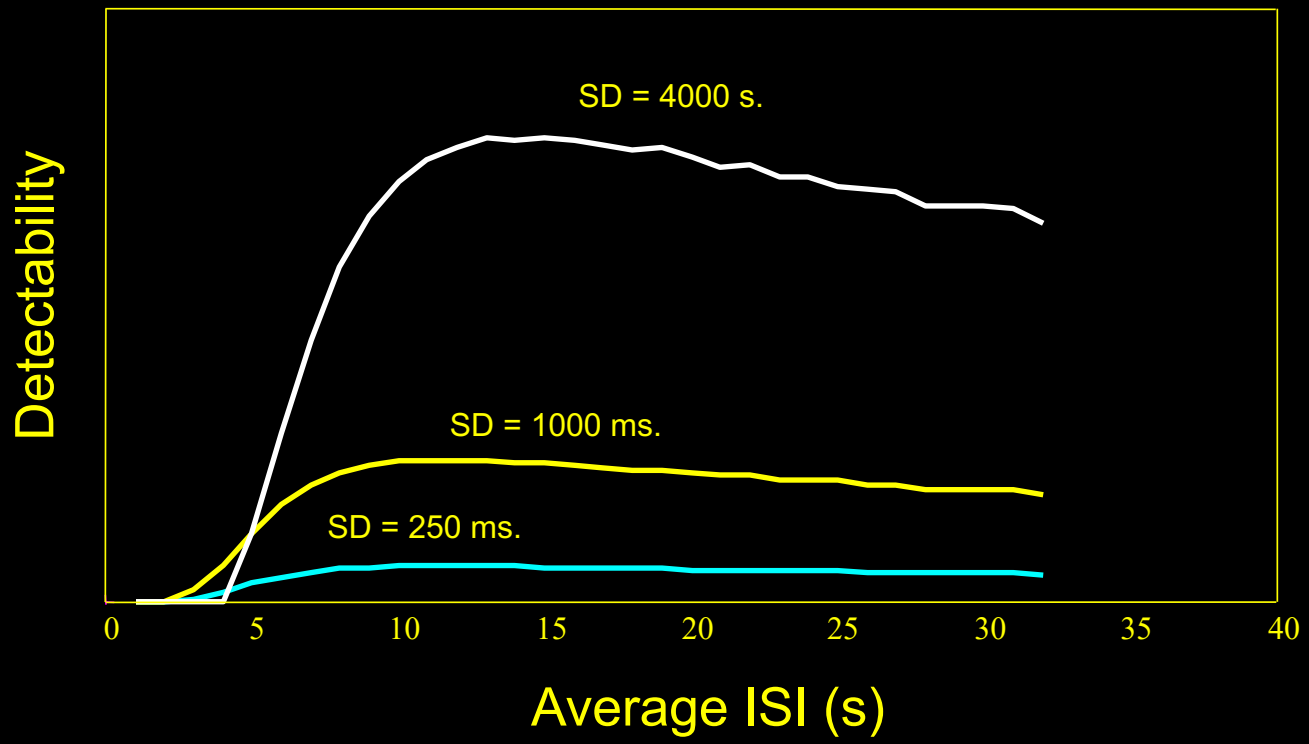
6. Free Behavior Design.

Detectability – constant ISI

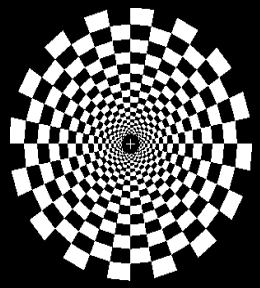
SD – stimulus duration

ISI – inter-stimulus interval

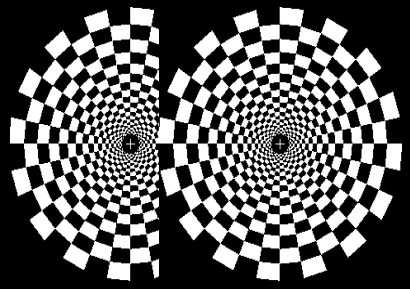




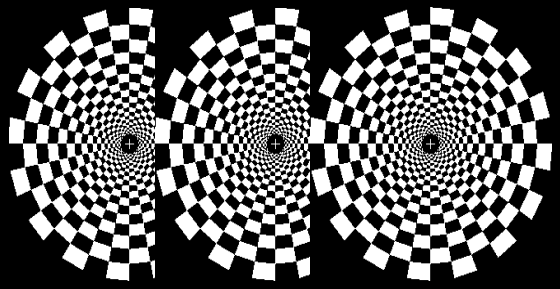
Visual Activation Paradigm: 1 , 2, & 3 Trials



0 sec 20 sec



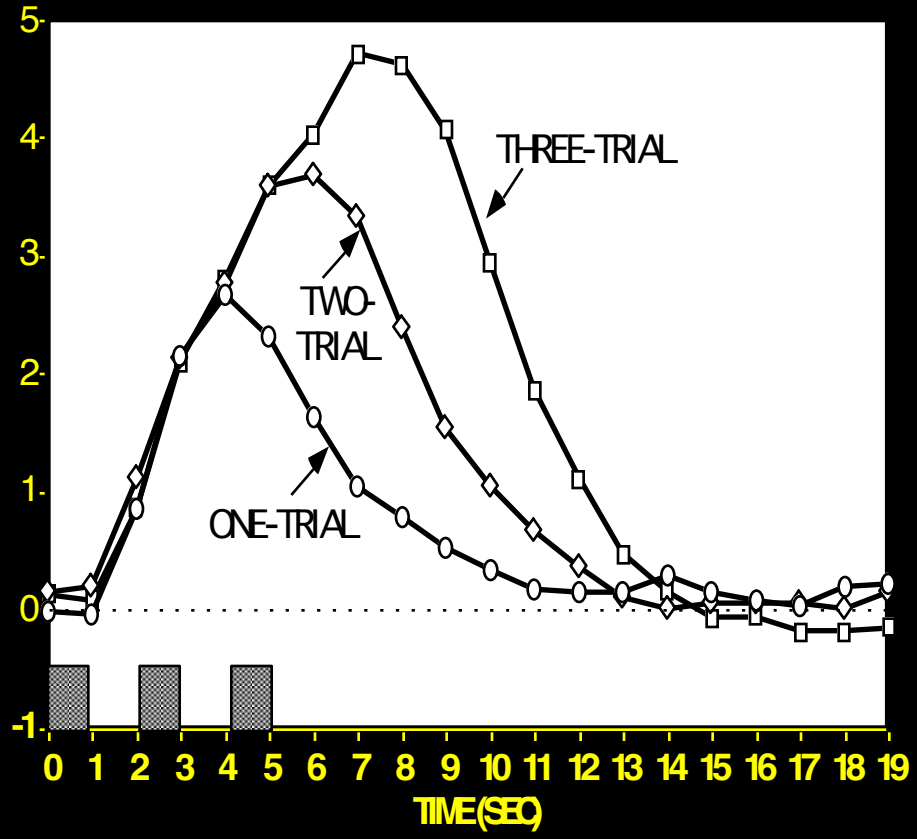
0 sec2 sec 20 sec



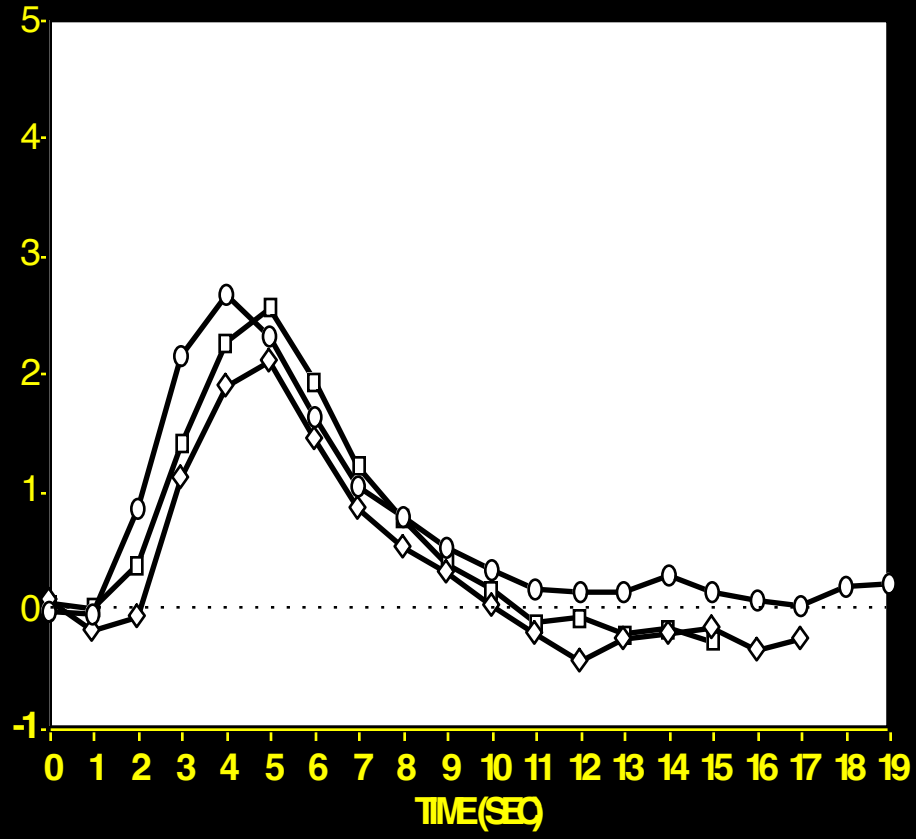
0 sec2 sec4 sec 20 sec

Response to Multiple Trials: Subject RW

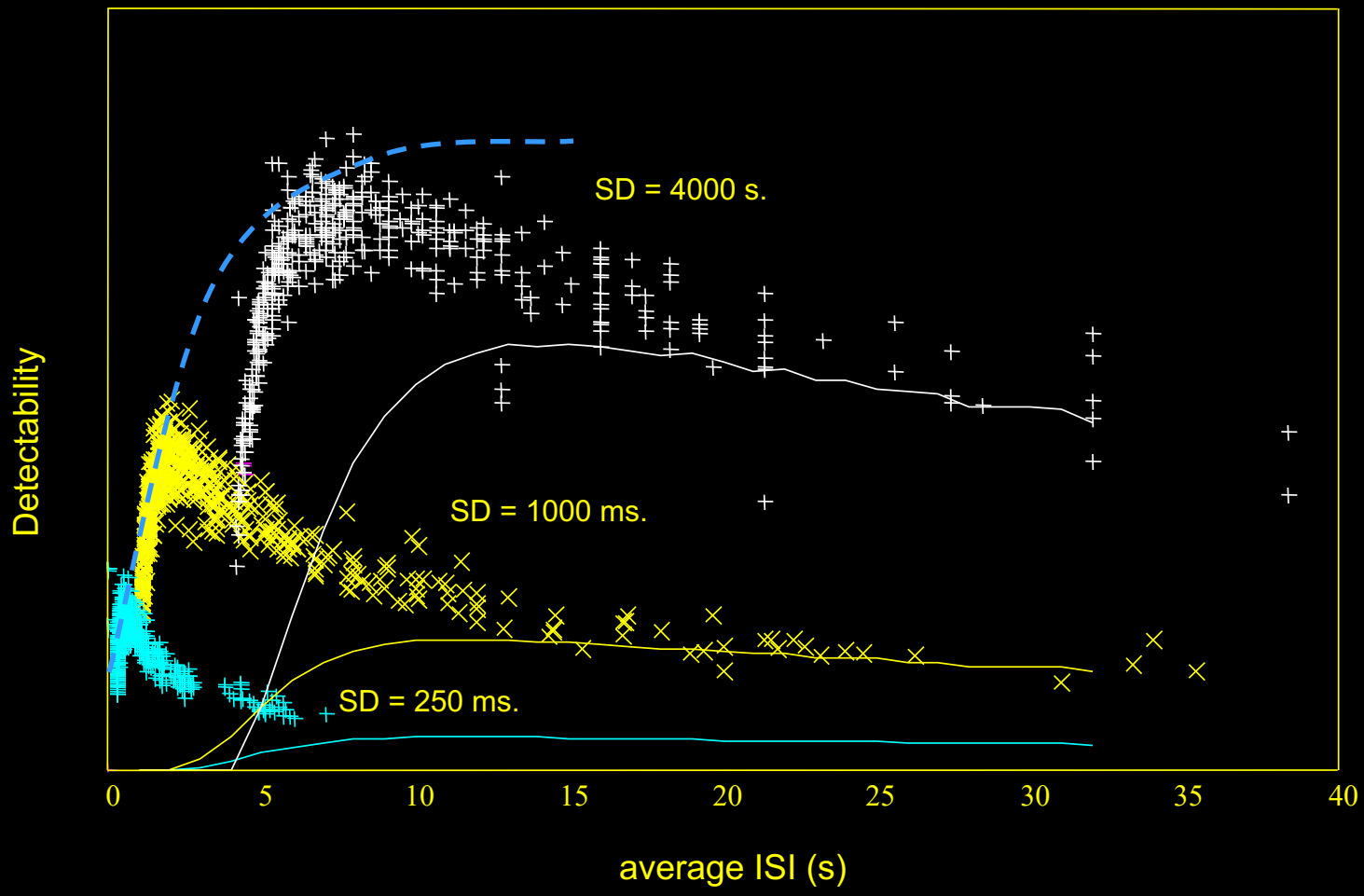
RAW DATA



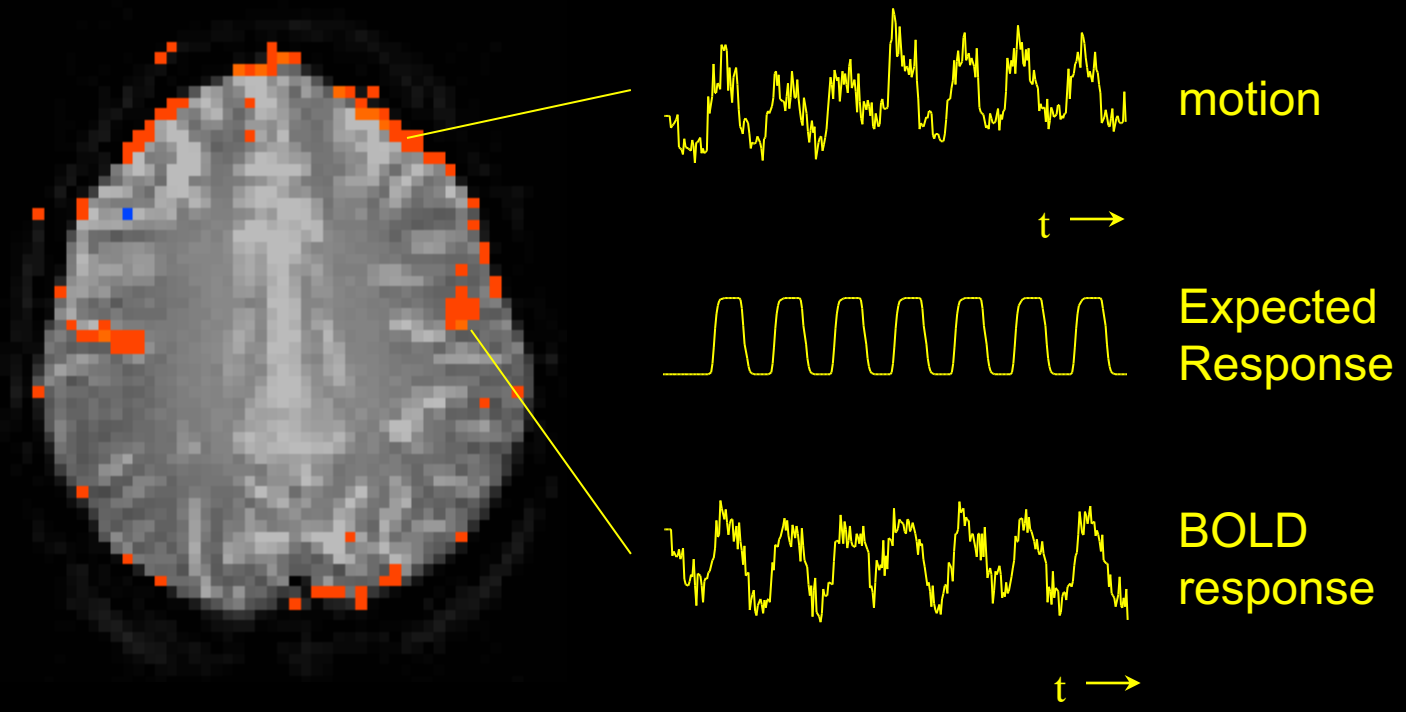
ESTIMATED RESPONSES



Detectability vs. Average ISI

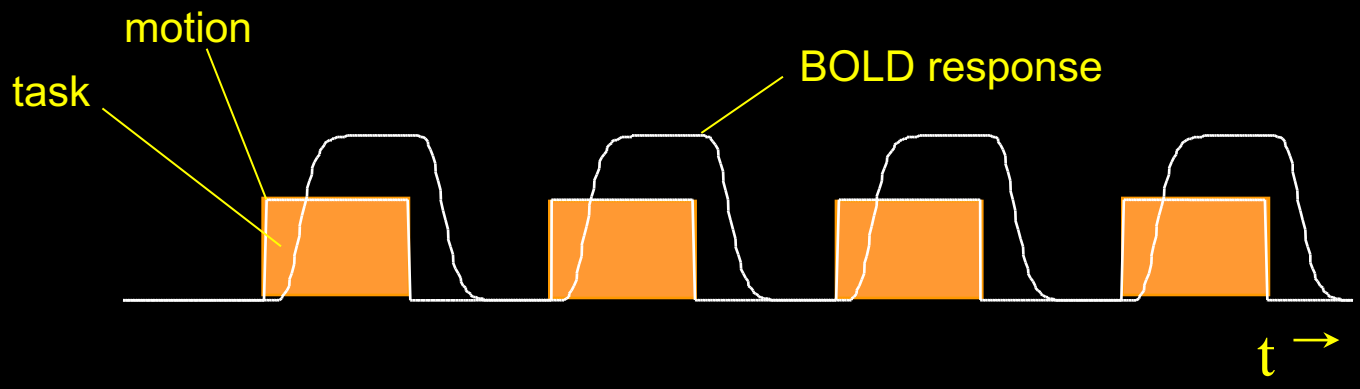


Speaking - Blocked Trial

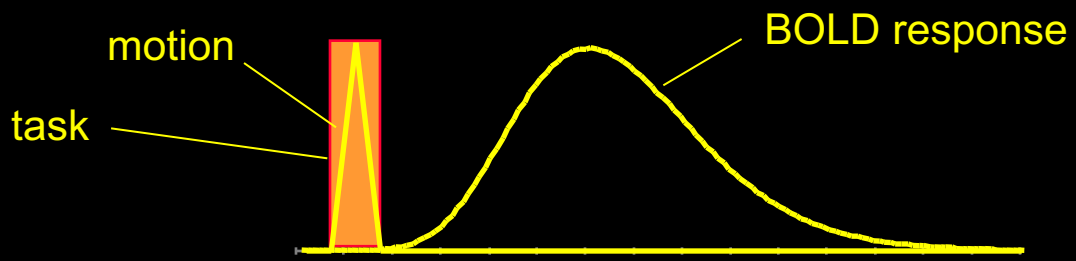


fMRI during tasks that involve brief motion

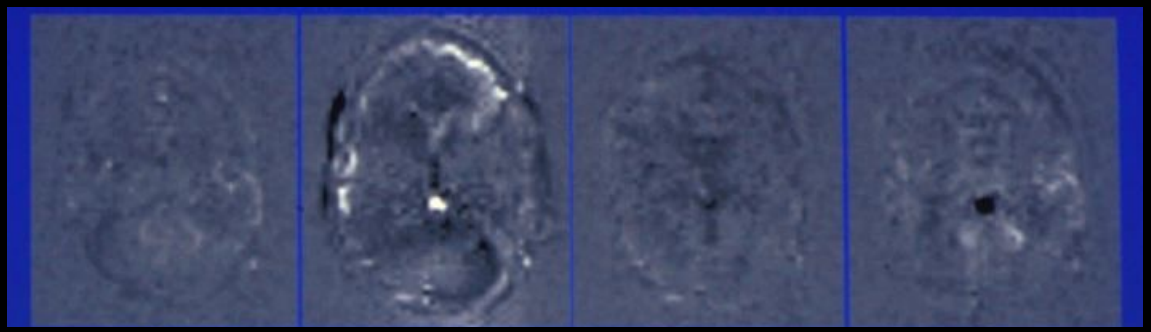
Blocked Design



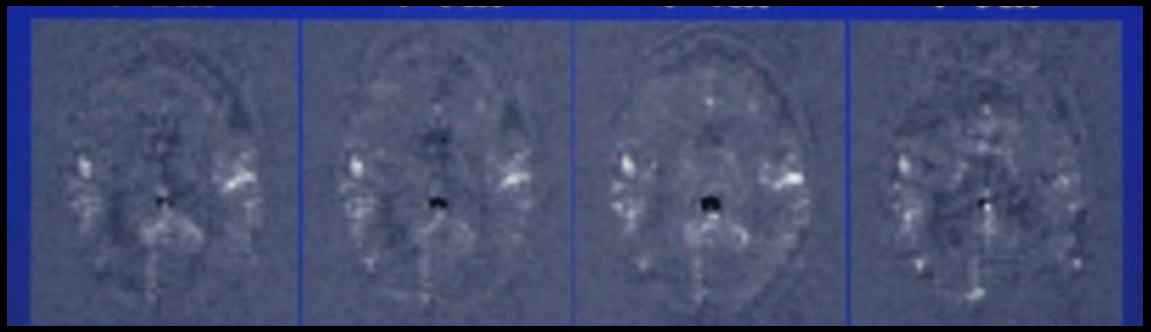
Event-Related Design



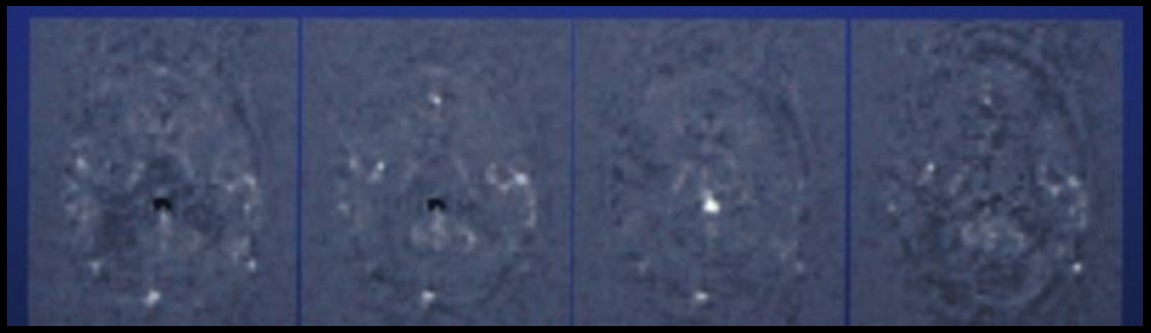
Overt Word Production



2 3 4 5

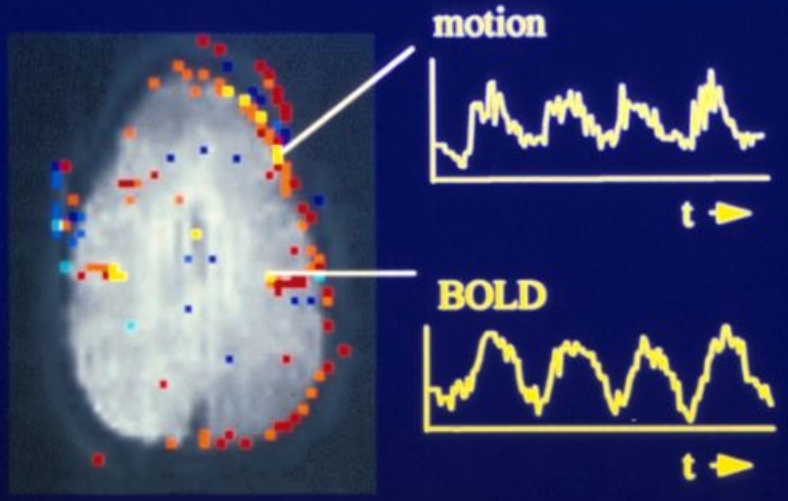


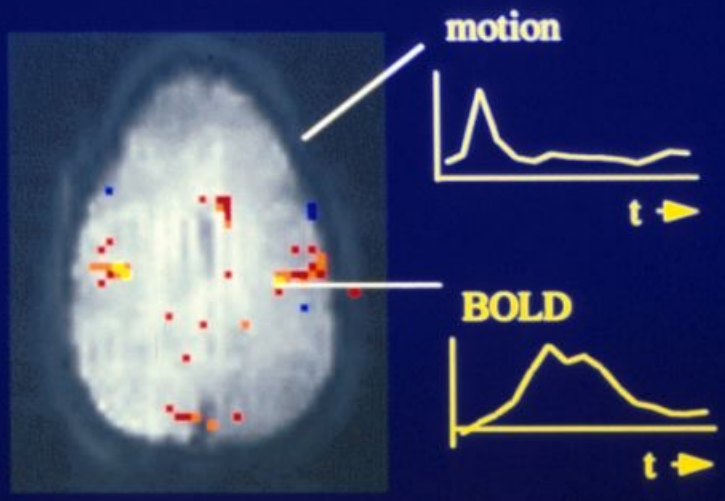
6 7 8 9



10 11 12 13

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





"block-trial" paradigm

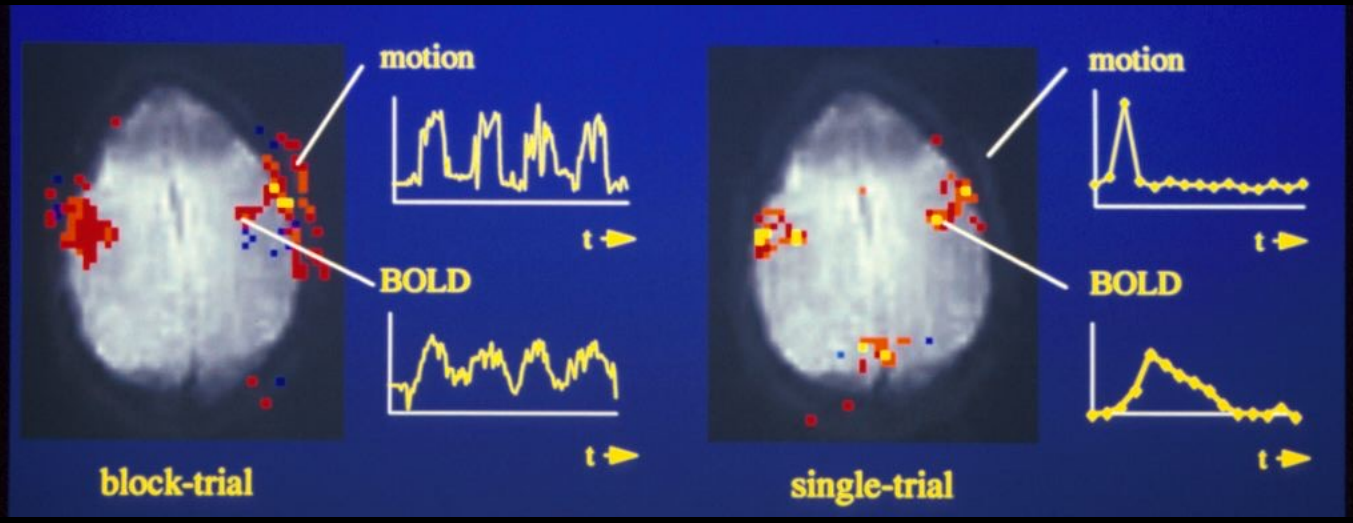
Motion induced signal changes resemble functional (BOLD) signal changes

"single-trial" paradigm

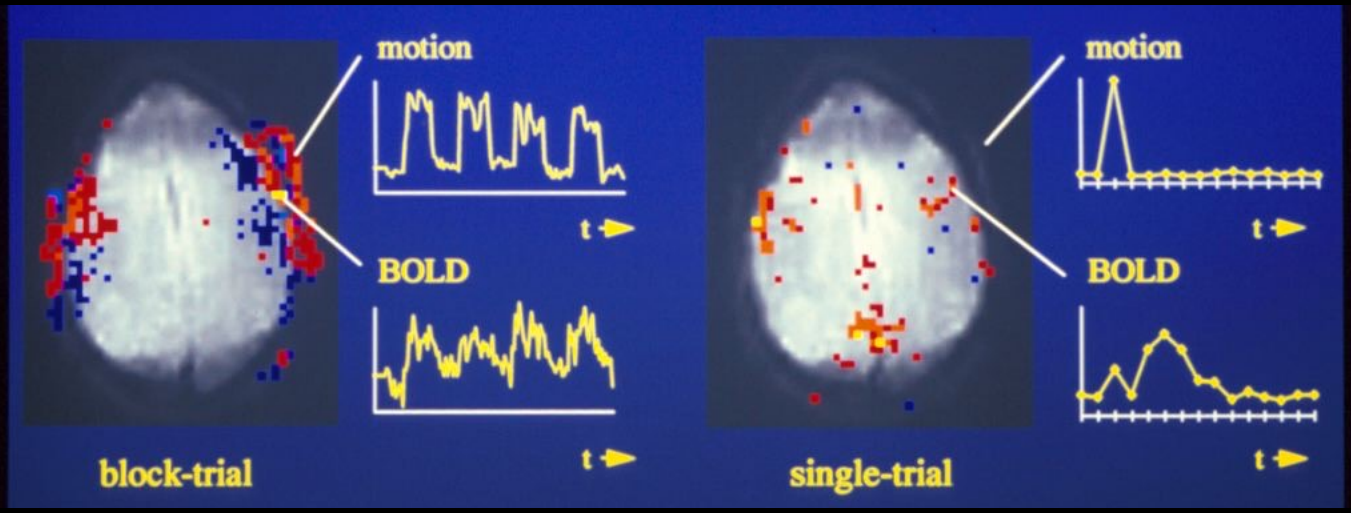
Motion induced and BOLD signal changes are separated in time

R.M. Birn, et al.

Tongue Movement

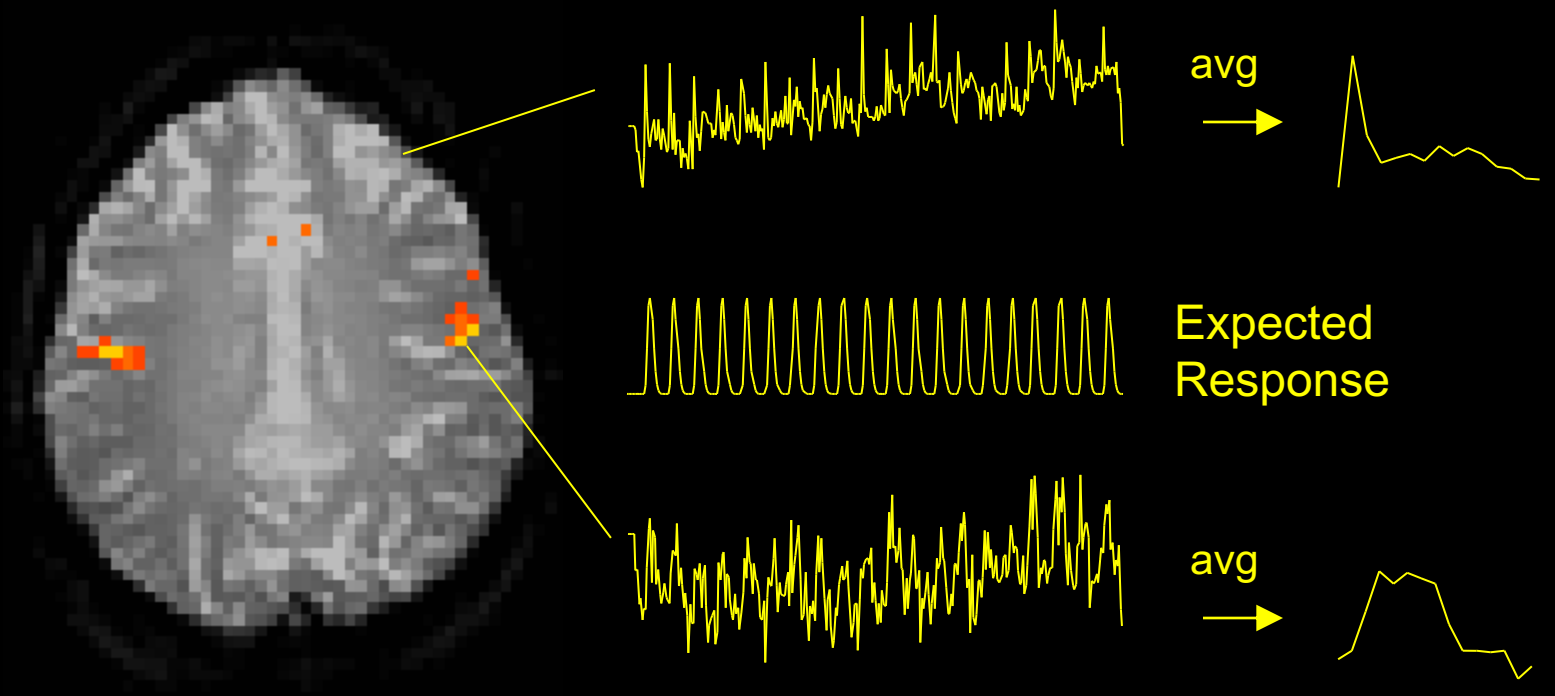


Jaw Clenching

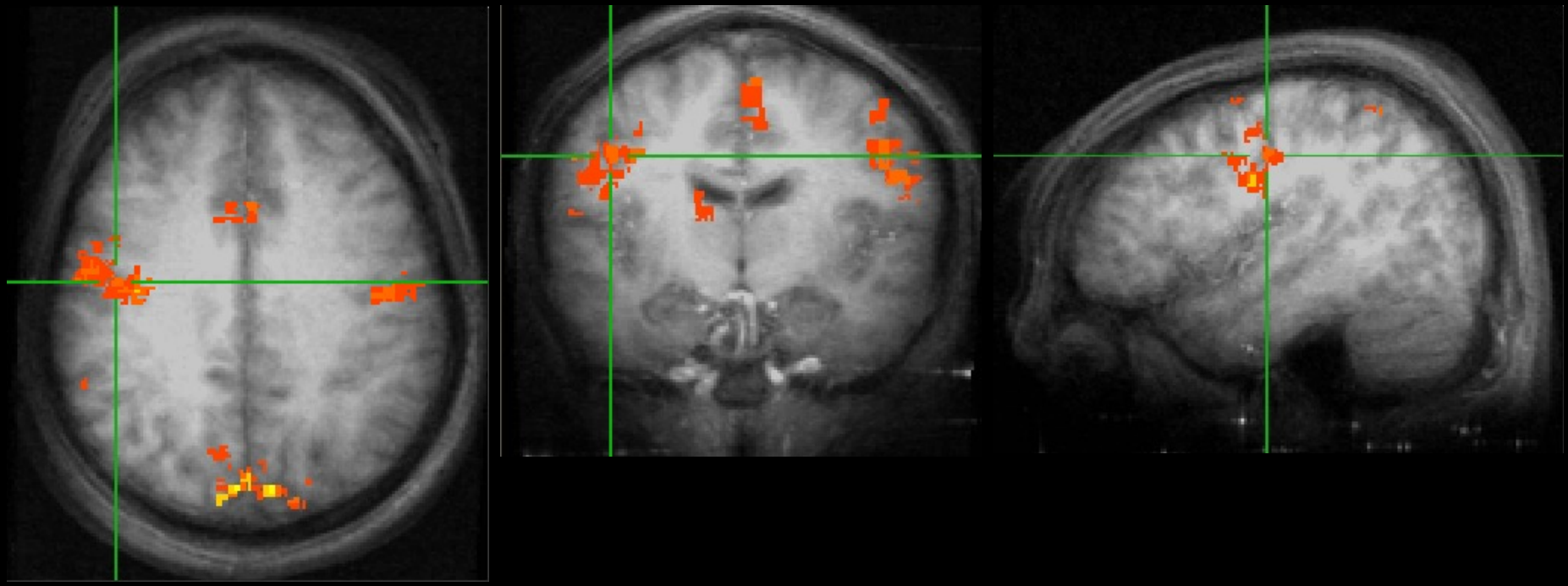


Constant ISI

Speaking - ER-fMRI



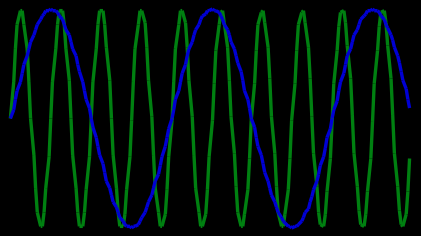
Swallowing - Event-Related



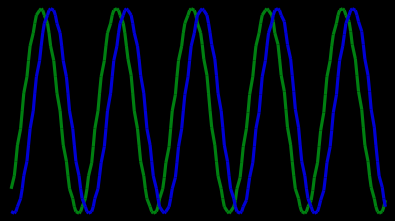
Neuronal Activation Input Strategies

1. Block Design

2. Frequency Encoding

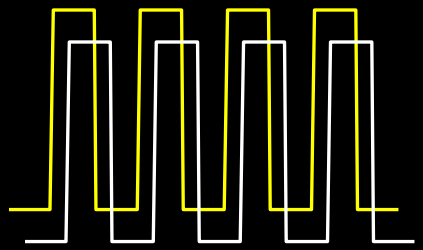


3. Phase Encoding



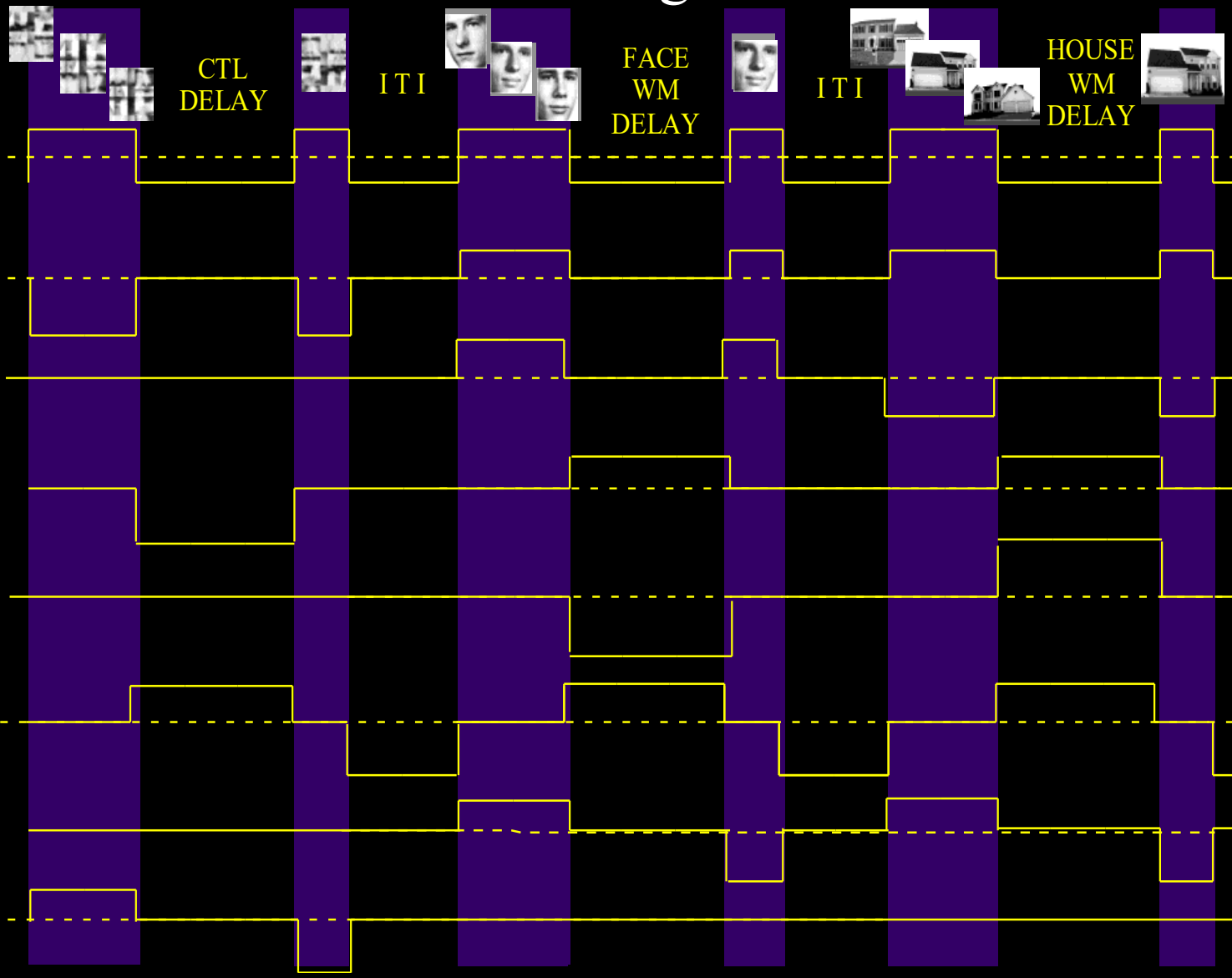
4. Single Event

5. Orthogonal Block Design



6. Free Behavior Design.

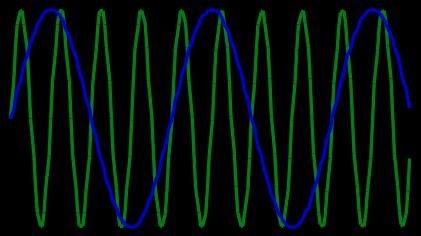
Example of a Set of Orthogonal Contrasts for Multiple Regression



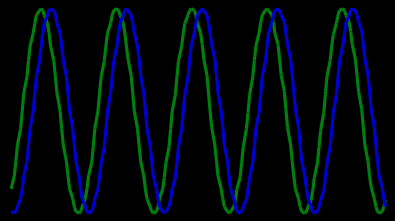
Neuronal Activation Input Strategies

1. Block Design

2. Frequency Encoding

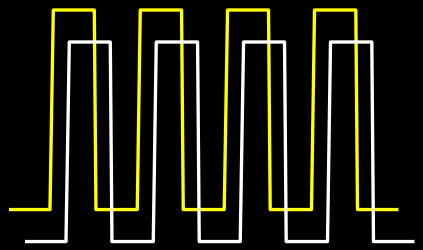


3. Phase Encoding



4. Single Event

5. Orthogonal Block Design



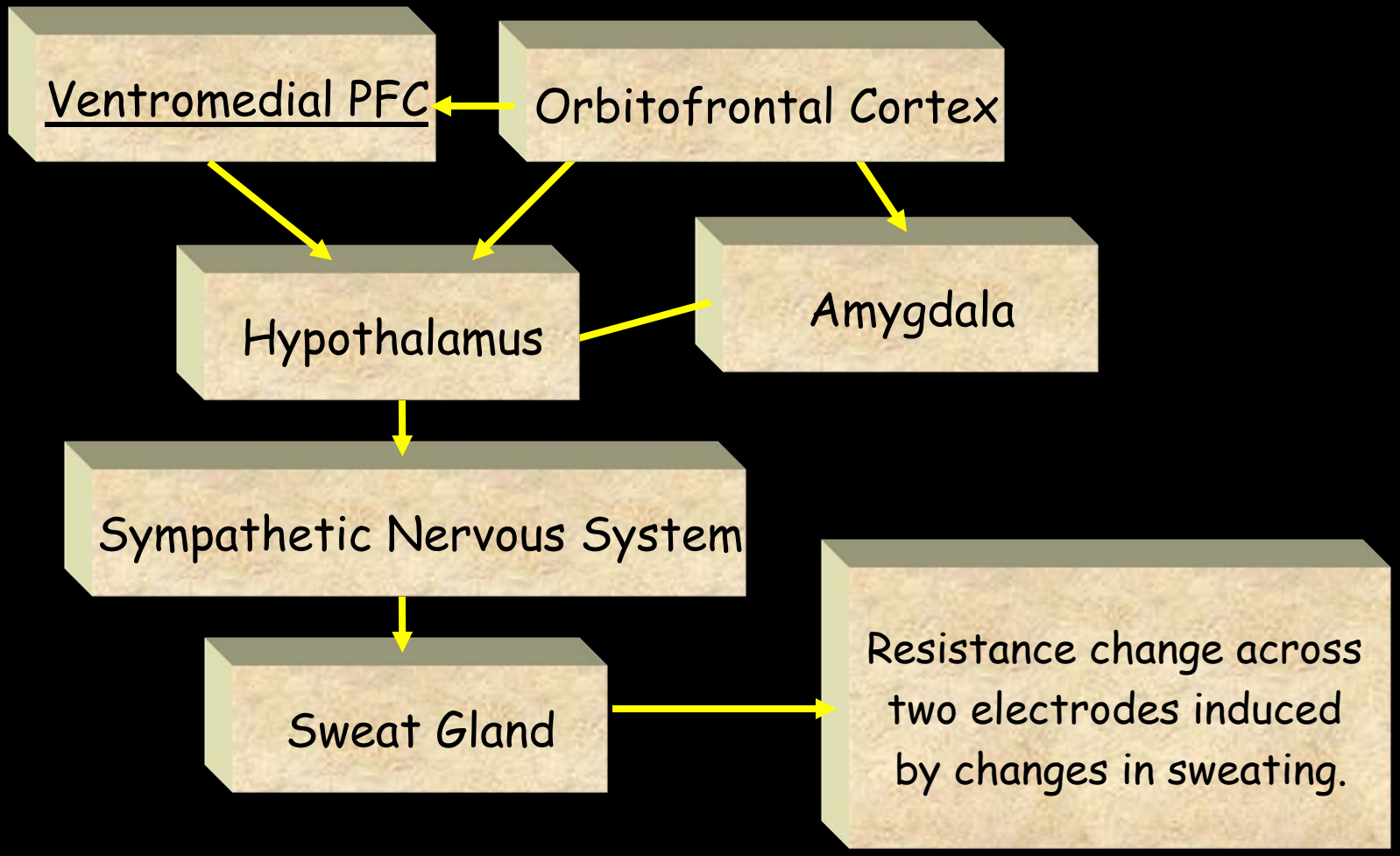
6. Free Behavior Design.

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 Dynamics

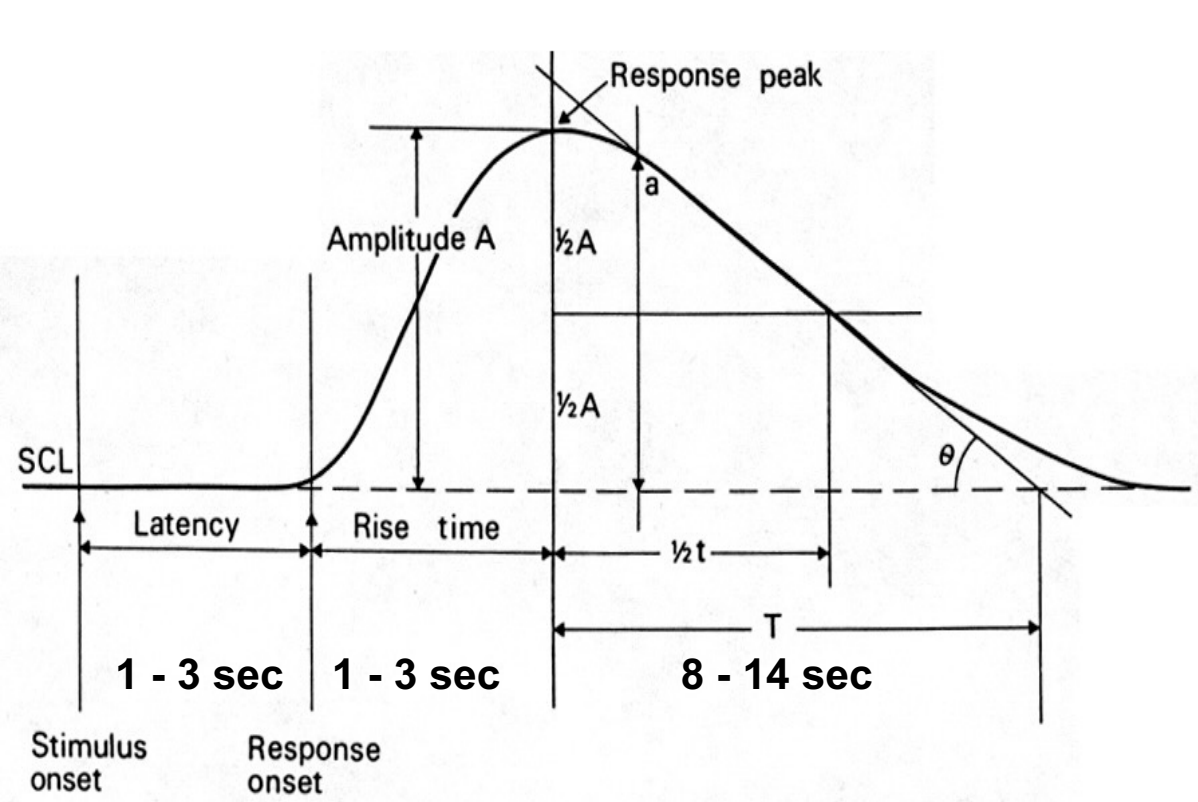
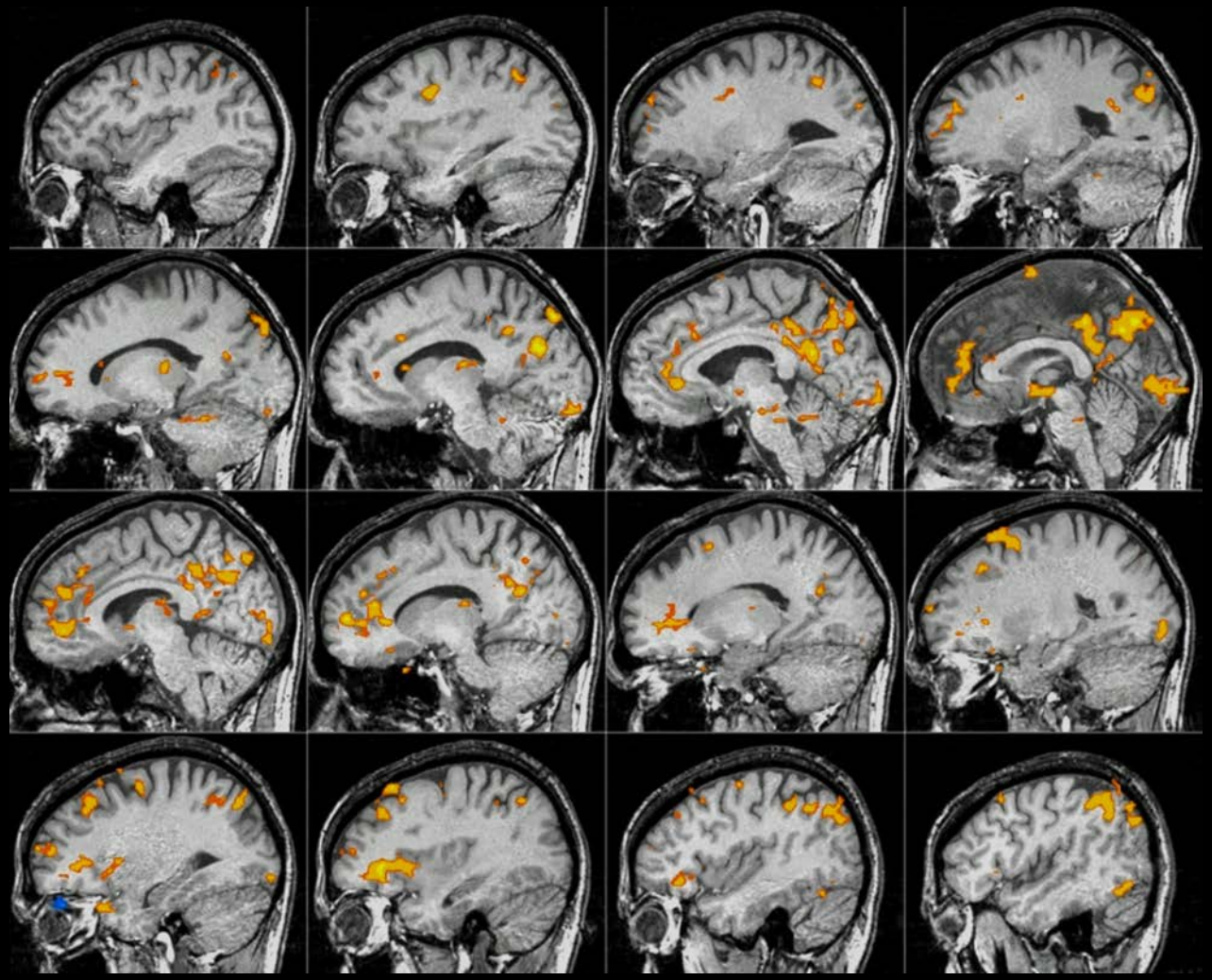


FIGURE 1. Diagrammatic skin conductance response.

•Boucsein, Wolfram (1992). Electrodermal Activity. Plenum Press, NY

•Venables, Peter, (1991). Autonomic Activity ANYAS 620:191-207.

Brain activity correlated with SCR during “Rest”



The 10 Things

1. The Scanning Technique (MRI)
2. Necessary Technical skills and/or People
3. Imaging and Processing steps
4. Types of Functional Contrast
5. Details of Functional Contrast
6. Types of Artifacts
7. Methods to Bypass or Remove Artifacts
8. Types of Applications
9. Limits of Techniques and Applications
10. Some “rules of thumb”

Types of Applications

- Clinical
  - presurgical mapping
  - perfusion mapping
  - correlation with disorders
- Physiology
- Basic Neuroscience
- Cognitive Neuroscience
- Psychiatry
- Psychology
- Pharmacology

The 10 Things

1. The Scanning Technique (MRI)
2. Necessary Technical skills and/or People
3. Imaging and Processing steps
4. Types of Functional Contrast
5. Details of Functional Contrast
6. Types of Artifacts
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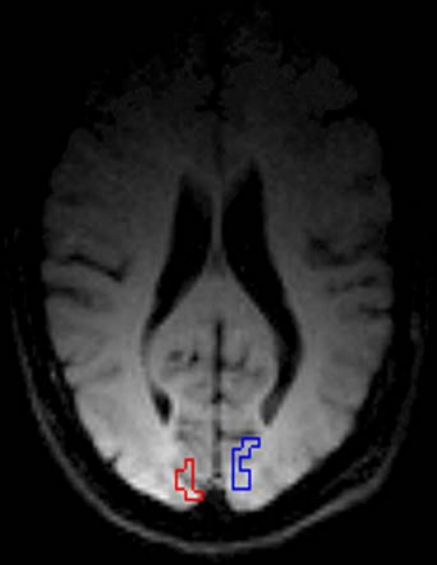
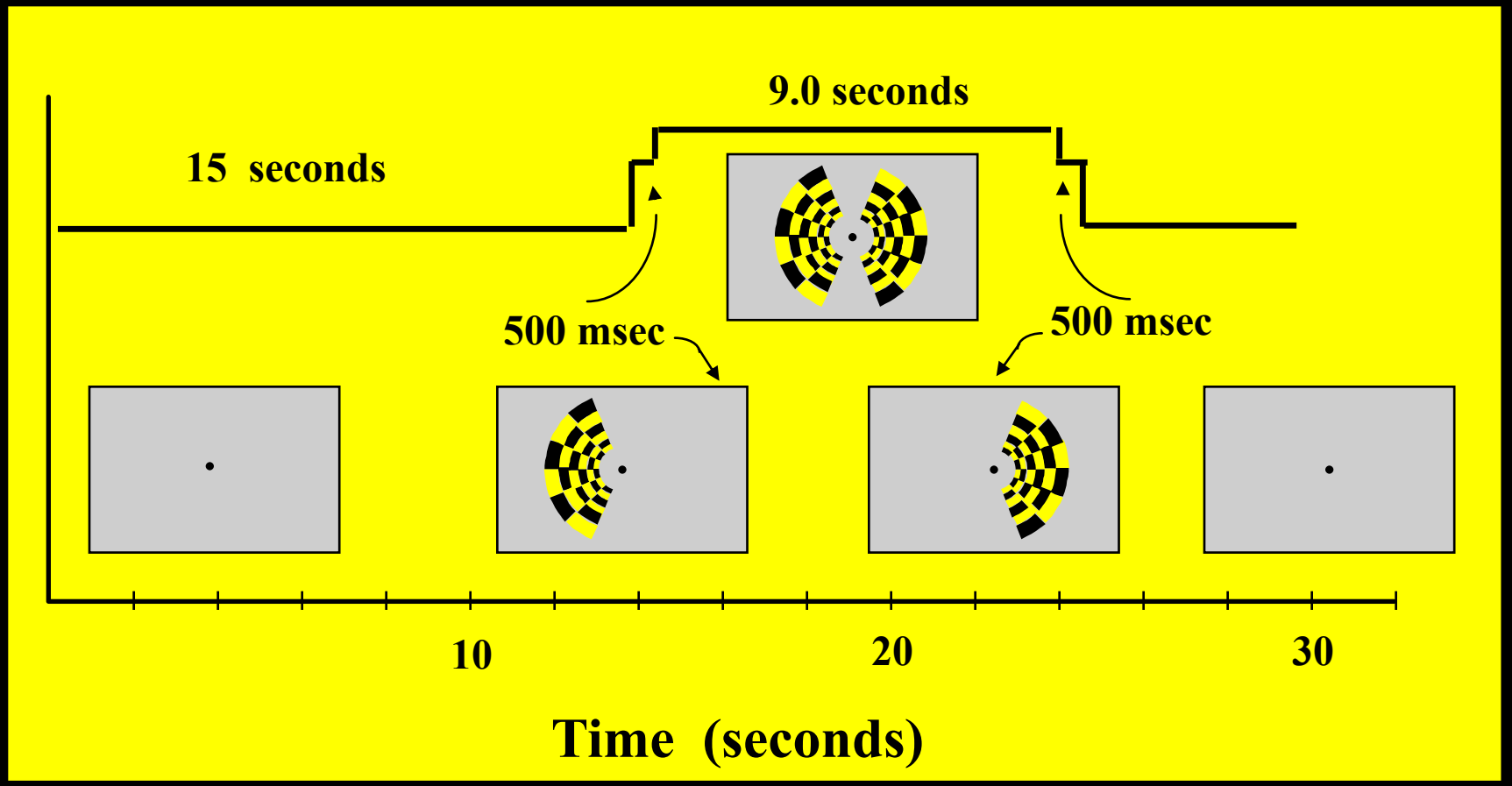
9. Limits of Techniques and Applications
10. Some “rules of thumb”

Regions of Interest Used for Hemi-Field Experiment

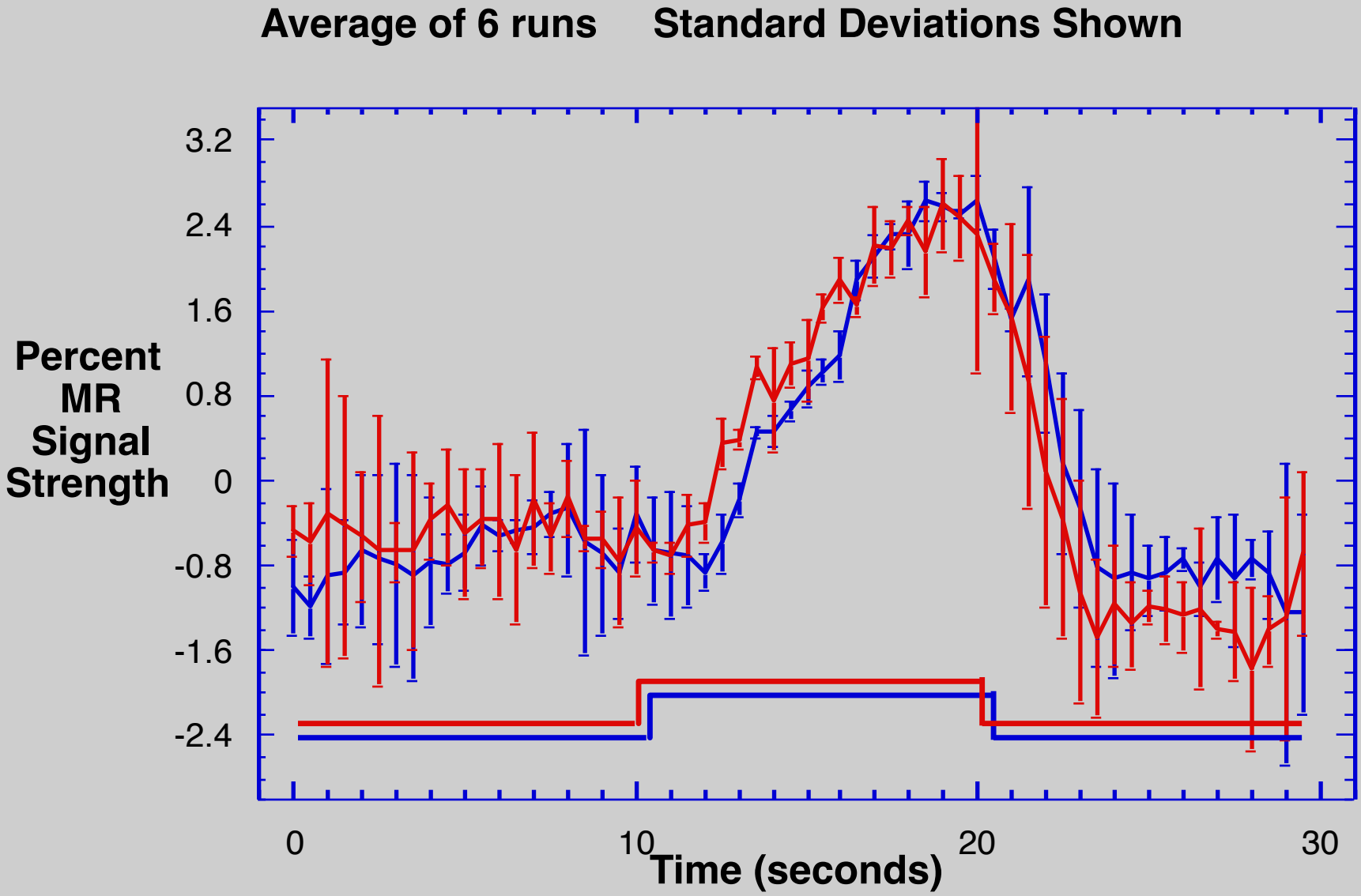


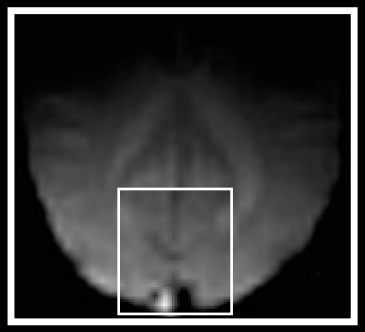
Right Hemisphere

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

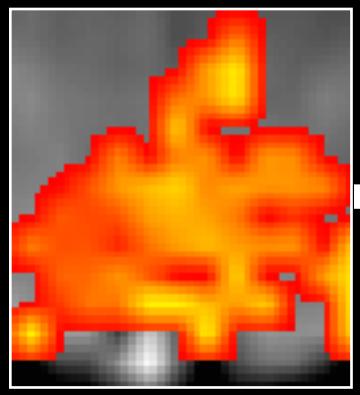
Right Hemifield

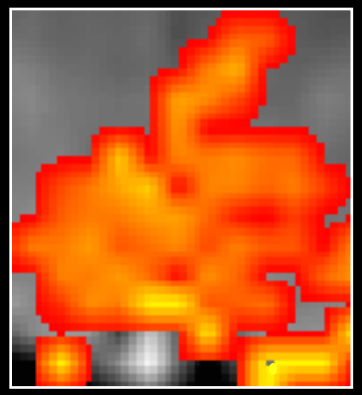
Left Hemifield

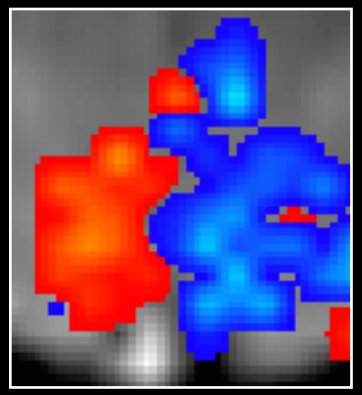
+ 2.5 s

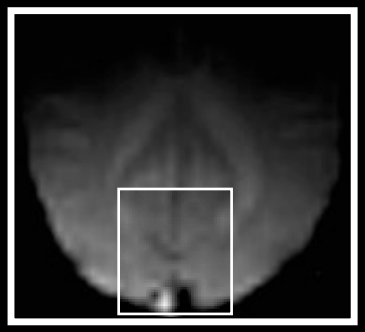
0 s

- 2.5 s





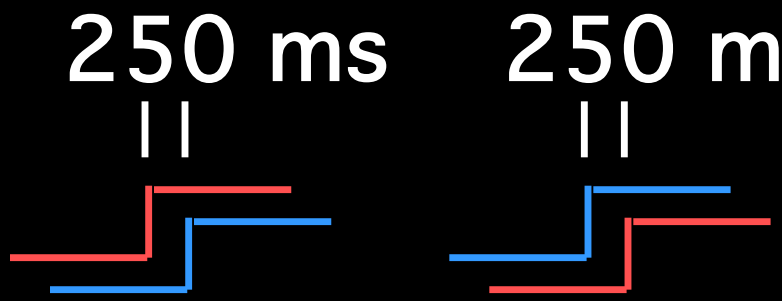




250 ms 250 ms

Right Hemifield

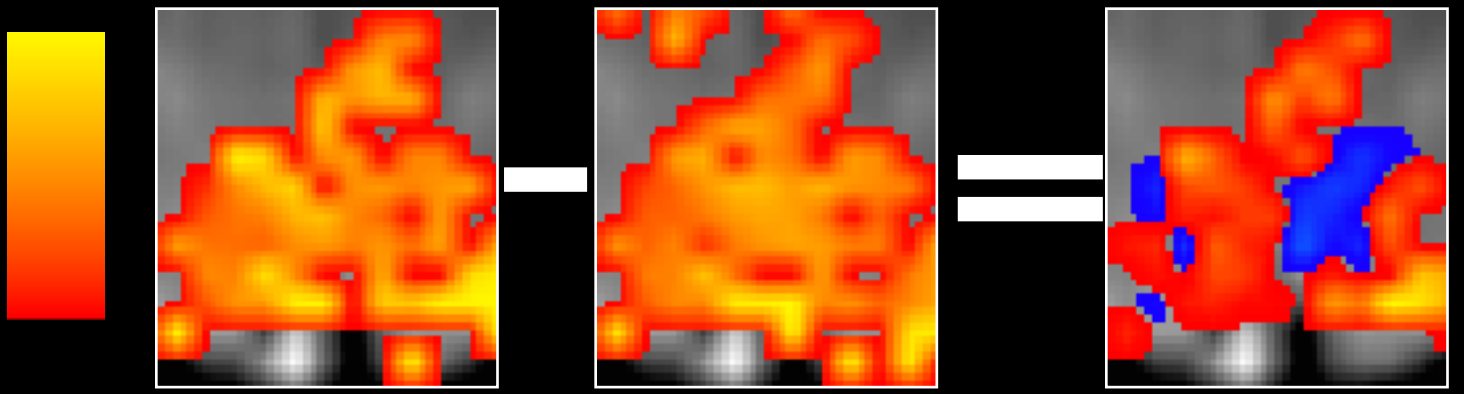
Left Hemifield



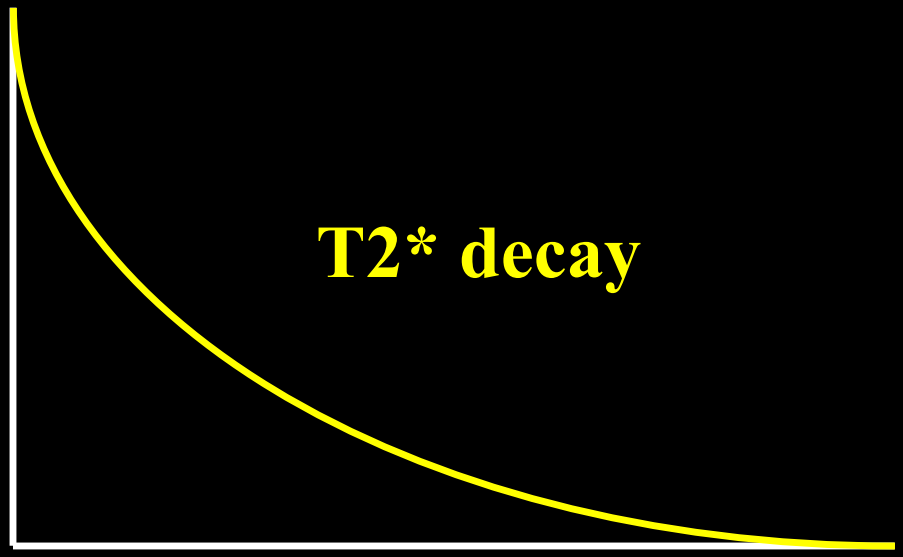
+ 2.5 s

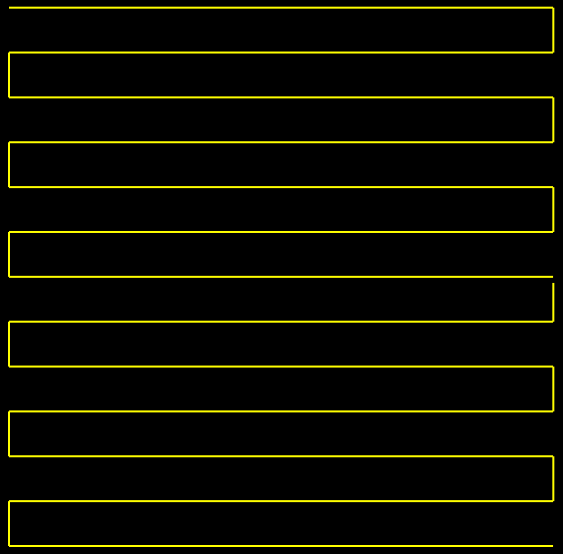
0 s

- 2.5 s



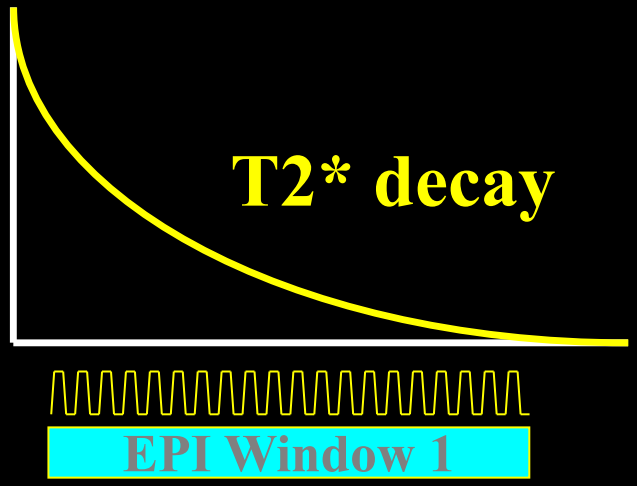
Single Shot Imaging

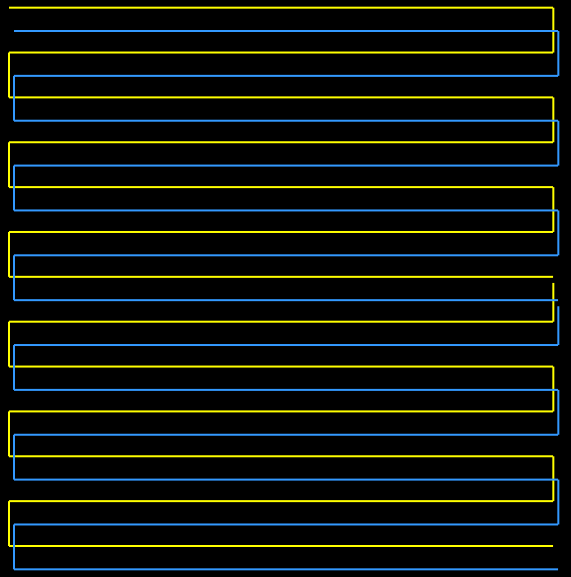


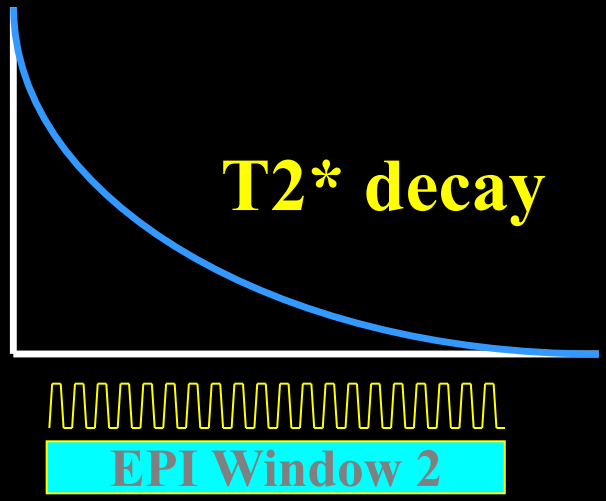


≈ 20 to 40 ms

Multishot Imaging

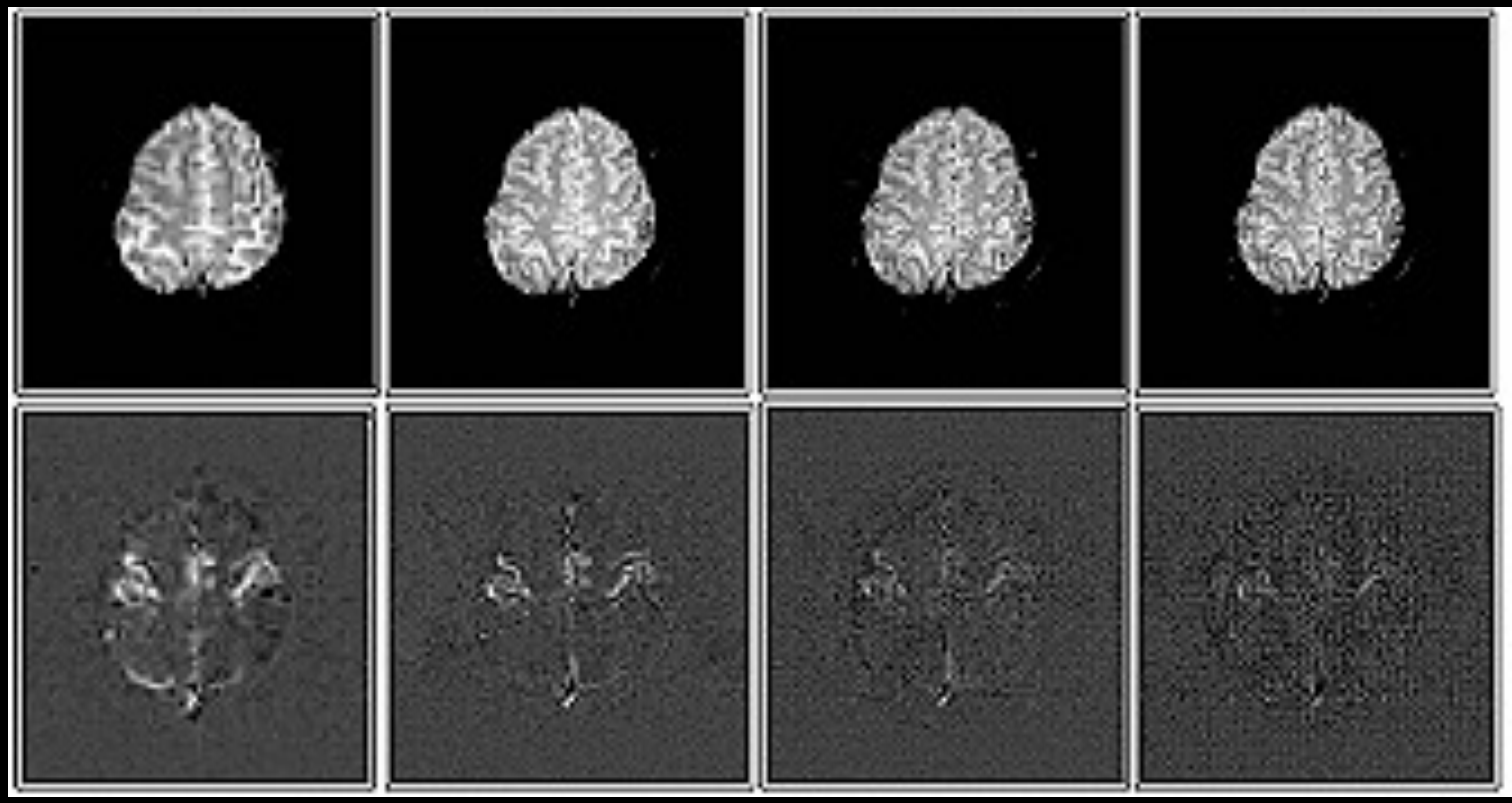




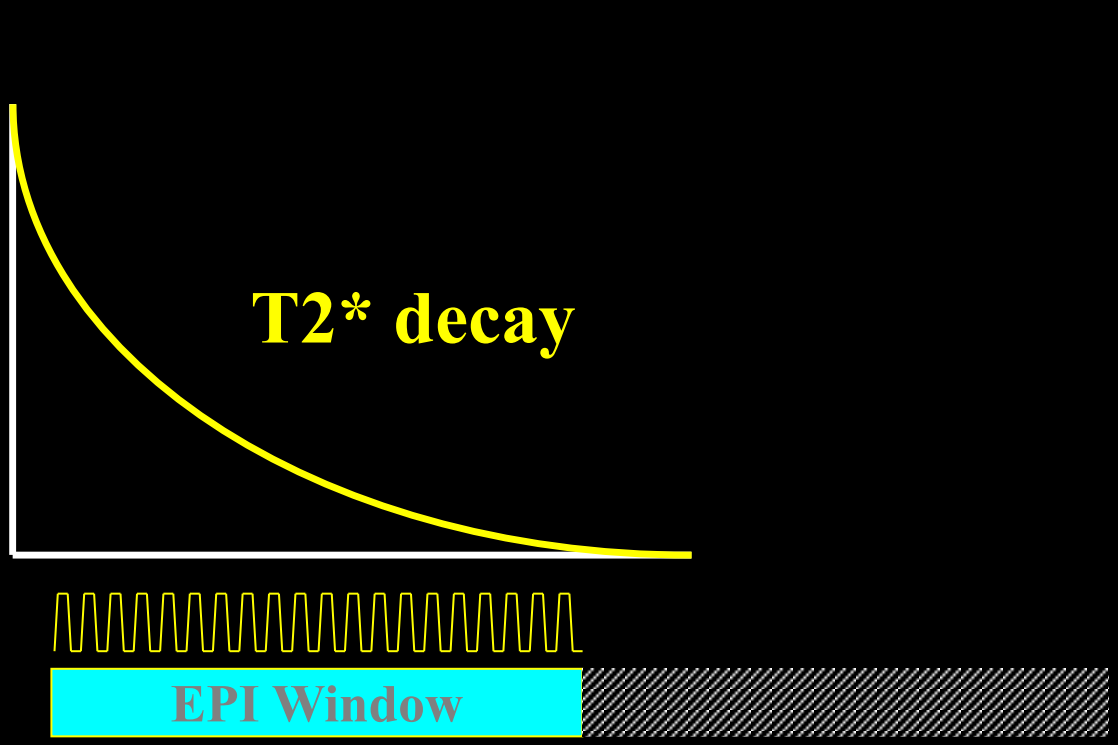


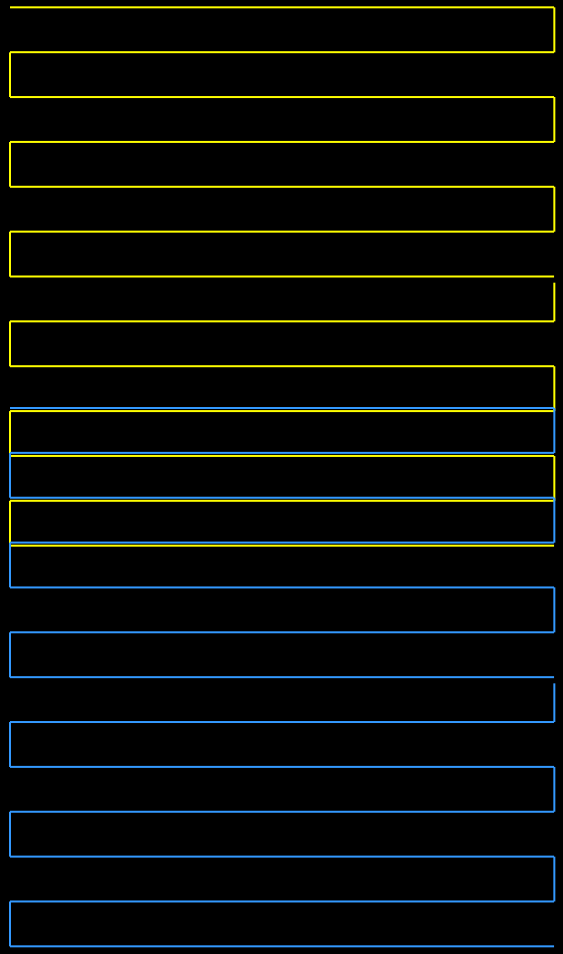
Multi Shot EPI

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

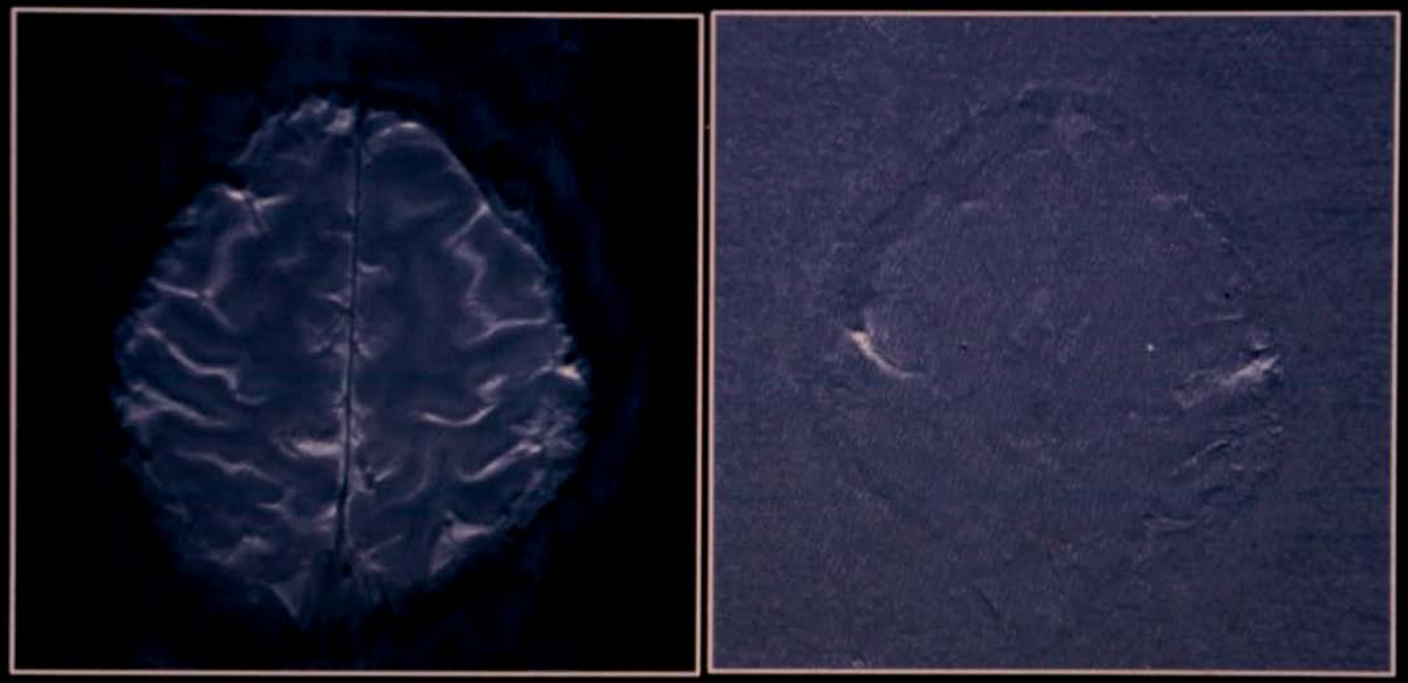


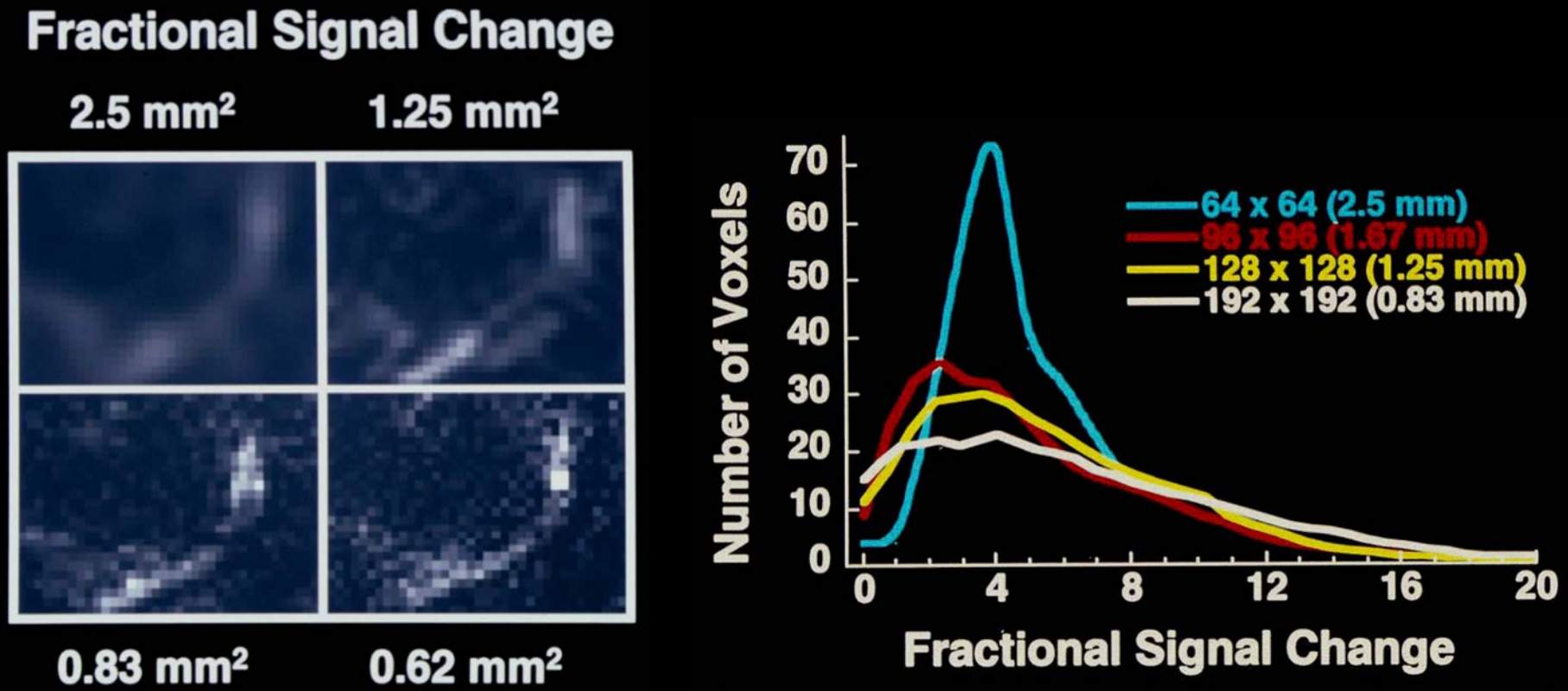
Partial k-space imaging



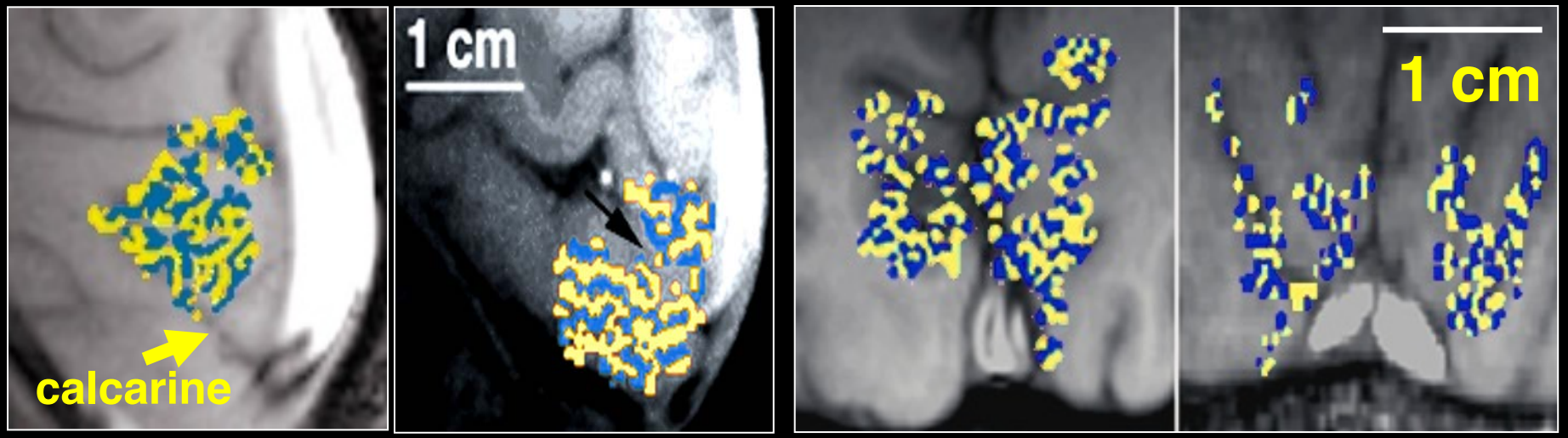


Single - Shot EPI at 3T:
Half NEX, 256 x 256, 16 cm FOV




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)

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).

The 10 Things

1. The Scanning Technique (MRI)
2. Necessary Technical skills and/or People
3. Imaging and Processing steps
4. Types of Functional Contrast
5. Details of Functional Contrast
6. Types of Artifacts
7. Methods to Bypass or Remove Artifacts
8. Types of Applications
9. Limits of Techniques and Applications
10. Some “rules of thumb”

“Rules of Thumb”

Signal Dropout – shimming limits
Image Warping
Resolution
Repetition Time (TR)
Echo Time (TE)
Time necessary for a slice
Amount of averaging necessary
Smoothing? (spatial, temporal)
RF coils
Comparisons within/across subjects

The 10 Things

1. The Scanning Technique (MRI)
2. Necessary Technical skills and/or People
3. Imaging and Processing steps
4. Types of Functional Contrast
5. Details of Functional Contrast
6. Types of Artifacts
7. Methods to Bypass or Remove Artifacts
8. Types of Applications
9. Limits of Techniques and Applications
10. Some “rules of thumb”

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