Choosing the Optimal Sequences and Strategies for Functional MRI

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Variables to Optimize

- Information Content
- Sensitivity
- Speed
- Resolution
- Image quality

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- Information Content
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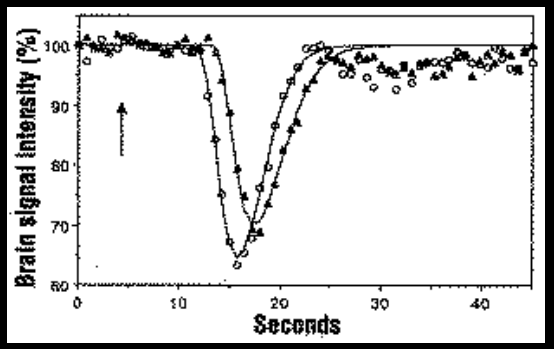
Information Content

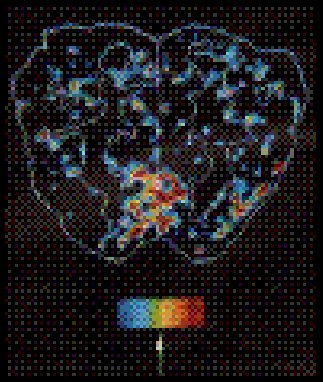
- Blood Volume
- Blood Oxygenation
- Blood Perfusion
- Hemodynamic Specificity
- Mapping of $CMRO_2$

Blood Volume

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

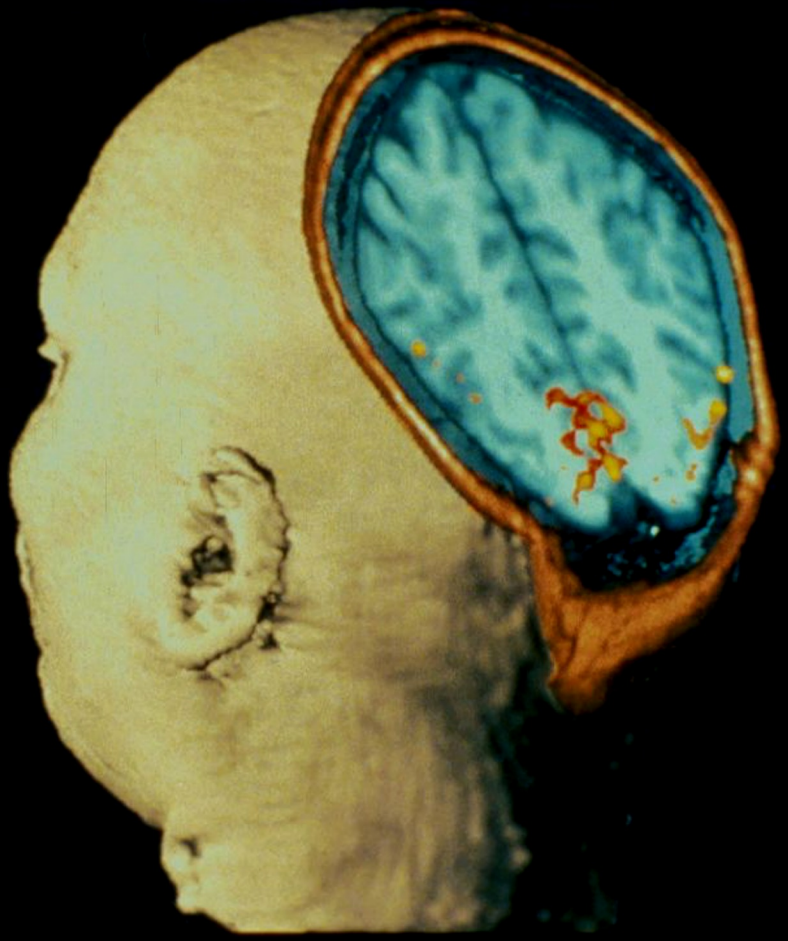
Resting Active





Blood Volume

Photic Stimulation



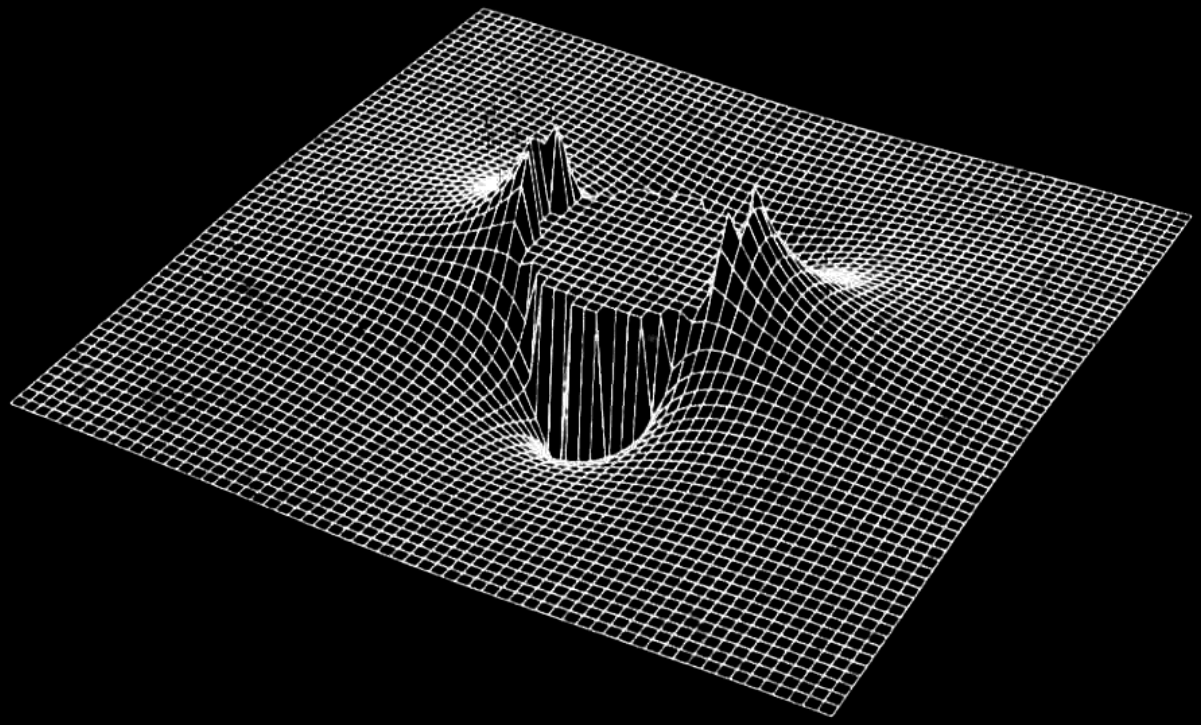
MRI Image showing activation of the Visual Cortex

From Belliveau, et al. Science Nov 1991

MSC - perfusion

Susceptibility Contrast

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



Blood Oxygenation

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

↓

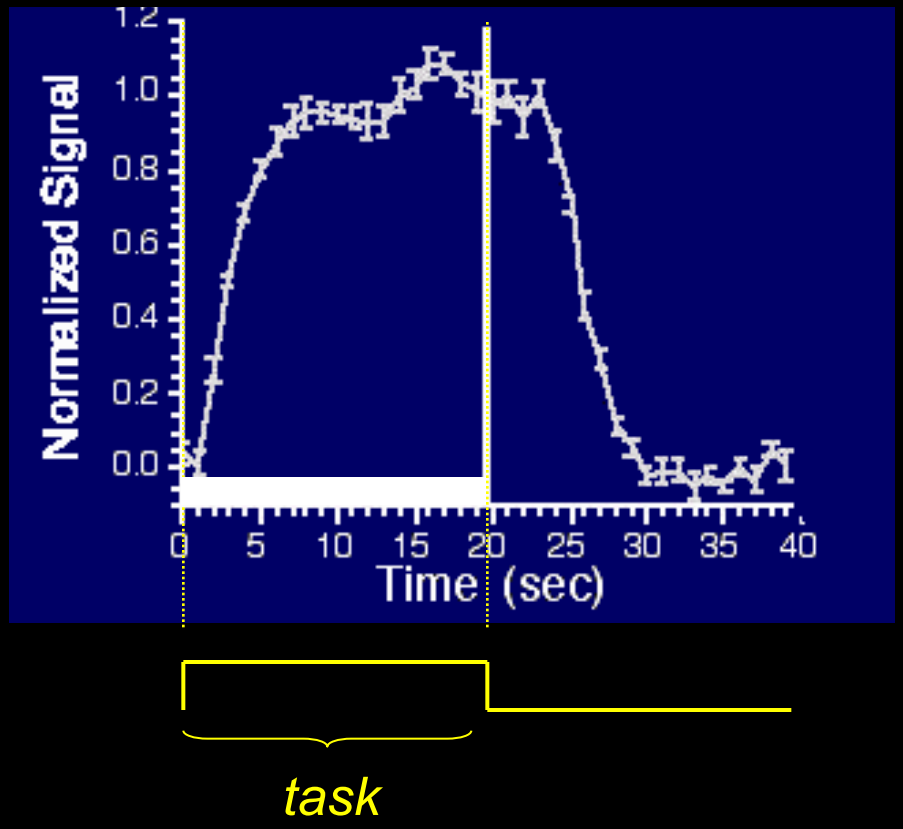
Decrease in susceptibility-related intravoxel dephasing → Increase in T2 and T2*

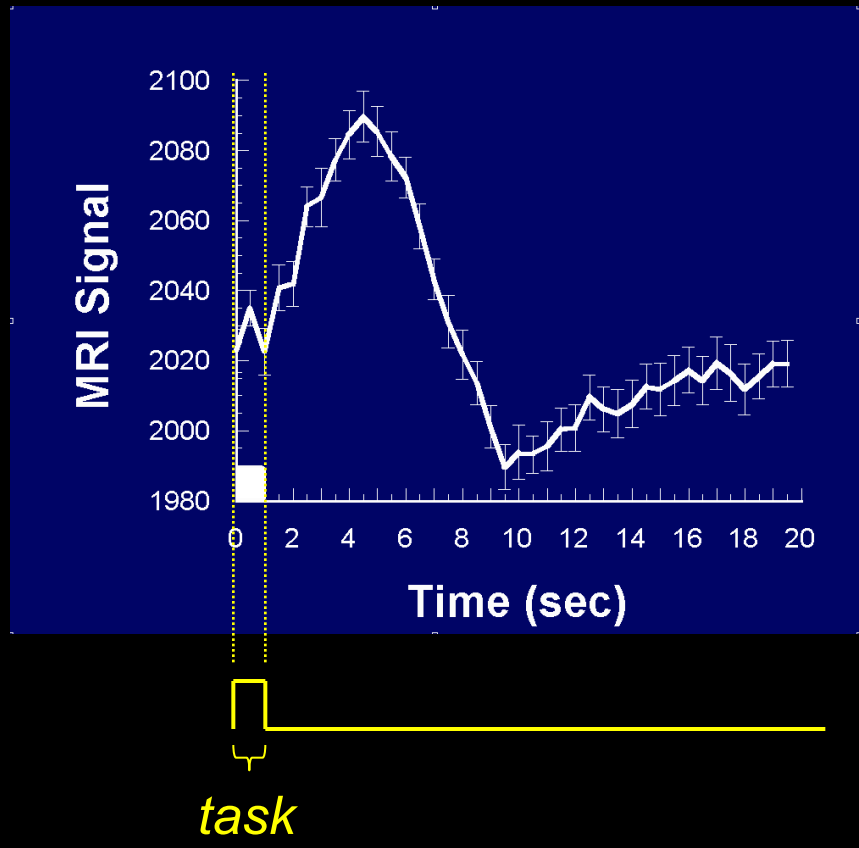
↓

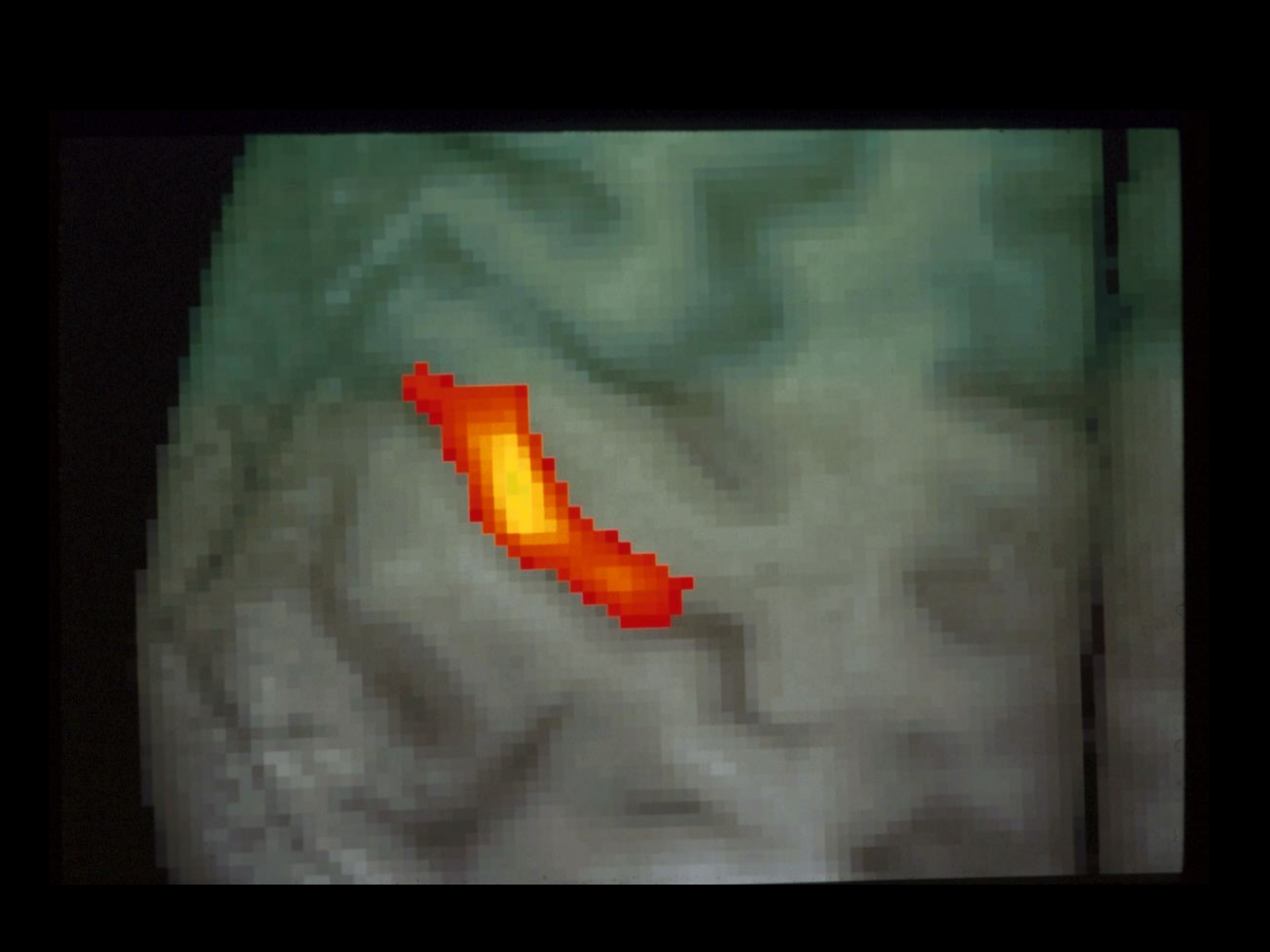
Local Signal Increase in T2 and T2* - weighted sequences

The BOLD Signal

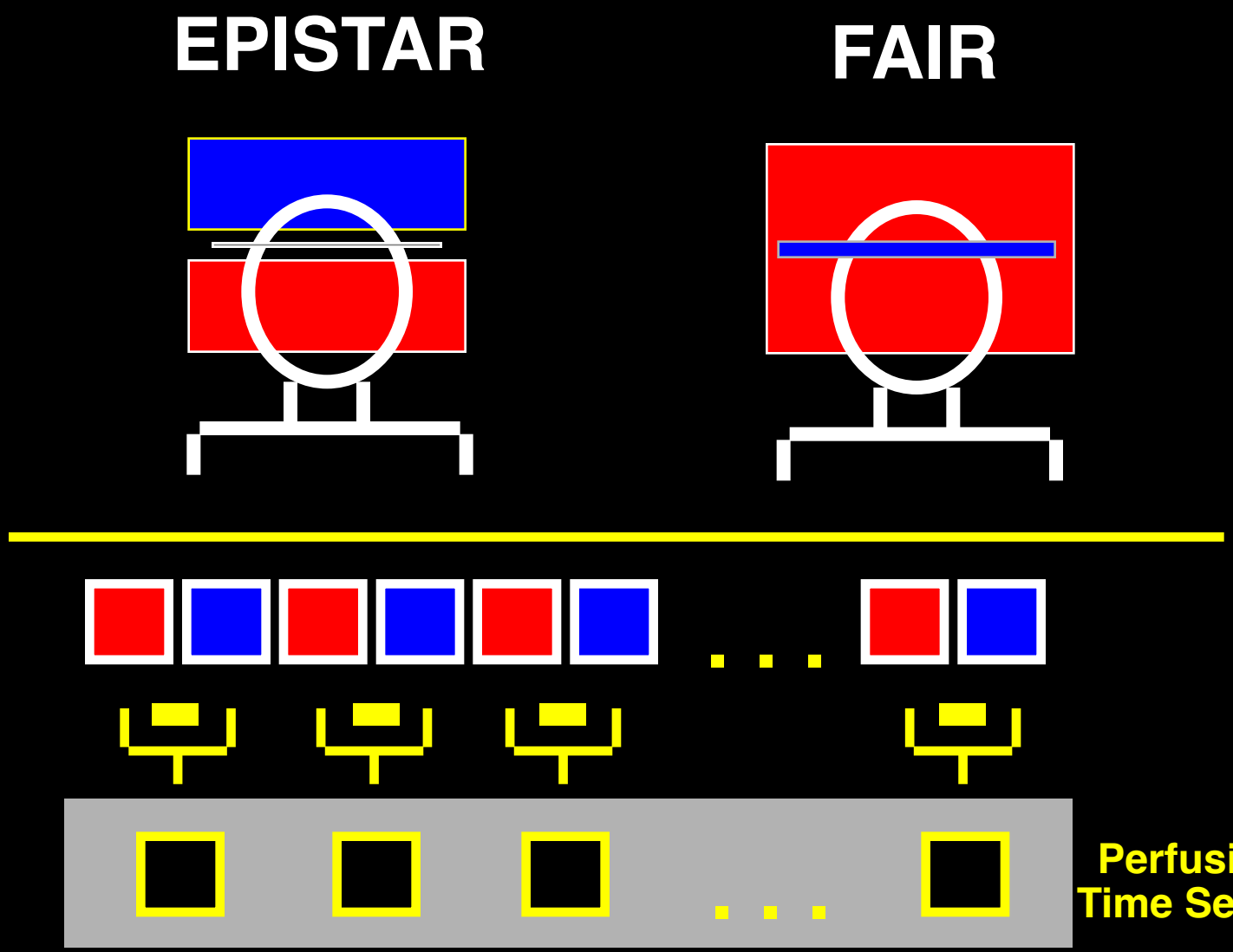
Blood Oxygenation Level Dependent (BOLD) signal changes

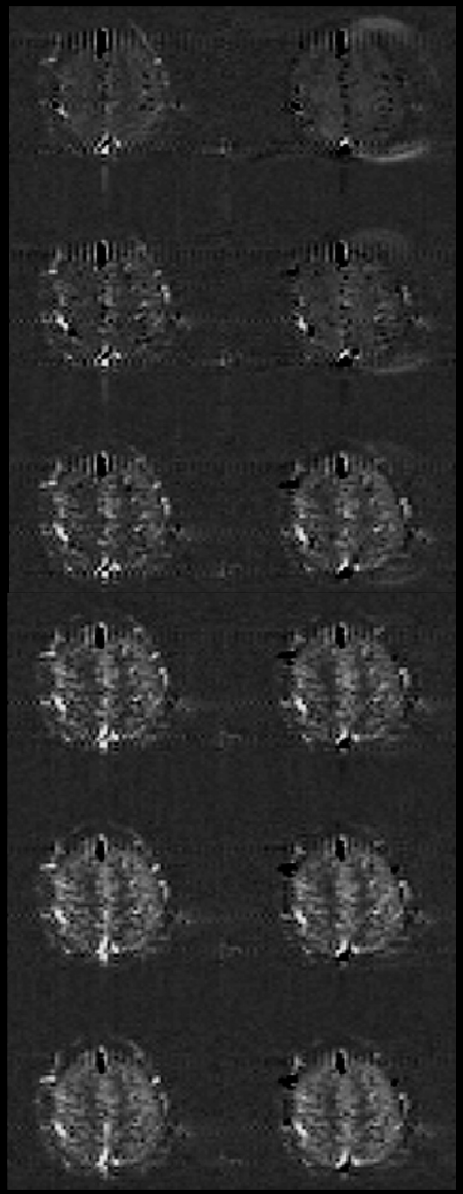






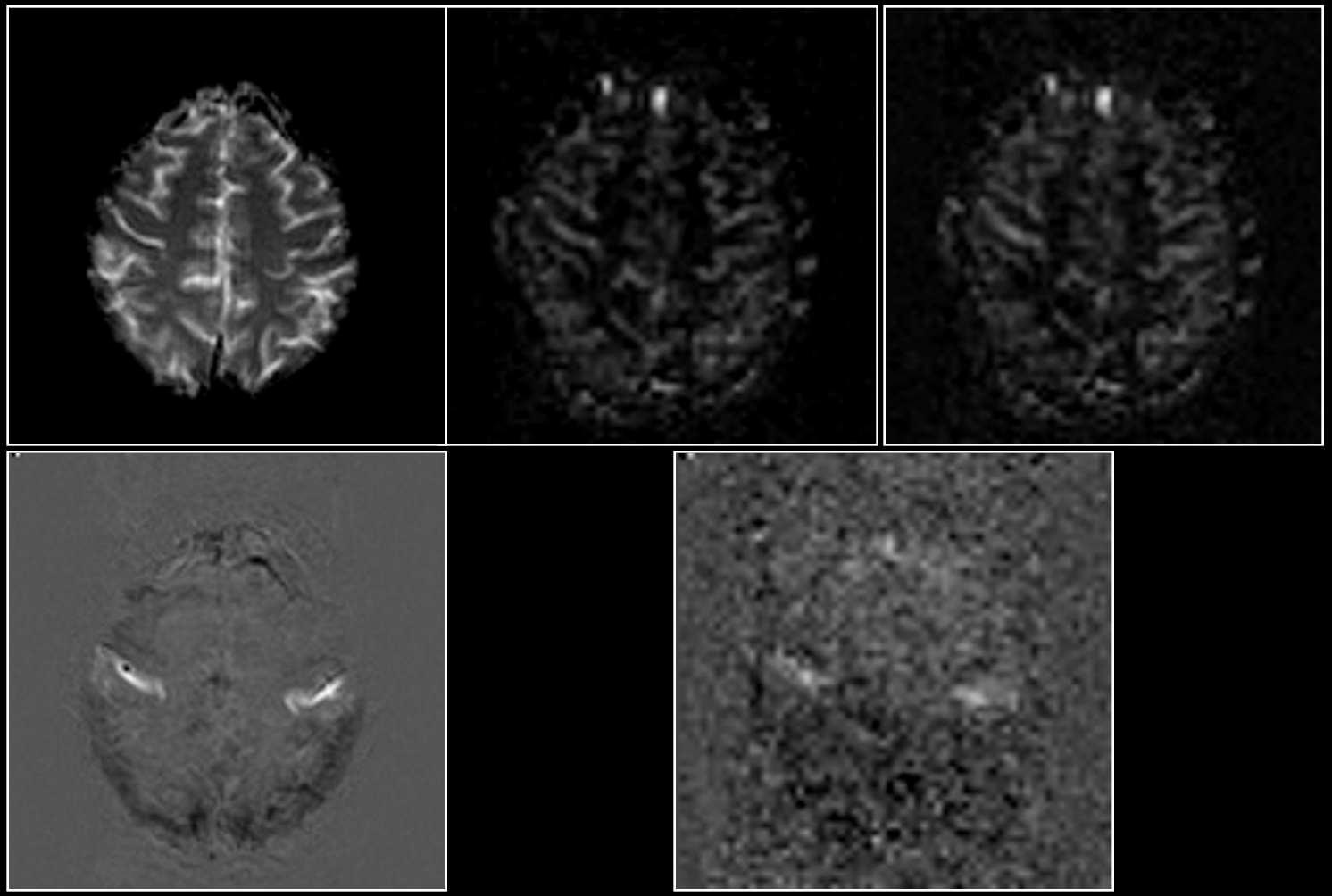
Blood Perfusion



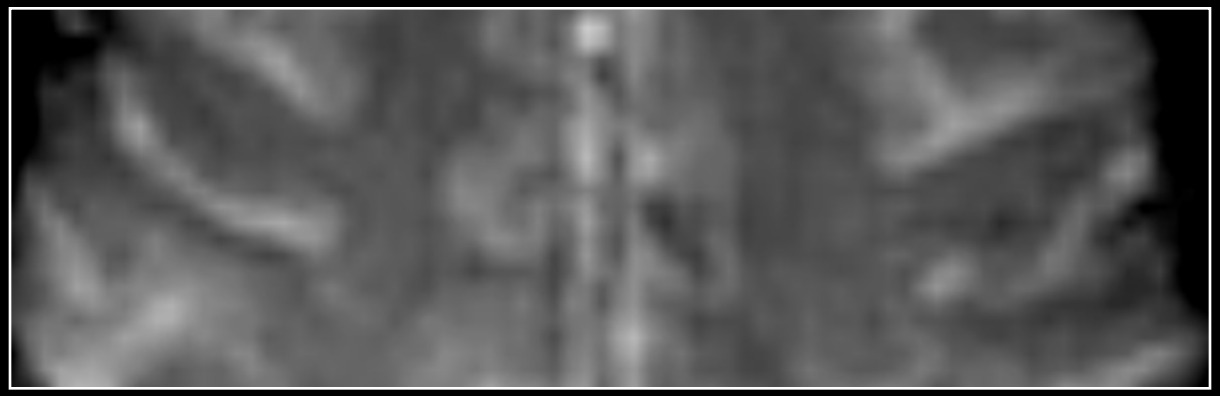
TI (ms)	FAIR	EPISTAR
200		
400		
600		
800		
1000		
1200		

Perfusion

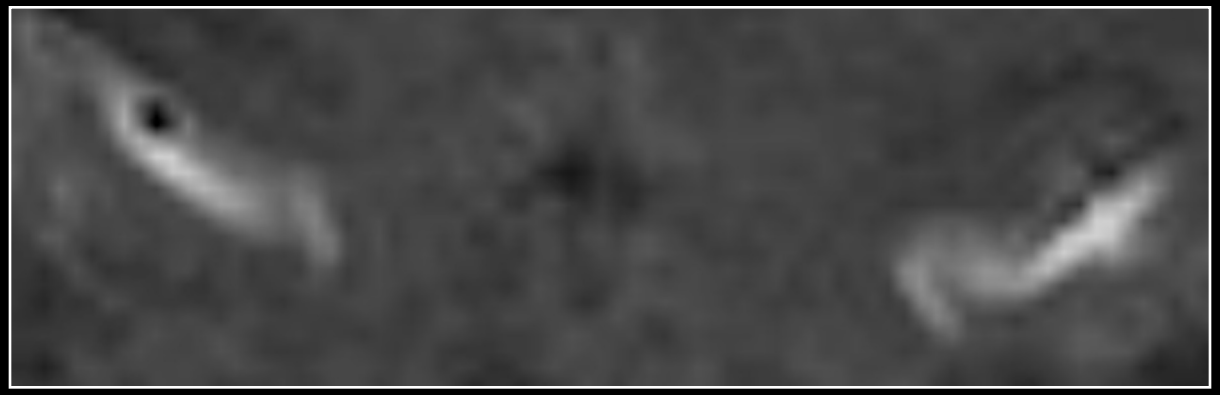
BOLD *Rest* *Activation*



Anatomy



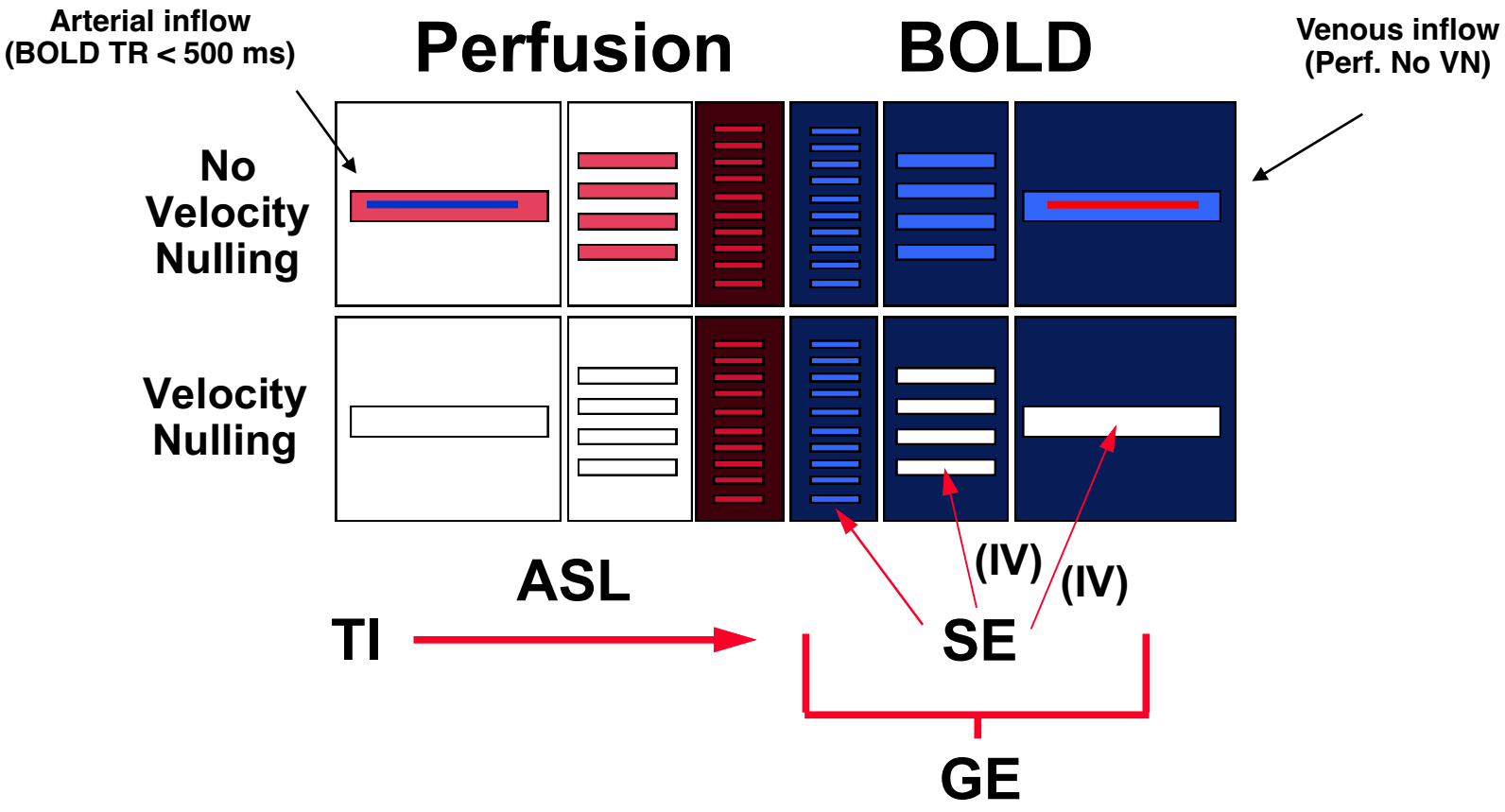
BOLD



Perfusion

	+	-
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

Hemodynamic Specificity

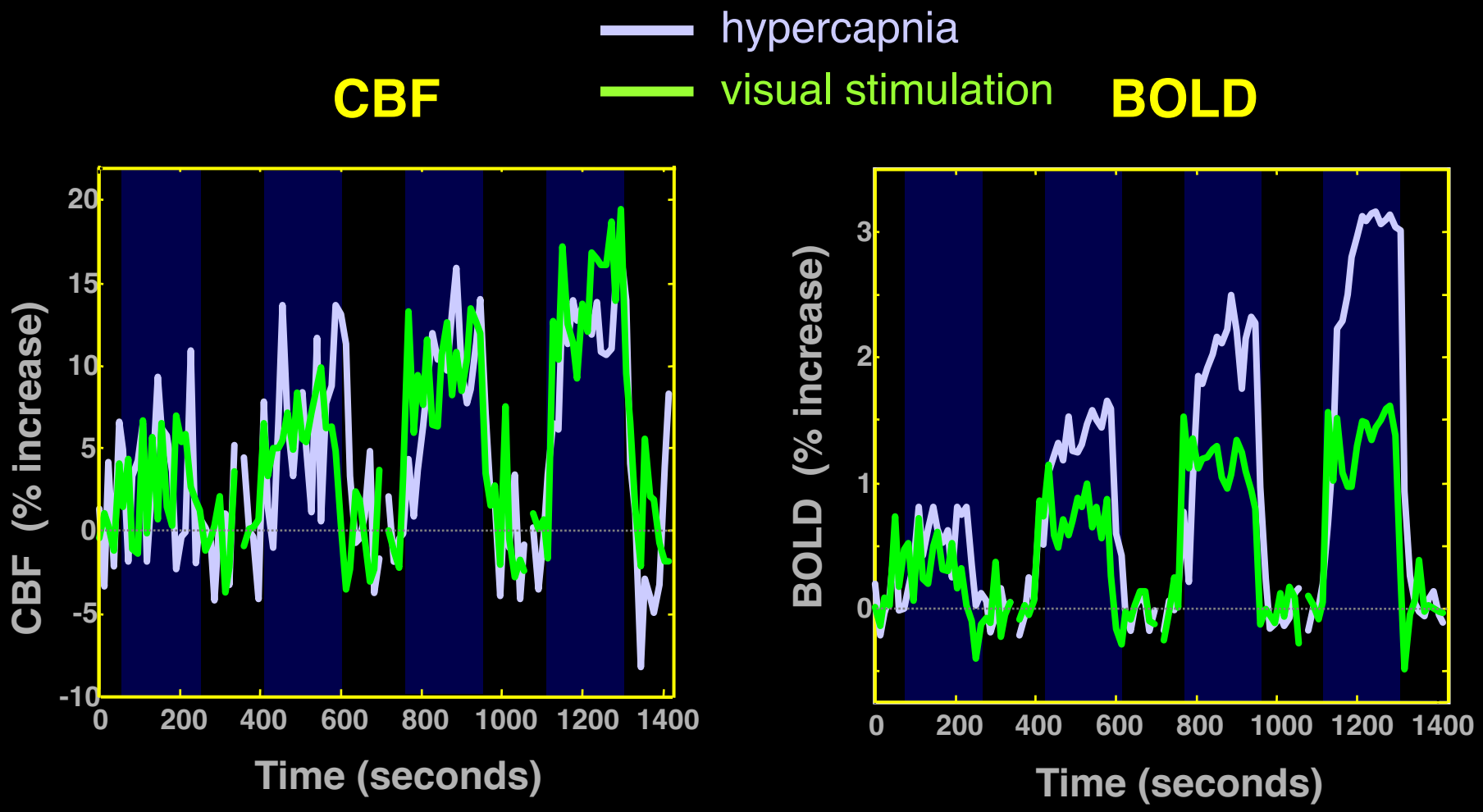


Mapping of $CMRO_2$

Activation:	Flow	⇑⇑
	$CMRO_2$	⇑
	Blood Oxygenation	⇑
CO_2 stress:	Flow	⇑⇑
	$CMRO_2$	⇒
	Blood Oxygenation	⇑⇑

$CMRO_2$-related BOLD signal deficit:

Hoge, et al.

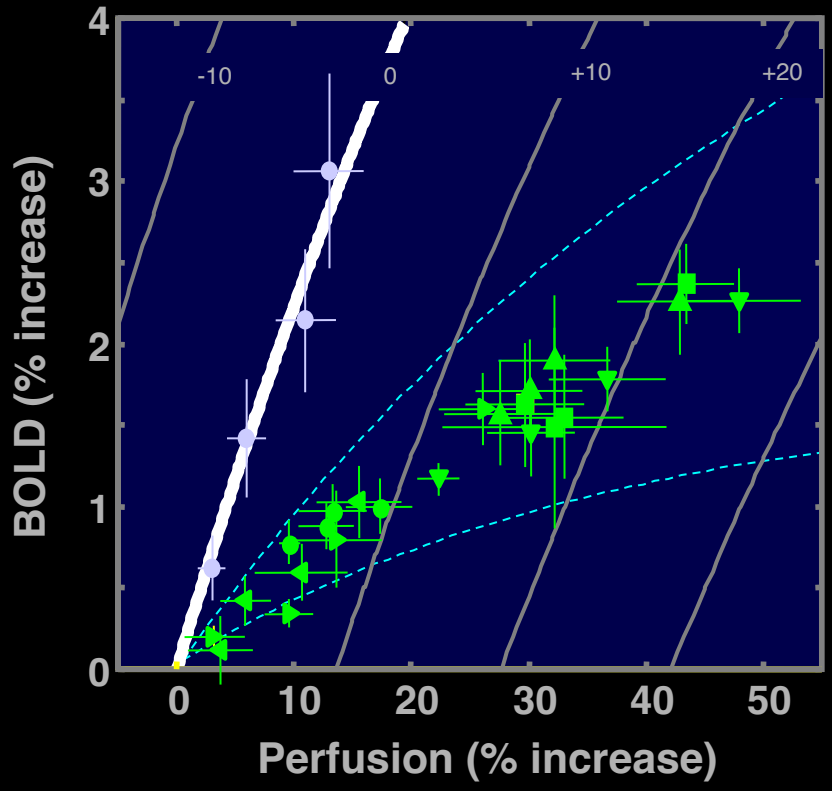


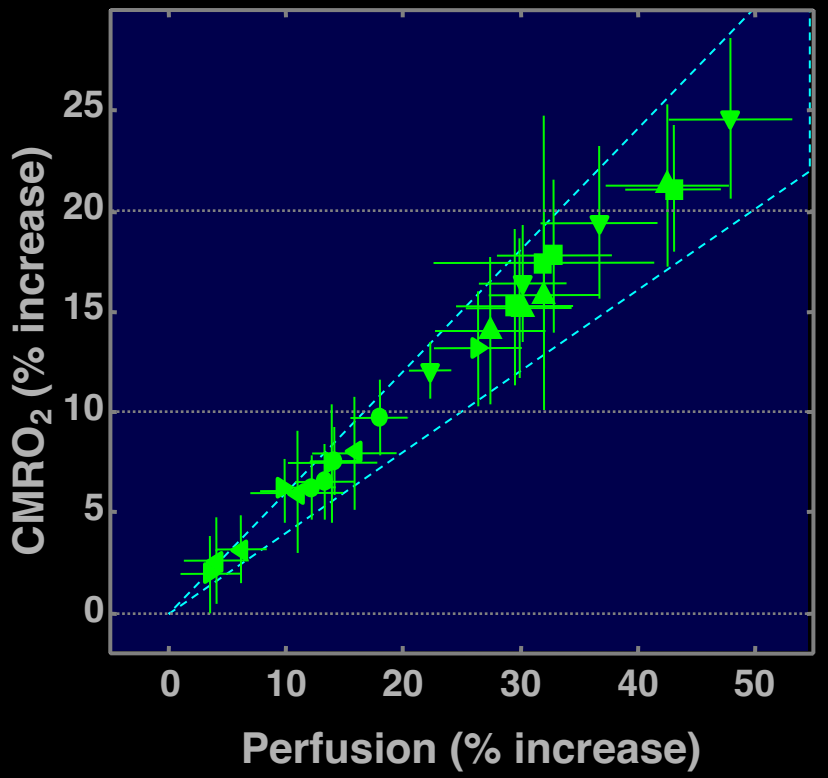
Simultaneous Perfusion and BOLD imaging during graded visual activation and hypercapnia

N=12

CBF-$CMRO_2$ coupling

Hoge, et al.

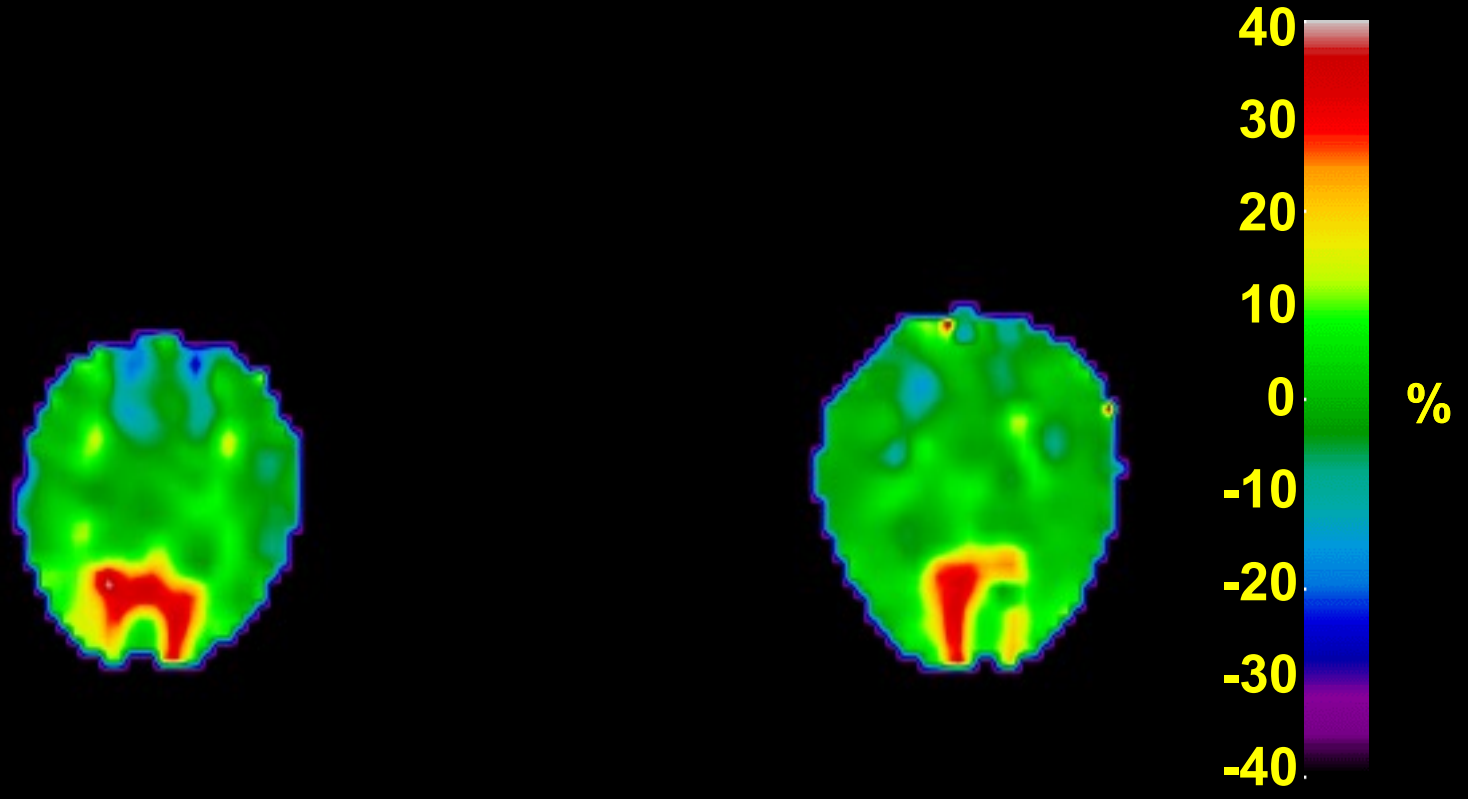




Characterizing Activation-induced $CMRO_2$ changes using calibration with hypercapnia

Hoge, et al.

Computed $CMRO_2$ Changes



Variables to Optimize

- Information Content
- Sensitivity
- Speed
- Resolution
- Image quality

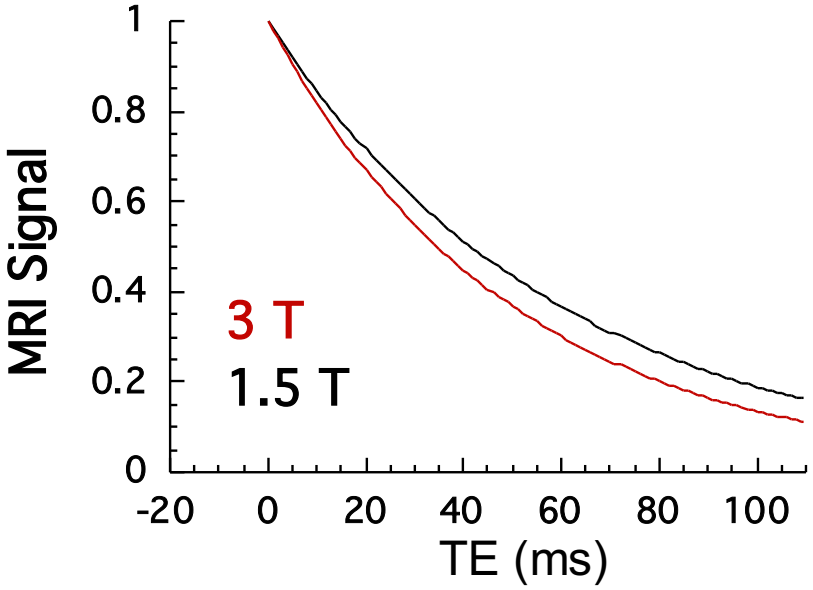
Sensitivity

- Optimizing fMRI Contrast
- Maximizing Signal
- Reducing Physiologic Fluctuations
- Minimizing Temporal Artifacts

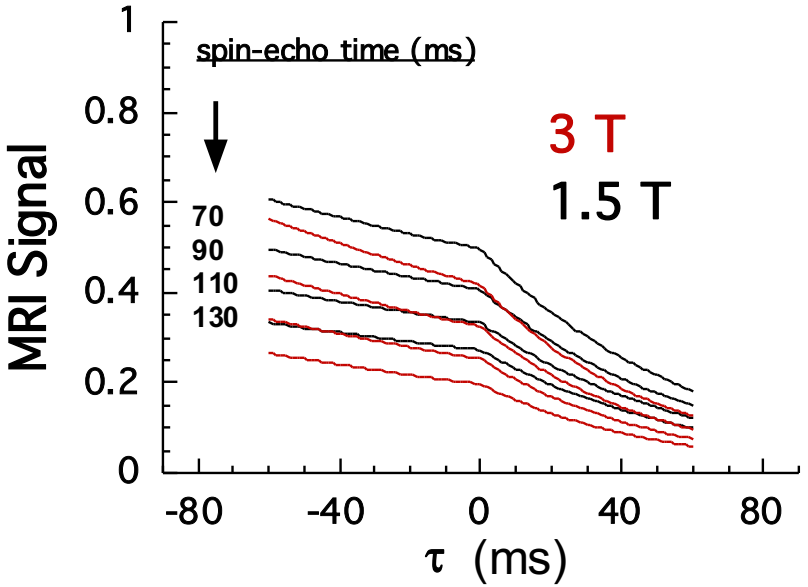
Optimizing fMRI Contrast

- Increase field strength
- Adjust pulse sequence timing (TE ≈ T2*)
- Adjust voxel volume (≈ activation volume)

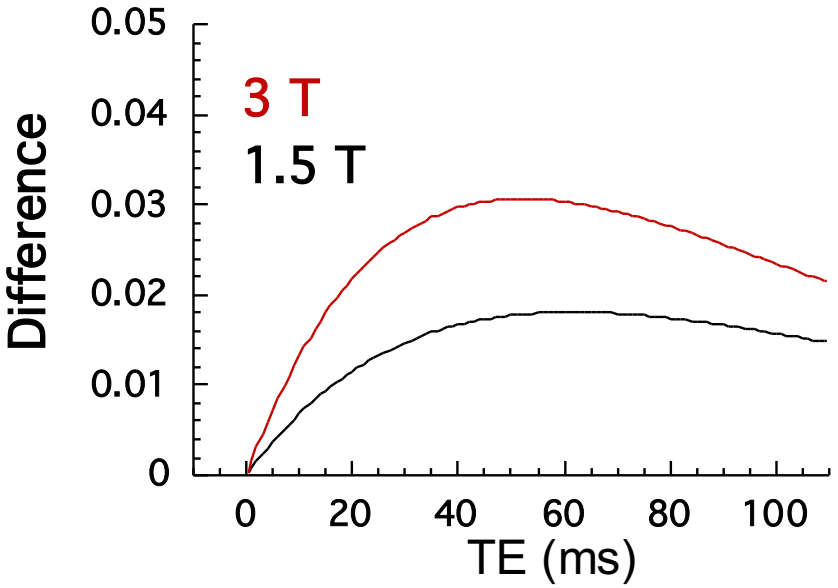
Gradient - Echo



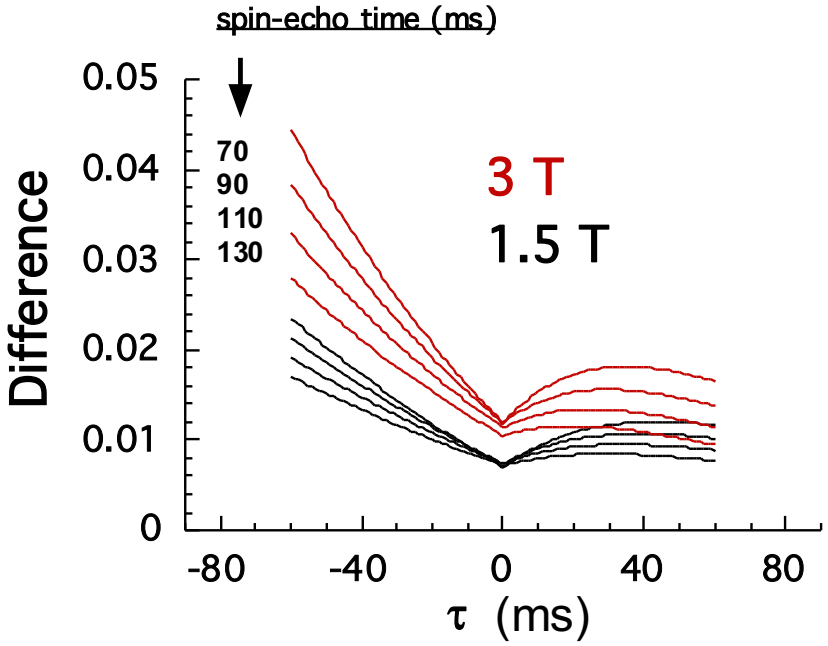
Asymmetric Spin - Echo



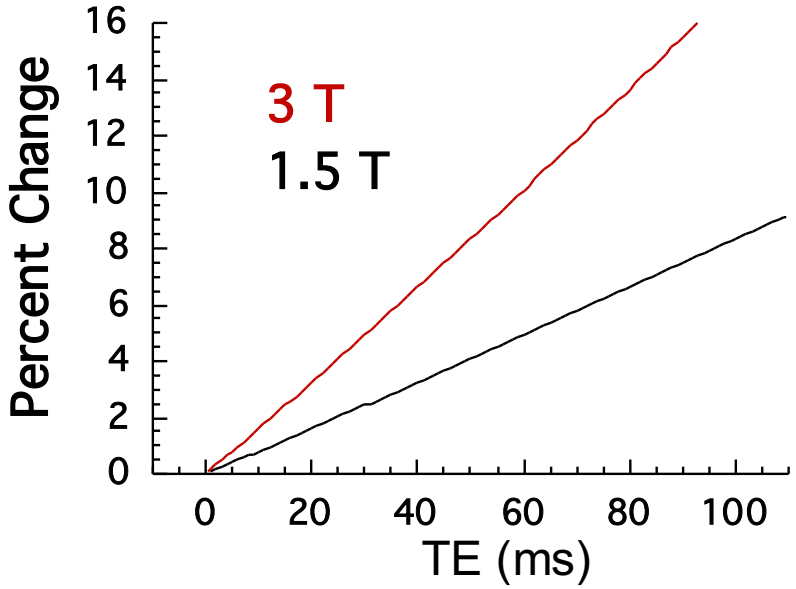
Gradient - Echo



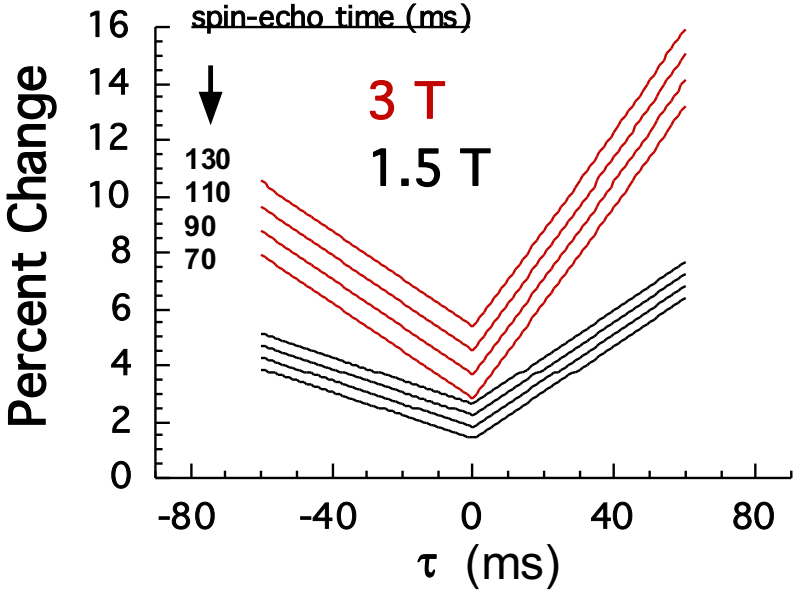
Asymmetric Spin - Echo



Gradient - Echo



Asymmetric Spin - Echo



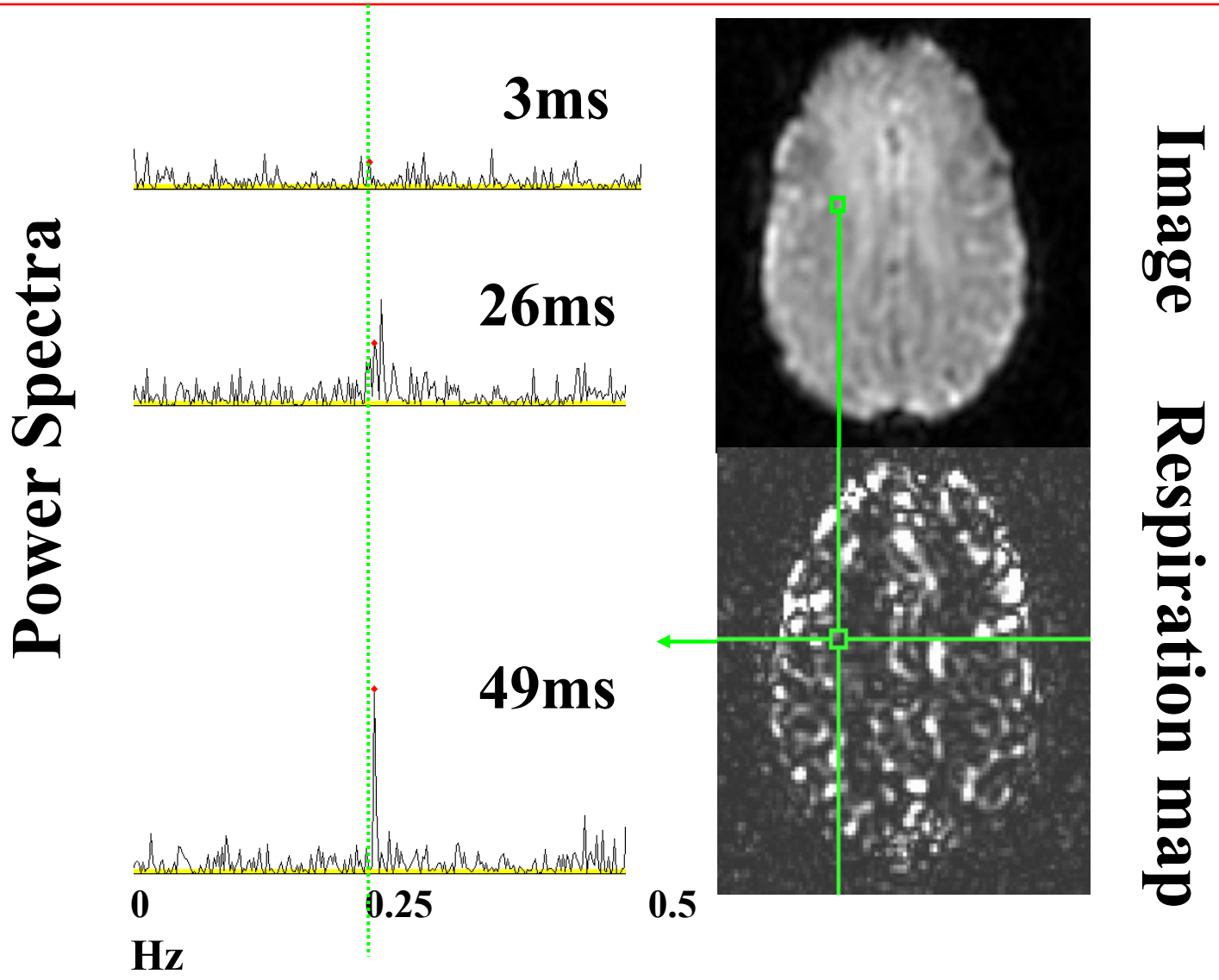
Maximizing Signal

- Higher Bo Field
- Radio frequency Coils
- Choice of repetition time (TR)
- Voxel volume

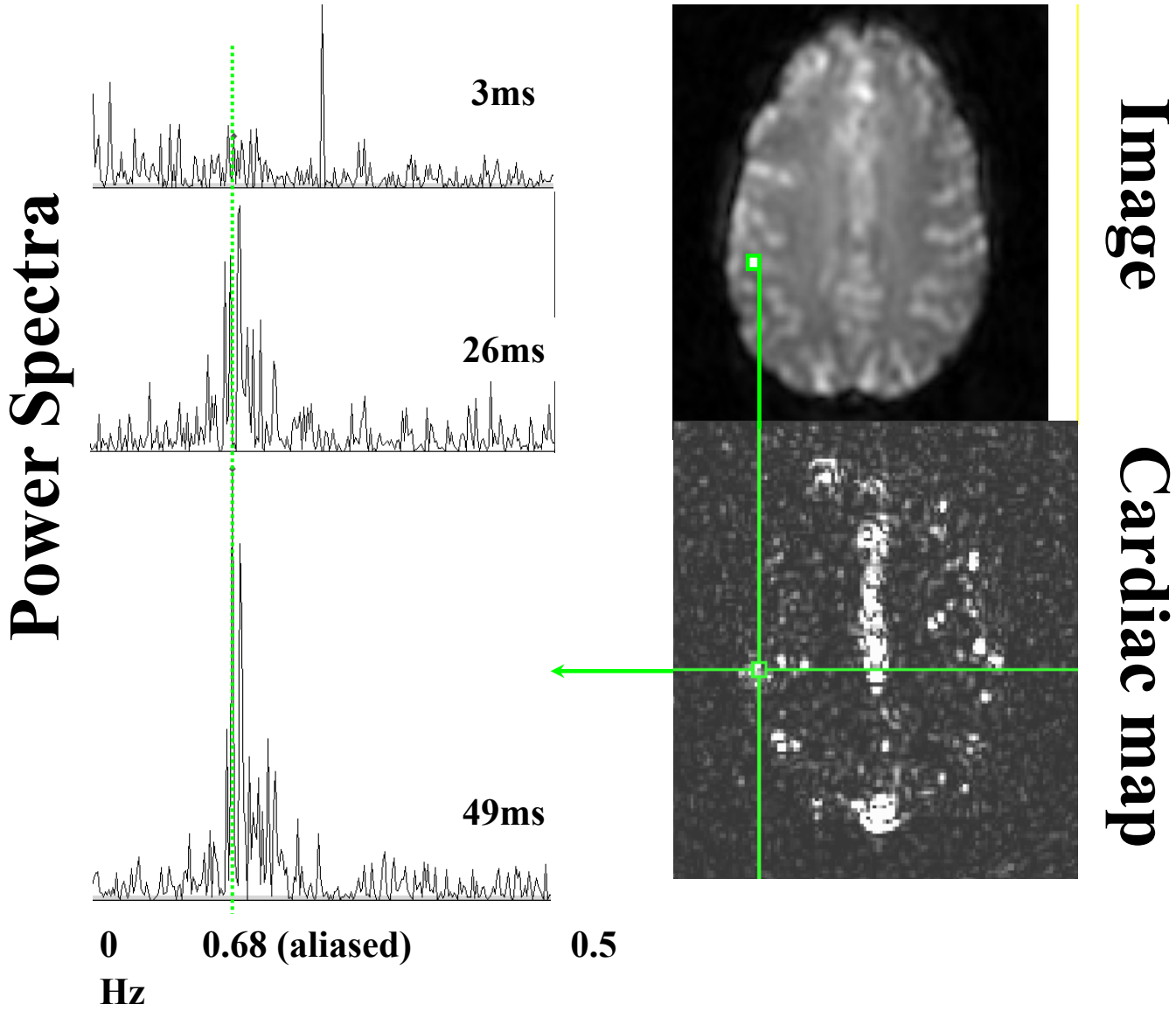
Physiologic Fluctuations

Cardiac	0.6 to 1.2 Hz
Respiratory	0.1 to 0.2 Hz
Low Frequency	0.0 to 0.1 Hz

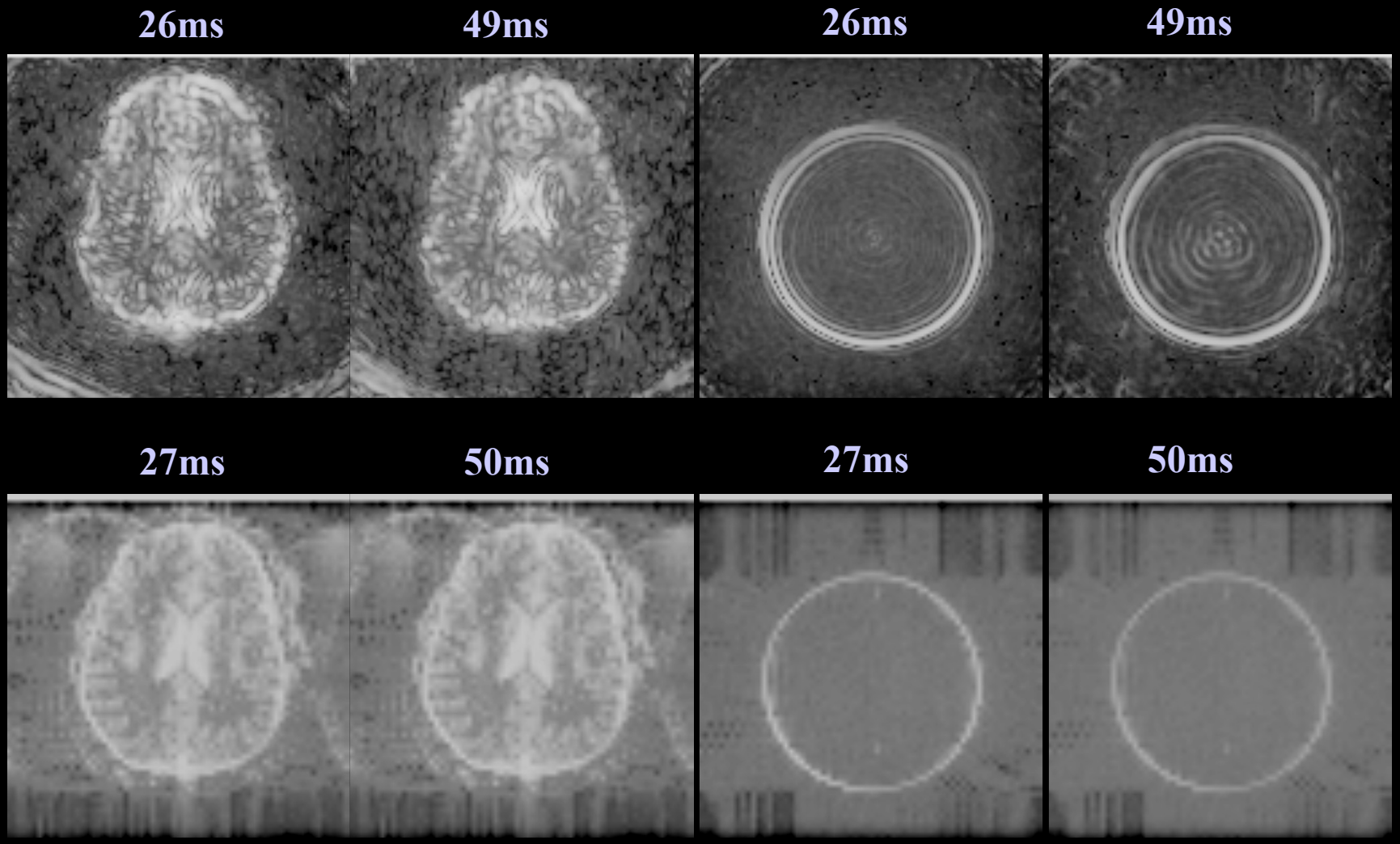
0.25 Hz Breathing at 1.5T



0.68 Hz Cardiac rate at 3T



Temporal vs. Spatial SNR- 3T



Reducing Physiologic Fluctuations

- Filtering
- Pulse sequence
  - single vs. multishot
  - strategies for multishot
- Gating with correction for variable TR

Temporal Artifacts

- System instabilities
- Motion
  - Drift
  - Stimulus correlated
  - Stimulus uncorrelated

Minimizing Temporal Artifacts

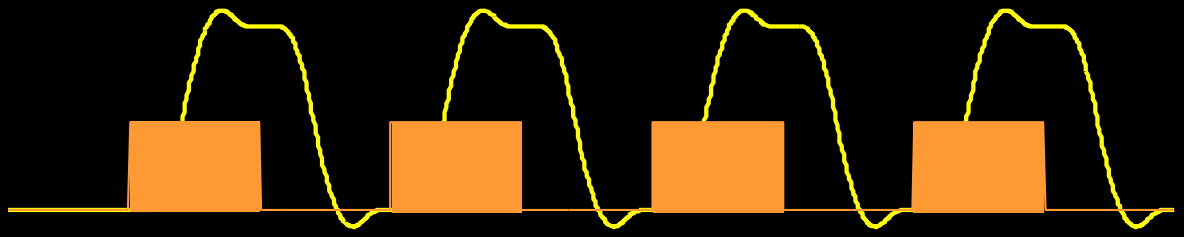
Recognize?
- Edge effects
- Shorter signal change latencies
- Unusually high signal changes
- External measuring devices

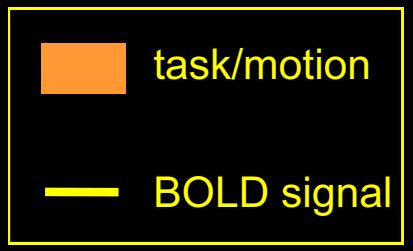
Correct?
- Image registration algorithms
- Orthogonalize to motion-related function *(cardiac, respiration, movement)*
- Navigator echo for k-space alignment *(for multishot techniques)*
- Re-do scan

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

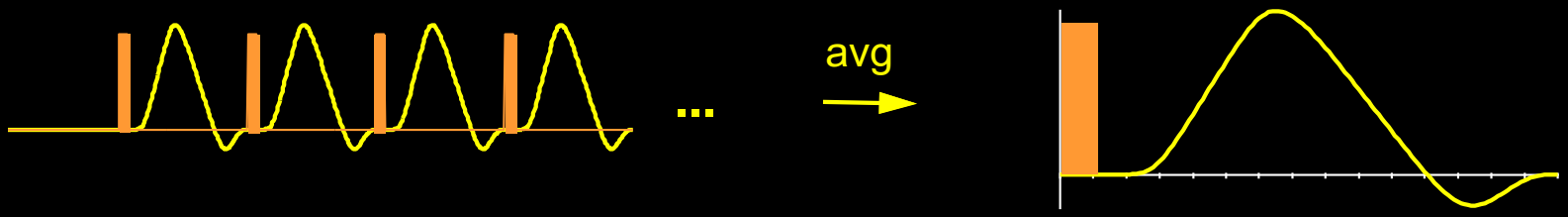
Suppress?
- Flatten image contrast
- Physical restraint
- Averaging, smoothing

Block-trial

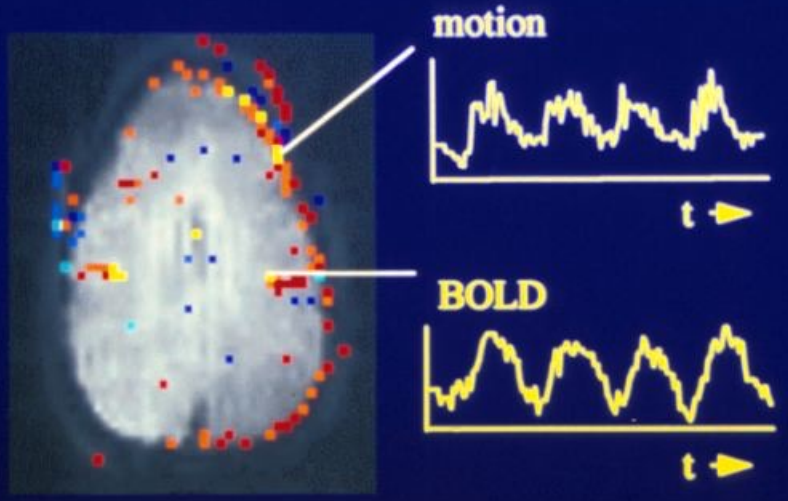


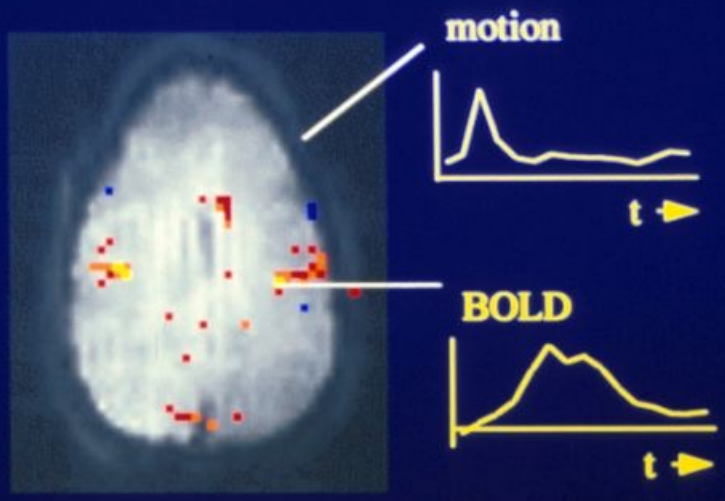


Single-trial (brief stimulus)



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





"block-trial" paradigm

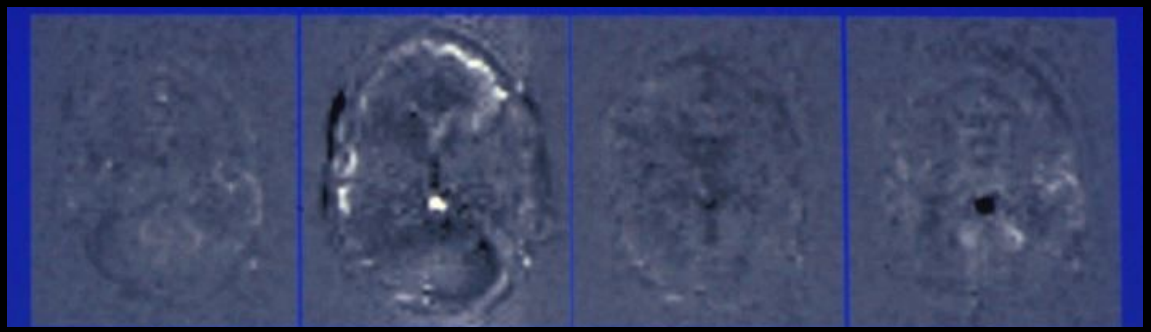
Motion induced signal changes resemble functional (BOLD) signal changes

"single-trial" paradigm

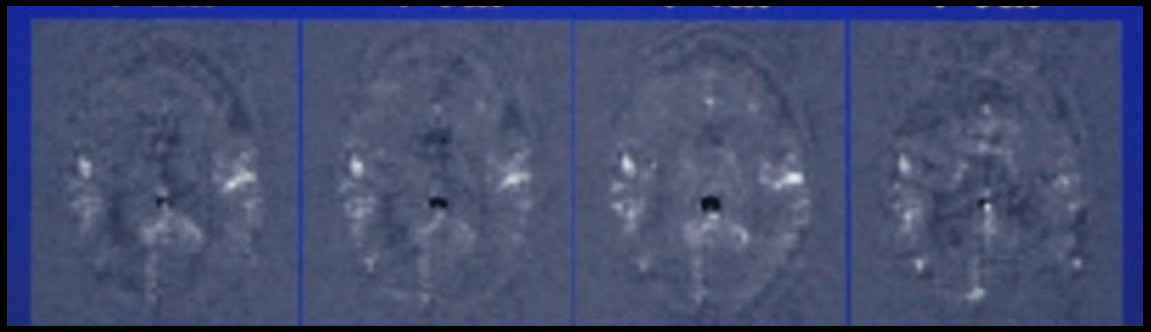
Motion induced and BOLD signal changes are separated in time

R.M. Birn, et al.

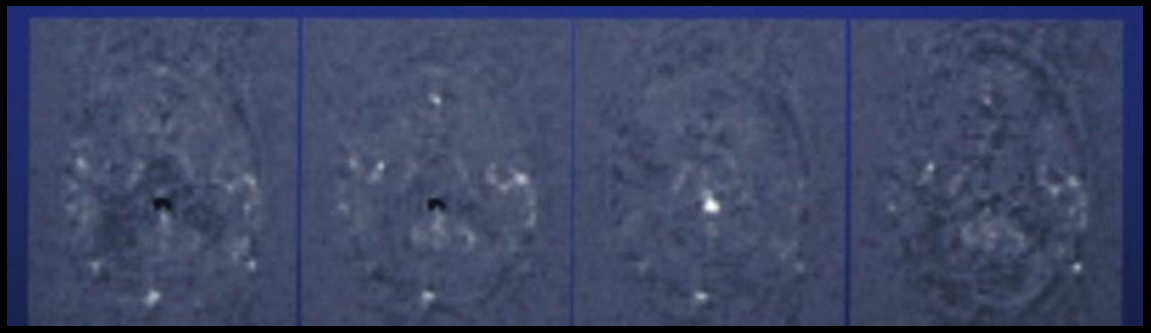
Overt Word Production



2 3 4 5

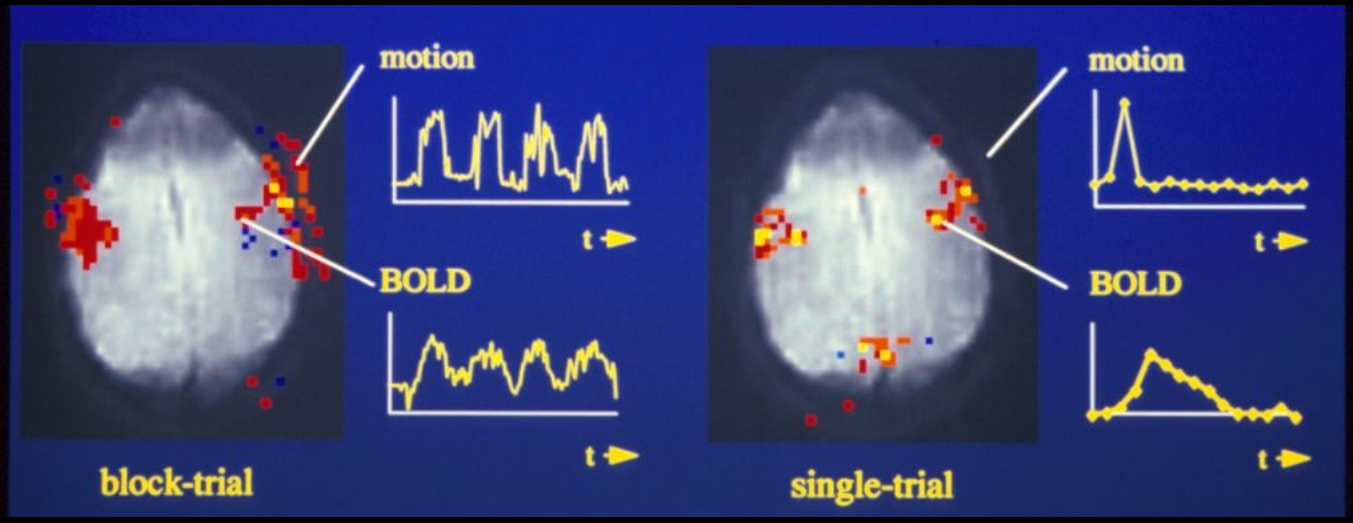


6 7 8 9

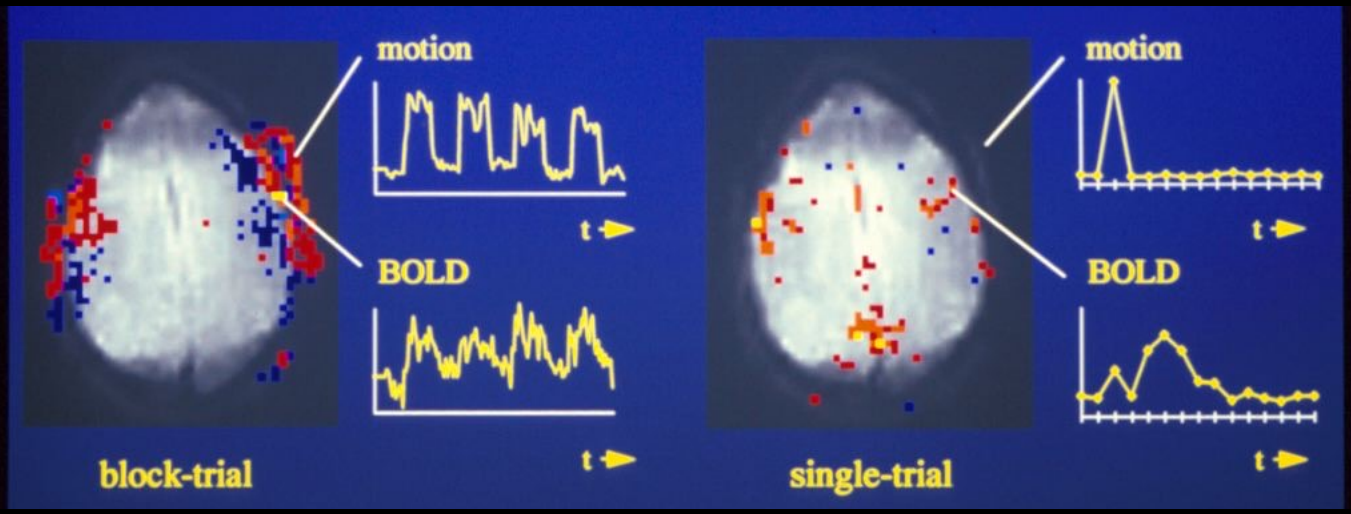


10 11 12 13

Tongue Movement



Jaw Clenching



Variables to Optimize

- Information Content
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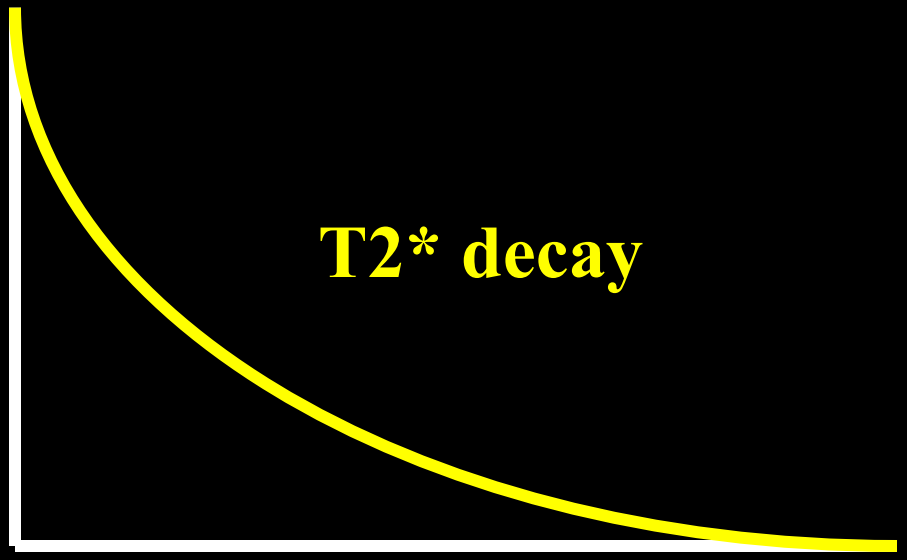
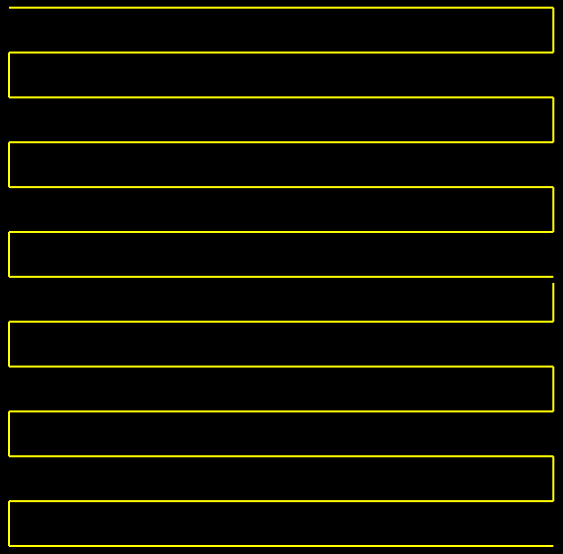
Speed

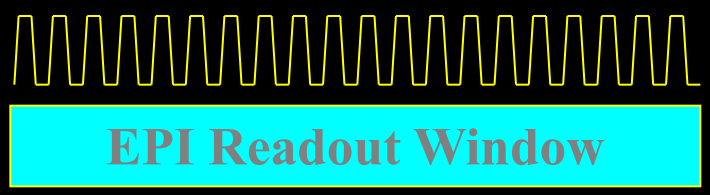
- Rapid imaging techniques:
  - Single shot imaging
  - TR vs. Brain coverage:

    min TR = (time/slice) x number of slices in volume
- Hemodynamic Issues
  - Paradigm timing
  - Event related fMRI
  - Timing modulation

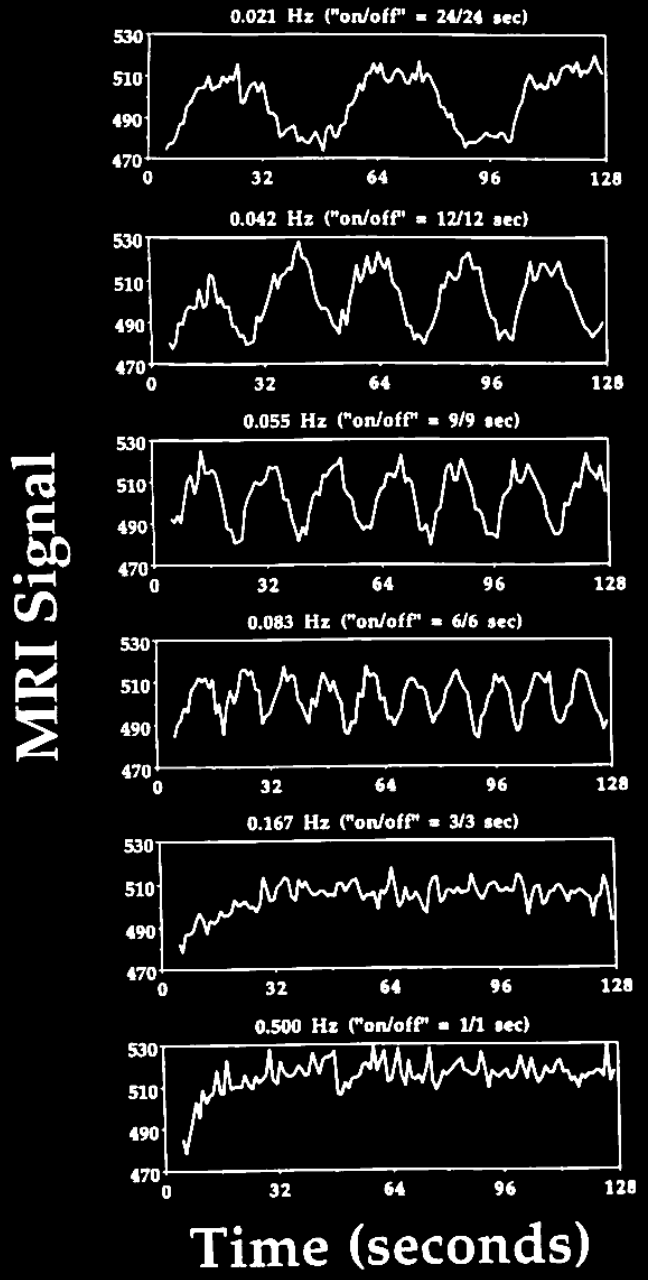
Single Shot Imaging

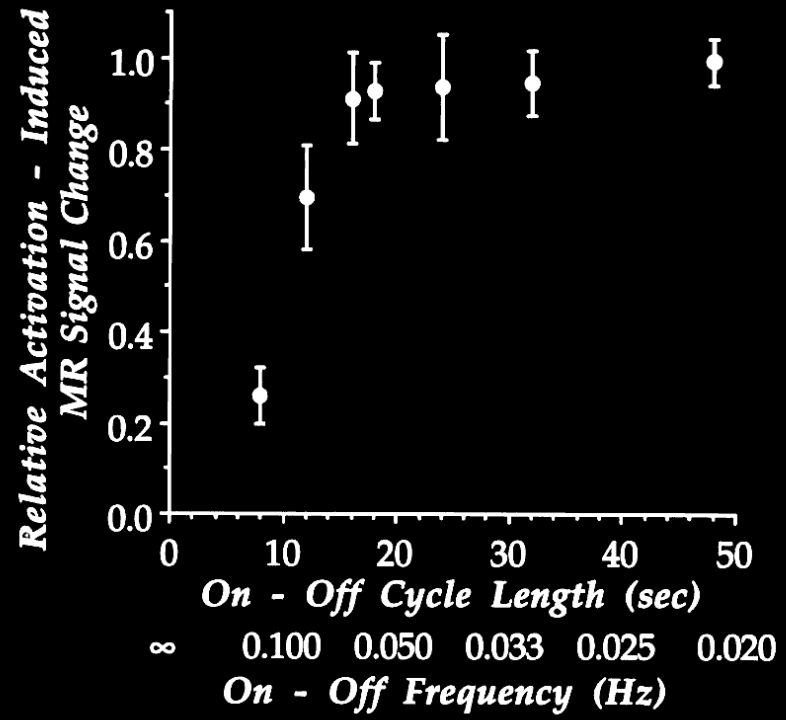


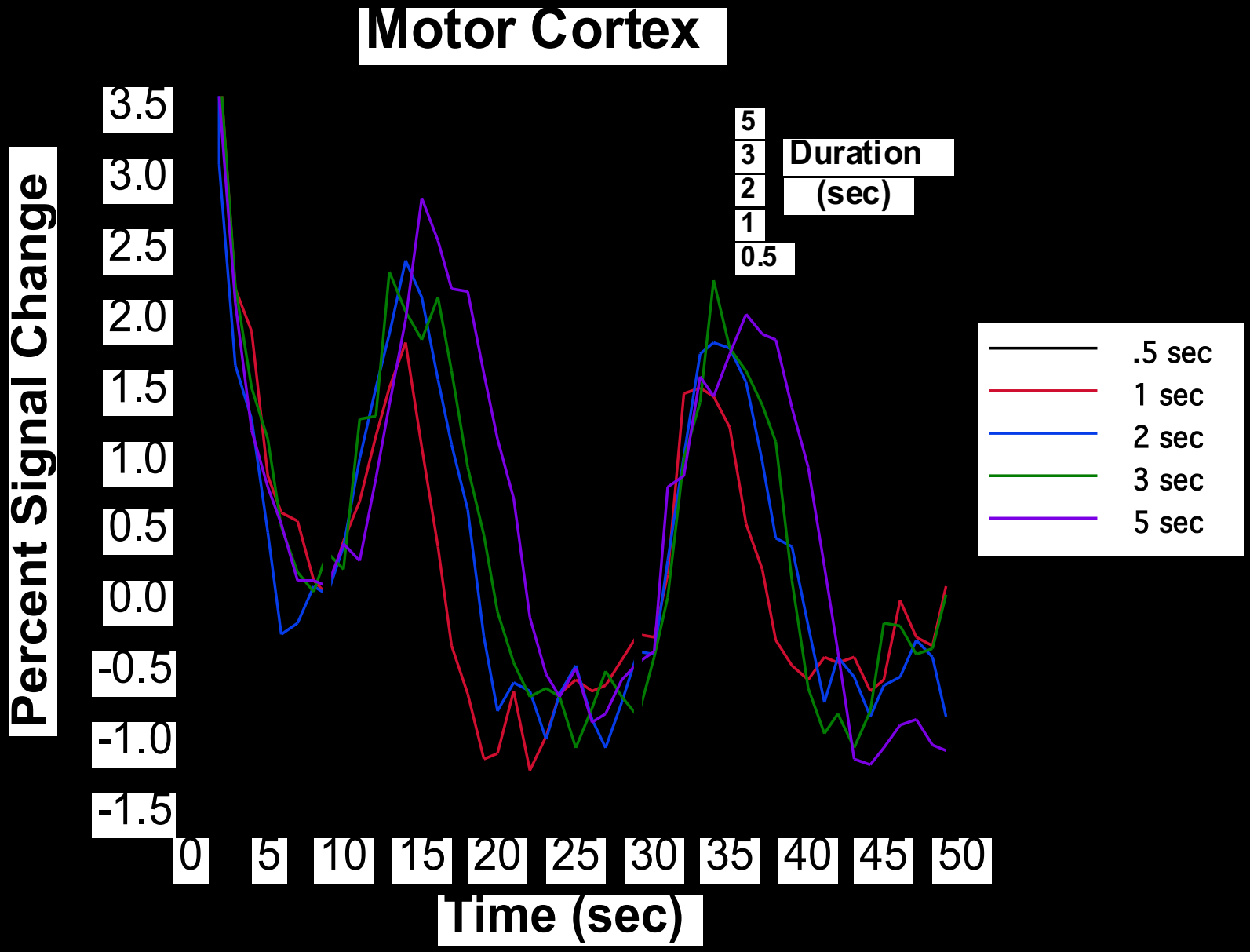


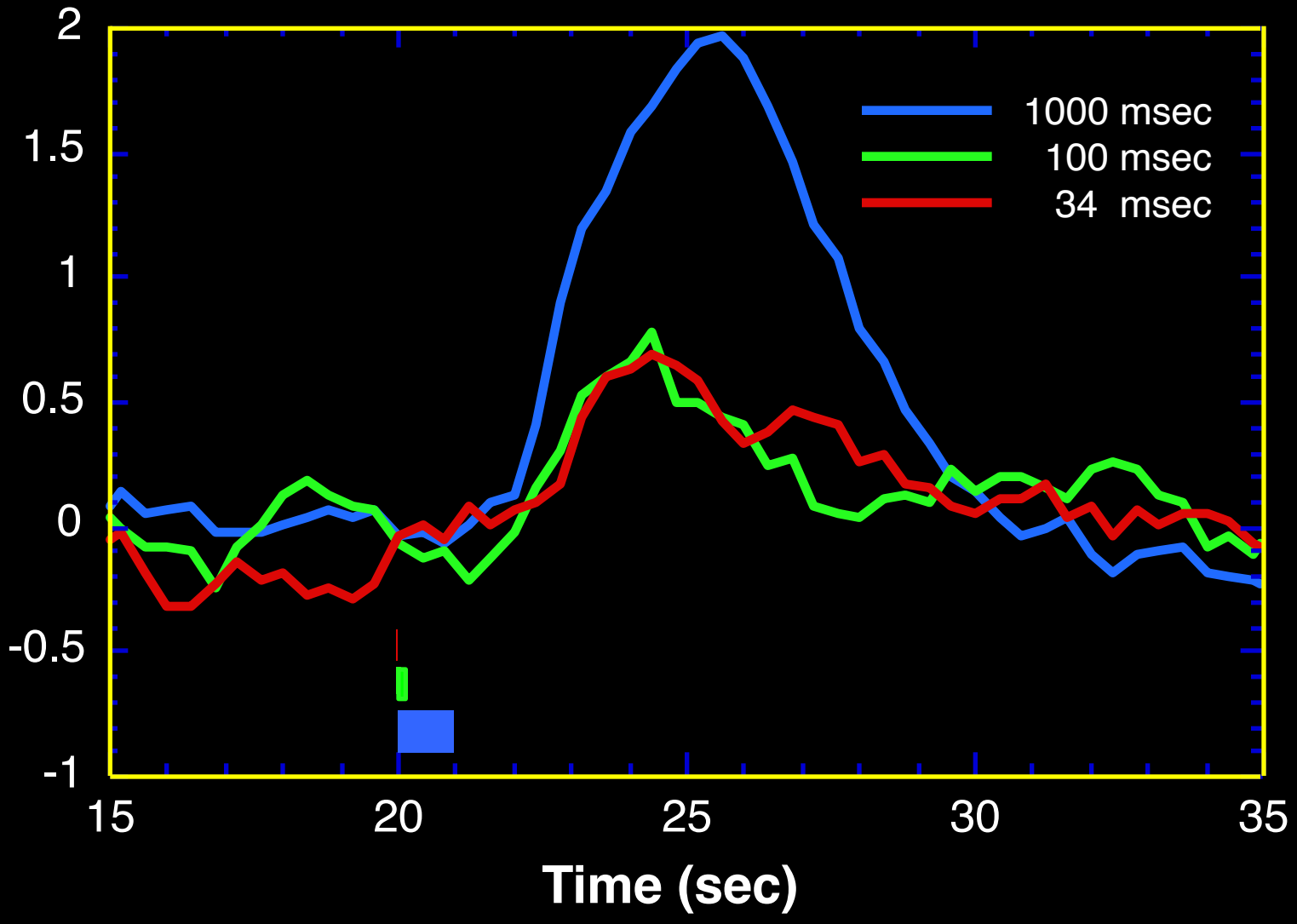


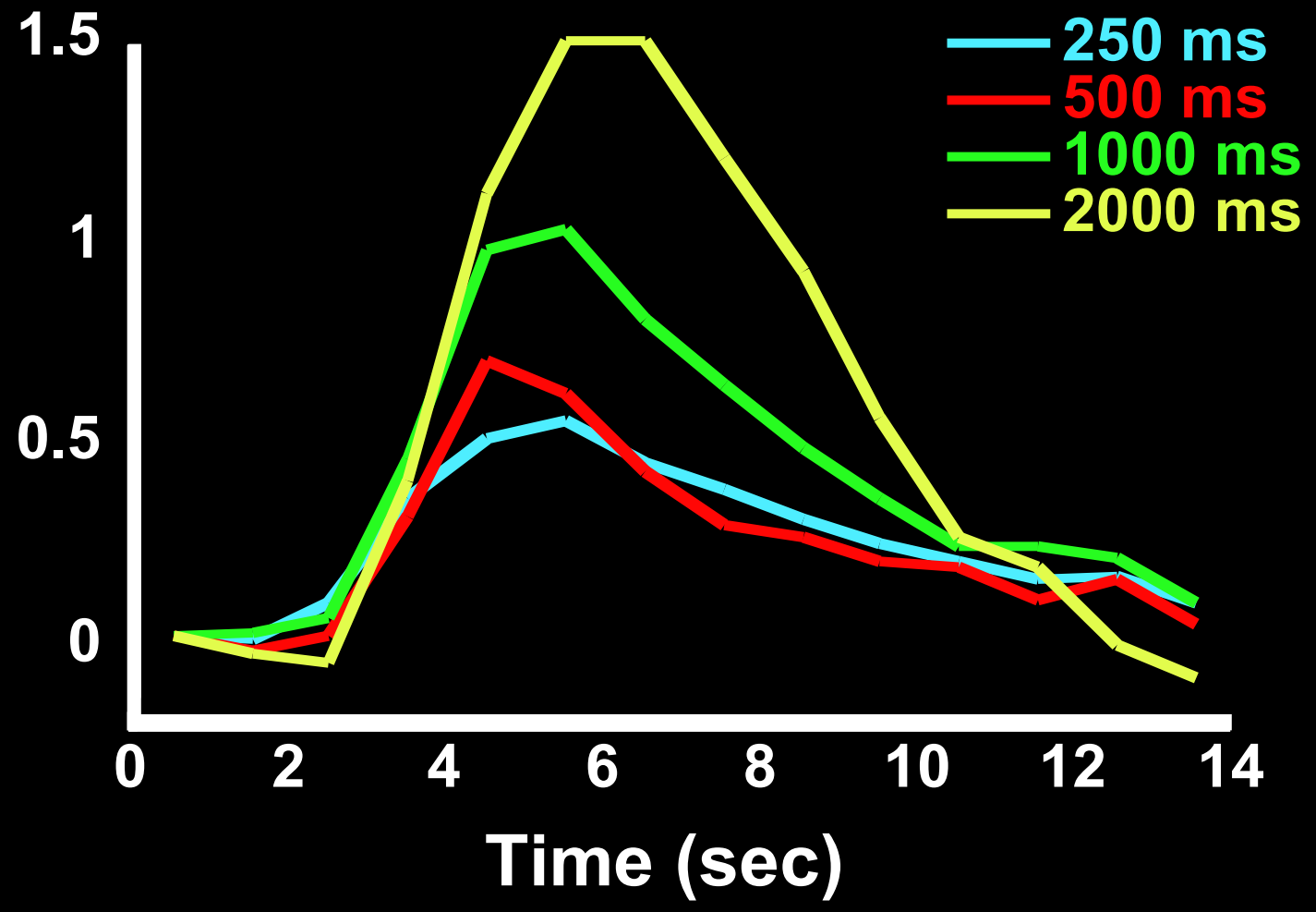
≈ 20 to 40 ms


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)

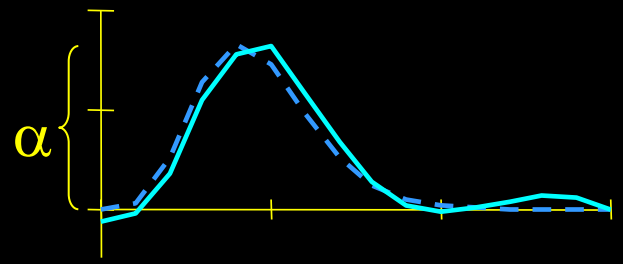

Motor Cortex
Percent Signal Change
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
0
5
10
15
20
25
30
35
40
45
50
Time (sec)
5
3
2
1
0.5
Duration
(sec)
.5 sec
1 sec
2 sec
3 sec
5 sec


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


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

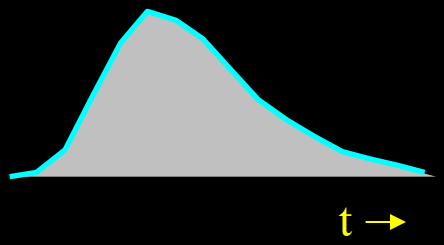
Compute nonlinearity *(for each voxel)*

- Amplitude of Response



Fit ideal (linear) to response

- Area under response / Stimulus Duration



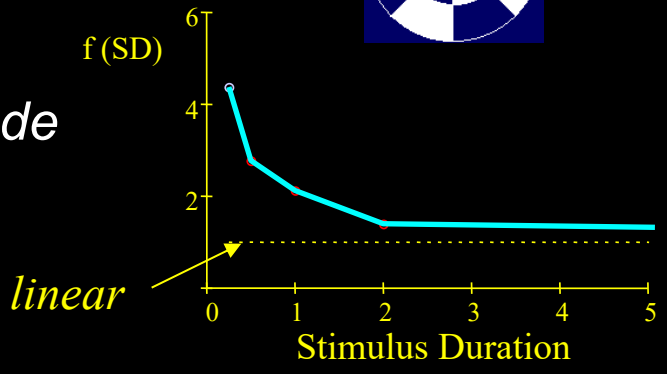
Output Area / Input Area

Nonlinearity

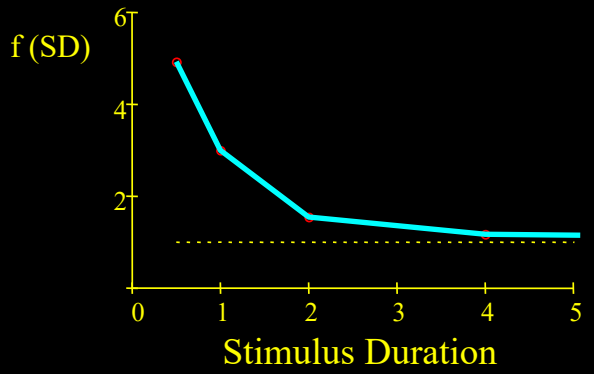
Visual

Motor

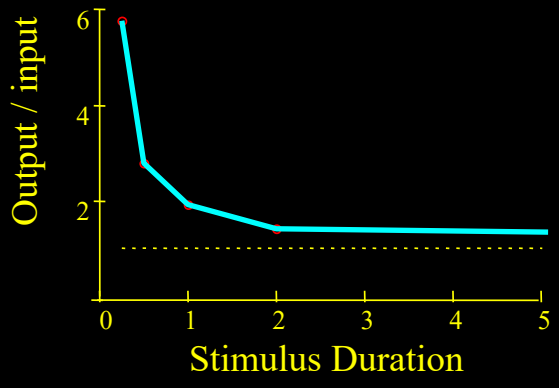
Magnitude

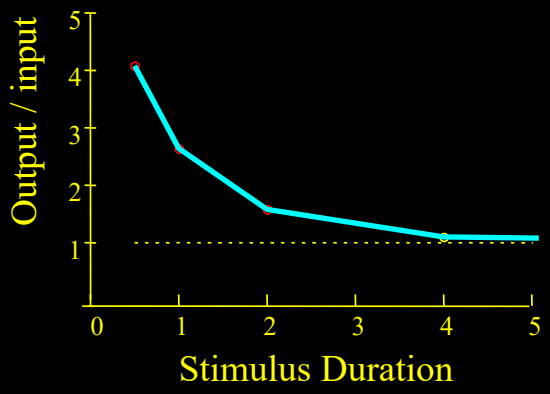


linear



Area



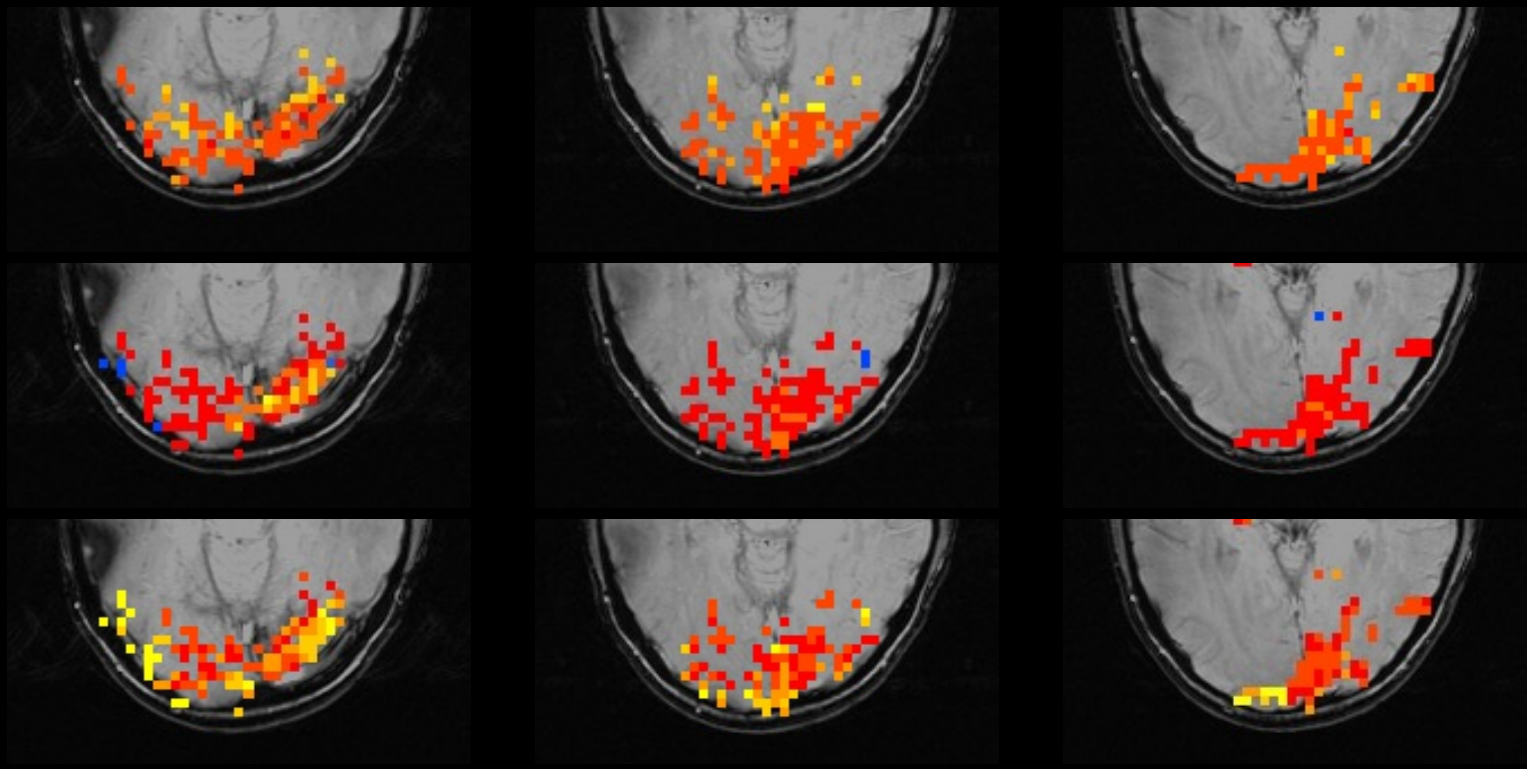


Results – visual task

Nonlinearity

Magnitude

Latency

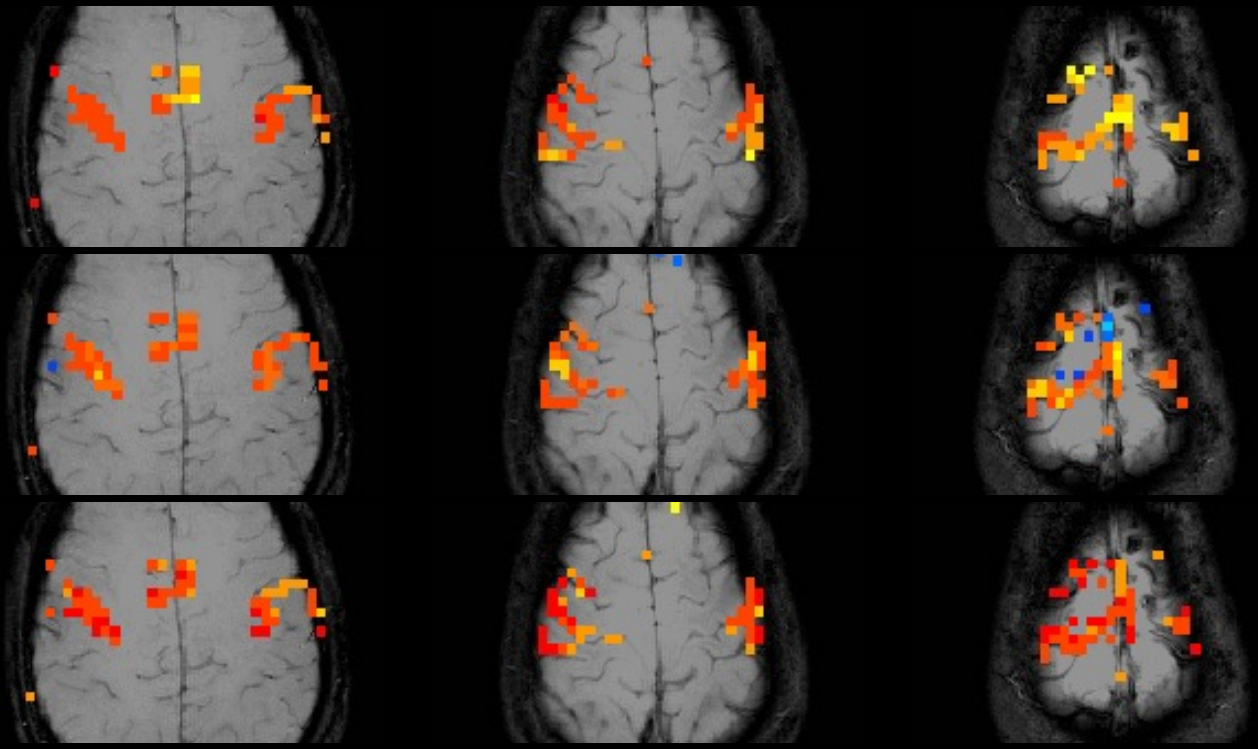


Results – motor task

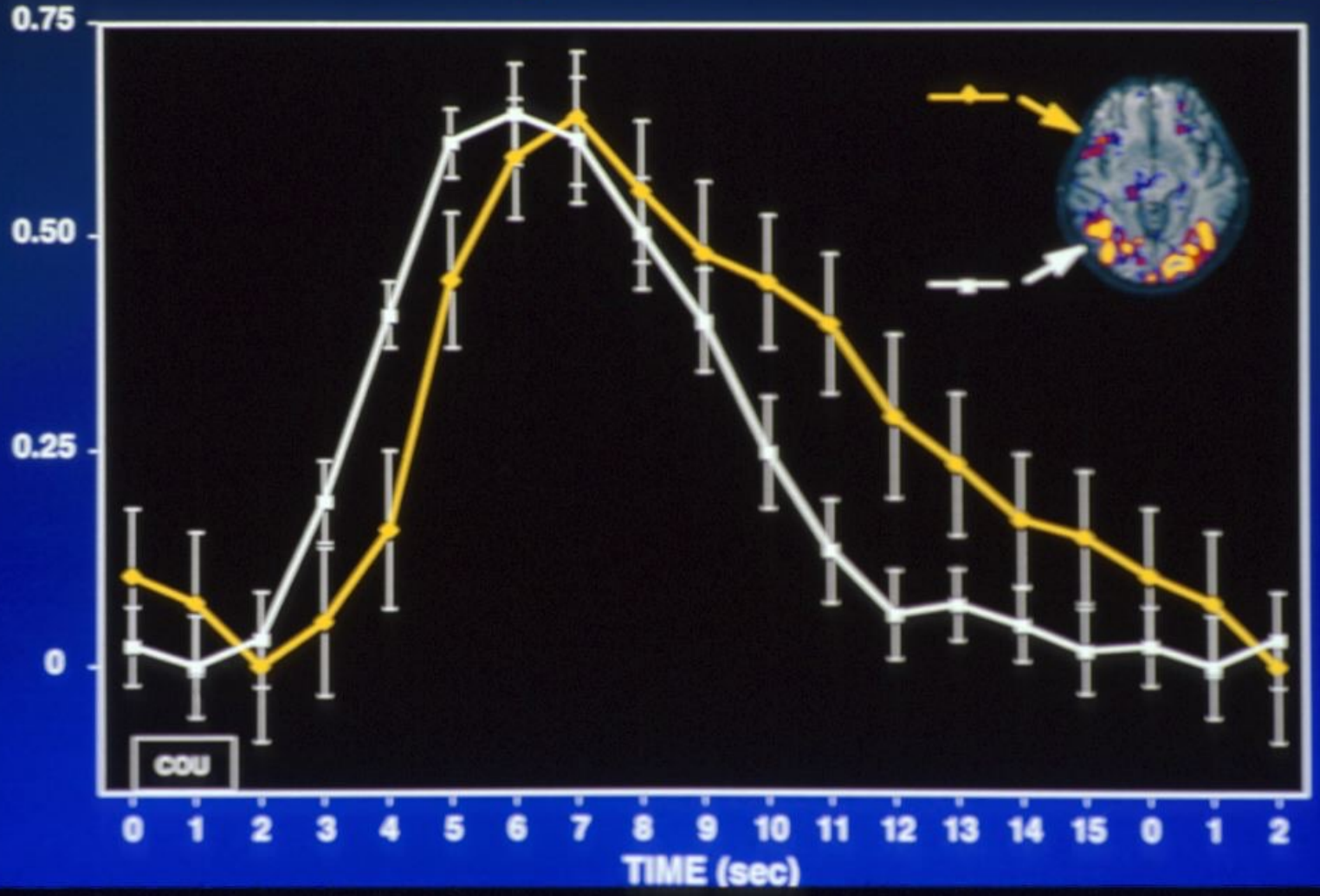
Nonlinearity

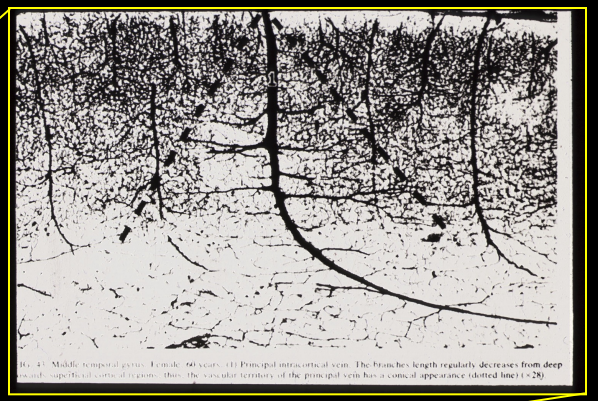
Magnitude

Latency



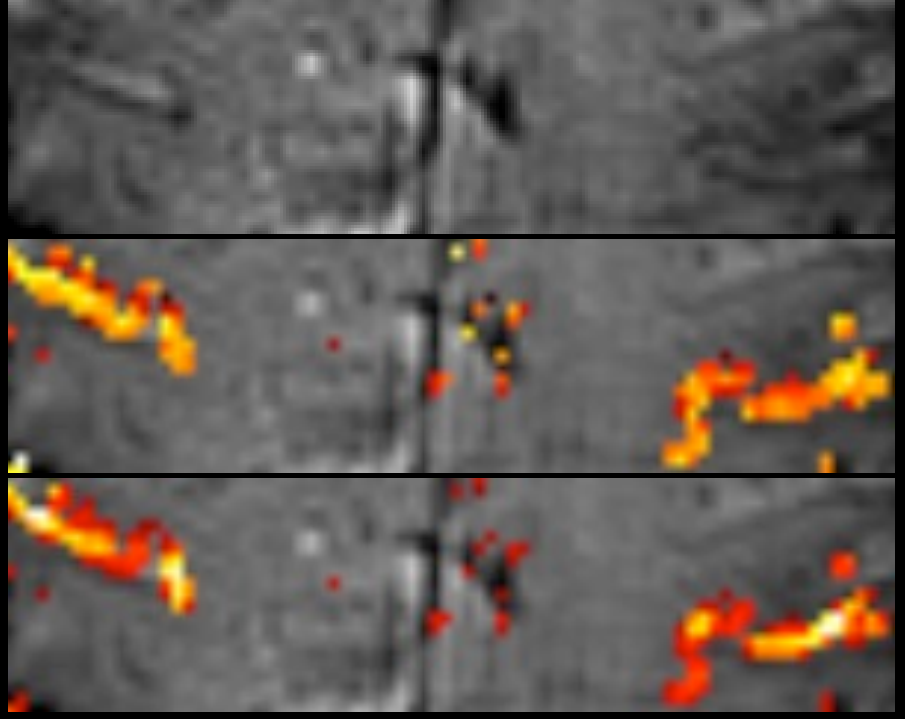
Time Course Comparison Across Brain Regions





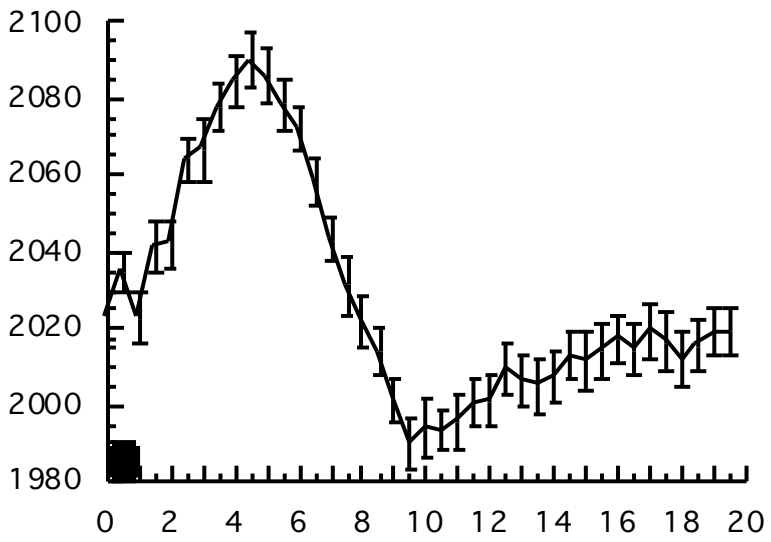
Latency

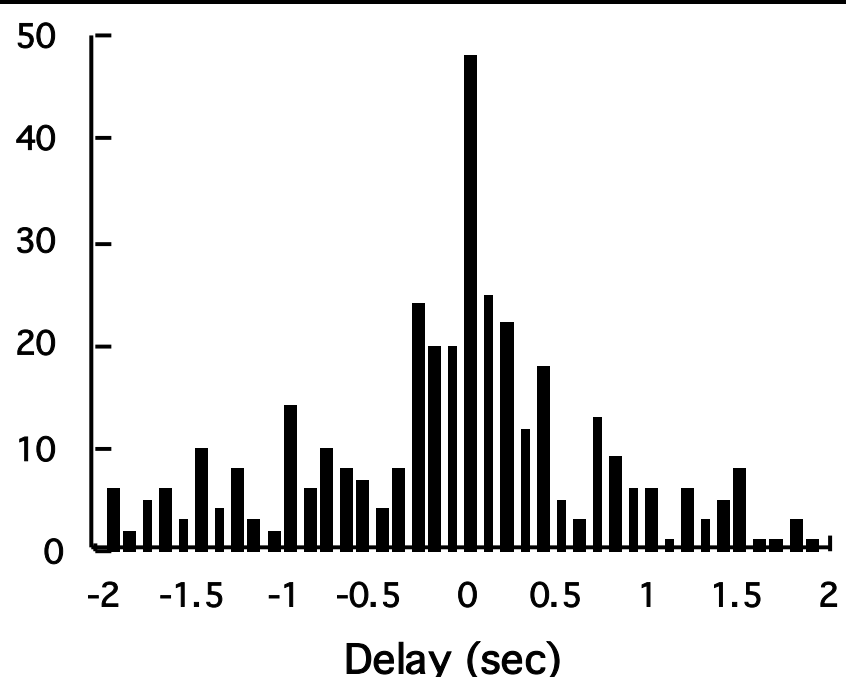
Magnitude



+ 2 sec

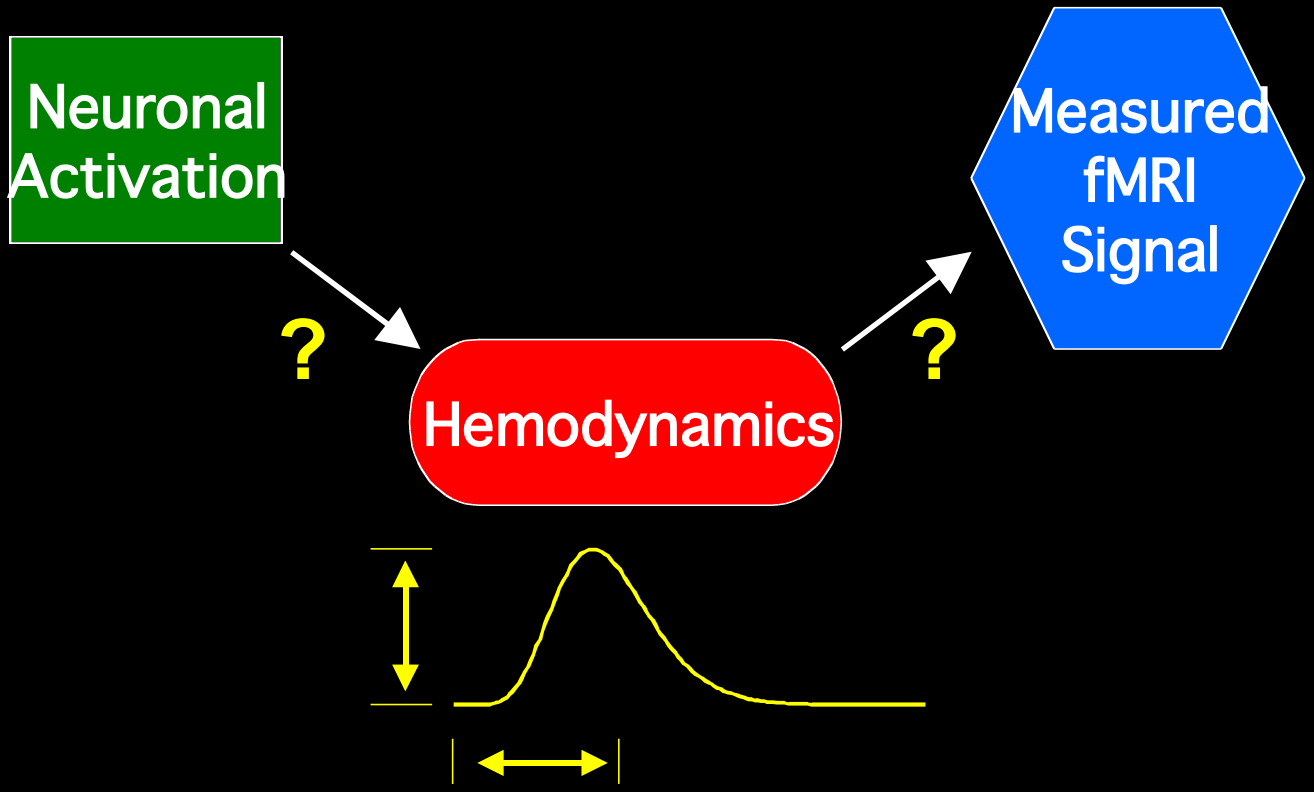
- 2 sec



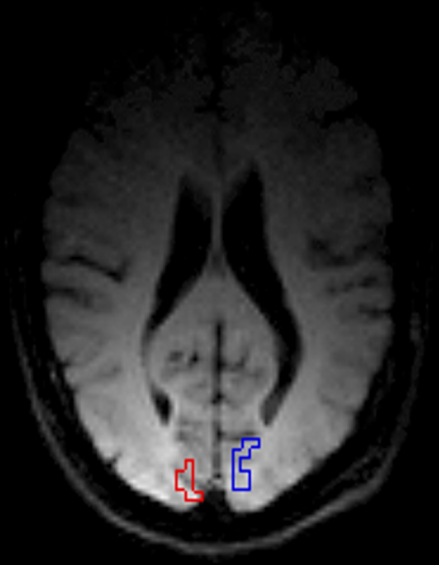


Temporal Normalization

Relative Timing

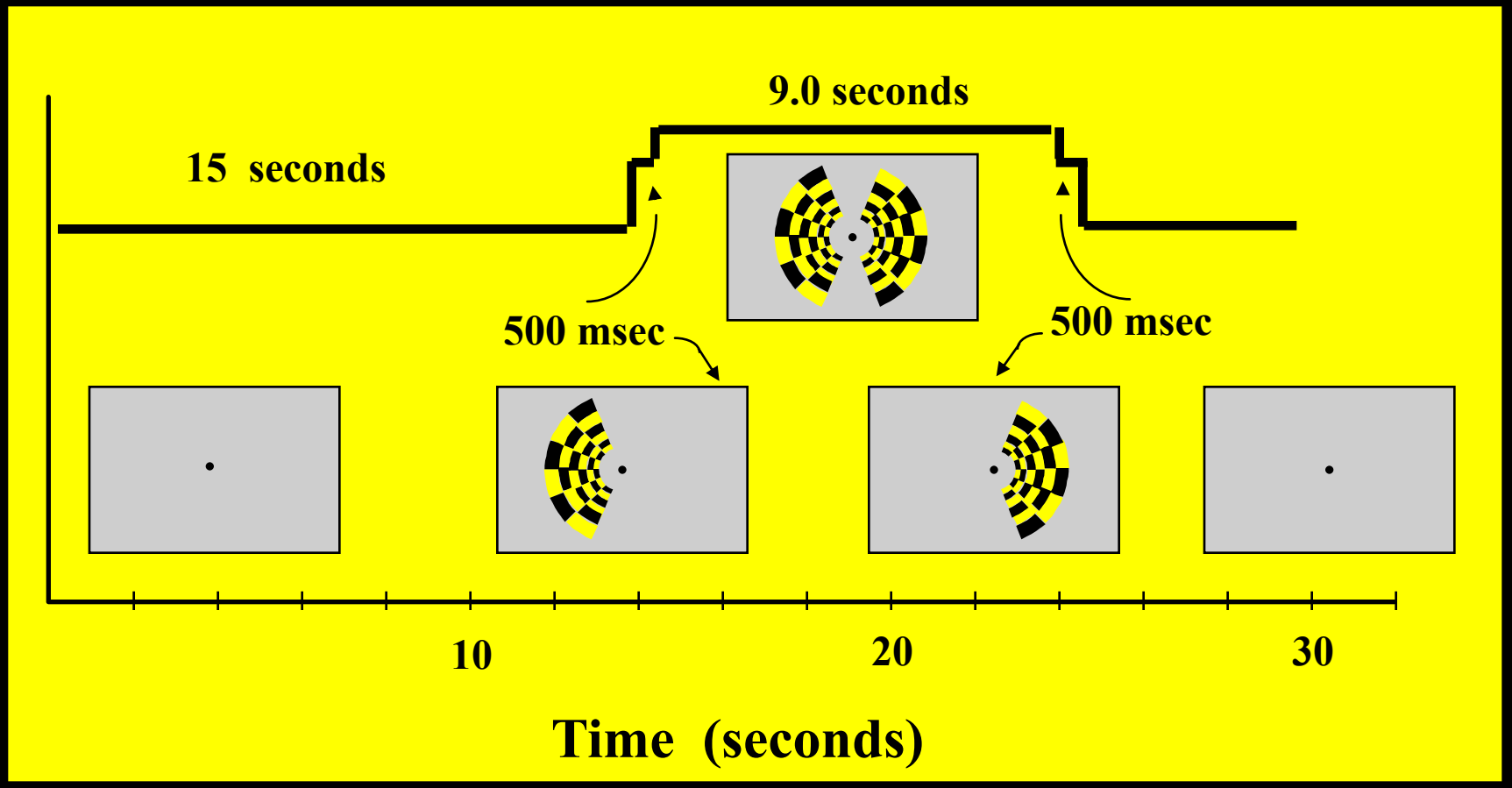


Regions of Interest Used for Hemi-Field Experiment

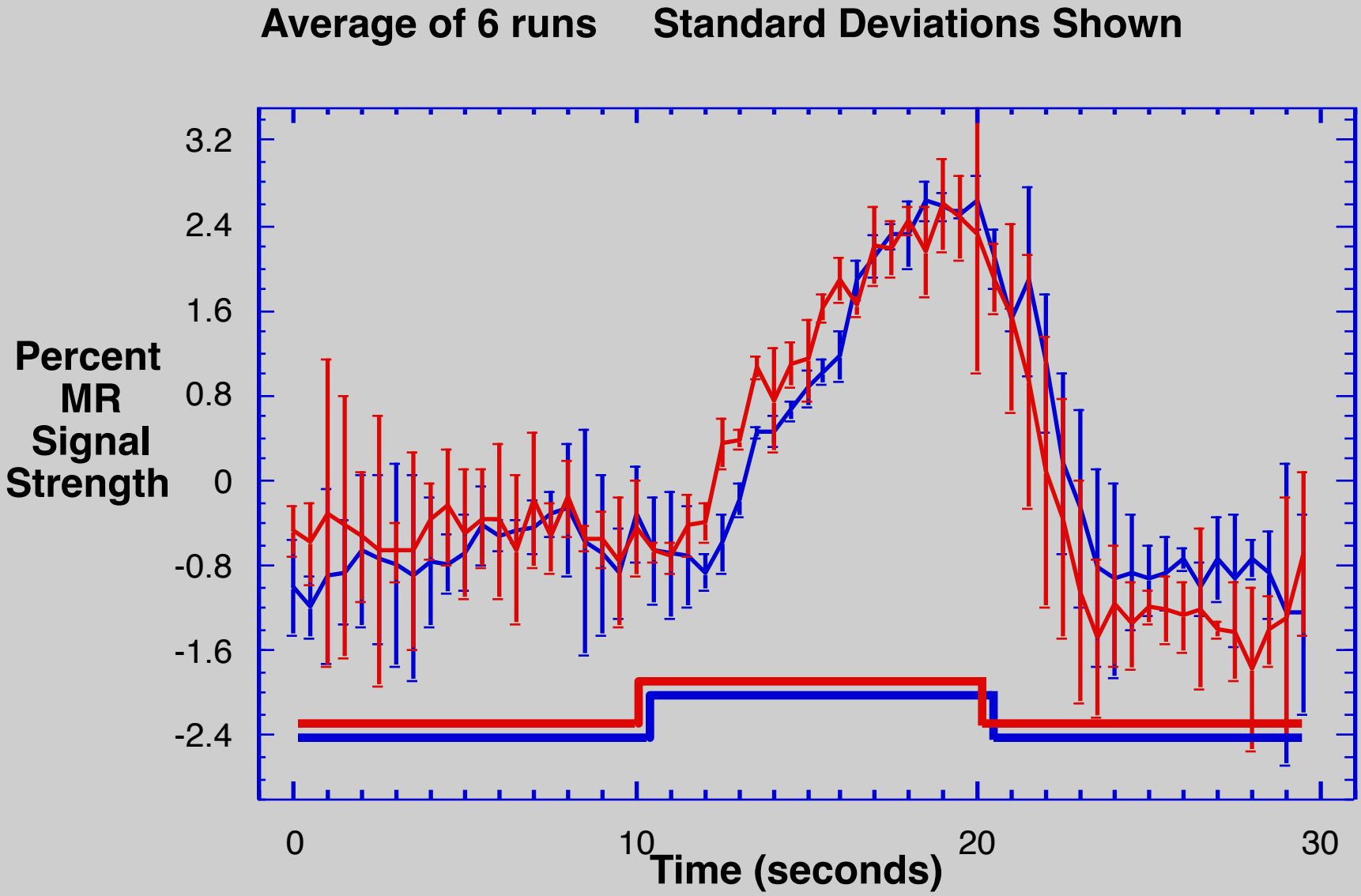


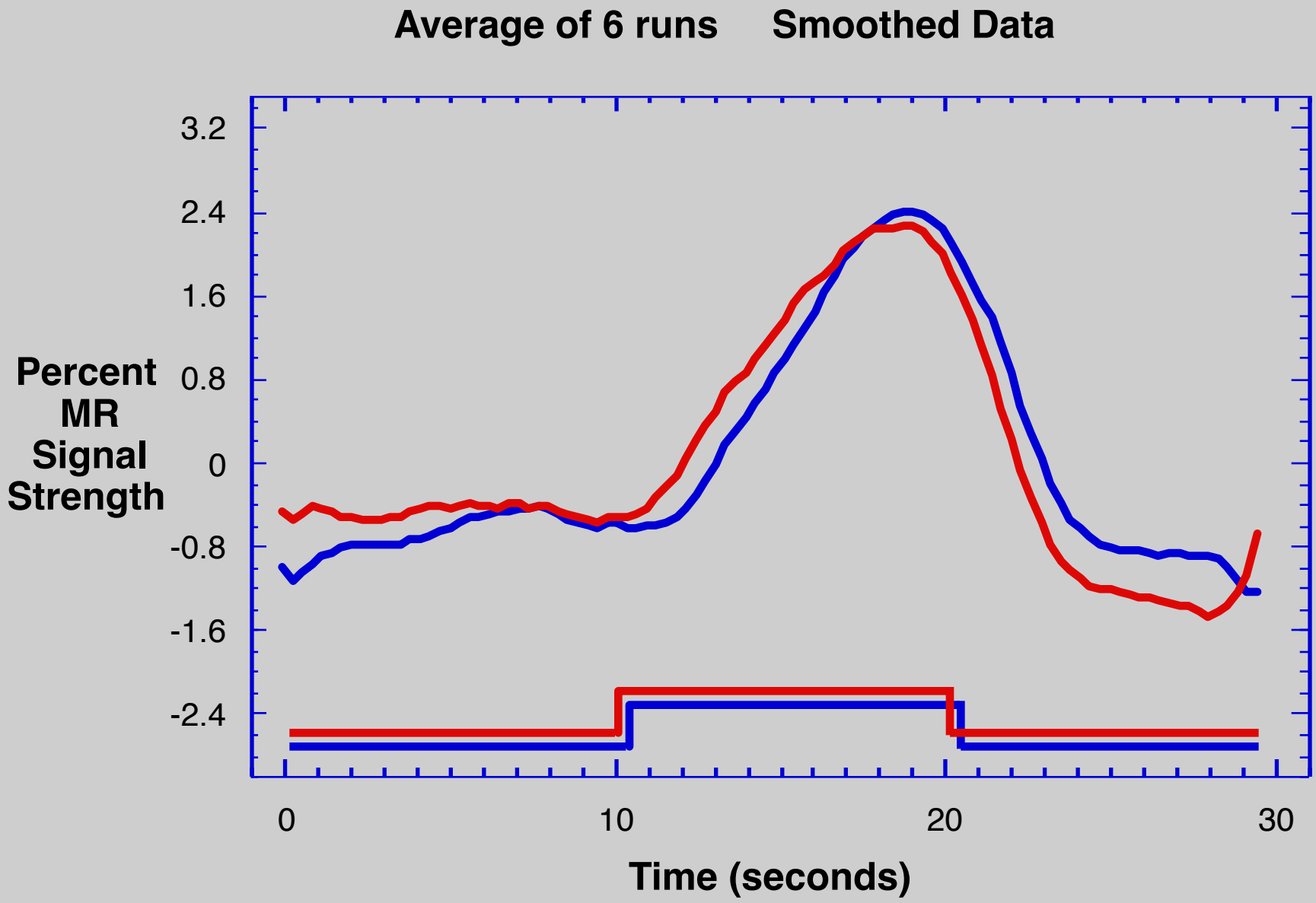
Right Hemisphere

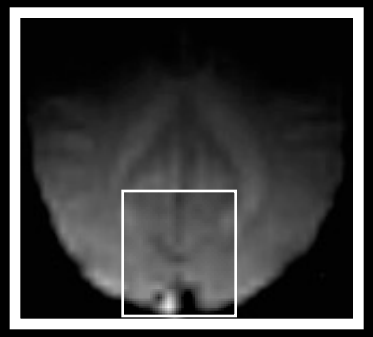
Left Hemisphere


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

Hemi-field with 500 msec asynchrony



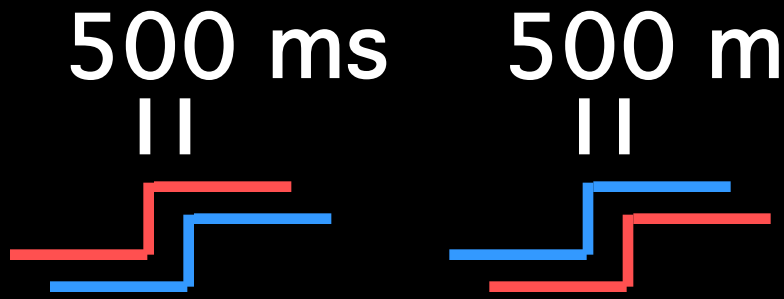

Average of 6 runs
Smoothed Data
Percent MR Signal Strength
3.2
2.4
1.6
0.8
0
-0.8
-1.6
-2.4
0
10
20
30
Time (seconds)



500 ms 500 ms

Right Hemifield

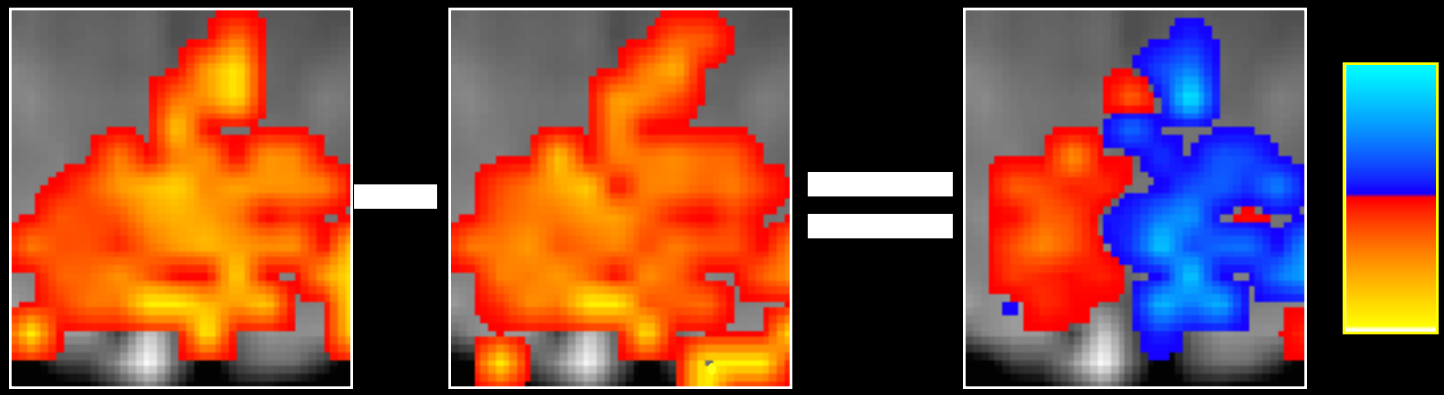
Left Hemifield

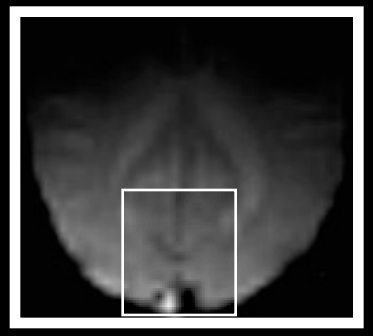


+ 2.5 s

0 s

- 2.5 s

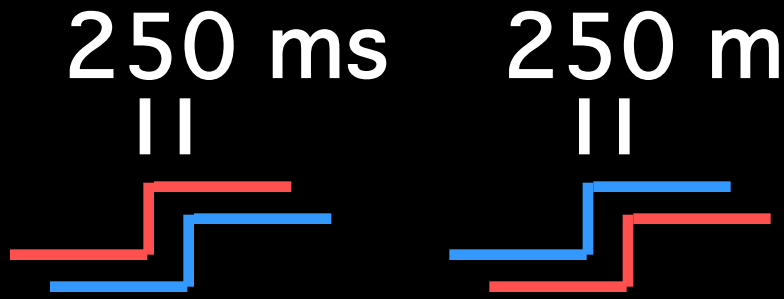




250 ms 250 ms

Right Hemifield

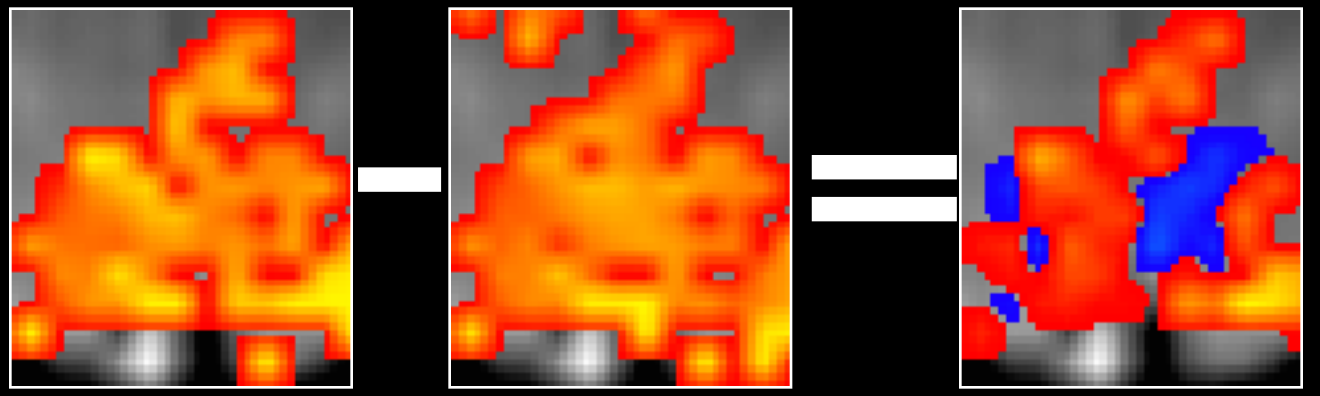
Left Hemifield



+ 2.5 s

0 s

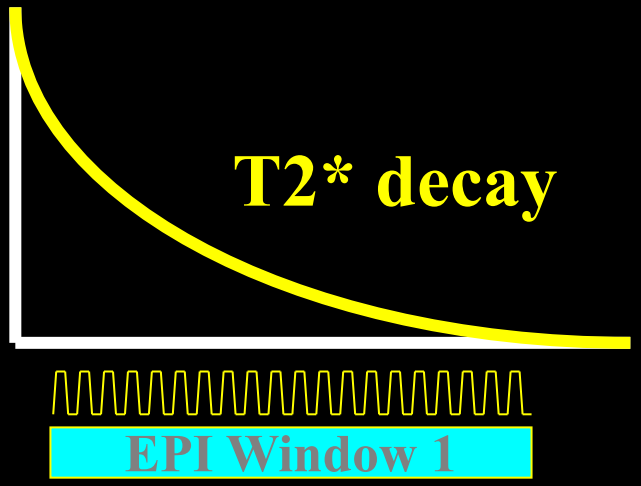
- 2.5 s

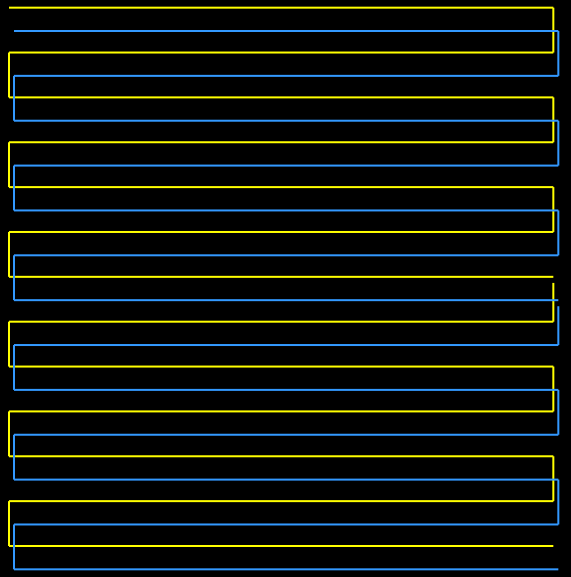


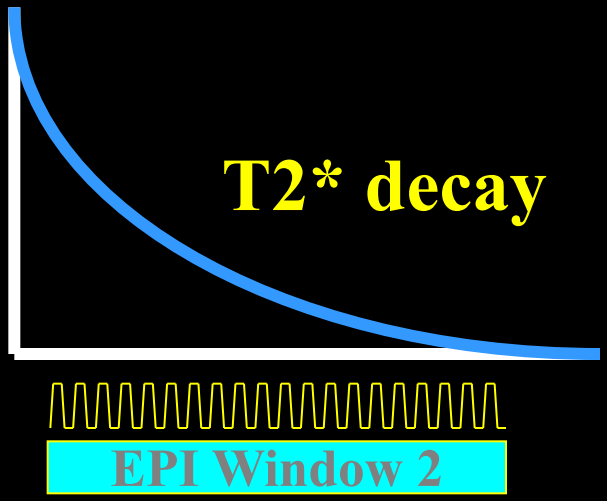
Variables to Optimize

- Information Content
- Sensitivity
- Acquisition Speed
- Resolution
- Image quality

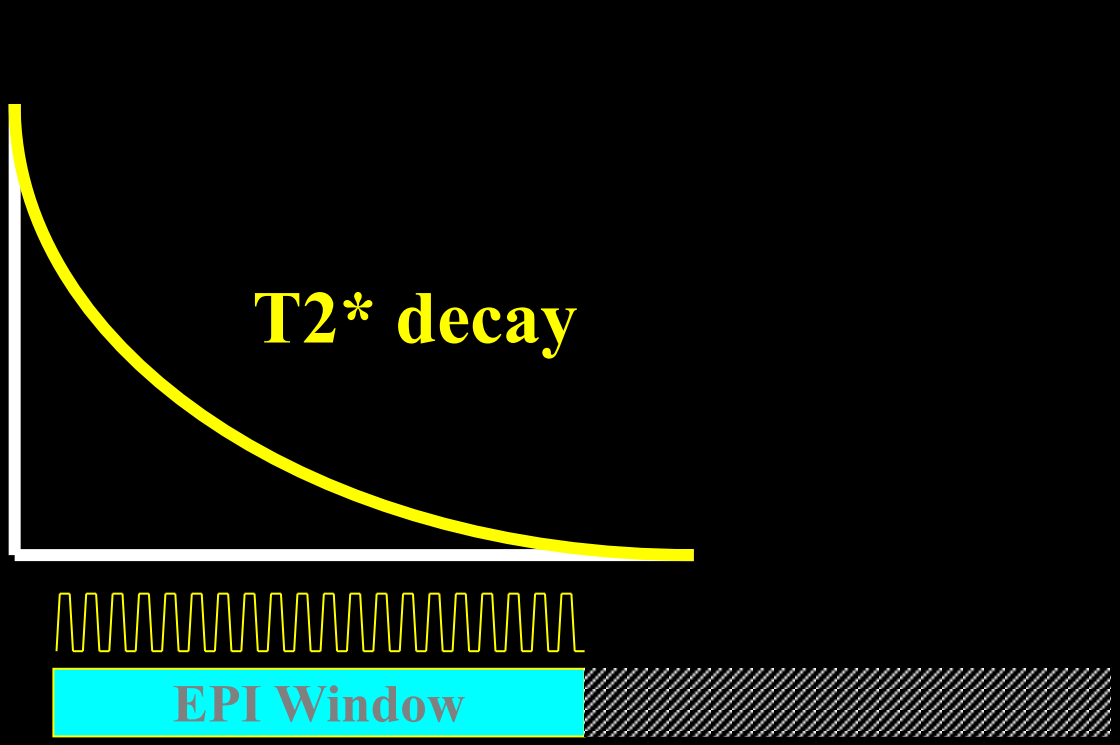
Multishot Imaging

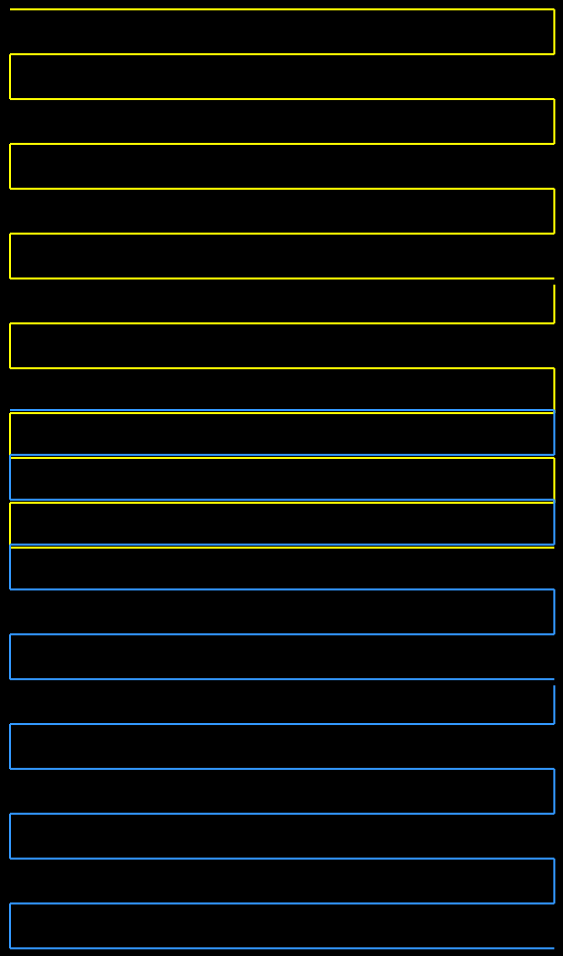




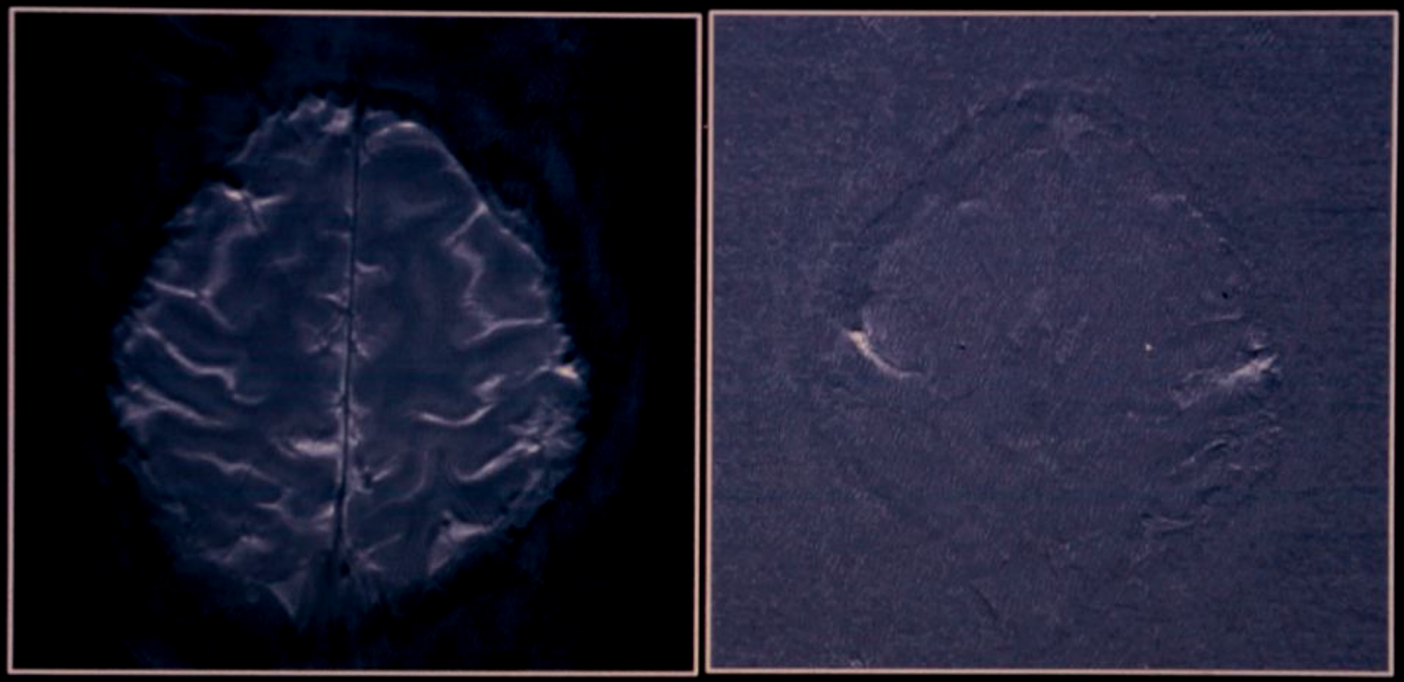


Partial k-space imaging

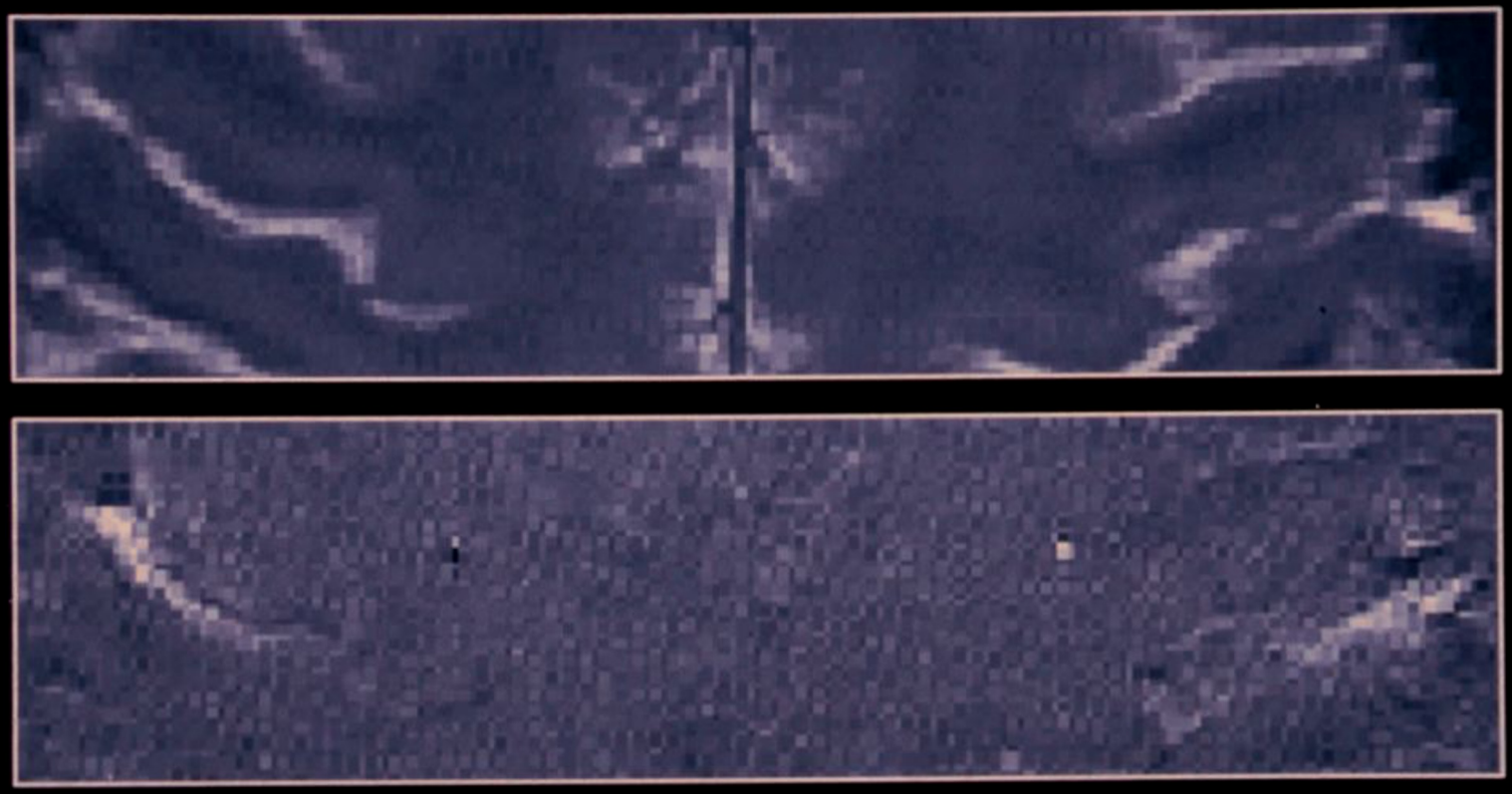




Single - Shot EPI at 3T:
Half NEX, 256 x 256, 16 cm FOV

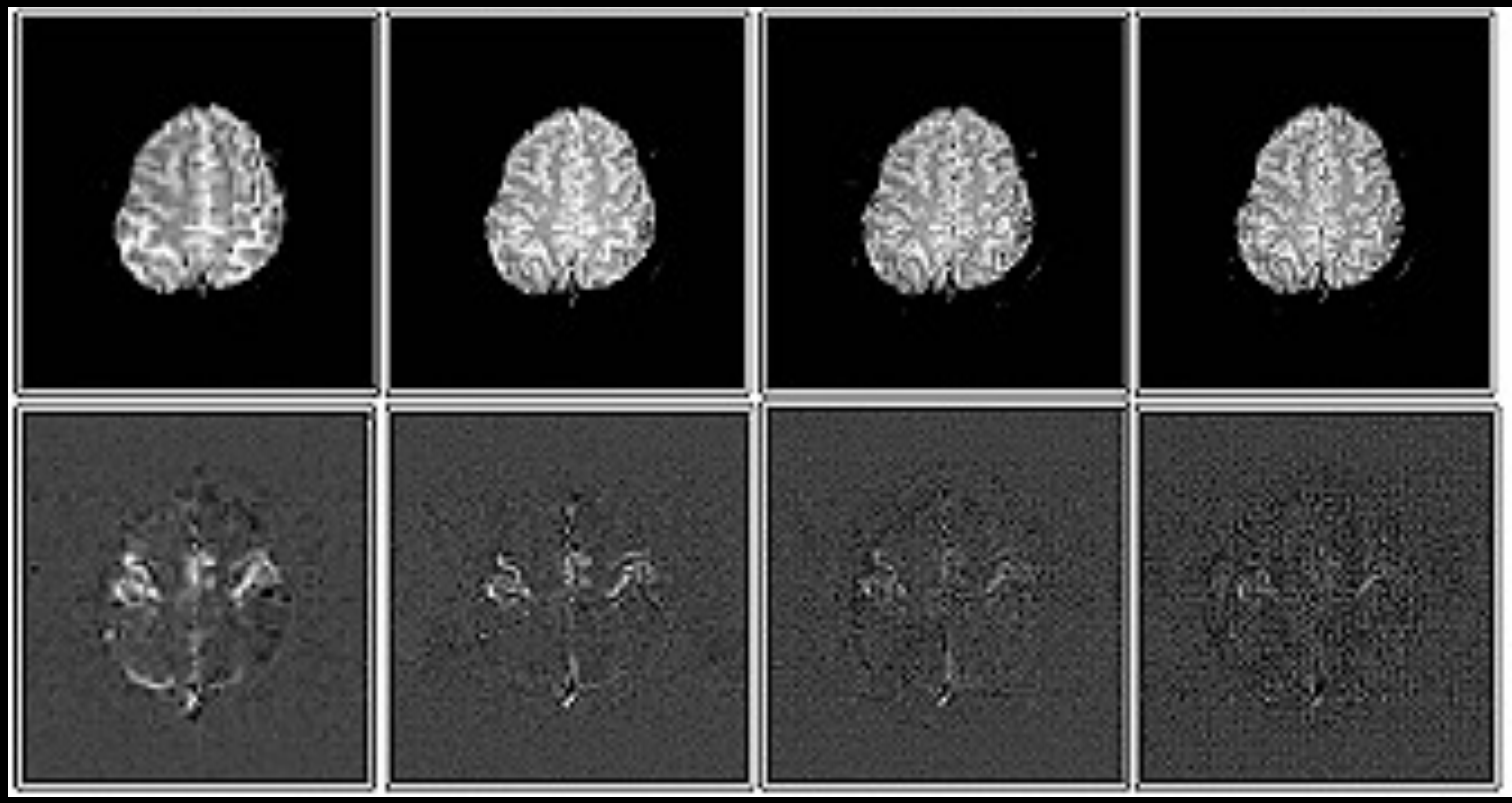


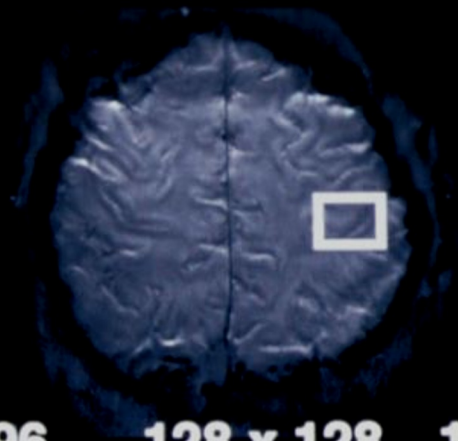
Single - Shot EPI at 3T:
Half NEX 256 x 256, 16 cm FOV



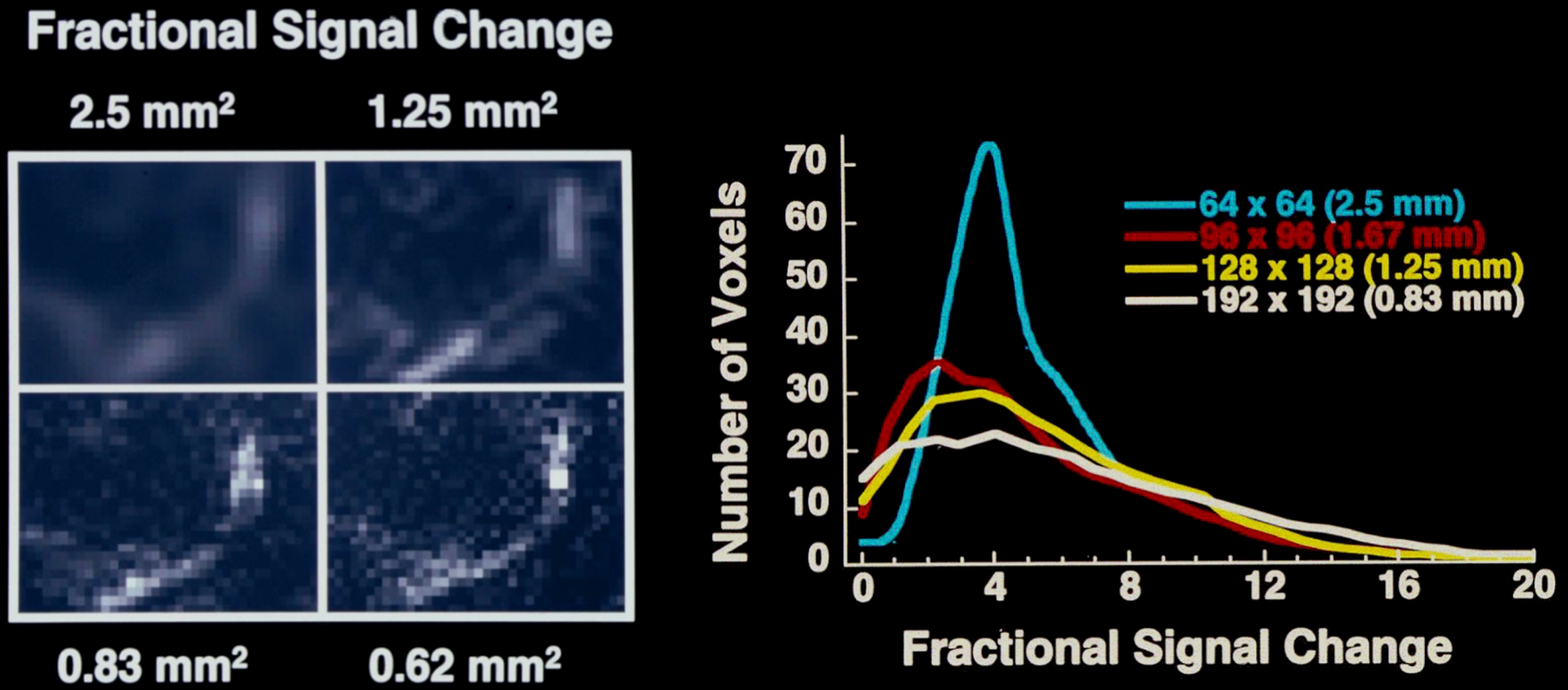
Multi Shot EPI

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

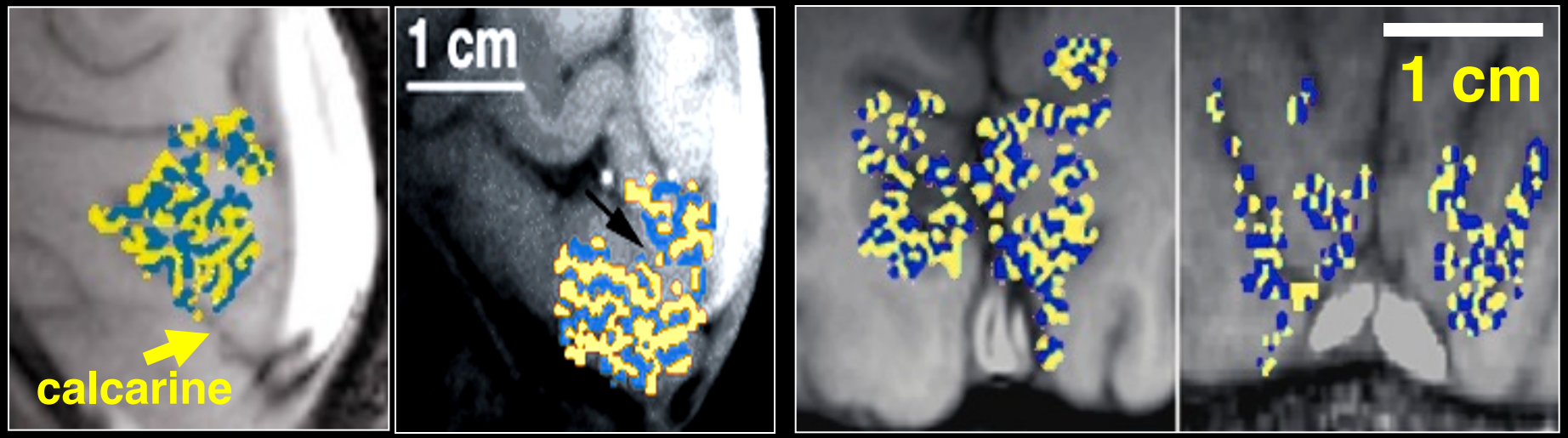




64 x 64	96 x 96	128 x 128	192 x 192	256 x 256
%				
C/N				
2.5 mm^2	1.67 mm^2	1.25 mm^2	0.83 mm^2	0.62 mm^2


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)

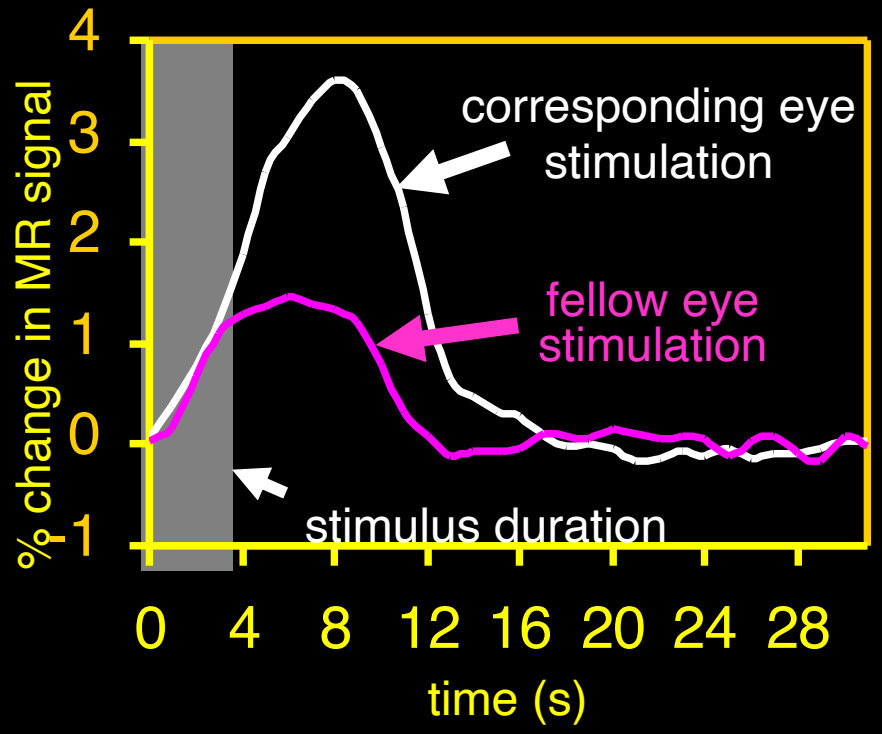
ODC Maps using fMRI



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

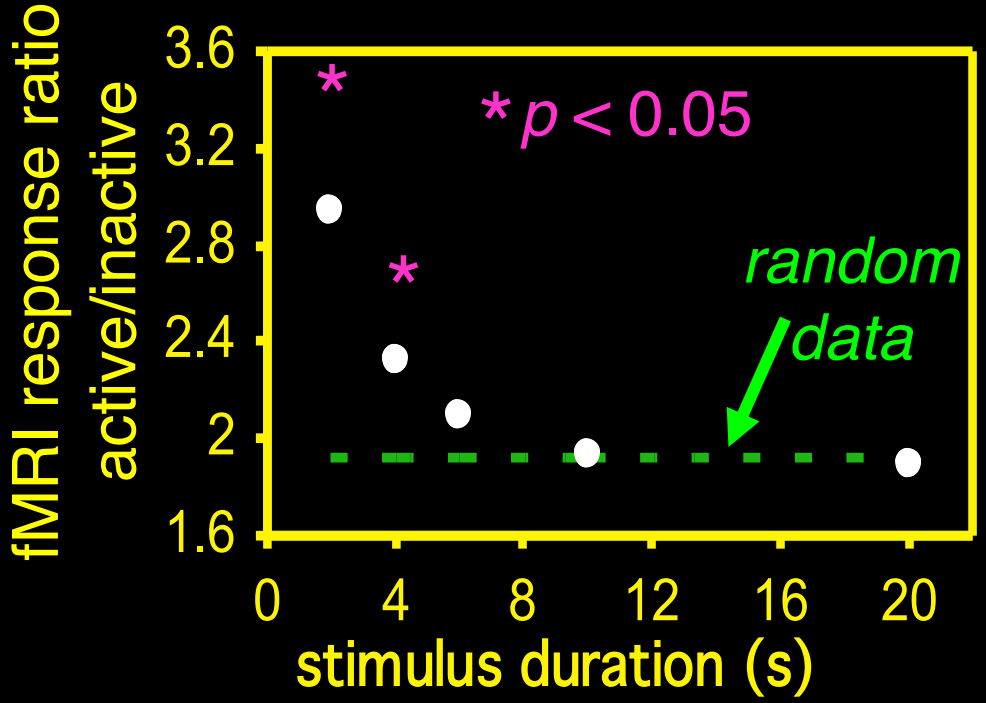
[1]Malonek D, Grinvald A. *Science* 272, 551-4 (1996).
[3]Horton JC, Hocking DR. *J Neurosci* 16, 7228-39 (1996).
[4]Horton JC, et al. *Arch Ophthalmol* 108, 1025-31 (1990).

fMRI Timecourse within an ODC



- For a 4 second stimulus, the hyperoxic response does not saturate (i.e., does not reach a plateau).
- The ratio of the peak magnitudes of the fMRI responses is nearly 3:1.

Experiment 2: Stimulus Duration



- The saturation of the hyperoxic response does not permit reliable mapping of ODCs.
- ODC maps obtained using the hyperoxic phase of the BOLD fMRI signal *are* reliable when stimulus duration is 4 seconds or less.

Variables to Optimize

- Information Content
- Sensitivity
- Speed
- Resolution
- Image quality

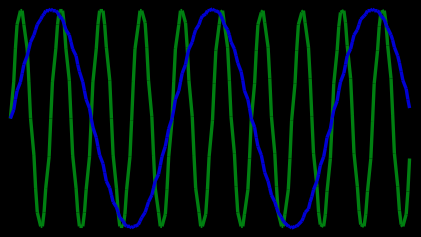
Image Quality

- Minimizing warping
  - Shimming
  - Reduced readout window duration
- Minimizing dropout
  - Shimming
  - Reduced TE
  - Adjust slice orientation
  - Increase resolution

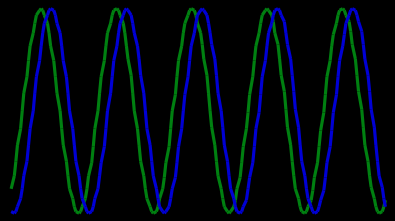
Neuronal Activation Input Strategies

1. Block Design

2. Frequency Encoding

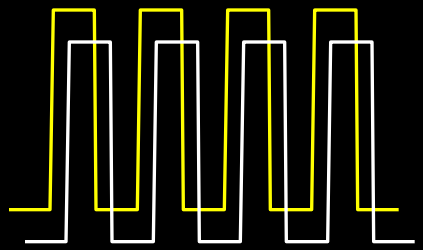


3. Phase Encoding



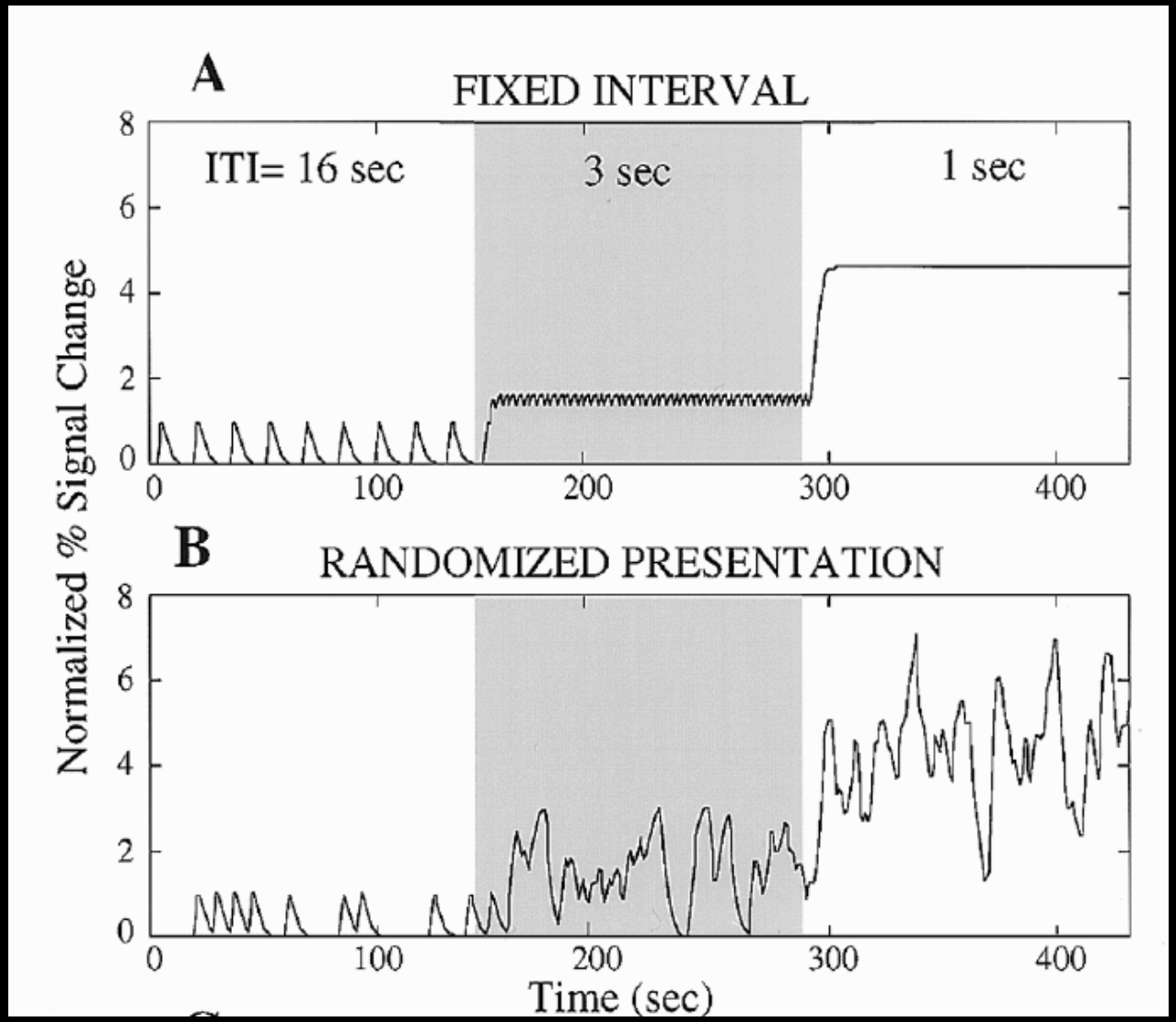
4. Event Related

5. Orthogonal Block Design



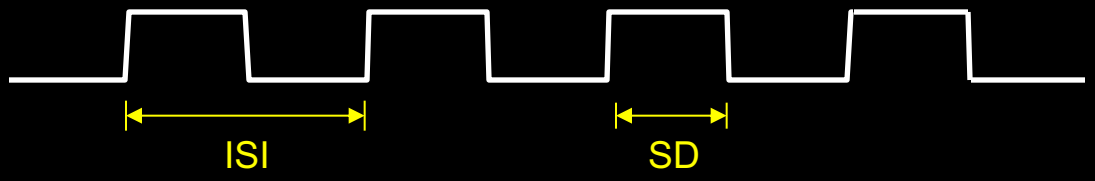
6. Free behavior Design.

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

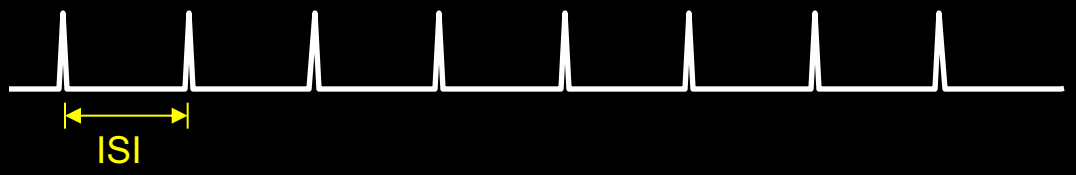


Definitions

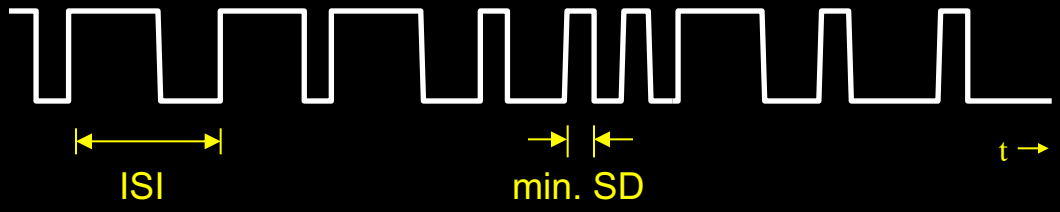
Blocked
Trial



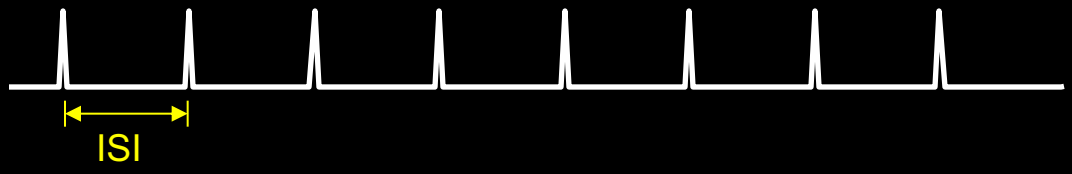
Event-Related
Constant ISI

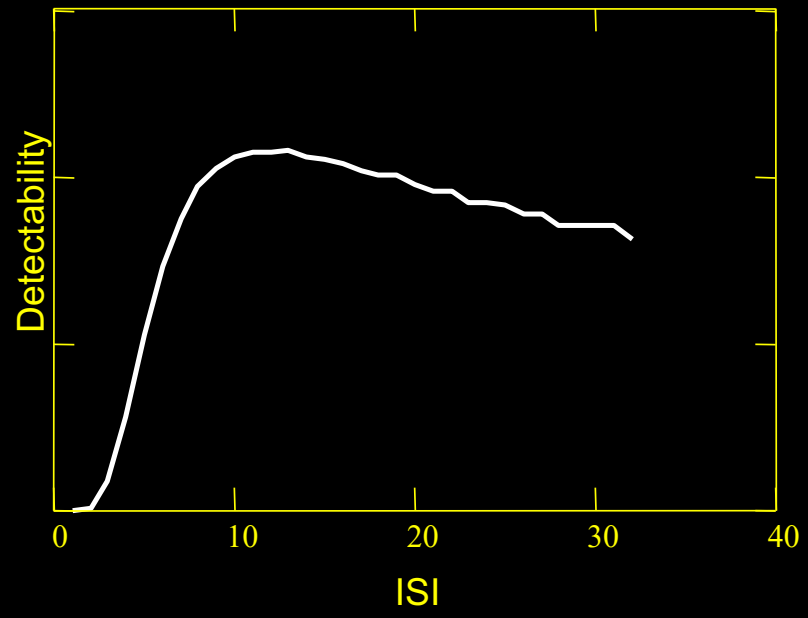


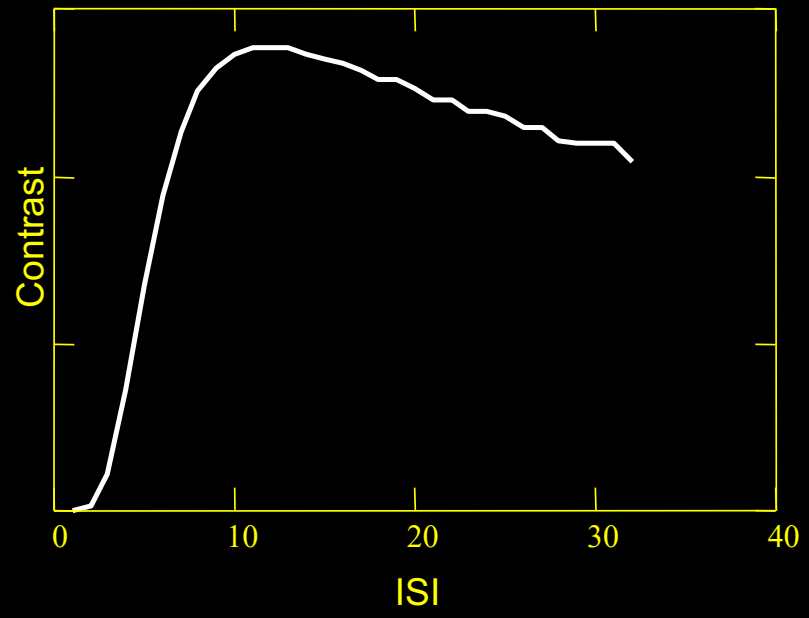
Event-Related
Variable ISI



Detection – constant ISI

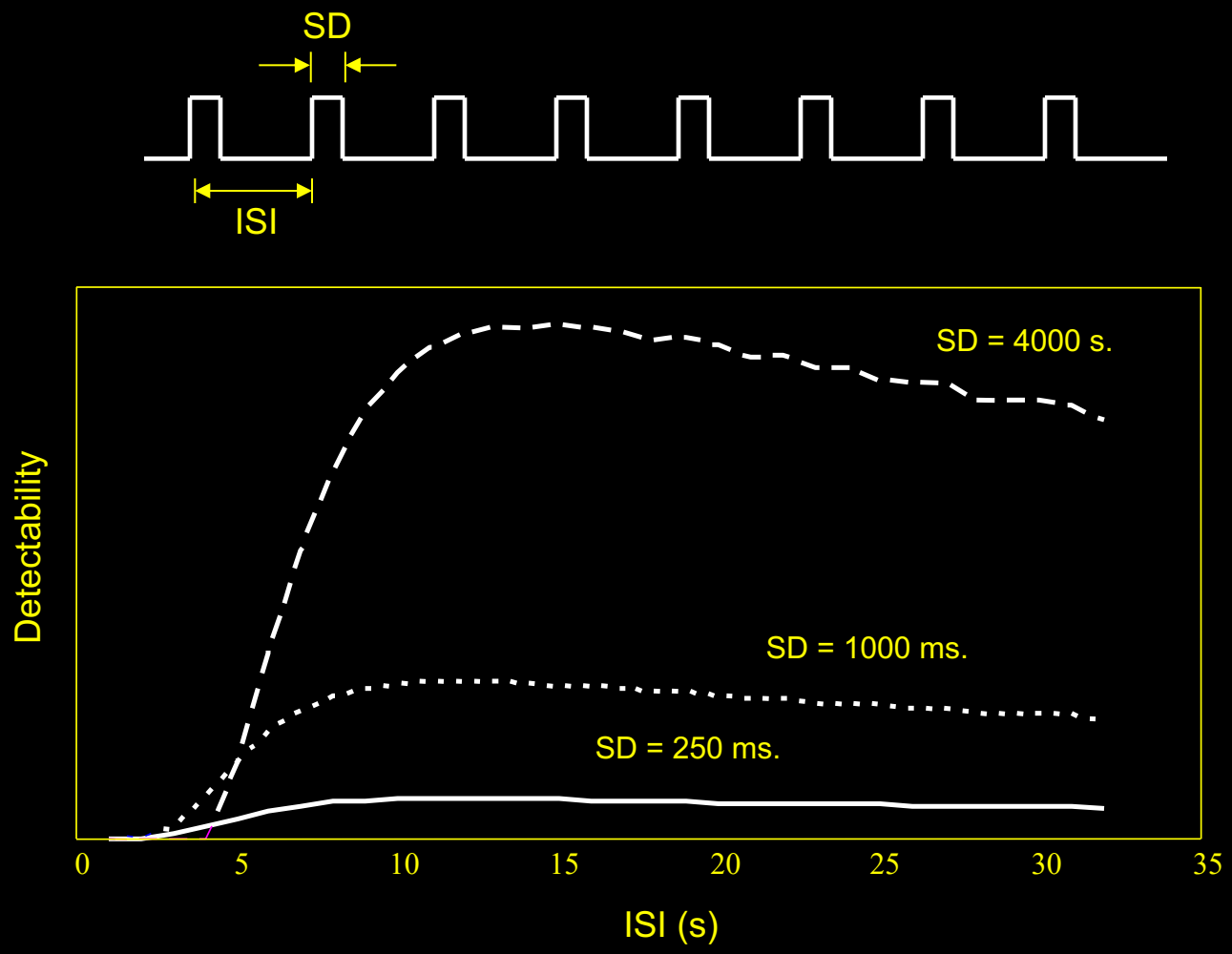






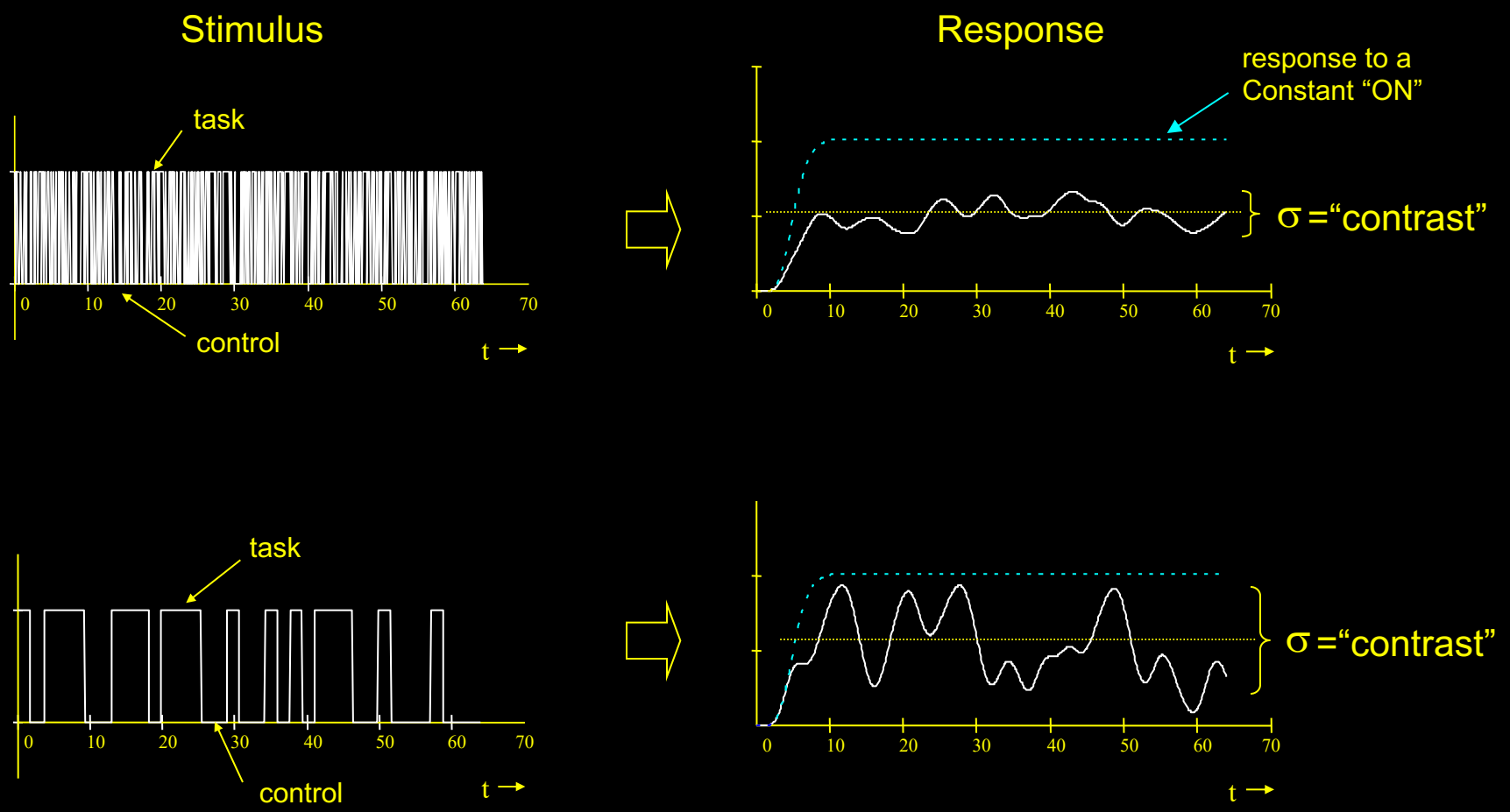
Optimal detection when there is no overlap

Detection vs. ISI – different SD

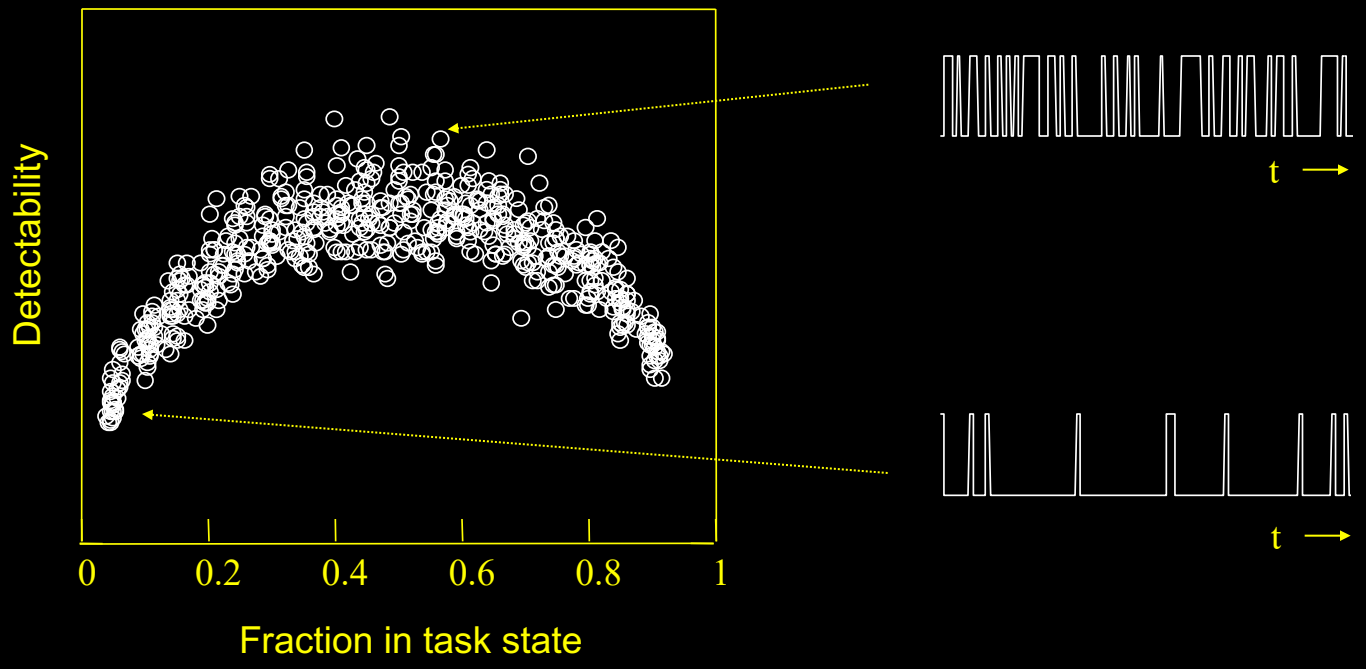


Optimal detection when there is no overlap

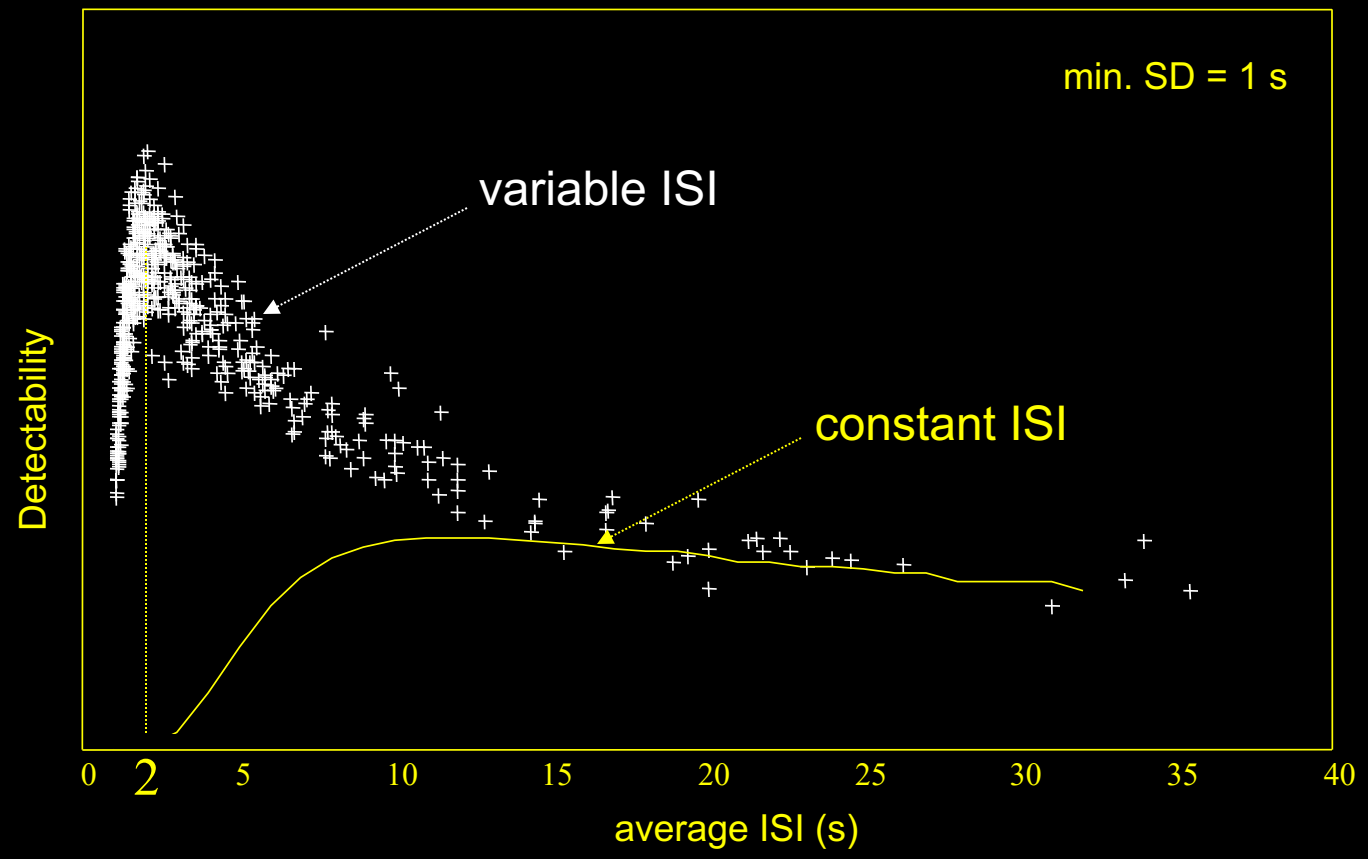
Detection: Contrast



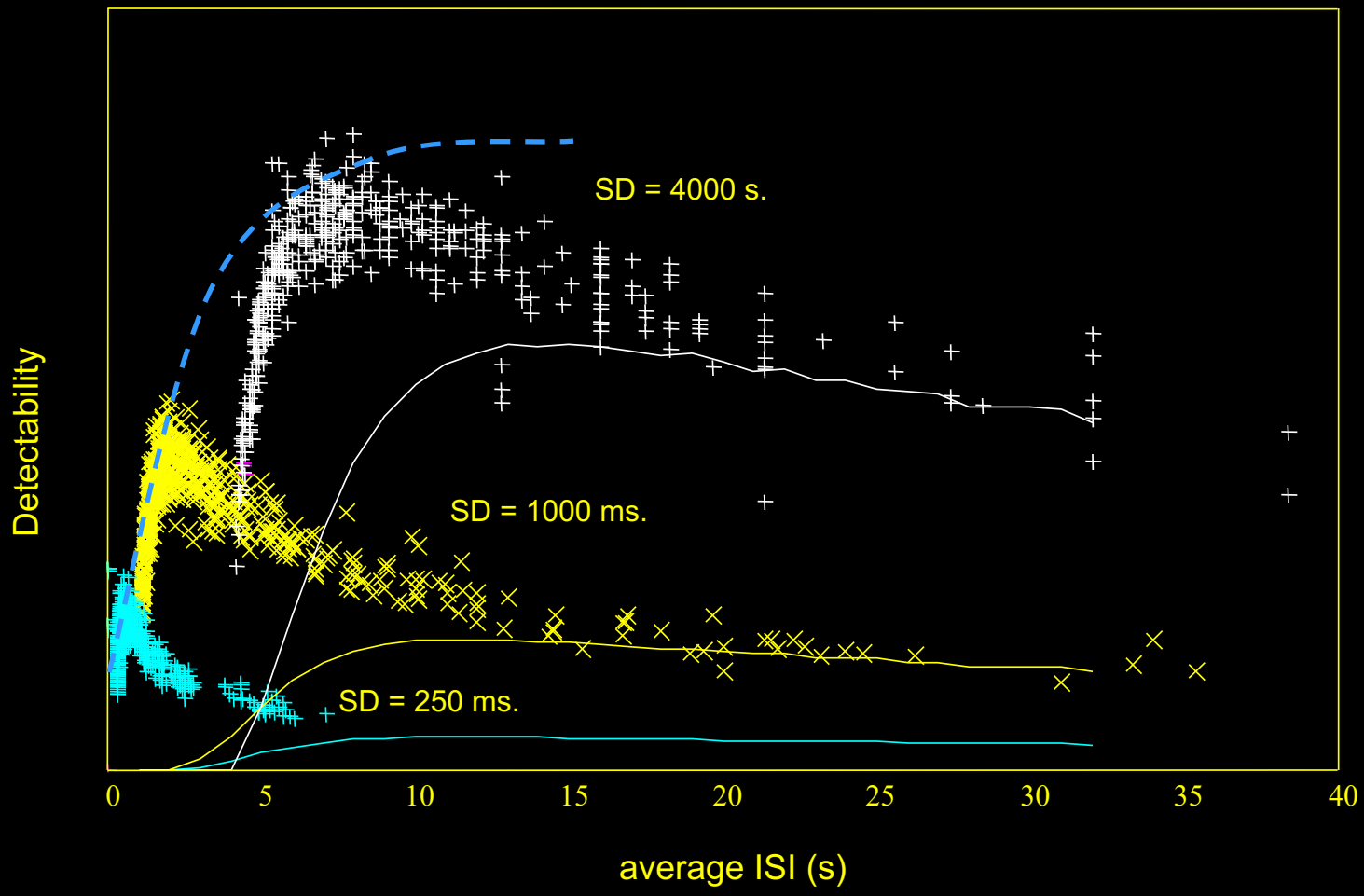
Detection vs. % “on” – variable ISI



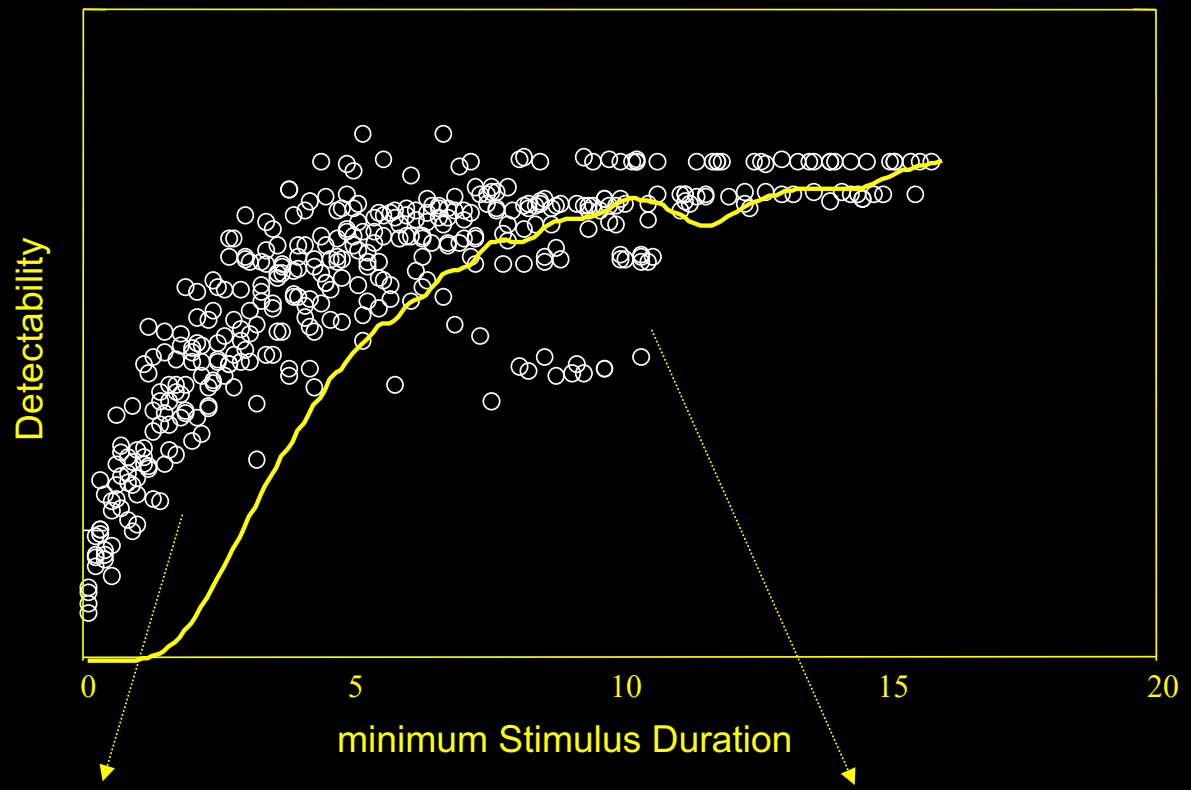
Detection vs. Average ISI



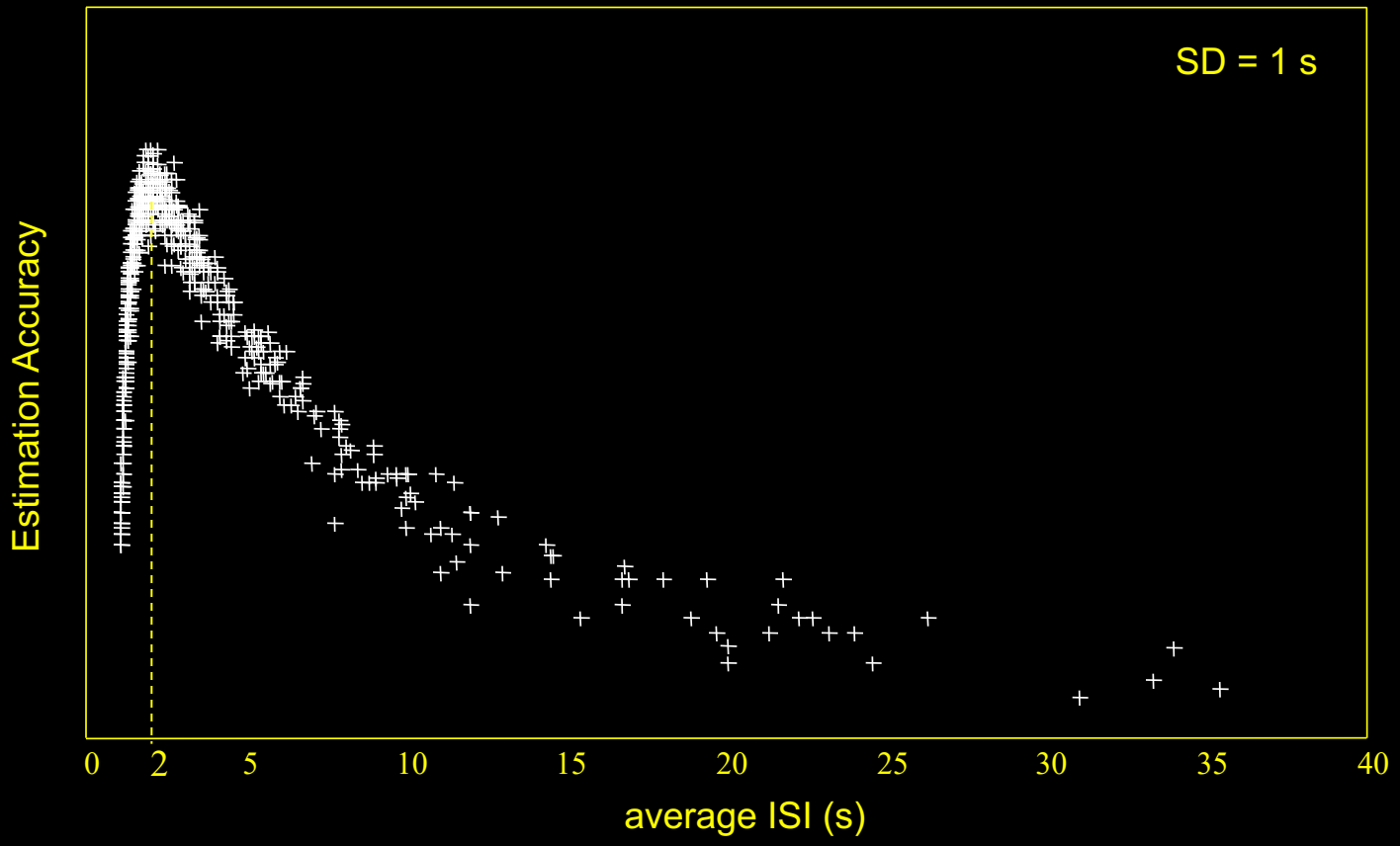
Detection vs. average ISI



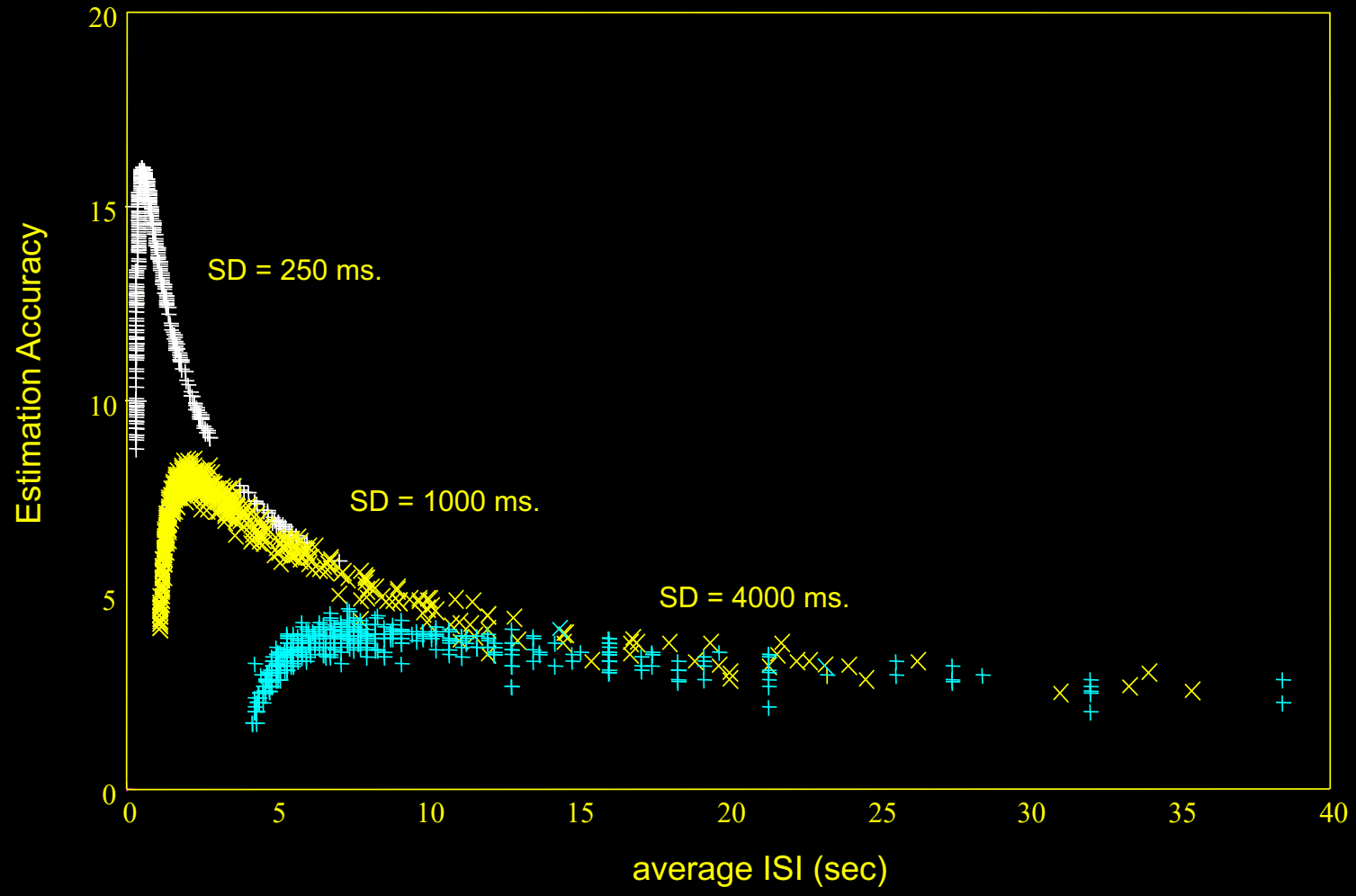
Detection – 50% “on”



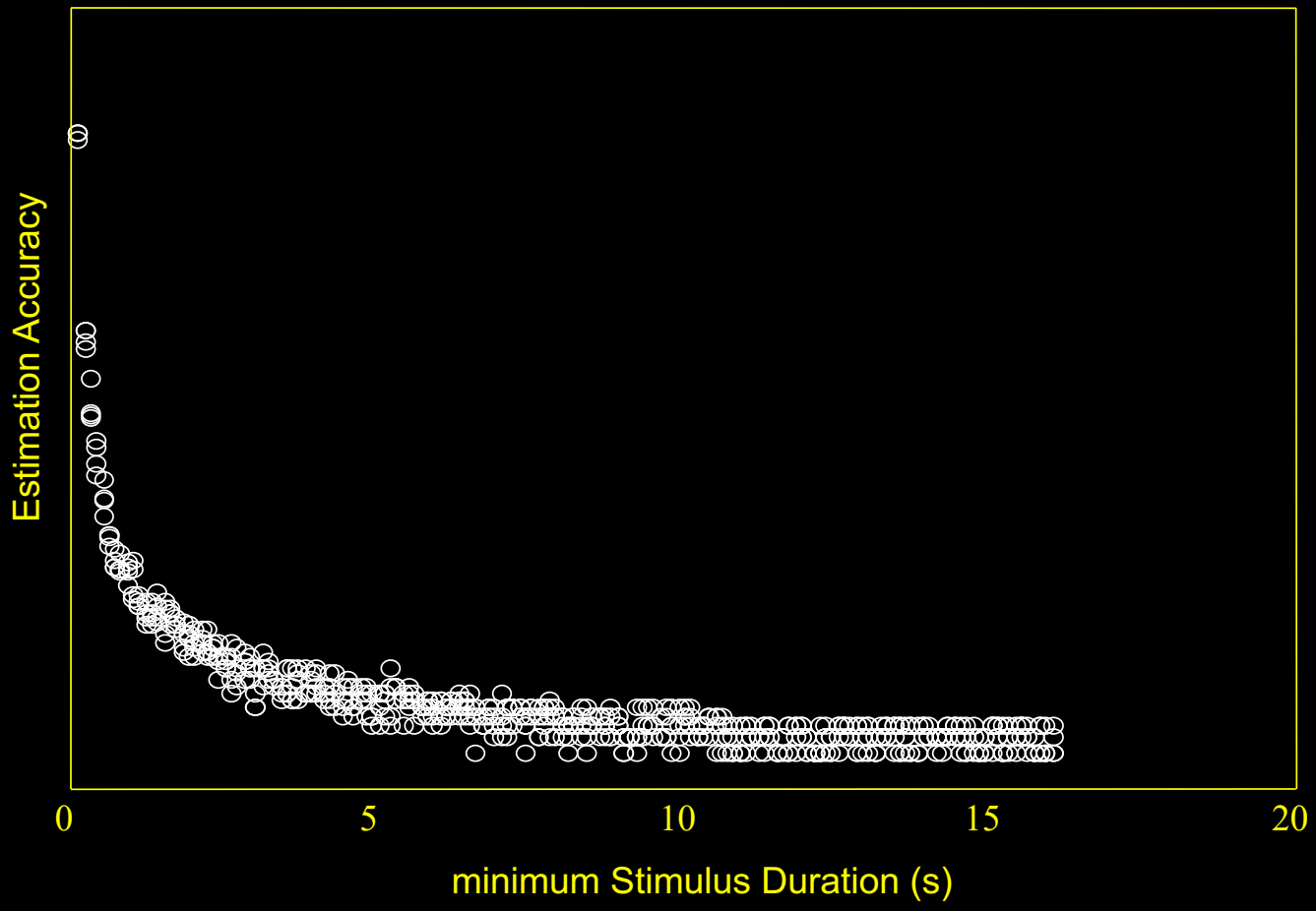
Estimation accuracy vs. average ISI



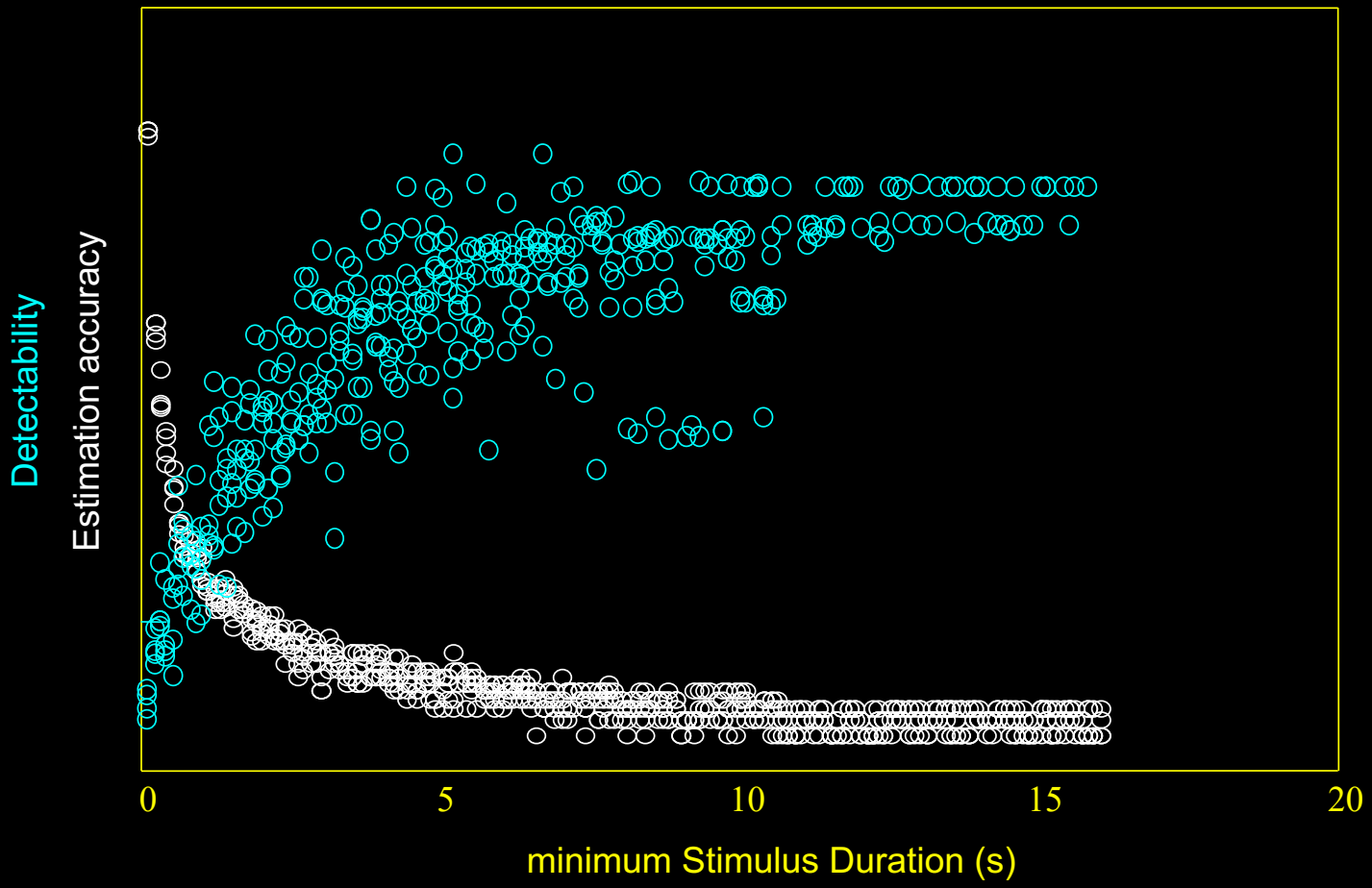
Estimation accuracy vs. average ISI



Estimation accuracy – 50% “on”



Detection and Estimation



Acknowledgements

Robert Savoy
Ravi Menon
Eric Wong
Rick Hoge

&...

Functional Imaging Methods / 3T Group

Staff Scientists:
Sean Marrett
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July 7, 2000