Basic Methodology and Information Content of Functional MRI

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Laboratory of Brain and Cognition
National Institute of Mental Health

Functional MRI

- Scanner and Hardware
- Anatomical Contrast and Image Formation
- Pulse sequences
  - *-functional contrast weighting*
  - *-functional time series image collection is*
- Neuronal Input / Information Display Strategie

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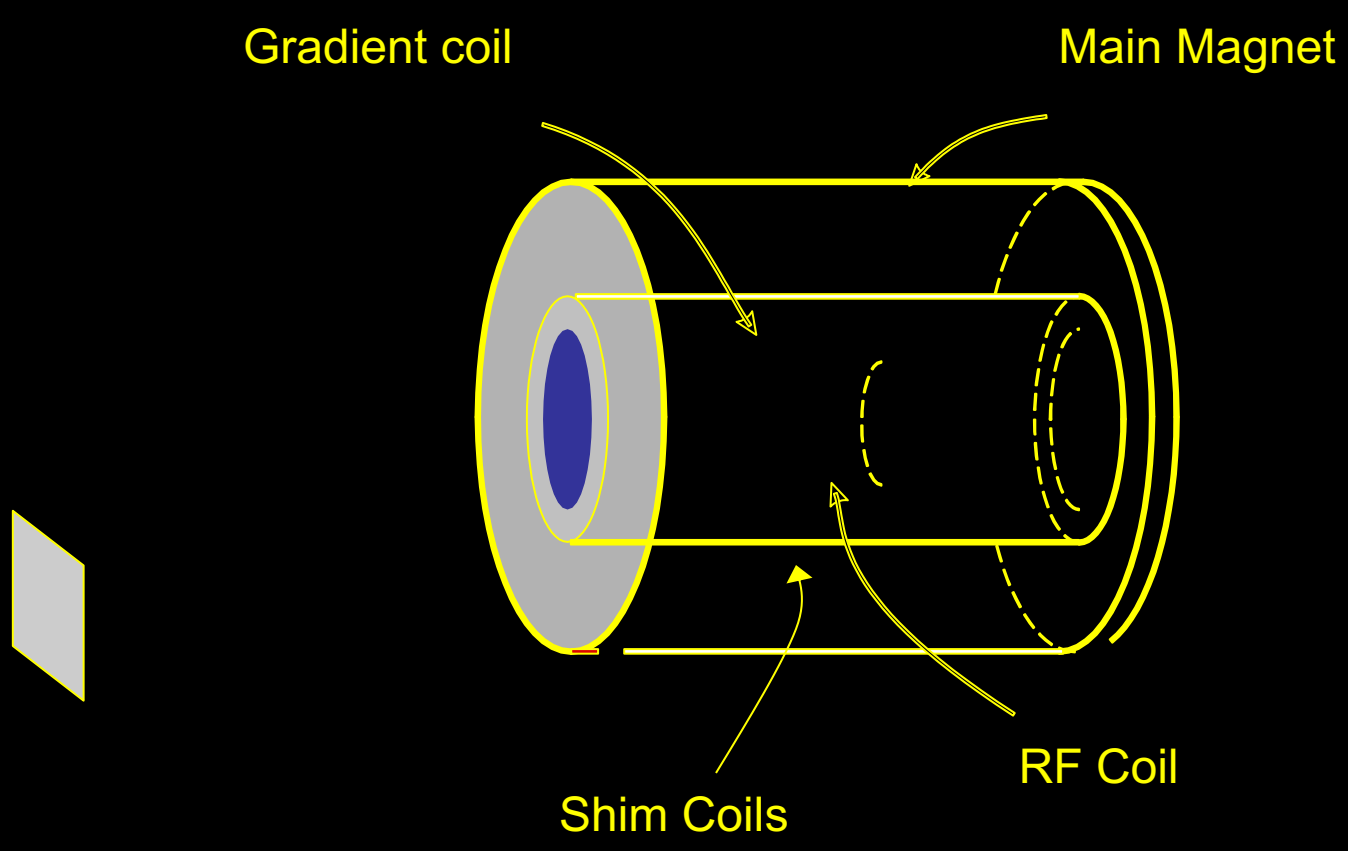
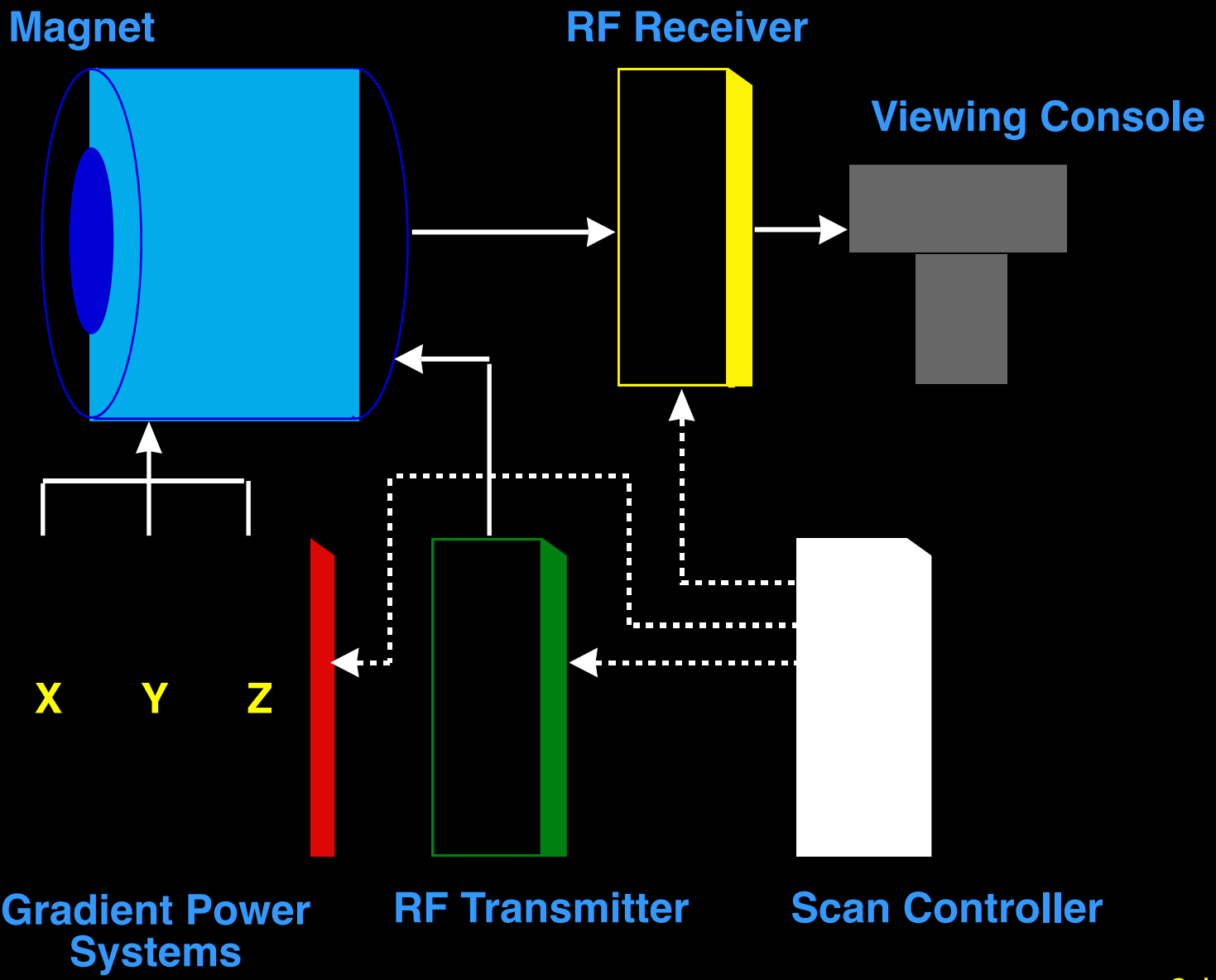
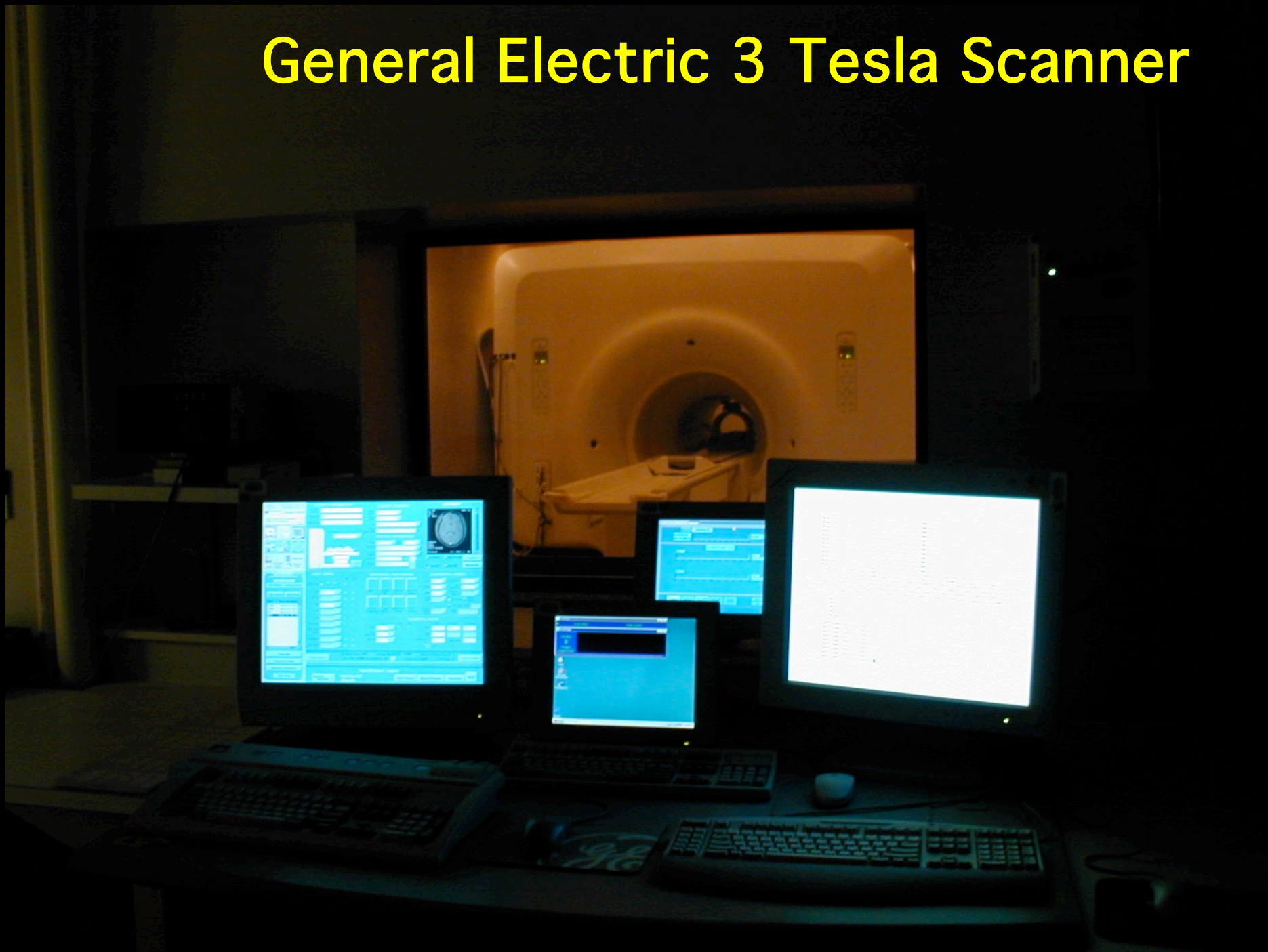

Gradient coil
Main Magnet
RF Coil
Shim Coils

Imaging System Components



Cohen et al

General Electric 3 Tesla Scanner



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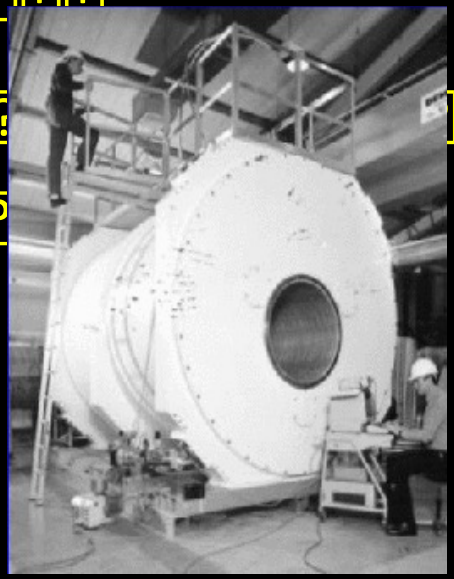

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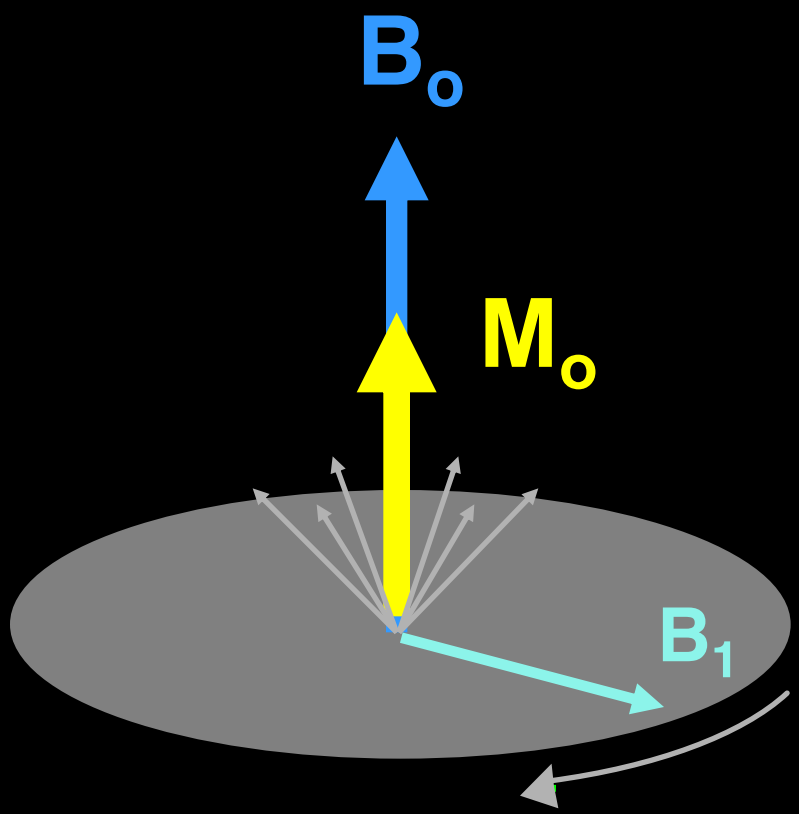
[illegible]

[illegible]

$$[illegible]_o = \gamma B_o$$

γ [illegible]

[illegible]$_{[illegible]}$ [illegible]


B_o
M_o
B_1

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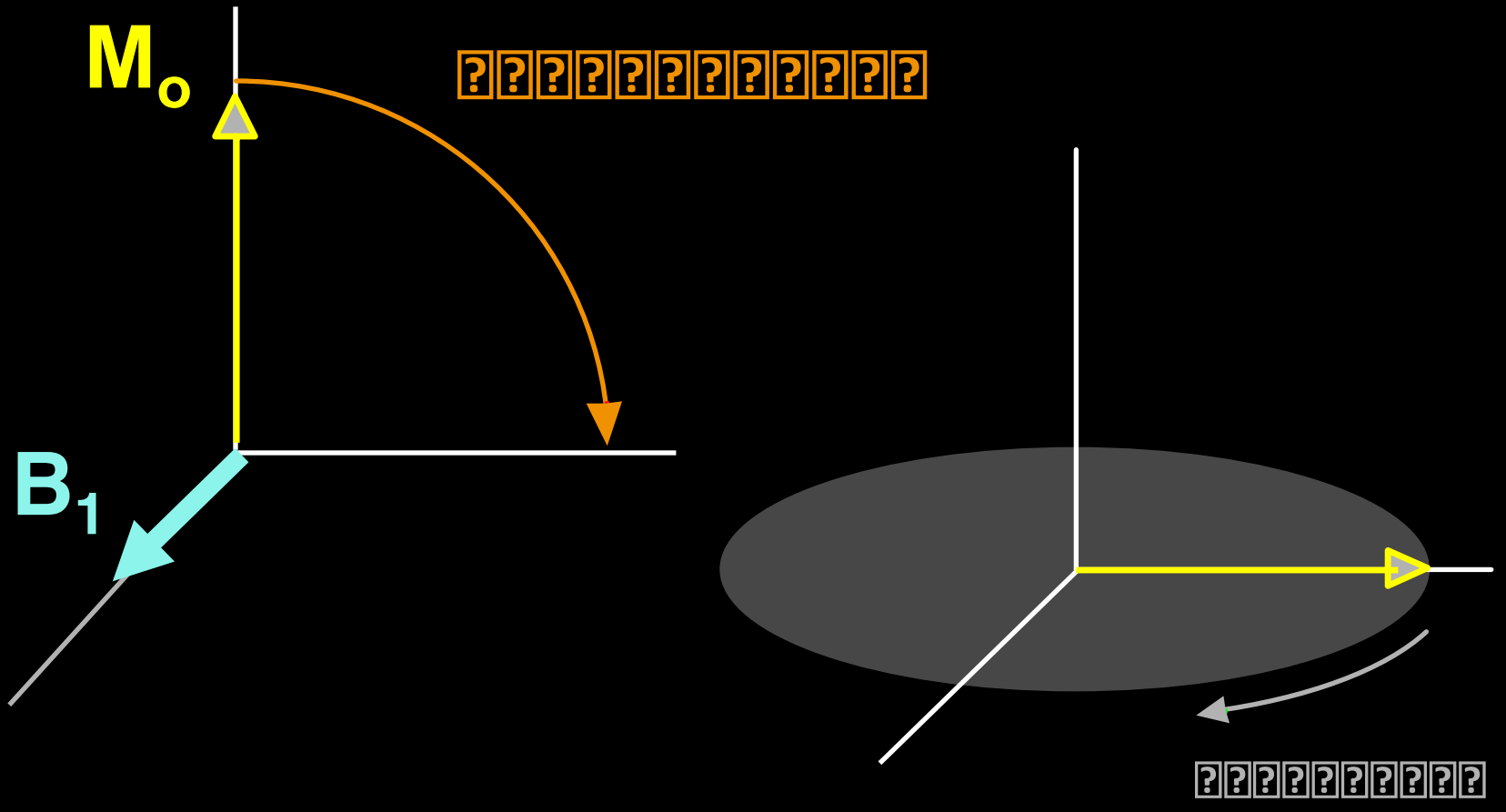
M_o
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B_1
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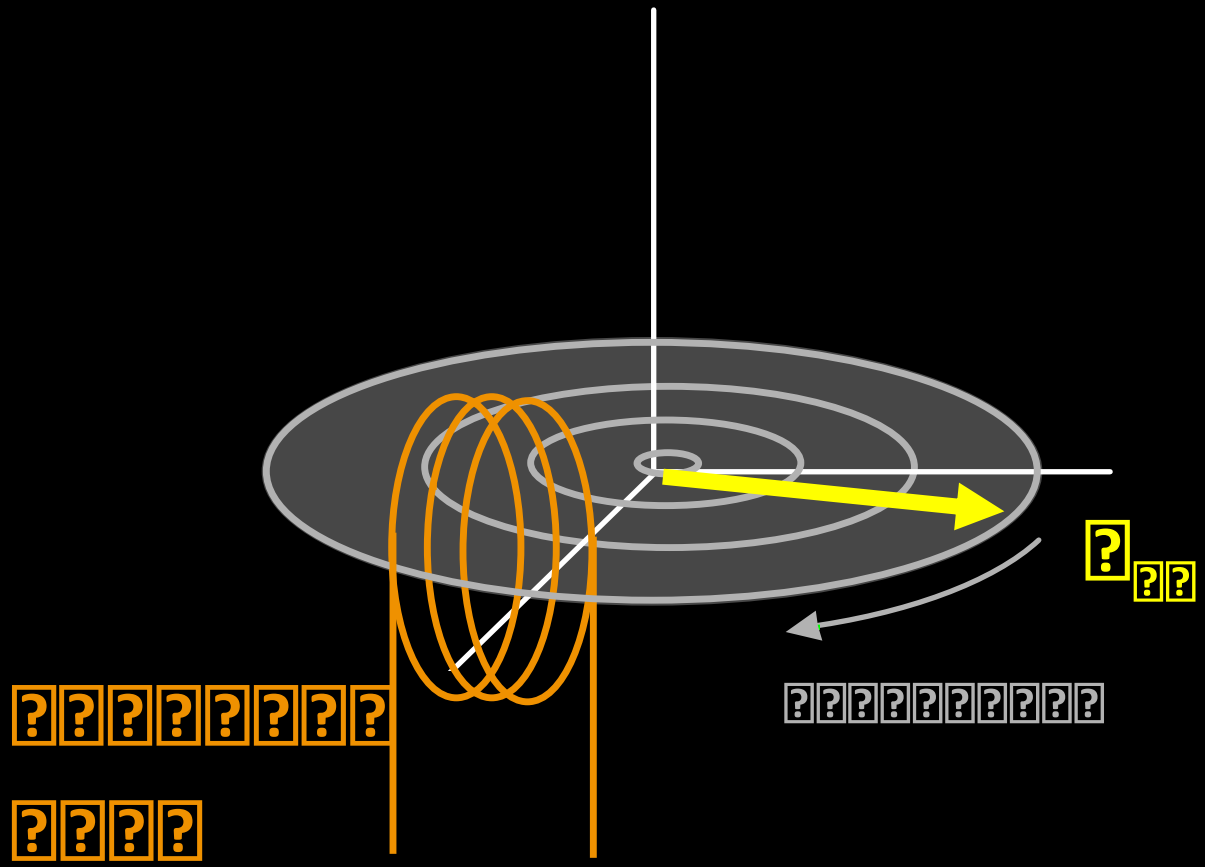

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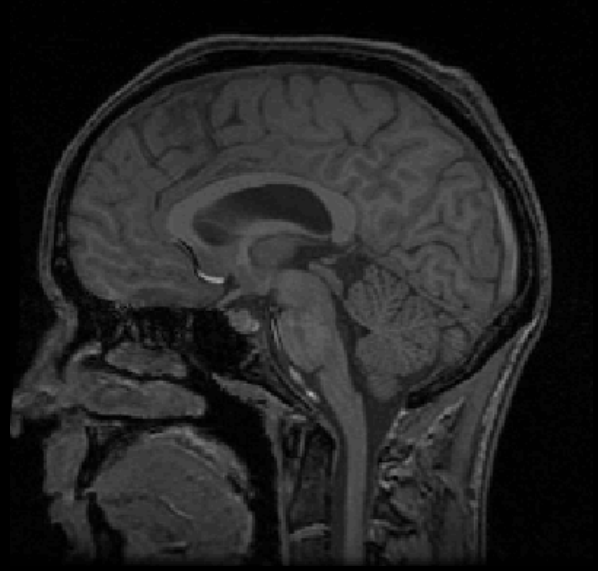

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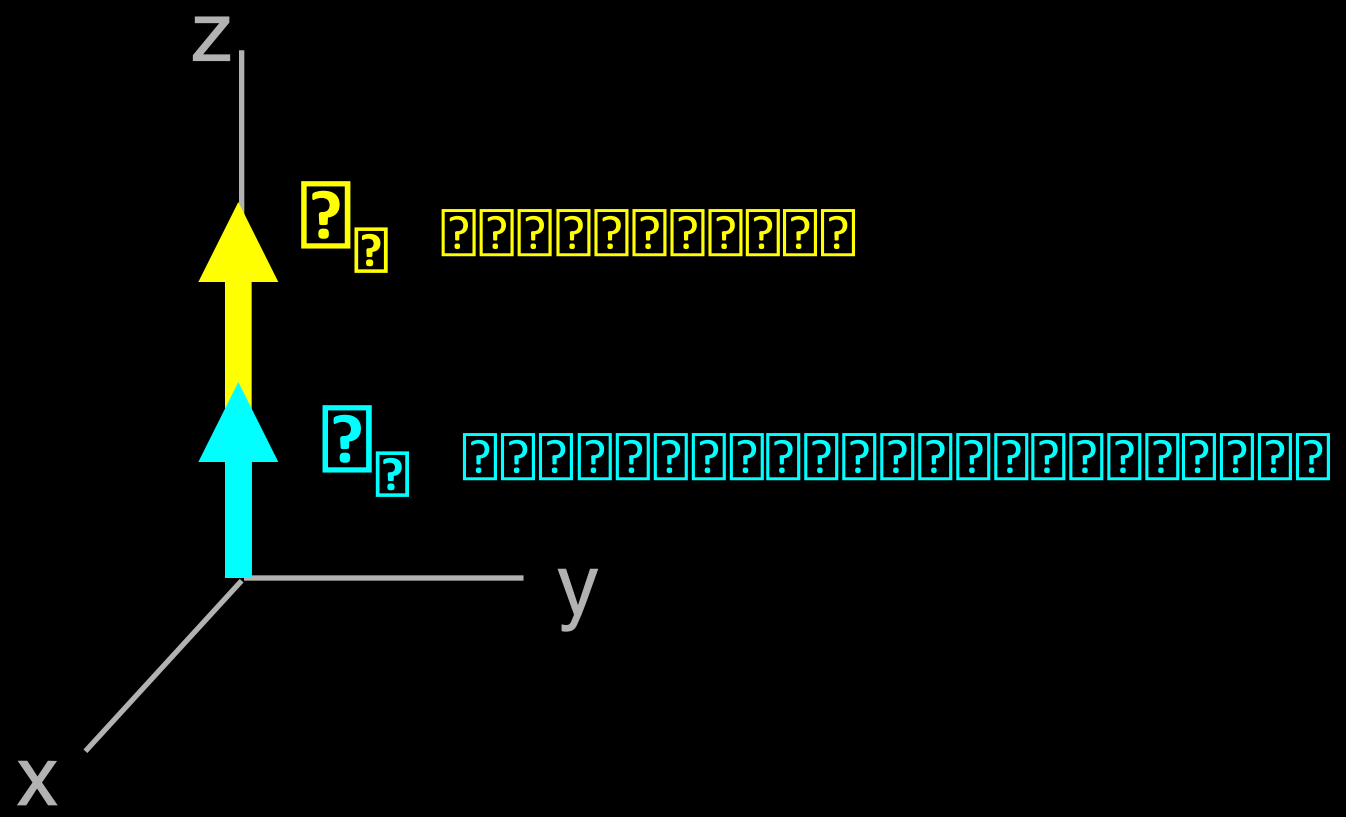
z
y
x

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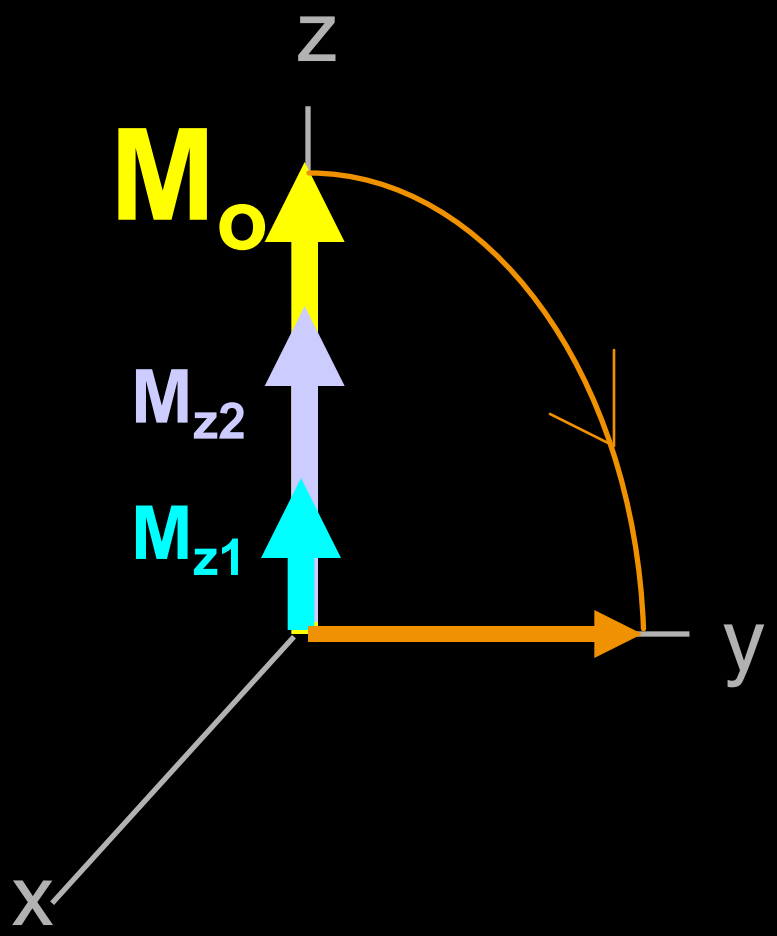
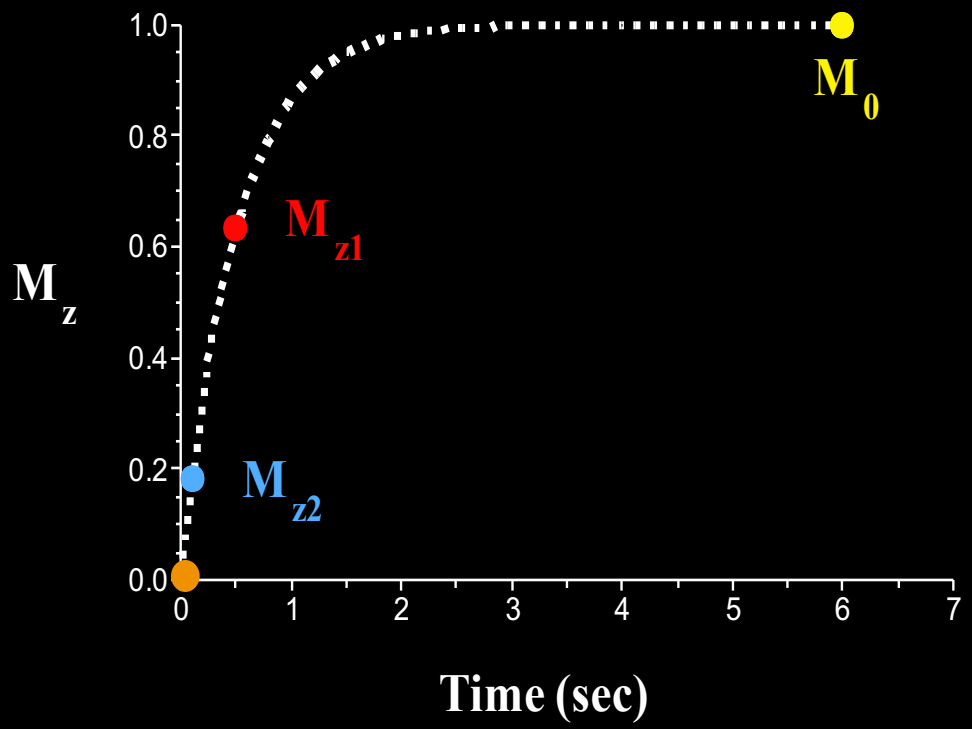
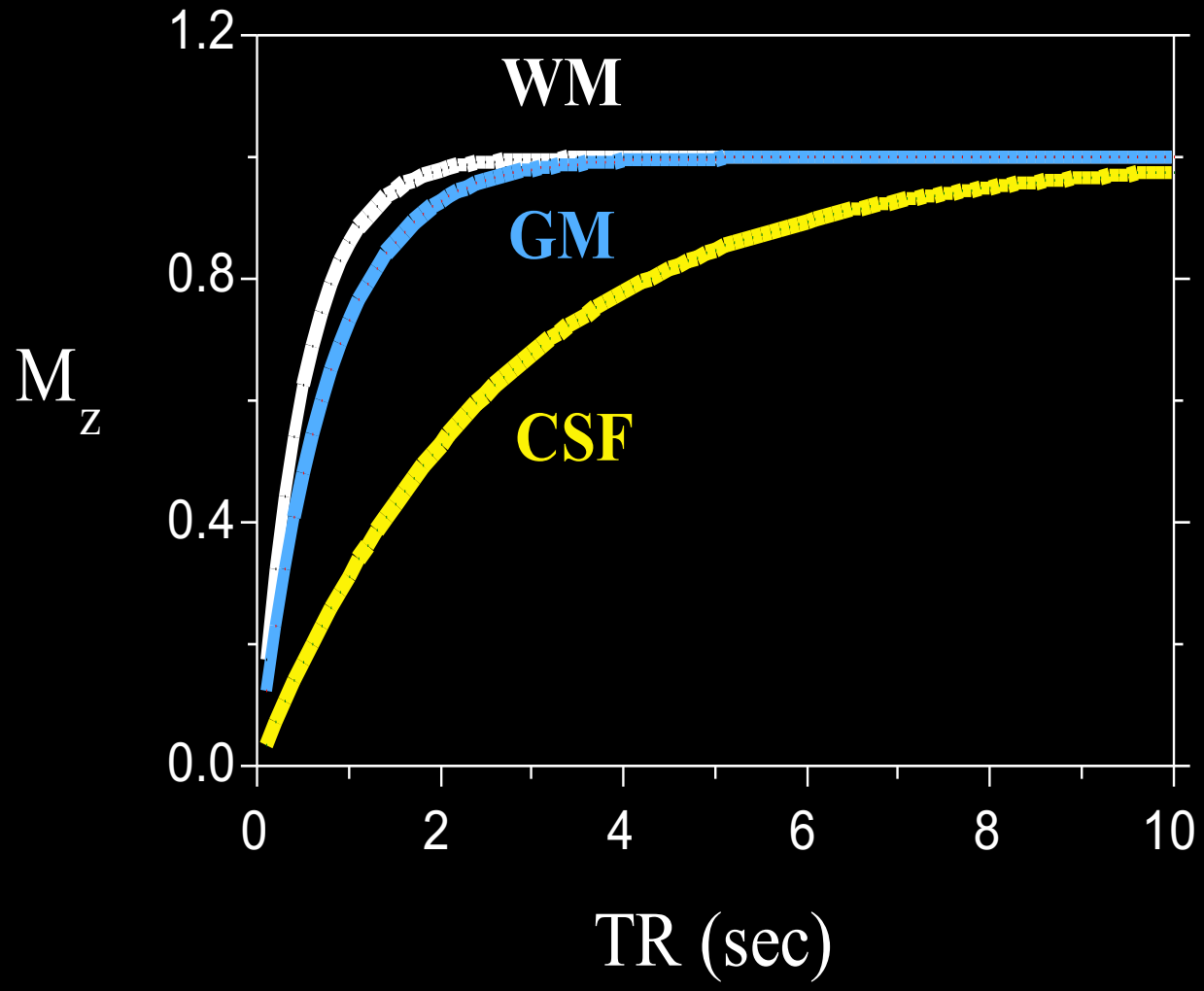

z
M_o
M_{z2}
M_{z1}
y
x


1.0
0.8
0.6
0.4
0.2
0.0
M_z
M_0
M_{z1}
M_{z2}
0
1
2
3
4
5
6
7
Time (sec)


1.2
0.8
0.4
0.0
M_z
WM
GM
CSF
0
2
4
6
8
10
TR (sec)

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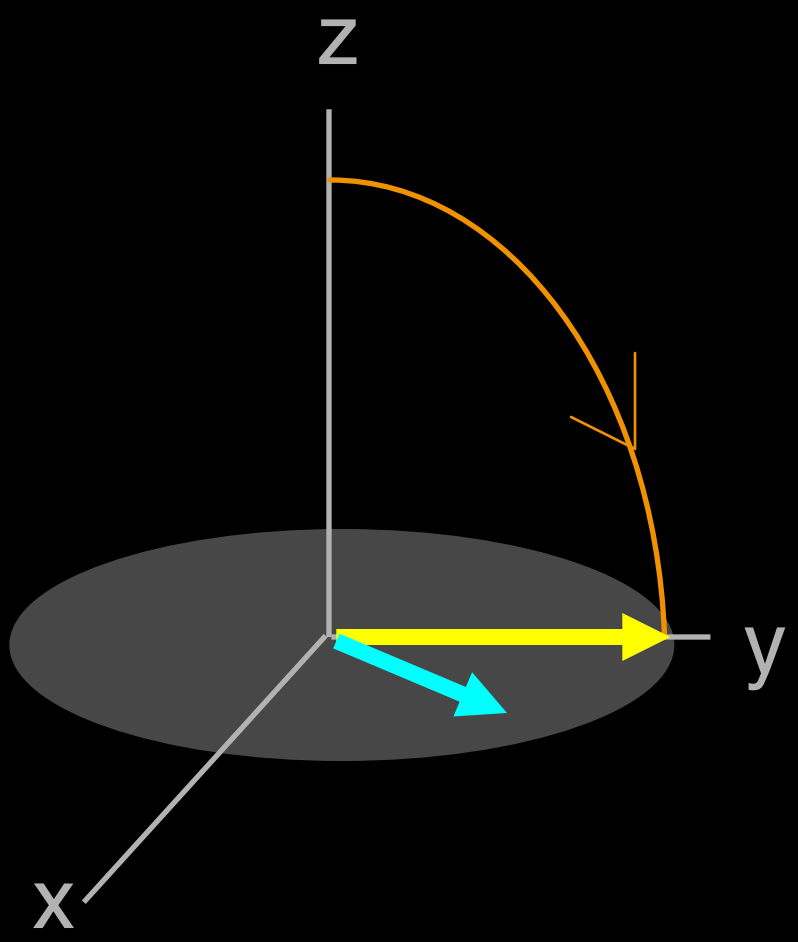
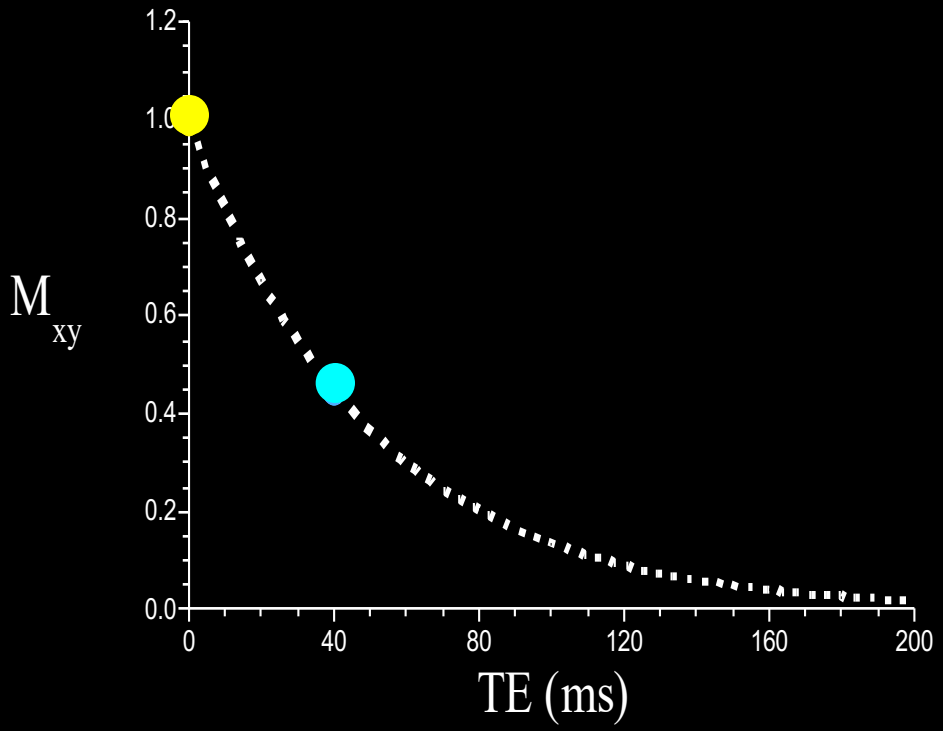
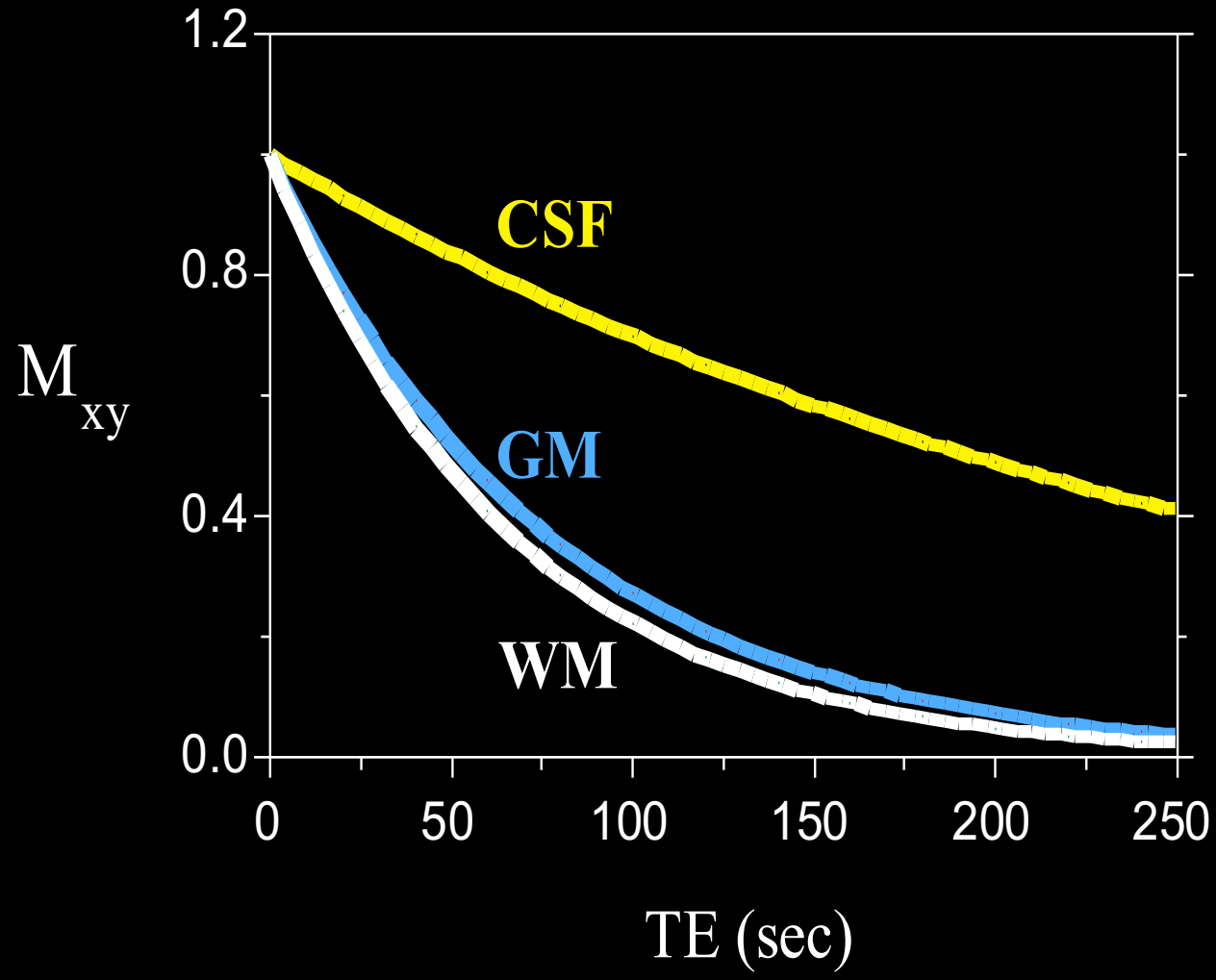
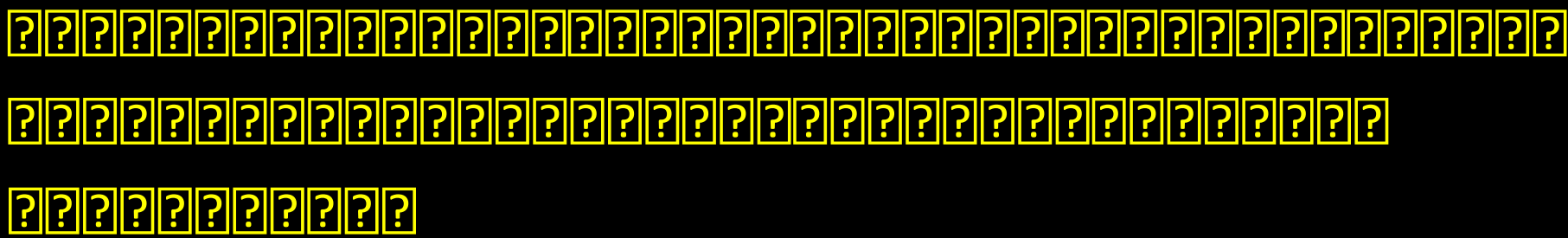
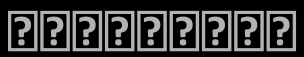

z
y
x


M
xy
1.2
1.0
0.8
0.6
0.4
0.2
0.0
0
40
80
120
160
200
TE (ms)


1.2
0.8
0.4
0.0
M_{xy}
CSF
GM
WM
0
50
100
150
200
250
TE (sec)



$$\frac{1}{T2^*} = \frac{1}{T2} + \frac{1}{T2'}$$



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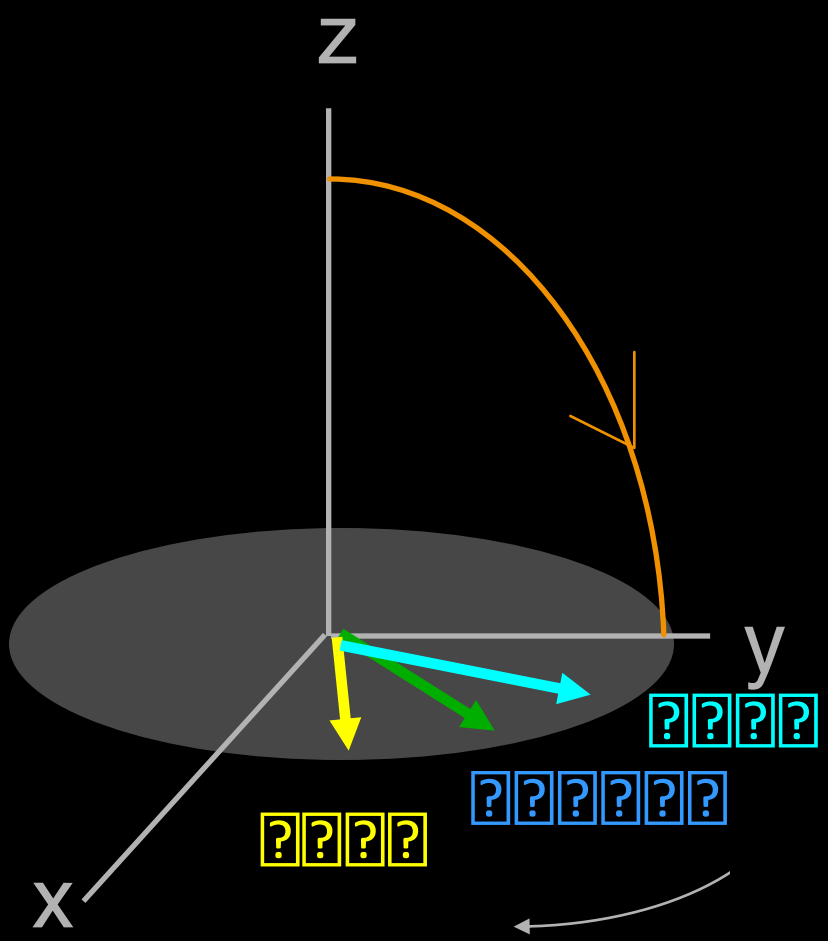
z
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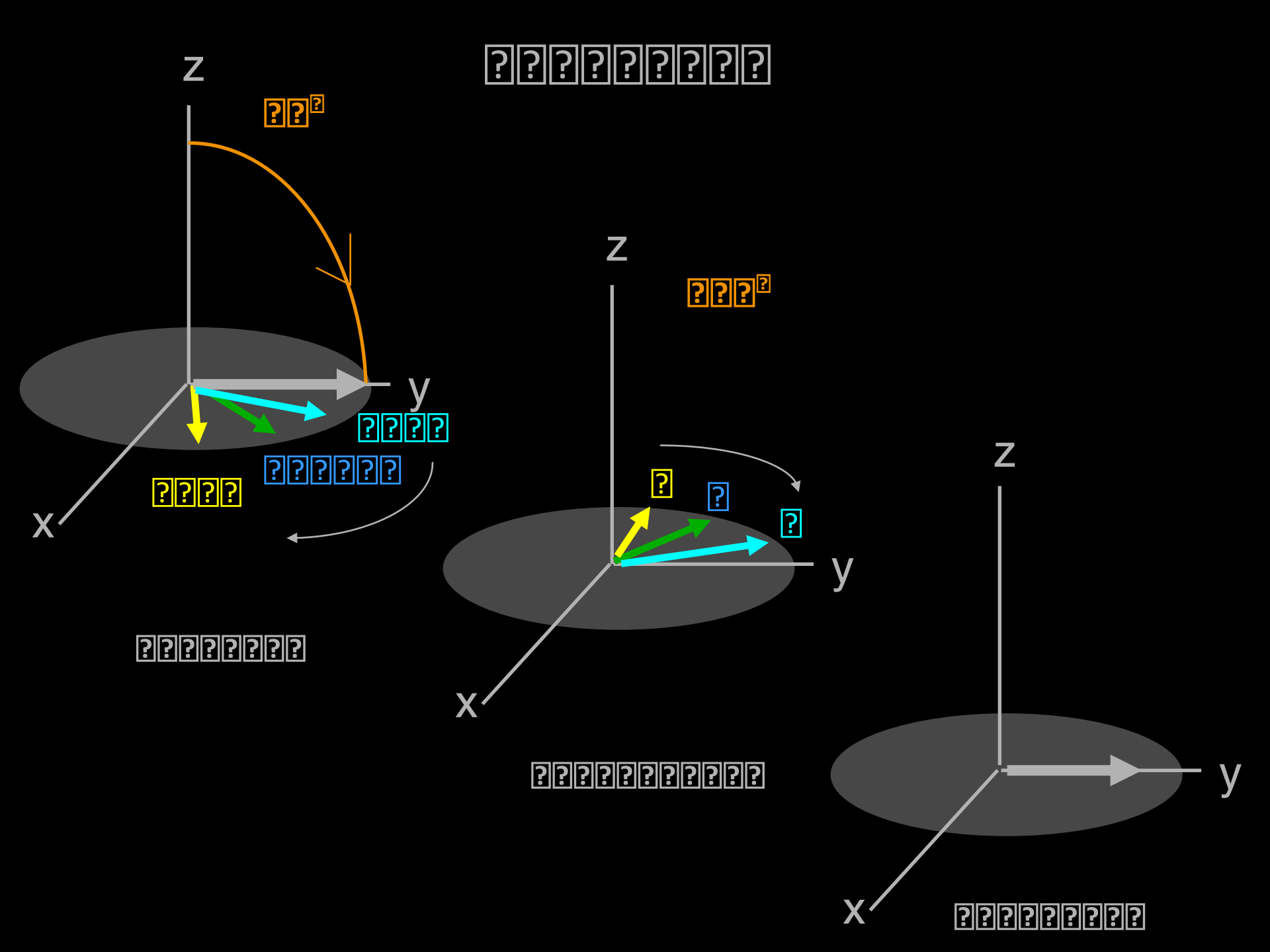
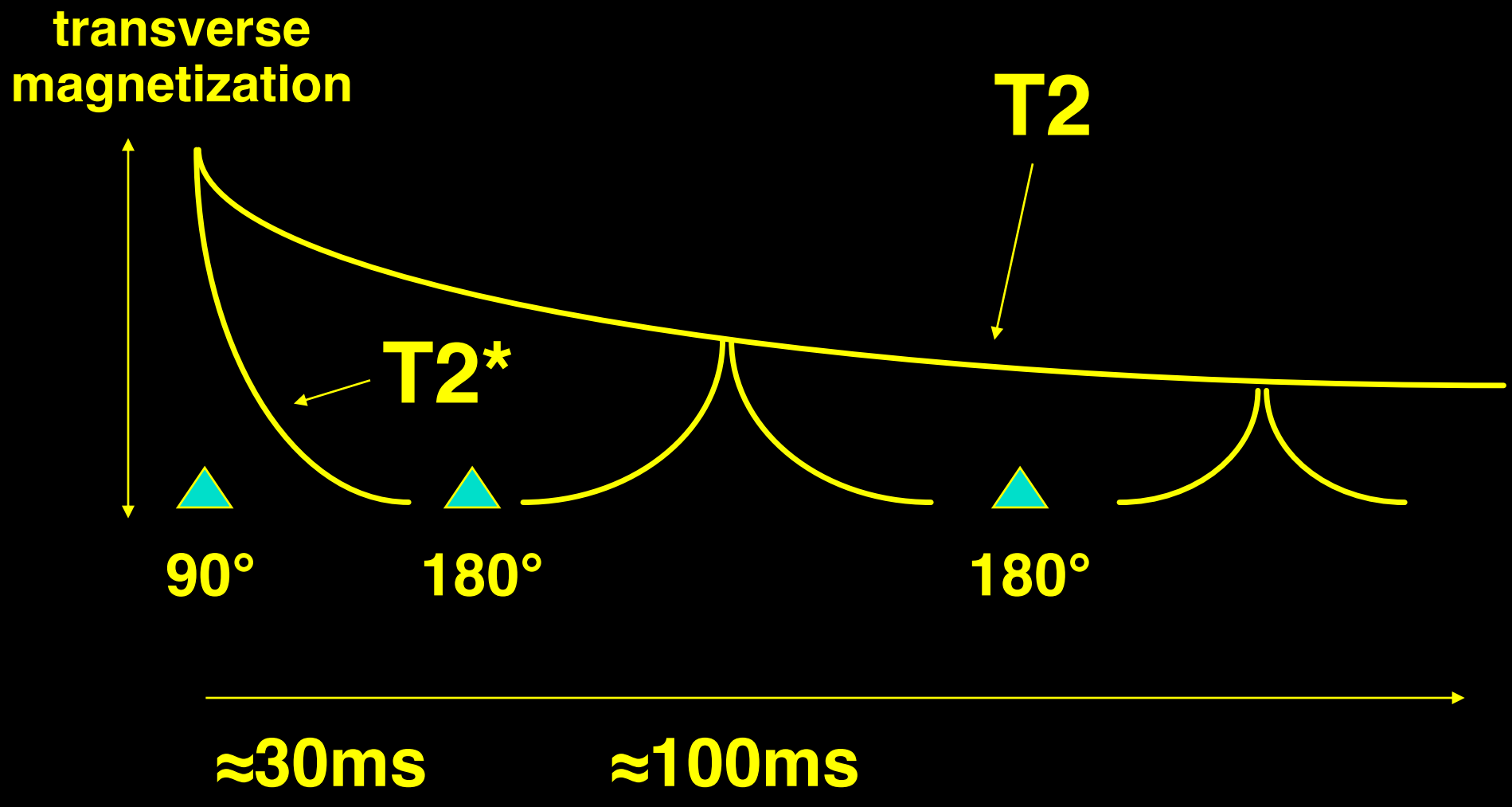
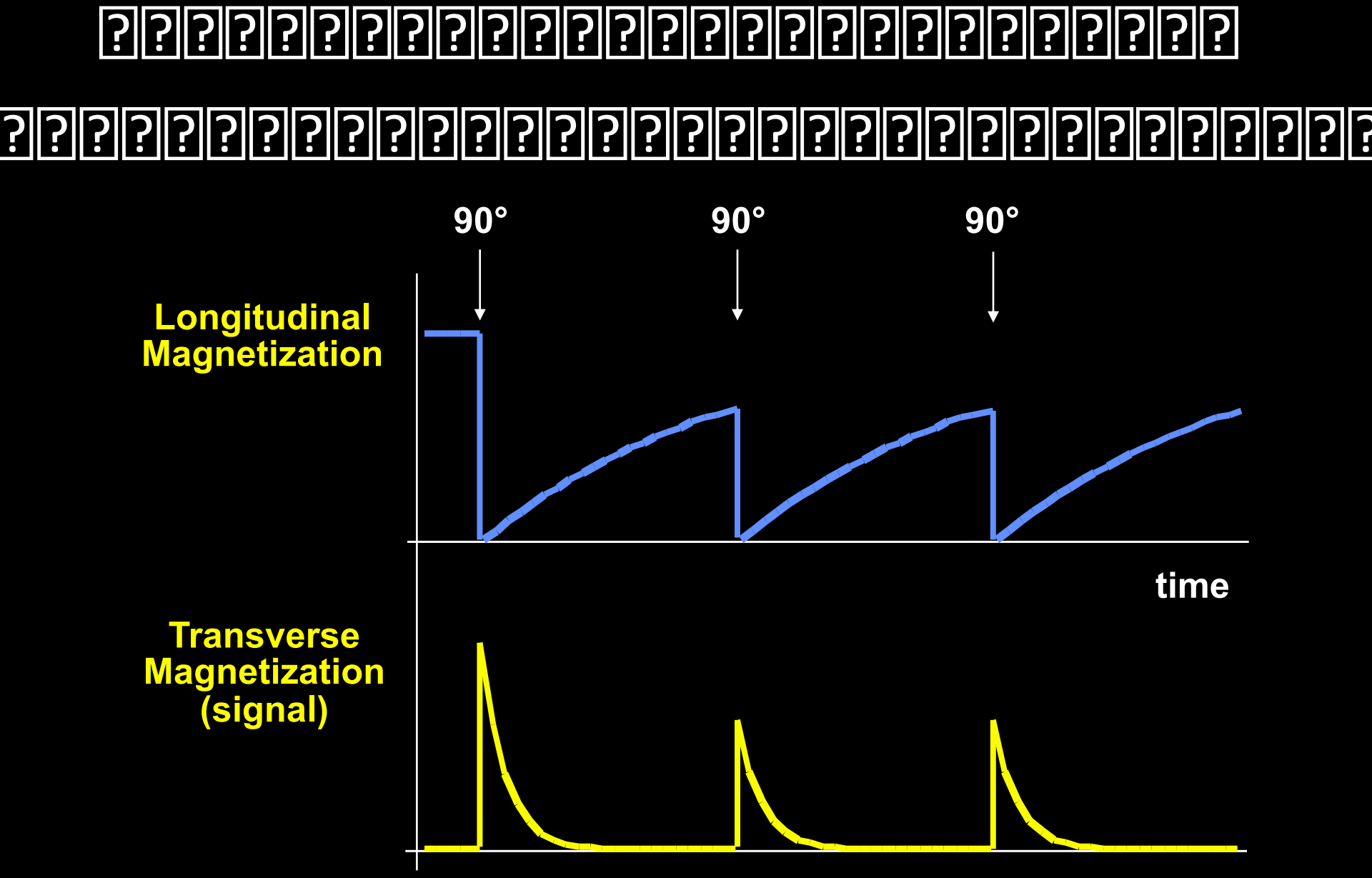

z
y
x
z
y
x
z
y
x

Transverse Relaxation




90°
90°
90°
Longitudinal Magnetization
time
Transverse Magnetization (signal)

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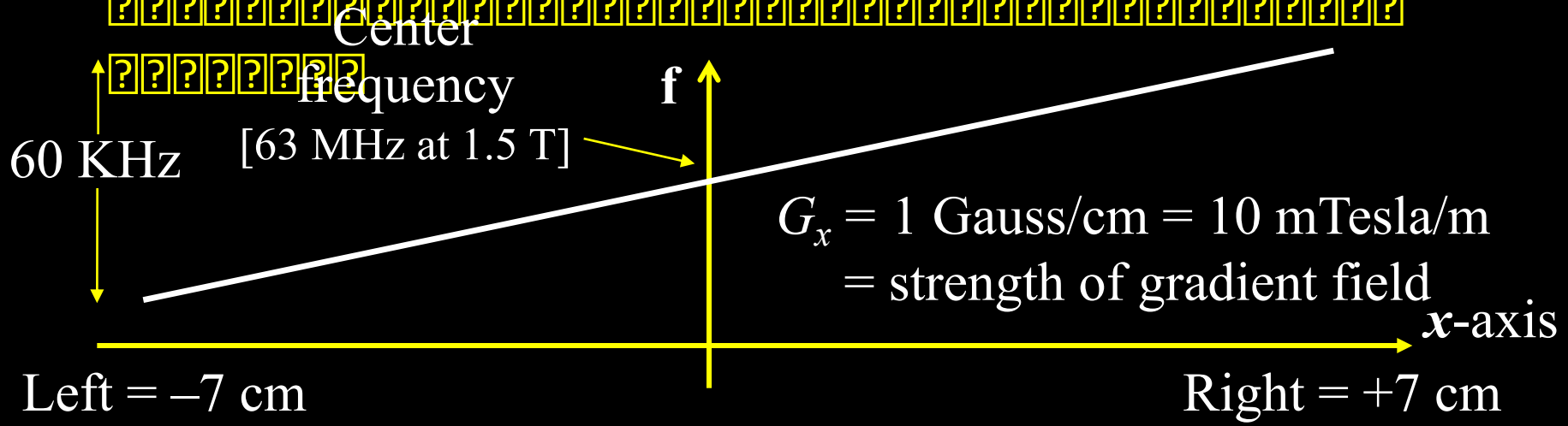
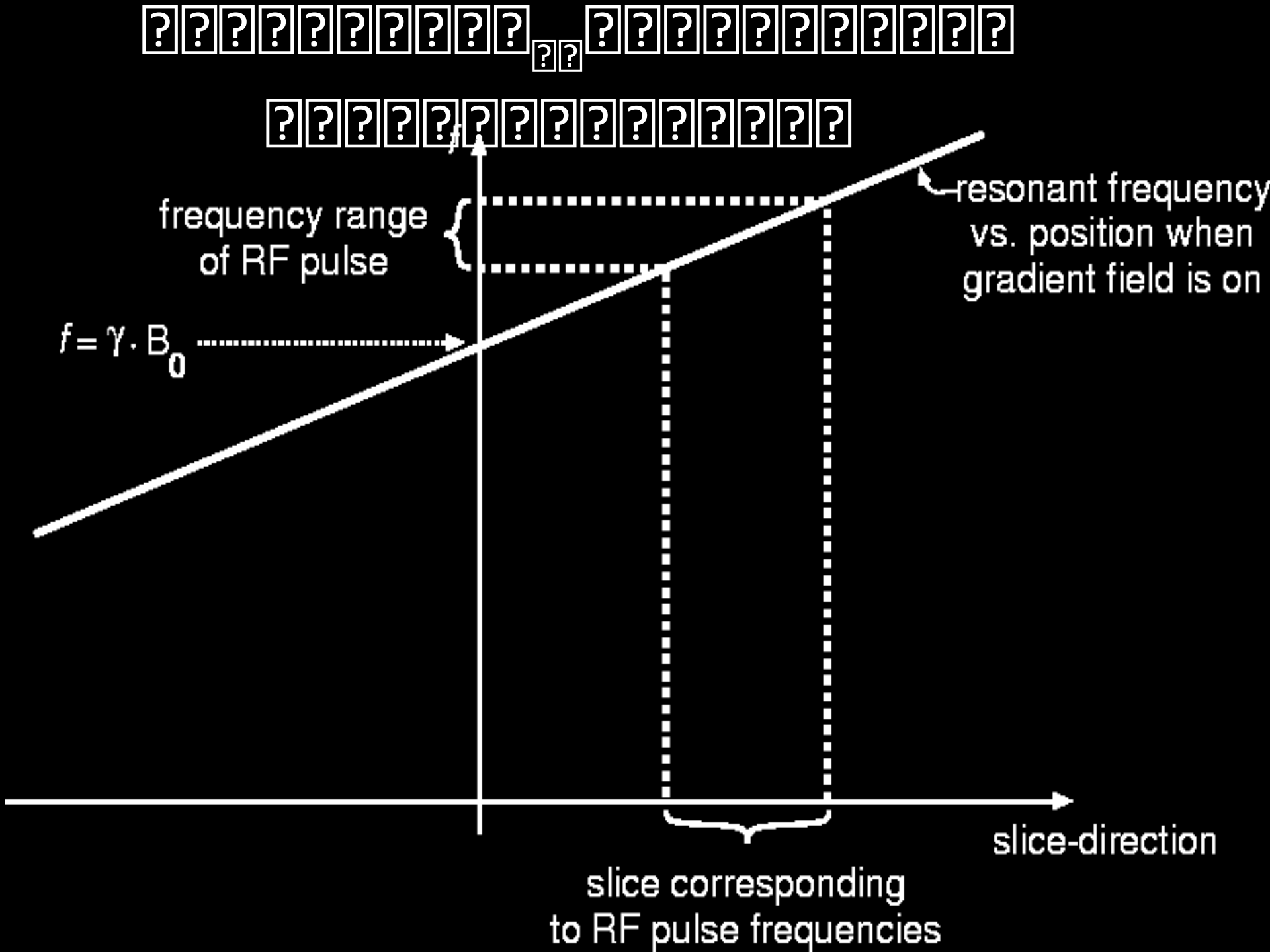

Center
frequency
[63 MHz at 1.5 T]
f
60 KHz
G_x = 1 Gauss/cm = 10 mTesla/m
= strength of gradient field
x-axis
Left = –7 cm
Right = +7 cm


f
frequency range
of RF pulse
resonant frequency
vs. position when
gradient field is on
$f = \gamma \cdot B_0$
slice-direction
slice corresponding
to RF pulse frequencies

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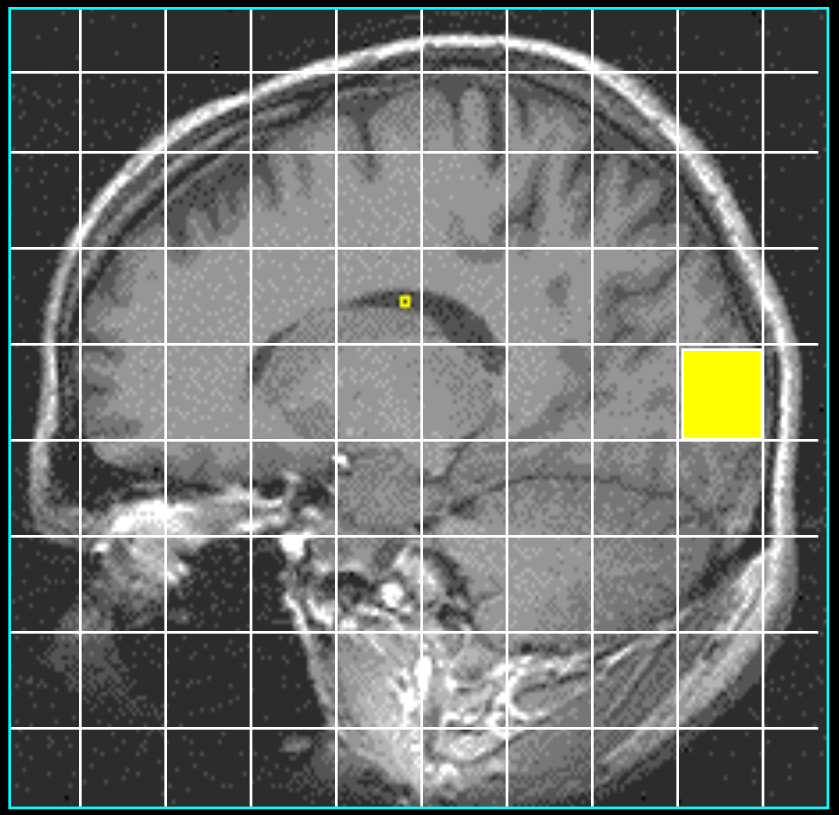

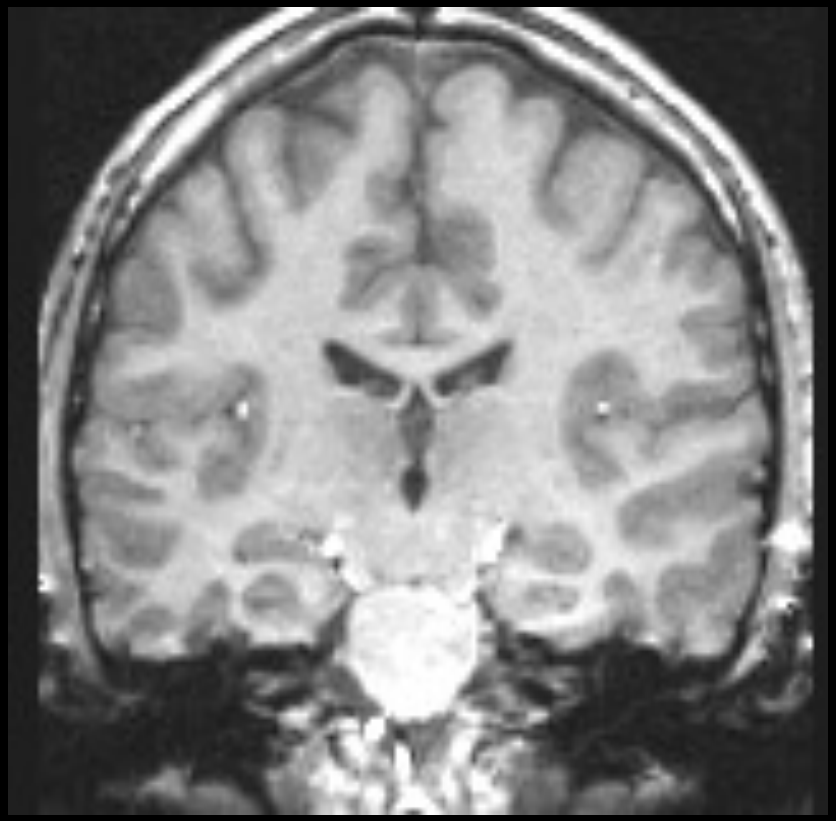

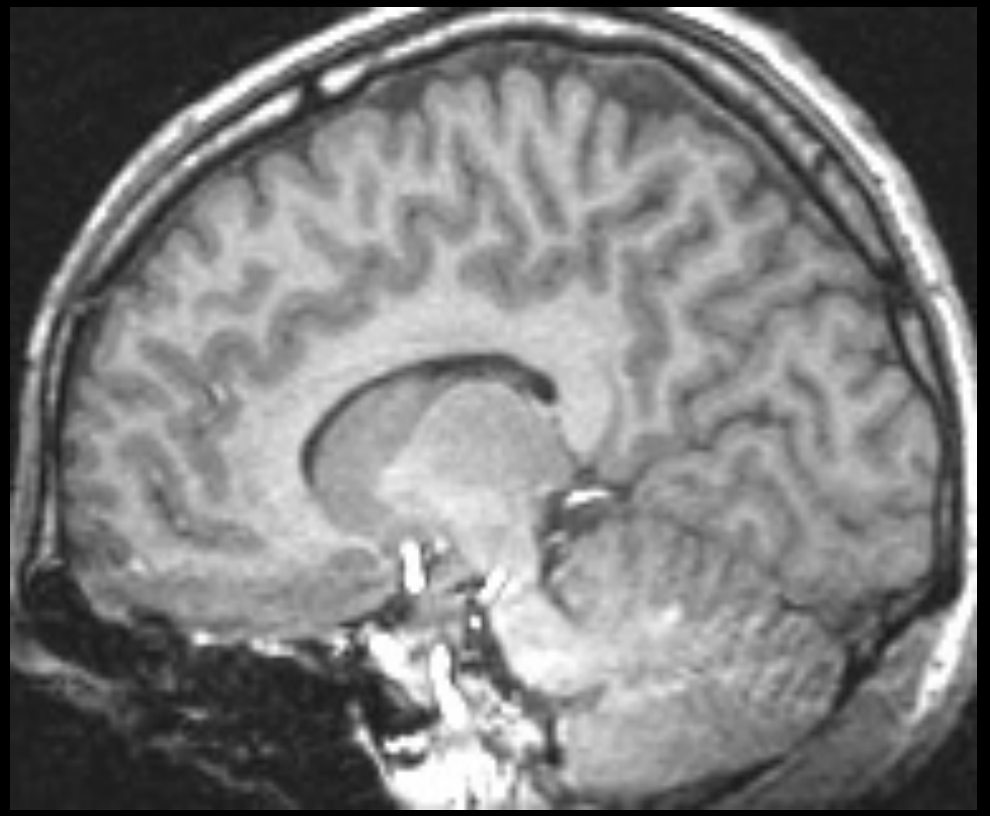

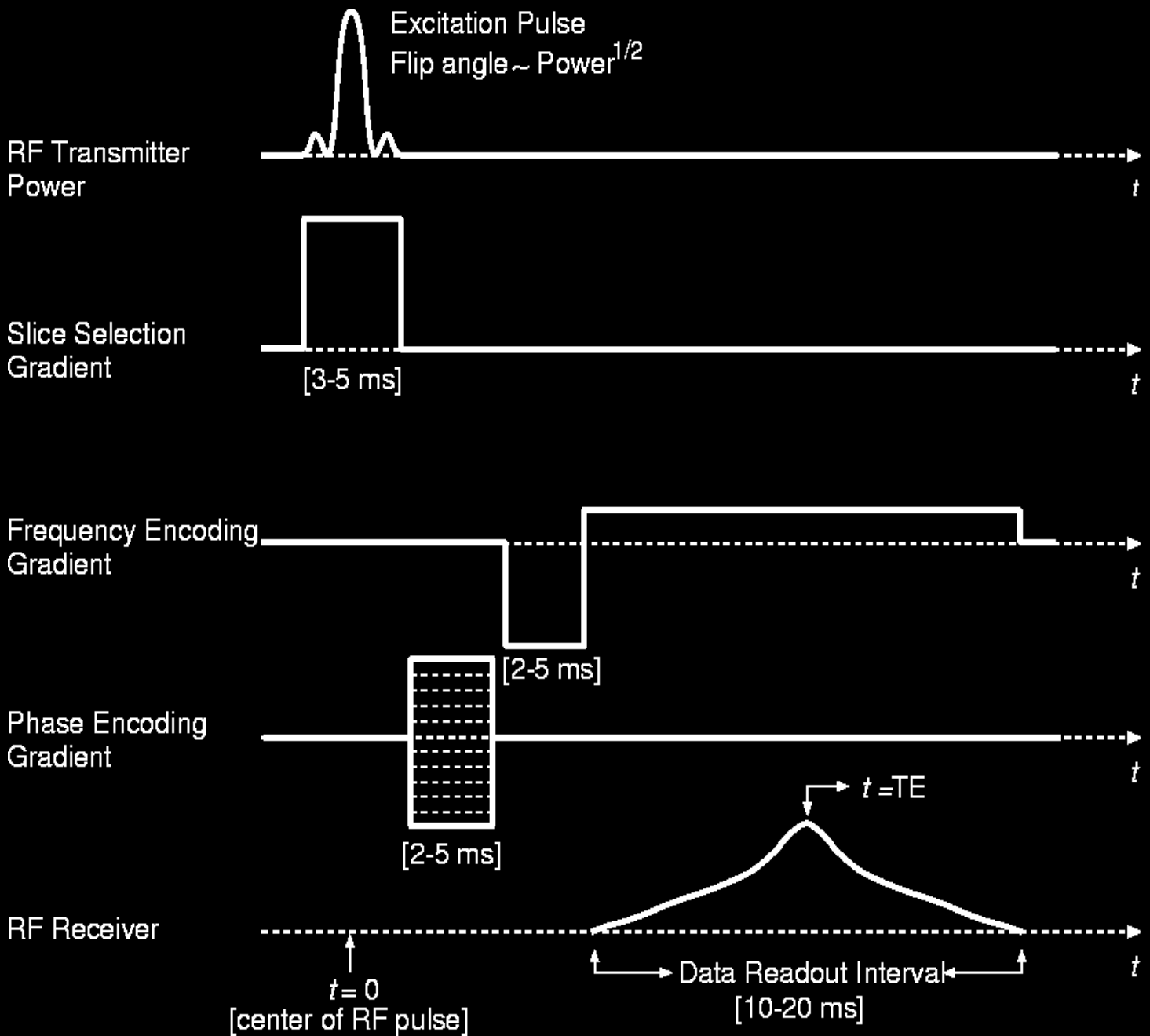

Illustrates sequence of events during scanning

As shown, this method (FLASH) takes 35 ms per RF shot, so would take 2.25 s for a 64×64 image

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[illegible]

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❷ [illegible]

❸ [illegible]

❹ [illegible]

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1
4
2
5
3

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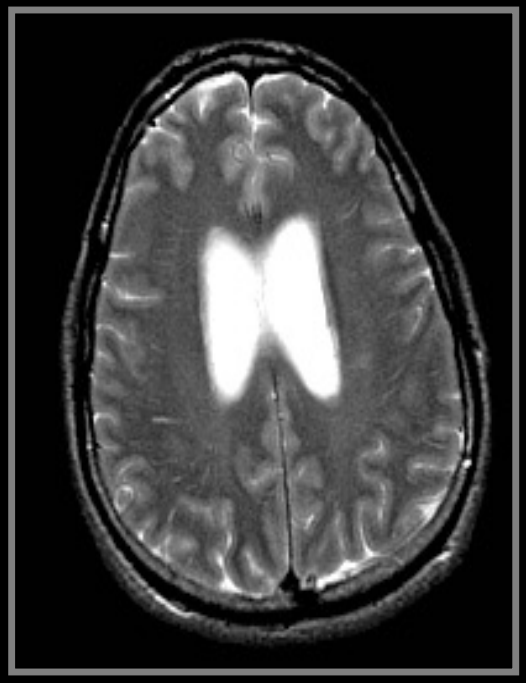
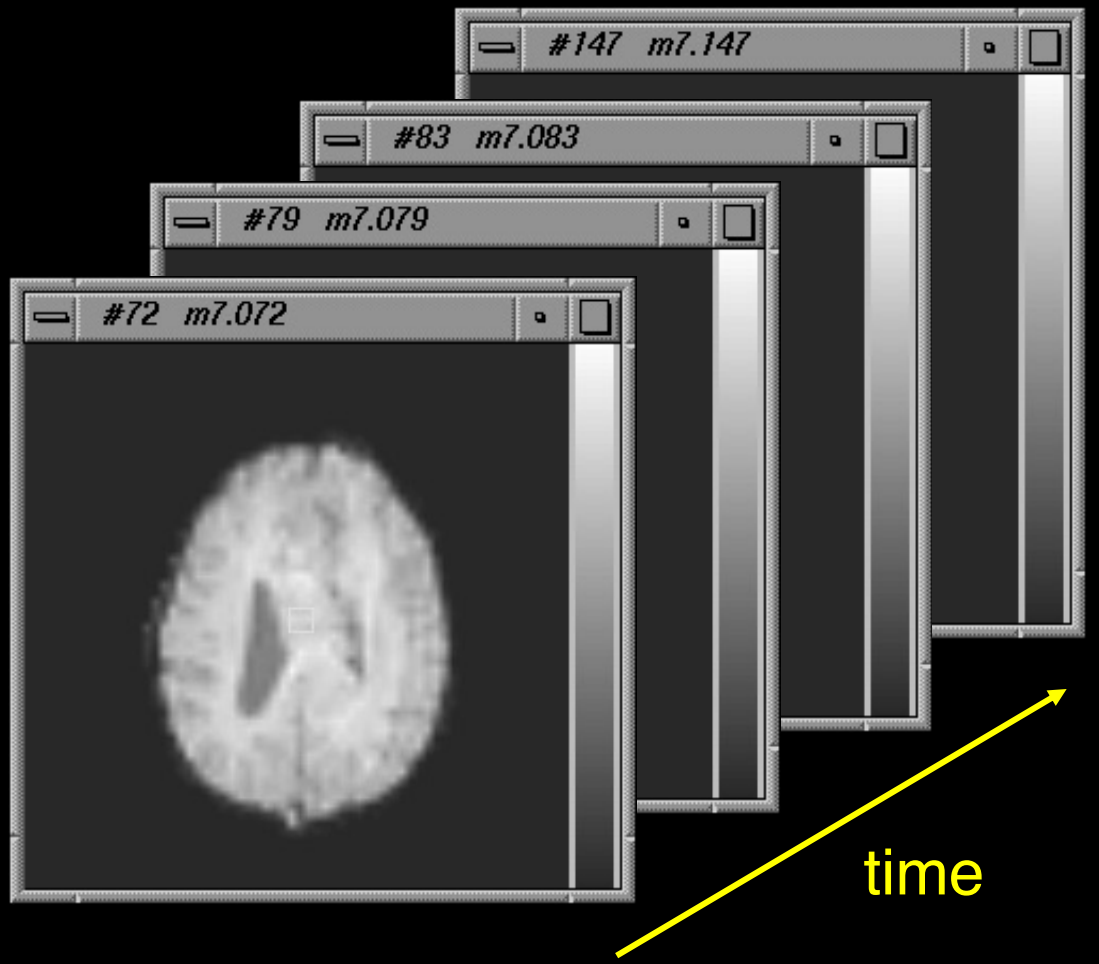
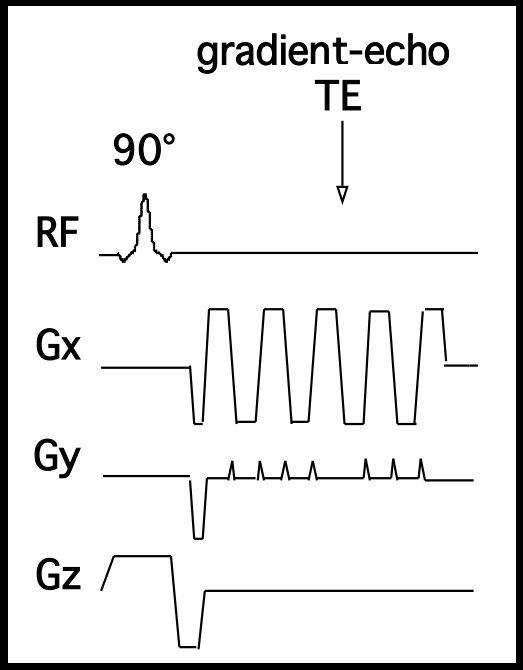


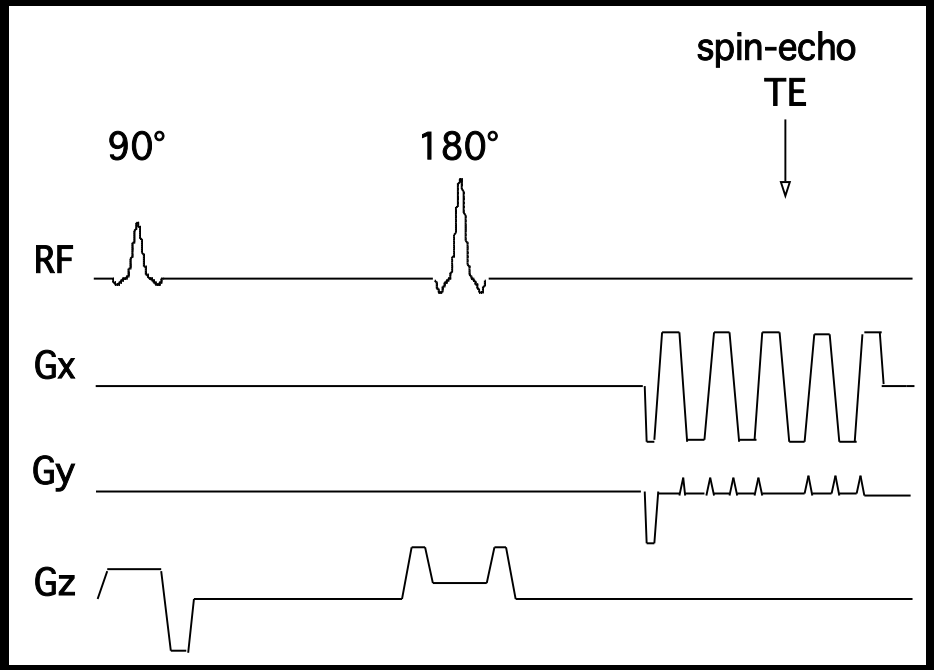


Anatomic

Functional

Echo-Planar Imaging





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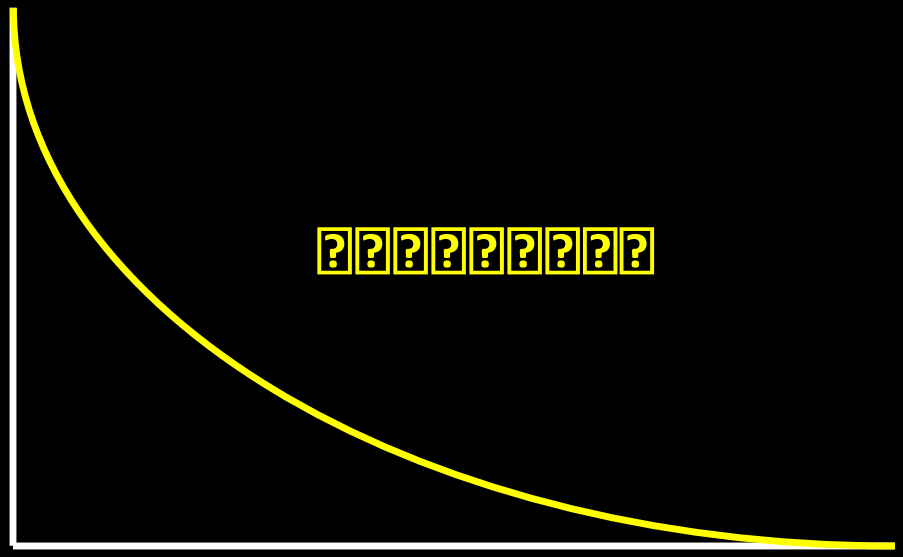

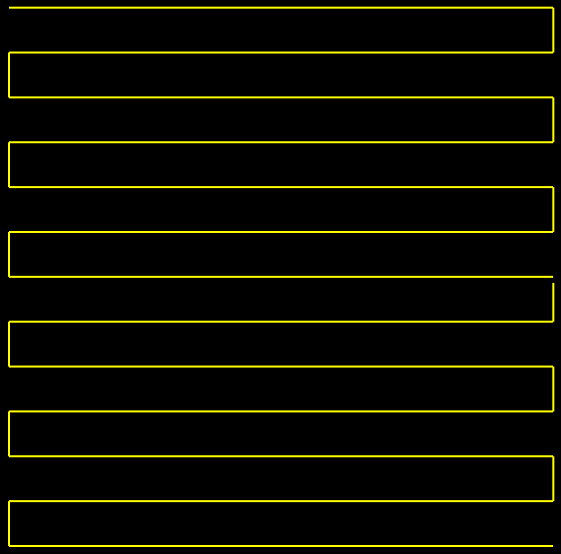

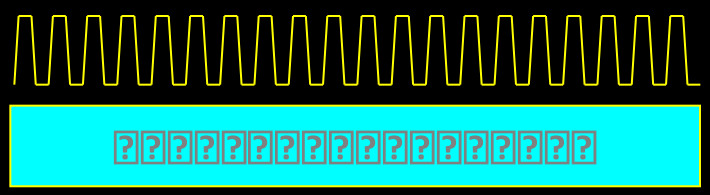

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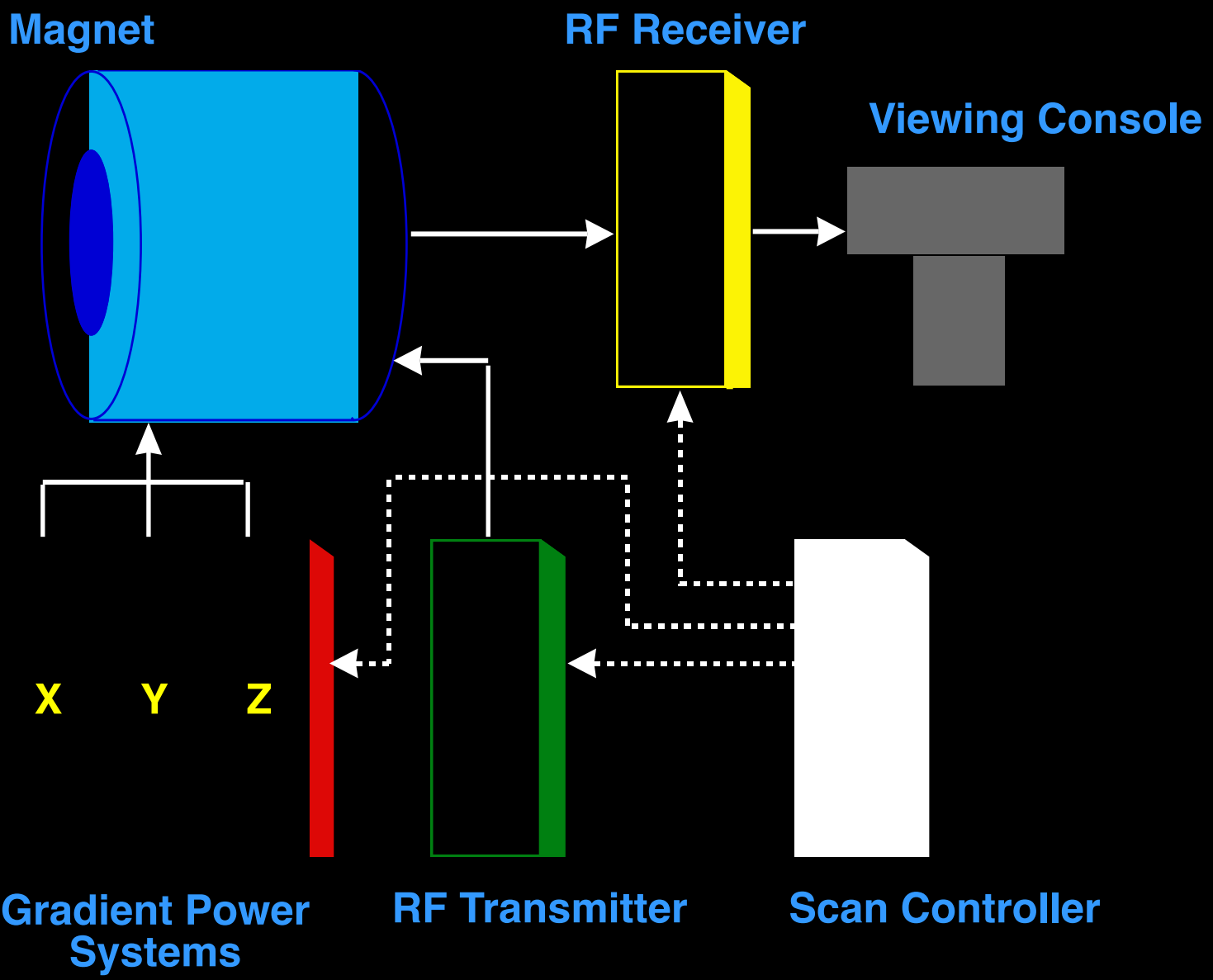
Imaging System Components



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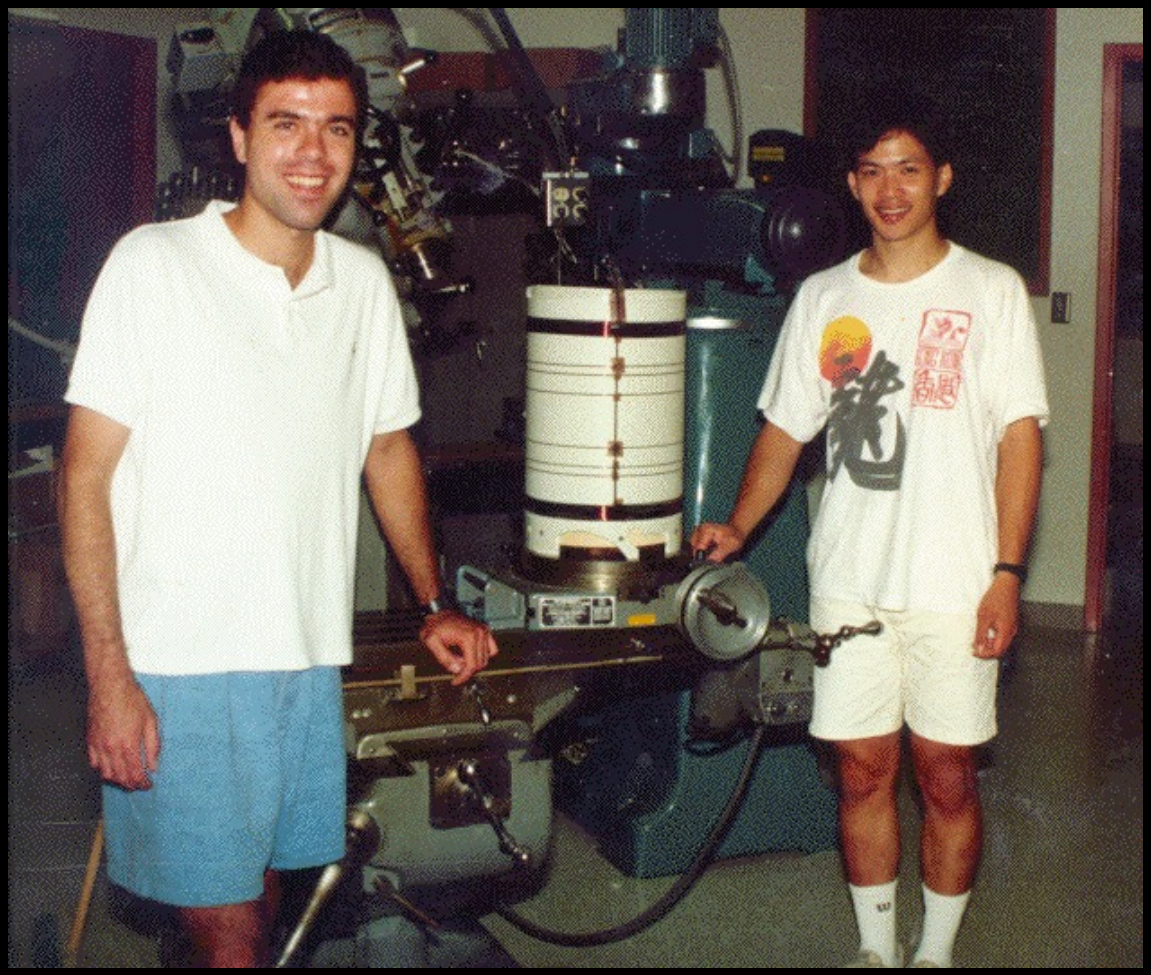

1991-1992

1992-1999

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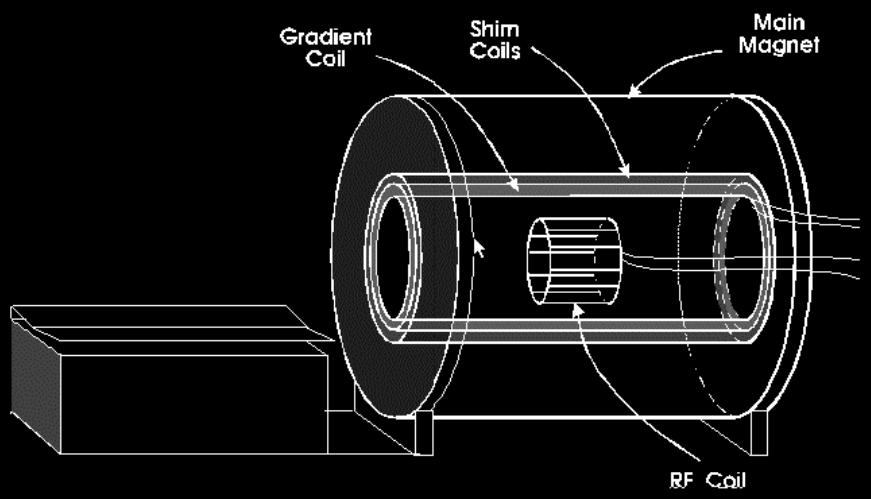
Gradient Coil
Shim Coils
Main Magnet
RF Coil

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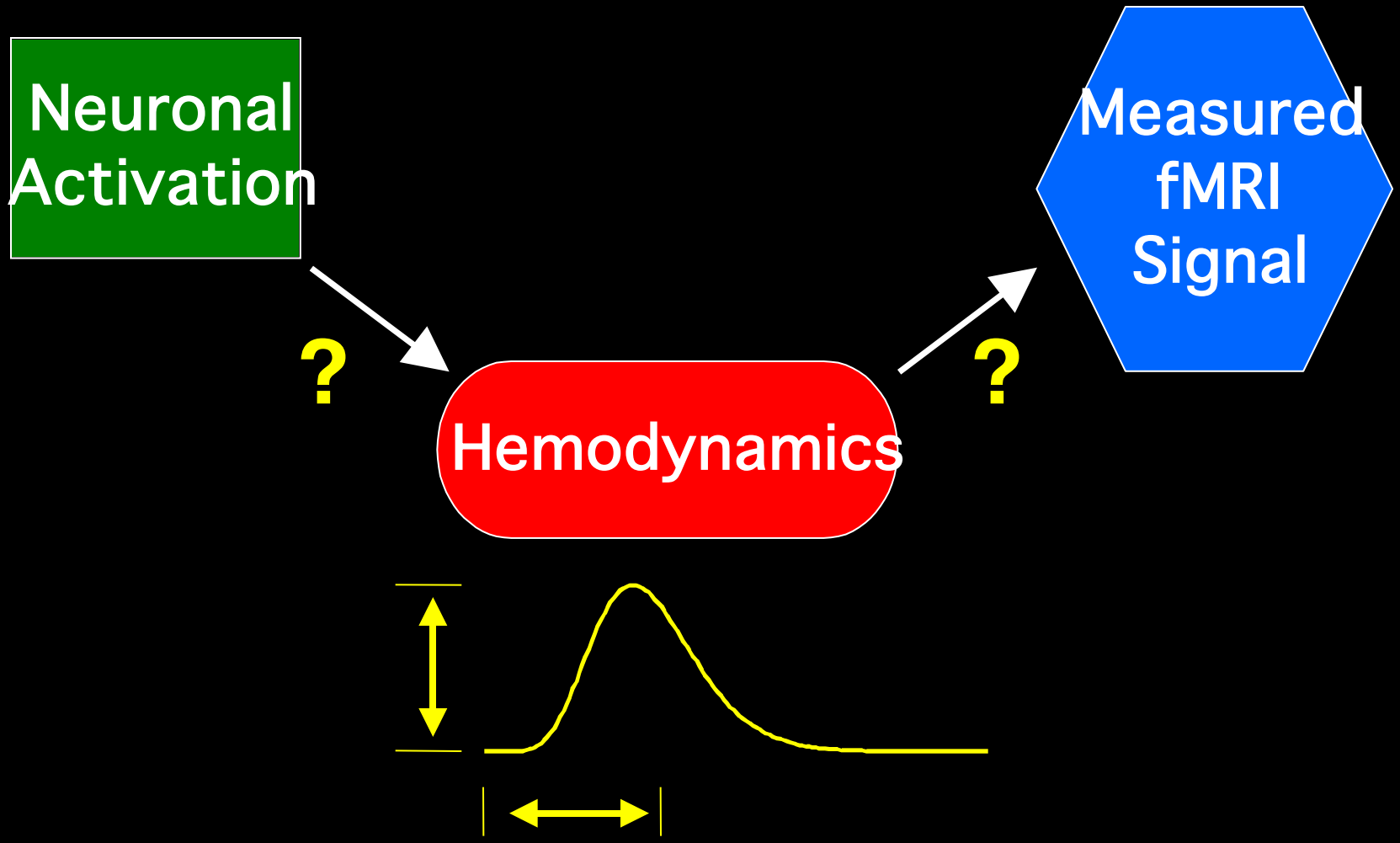
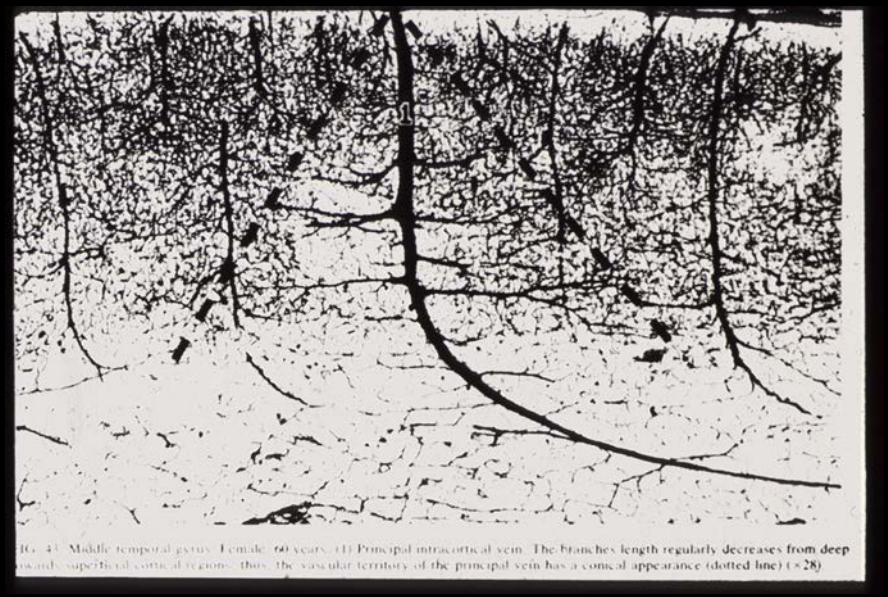
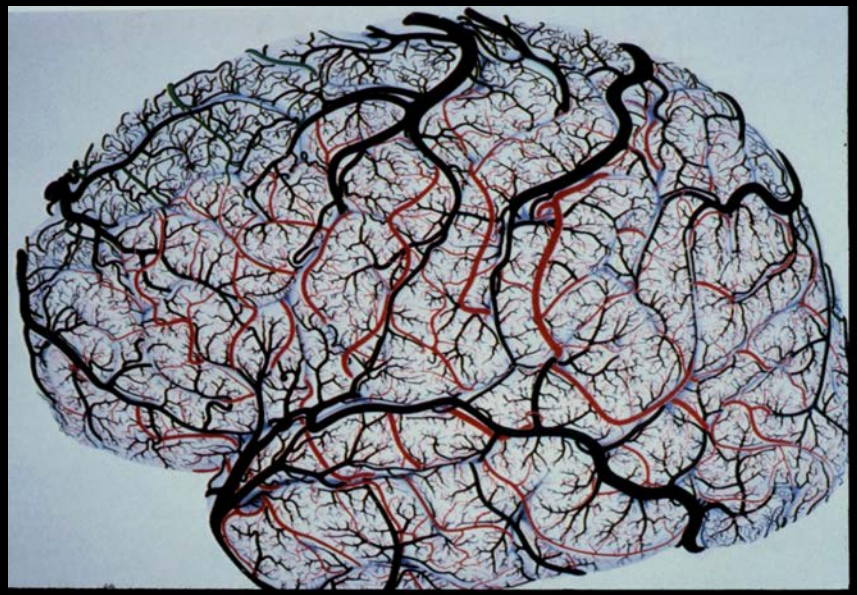

Neuronal Activation
?
Hemodynamics
?
Measured fMRI Signal
Physiologic Factors

A Primary Challenge:

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





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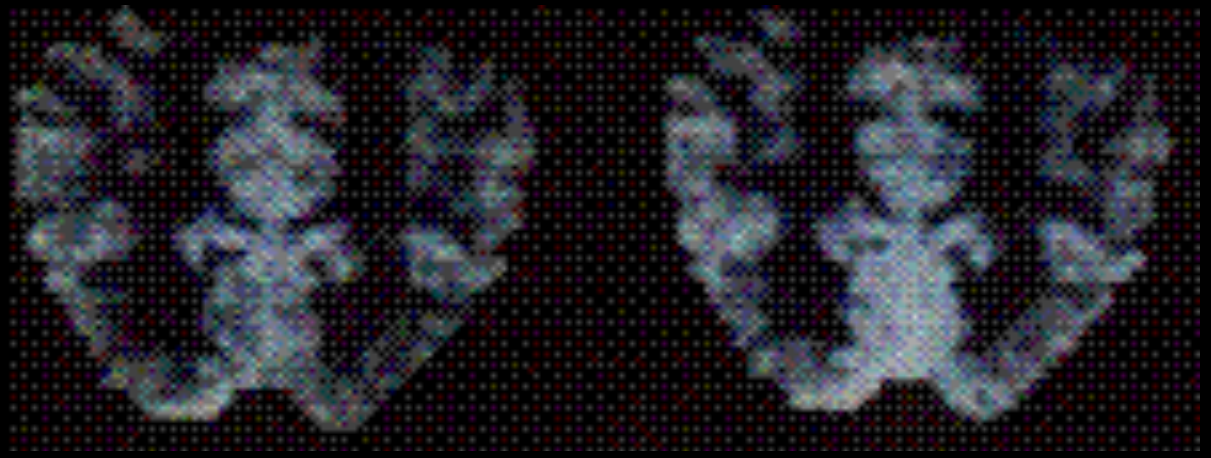
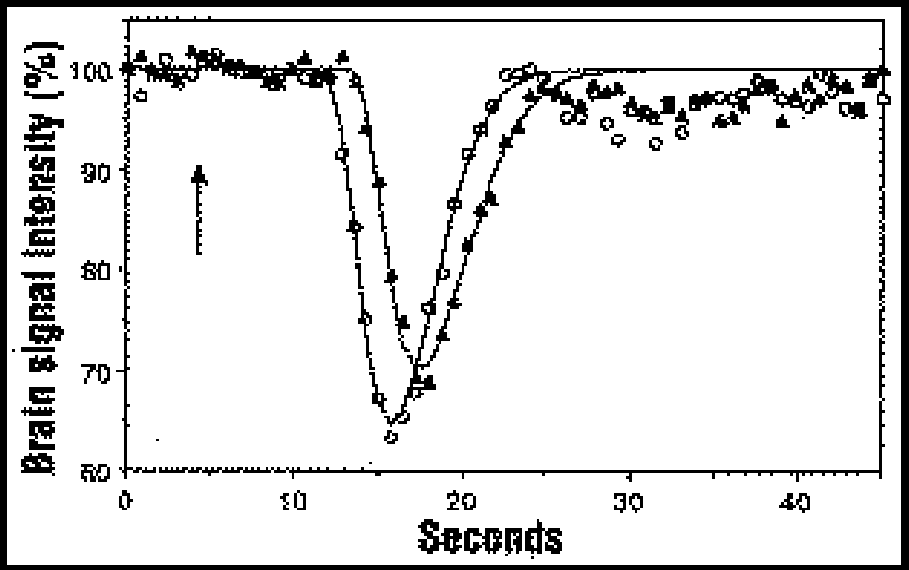
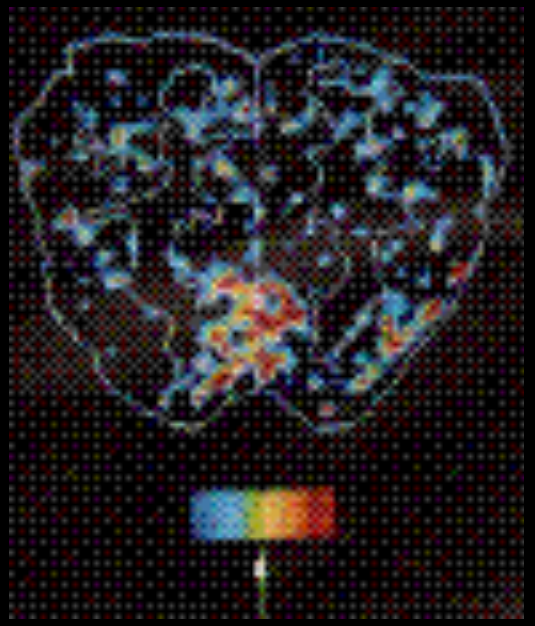
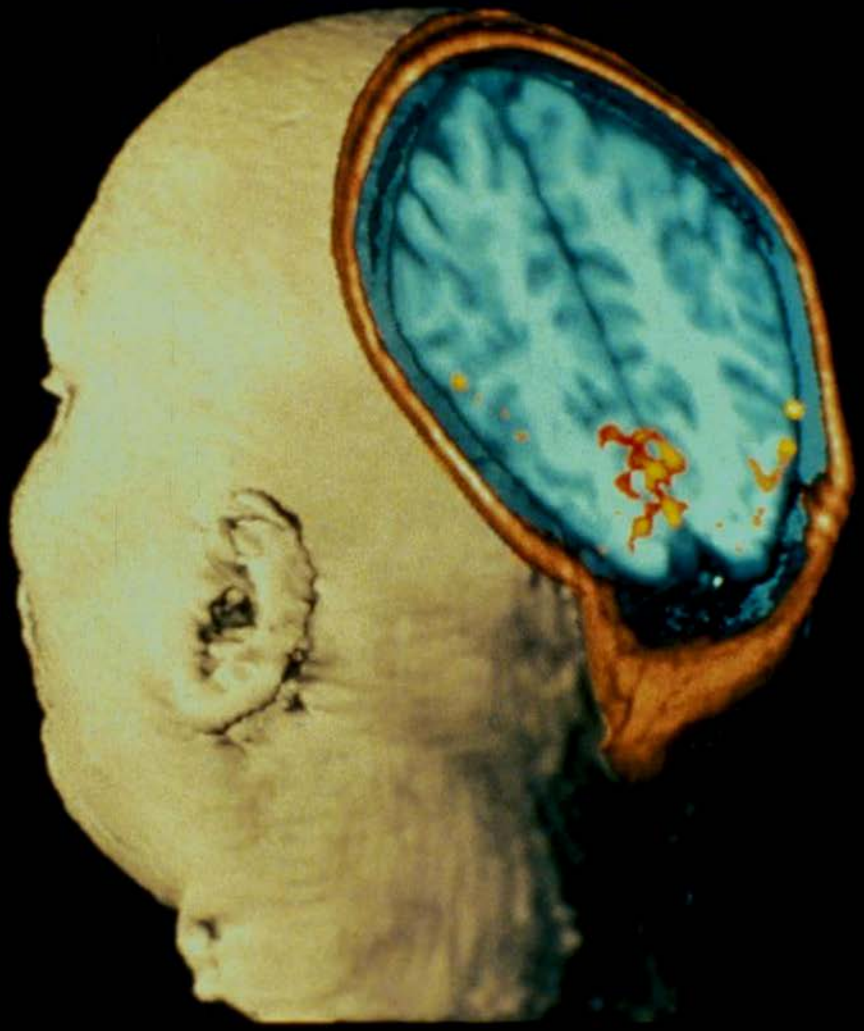
Resting Active







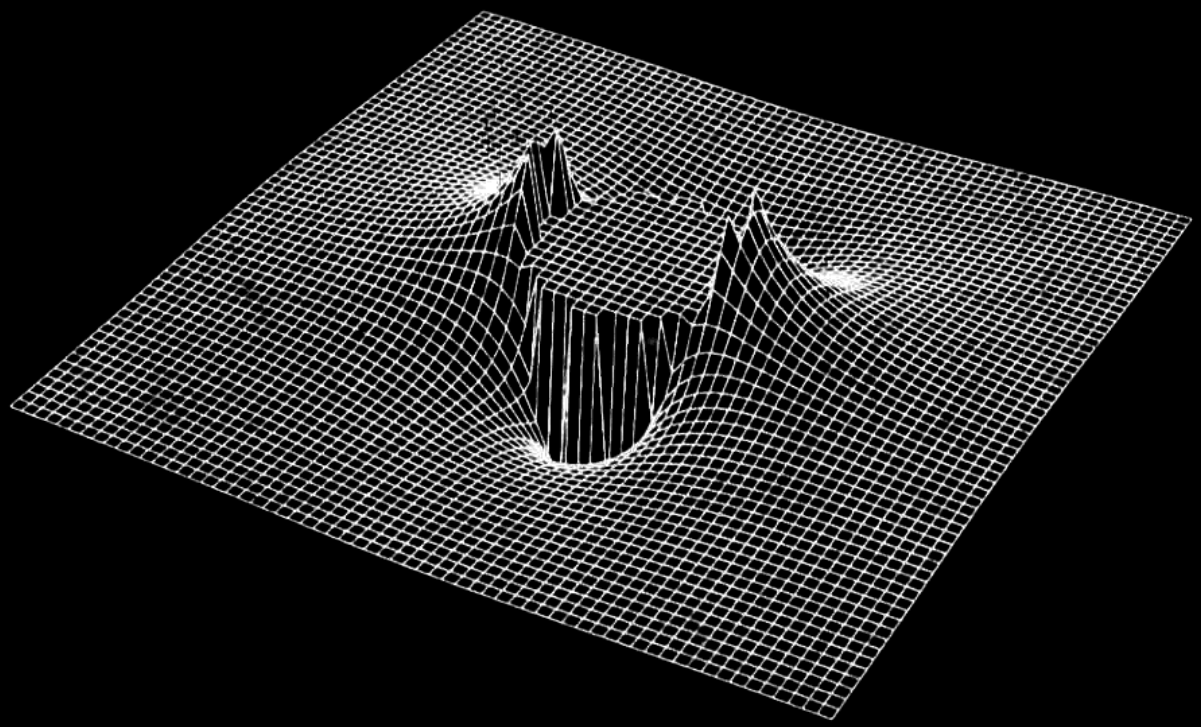
Photic Stimulation



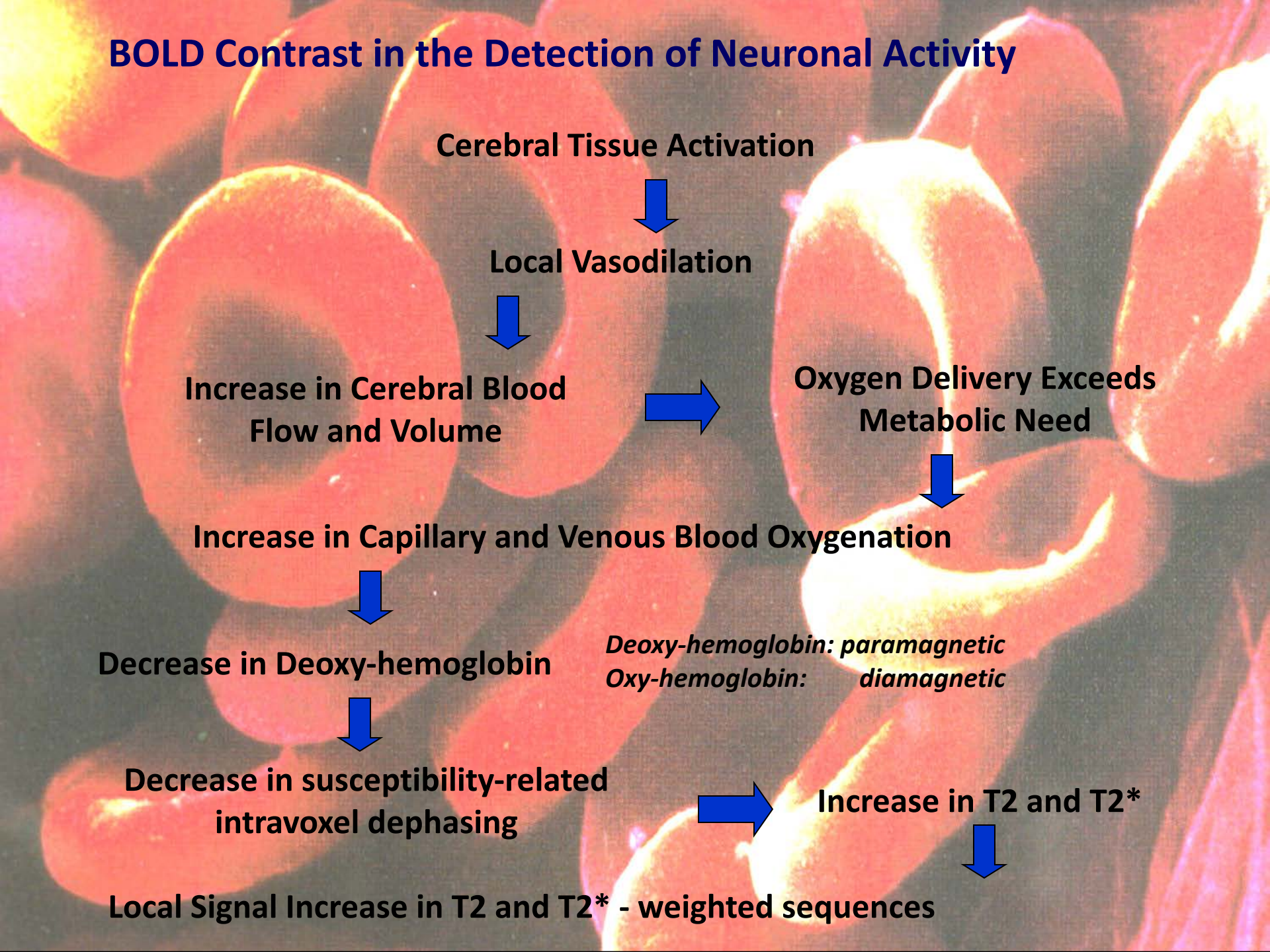
MRI Image showing activation of the Visual Cortex

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



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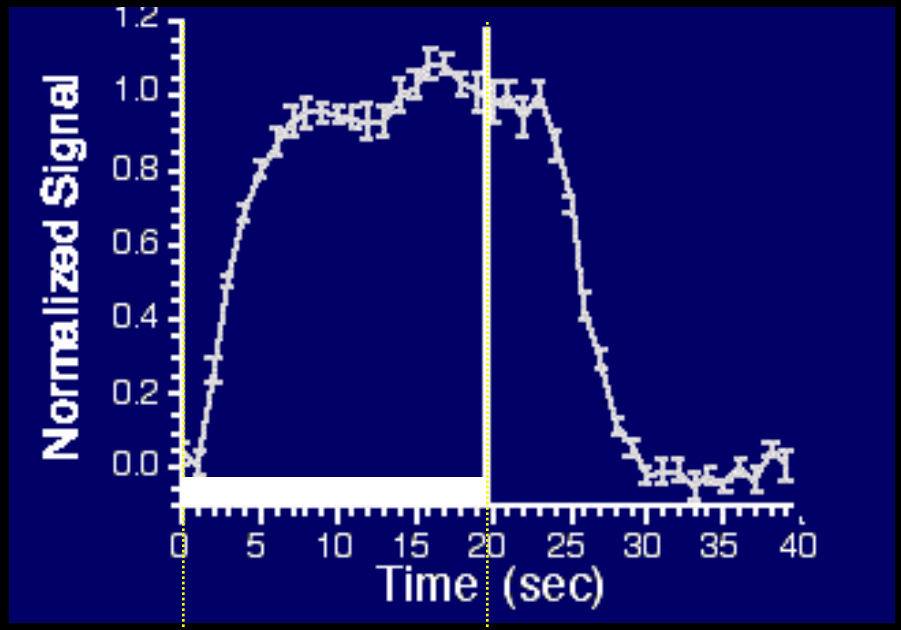
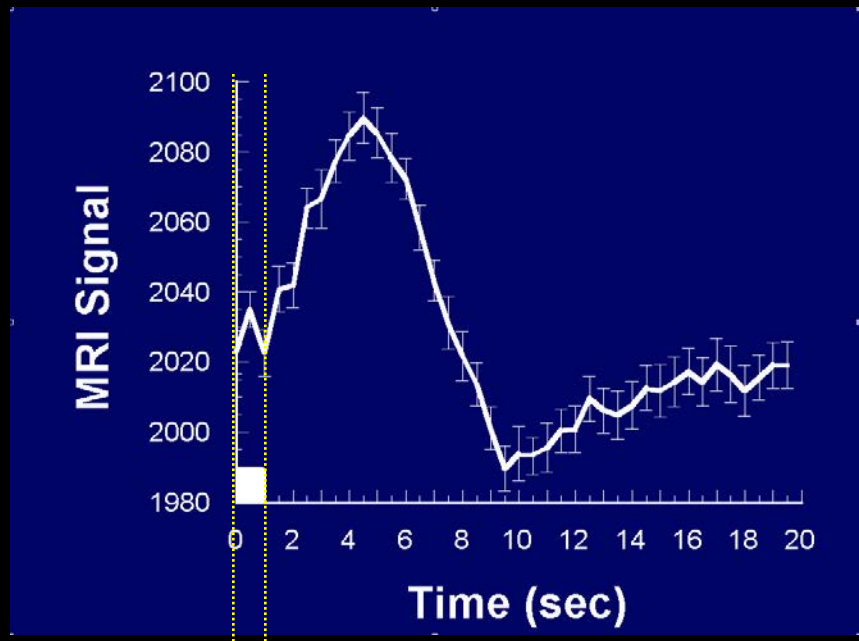
Blood Oxygenation Level Dependent (BOLD) signal changes





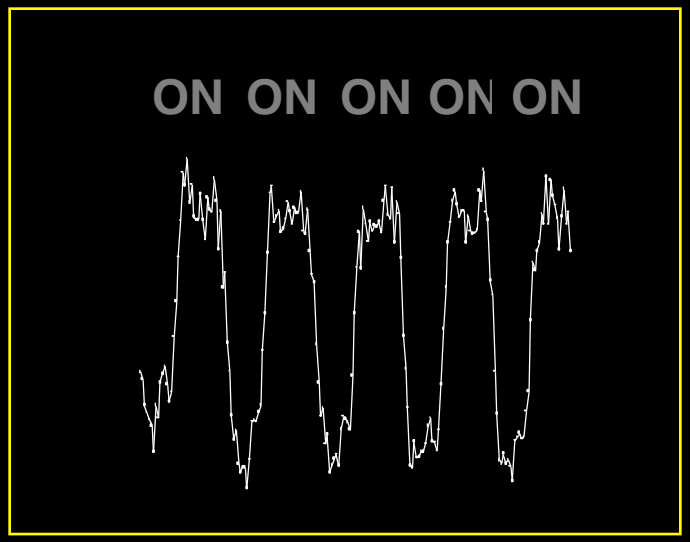
task

task

Alternating Left and Right Finger Tapping

~ 1992

Creating a Functional Image



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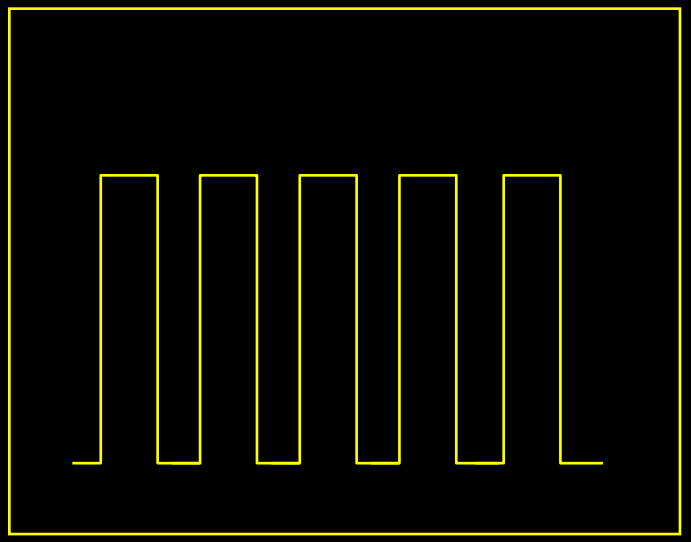

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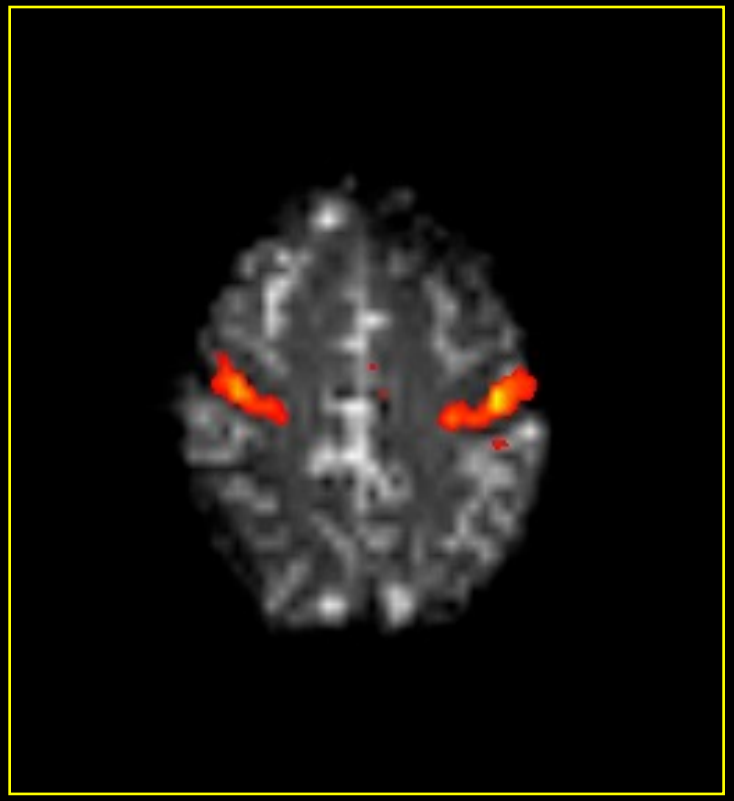

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Statistical Map

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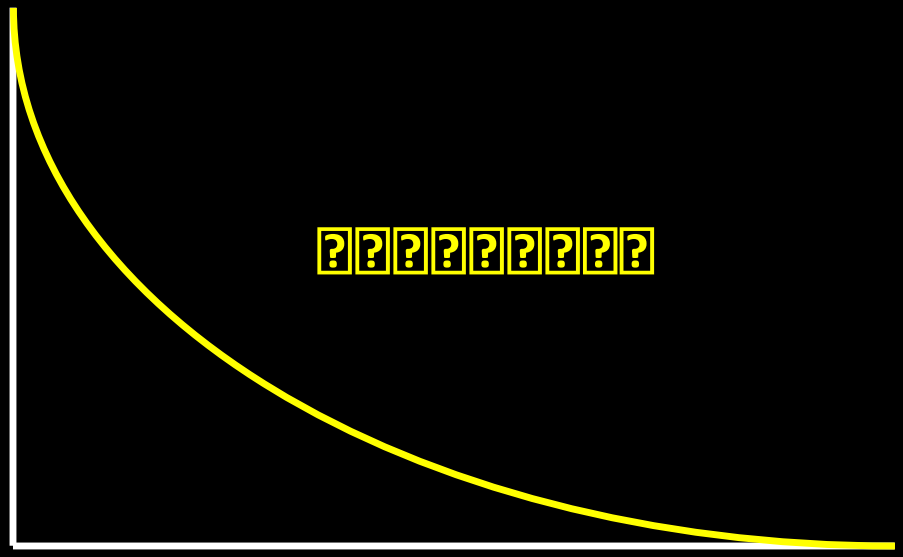

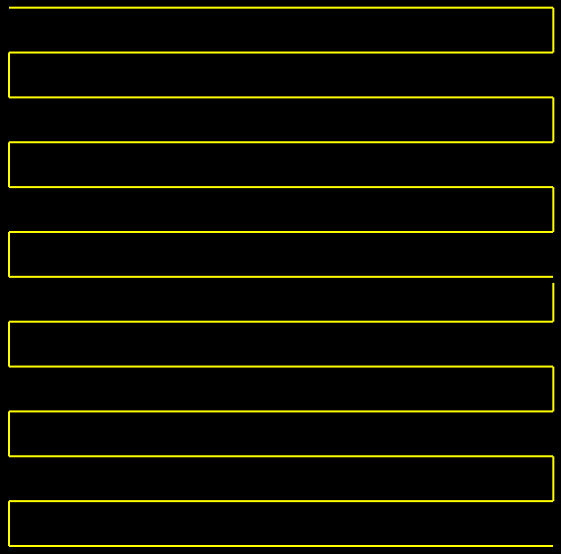

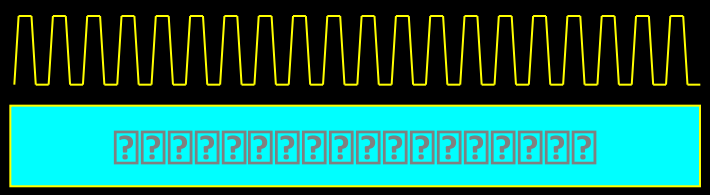

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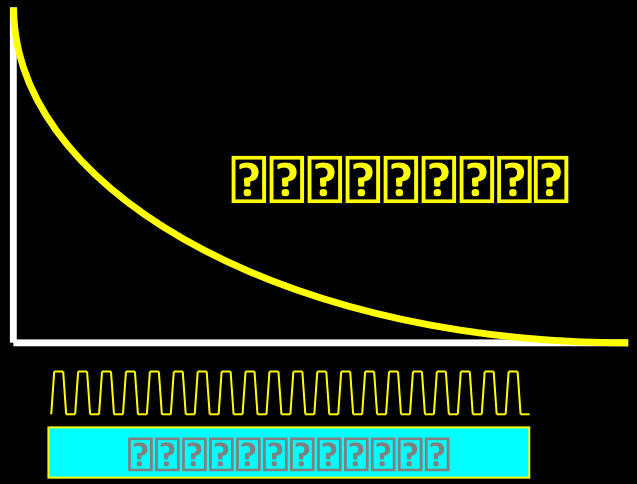
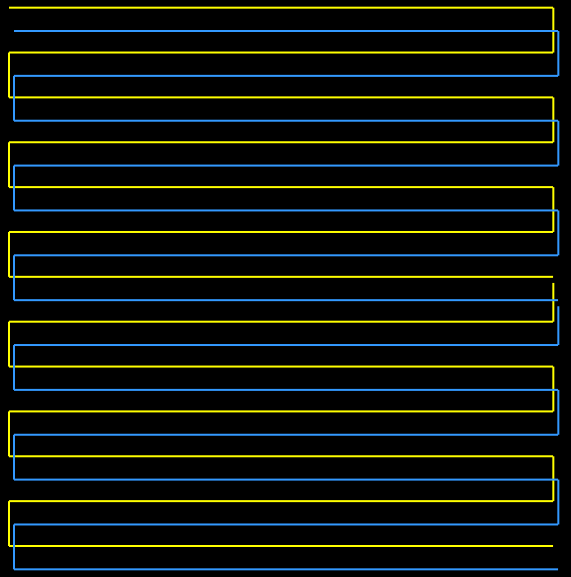
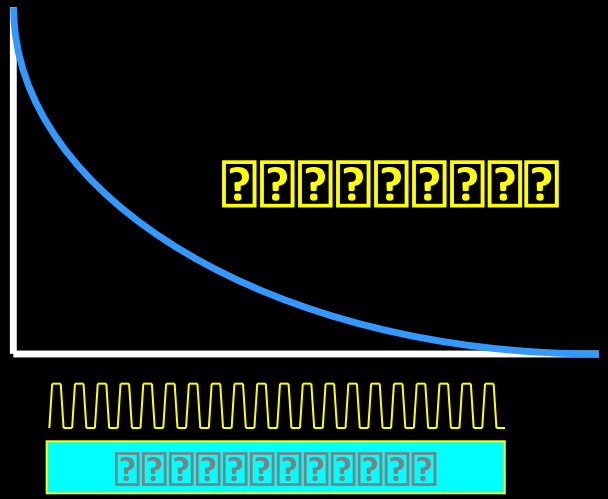
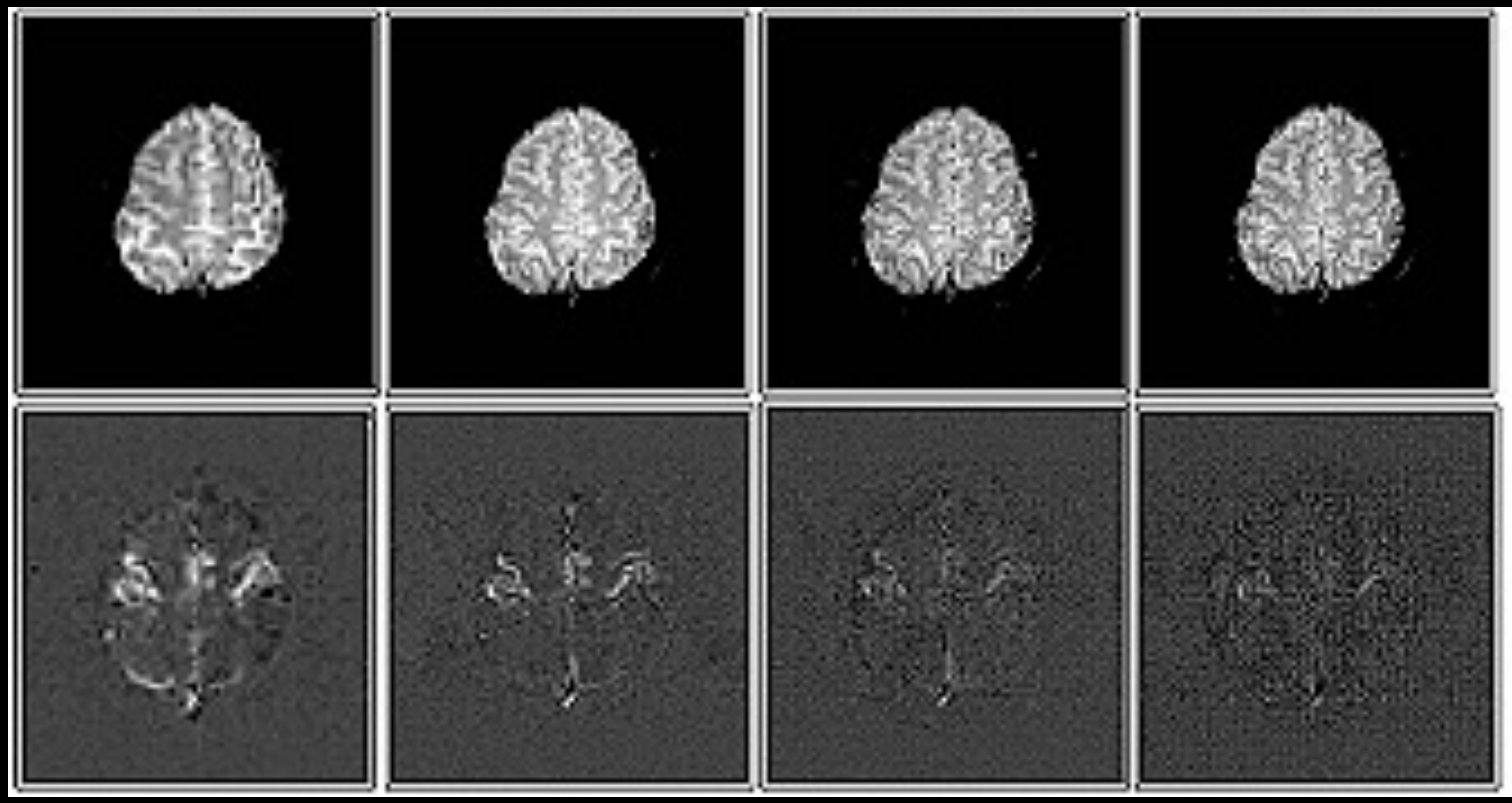






Multi Shot EPI

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



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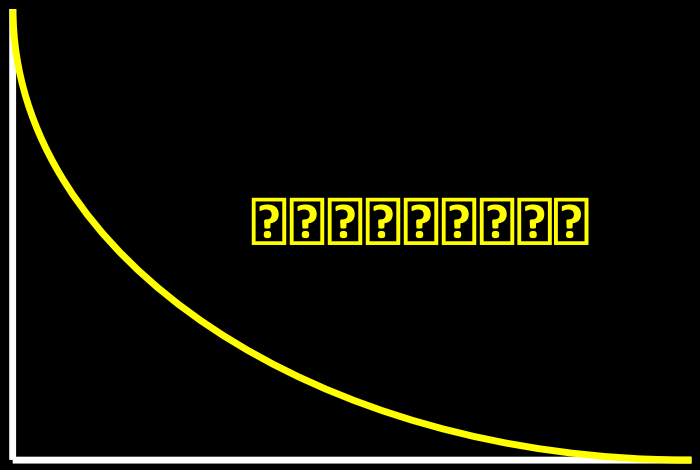
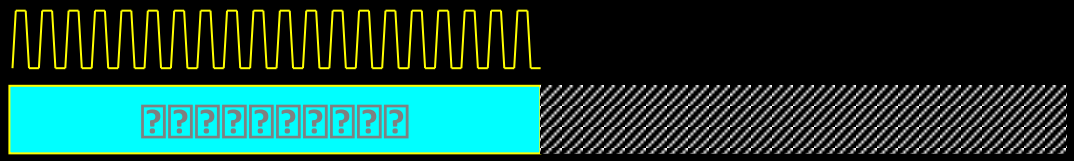
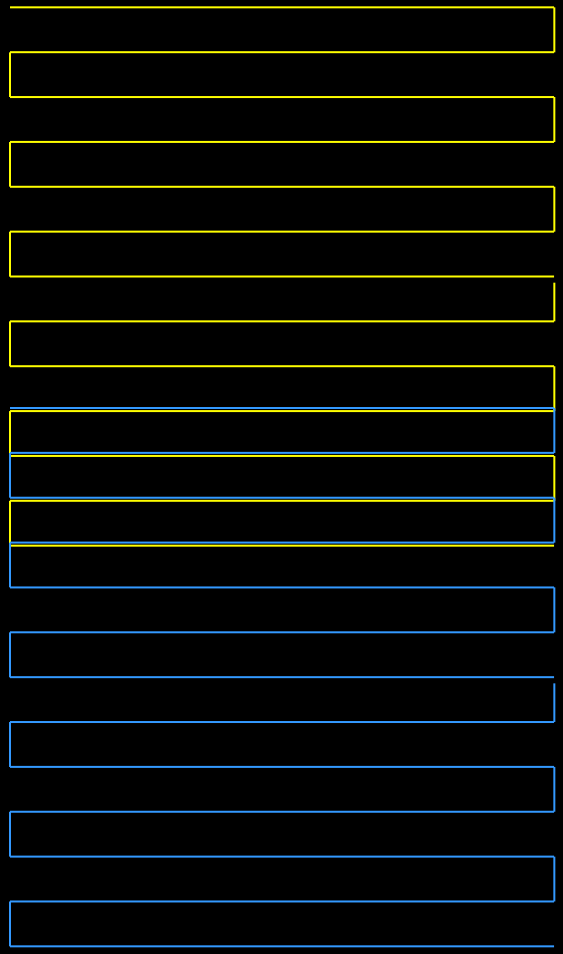
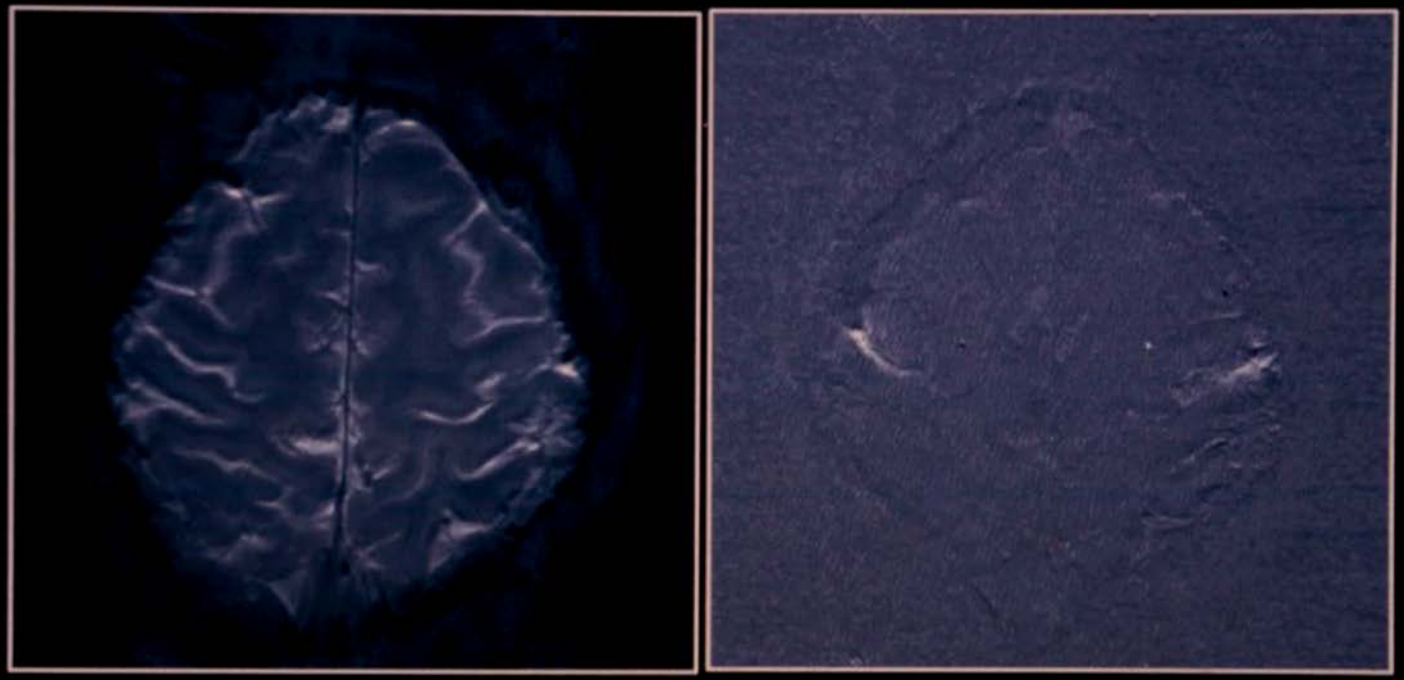






Single - Shot EPI at 3T:
Half NEX, 256 x 256, 16 cm FOV



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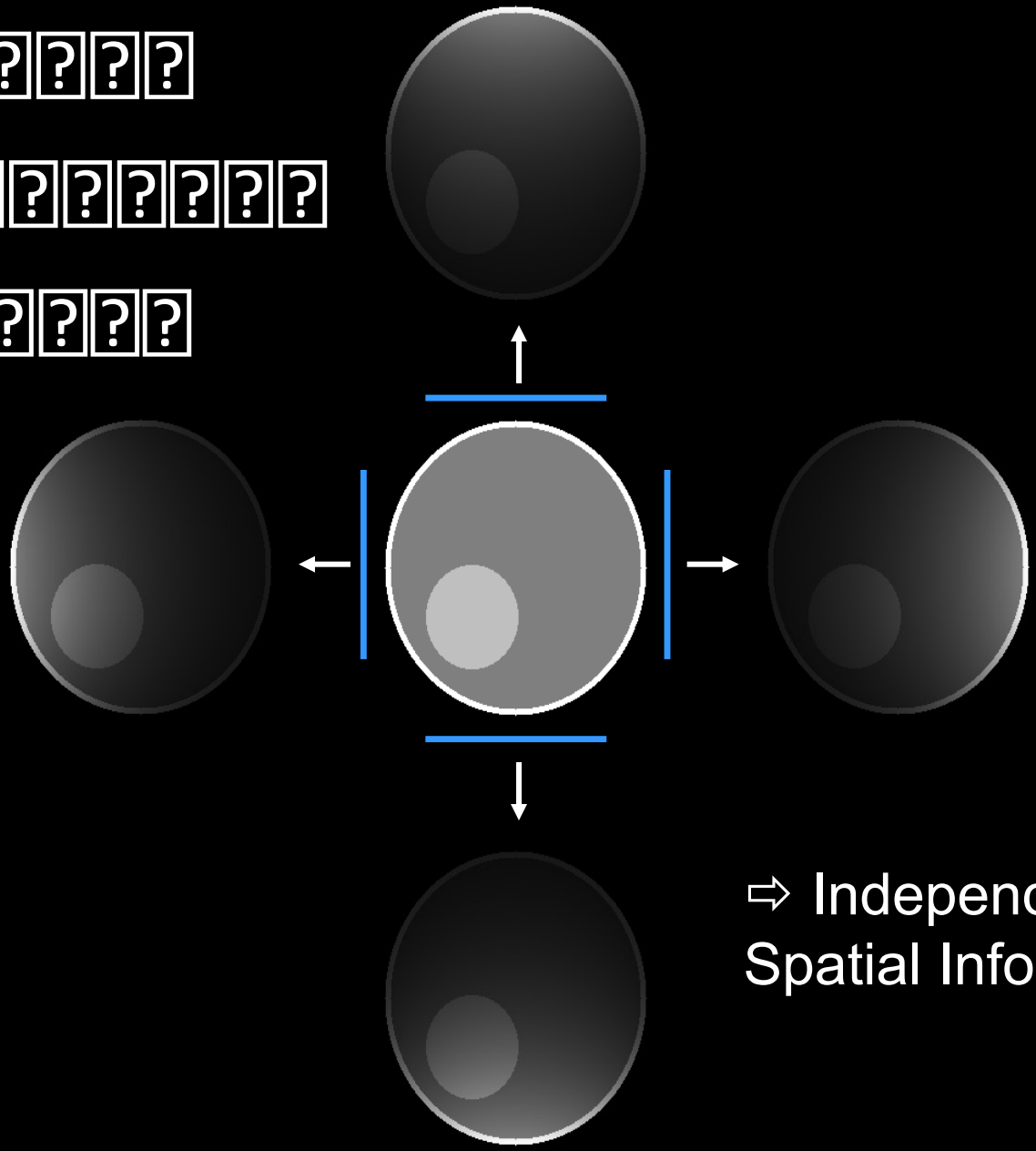
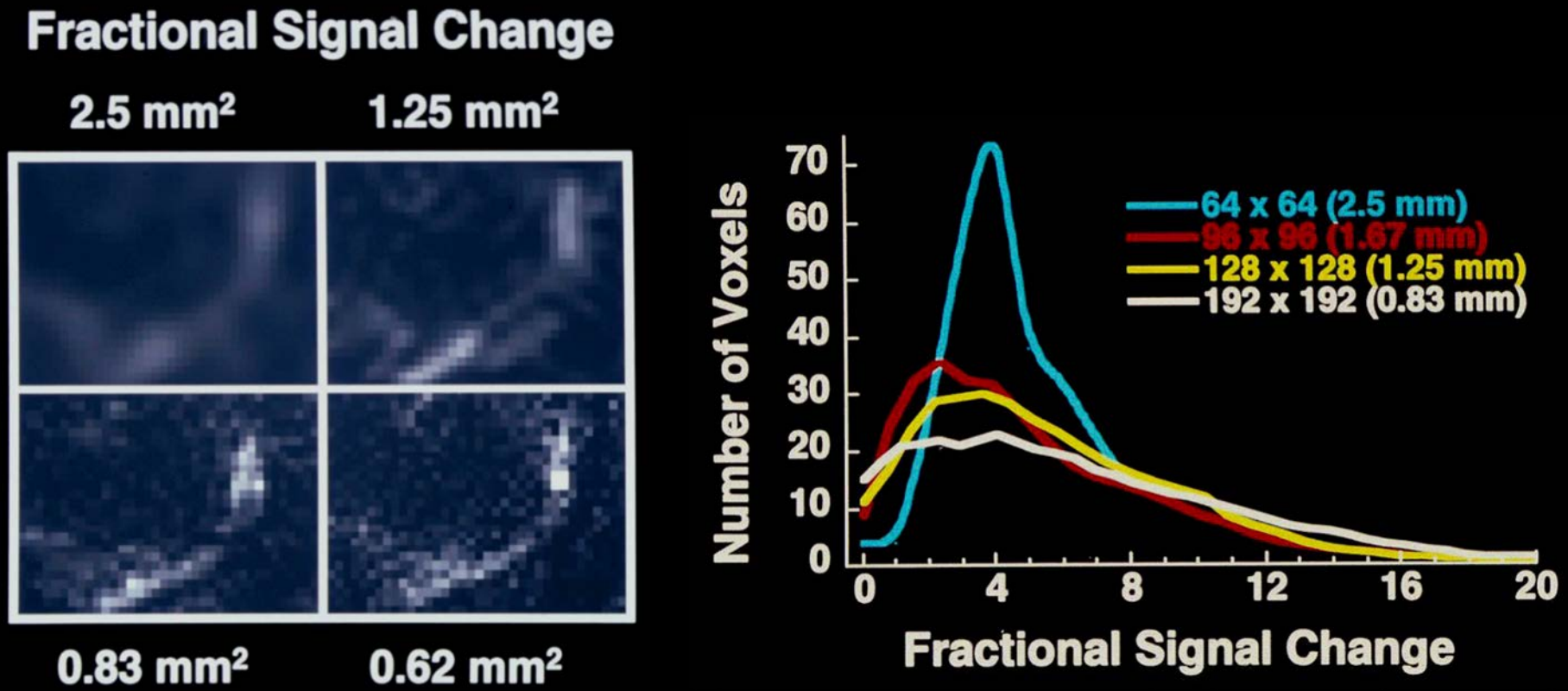
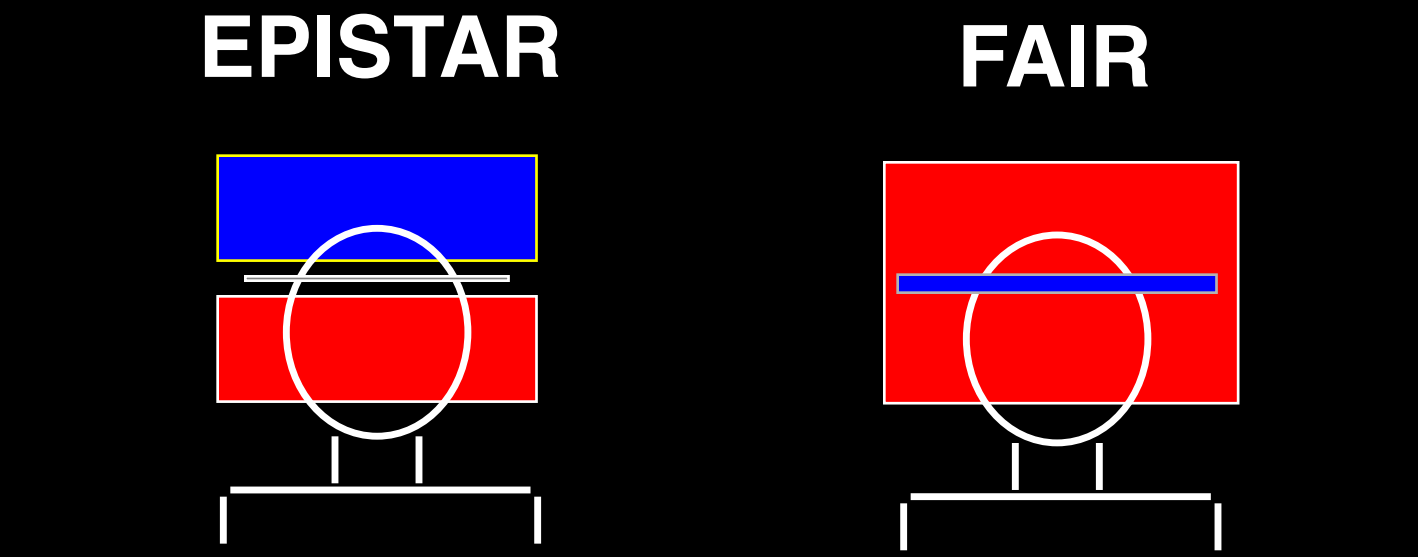
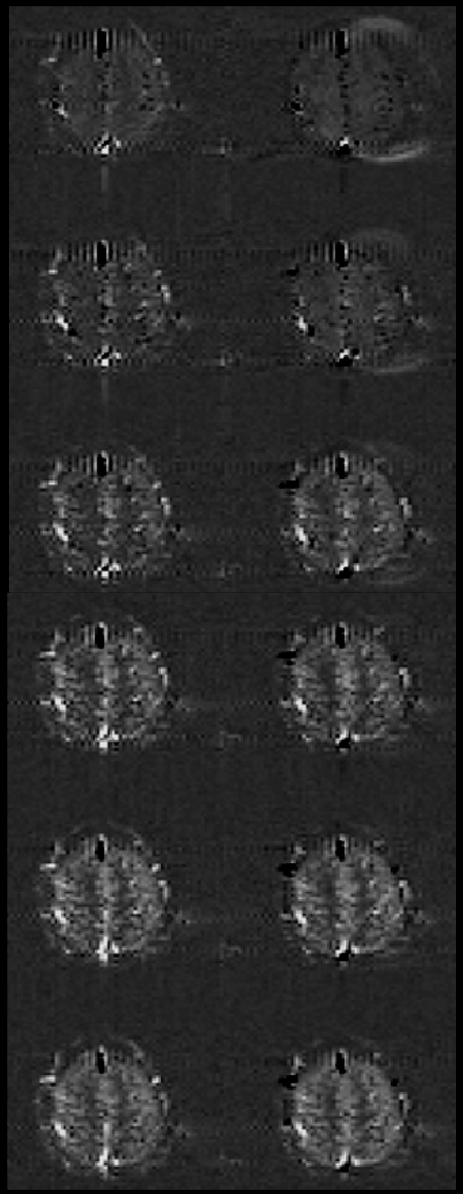


⇨ Independent
Spatial Information

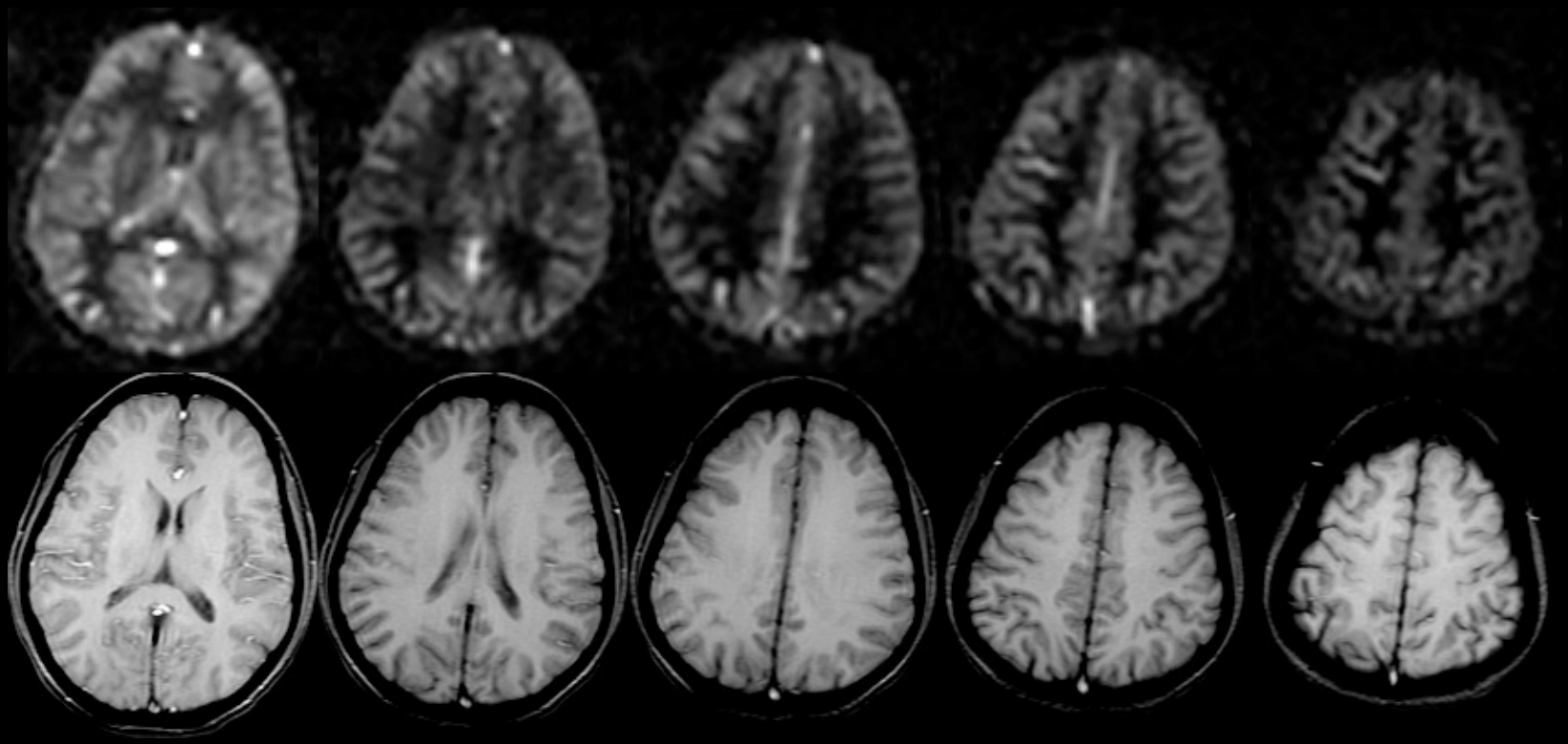

Fractional Signal Change
2.5 mm²
1.25 mm²
0.83 mm²
0.62 mm²
Number of Voxels
0
10
20
30
40
50
60
70
0
4
8
12
16
20
Fractional Signal Change
64 x 64 (2.5 mm)
96 x 96 (1.67 mm)
128 x 128 (1.25 mm)
192 x 192 (0.83 mm)

Perfusion / Flow Imaging

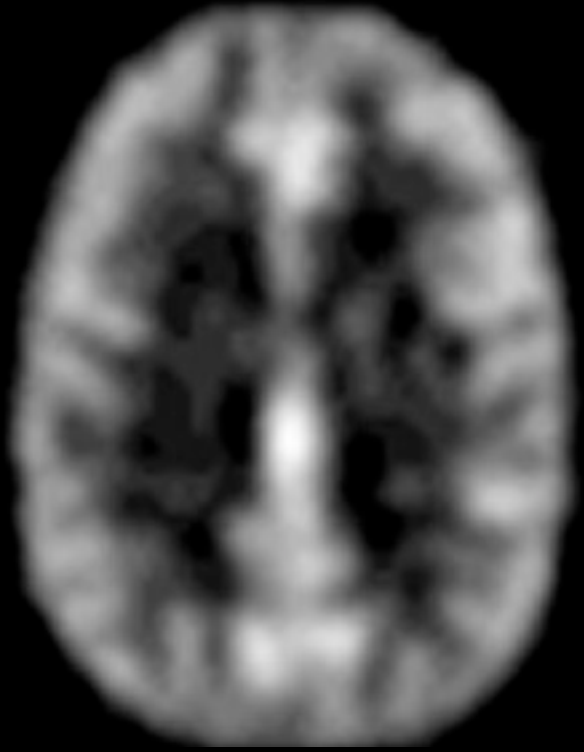


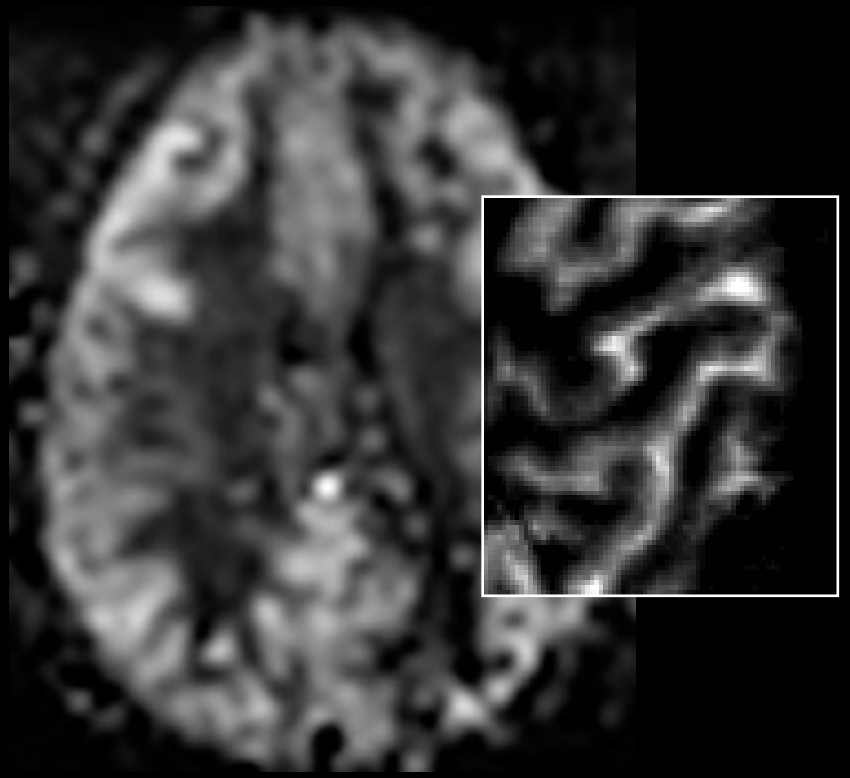
TI (ms)	FAIR	EPISTAR
200		
400		
600		
800		
1000		
1200		

Resting ASL Signal



Comparison with Positron Emission Tomography



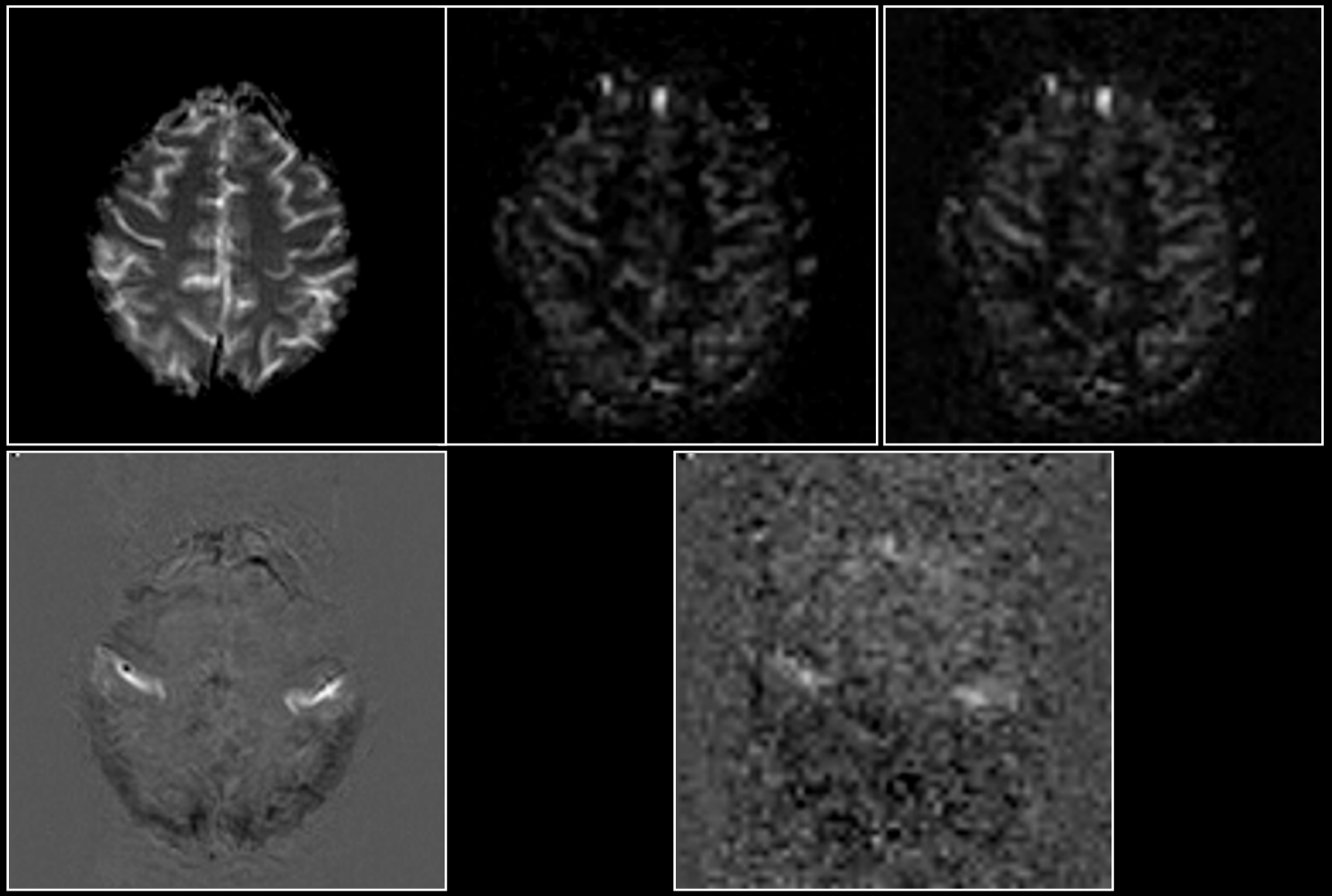


[illegible]

[illegible]

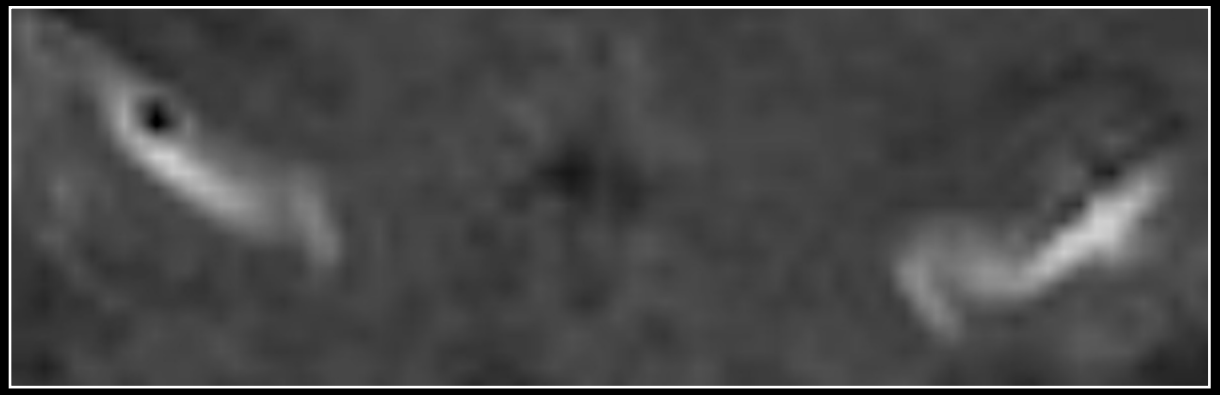
Perfusion

BOLD *Rest* *Activation*



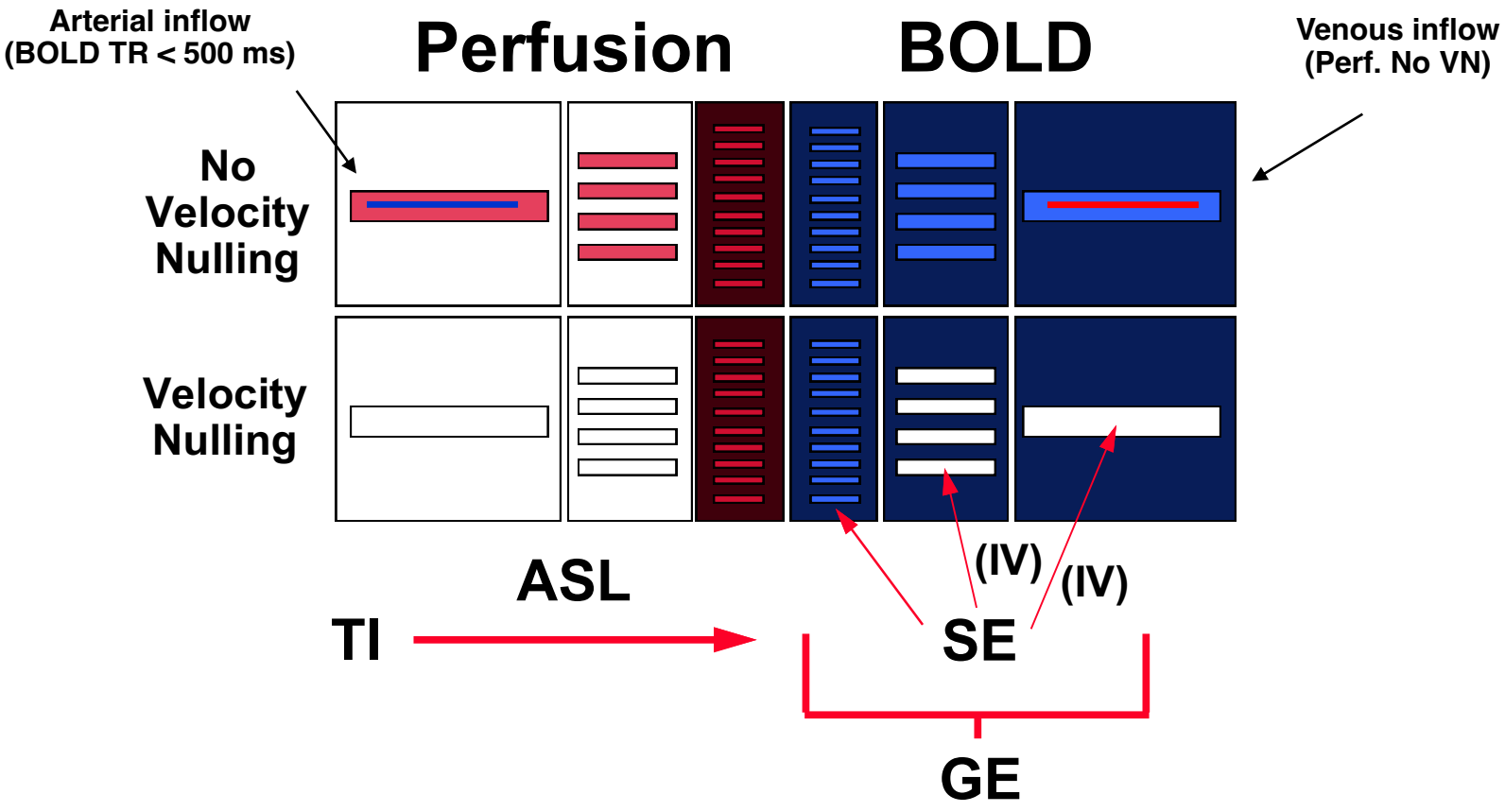
Anatomy

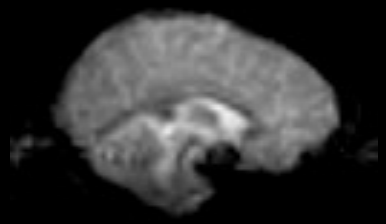
BOLD

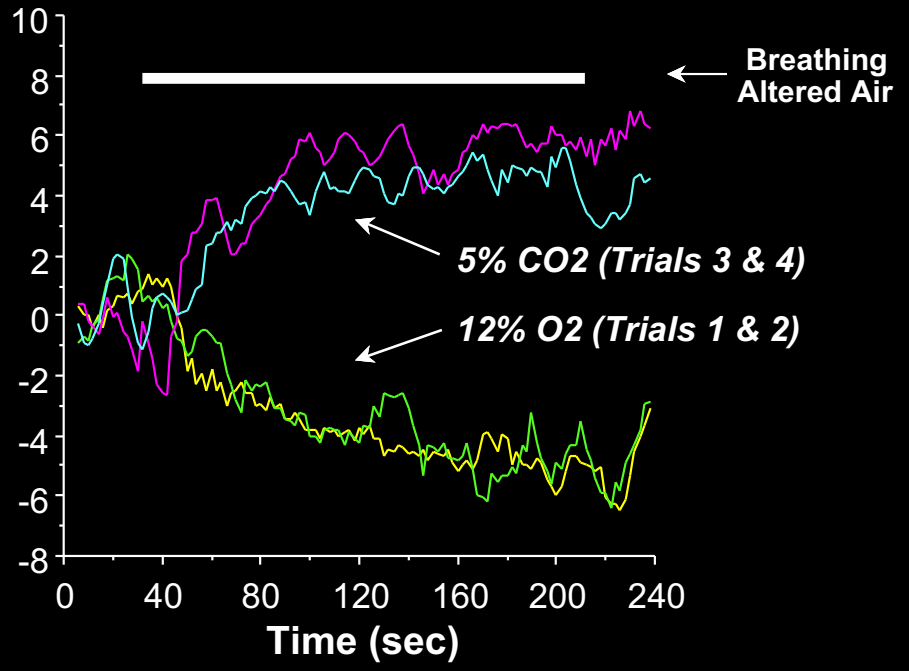


Perfusion

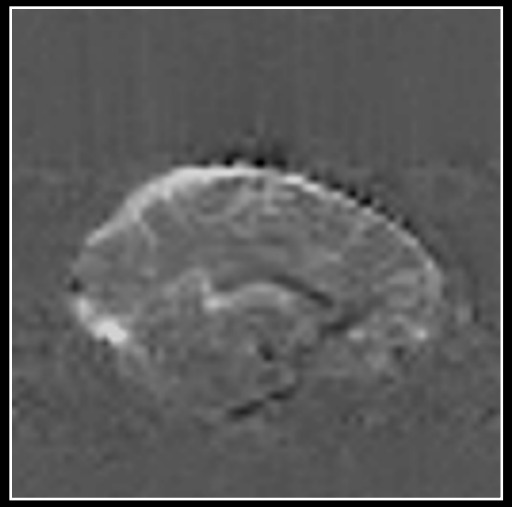
Hemodynamic Specificity

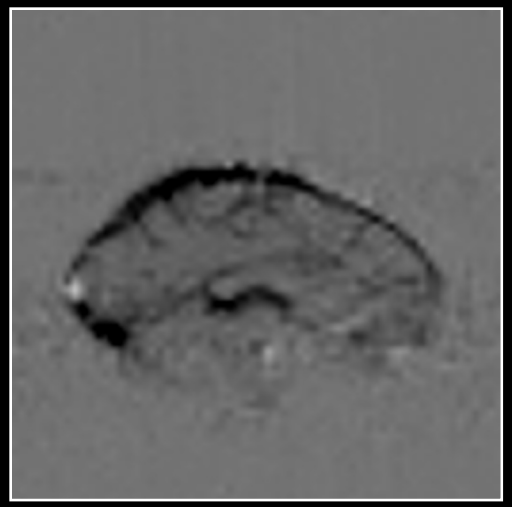





10
8
6
4
2
0
-2
-4
-6
-8
0
40
80
120
160
200
240
Time (sec)
Breathing
Altered Air
5% CO2 (Trials 3 & 4)
12% O2 (Trials 1 & 2)

5% CO2

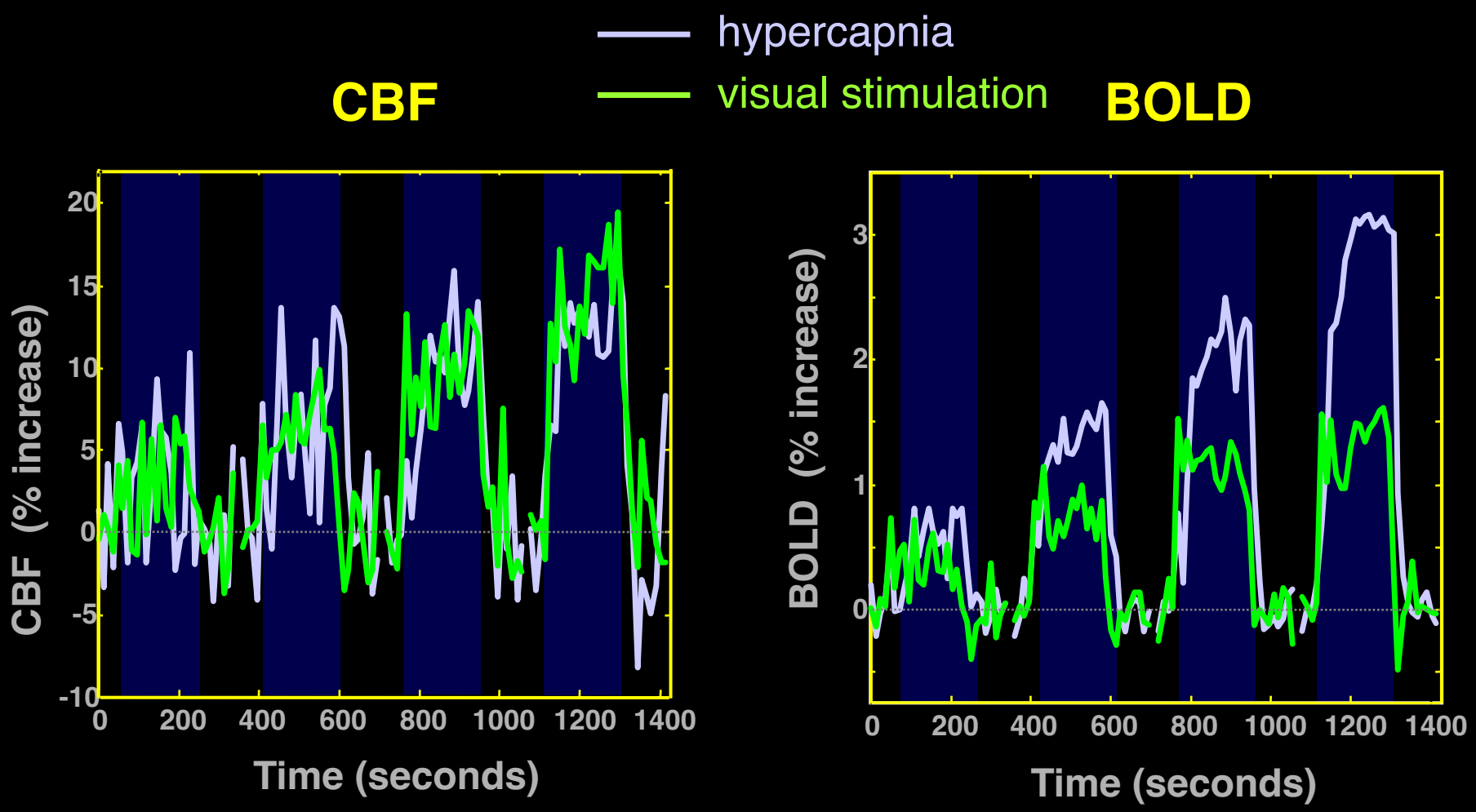




12% O2

$CMRO_2$-related BOLD signal deficit:

Hoge, et al.

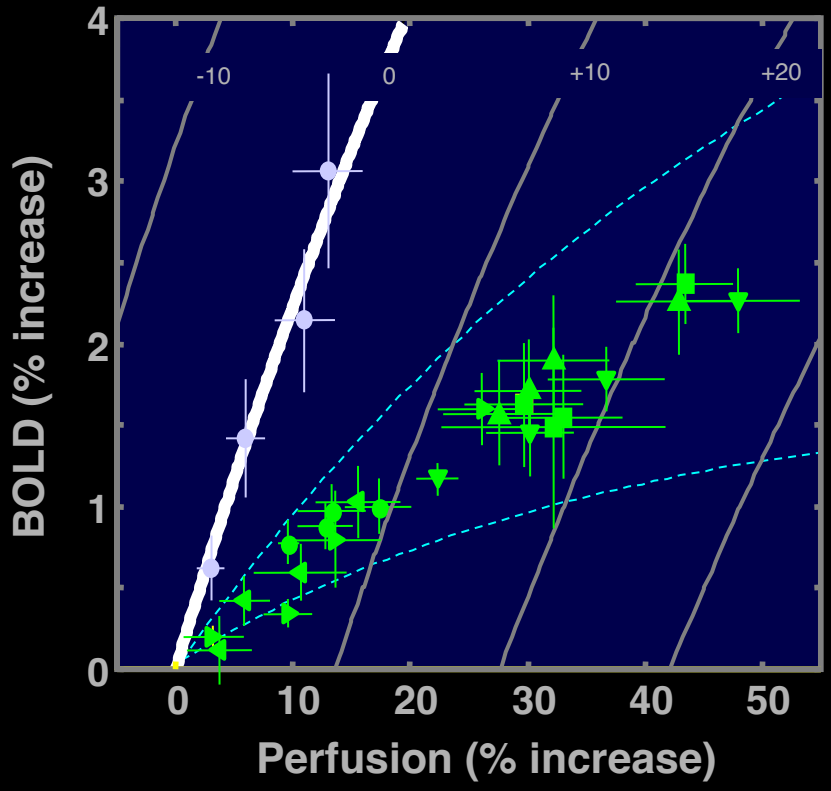


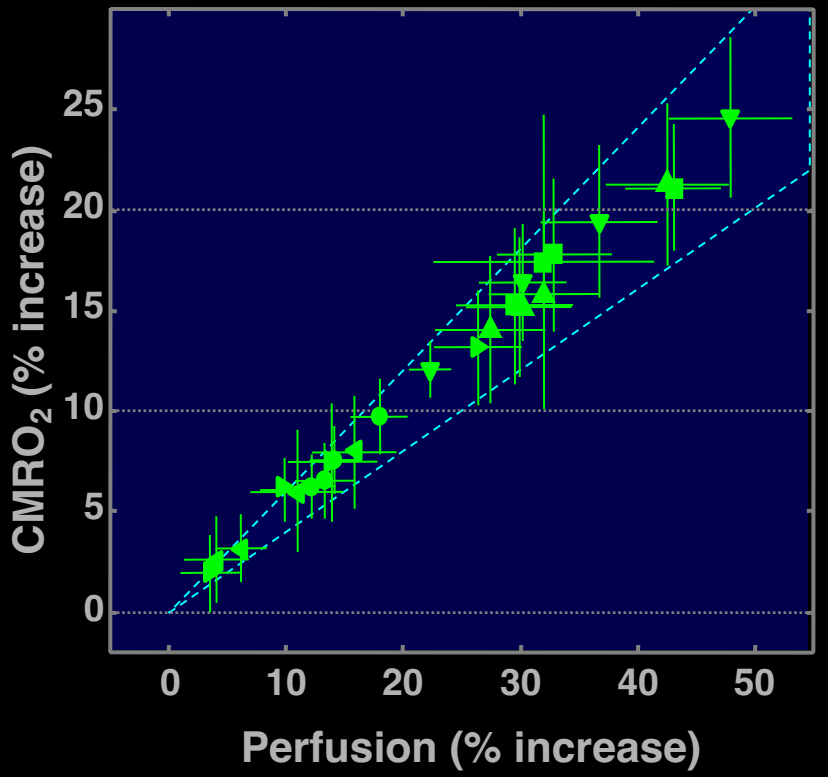
Simultaneous Perfusion and BOLD imaging during graded visual activation and hypercapnia

N=12

CBF-CMRO$_2$ coupling

Hoge, et al.





Characterizing Activation-induced CMRO$_2$ changes using calibration with hypercapnia

Hoge, et al.

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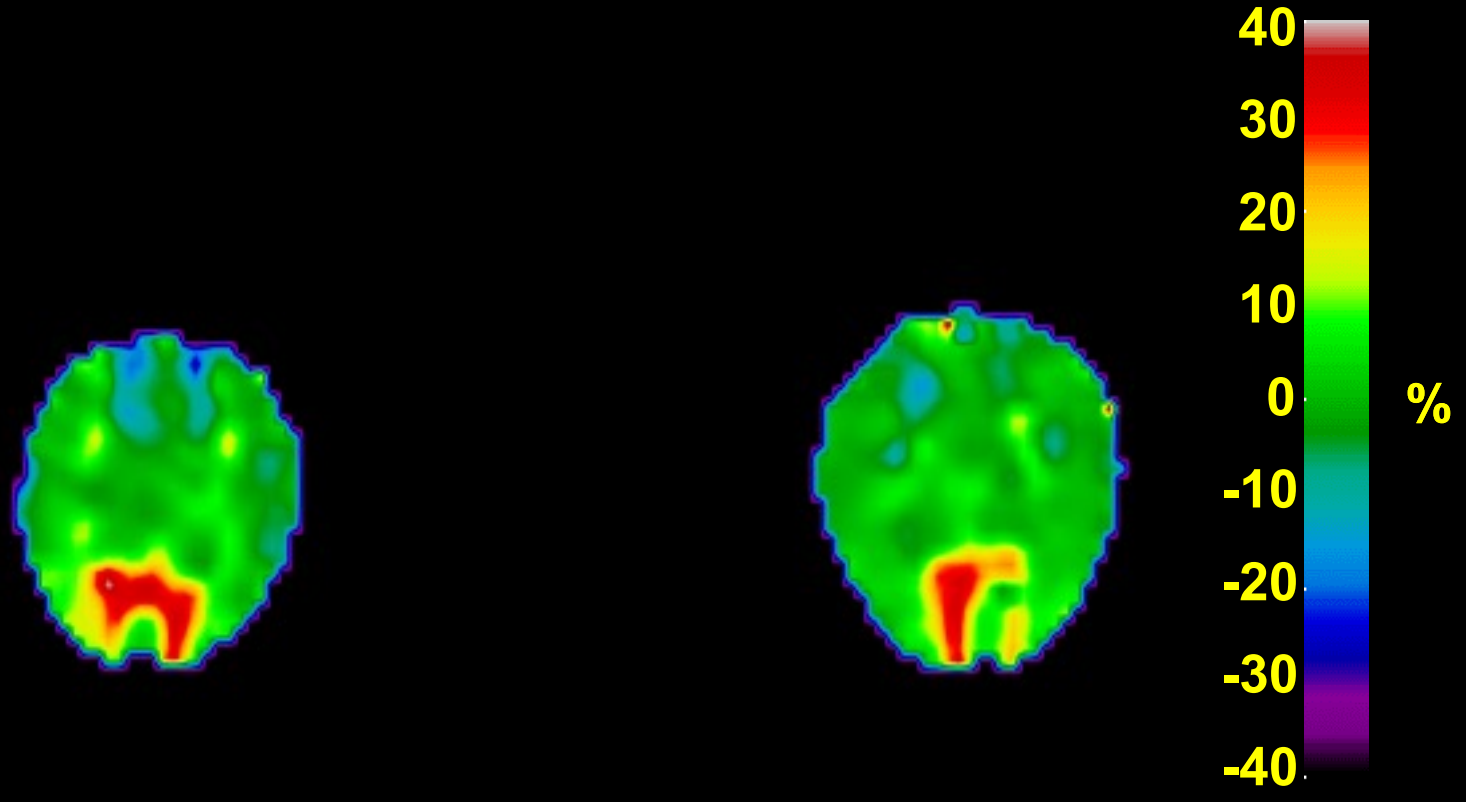
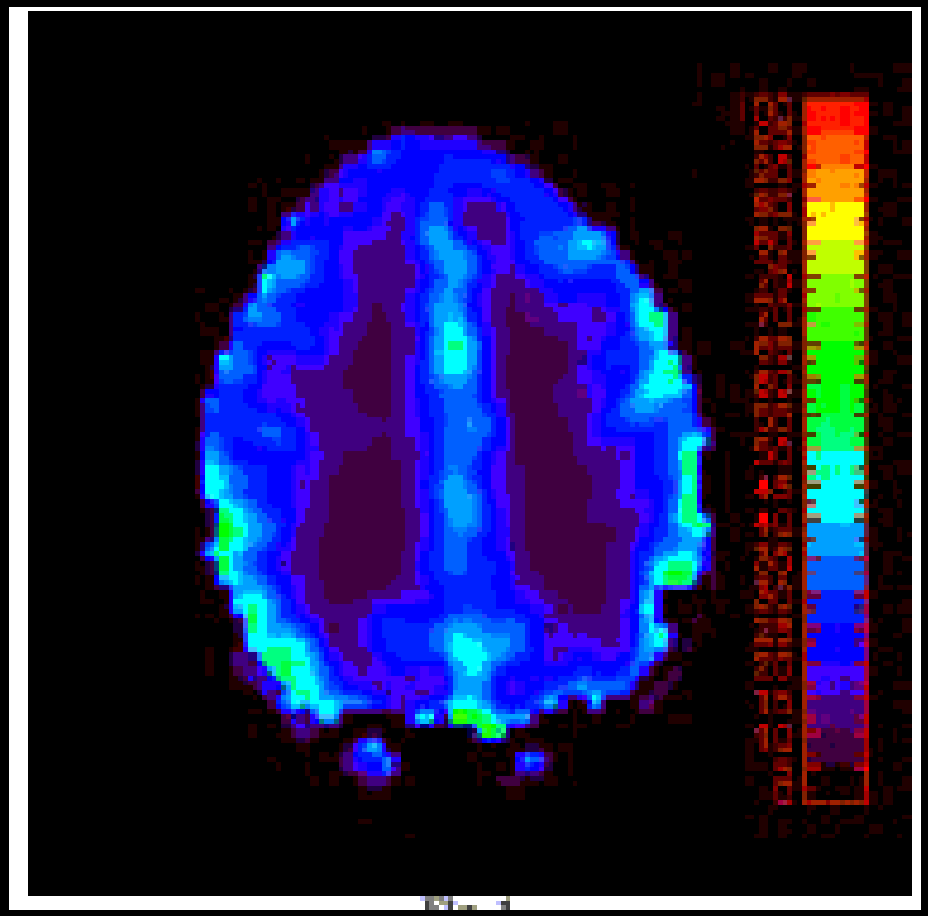


Quantitative Measurements of Cerebral Metabolic Rate of Oxygen (CMRO2) Using MRI: A Volunteer Study

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

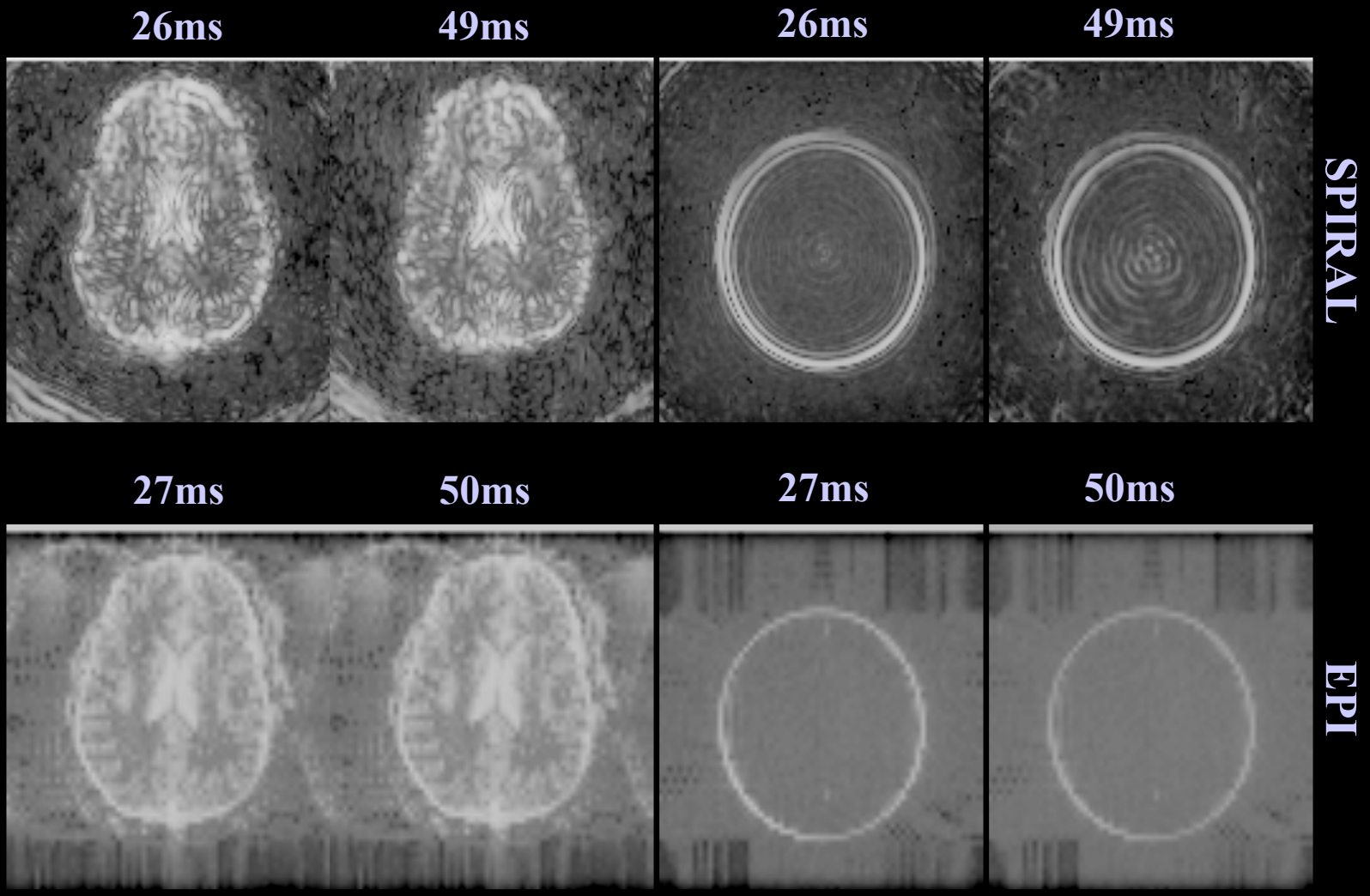
[1]Washington University, 600 Airport Road, Chapel Hill, NC USA; [2]UNC-Chapel Hill, Department of Radiology, CB#7515, Chapel Hill, NC USA; [3]GE Medical Systems, ; [4]UNC-Chapel Hill, ;



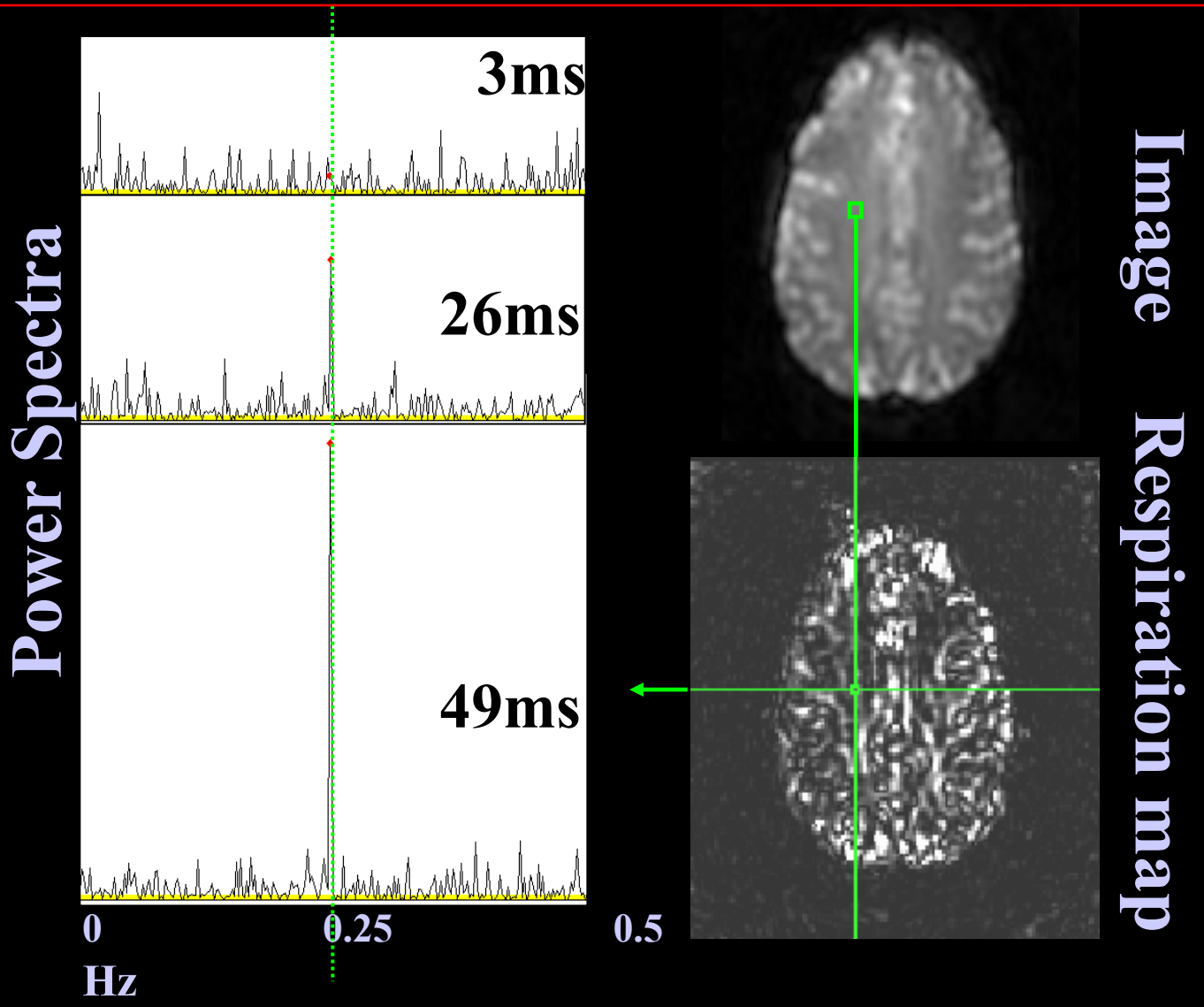
Functional MRI

- Scanner and Hardware
- Anatomical Contrast and Image Formation
- Pulse sequences
  - *-functional contrast weighting*
  - *-functional time series image collection is*
- Neuronal Input / Information Display Strategi

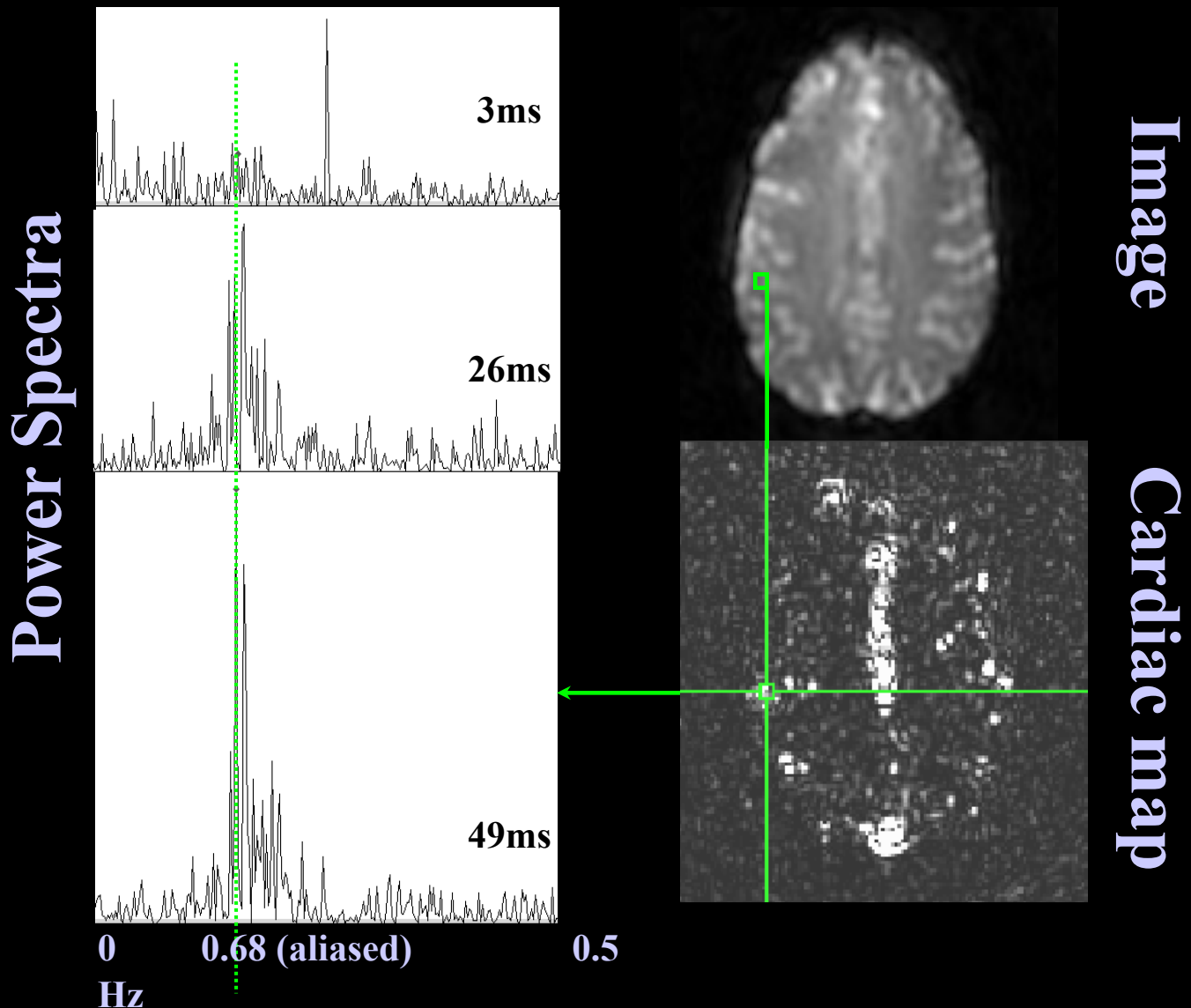
Temporal vs. Spatial SNR- 3T



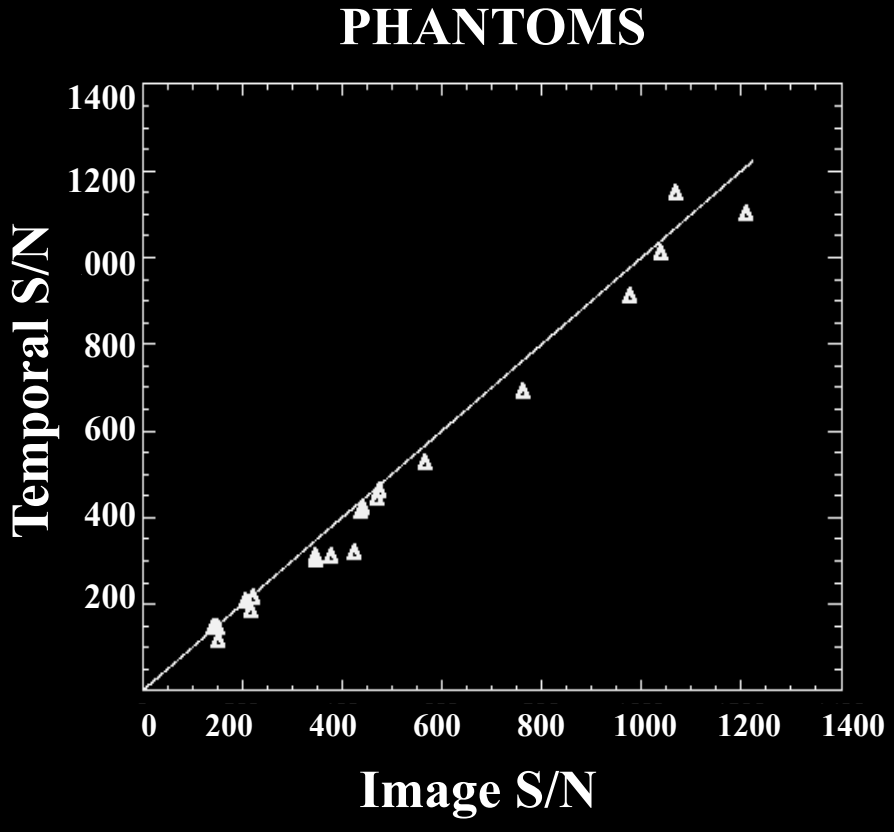
0.25 Hz Breathing at 3T

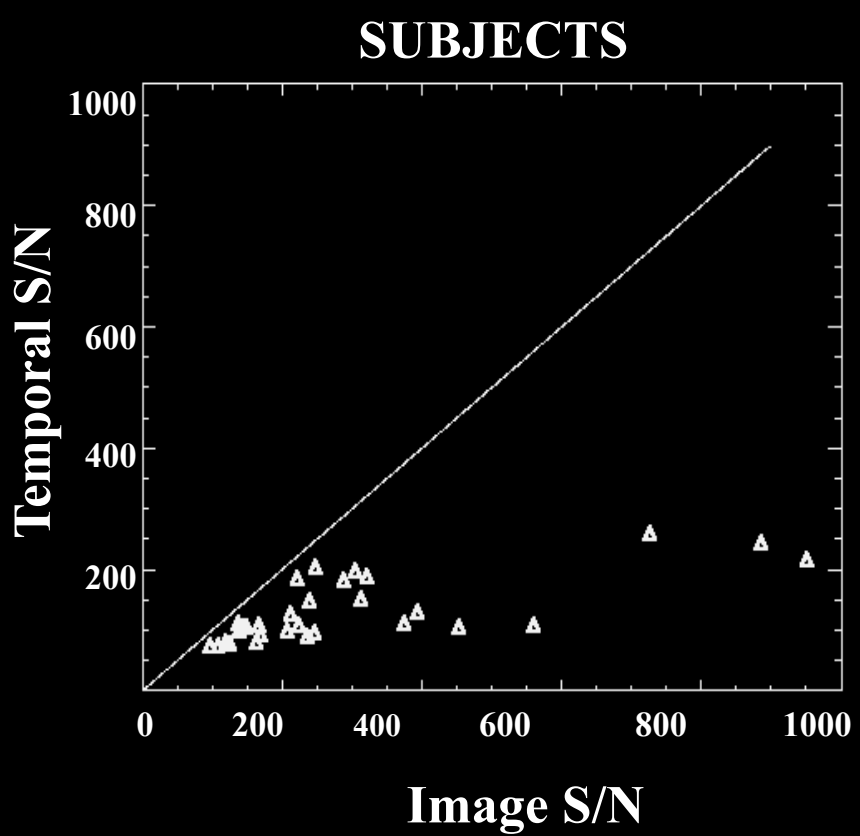


0.68 Hz Cardiac rate at 3T



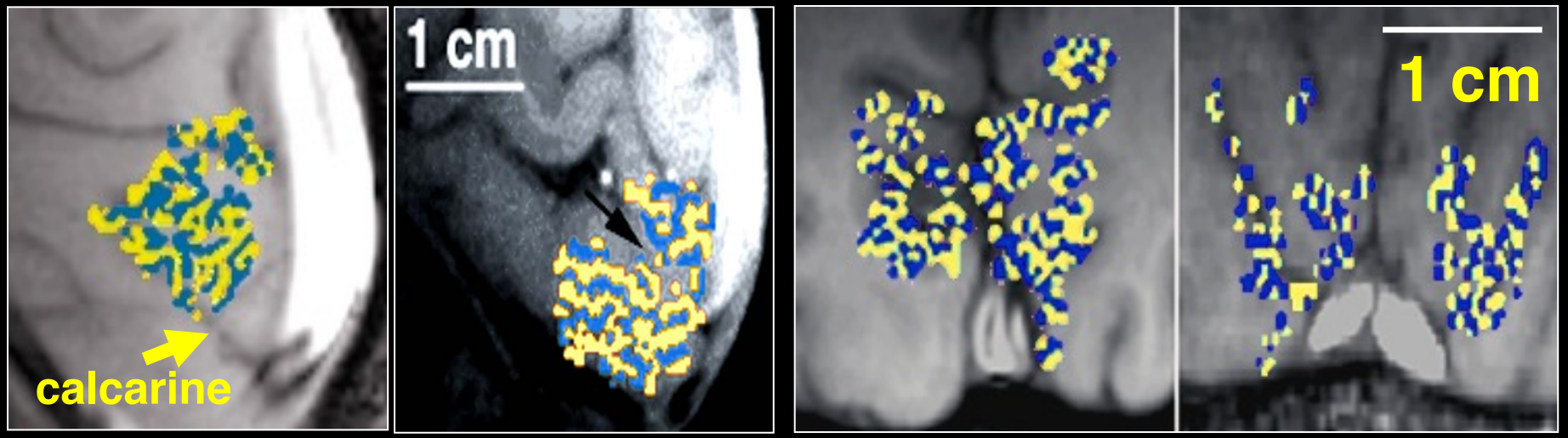
Temporal S/N vs. Image S/N





N. Petridou

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).

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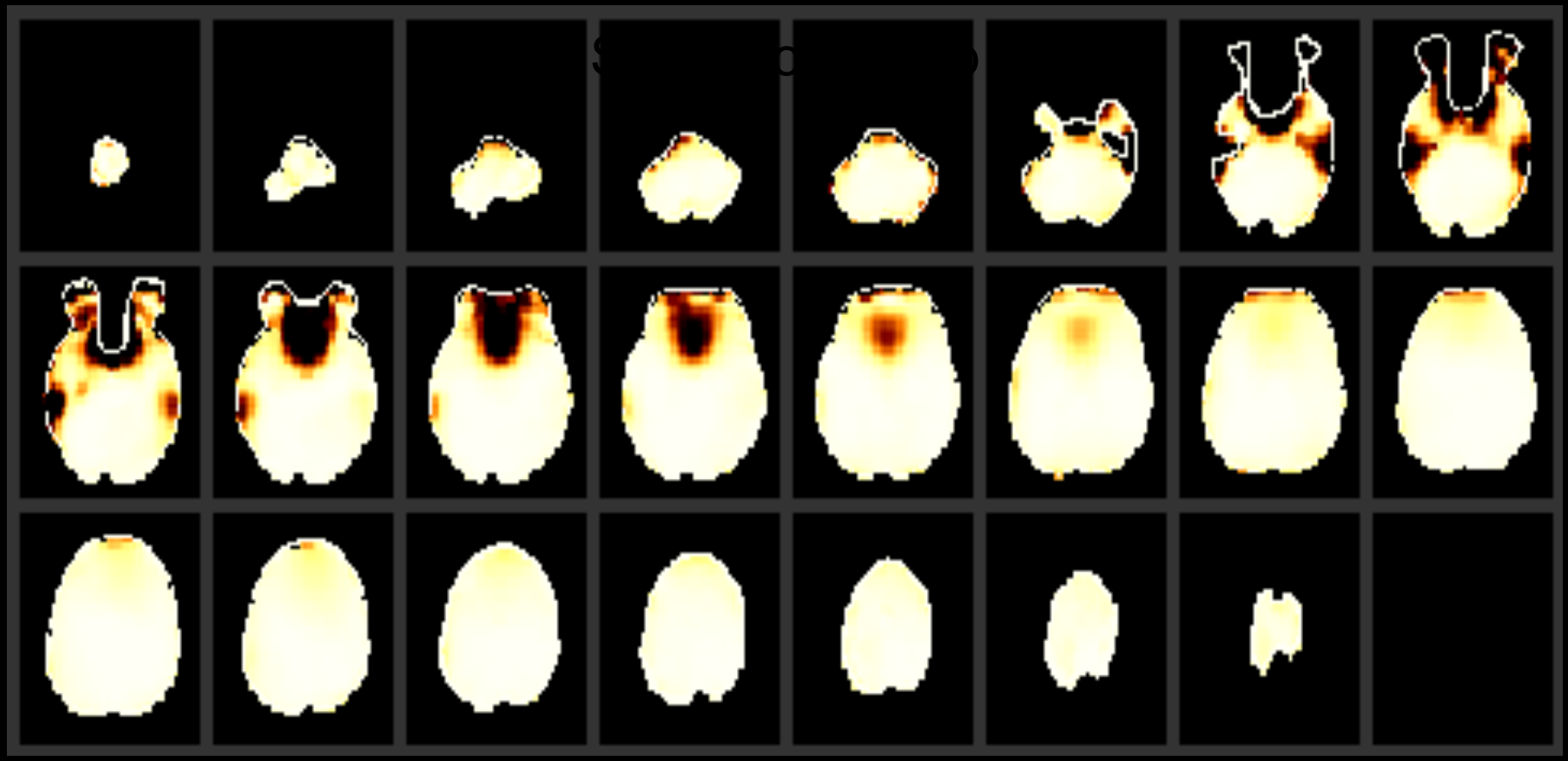

Functional MRI

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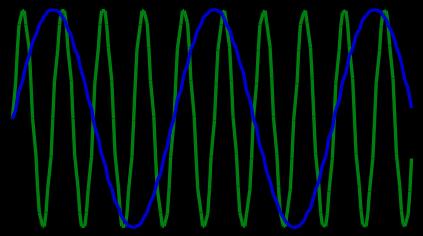
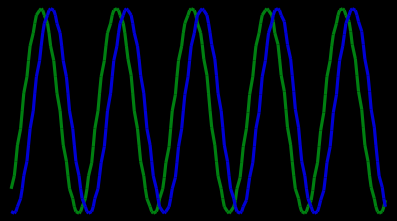
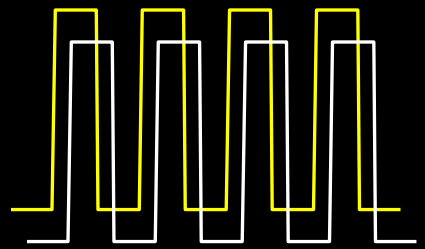
- Anatomical Contrast and Image Formation
- Pulse sequences
  - *-functional contrast weighting*
  - *-functional time series image collection is*
- Neuronal Input / Information Display Strategi

Neuronal Activation Input Strategies

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



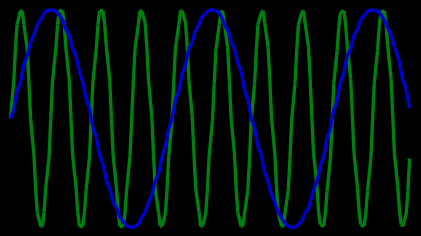




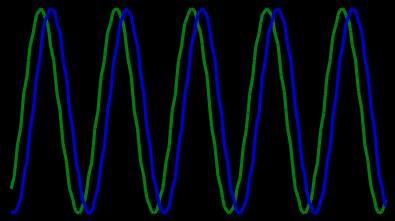
Neuronal Activation Input Strategies

1. Block Design

2. Frequency Encoding

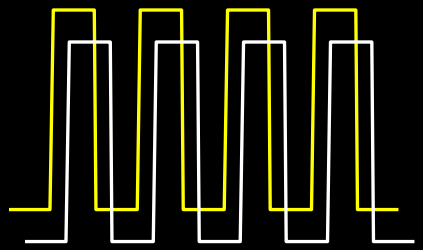


3. Phase Encoding

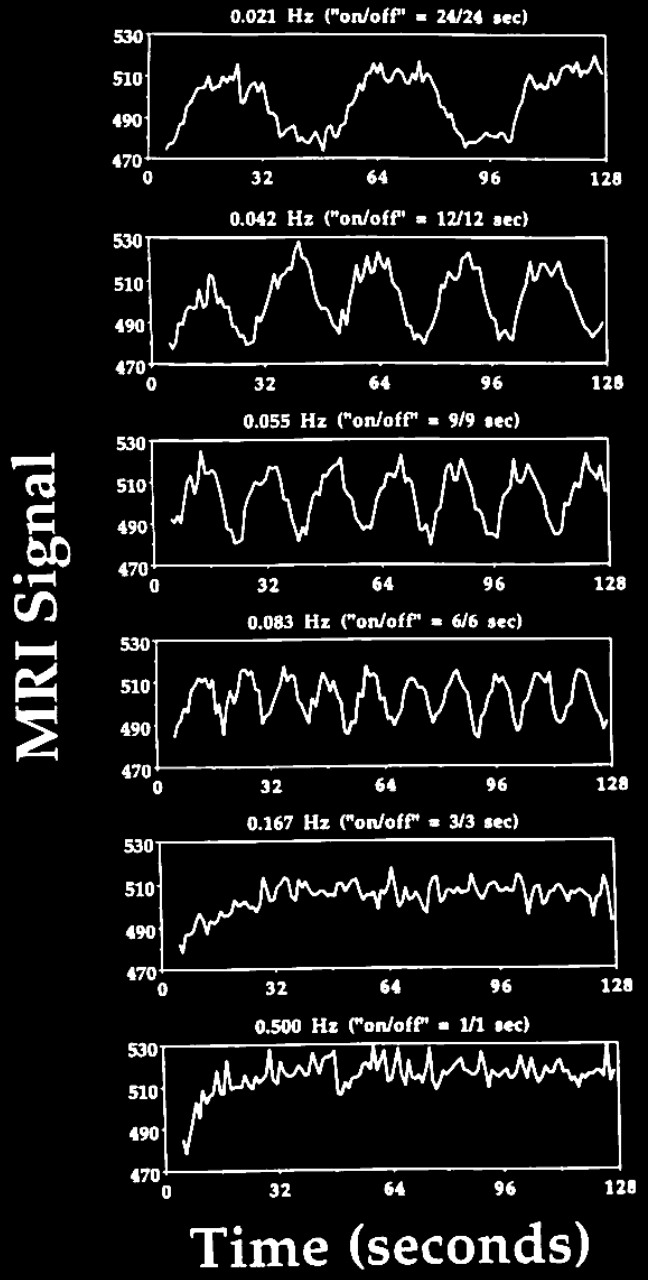


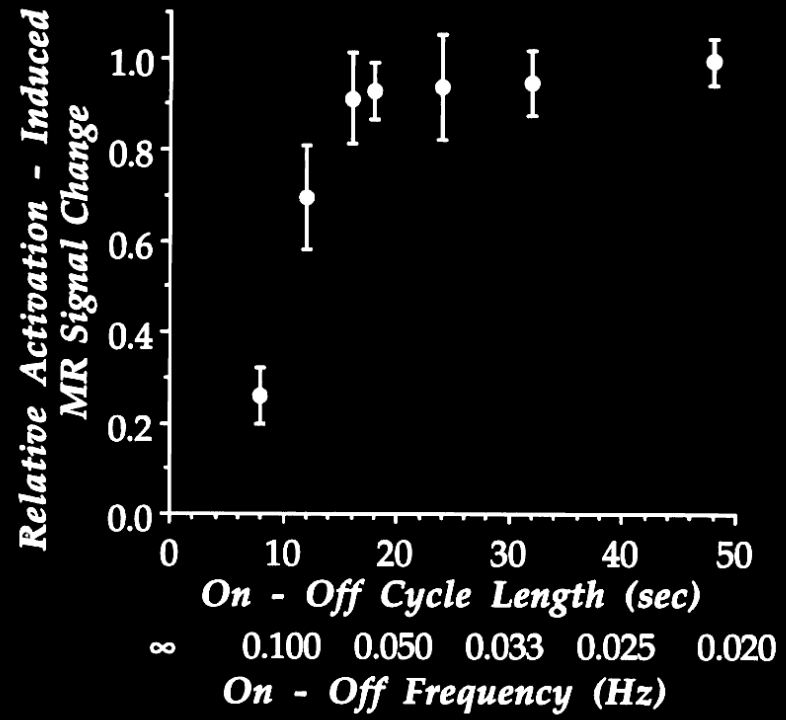
4. Single Event

5. Orthogonal Block Design

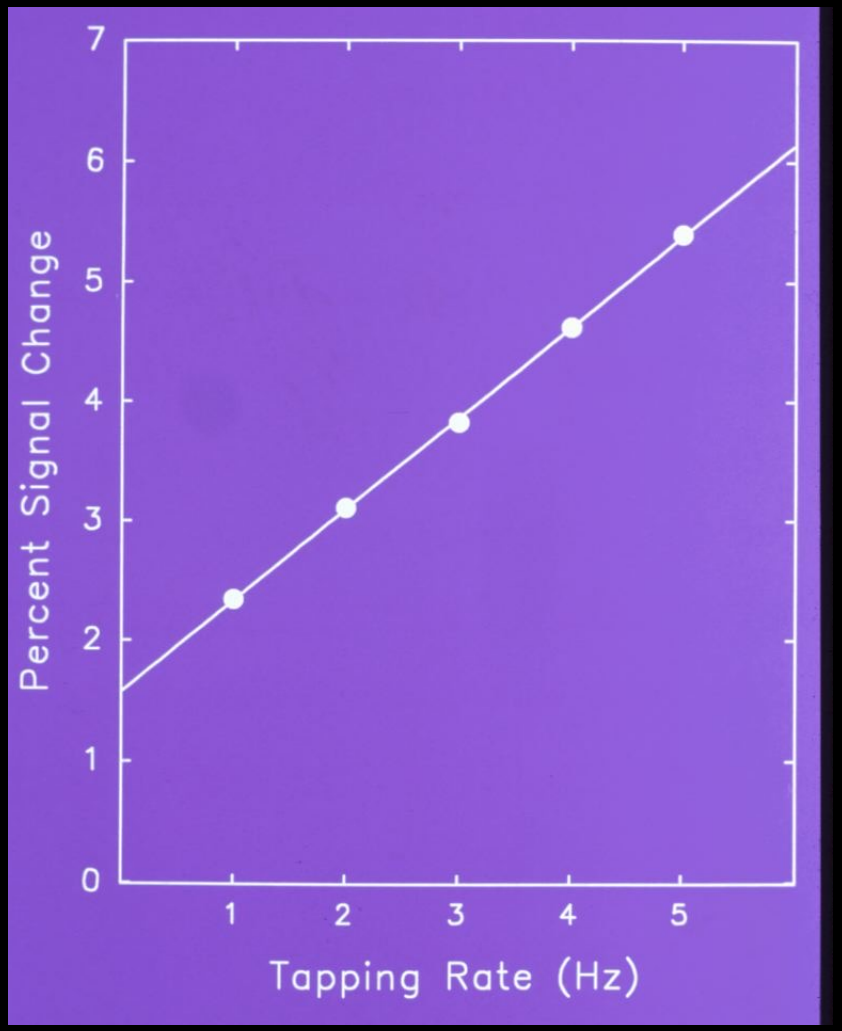


6. Free Behavior Design.

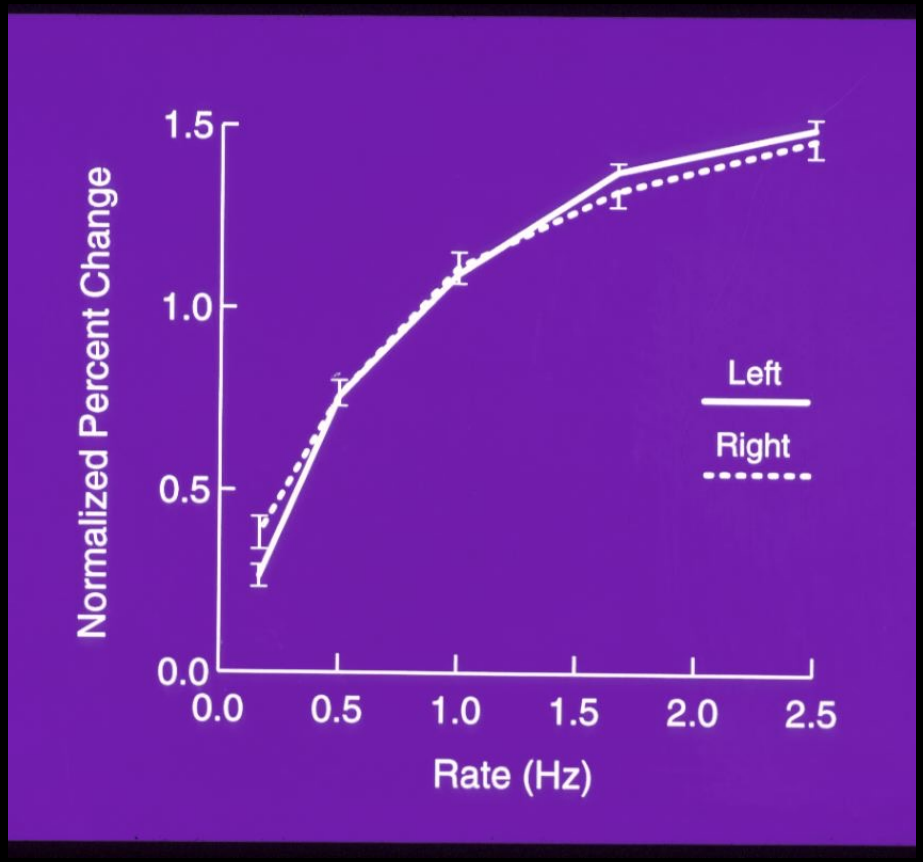

0.021 Hz ("on/off" = 24/24 sec)
0.042 Hz ("on/off" = 12/12 sec)
0.055 Hz ("on/off" = 9/9 sec)
0.083 Hz ("on/off" = 6/6 sec)
0.167 Hz ("on/off" = 3/3 sec)
0.500 Hz ("on/off" = 1/1 sec)
530
510
490
470
0
32
64
96
128
MRI Signal
Time (seconds)

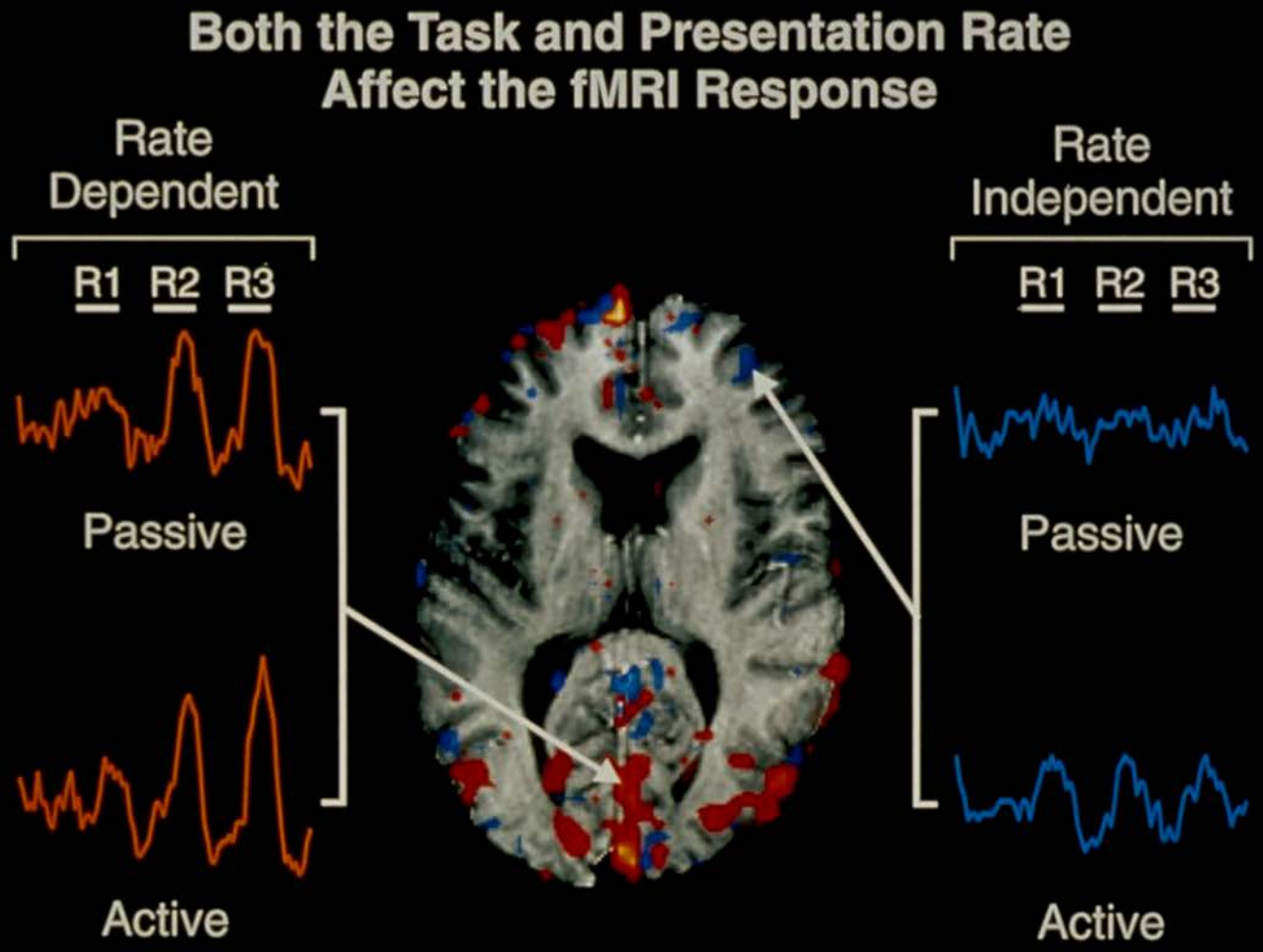

Relative Activation - Induced MR Signal Change
1.0
0.8
0.6
0.4
0.2
0.0
0
10
20
30
40
50
On - Off Cycle Length (sec)
∞
0.100
0.050
0.033
0.025
0.020
On - Off Frequency (Hz)

Motor Cortex



Auditory Cortex

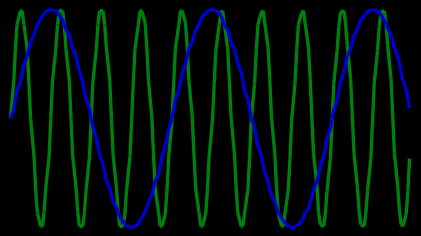



Both the Task and Presentation Rate
Affect the fMRI Response
Rate
Dependent
R1 R2 R3
Passive
Active
Rate
Independent
R1 R2 R3
Passive
Active

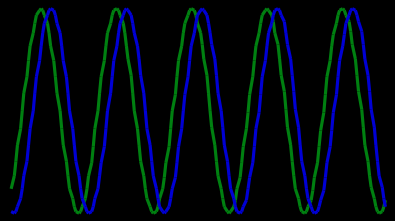
DeYoe et al.

Neuronal Activation Input Strategies

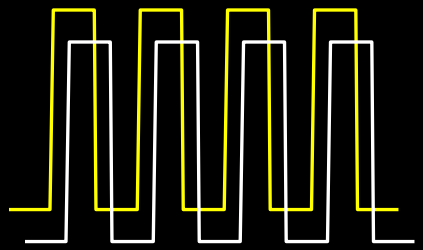
1. Block Design
2. Frequency Encoding



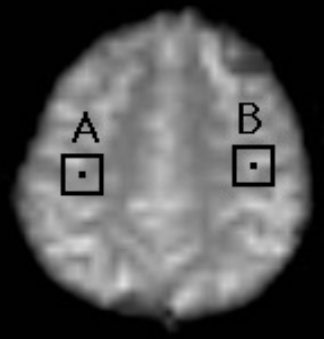
3. Phase Encoding

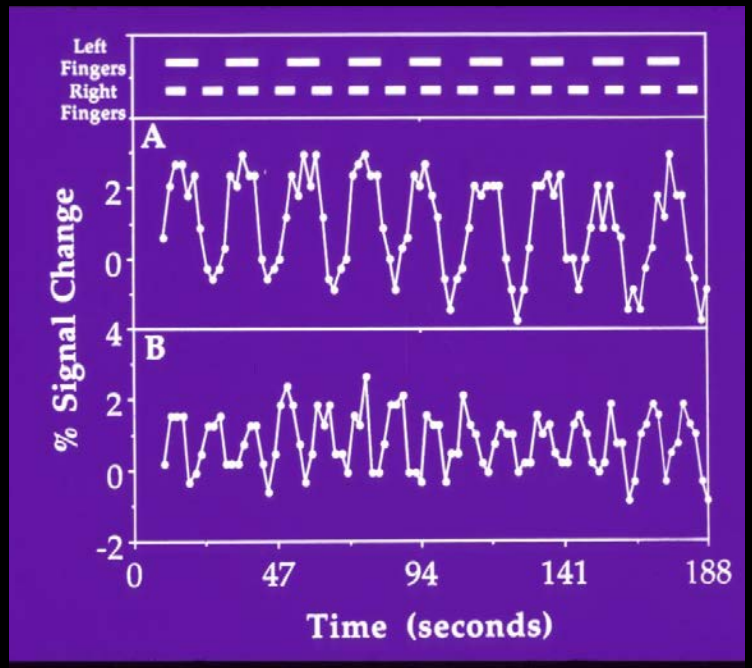


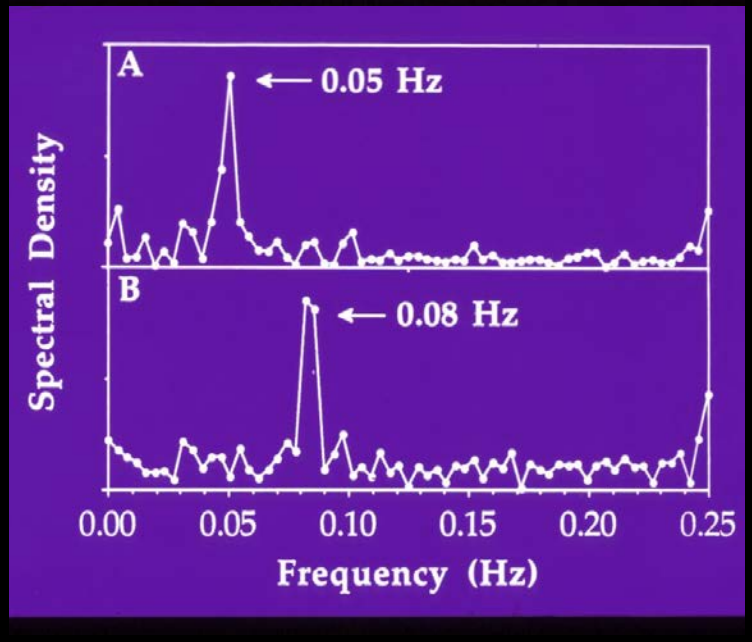
4. Single Event
5. Orthogonal Block Design

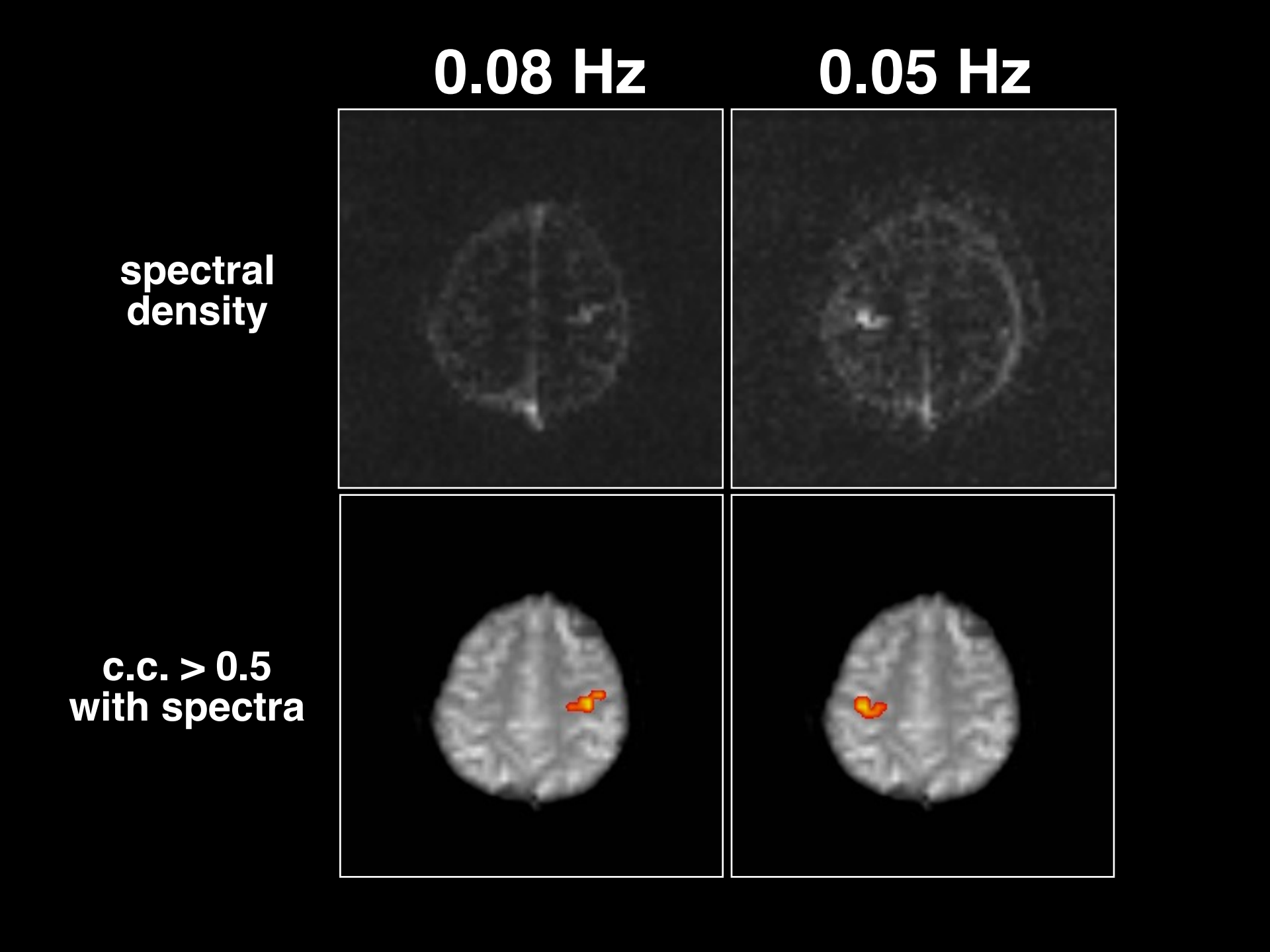


6. Free Behavior Design.


A
B

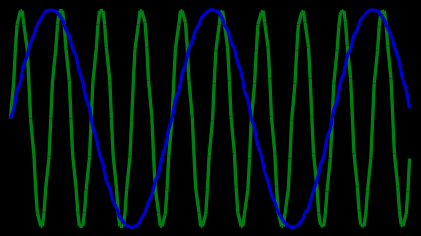

Left Fingers
Right Fingers
A
B
% Signal Change
2
0
4
2
0
-2
0
47
94
141
188
Time (seconds)


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

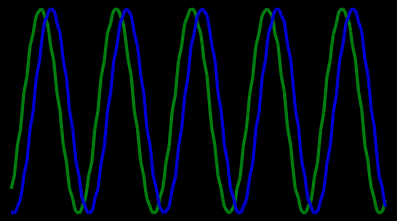

0.08 Hz
0.05 Hz
spectral density
c.c. > 0.5 with spectra

Neuronal Activation Input Strategies

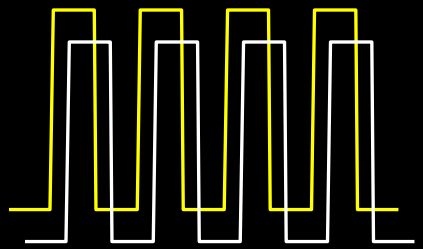
1. Block Design
2. Frequency Encoding



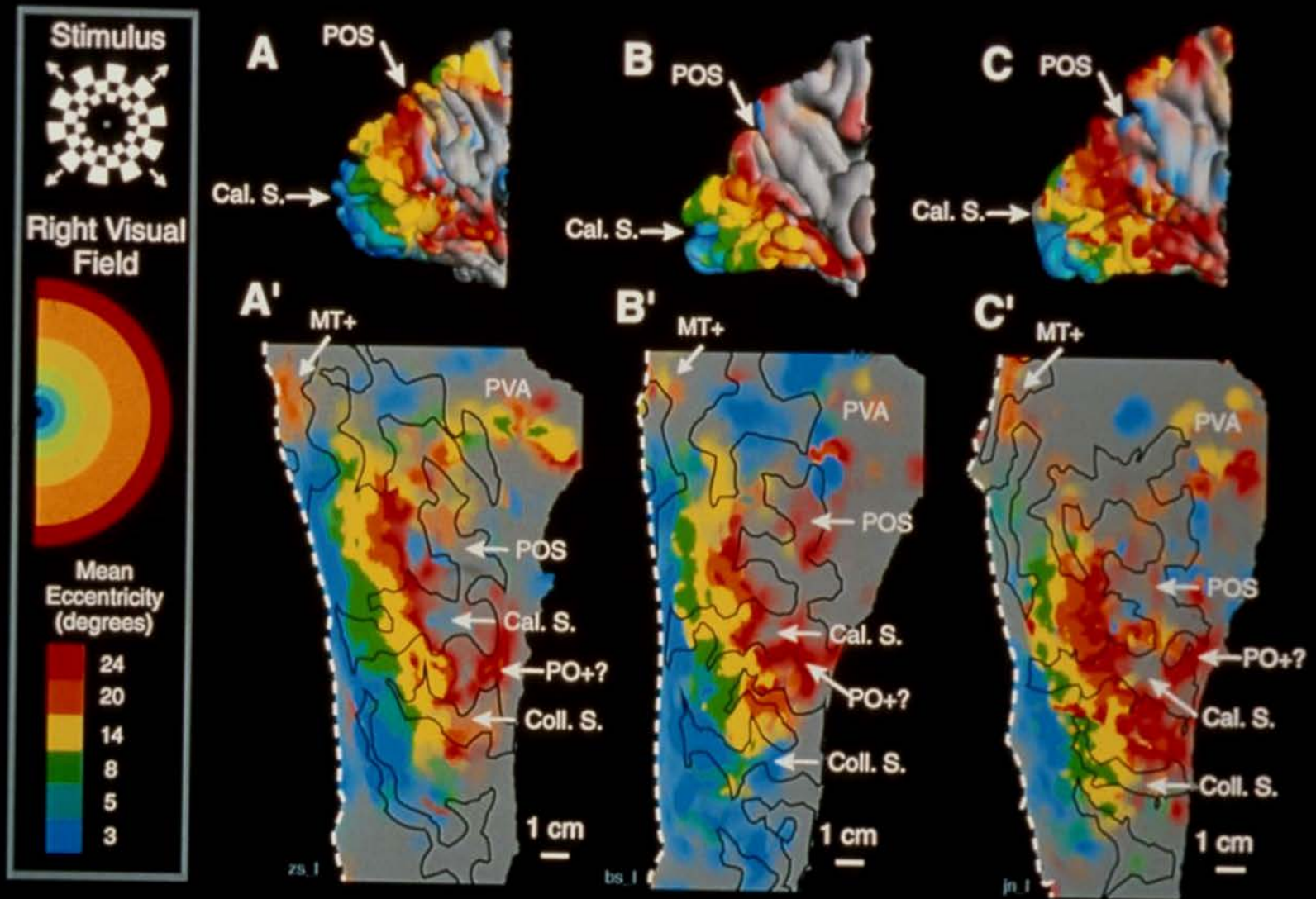
3. Phase Encoding

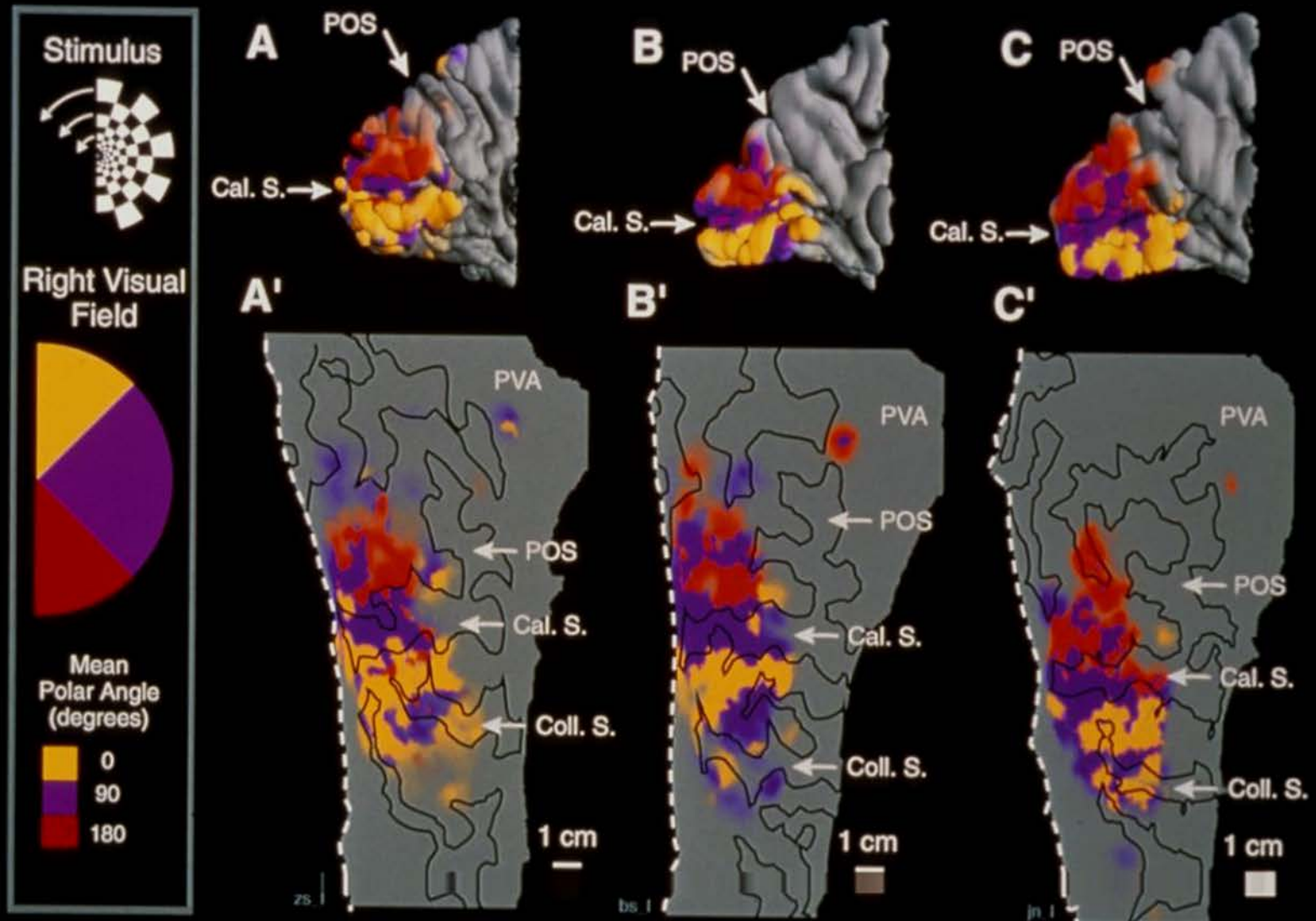


4. Single Event
5. Orthogonal Block Design



6. Free Behavior Design.

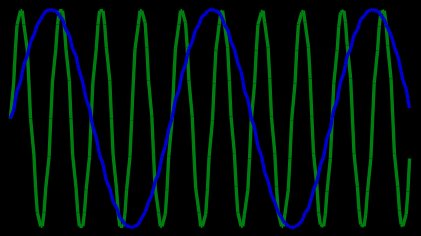

Stimulus
Right Visual Field
Mean Eccentricity (degrees)
24
20
14
8
5
3
A
POS
Cal. S.
B
POS
Cal. S.
C
POS
Cal. S.
A'
MT+
PVA
POS
Cal. S.
PO+?
Coll. S.
1 cm
zs_l
B'
MT+
PVA
POS
Cal. S.
PO+?
Coll. S.
1 cm
bs_l
C'
MT+
PVA
POS
PO+?
Cal. S.
Coll. S.
1 cm
jn_l


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

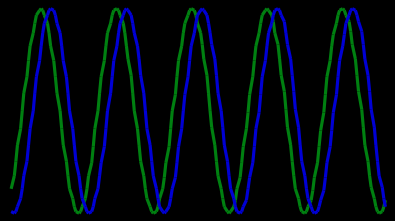
Neuronal Activation Input Strategies

1. Block Design

2. Frequency Encoding

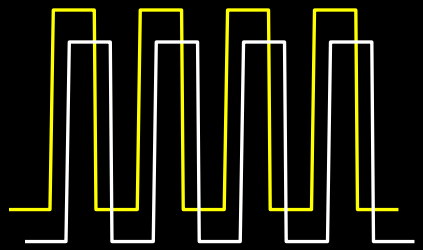


3. Phase Encoding

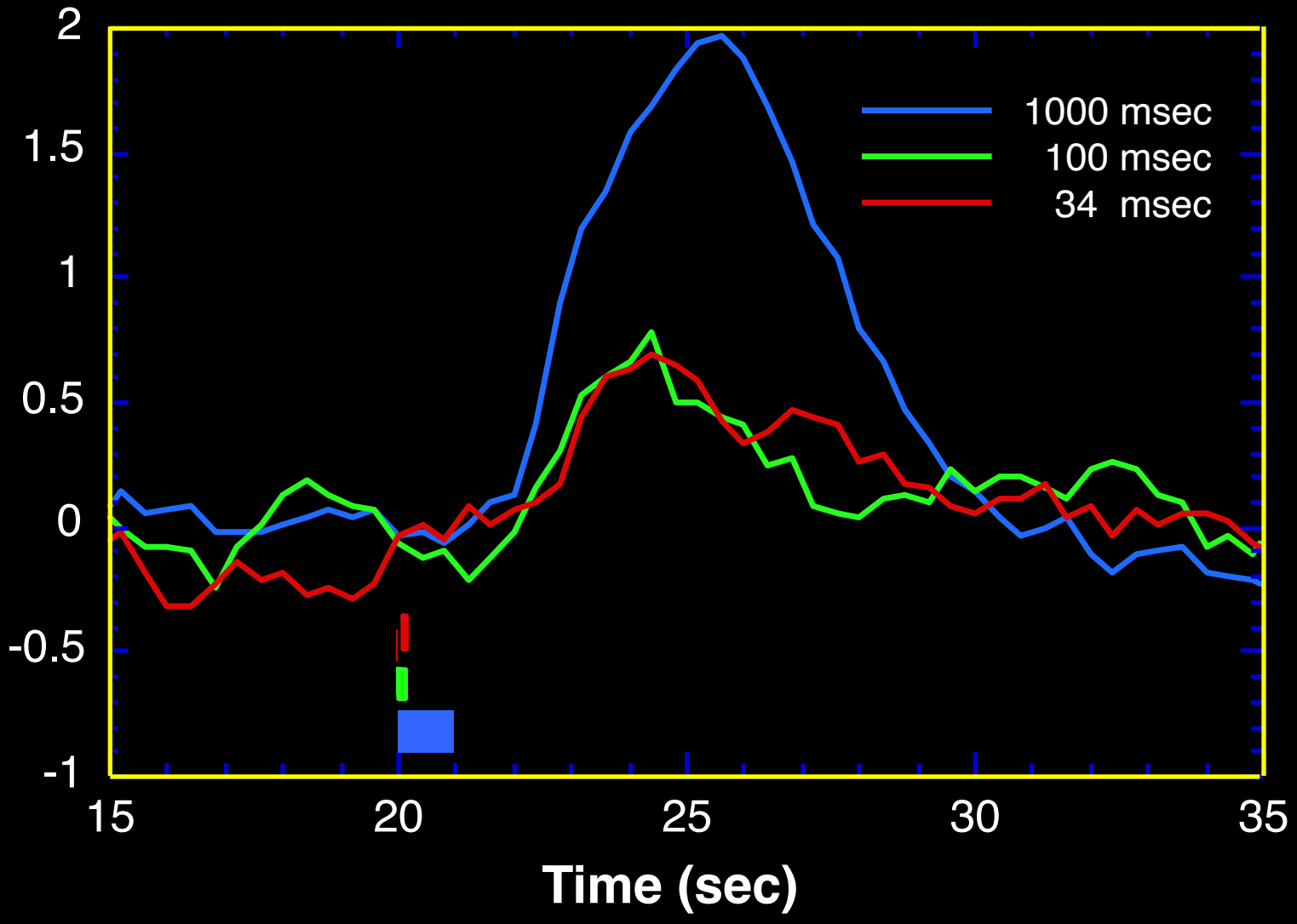


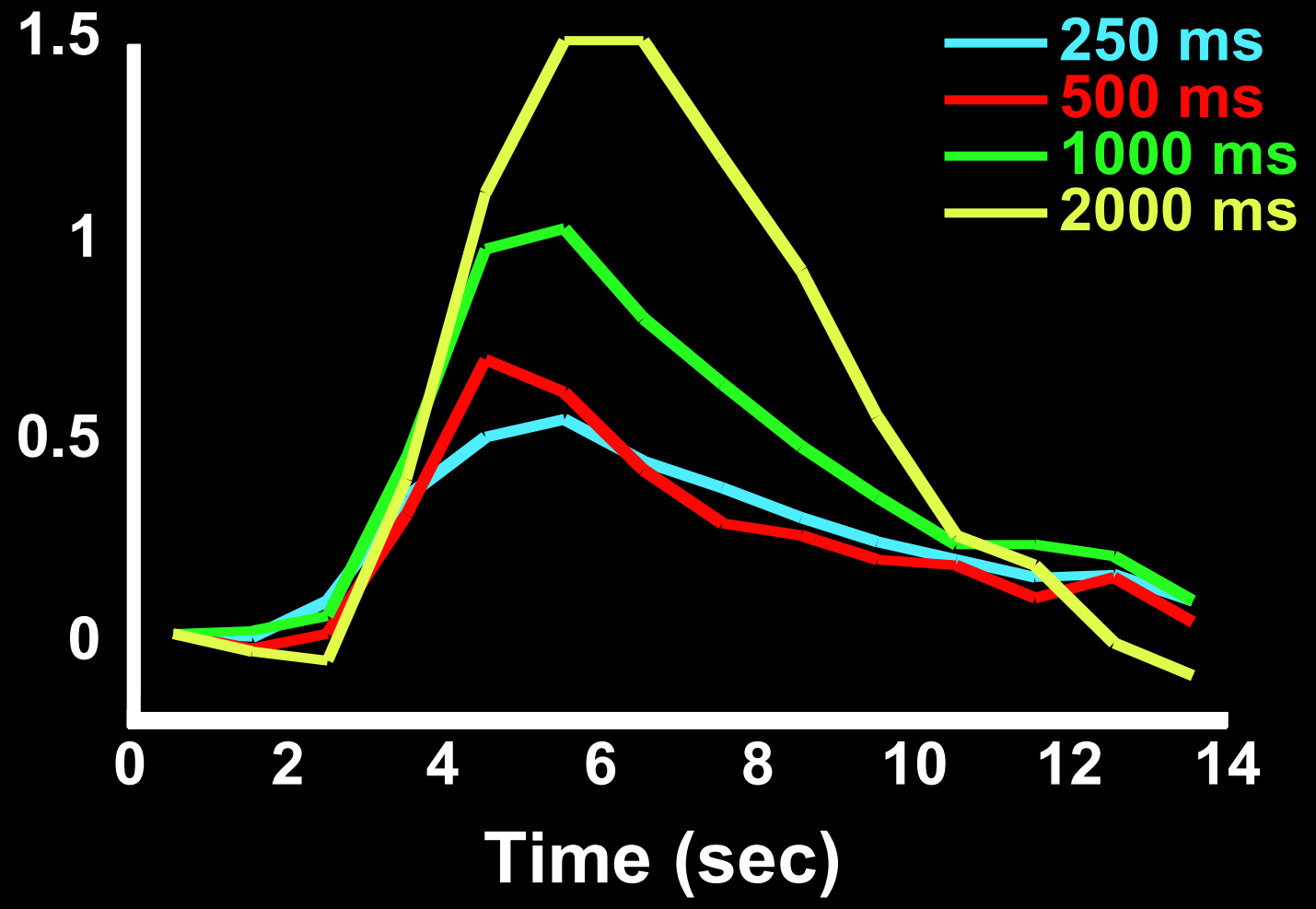
4. Single Event

5. Orthogonal Block Design



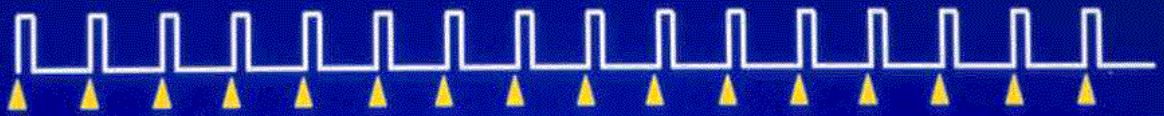
6. Free Behavior Design.

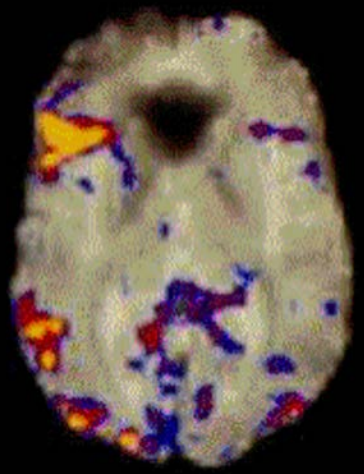

2
1.5
1
0.5
0
-0.5
-1
15
20
25
30
35
Time (sec)
1000 msec
100 msec
34 msec

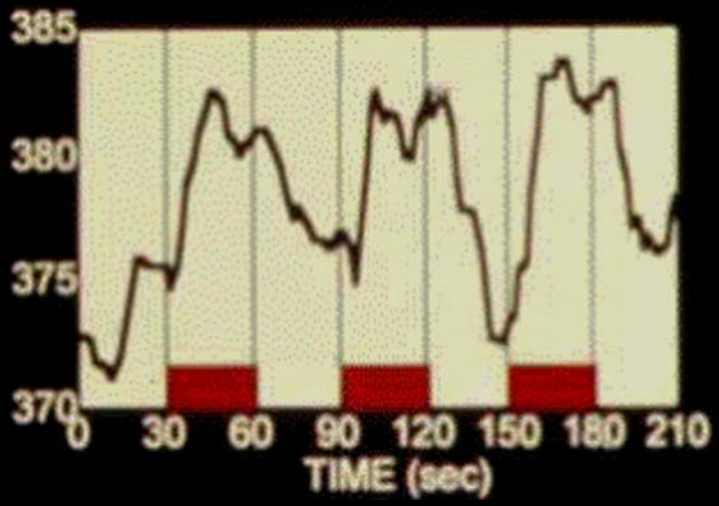

1.5
1
0.5
0
0
2
4
6
8
10
12
14
Time (sec)
250 ms
500 ms
1000 ms
2000 ms

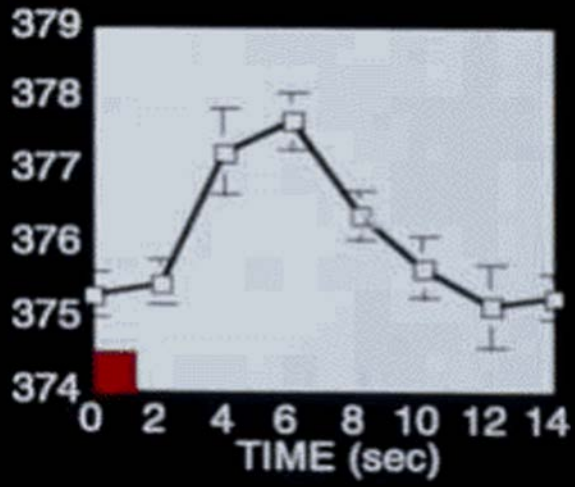
BLOCKED:

SINGLE TRIAL:

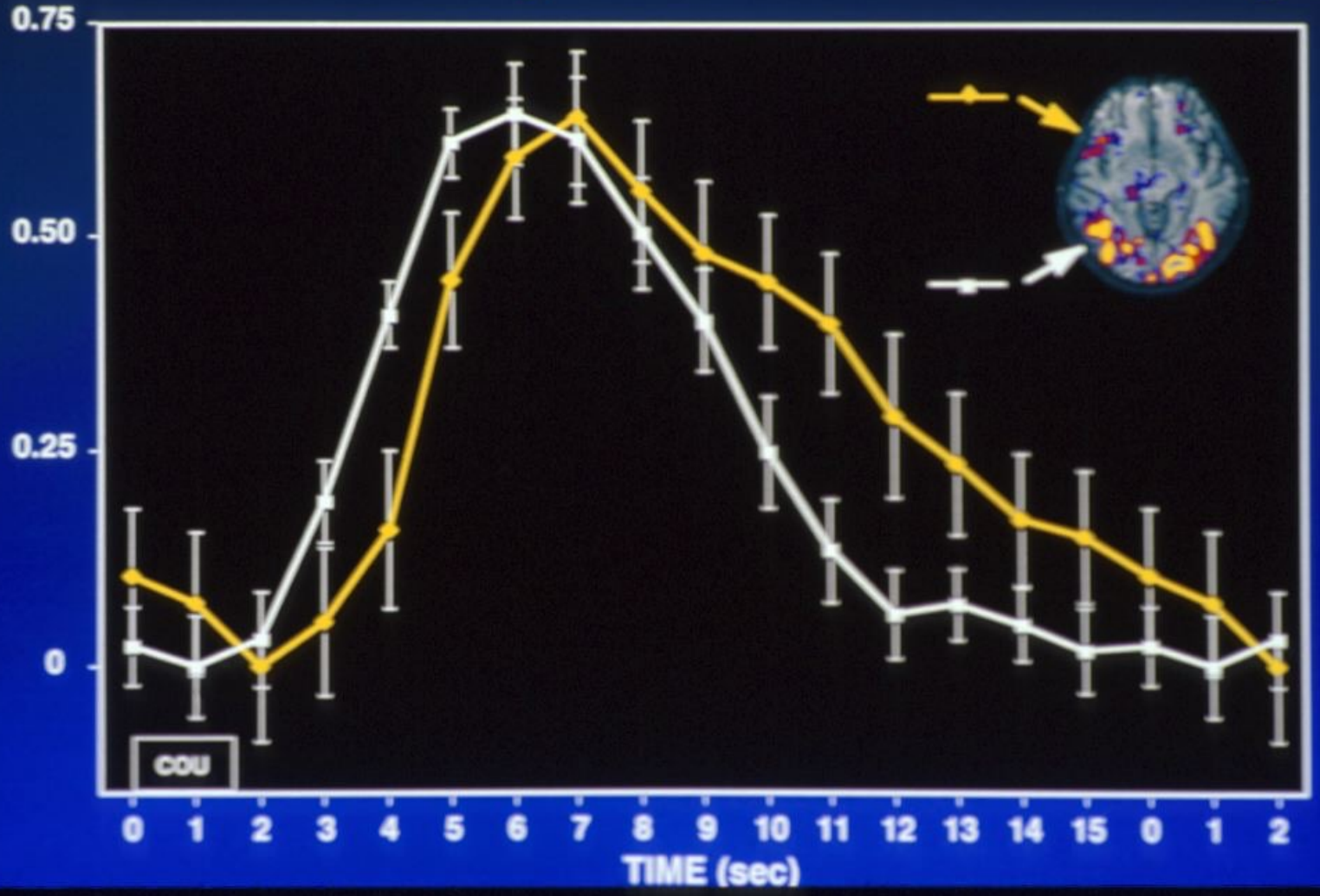


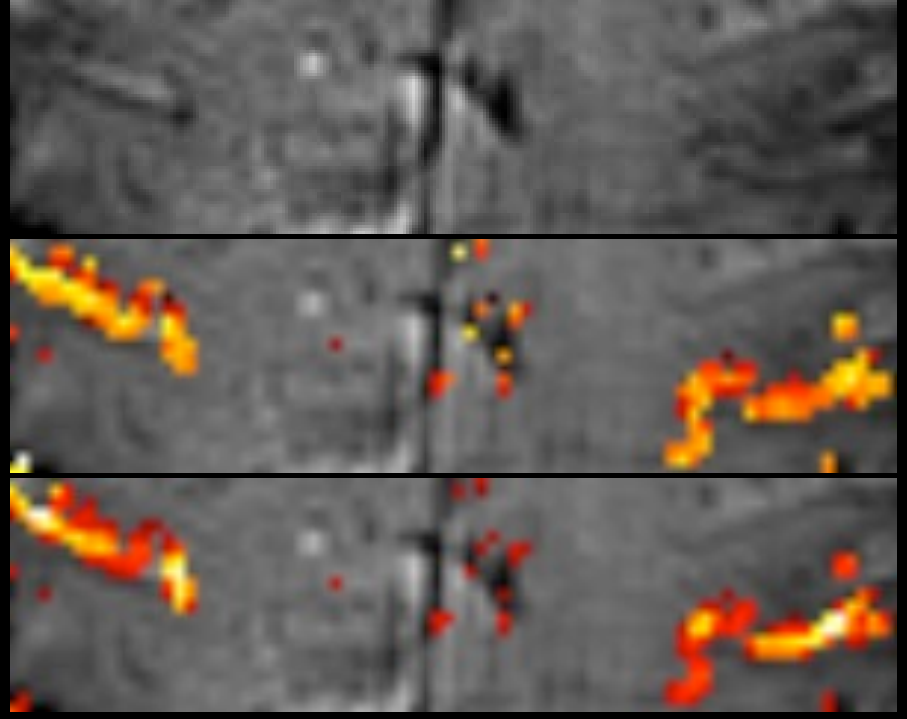


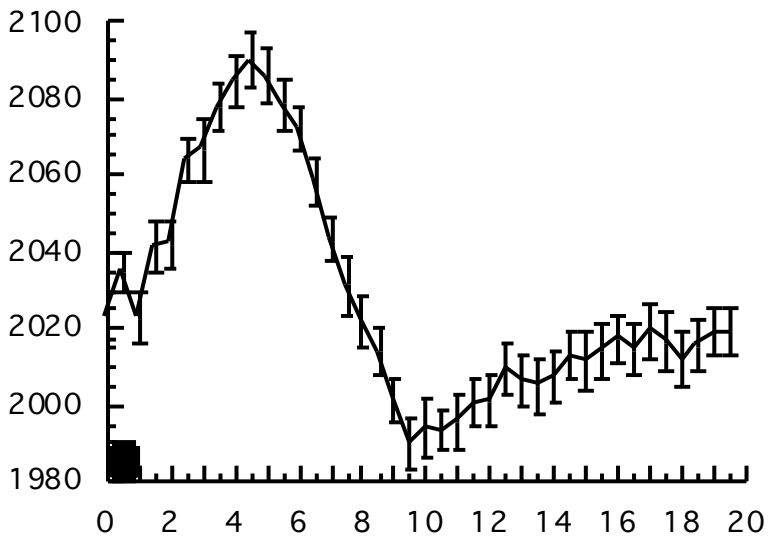


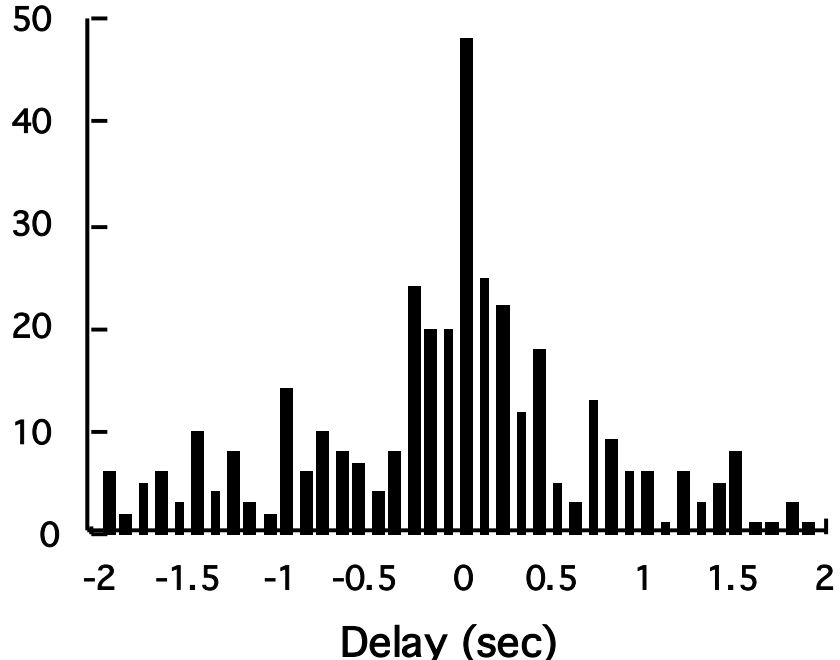


Time Course Comparison Across Brain Regions

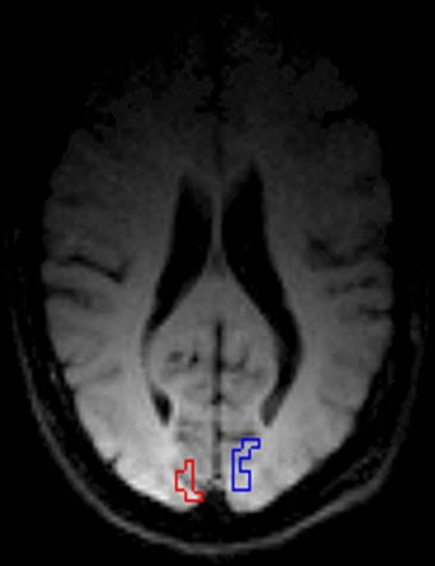



Latency
Magnitude
+ 2 sec
- 2 sec


2100
2080
2060
2040
2020
2000
1980
0 2 4 6 8 10 12 14 16 18 20
Time (sec)

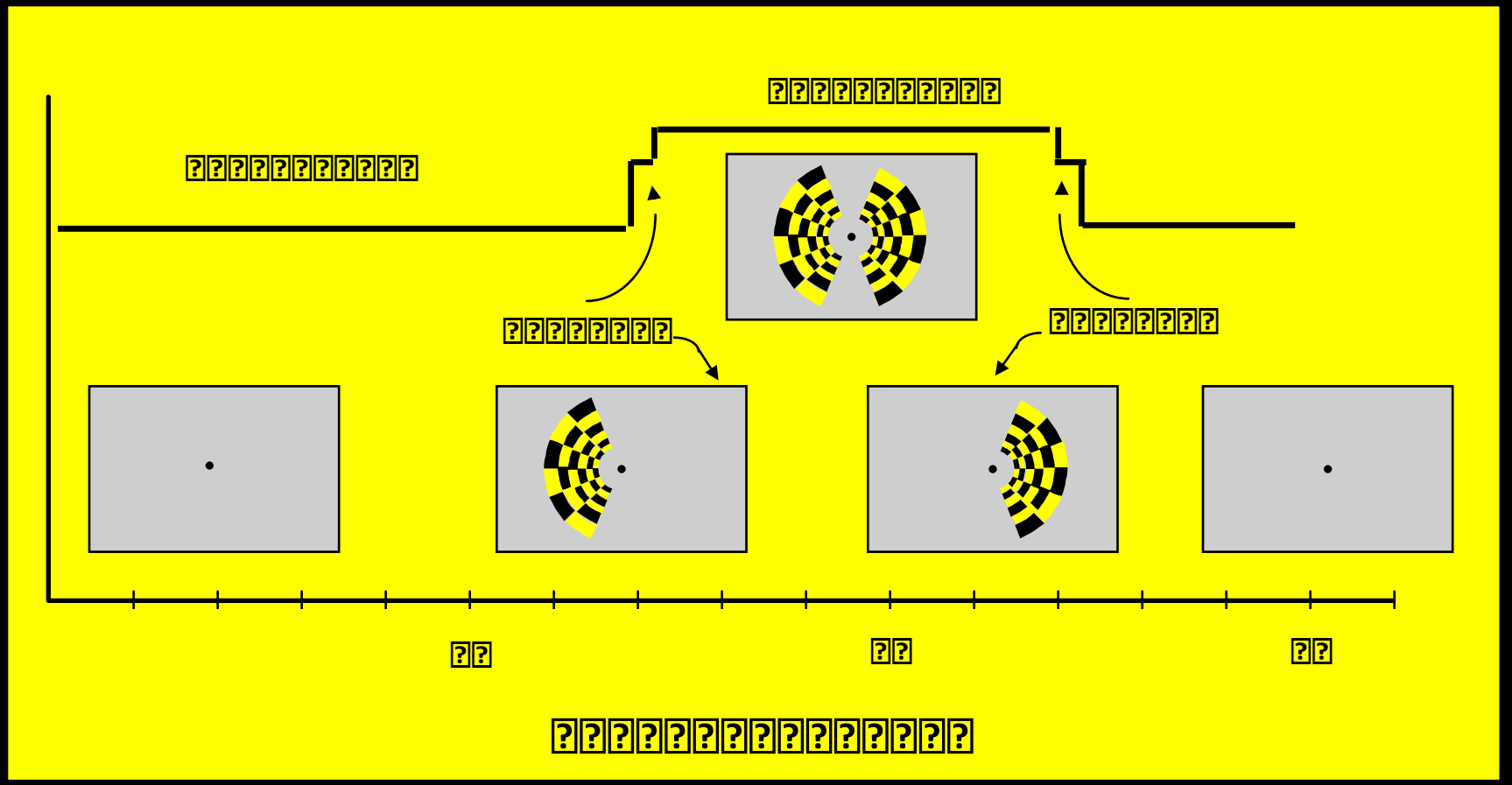

50
40
30
20
10
0
-2 -1.5 -1 -0.5 0 0.5 1 1.5 2
Delay (sec)

Regions of Interest Used for Hemi-Field Experiment

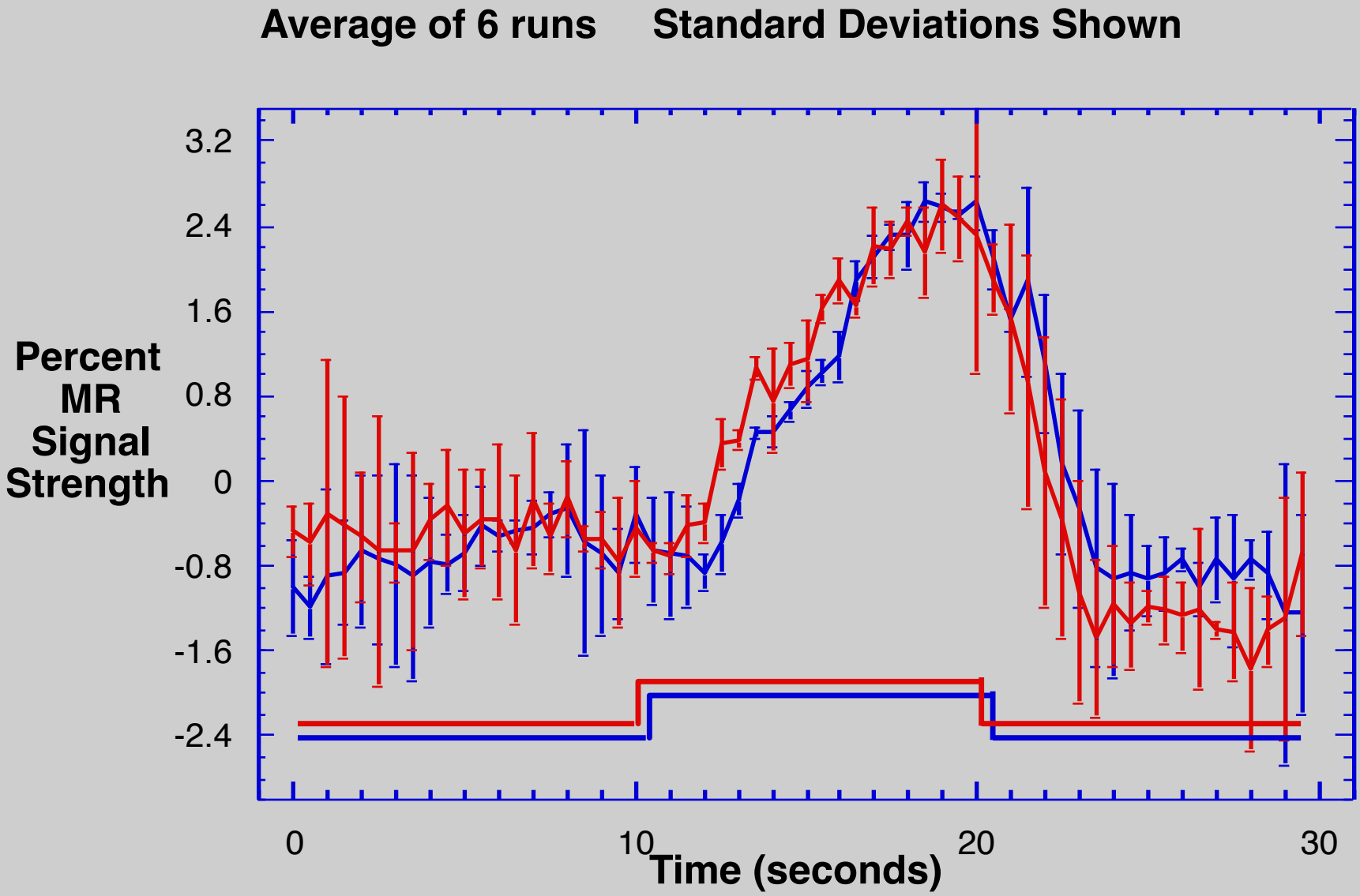


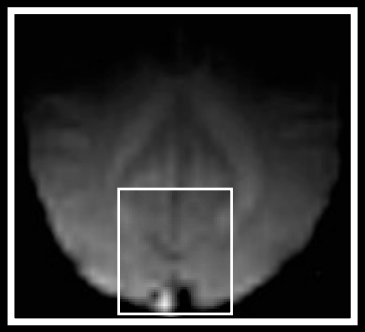
Right Hemisphere

Left Hemisphere



Hemi-field with 500 msec asynchrony





500 ms

500 ms

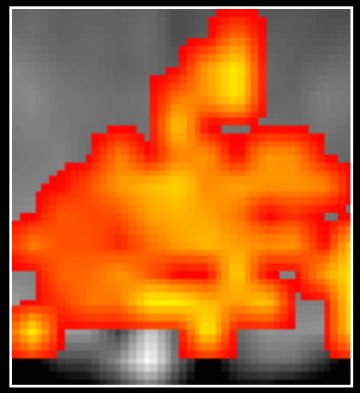
Right Hemifield

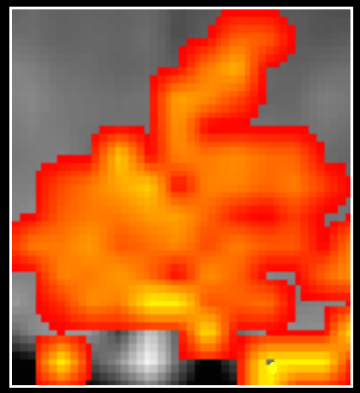
Left Hemifield

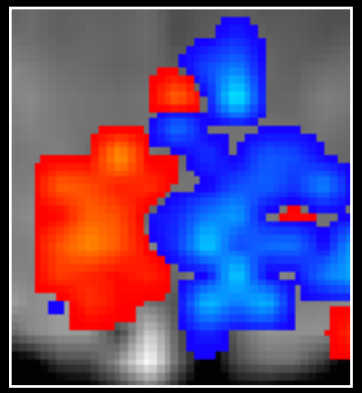
+ 2.5 s

0 s

- 2.5 s







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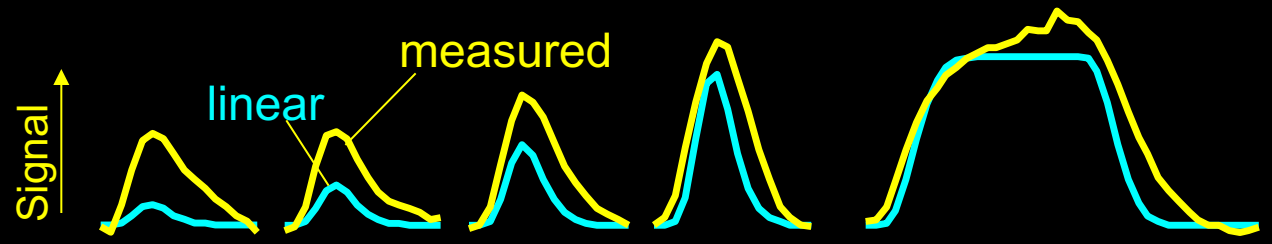
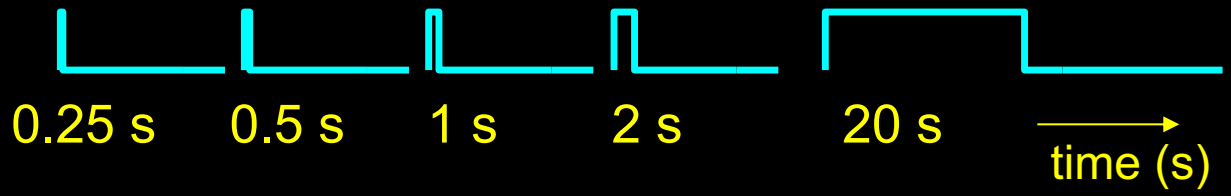
BOLD Response

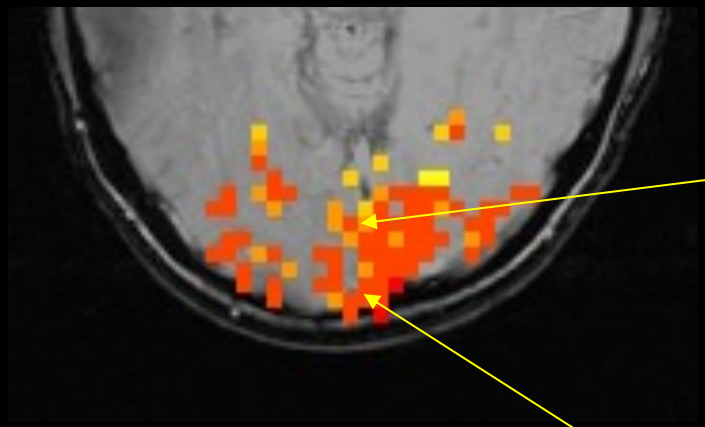


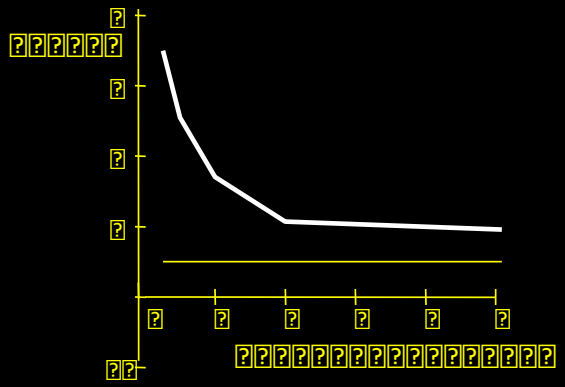
Stimulus timing

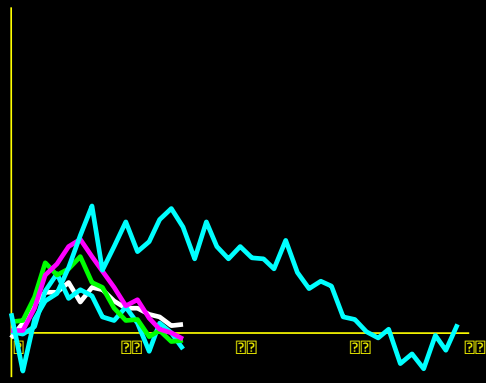


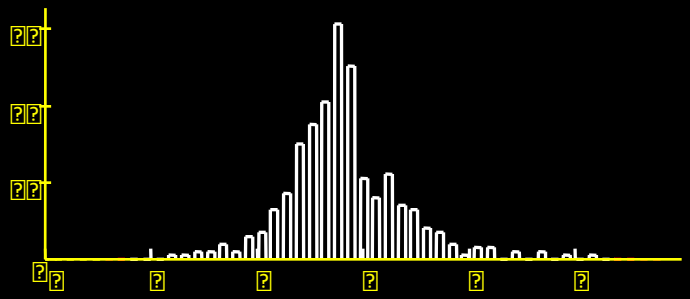
Brief stimuli produce larger responses than expected

Results – visual task

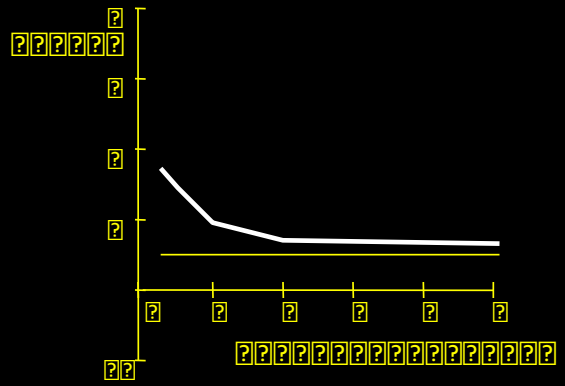


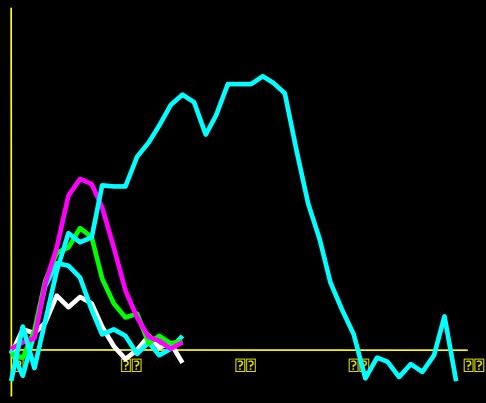






nonlinearity





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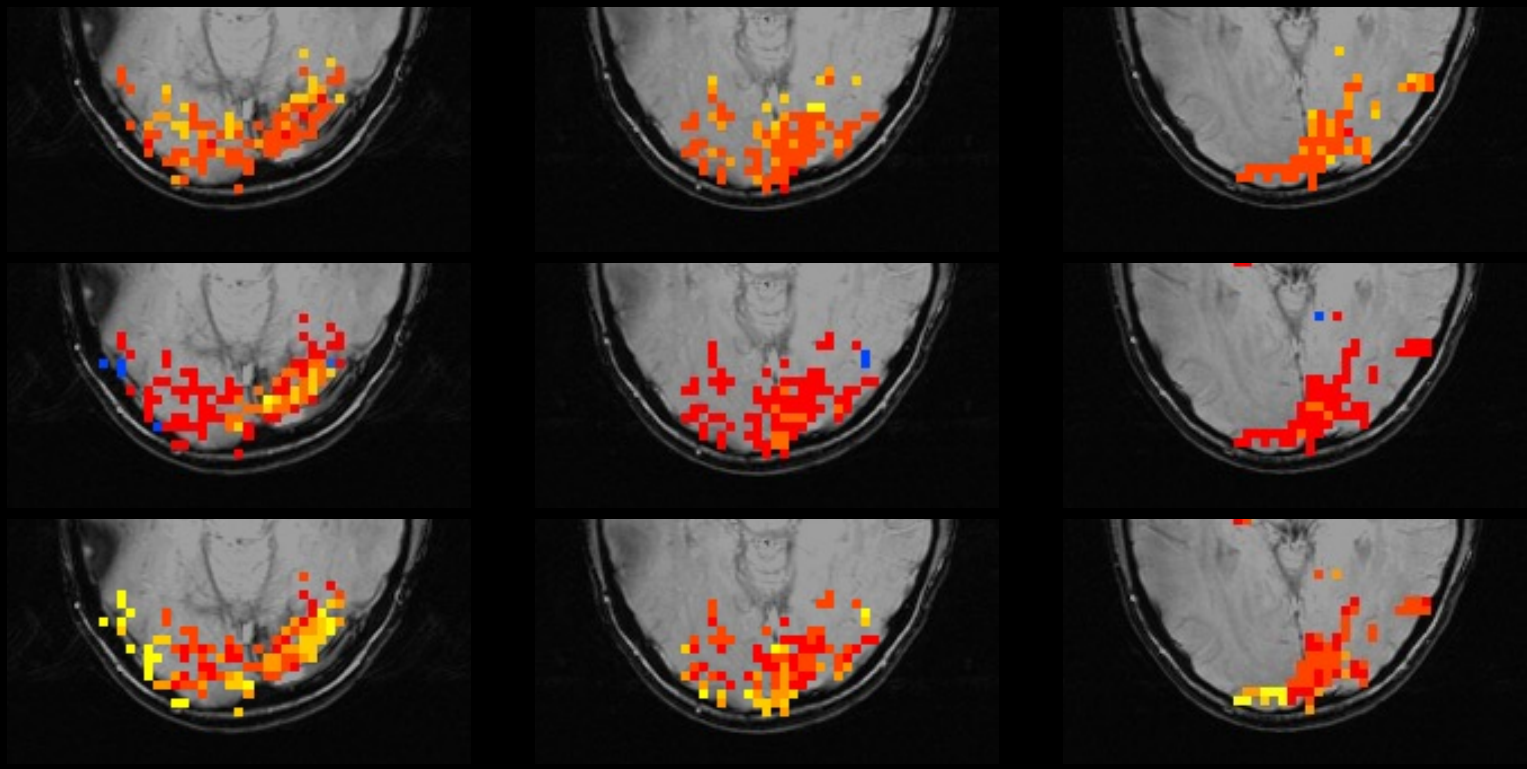
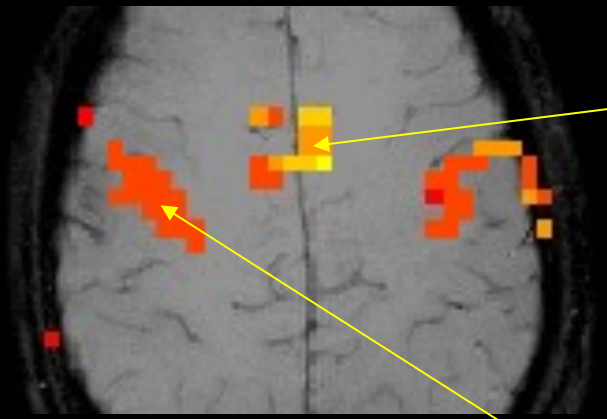
Nonlinearity

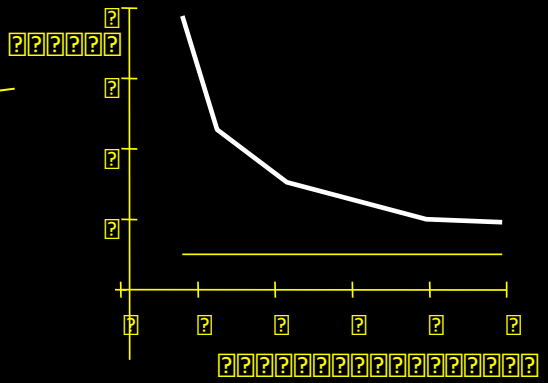
Magnitude

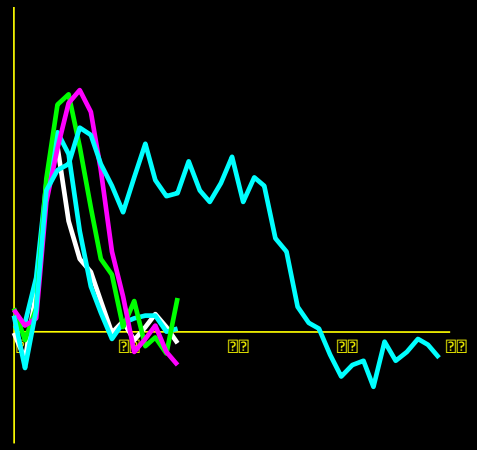
Latency

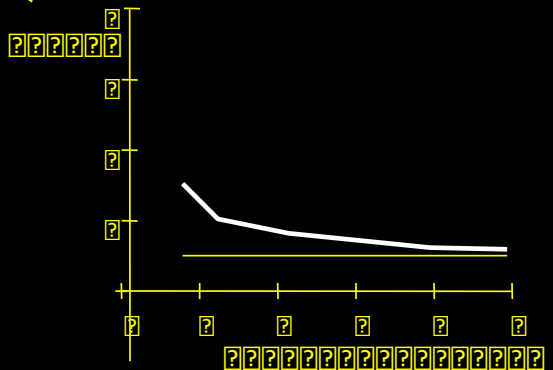


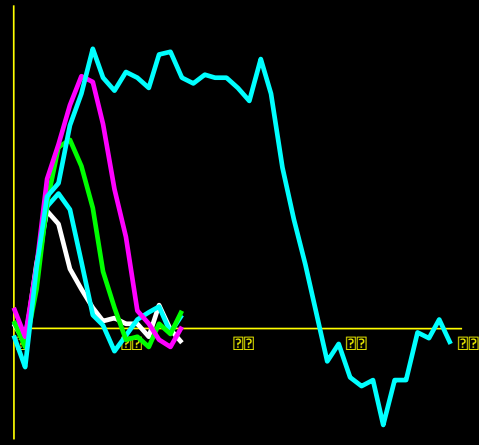
Results – motor task

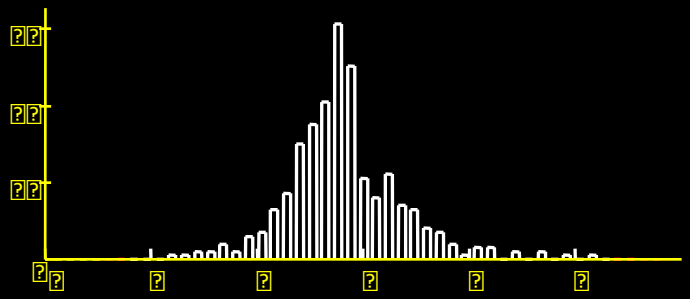












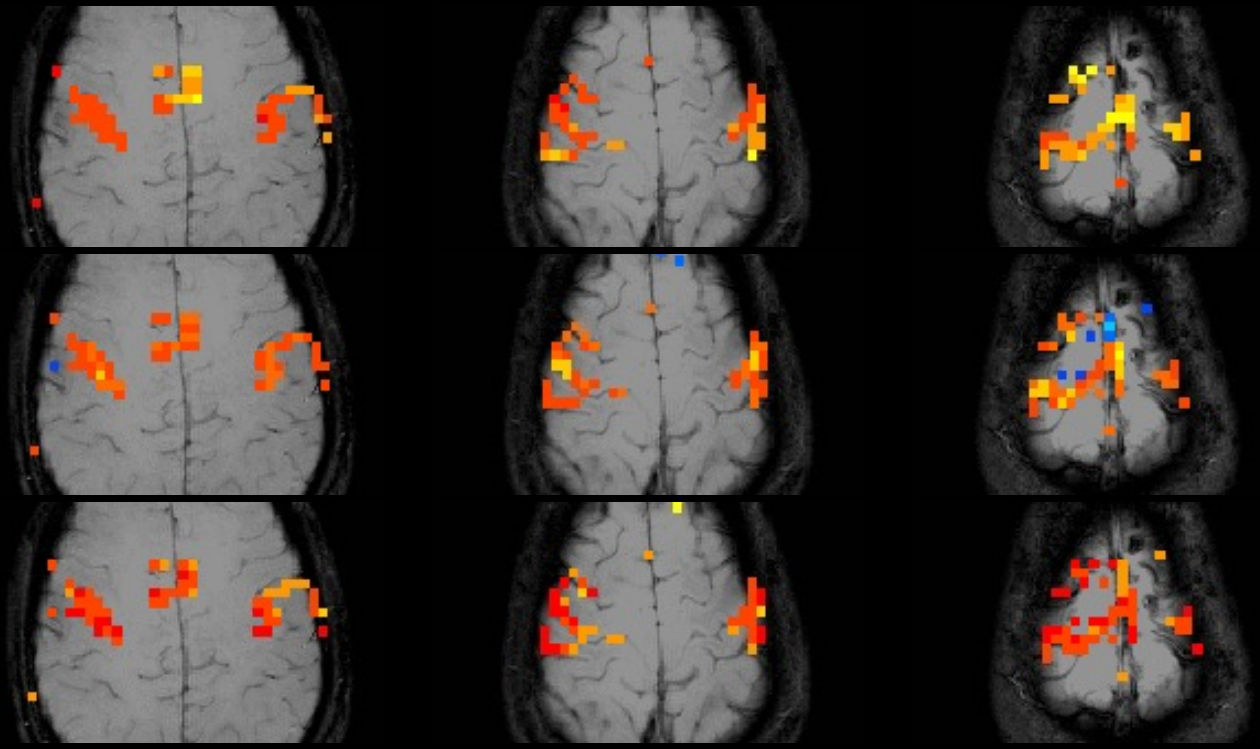
nonlinearity

????????????????????

Nonlinearity

Magnitude

Latency



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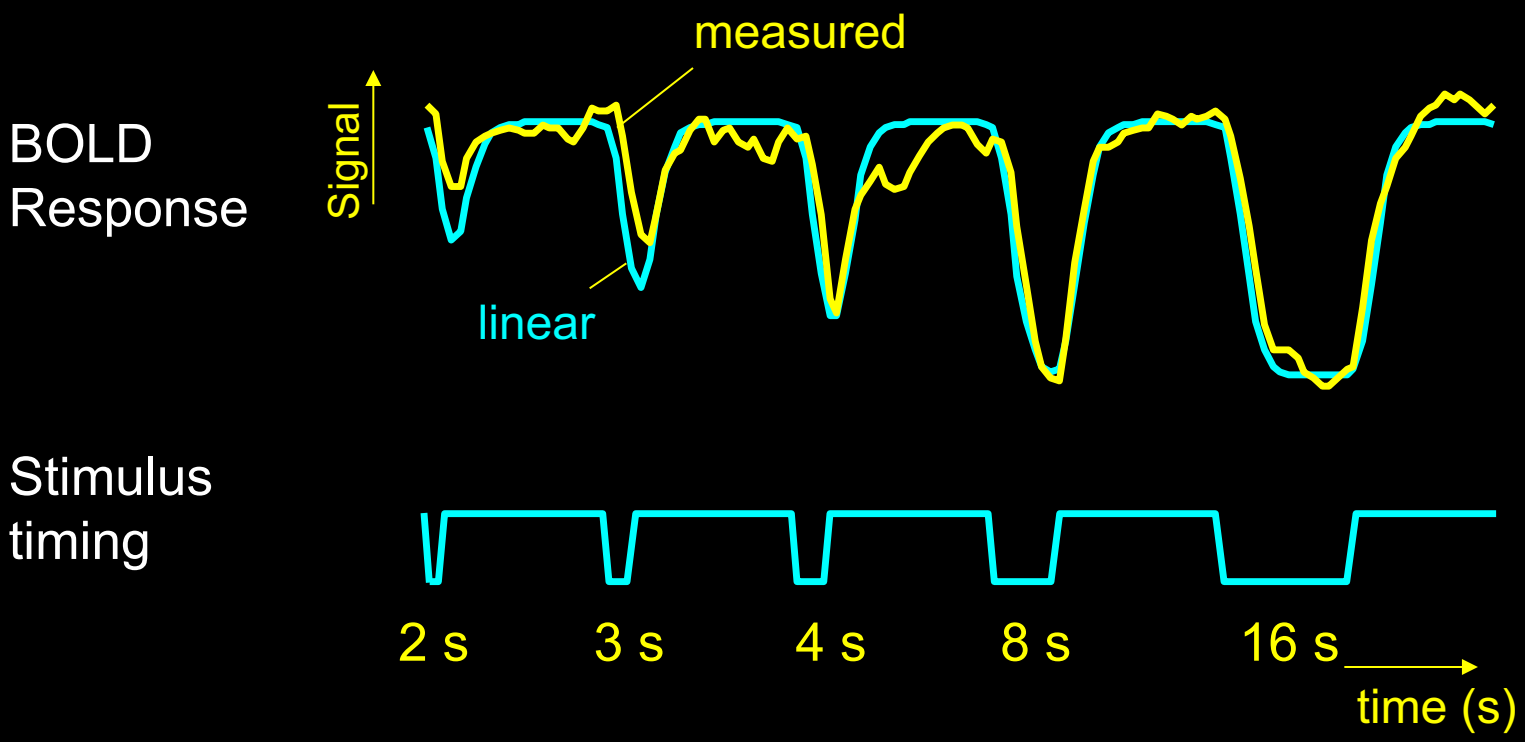
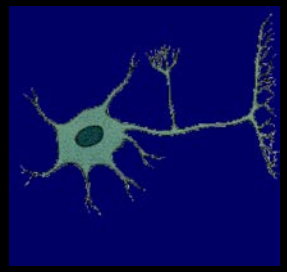
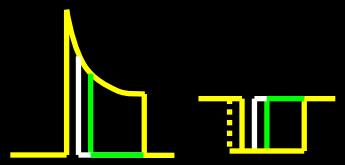


Brief stimulus OFF periods produce smaller decreases than expecte

??????????????????????????

- ????????





- ??????????

  - ??????????????????
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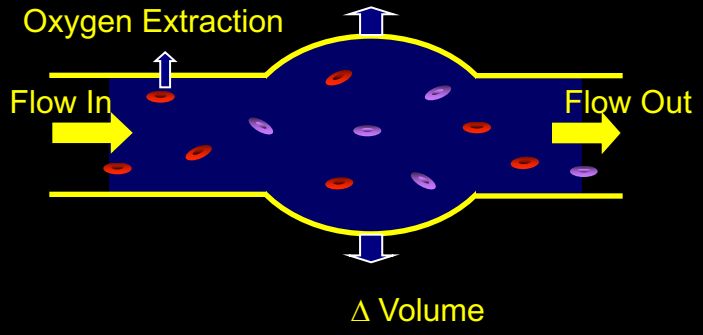
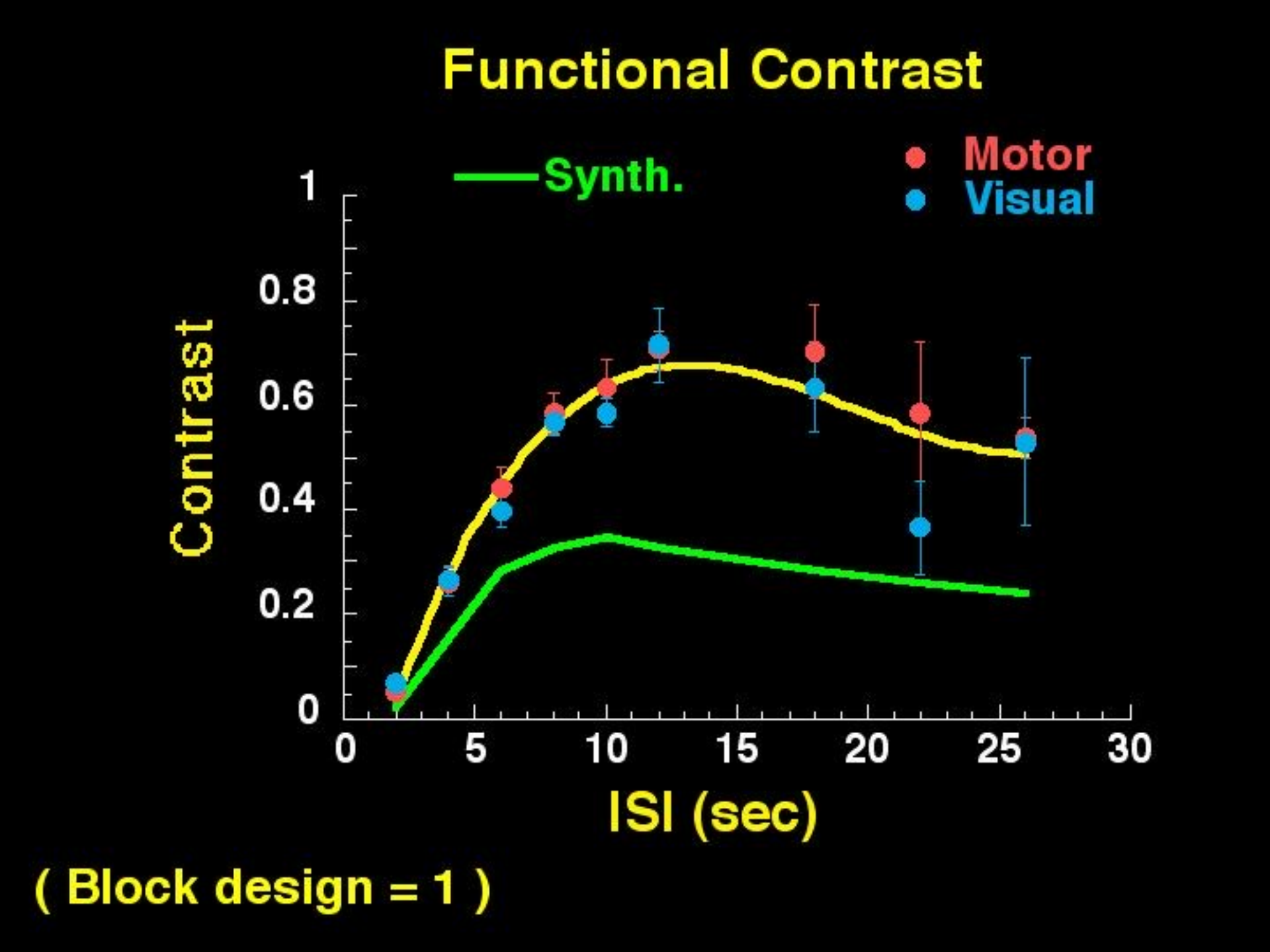
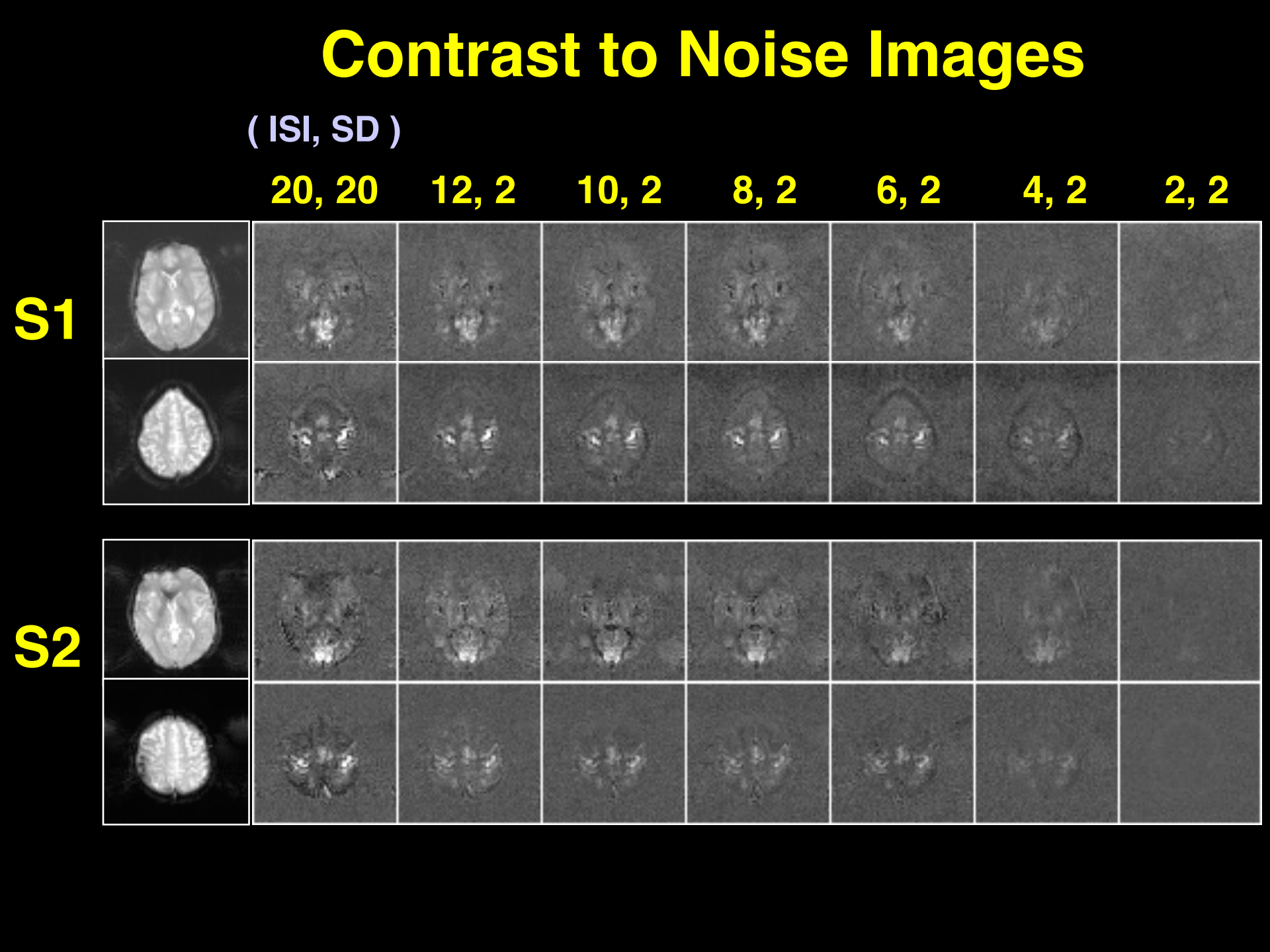

Oxygen Extraction
Flow In
Flow Out
Δ Volume


Functional Contrast
Synth.
Motor
Visual
Contrast
1
0.8
0.6
0.4
0.2
0
0
5
10
15
20
25
30
ISI (sec)
(Block design = 1)

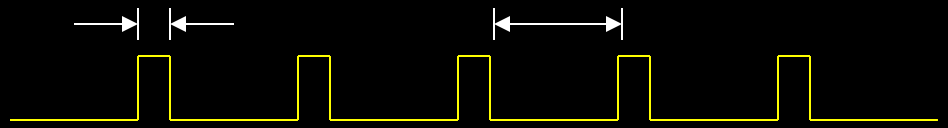
Contrast to Noise Images

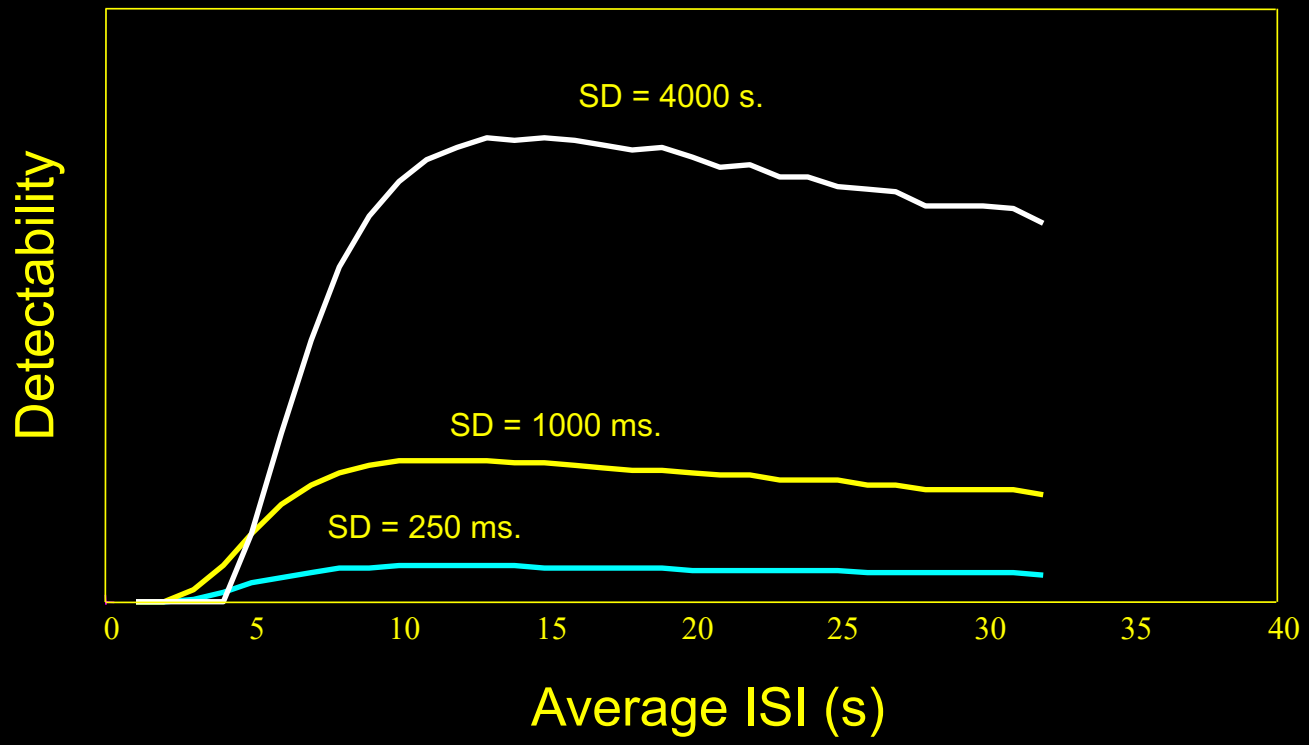


Detectability – constant ISI

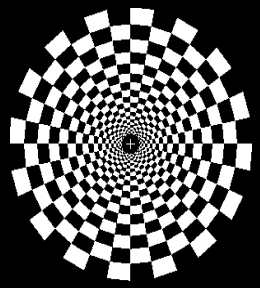
SD – stimulus duration

ISI – inter-stimulus interval

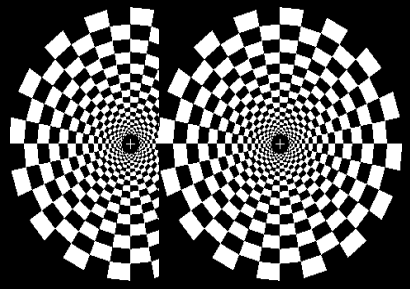




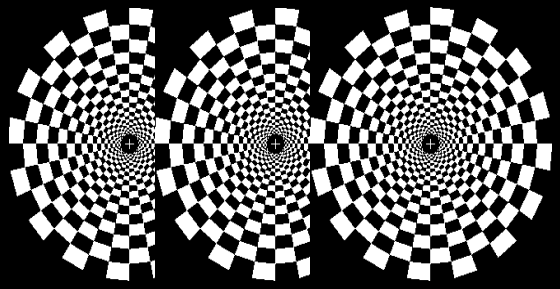
Visual Activation Paradigm: 1 , 2, & 3 Trials



0 sec 20 sec



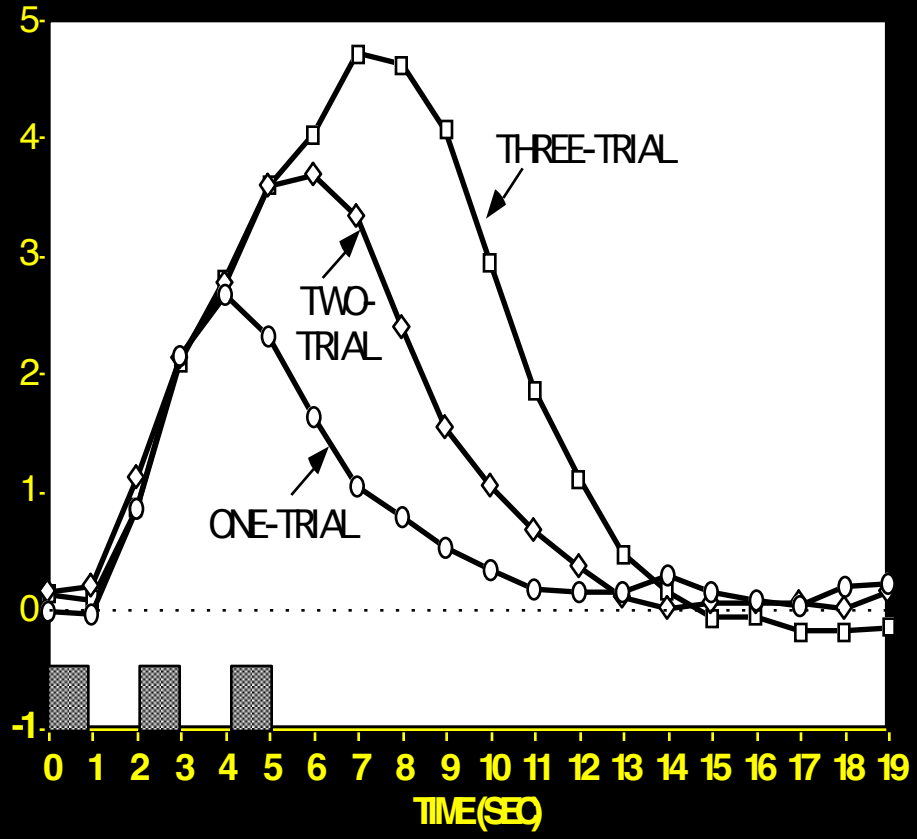
0 sec2 sec 20 sec



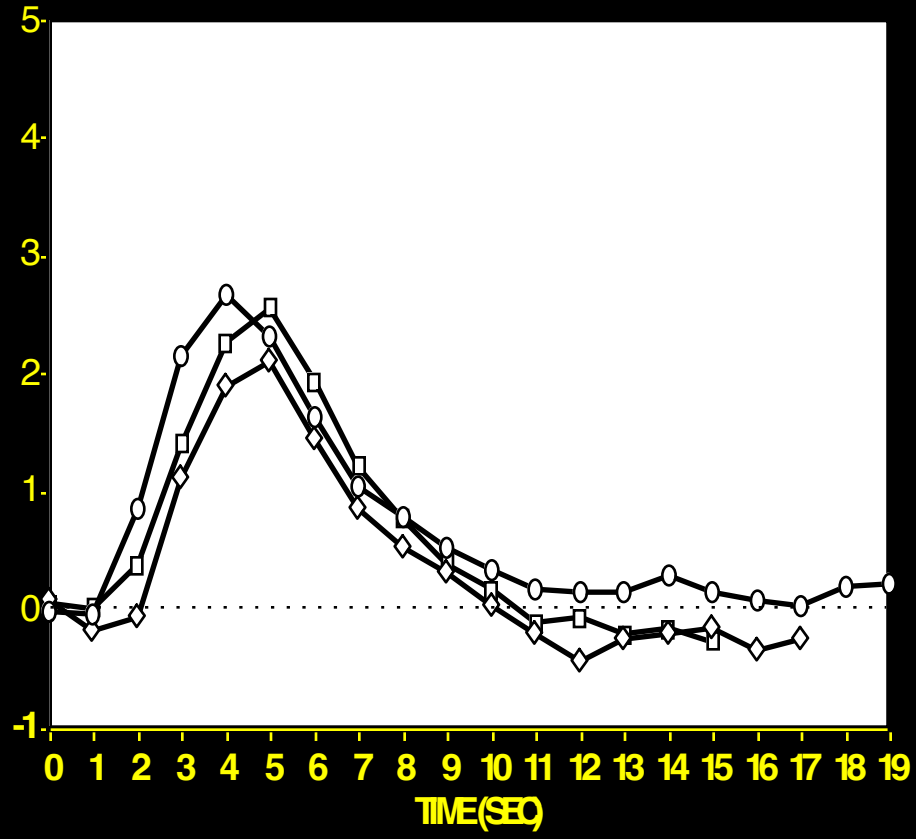
0 sec2 sec4 sec 20 sec

Response to Multiple Trials: Subject RW

RAW DATA



ESTIMATED RESPONSES



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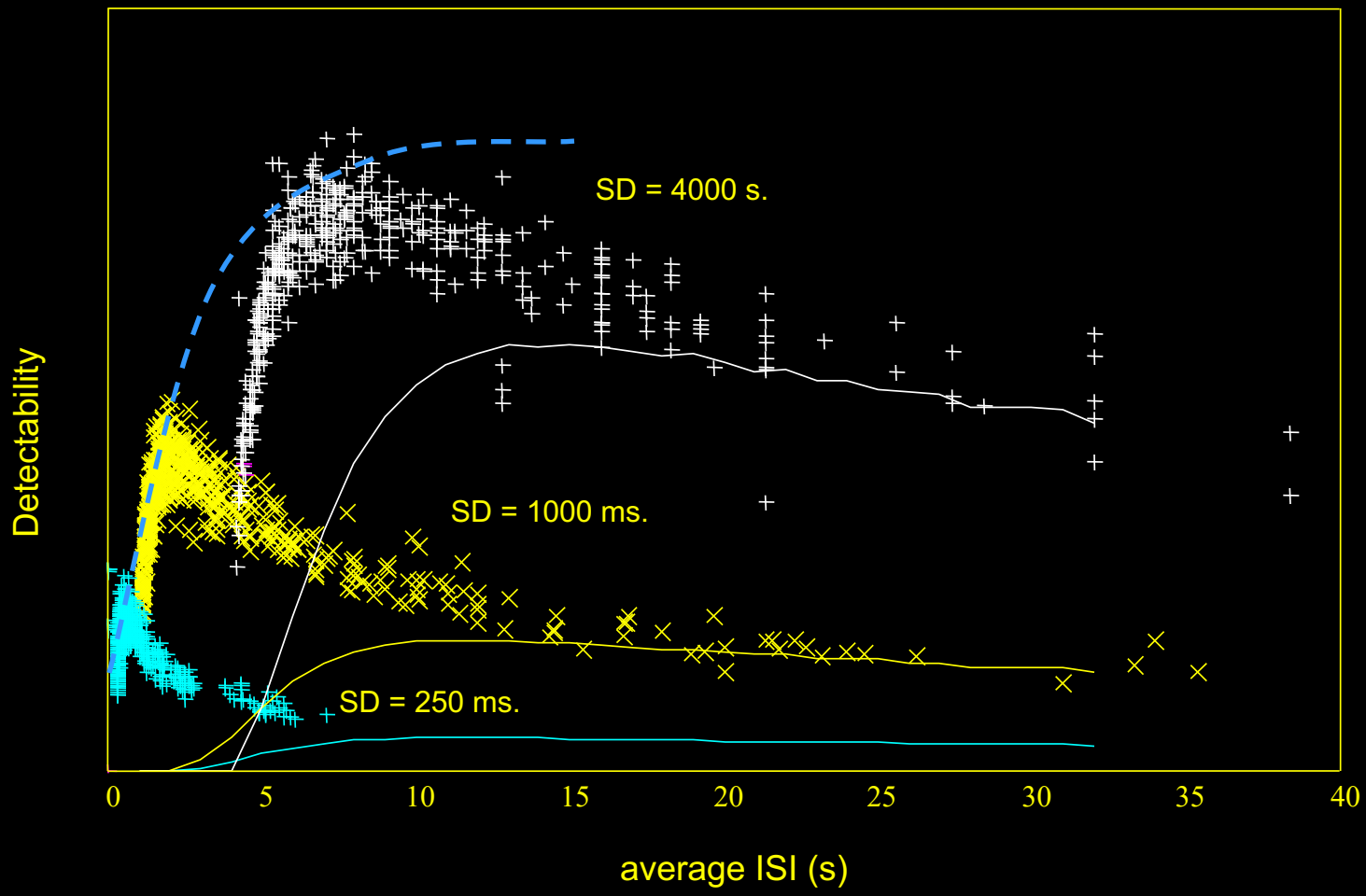
SD = 4000 s.
SD = 1000 ms.
SD = 250 ms.
Detectability
0
5
10
15
20
25
30
35
40
average ISI (s)

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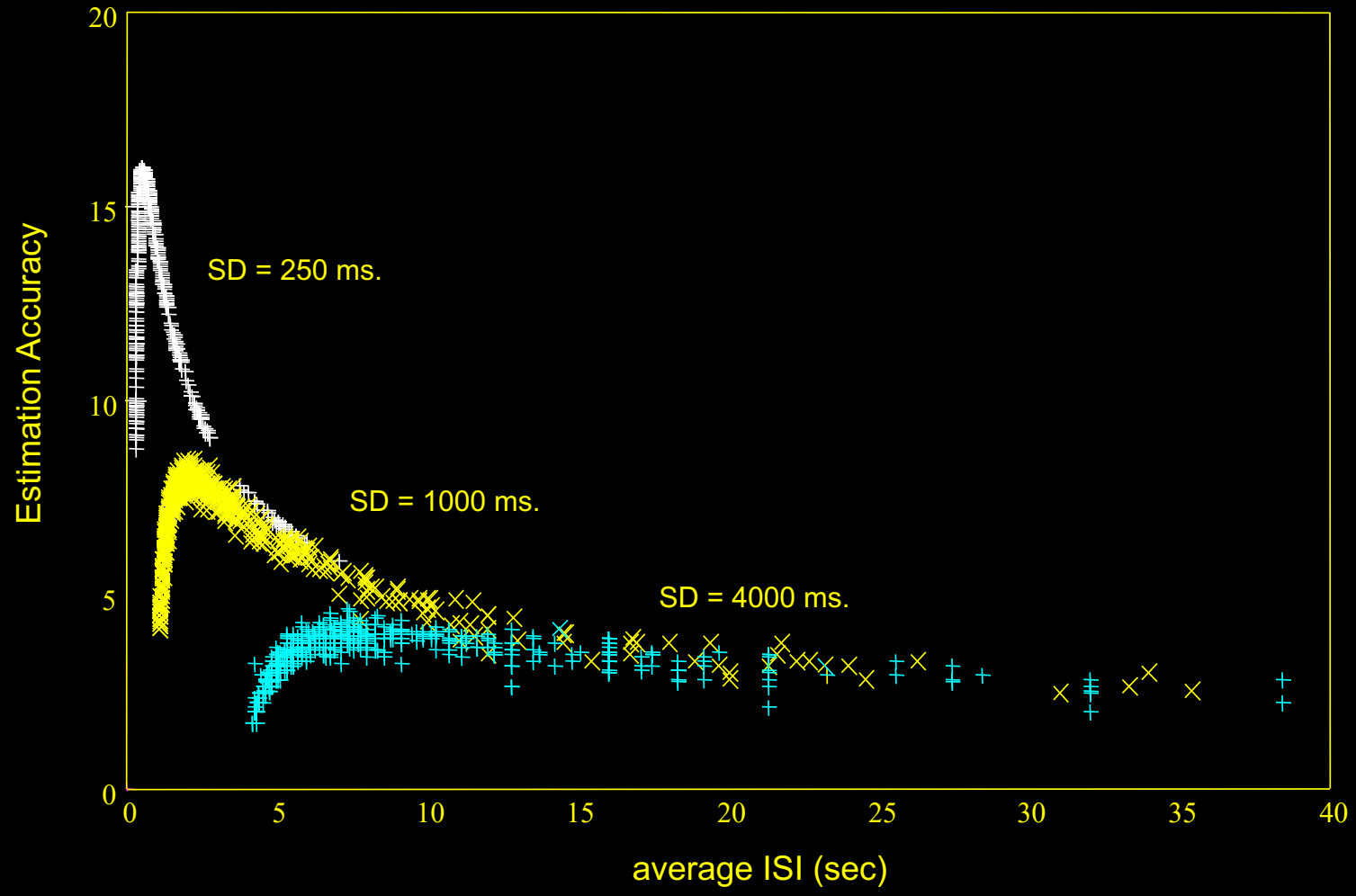
Estimation Accuracy
SD = 250 ms.
SD = 1000 ms.
SD = 4000 ms.
average ISI (sec)
0
5
10
15
20
25
30
35
40

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

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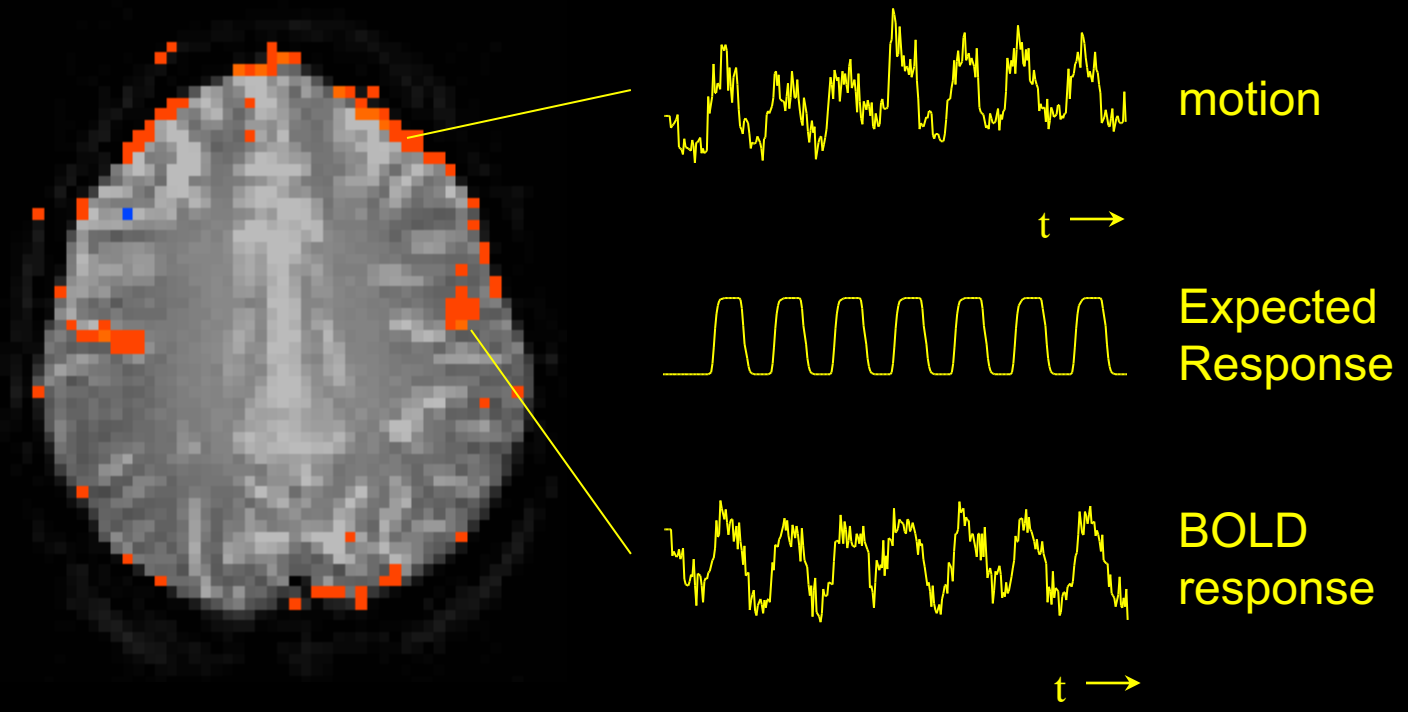
motion
t
Expected
Response
BOLD
response
t

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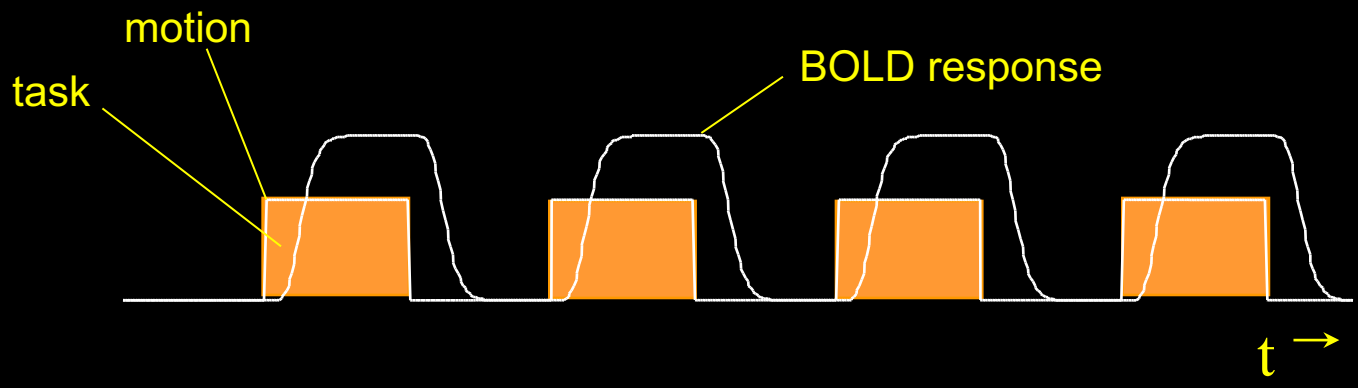
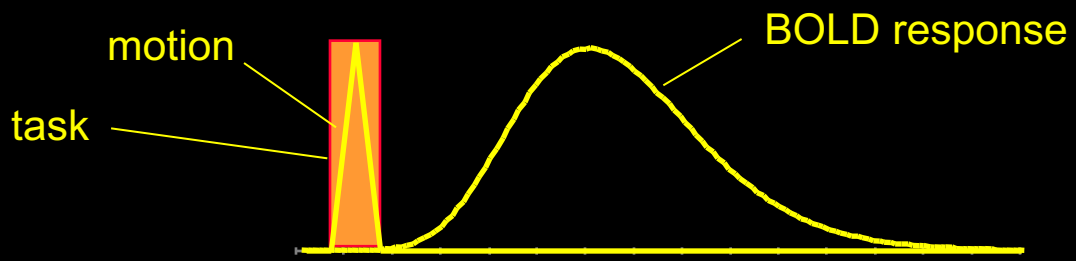
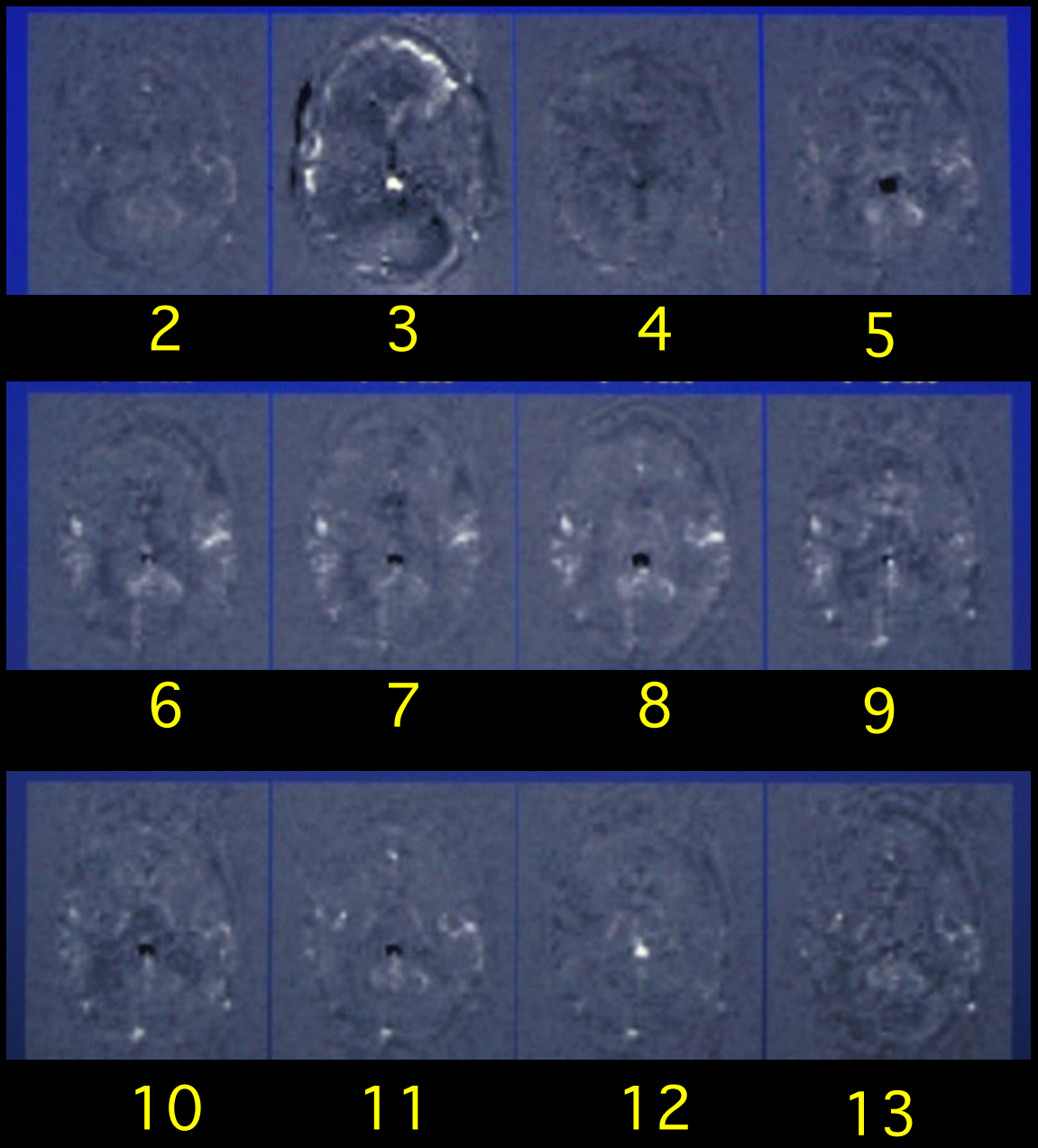
Blocked Design



Event-Related Design



Overt Word Production



Constant ISI

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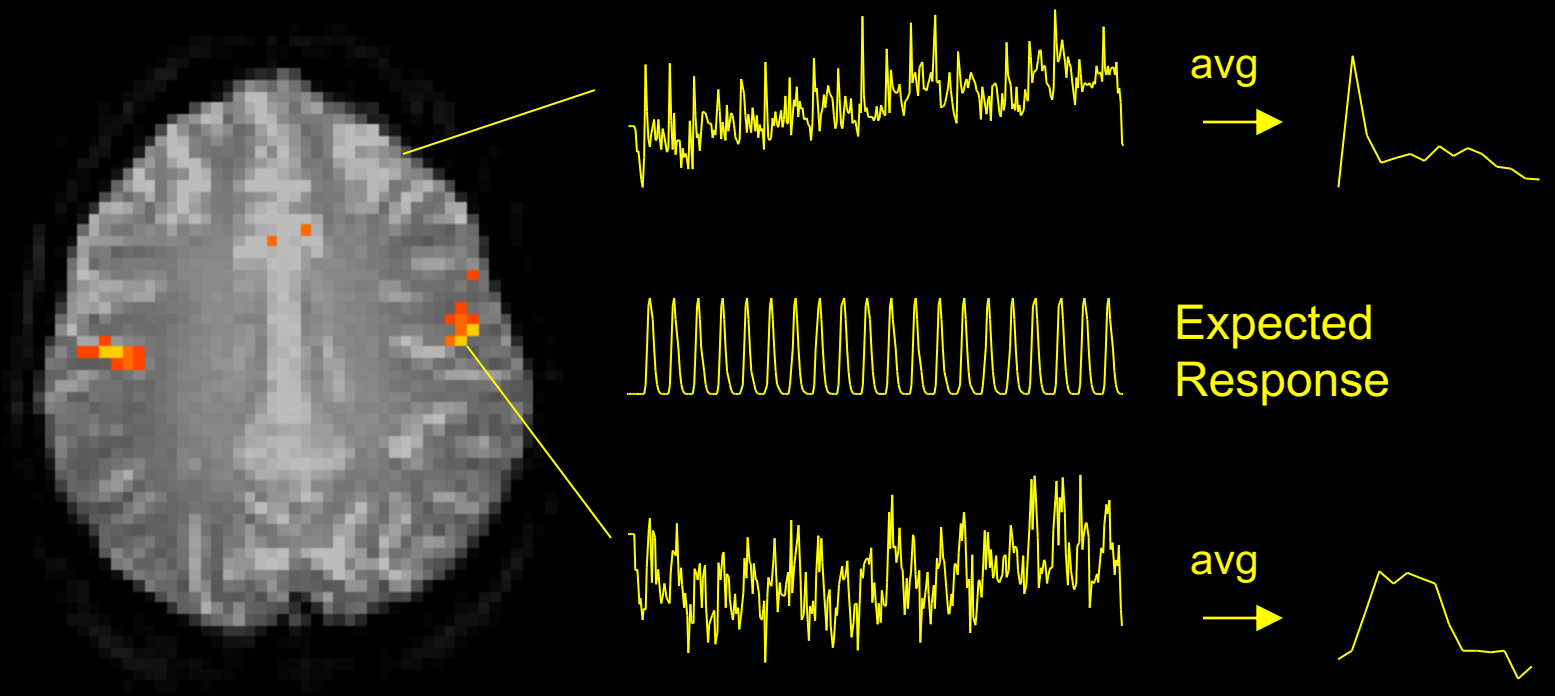

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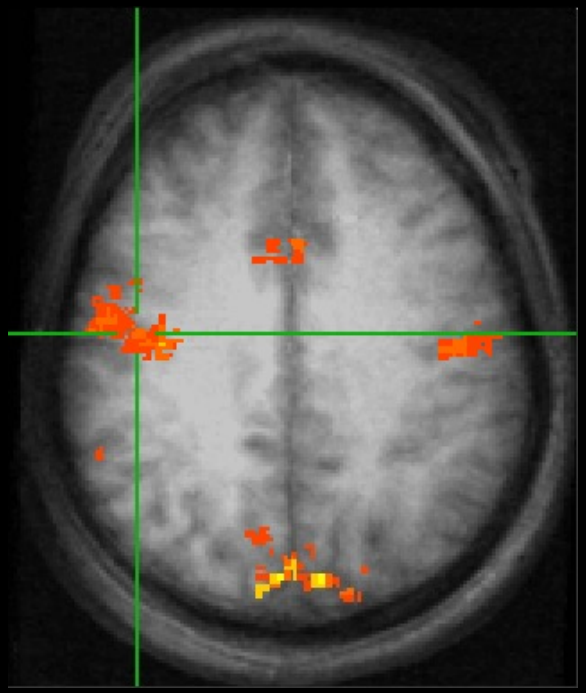
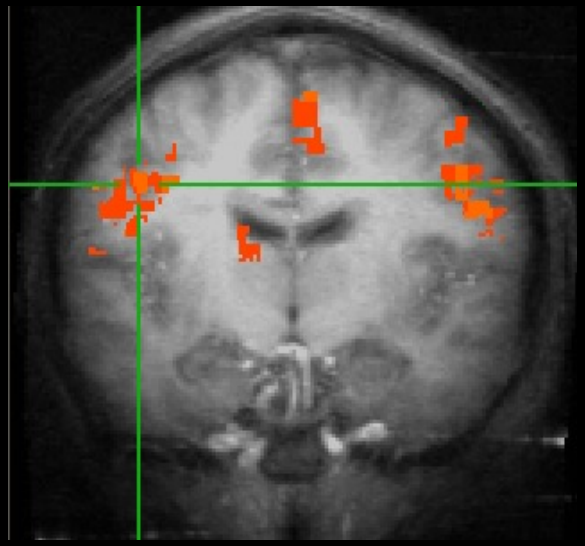
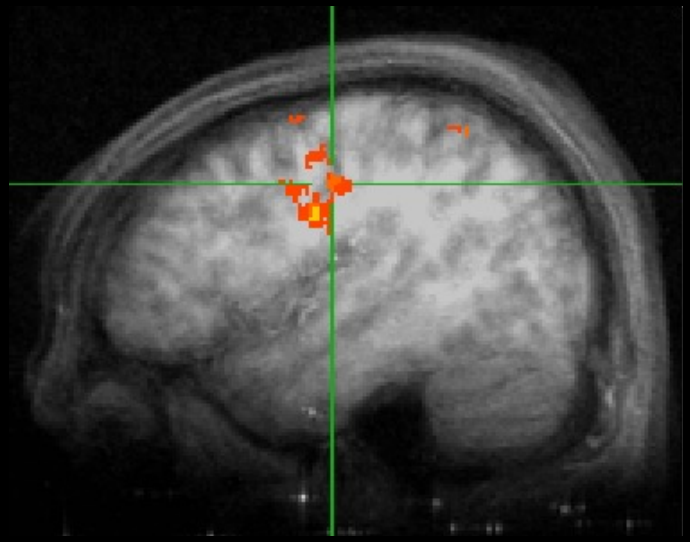
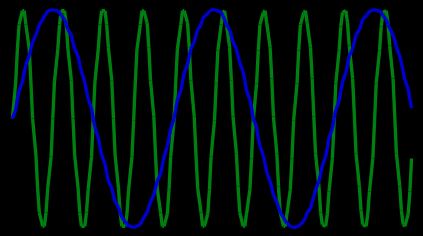


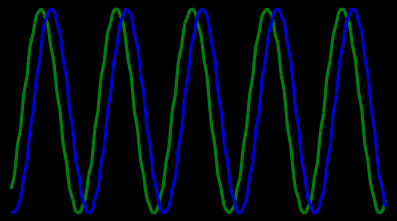


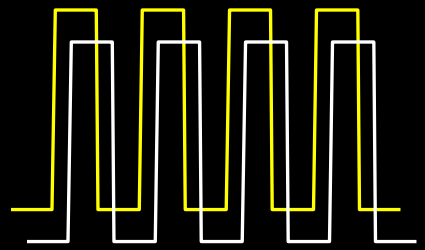


Neuronal Activation Input Strategies

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







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Nonselective Visual Stimulation

Faces & Houses vs Ctl. Stimuli

Face Stimuli vs House Stimuli

Memory delays vs. ctl. delays

Face WM delays vs House WM delays

Anticipatory delays vs ITIs

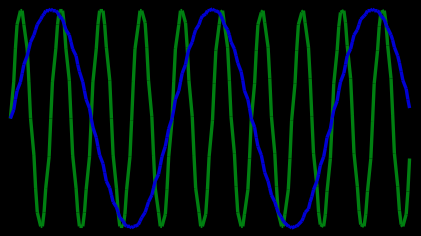
Encoding vs. Recognition

Ctl. Stim. vs. Ctl. Response

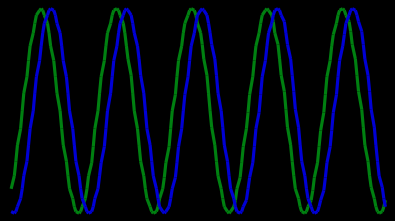
Neuronal Activation Input Strategies

1. Block Design

2. Frequency Encoding

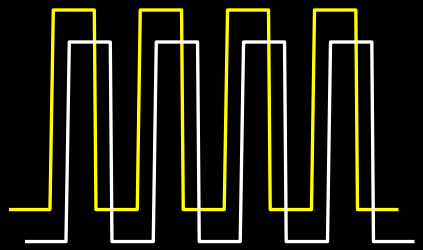


3. Phase Encoding



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

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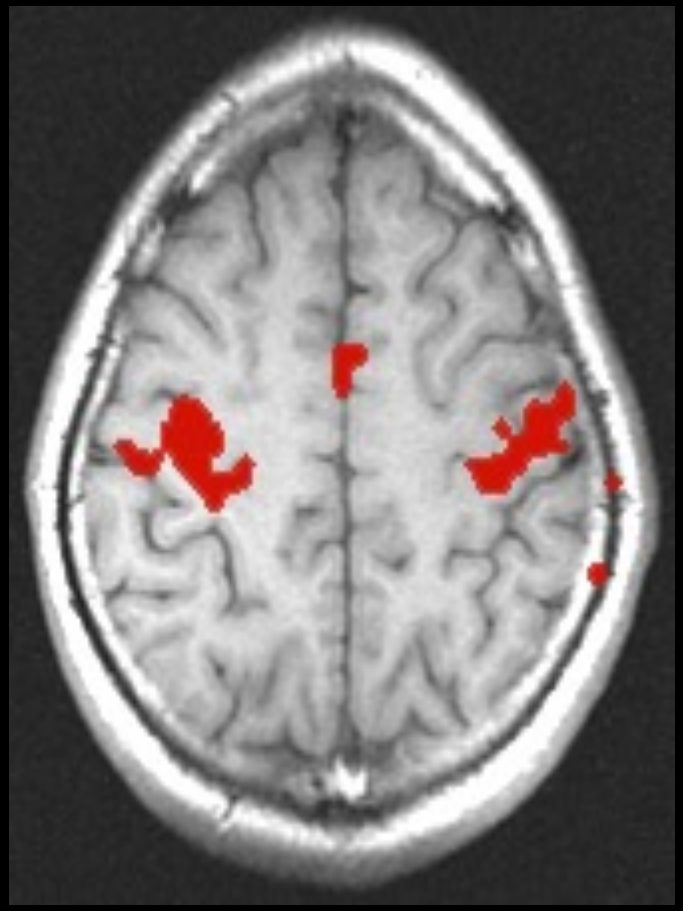

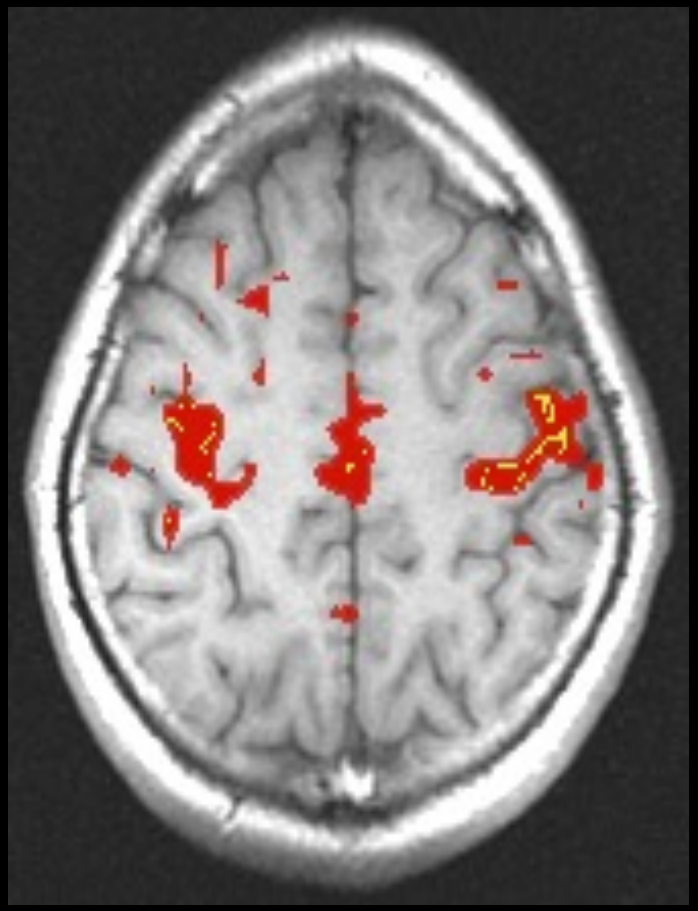

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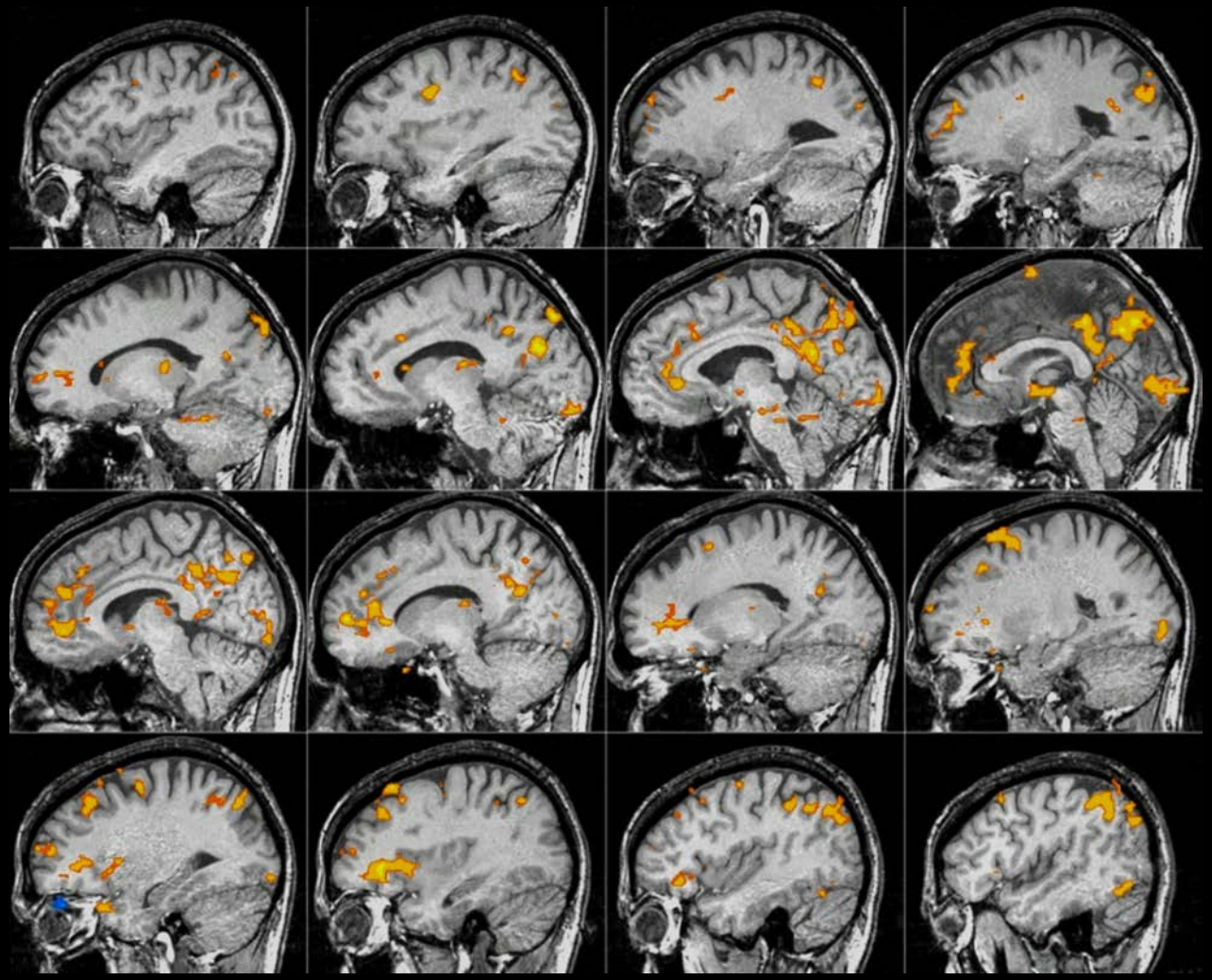

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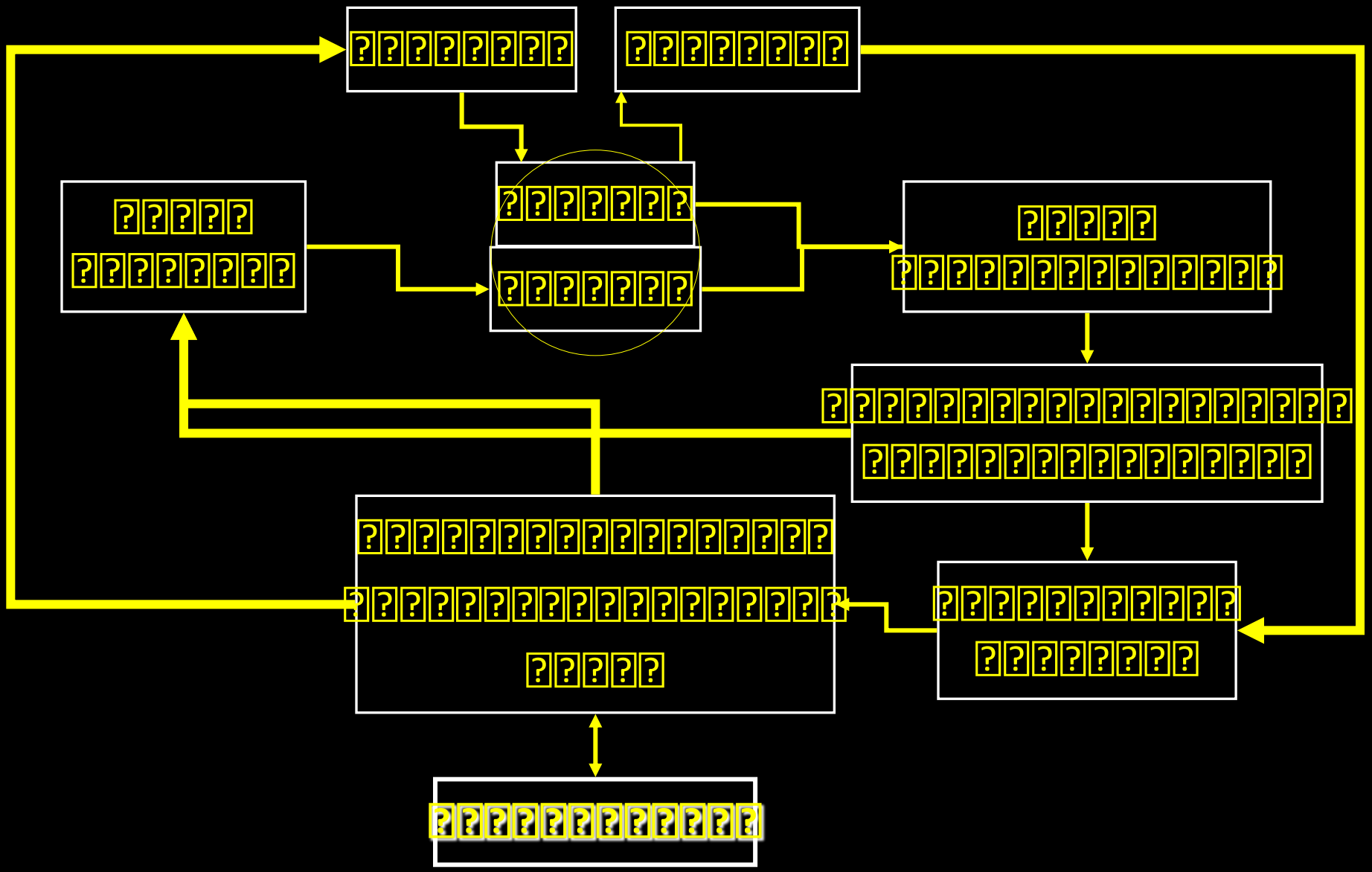
Processing Stream with Real Time fMRI



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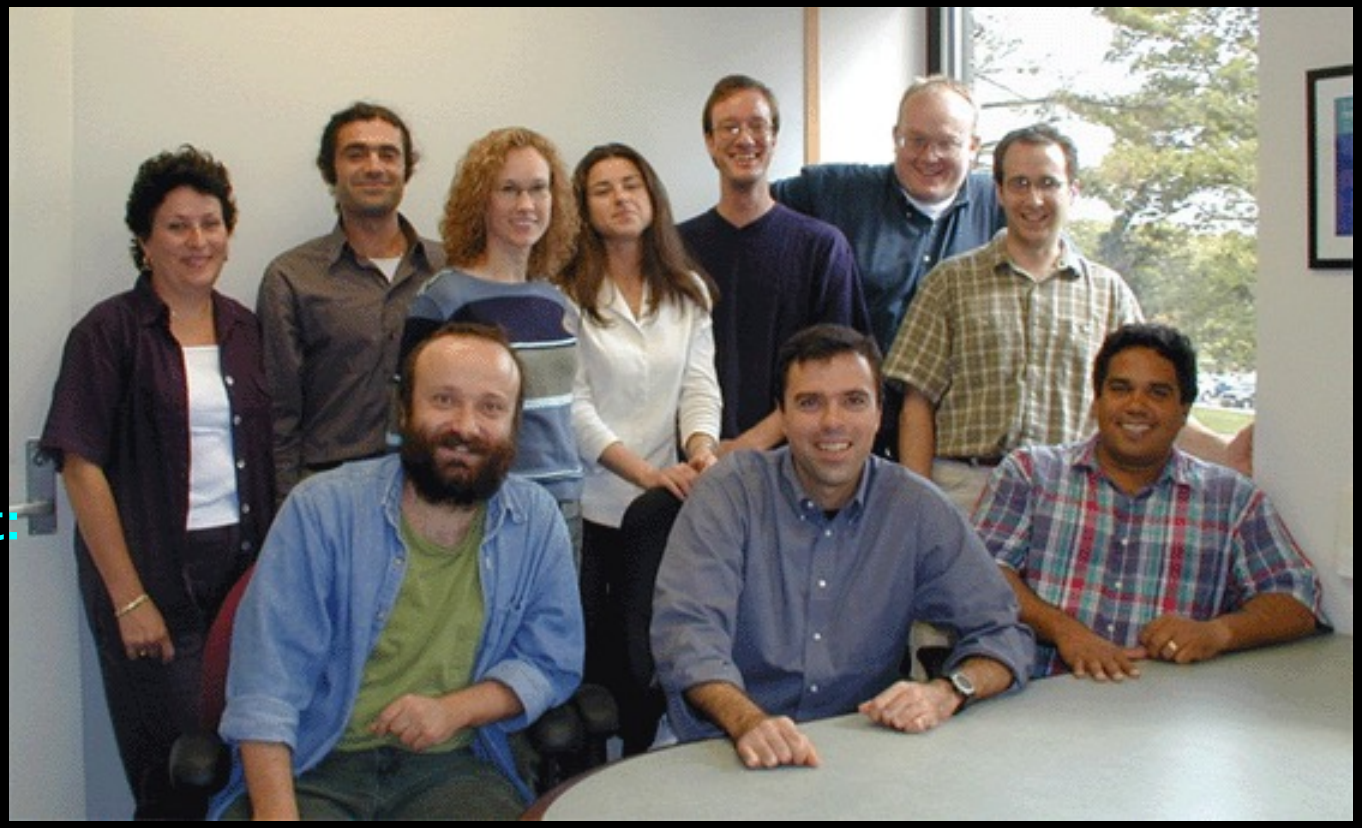

August, 2000

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