fMRI Contrast: How Much More Information Can We Obtain?

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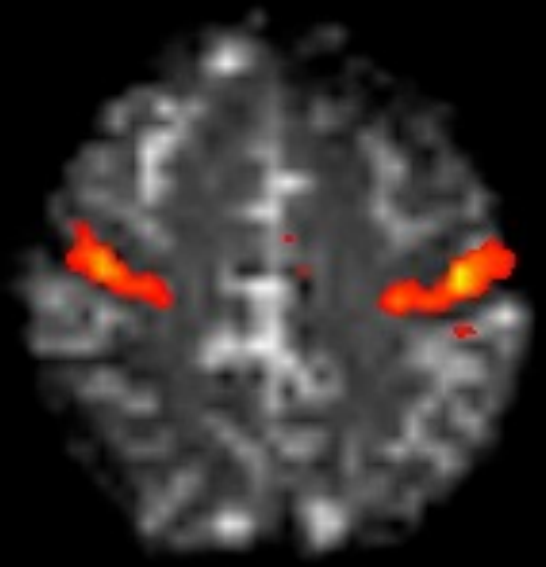
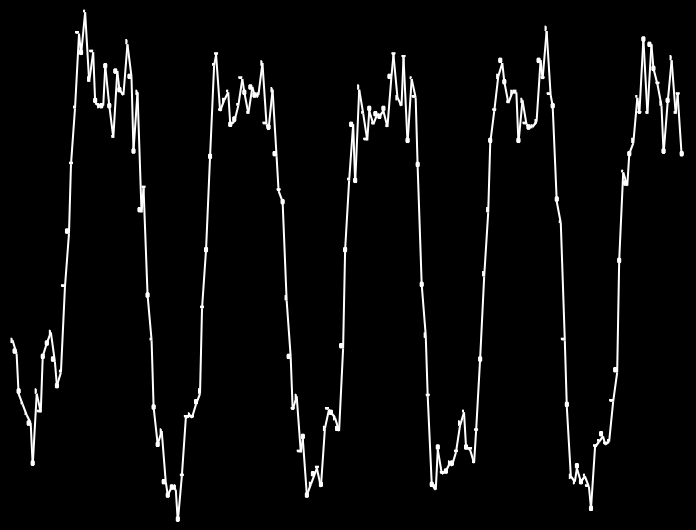
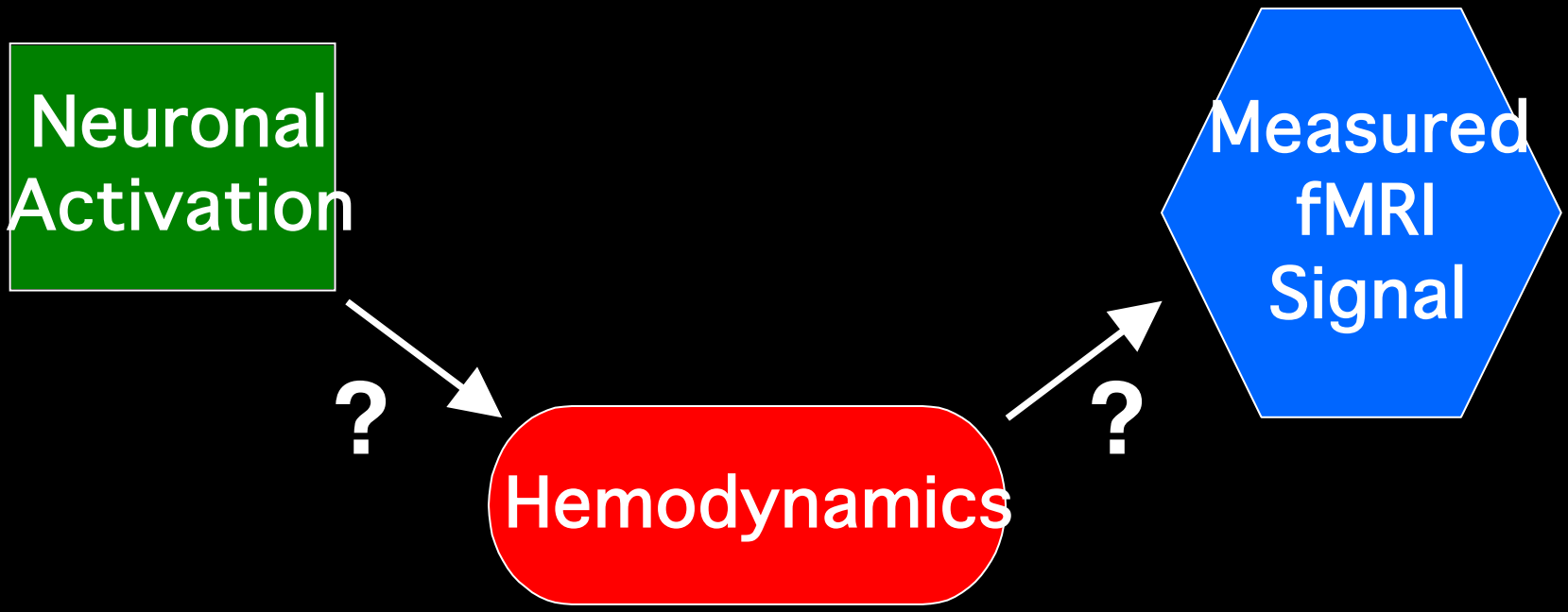
National Institute of Mental Health

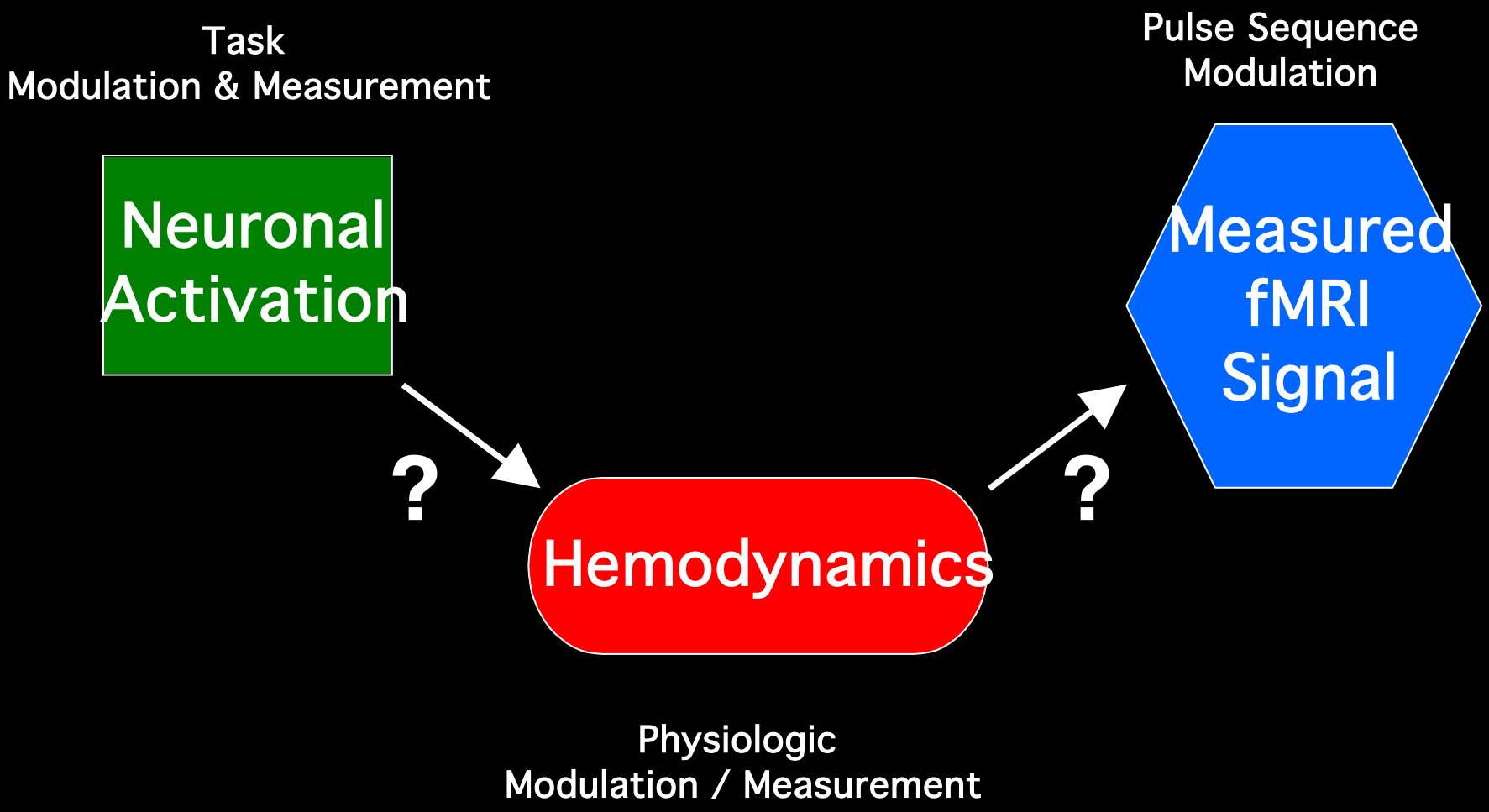
BOLD Contrast





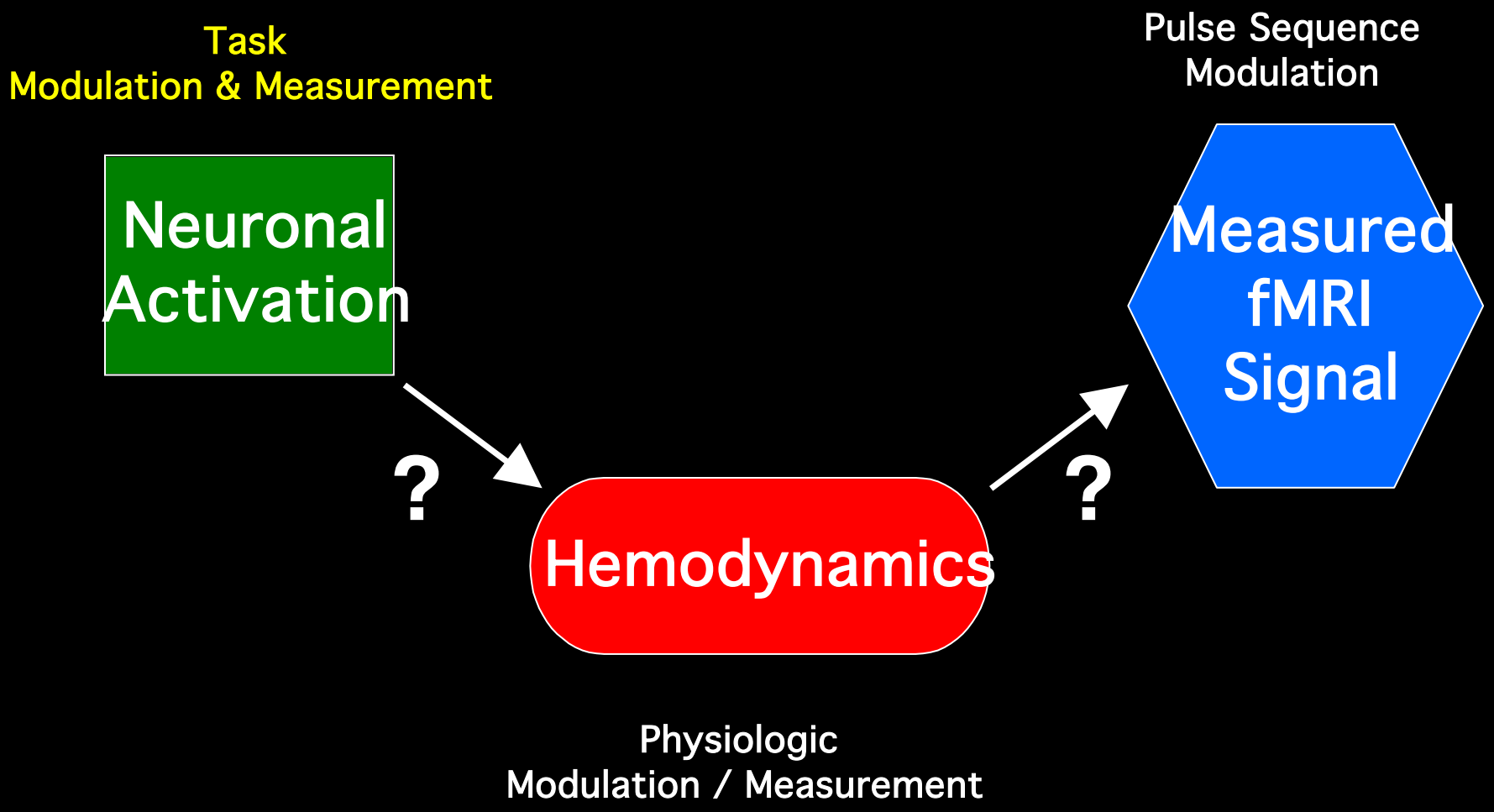


The continuing challenge is to make progressively more precise neuronal, metabolic, and hemodynamic inferences across spatial and temporal scales.


Task
Modulation & Measurement
Pulse Sequence
Modulation
Neuronal
Activation
Measured
fMRI
Signal
?
?
Hemodynamics
Physiologic
Modulation / Measurement

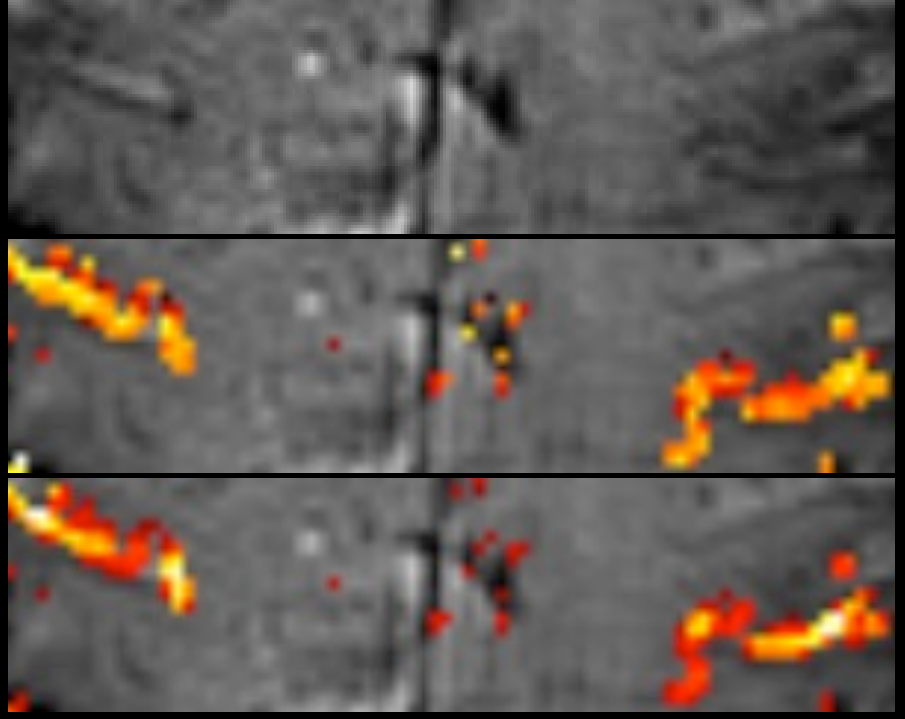
BOLD Contrast Advancements

1991- 2	•TE dependence •Field Strength Dependence •Resolution Dependence •Pulse sequence dependence (T2 and T2*) •Dynamics: latency and return to baseline •First BOLD models •Correlation of BOLD with parametric task manipulation
1992- 3	•Post undershoot •NMR phase shift observation •Angio and venogram correlation
1993- 4	•Effects of Physiologic Stress •Retinotopy •Cognitive mapping
1994 - 5	•Event - related fMRI •Parametric task design •Sub-millimeter resolution fMRI
1995 - 6	•Diffusion weighting dependence (IV contribution) •Physiologic fluctuations
1996 - 7	•Extended duration stimulation effects •Pre undershoot
1997- 8	•Flow and BOLD comparisons (dynamics and magnitude) •Blood volume dynamics •Simultaneous flow and BOLD acquisition
1998 - 9	•Ocular Dominance Column Mapping •$CMRO_2$ Mapping •Randomized ER-fMRI task design •Balloon Model
1999 - 2000	•Baseline Blood Oxygenation Quantitation •Mental Chronomitry •Linearity of BOLD signal change


Task
Modulation & Measurement
Neuronal Activation
?
Hemodynamics
?
Pulse Sequence
Modulation
Measured fMRI Signal
Physiologic
Modulation / Measurement

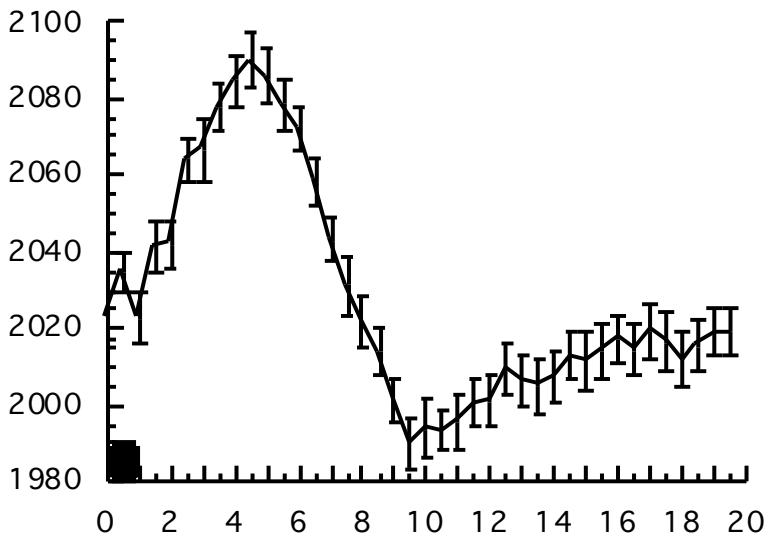
Latency

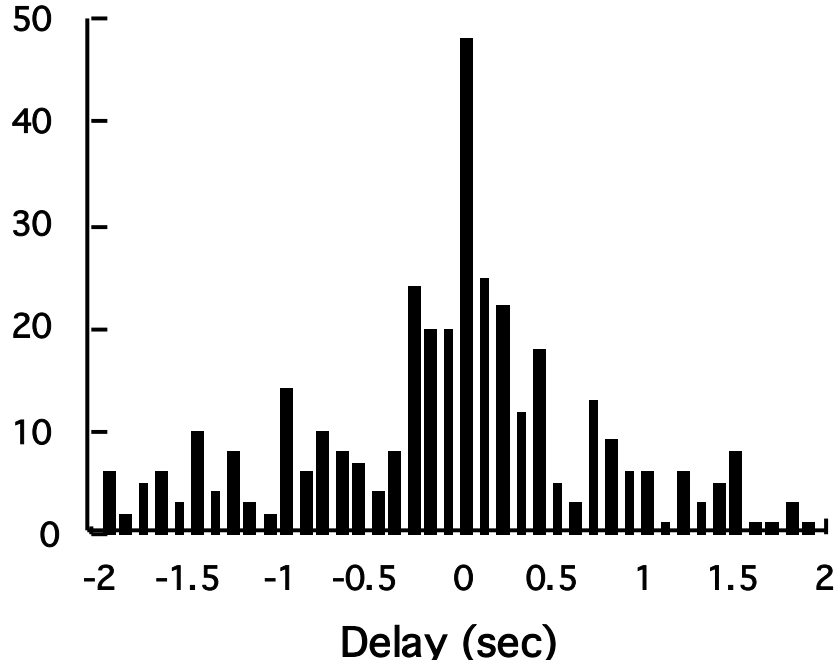
Magnitude

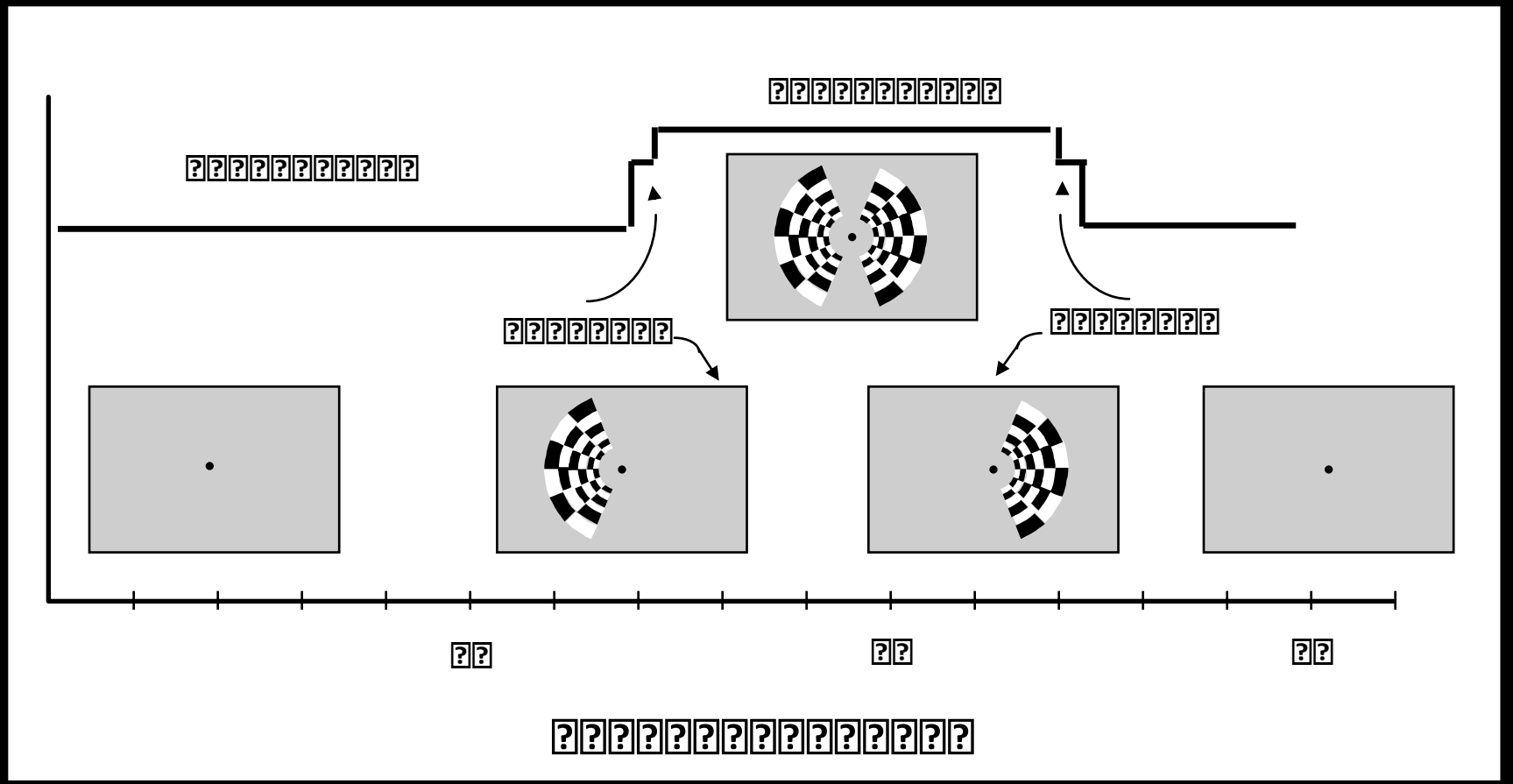


+ 2 sec

- 2 sec







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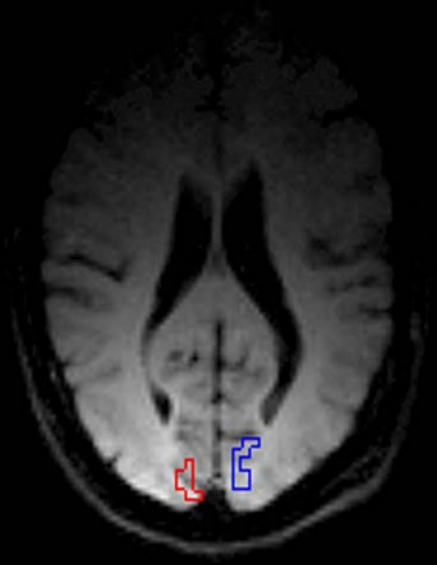
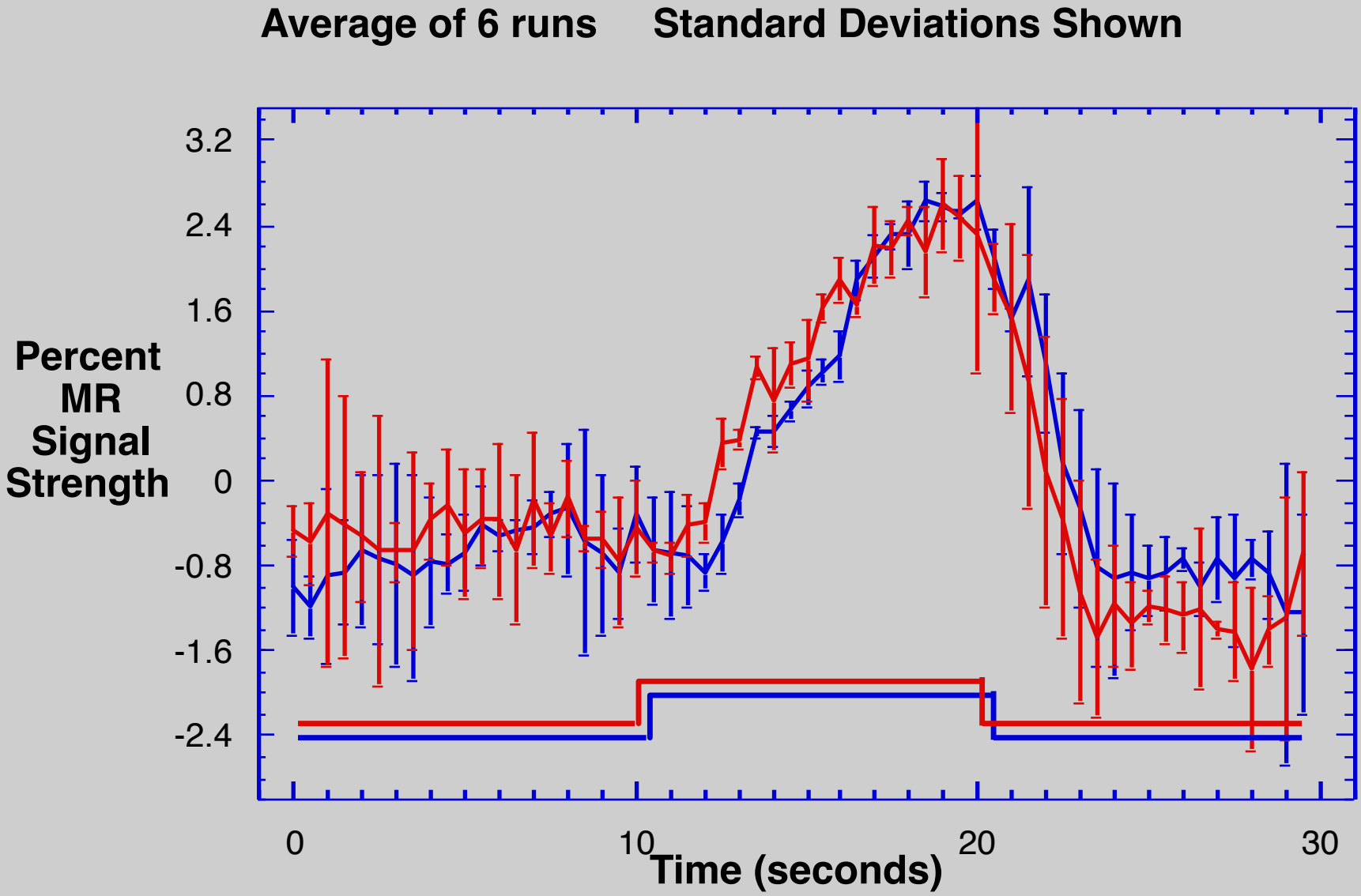
Regions of Interest Used for Hemi-Field Experiment

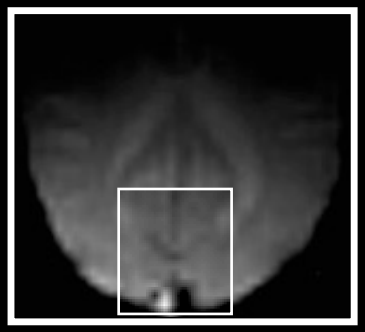


Right Hemisphere

Left Hemisphere

Hemi-field with 500 msec asynchrony





500 ms

500 ms

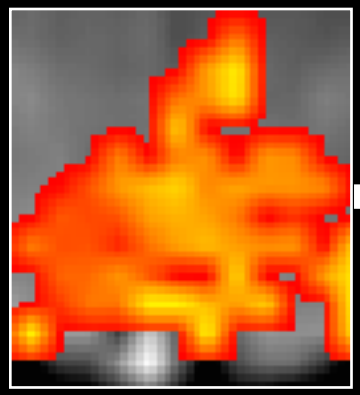
Right Hemifield

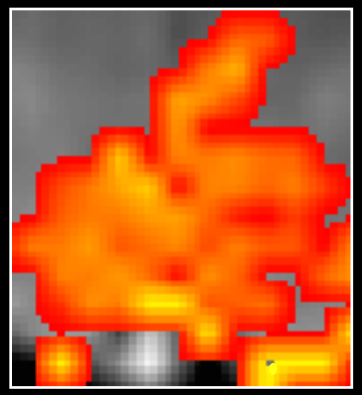
Left Hemifield

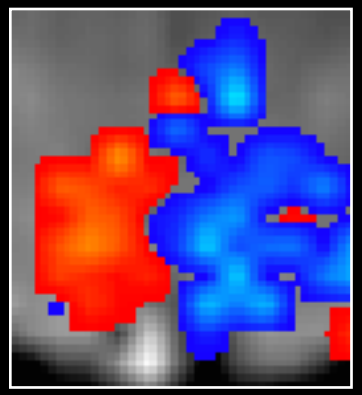
+ 2.5 s

0 s

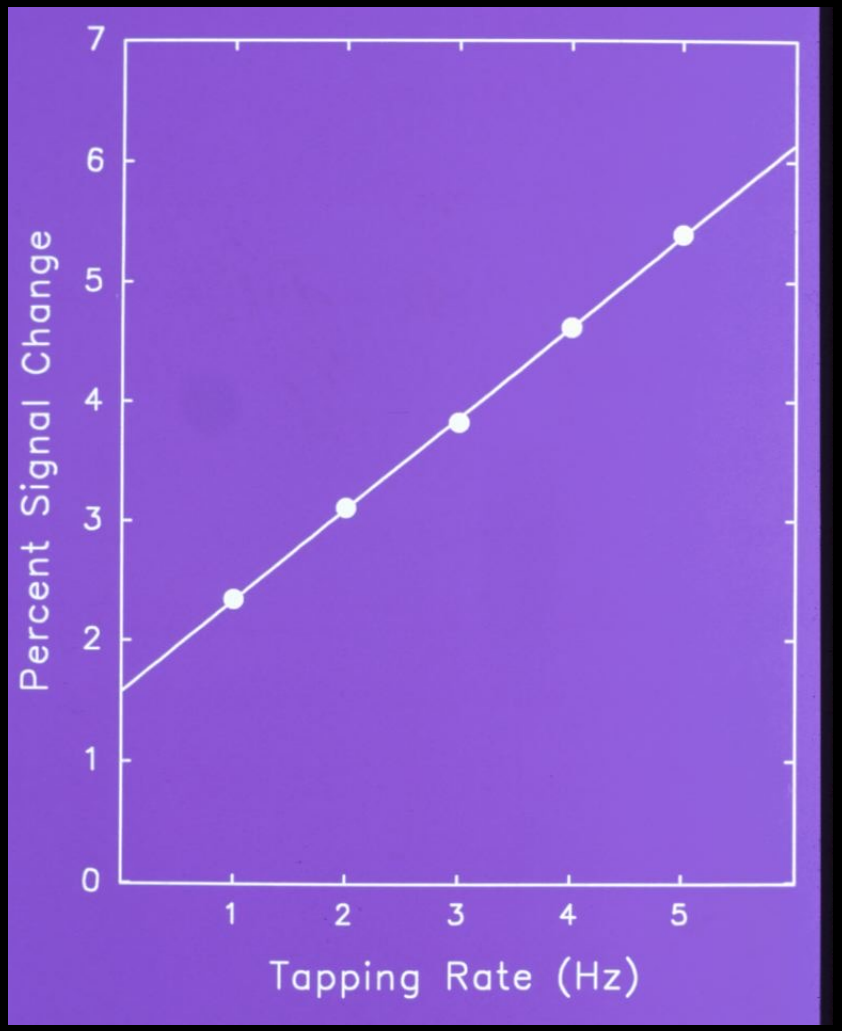
- 2.5 s



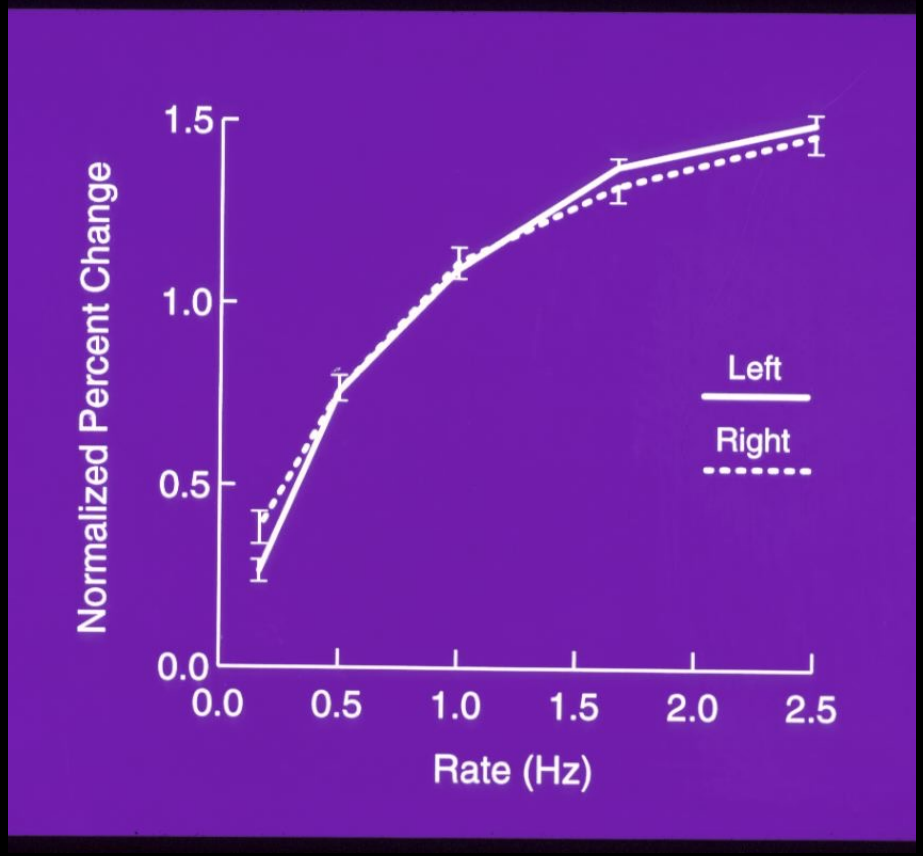


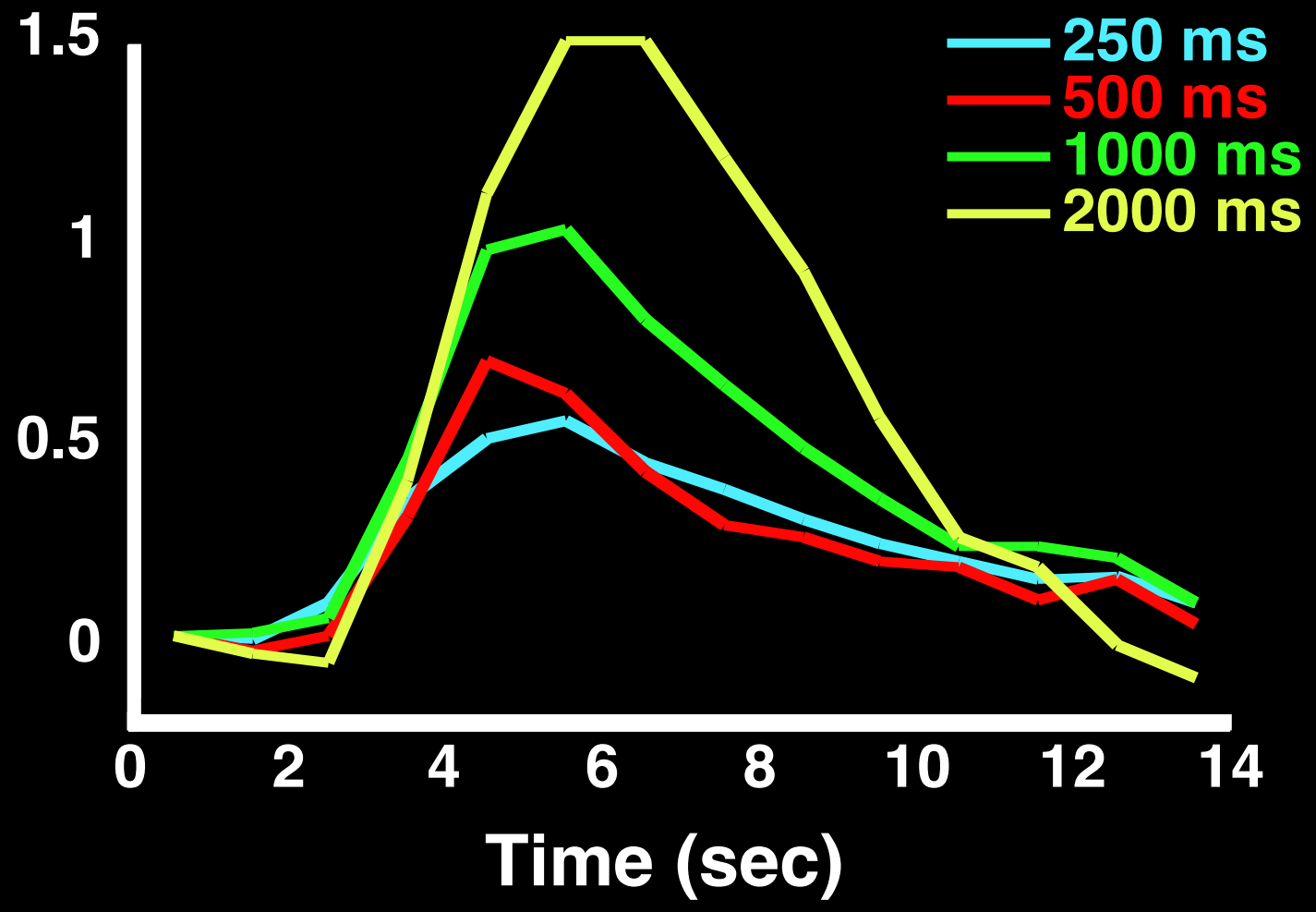


Motor Cortex

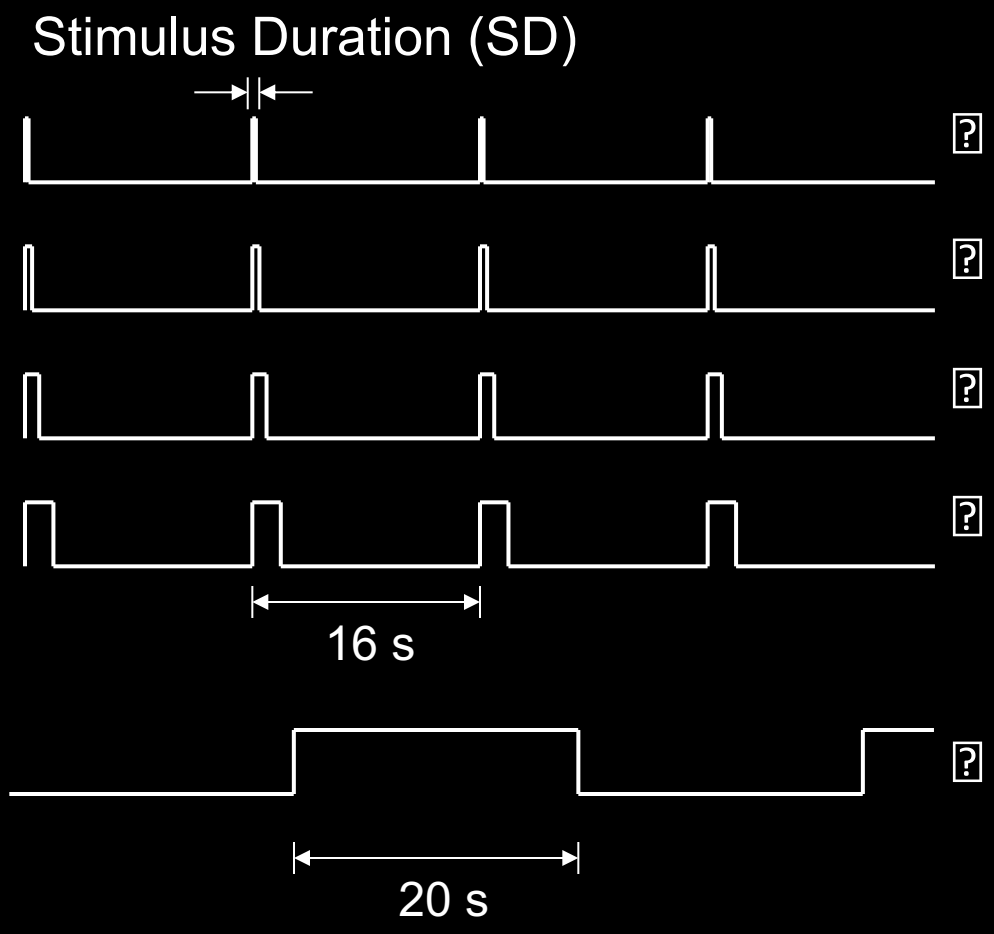


Auditory Cortex




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

Methods



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SD = 250 ms SD = 500 ms

SD = 500 ms SD = 1000 ms

SD = 1000 ms SD = 2000 ms

SD = 2000 ms SD = 4000 ms

Blocked Trial

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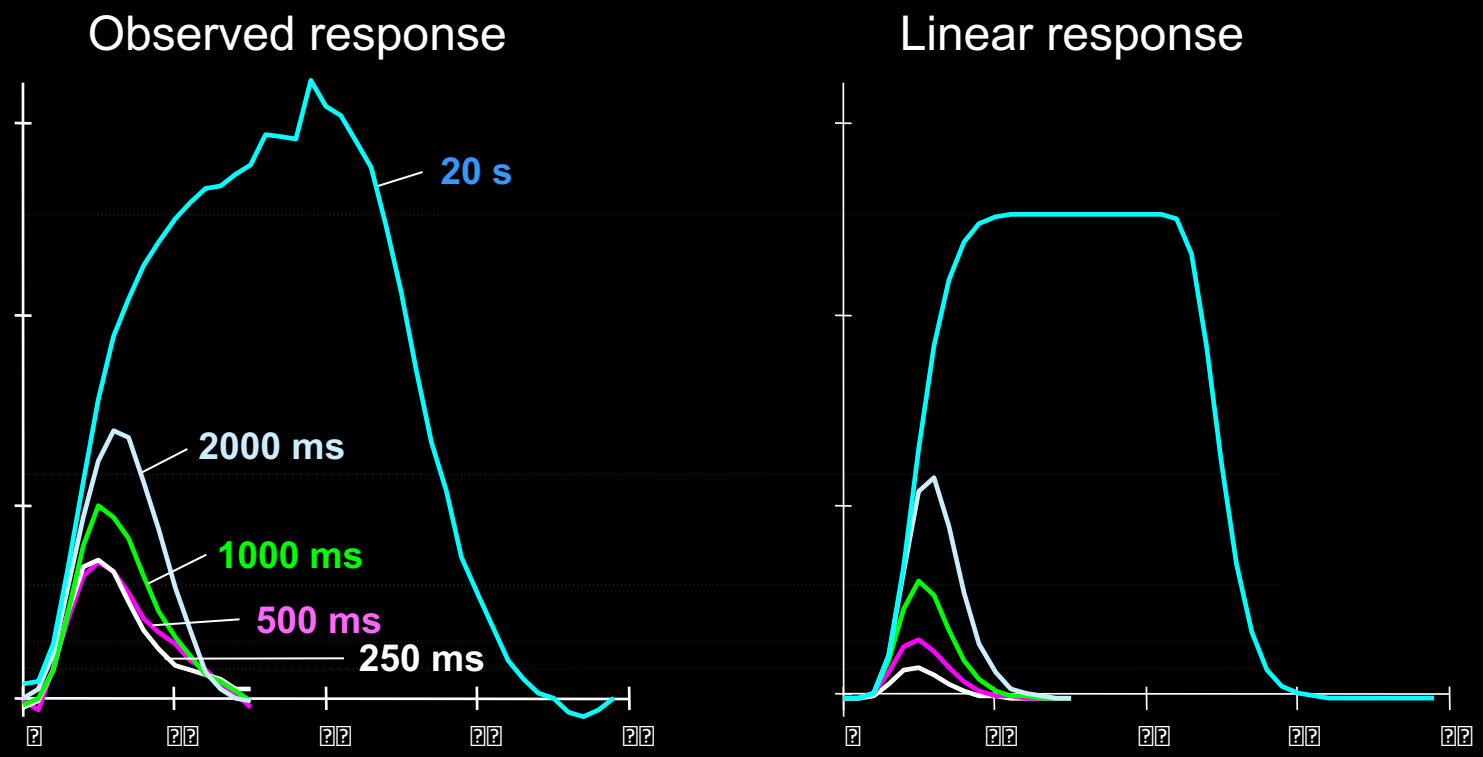

Short duration stimuli produce larger responses than expected

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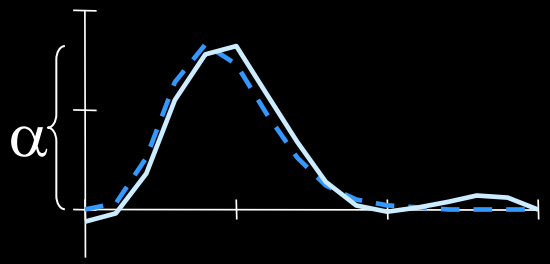
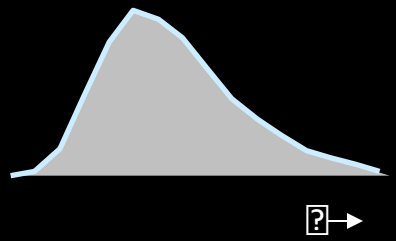
- Amplitude of Response



Fit ideal (linear) to response

- Area under response / Stimulus Duration



Output Area / Input Area

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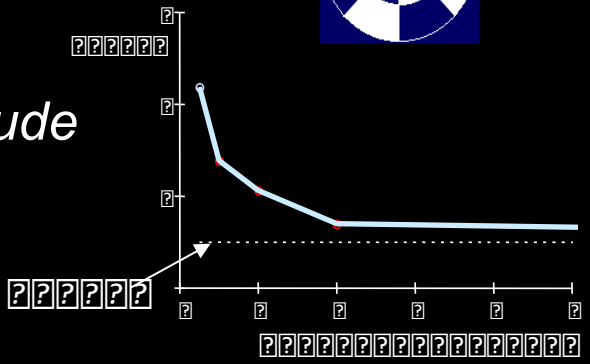
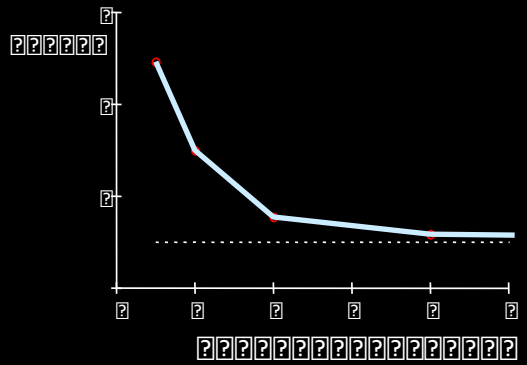
Visual

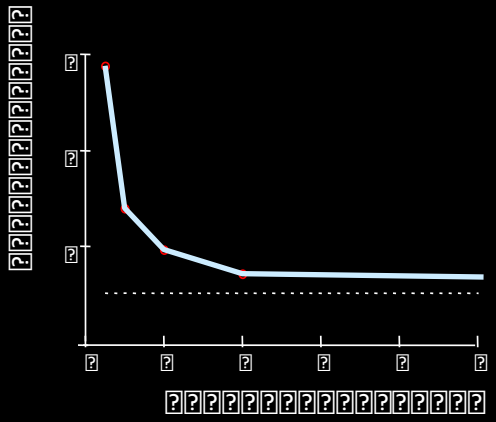
Motor

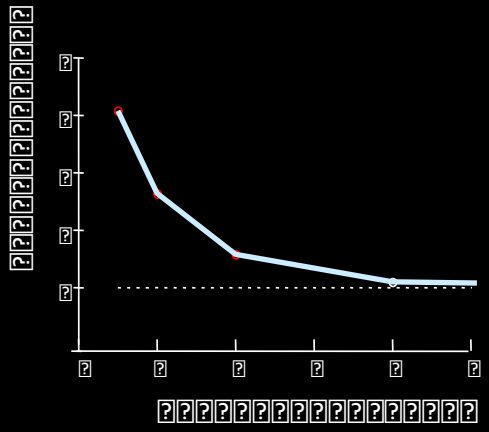
Magnitude





Area





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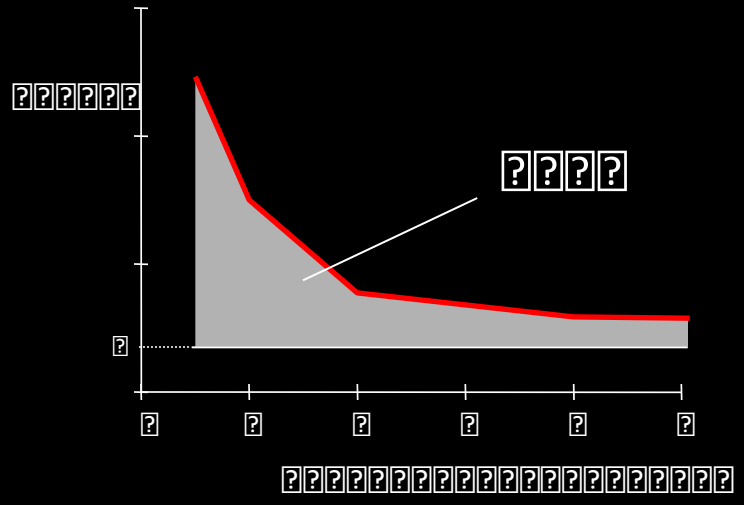
- Area under nonlinearity curve



- Slope of nonlinearity curve

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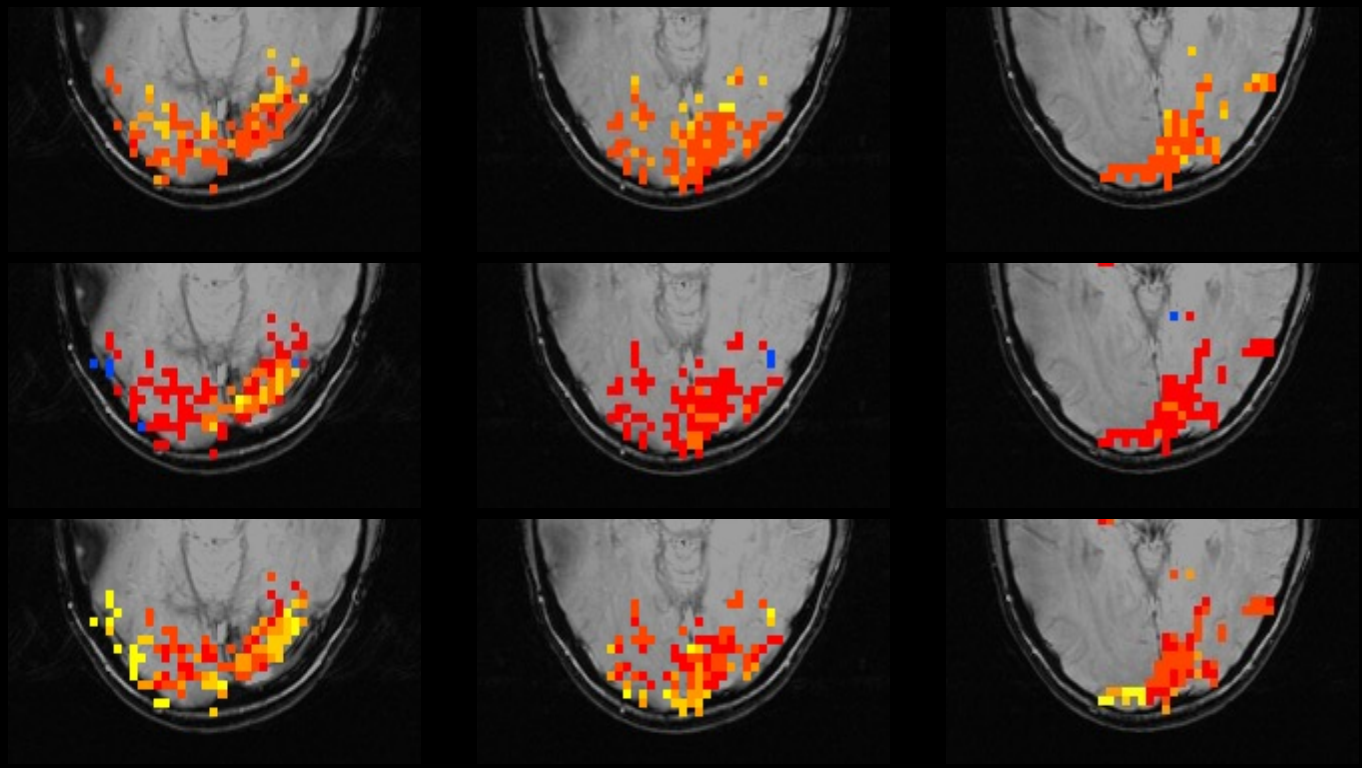
Nonlinearity

Magnitude

Latency



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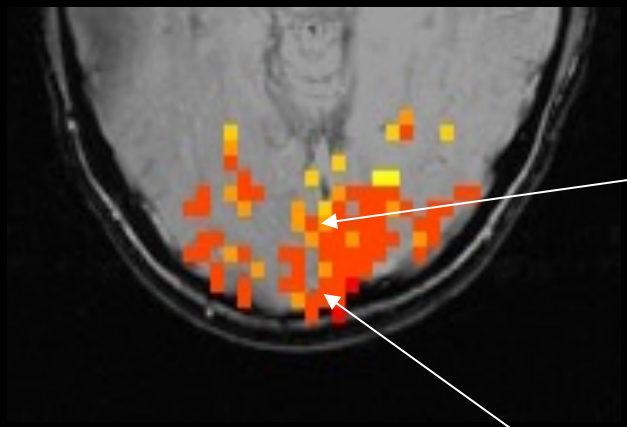
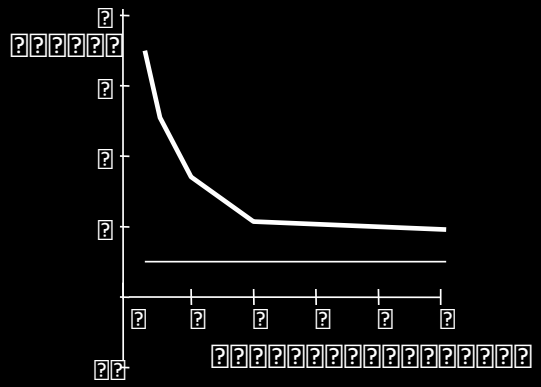
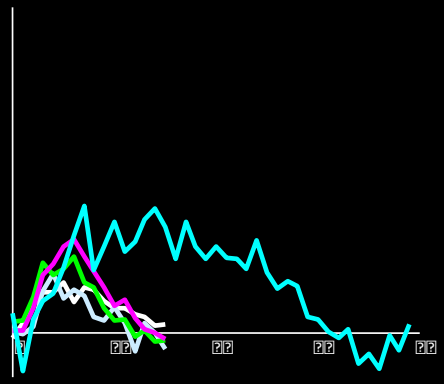
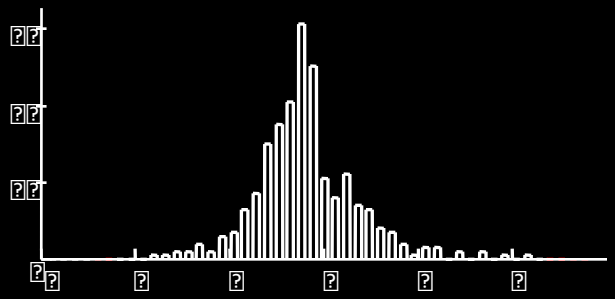
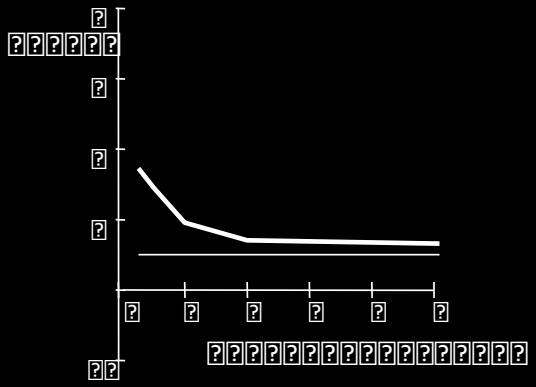


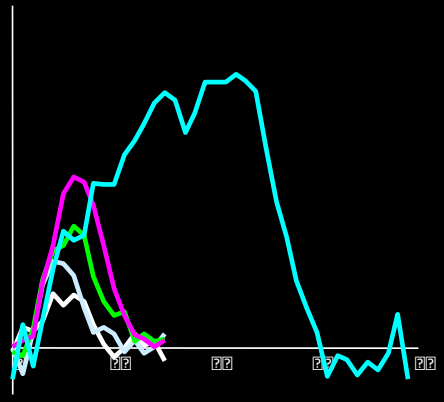






nonlinearity





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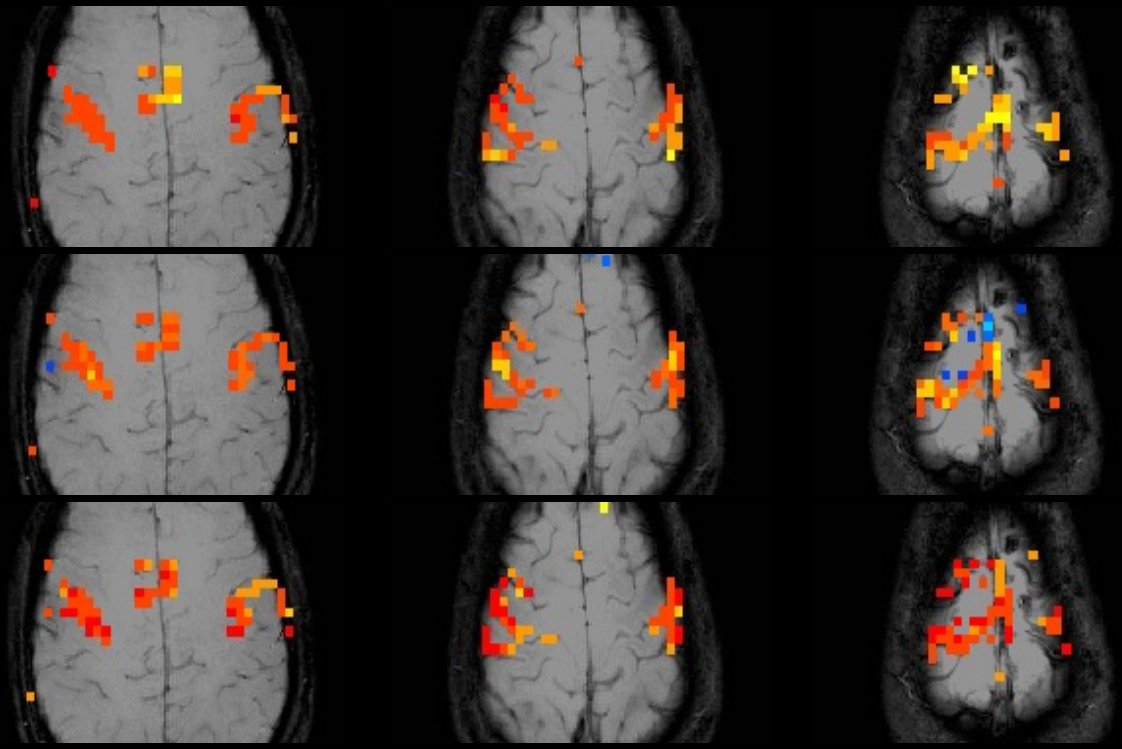
Nonlinearity

Magnitude

Latency



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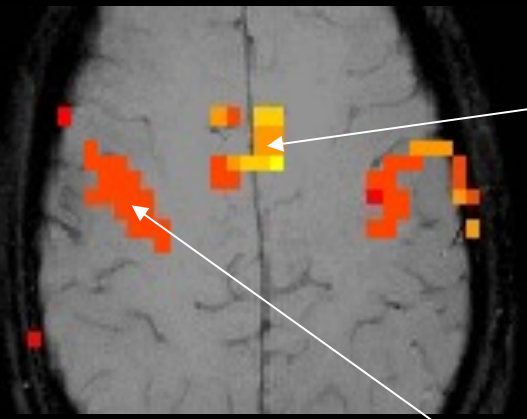
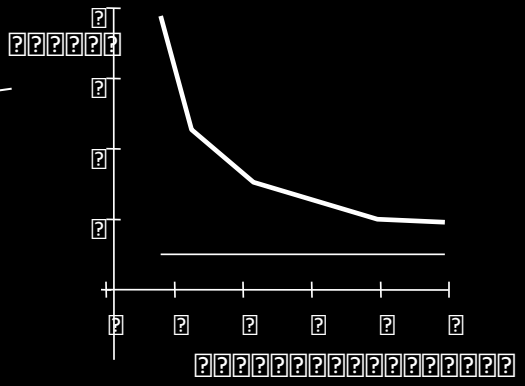
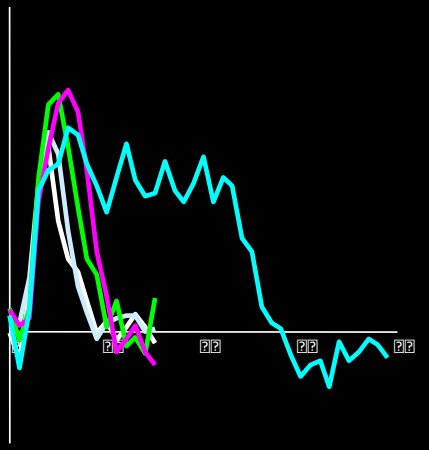
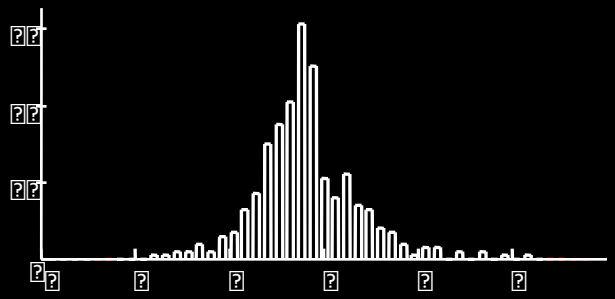
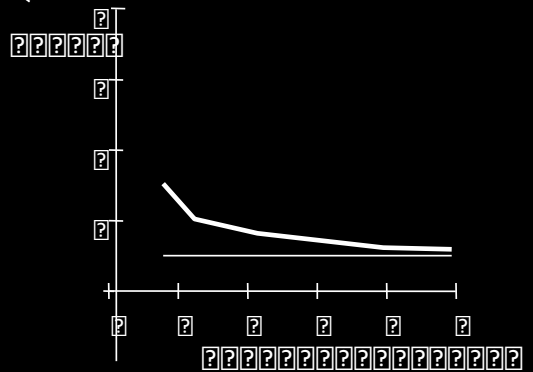


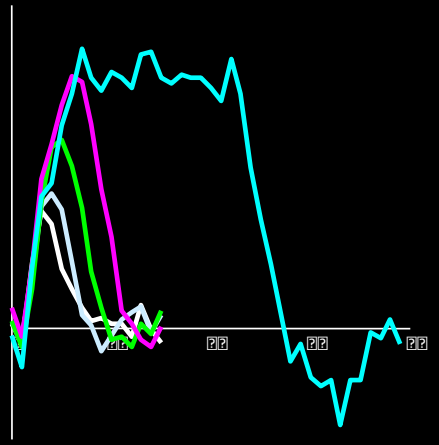






nonlinearity





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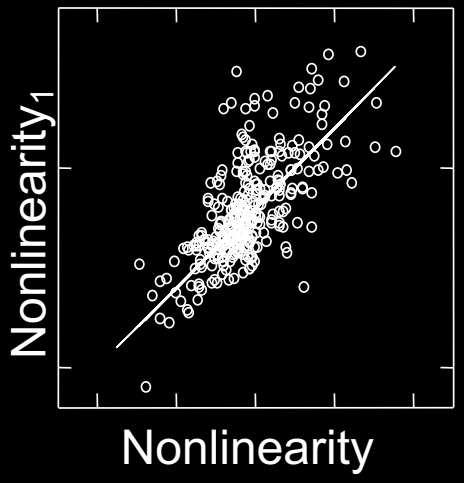
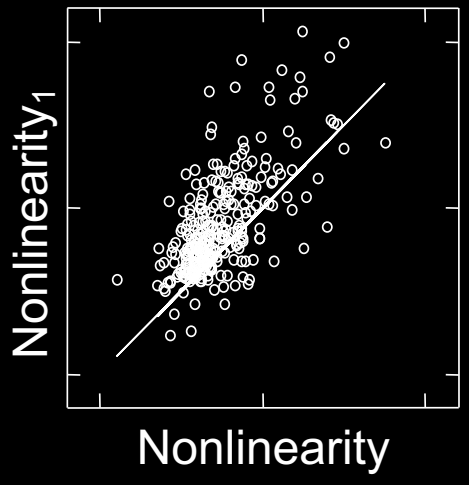
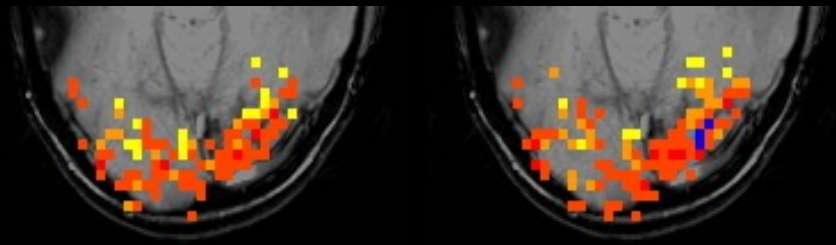
Visual task

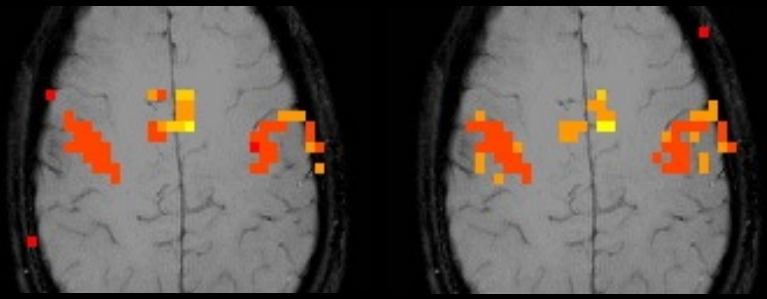


Motor task





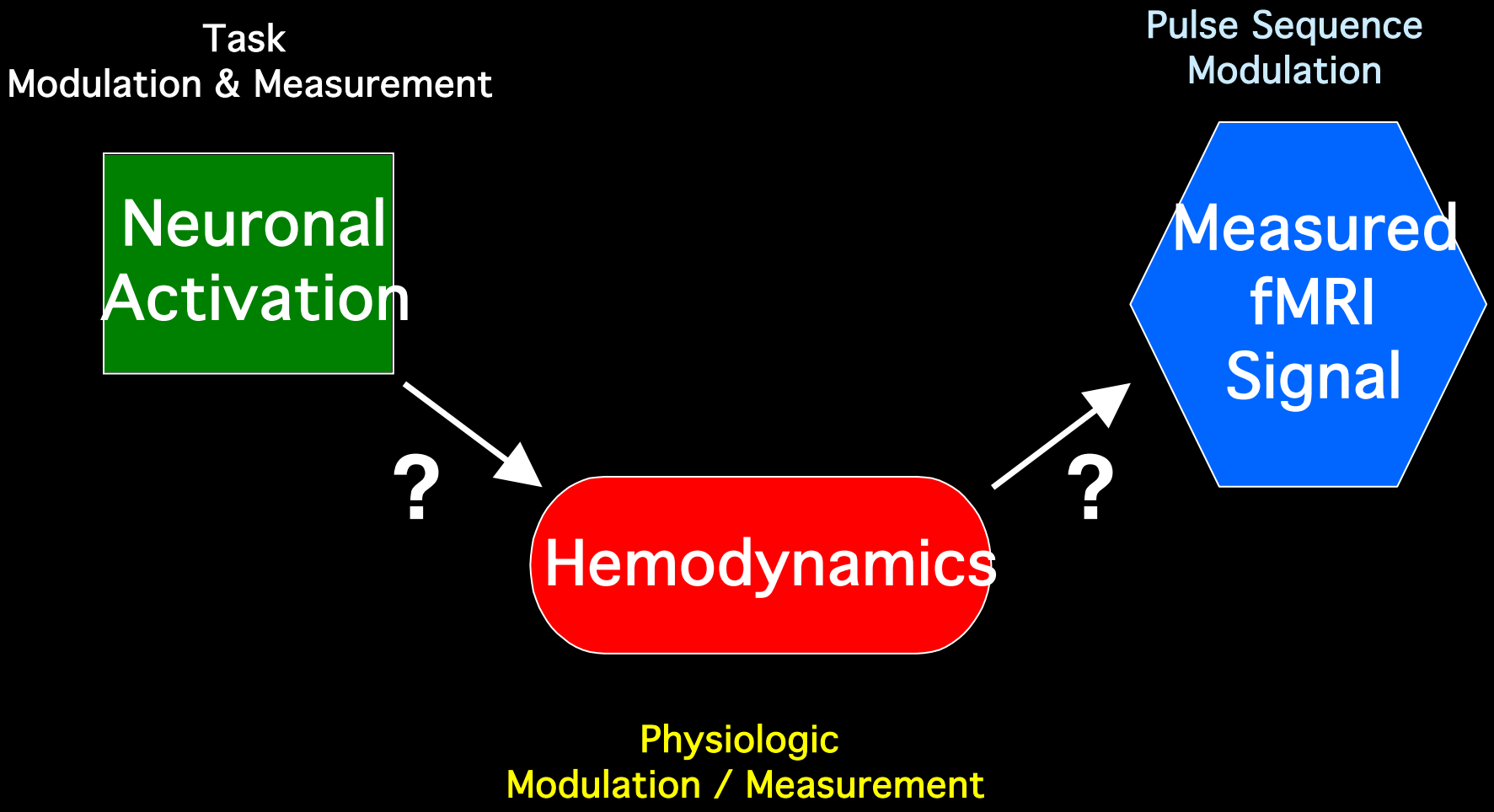
Experiment 1 Experiment 2

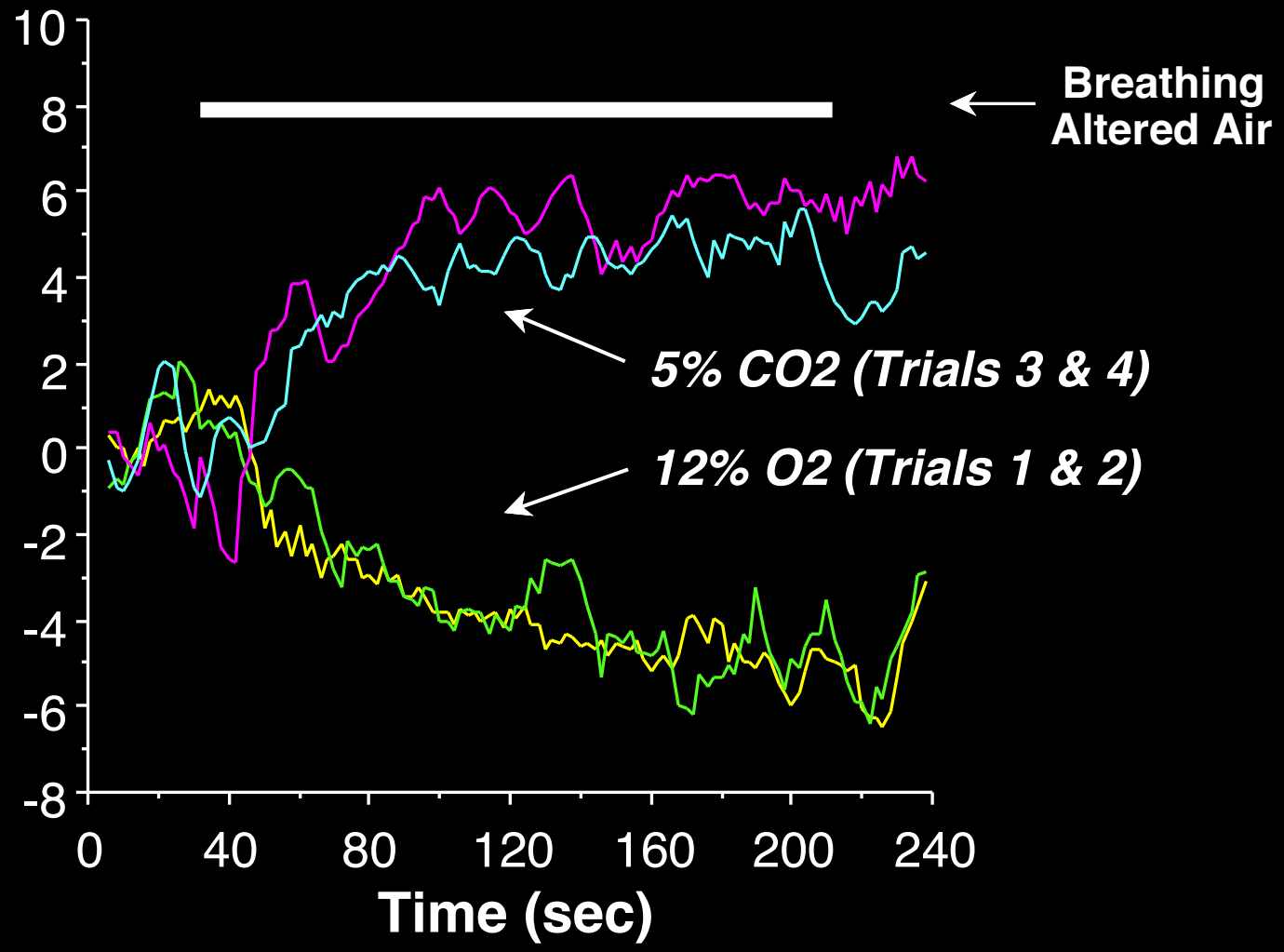


Experiment 1 Experiment 2

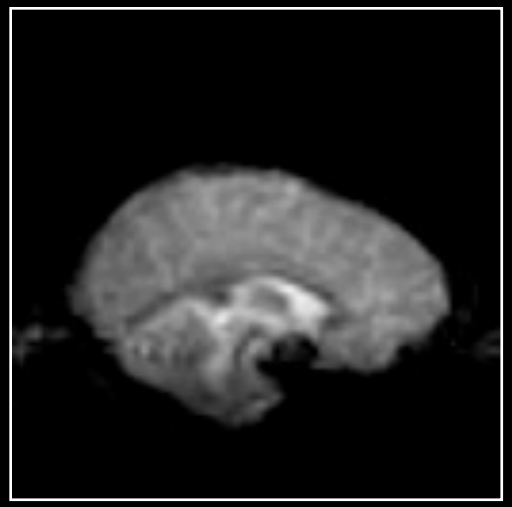
Conclusions

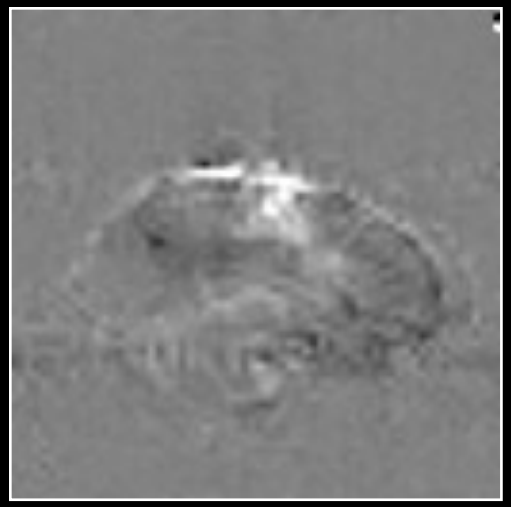
- Responses to short duration stimuli are larger than predicted from a linear system
- Spatial variation in this nonlinear relationship is seen
- The variation in nonlinearity is not significantly correlated with magnitude or latency


Task
Modulation & Measurement
Pulse Sequence
Modulation
Neuronal
Activation
Measured
fMRI
Signal
?
?
Hemodynamics
Physiologic
Modulation / Measurement


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)

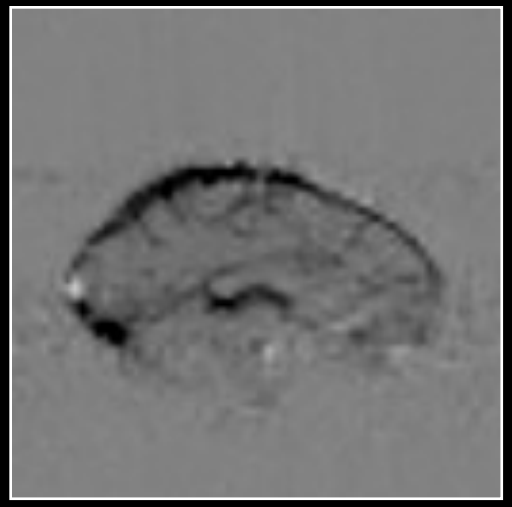
Anatomical

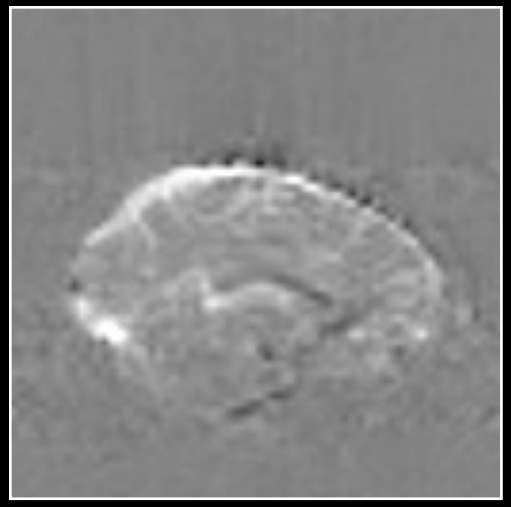




Finger Movement

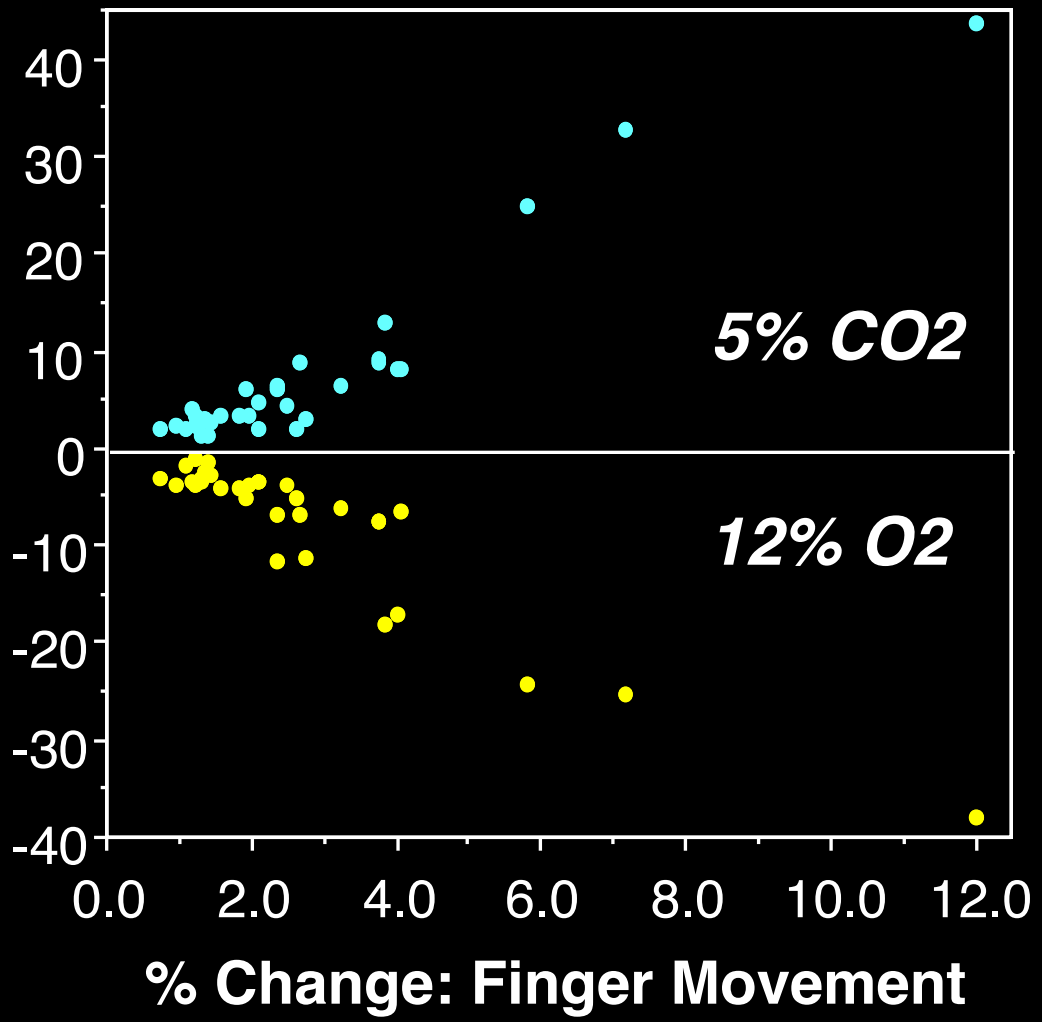
12% O2

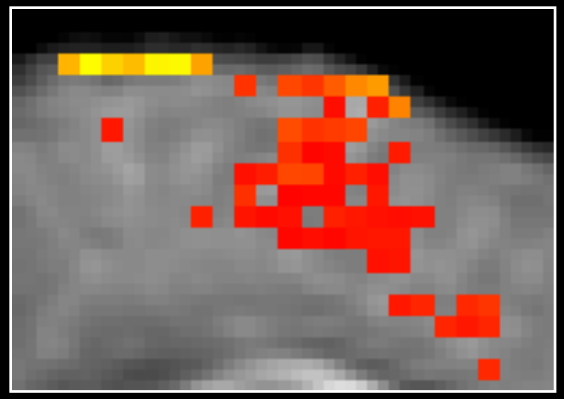




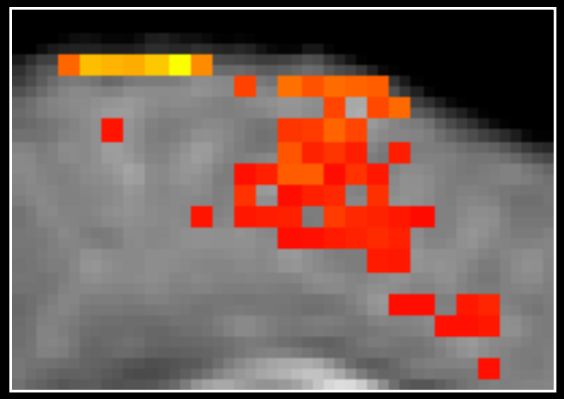
5% CO2

Resting State Blood Volume Weighting





?



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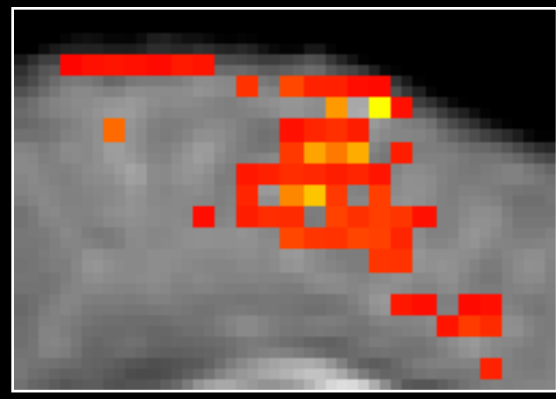
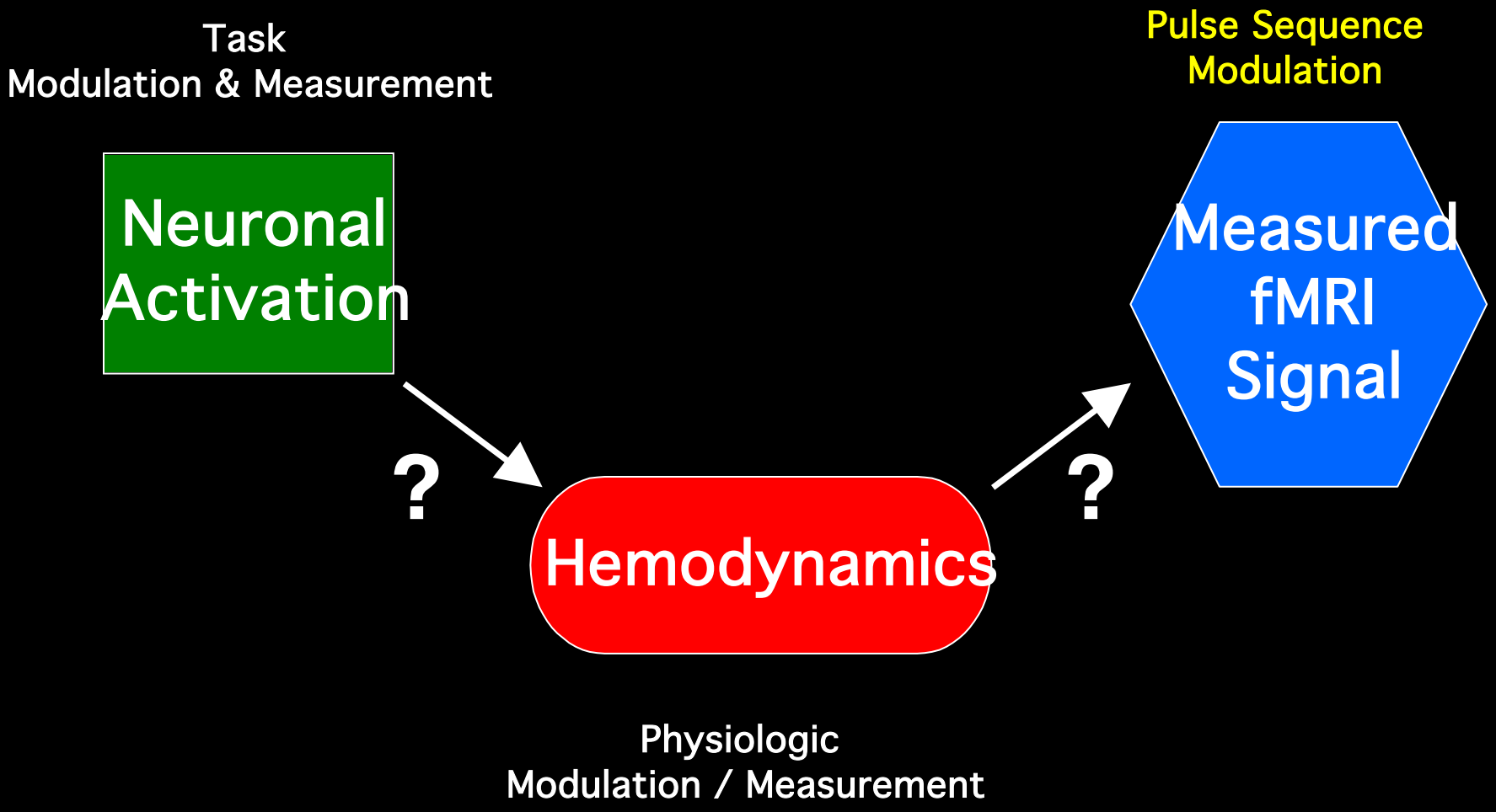



Task
Modulation & Measurement
Neuronal Activation
?
Hemodynamics
?
Pulse Sequence
Modulation
Measured fMRI Signal
Physiologic
Modulation / Measurement

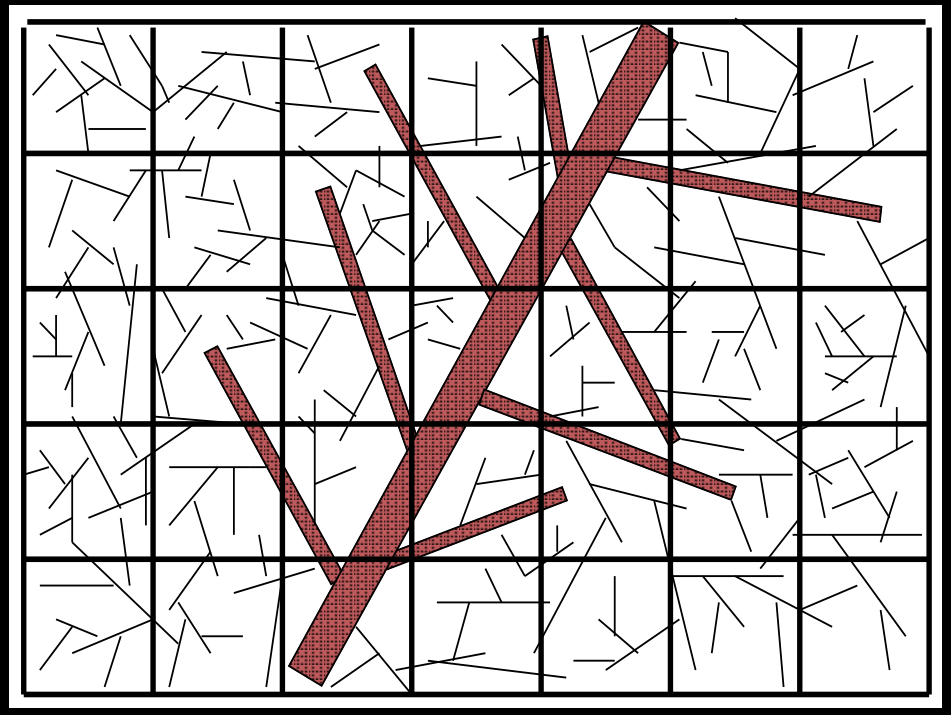
Activation-induced MR Signal Change Mechanisms

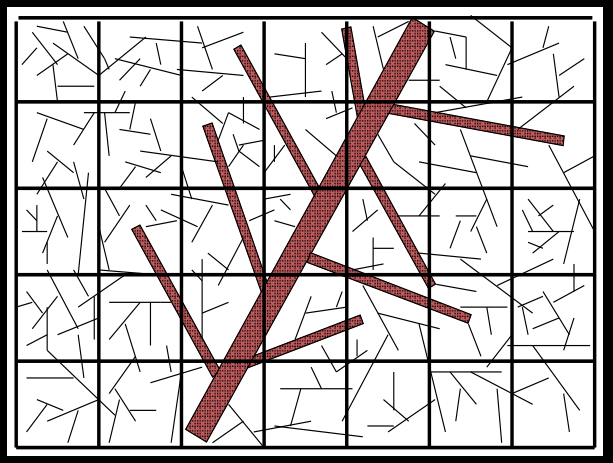
T1

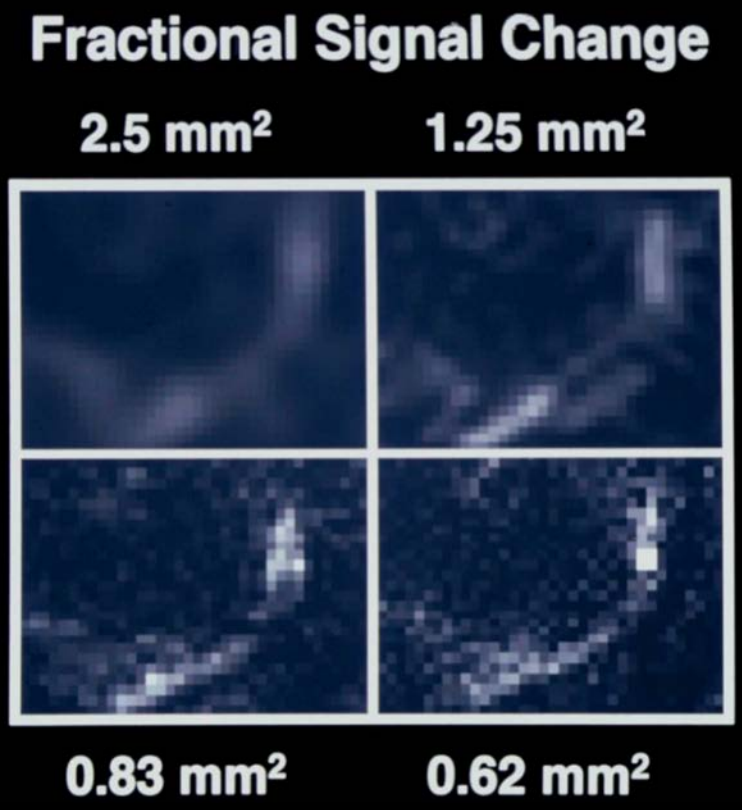
Inflow

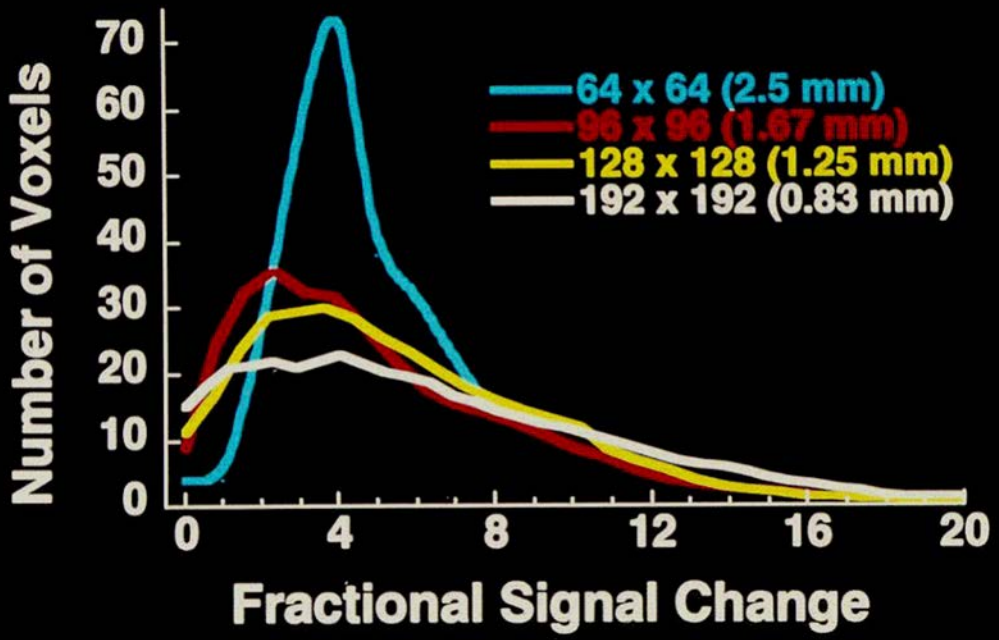
T2

T2*






Fractional Signal Change
2.5 mm²
1.25 mm²
0.83 mm²
0.62 mm²


Number of Voxels
70
60
50
40
30
20
10
0
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)

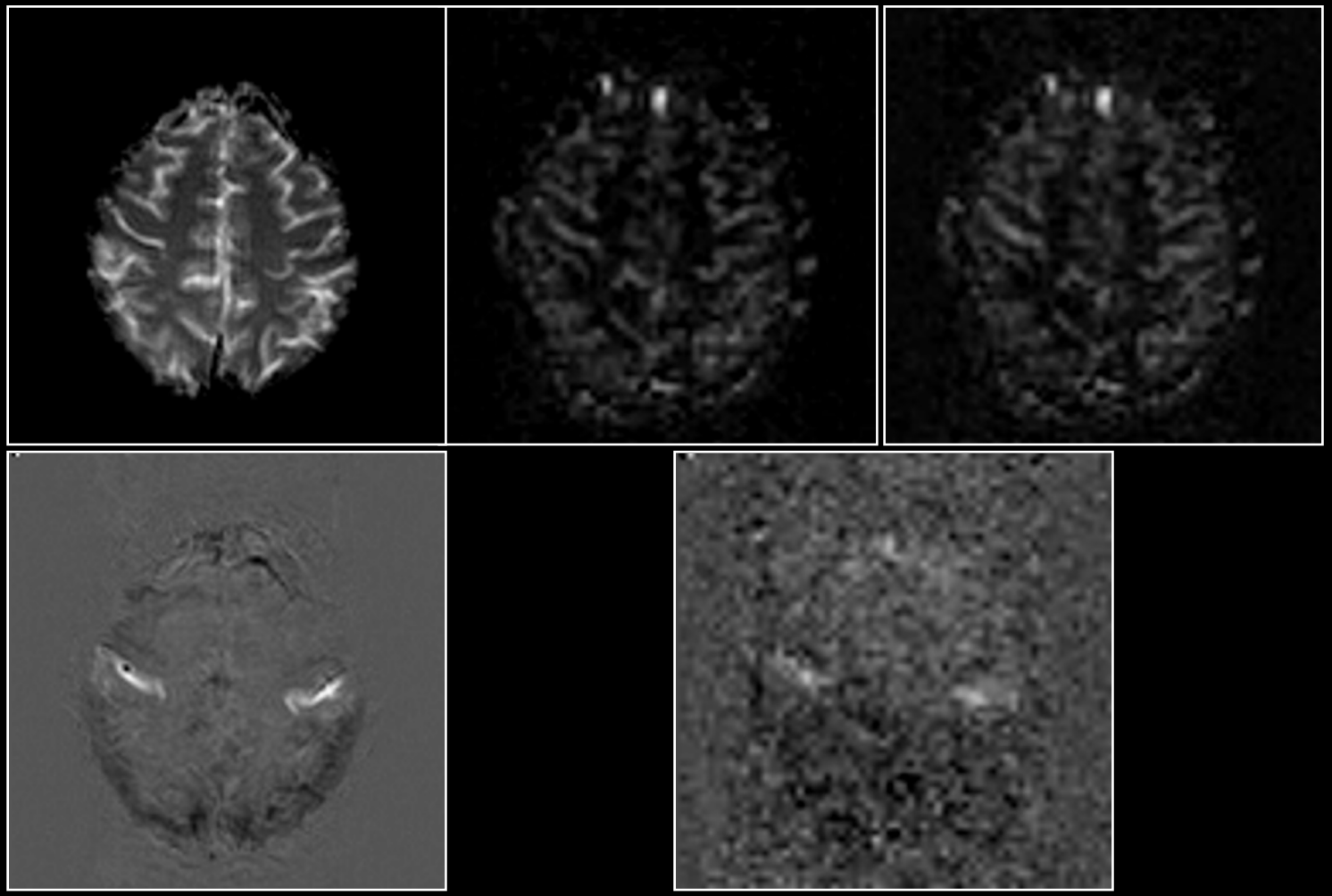
T1 - weighted

T2* weighted

T1 and T2* weighted

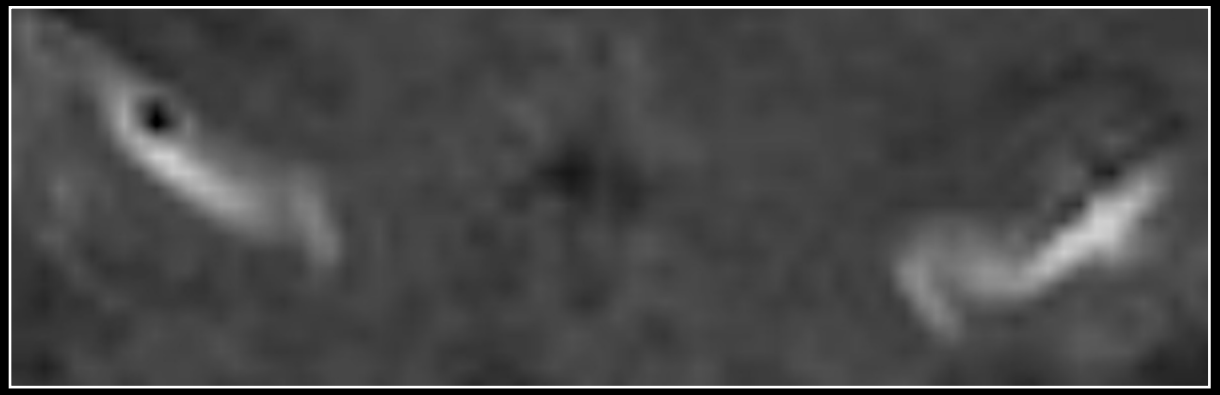
Perfusion

BOLD *Rest* *Activation*



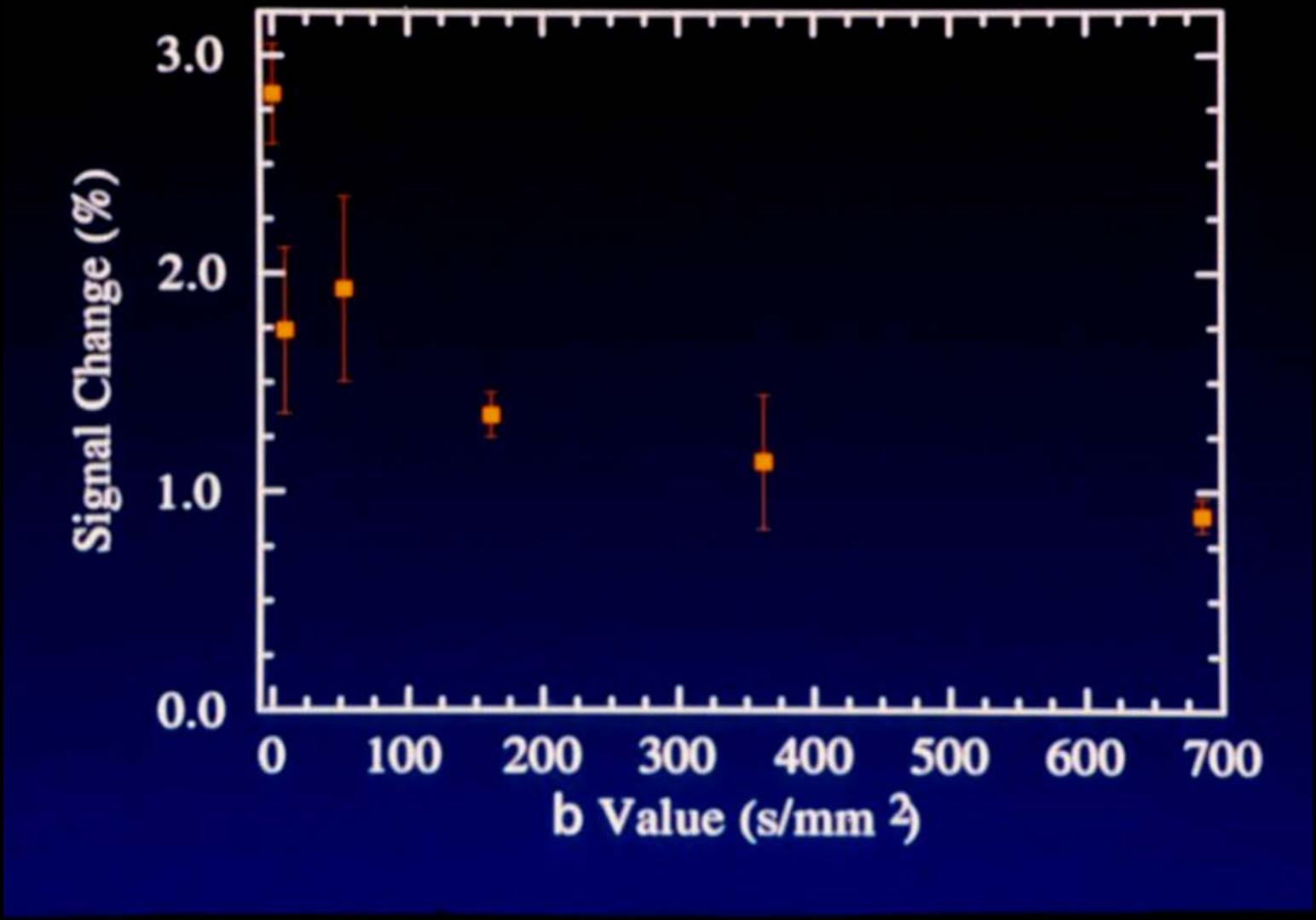
Anatomy

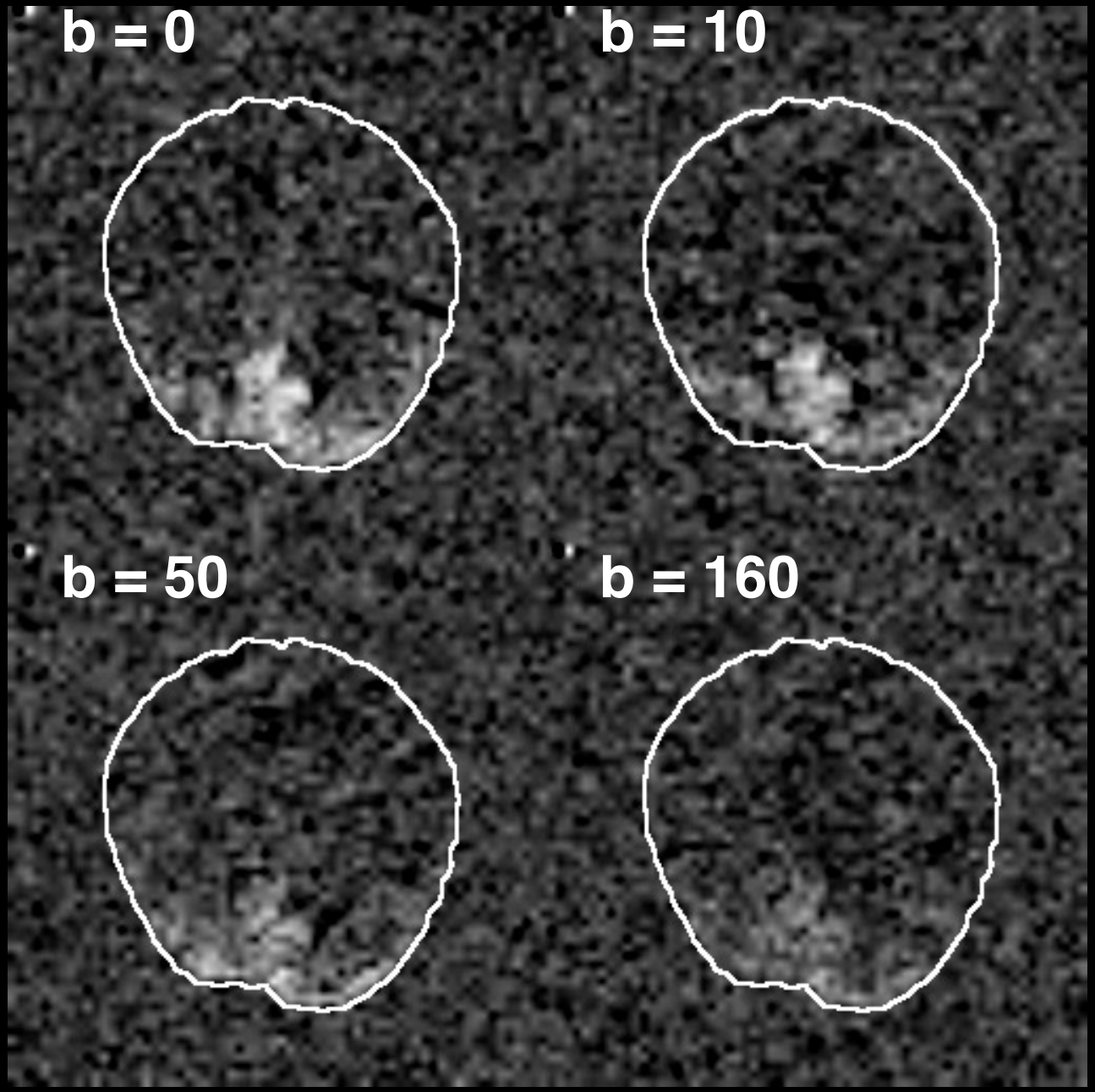
BOLD

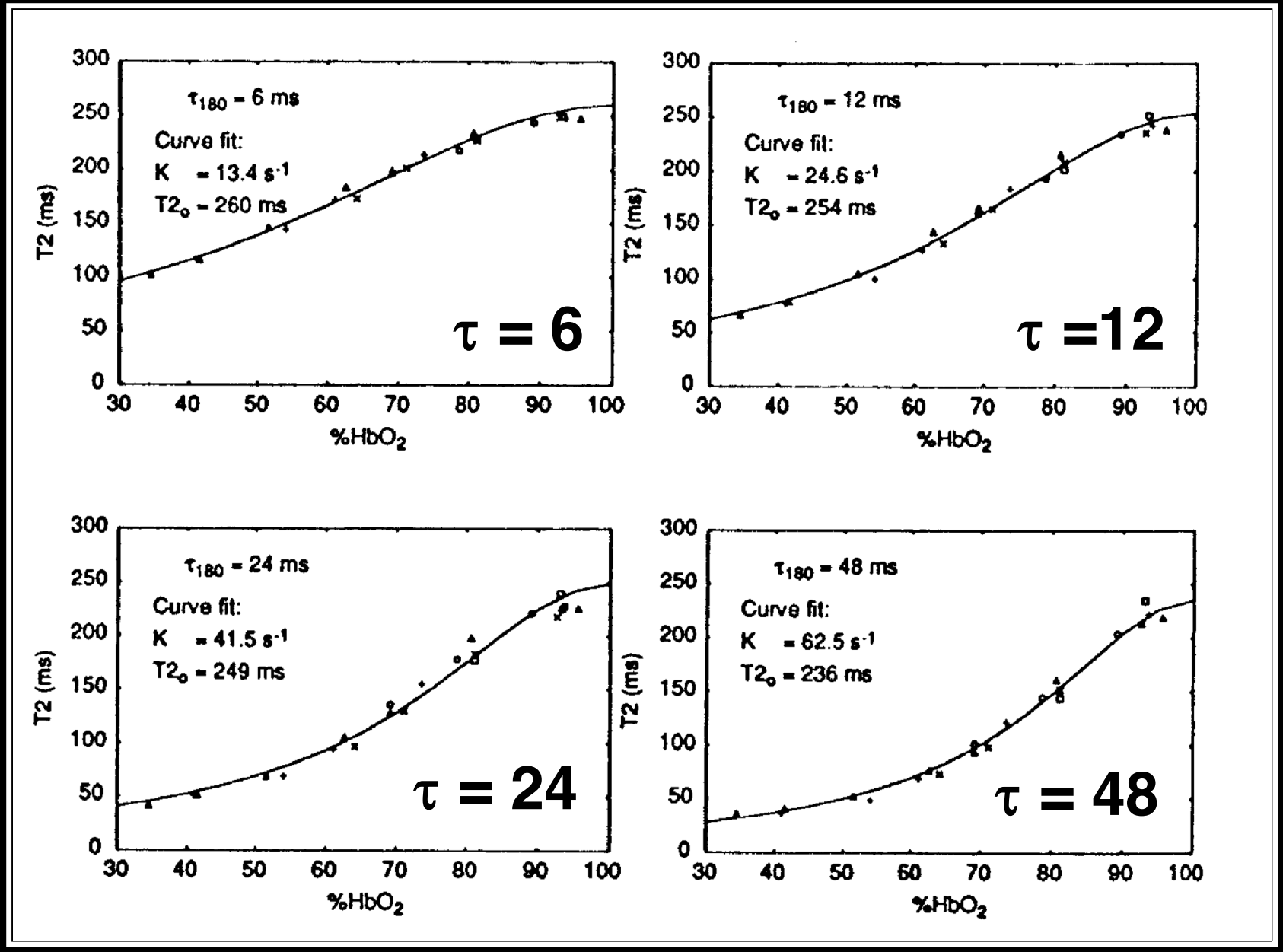


Perfusion

Velocity Nulling at 1.5T

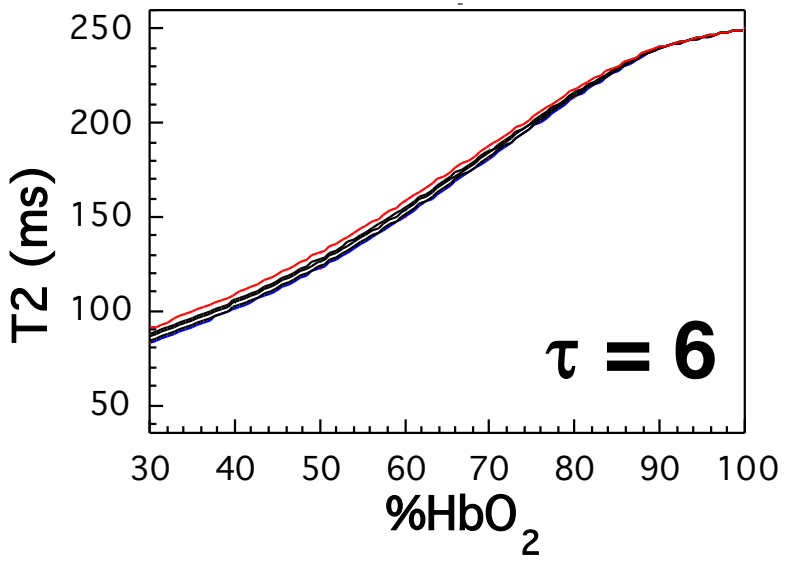


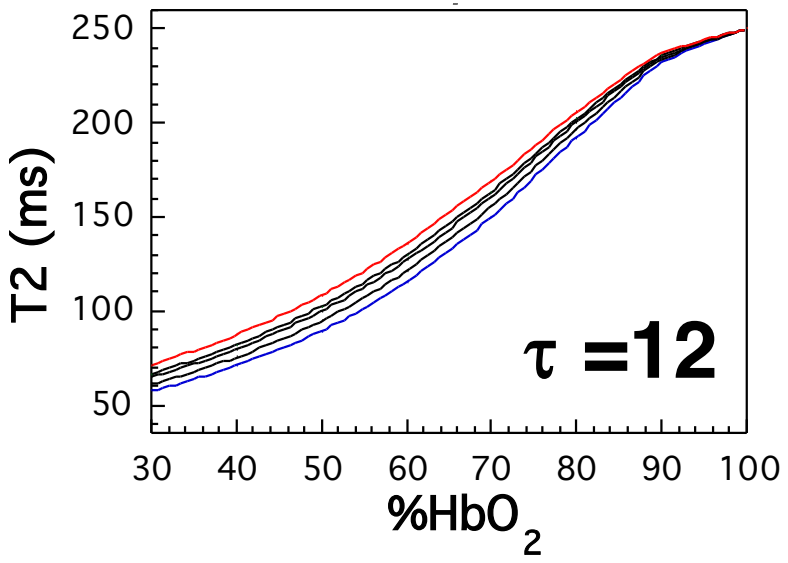

b = 0
b = 10
b = 50
b = 160

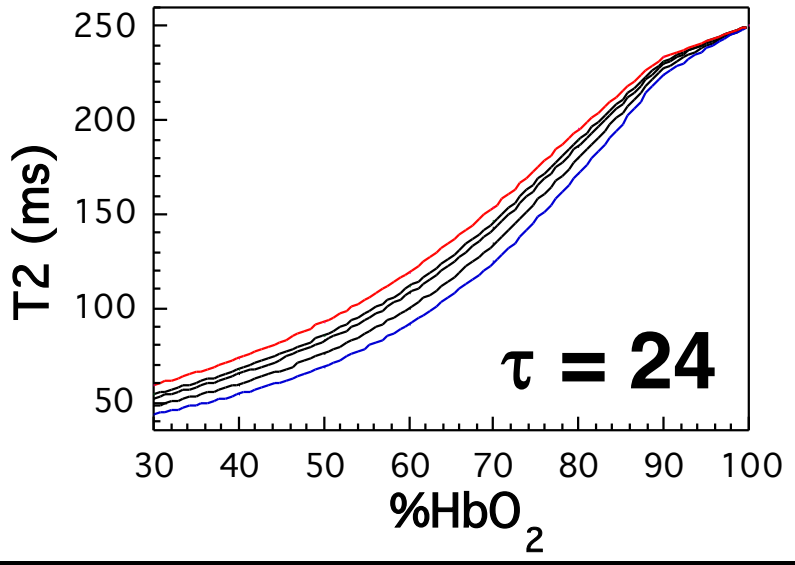


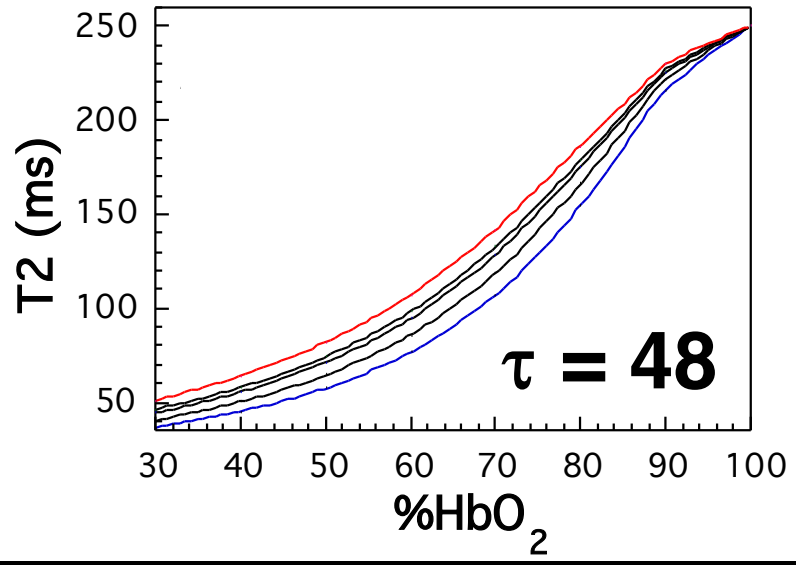
Wright et al. JMRI, 1: 275-228, 1991

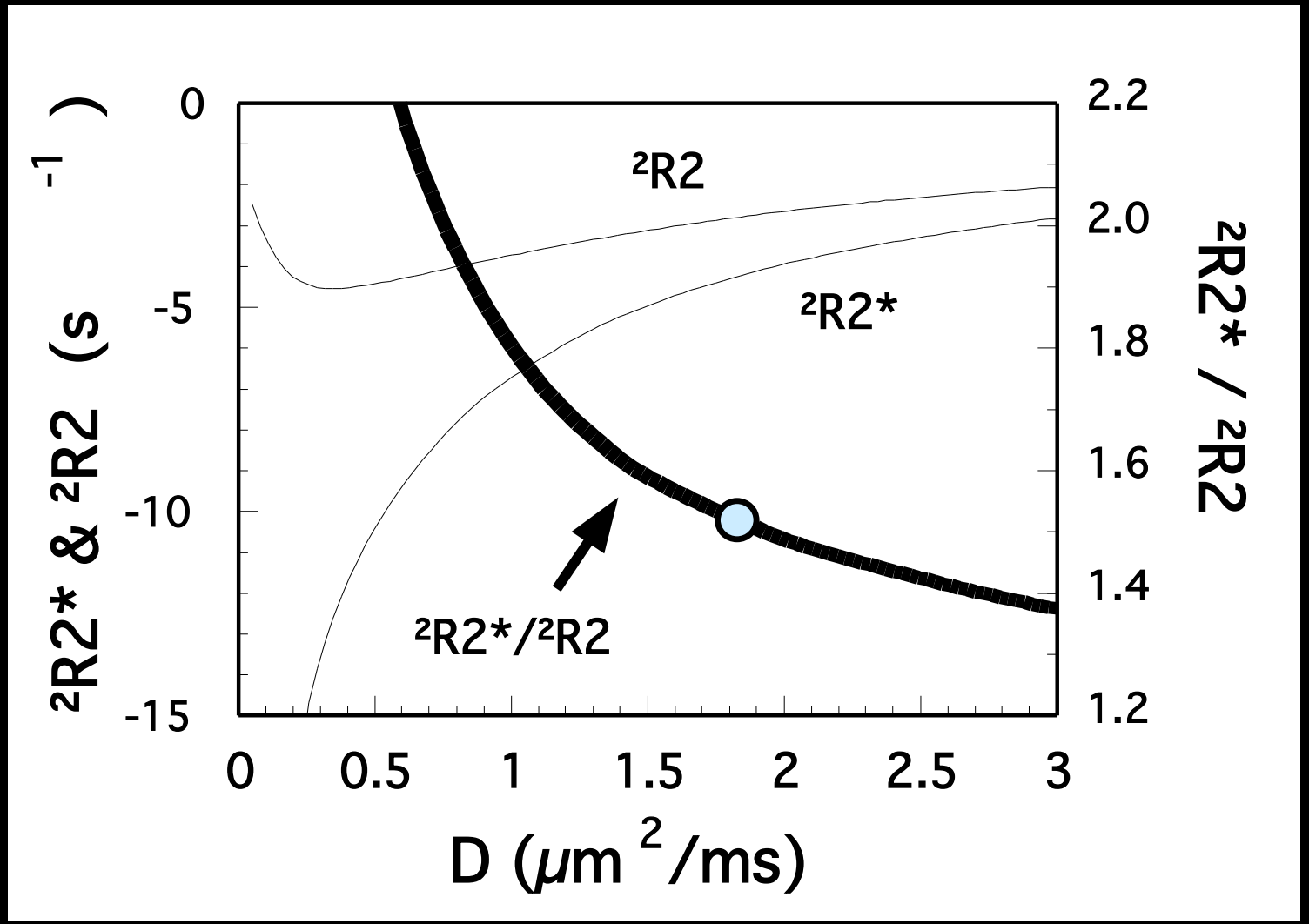
D = 1 μm^2 / ms -> 2.5 μm^2 / ms



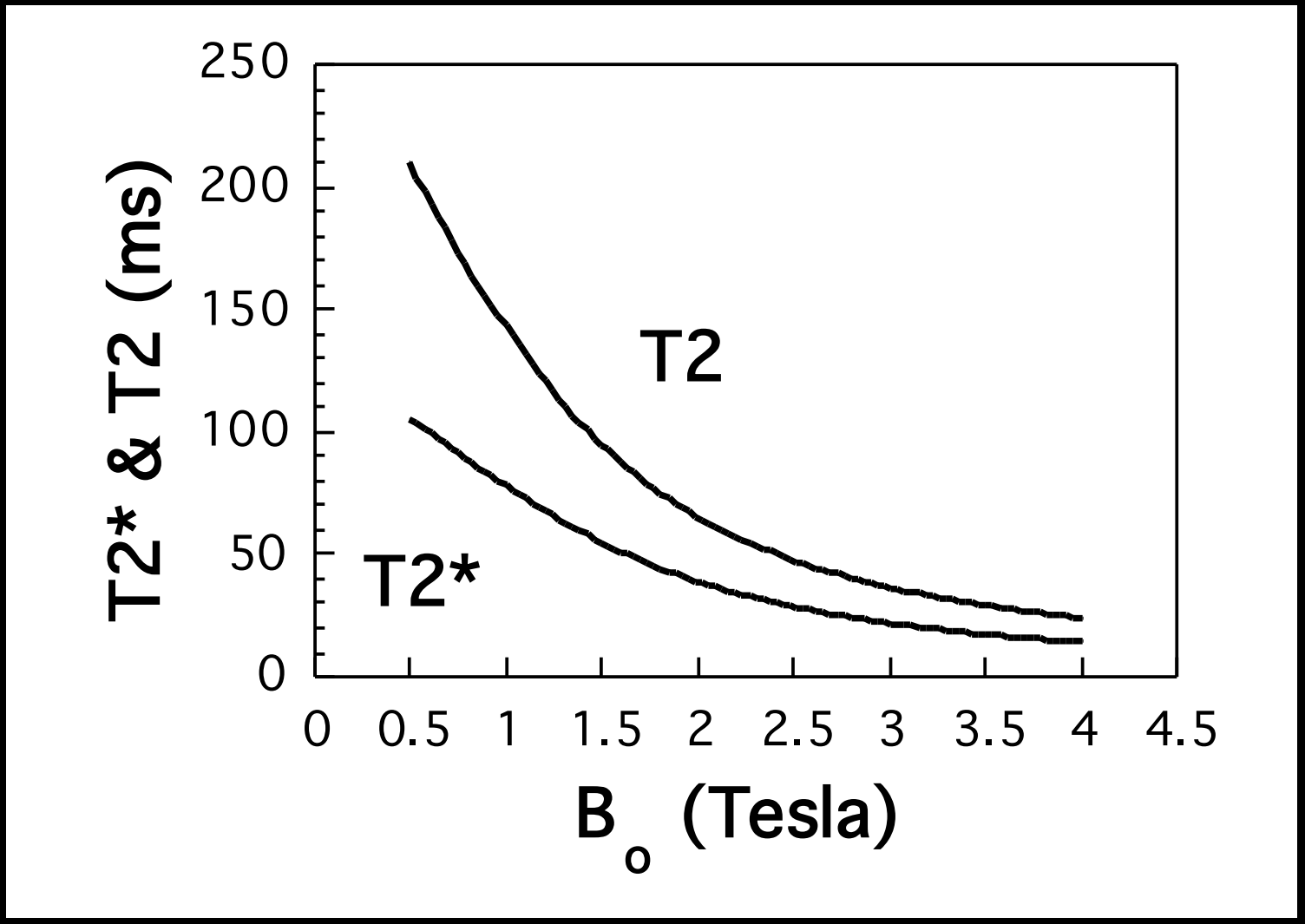






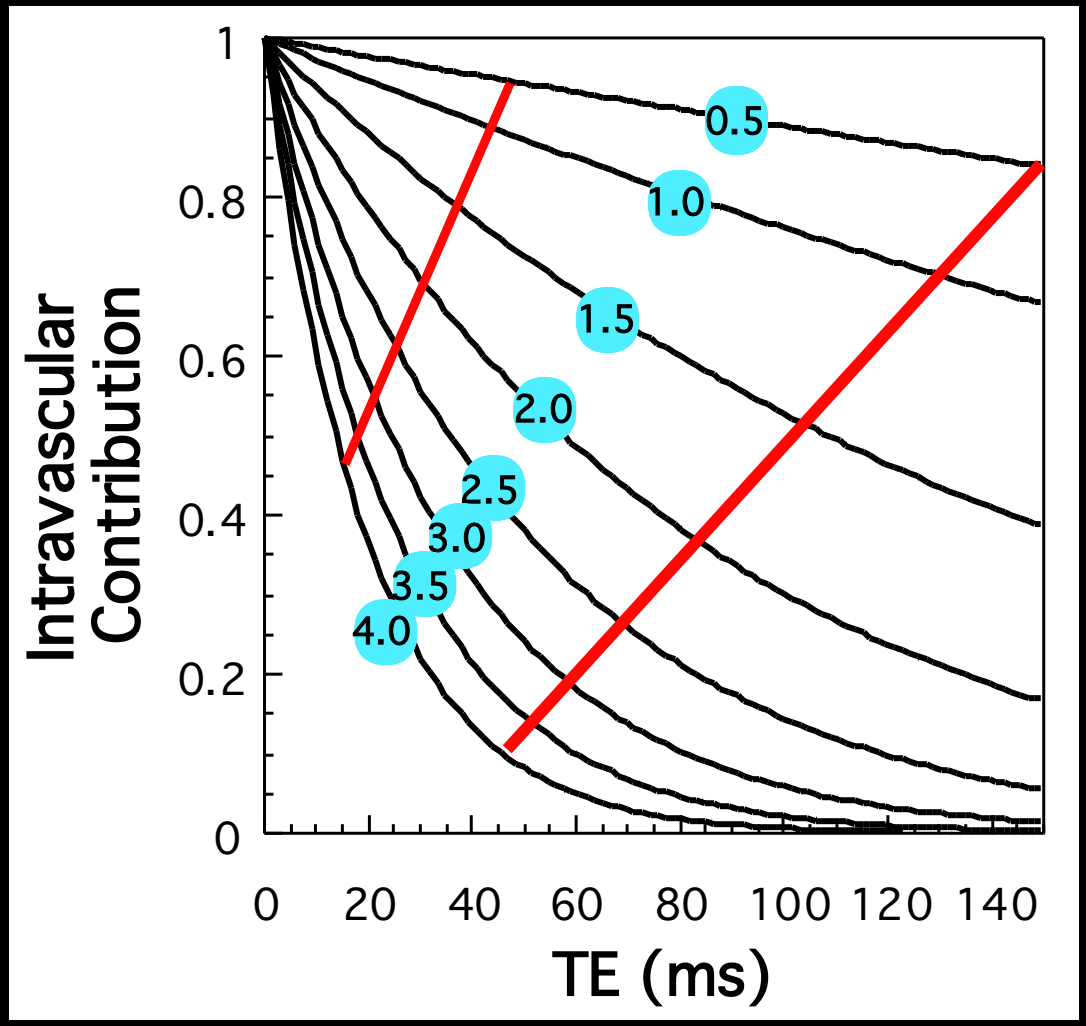

0
-5
-10
-15
2.2
2.0
1.8
1.6
1.4
1.2
0
0.5
1
1.5
2
2.5
3
²R2
²R2*
²R2*/²R2
²R2* & ²R2 (s⁻¹)
²R2* / ²R2
D (μm²/ms)

Field -Strength Dependence of T2* and T2

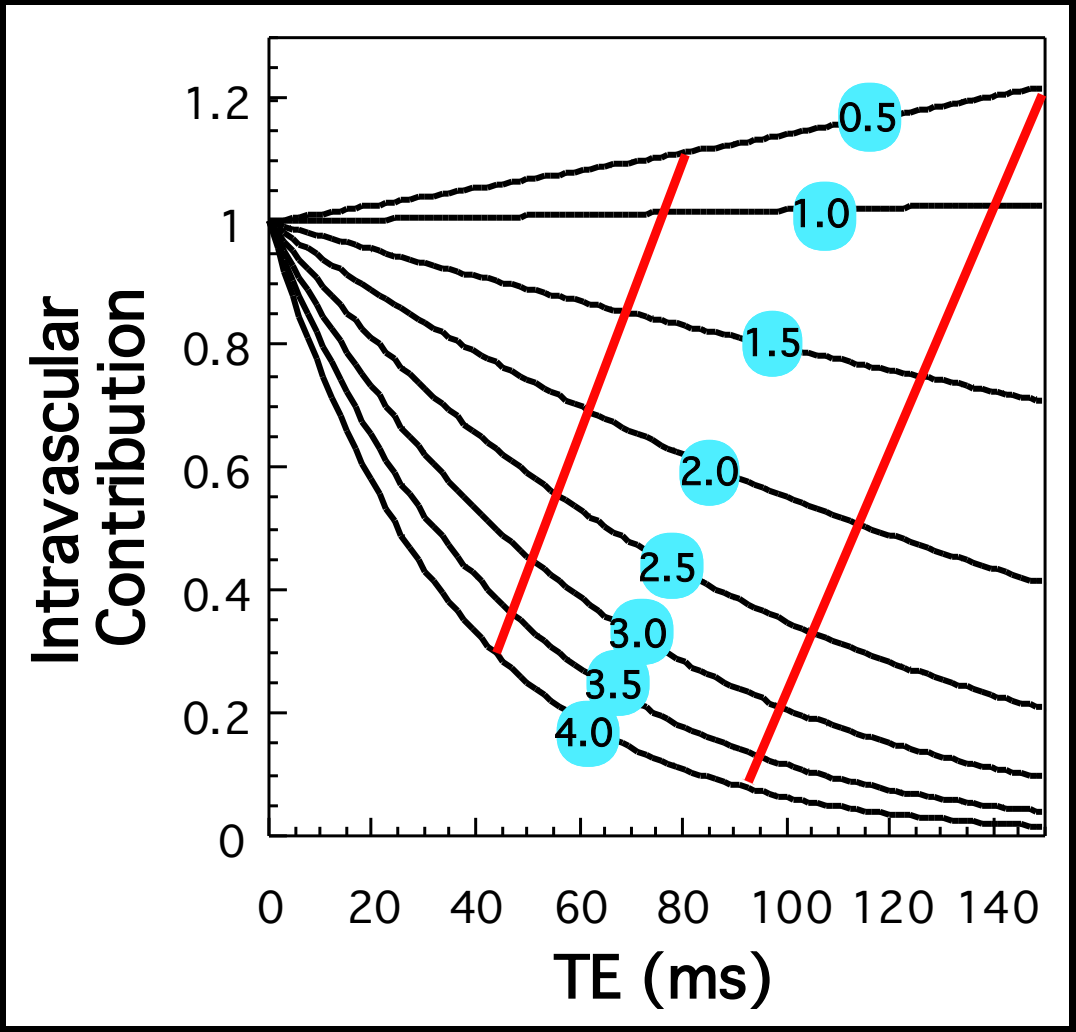


Hct = 44, τ = 48, %HbO_2 = 60, $T2_o$ = 250 ms, T2' = 120 ms

Gradient-echo, %HbO_2 = 60



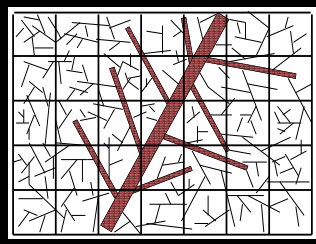
Spin-echo, %HbO_2 = 60



3T

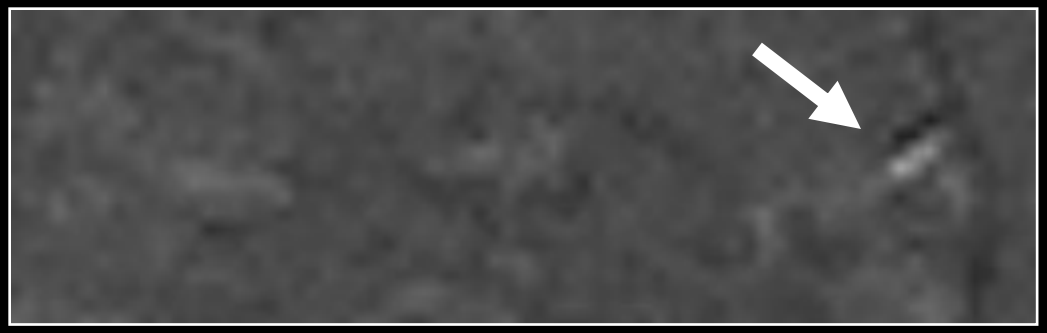
Spin-Echo
TE = 105 ms
TR = ∞

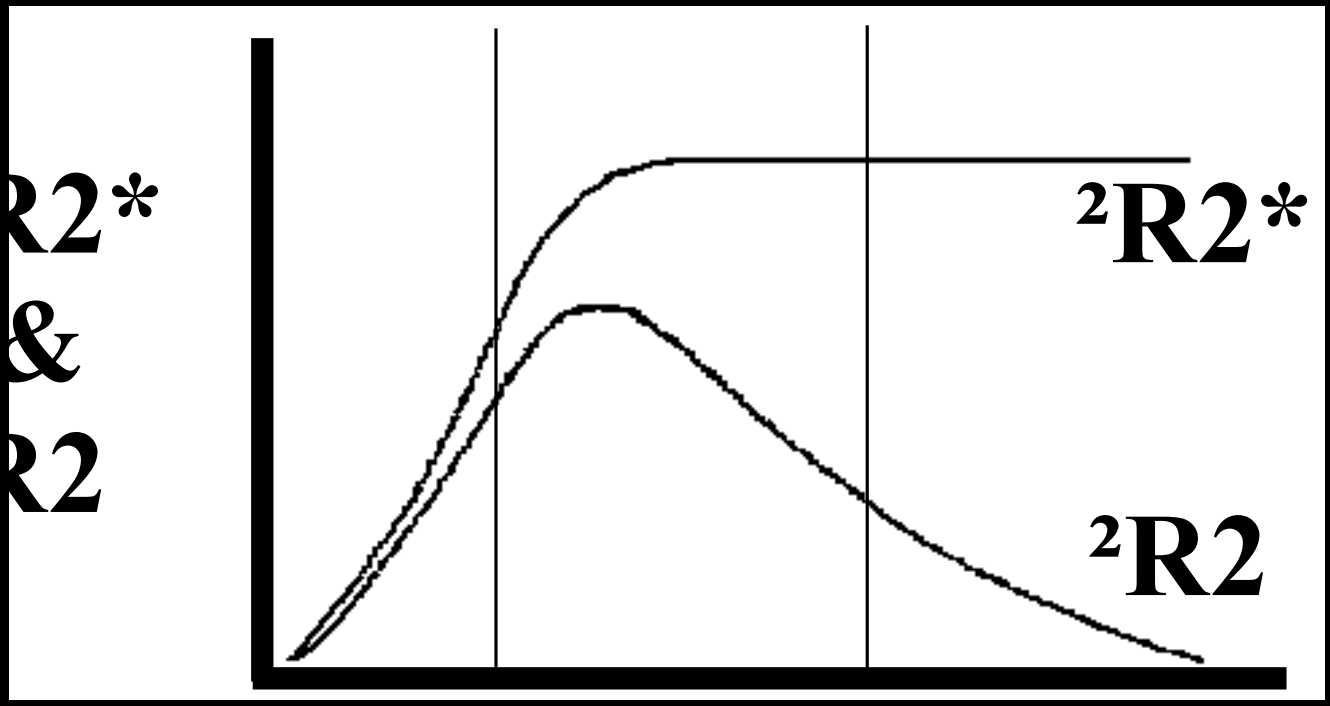
Gradient-Echo
TE = 50 ms



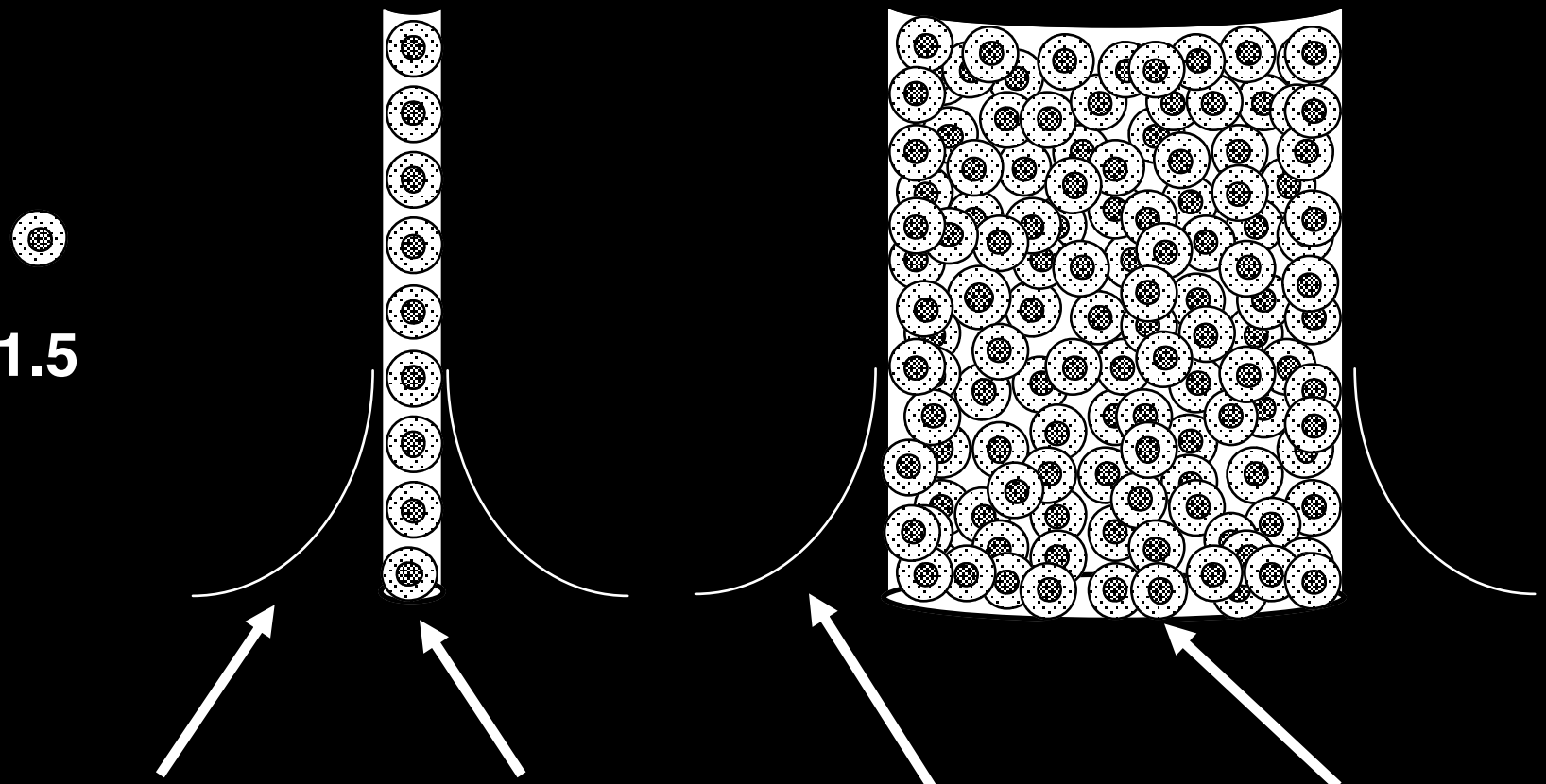
Gradient-Echo
functional
TE = 50 ms

Spin-Echo
functional
TE = 105 ms



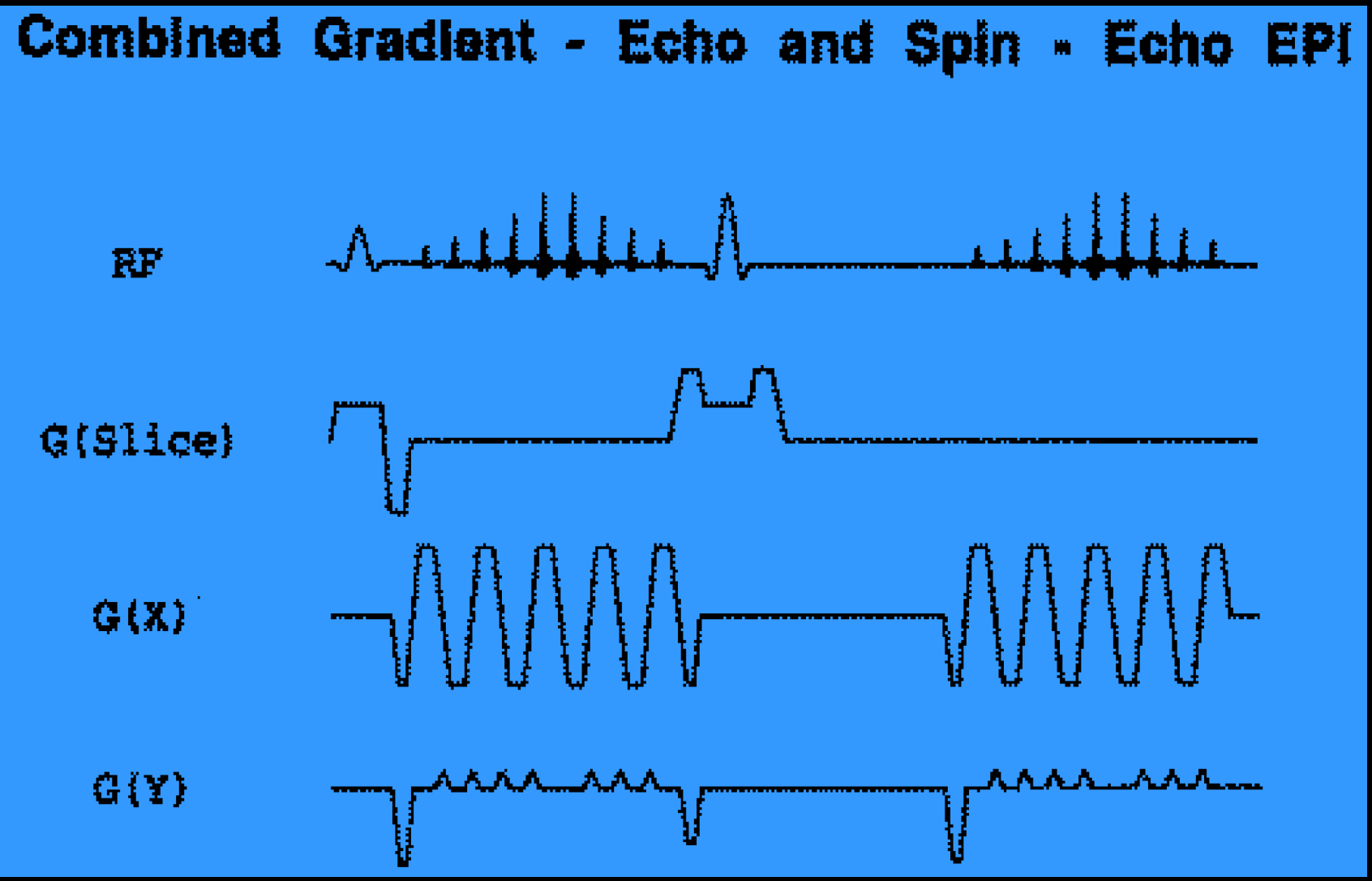

R2*
&
R2
²R2*
²R2

ΔR2* / ΔR2



average ΔR2 / ΔR2 ≈ 3 to 4*

Combined Gradient - Echo and Spin - Echo EPI

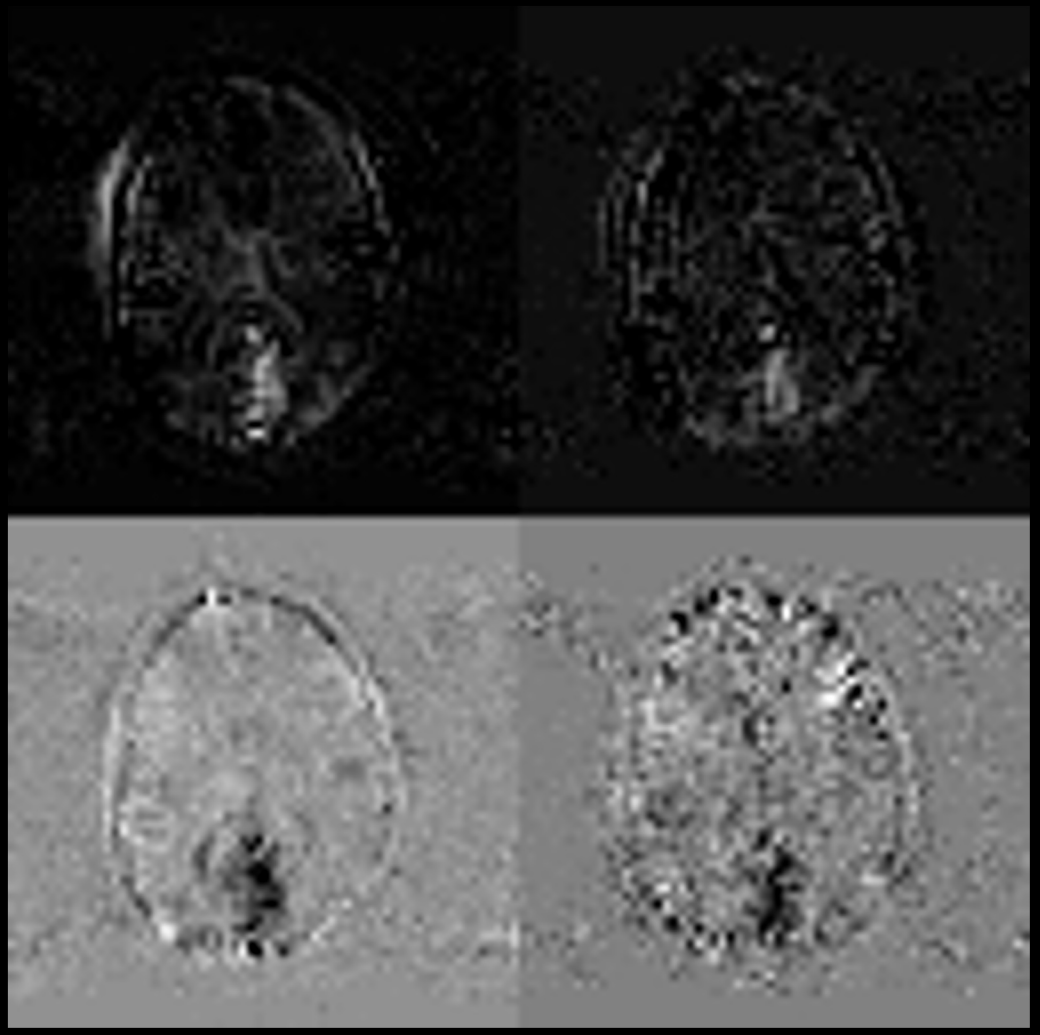


Gradient - Echo

Spin - Echo

During Activation Increase

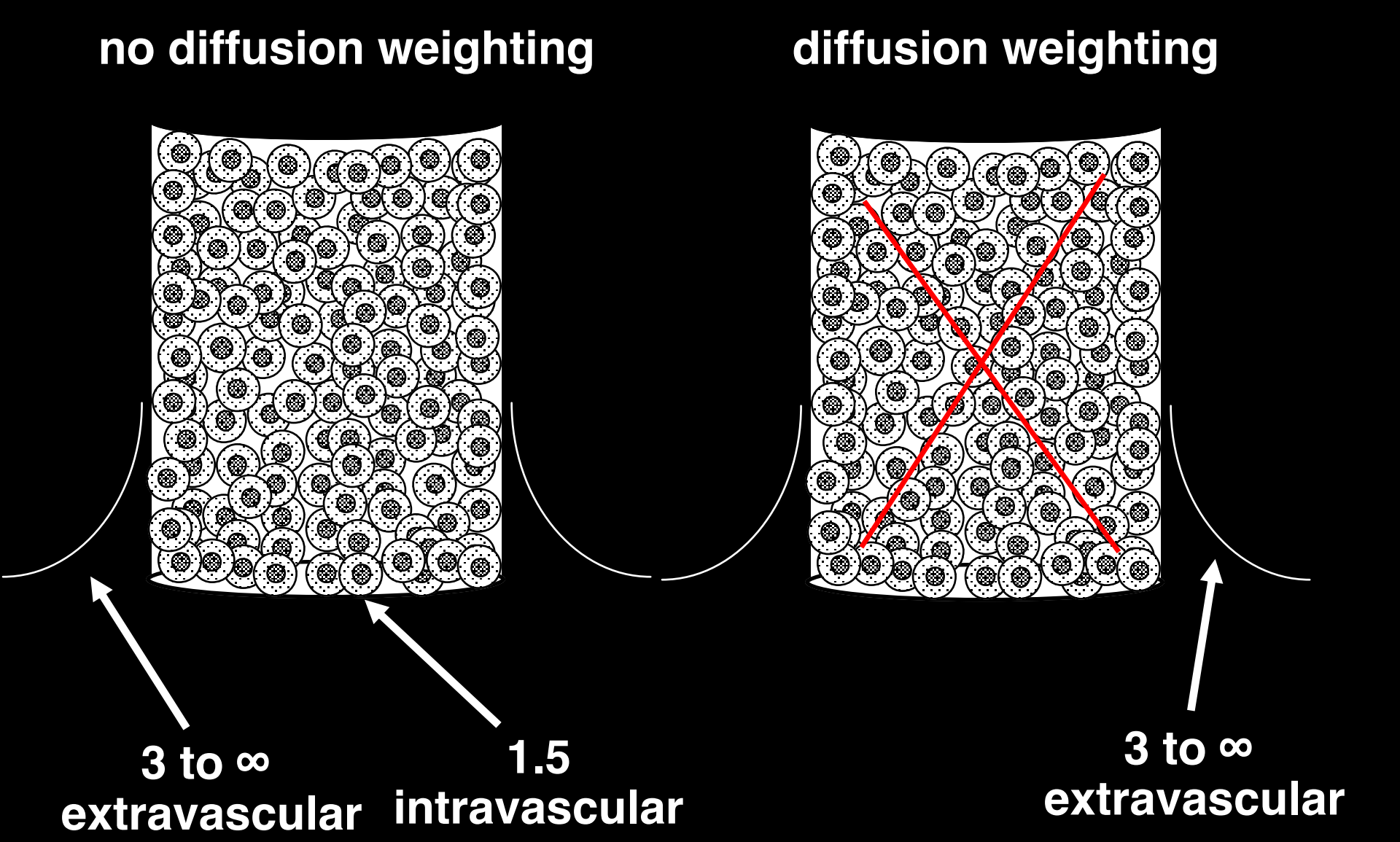
Post Activation Undershoot



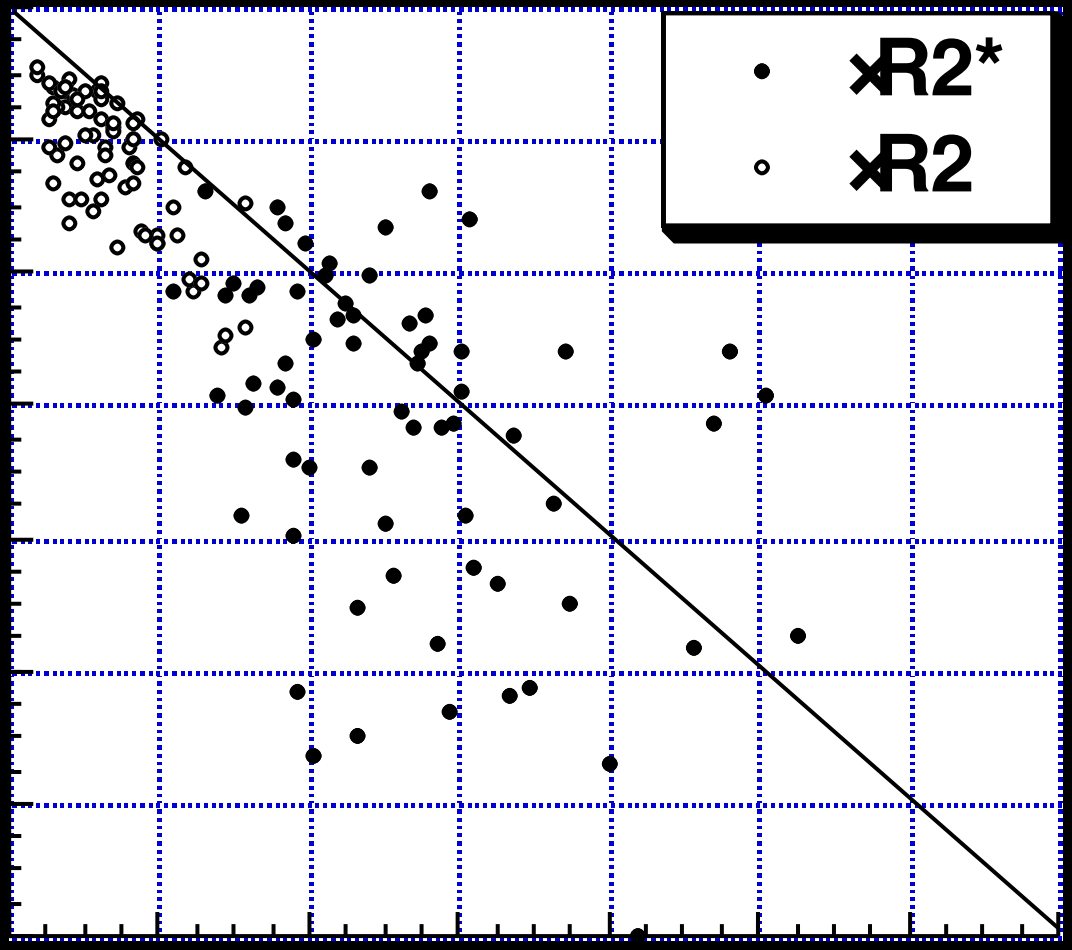
Gradient - Echo Spin - Echo

During Activation Increase

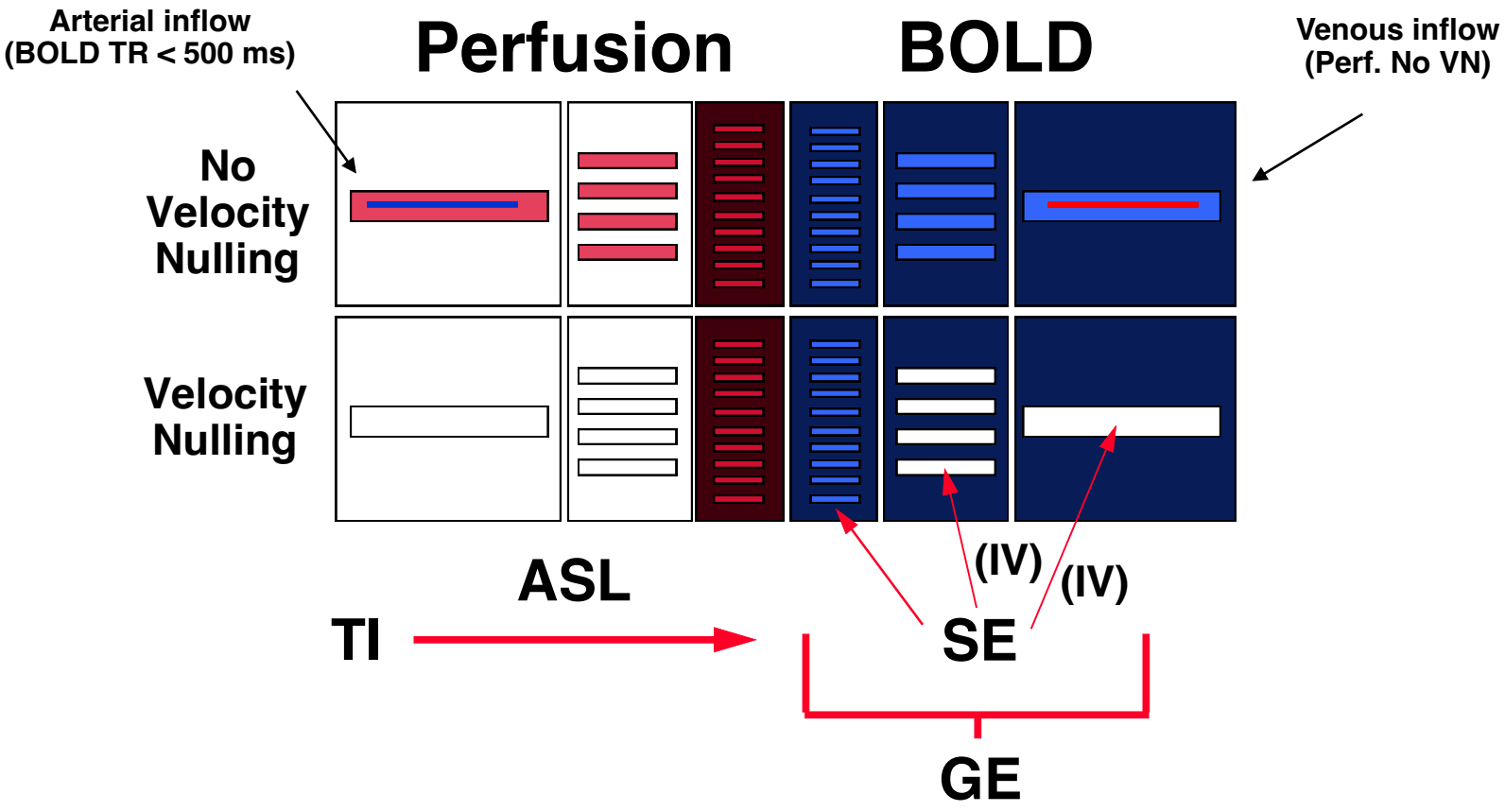
Post Activation Undershoot



ΔR2* / ΔR2:	*ΔR2* / ΔR2 should increase*
= IV and EV	= EV only


R2*
R2

Hemodynamic Specificity



How Much More Information Can we Obtain?

Neuronal Firing Rates
Hemodynamics:

will eventually have quantitative maps of flow, oxygenation, volume, and CMRO2 as well as other parameters such as velocity, exchange, hematocrit, and vascular responsivity.

Resolution: < 1mm and < 100 ms.

Key:

Neuronal, Physiologic, and Pulse Sequence Modulation

Needs...

More “embedded information” pulse sequences
More specific neuronal activation and physiologic stresses

Which requires...

Extreme sensitivity (high field strength)

Functional Imaging Methods / 3T Group

Staff Scientists
Jerzy Bodurka
Sean Marrett

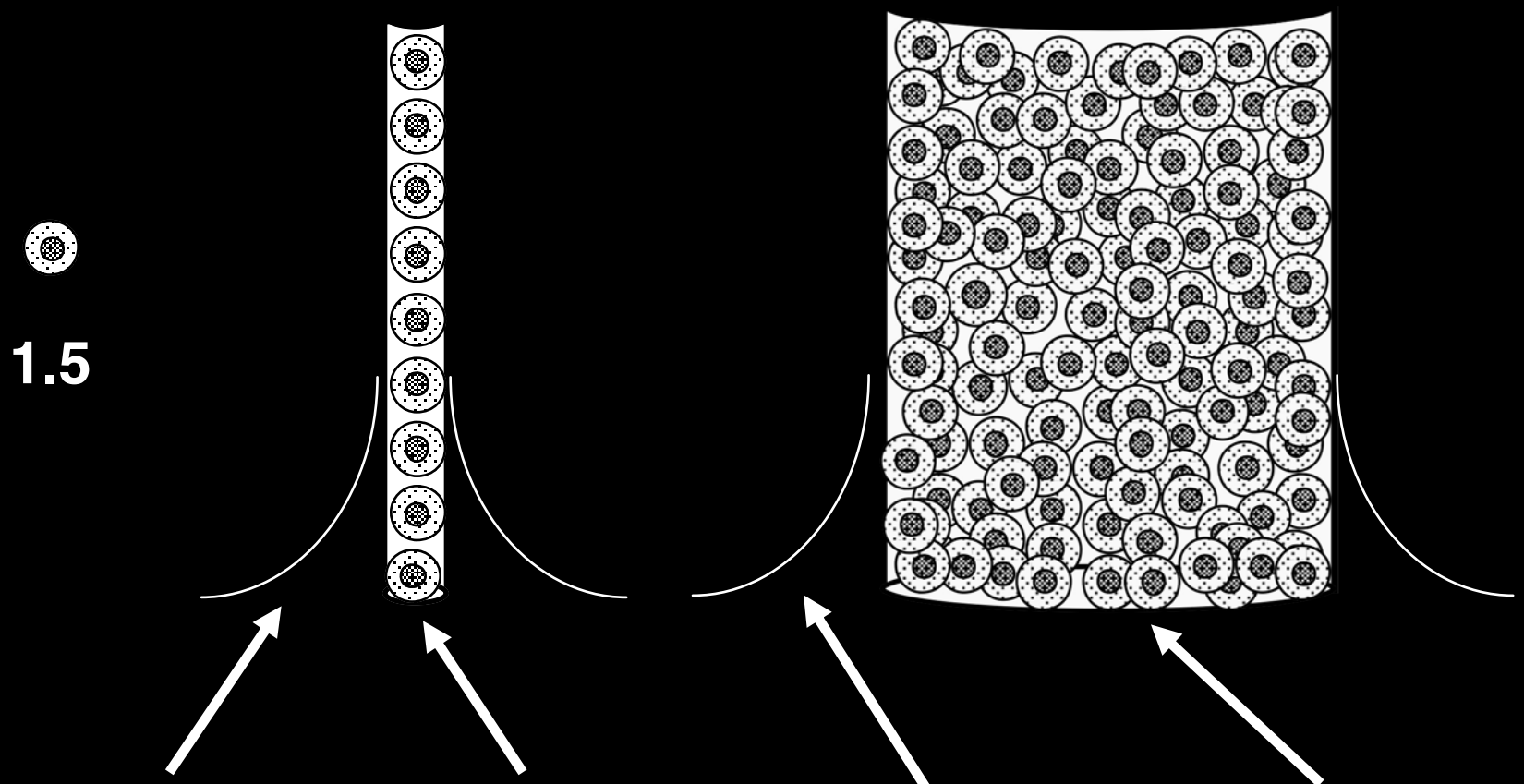
Post Docs
Rasmus Birn
Patrick Frost-Bellgowan
Ziad Saad

Graduate Student
Natalia Petridou

Psychologist
Julie Frost-Bellgowan

Program Assistant
Kay Kuhns

ΔR2* /ΔR2



average ΔR2 / ΔR2 ≈ 3 to 4*

Further Advancements?

More pulse sequence modulation
Model fitting and constraining
Simultaneous collection of multiple types of baseline and time series informatin
Spatial mapping of dynamic characteristics with well controlled stimuli

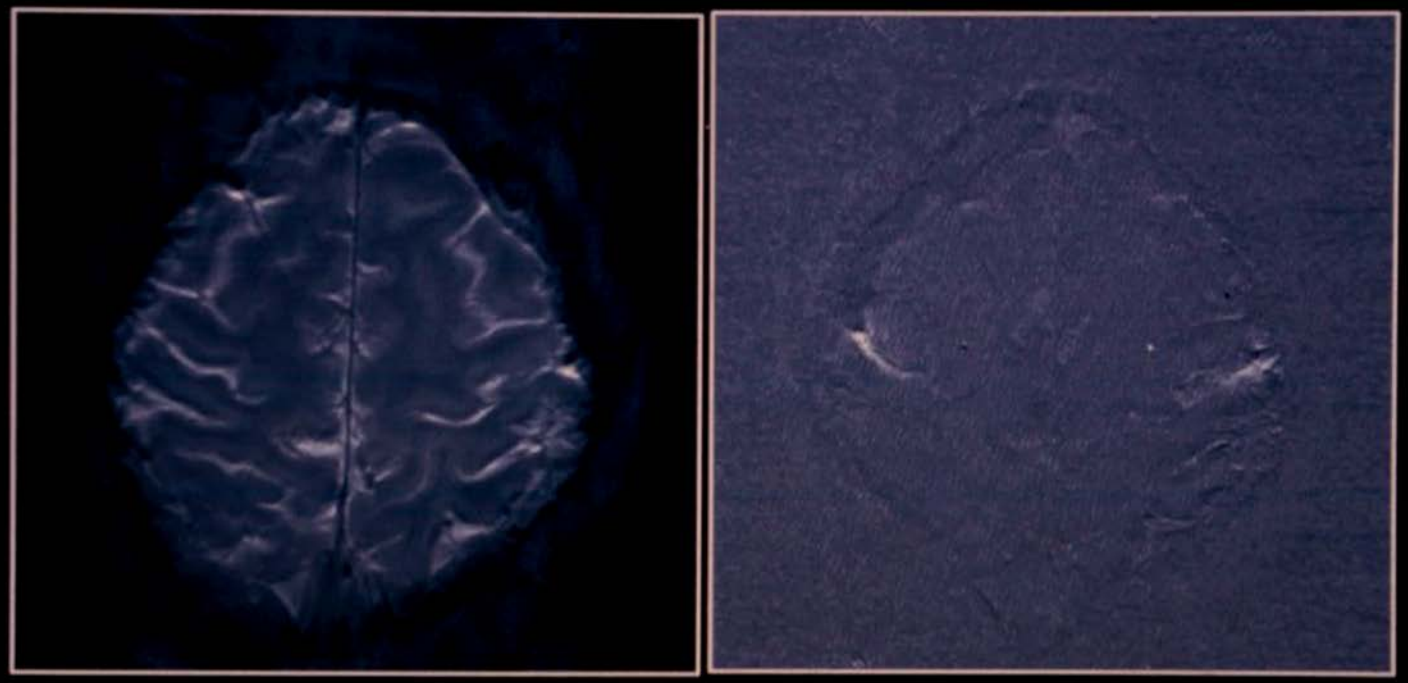
High Field Strength:

Ask questions across spatial resolution scales
Ask more subtle questions about dynamics and magnitudes
Reduced intravascular effects
Create MAPS of these effects..

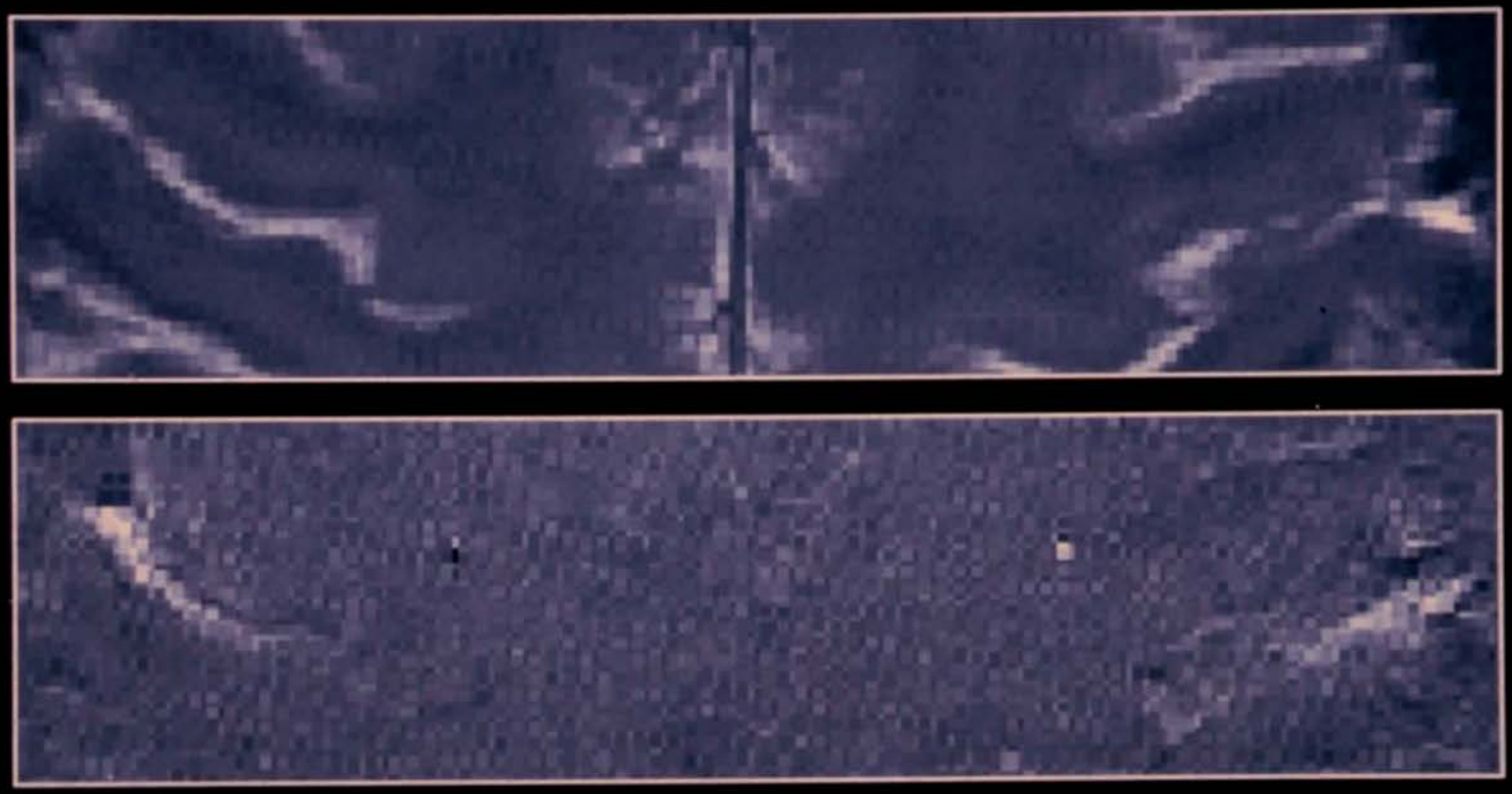
Maps:

Spin-echo vs. gradient-echo
Flow vs. BOLD
Latency
Post undershoot
Pre undershoot
Balloon model parameters
Diffusion attenuation
Correlation with parametric task modulation
Noise correlation

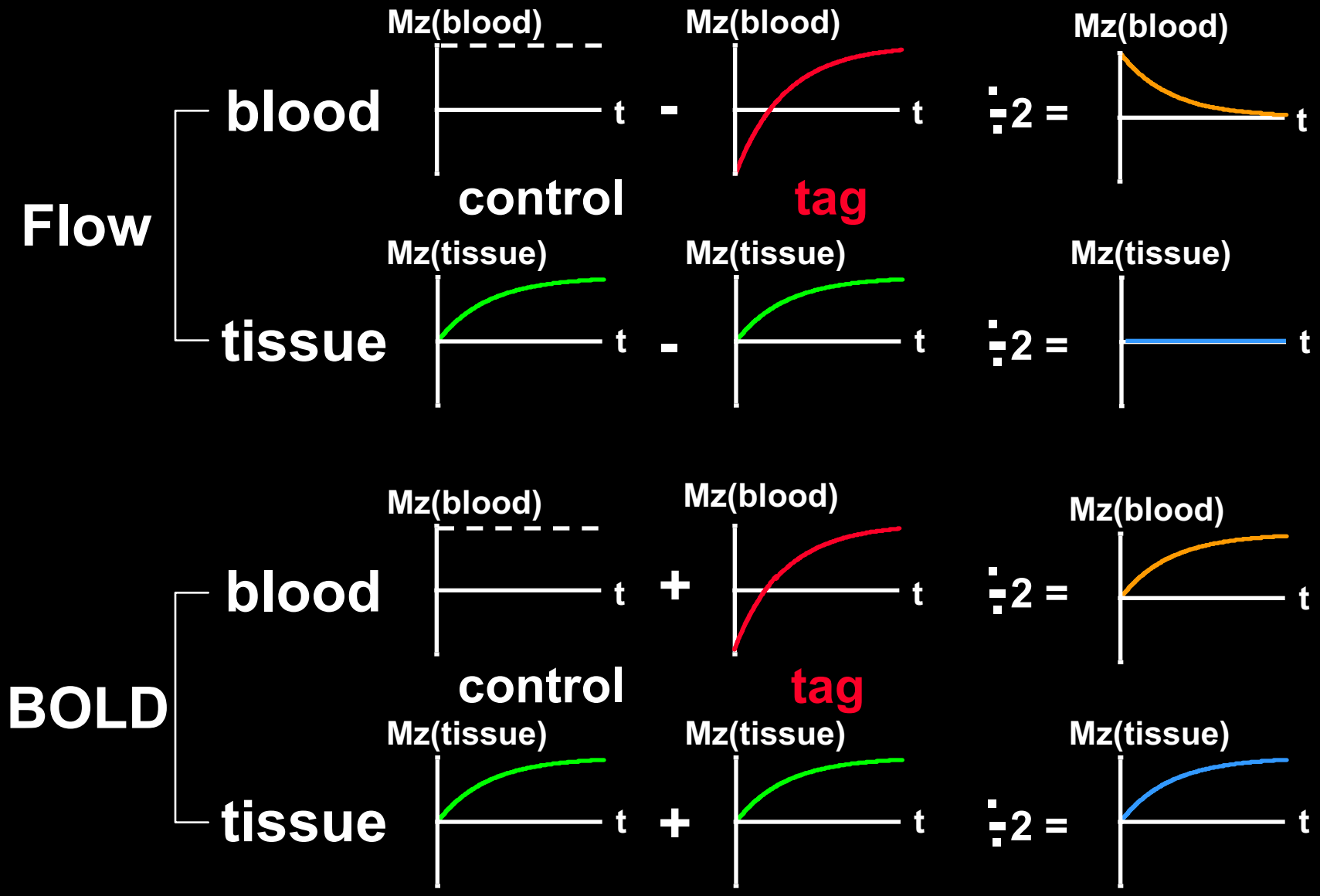
Single - Shot EPI at 3T:
Half NEX, 256 x 256, 16 cm FOV



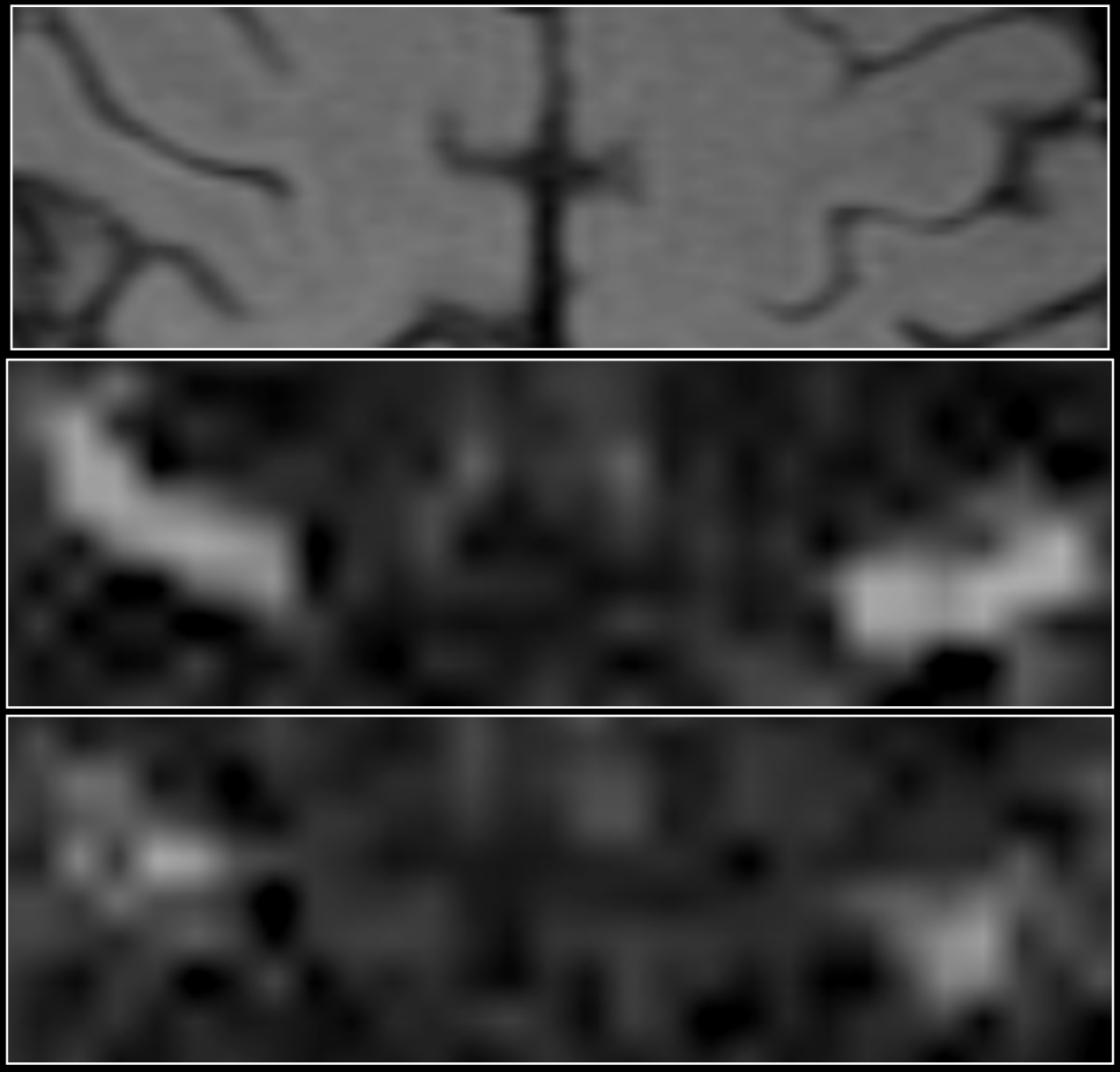
Single - Shot EPI at 3T:
Half NEX 256 x 256, 16 cm FOV



Simultaneous Flow and BOLD



Simultaneous BOLD and Perfusion



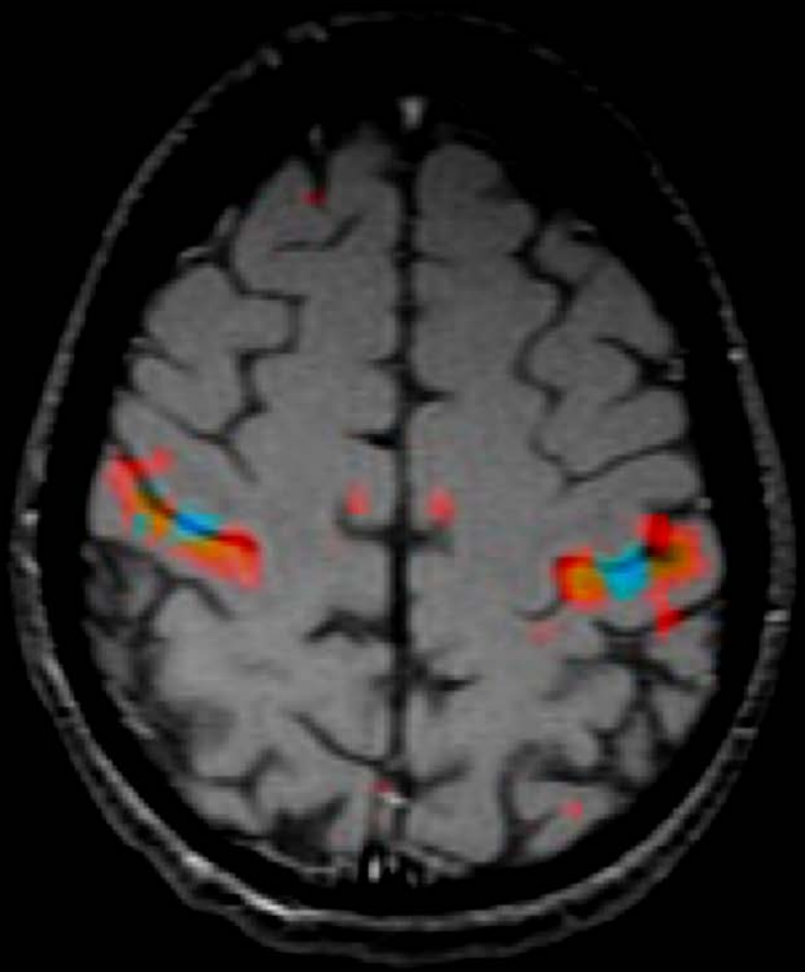
BOLD

Perfusion

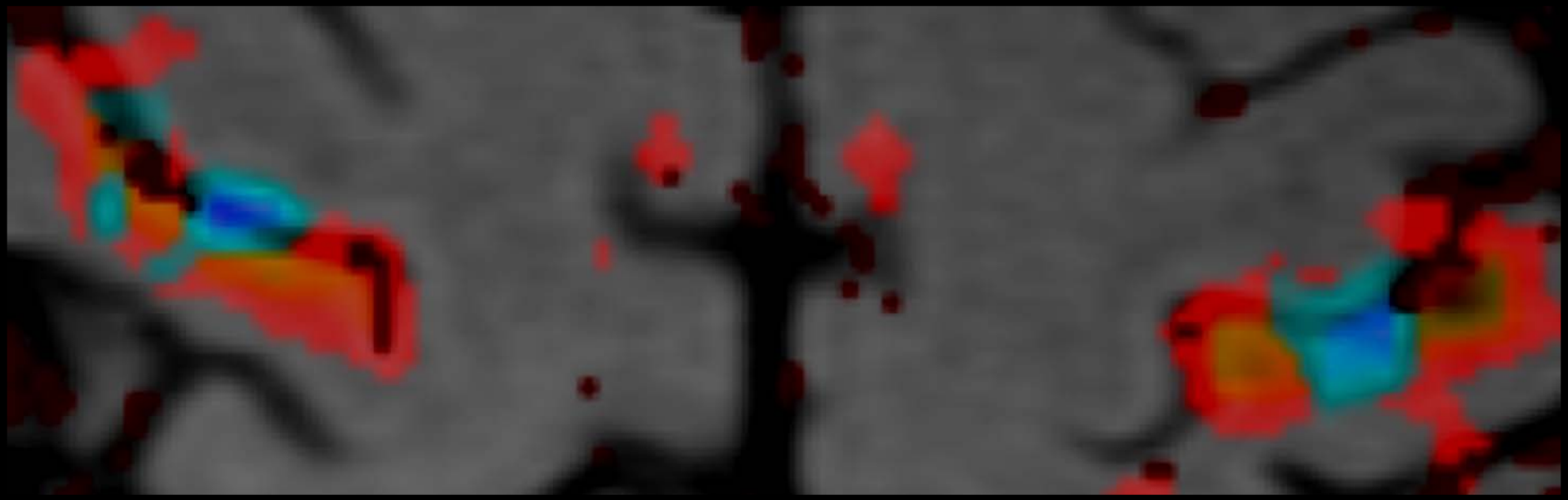
Simultaneous BOLD and Perfusion

perfusion

BOLD



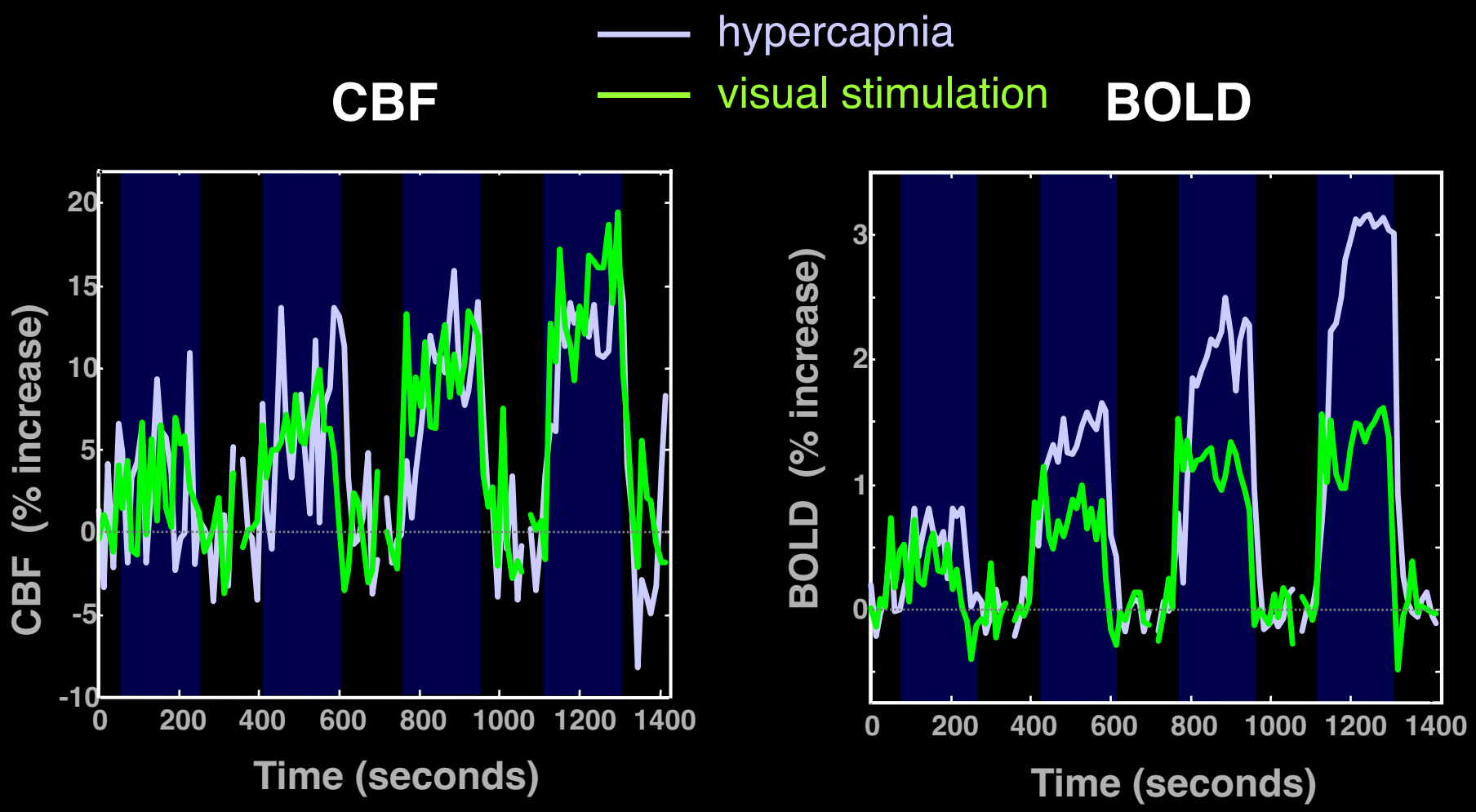
Angiogram
Perfusion
BOLD



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

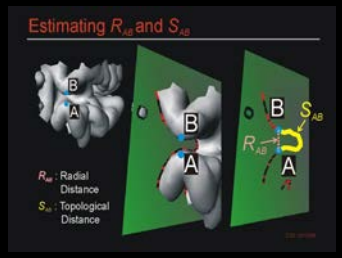
$CMRO_2$-related BOLD signal deficit:

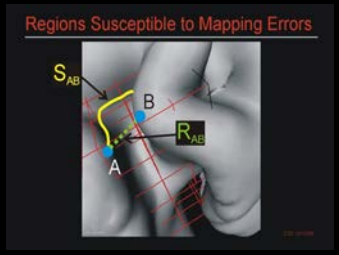
Hoge, et al.

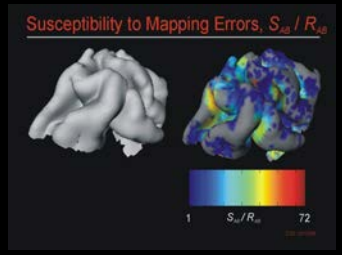


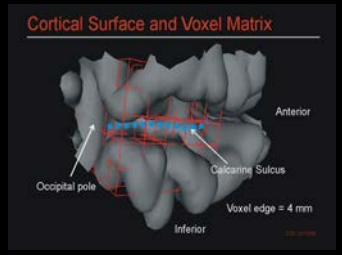
Simultaneous Perfusion and BOLD imaging during graded visual activation and hypercapnia

N=12

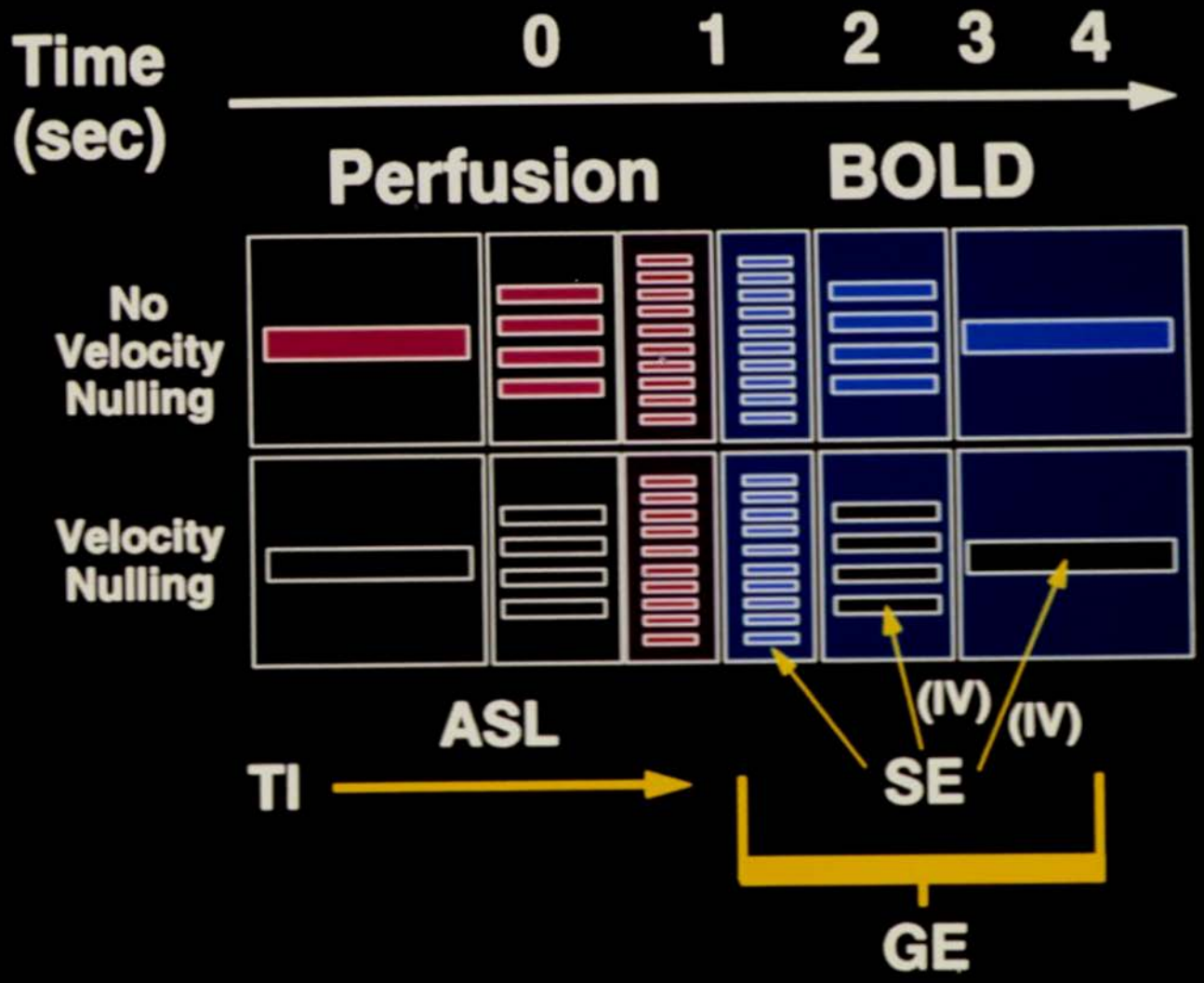

Estimating R_{AB} and S_{AB}
B
A
B
A
B
S_{AB}
R_{AB}
A
R_{AB} : Radial Distance
S_{AB} : Topological Distance


Regions Susceptible to Mapping Errors
S_{AB}
B
R_{AB}
A


Susceptibility to Mapping Errors, S_{AB} / R_{AB}
1
S_{AB} / R_{AB}
72

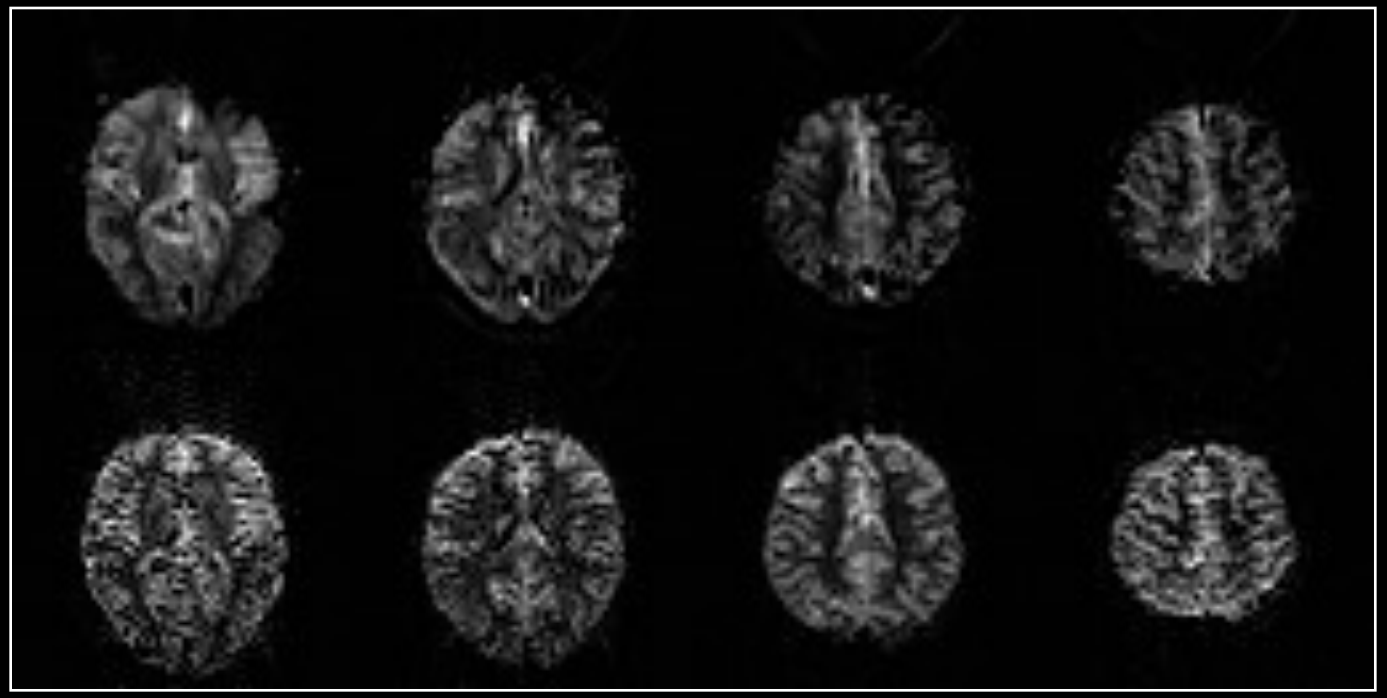

Cortical Surface and Voxel Matrix
Anterior
Calcarine Sulcus
Occipital pole
Voxel edge = 4 mm
Inferior

Vascular Sensitization

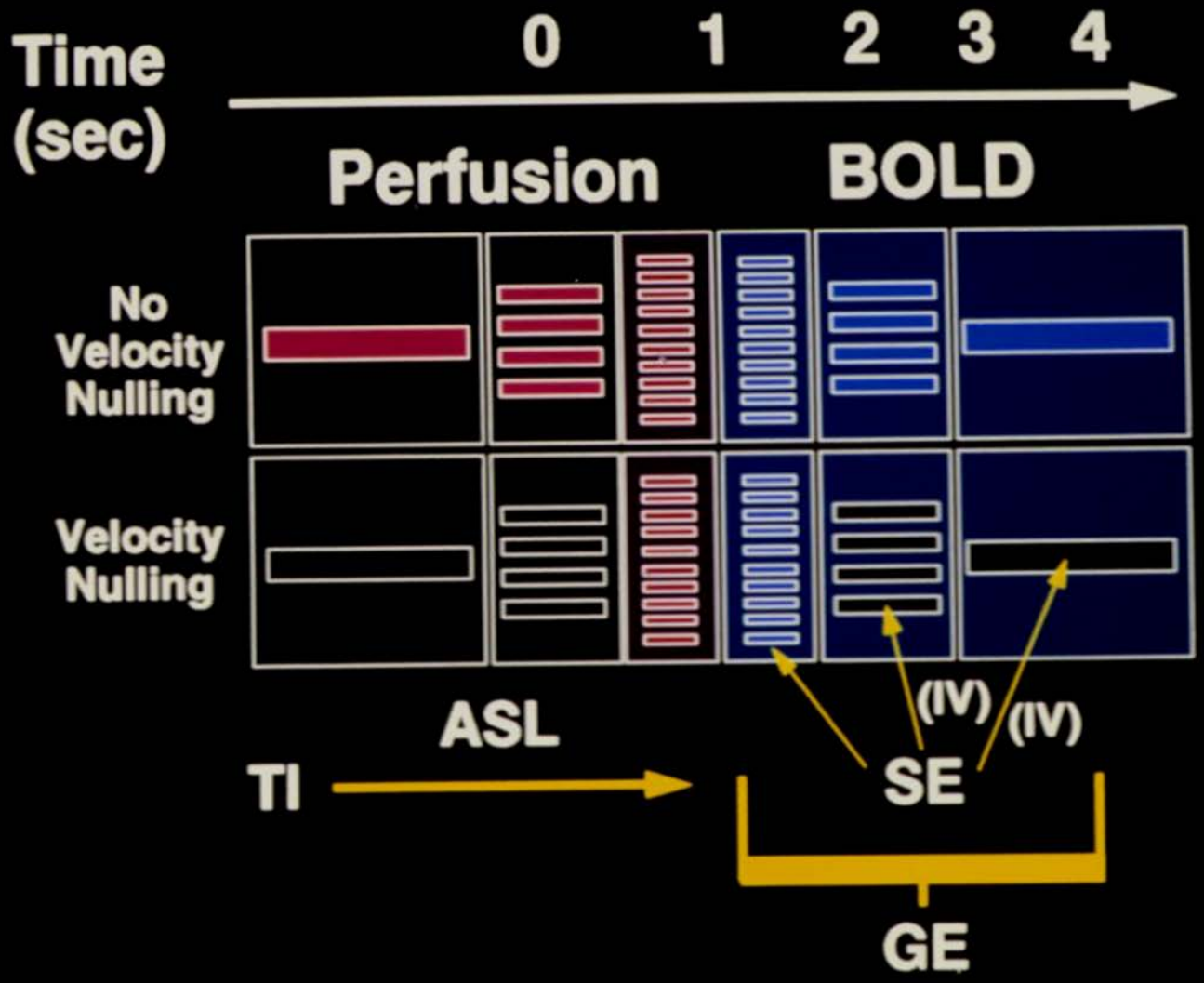


GE
TE = 30 ms

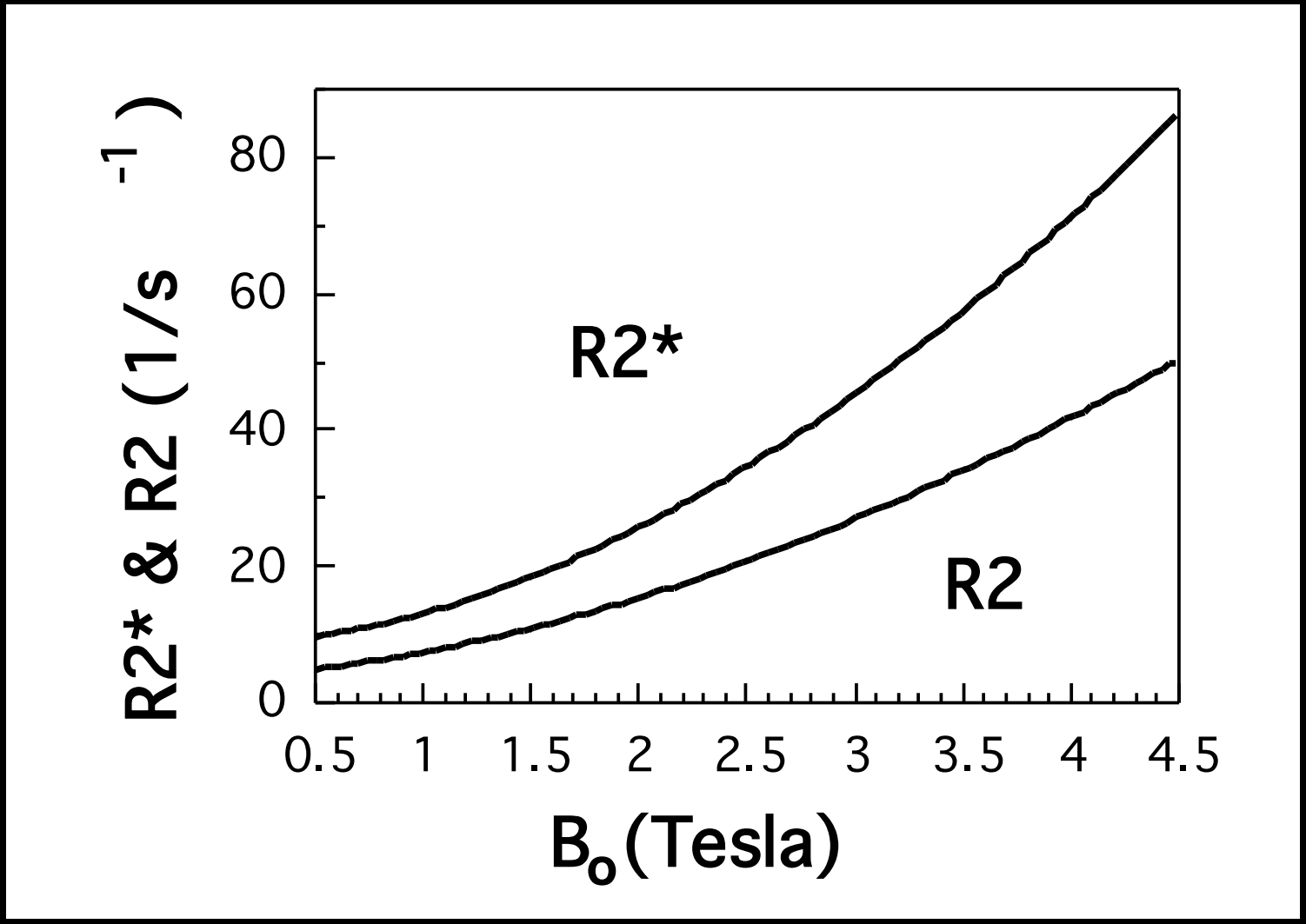
SE
TE = 110 ms



Vascular Sensitization

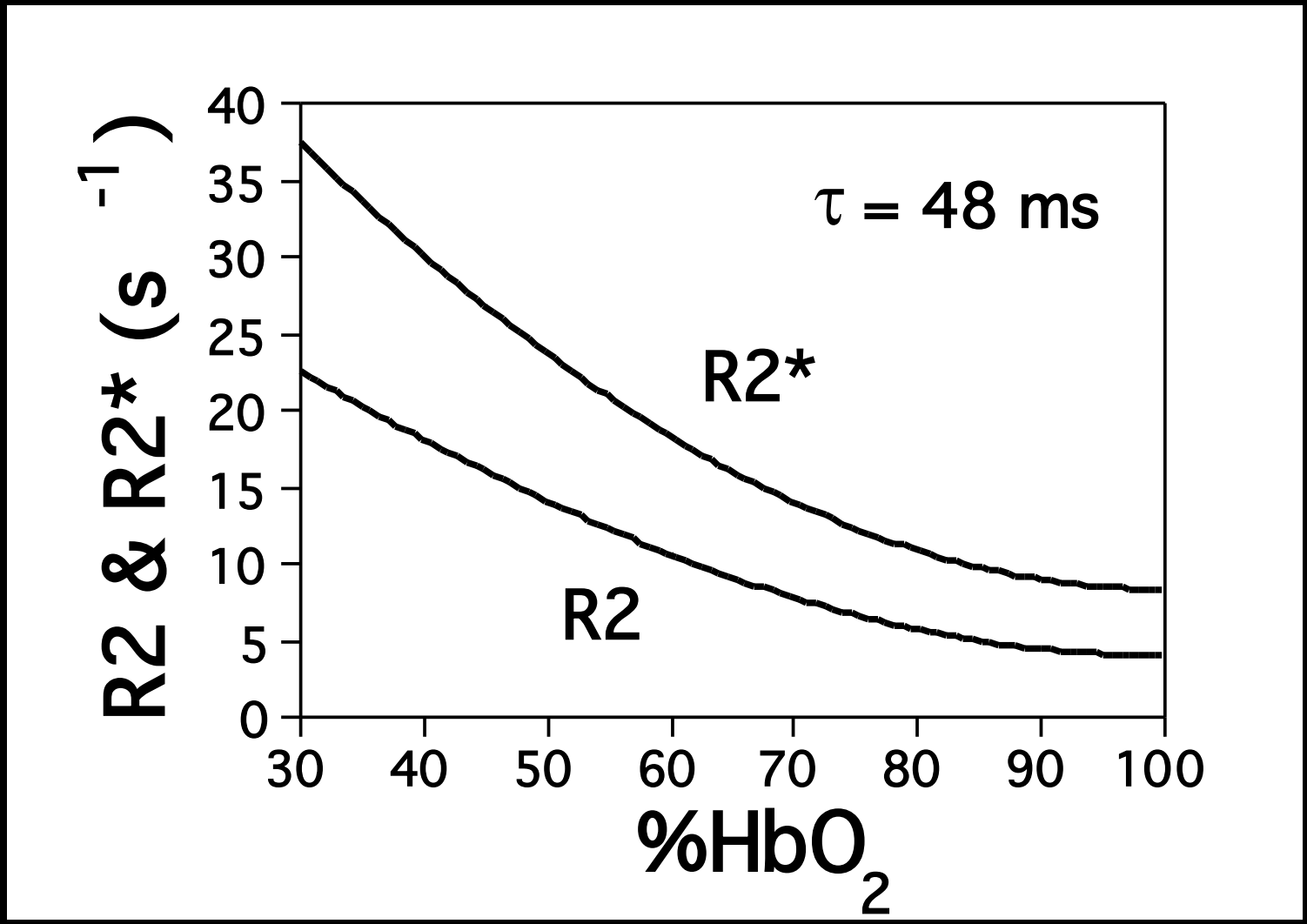


Field -Strength Dependence of R2* and R2



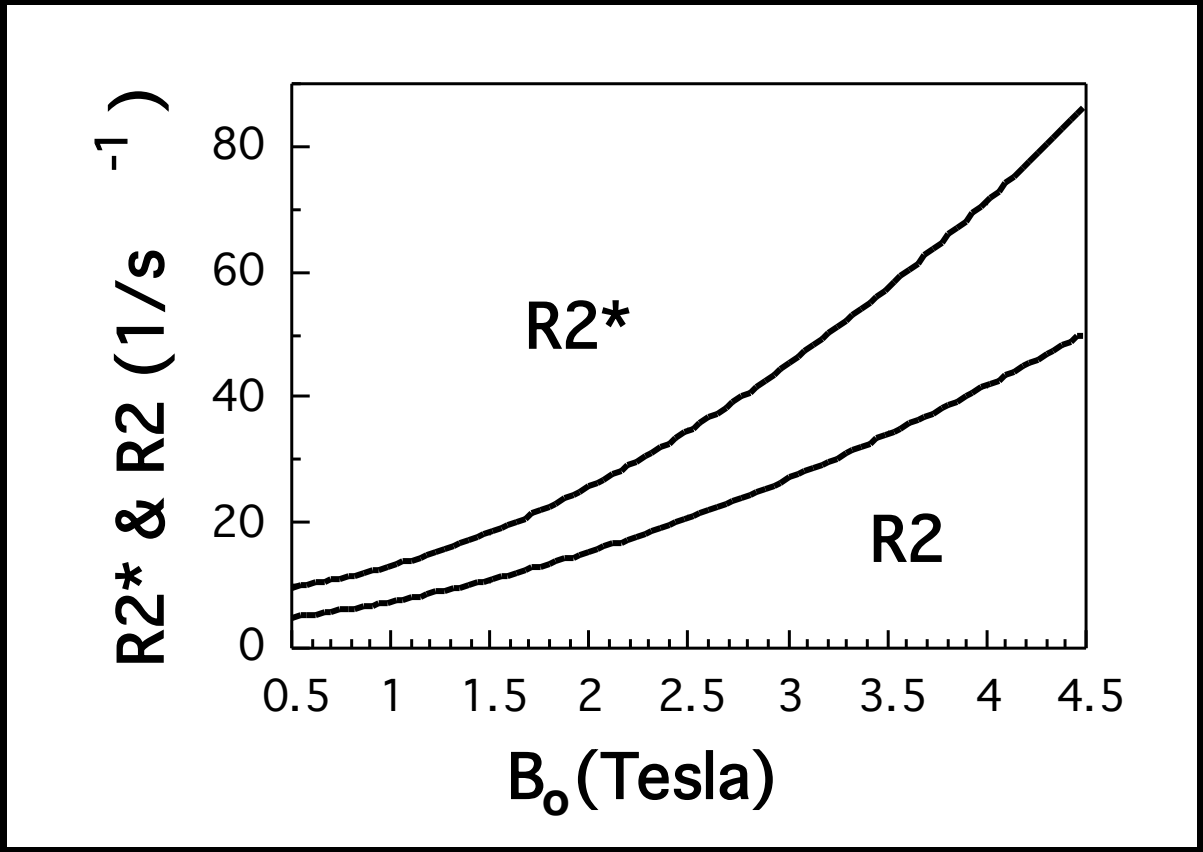
Hct = 44, τ = 48, %HbO_2 = 60, $R2_o$ = 4.0 s^{-1}, $R2'_o$ = 8.3 s^{-1}

Relative R2* and R2 dependence on %HbO_2



Hct = 44, D = 1.8 μm ^{2} / ms, $R2_o$ = 4.0 s^{-1}, $R2'_o$ = 8.3 s^{-1}

Field -Strength Dependence of R2* and R2

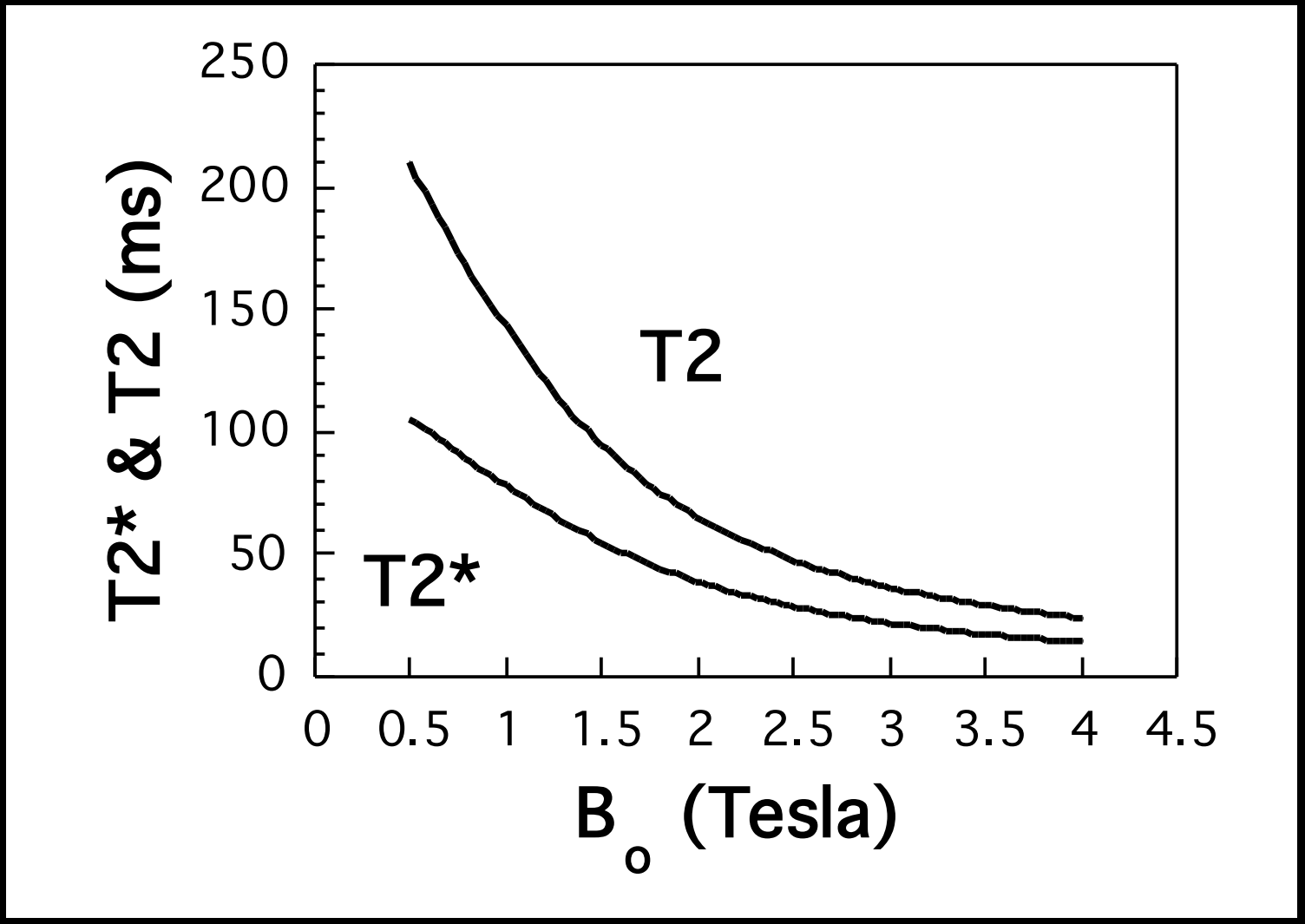


$R2^* = 8.33 + 4.8 \times B_o^{1.85}$

$R2 = 4.0 + 4.8 \times B_o^{1.73}$

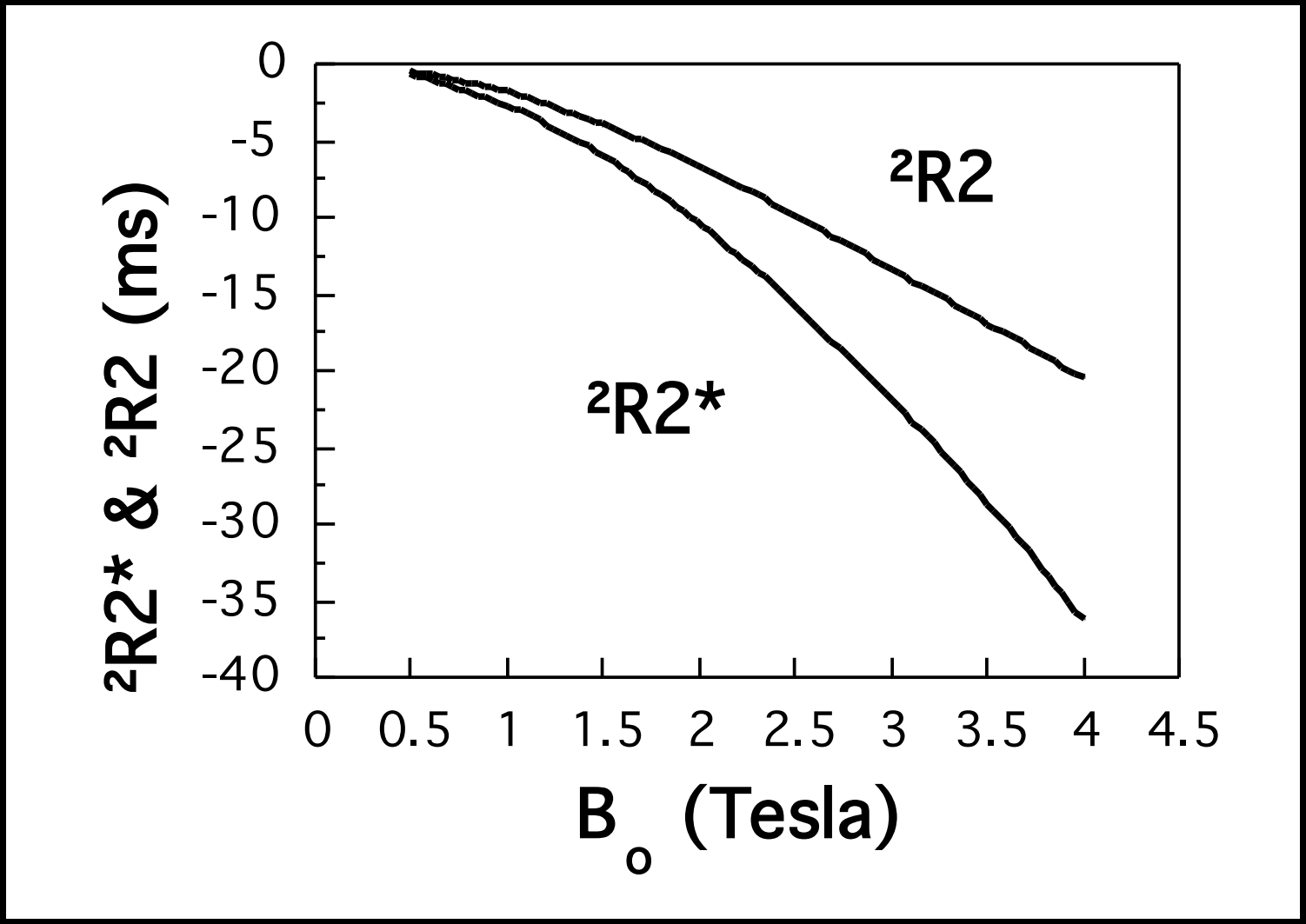
Hct = 44, τ = 48, $\%HbO_2$ = 60, $R2_o = 4.0\ s^{-1}$, $R2'_o = 8.3\ s^{-1}$

Field -Strength Dependence of T2* and T2

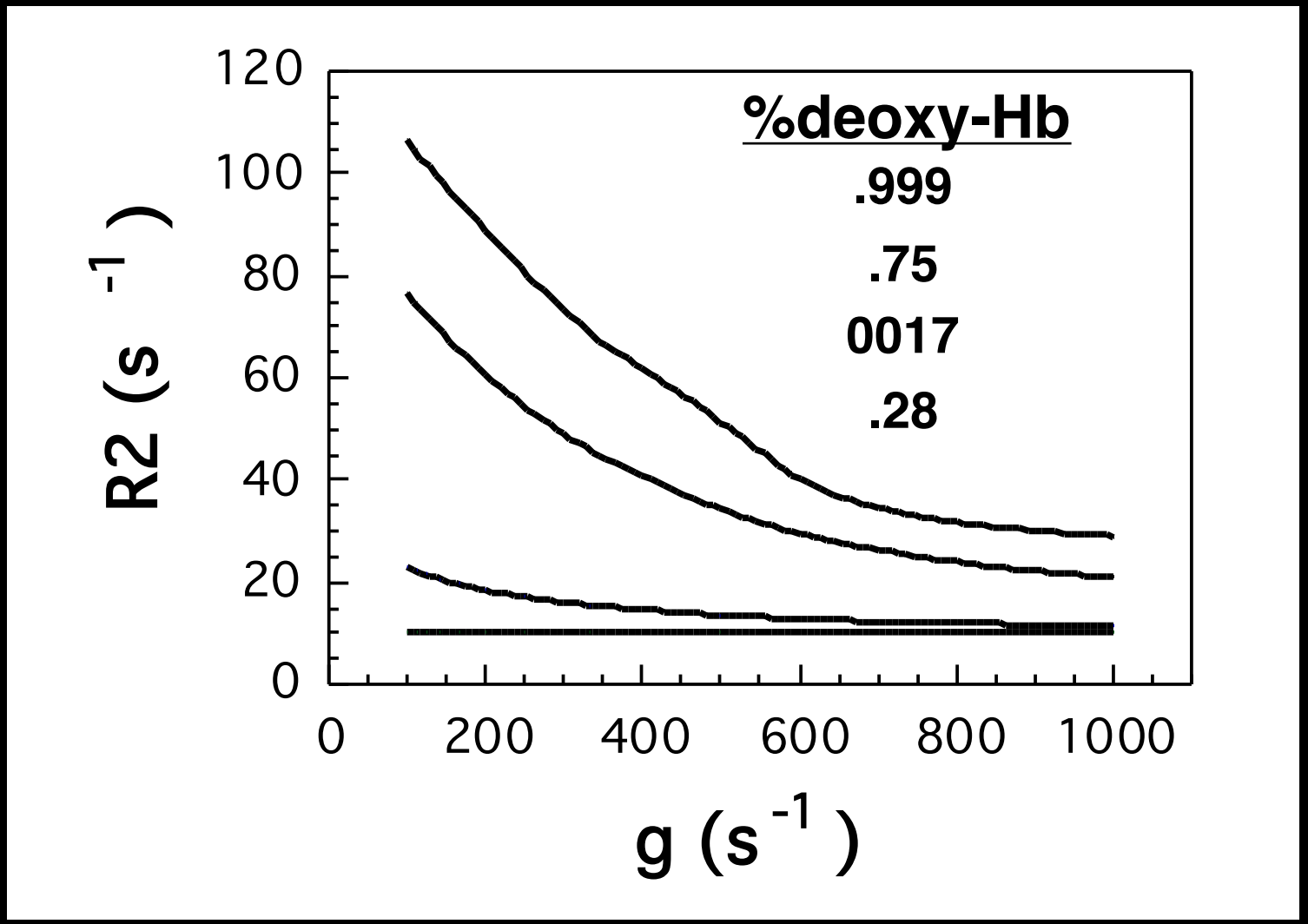


Hct = 44, τ = 48, %HbO_2 = 60, $T2_o$ = 250 ms, T2' = 120 ms

Relaxation rate *change* dependence on field strength

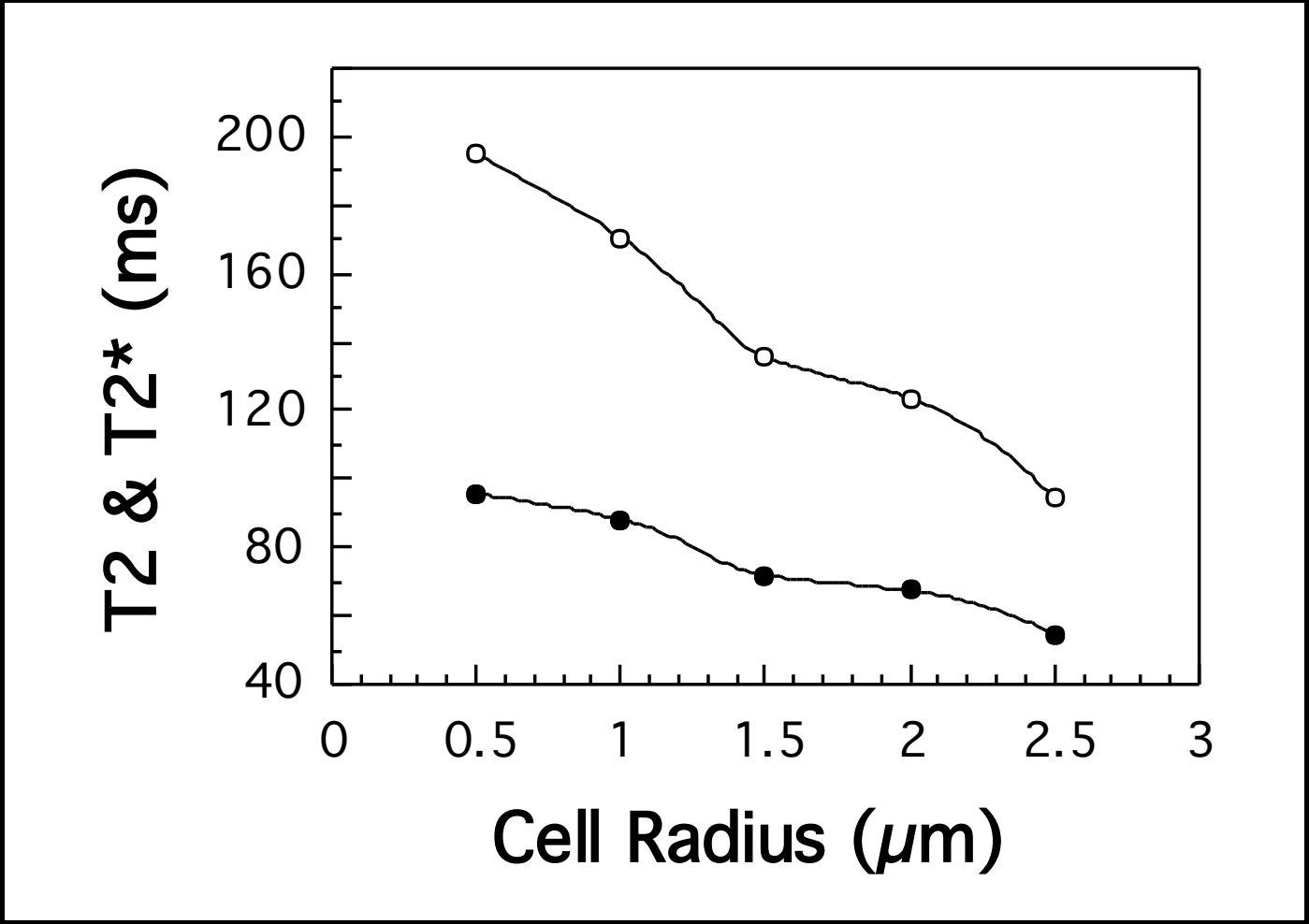


%HbO_2 = 60 -> 75, Hct = 44, τ = 48



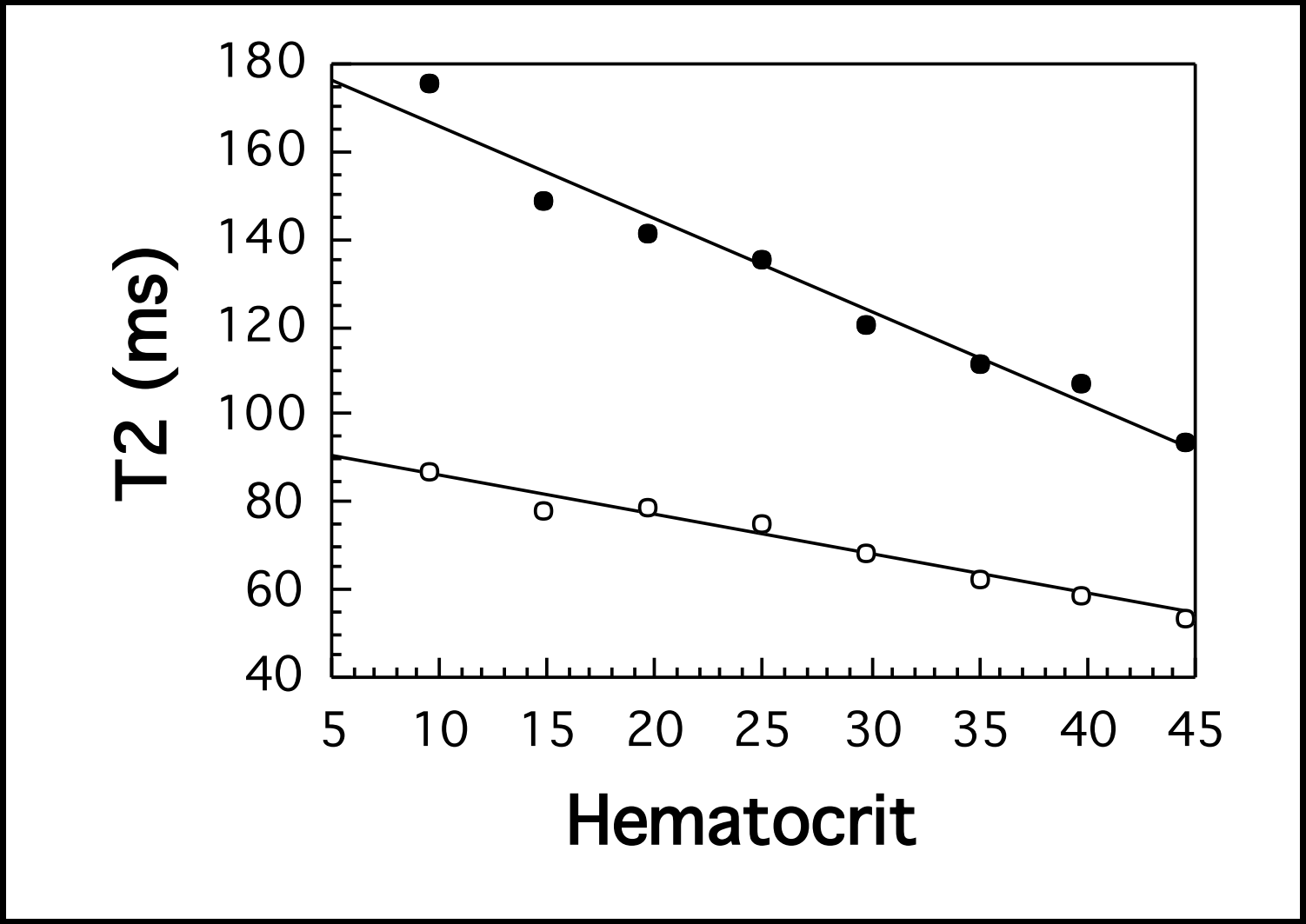
Hct = 44, $R2_o$ = 4.0 s^{-1}

Cell Radius Effect



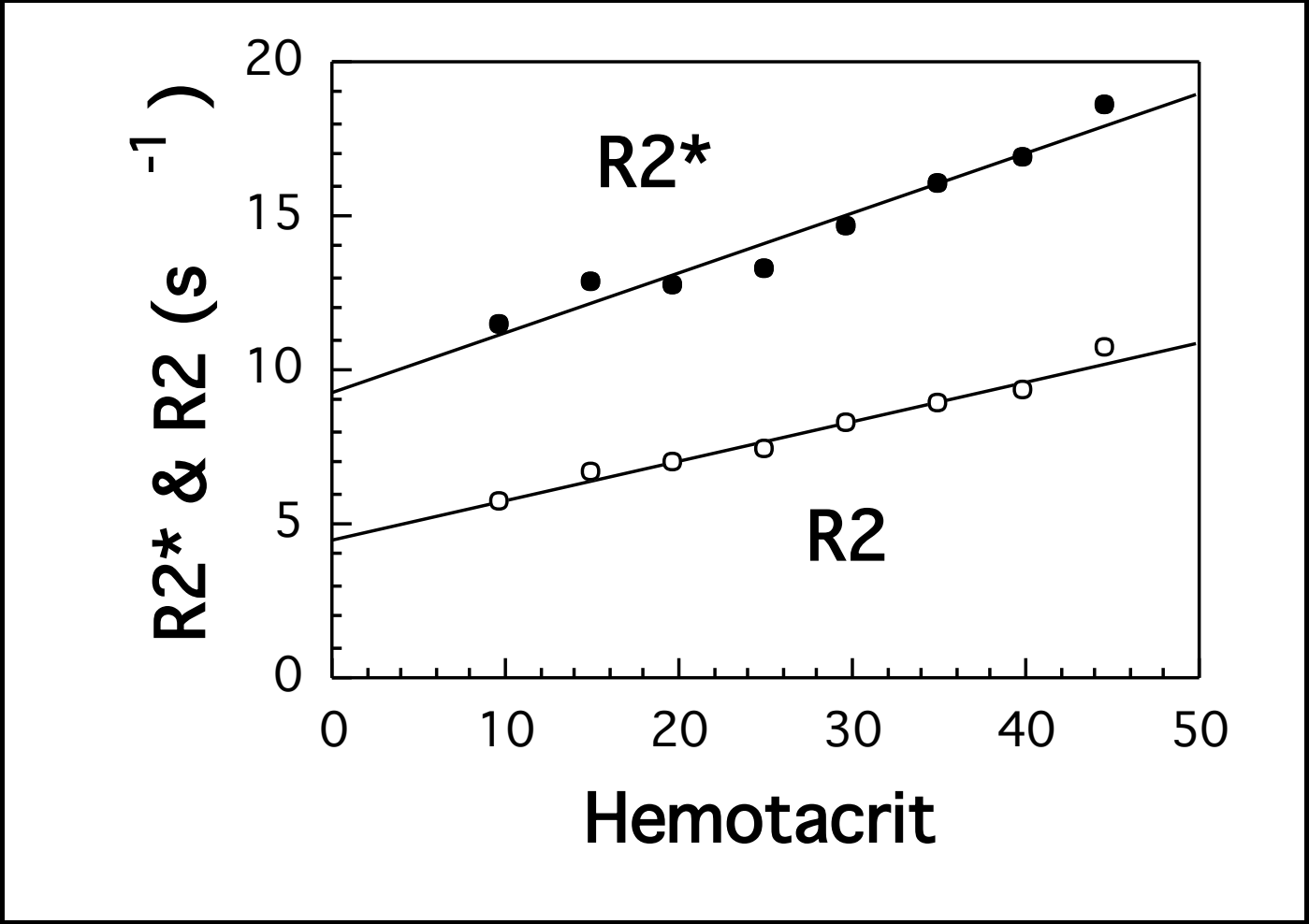
Hct = 44, τ = 48, %HbO_2 = 60, $T2_o$ = 250 ms, T2' = 120 ms

Hematocrit Effect



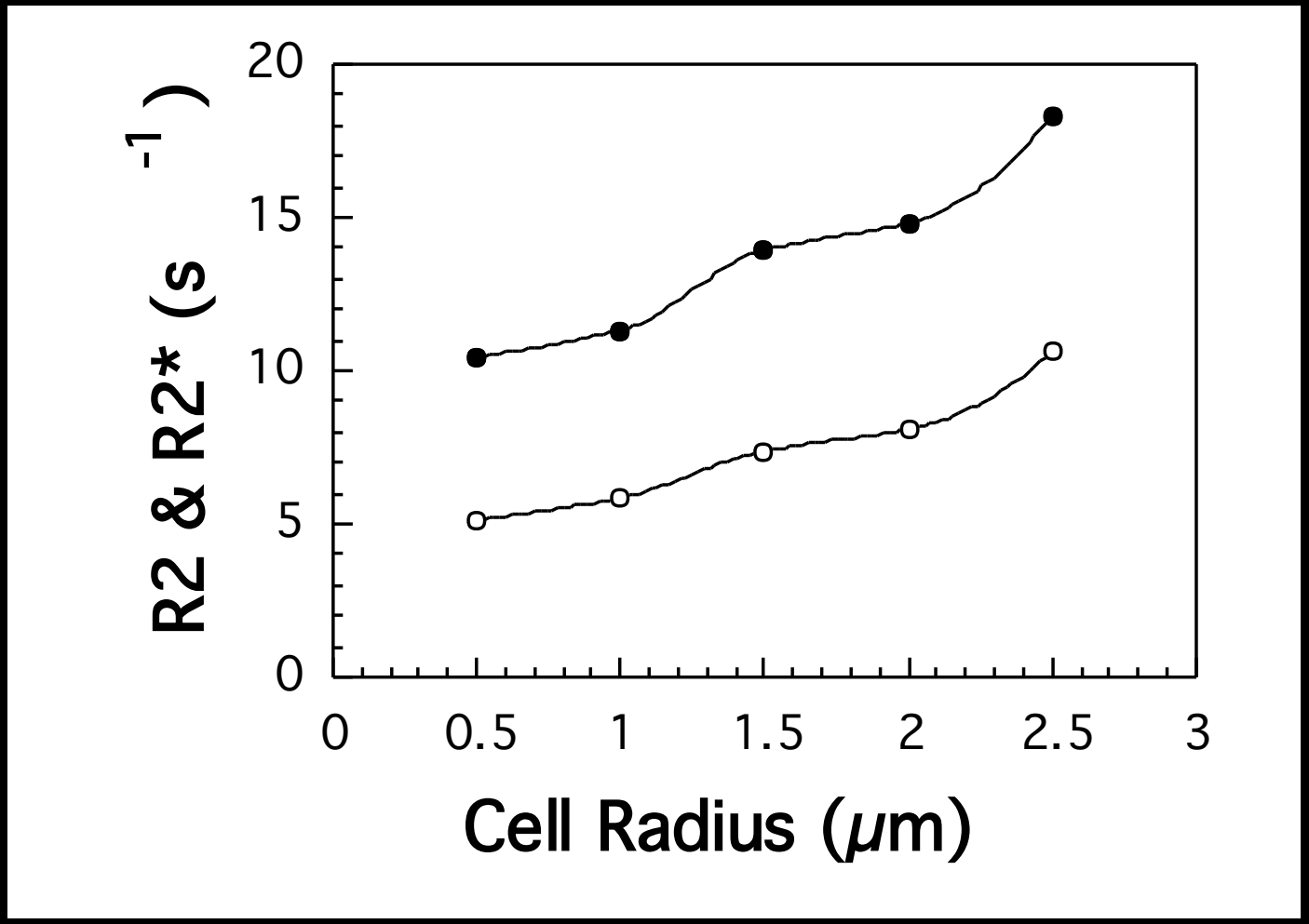
τ = 48, %HbO_2 = 60, $T2_o$ = 250 ms, T2' = 120 ms

Hematocrit Effect



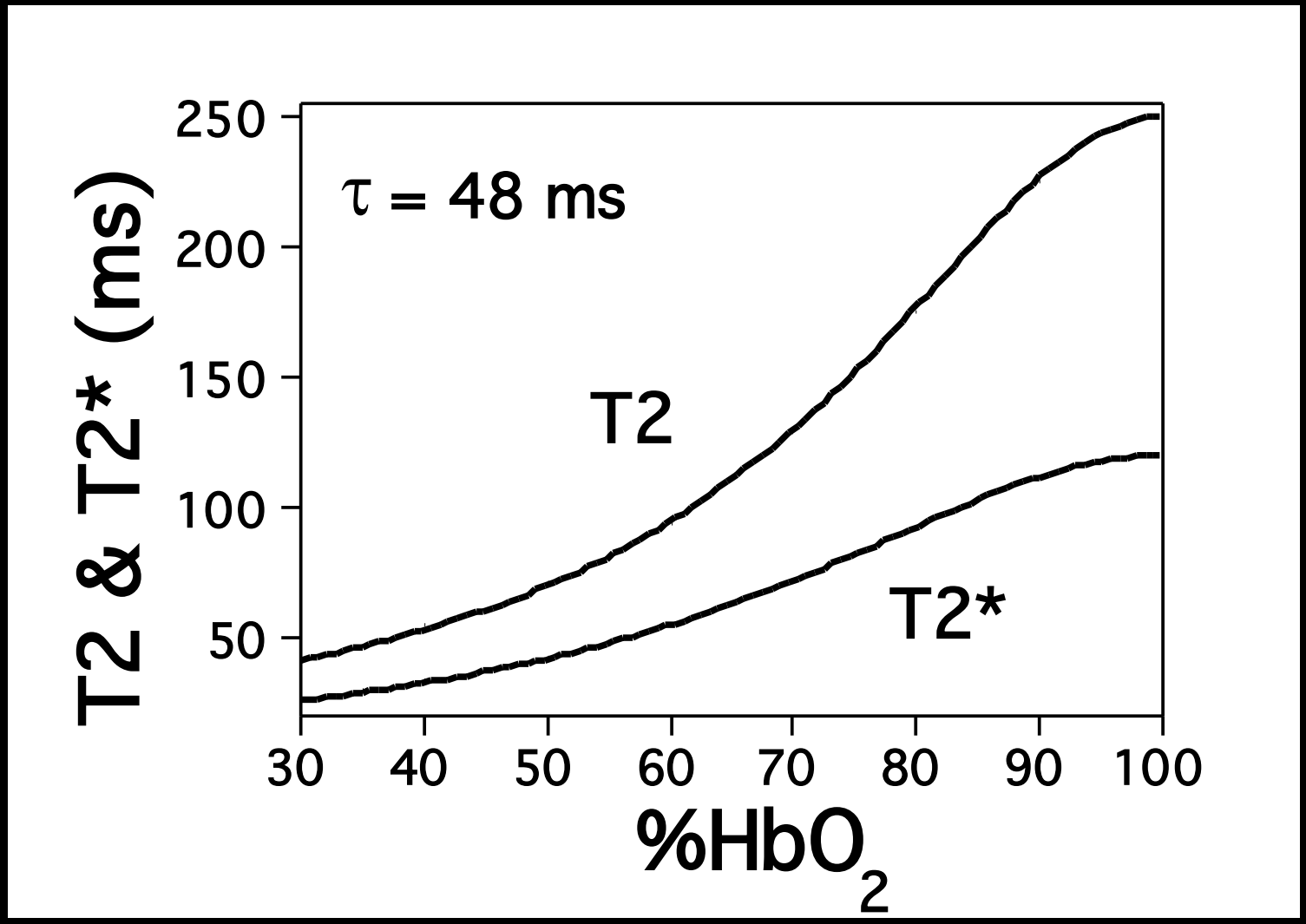
$\tau = 48$, $\%HbO_2 = 60$, $R2_o = 4.0\ s^{-1}$, $R2'_o = 8.3\ s^{-1}$

Cell Radius Effect



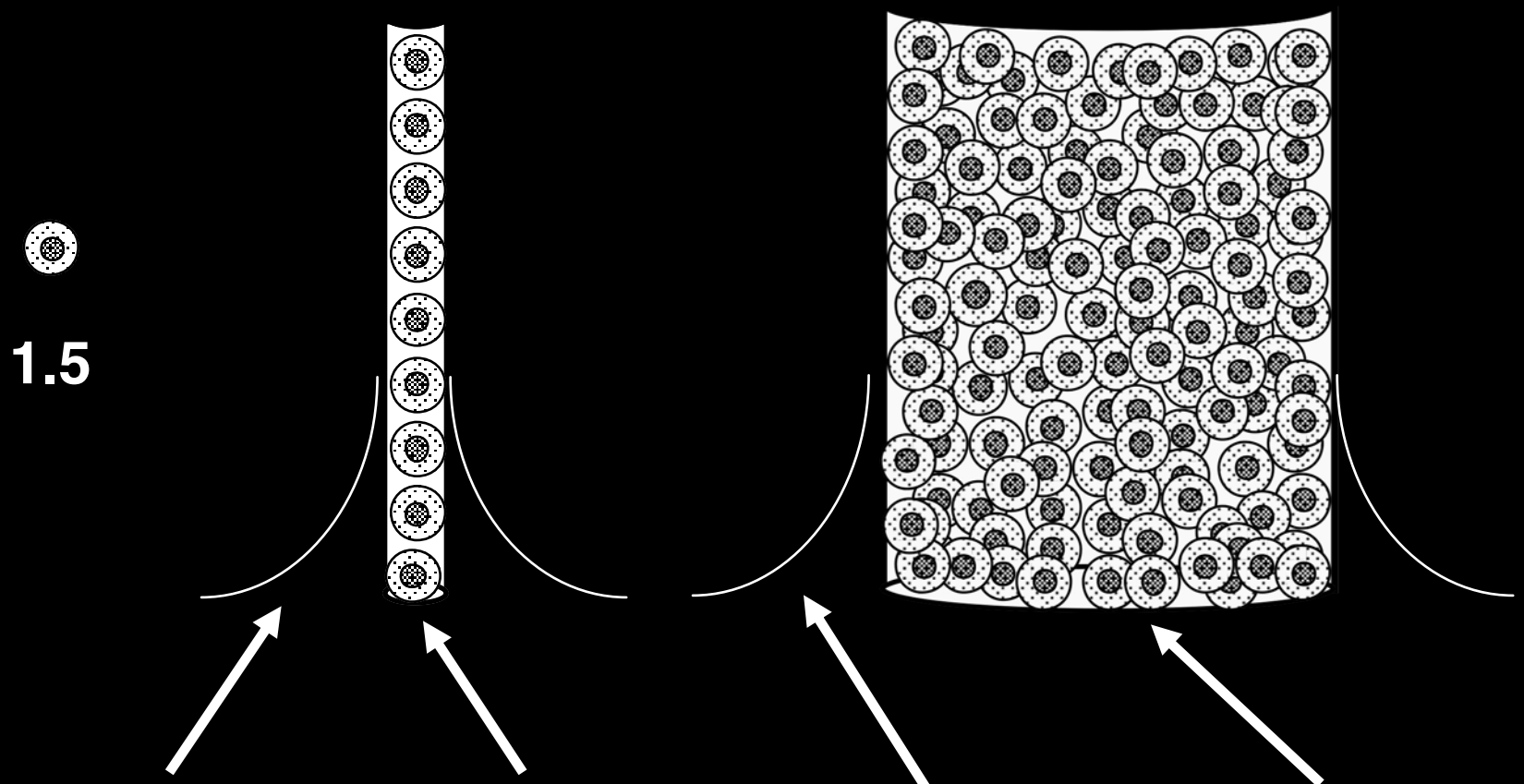
Hct = 44, τ = 48, %HbO_2 = 60, $R2_o$ = 4.0 s^{-1}, $R2'_o$ = 8.3 s^{-1}

Relative T2* and T2 dependence on $\%HbO_2$



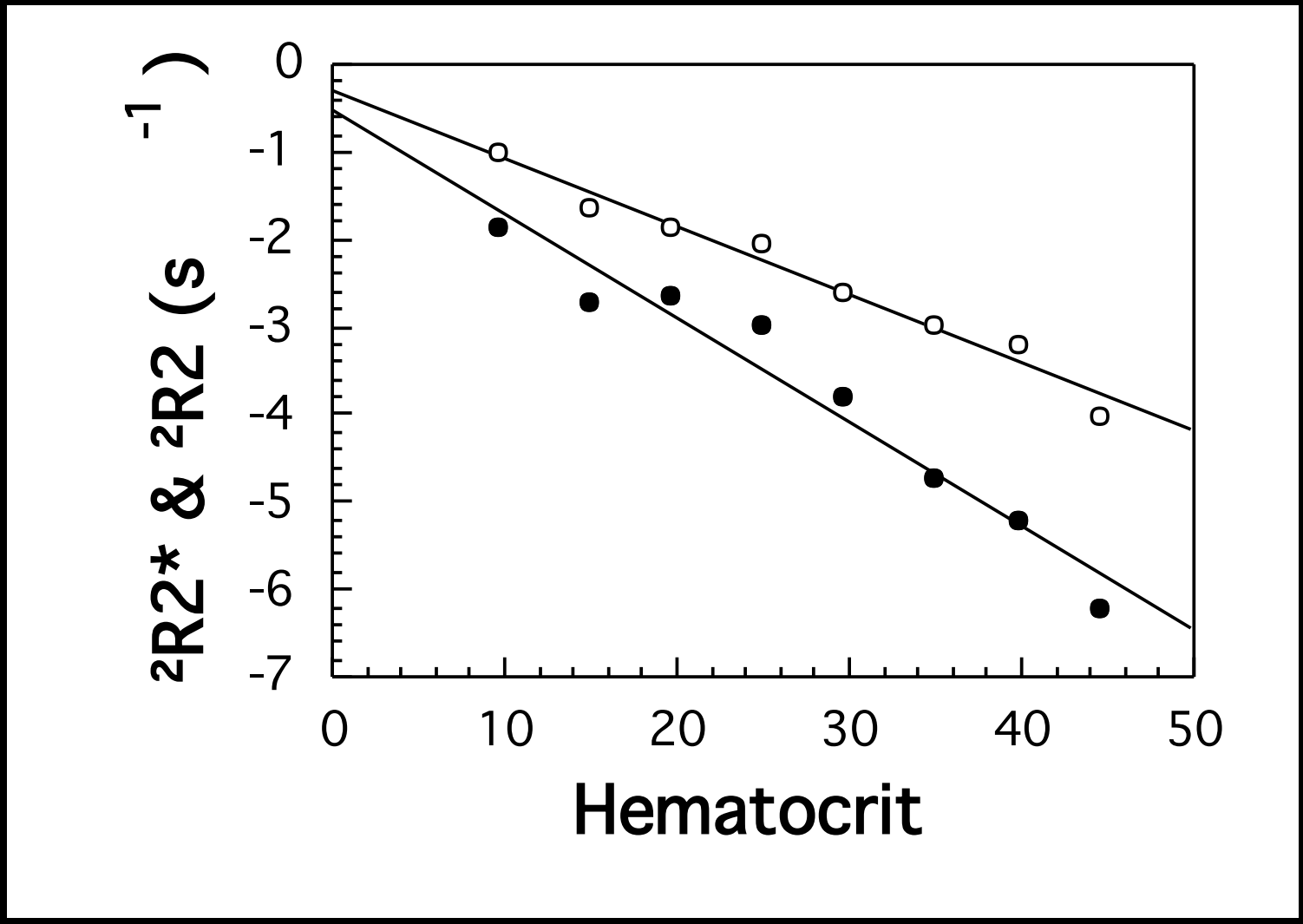
Hct = 44, D = 1.8 μm^2 / ms, $T2_o$ = 250 ms, $T2'_o$ = 120 ms

ΔR2* /ΔR2



average ΔR2 / ΔR2 ≈ 3 to 4*

Hematocrit Effect Relaxation Rate Changes with and Oxygenation Change



τ = 48, %HbO_2 = 60 -> 75

Numerical Simulations of the Oxygenation Dependence of the T2 and T2* of Whole Blood using a Deterministic Diffusion Model

P. A. Bandettini [1] J. L. Boxerman [1, 2] E. C. Wong [3]

R. M. Weisskoff [1] and B. R. Rosen [1]

[1] Massachusetts General Hospital - NMR Center

[2] Harvard - MIT Division of
Health Sciences and Technology

[3] University of California - San Diego

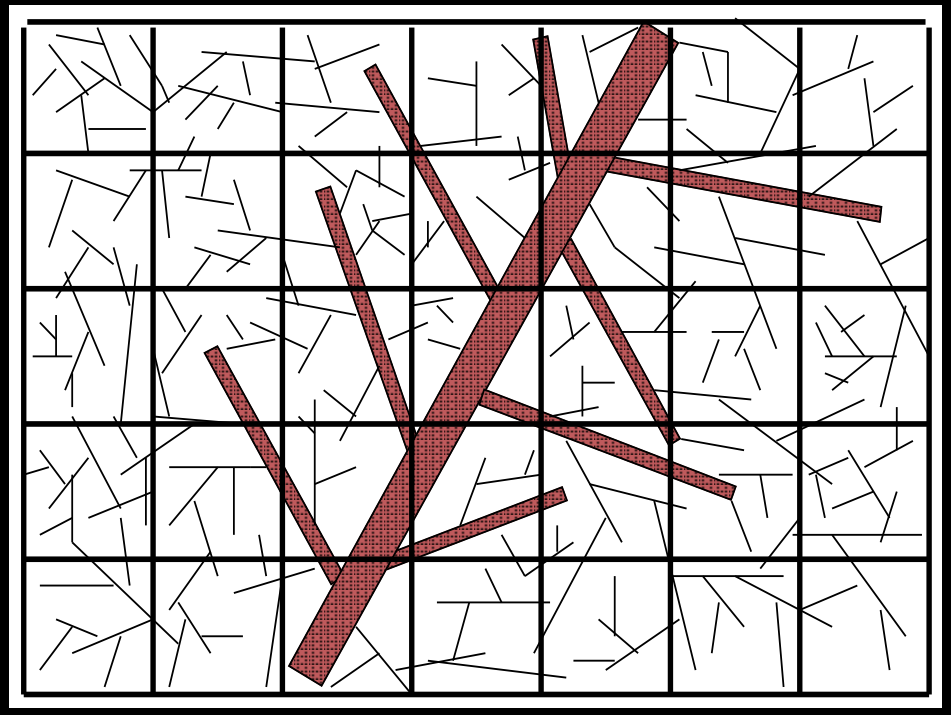
Activation-induced MR Signal Change Mechanisms

T1

Inflow

T2

T2*



•compartment sizes	2.5 μ m -> 380 μm
•proton dynamics	Diffusion, Exchange, Flow, Pulsation
•orientation	Random -> Single Orientation
•oxygen saturation	0.6 -> 0.95
•volume	2% -> 100% (per voxel)
•hematocrit	10 -> 50

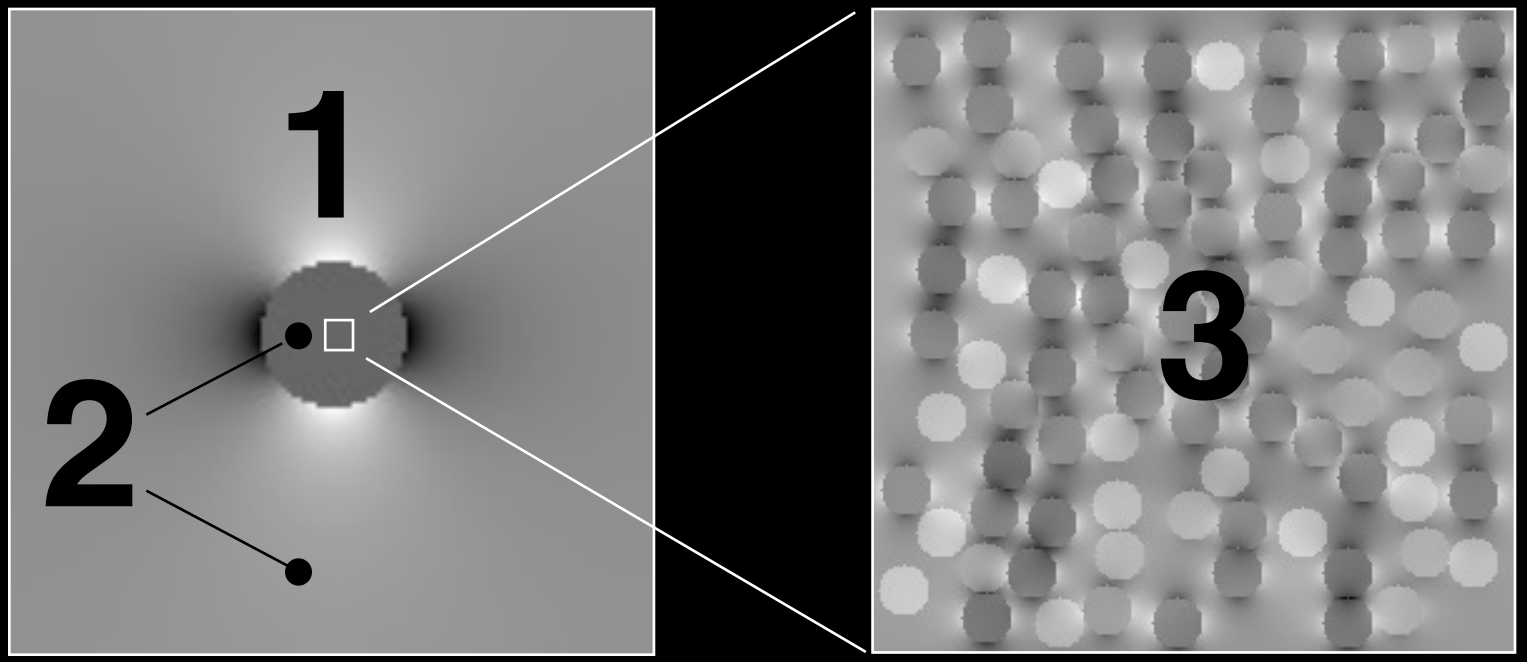
also

relative intravascular and extravascular effects

Intravascular and Extravascular T2* Effects

vessel in tissue

red blood cells in vessel



Δω maps

Intravascular and Extravascular T2* Effects

1. extravascular dephasing
2. intravascular / intravascular dephasing
3. intravascular dephasing

|

(dependent on the T2 of blood)*

Blood T2

- Thulborn et al. Biochim Biophys Acta, 714: 265-270, 1982
- Gomori et al. JCAT, 11: 684-690, 1987
- Wright et al. JMRI, 1: 275-228, 1991
- Ogawa et al. MRM, 29: 205-210, 1993
- Gilles et al. MRM 33: 93-100, 1995
- Brooks et al. JMRI 4: 446-450,1995
- Meyer et al. MRM 34: 234-241, 1995

Blood T2* ?

Most fMRI is performed using gradient-echo sequences.

Calculating T2* of Fully Oxygenated Blood

Assumption:

T2’ of fully oxygenated blood ≈ T2’ of cortex

T2 ’ of cortex:

$1 / T2' = 1 / T2^* - 1 / T2 \approx 1 / 60\ ms - 1 / 80\ ms \approx 1 / 240\ ms$

T2 * of fully oxygenated blood (at 1.5T):

$1 / T2^* \approx 1 / T2' + 1 / T2 \approx 1 / 240\ ms + 1 / 250\ ms \approx 1 / 120\ ms$

Basic Approach

1. Simplified model based on literature values.

Physiologic:	MR:
hematocrit	inter-180 time
oxygenation	field strength
geometry	
susceptibility	

3. Adjust *diffusion coefficient* to "match" results of:

- Wright et al. JMRI, 1: 275-228, 1991 (T2)

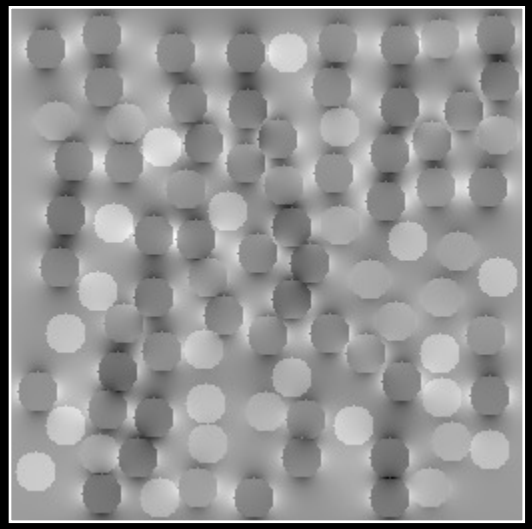
and

- Hoppel et al. MRM, 30: 715-723, 1993 (ΔR2* / ΔR2)

4. Using matched parameters, simulate T2* effects.

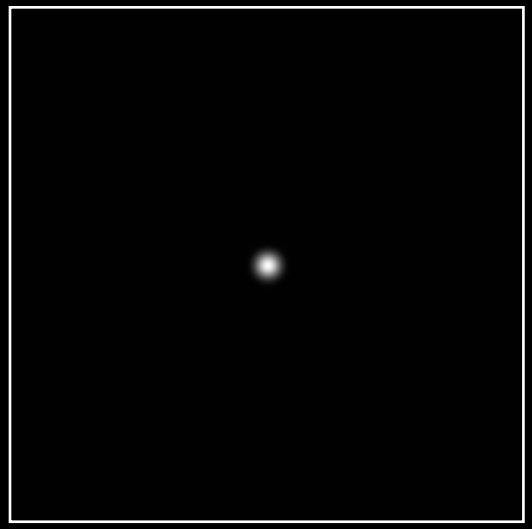
Deterministic Diffusion Model

Frequency Offset



- Randomly oriented cylinders
- Feely permeable
- Overlapping fields
- Red blood cell radius:
  (2.5 μm = 10 voxels)
- Hct. determines number of cells

Spin Probability Distribution



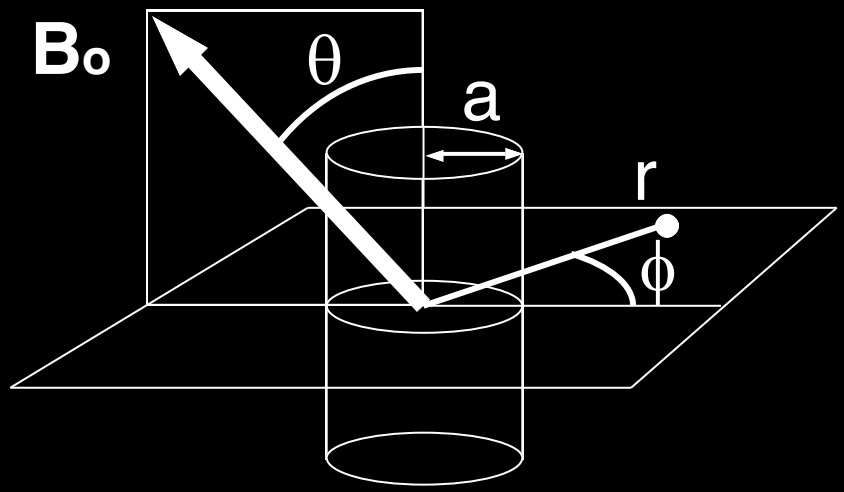
- Gaussian distribution
- Step time increment:
  (0.1 ms to 0.25 ms)

$$\text{prob}(x,y) = \left(\frac{LX \times LY}{2\,\check{s}}\right)\frac{1}{\sigma^2}\,e^{-\left(\frac{x^2+y^2}{2\sigma^2}\right)}$$

$$\sigma = \sqrt{2Dt}$$

matrix sizes = 256 x 256 voxels

Frequency Offset Map



$$\Delta\omega' = 2\pi \left[(42.57 \times 10^{6}) \, 2\pi B_o \right] [\Delta\chi] (1 - Y)$$

rbc

$\Delta\chi = 0.180 \times 10^{-6}$

$$\Delta\omega \text{ (outside)} = \Delta\omega' \sin(\theta)^2 (a/r)^2 \cos(2\phi)$$

$$\Delta\omega \text{ (inside)} = \Delta\omega' (3\cos(\theta) - 1)^2 / 3$$

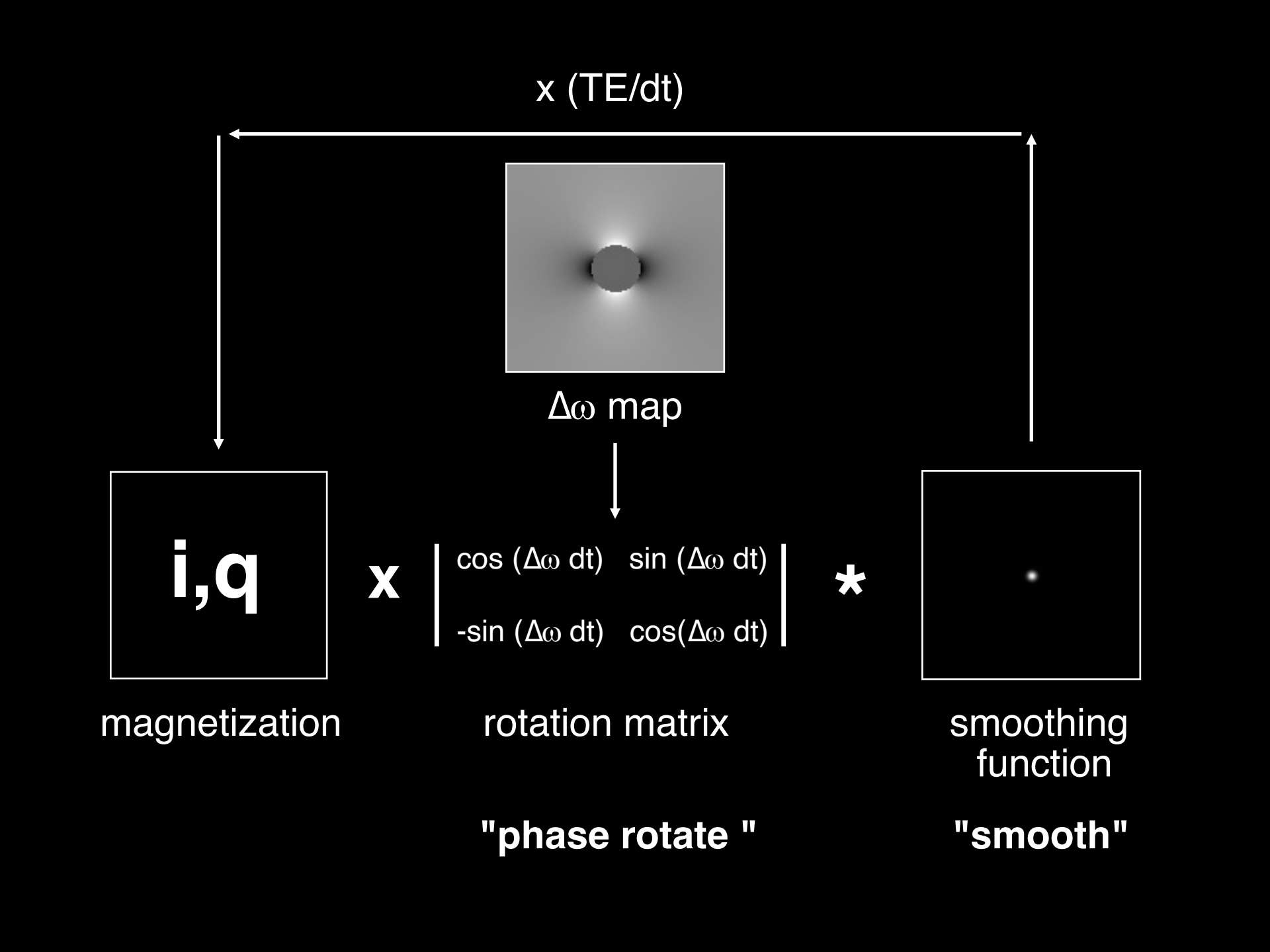
S. Ogawa et al.
Biophys J. 64, 803-812 (1993).

Spin Probablility Distribution

$$\text{prob}(x,y) = \left(\frac{LX \times LY}{2\,\check{s}}\right)\frac{1}{\sigma^2}\,e^{-\left(\frac{x^2+y^2}{2\sigma^2}\right)}$$

$$\sigma = \sqrt{2Dt}$$

$$D\,(\text{pixels}^2/\text{ms}) = \frac{D\,(\mu\text{m}^2/\text{ms})}{\left(\frac{\text{cell radius}\ \ (\text{pixels})}{\text{cell radius}\ \ (\mu\text{m})}\right)^2}$$


x (TE/dt)
Δω map
i,q
x
cos (Δω dt) sin (Δω dt)
-sin (Δω dt) cos(Δω dt)
*
magnetization
rotation matrix
smoothing function
"phase rotate "
"smooth"

"Phase Rotate" and "Smooth" Simulation

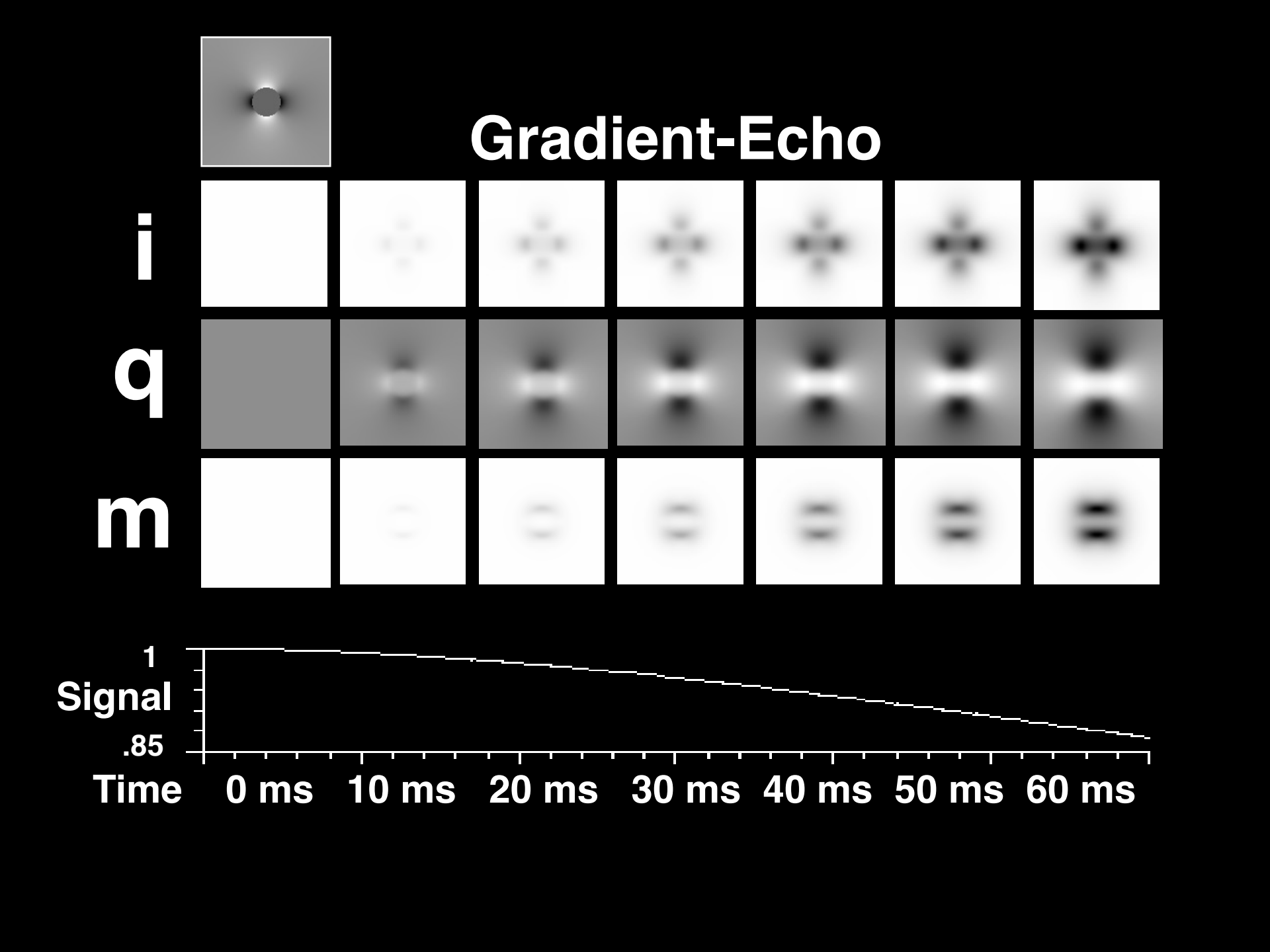
1) Start with maps of uniform, coherent transverse magnetization (i = 1, q = 0).

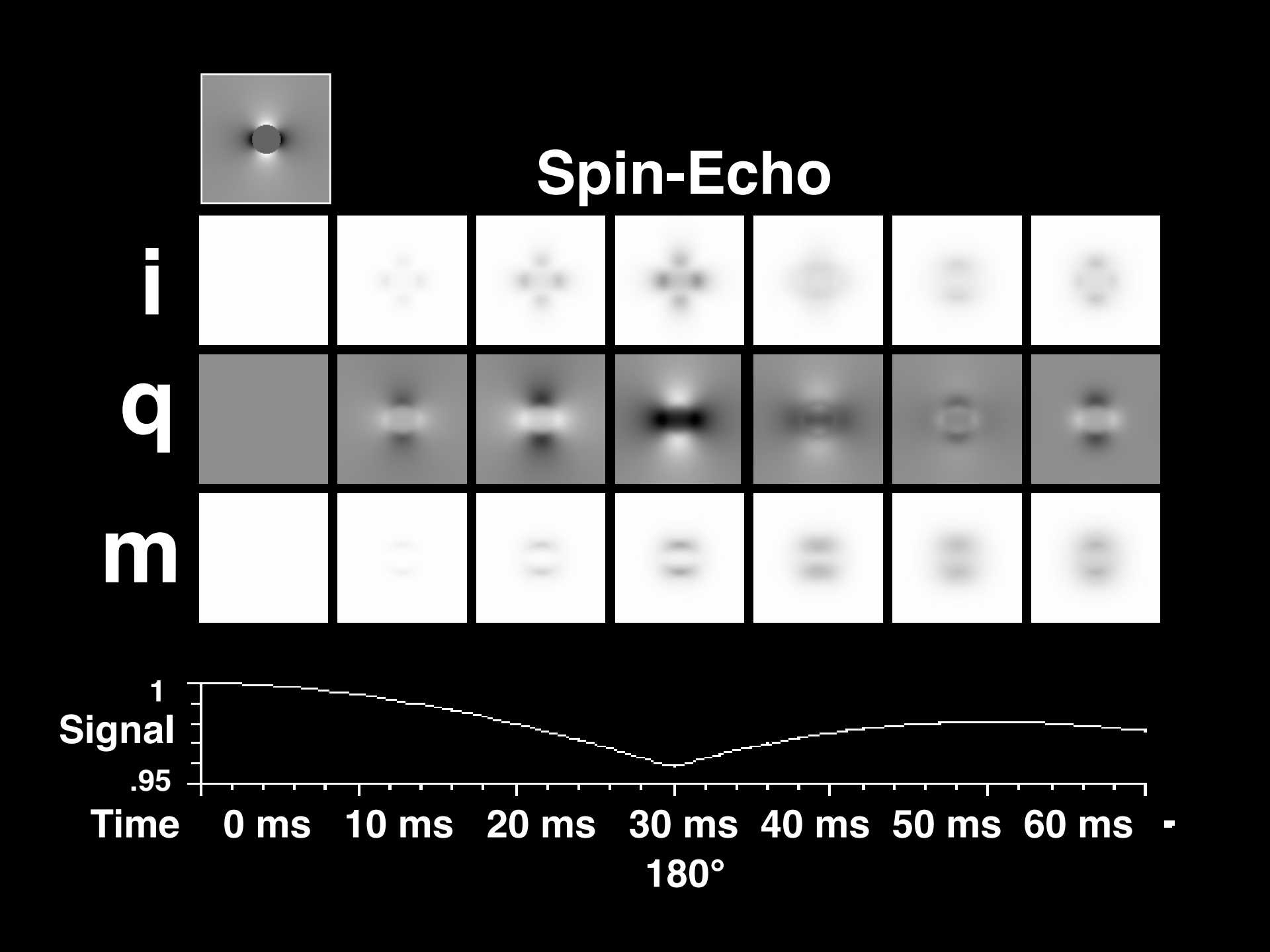
2) For each time interval, dt, perform:

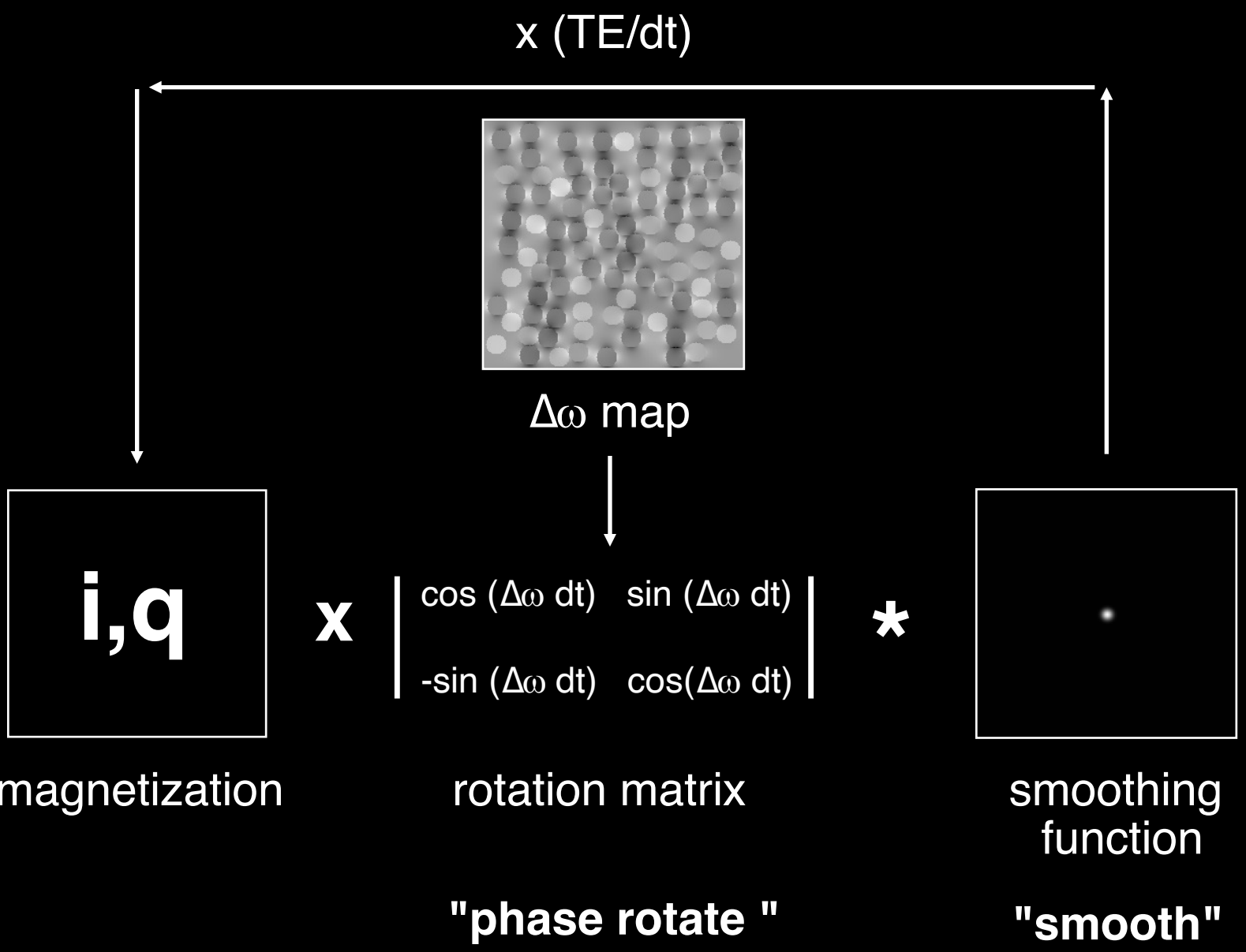
   a) Spatially - dependent phase rotation.
   (using $\Delta\omega$ maps)

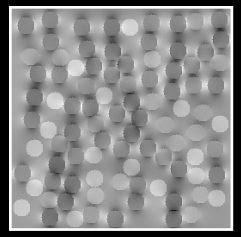
   b) Convolution with gaussian smoothing function.
   (representing diffusion during time, dt)

   c) Signal magnitude calculation by complex addition of every matrix element.

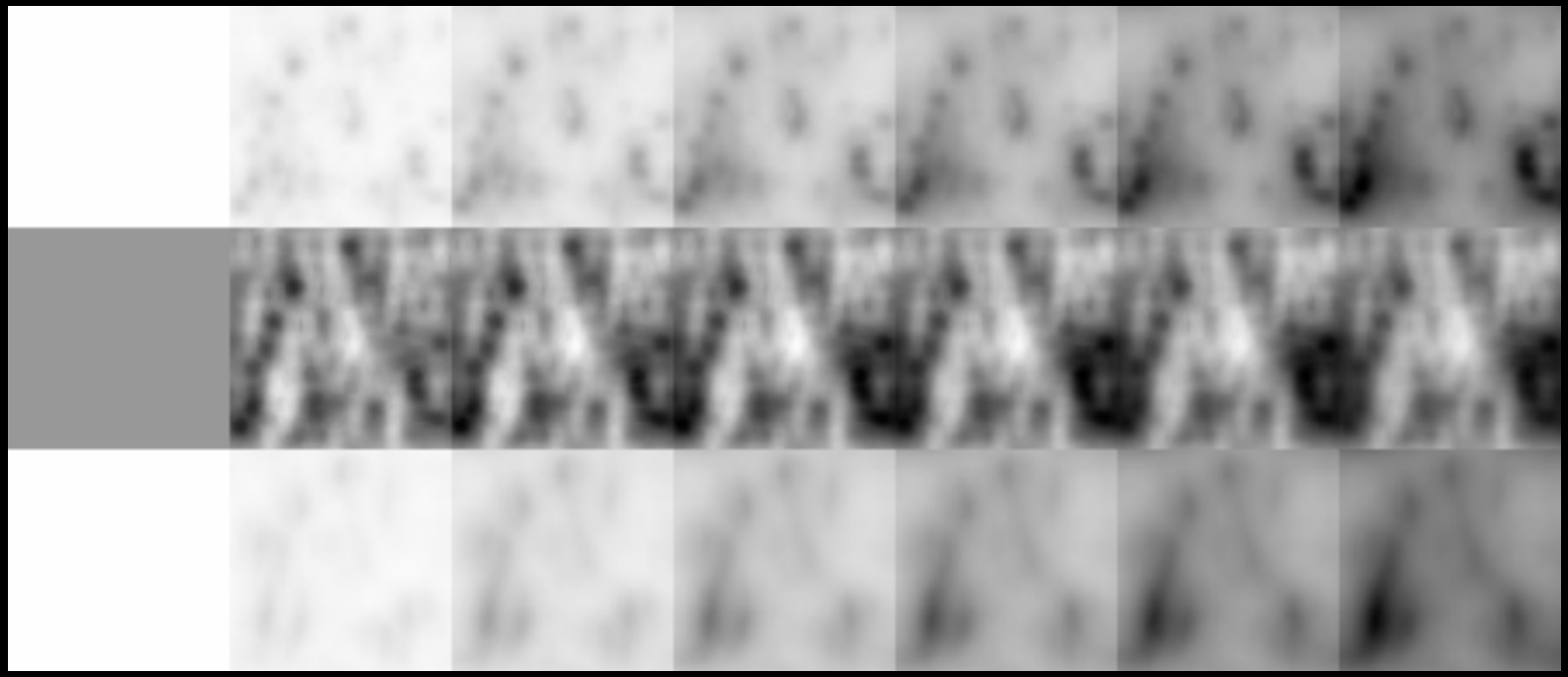

Gradient-Echo
i
q
m
1
Signal
.85
Time
0 ms
10 ms
20 ms
30 ms
40 ms
50 ms
60 ms

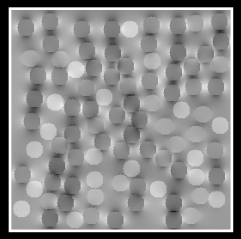

Spin-Echo
i
q
m
1
Signal
.95
Time
0 ms
10 ms
20 ms
30 ms
40 ms
50 ms
60 ms
180°


x (TE/dt)
Δω map
i,q
x
cos (Δω dt) sin (Δω dt)
-sin (Δω dt) cos(Δω dt)
*
magnetization
rotation matrix
smoothing function
"phase rotate "
"smooth"

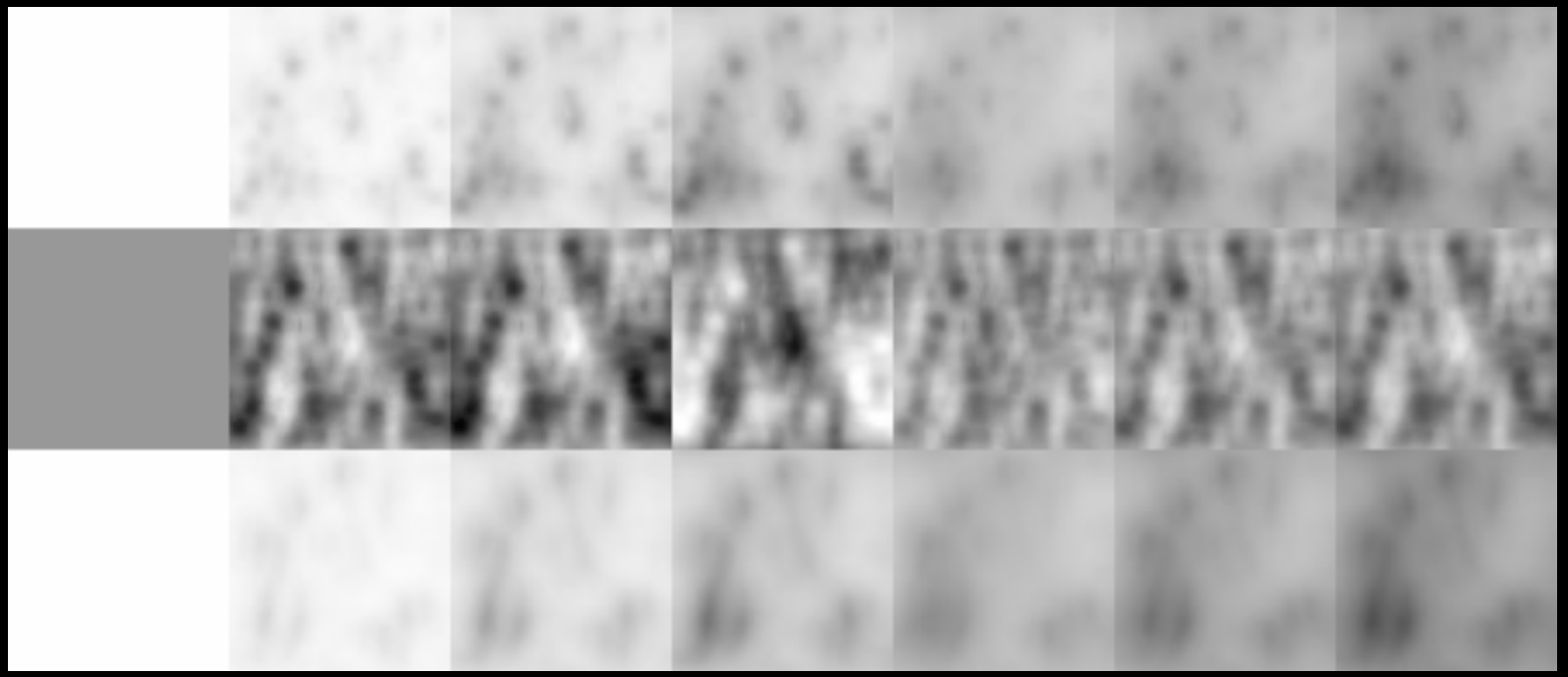


Gradient-Echo

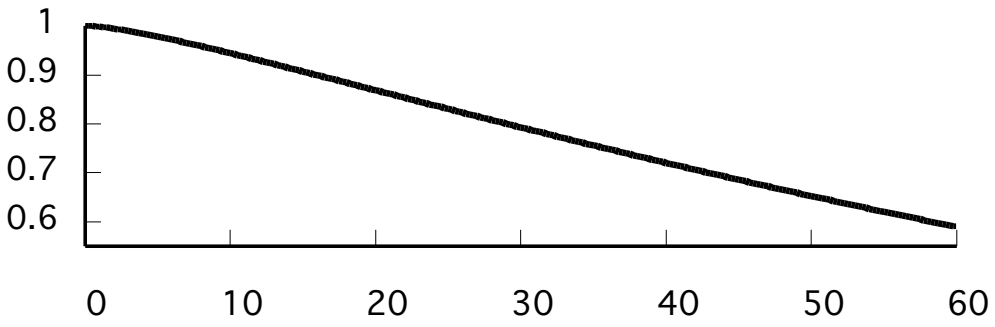




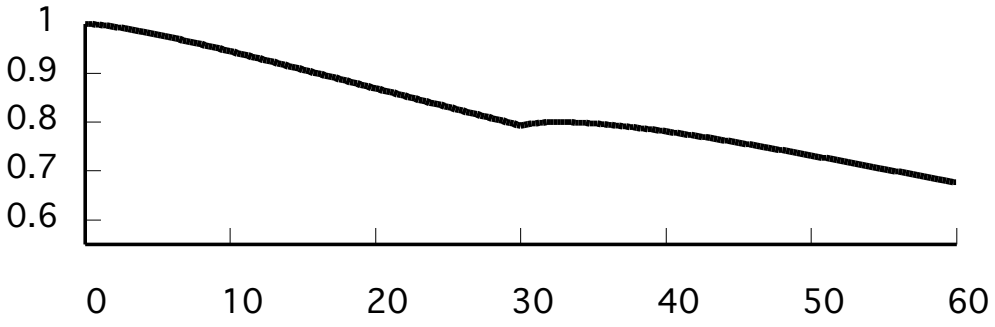
Spin-Echo



GE



SE

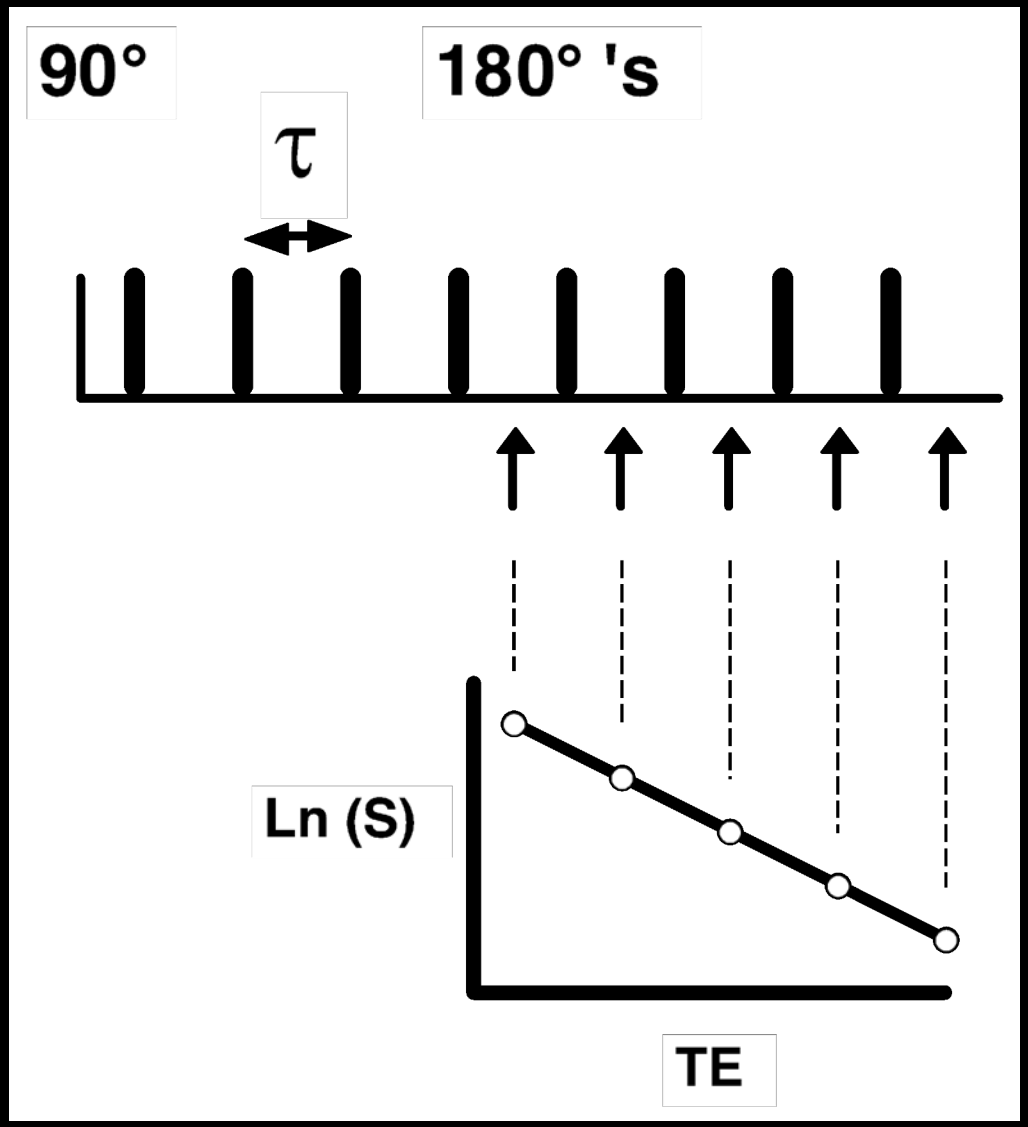


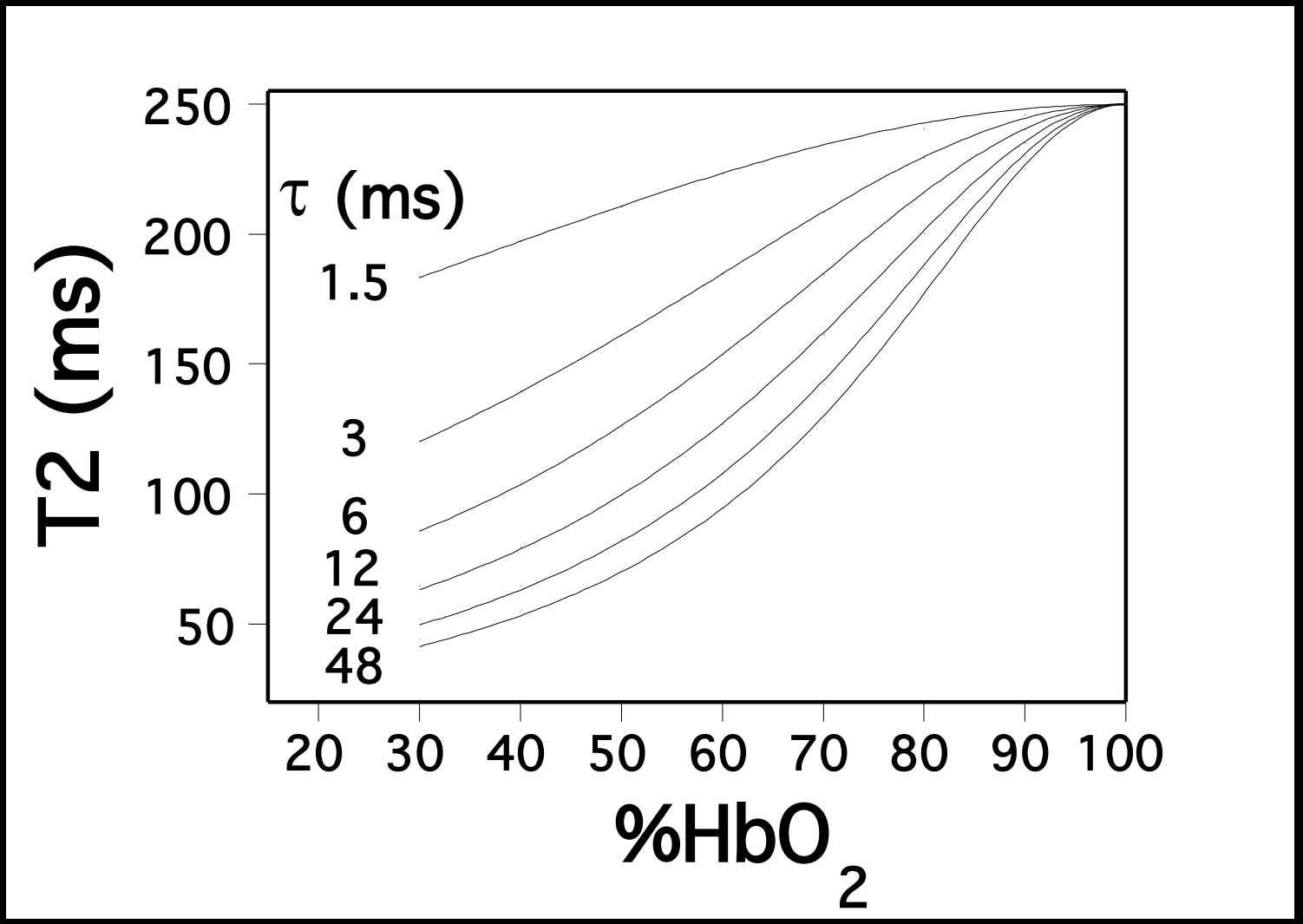
Comparison #1

•Wright et al. JMRI, 1: 275-228, 1991

- **Hct = 44**
- **Field Strength = 1.5 T**
- **5 echo measurement**
- **inter-180 time (τ) from 1.5 ms to 48 ms.**
- **$T2_o$ set to 250 ms.**
- **%HbO_2 varied from 30% to 100%**

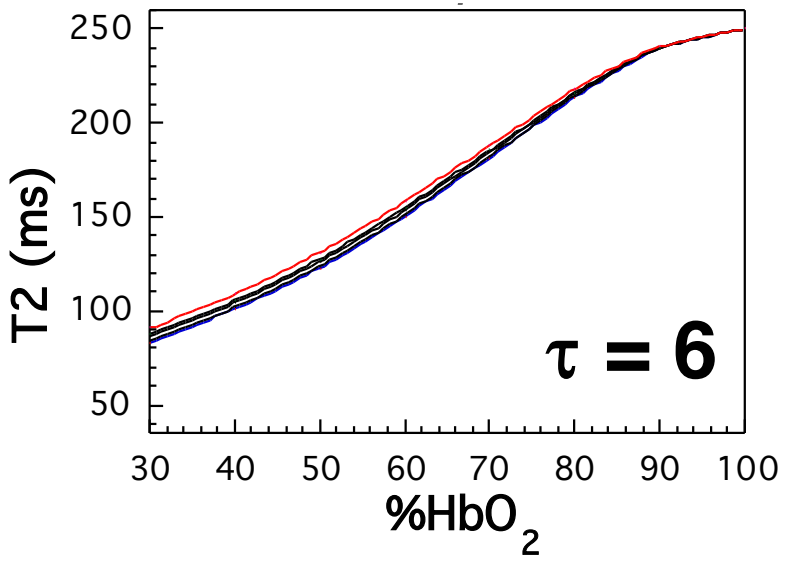
Simulated Multi - Echo Collection

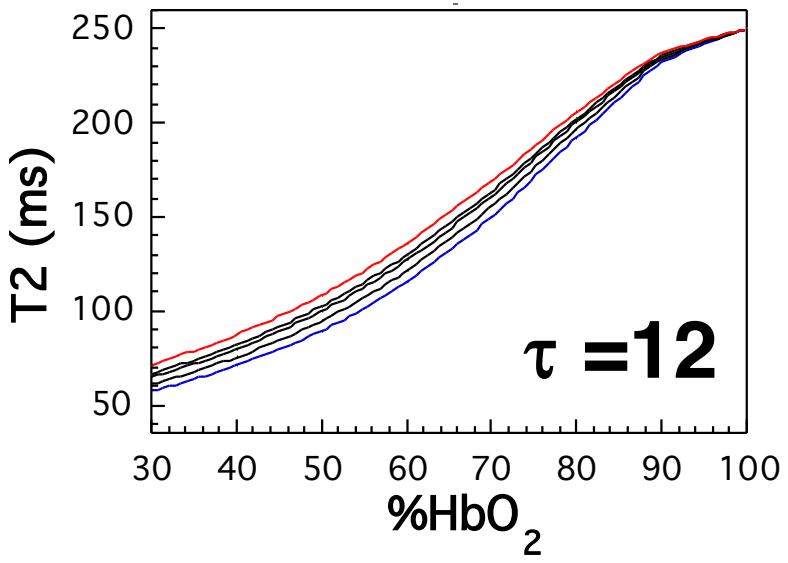


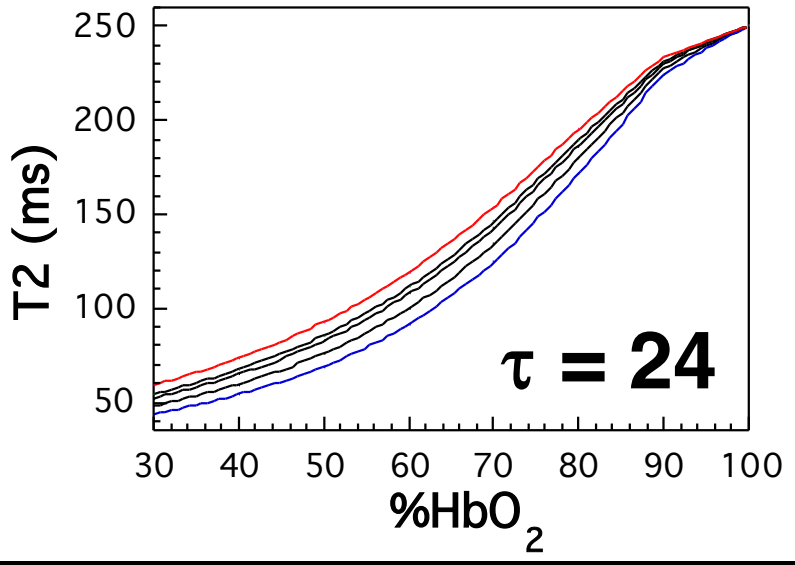

250
200
150
100
50
T2 (ms)
τ (ms)
1.5
3
6
12
24
48
20 30 40 50 60 70 80 90 100
%HbO2

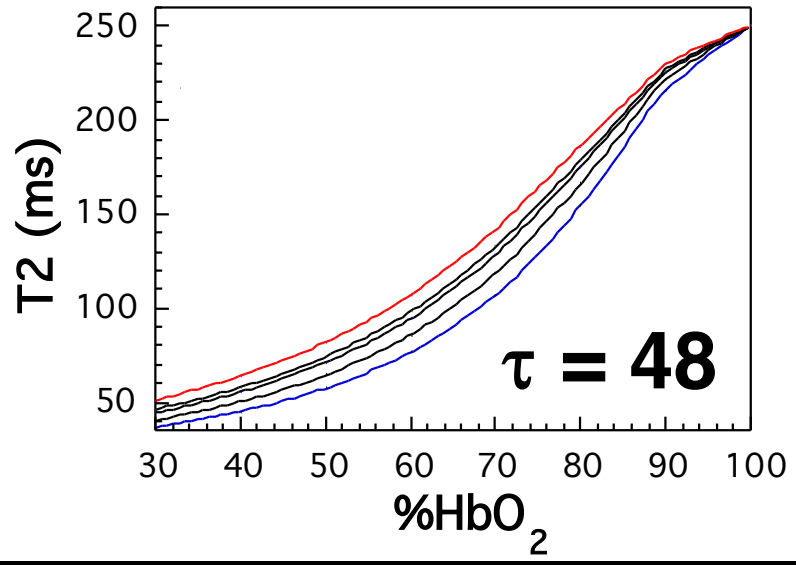
D = 1.8 μm^2 / ms

D = 1 μm^2 / ms -> 2.5 μm^2 / ms









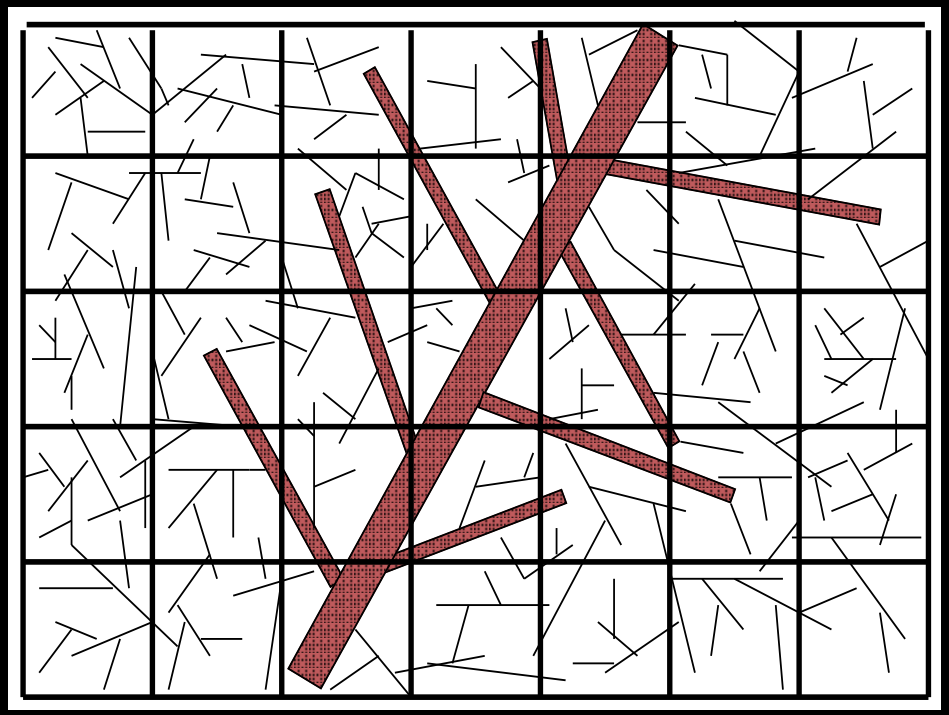
Comparison #2

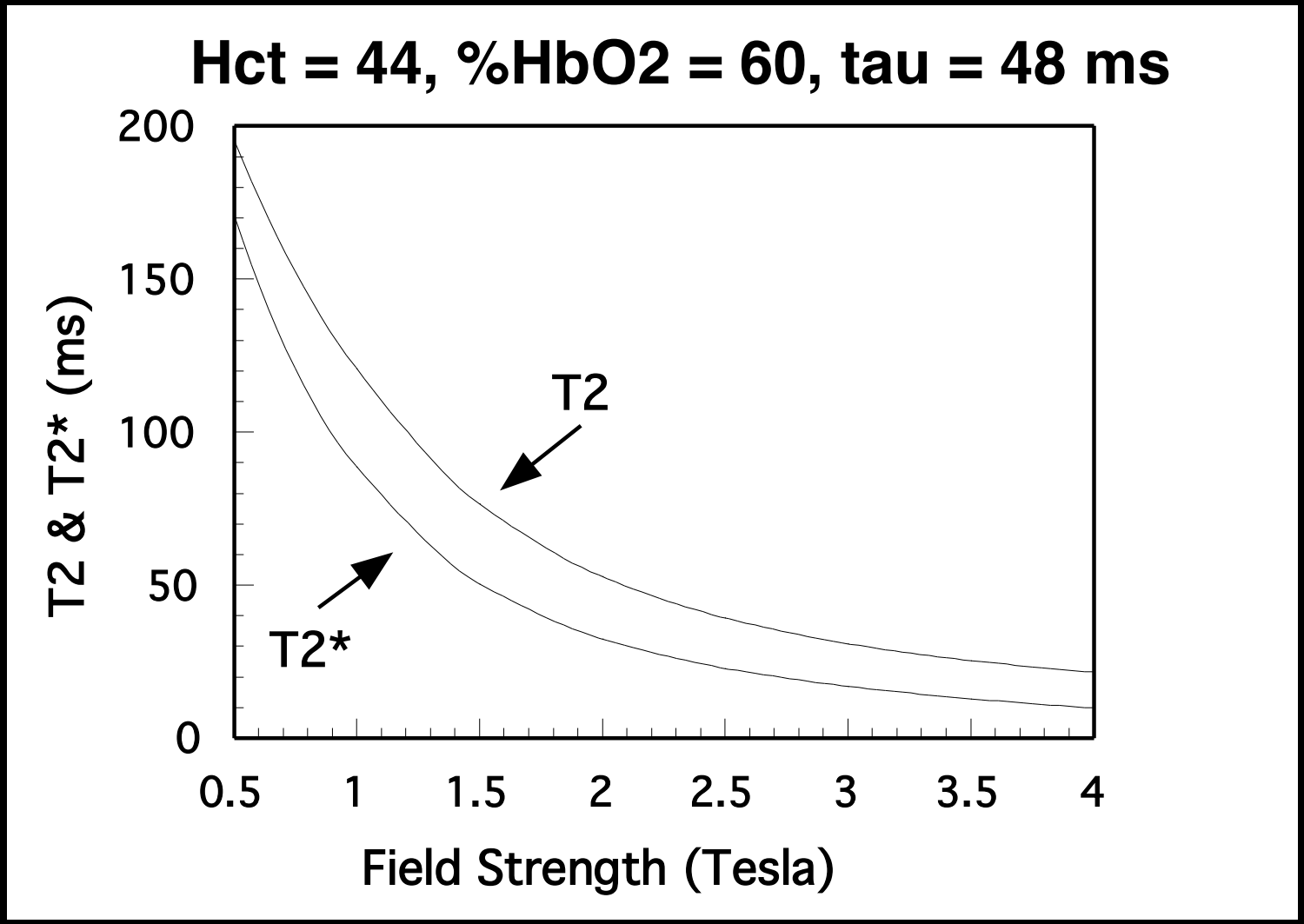
•Hoppel et al. MRM, 30: 715-723, 1993

- **Hct = 44**
- **Field Strength = 1.5 T**
- **Determine ΔR2*/ΔR2**
- **5 echo measurement**
- **Spin-echo: τ = 48 ms.**
- **Gradient-echo: center echo TE = 48 ms.**
- **ΔR2* and ΔR2 relating to %HbO_2 change from 60% to 70%.**

- Large vessel effect not removed by spin-echo.

- FMRI signal change magnitude (for SE and GE) is likely to be most strongly weighted by blood volume in each voxel




Hct = 44, %HbO2 = 60, tau = 48 ms
200
150
100
50
0
T2 & T2* (ms)
T2
T2*
0.5
1
1.5
2
2.5
3
3.5
4
Field Strength (Tesla)

Conclusions

1. Intravascular T2* and T2 effects are simulated with a deterministic diffusion model.

-simplified geometry and proton dynamics.

-simplified dephasing mechanism:

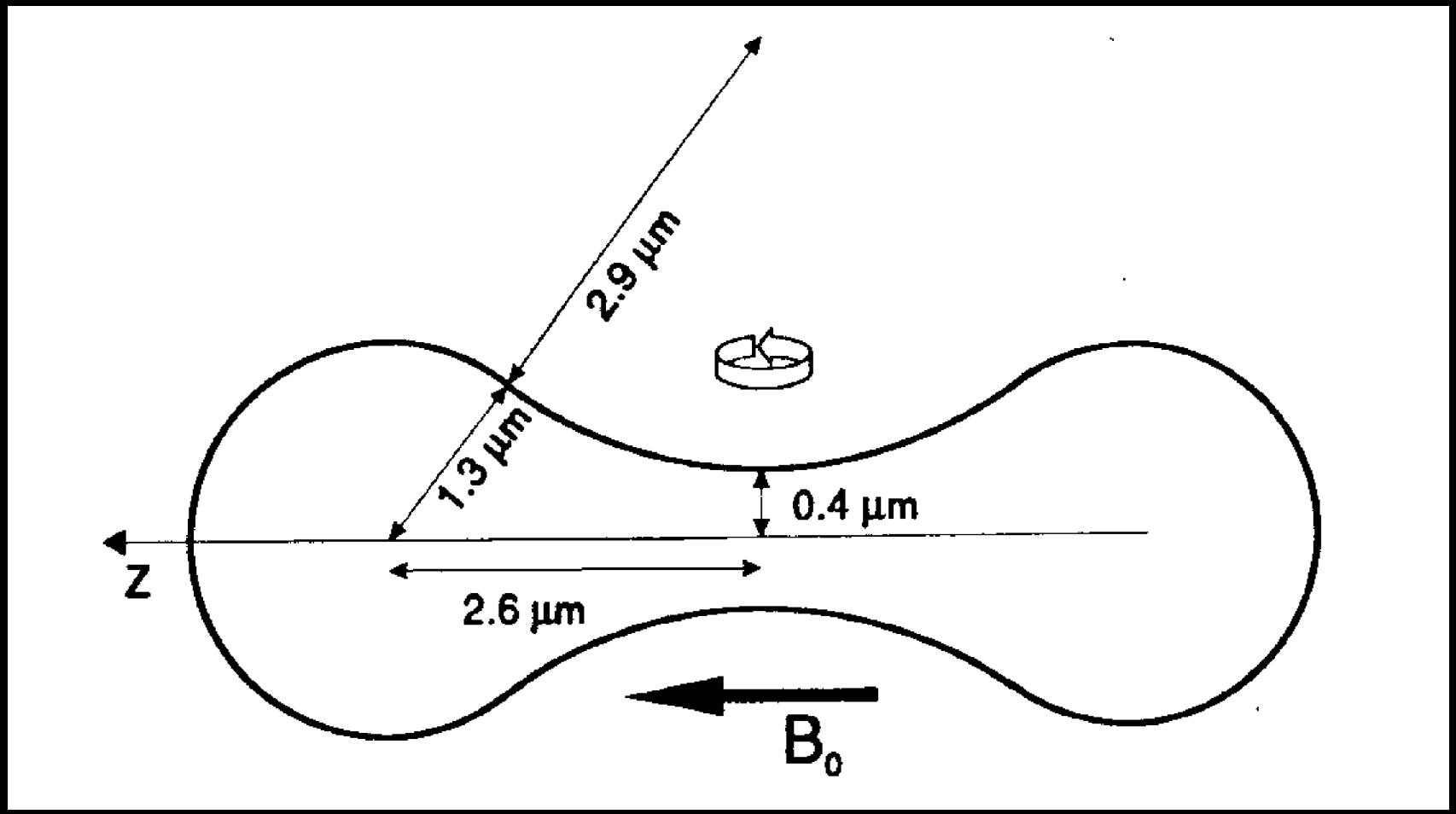
(diffusion in, through, and around red blood cells)

2. Results show general agreement with literature at D = 1.8 μm^2 / ms and radius = 2.5 μm.

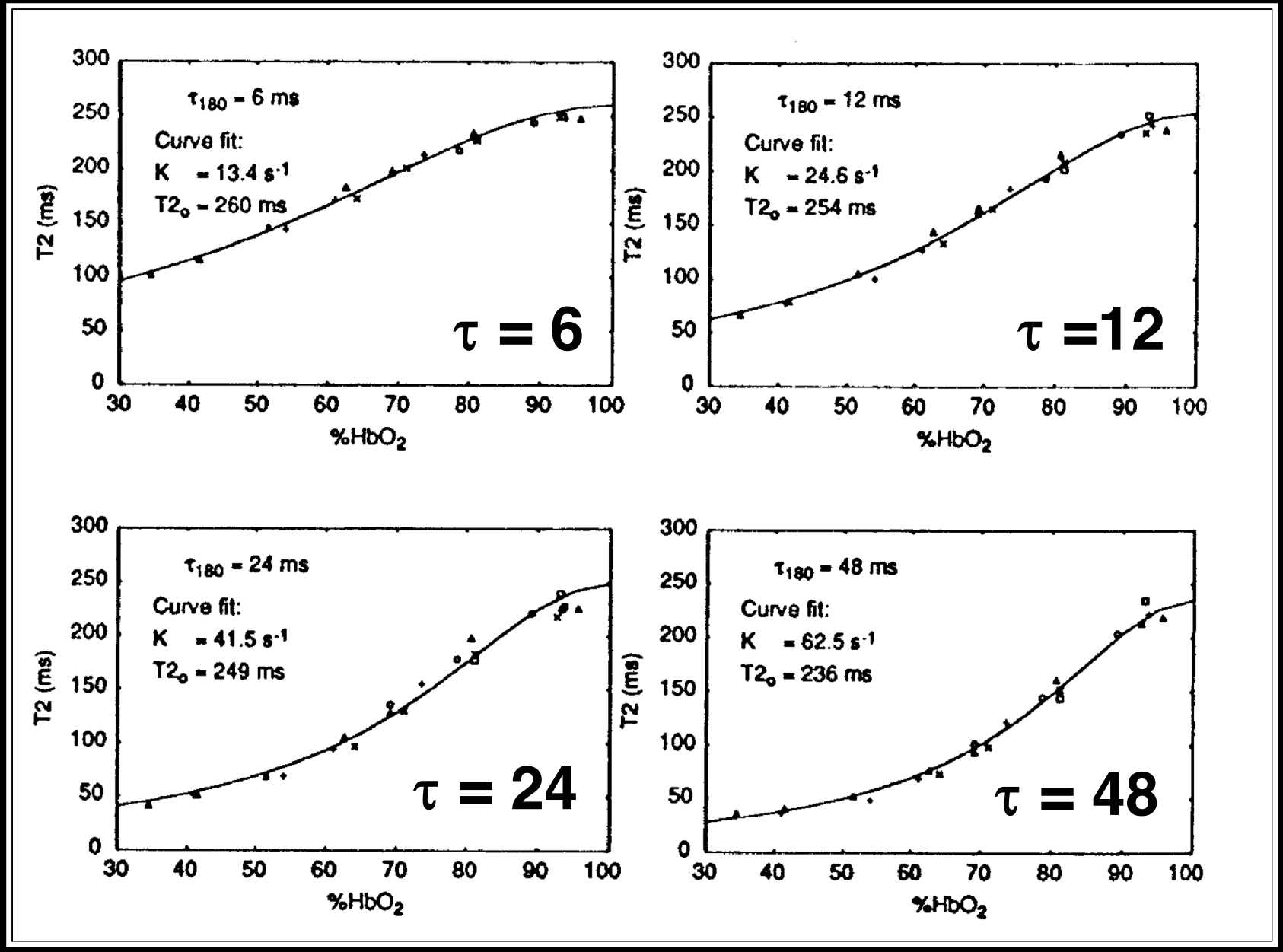
3. Because of intravascular effects, spin-echo sequences do not remove large vessel effects.

4. T2* of blood is significant when considering field strength fMRI dependence.

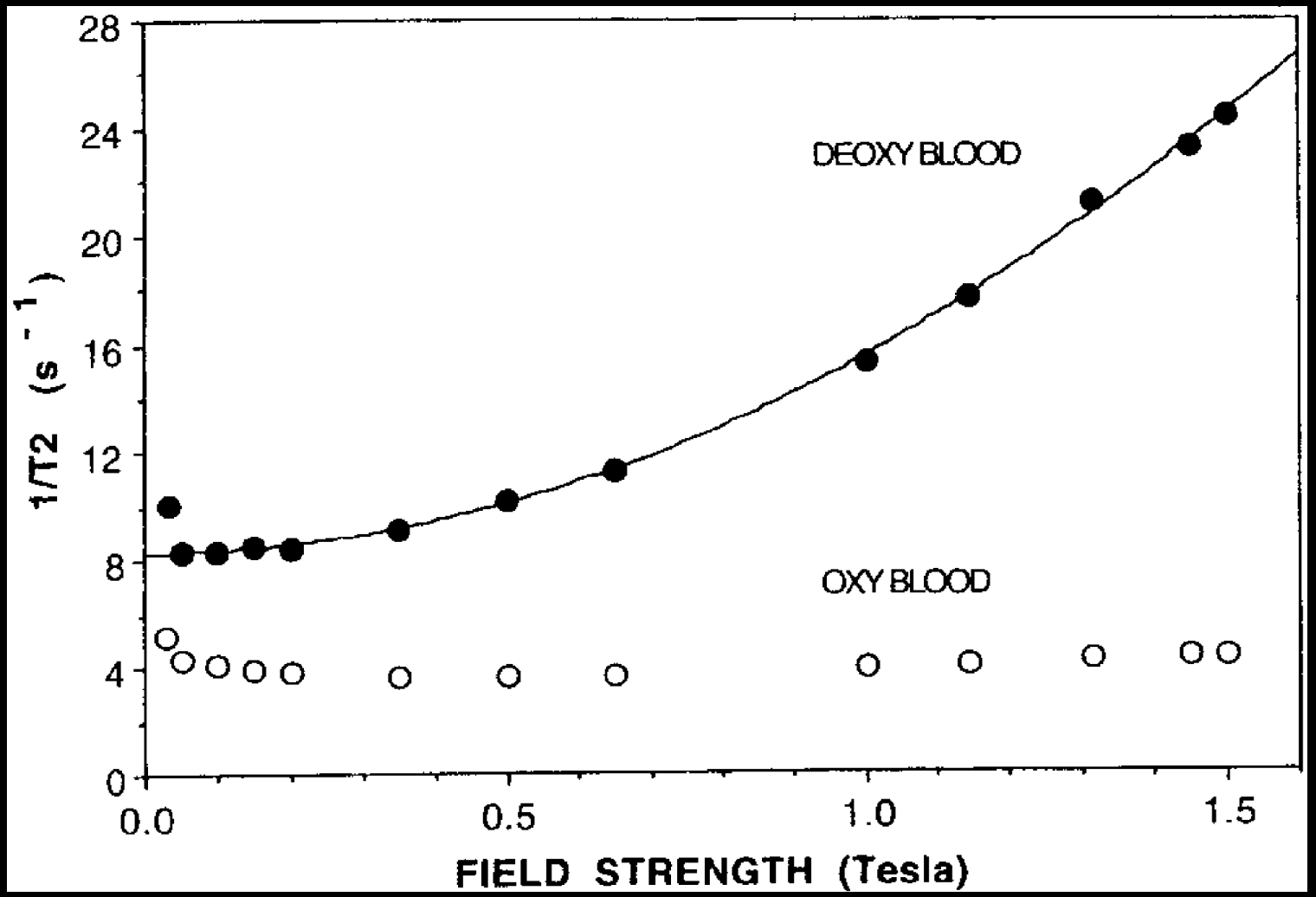
Red Blood Cell



Gilles et al. MRM 33: 93-100, 1995



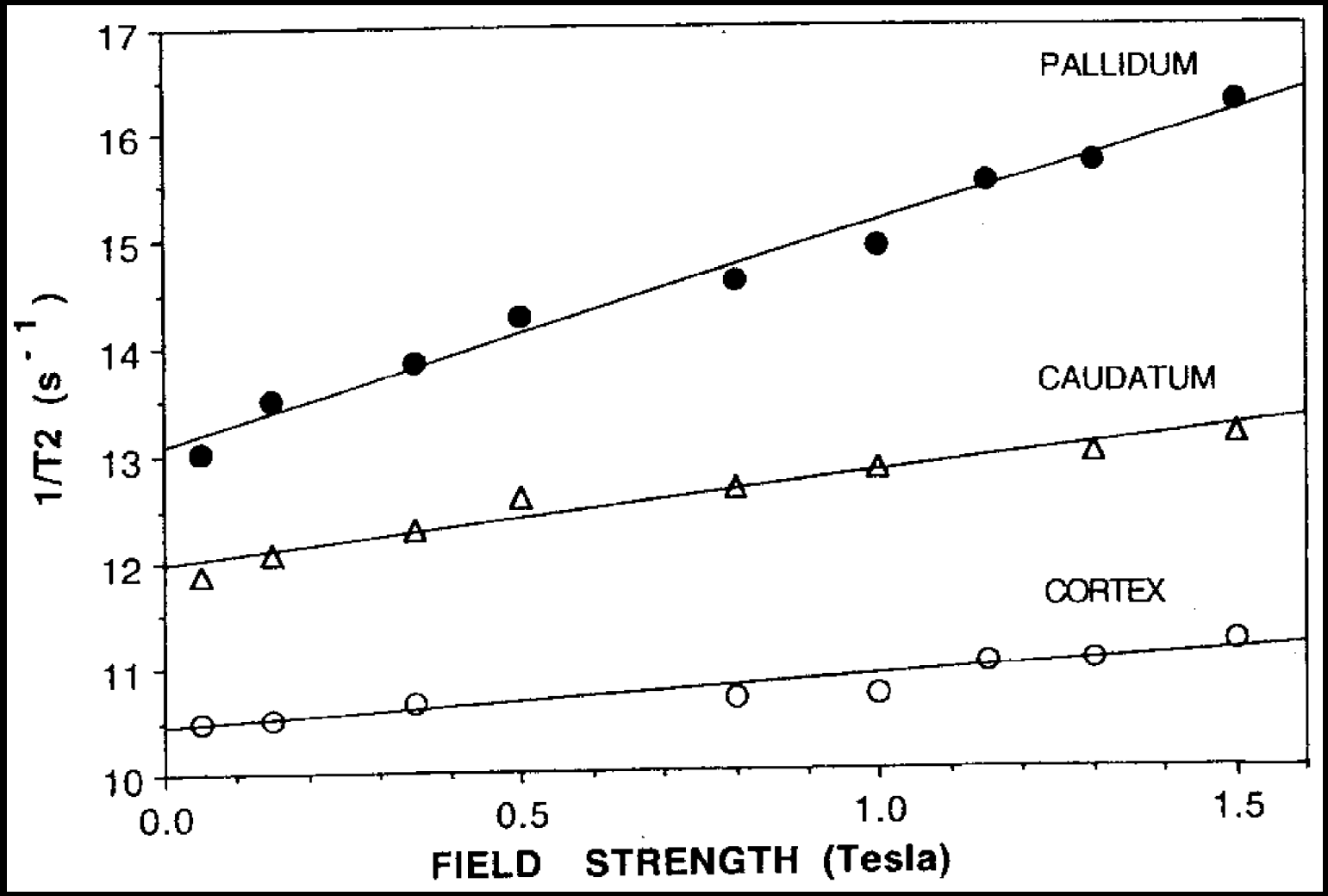
Wright et al. JMRI, 1: 275-228, 1991



Brooks et al. JMRI 4: 446-450,1995

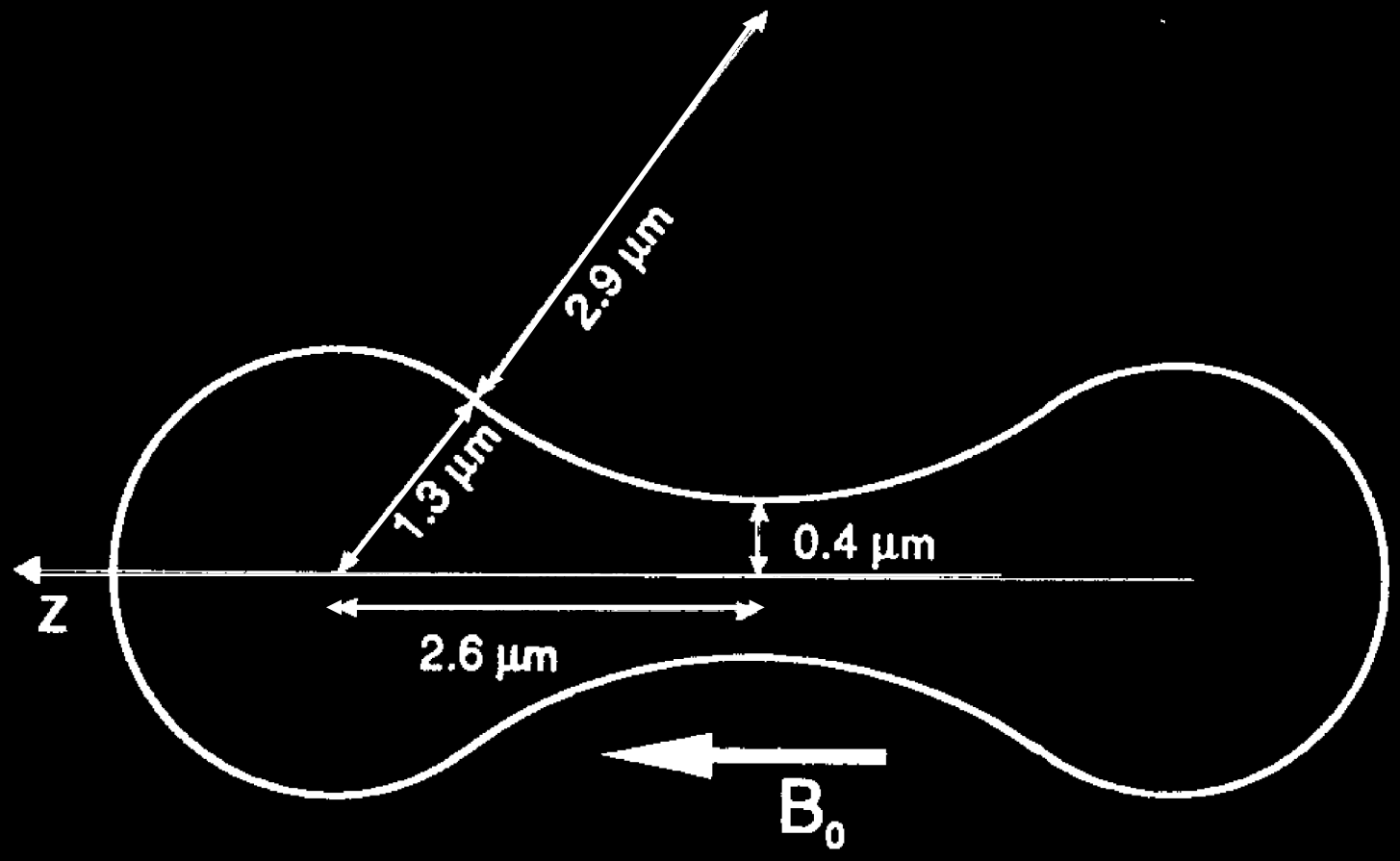
Future Work

- Model the relative intravascular and extravascular effects using the deterministic diffusion model.
- Characterize the differences between exchange and diffusion mechanisms.



Brooks et al. JMRI 4: 446-450,1995

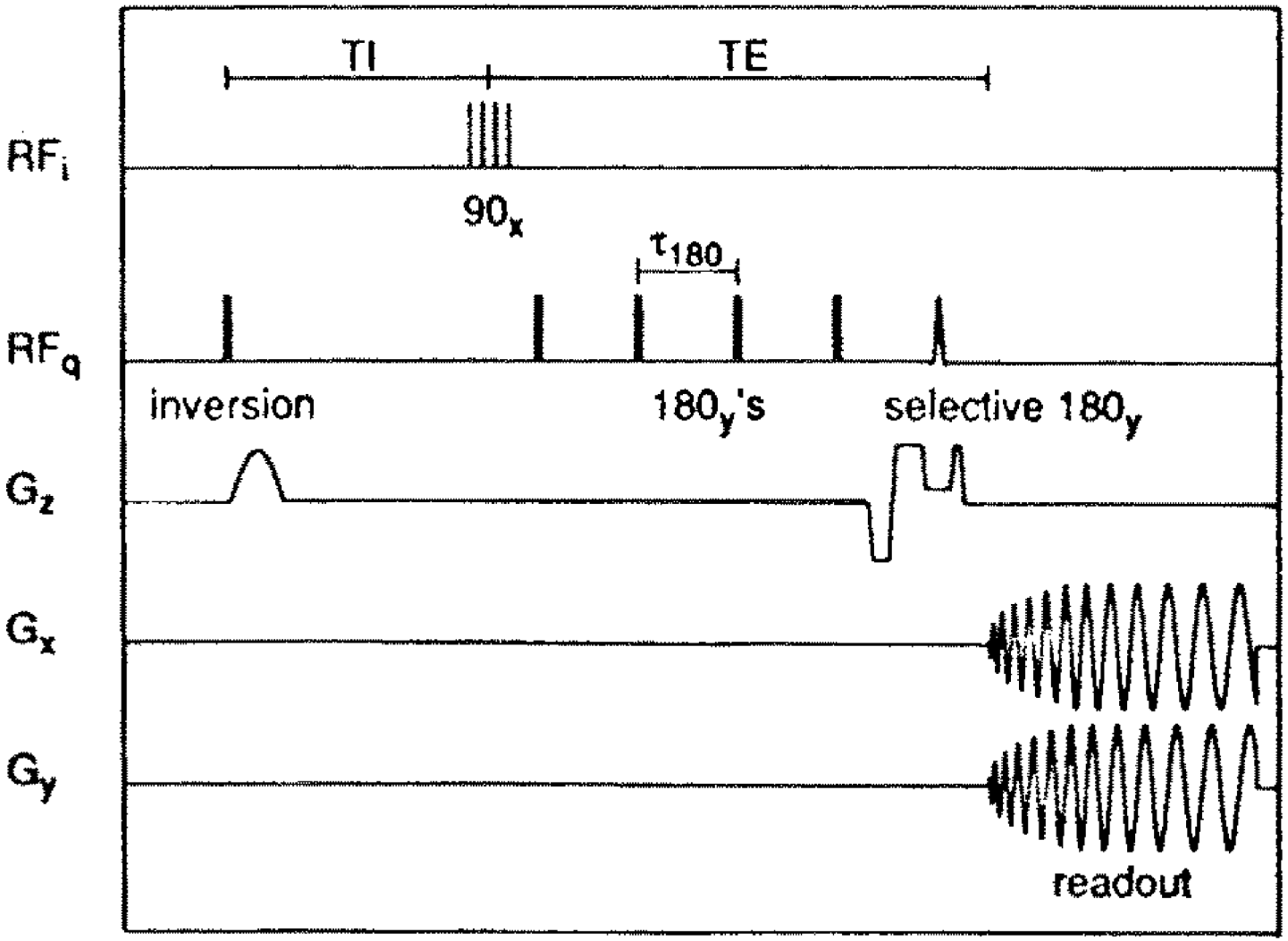
Red Blood Cell



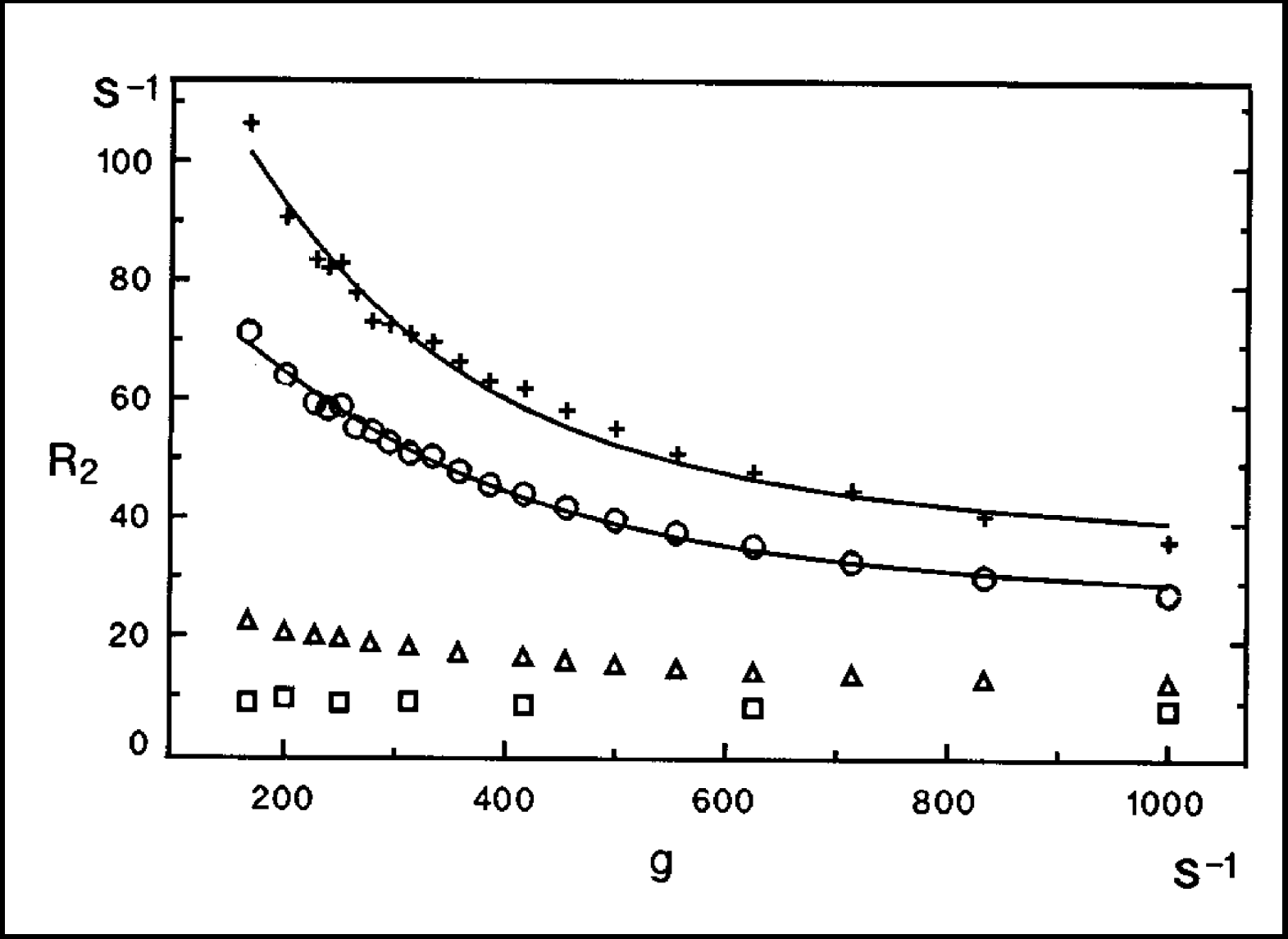
Gilles et al. MRM 33: 93-100, 1995

$$\frac{1}{T2_b} = \frac{1}{T2_o} + K(\tau_{180}, \omega_0)\left(1 - \frac{\%HbO_2}{100\%}\right)^2$$

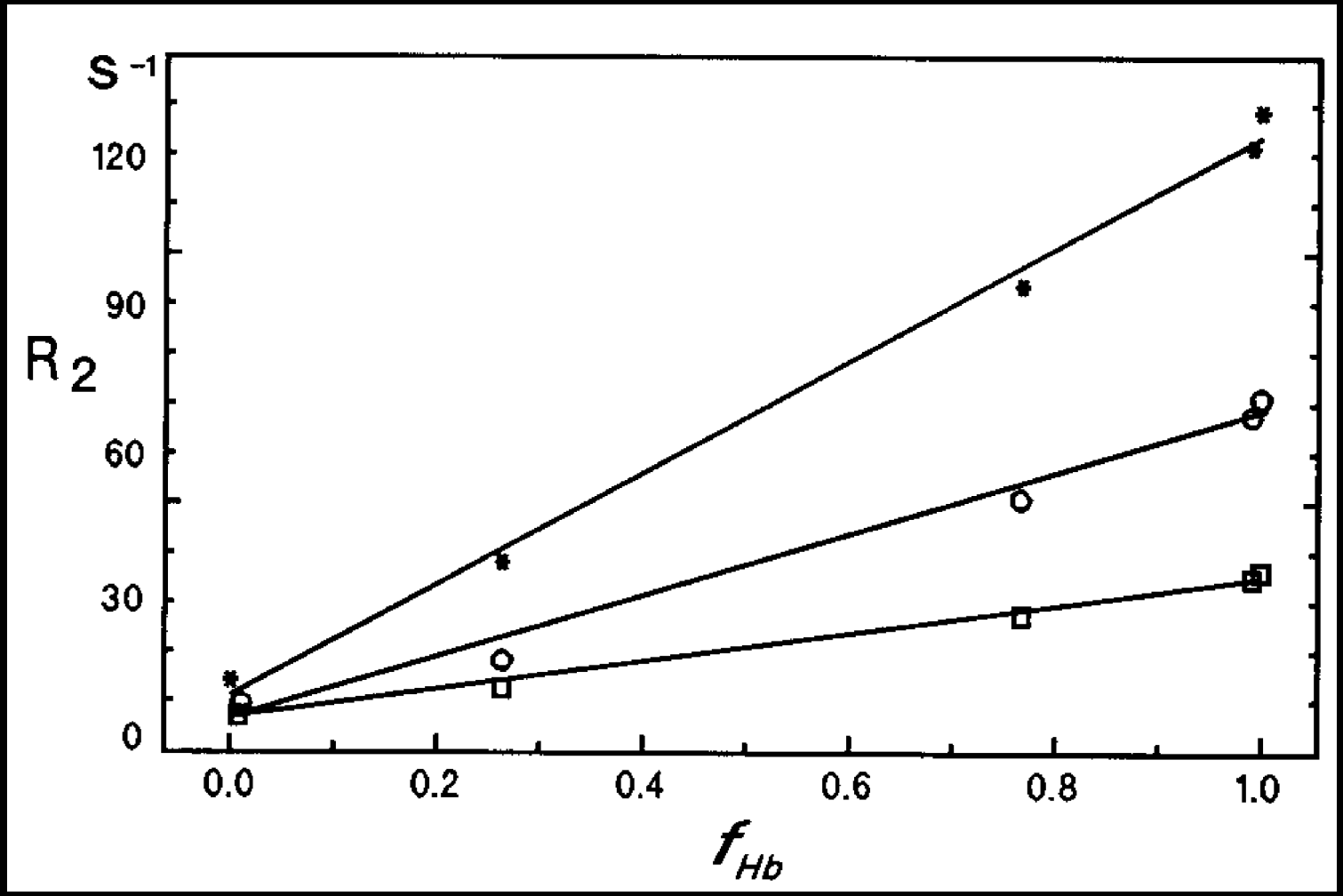
Luz - Meiboom Model



Wright et al. JMRI, 1: 275-228, 1991



Meyer et al. MRM 34: 234-241, 1995



Meyer et al. MRM 34: 234-241, 1995

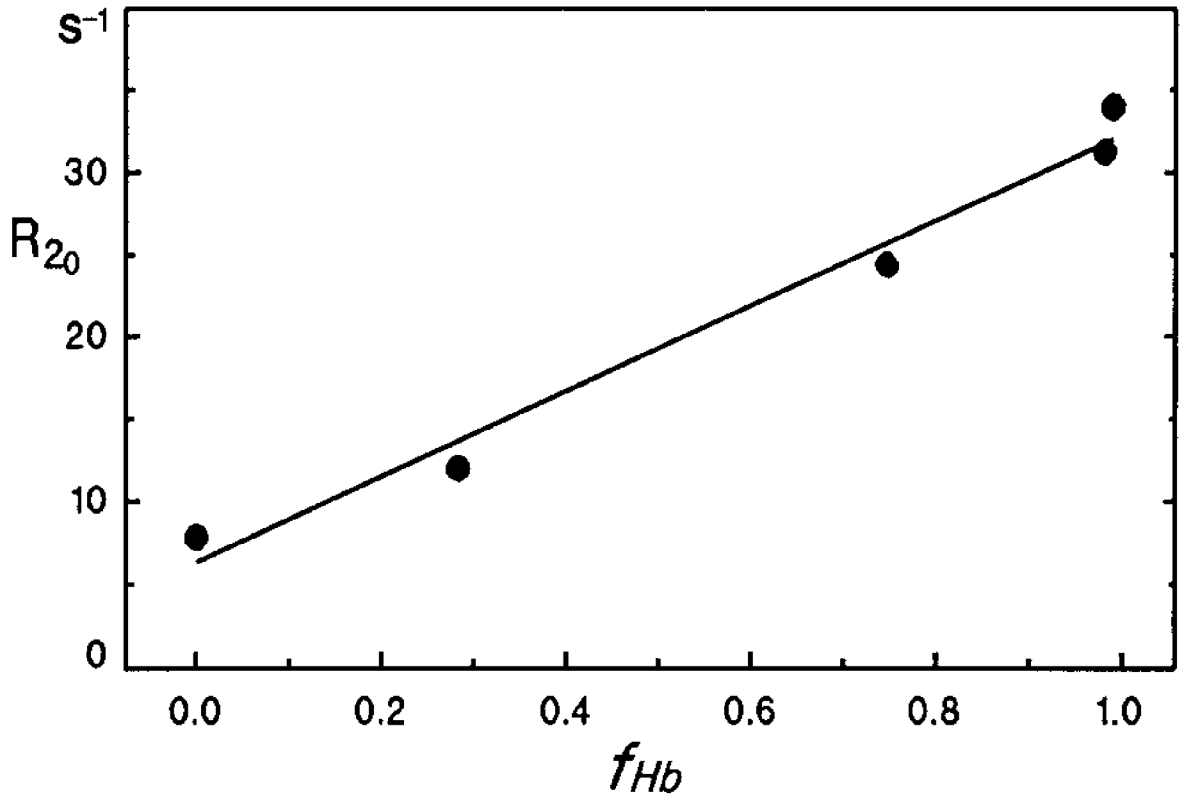
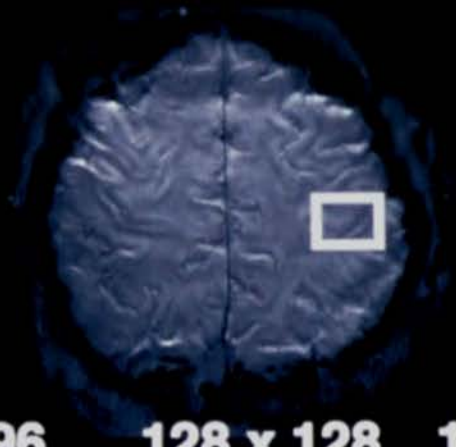
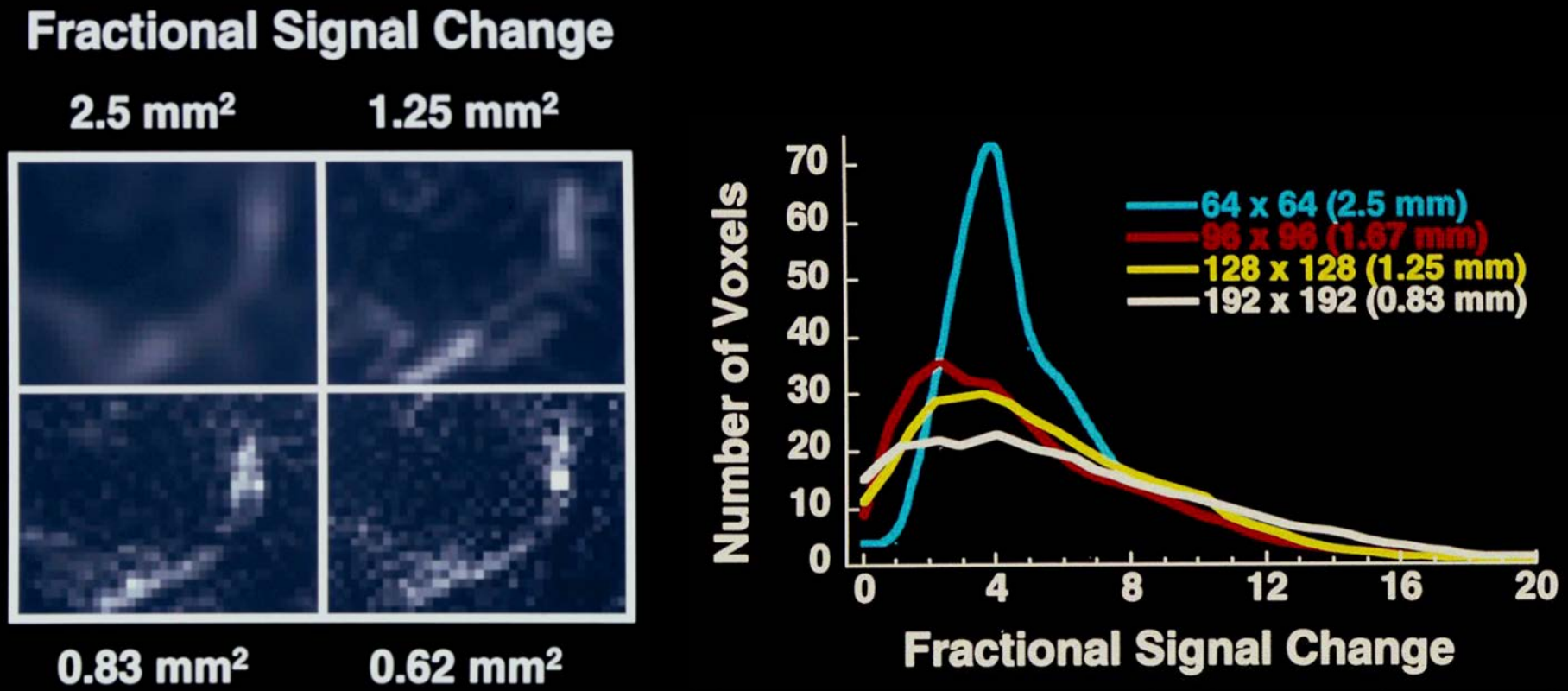


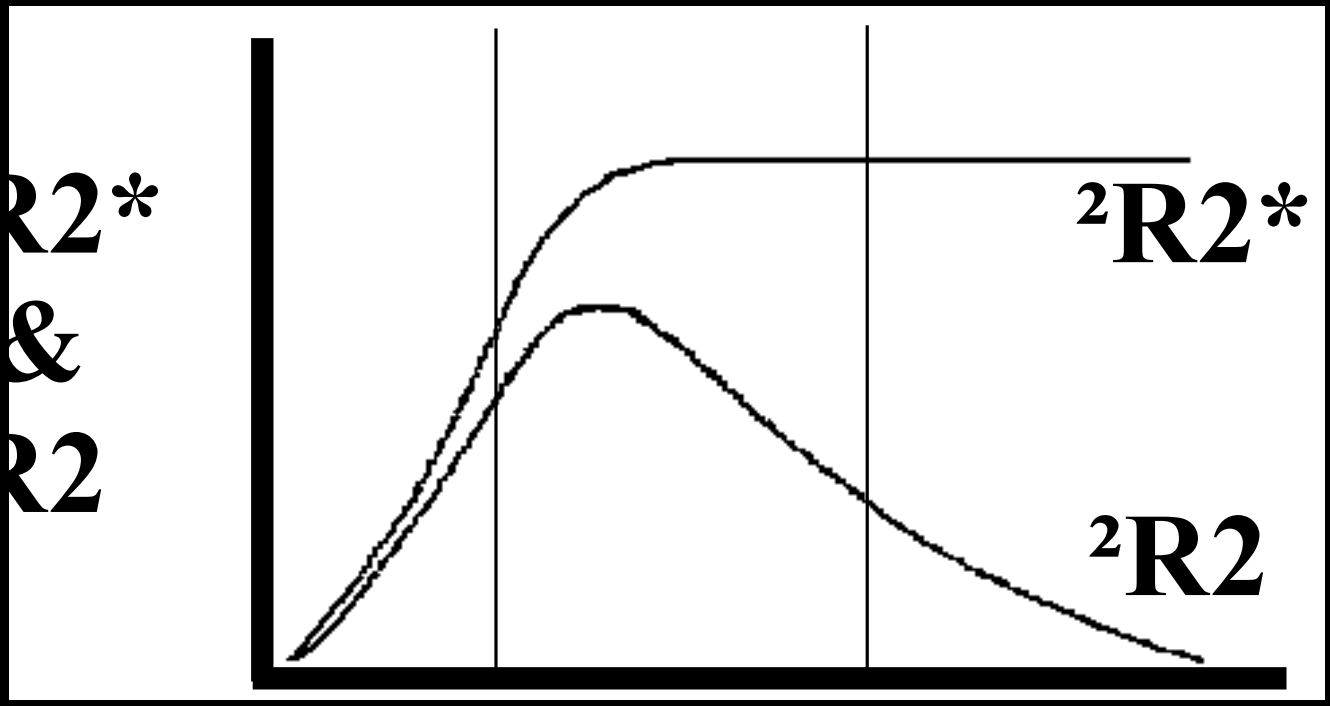
FIG. 4. Dependence of the relaxation rate in the absence of exchange ($A = R_{2_0}$, in Eq. [3]) on the fraction of deoxyhemoglobin in whole blood (f_{Hb}). The linear regression of this plot is $R_{2_0} = (26 \pm 2.13)\ f_{Hb} + (6.28 \pm 1.84)$; $r^2 = 0.98$.

Meyer et al. MRM 34: 234-241, 1995

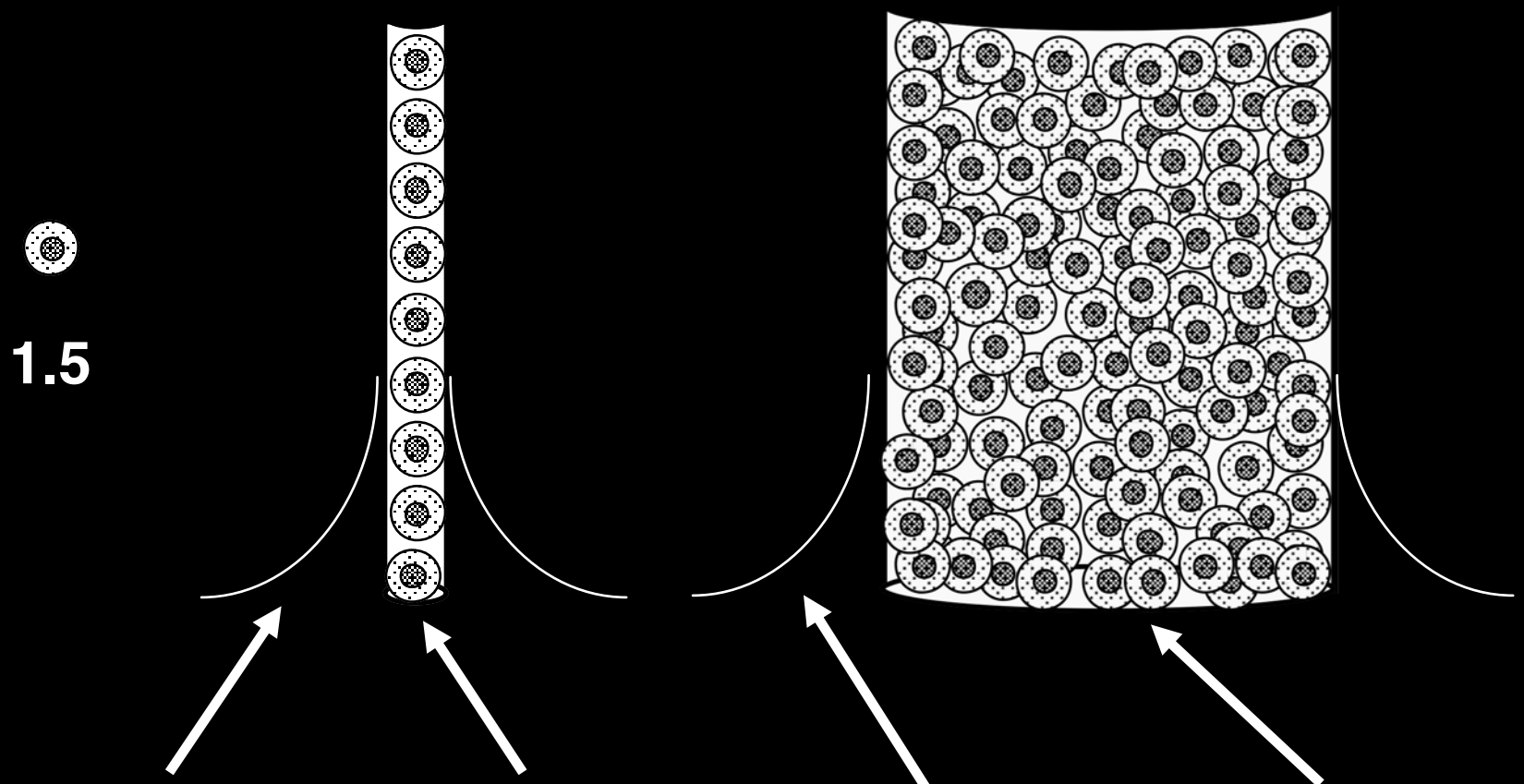


	64 x 64	96 x 96	128 x 128	192 x 192	256 x 256
%					
C/N					
	2.5 mm^2	1.67 mm^2	1.25 mm^2	0.83 mm^2	0.62 mm^2

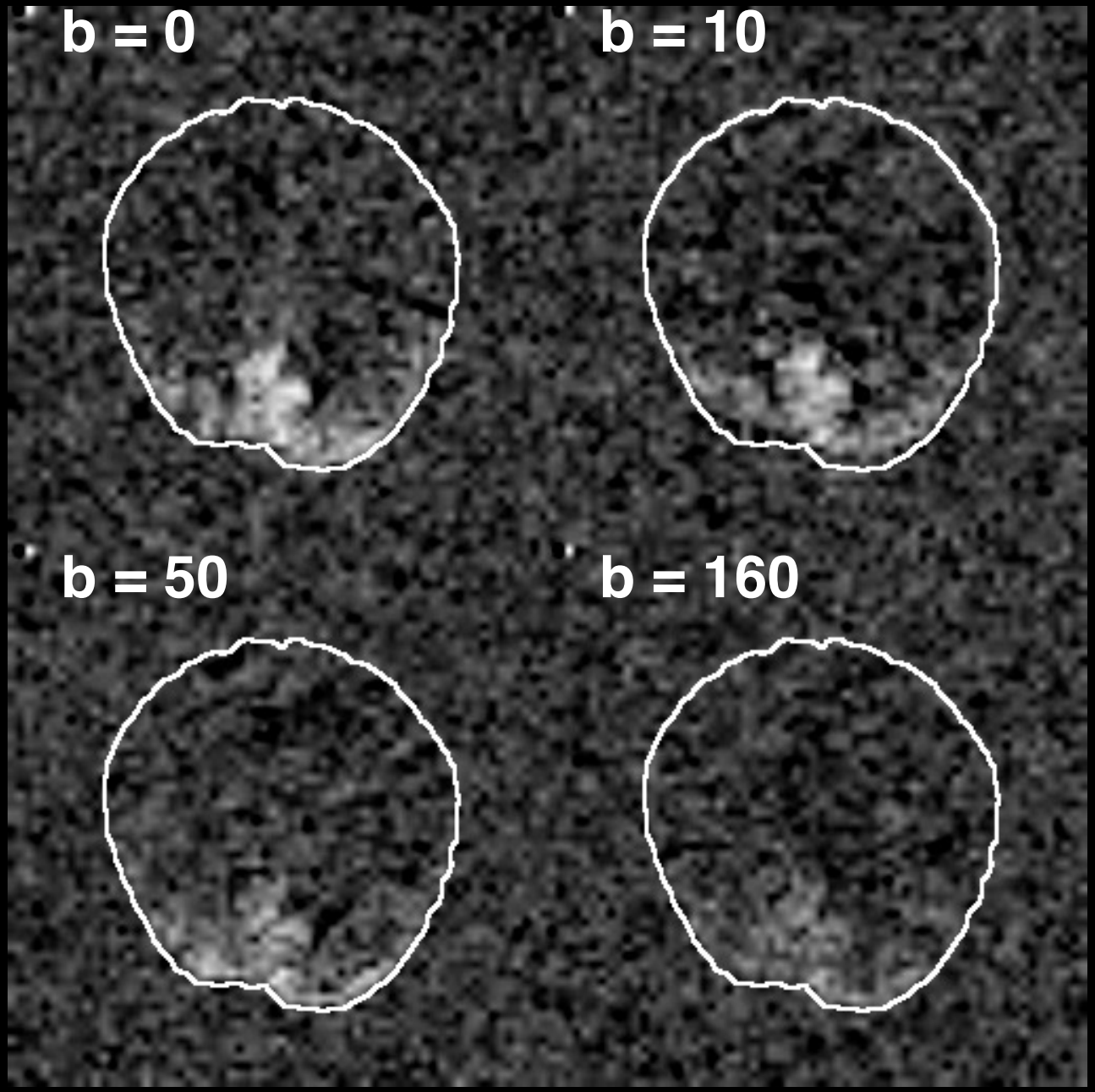

Fractional Signal Change
2.5 mm²
1.25 mm²
0.83 mm²
0.62 mm²
Number of Voxels
0
10
20
30
40
50
60
70
0
4
8
12
16
20
Fractional Signal Change
64 x 64 (2.5 mm)
96 x 96 (1.67 mm)
128 x 128 (1.25 mm)
192 x 192 (0.83 mm)


R2*
&
R2
²R2*
²R2

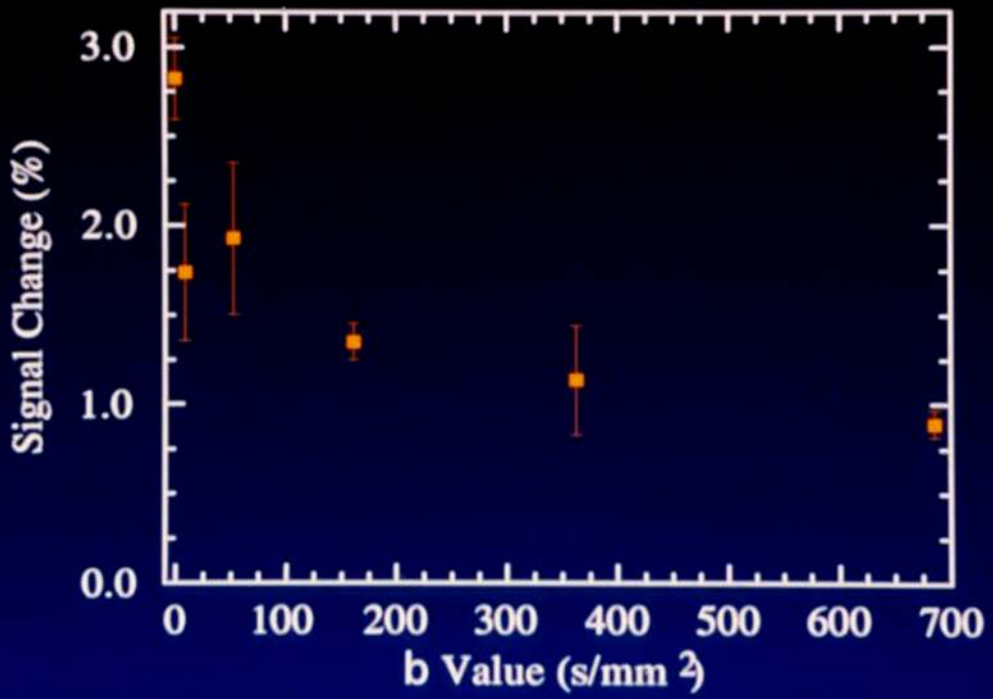
ΔR2* /ΔR2



average ΔR2 / ΔR2 ≈ 3 to 4*

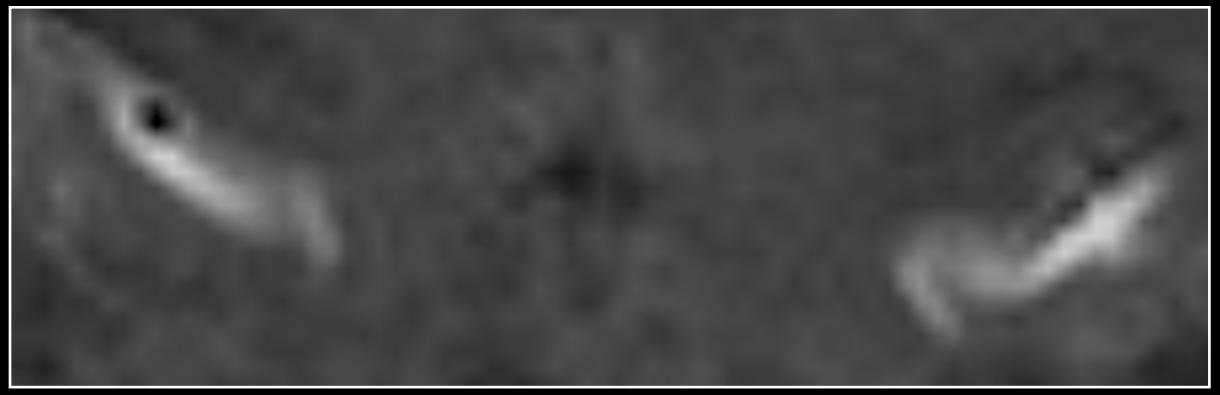

b = 0
b = 10
b = 50
b = 160

Summary of Diffusion-Weighted fMRI Data



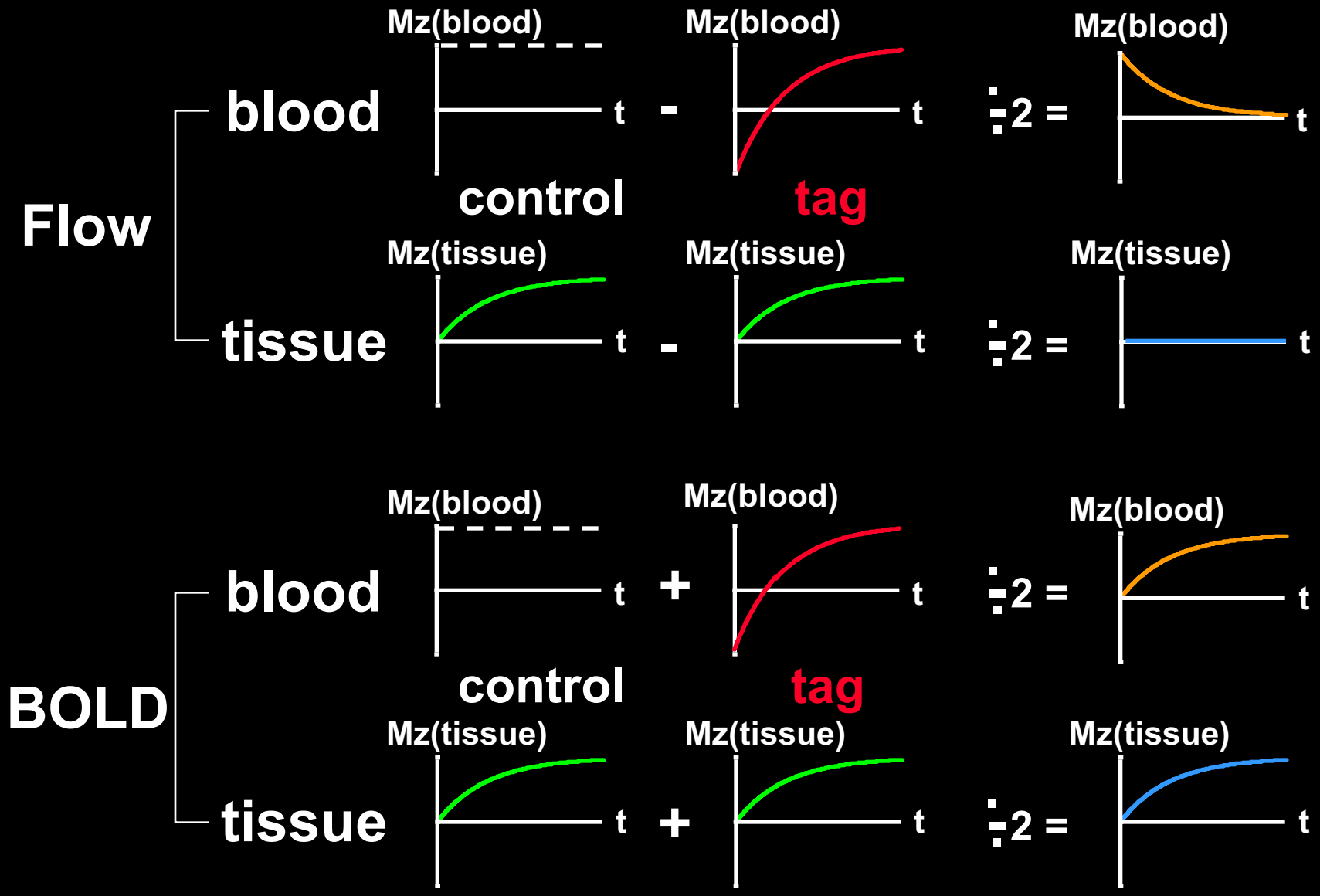
Anatomy

BOLD



Perfusion

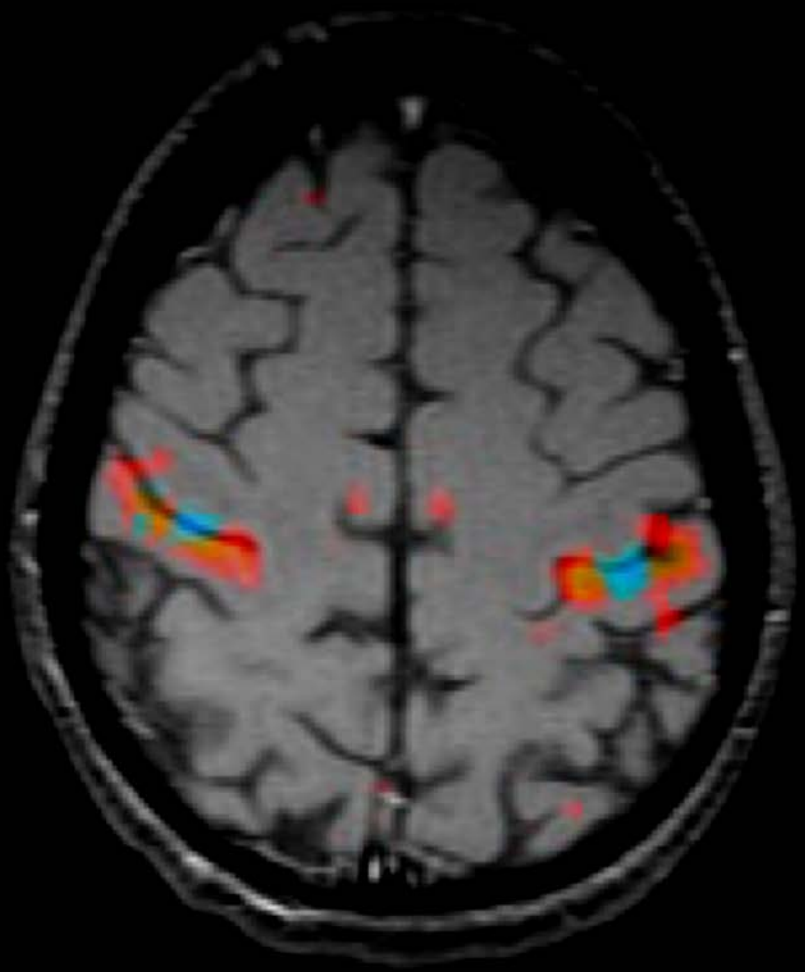
Simultaneous Flow and BOLD



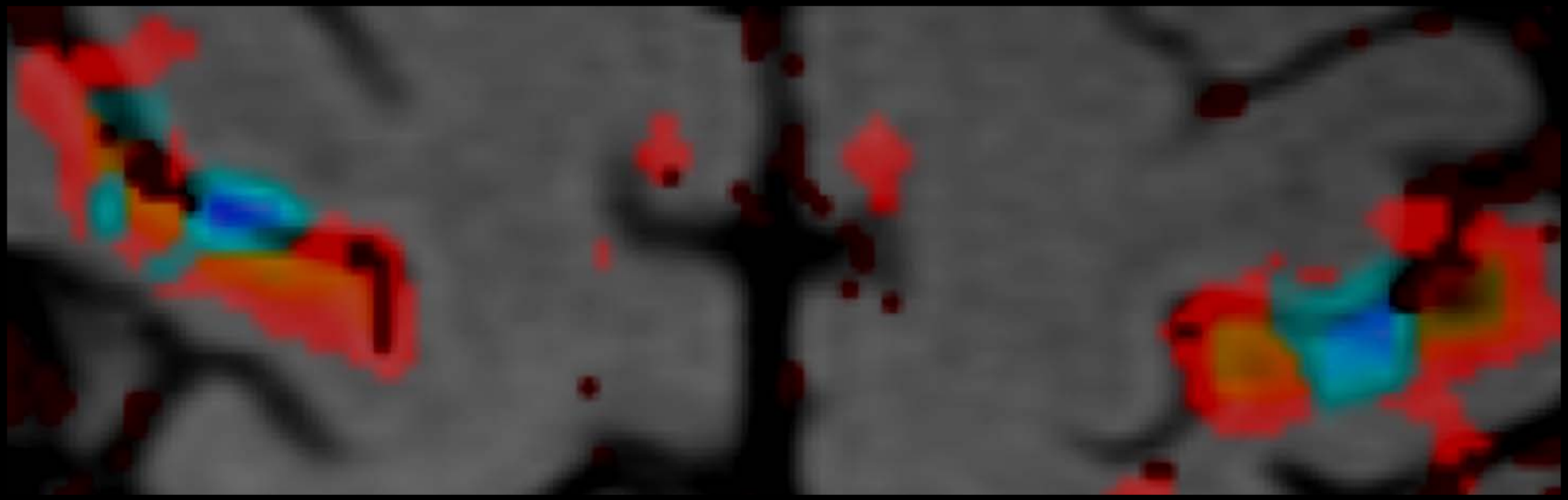
Simultaneous BOLD and Perfusion

perfusion

BOLD



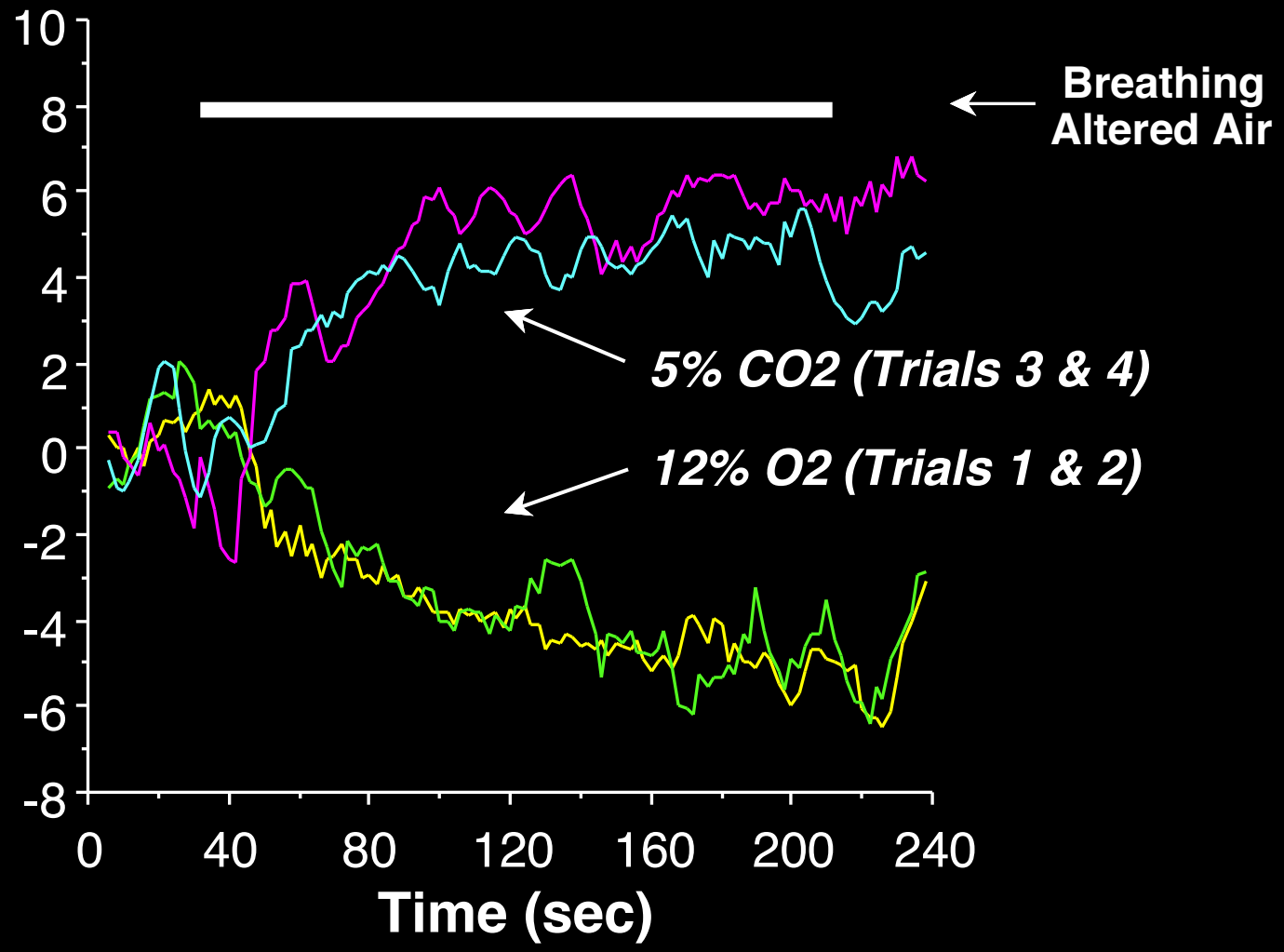
Angiogram
Perfusion
BOLD



T1 - weighted

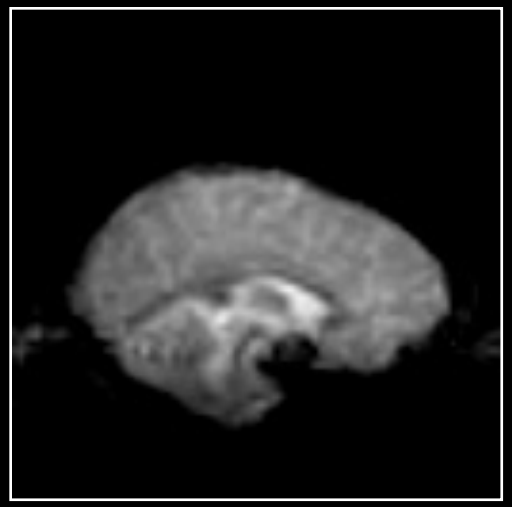
T2* weighted

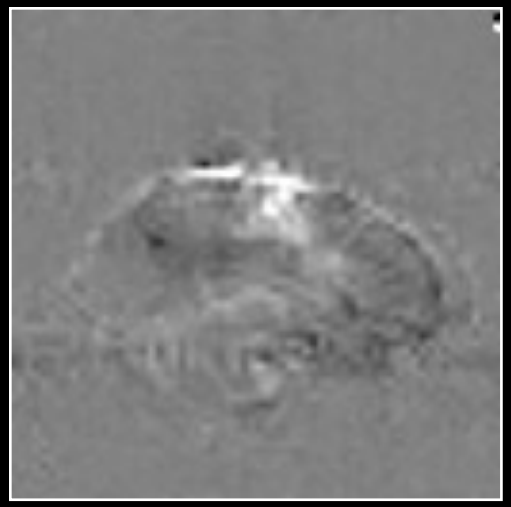
T1 and T2* weighted


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)

,

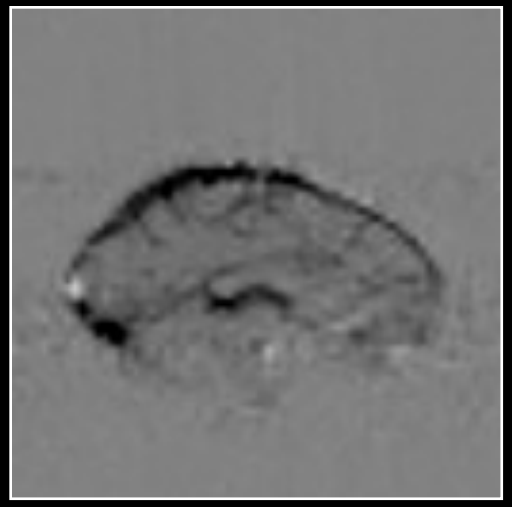
Anatomical

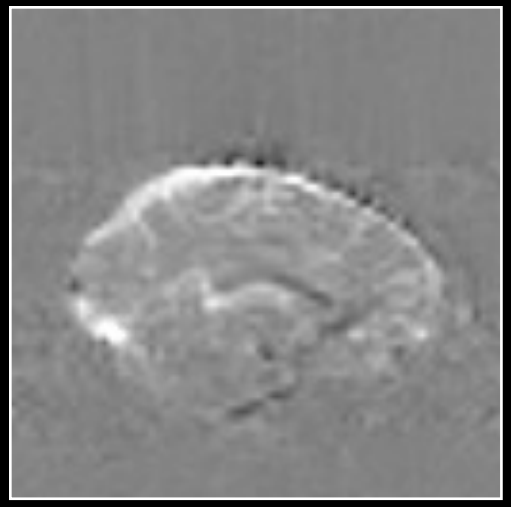




Finger Movement

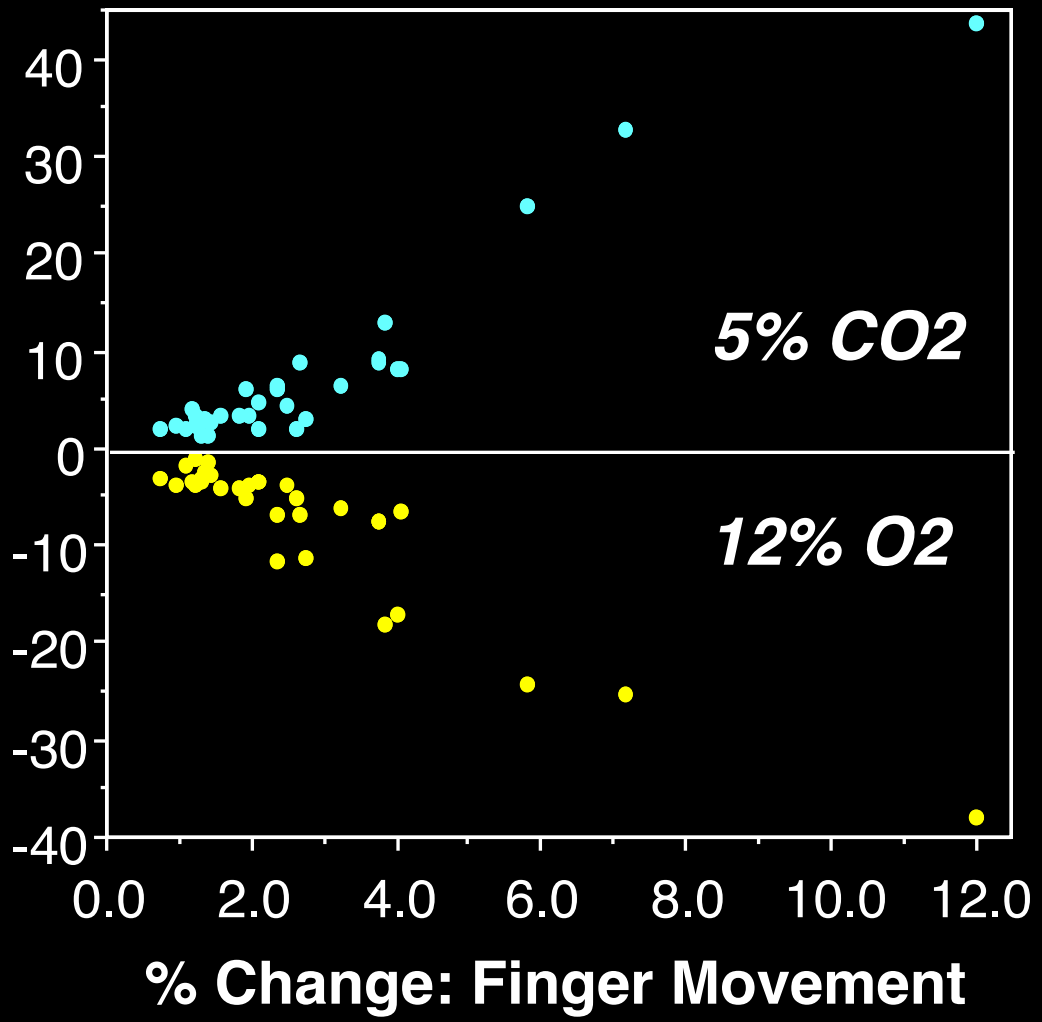
12% O2

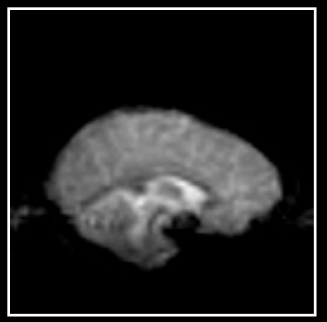




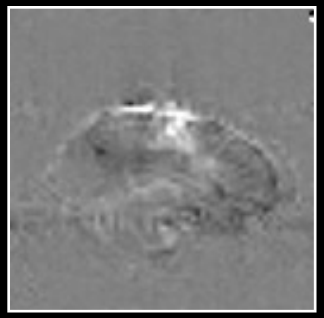
5% CO2

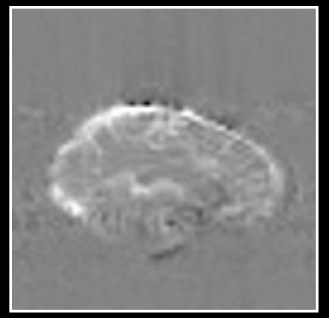
Resting State Blood Volume Weighting

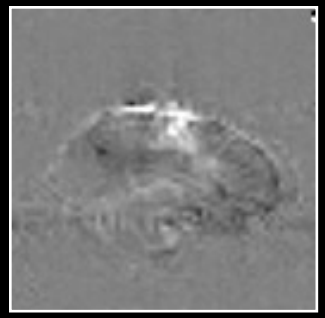


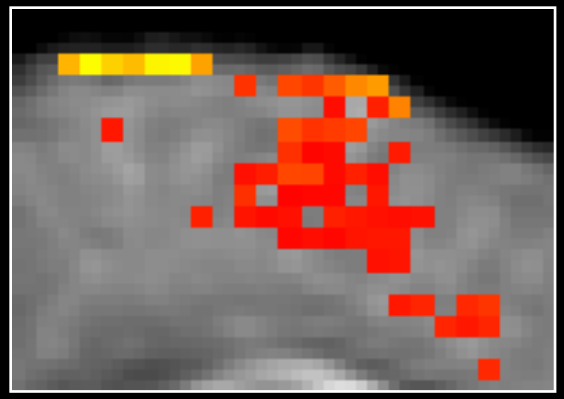


Capillaries
Veins









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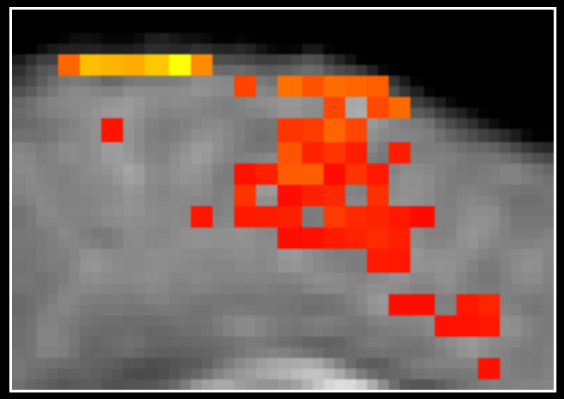

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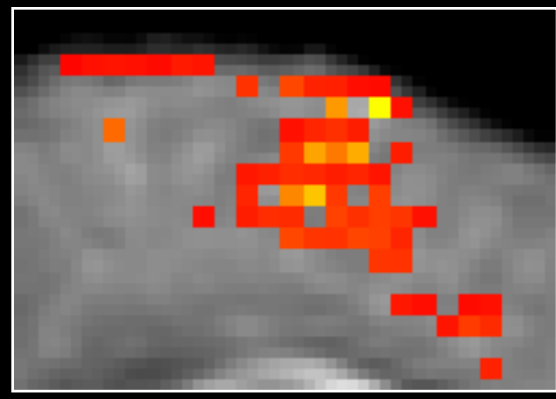
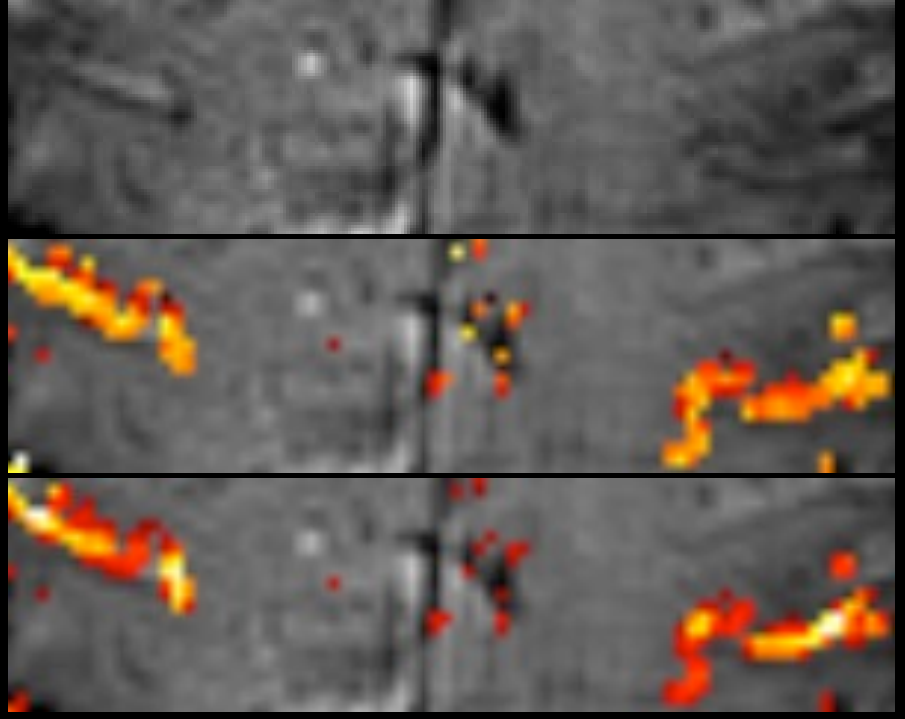


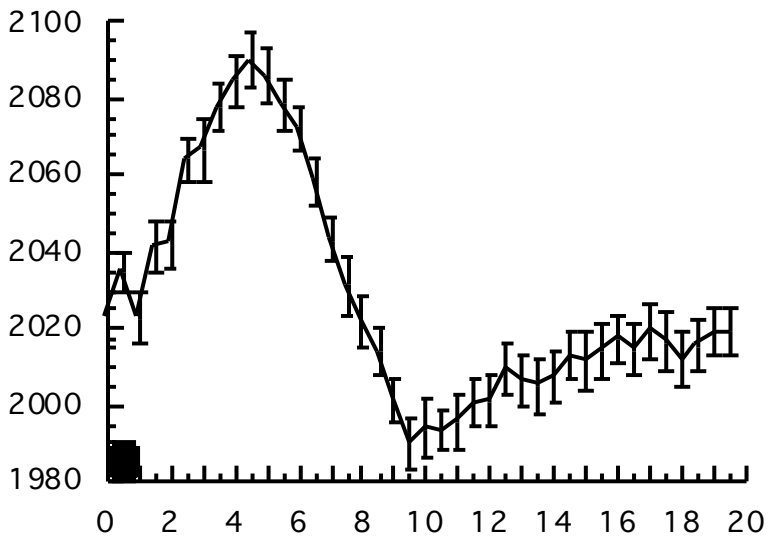
Latency

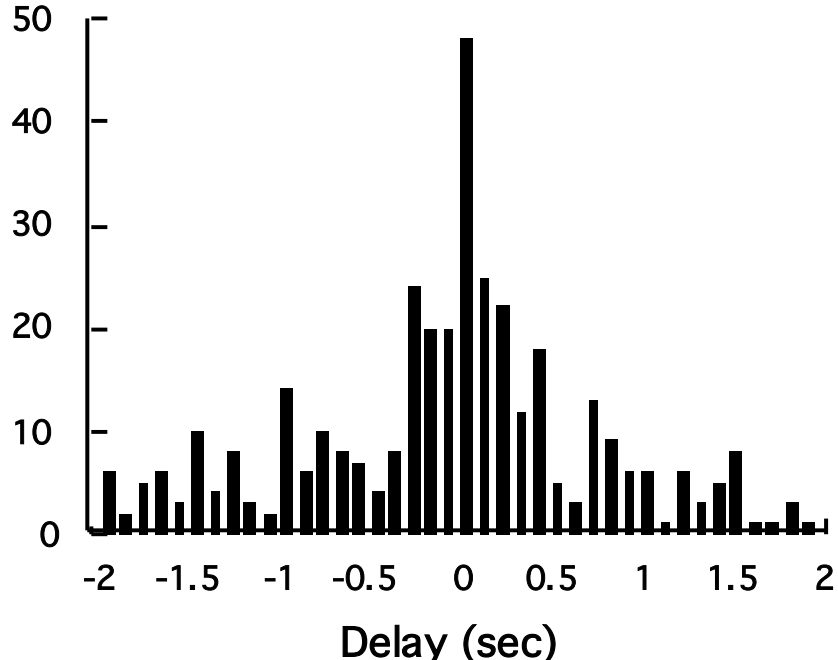
Magnitude



+ 2 sec

- 2 sec



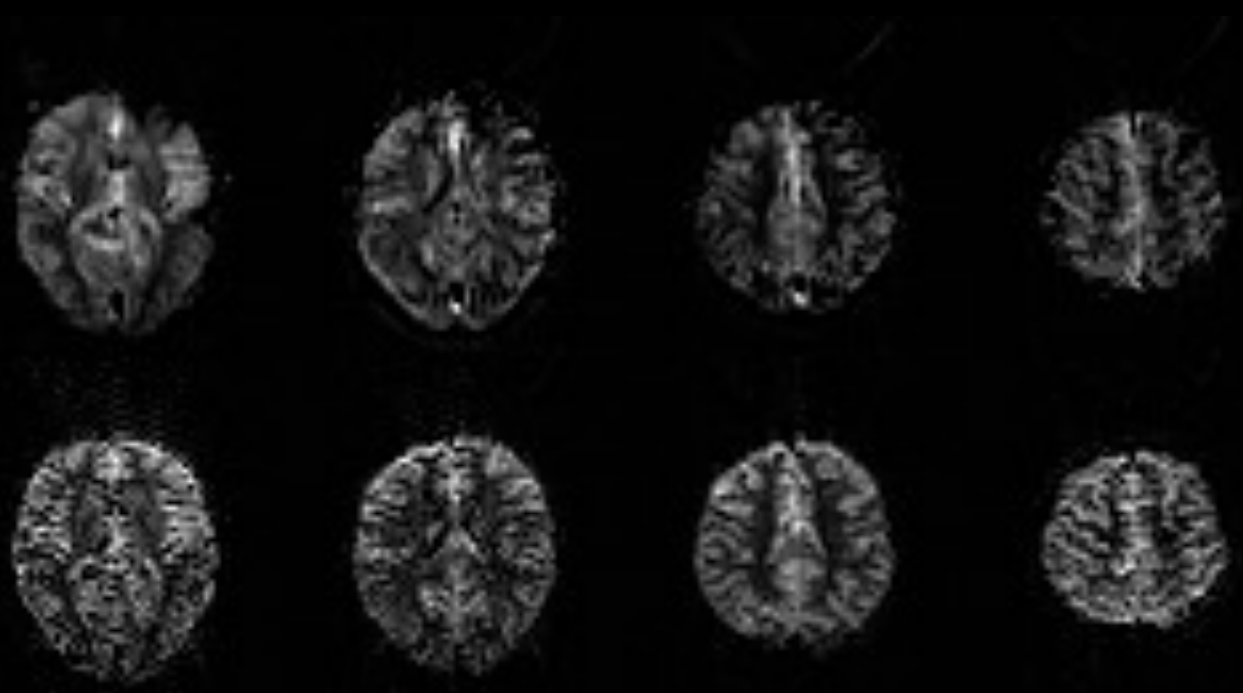


1991-1992

1992-1999

GE
TE = 30 ms

SE
TE = 110 ms

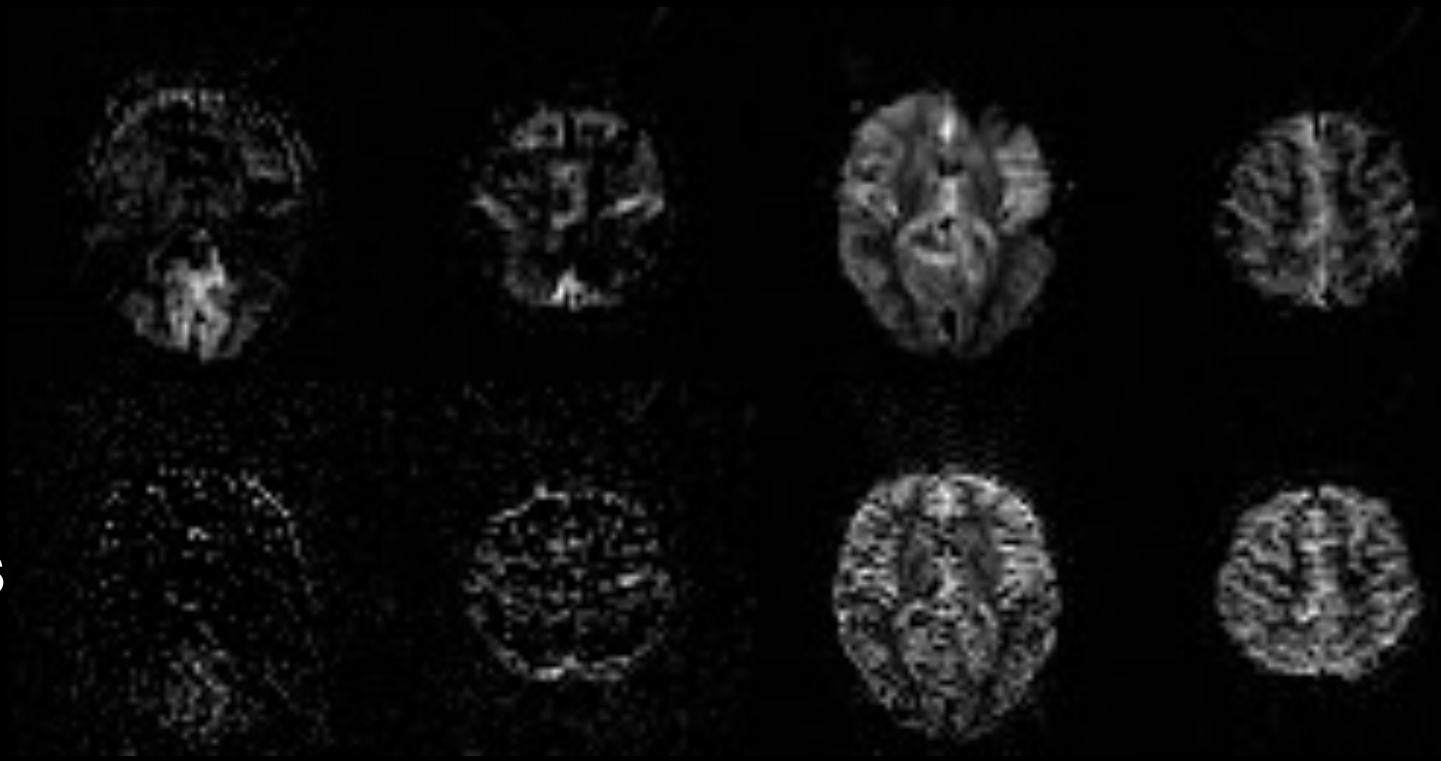


BOLD

BALD

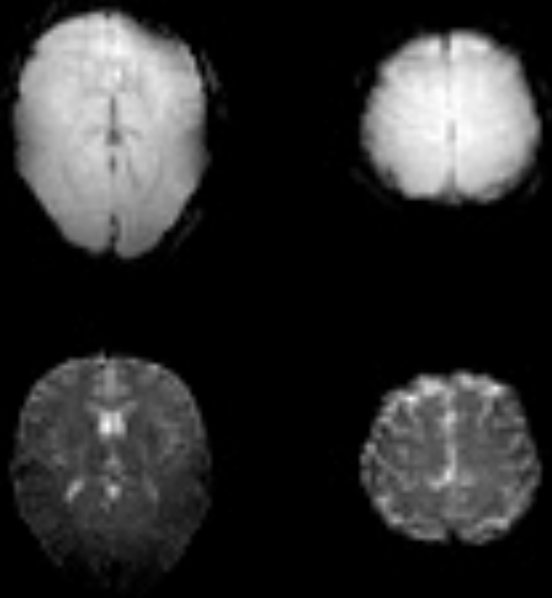
GE
TE=30 ms

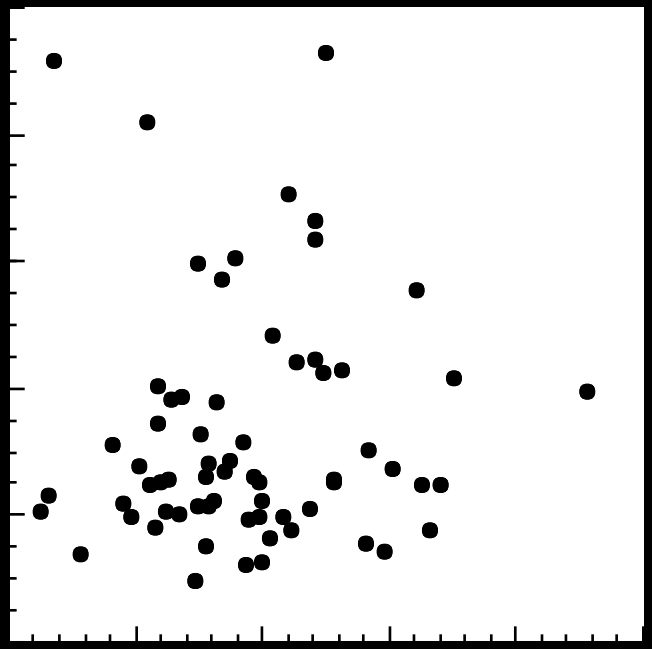
SE
TE=110 ms

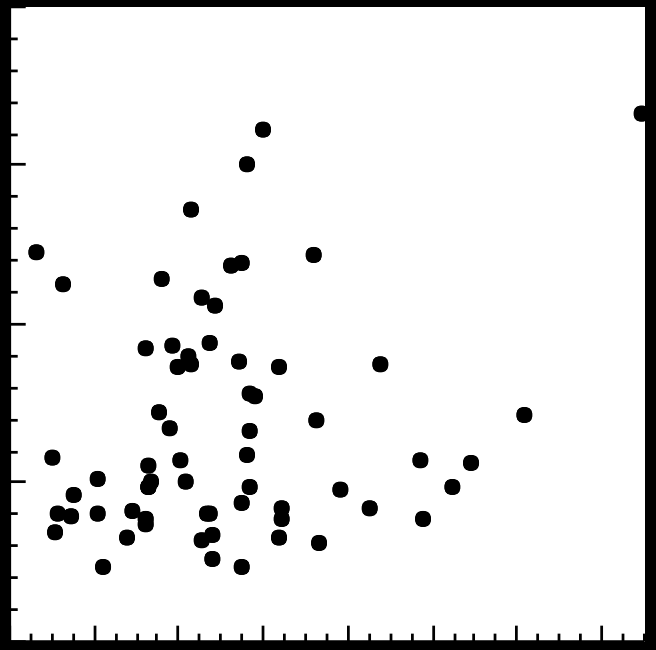


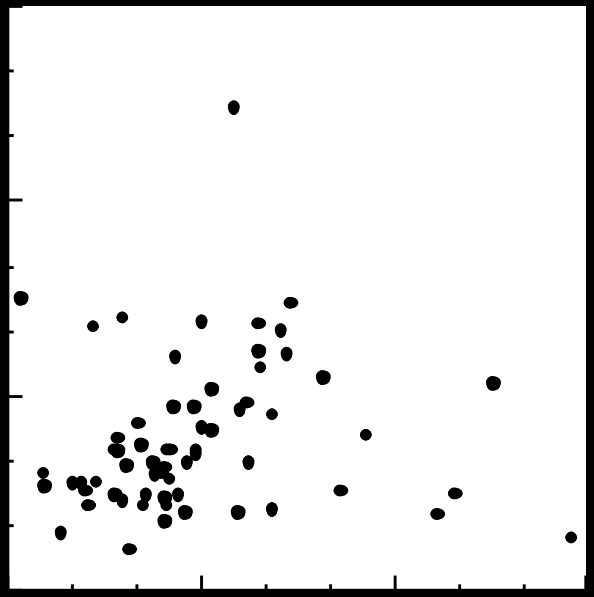
GE
TE = 30 ms

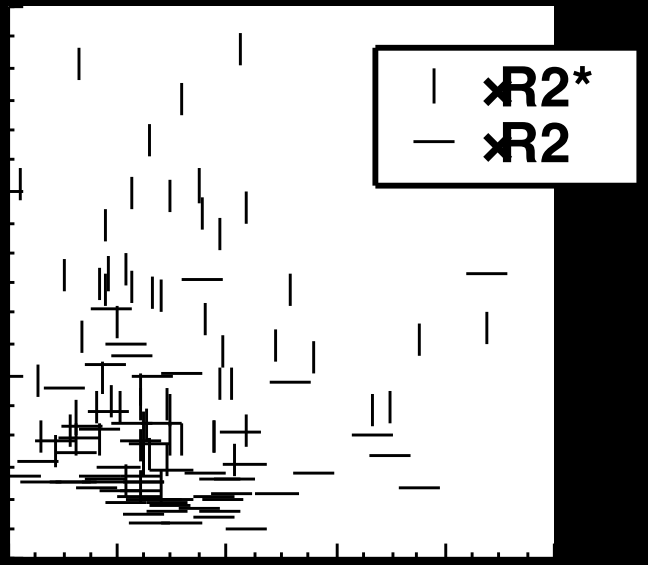
SE
TE = 110 ms

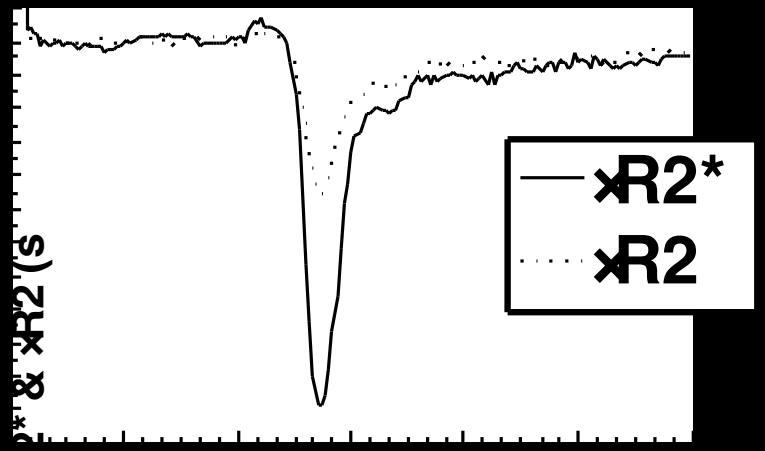


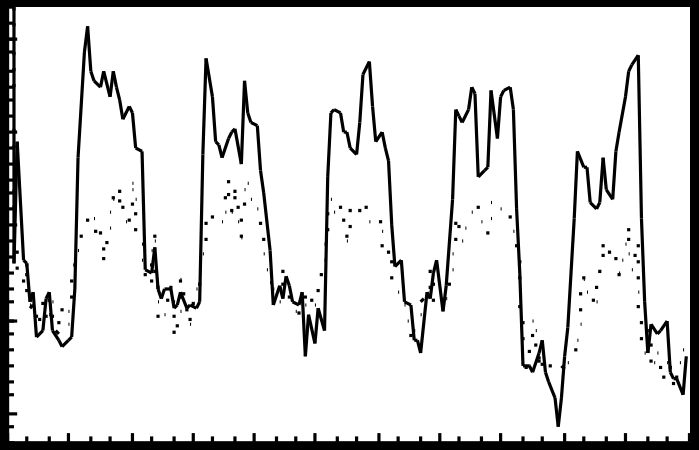







R2*
R2


R2*
R2

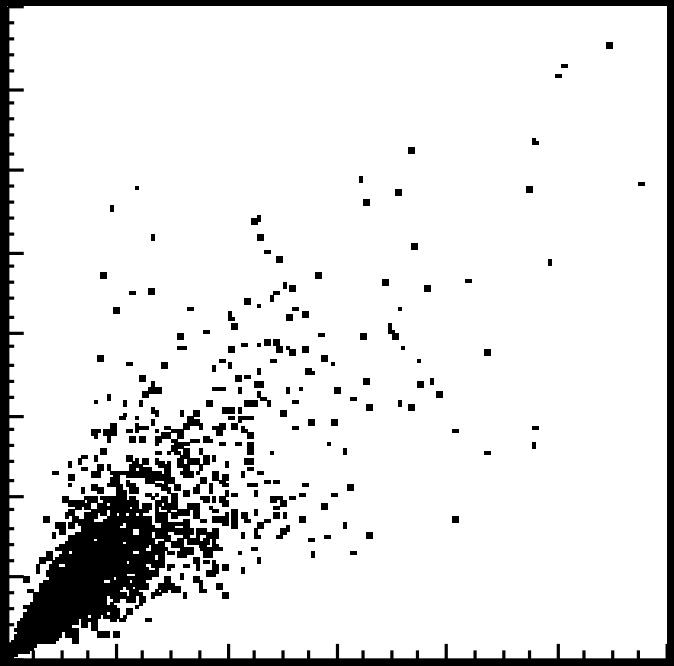


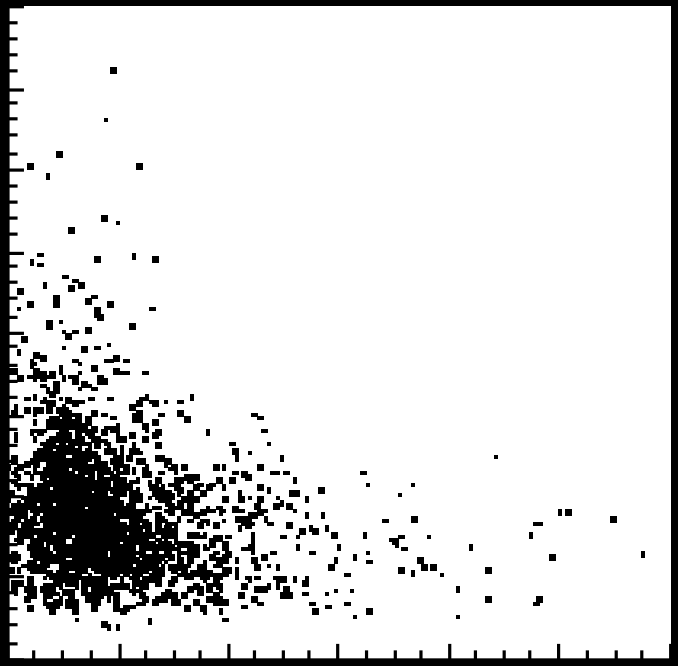
GE
(TE = 30 ms)

SE
(TE = 110 ms)

Subject 1

Subject 2





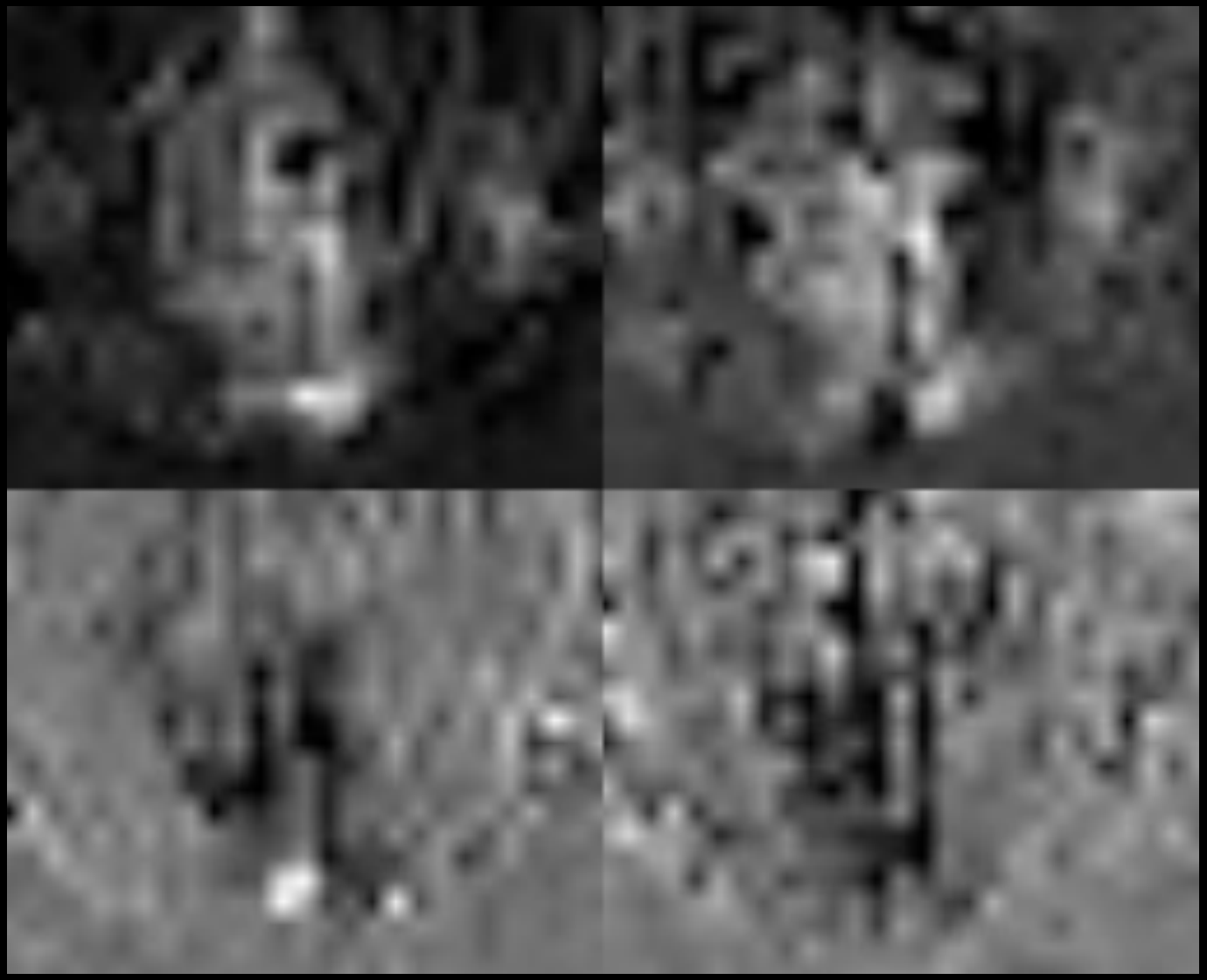
S2

Gradient - Echo

Spin - Echo

During Activation Increase

Post Activation Undershoot

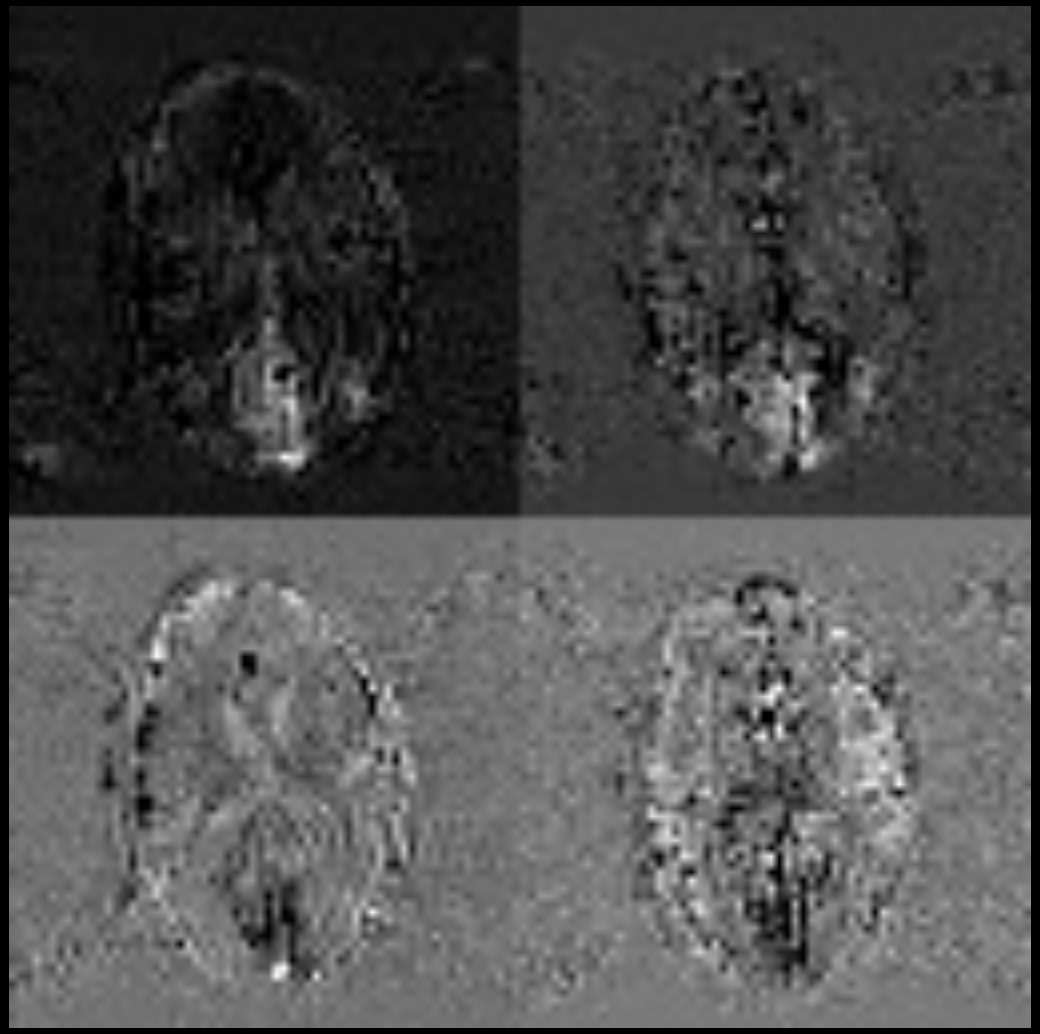


Gradient - Echo

Spin - Echo

During Activation Increase

Post Activation Undershoot



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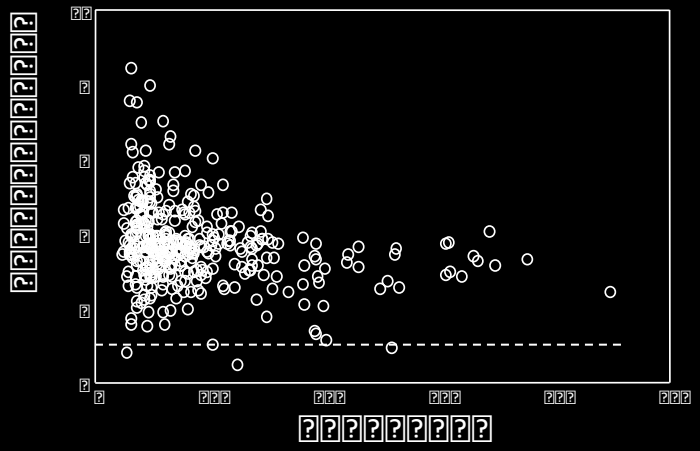
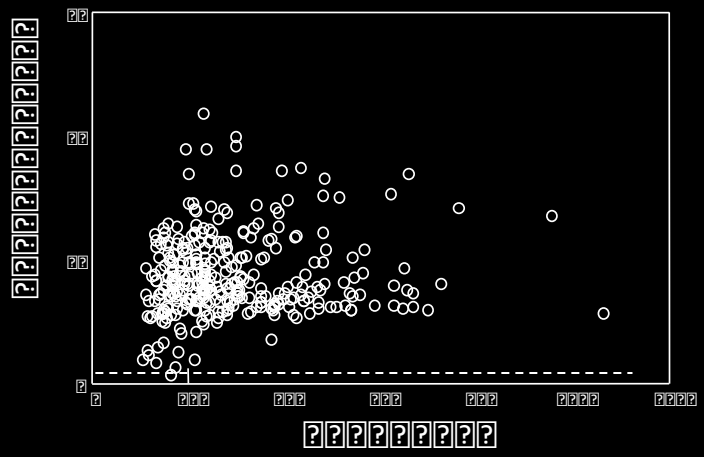
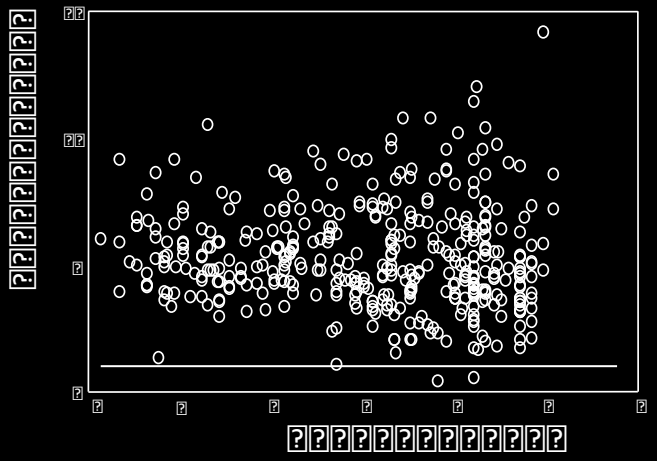
???????

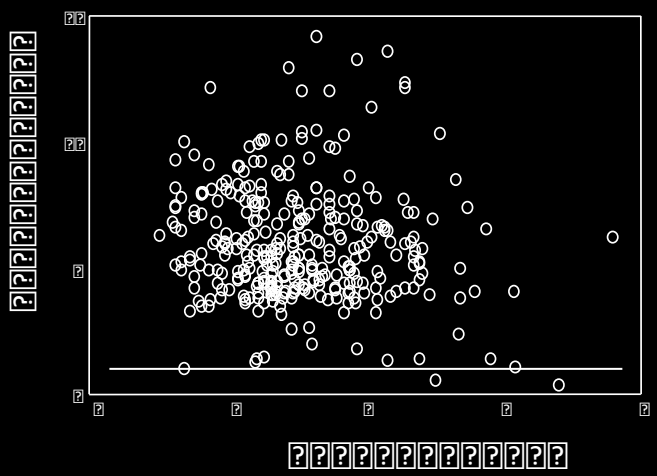
Visual task

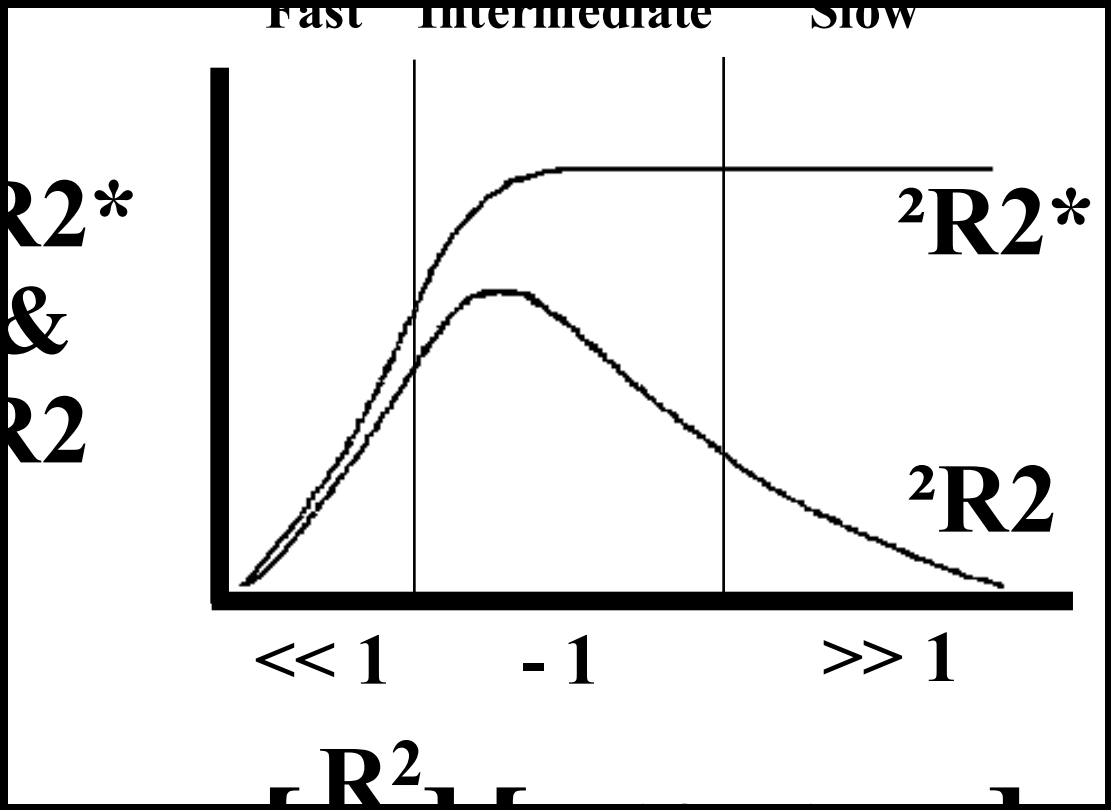


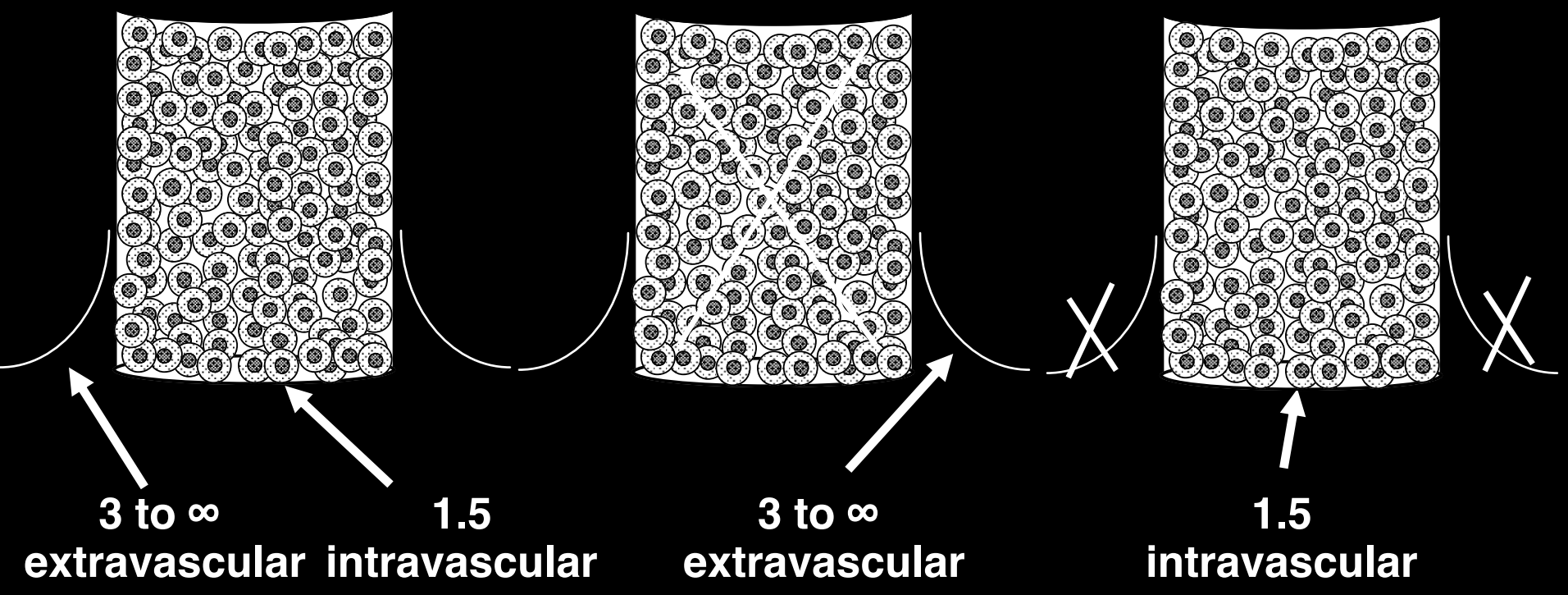
Motor task





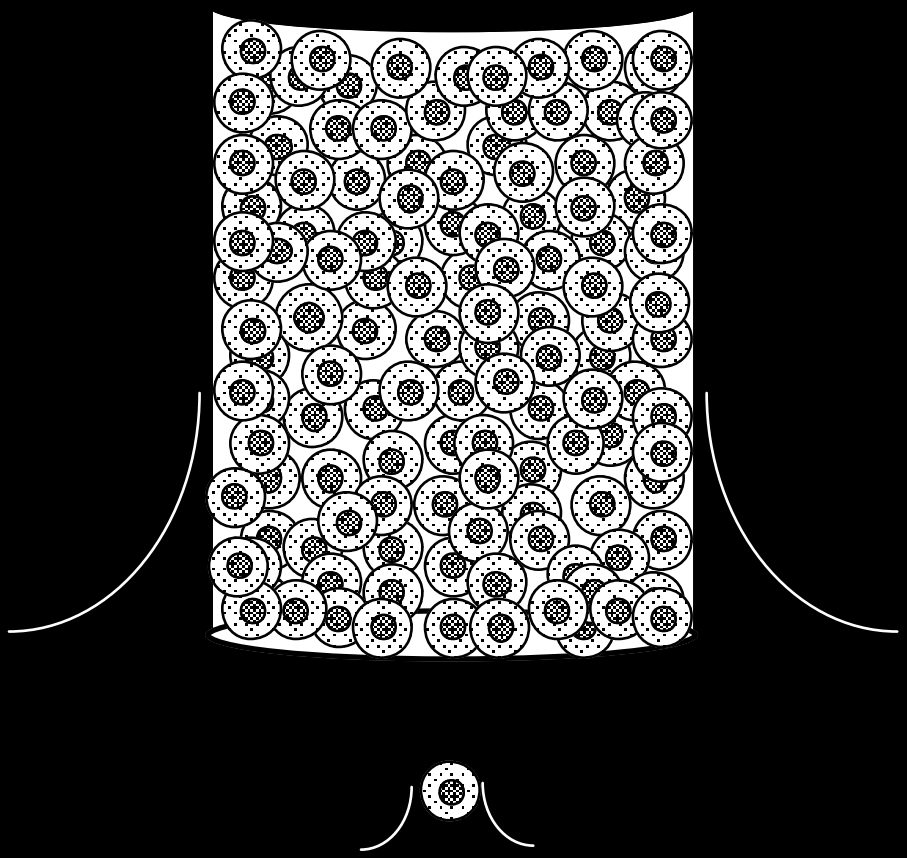



Fast
Intermediate
Slow
R2*
&
R2
²R2*
²R2
<< 1
- 1
>> 1
[R²]



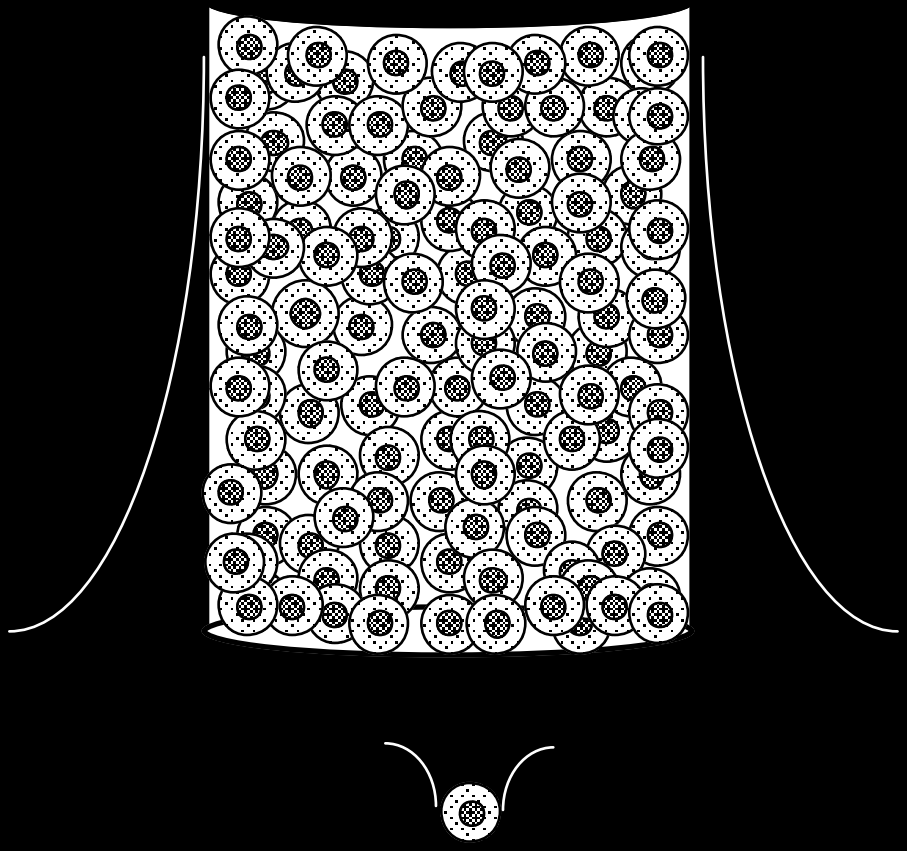
ΔR2* / ΔR2:	*ΔR2* / ΔR2 increase*	*ΔR2*/ ΔR2 decrease*
= IV and EV	= EV only	= IV only

BOLD

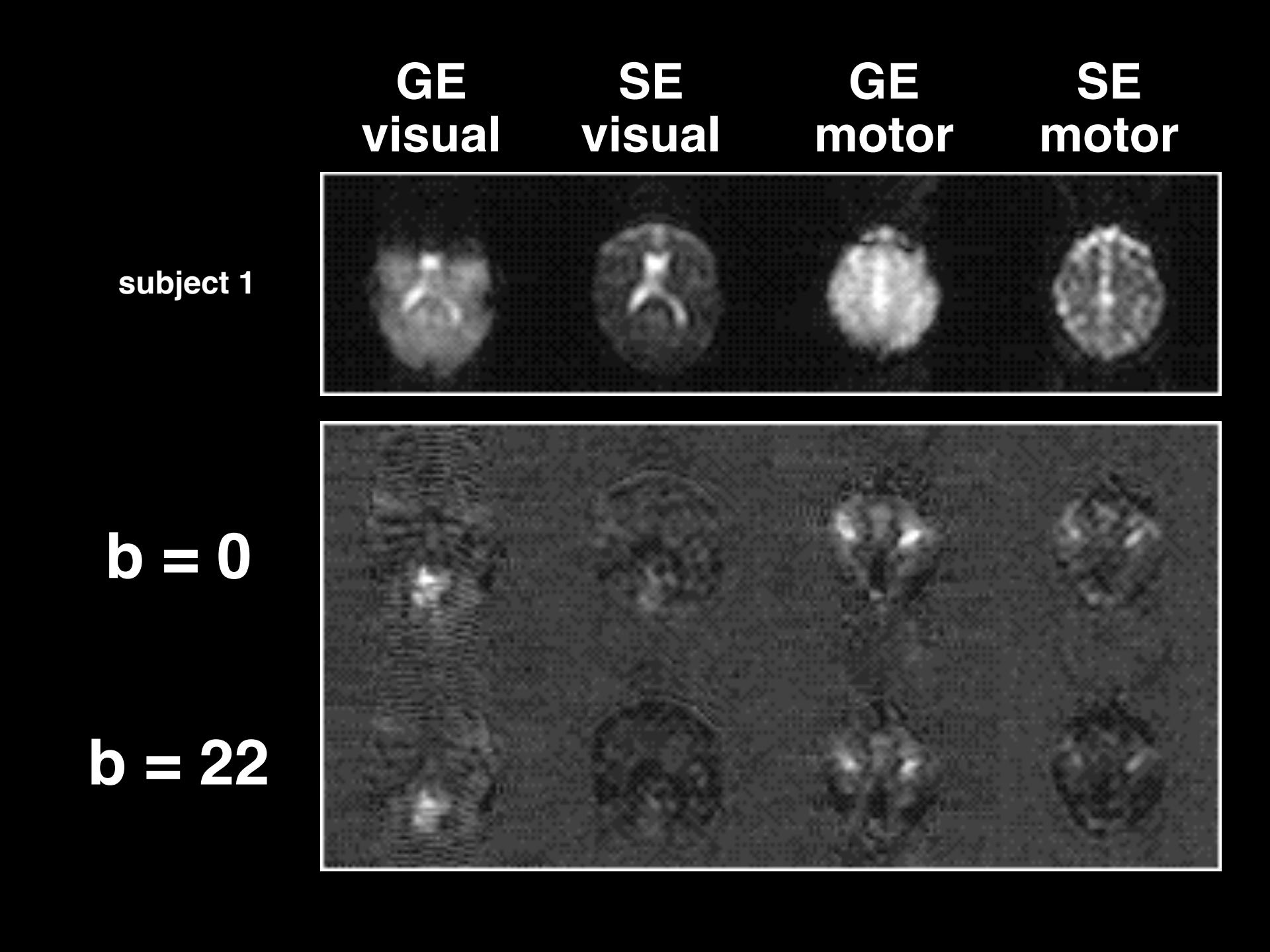


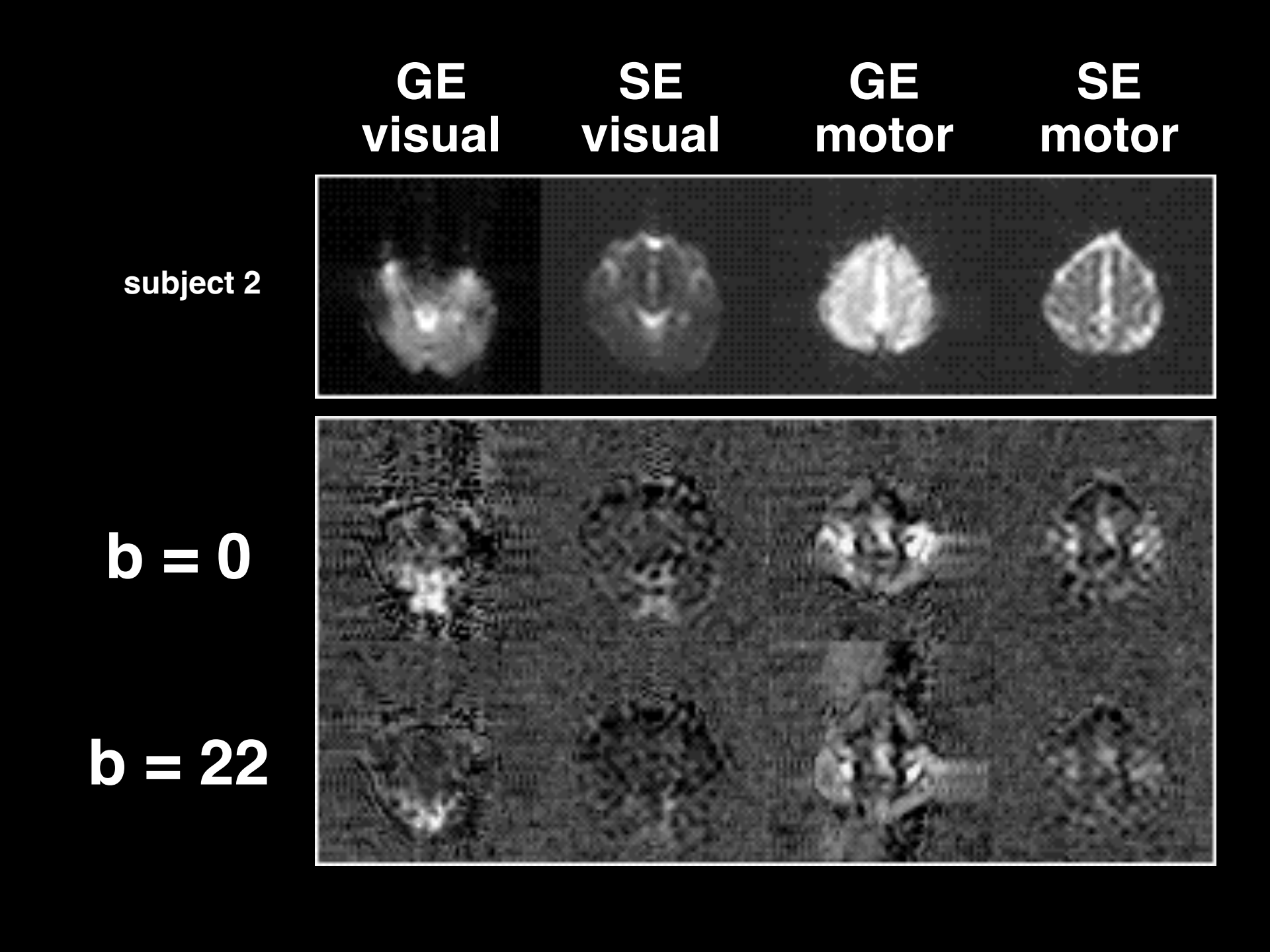
plasma χ < rbc χ

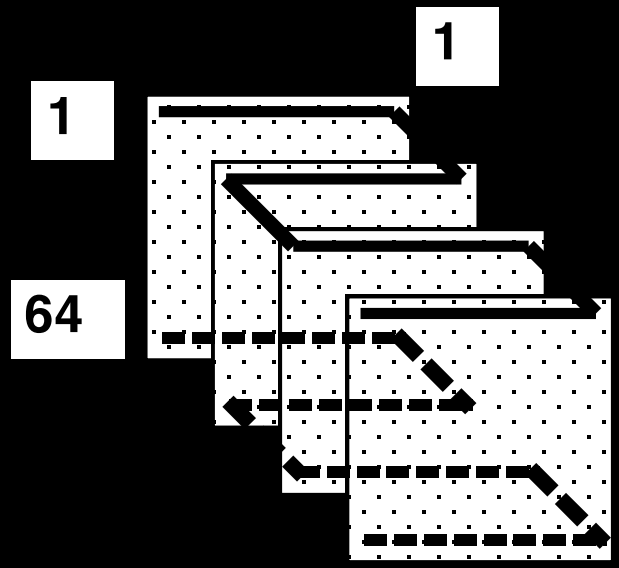
BALD



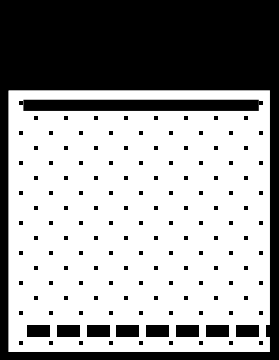
plasma χ > rbc χ


GE visual
SE visual
GE motor
SE motor
subject 1
b = 0
b = 22

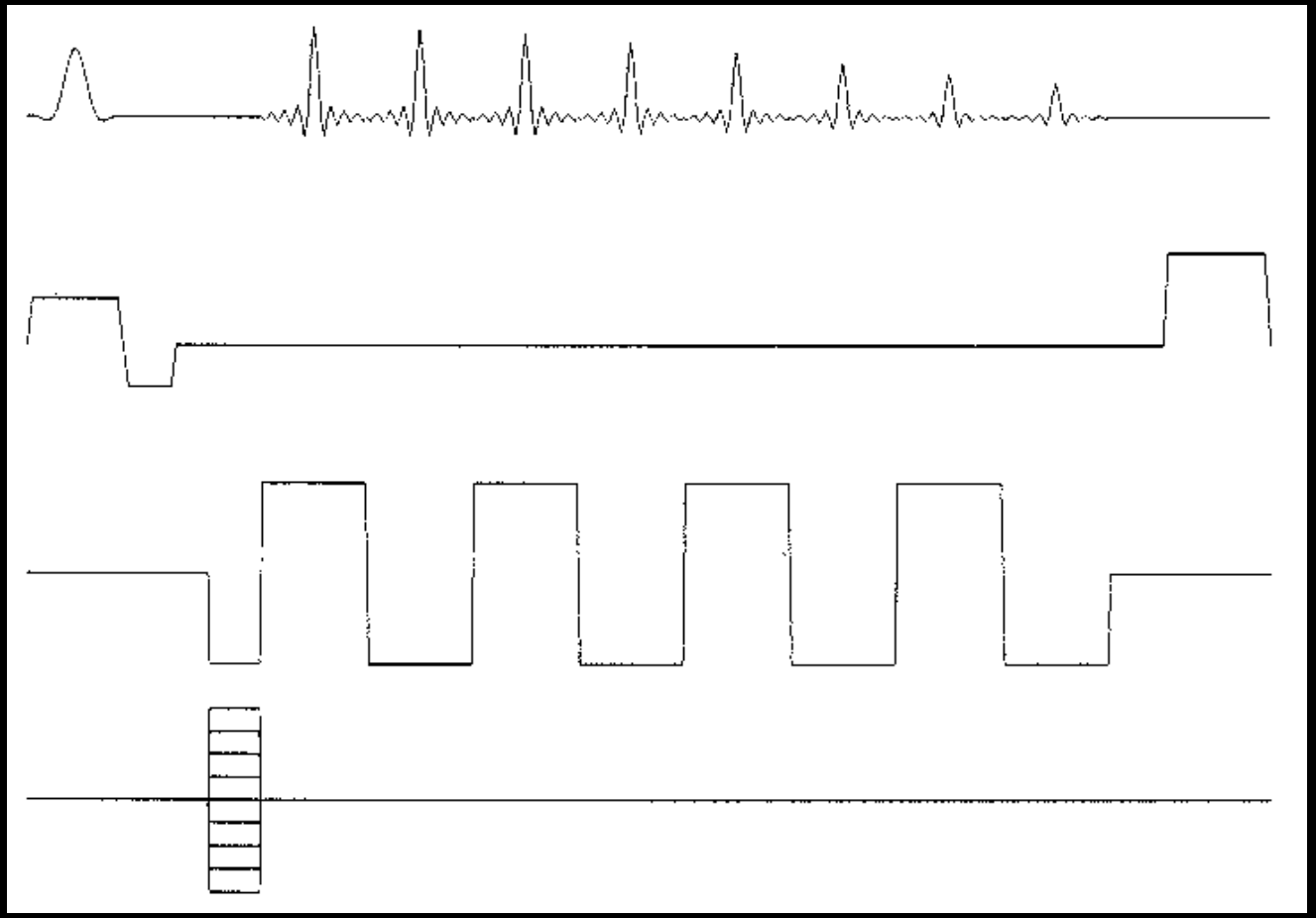

GE visual
SE visual
GE motor
SE motor
subject 2
b = 0
b = 22

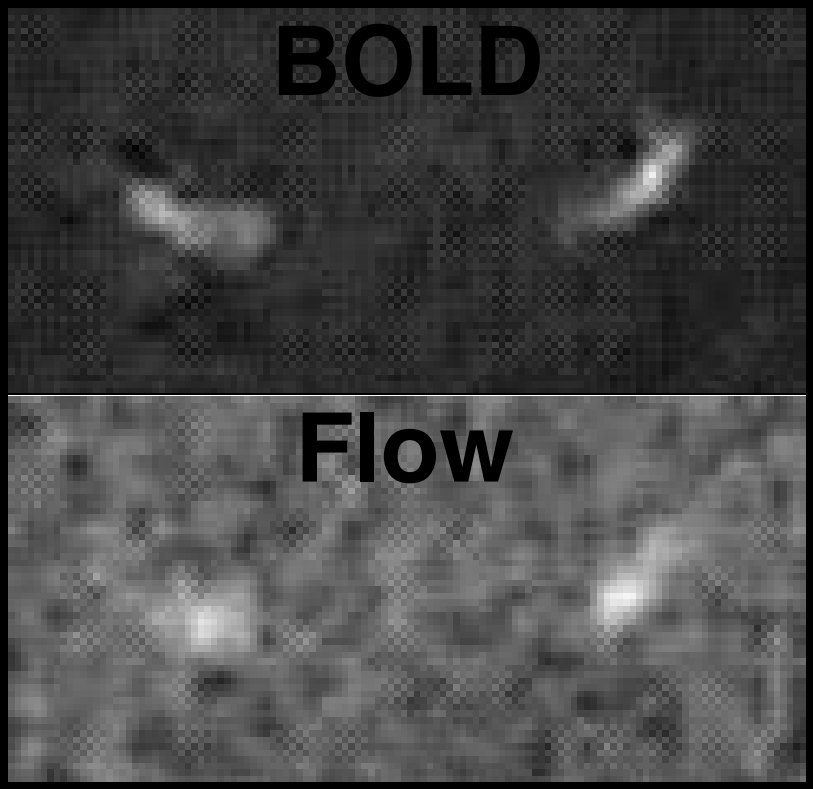


TE = 5.0

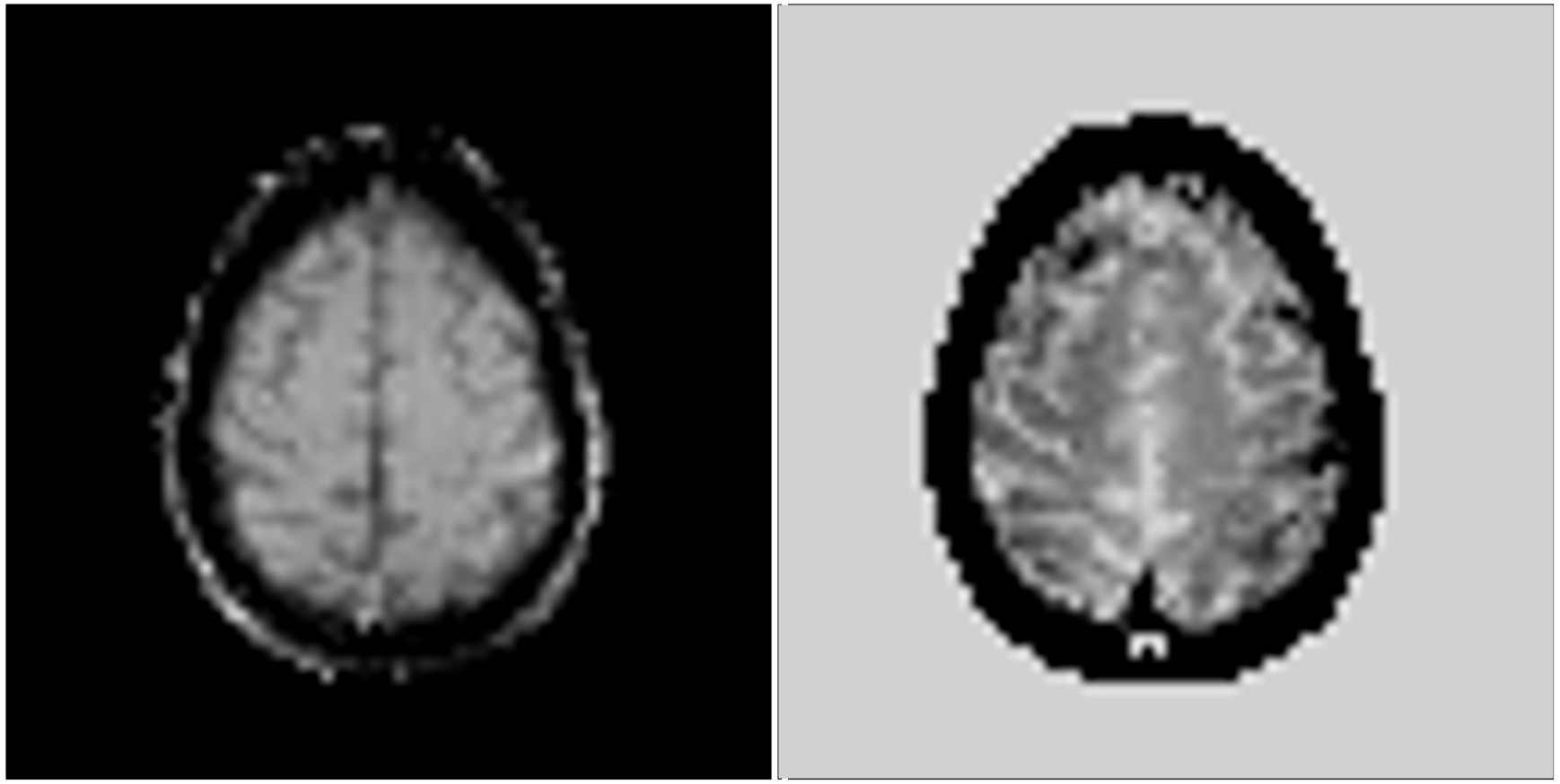


TE = 44.3

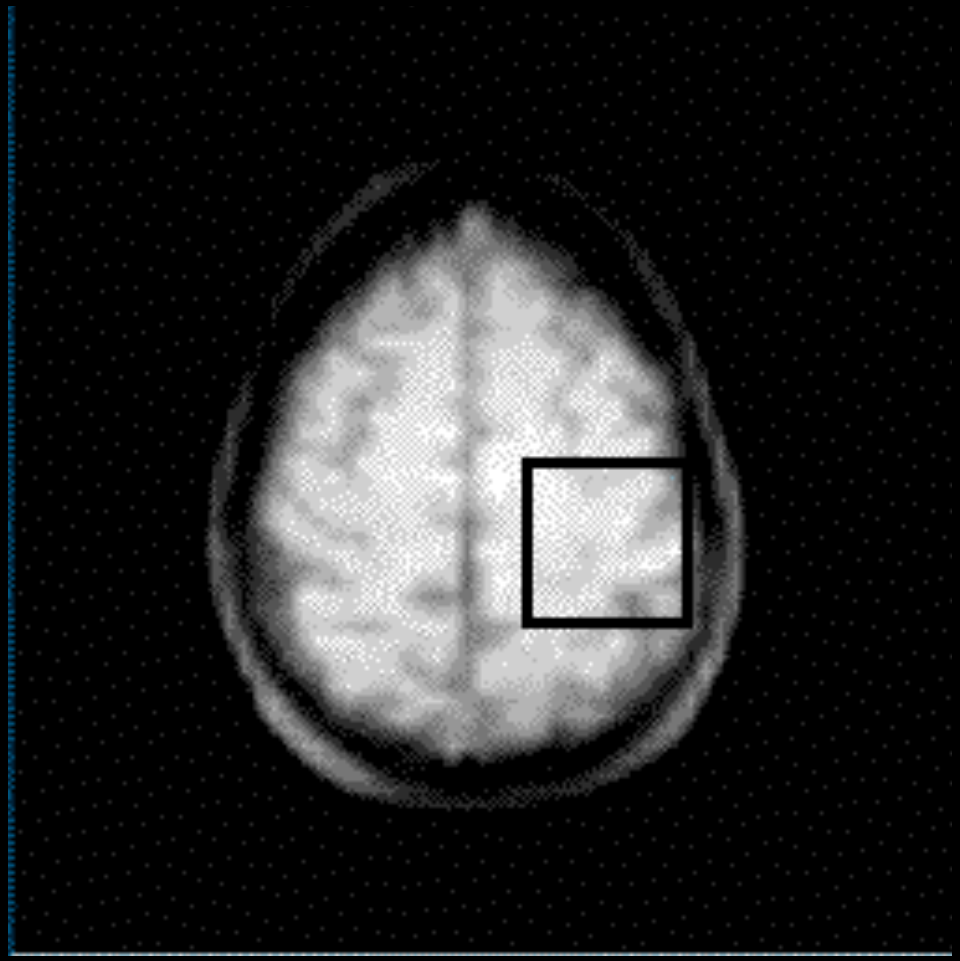

RF
G slice
G freq
G phase

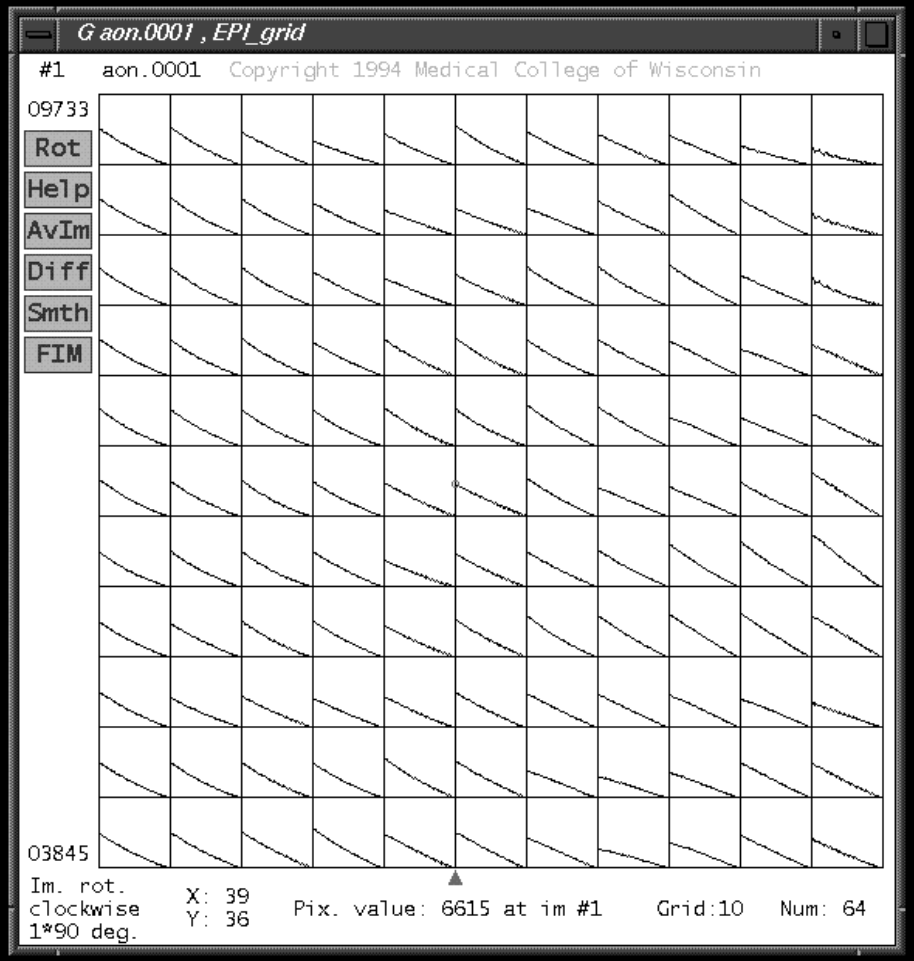

BOLD
Flow

M_o T2*



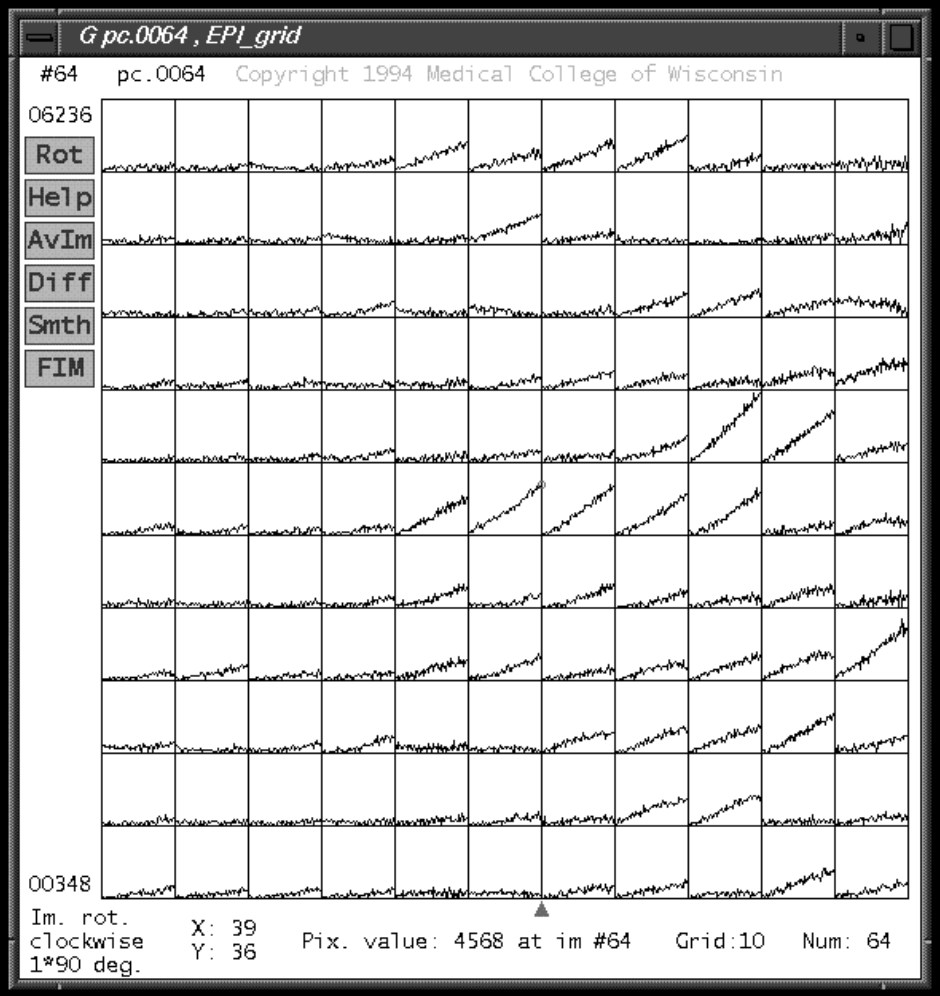
MR Signal



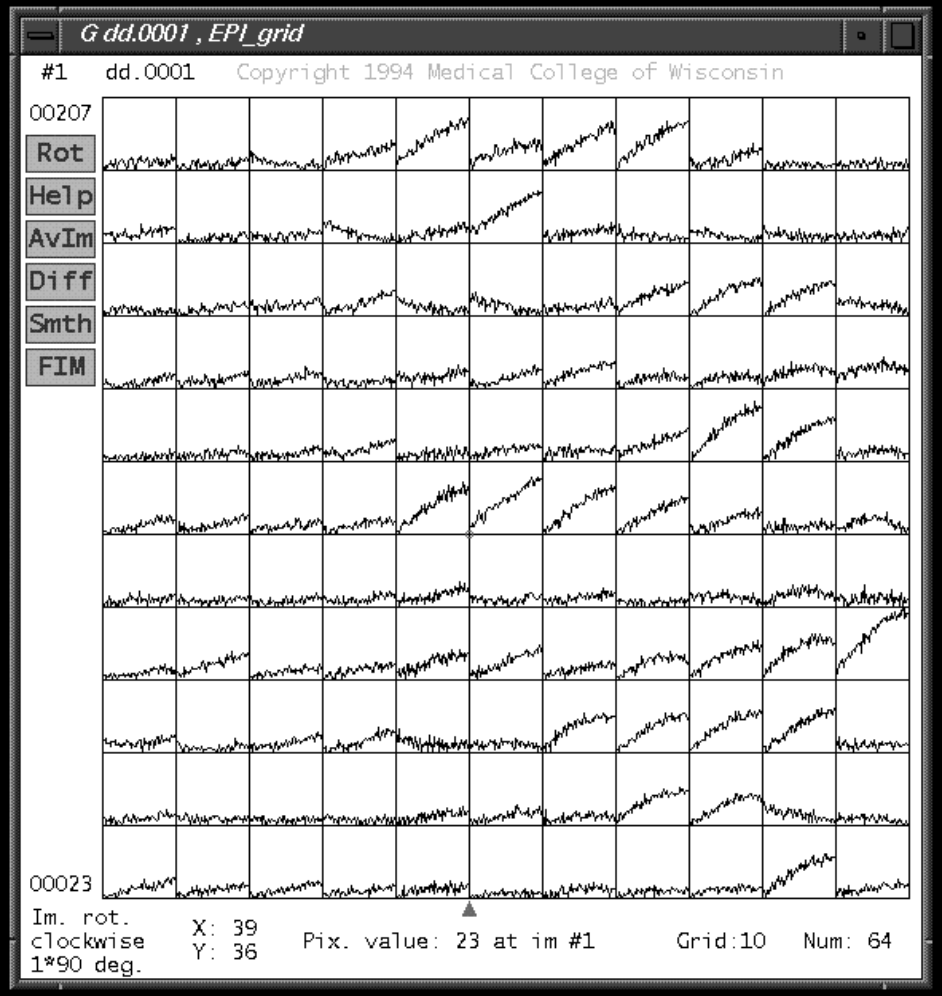


TE (5 to 44 ms)

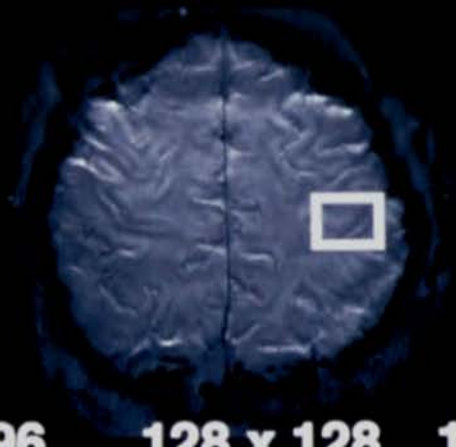
Percent Change



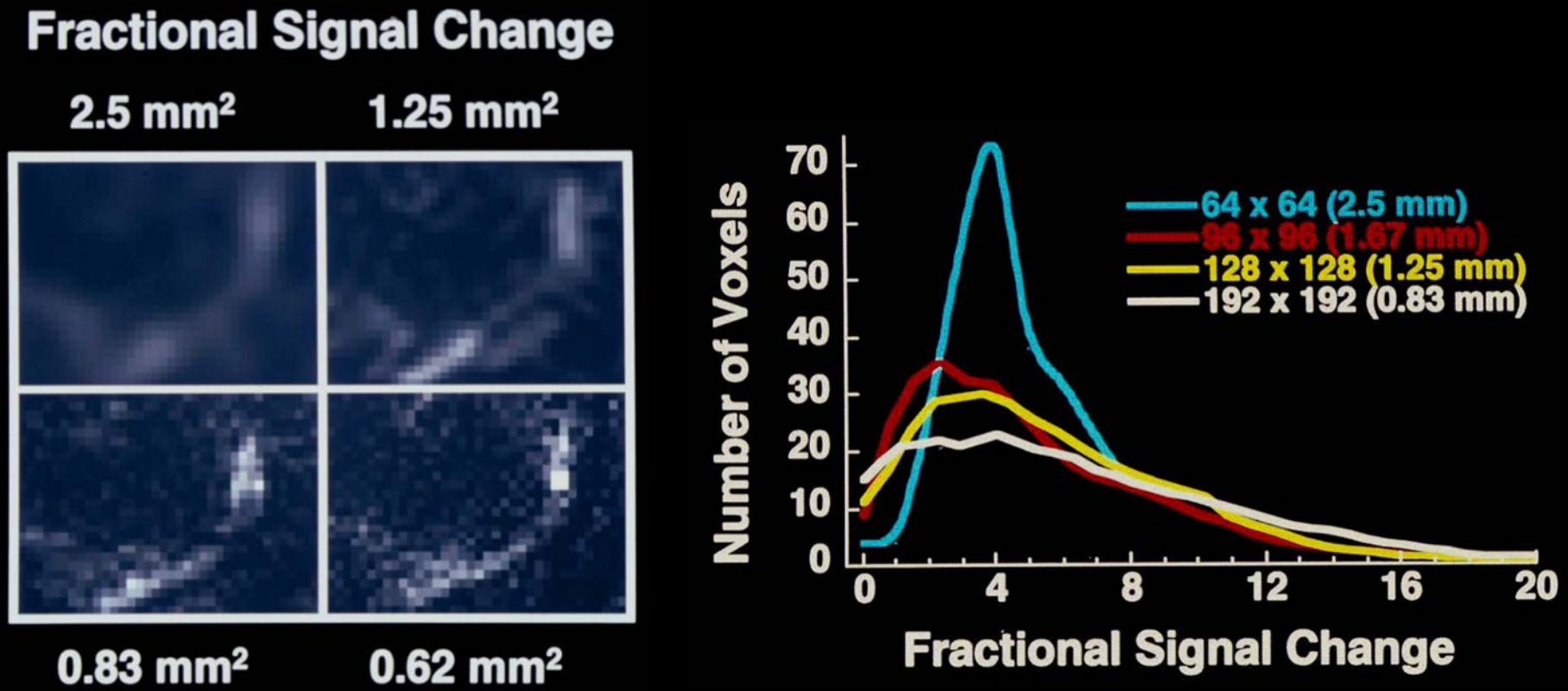
Difference



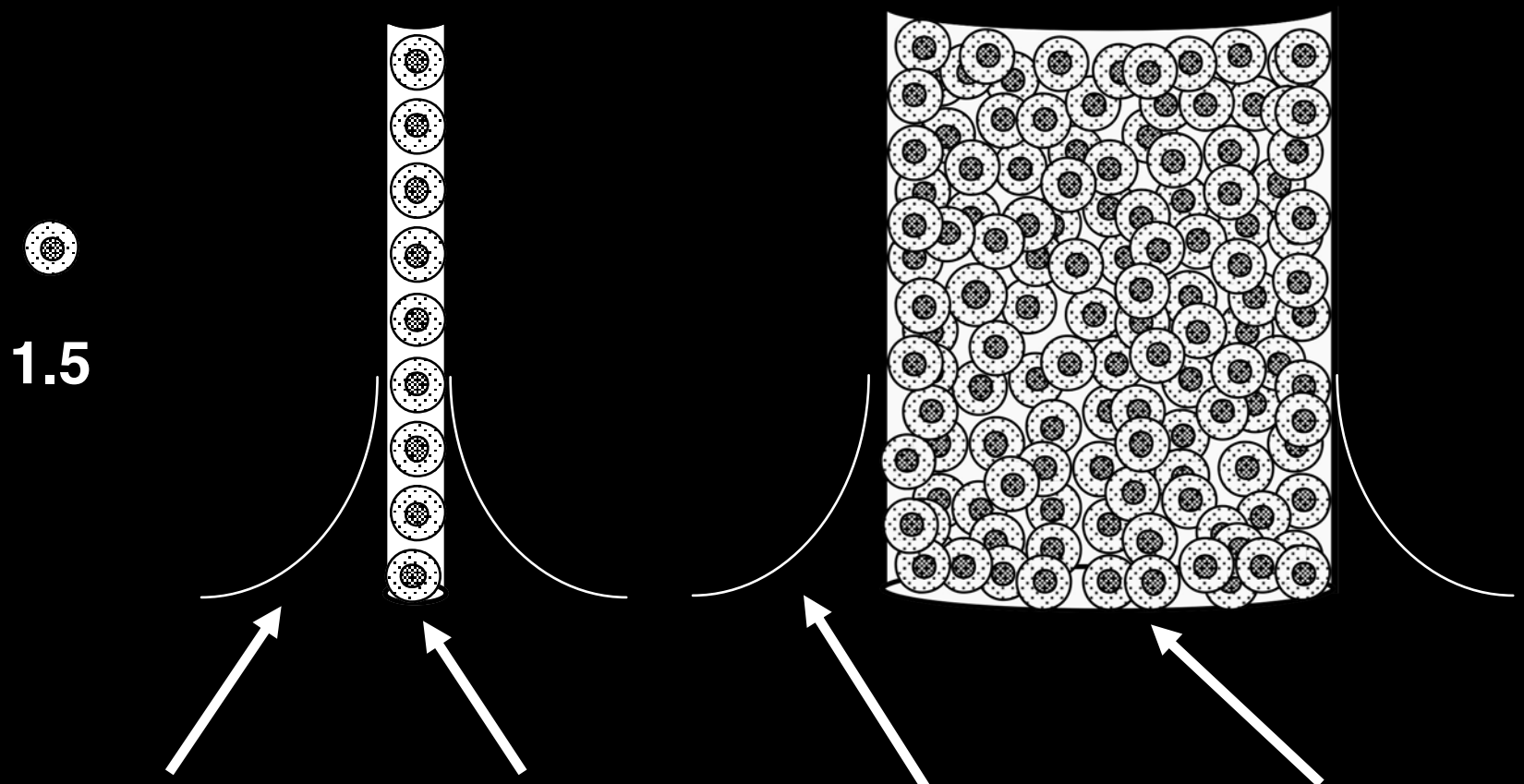
TE (5 to 44 ms)



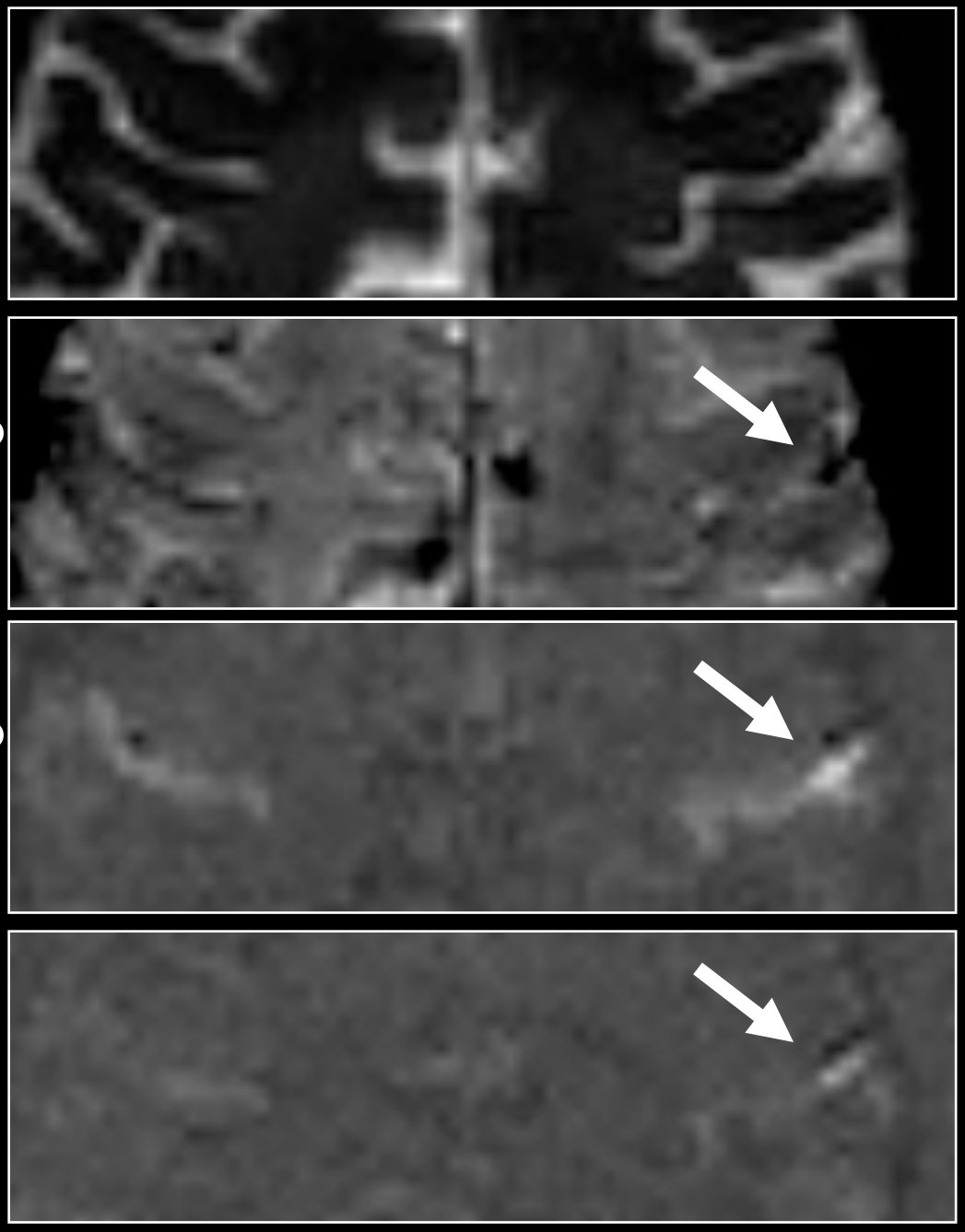
	64 x 64	96 x 96	128 x 128	192 x 192	256 x 256
%					
C/N					
	2.5 mm^2	1.67 mm^2	1.25 mm^2	0.83 mm^2	0.62 mm^2

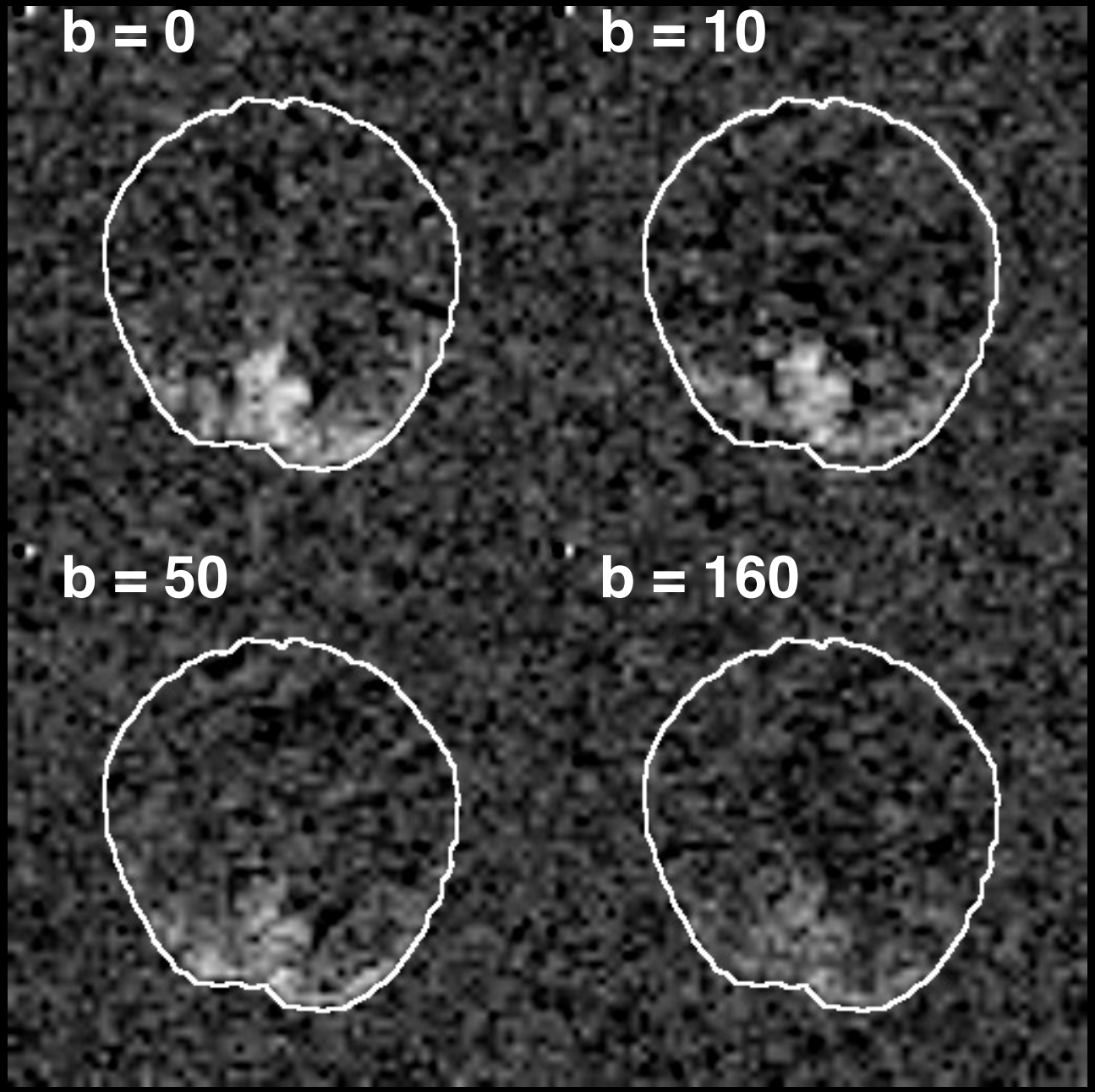

Fractional Signal Change
2.5 mm²
1.25 mm²
0.83 mm²
0.62 mm²
Number of Voxels
0
10
20
30
40
50
60
70
0
4
8
12
16
20
Fractional Signal Change
64 x 64 (2.5 mm)
96 x 96 (1.67 mm)
128 x 128 (1.25 mm)
192 x 192 (0.83 mm)

ΔR2* /ΔR2

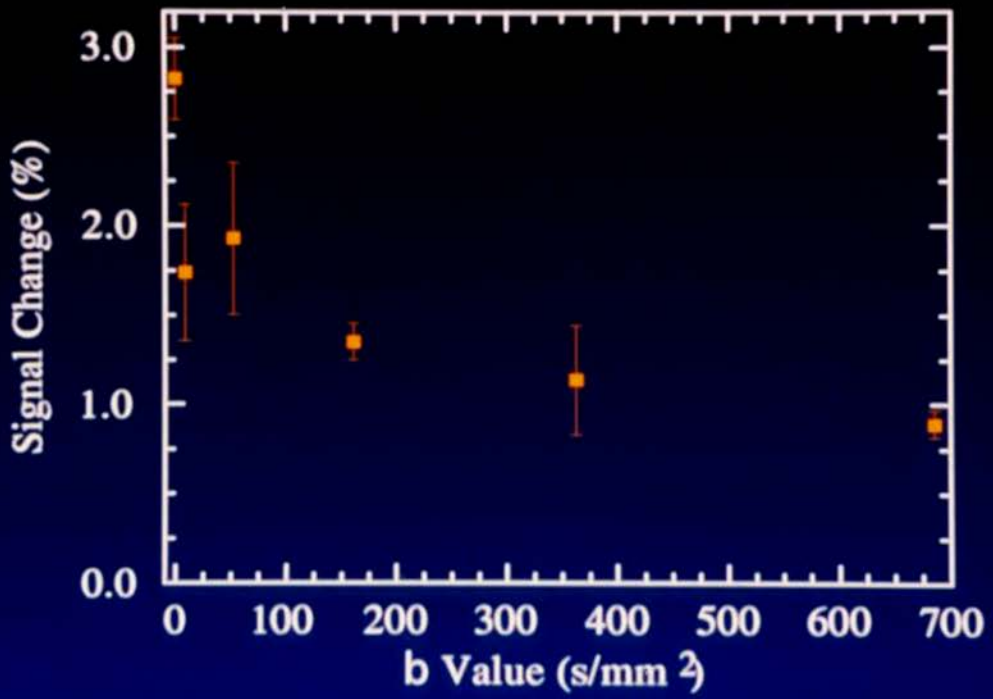


average ΔR2 / ΔR2 ≈ 3 to 4*


Spin-Echo
TE = 105 ms
TR = ∞
Gradient-Echo
TE = 50 ms
Gradient-Echo
functional
TE = 50 ms
Spin-Echo
functional
TE = 105 ms
3T

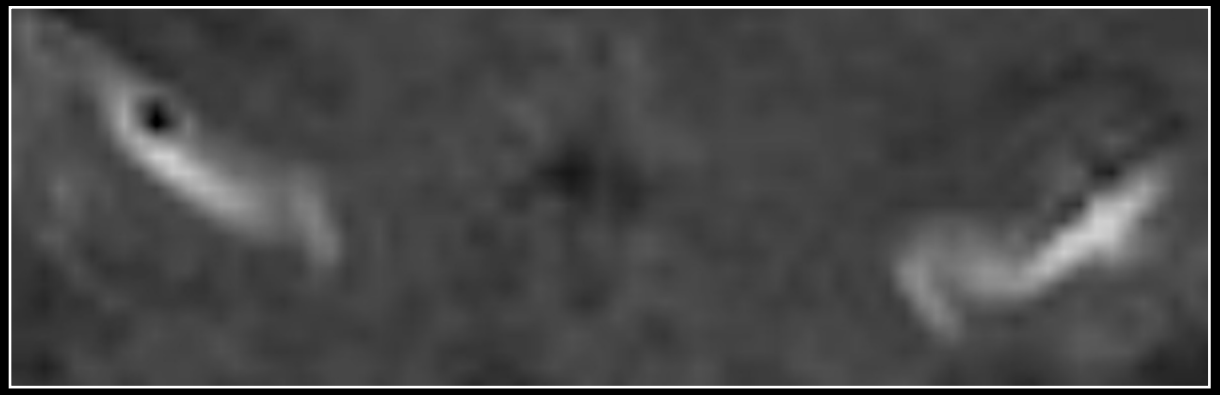

b = 0
b = 10
b = 50
b = 160

Summary of Diffusion-Weighted fMRI Data



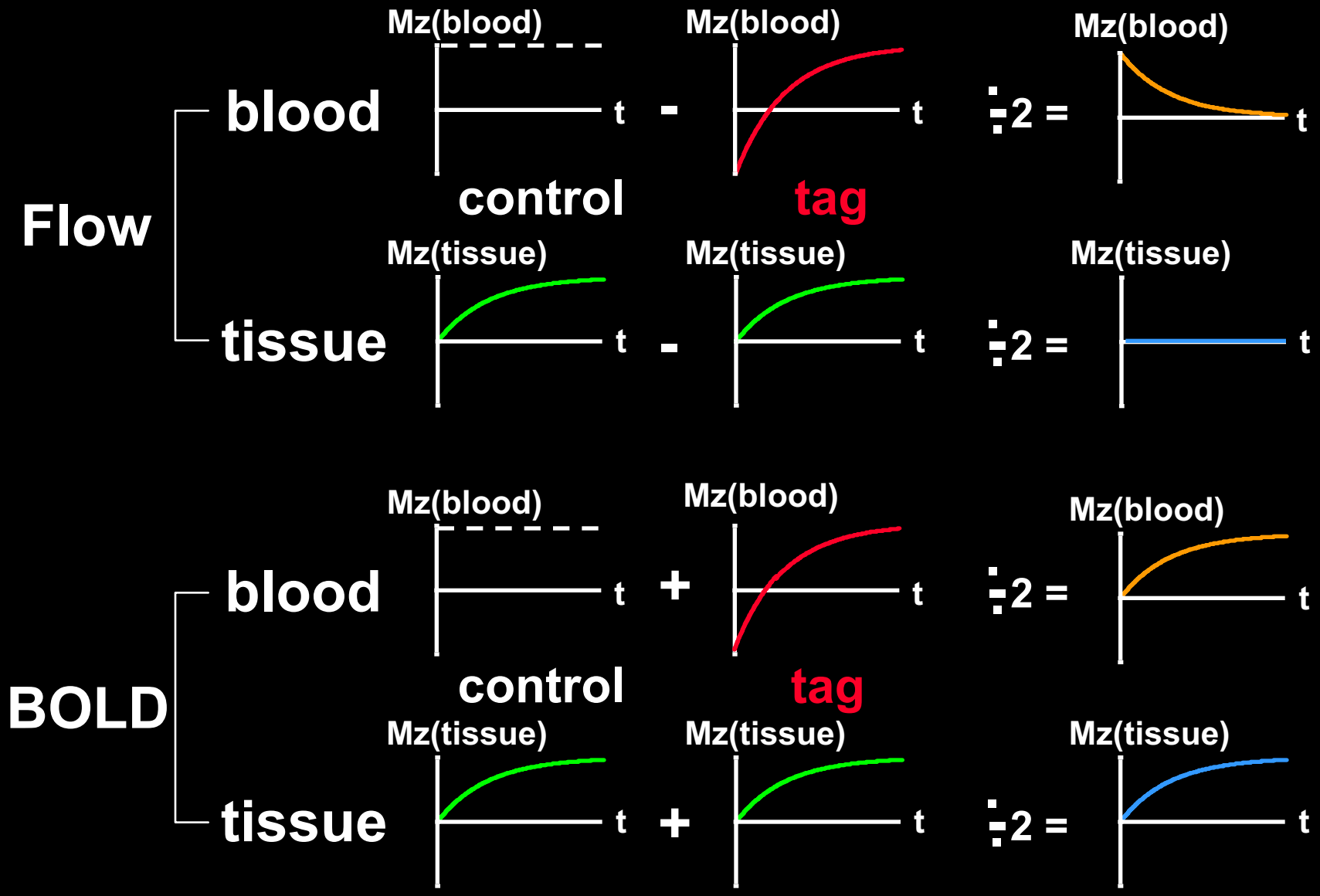
Anatomy

BOLD



Perfusion

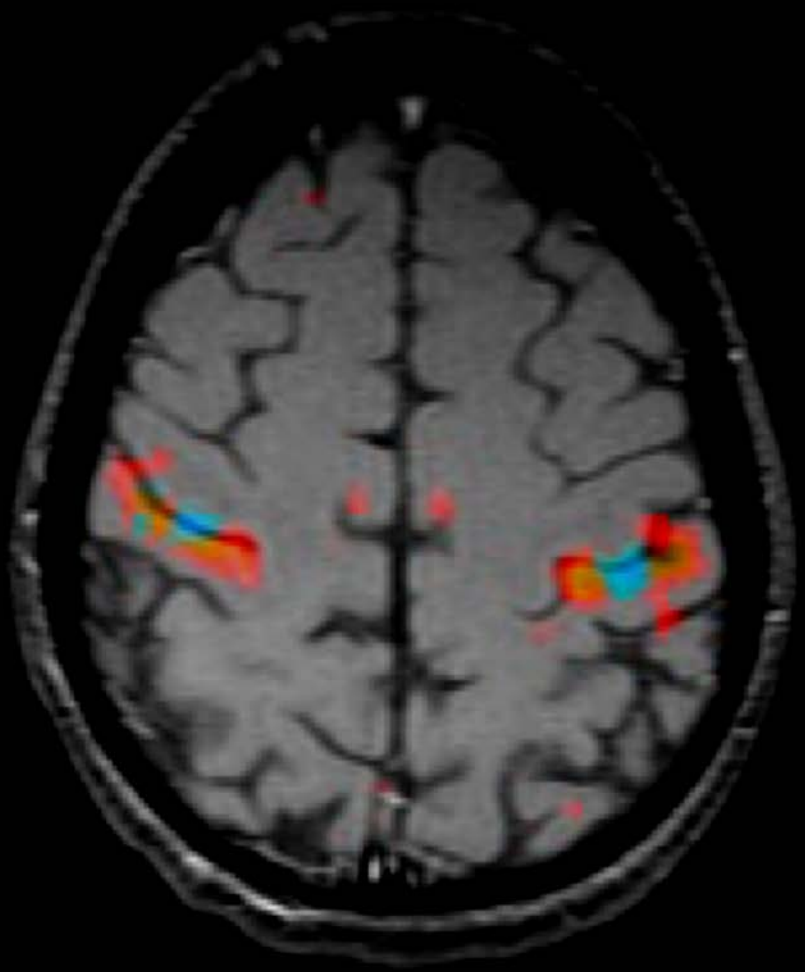
Simultaneous Flow and BOLD



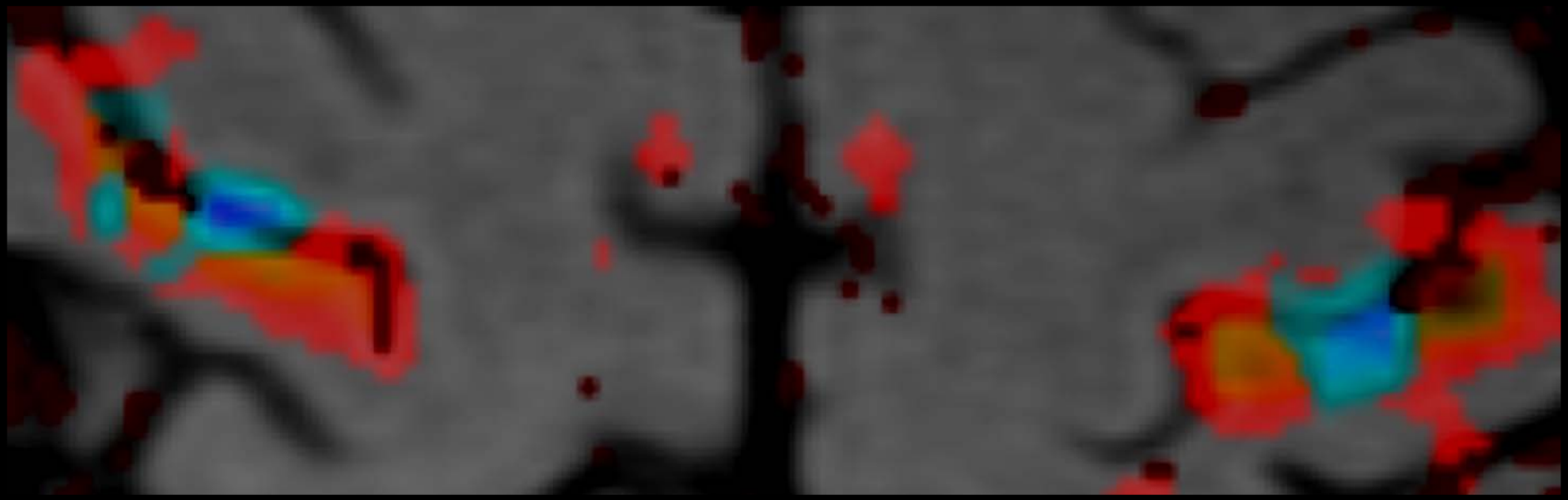
Simultaneous BOLD and Perfusion

perfusion

BOLD



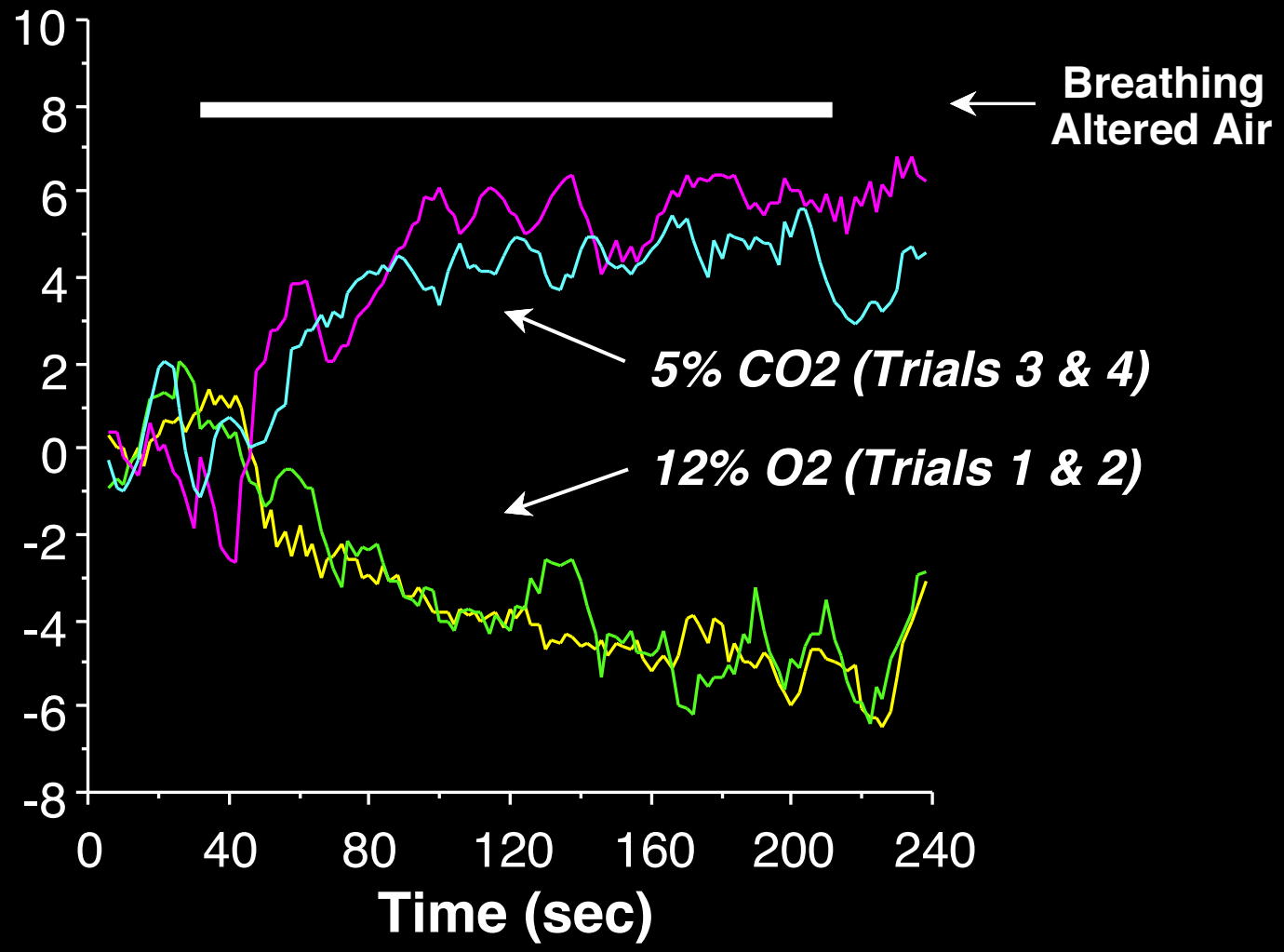
Angiogram
Perfusion
BOLD



T1 - weighted

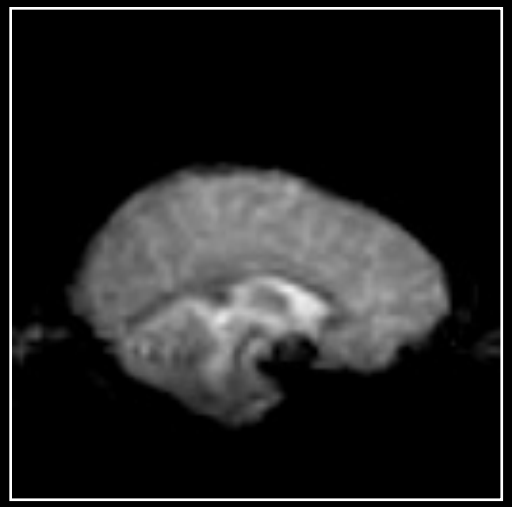
T2* weighted

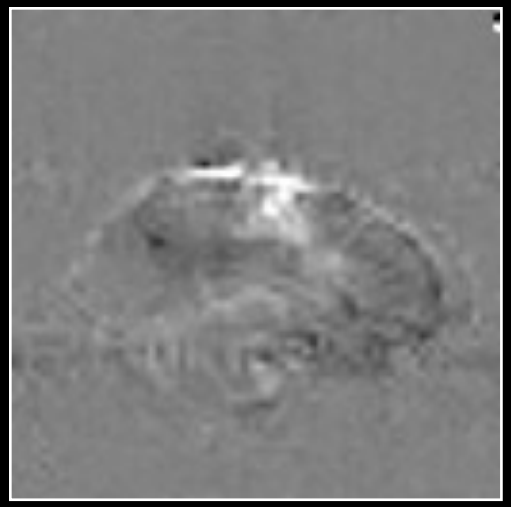
T1 and T2* weighted


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)

,

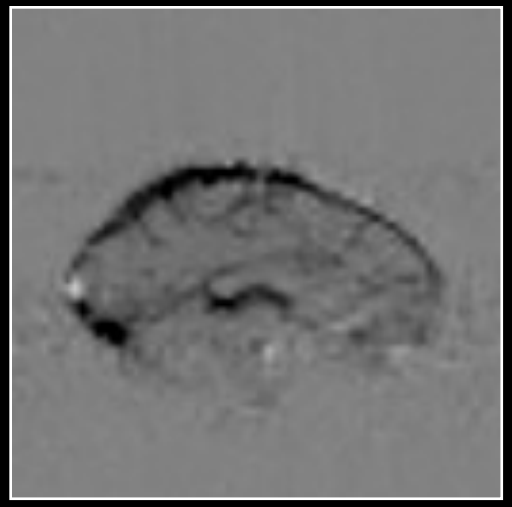
Anatomical

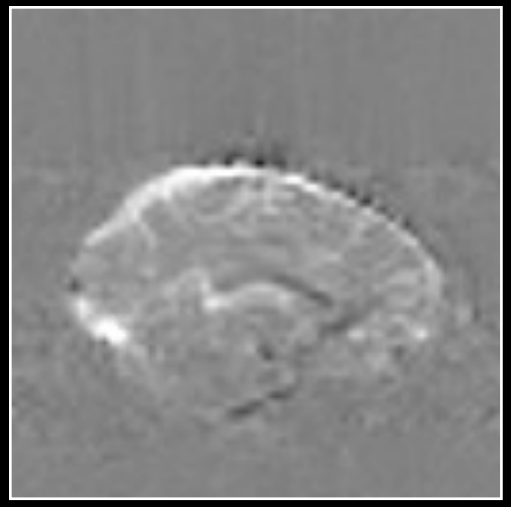




Finger Movement

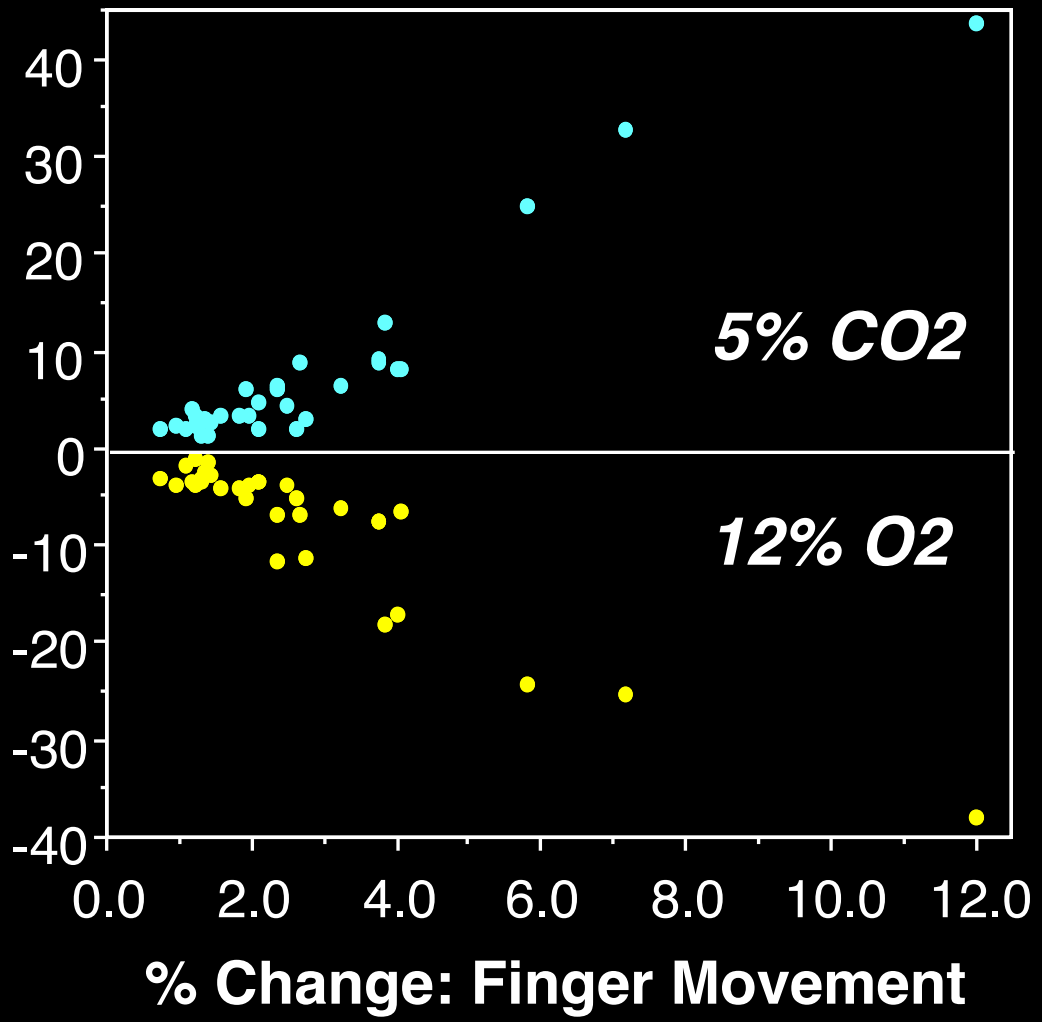
12% O2

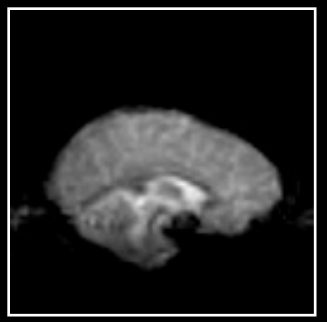




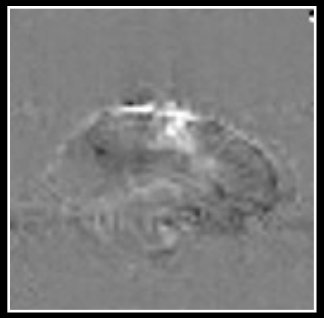
5% CO2

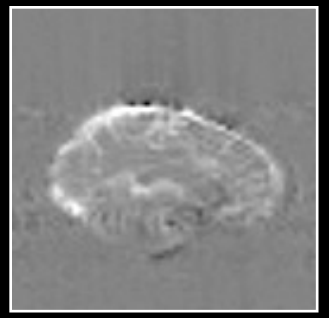
Resting State Blood Volume Weighting

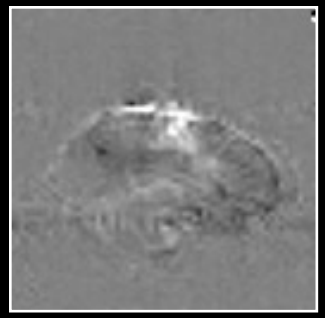


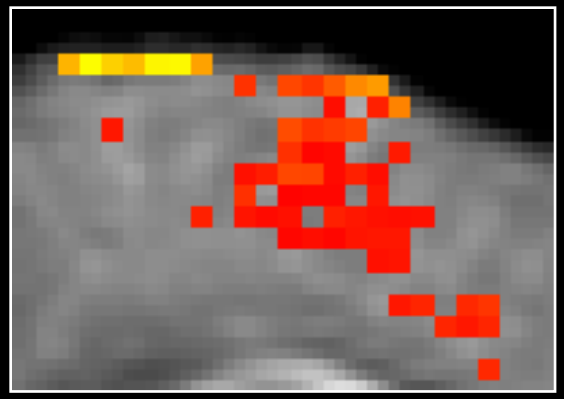


Capillaries
Veins









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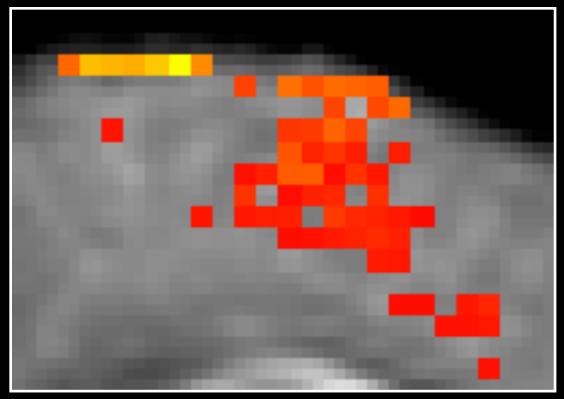

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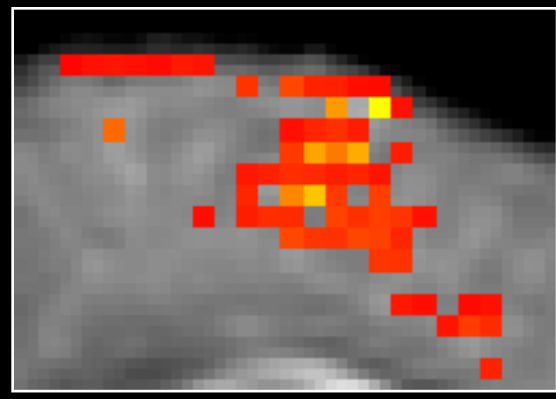
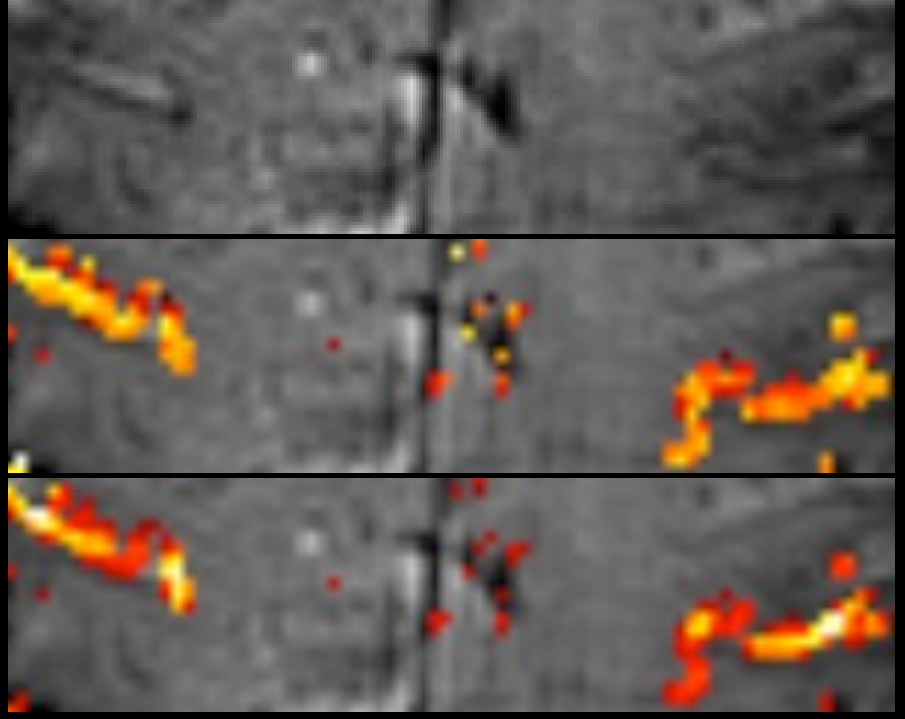


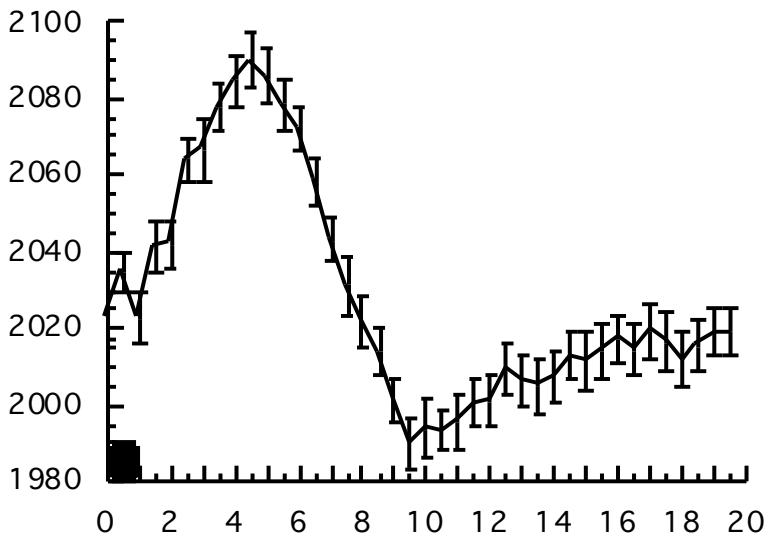
Latency

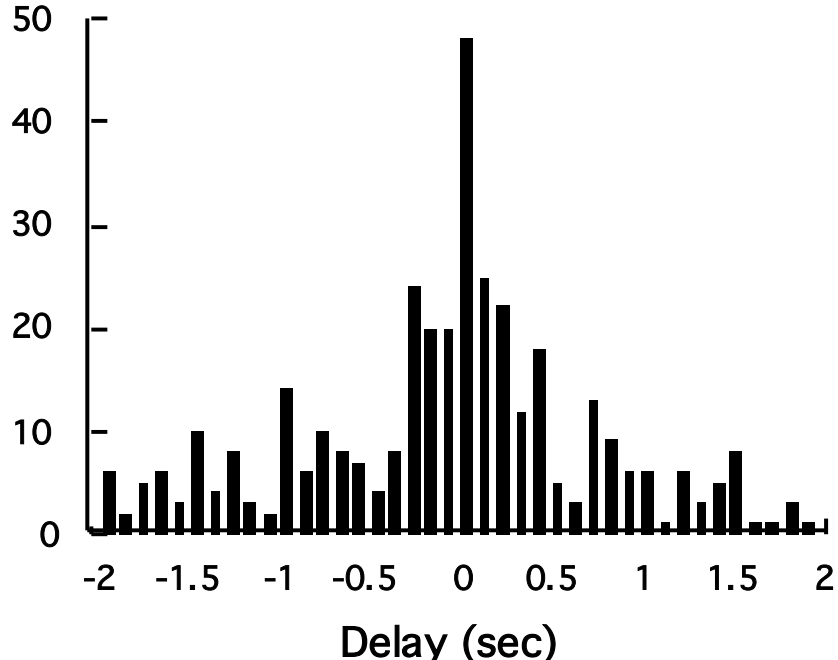
Magnitude



+ 2 sec

- 2 sec





1991-1992

1992-1999

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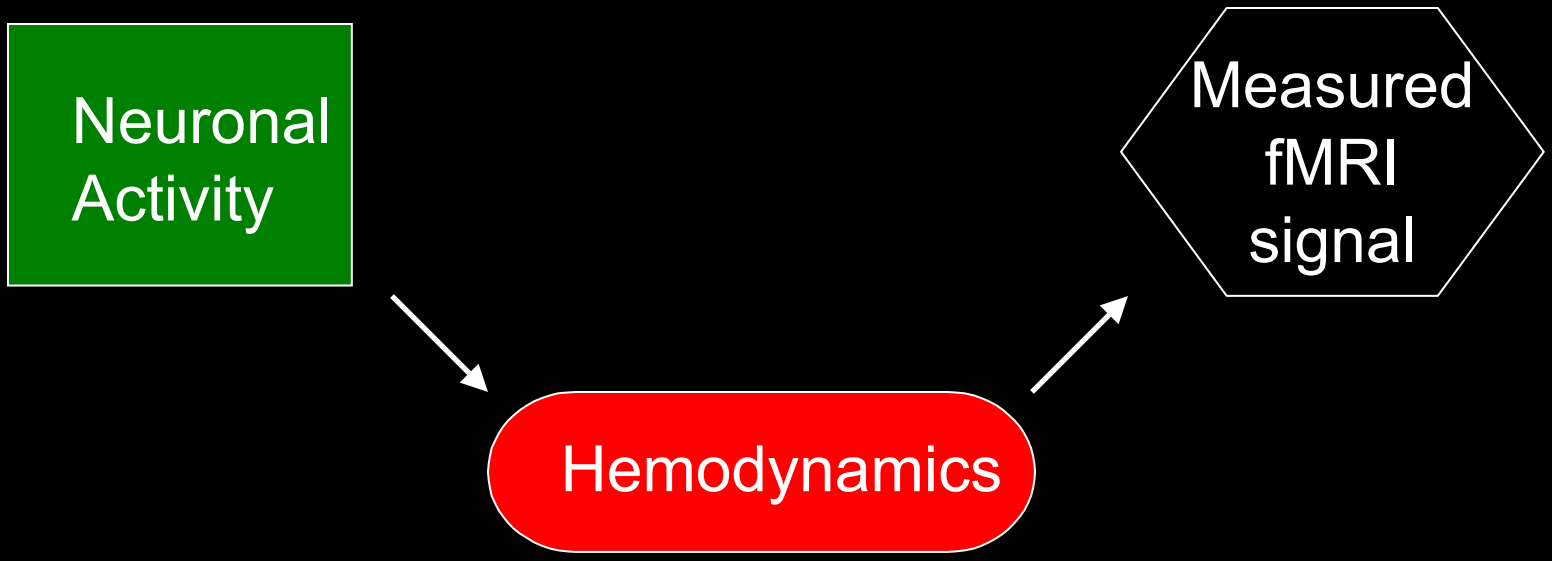


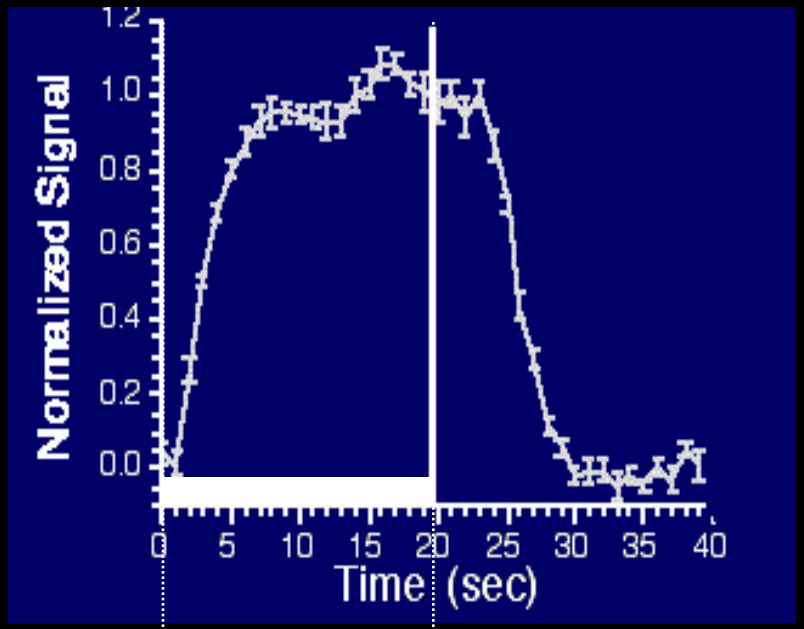
Δ Blood Flow (CBF)

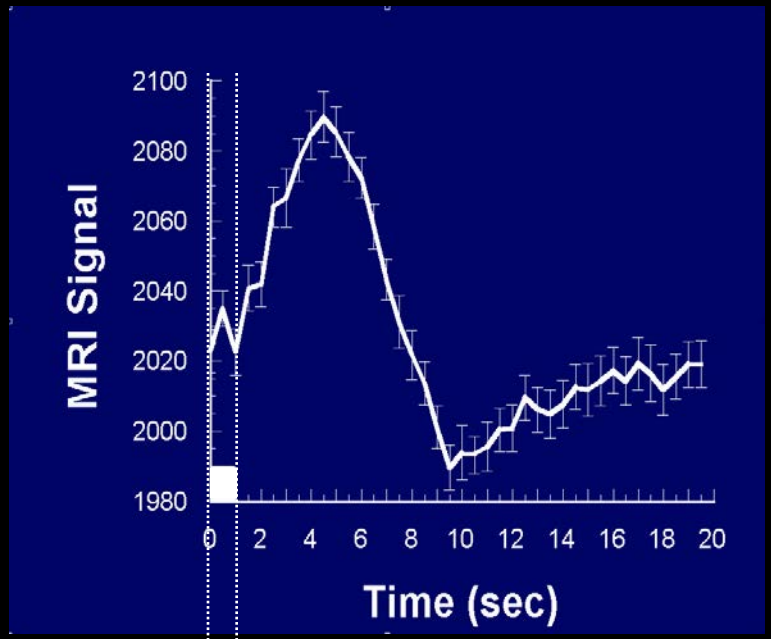
Δ Blood Volume (CBV)

Δ Oxygen Consumption (CMRO2)

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

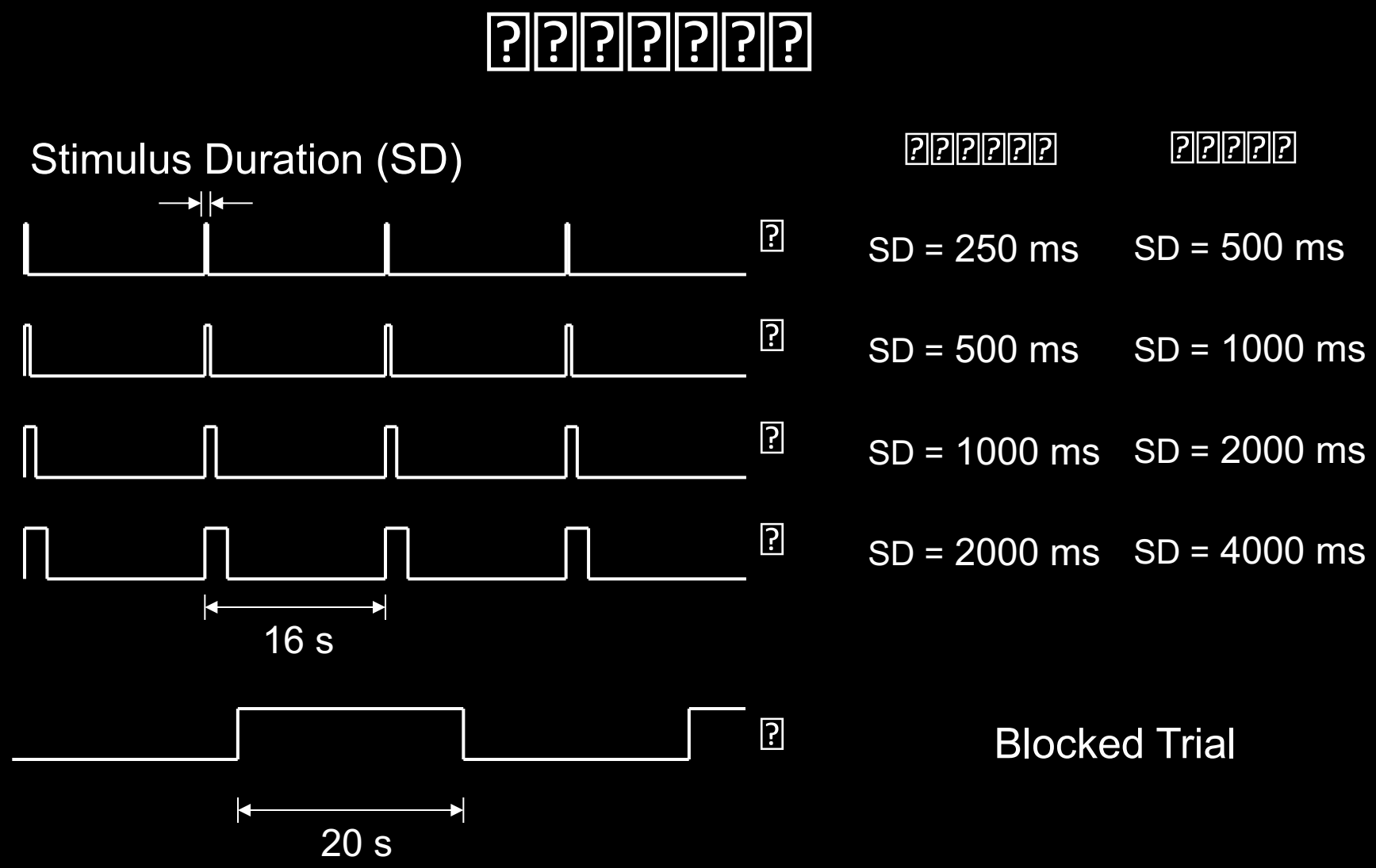
Blood Oxygenation Level Dependent (BOLD) signal changes



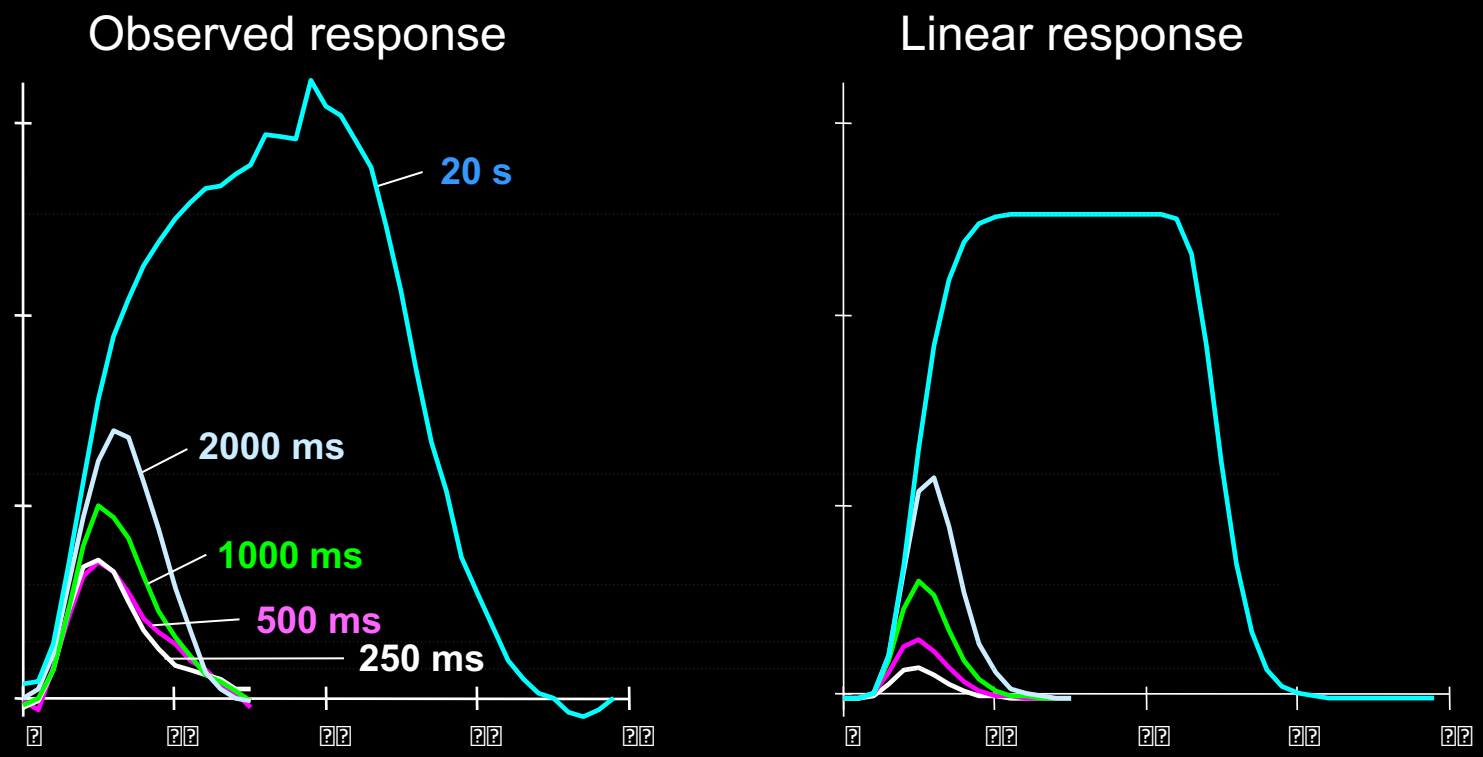


task

task


Stimulus Duration (SD)
16 s
20 s
SD = 250 ms
SD = 500 ms
SD = 500 ms
SD = 1000 ms
SD = 1000 ms
SD = 2000 ms
SD = 2000 ms
SD = 4000 ms
Blocked Trial

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



Short duration stimuli produce larger responses than expected

???????

Tasks

Visual Stimulation

Finger tapping

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

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Imaging Parameters

3 Tesla
EPI
64x64
24 cm FOV
5 mm slice thickness
8 slices

TR: 1000 ms
TE: 30 ms

320 time points

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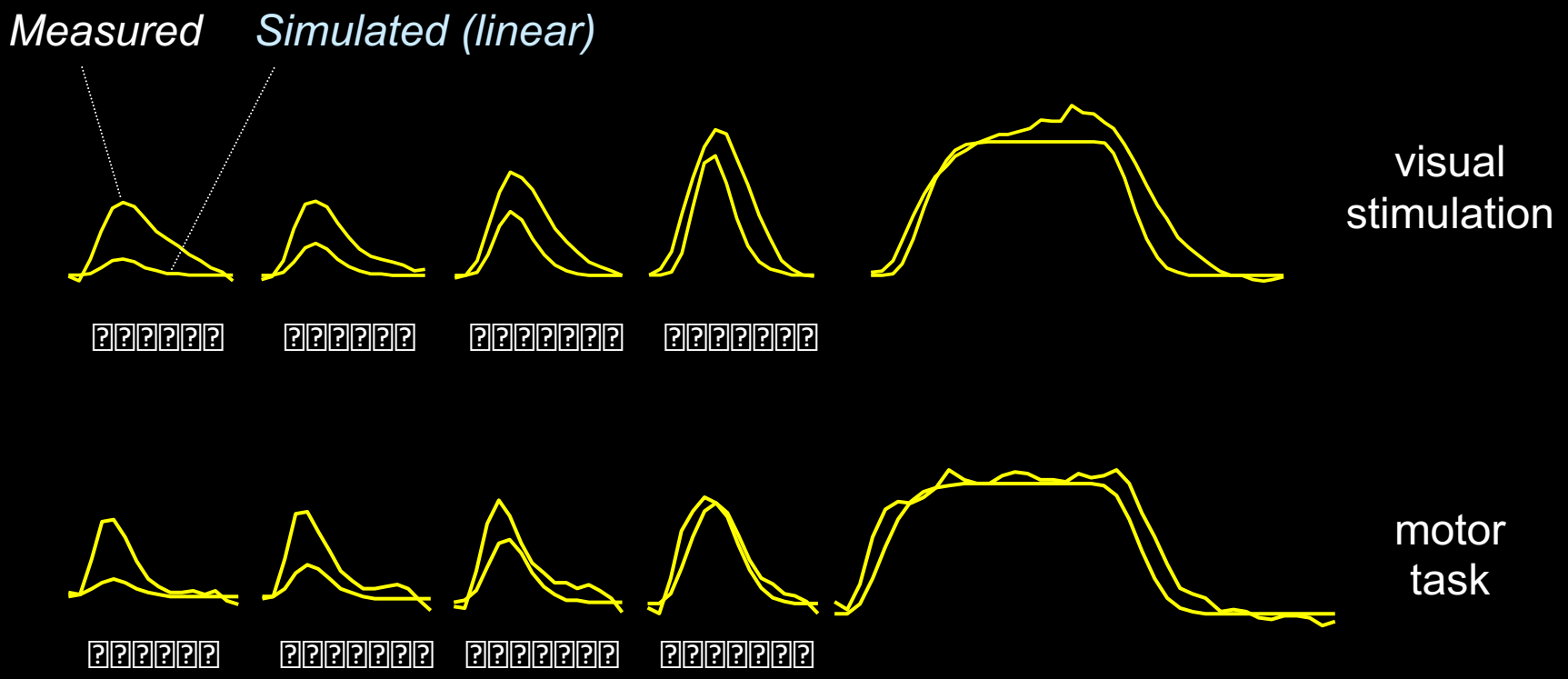
Measured
Simulated (linear)
visual stimulation
motor task

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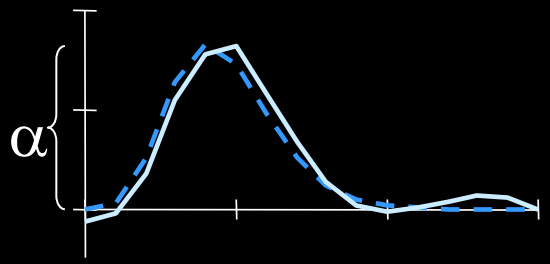
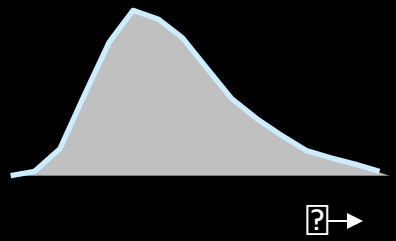
- Amplitude of Response



Fit ideal (linear) to response

- Area under response / Stimulus Duration



Output Area / Input Area

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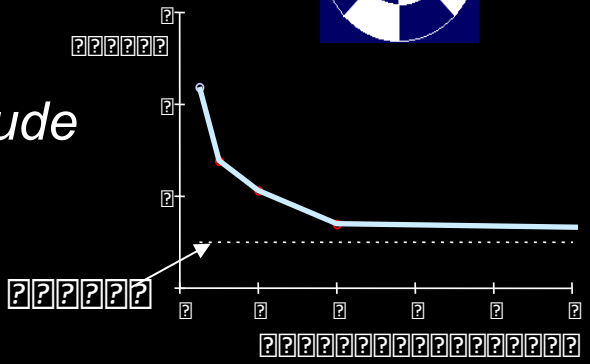
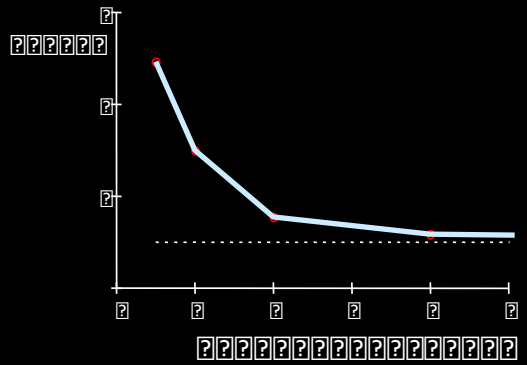
Visual

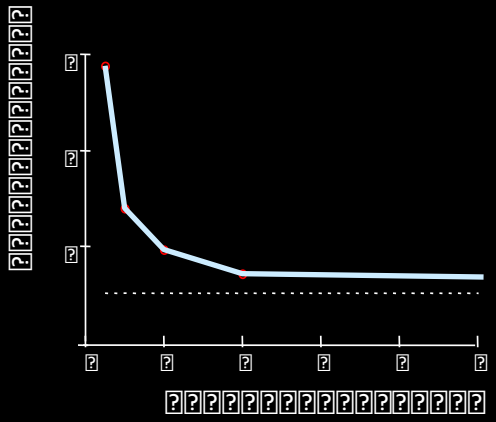
Motor

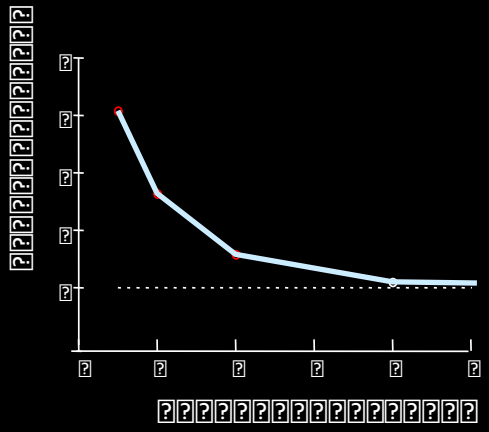
Magnitude





Area





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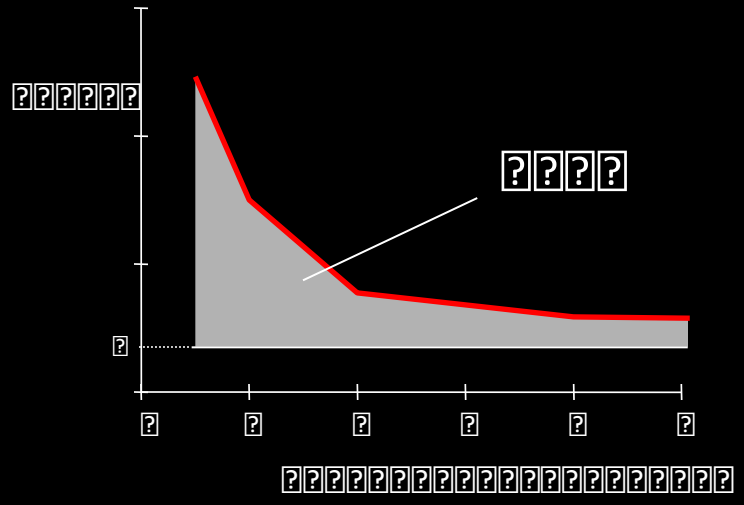
- Area under nonlinearity curve



- Slope of nonlinearity curve

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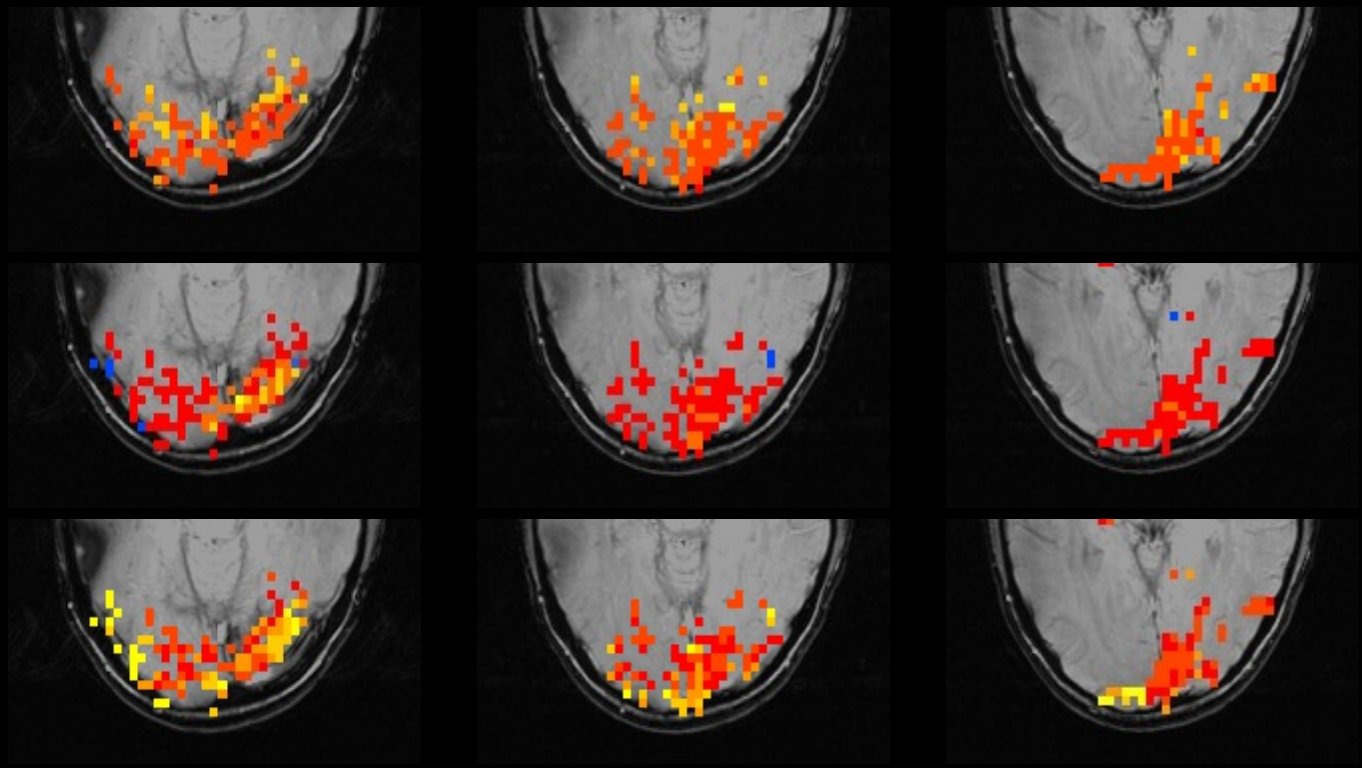
Nonlinearity

Magnitude

Latency



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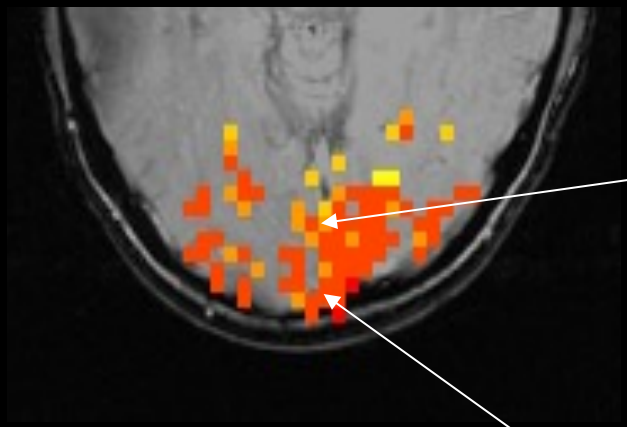
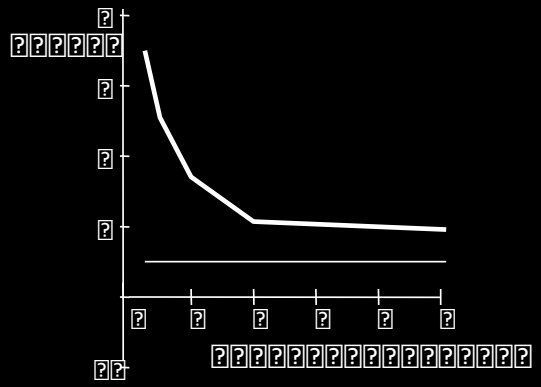
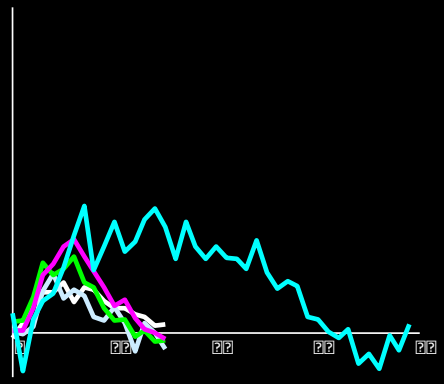
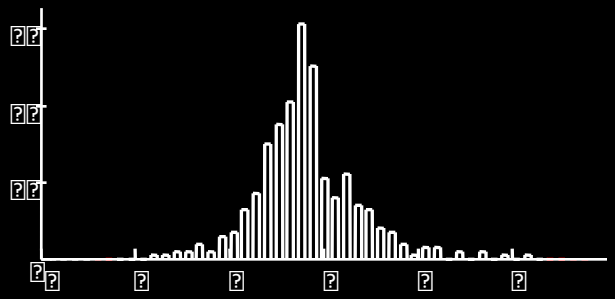
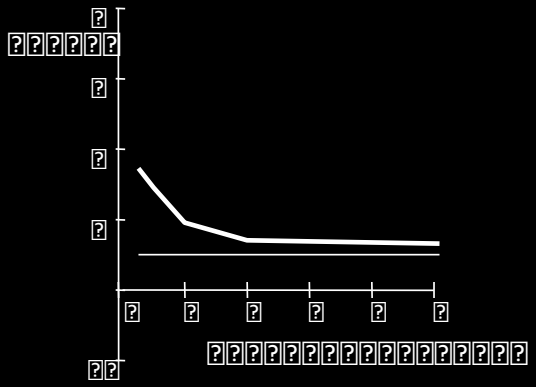


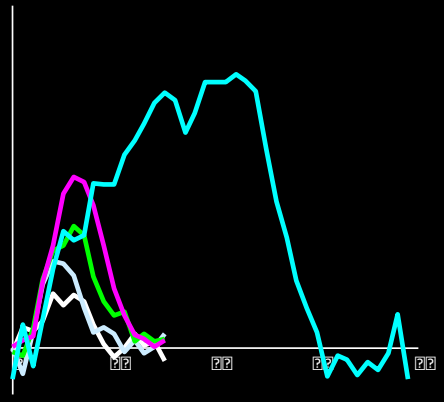






nonlinearity





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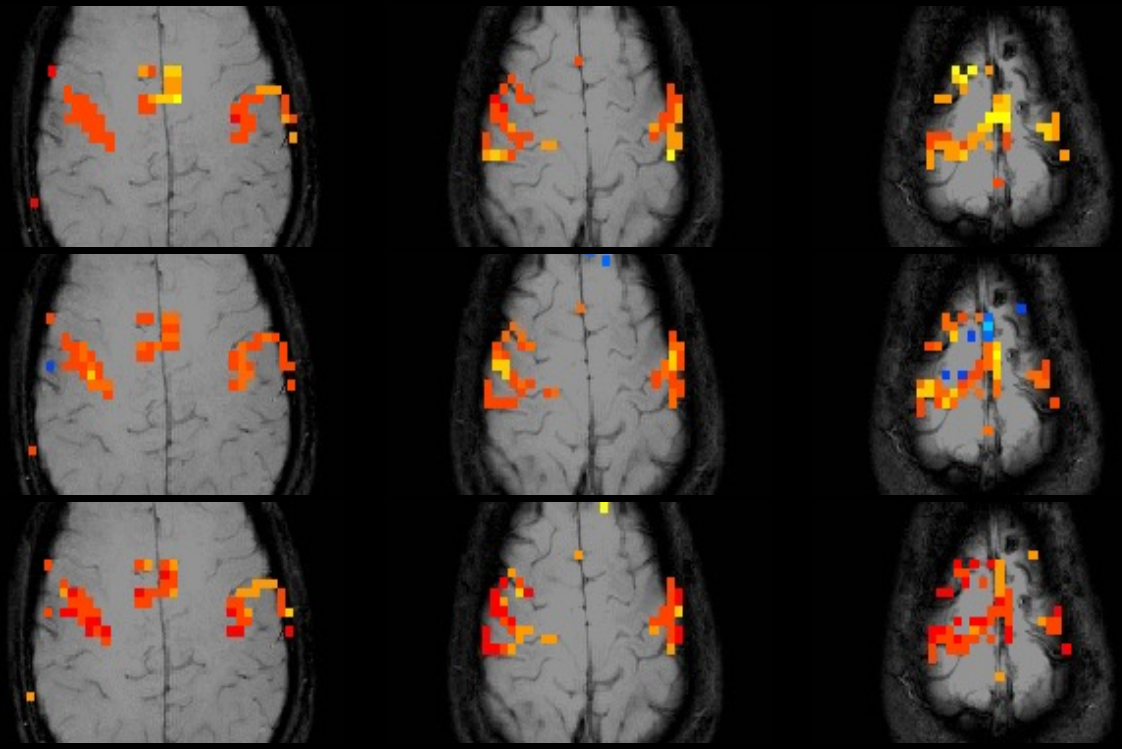
Nonlinearity

Magnitude

Latency



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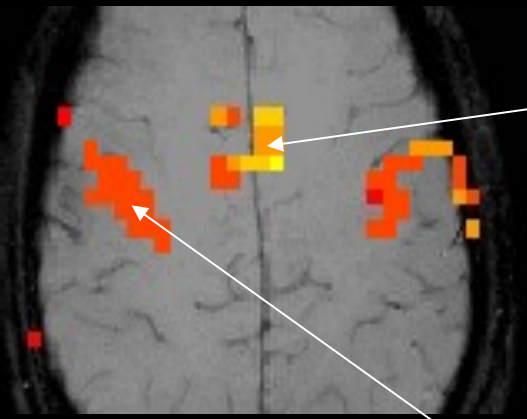
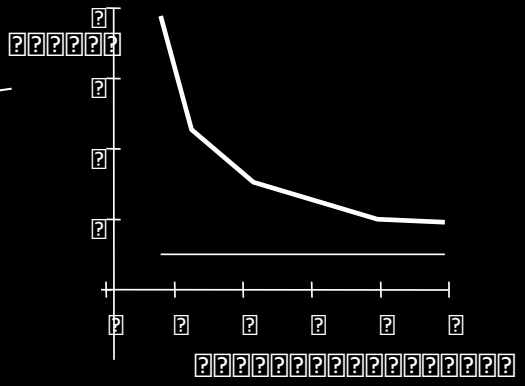
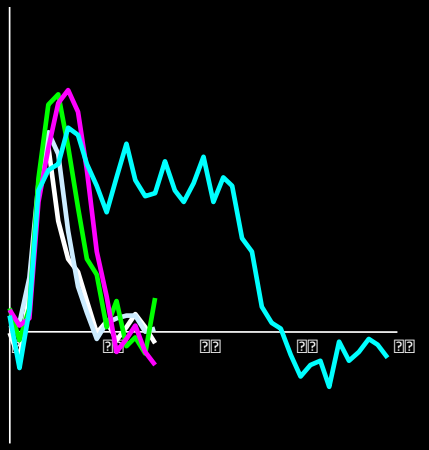
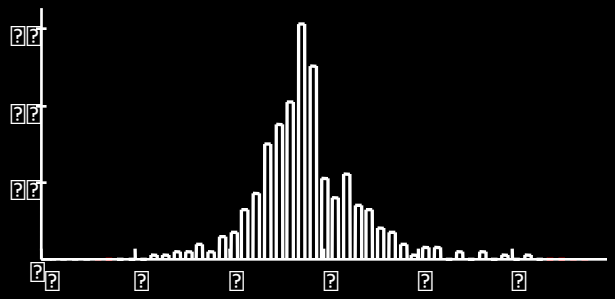
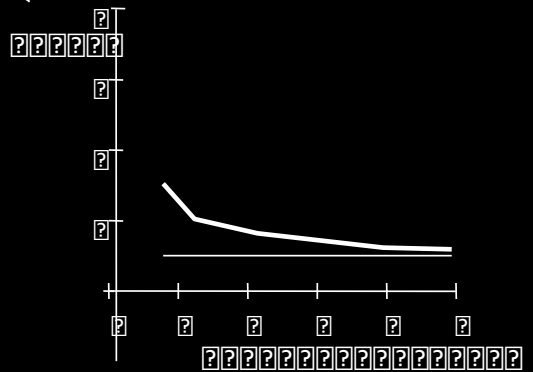


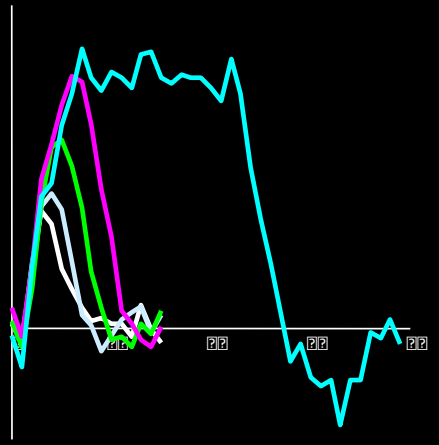


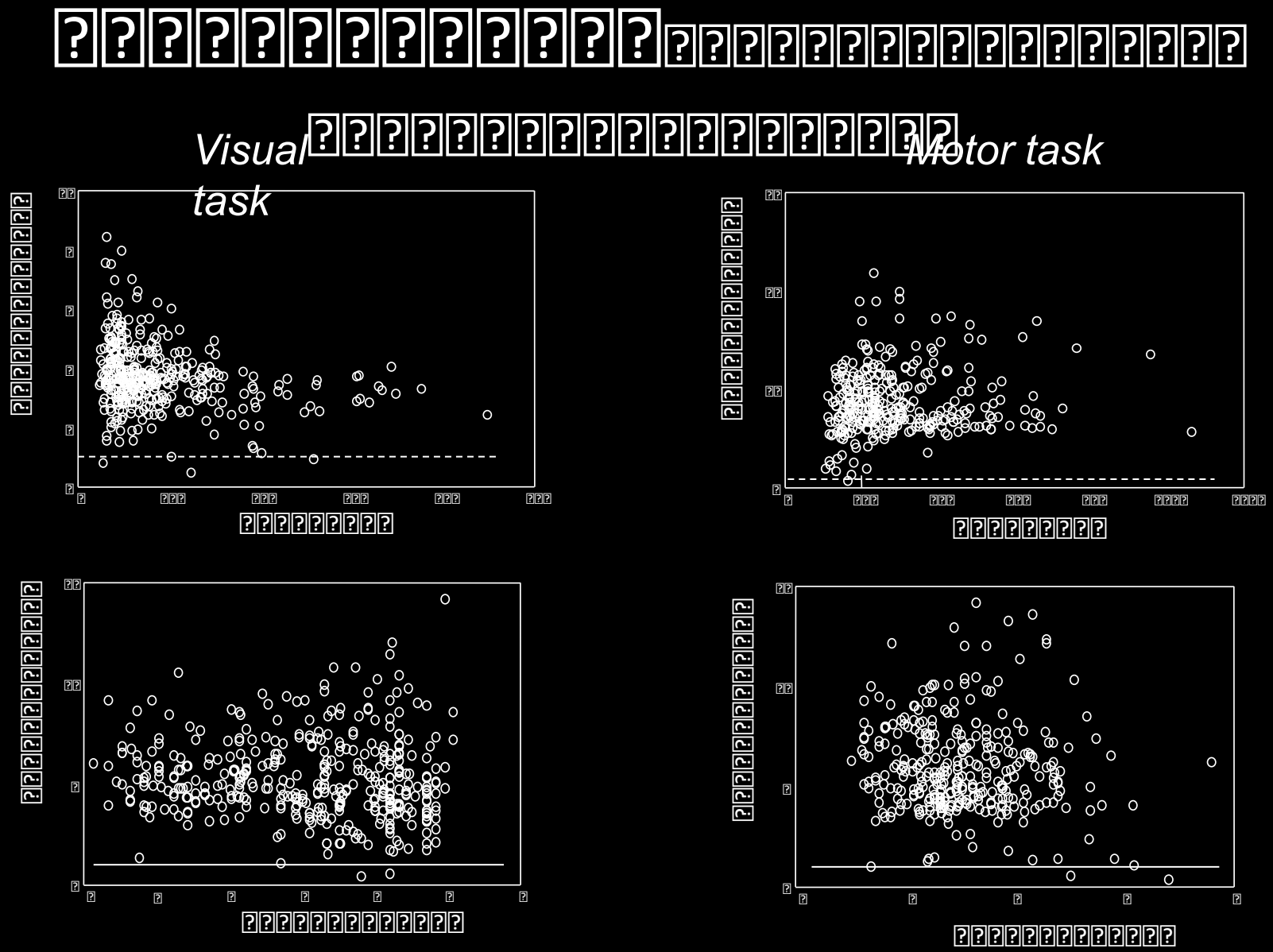




nonlinearity






Visual task
Motor task

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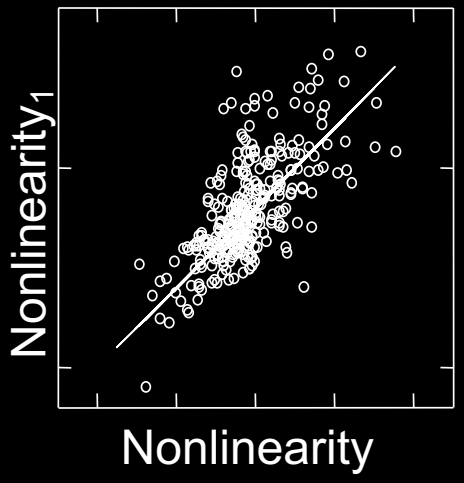
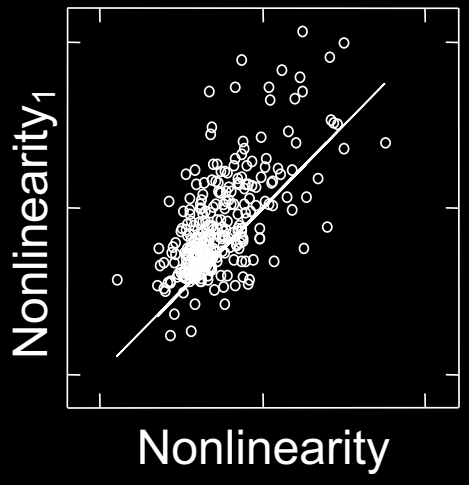
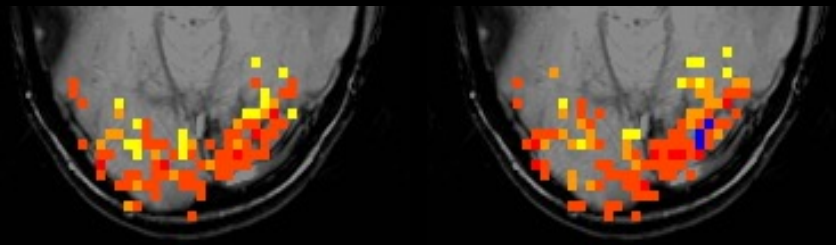
Visual task

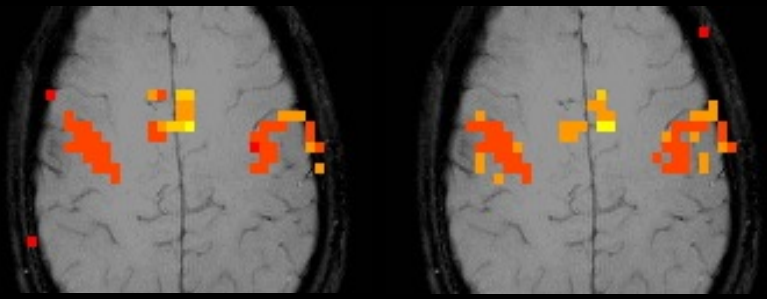


Motor task





Experiment 1 Experiment 2



Experiment 1 Experiment 2

Conclusions

- Responses to short duration stimuli are larger than predicted from a linear system
- Spatial variation in this nonlinear relationship is seen
- The variation in nonlinearity is not significantly correlated with magnitude or latency

Implications

- Nonlinearity is primarily neuronal in origin

or

- Magnitude and latency do not accurately reflect underlying vasculature