

# A closer look at fMRI

dynamics, fluctuations, and patterns

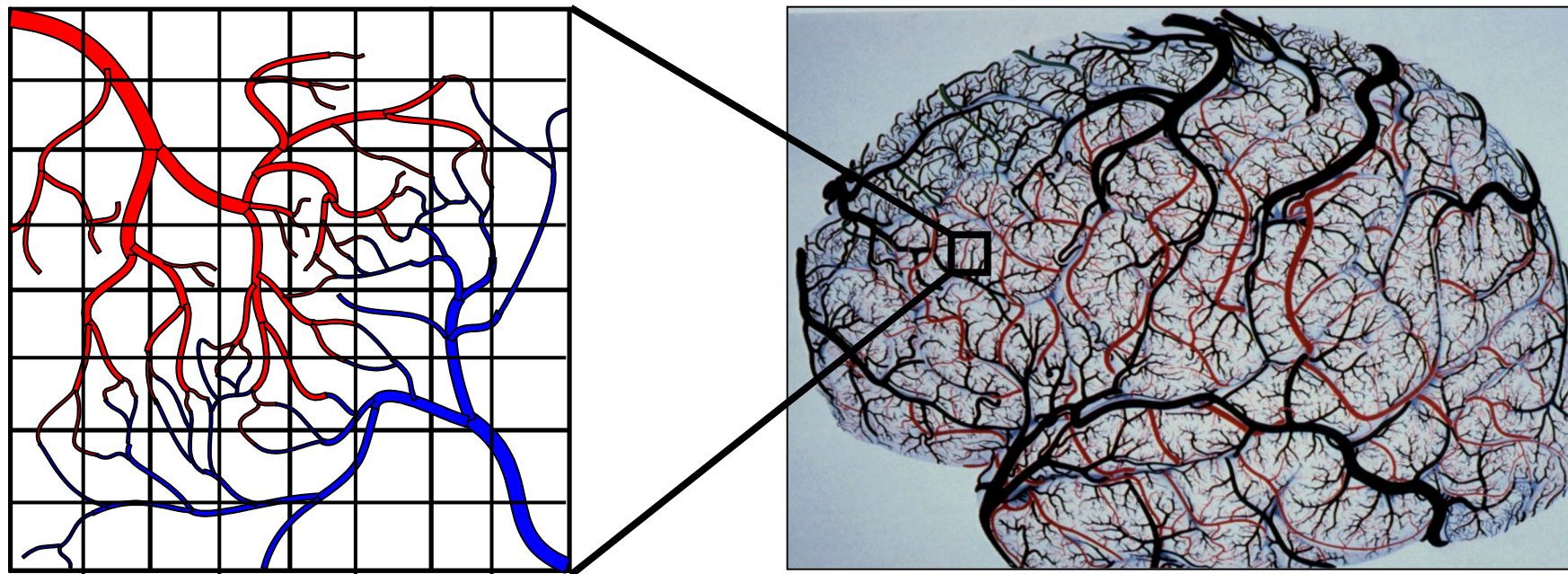
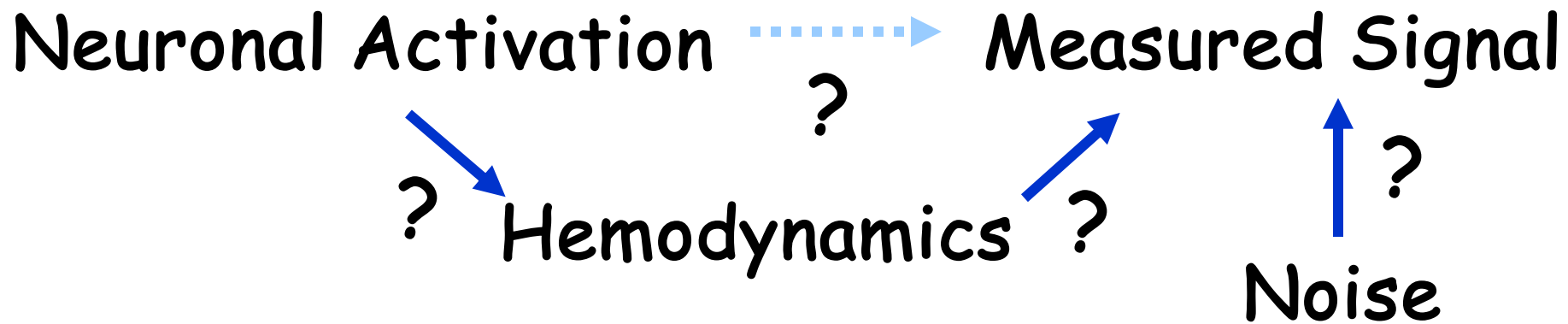
Peter A. Bandettini, Ph.D.

Section on Functional Imaging Methods  
Laboratory of Brain and Cognition, NIMH  
&  
Functional MRI Facility, NIMH





1991



1. Dynamics

2. Fluctuations

3. Experimental Design

4. Pattern Information

5. Neuronal Current MRI

# 1. Dynamics

## Motivation:

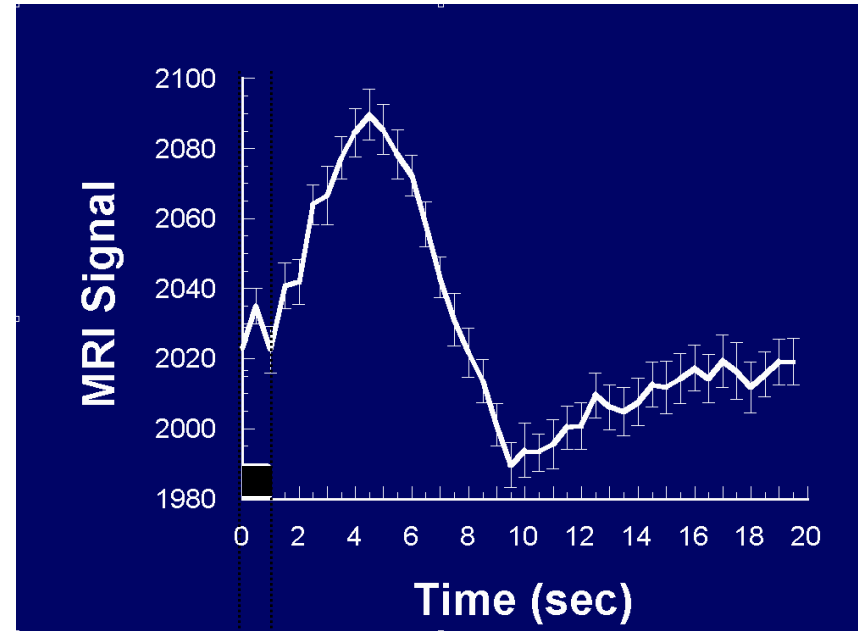
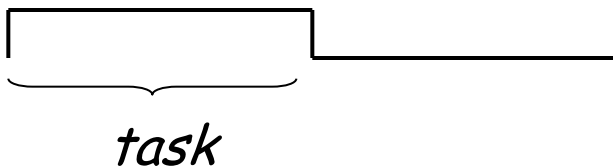
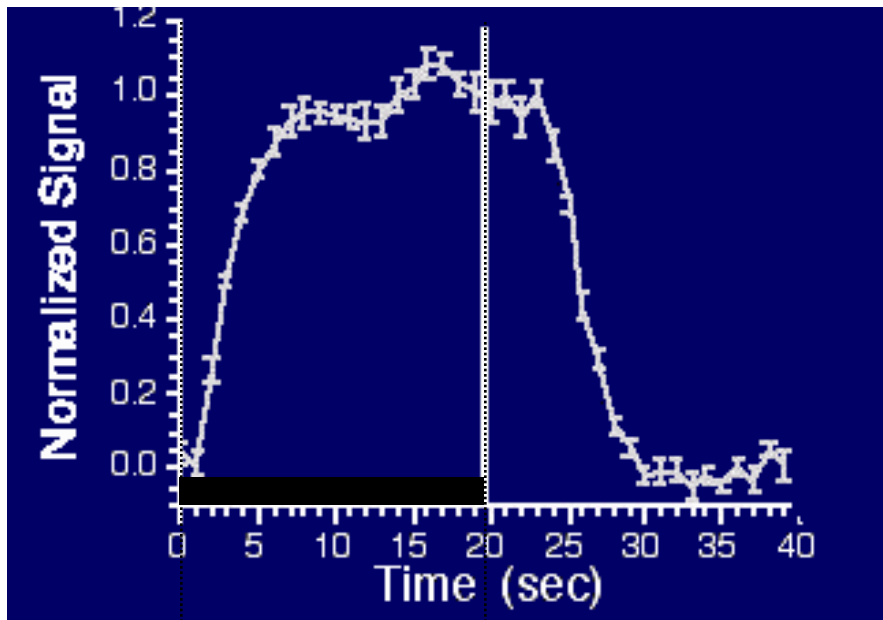
- To understand the neuronal and non-neuronal influences on the fMRI signal.

## Studies:

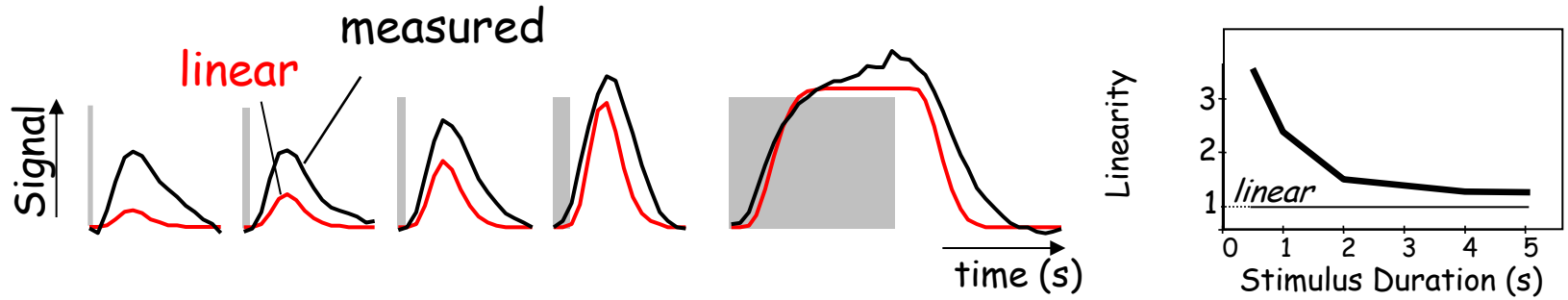
- Modulate timing: "on" duration, "off" duration, and duty cycle of visual cortex activation.
- Neuronal and Hemodynamic Modeling.
- MEG and fMRI Comparison.

# The BOLD Signal

Blood Oxygenation Level Dependent (BOLD) signal changes

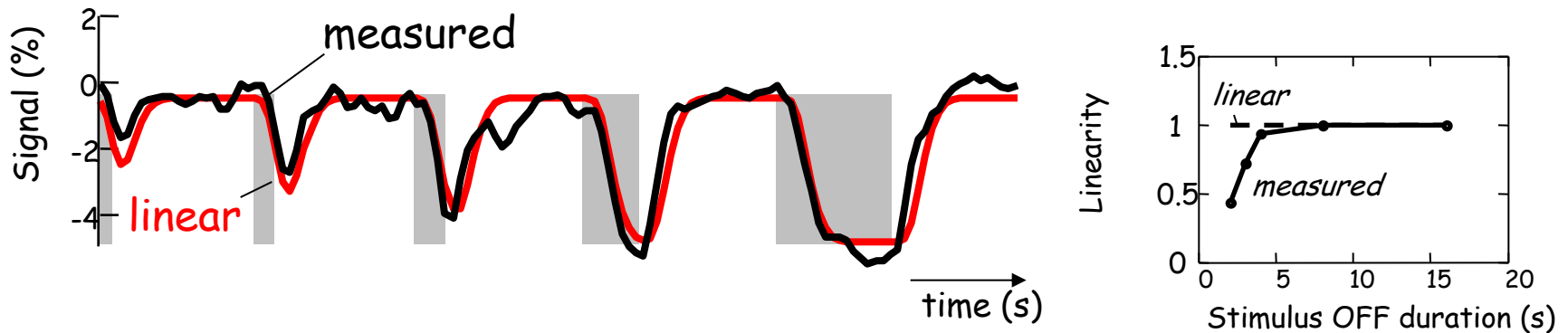


Brief "on" periods produce **larger** increases than expected.



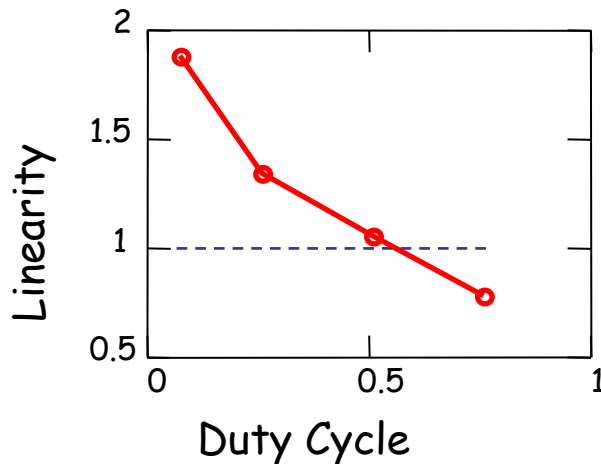
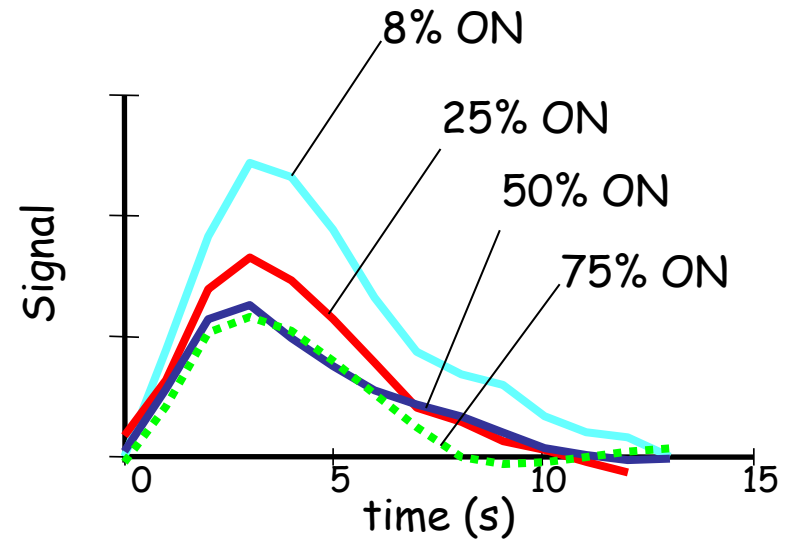
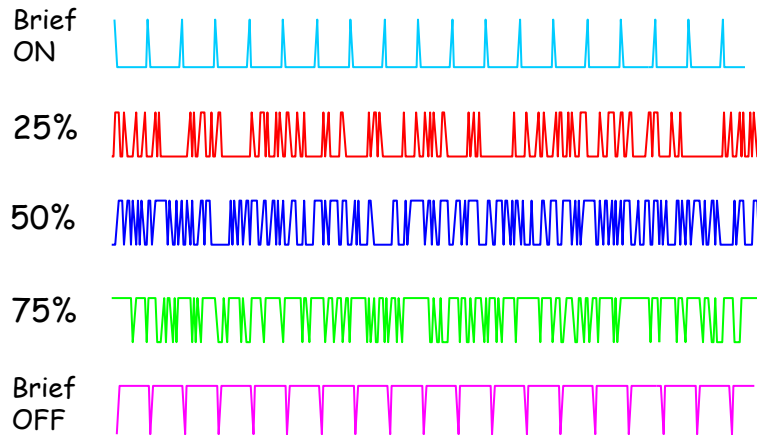
R. M. Birn, Z. Saad, P. A. Bandettini, *NeuroImage*, 14: 817-826, (2001)

Brief "off" periods produce **smaller** decreases than expected.



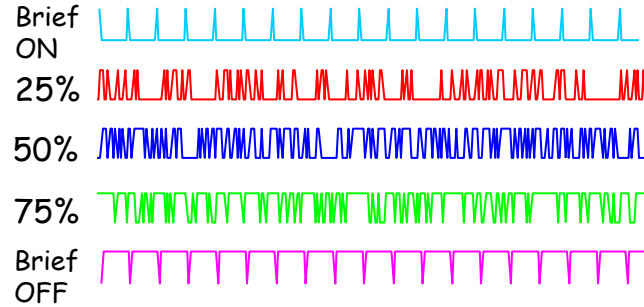
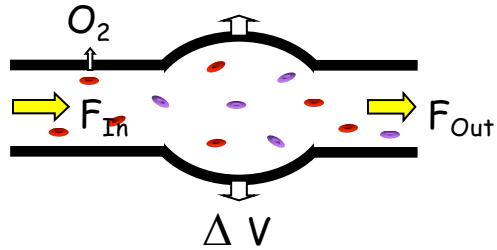
R.M. Birn, P. A. Bandettini, *NeuroImage*, 27, 70-82 (2005)

# Varying the Duty Cycle



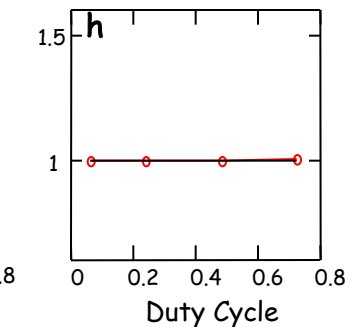
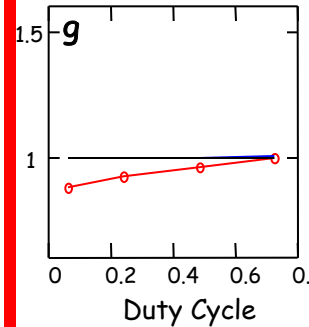
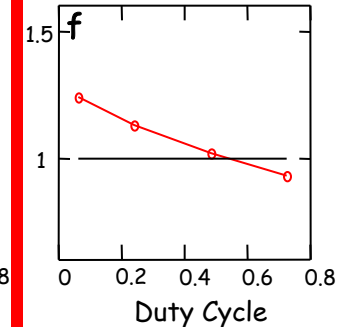
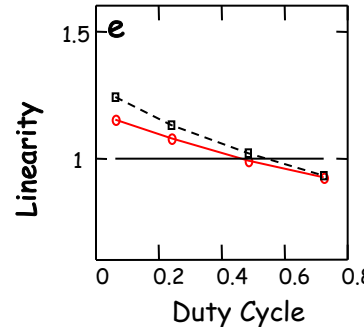
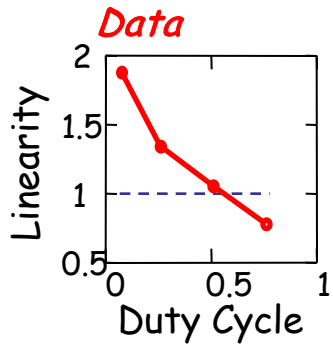
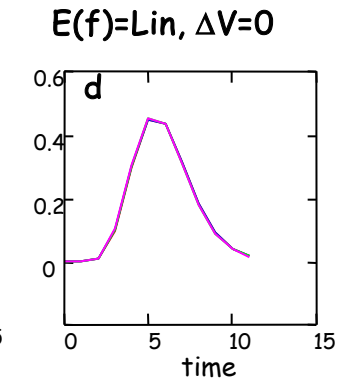
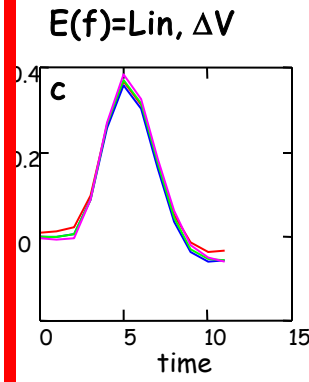
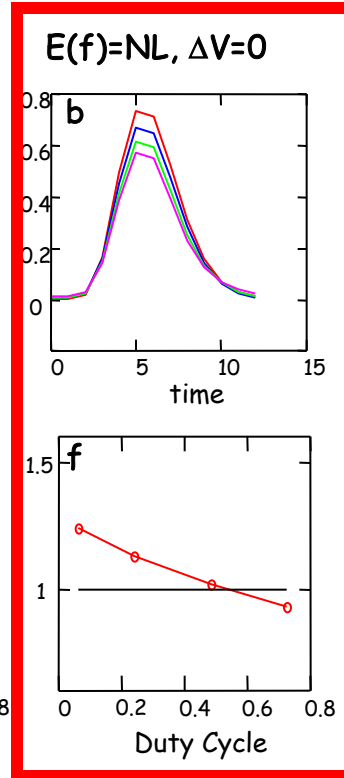
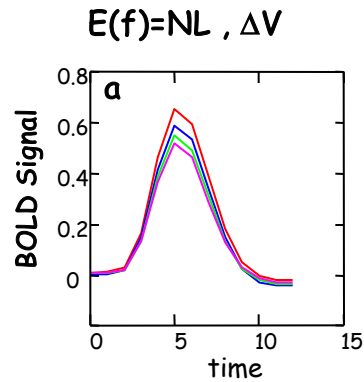


# Simulation of Hemodynamic Mechanisms (Balloon model)

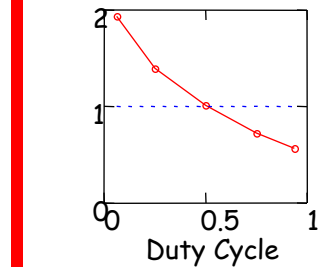
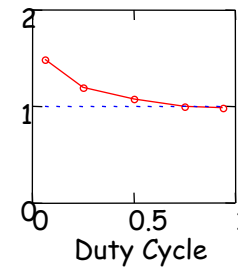
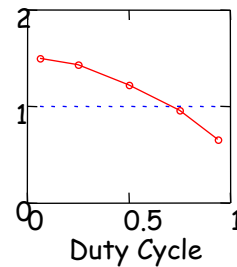
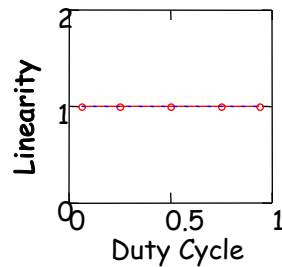
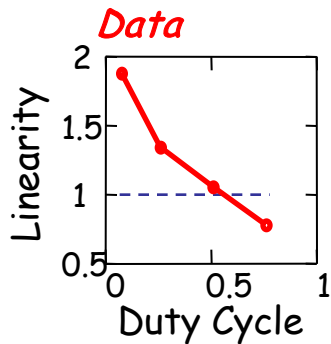
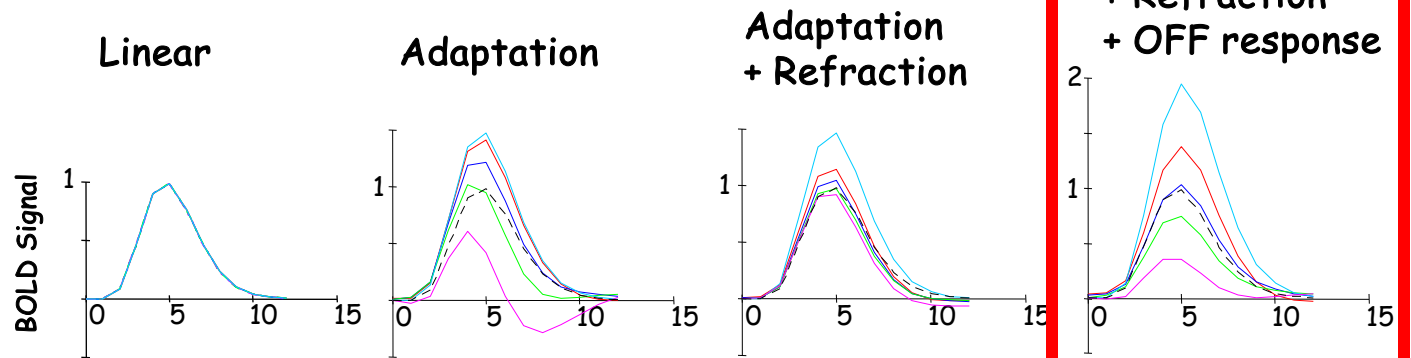
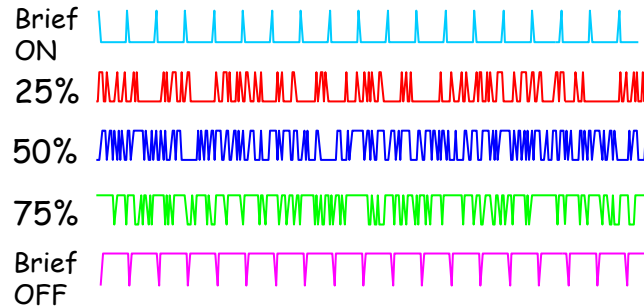
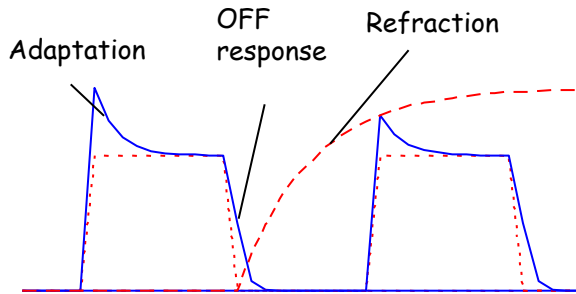


$E(f)$  = oxygen extraction fraction

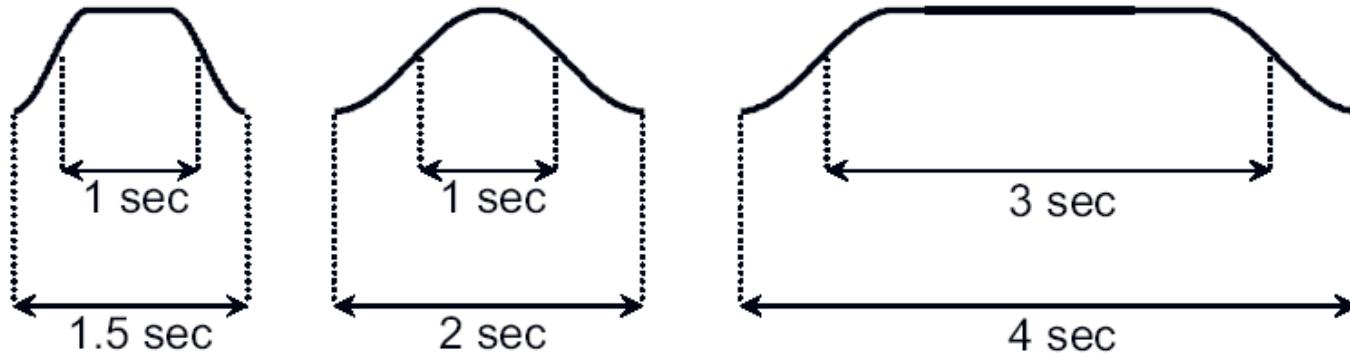
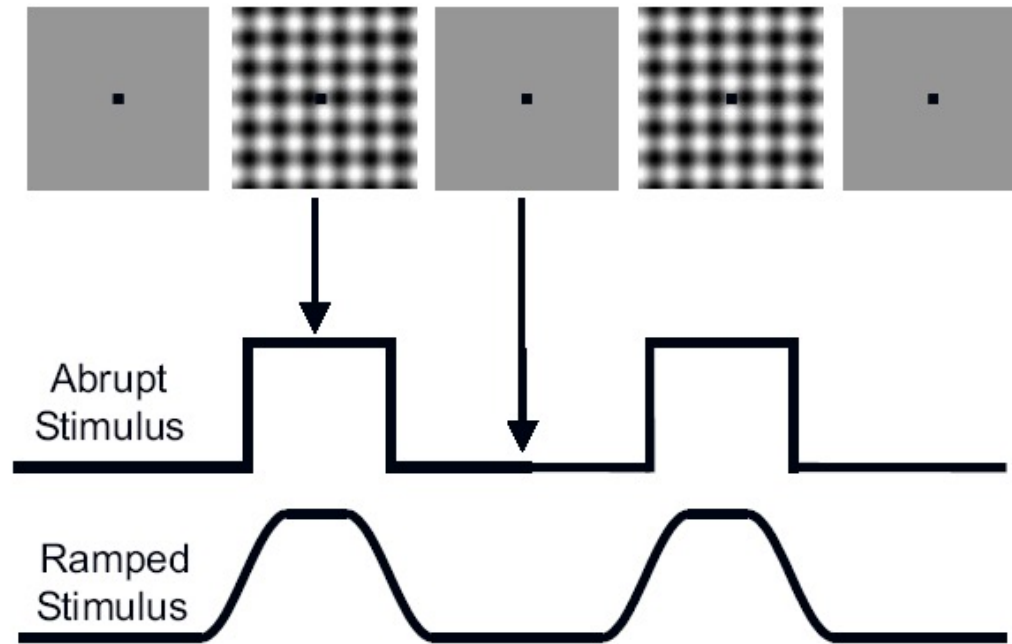
$V$  = blood volume



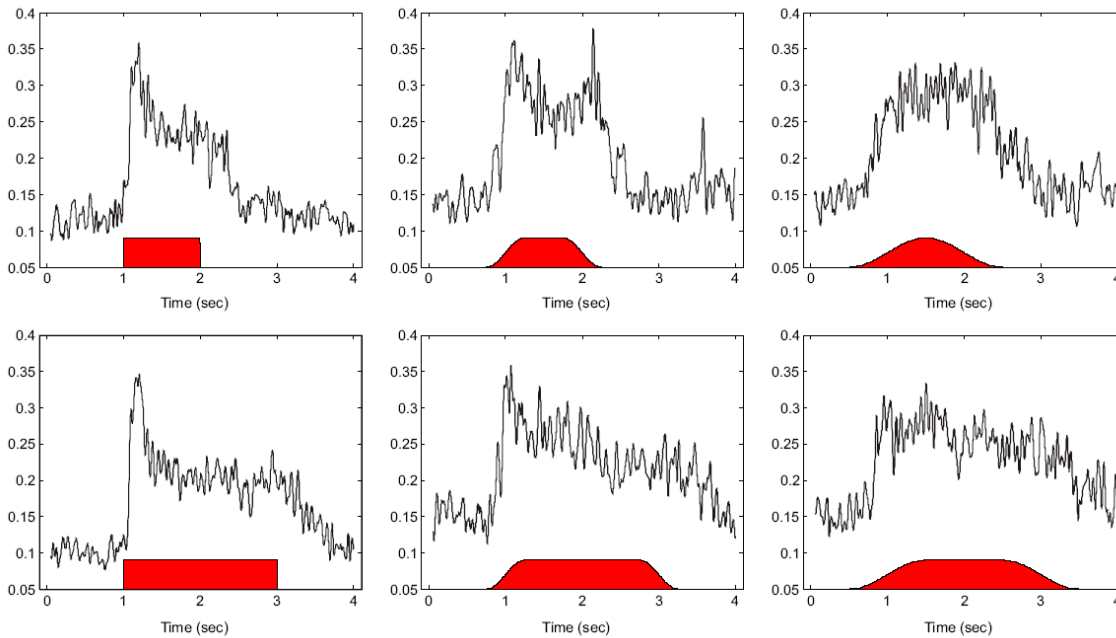
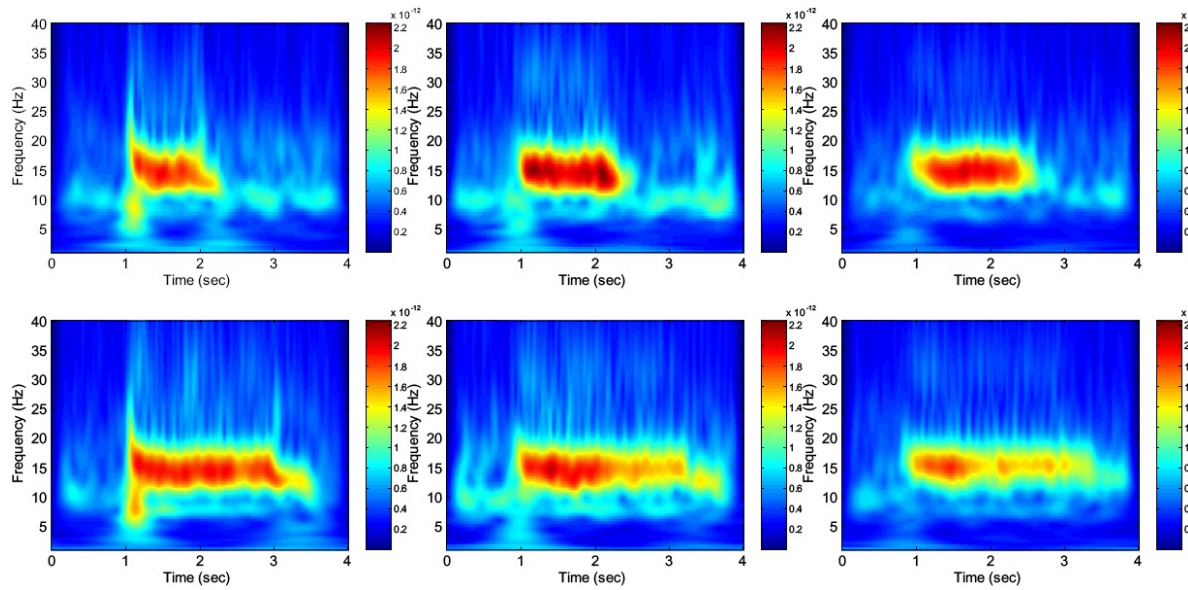
# Simulation of Neuronal Mechanisms



# MEG & fMRI Linearity Comparison



# MEG Results

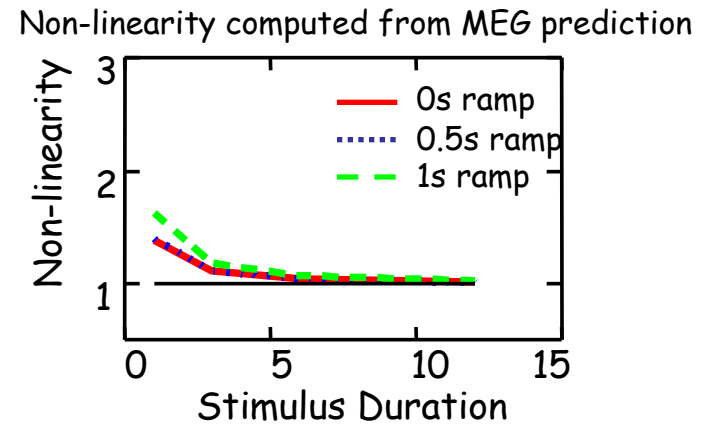
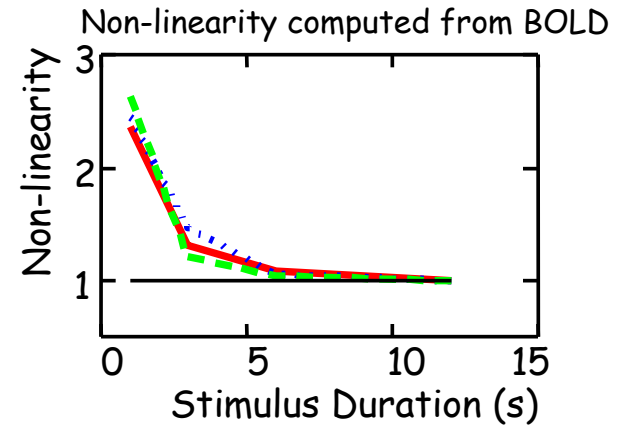
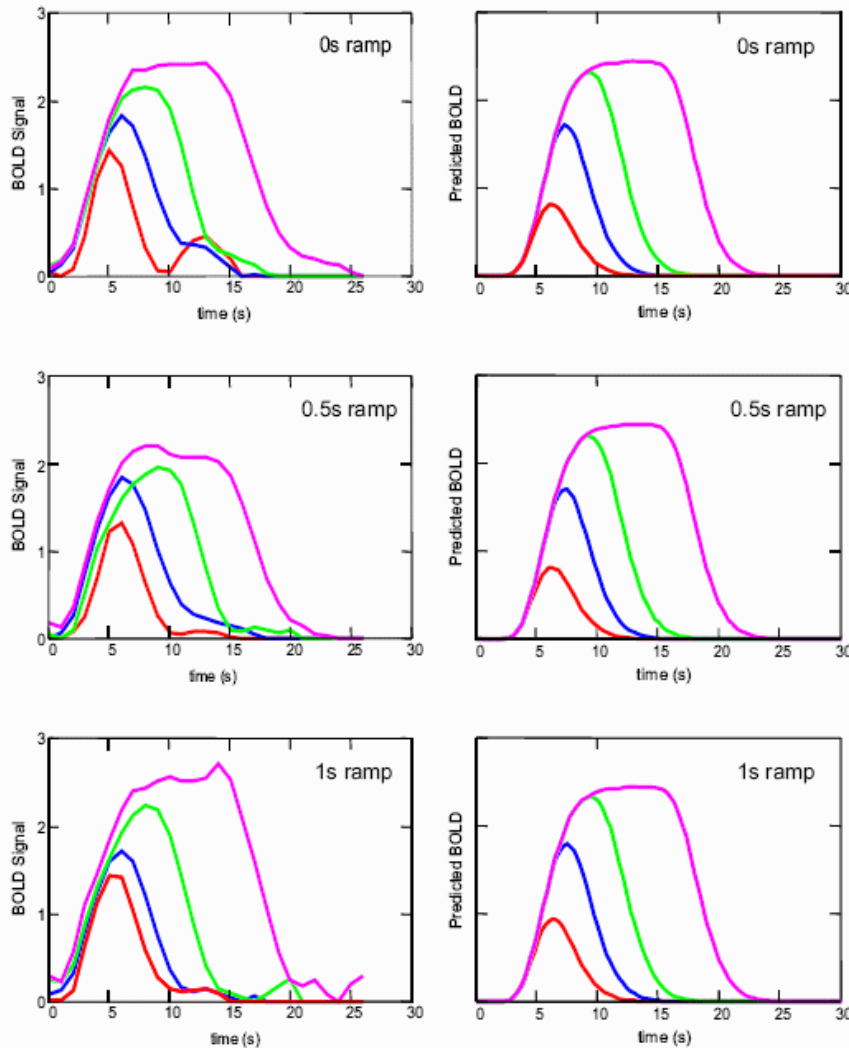


A. Tuan, R. M. Birn, P. A. Bandettini, G. M. Boynton, (submitted)

# Measured and Predicted BOLD responses

**BOLD**

**MEG**



# 2. Fluctuations

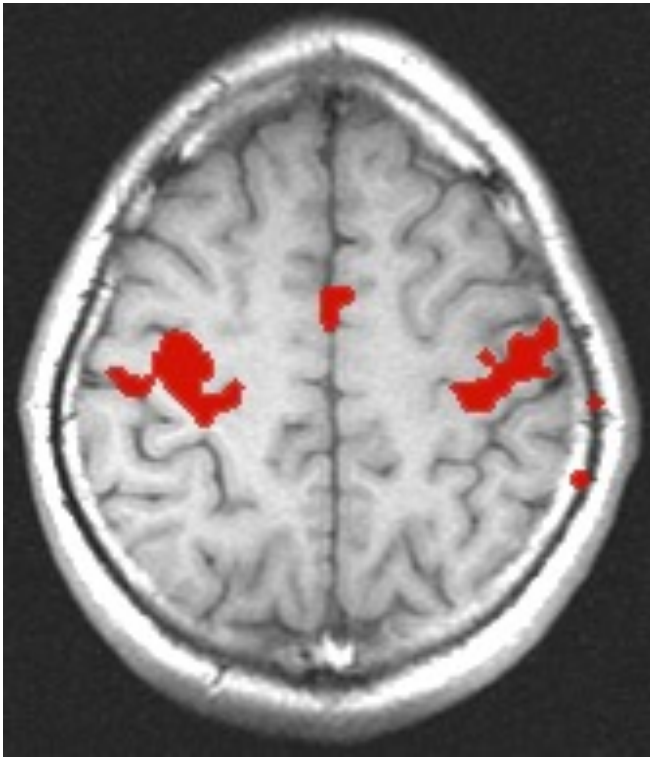
## Motivation:

- Applications of connectivity mapping (autism, schizophrenia, Alzheimer's, ADHD) have exploded - need for better interpretation.
- Distinguish neuronal activity-related fluctuations from non-neuronal physiological fluctuations.
  - reduce false positives in resting state connectivity maps*
  - increase functional contrast to noise for activation maps*
- *fMRI activation magnitude* calibration using fluctuations rather than hypercapnic or breath-hold stress.

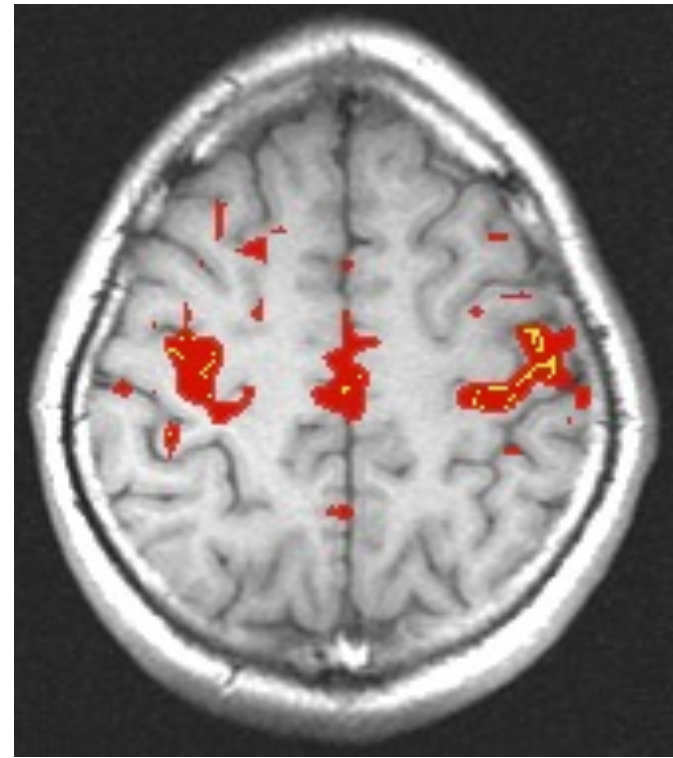
## Studies:

- Time course of respiration volume per unit time (RVT)
- The Respiration Response Function (RRF)
- fMRI Calibration using RRF

## Resting State Correlations

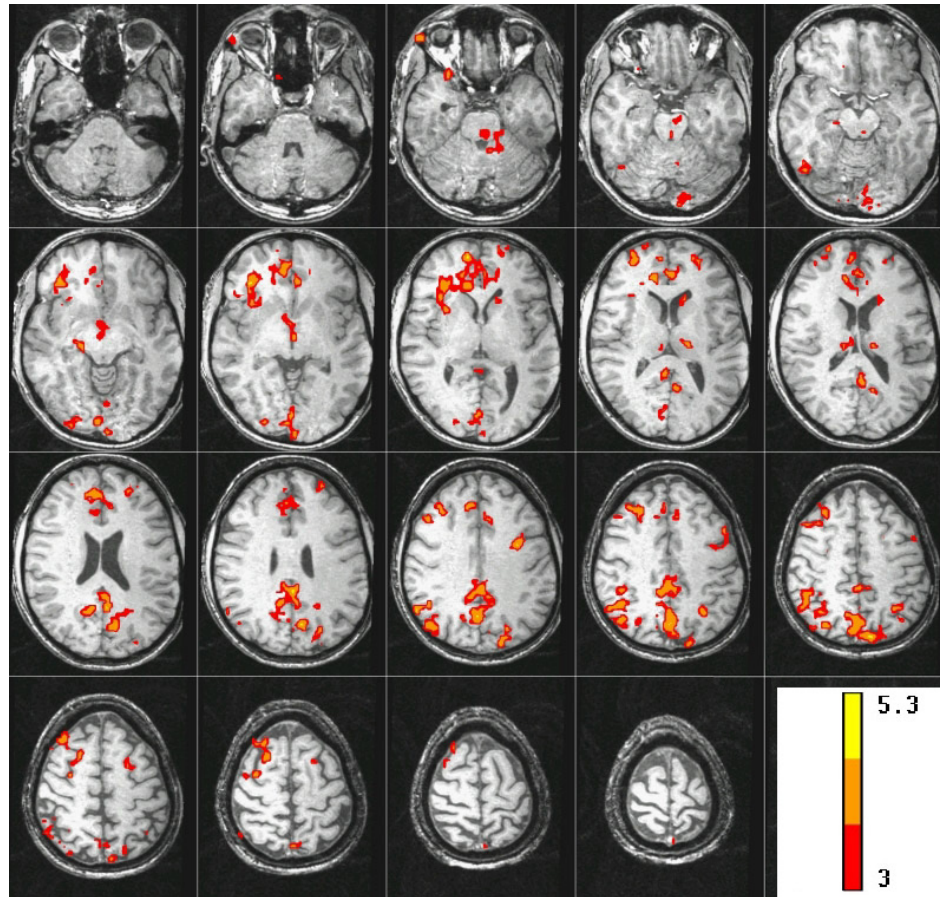


Activation:  
correlation with reference function



Rest:  
seed voxel in motor cortex

## BOLD correlated with SCR during "Rest"



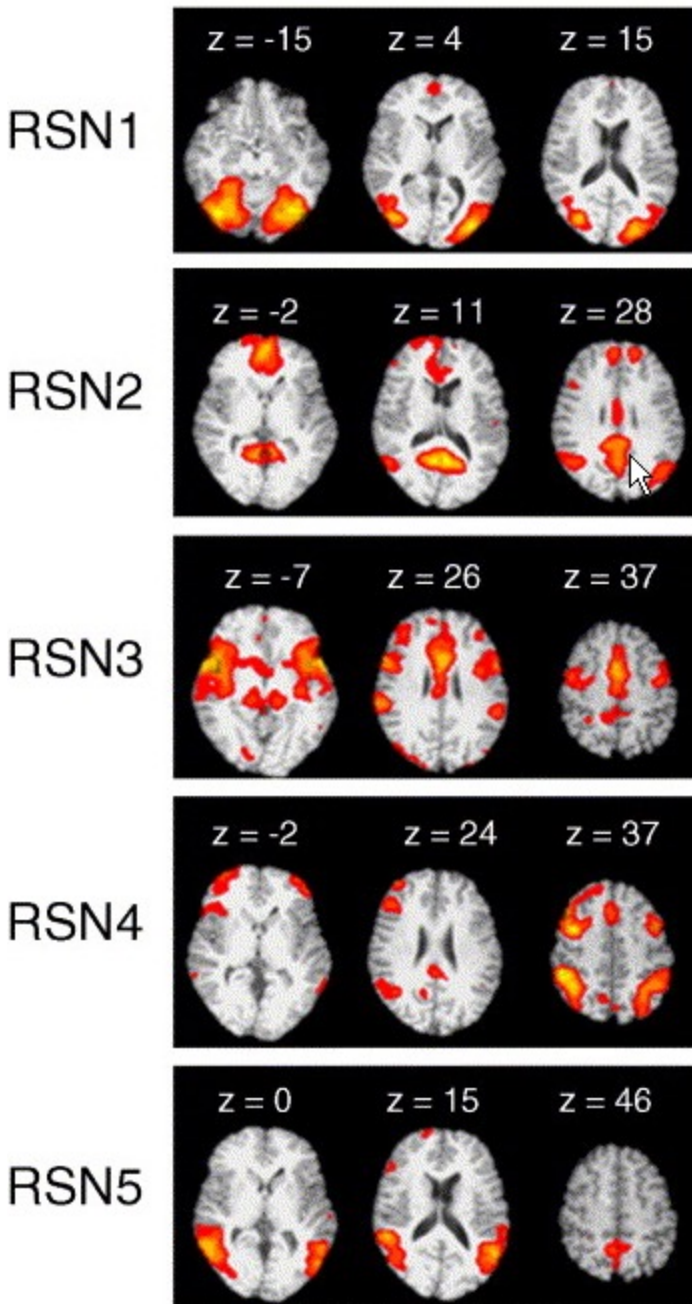
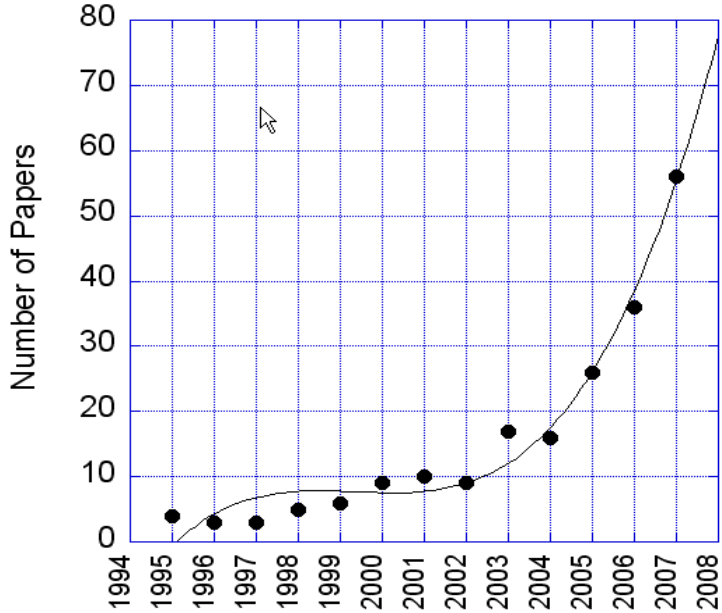
J. C. Patterson II, L. G. Ungerleider, and P. A. Bandettini,  
*NeuroImage* 17: 1787-1806, (2002).



# Methodology

## Resting state networks identified with ICA

M. DeLuca, C.F. Beckmann, N. De Stefano, P.M. Matthews, S.M. Smith, *fMRI resting state networks define distinct modes of long-distance interactions in the human brain*. *NeuroImage*, 29, 1359-1367

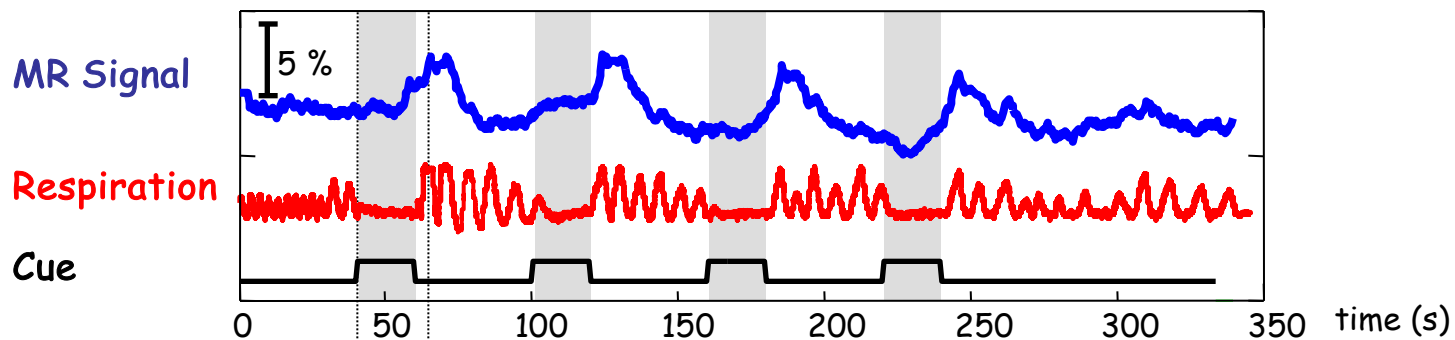


## Sources of time series fluctuations:

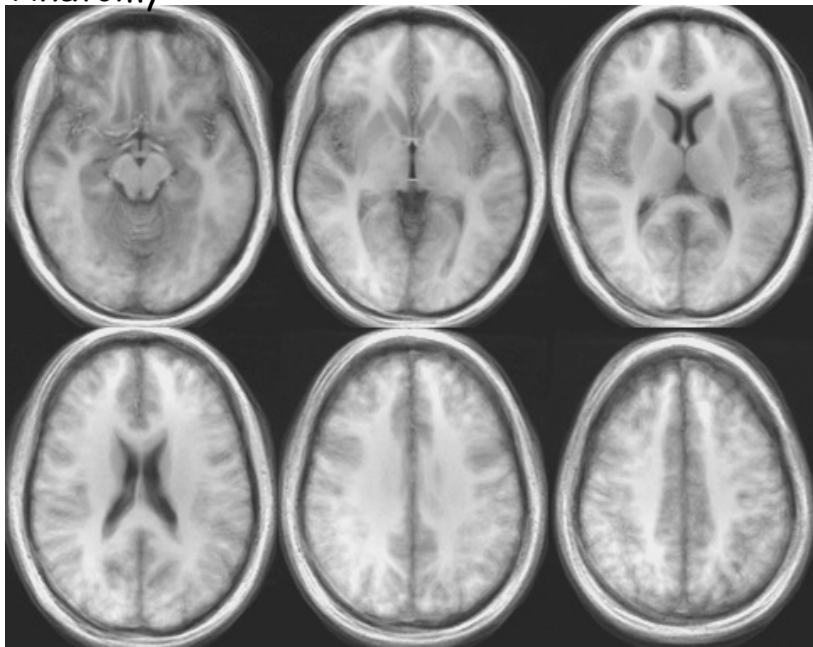
- Blood, brain and CSF pulsation
- Vasomotion
- Breathing cycle ( $B_0$  shifts with lung expansion)
- Bulk motion
- Scanner instabilities
- Changes in blood  $CO_2$  (changes in breathing)
- Spontaneous neuronal activity

# Breath-holding

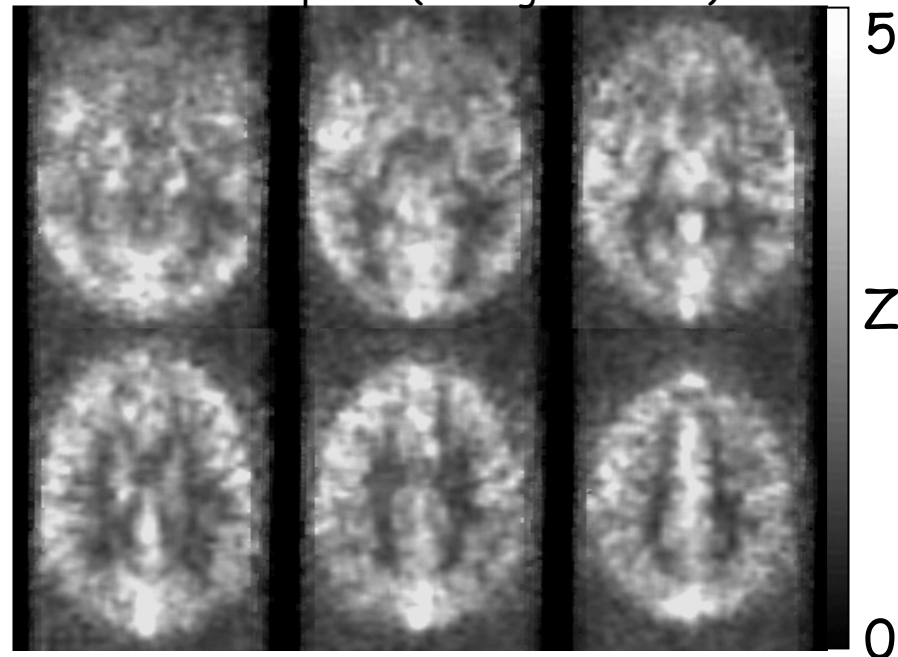
Group Maps (N = 7)



Anatomy

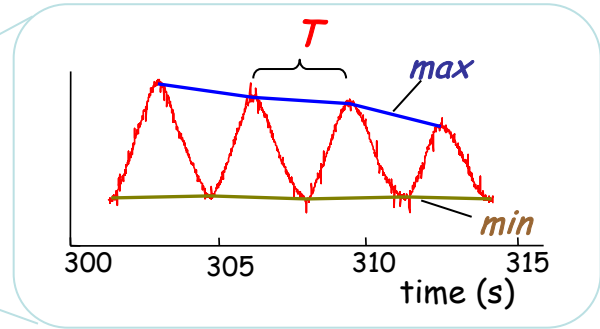
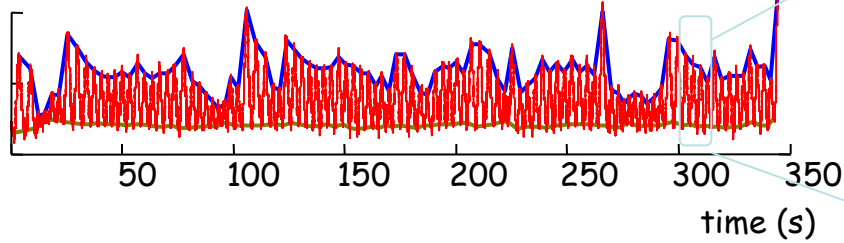


Breath-hold response (average Z-score)

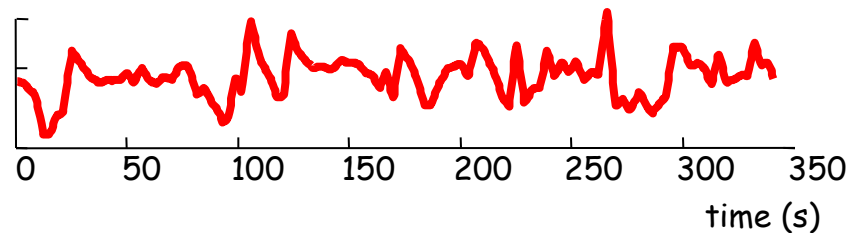


# Estimating respiration volume changes

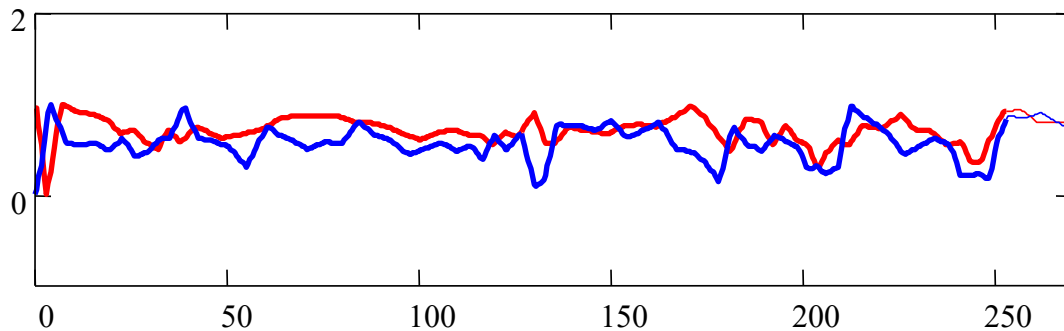
Respiration



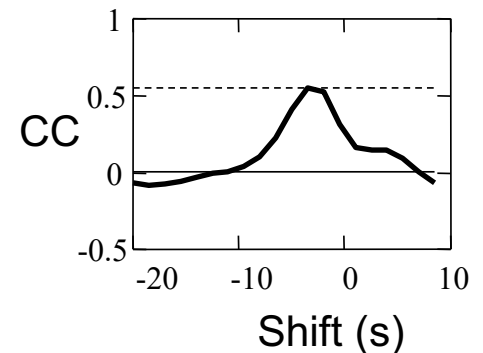
Respiration Volume / Time (RVT)



$$RVT = \frac{\text{max} - \text{min}}{T}$$



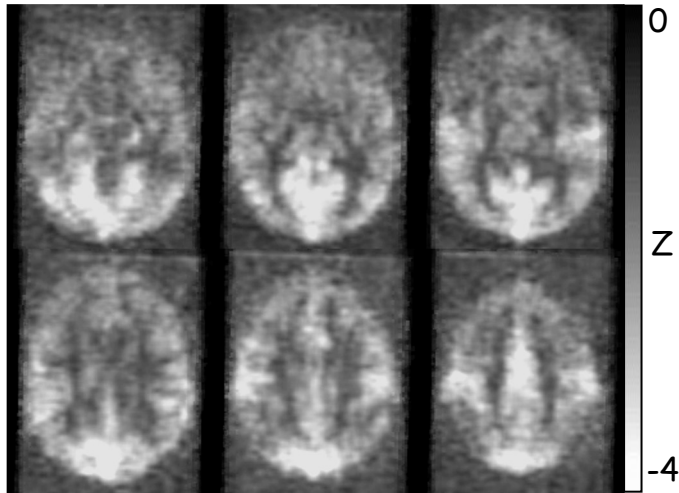
— CO<sub>2</sub>  
— RVT



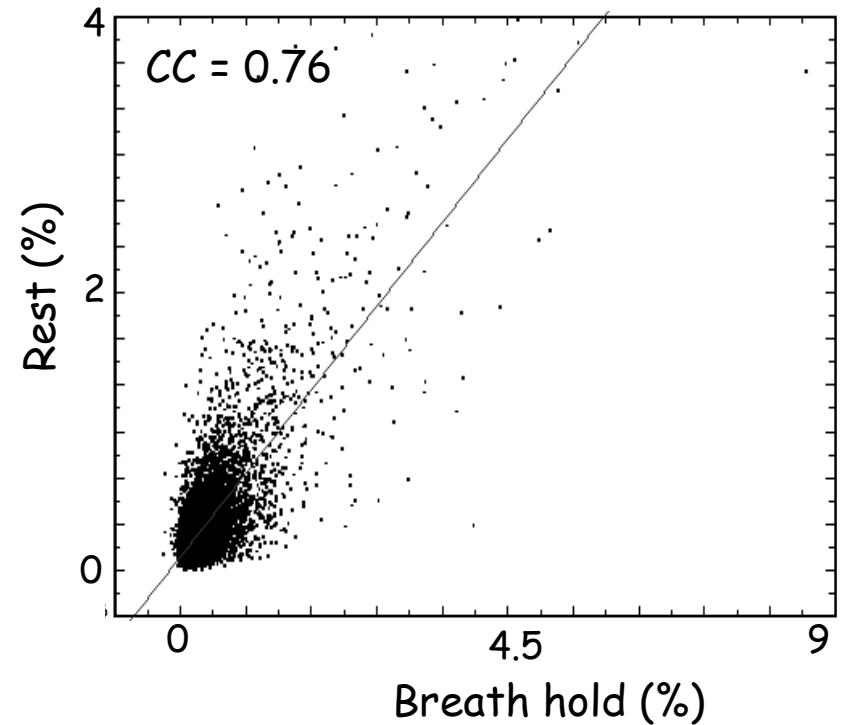
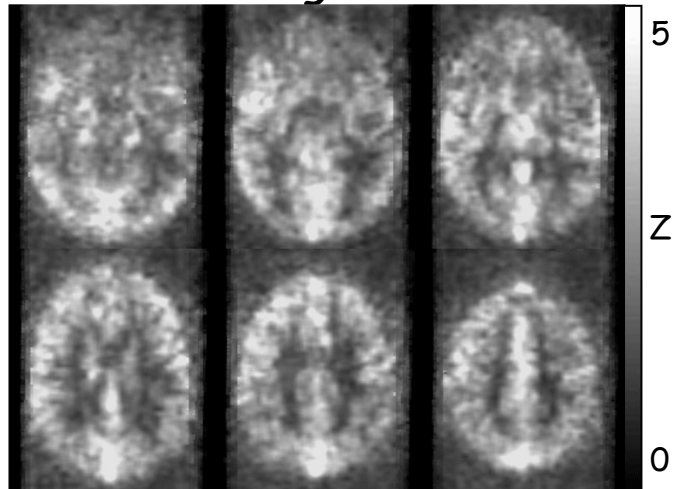
RVT precedes end tidal CO<sub>2</sub> by 5 sec.

# Respiration induced signal changes

*Rest*



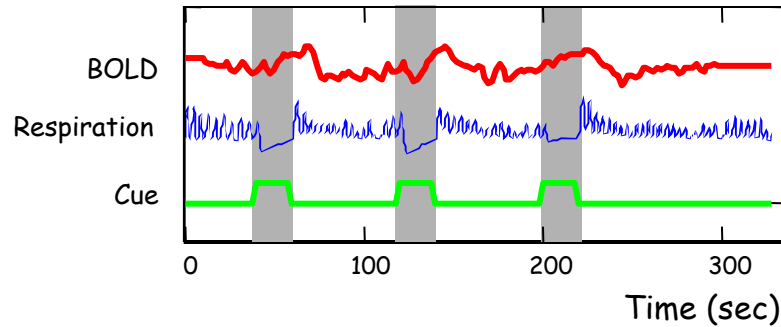
*Breath-holding*



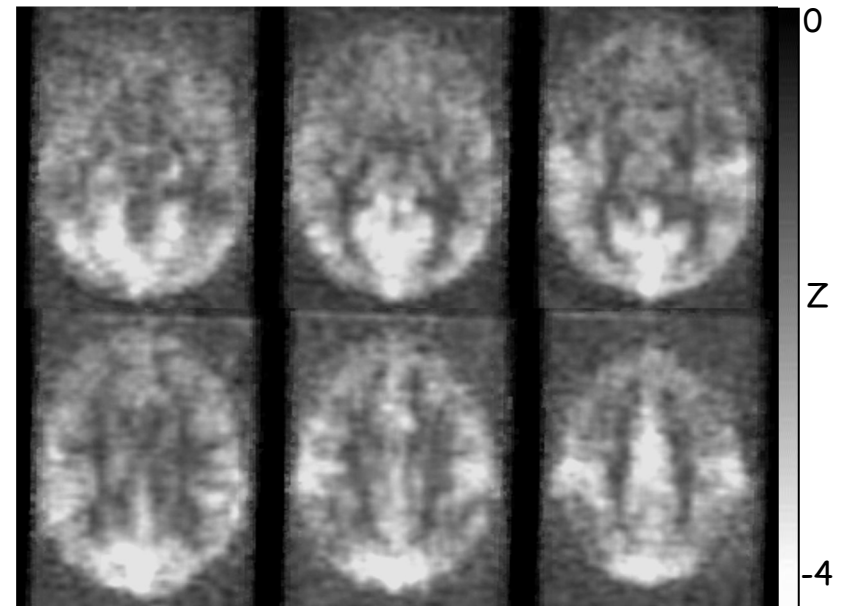
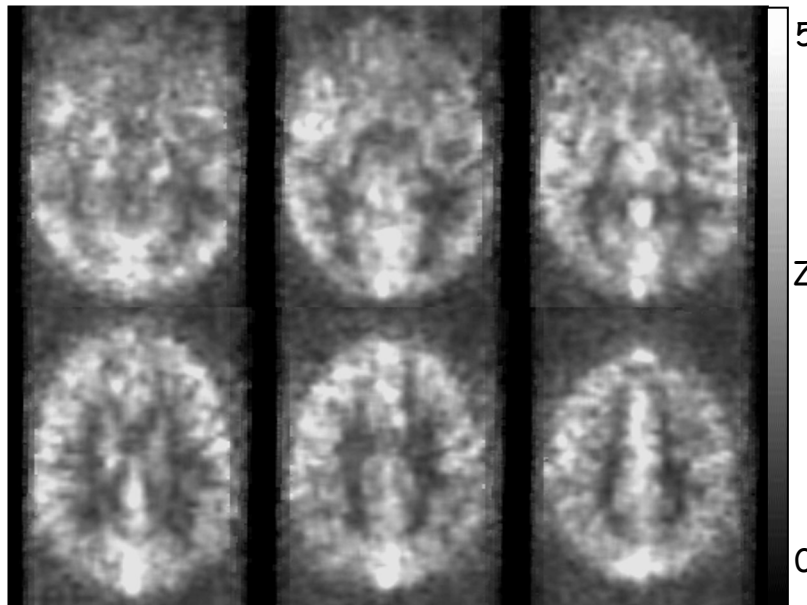
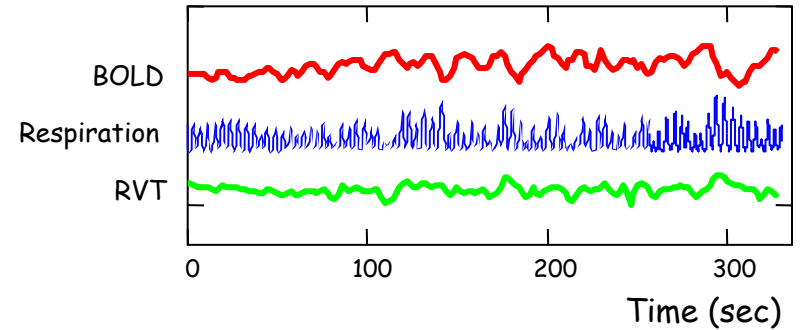
(N=7)

# Respiration induced signal changes

## *Breath-holding*



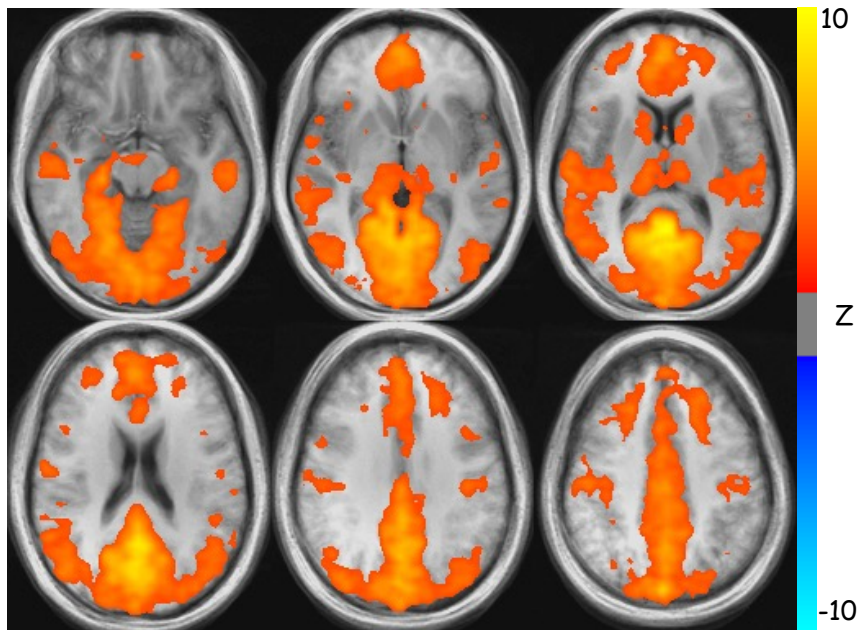
## *Rest*



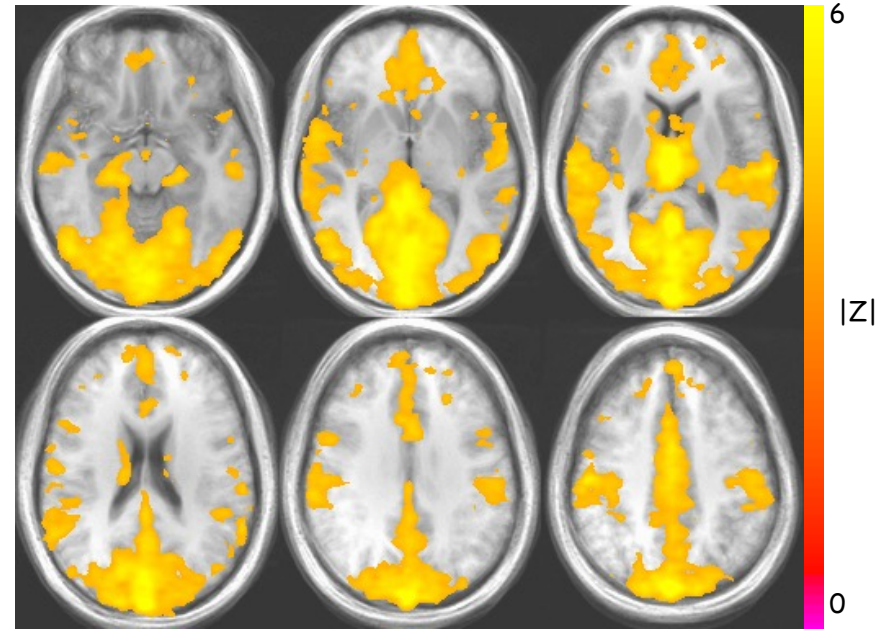
(N=7)

# RVT Correlation Maps & Functional Connectivity Maps

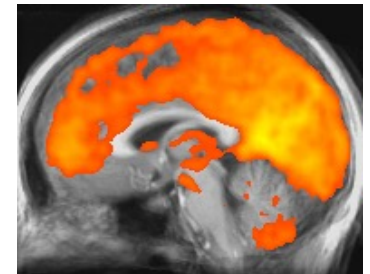
Resting state correlation with signal from posterior cingulate



Resting state correlation with RVT signal



*Group (n=10)*

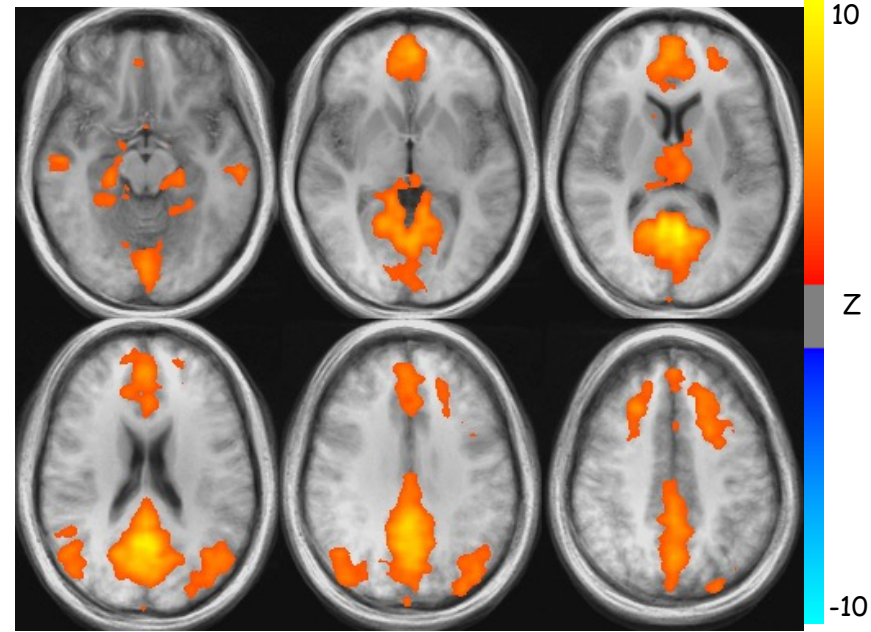
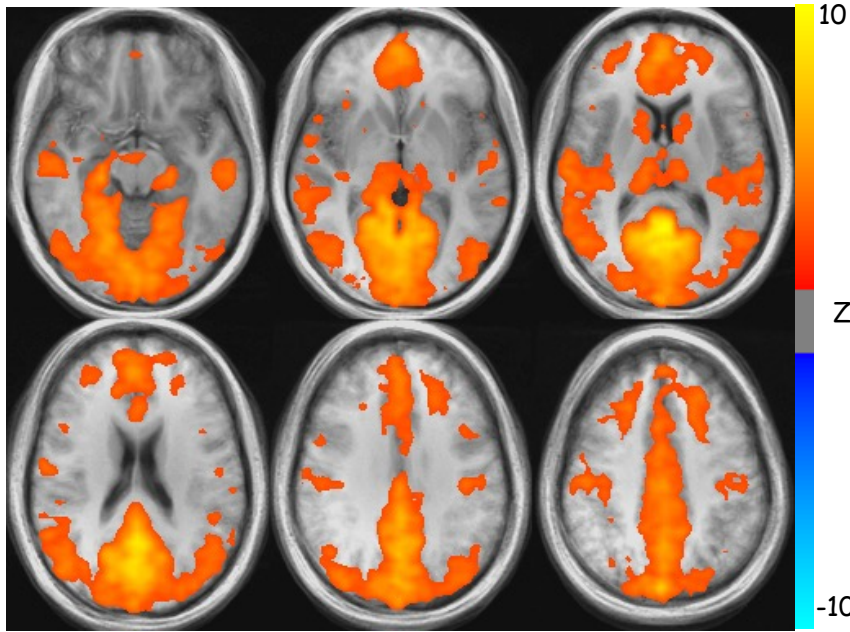


R.M. Birn, J. A. Diamond, M. A. Smith, P. A. Bandettini,  
*NeuroImage*, 31, 1536-1548 (2006)

# Effect of Respiration Rate Consistency on Resting Correlation Maps

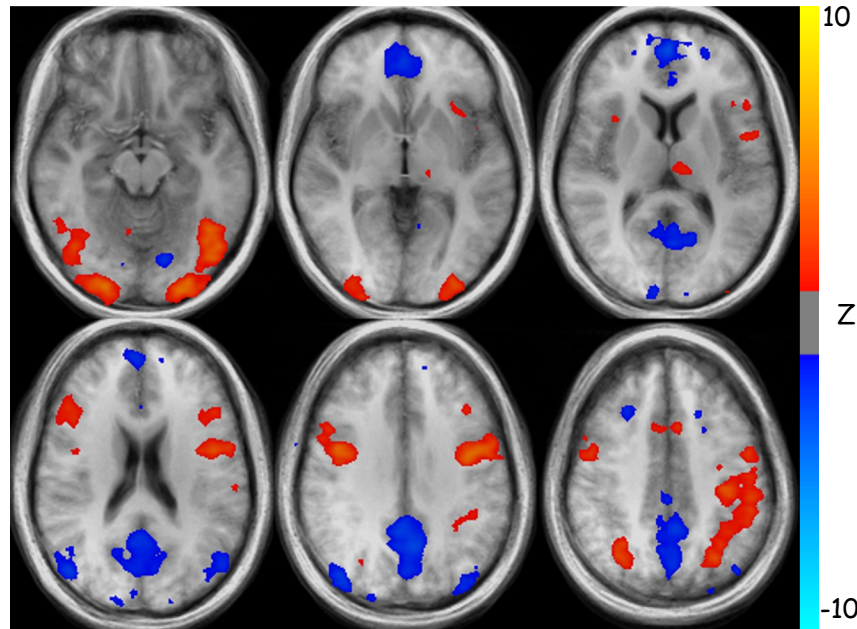
Spontaneously Varying Respiration Rate

Constant Respiration Rate



Lexical Decision Making Task

Group (n=10)

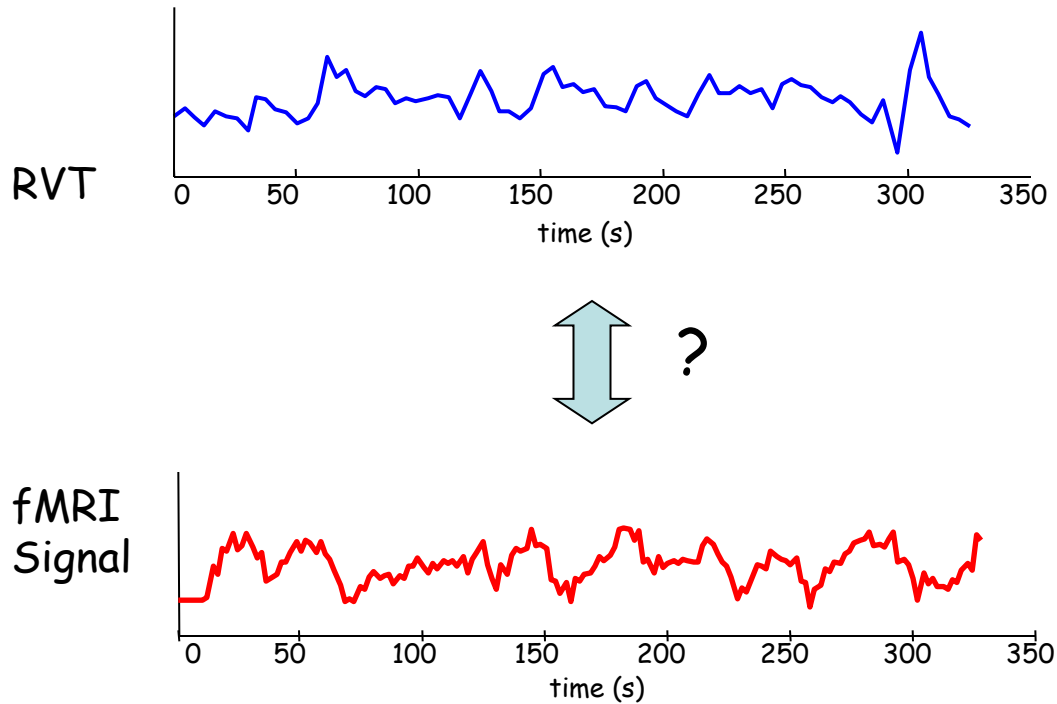


Blue: deactivated network



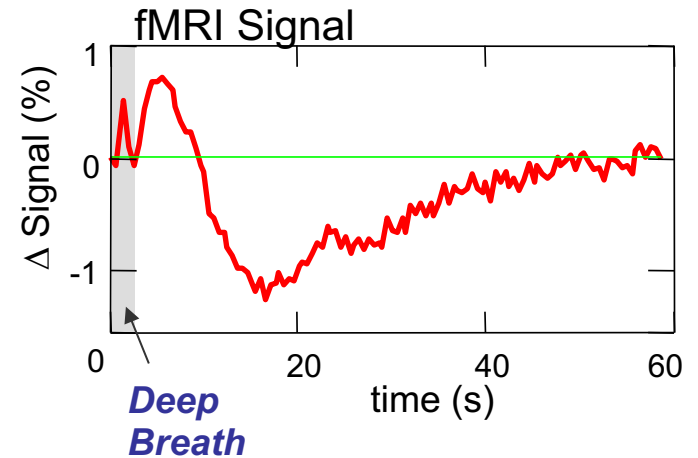
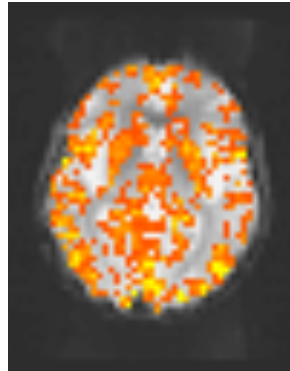
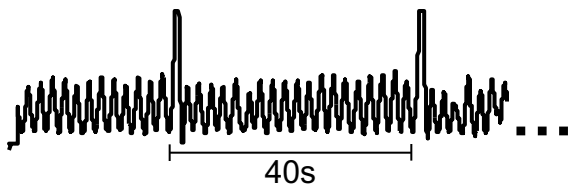
# Respiration Changes vs. BOLD

*How are the BOLD changes related to respiration variations?*

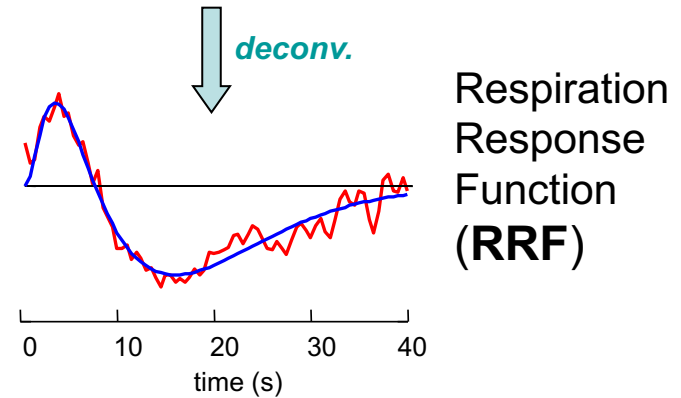


# fMRI response to a single Deep Breath

Respiration

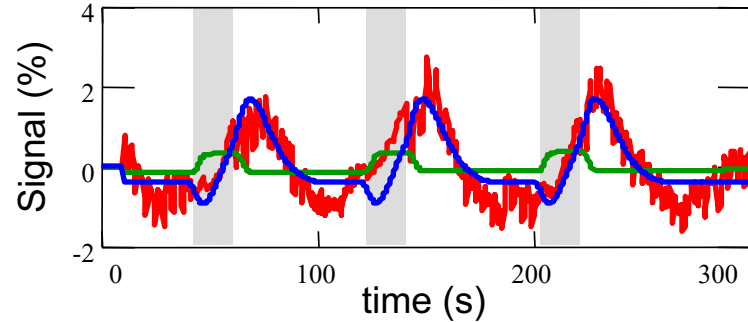
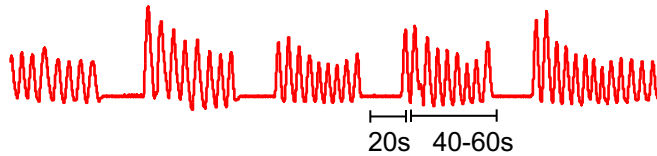


$$\text{RRF}(t) = 0.6 t^{2.1} e^{-1.6 t} - 0.0023 t^{3.54} e^{-4.25 t}$$

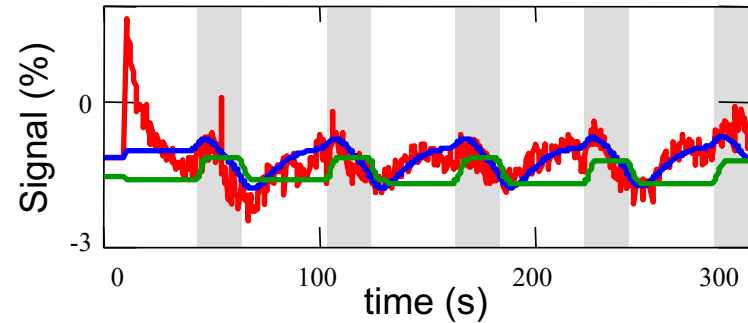
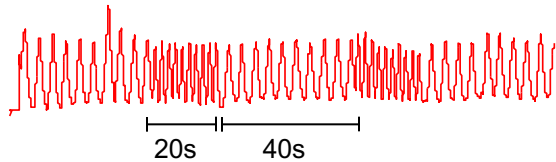


Respiration response function predicts BOLD signal associated with breathing changes better than activation response function.

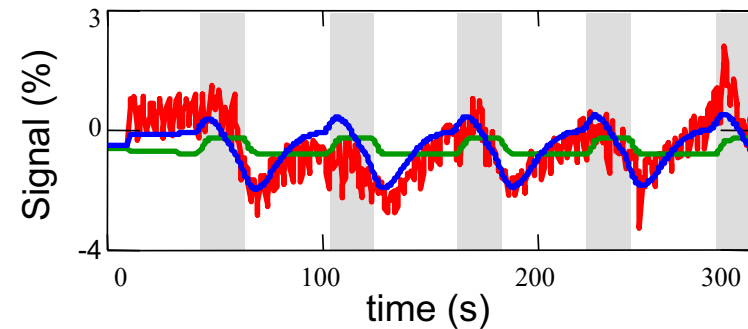
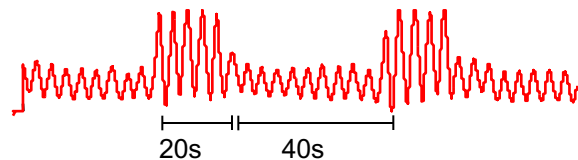
### Breath-holding

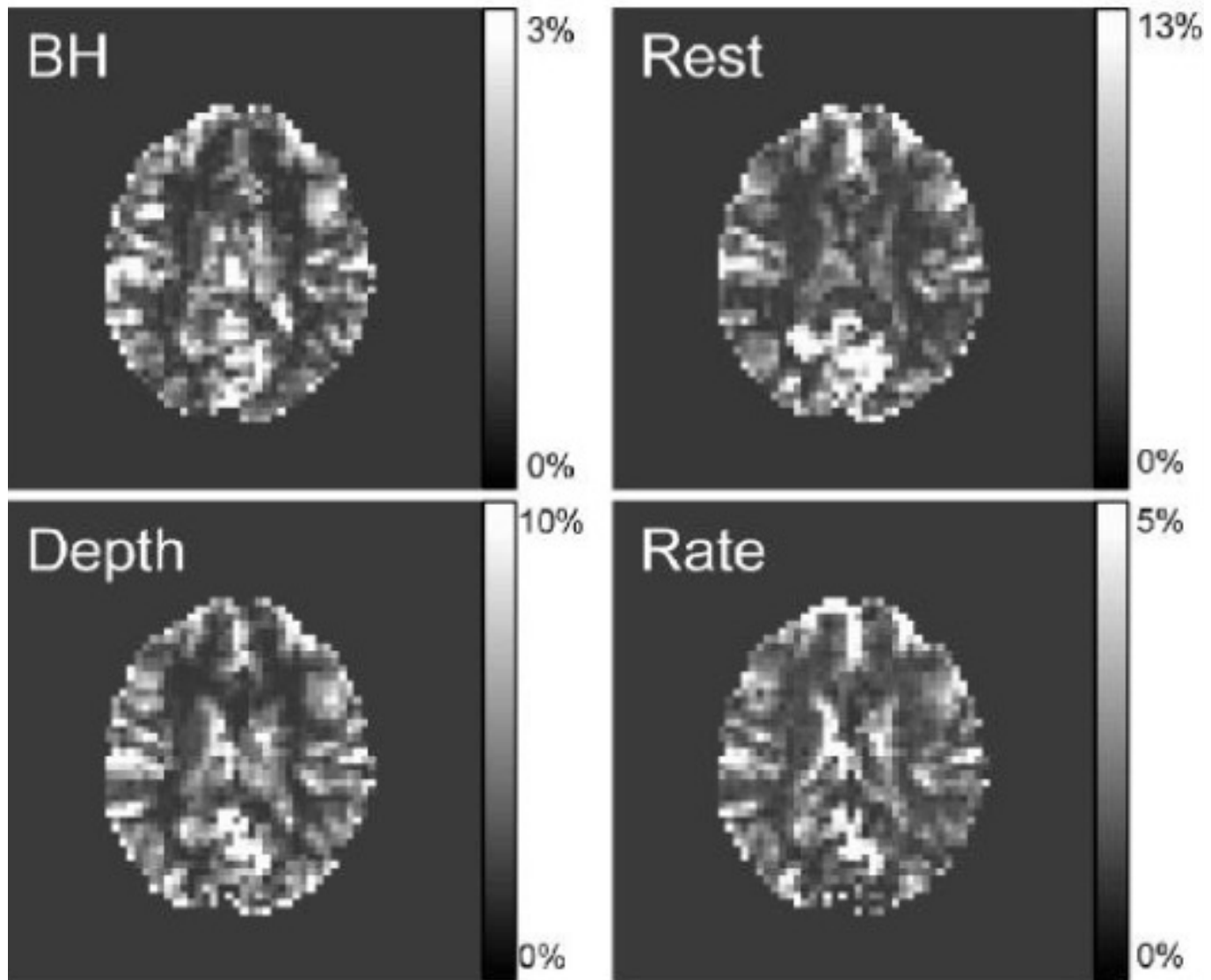


### Rate Changes

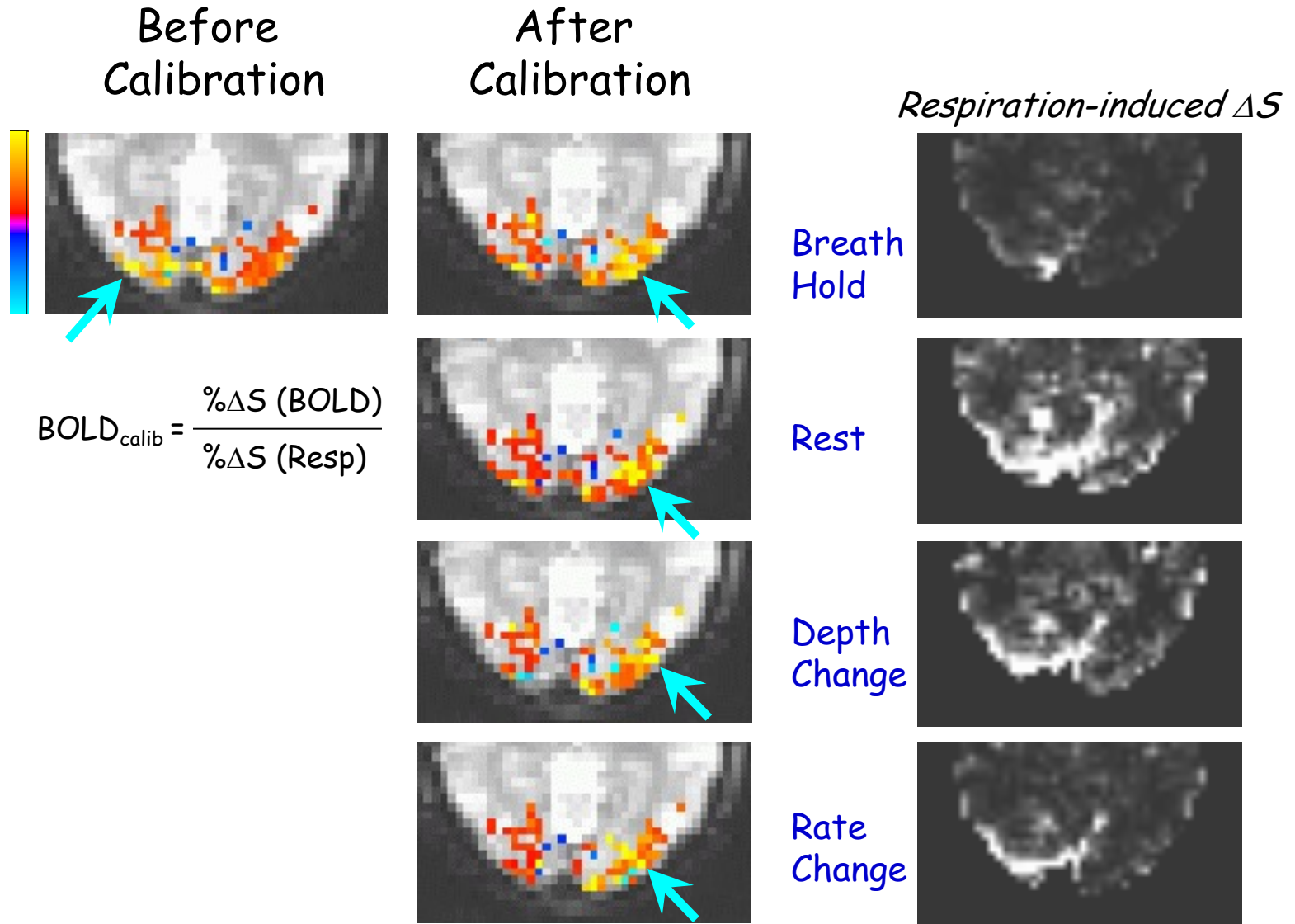


### Depth Changes





# BOLD magnitude calibration



# 3. Experimental Design

## Motivation:

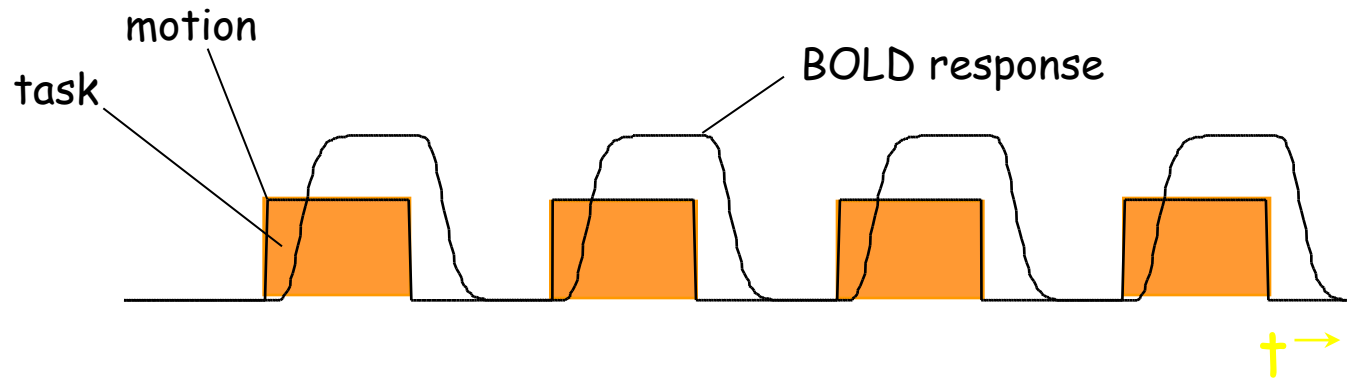
- Guides for *individual* subject scanning at the limits of detectability, resolution, available time, and subject performance.

## Studies:

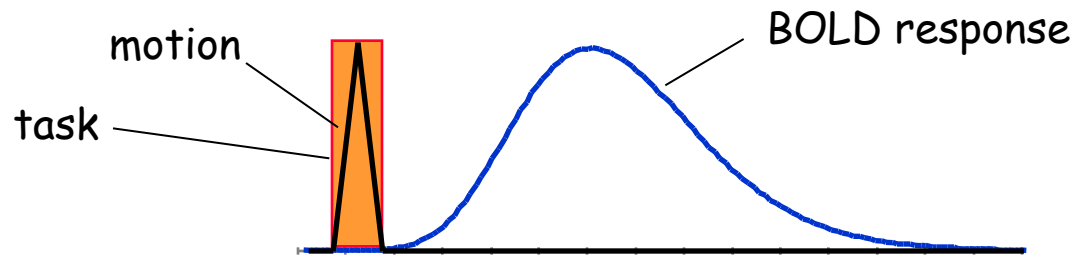
- Overt response timing
- Suggested resolution

# fMRI during tasks that involve brief motion

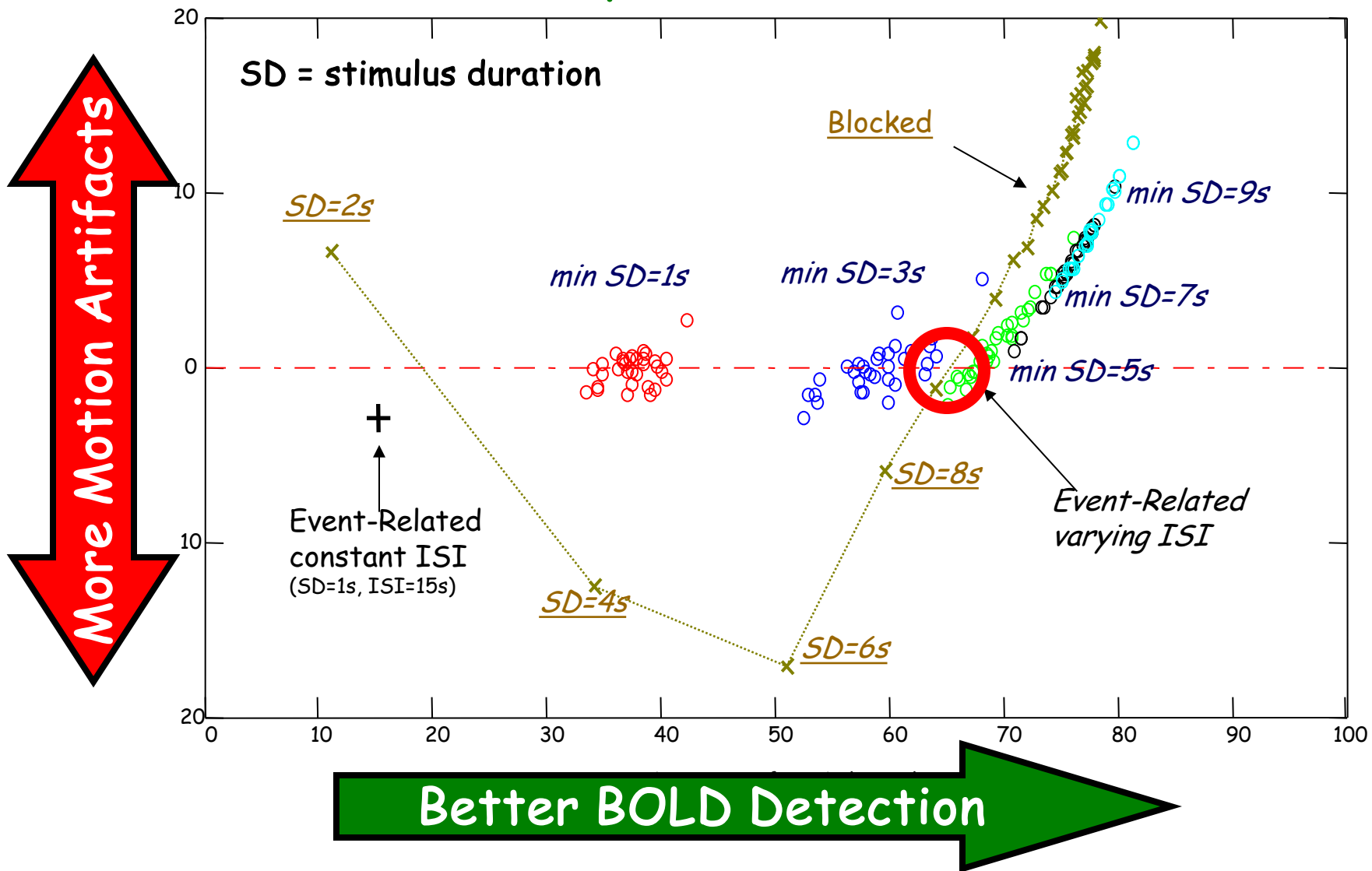
## Blocked Design



## Event-Related Design

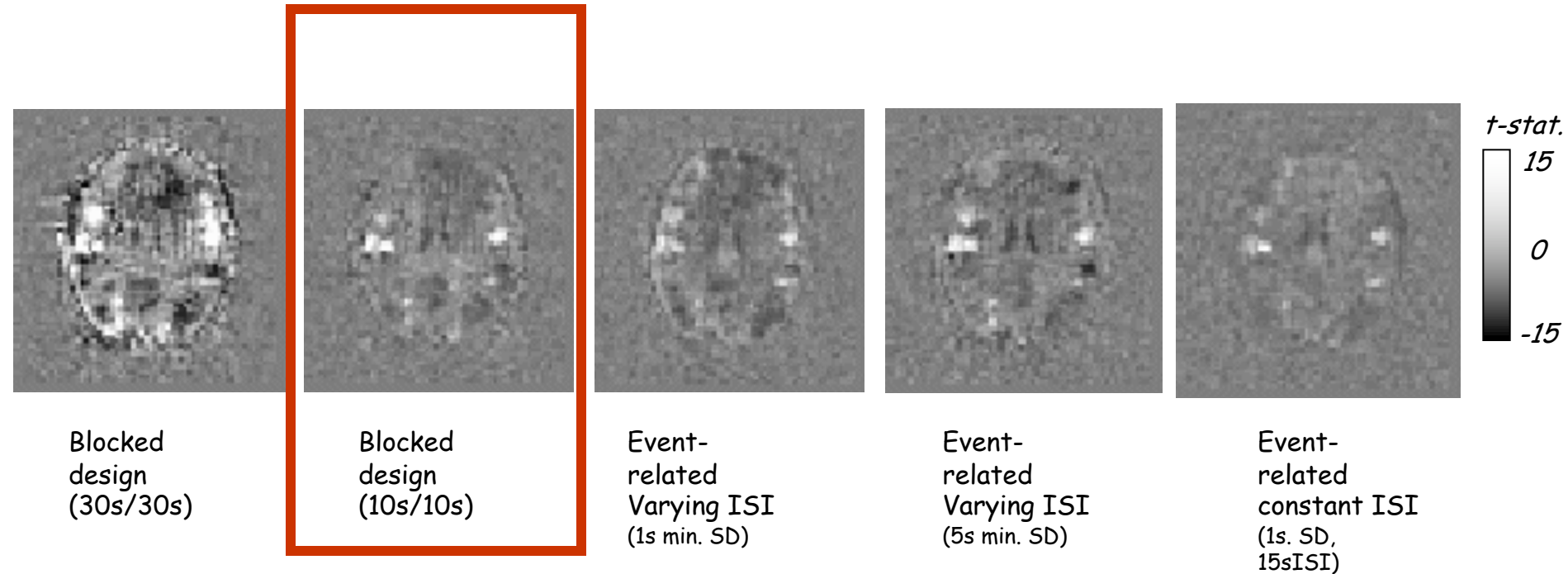


# Overt Responses - Simulations





# Overt Responses



Blocked design  
(30s/30s)

Blocked design  
(10s/10s)

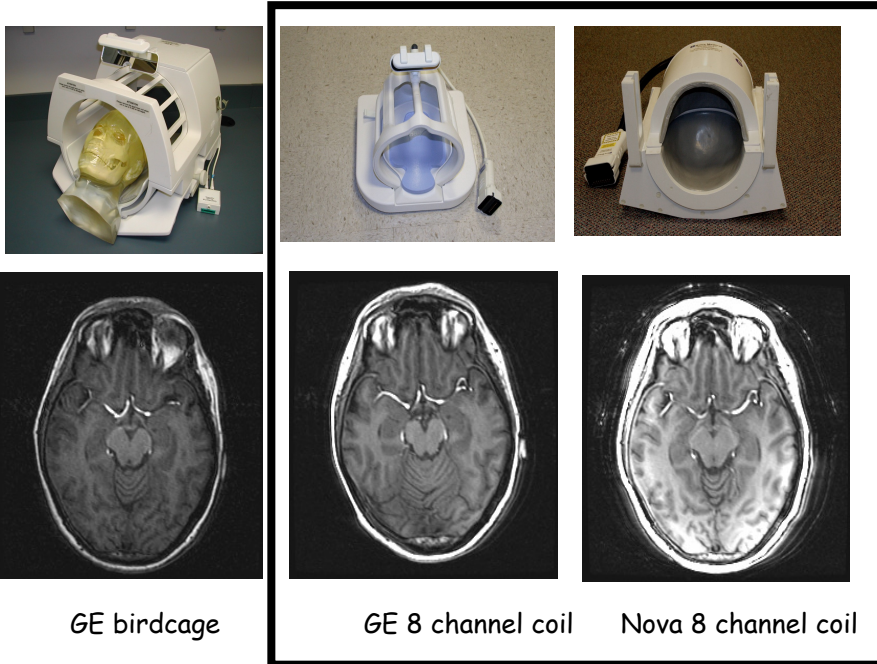
Event-related  
Varying ISI  
(1s min. SD)

Event-related  
Varying ISI  
(5s min. SD)

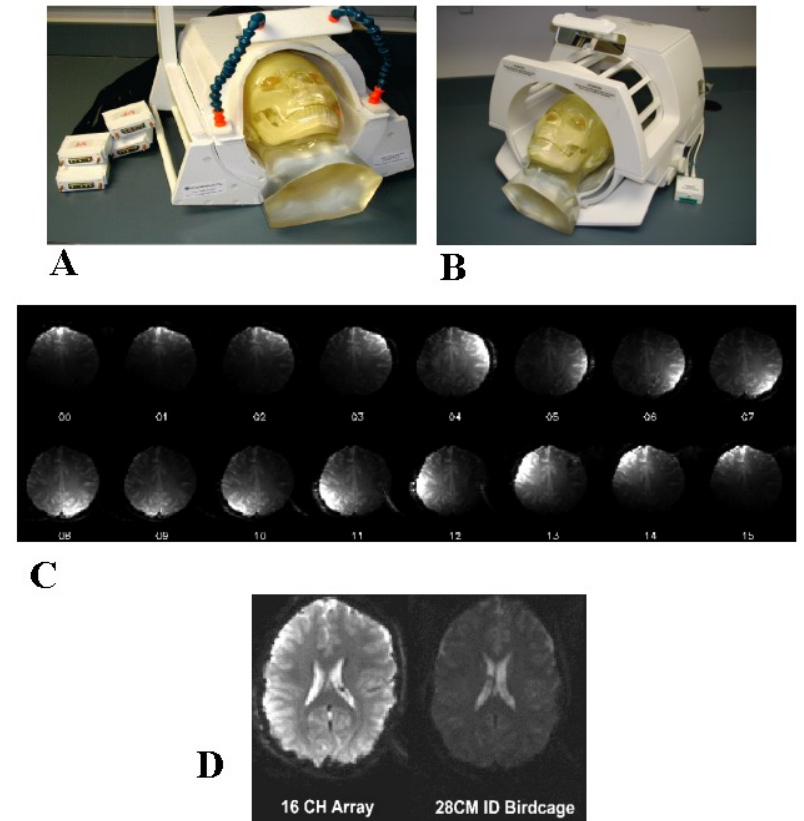
Event-related  
constant ISI  
(1s. SD,  
15sISI)

*t-stat.*  
15  
0  
-15

## 8 channel parallel receiver coil

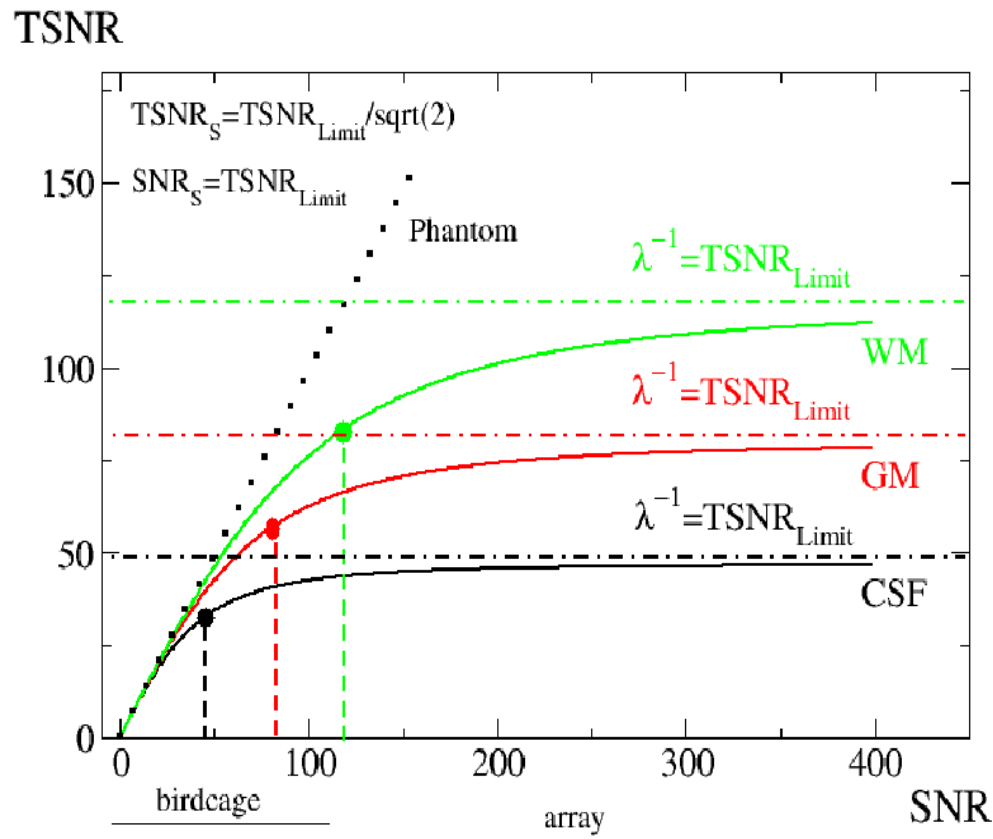


## 16 channel parallel receiver coil



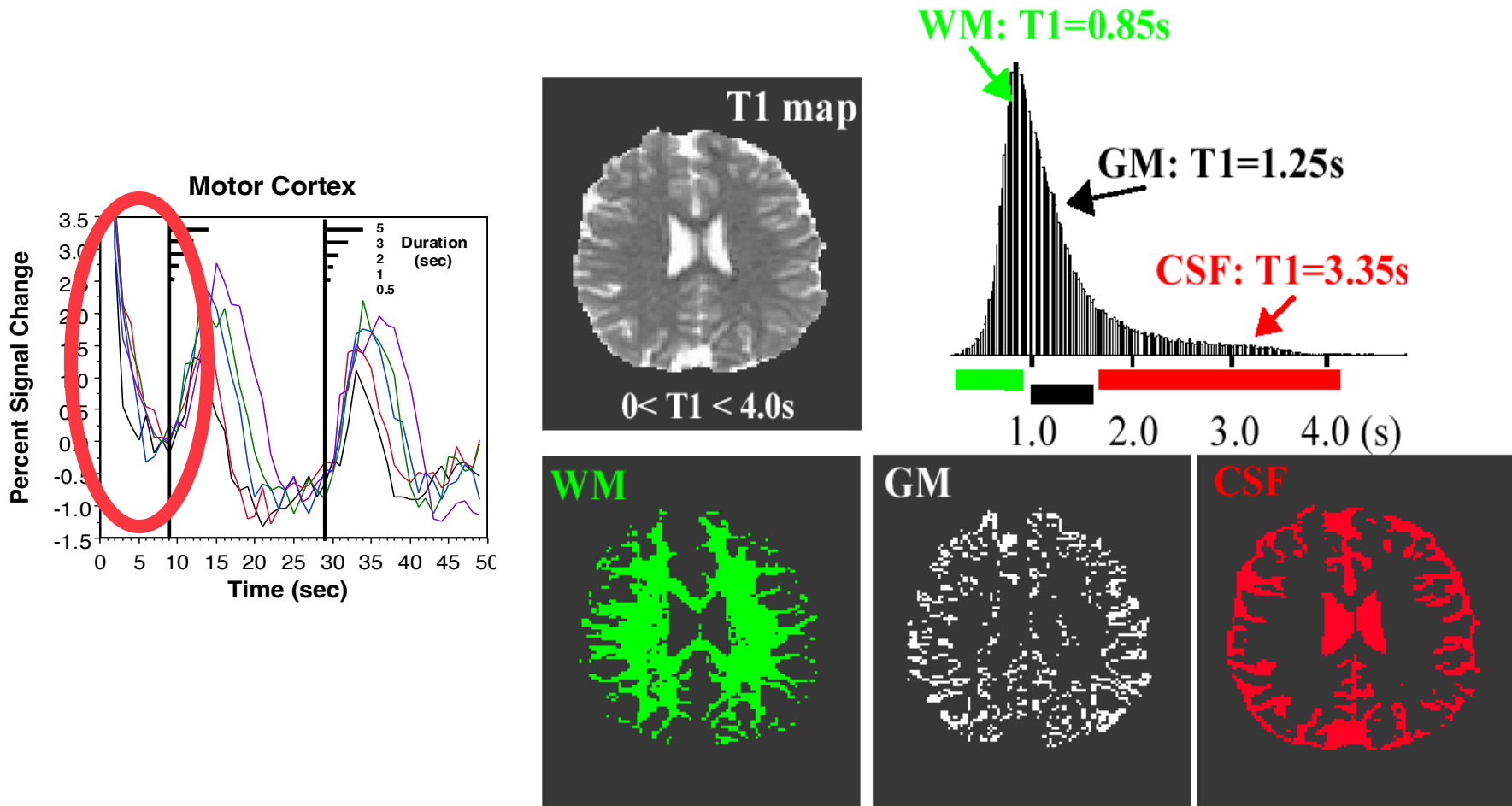
# Finding the "suggested voxel volume"

Temporal Signal to Noise Ratio (TSNR) vs. Signal to Noise Ratio (SNR)

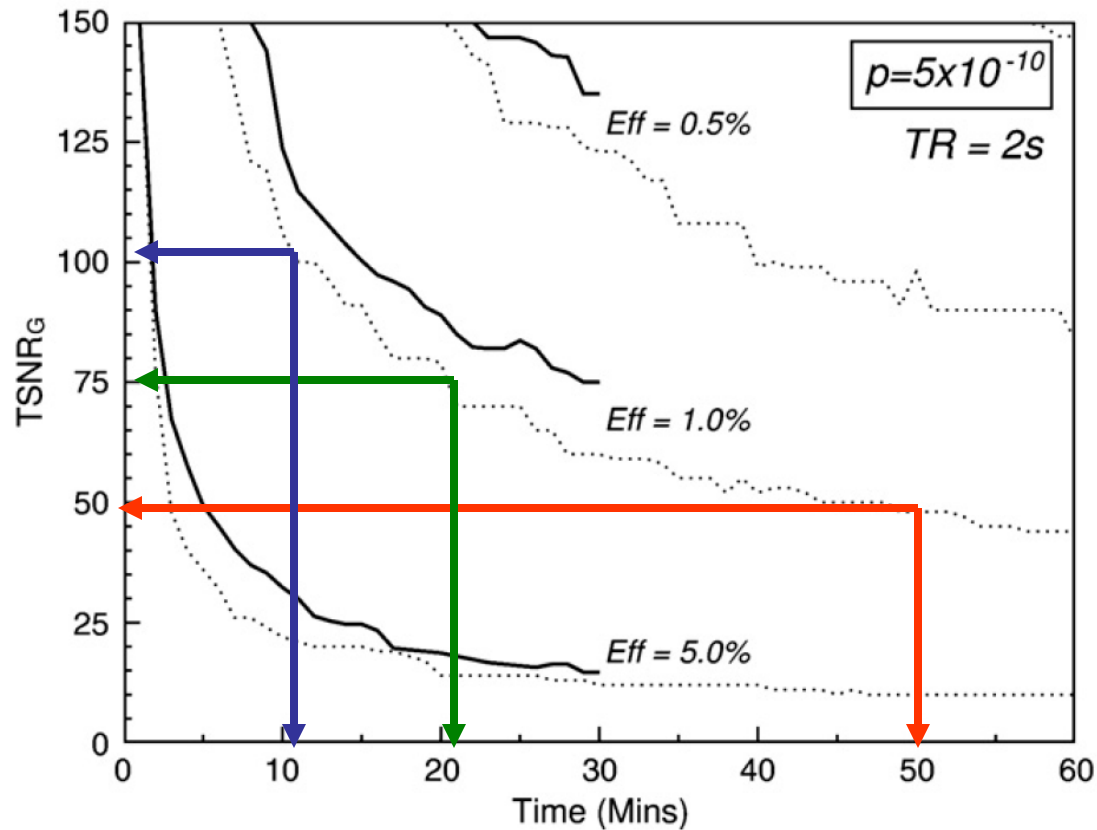


3T, birdcage:	2.5 mm <sup>3</sup>
3T, 16 channel:	1.8 mm <sup>3</sup>
7T, 16 channel:	1.4 mm <sup>3</sup>

# Segmentation using EPI Transient



# Sensitivity, Scan Time, and Temporal Signal to Noise



# 4. Pattern-Information Analysis

## Motivation:

- Classical fMRI analysis:  
*Is a region activated during a task?*
- Pattern-information analysis:  
*Does a region carry a particular kind of information?*

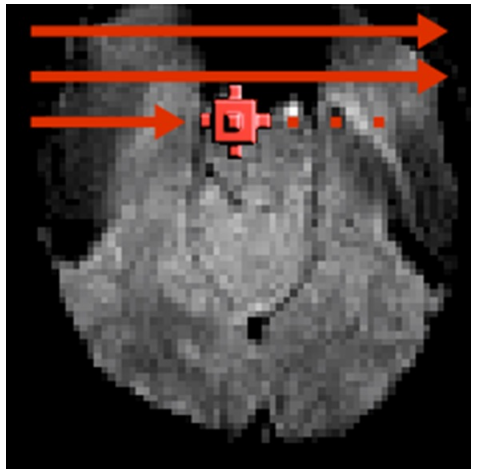
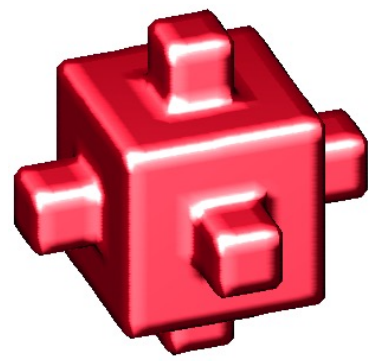
## Study:

- Pattern-Information Mapping
- Dis-similarity matrix



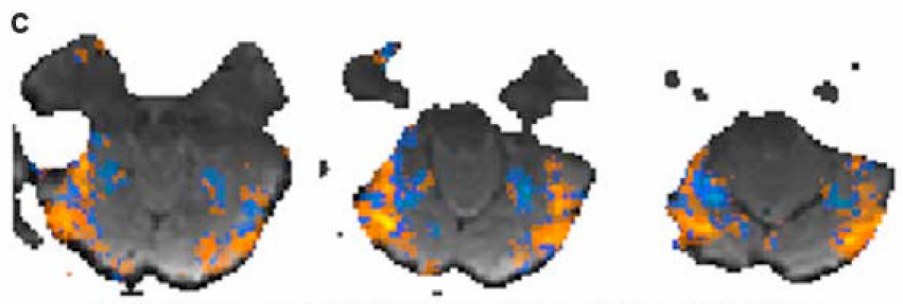
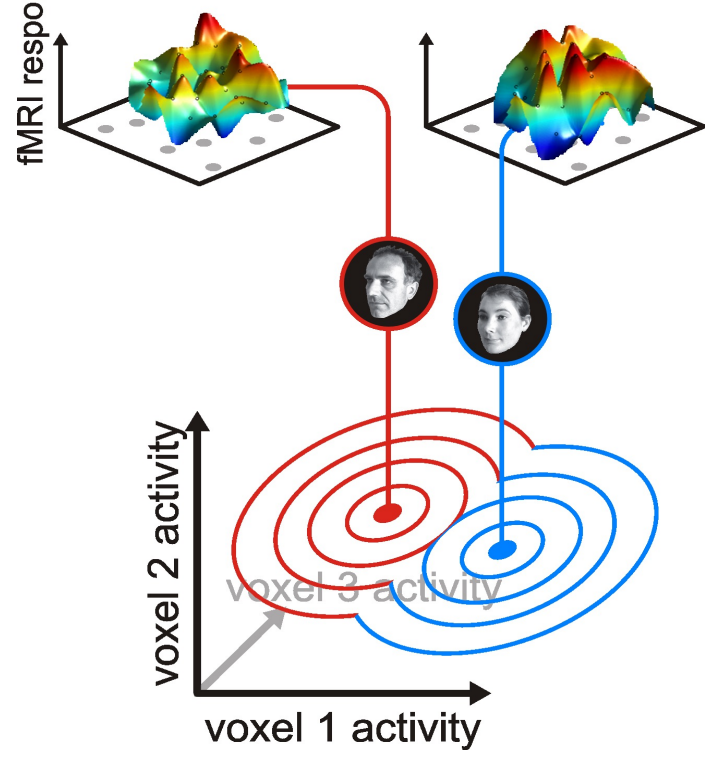
# Pattern Information Mapping

"searchlight" ROI →



From fixed ROI

event-related spatial response patterns

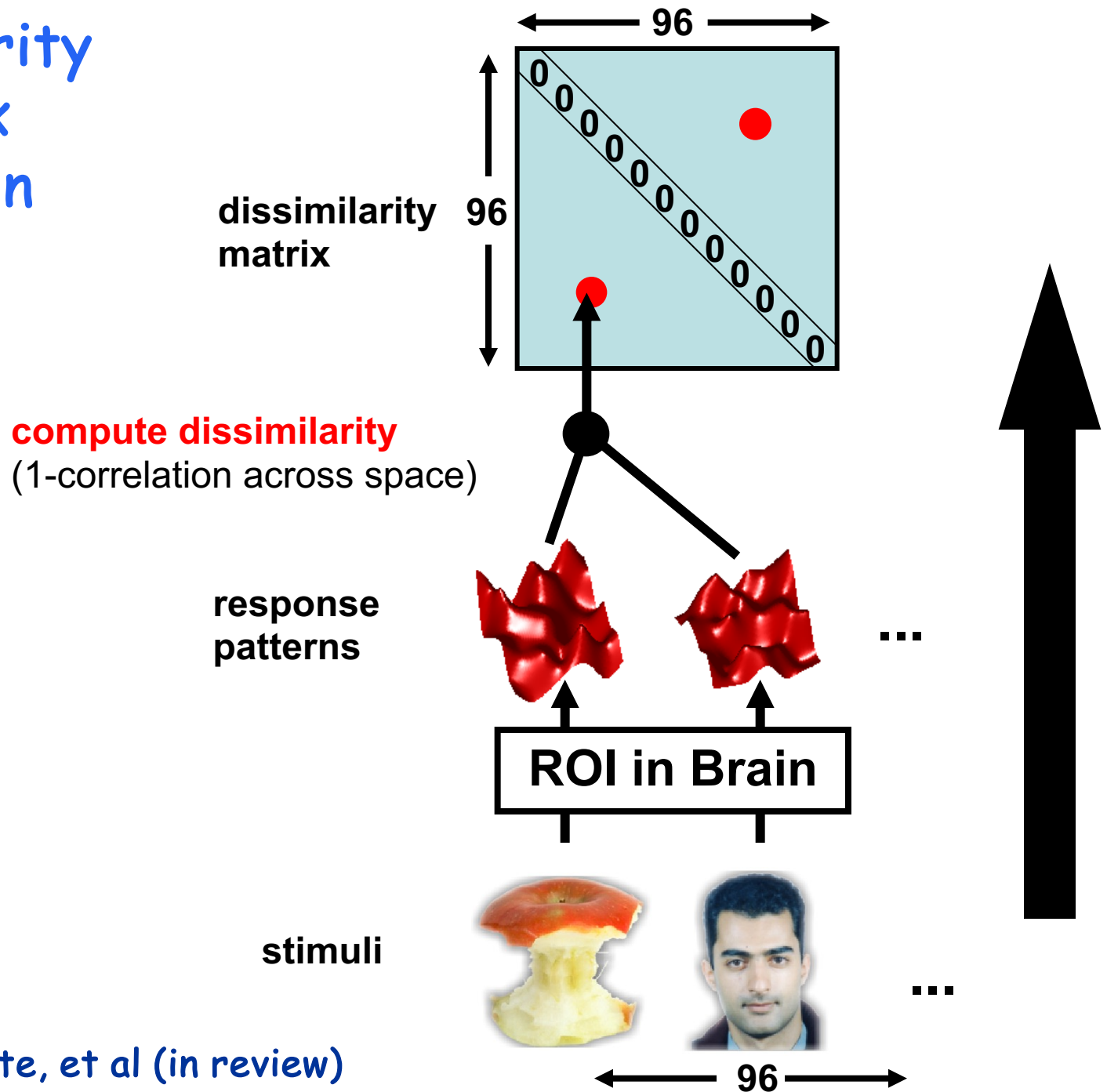


Information-based searchlight map with t-map texture (FDR  $q < 0.05$ )



Unsmoothed-data t map (same number of voxels marked)

# Dissimilarity Matrix Creation



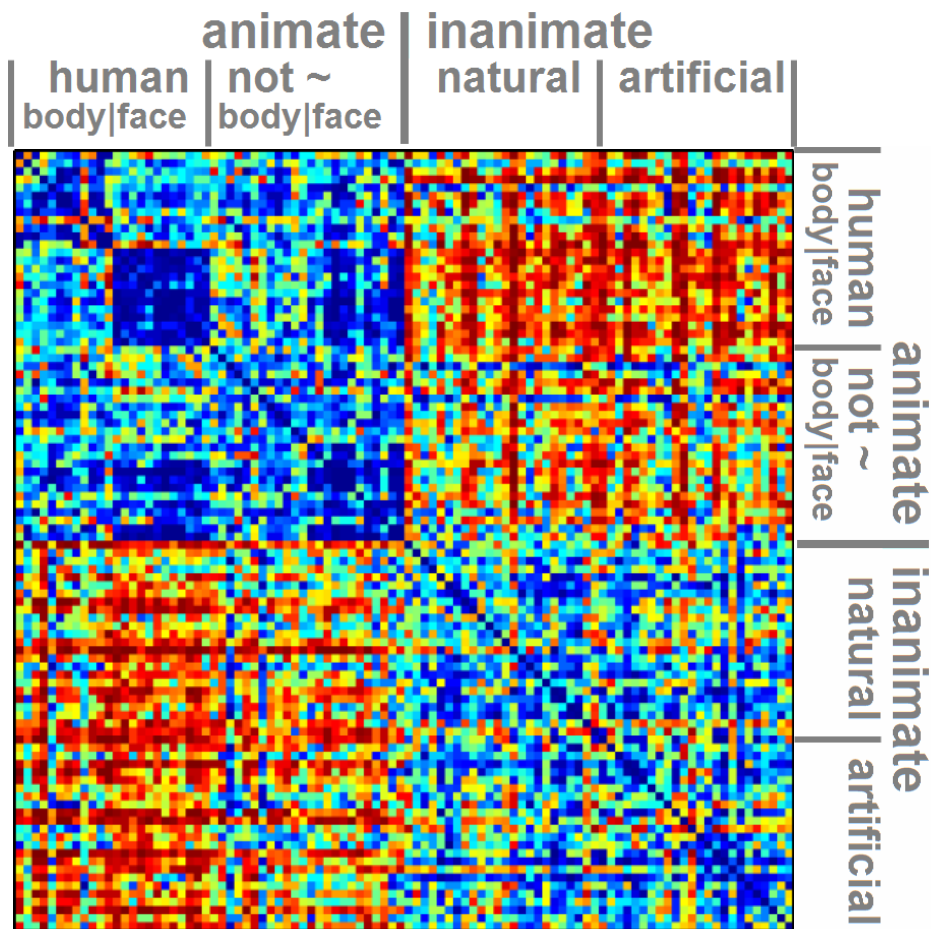


# Visual Stimuli



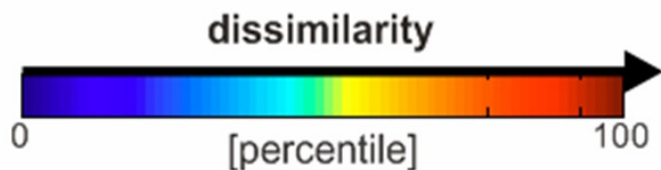
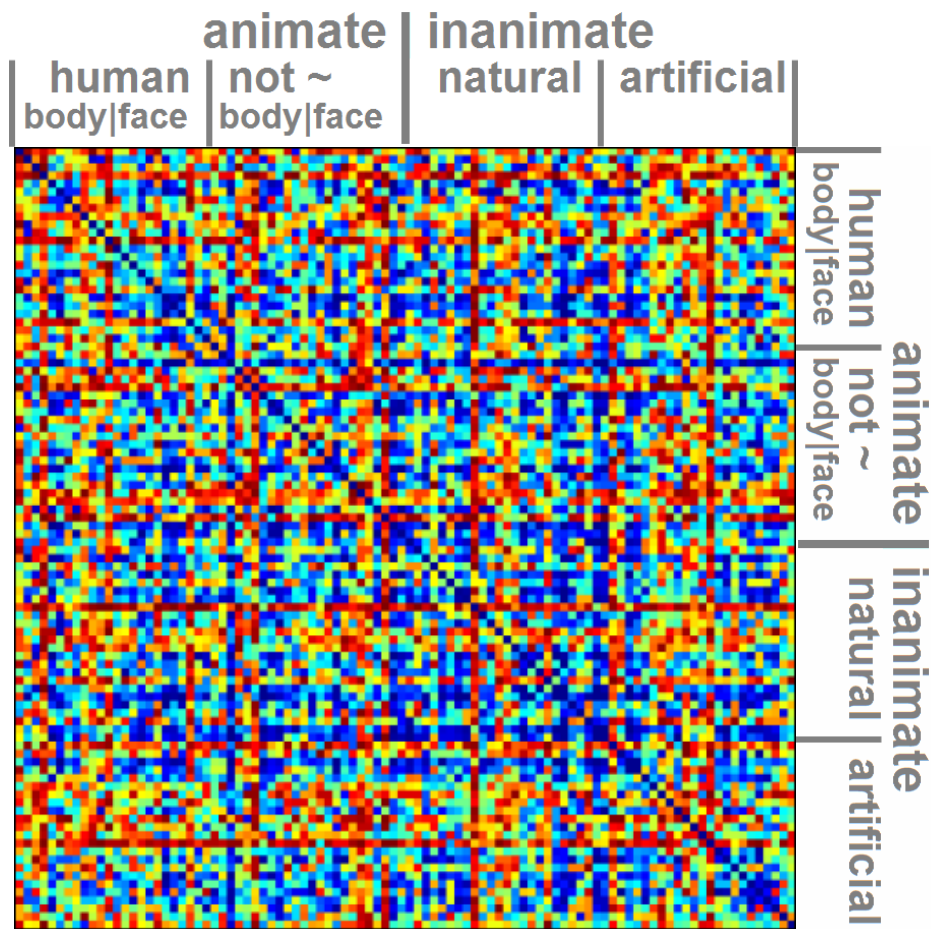
# Human IT

(1000 visually most responsive voxels)



# Human Early Visual Cortex

(1057 visually most responsive voxels)



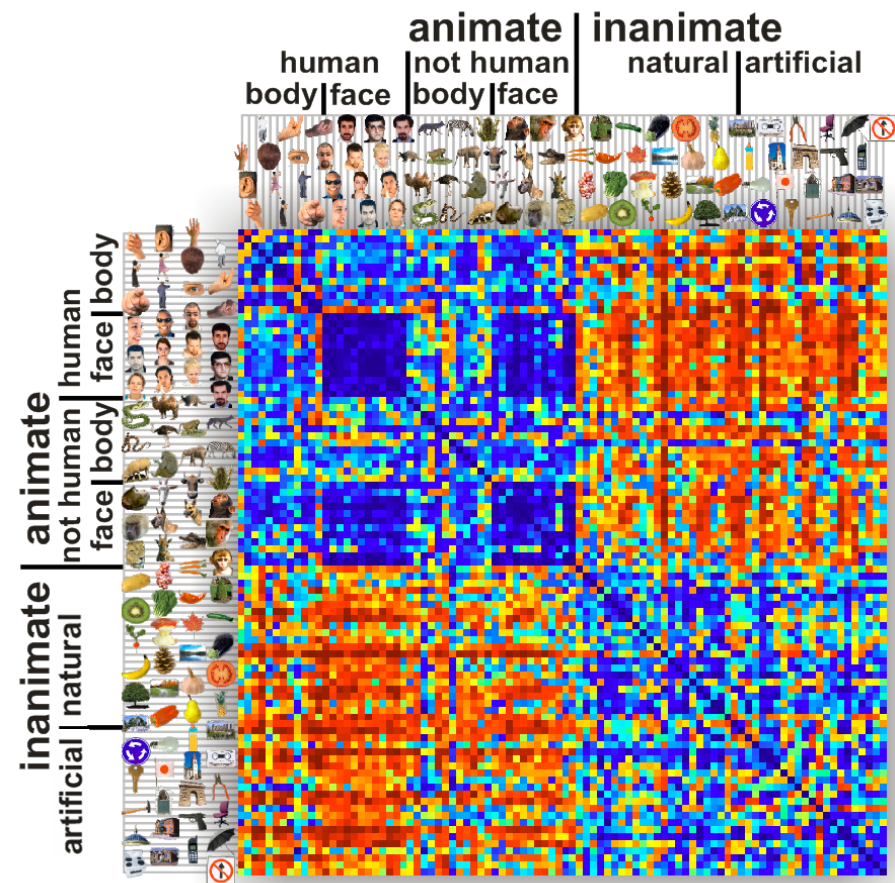
# Monkey-Human Comparison Procedure

## Human

- fMRI in four subjects  
(repeated sessions,  
>12 runs per subject)
- "quick" event-related  
design  
(stimulus duration: 300ms,  
stimulus onset asynchrony: 4s)
- fixation task  
(with discrimination of fixation-point  
color changes)
- occipitotemporal  
measurement slab  
(5-cm thick)
- small voxels ( $1.95 \times 1.95 \times 2 \text{mm}^3$ )
- 3T magnet, 16-channel coil  
(SENSE, acc. fac. 2)

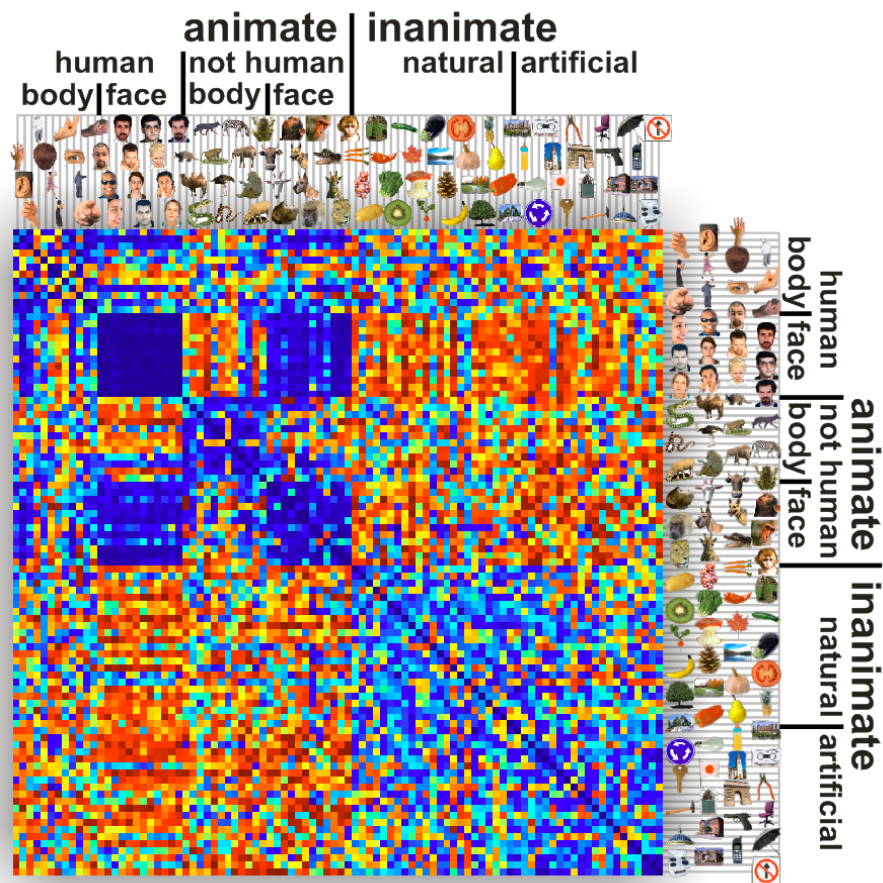
## Monkey (Kiani et al. 2007)

- single-cell recordings  
in two monkeys
- rapid serial presentation  
(stimulus duration: 105ms)
- fixation task
- electrodes in anterior IT  
(left in monkey 1, right in monkey 2)
- 674 cells total
- windowed spike count  
(140-ms window starting 71ms after  
stimulus onset)



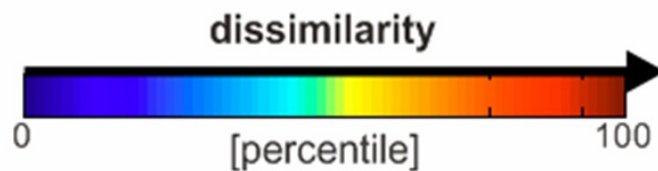
average of 4 subjects  
fixation-color task  
316 voxels

**man**



average of 2 monkeys  
fixation task  
>600 cells

**monkey**



# 5. Neuronal Current MRI

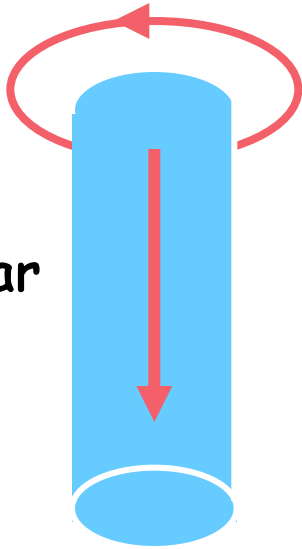
## Motivation:

- Direct fMRI of neuronal activity.

## Studies:

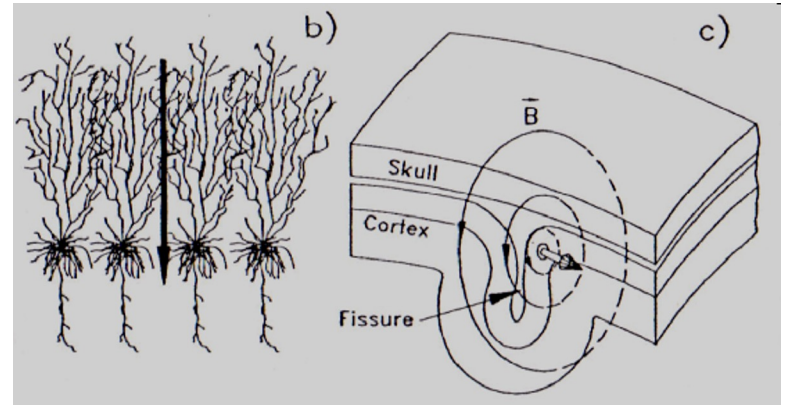
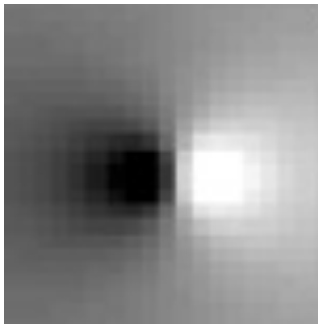
- Model
- Phantom Studies
- Cell Cultures at 7T and 3T

Magnetic Field



Intracellular  
Current

Surface Fields

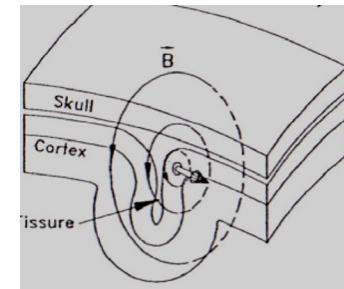


100 fT at on the scalp

J.P. Wikswo Jr et al. *J Clin  
Neurophys* 8(2): 170-188, 1991

# Magnetic field associated with a bundle of dendrites

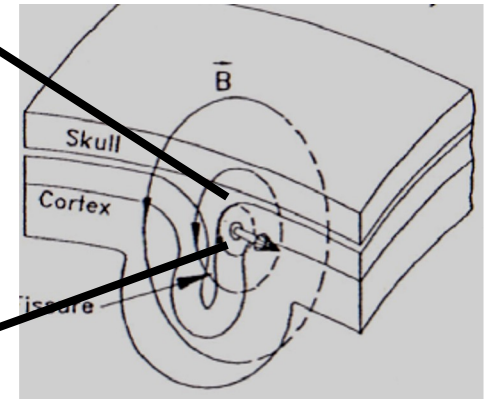
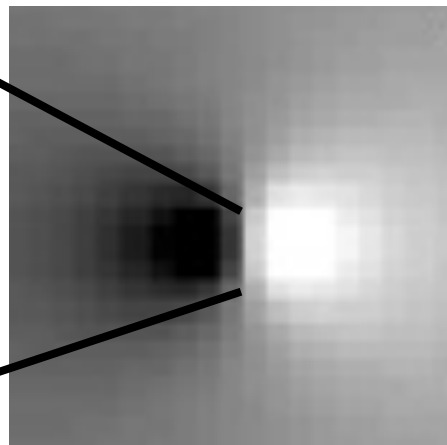
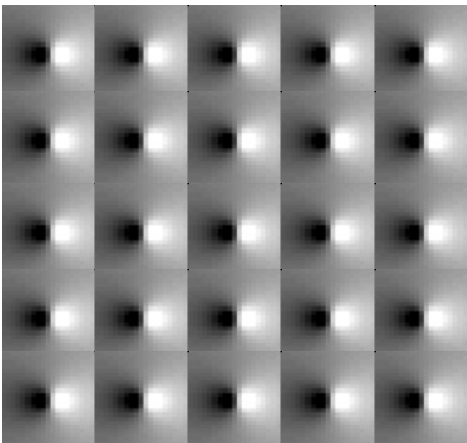
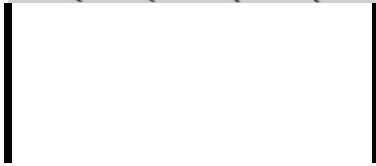
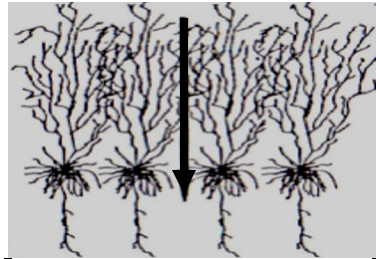
Because  $B_{MEG} = 100 \text{ fT}$  is measured by MEG on the scalp



at least 50,000 neurons ( $0.002 \text{ fT}$  (per dendrite)  $\times 50,000 = 100 \text{ fT}$ ), must coherently act to generate such field. These bundles of neurons produce, within a typical voxel,  $1 \text{ mm} \times 1 \text{ mm} \times 1 \text{ mm}$ , a field of order:

$$B_{MRI} = B_{MEG} \left( \frac{r_{MEG}}{r_{MRI}} \right)^2 = B_{MEG} \left( \frac{4 \text{ cm}}{0.1 \text{ cm}} \right)^2 = 1600 B_{MEG} \quad B_{MRI} \approx 0.2 \text{ nT}$$

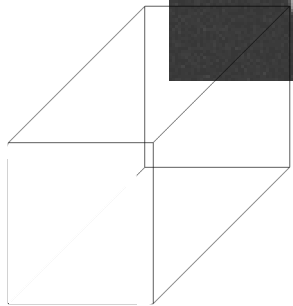
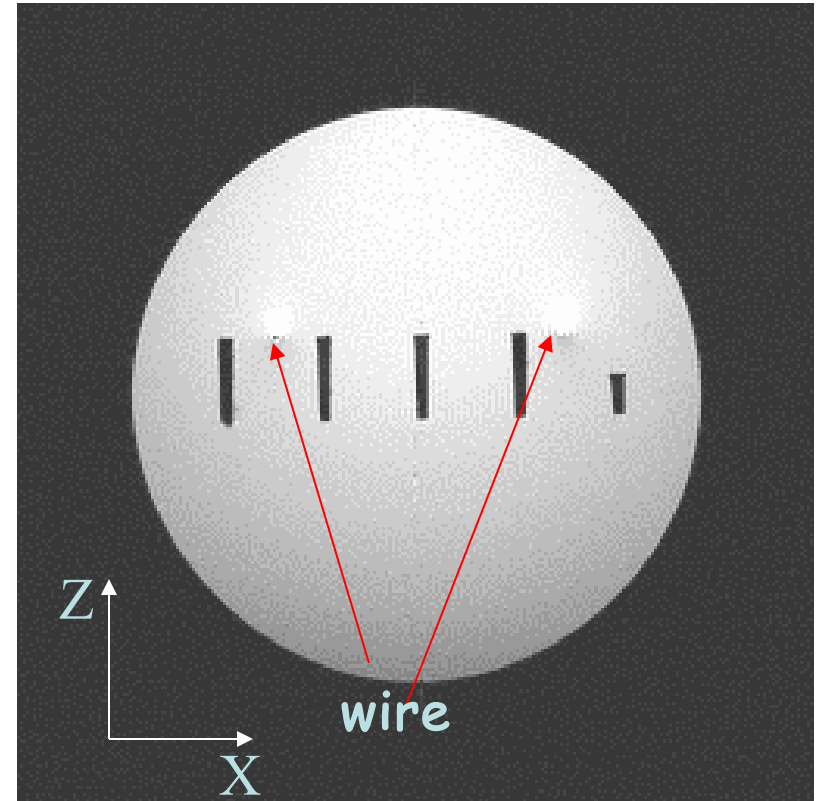
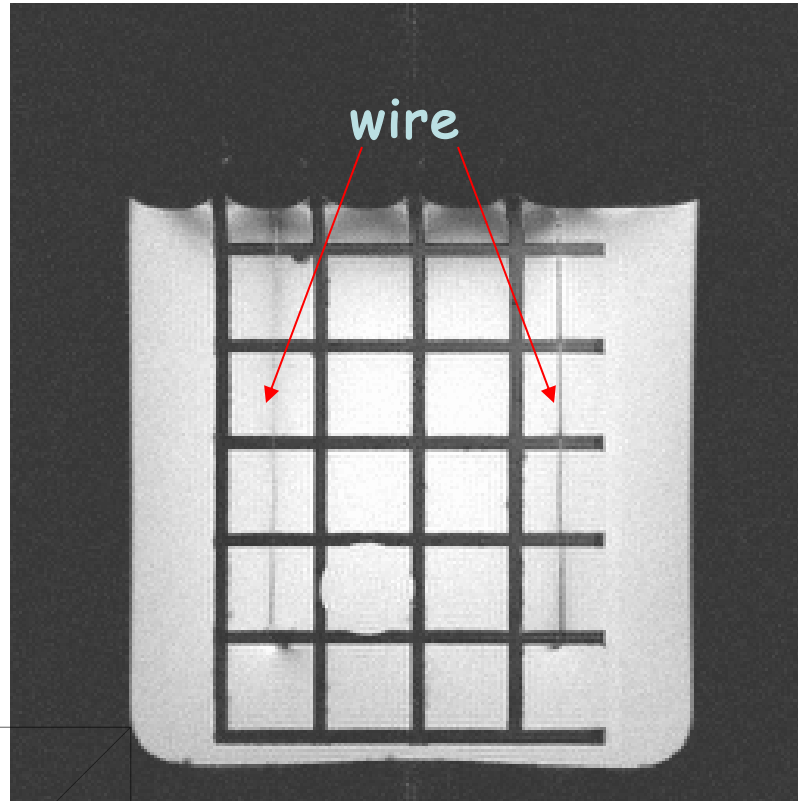
## Surface Field Distribution Across Spatial Scales



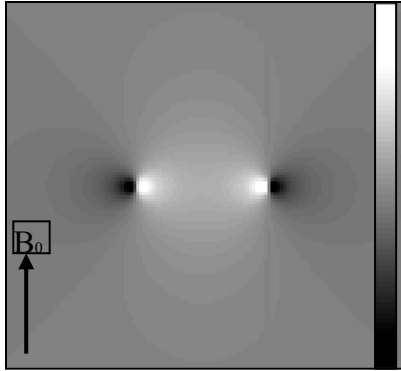
Adapted from: J.P. Wikswo Jr et al.  
*J Clin Neurophy* 8(2): 170-188, 1991



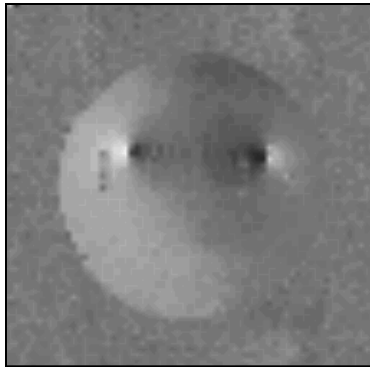
# Current Phantom Experiment



calculated  $B_c \parallel B_0$

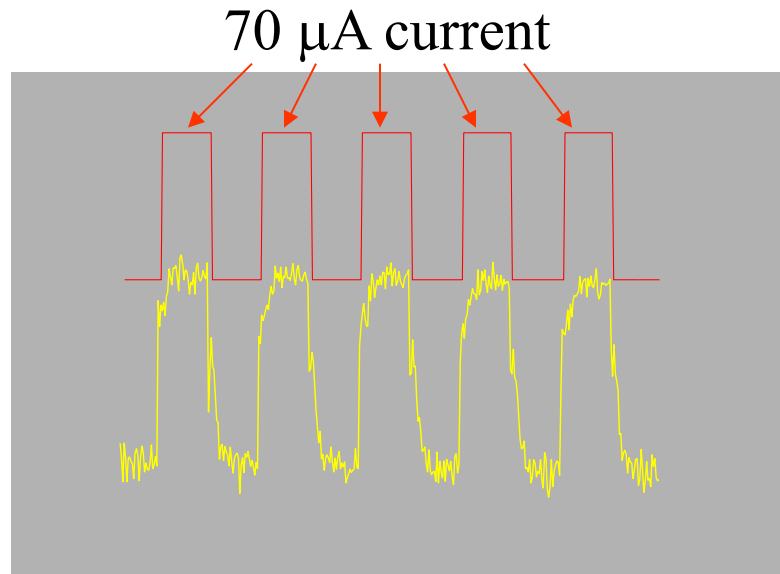


$\Delta\phi \cong 20^\circ$

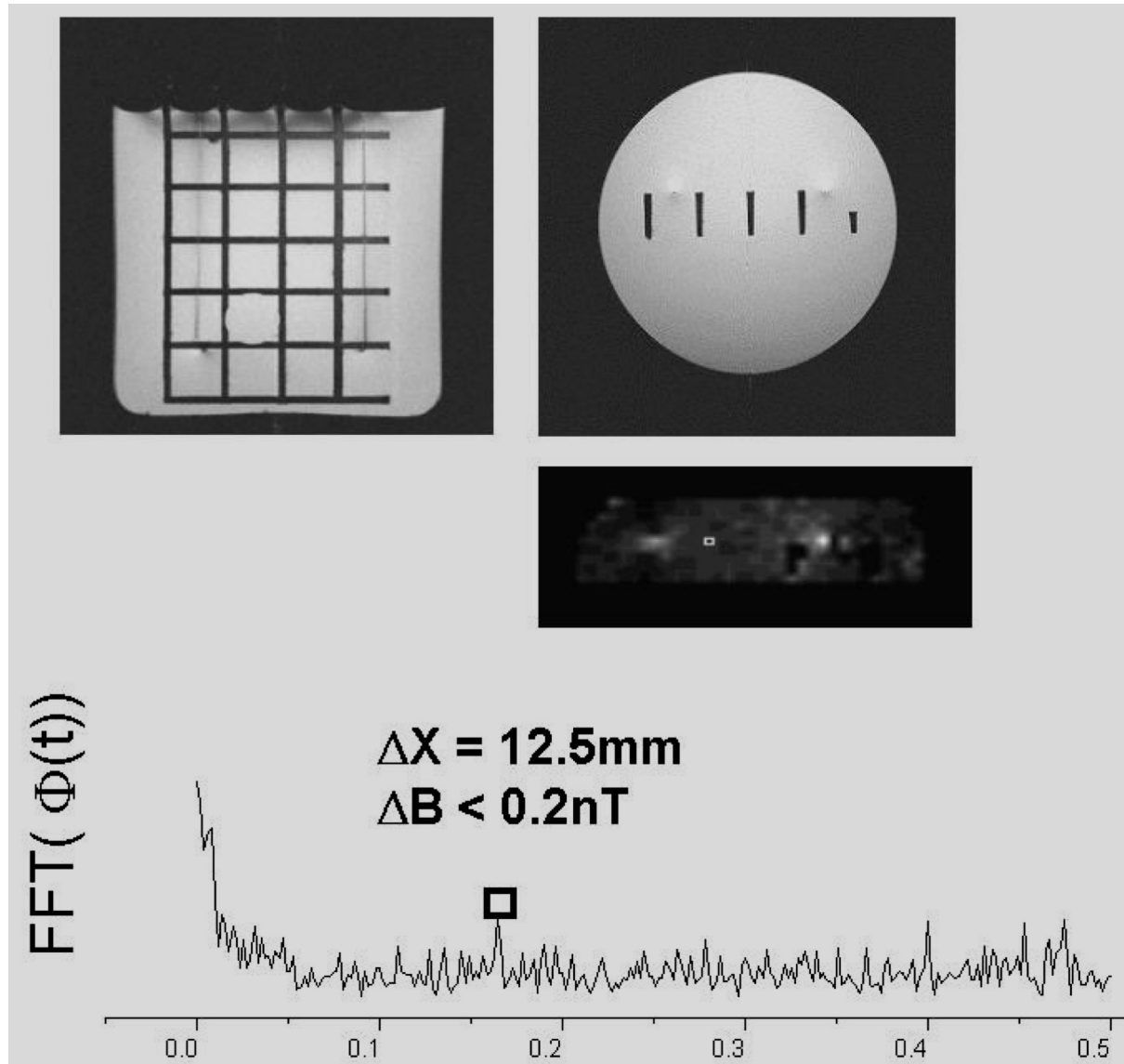


Correlation image

Measurement



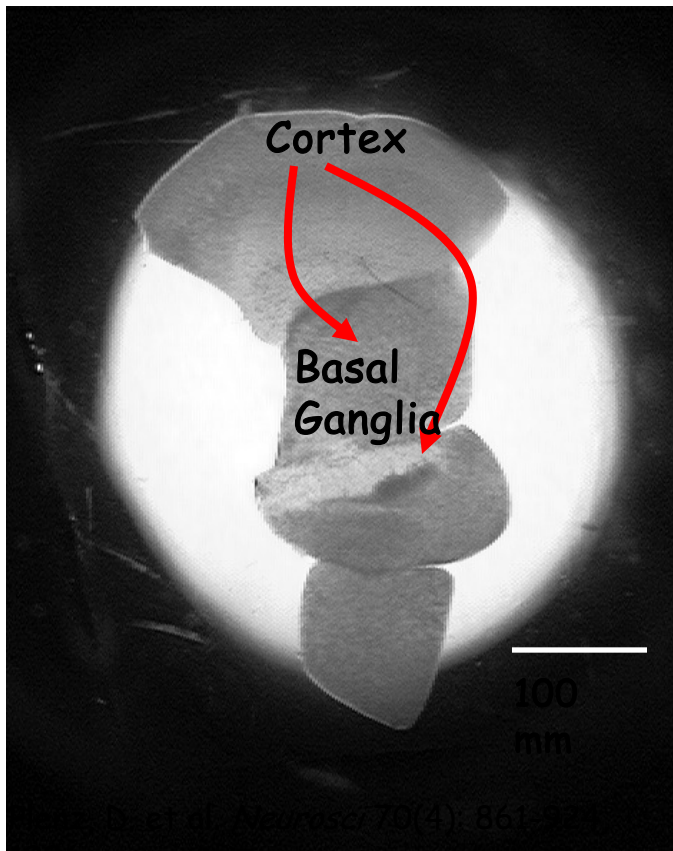
Single shot GE EPI



J. Bodurka, P. A. Bandettini. *Magn. Reson. Med.* 47: 1052-1058, (2002).

## in vitro model

Organotypic (*no blood supply or hemoglobin traces*) sections of newborn-rat somato-sensory Cortex & Basal Ganglia



- Size: in-plane: ~1-2mm<sup>2</sup>, thickness: 60-100μm
- Neuronal Population: 10,000-100,000
- Spontaneous synchronized activity < 2Hz
- Epileptiform activity
- Spontaneous beta freq. activity (20-30Hz)
- Network Activity Range: ~ 0.5-15μV

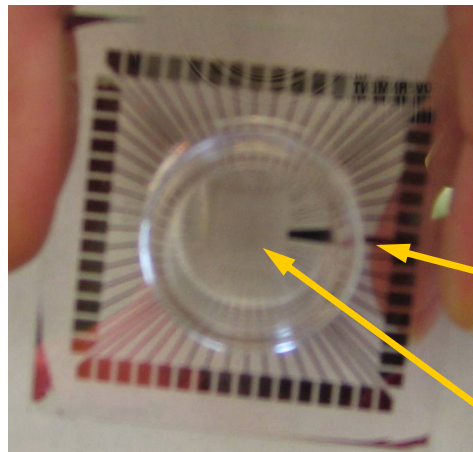
## *Culture Preparation*

### Multi-Electrode Arrays (MEA)

Multichannelsystems Germany 8x8 electrodes

0.8ml culture medium

#### Multi-Electrode Array



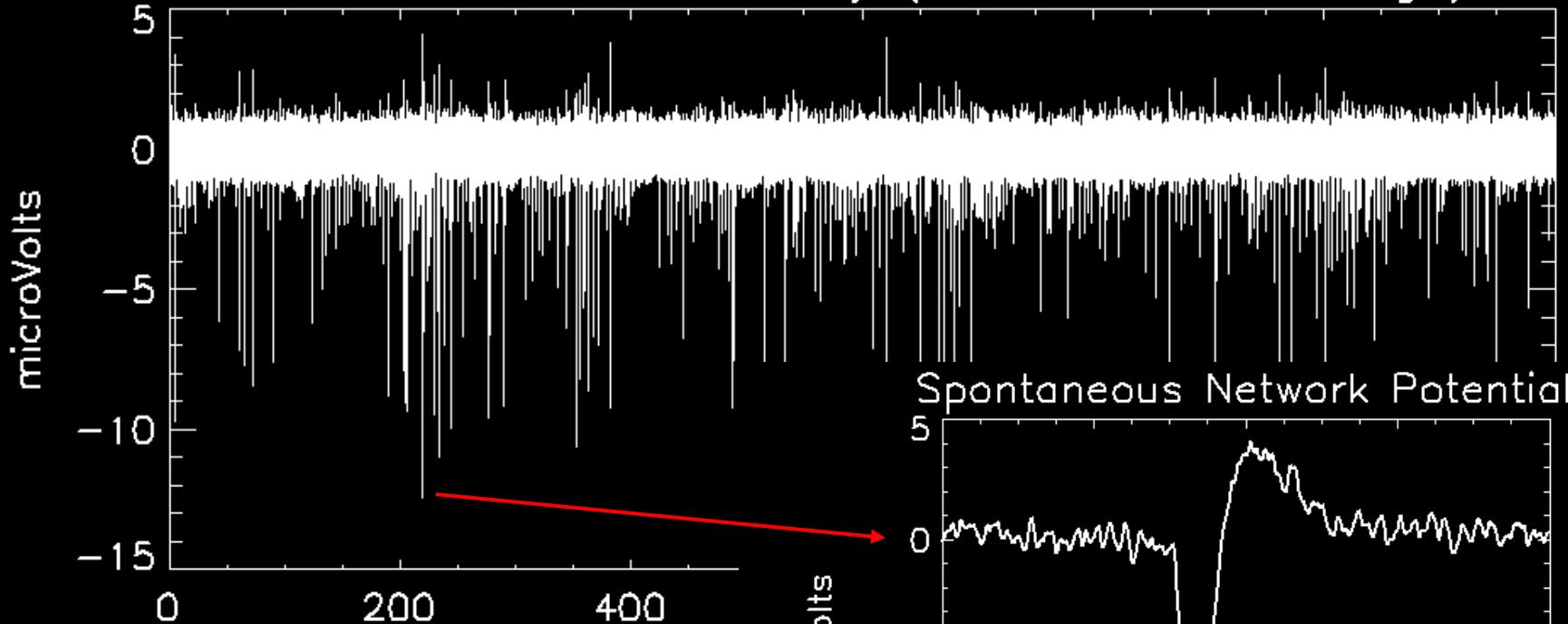
Reference  
electrode

Culture site

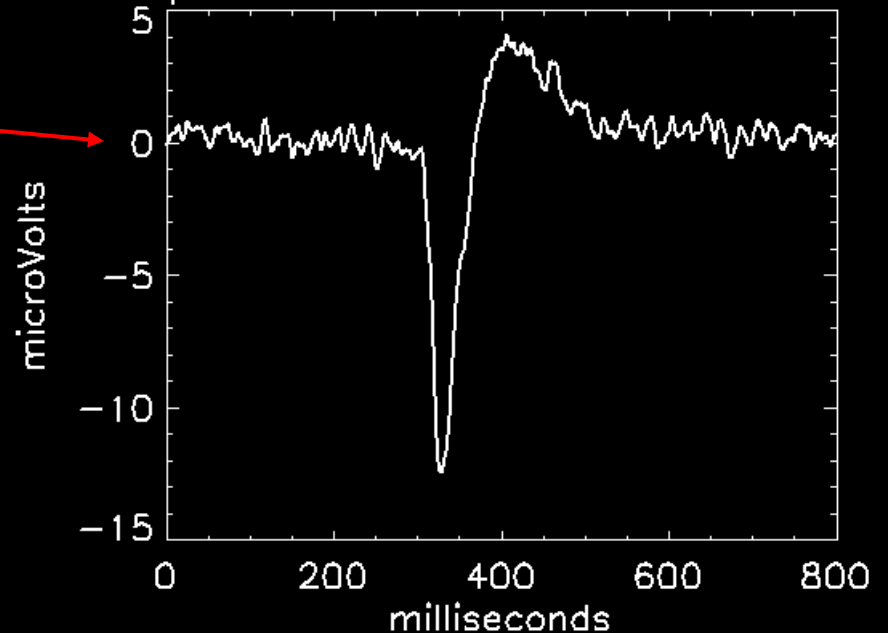
10mm

# Multi-Electrode Array EEG recording

Neuronal Network Activity (64 electrode average)



Spontaneous Network Potential



Multi-Electrode Array (MEA)  
EEG Recording  
1 kHz sampling rate, 20 minutes  
8x8 electrode configuration

## in vitro MR protocol

### Imaging (3T)

- Spin-Echo EchoPlanar Imaging

SE EPI  
image

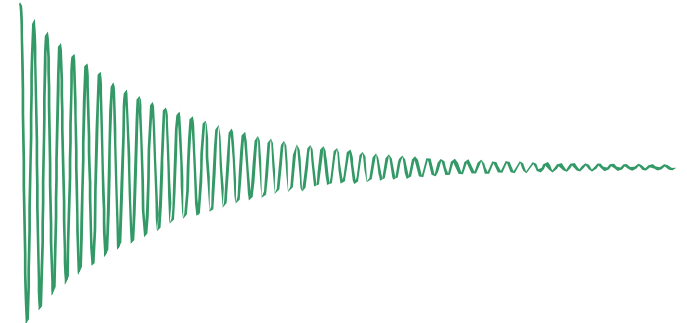


- voxel size:  $\sim 3 \times 3 \times 3$  mm
- Sampling Rate :1 Hz (TR: 1sec)
- TE: 60 ms
- Readout :44 ms

### NMR (7T)

- free induction decay (FID) acquisition

FID



- slab size:  $\sim 2 \times 10 \times 1$  mm
- Sampling Rate :10 Hz (TR: 100ms)
- TE : 30 ms
- Readout : 41 ms

# in vitro MR experiment design

## Imaging (3T)

### Six Experiments

Active : 10 min (600 images) neuronal activity present

Inactive : 10 min (600 images) neuronal activity terminated via TTX administration

## NMR (7T)

### Six Experiments

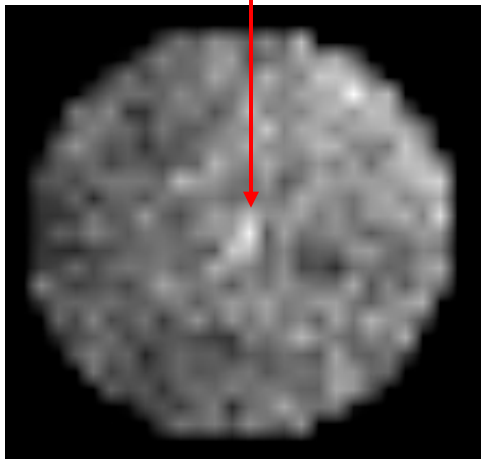
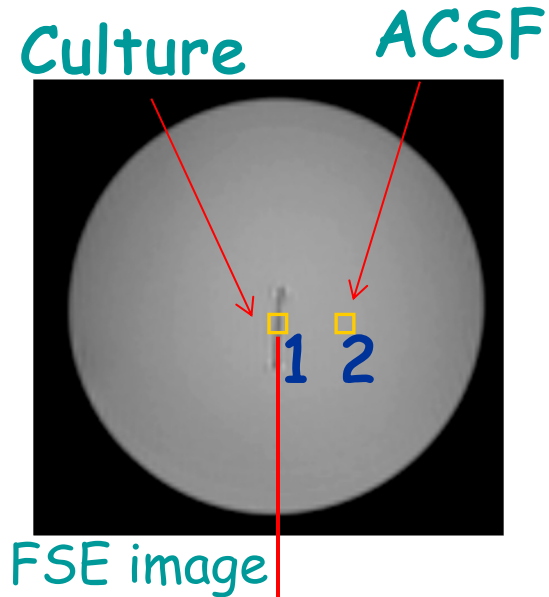
Active : ~17 min (10,000 images) neuronal activity present

Inactive : ~17 min (10,000 images) neuronal activity terminated via TTX administration

*Pre- and Post- MR scan electrical recordings*

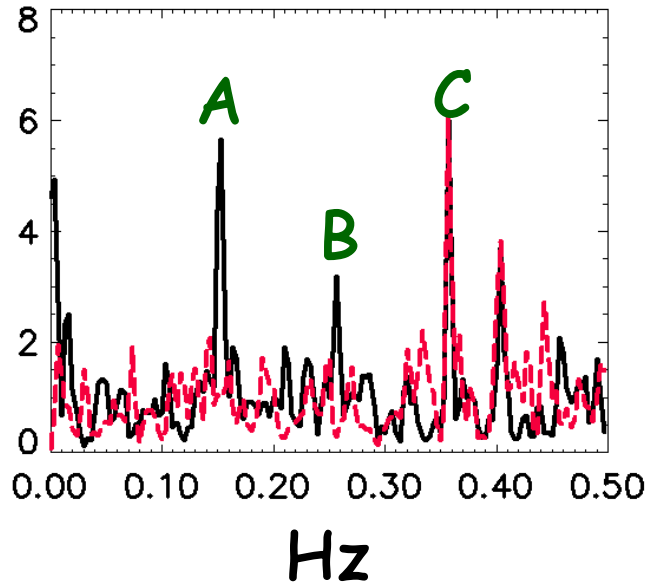


# 3 Tesla data

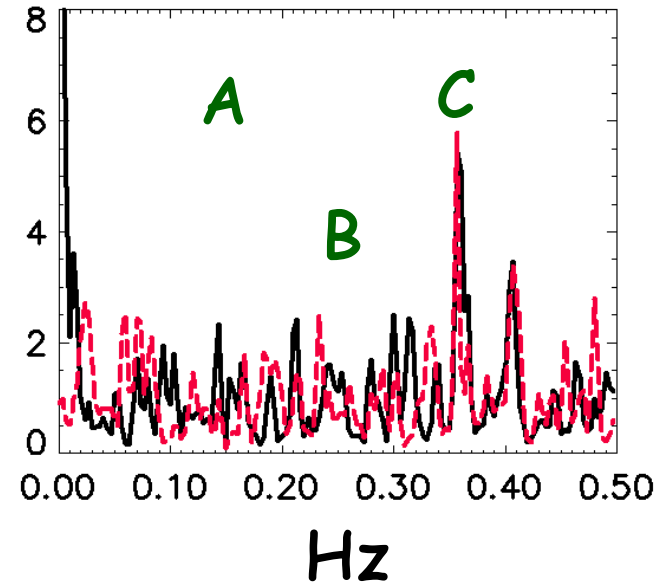


0.15Hz map

1: culture



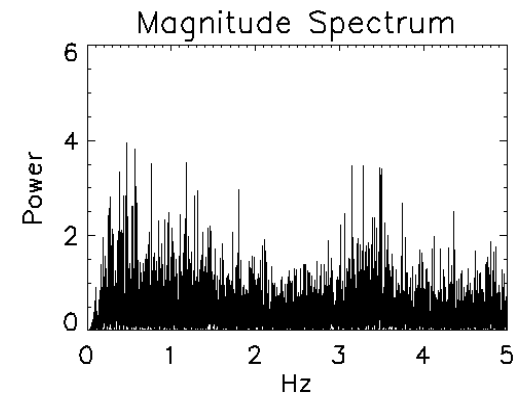
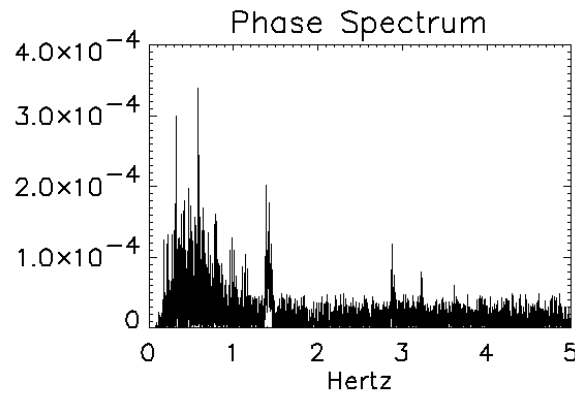
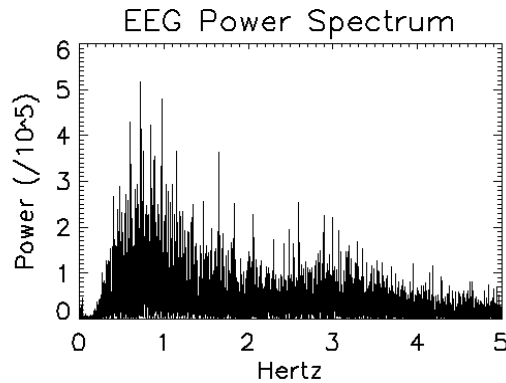
2: ACSF



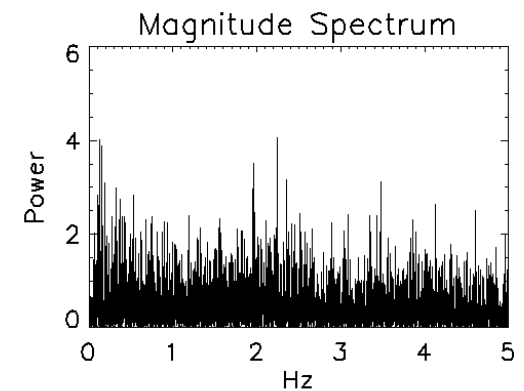
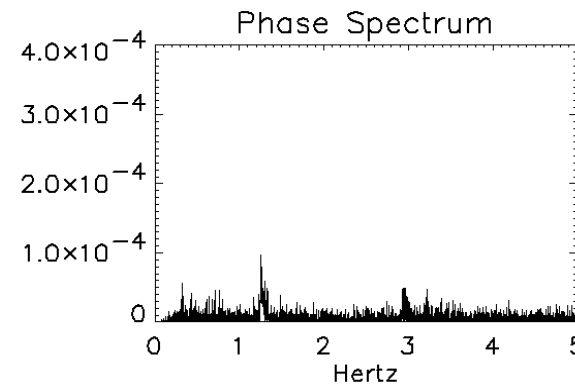
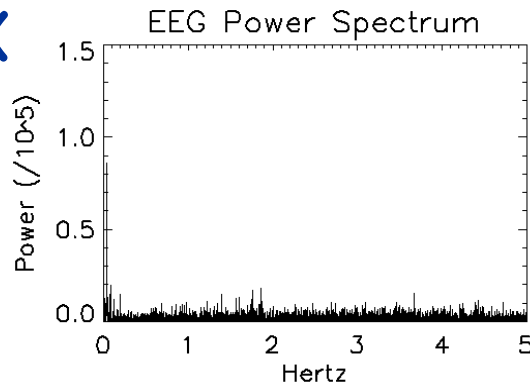
Active condition: black line  
Inactive condition: red line

A: 0.15 Hz activity, on/off frequency  
B: activity  
C: scanner noise (cooling-pump)

# 7 Tesla data



TTX



Power decrease between PRE & TTX EEG : ~ 81%    Decrease between PRE & TTX MR phase: ~ 70%    Decrease between PRE & TTX MR magnitude: ~ 8%

N. Petridou, D. Plenz, A. C. Silva, J. Bodurka, M. Loew, P. A. Bandettini,  
*Proc. Nat'l. Acad. Sci. USA.* 103, 16015-16020 (2006).

1. Dynamics

2. Fluctuations

3. Experimental Design

4. Pattern Information

5. Neuronal Current MRI



September, 1991

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<b>Youn Kim</b>	<b>post bac IRTA</b>
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<b>Naja Waters</b>	<b>post bac IRTA</b>

## Functional MRI Facility

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<b>Kenny Kan</b>	<b>technologist</b>
<b>Kay Kuhns</b>	<b>admin. lab manager</b>
<b>Wenming Luh</b>	<b>staff scientist</b>
<b>Sean Marrett</b>	<b>staff scientist</b>
<b>Marcela Montequin</b>	<b>technologist</b>
<b>Sandra Moore</b>	<b>technologist</b>
<b>Sahra Omar</b>	<b>technologist</b>
<b>Alda Ottley</b>	<b>technologist</b>
<b>Paula Rowser</b>	<b>technologist</b>
<b>Adam Thomas</b>	<b>system admin</b>
<b>Karen Bove-Bettis</b>	<b>technologist</b>
<b>James Hoske</b>	<b>technologist</b>

Parameter	Description	Default value	Range evaluated
$E_0$	Resting oxygen extraction fraction	0.4	0.3–0.6
$v_0$	Resting blood volume fraction	0.03	0.03–0.18
$f_0$	Resting relative blood flow	$0.01 \text{ s}^{-1}$	0.01 s–0.16 s
$\Delta f$	Fractional blood flow change	0.4	–
$\alpha$	Steady-state flow–volume relationship	0.4	0.25–1.0
$\tau_{\text{MTT}}$	Blood mean transit time ( $v_0/f_0$ )	3 s	1.1 s–18 s
$\tau_+$	Viscoelastic time constant (inflation)	20 s	10 s–40 s
$\tau_-$	Viscoelastic time constant (deflation)	20 s	10 s–40 s
$a_1$	Weight for deoxyhemoglobin change	3.7	2.8–5.6
$a_2$	Weight for blood volume change	1.1	0.7–1.9

ON response amplitude: initial amp:	1.5 times steady state amp
Adaptation time constant:	1.5s
Refractory period:	5s
OFF response amplitude:	initial amp 0.5 times steady state amp
OFF response time constant:	0.5s

The initial overshoot amplitude and decay time were chosen to roughly match the local field potential change measured in macaque visual cortex in response to rotating checkerboard, as measured by Logothetis et al. (2001).

The refractory period was chosen to produce results somewhat consistent with observed BOLD refractory period (Huettel et al., 2000).

