

A closer look at fMRI

dynamics, fluctuations, and patterns

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1991

Neuronal Activation



Measured Signal

?

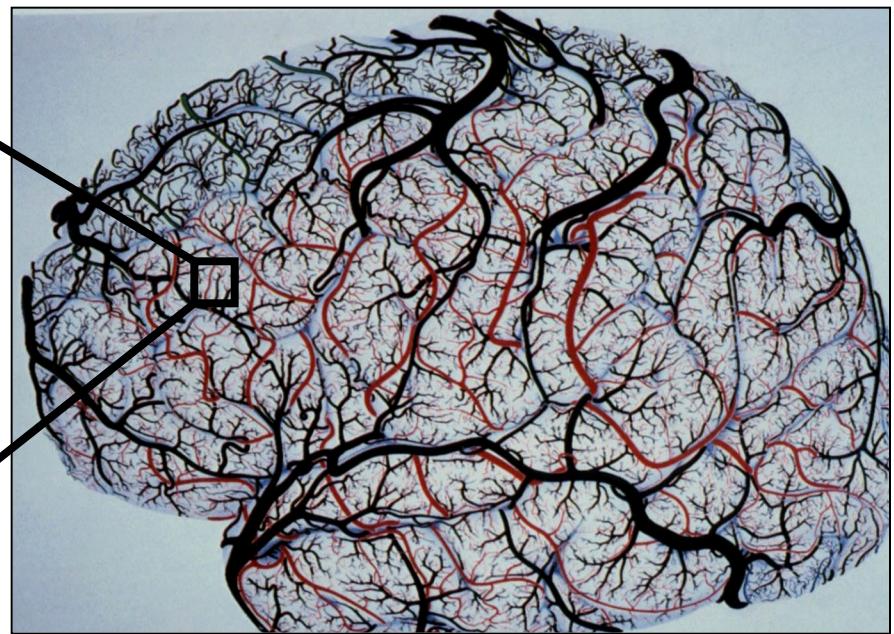
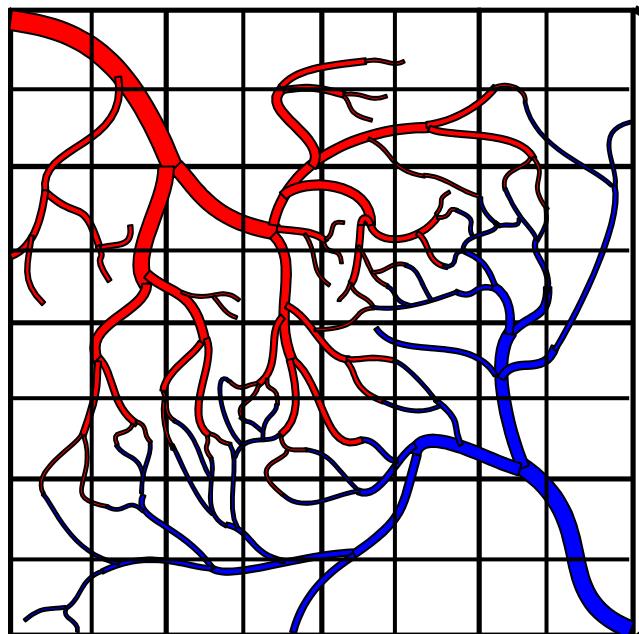


Hemodynamics

?



Noise



1. Dynamics

2. Fluctuations

3. Experimental Design

4. Pattern Information

5. Neuronal Current MRI

1. Dynamics

Motivation:

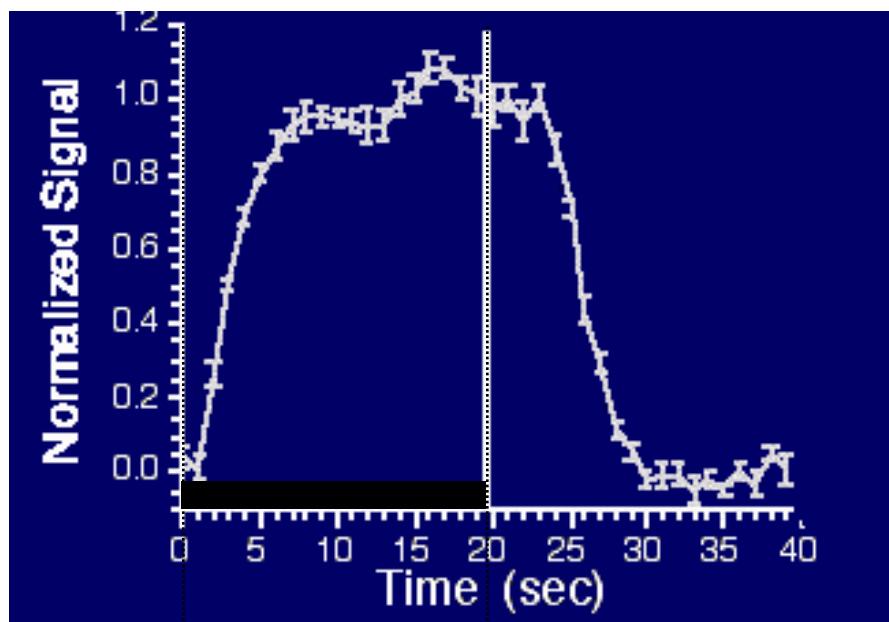
- To understand the neuronal and non-neuronal influences on the fMRI signal.

Studies:

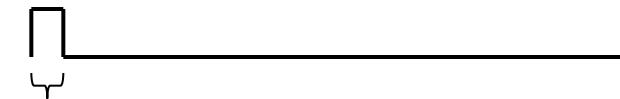
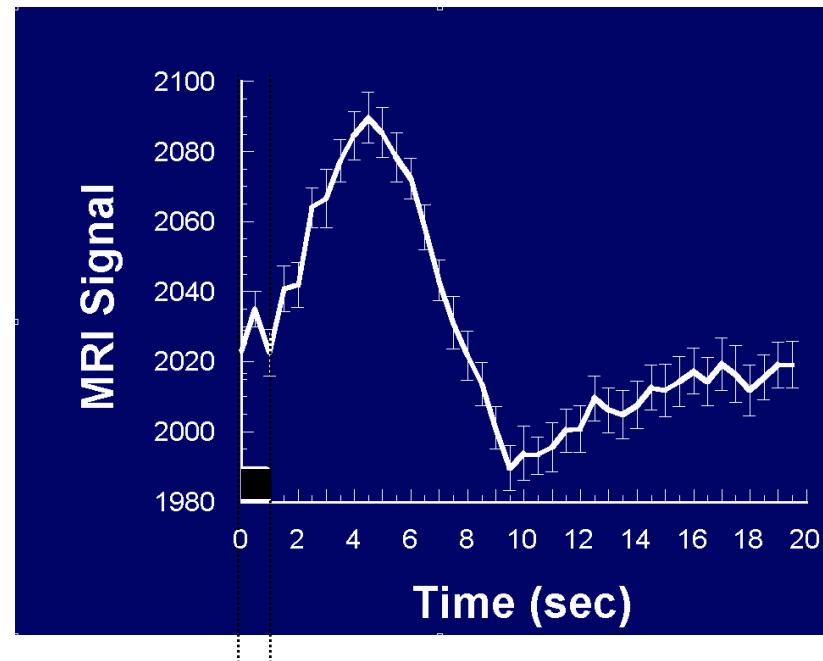
- Modulate timing: "on" duration, "off" duration, and duty cycle of visual cortex activation.
- Neuronal and Hemodynamic Modeling.
- MEG and fMRI Comparison.

The BOLD Signal

Blood Oxygenation Level Dependent (BOLD) signal changes

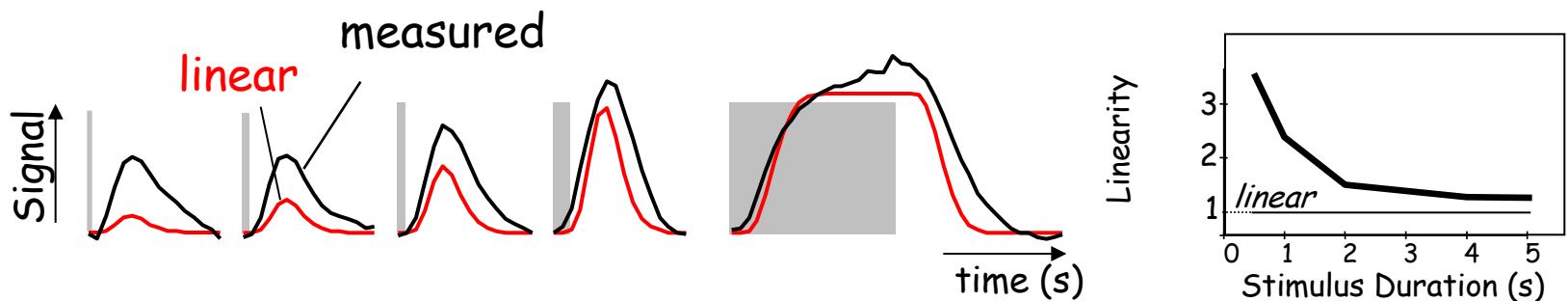


task



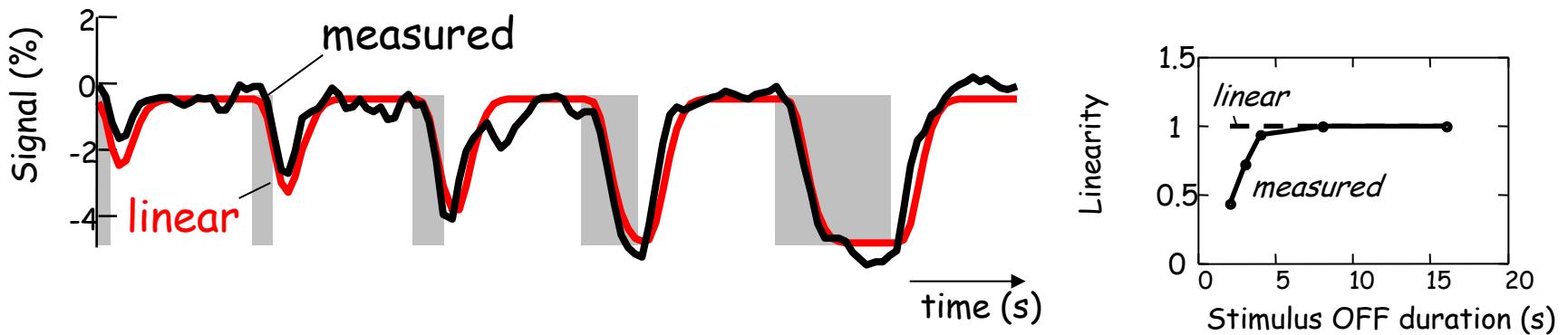
task

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



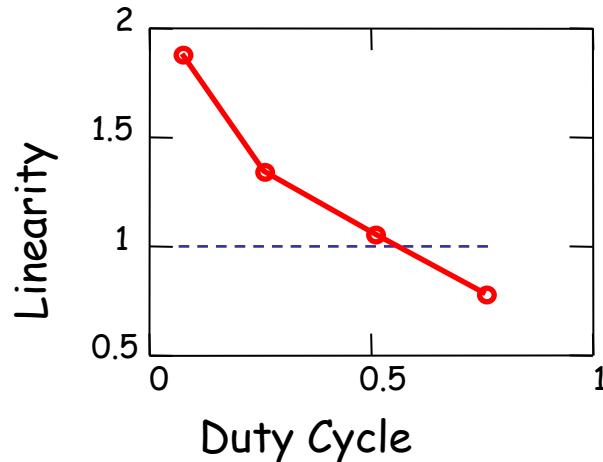
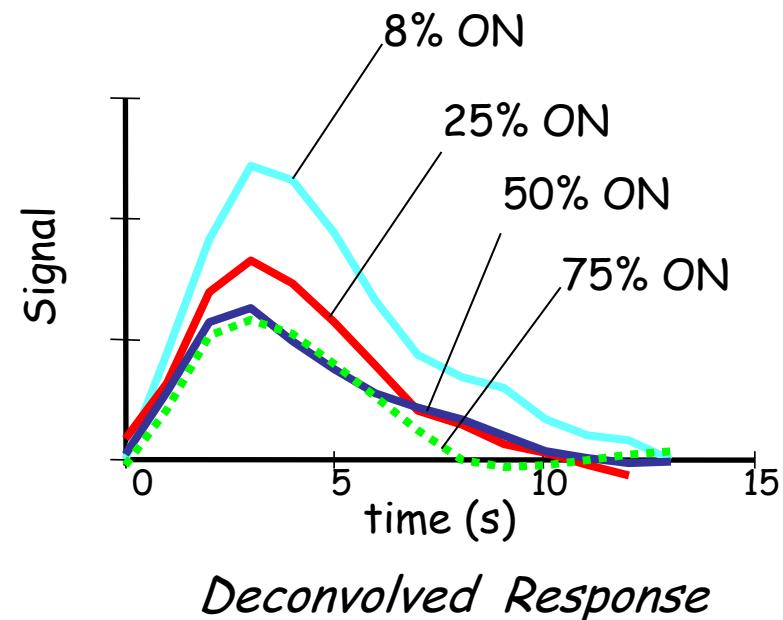
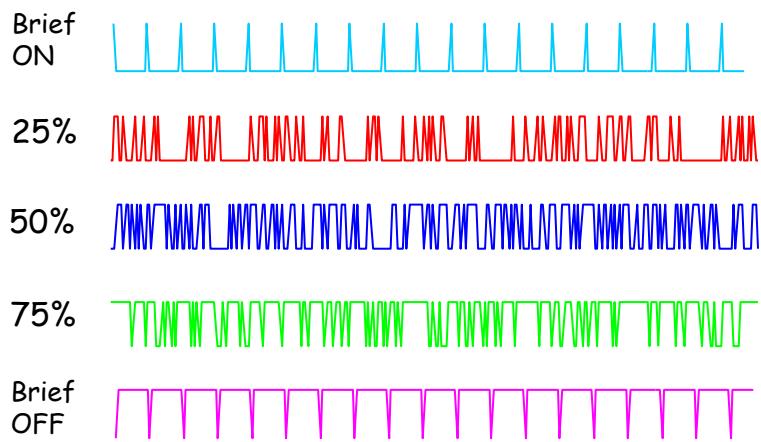
R. M. Birn, Z. Saad, P. A. Bandettini, NeuroImage, 14: 817-826, (2001)

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

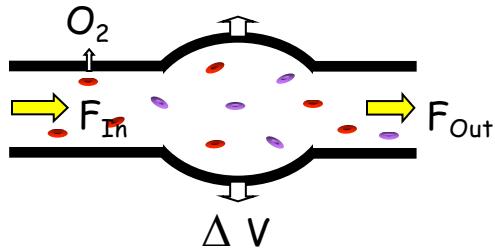


R.M. Birn, P. A. Bandettini, NeuroImage, 27, 70-82 (2005)

Varying the Duty Cycle

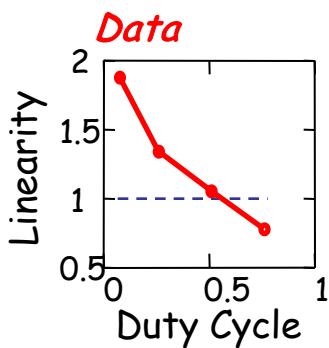
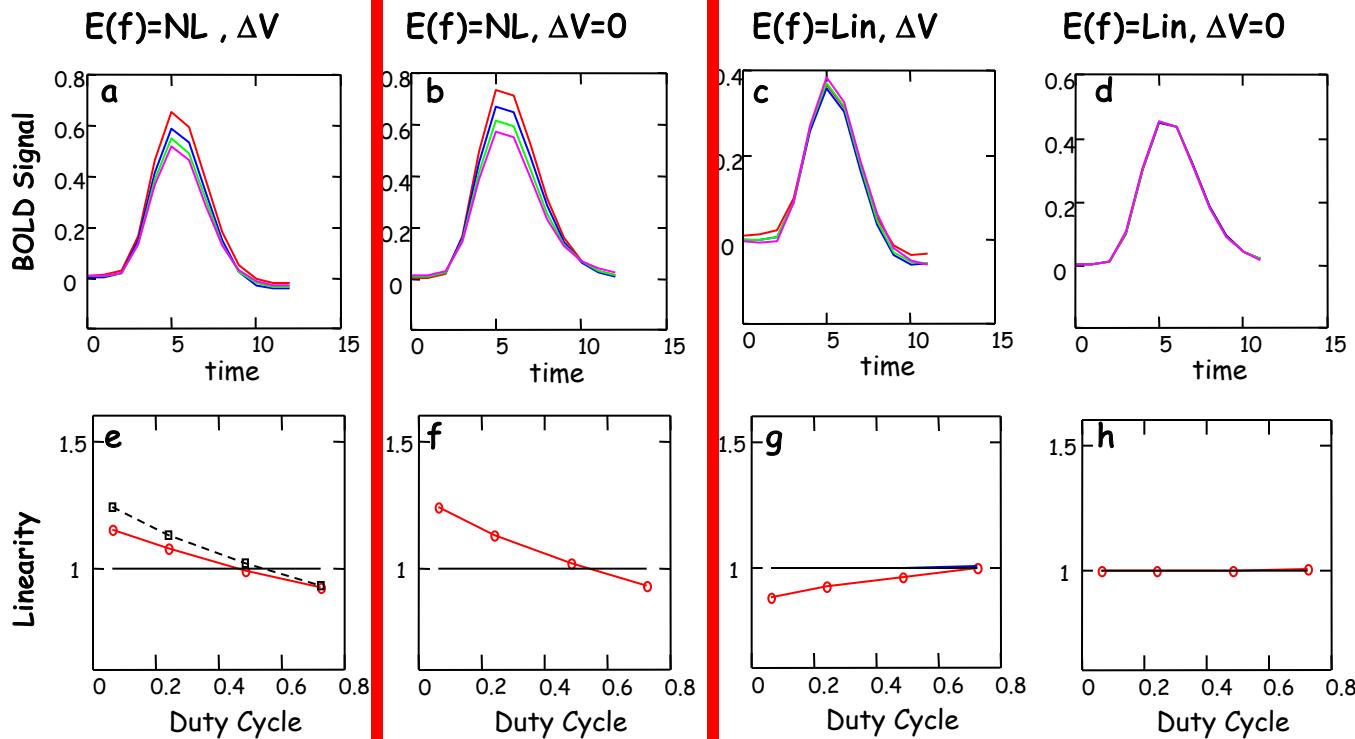
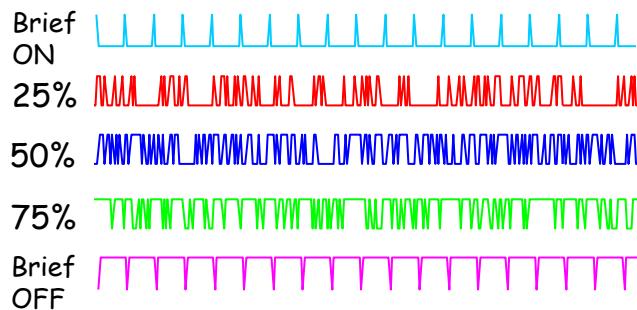


Simulation of Hemodynamic Mechanisms (Balloon model)

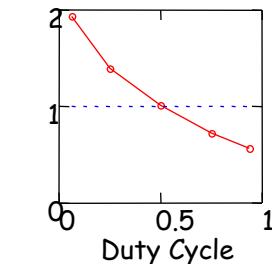
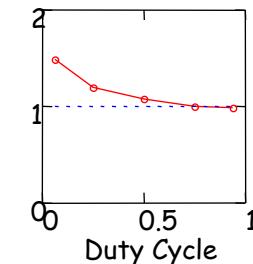
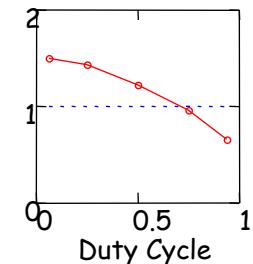
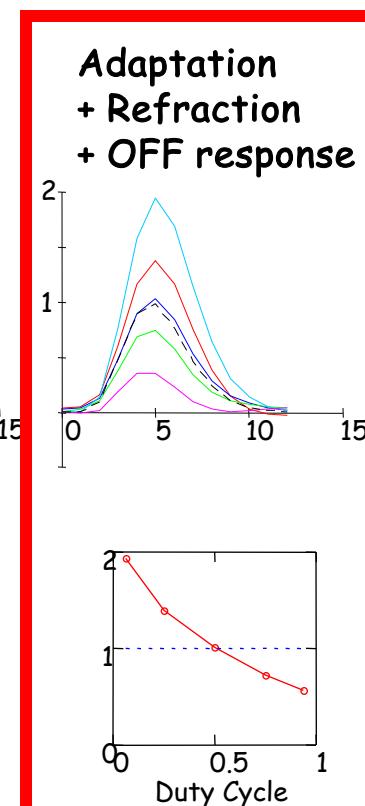
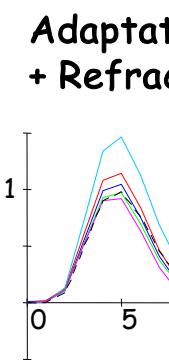
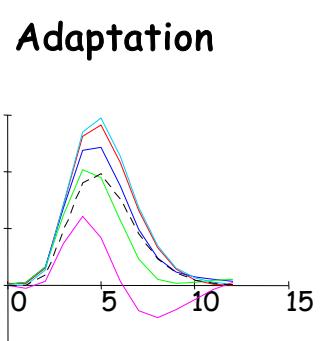
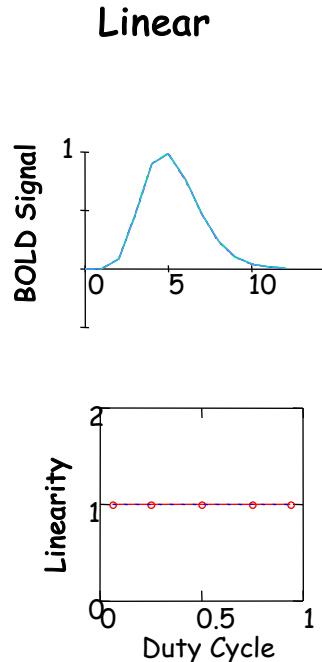
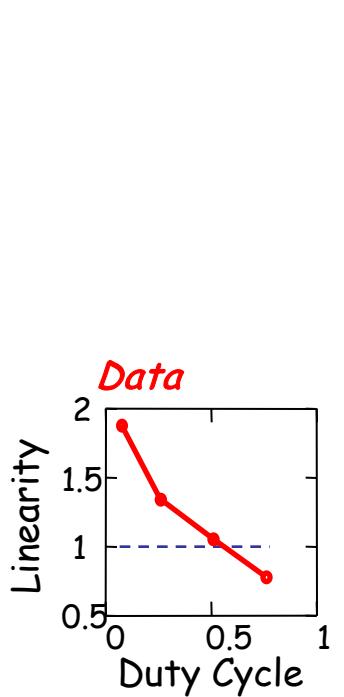
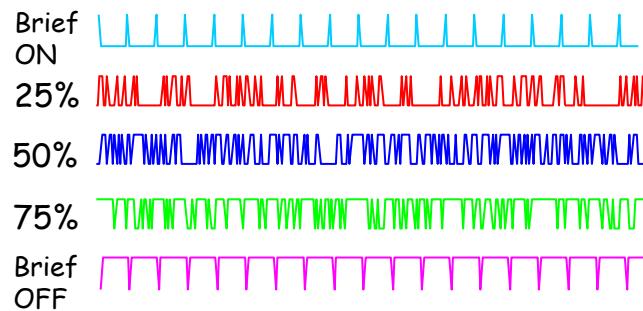
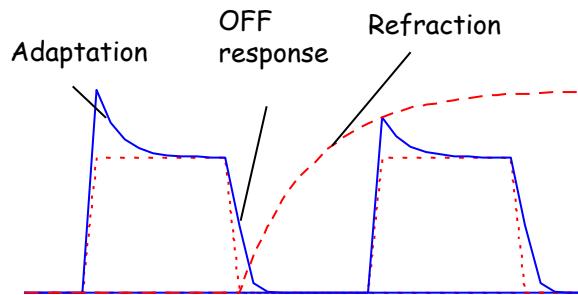


$E(f)$ = oxygen extraction fraction

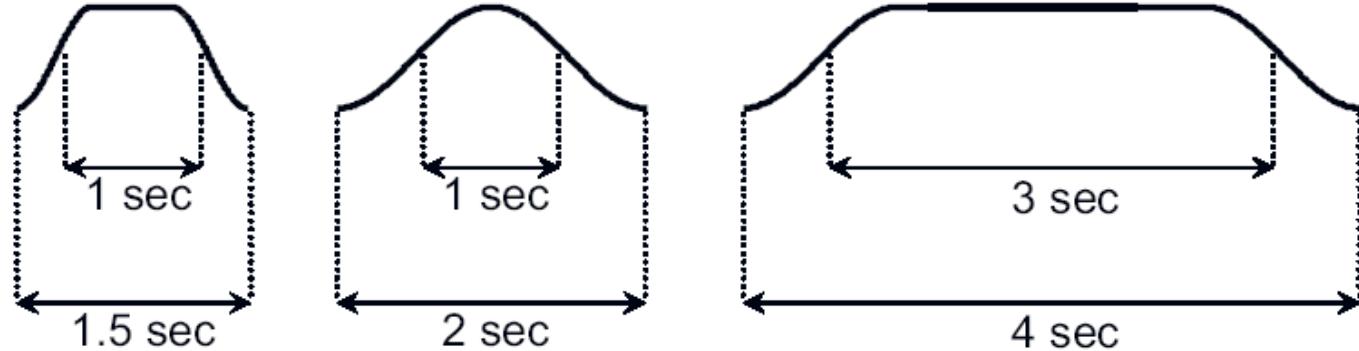
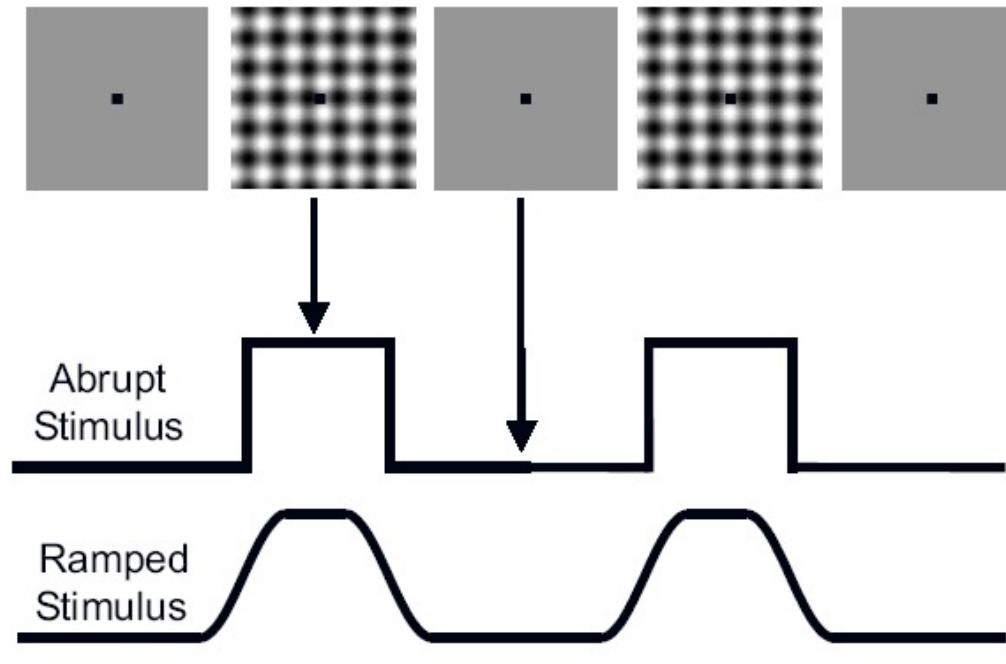
V = blood volume



Simulation of Neuronal Mechanisms

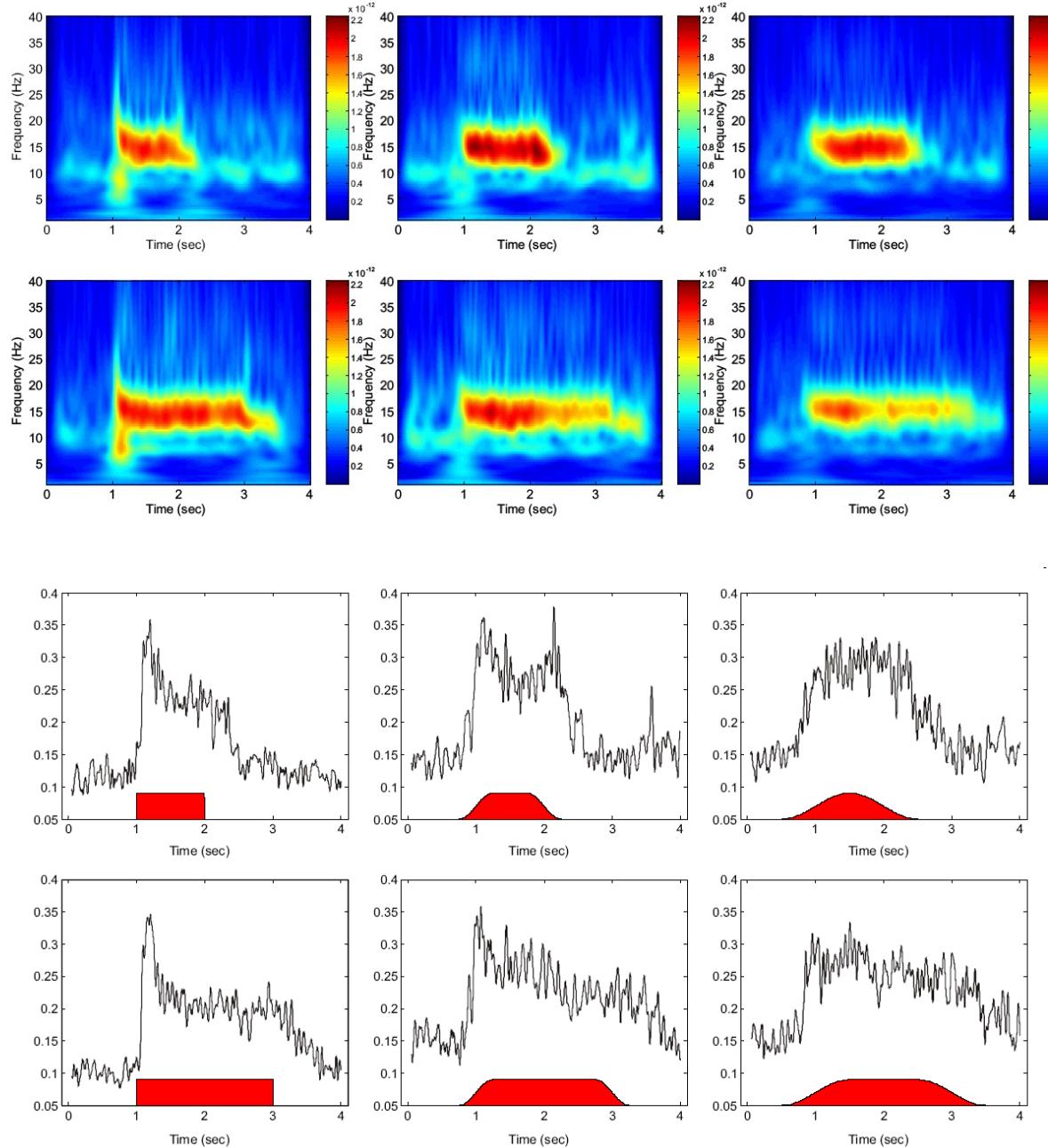


MEG & fMRI Linearity Comparison



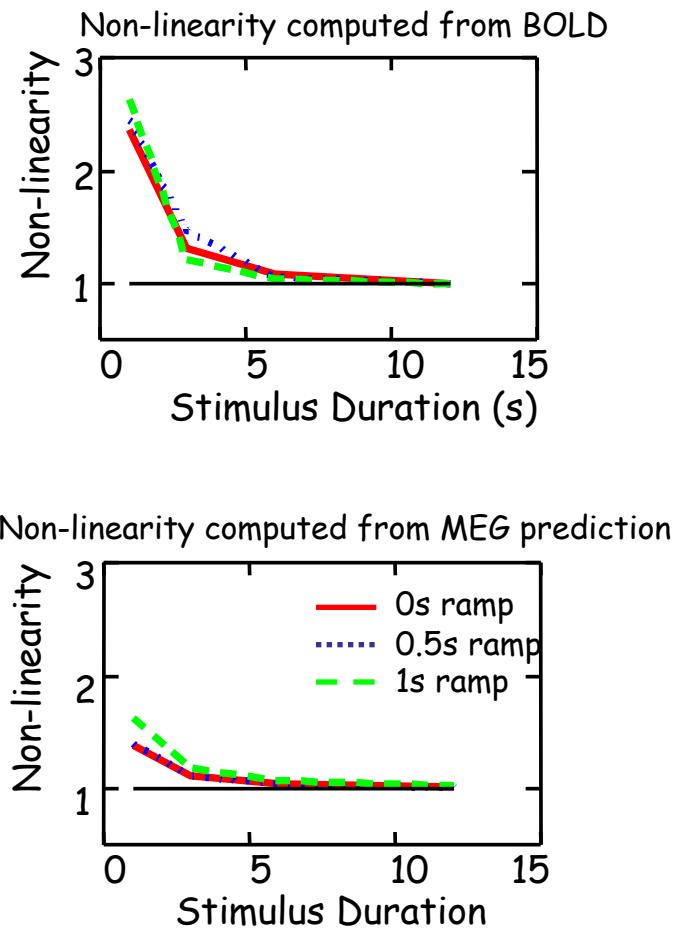
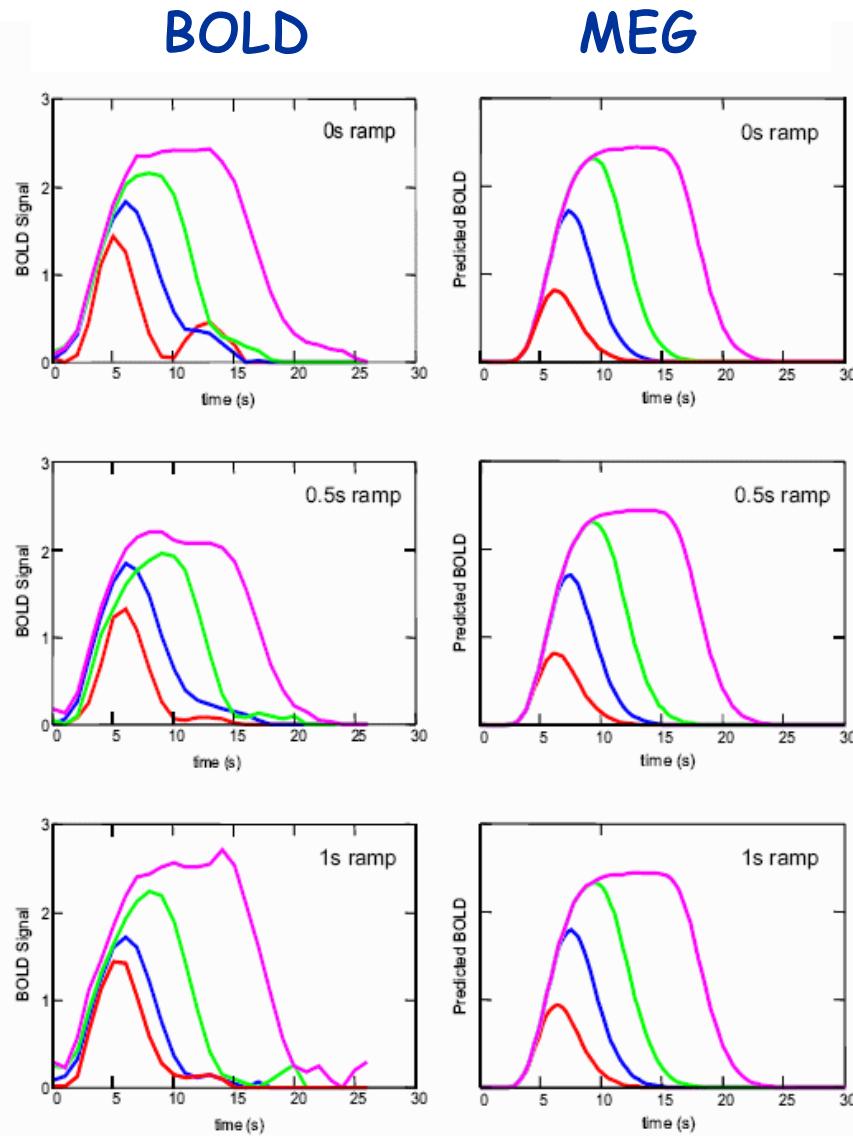
A. Tuan, R. M. Birn, P. A. Bandettini, G. M. Boynton, (submitted)

MEG Results



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

Measured and Predicted BOLD responses



2. Fluctuations

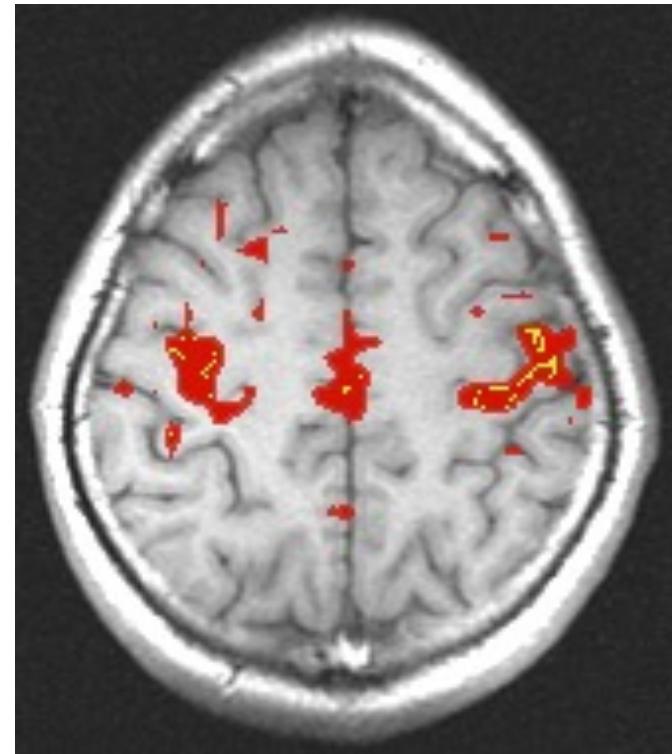
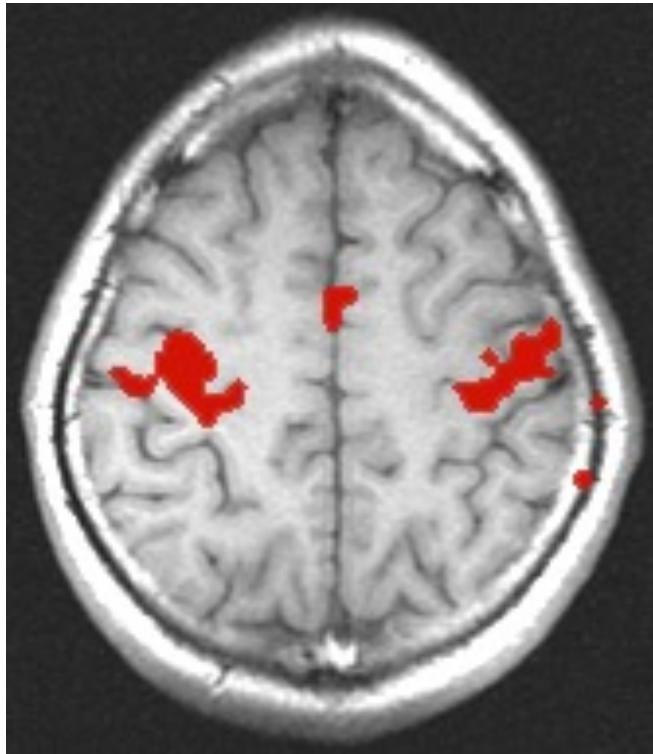
Motivation:

- 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

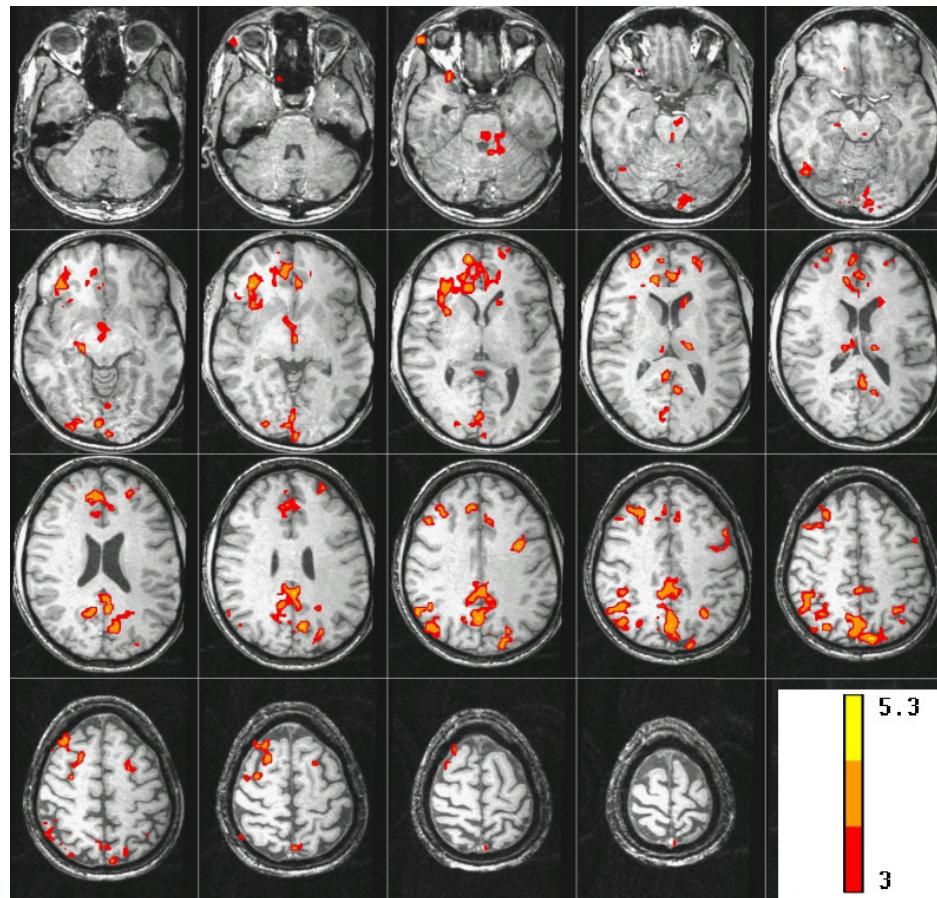
Resting State Correlations



Activation:
correlation with reference function

Rest:
seed voxel in motor cortex

BOLD correlated with SCR during "Rest"

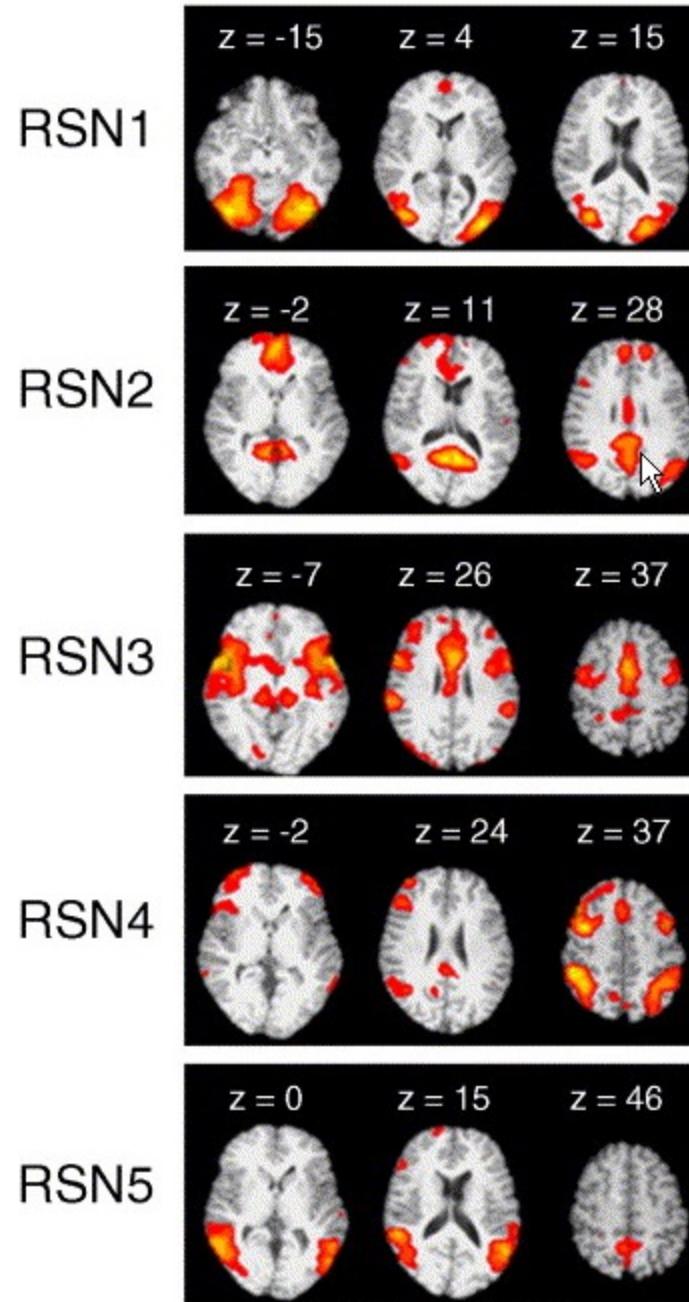
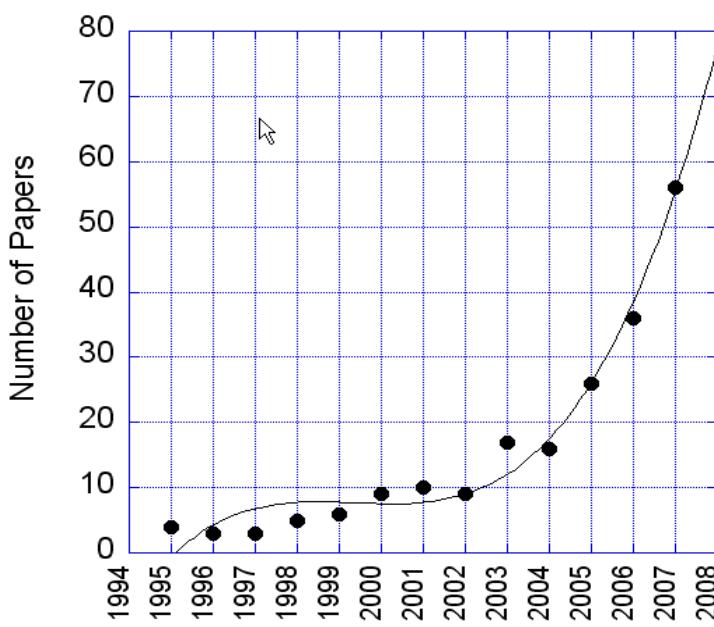


J. C. Patterson II, L. G. Ungerleider, and P. A Bandettini,
NeuroImage 17: 1787-1806, (2002).

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

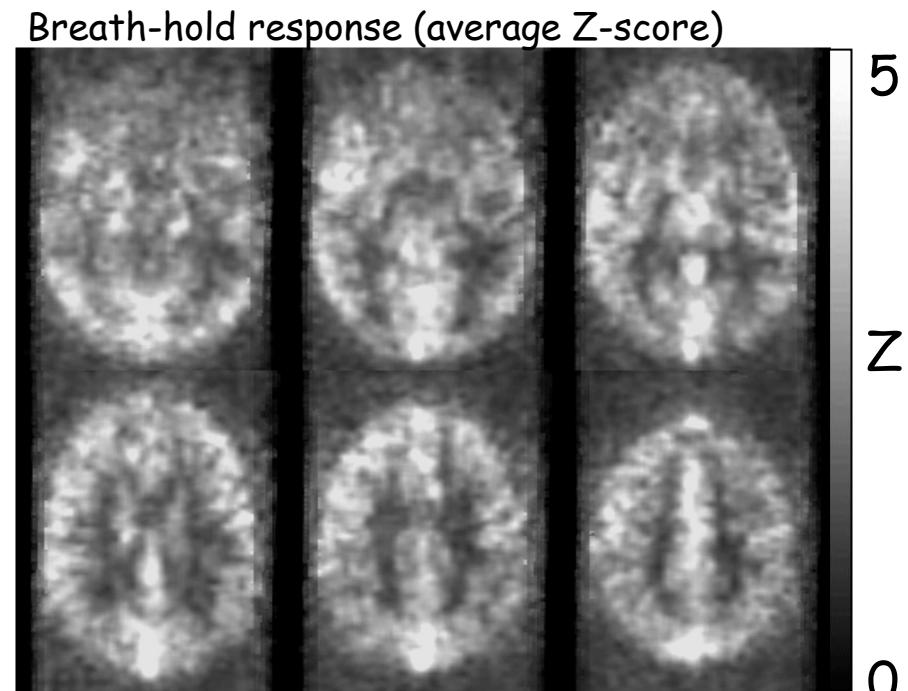
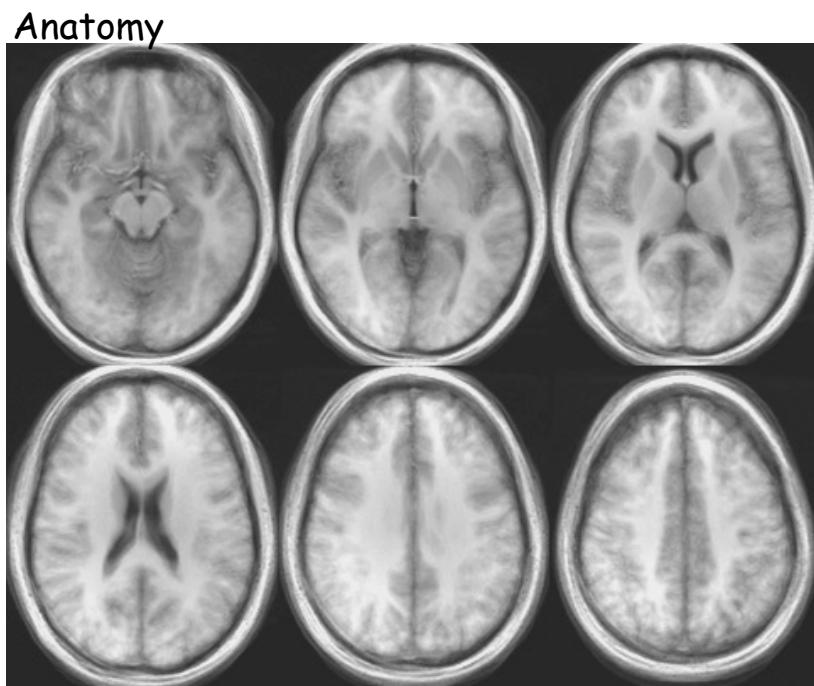
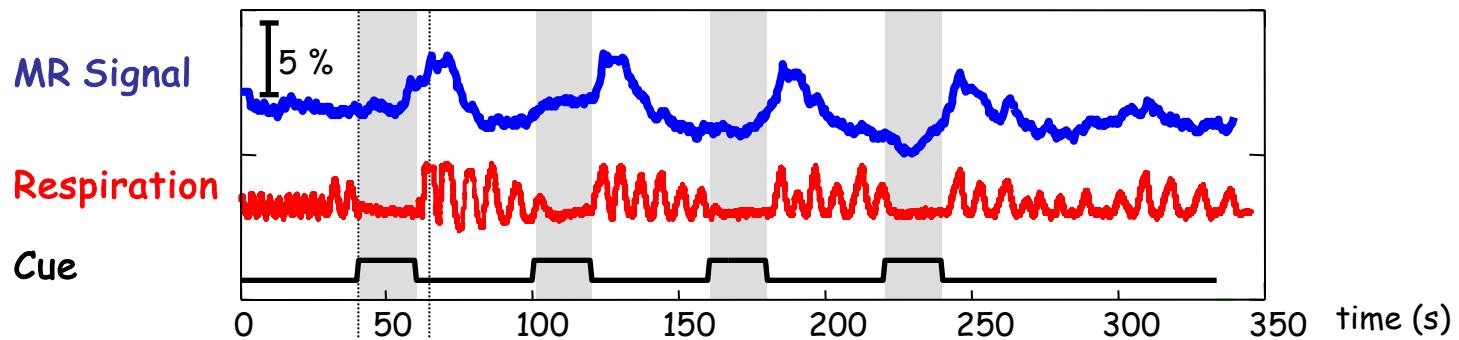


Sources of time series fluctuations:

- 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

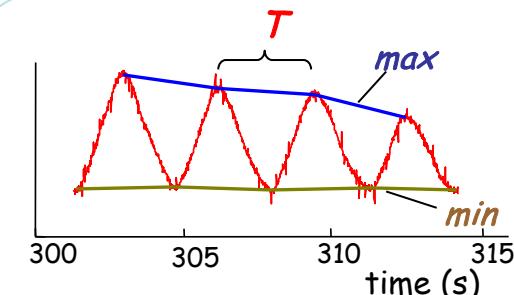
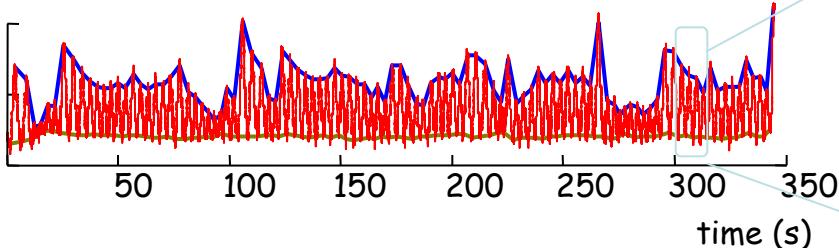
Breath-holding

Group Maps (N = 7)

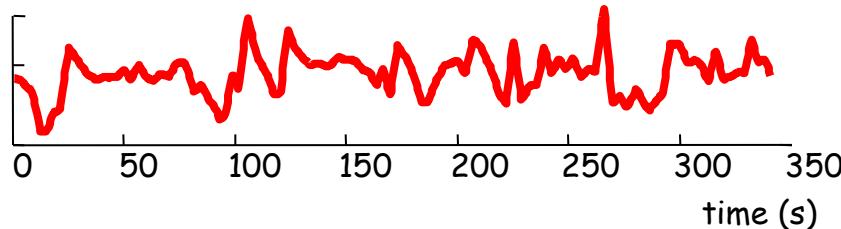


Estimating respiration volume changes

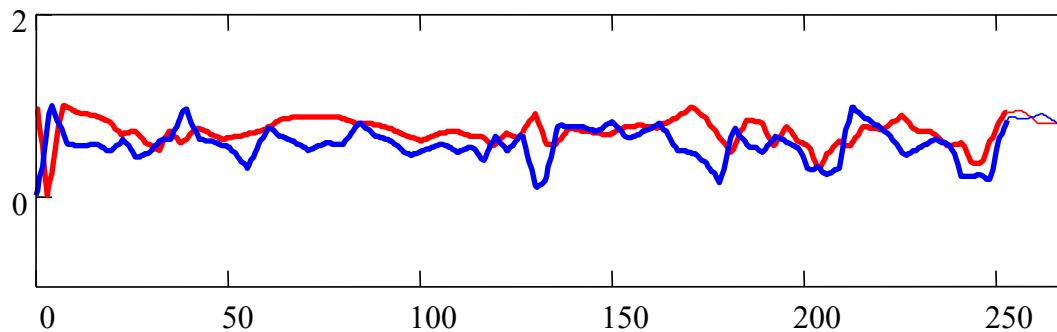
Respiration



Respiration Volume / Time (RVT)

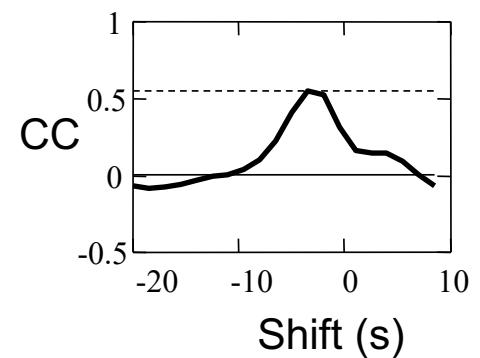


$$RVT = \frac{\text{max} - \text{min}}{T}$$



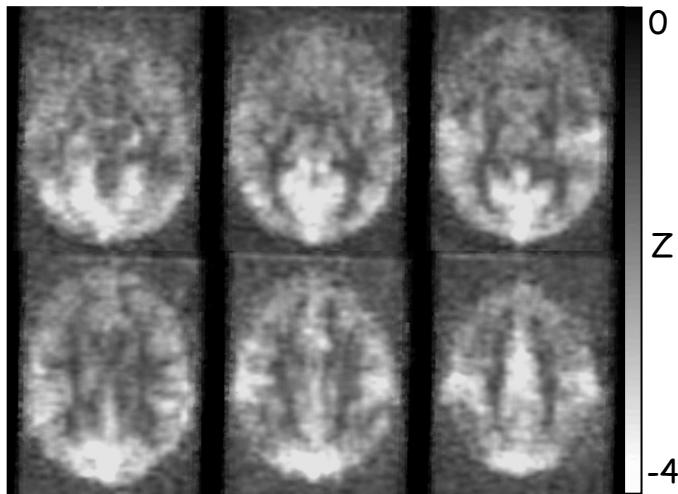
— CO_2
— RVT

RVT precedes end tidal CO_2 by 5 sec.

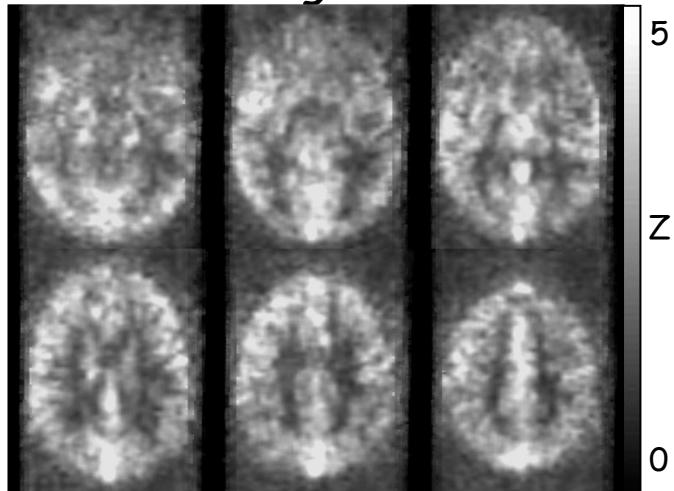


Respiration induced signal changes

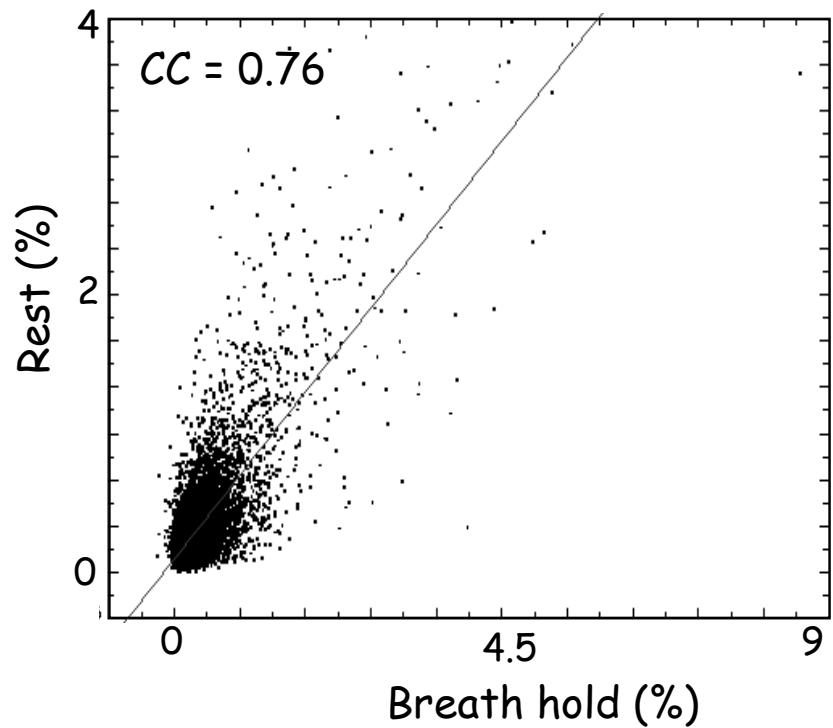
Rest



Breath-holding

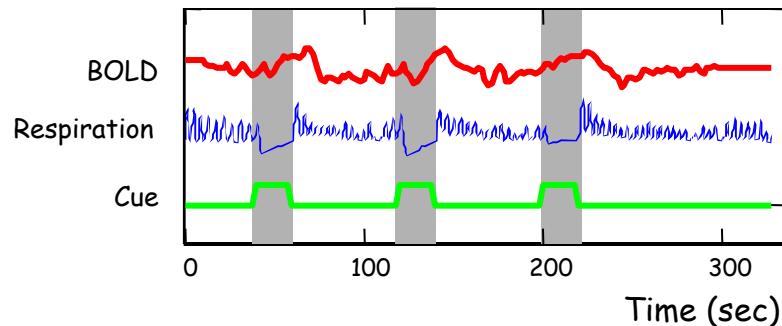


(N=7)

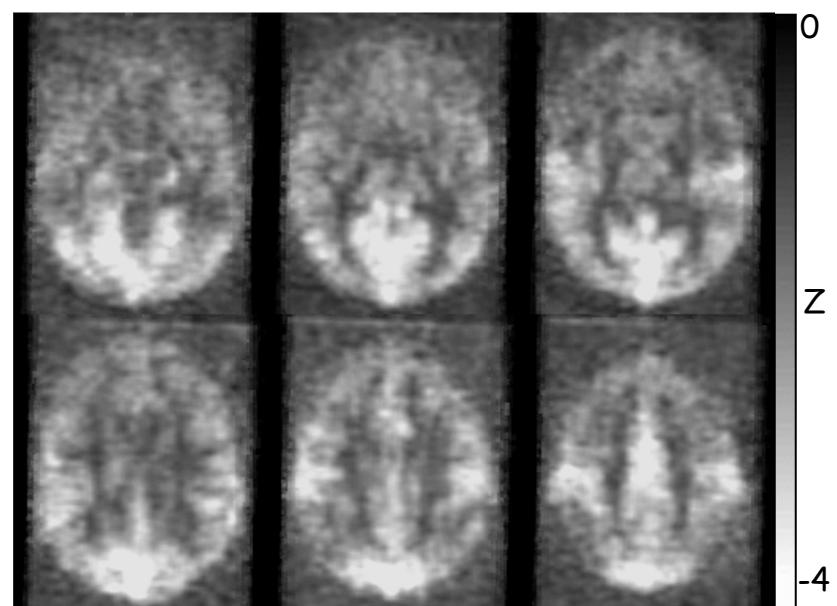
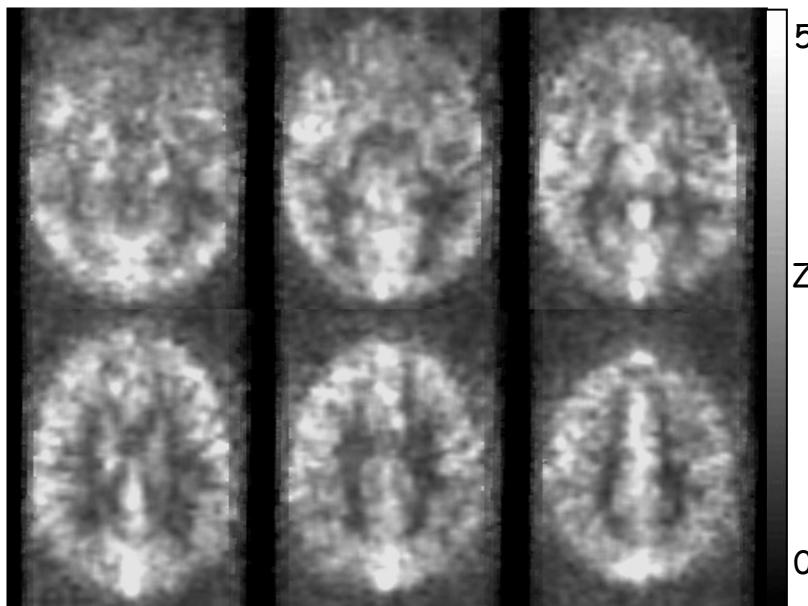
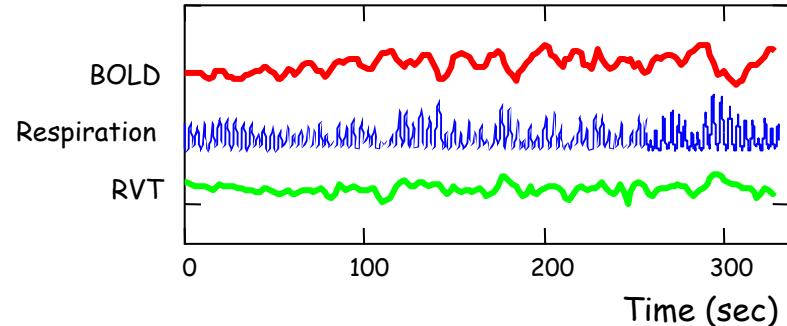


Respiration induced signal changes

Breath-holding

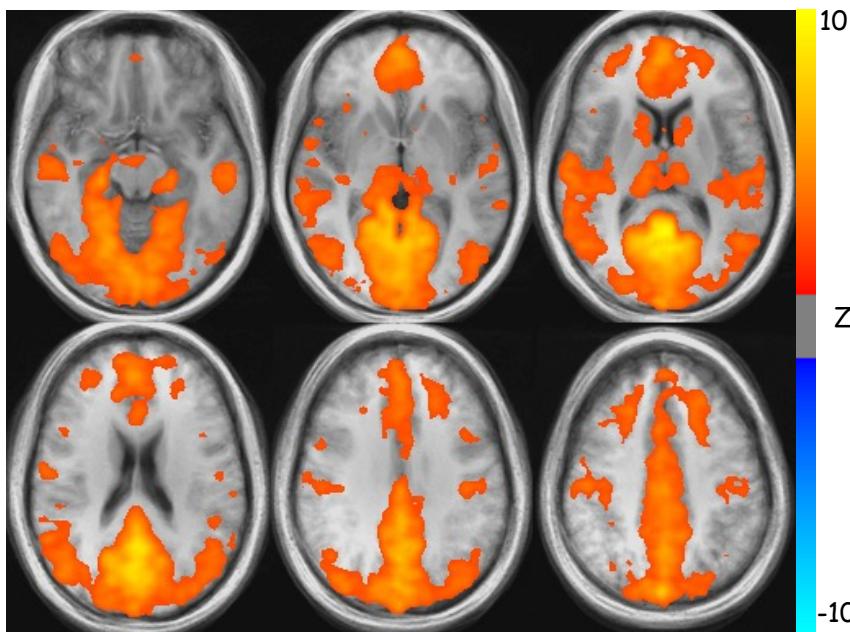


Rest

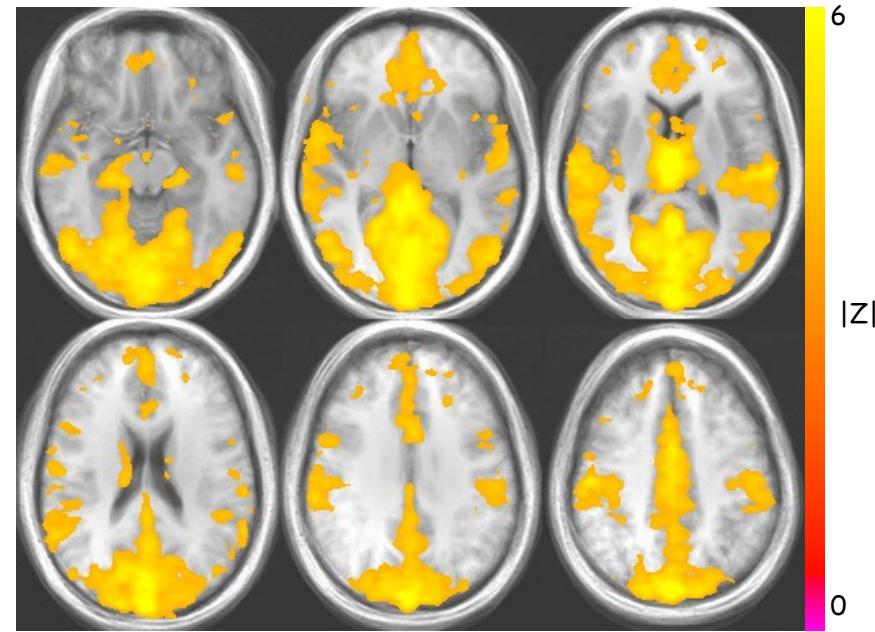


RVT Correlation Maps & Functional Connectivity Maps

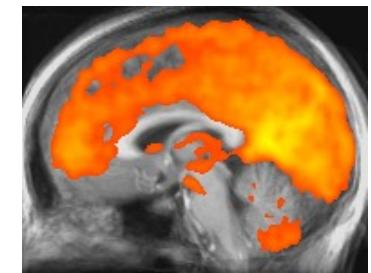
Resting state correlation with signal from posterior cingulate



Resting state correlation with RVT signal



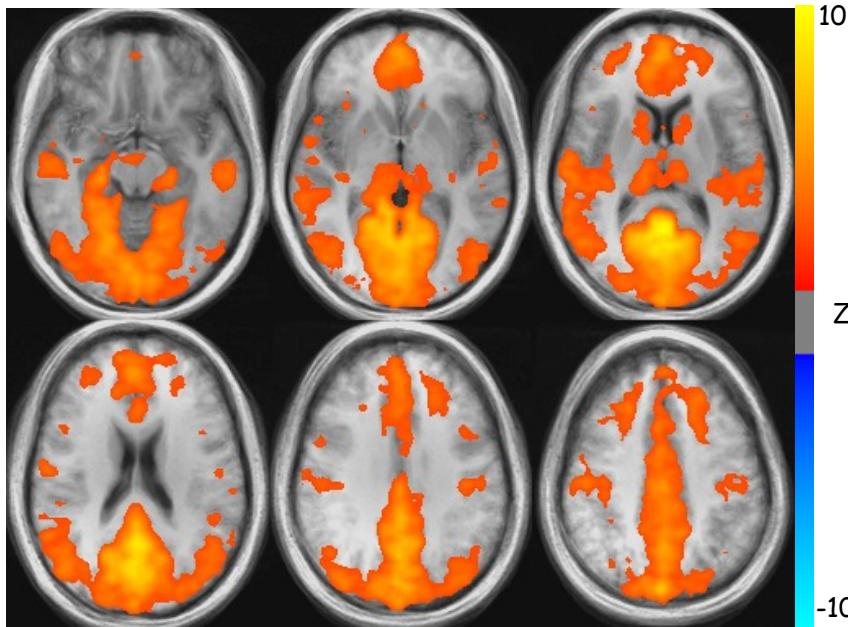
Group (n=10)



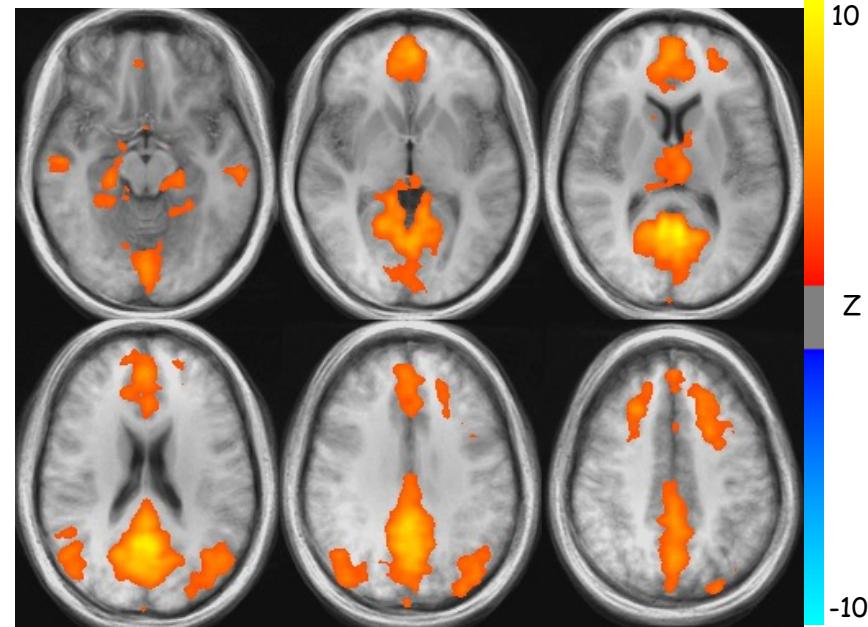
R.M. Birn, J. A. Diamond, M. A. Smith, P. A. Bandettini,
NeuroImage, 31, 1536-1548 (2006)

Effect of Respiration Rate Consistency on Resting Correlation Maps

Spontaneously Varying Respiration Rate

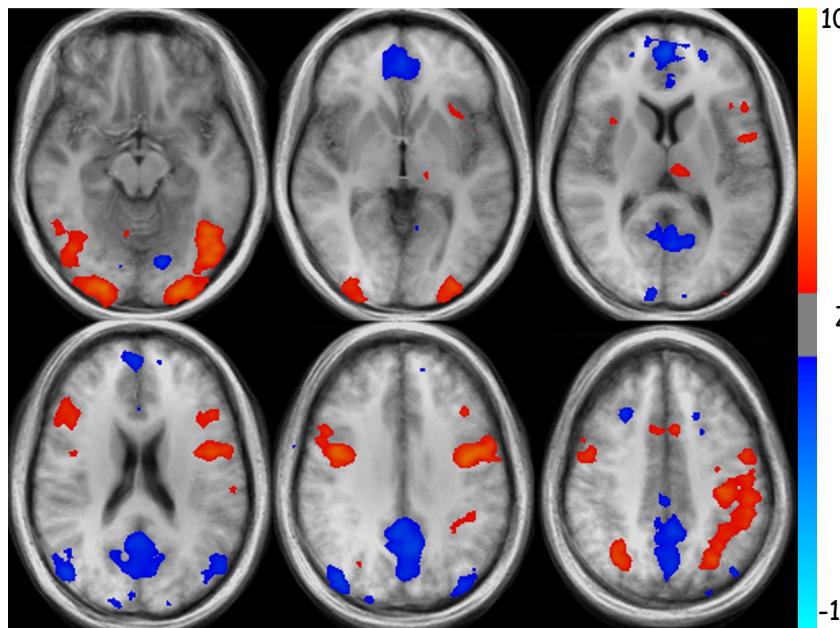


Constant Respiration Rate



Lexical Decision
Making Task

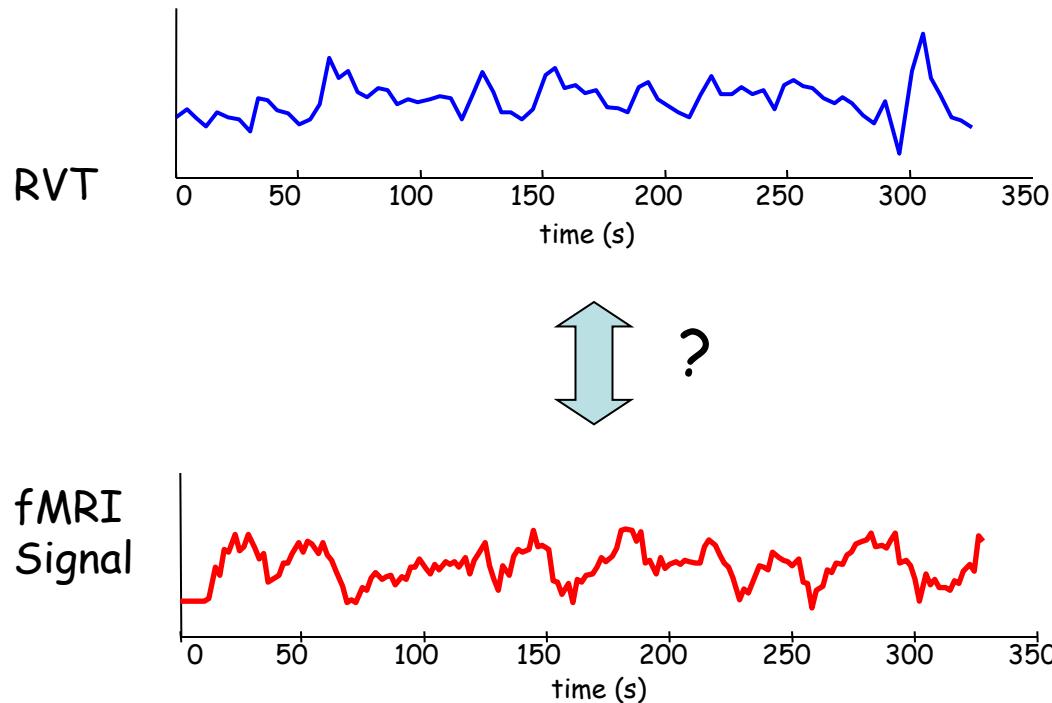
Group ($n=10$)



Blue: deactivated
network

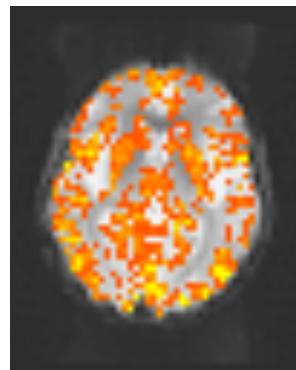
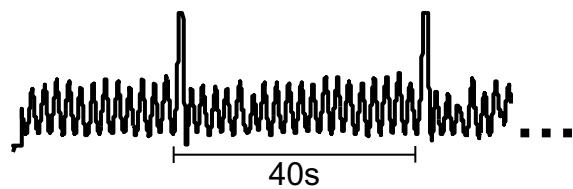
Respiration Changes vs. BOLD

How are the BOLD changes related to respiration variations?

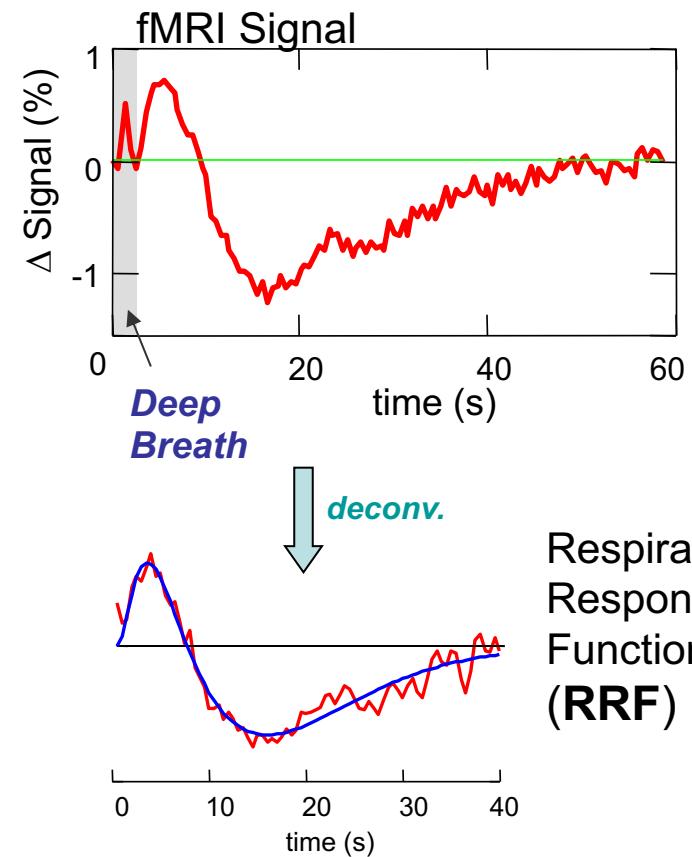


fMRI response to a single Deep Breath

Respiration



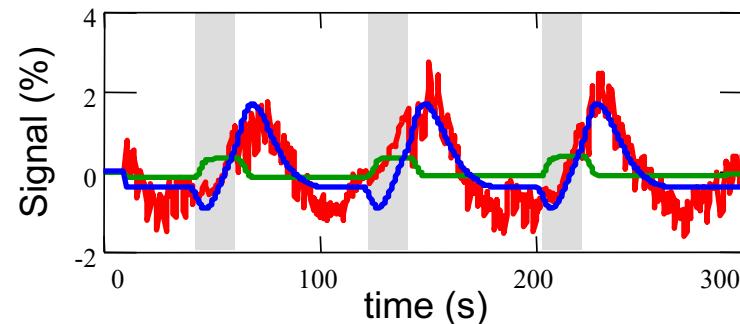
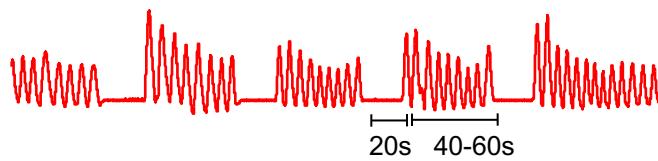
$$RRF(t) = 0.6 t^{2.1} e^{-1.6} - 0.0023 t^{3.54} e^{-4.25}$$



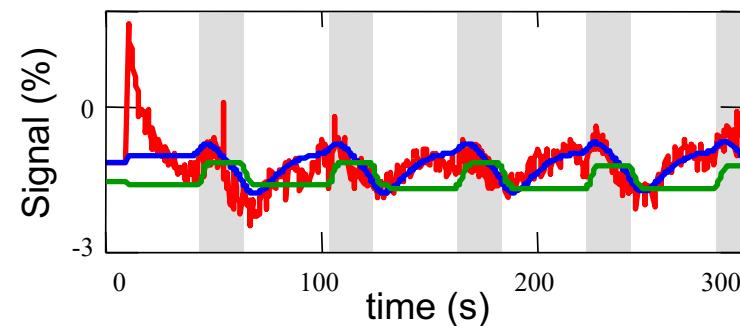
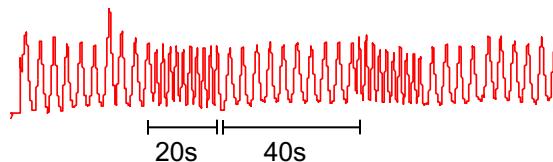
Respiration
Response
Function
(RRF)

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

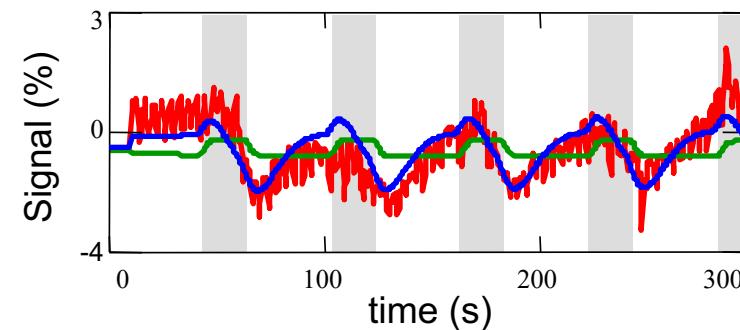
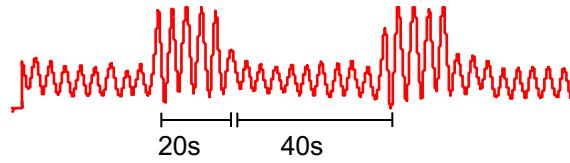
Breath-holding

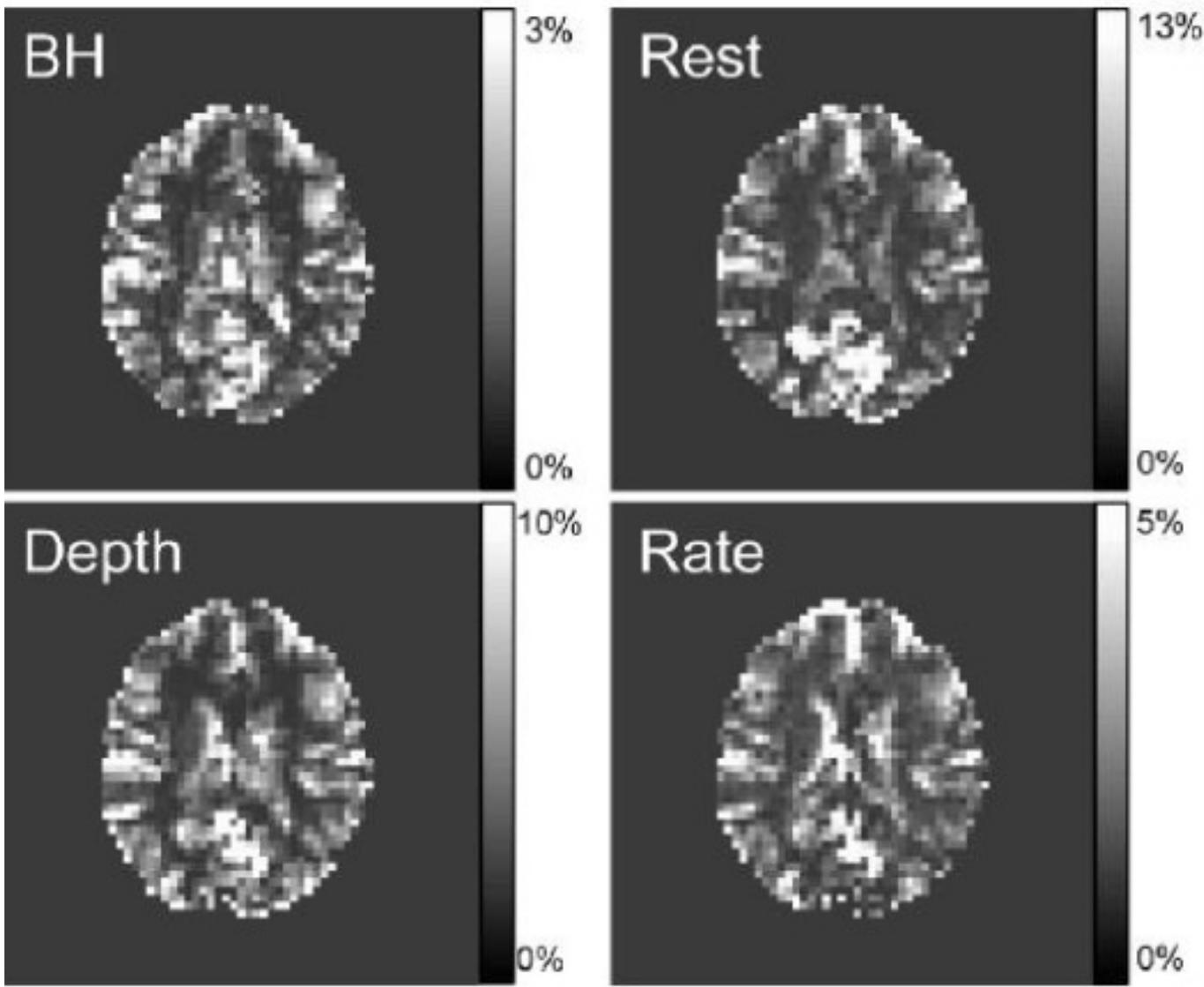


Rate Changes

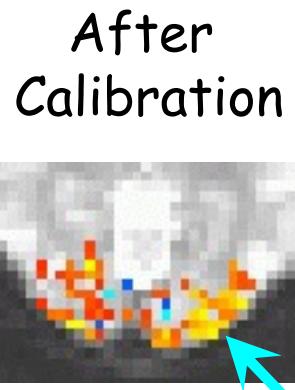
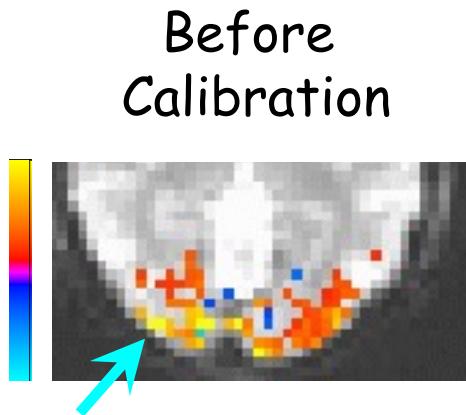


Depth Changes

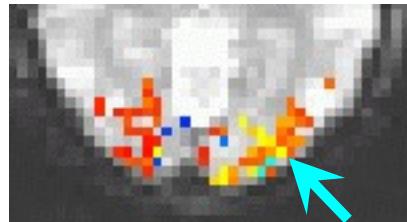
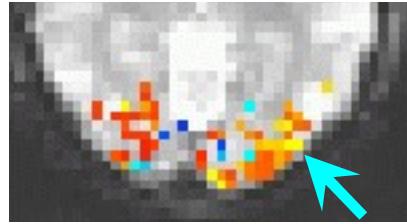
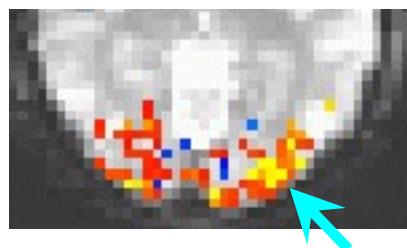




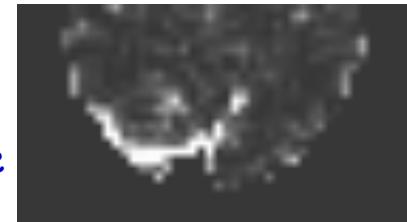
BOLD magnitude calibration



$$\text{BOLD}_{\text{calib}} = \frac{\% \Delta S (\text{BOLD})}{\% \Delta S (\text{Resp})}$$



Respiration-induced ΔS



3. Experimental Design

Motivation:

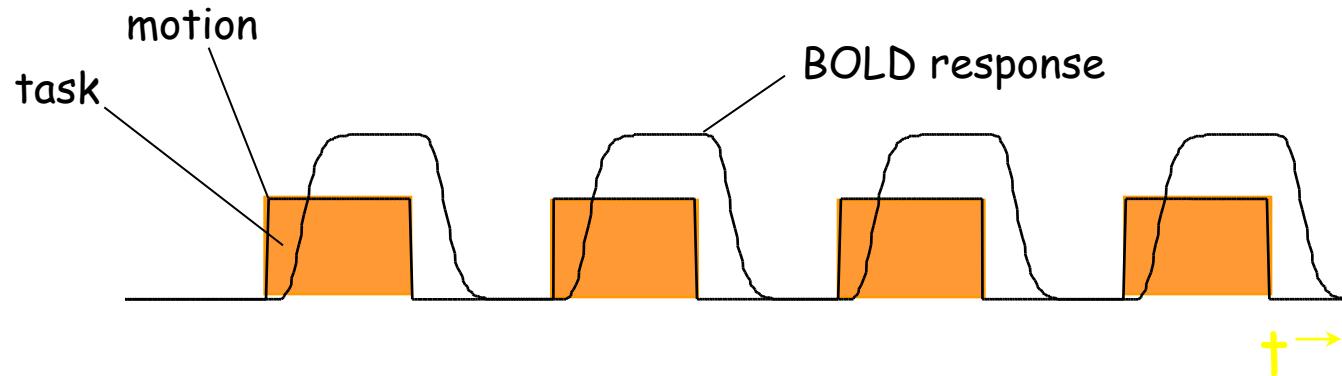
- Guides for *individual* subject scanning at the limits of detectability, resolution, available time, and subject performance.

Studies:

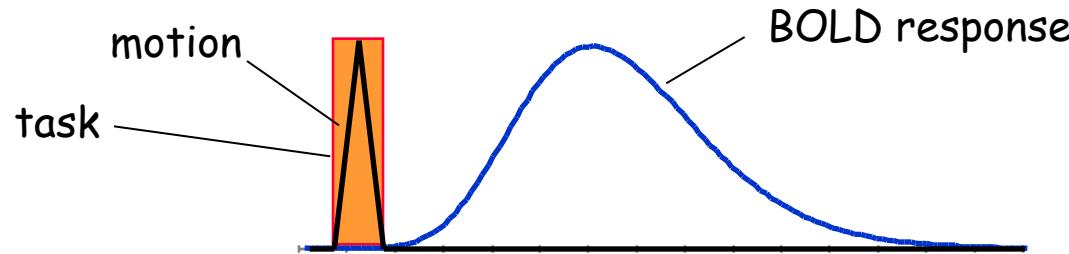
- Overt response timing
- Suggested resolution

fMRI during tasks that involve brief motion

Blocked Design

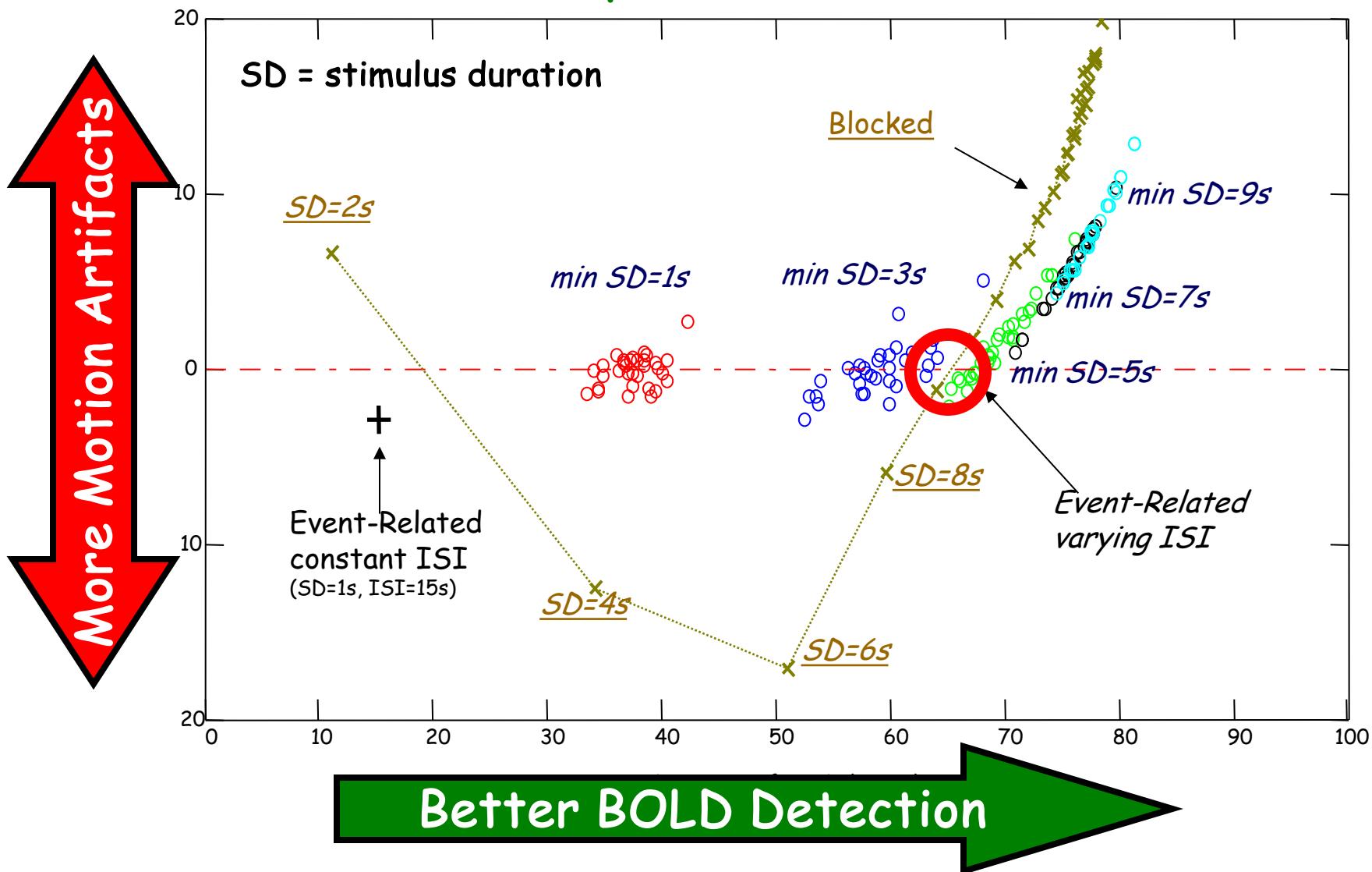


Event-Related Design

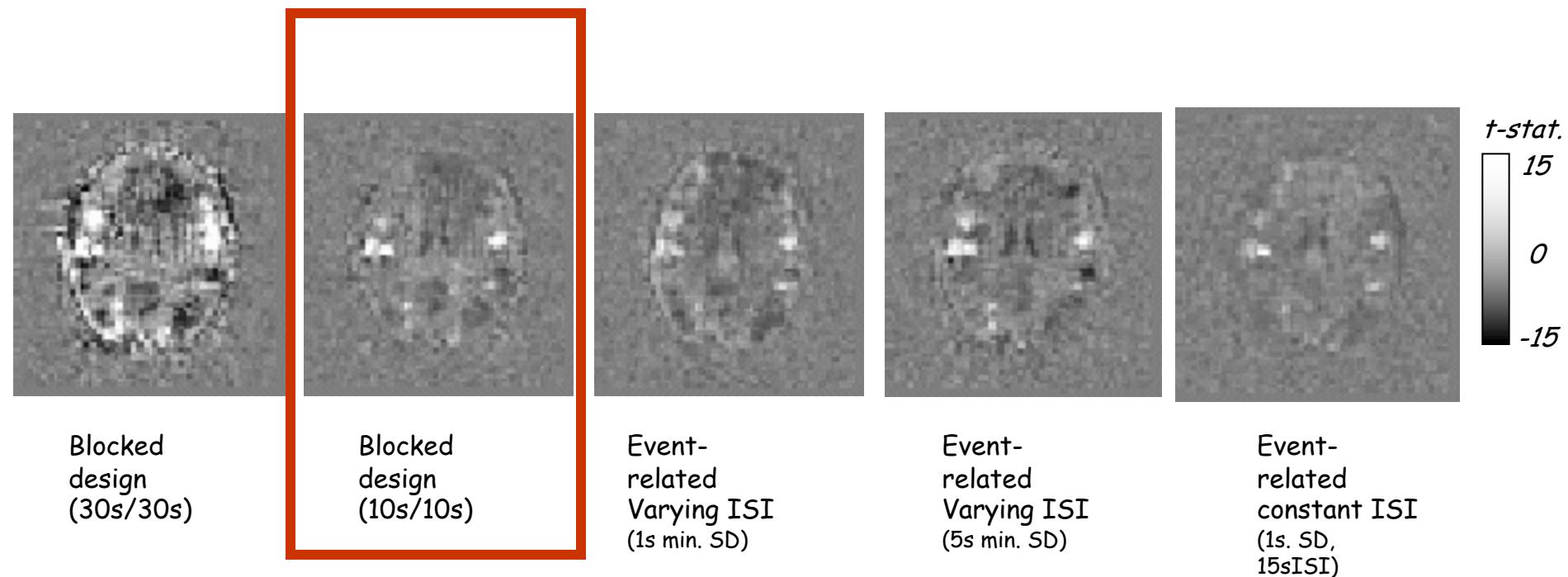


R. M. Birn, P. A. Bandettini, R. W. Cox, R. Shaker, *Human Brain Mapping* 7: 106-114 (1999).

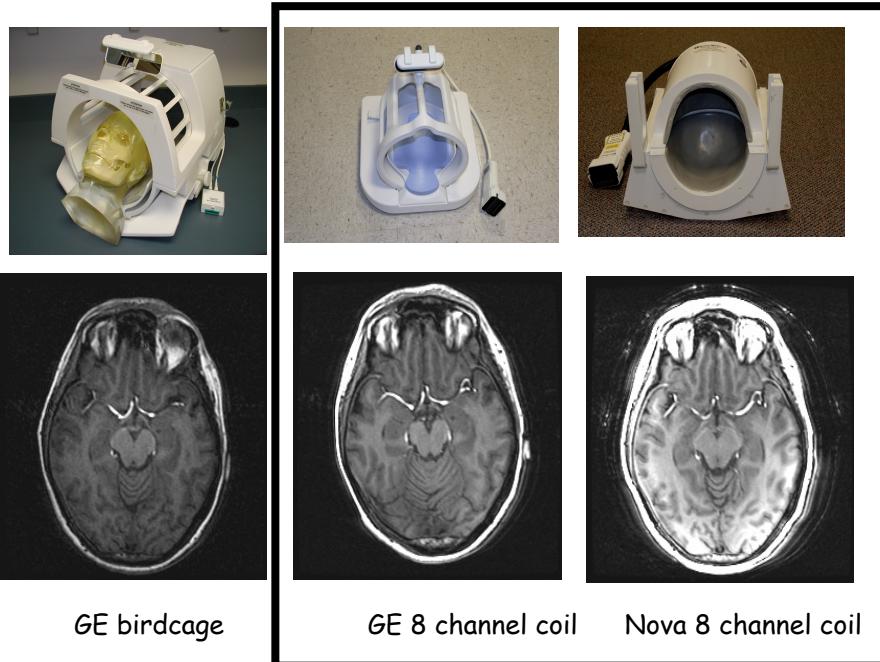
Overt Responses - Simulations



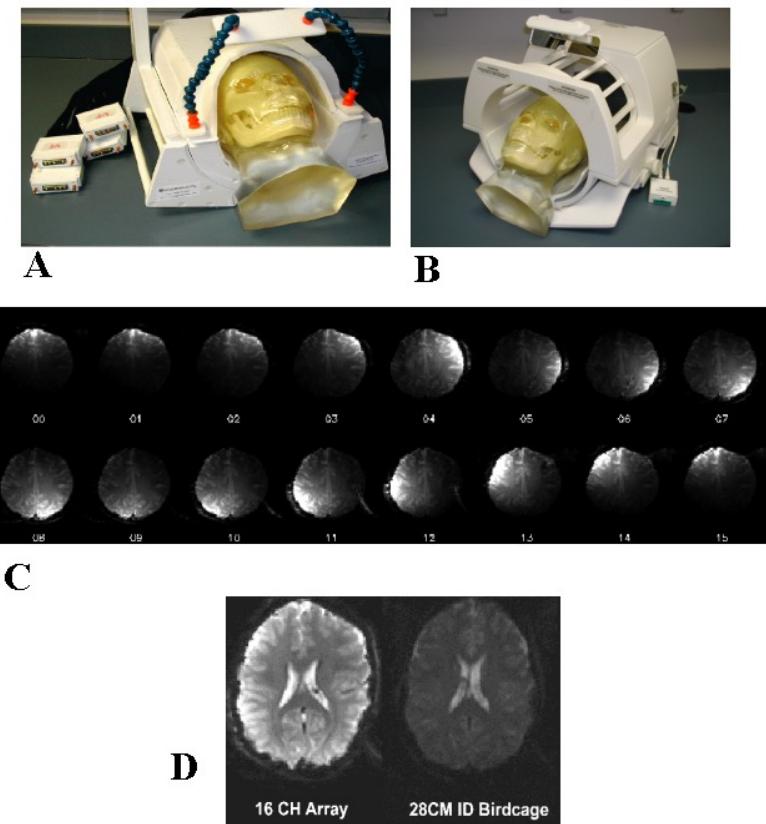
Overt Responses



8 channel parallel receiver coil



16 channel parallel receiver coil

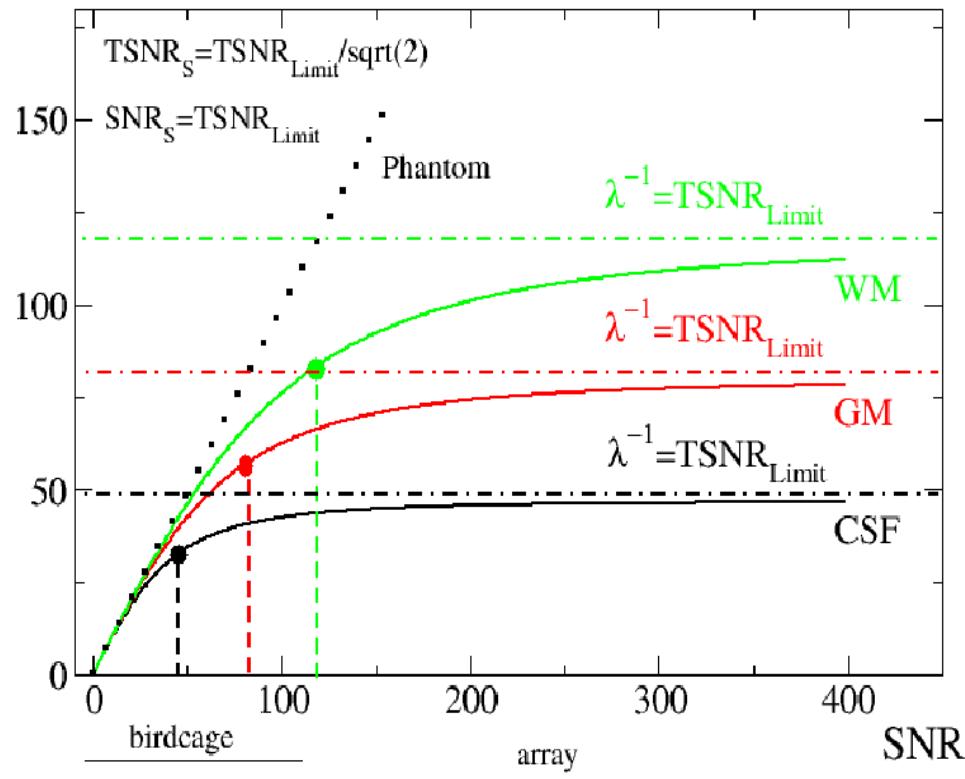


J. Bodurka, et al, Magnetic Resonance in Medicine 51 (2004) 165-171.

Finding the “suggested voxel volume”

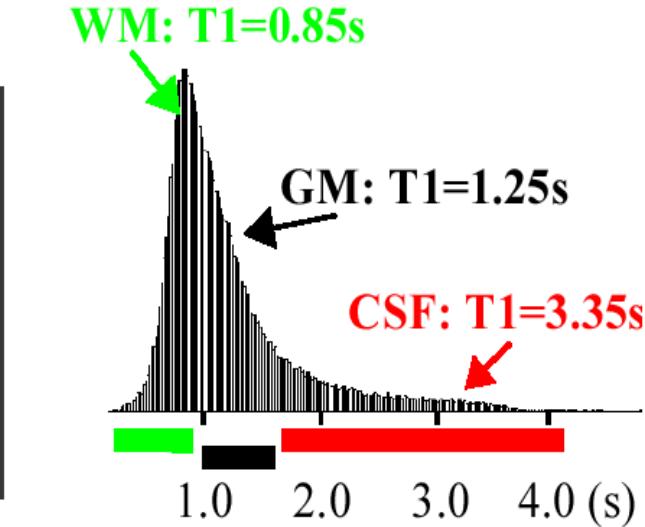
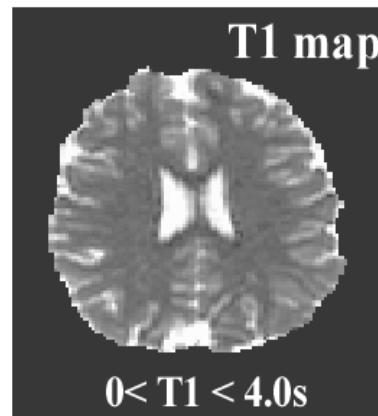
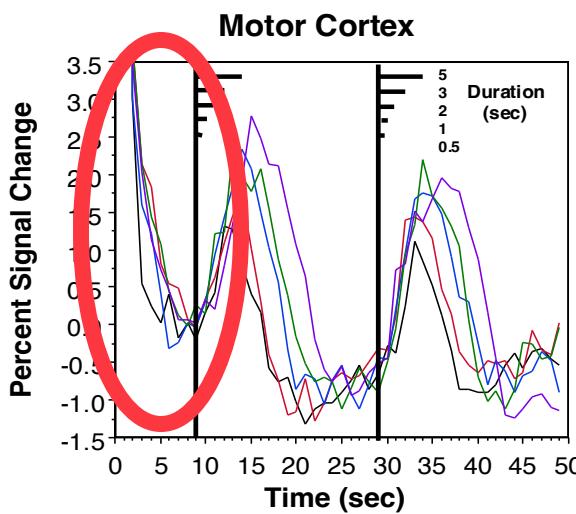
Temporal Signal to Noise Ratio (TSNR) vs. Signal to Noise Ratio (SNR)

TSNR

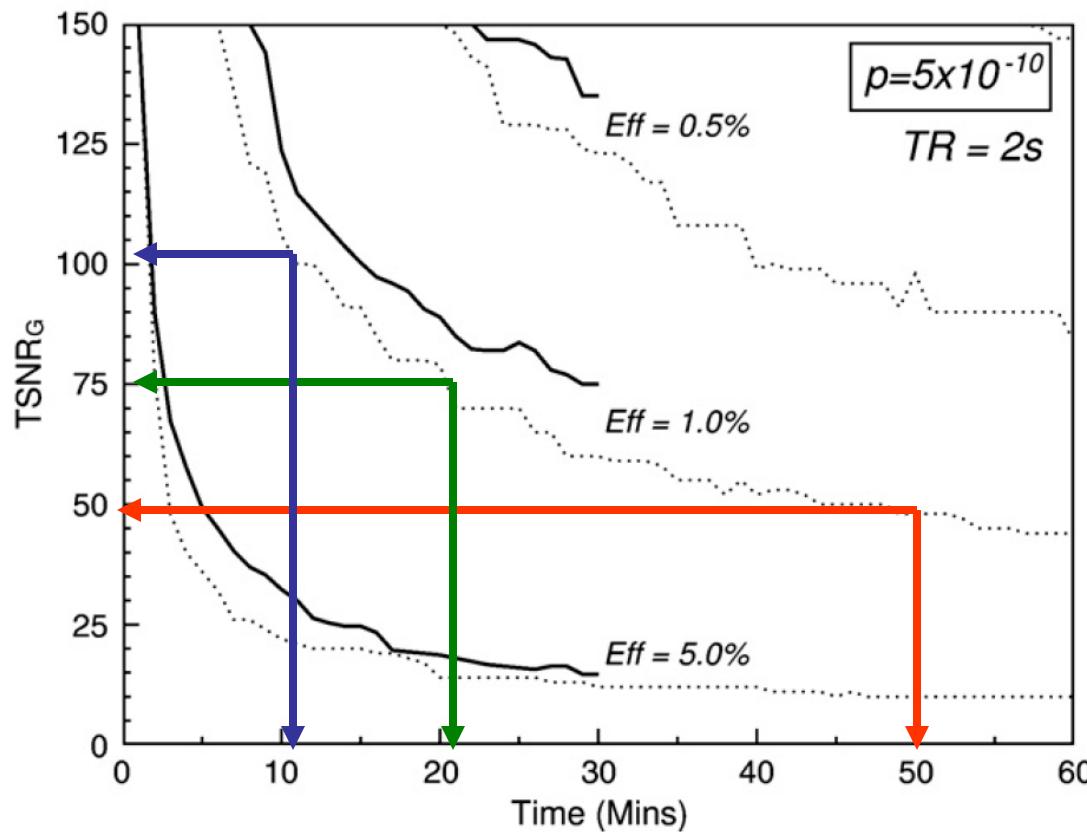


3T, birdcage:	2.5 mm ³
3T, 16 channel:	1.8 mm ³
7T, 16 channel:	1.4 mm ³

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:

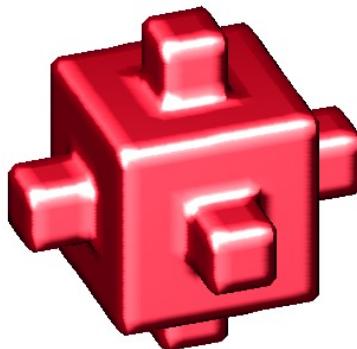
- Pattern-Information Mapping

- Dis-similarity matrix

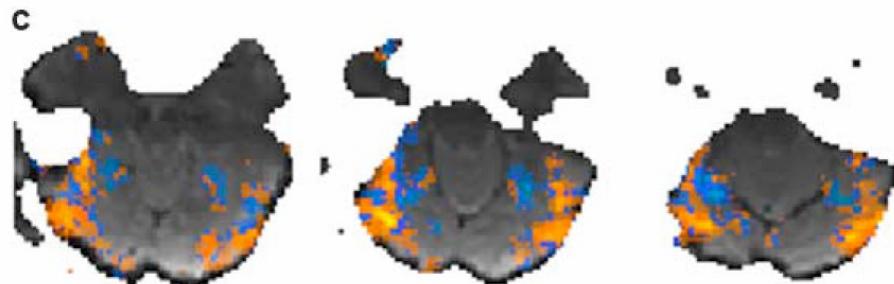
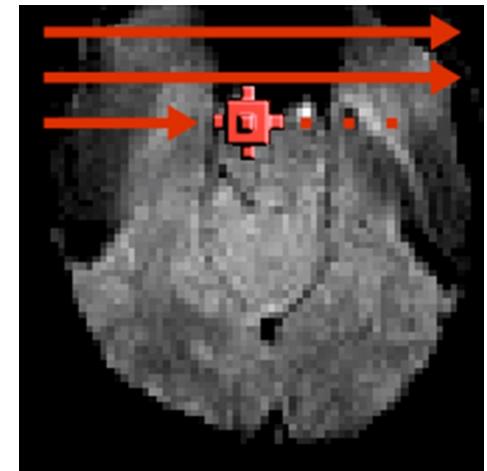
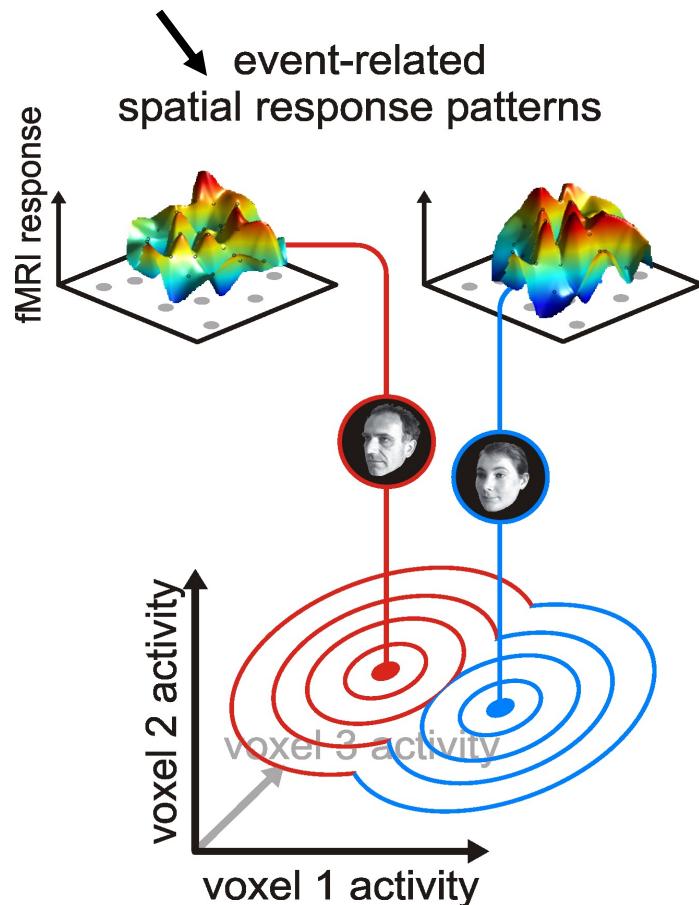


Pattern Information Mapping

"searchlight" ROI →

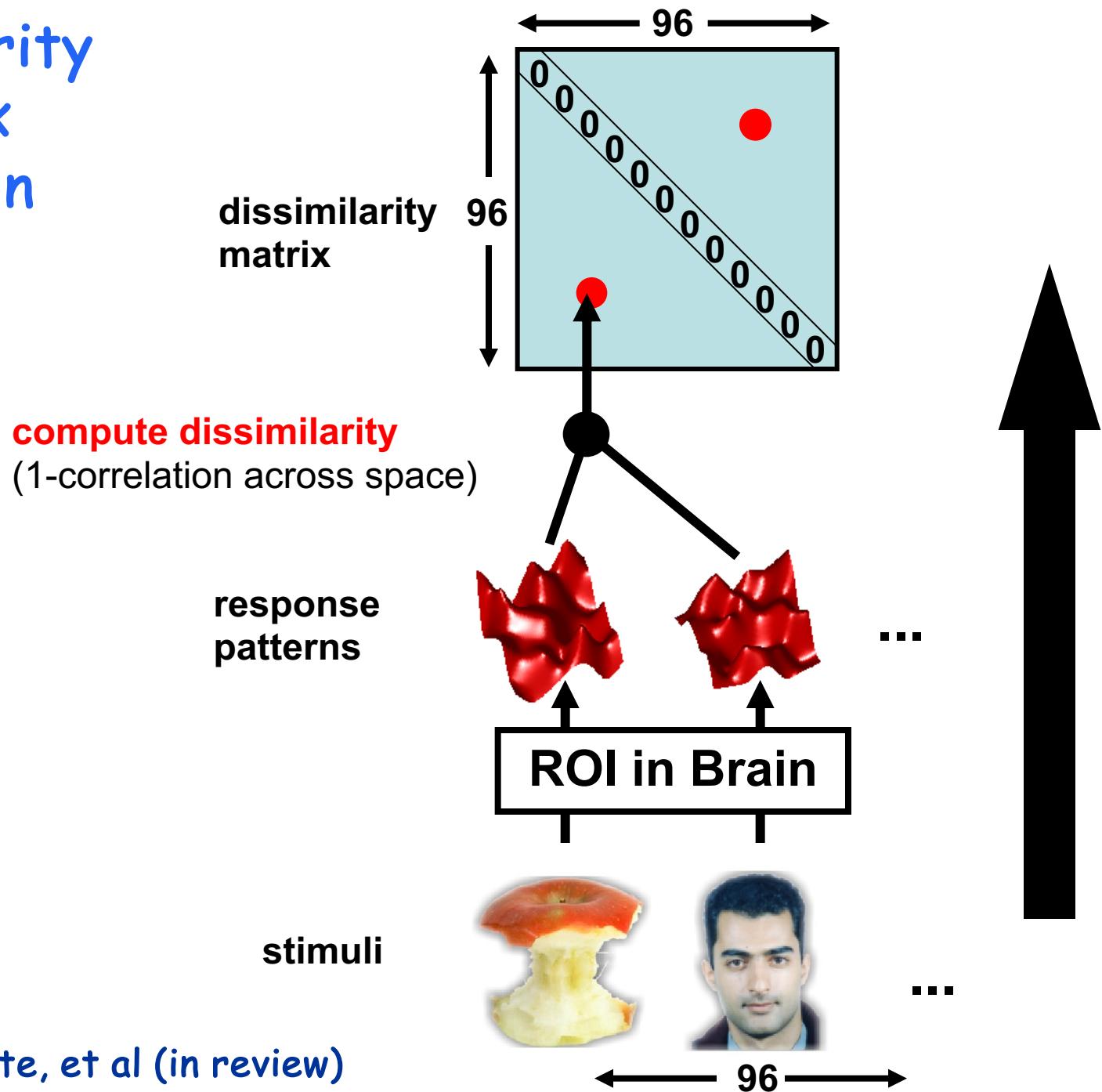


From fixed ROI



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

Dissimilarity Matrix Creation

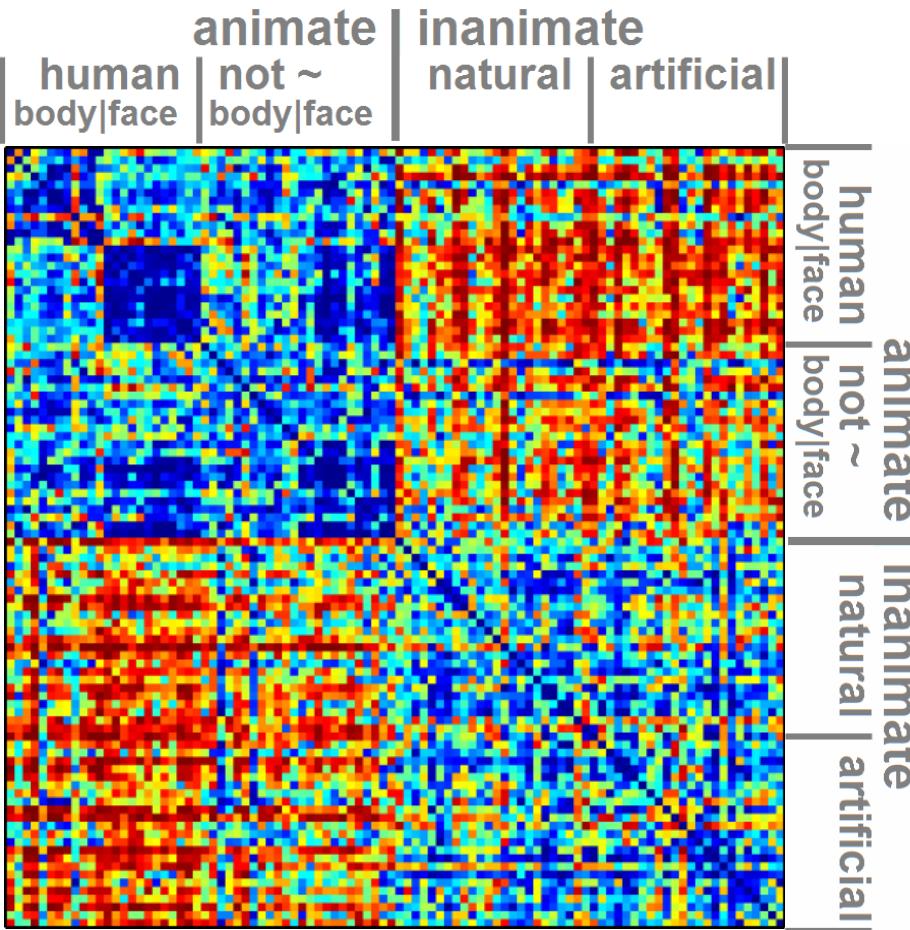


Visual Stimuli



Human IT

(1000 visually most responsive voxels)



dissimilarity

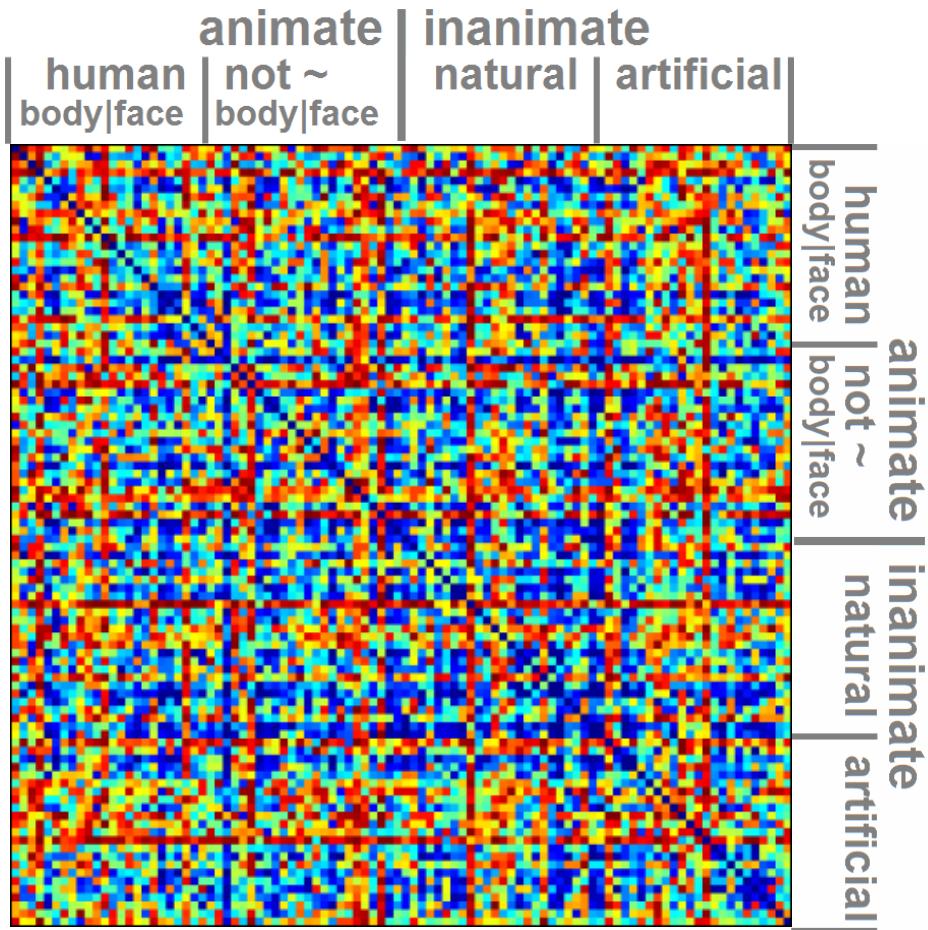
0

[percentile]

100

Human Early Visual Cortex

(1057 visually most responsive voxels)



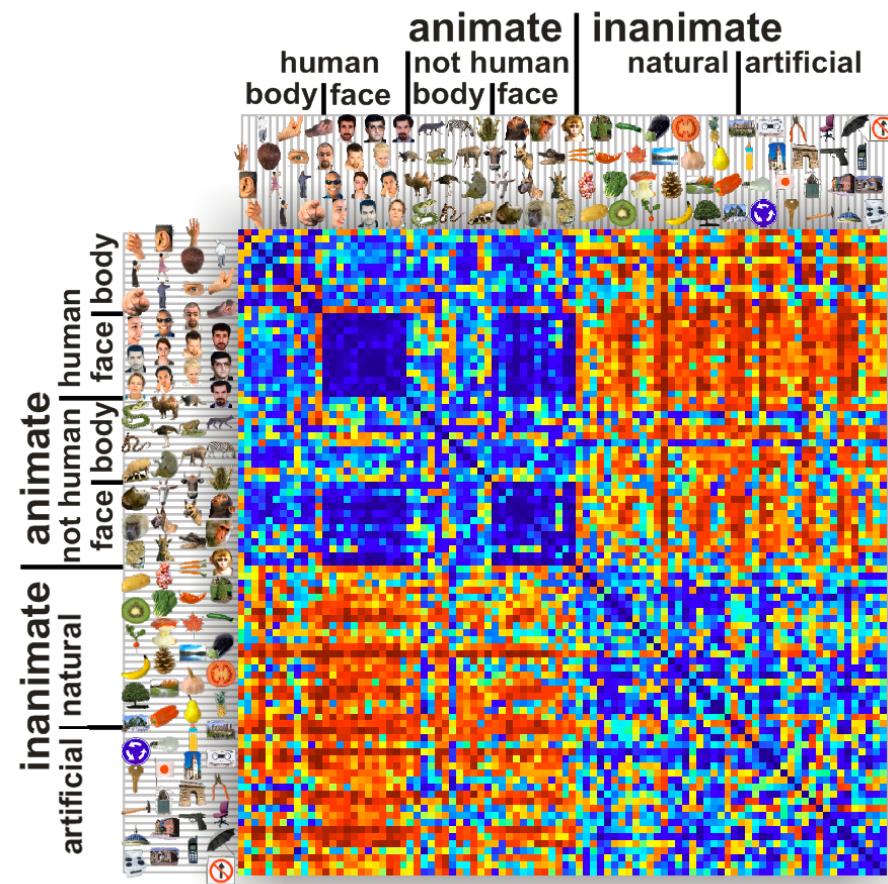
Monkey-Human Comparison Procedure

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)

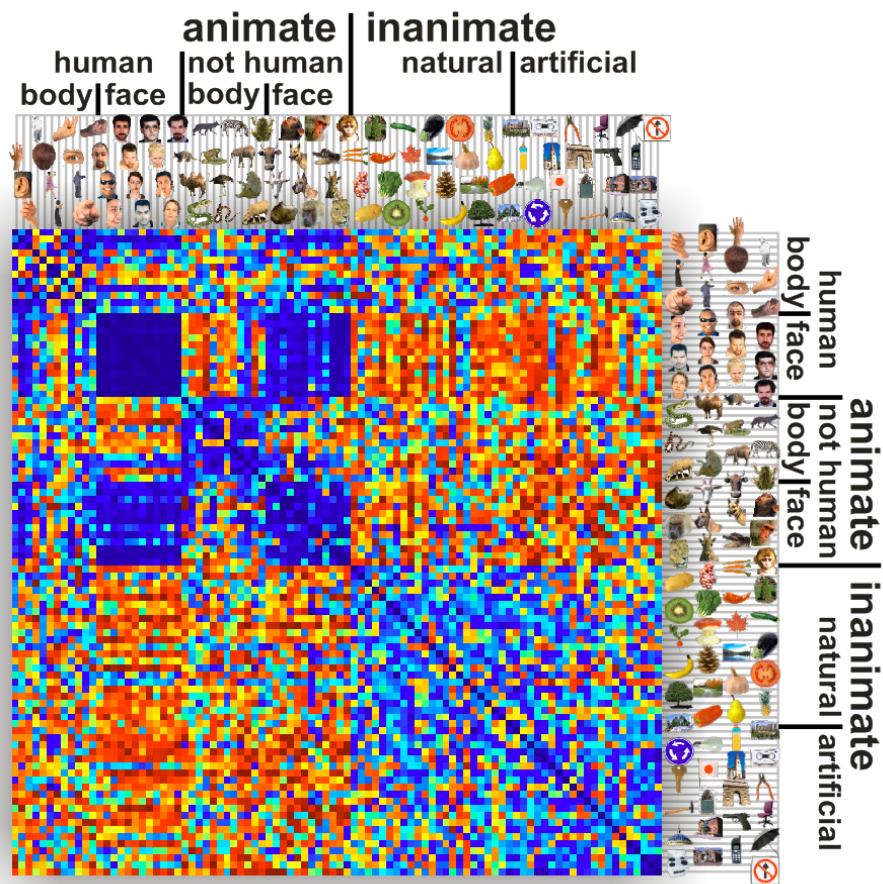
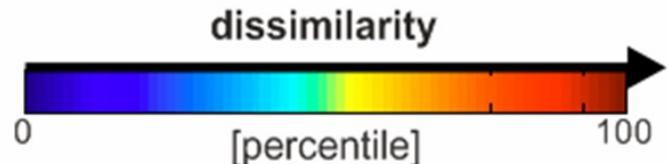
Monkey (Kiani et al. 2007)

- 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:

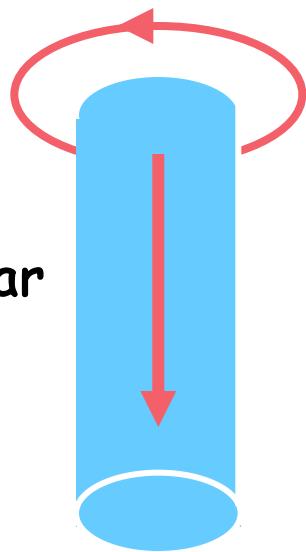
- Direct fMRI of neuronal activity.

Studies:

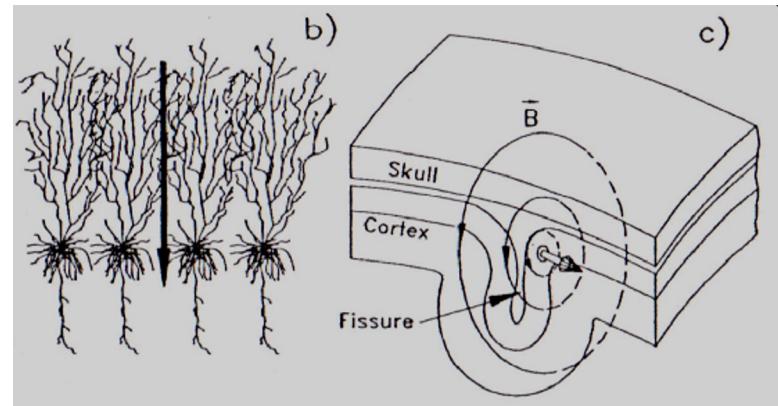
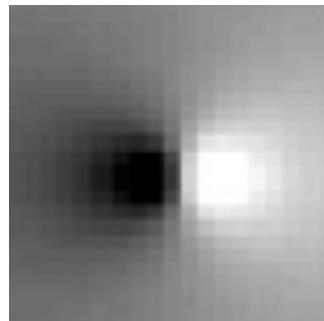
- Model
- Phantom Studies
- Cell Cultures at 7T and 3T

Magnetic Field

Intracellular Current



Surface Fields

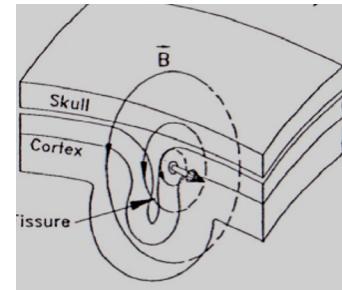


100 fT at on the scalp

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

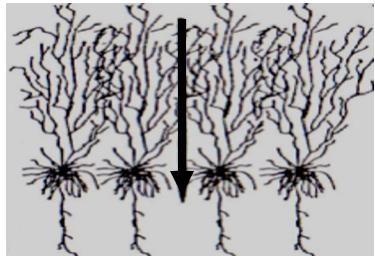
Magnetic field associated with a bundle of dendrites

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

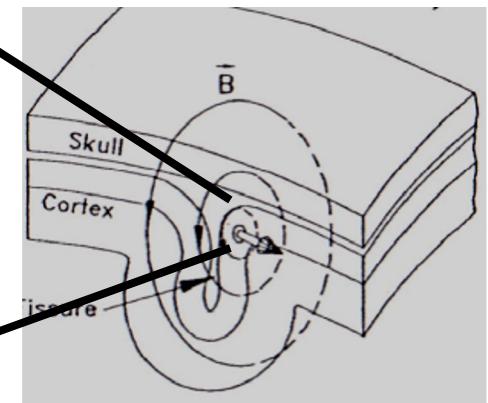
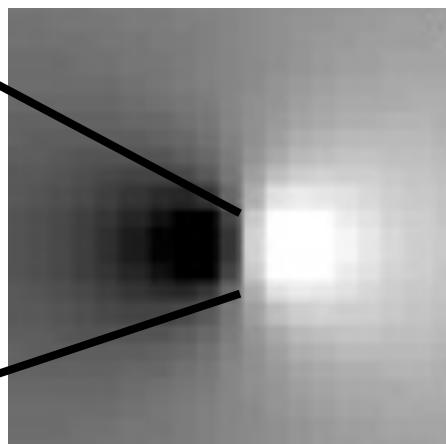
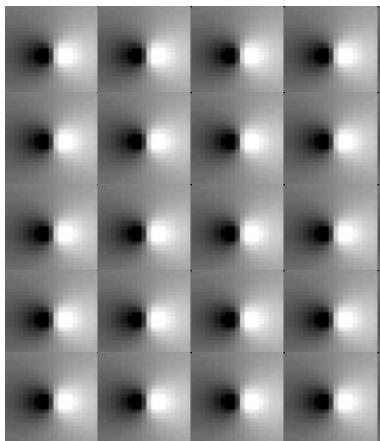


at least 50,000 neurons (0.002 fT (per dendrite) $\times 50,000 = 100 \text{ fT}$), must coherently act to generate such field. These bundles of neurons produce, within a typical voxel, $1 \text{ mm} \times 1 \text{ mm} \times 1 \text{ mm}$, a field of order:

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

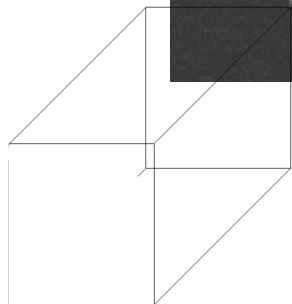
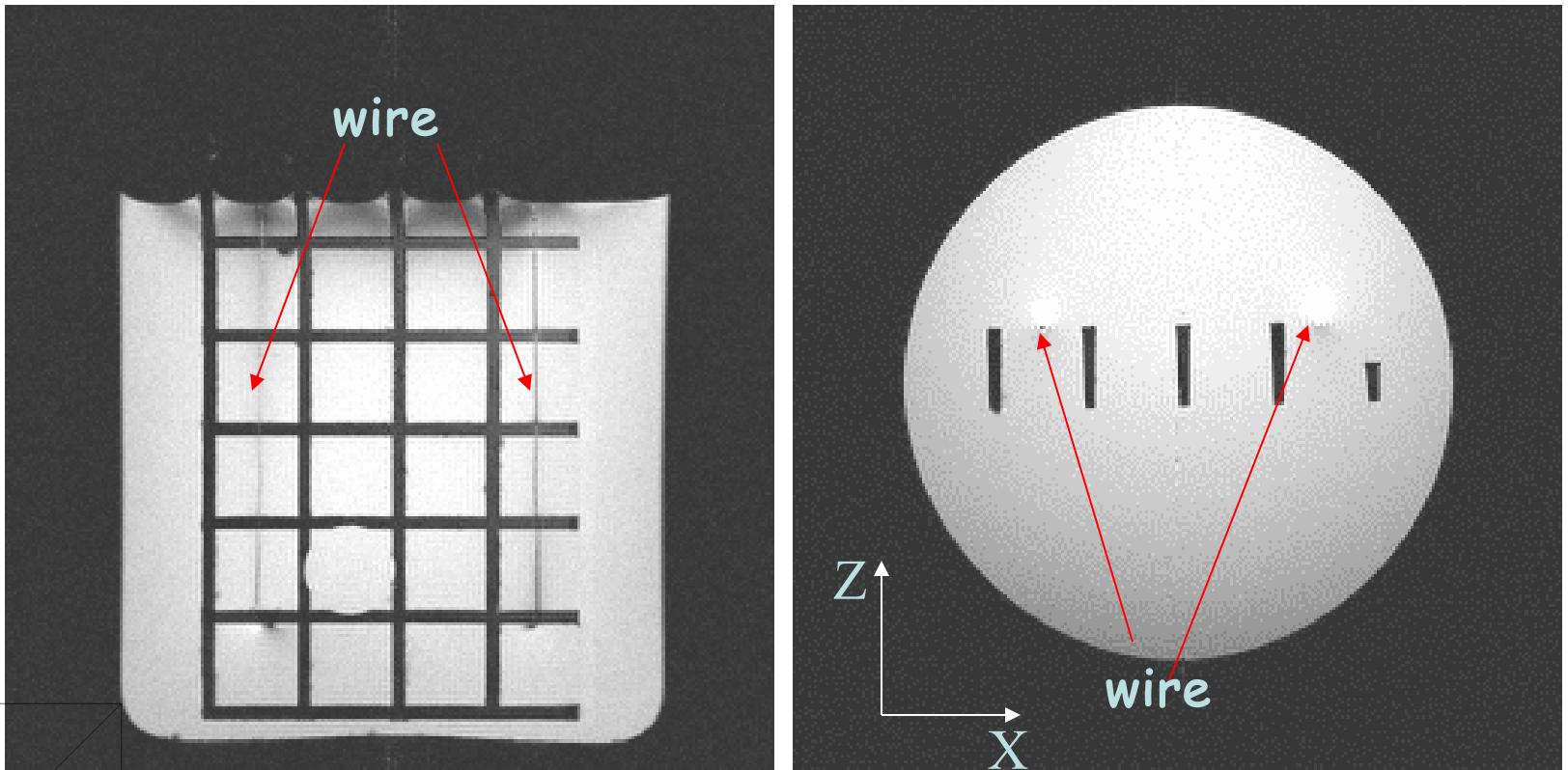


Surface Field Distribution Across Spatial Scales

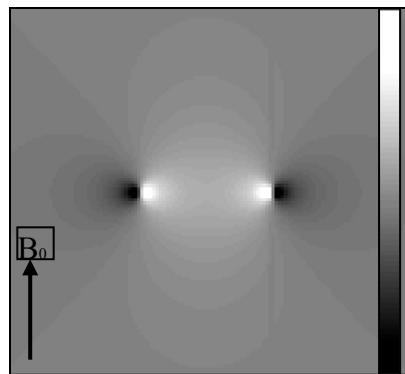


Adapted from: J.P. Wikswo Jr et al.
J Clin Neurophys 8(2): 170-188, 1991

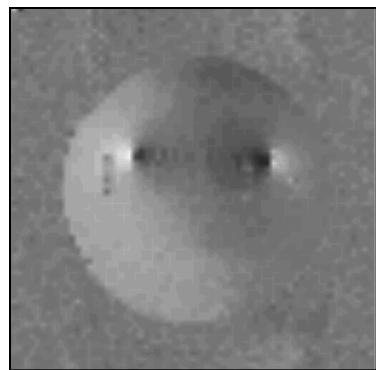
Current Phantom Experiment



calculated $B_c \parallel B_0$

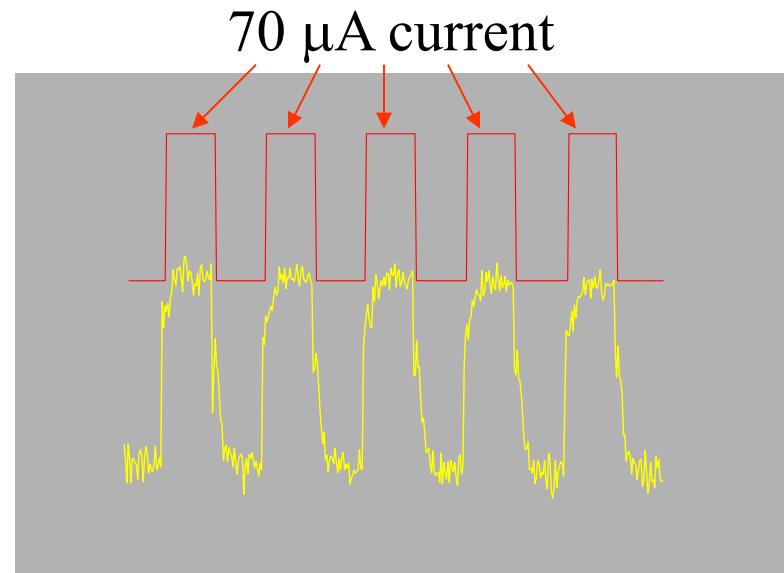


$$\Delta\phi \approx 20^\circ$$



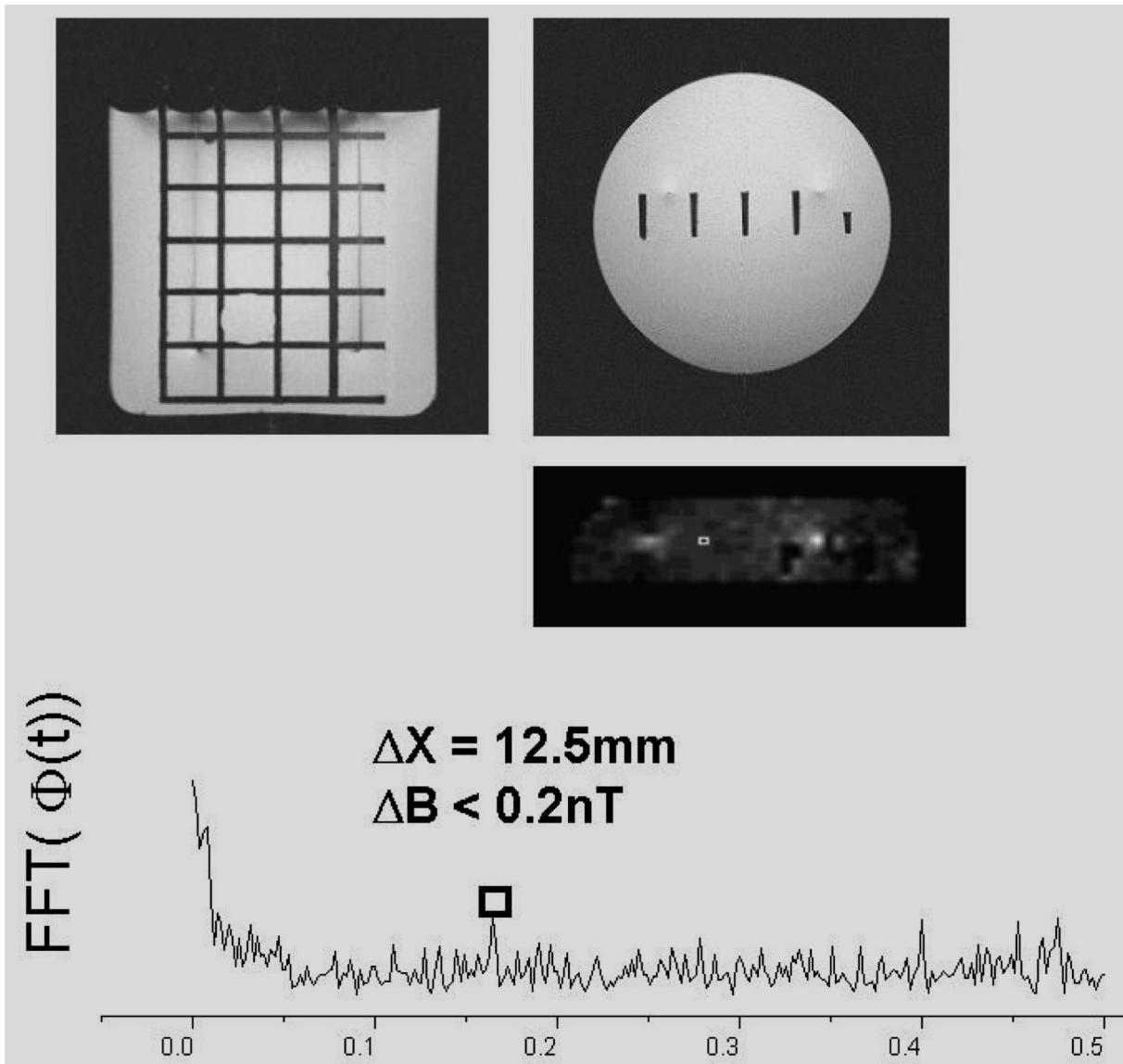
Correlation image

Measurement



Single shot GE EPI

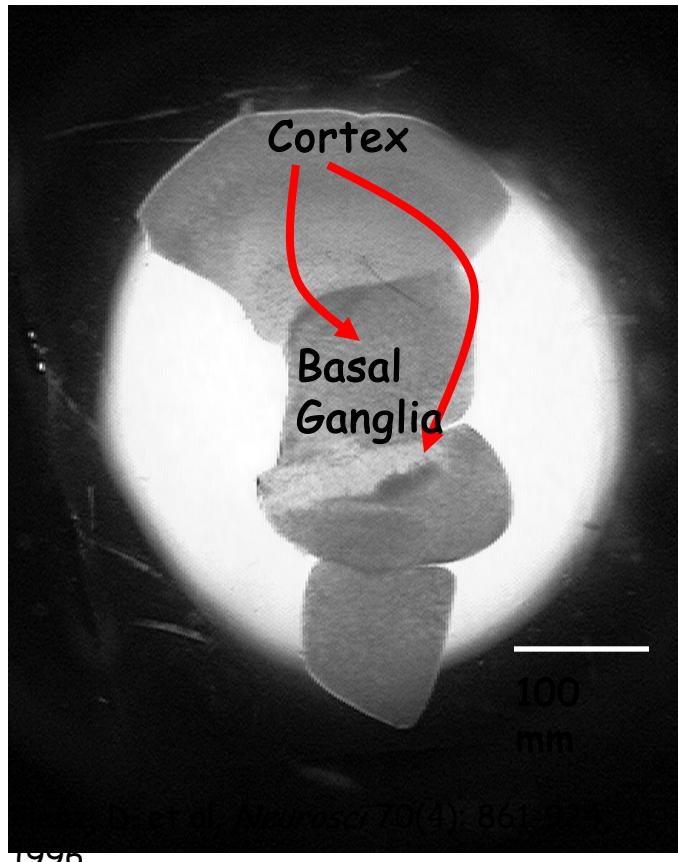
J. Bodurka, P. A. Bandettini. Magn. Reson. Med. 47: 1052-1058, (2002).



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:~1-2mm², 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

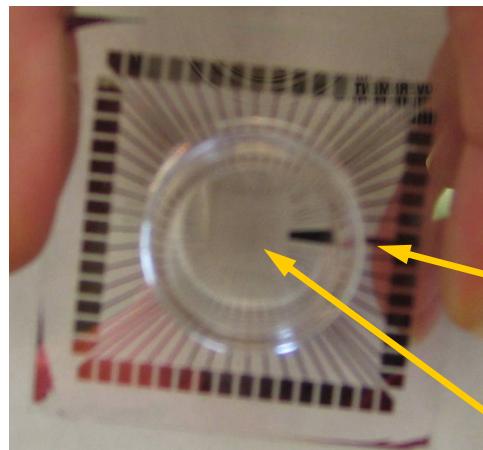
Culture Preparation

Multi-Electrode Arrays (MEA)

Multichannelsystems Germany 8x8 electrodes

0.8ml culture medium

Multi-Electrode Array

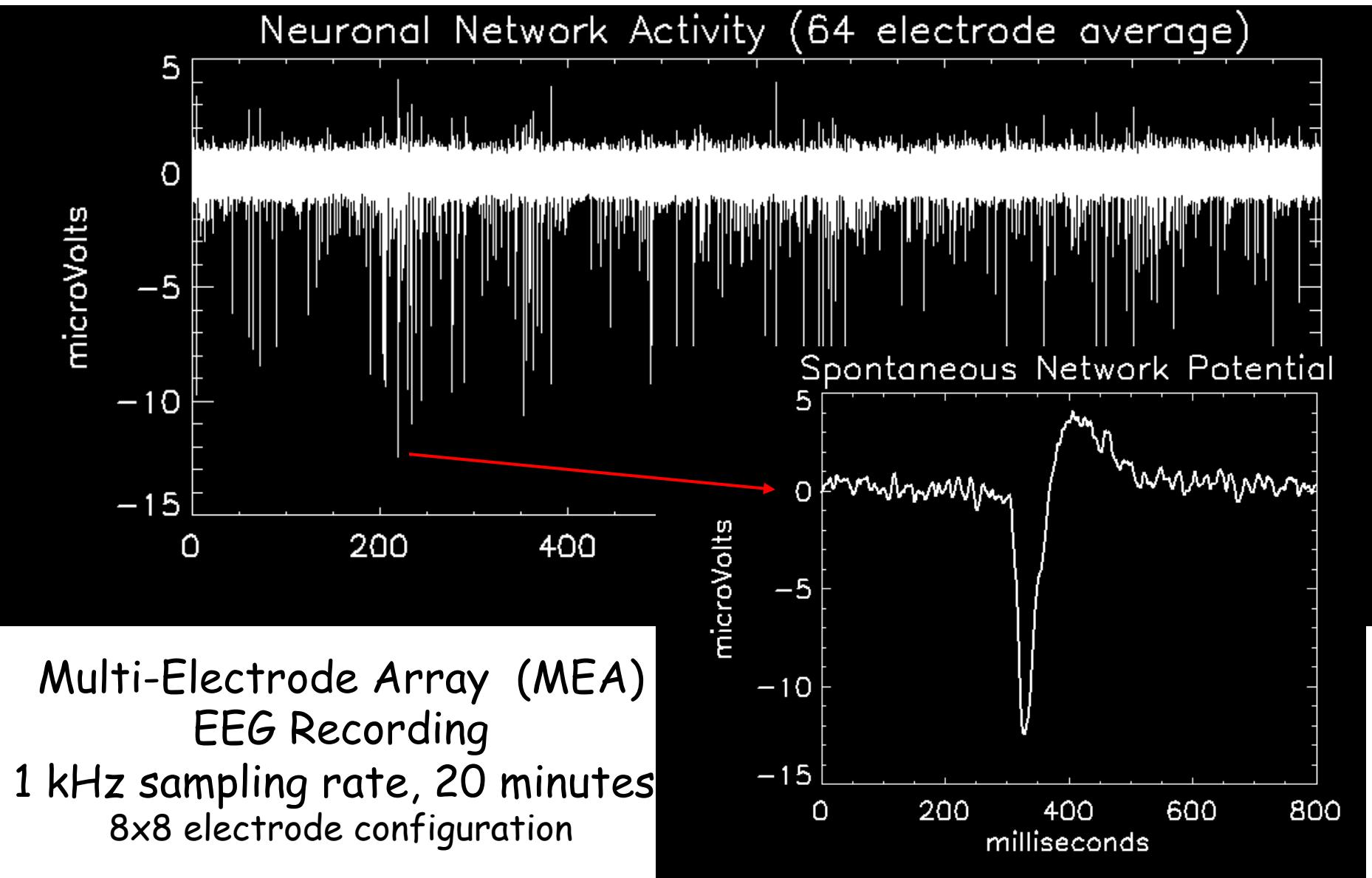


Reference
electrode

Culture site

10mm

Multi-Electrode Array EEG recording



in vitro MR protocol

Imaging (3T)

- Spin-Echo EchoPlanar Imaging

SE EPI
image

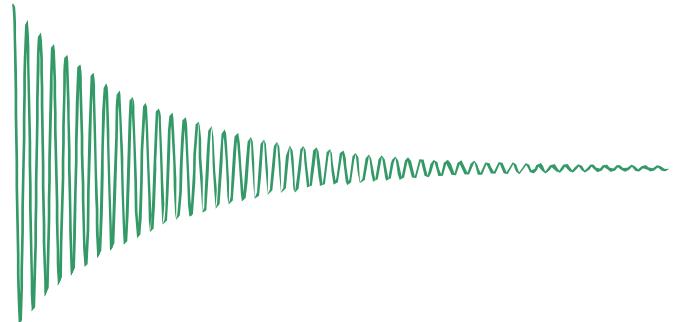


- voxel size: ~3x3x3 mm
- Sampling Rate :1 Hz (TR: 1sec)
- TE: 60 ms
- Readout :44 ms

NMR (7T)

- free induction decay (FID) acquisition

FID



- slab size: ~2x10x1mm
- 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

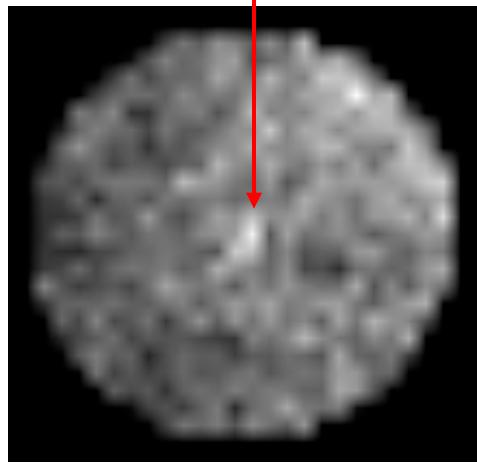
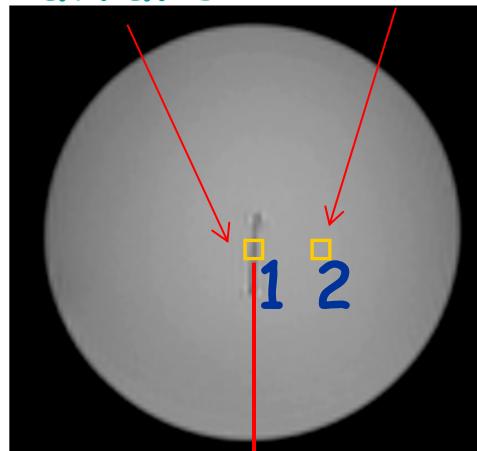
Active : ~17 min (10,000 images) neuronal activity present

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

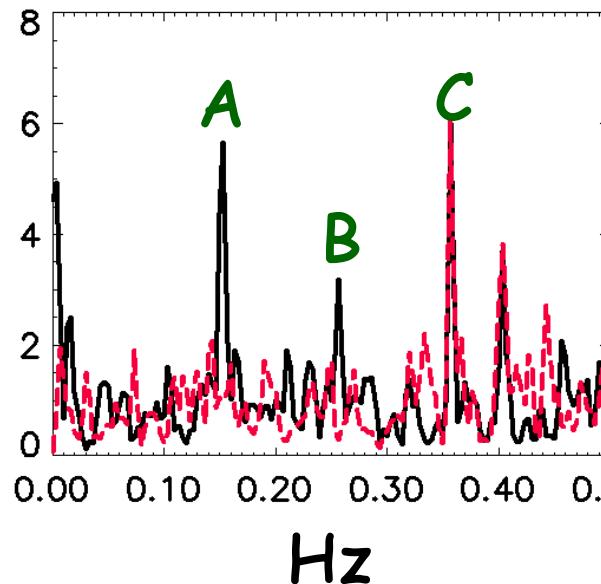
Pre- and Post- MR scan electrical recordings

3 Tesla data

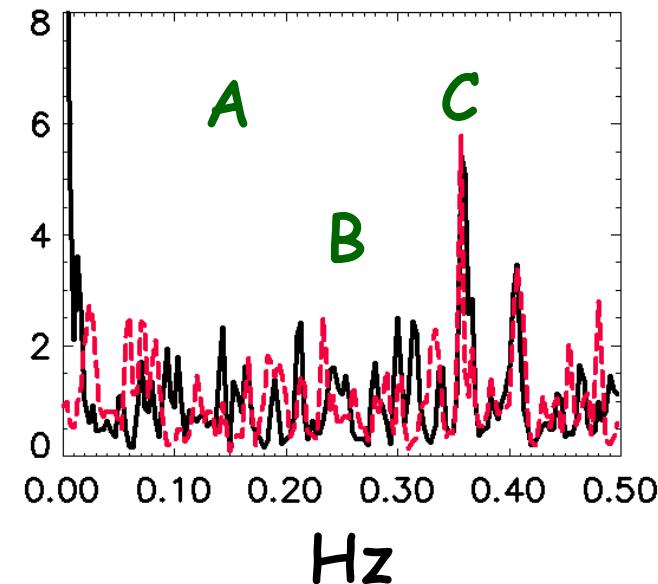
Culture ACSF



1: culture



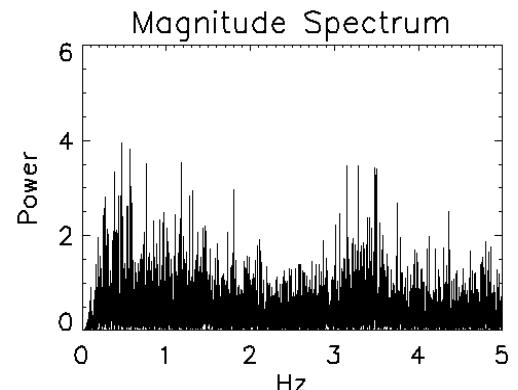
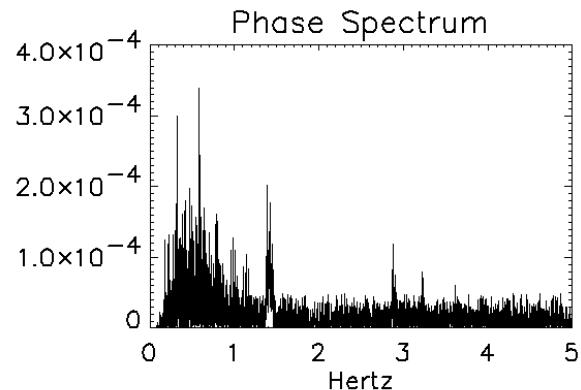
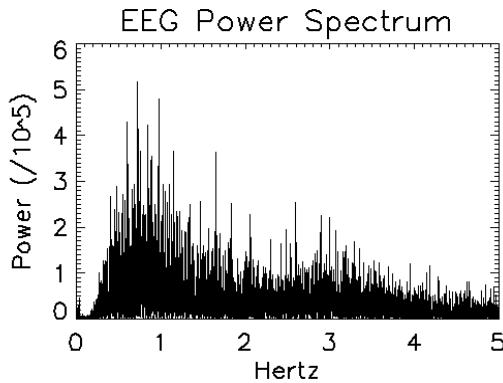
2: ACSF



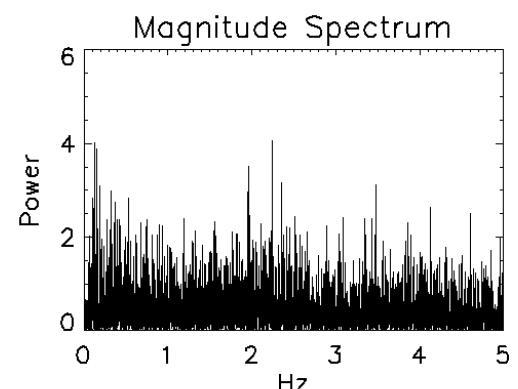
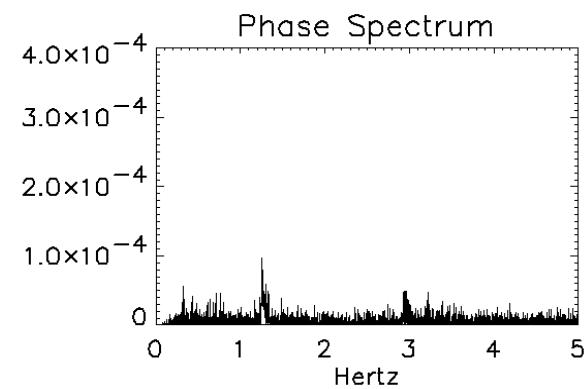
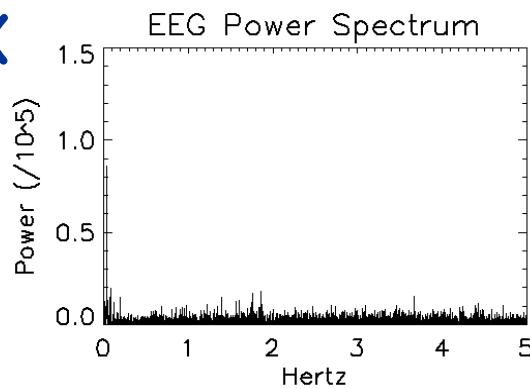
Active condition: black line
Inactive condition: red line

- 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

Section on Functional Imaging Methods

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Anthony Boemio	post doc
Justin Edmands	system admin
Dan Handwerker	post doc
Tyler Jones	post bac IRTA
Youn Kim	post bac IRTA
Niko Kriegeskorte	post doc
Marieke Mur	student IRTA
Kevin Murphy	post doc
Alissa Par	post bac IRTA
Vikas Patel	system admin
Dorian Van Tassell	program assistant

Javier Castillo-Gonzalez Summer Student	
Jason Diamond	Howard Hughes Fellow
Thomas Gallo	Summer Student
Hauke Heekeren	post doc
David Knight	post doc
Ilana Levy	post bac IRTA
Marta Maierow	visiting fellow
Hanh Nguyen	post bac IRTA
Natalia Petridou	student IRTA
Douglass Ruff	post bac IRTA
Monica Smith	post bac IRTA
August Tuan	post bac IRTA
Naja Waters	post bac IRTA

Functional MRI Facility

Jerzy Bodurka	staff scientist
Ellen Condon	technologist
Janet Ebron	technologist
Kenny Kan	technologist
Kay Kuhns	admin. lab manager
Wenming Luh	staff scientist
Sean Marrett	staff scientist
Marcela Montequin	technologist
Sandra Moore	technologist
Sahra Omar	technologist
Alda Ottley	technologist
Paula Rowser	technologist
Adam Thomas	system admin

Karen Bove-Bettis	technologist
James Hoske	technologist

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 s ⁻¹	0.01 s–0.16 s
Δf	Fractional blood flow change	0.4	—
α	Steady-state flow–volume relationship	0.4	0.25–1.0
τ_{MTT}	Blood mean transit time (v_0/f_0)	3 s	1.1 s–18 s
τ_+	Viscoelastic time constant (inflation)	20 s	10 s–40 s
τ_-	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).