A closer look at fMRI

dynamics, fluctuations, and patterns

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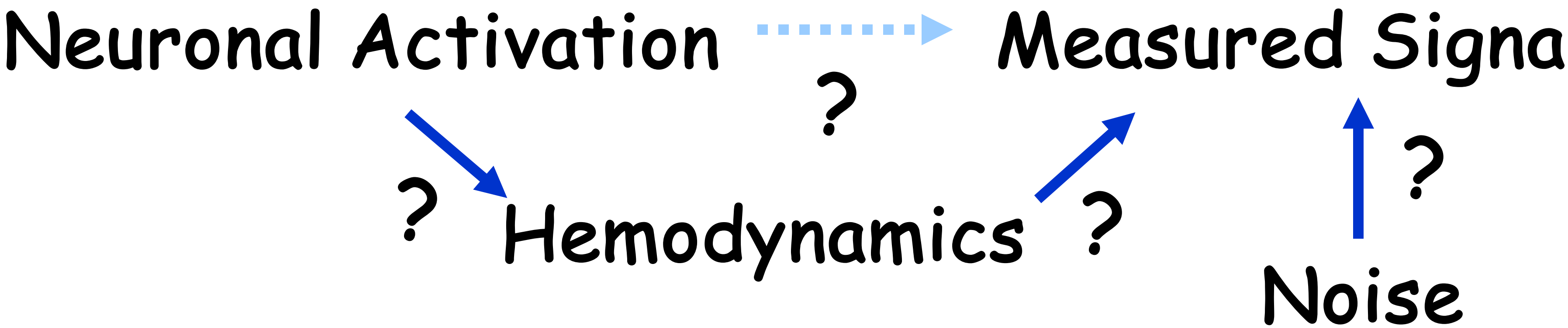
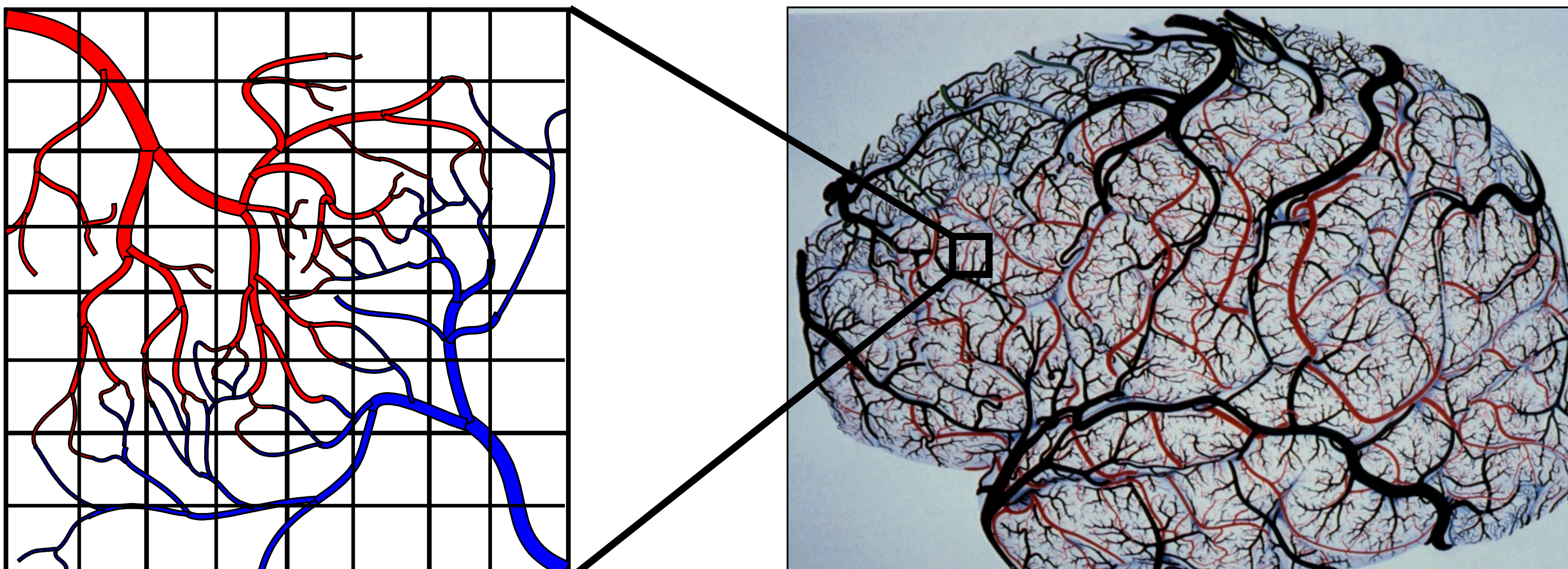
September, 1991


Neuronal Activation
Measured Signal
?
?
Hemodynamics
?
?
Noise



1. Dynamics
2. Fluctuations
3. Experimental Design
4. Pattern Information
5. Neuronal Current MRI

1. Dynamics

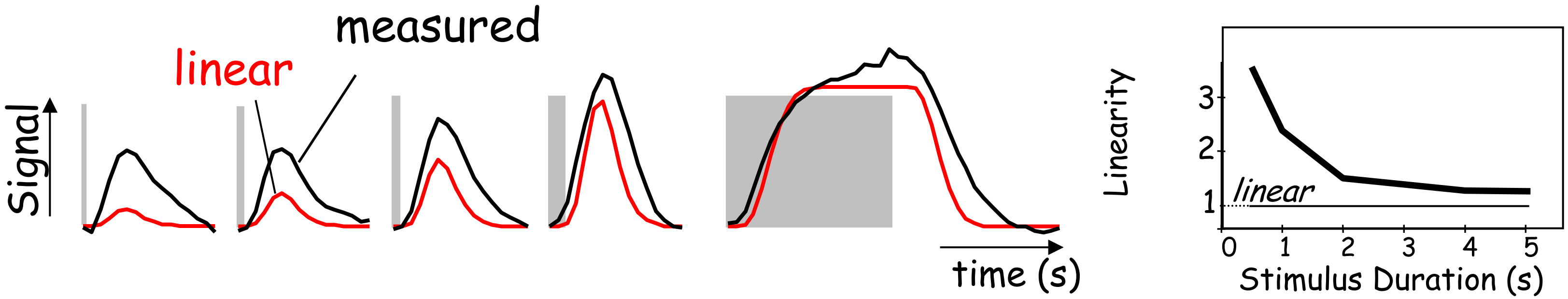
Motivation:

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

Studies:

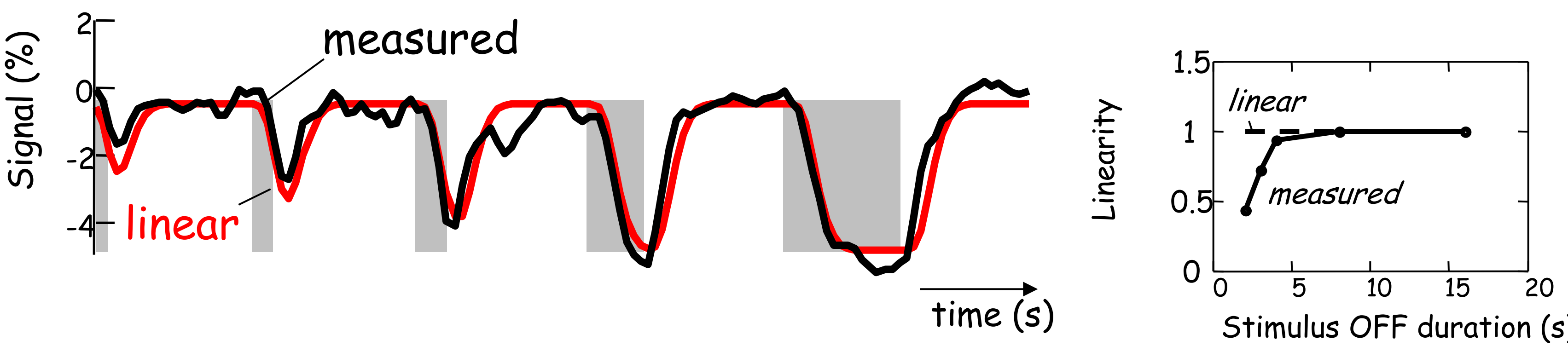
- Modulate timing: “on” duration, “off” duration, and duty cycle of visual cortex activation.
- Neuronal and Hemodynamic Modeling.
- MEG and fMRI Comparison.

Brief "on" periods produce larger increases than expected.



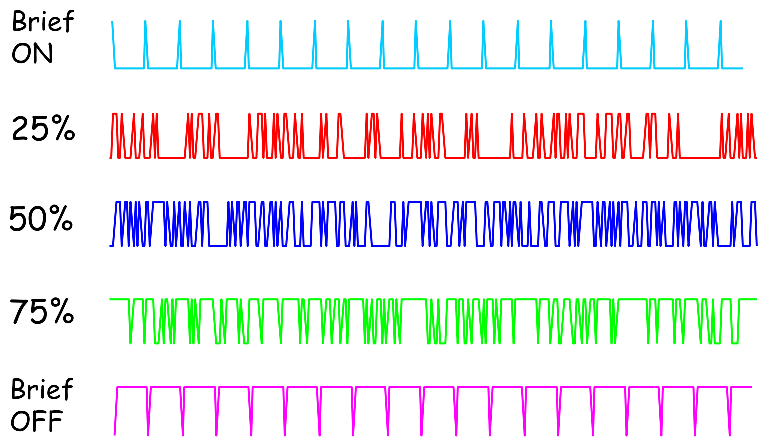
R. M. Birn, Z. Saad, P. A. Bandettini, NeuroImage, 14: 817-826, (2001)

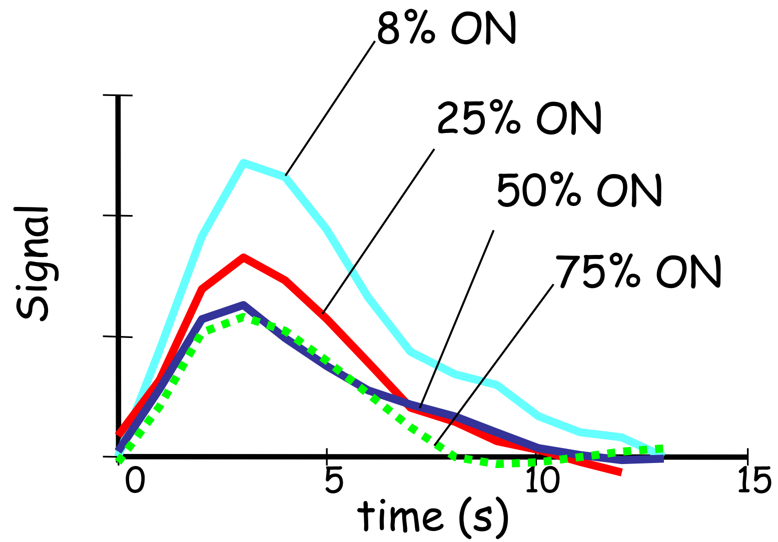
Brief "off" periods produce smaller decreases than expected.



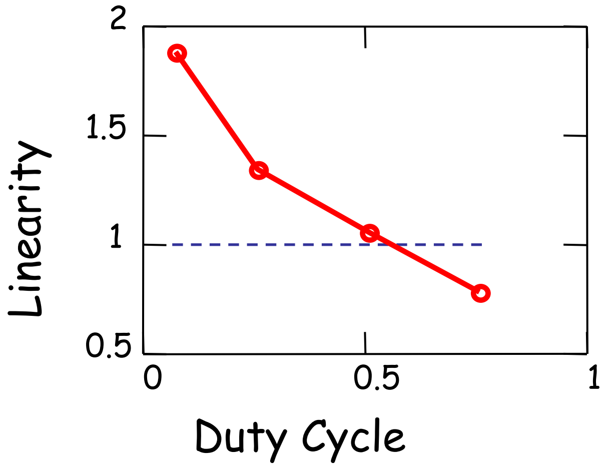
R.M. Birn, P. A. Bandettini, NeuroImage, 27, 70-82 (2005)

Varying the Duty Cycle



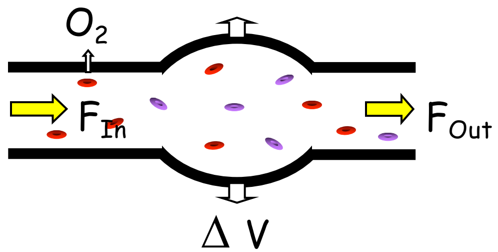


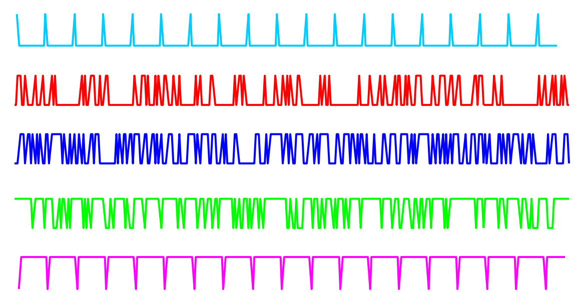
Deconvolved Response



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

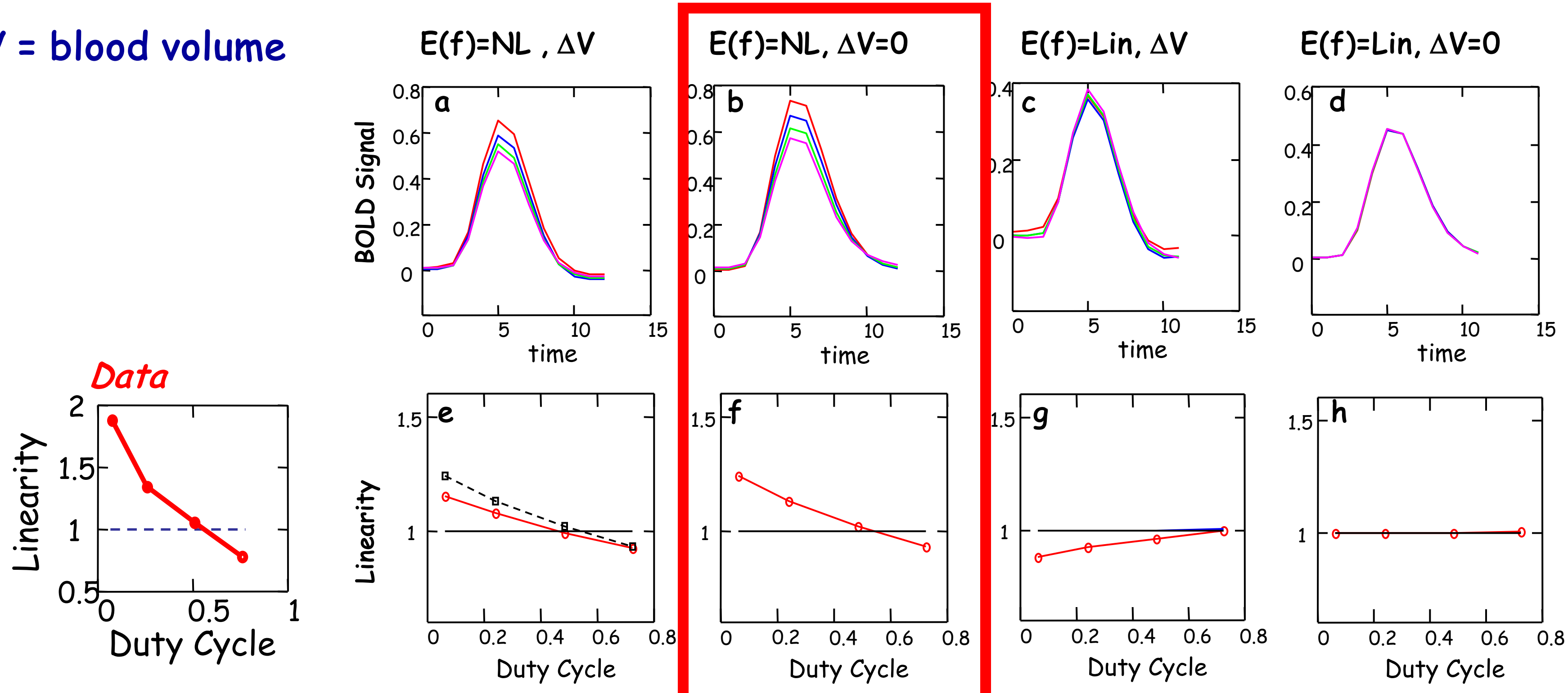
Simulation of Hemodynamic Mechanisms
(Balloon model)



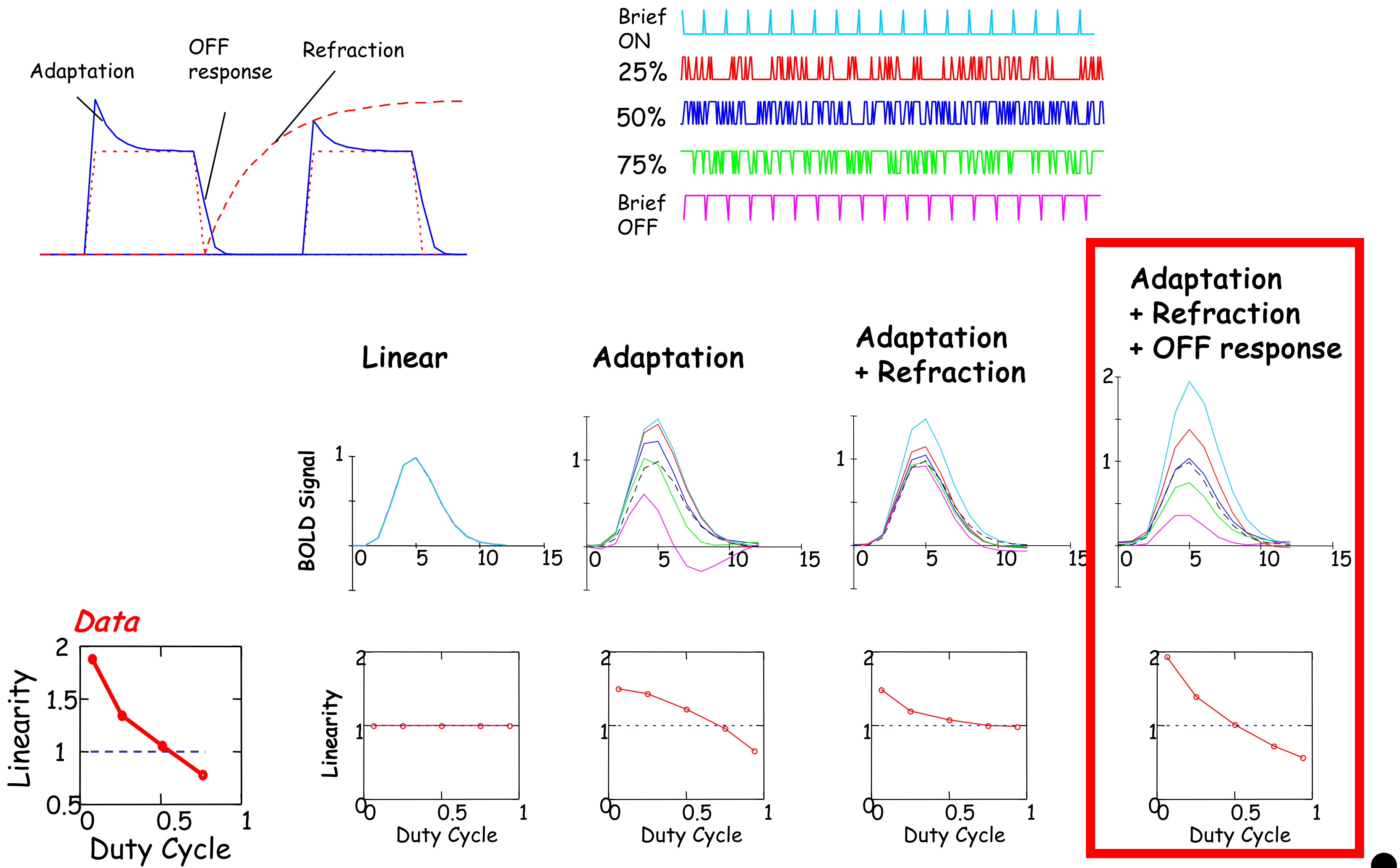


E(f) = oxygen extraction fraction

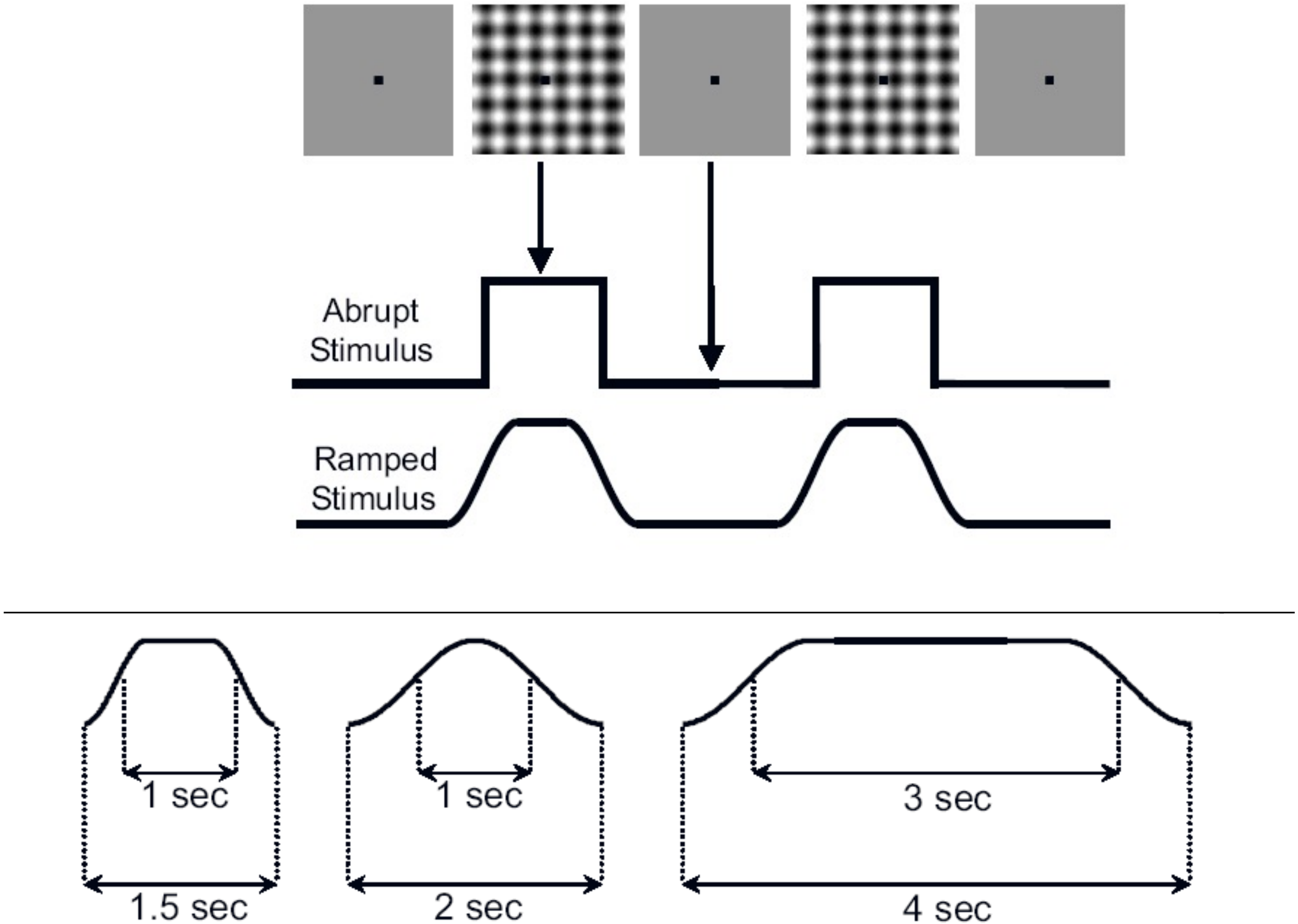
V = blood volume



Simulation of Neuronal Mechanisms

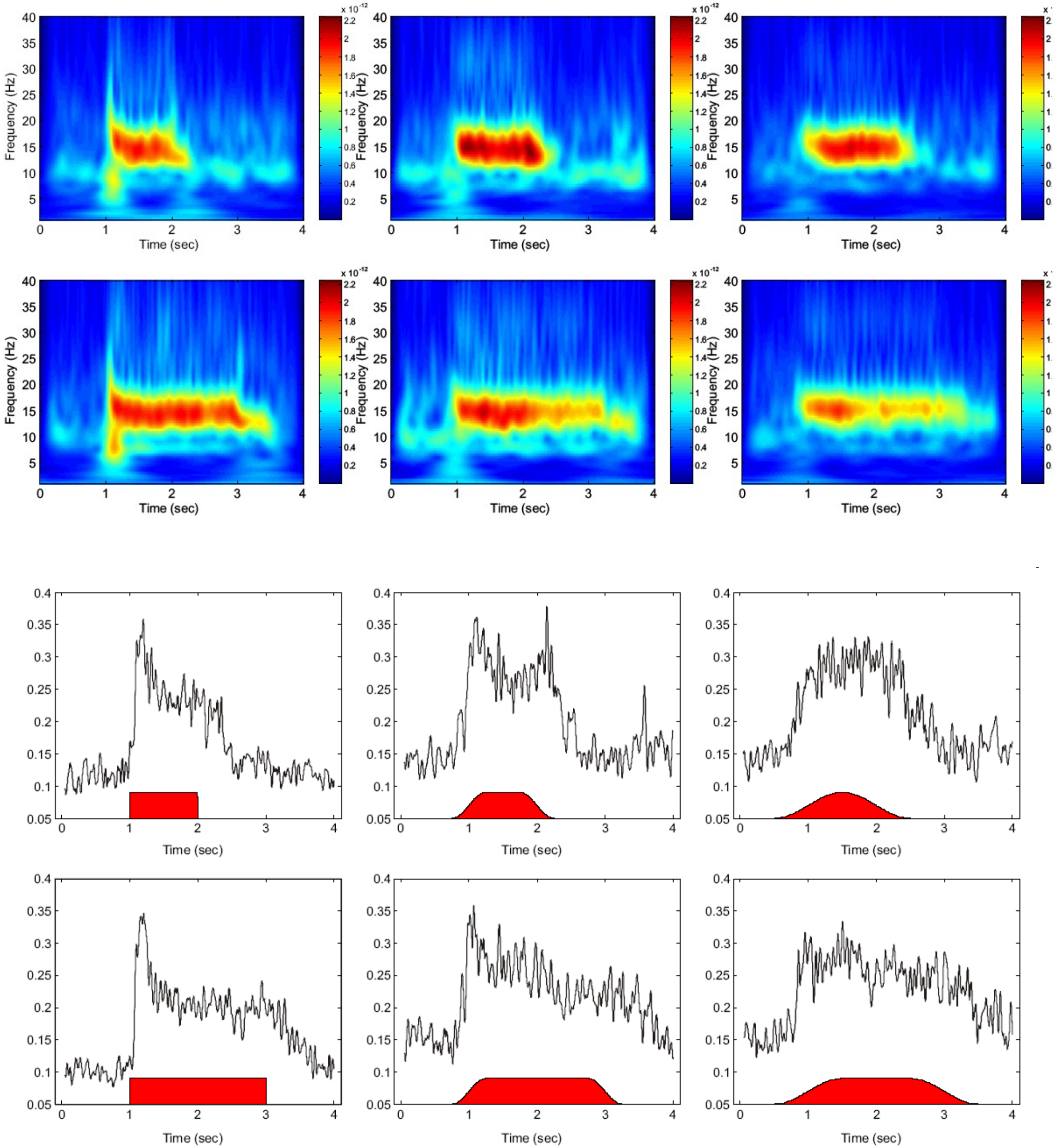


MEG & fMRI Linearity Comparison



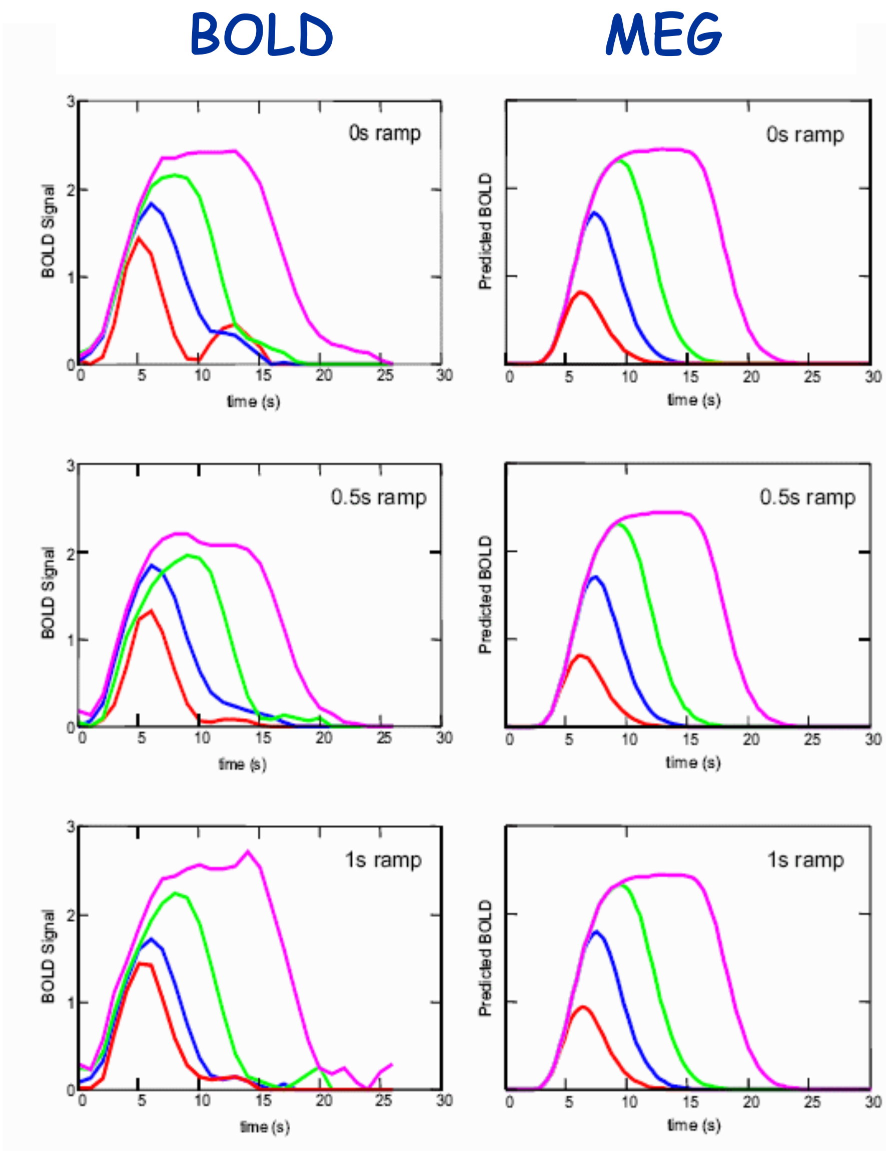
A. Tuan, R. M. Birn, P. A. Bandettini, G. M. Boynton, (submitted)

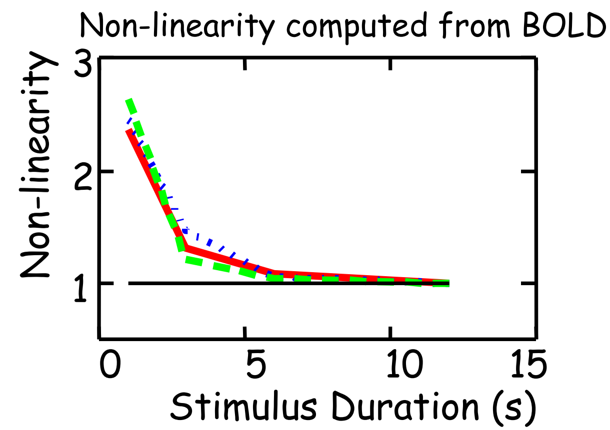
MEG Results

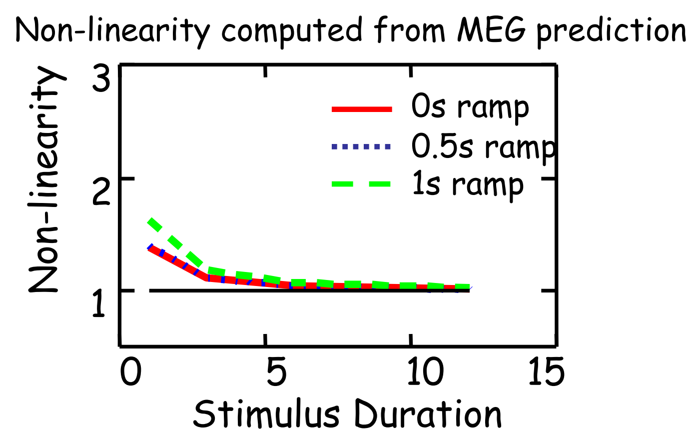


A. Tuan, R. M. Birn, P. A. Bandettini, G. M. Boynton, (submitted)

Measured and Predicted BOLD responses







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

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.

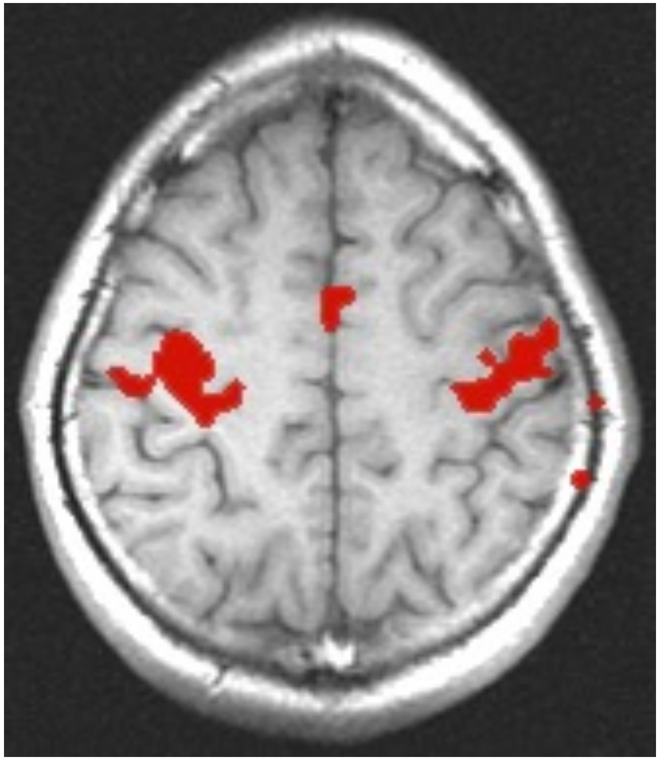
Studies:

- Time course of respiration volume per unit time (RVT)

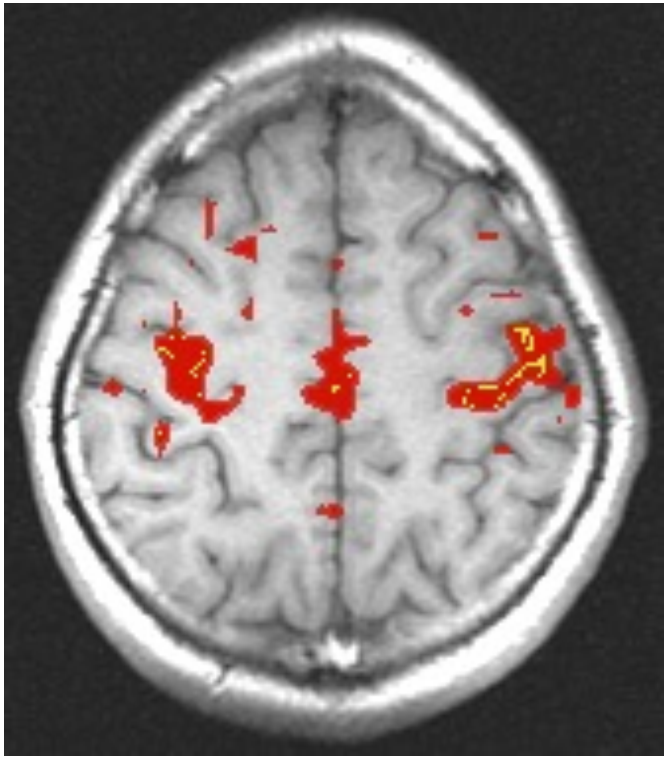
- The Respiration Response Function (RRF)

- FMRI Calibration using RRF

Resting State Correlations



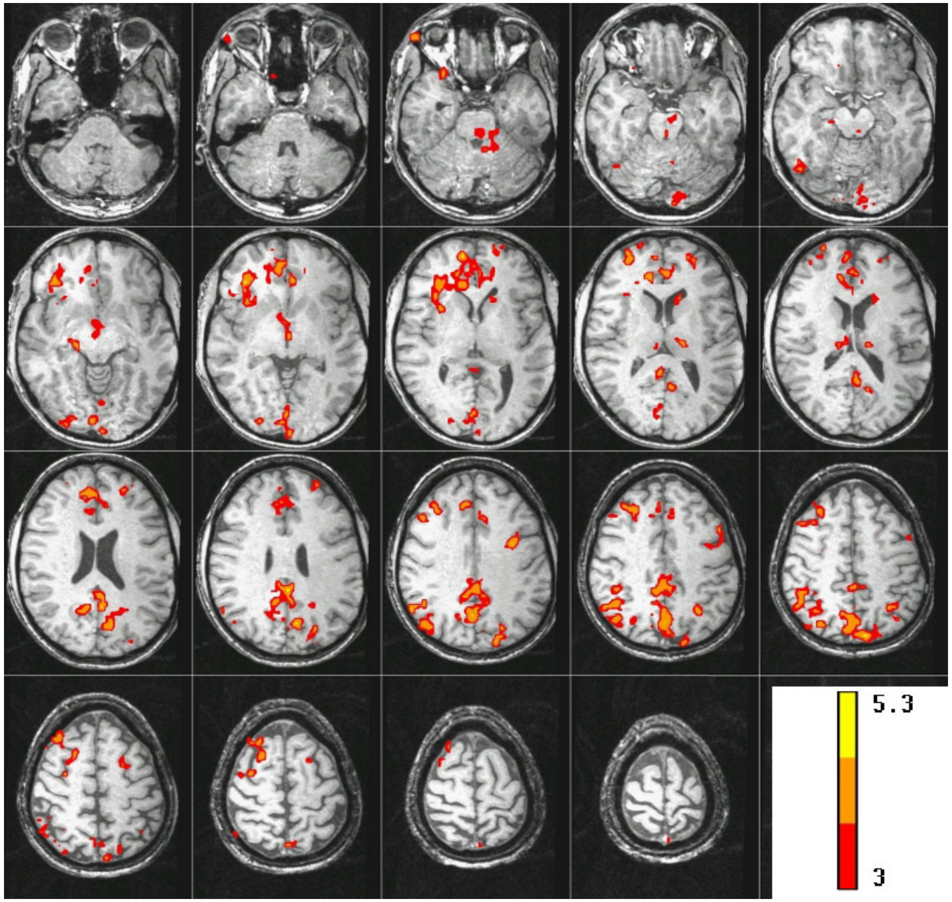
Activation:
correlation with reference function



Rest:
seed voxel in motor cortex

B. Biswal *et al.*, MRM, 34:537 (1995)

BOLD correlated with SCR during "Rest"

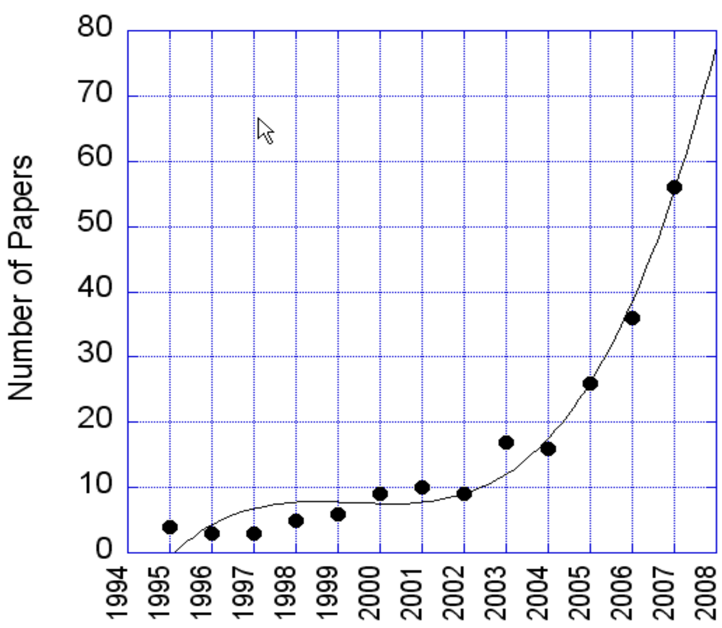


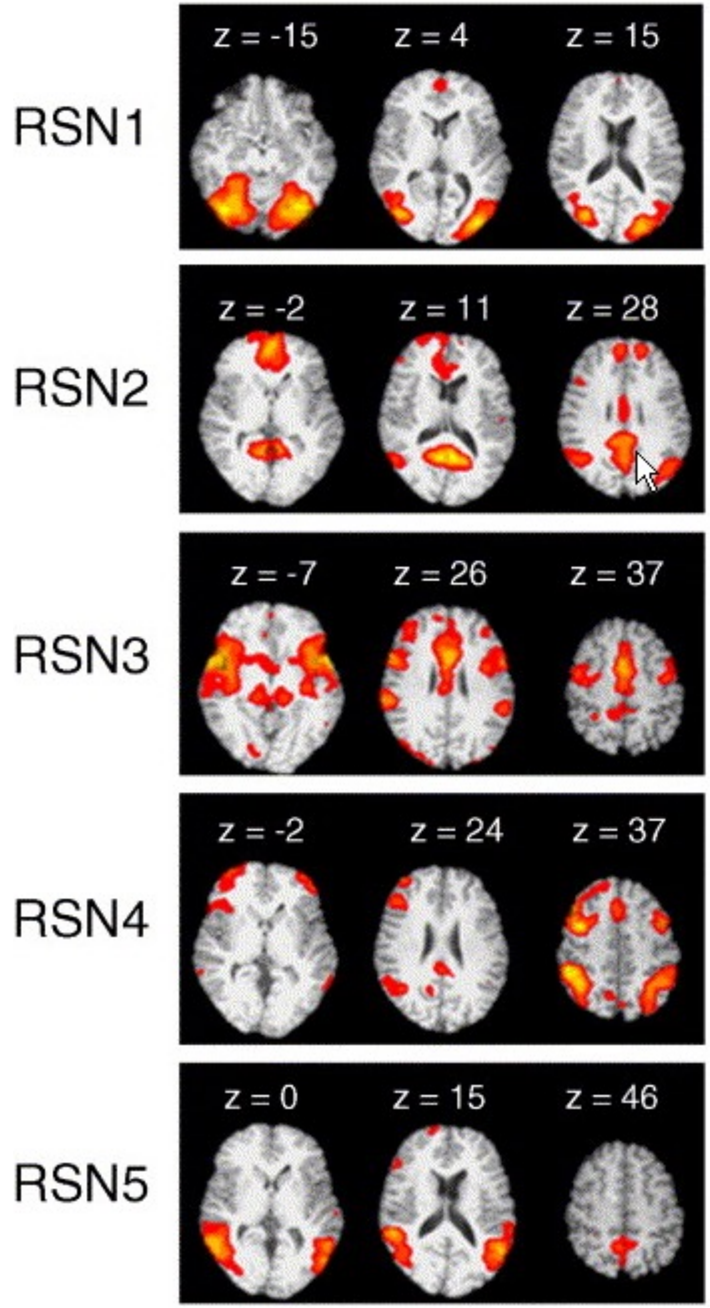
J. C. Patterson II, L. G. Ungerleider, and P. A Bandettini, *NeuroImage 17: 1787-1806, (2002).*

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



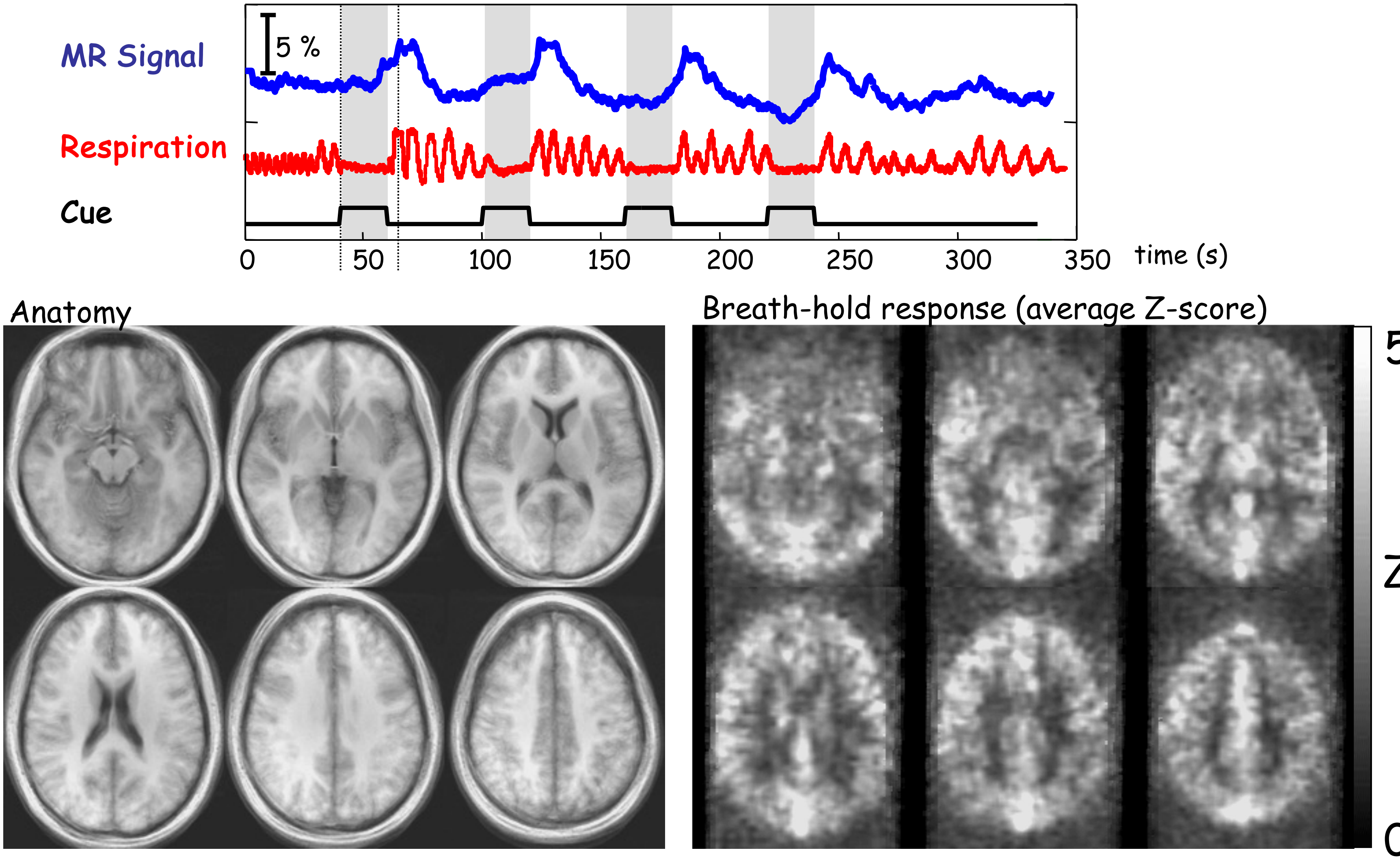


Sources of time series fluctuations:

- 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

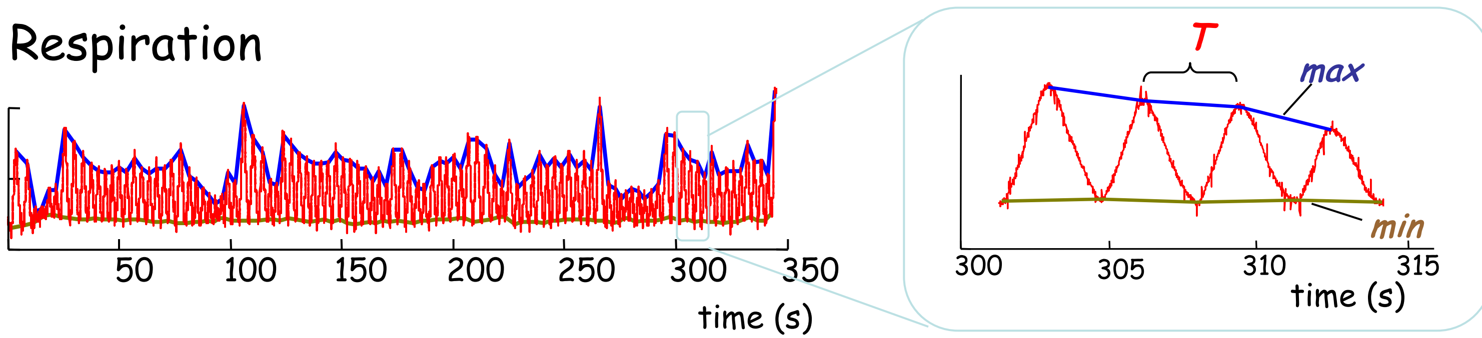
Group Maps (N = 7)



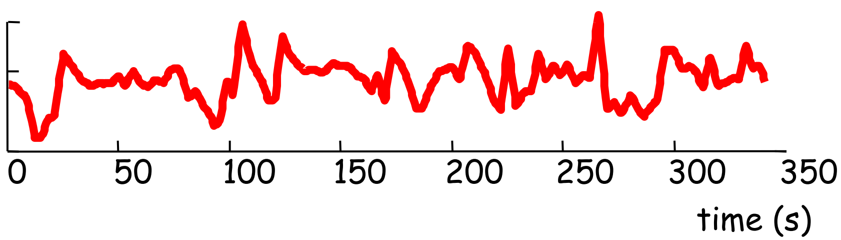
R.M. Birn, J. A. Diamond, M. A. Smith, P. A. Bandettini, *NeuroImage*, 31, 1536-1548

Estimating respiration volume changes

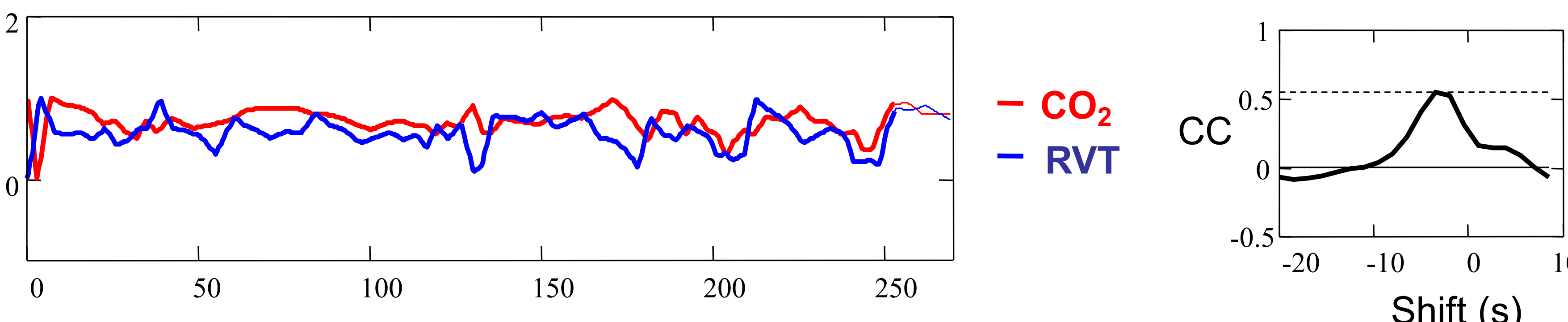
Respiration



Respiration Volume / Time (RVT)

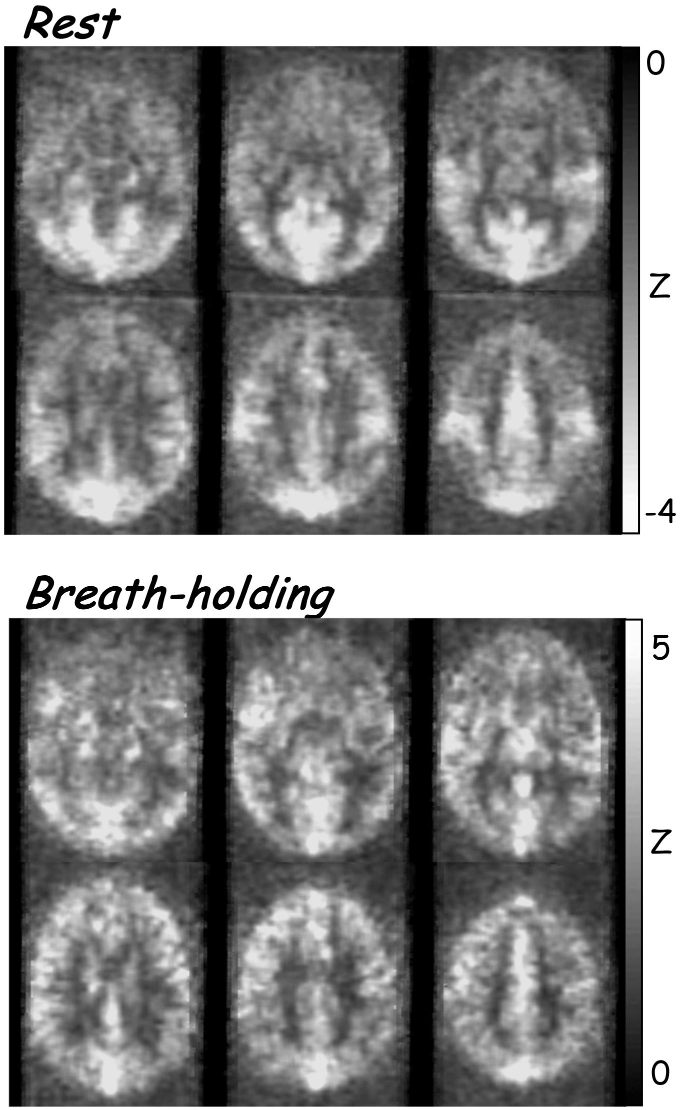


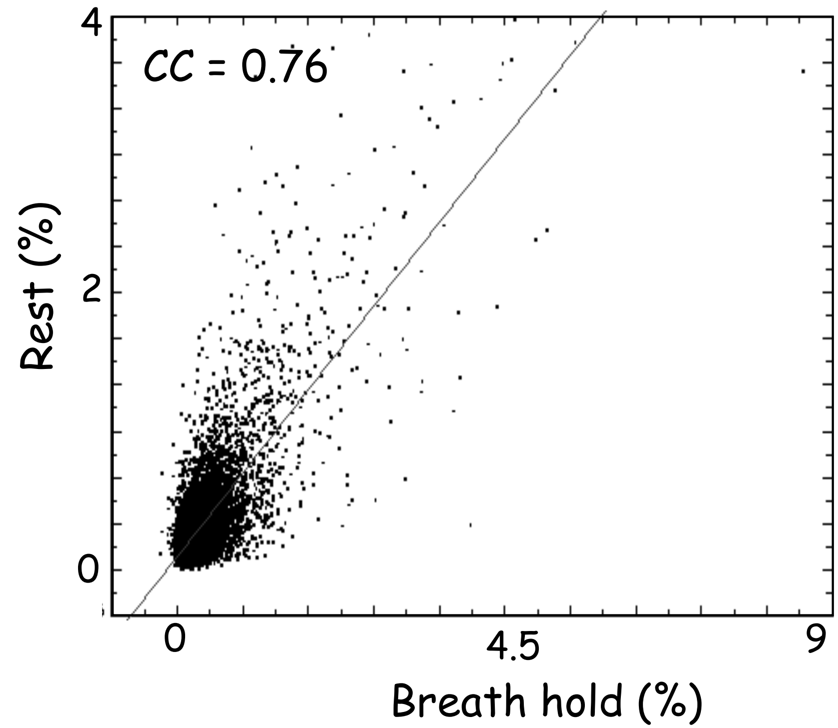
$$RVT = \frac{max - min}{T}$$



RVT precedes end tidal CO_2 by 5 sec.

Respiration induced signal changes

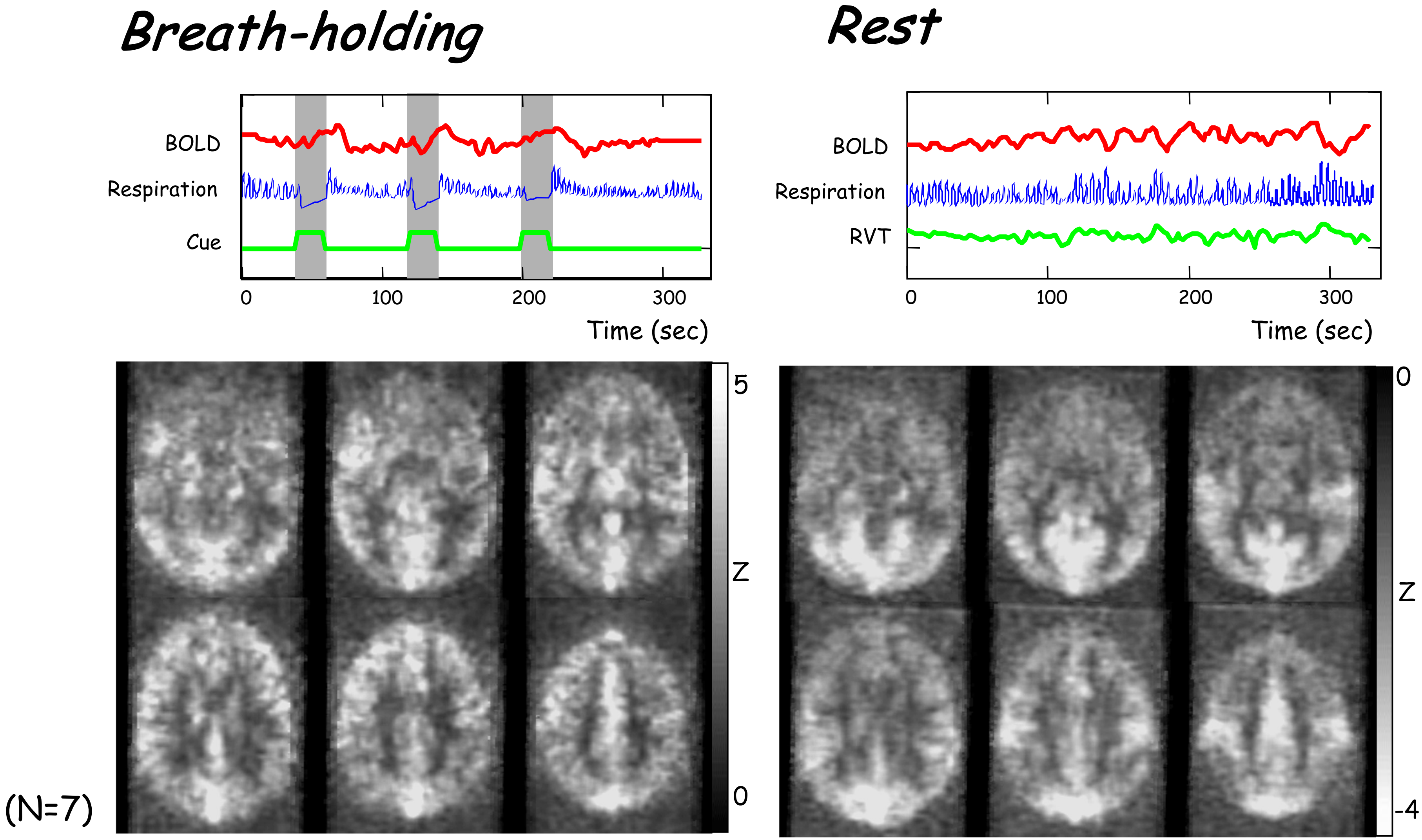




(N=7)

Methodology

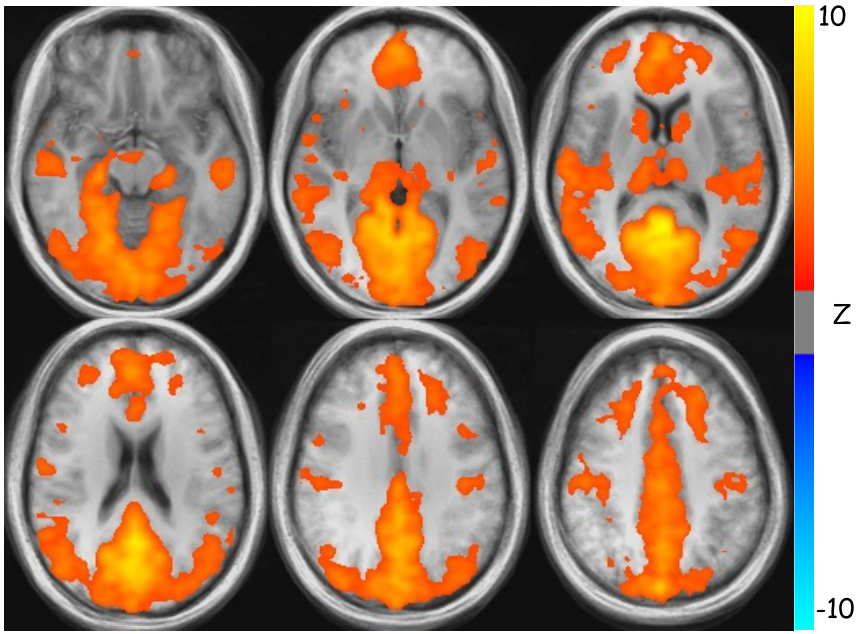
Respiration induced signal changes



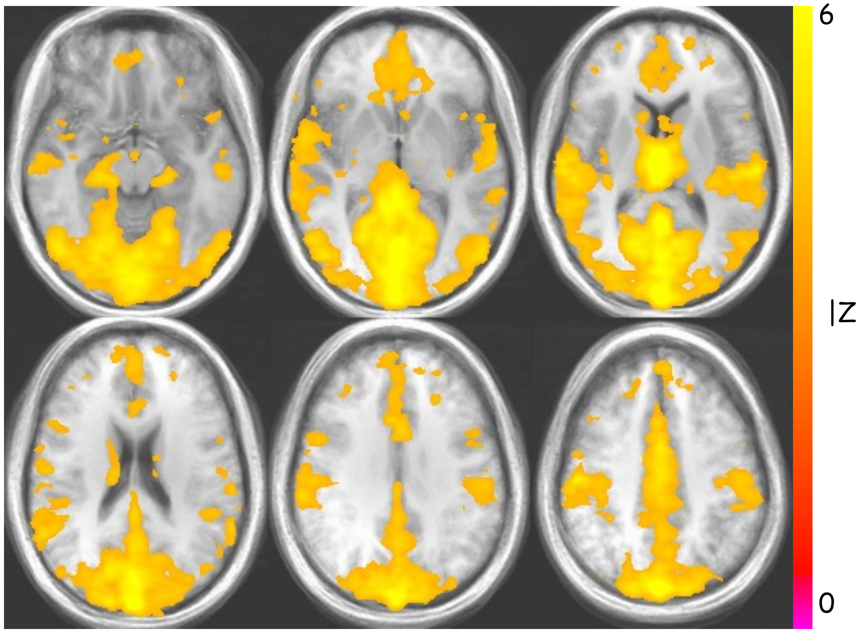
R.M. Birn, J. A. Diamond, M. A. Smith, P. A. Bandettini, *NeuroImage*, 31, 1536-1548 (2006)

RVT Correlation Maps & Functional Connectivity Maps

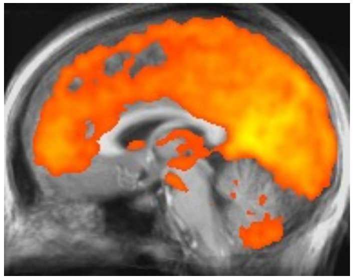
Resting state correlation with signal from posterior cingulate



Resting state correlation with RVT signal



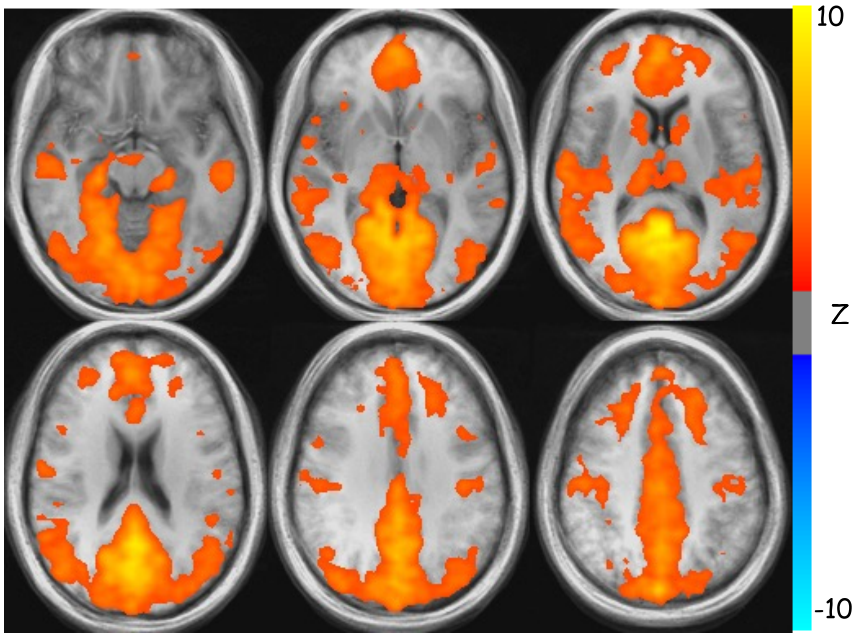
Group (n=10)



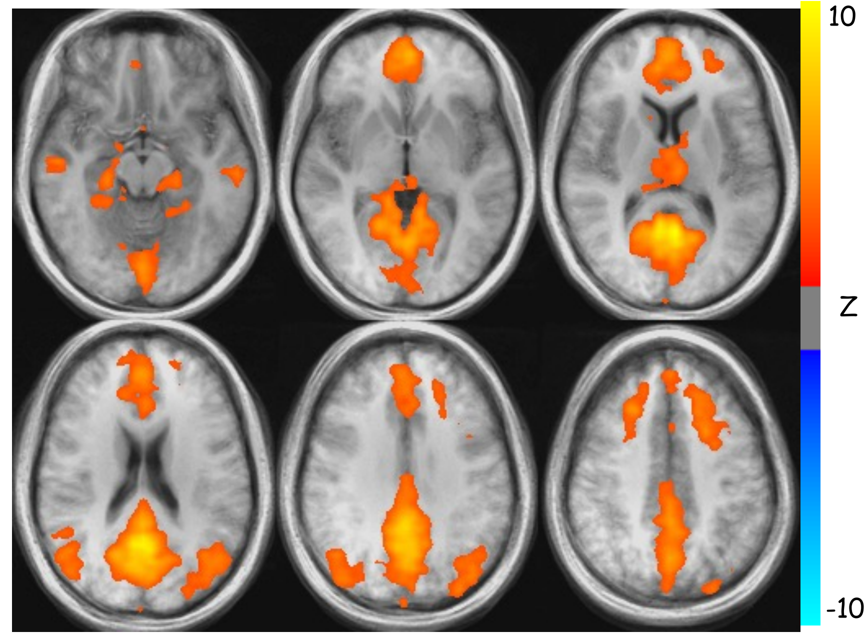
R.M. Birn, J. A. Diamond, M. A. Smith, P. A. Bandettini,
NeuroImage, 31, 1536-1548 (2006)

Effect of Respiration Rate Consistency on Resting Correlation Maps

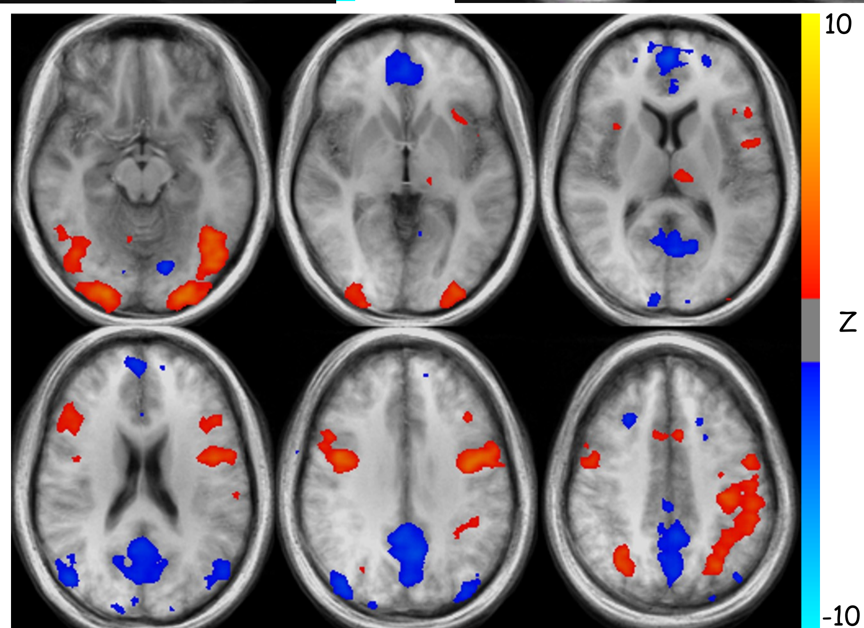
Spontaneously Varying Respiration Rate



Constant Respiration Rate



Lexical Decision Making Task

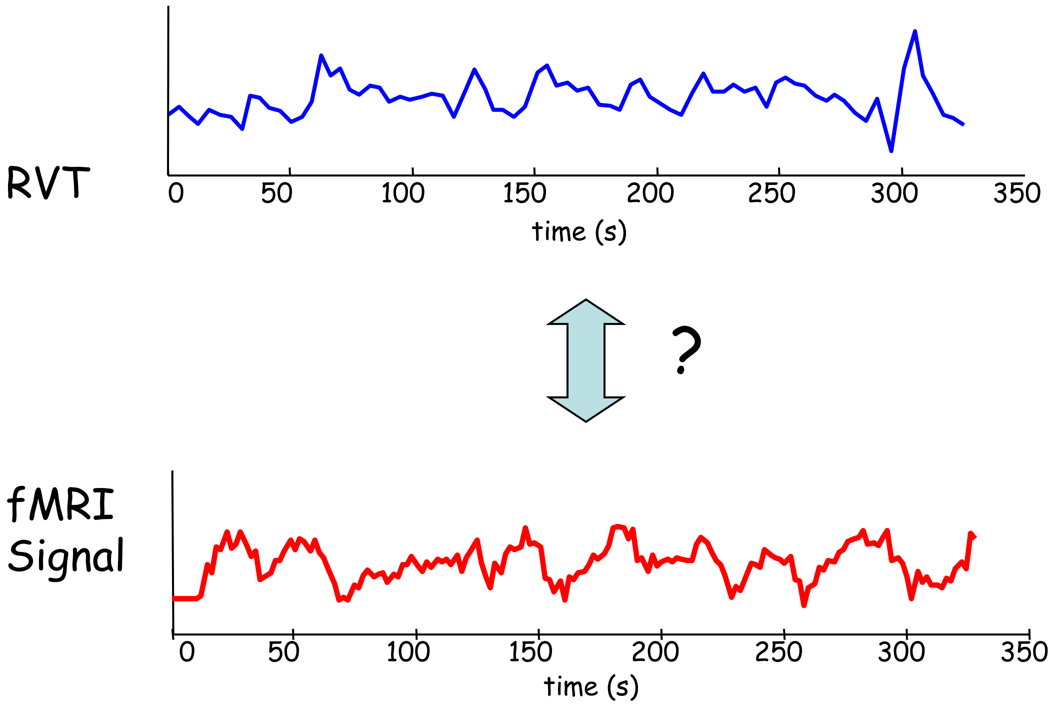


Blue: deactivated network

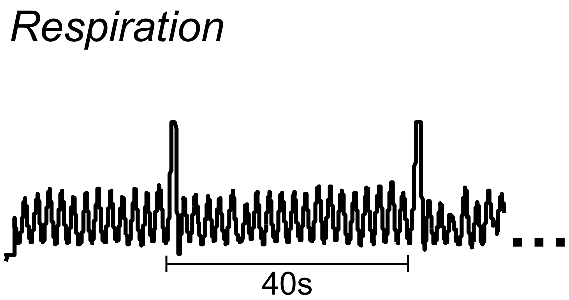
Group (n=10)

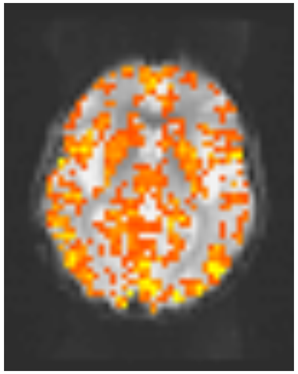
Respiration Changes vs. BOLD

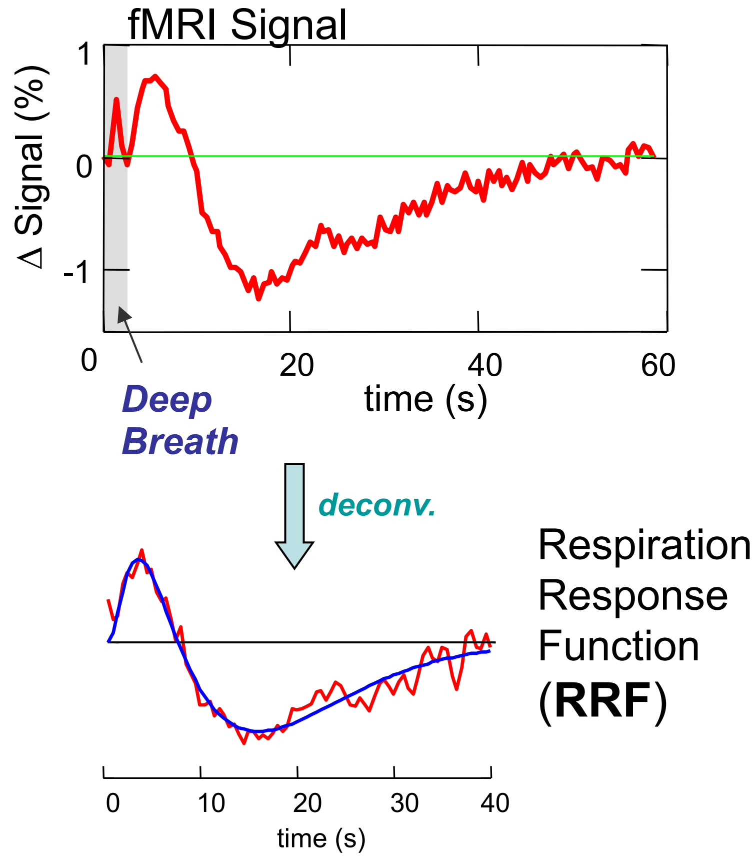
How are the BOLD changes related to respiration variations?



fMRI response to a single Deep Breath





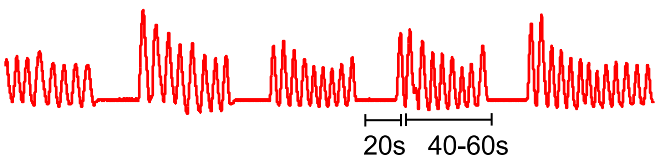


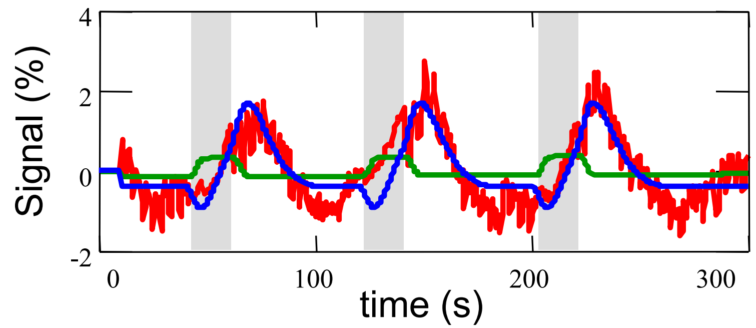
$$\mathrm{RRF}(t) = 0.6\ t^{2.1}\, e^{\frac{t}{1.6}} - 0.0023\ t^{3.54}\, e^{\frac{t}{4.25}}$$

R.M. Birn, M. A. Smith, T. B. Jones, P. A. Bandettini, *NeuroImage*, (in press)

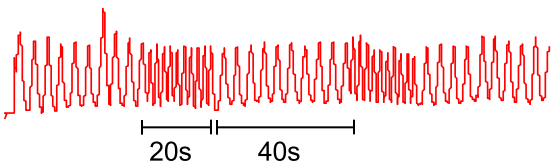
Respiration response function predicts BOLD signal associated with breathing changes better than activation response function.

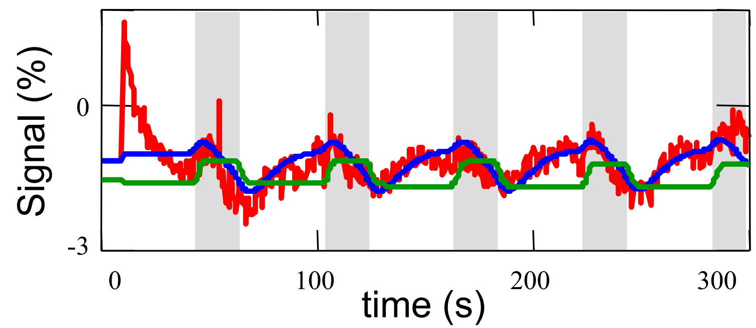
Breath-holding



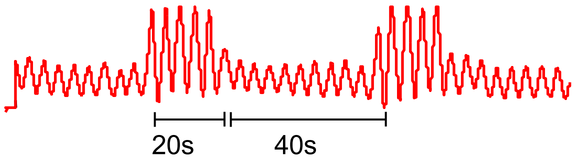


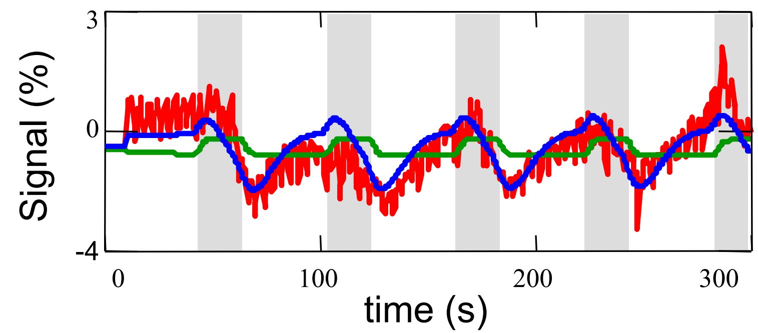
Rate Changes



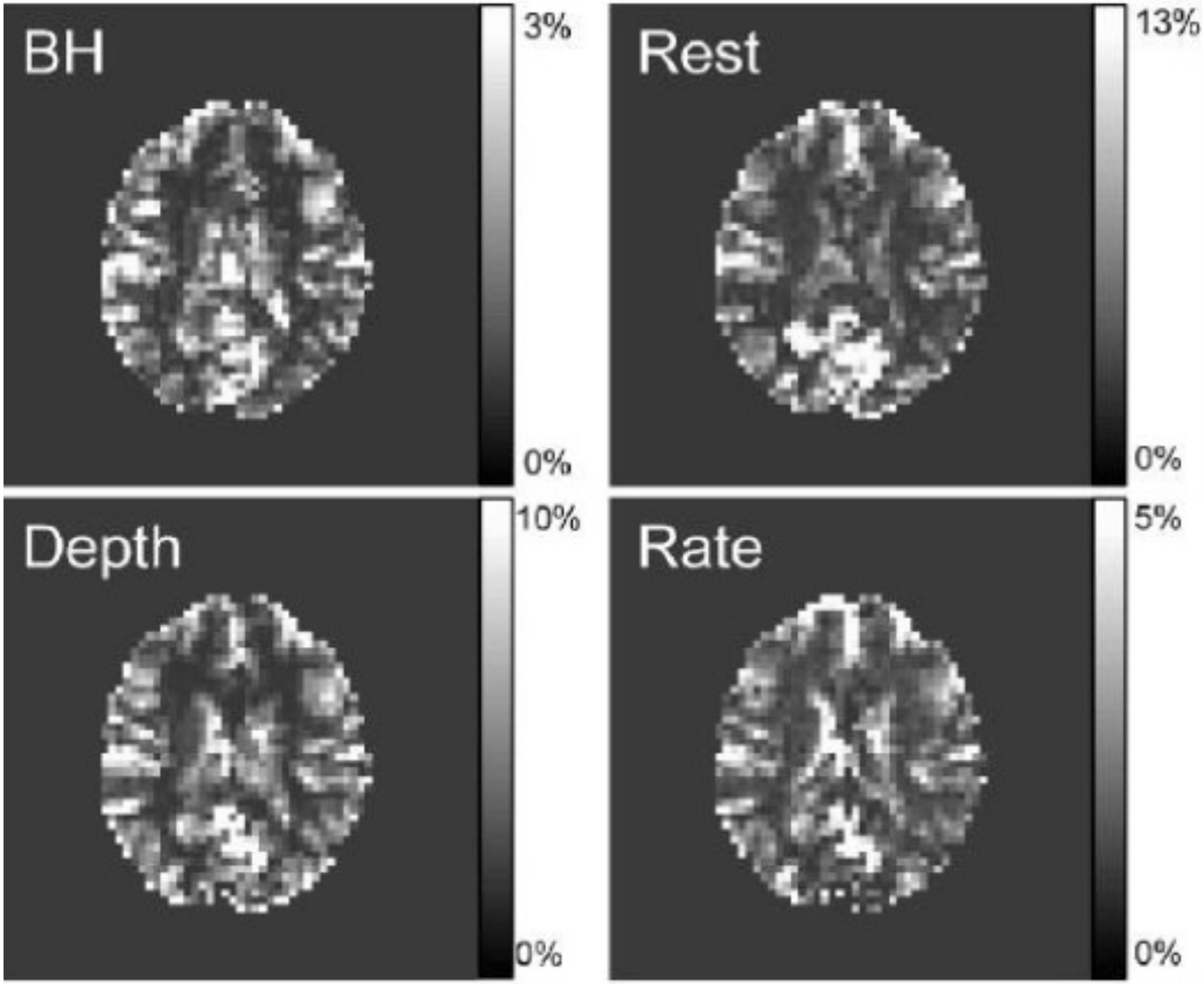


Depth Changes



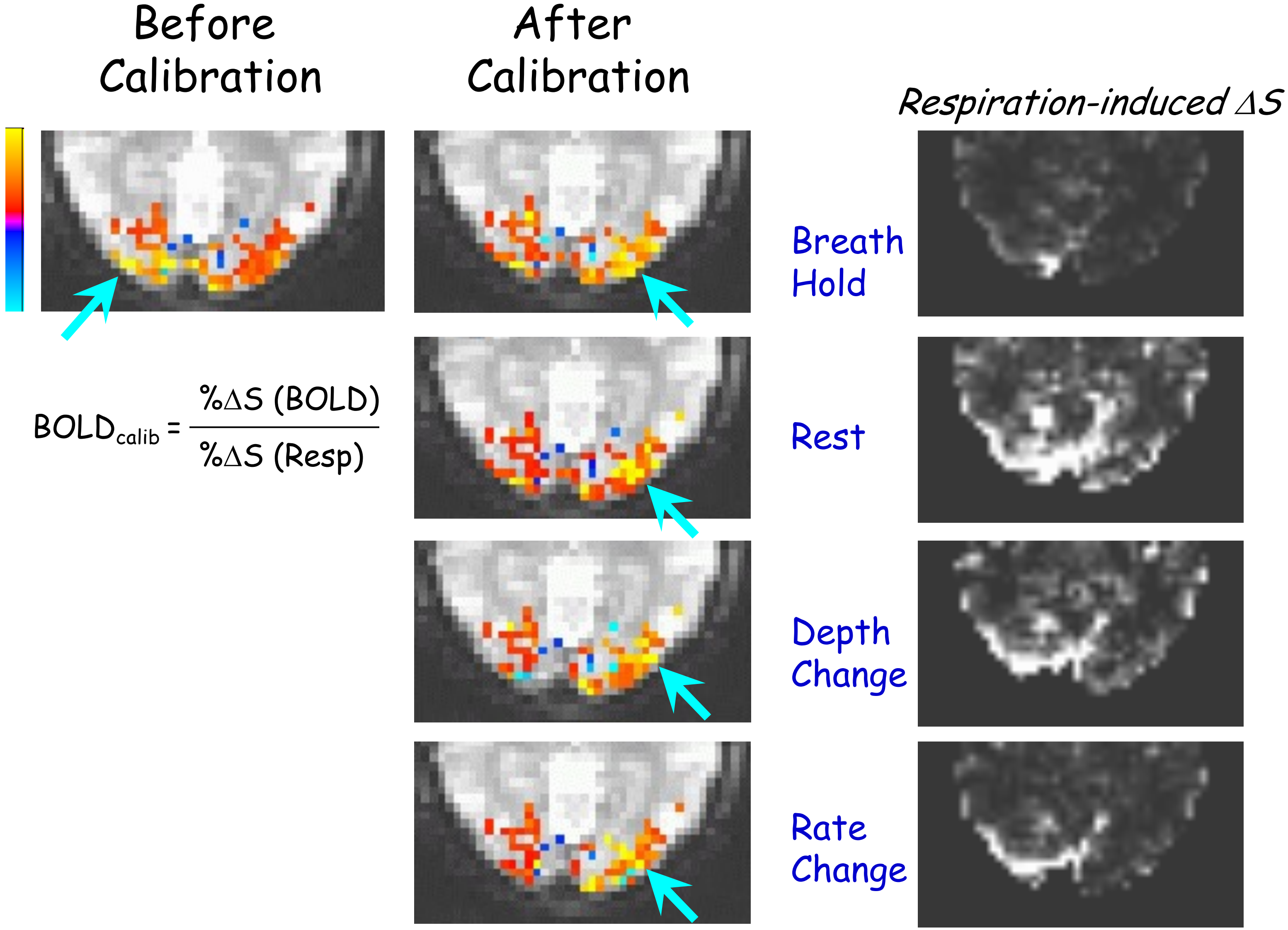


R.M. Birn, M. A. Smith, T. B. Jones, P. A. Bandettini, *NeuroImage*, (in press)



R.M. Birn, M. A. Smith, T. B. Jones, P. A. Bandettini, *NeuroImage*, (in press)

BOLD magnitude calibration



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

R.M. Birn, M. A. Smith, T. B. Jones, P. A. Bandettini, *NeuroImage*, (in press)

3. Experimental Design

Motivation:

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

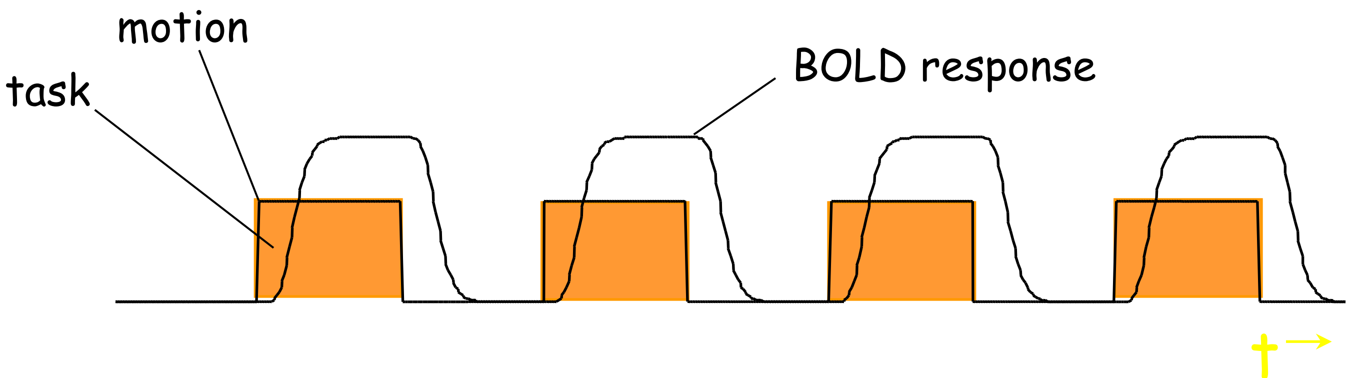
Studies:

- Overt response timing

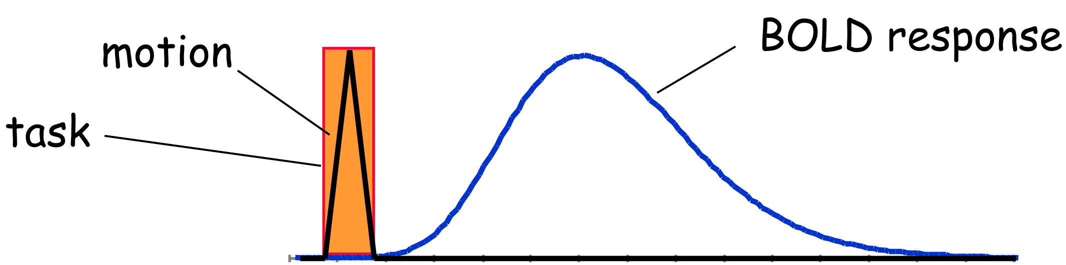
- Suggested resolution

fMRI during tasks that involve brief motion

Blocked Design

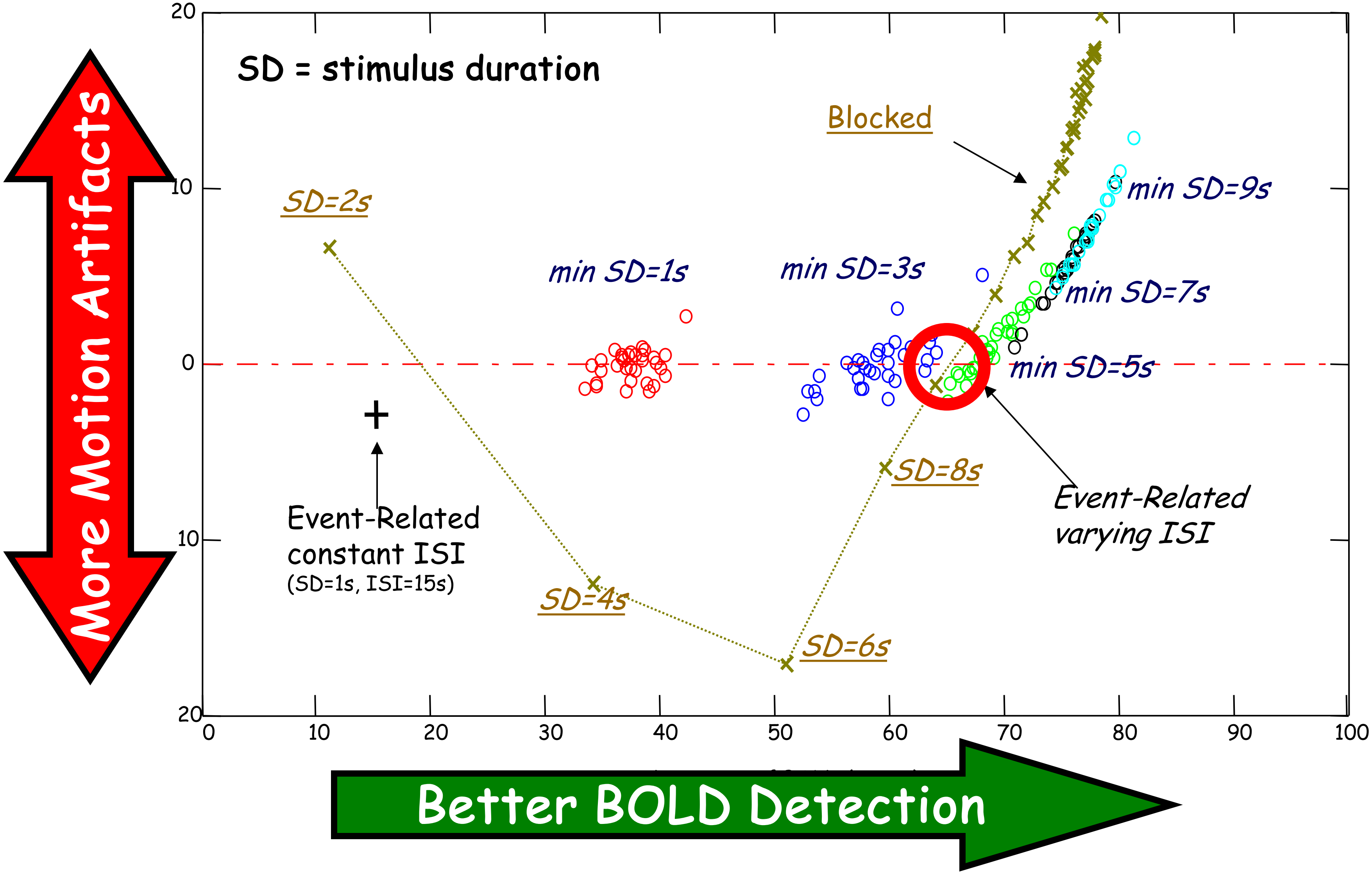


Event-Related Design



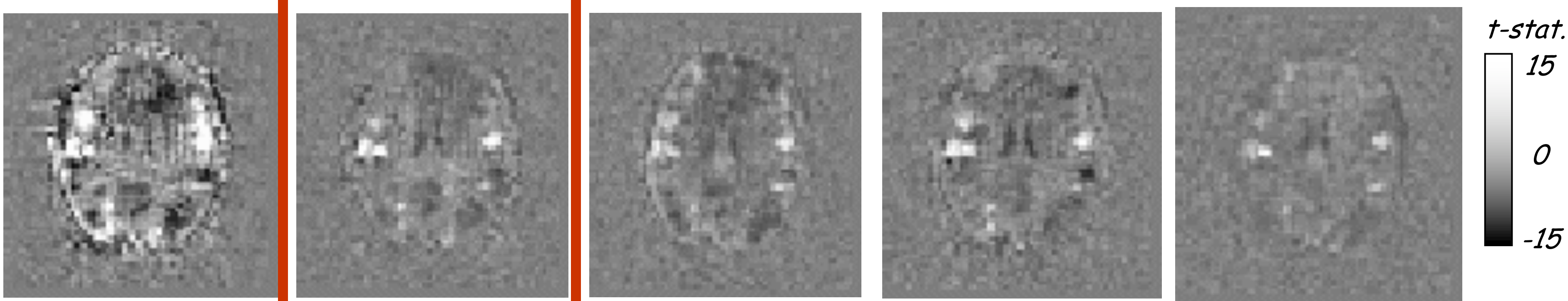
R. M. Birn, P. A. Bandettini, R. W. Cox, R. Shaker, *Human Brain Mapping* 7: 106-114 (1999).

Overt Responses - Simulations



R.M. Birn, R. W. Cox, P. A. Bandettini, *NeuroImage*, 23, 1046-1058 (2004)

Overt Responses



Blocked design (30s/30s)

Blocked design (10s/10s)

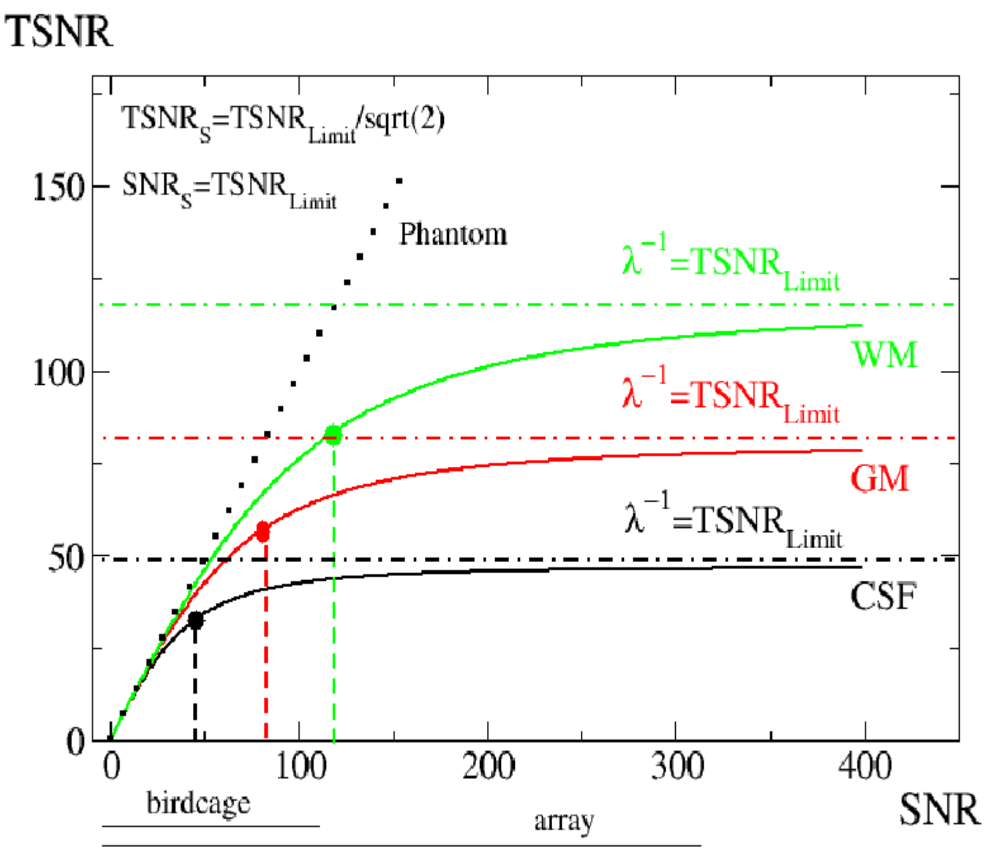
Event-related Varying ISI (1s min. SD)

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

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

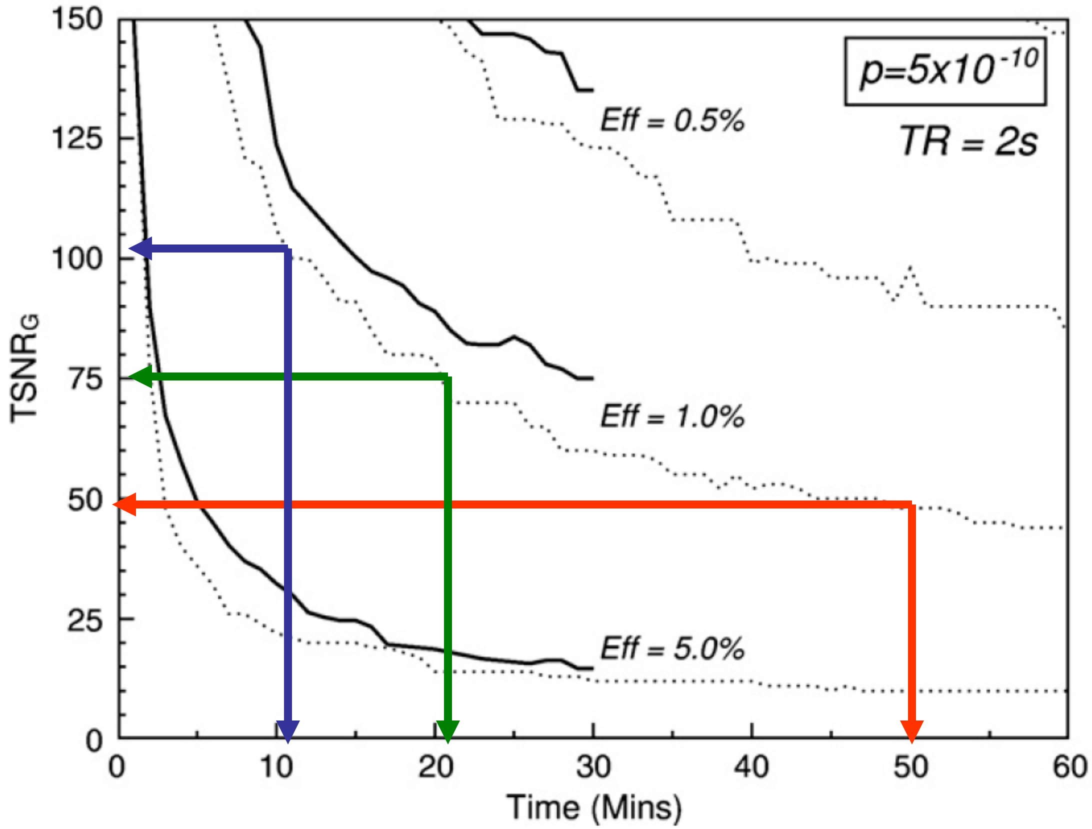
Finding the "suggested voxel volume"

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



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

J. Bodurka, F. Ye, N Petridou, K. Murphy, P. A. Bandettini, *NeuroImage,* 34, 542-549 (2007)



K. Murphy, J. Bodurka, P. A. Bandettini, How long to scan? The relationship between fMRI temporal signal to noise and the necessary scan duration. *NeuroImage*, 34, 565-574 (2007)

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?

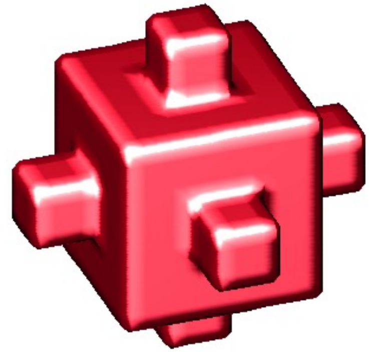
Study:

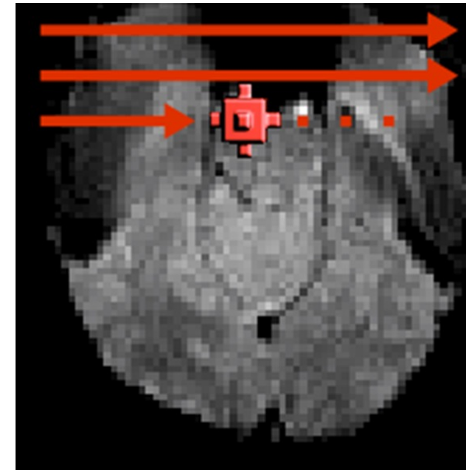
- Pattern-Information Mapping

- Dis-similarity matrix

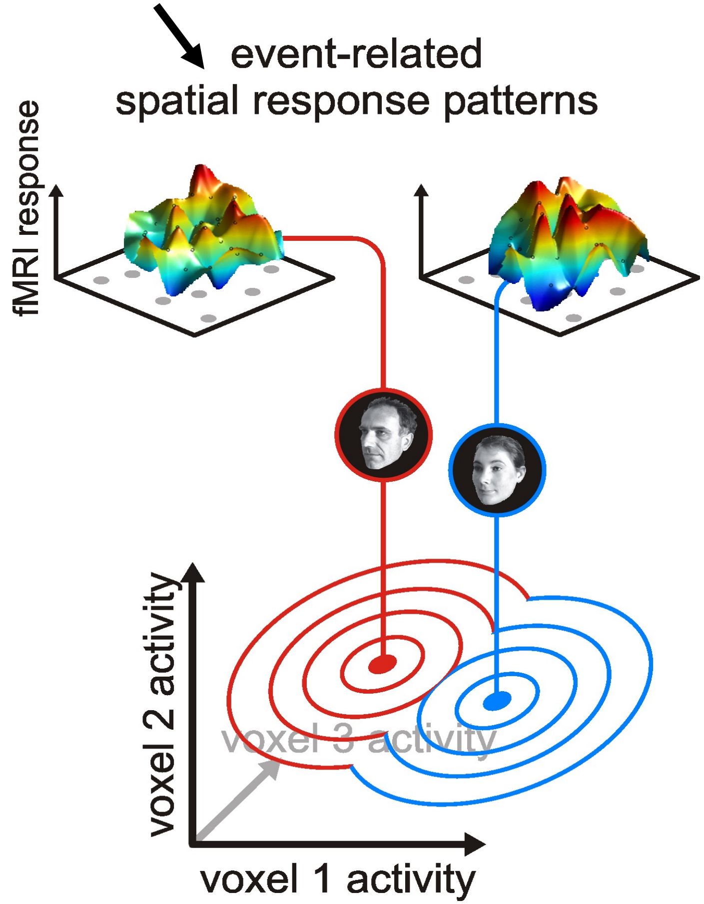
Pattern Information Mapping

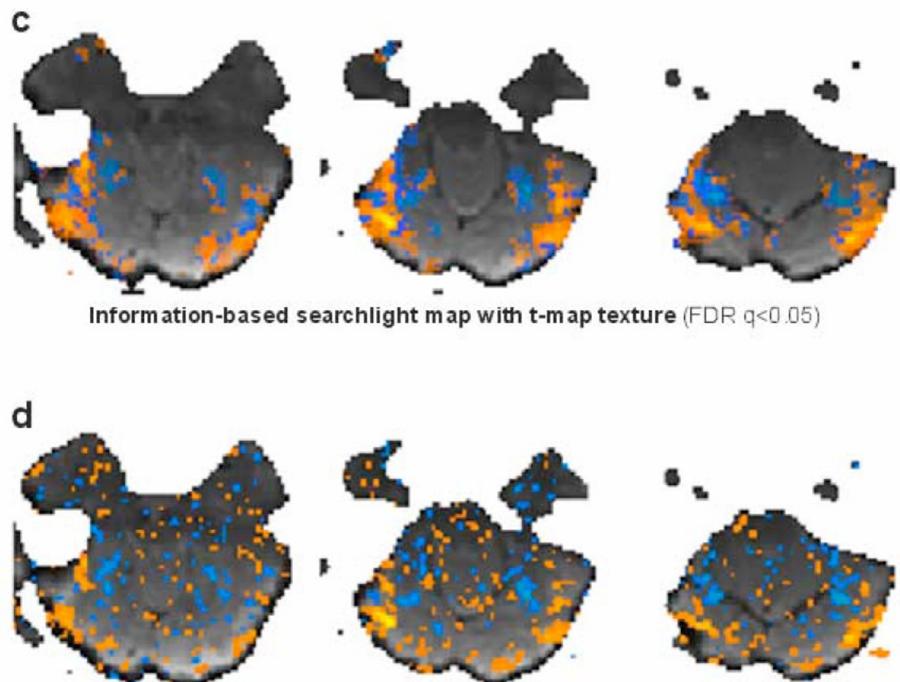
"searchlight" ROI





From fixed ROI



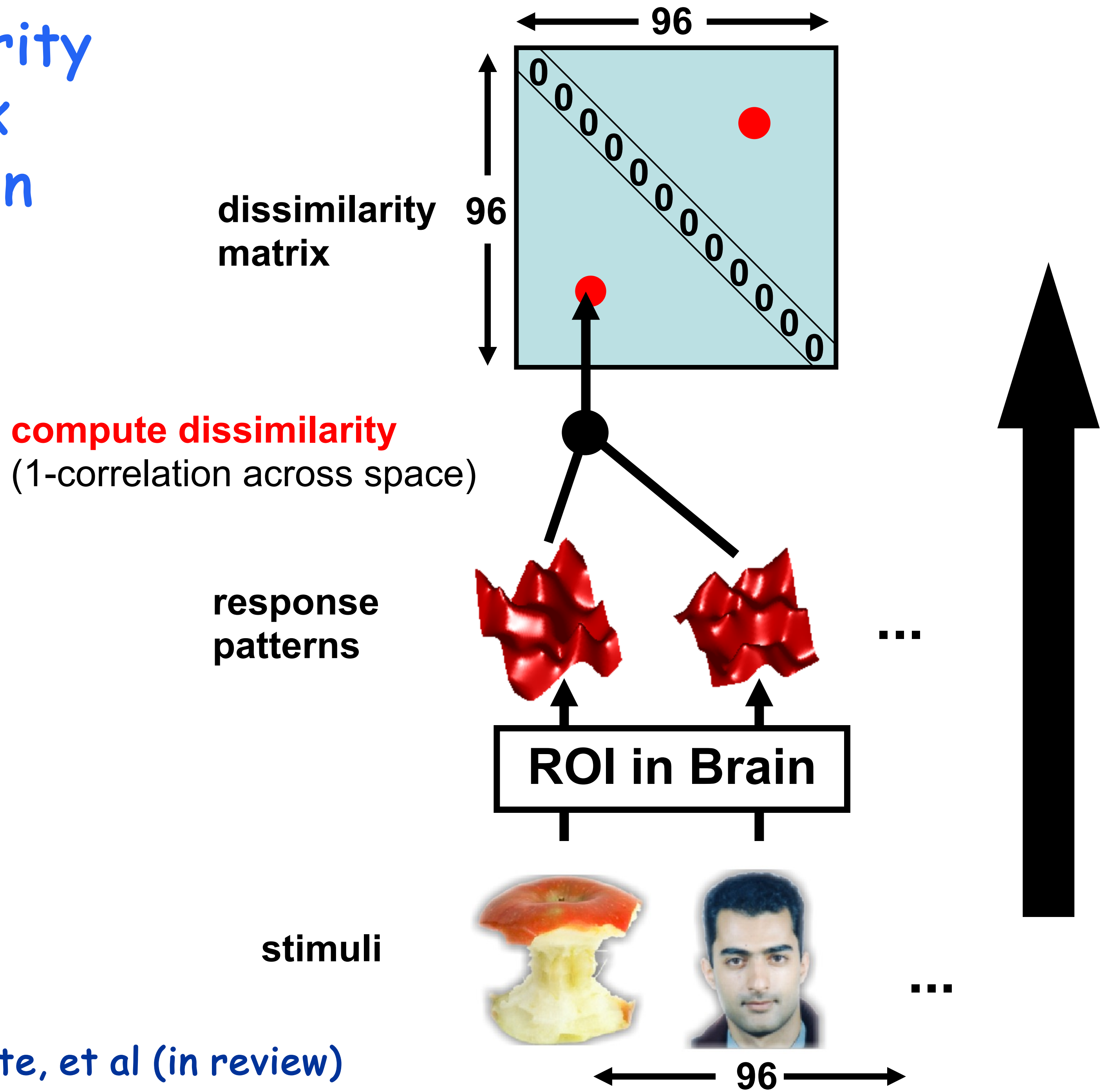


Information-based searchlight map with t-map texture (FDR q<0.05)

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

N. Kriegeskorte, R. Goebel, P. Bandettini, *Proc. Nat'l. Acad. Sci. USA*, 103, 3863-3868 (2006)

Dissimilarity Matrix Creation



N. Kriegeskorte, et al (in review)

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 ($1.95 \times 1.95 \times 2 mm^3$)
- 3T magnet, 16-channel coil
  (SENSE, acc. fac. 2)

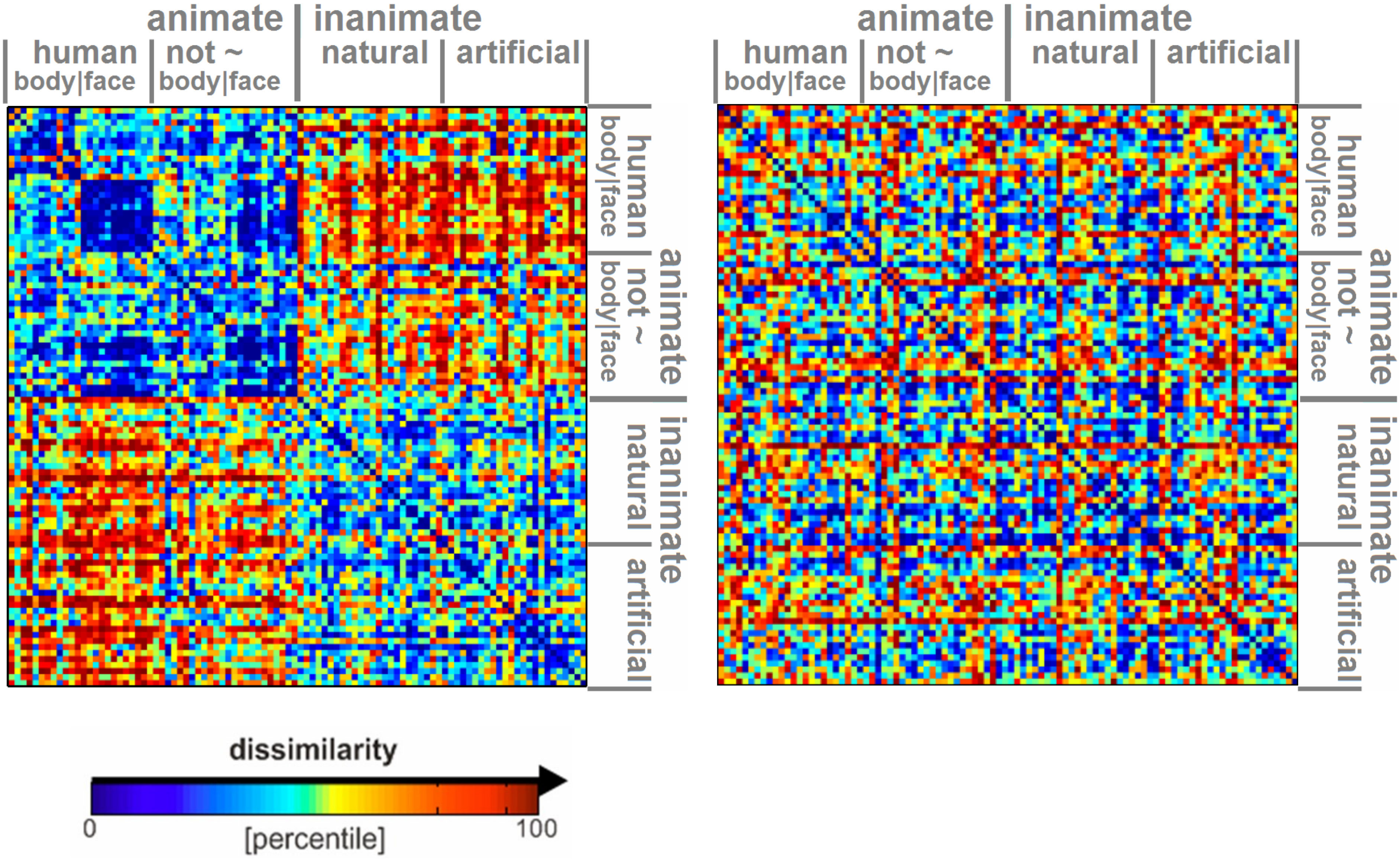
Monkey (Kiani et al. 2007)

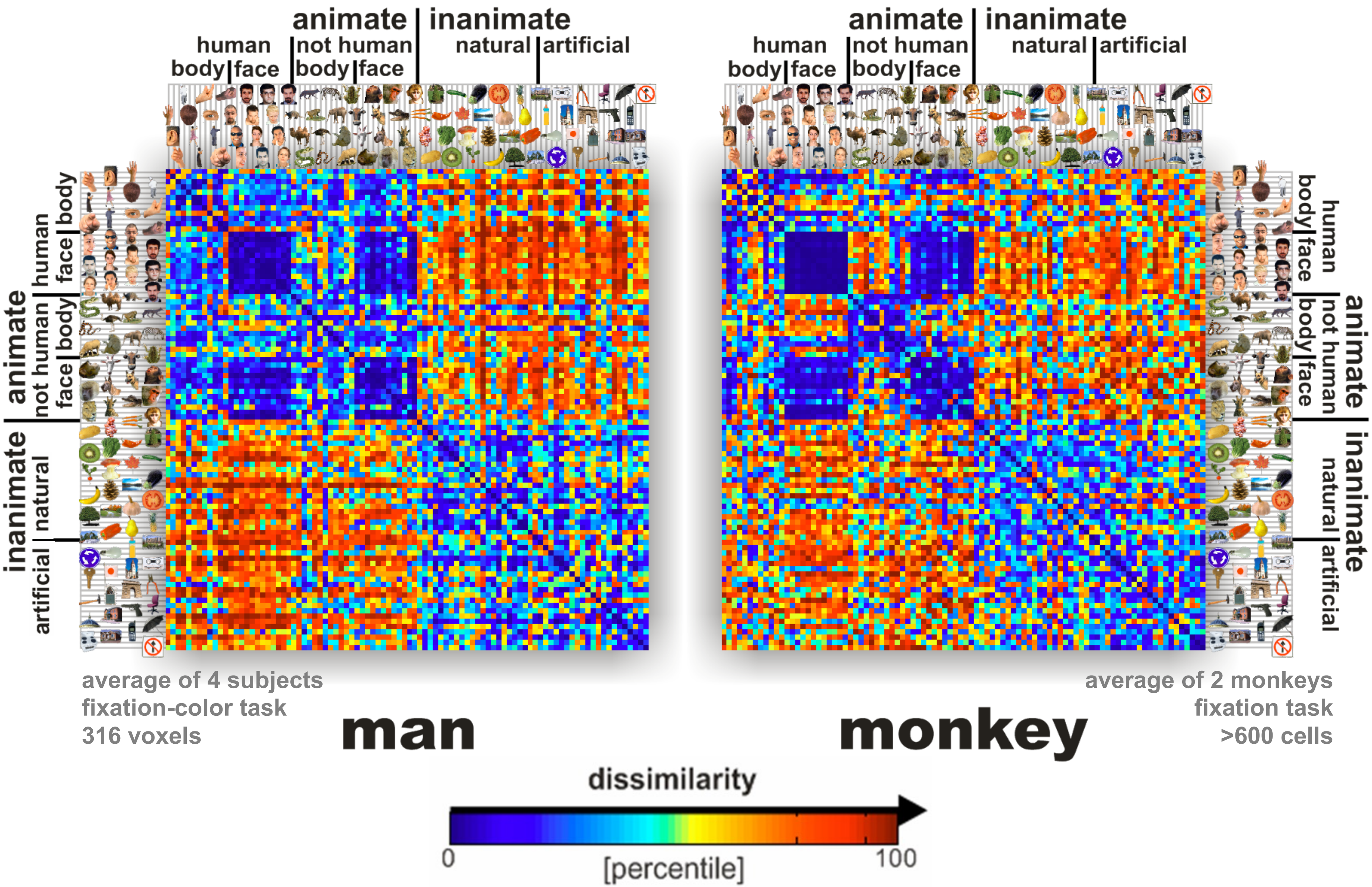
- single-cell recordings in two monkeys
- rapid serial presentation
  (stimulus duration: 105ms)
- fixation task
- electrodes in anterior IT
  (left in monkey 1, right in monkey 2)
- 674 cells total
- windowed spike count
  (140-ms window starting 71ms after stimulus onset)

Visual Stimuli

Human IT
(1000 visually most responsive voxels)

Human Early Visual Cortex
(1057 visually most responsive voxels)





N. Kriegeskorte, et al (in review)

5. Neuronal Current MRI

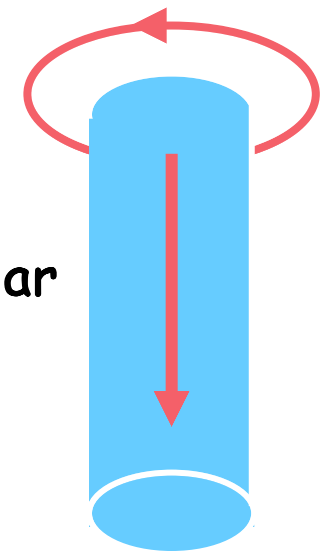
Motivation:

- Direct fMRI of neuronal activity.

Studies:

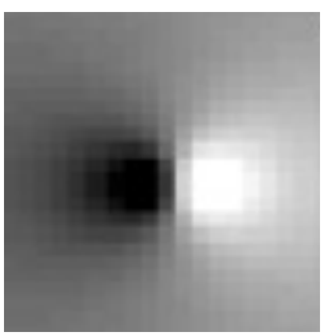
- Model
- Phantom Studies
- Cell Cultures at 7T and 3T

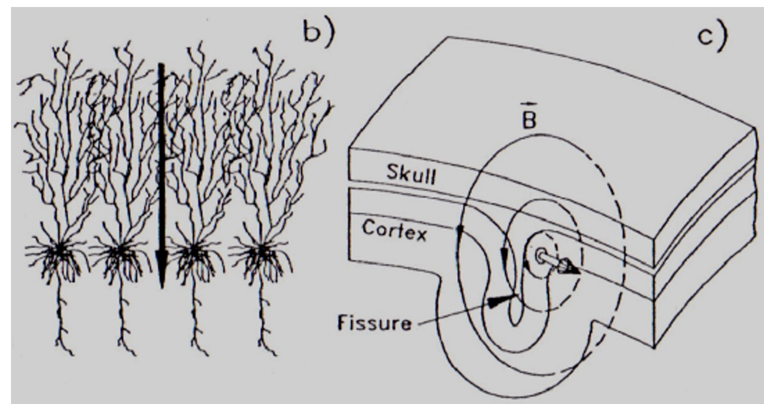
Magnetic Field



Intracellular Current

Surface Fields



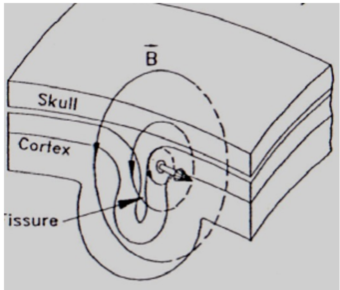


100 fT at on the scalp

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

Magnetic field associated with a bundle of dendrites

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

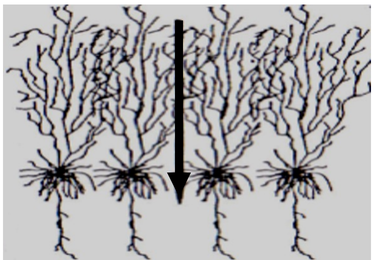


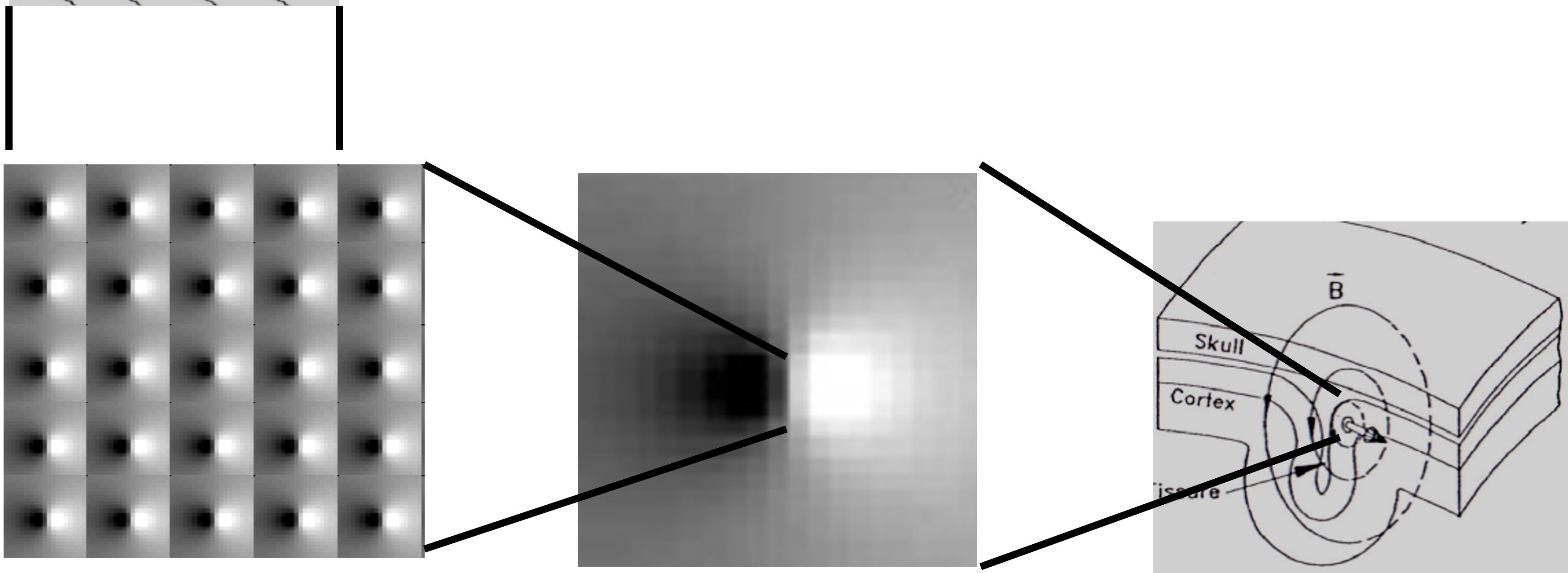
at least 50,000 neurons (0.002 fT (per dendrite) x 50,000 = 100 fT), must coherently act to generate such field. These bundles of neurons produce, within a typical voxel, 1 mm x 1 mm x 1 mm, a field of order:

$$B_{MRI} = B_{MEG}\left(\frac{r_{MEG}}{r_{MRI}}\right)^2 = B_{MEG}\left(\frac{4\,cm}{0.1\,cm}\right)^2 = 1600\,B_{MEG}$$

$B_{MRI} \approx 0.2$nT

Surface Field Distribution Across Spatial Scales

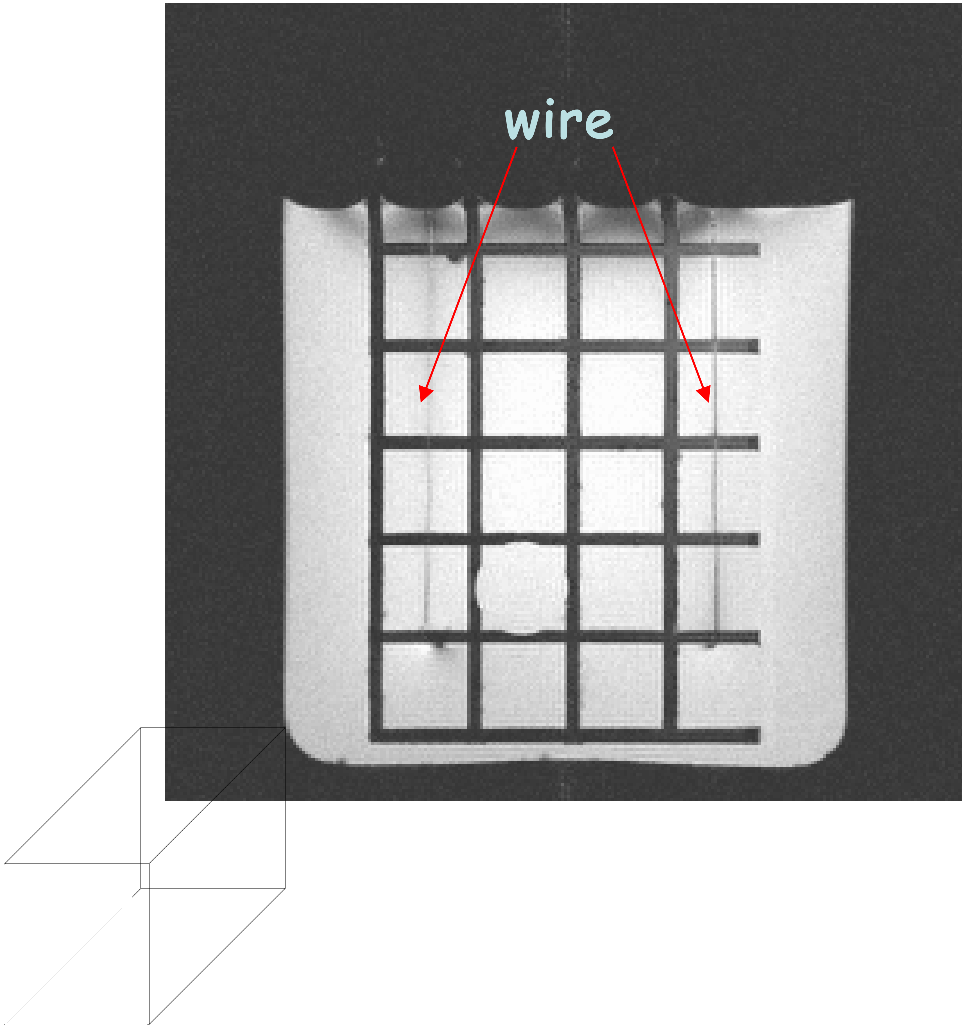


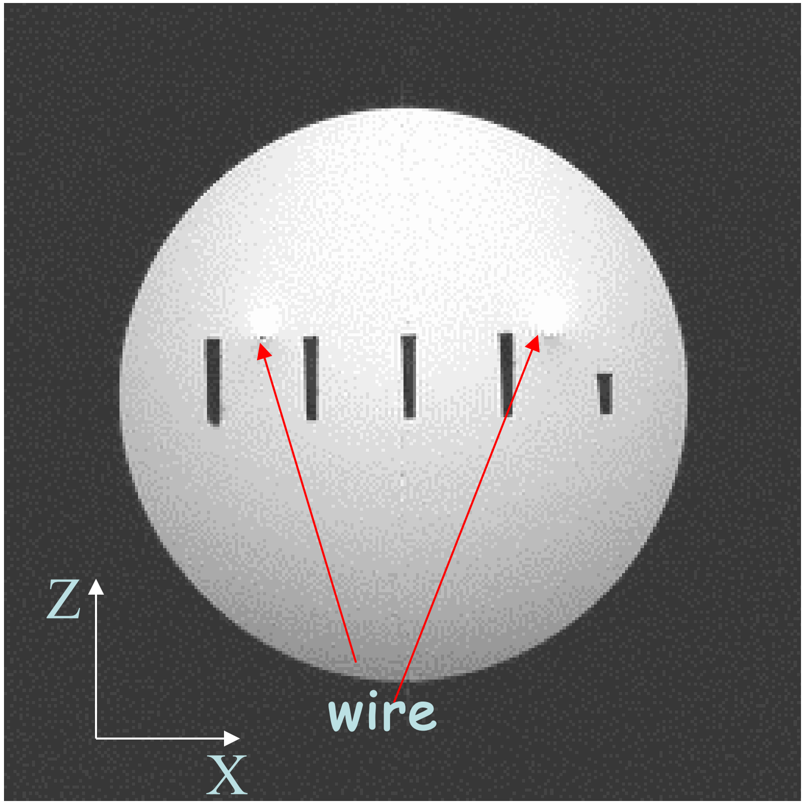


Adapted from: J.P. Wikswo Jr et al.

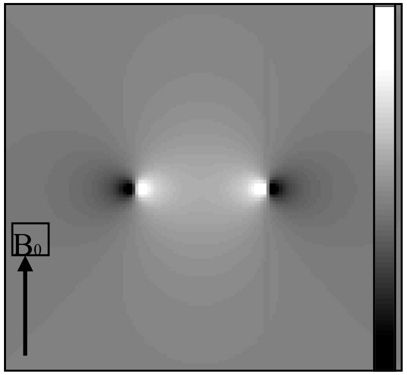
J Clin Neurophy 8(2): 170-188, 1991

Current Phantom Experiment

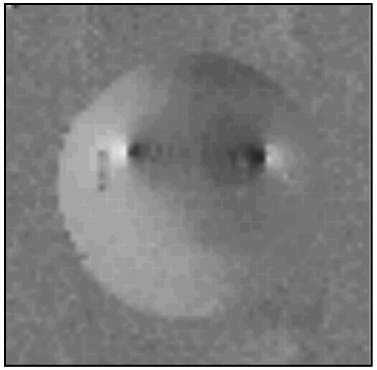




calculated $B_c \parallel B_0$



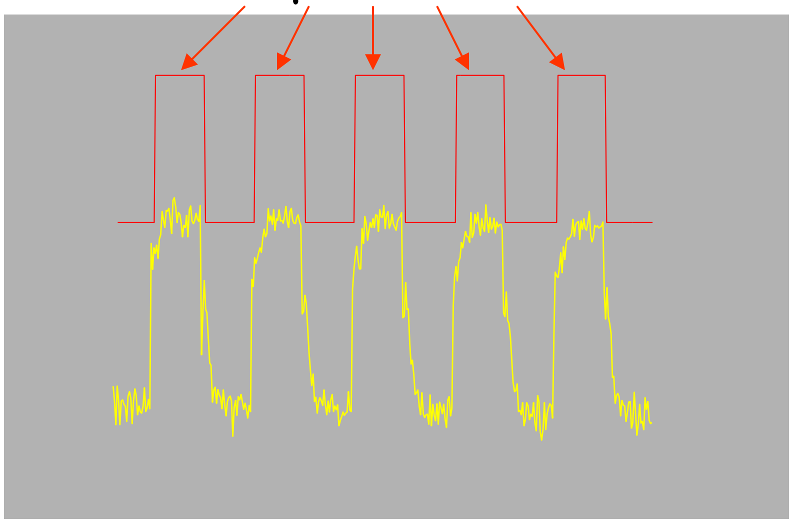
$\Delta\phi \cong 20^0$



Correlation image

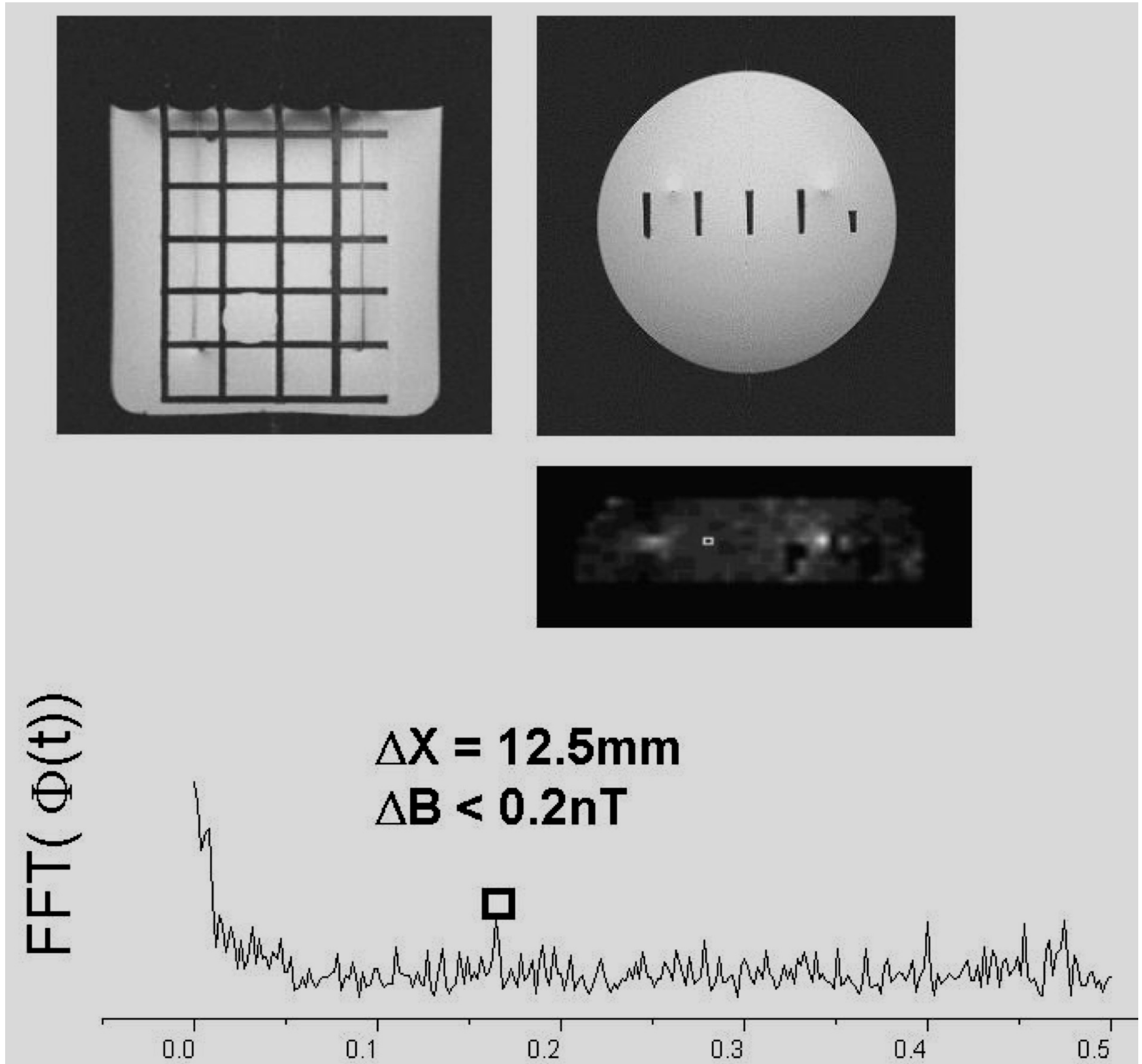
Measurement

70 μA current



Single shot GE EPI

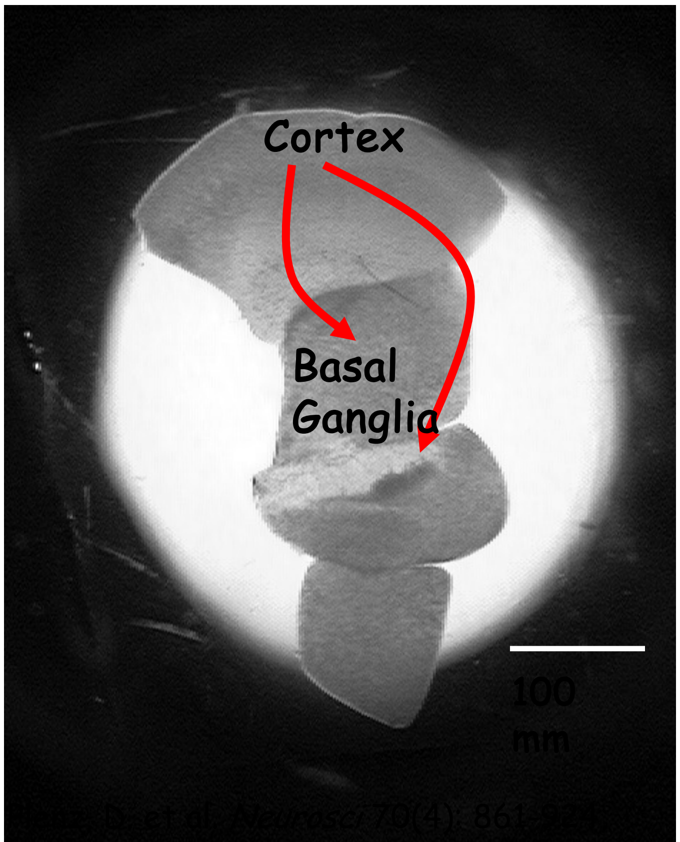
J. Bodurka, P. A. Bandettini. Magn. Reson. Med. 47: 1052-1058, (2002).



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



1996

- Size: in-plane:~1-2mm^2, 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

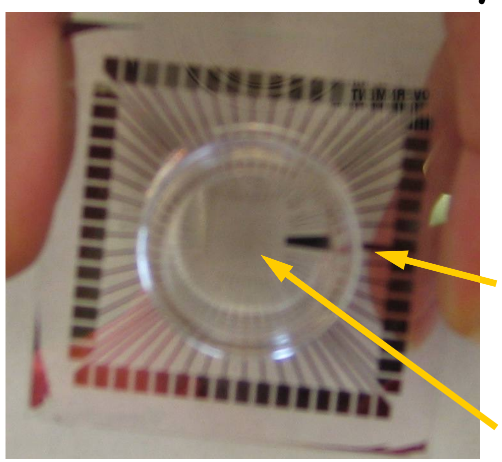
Culture Preparation

Multi-Electrode Arrays (MEA)

Multichannelsystems Germany 8x8 electrodes

0.8ml culture medium

Multi-Electrode Array

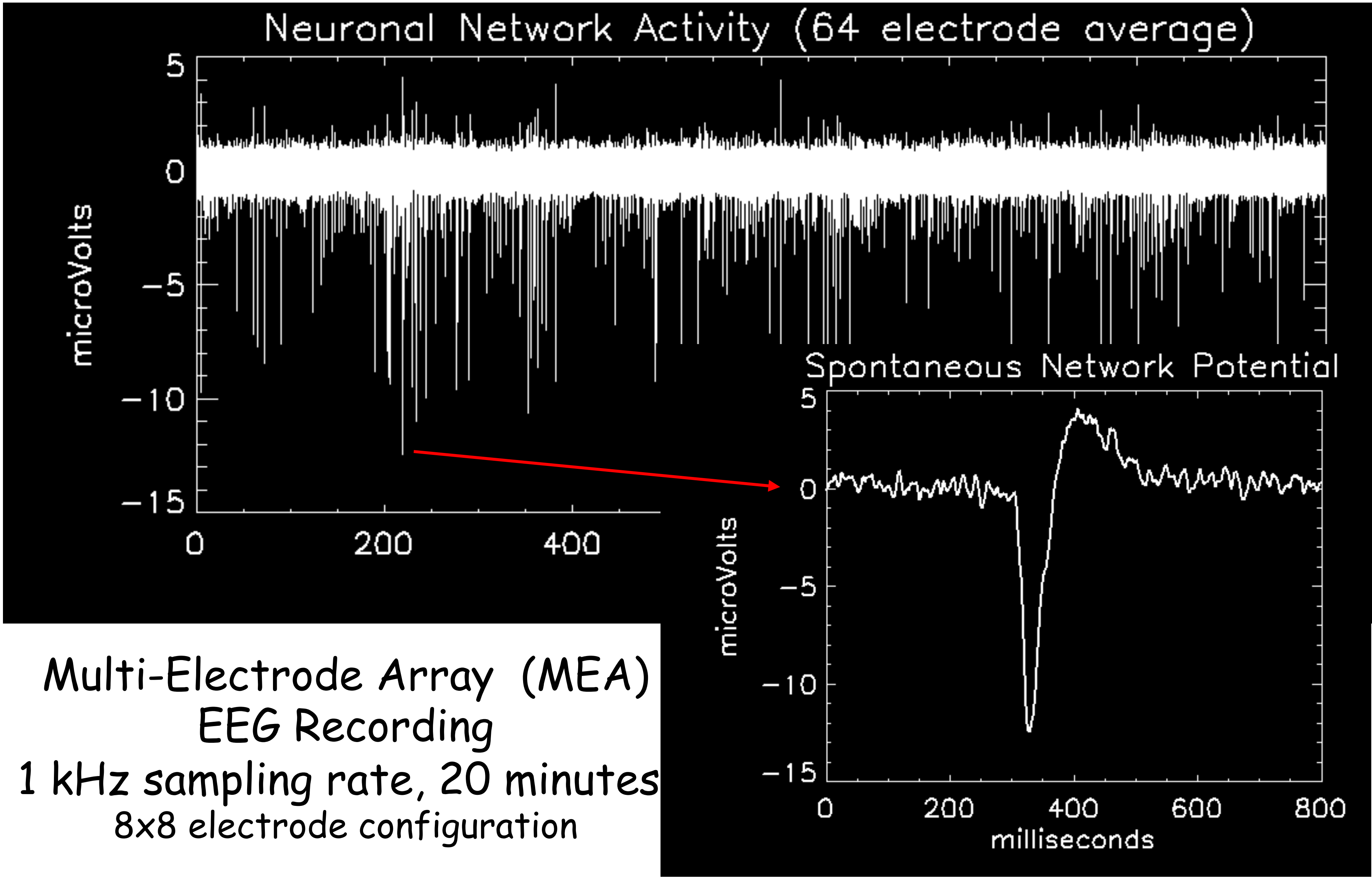


Reference electrode

Culture site

10mm

Multi-Electrode Array EEG recording



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

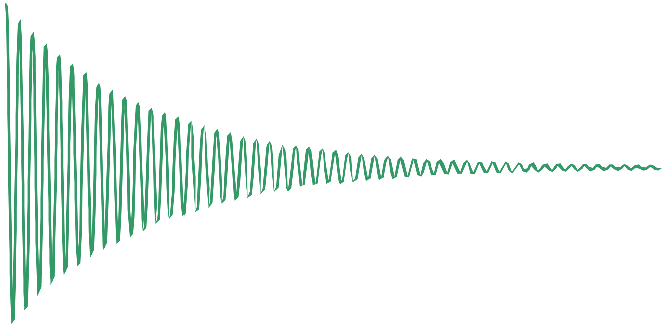
SE EPI image

- voxel size: ~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)

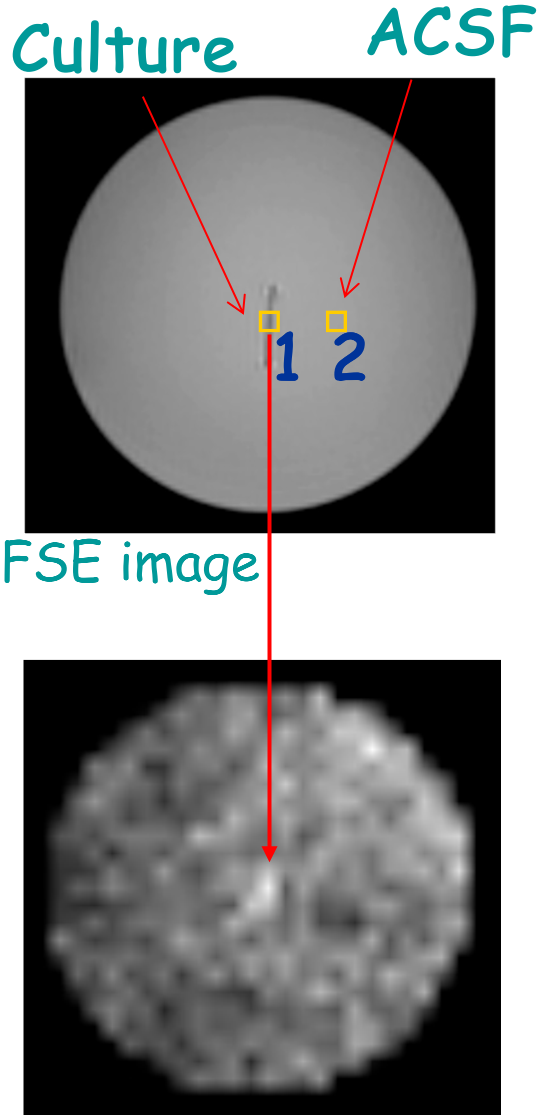
Six Experiments

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

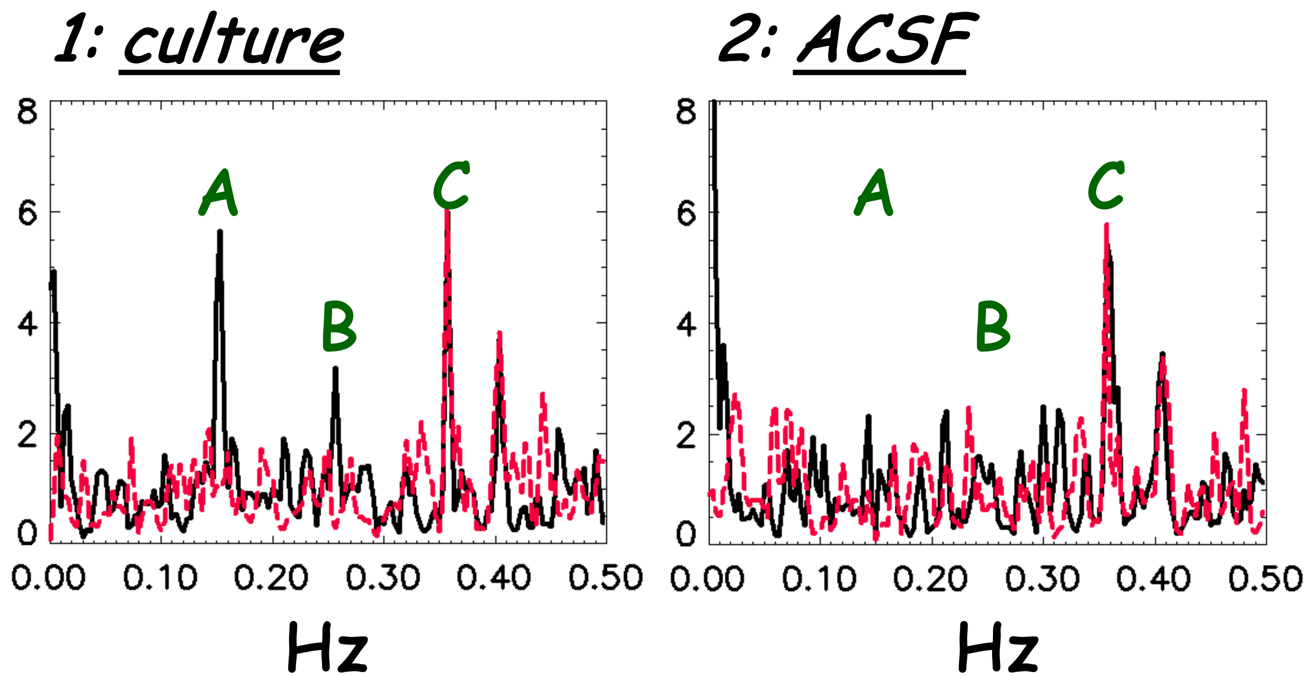
Inactive : ~17 min (10,000 images) neuronal activity terminated via TTX administration

Pre- and Post- MR scan electrical recordings

3 Tesla data



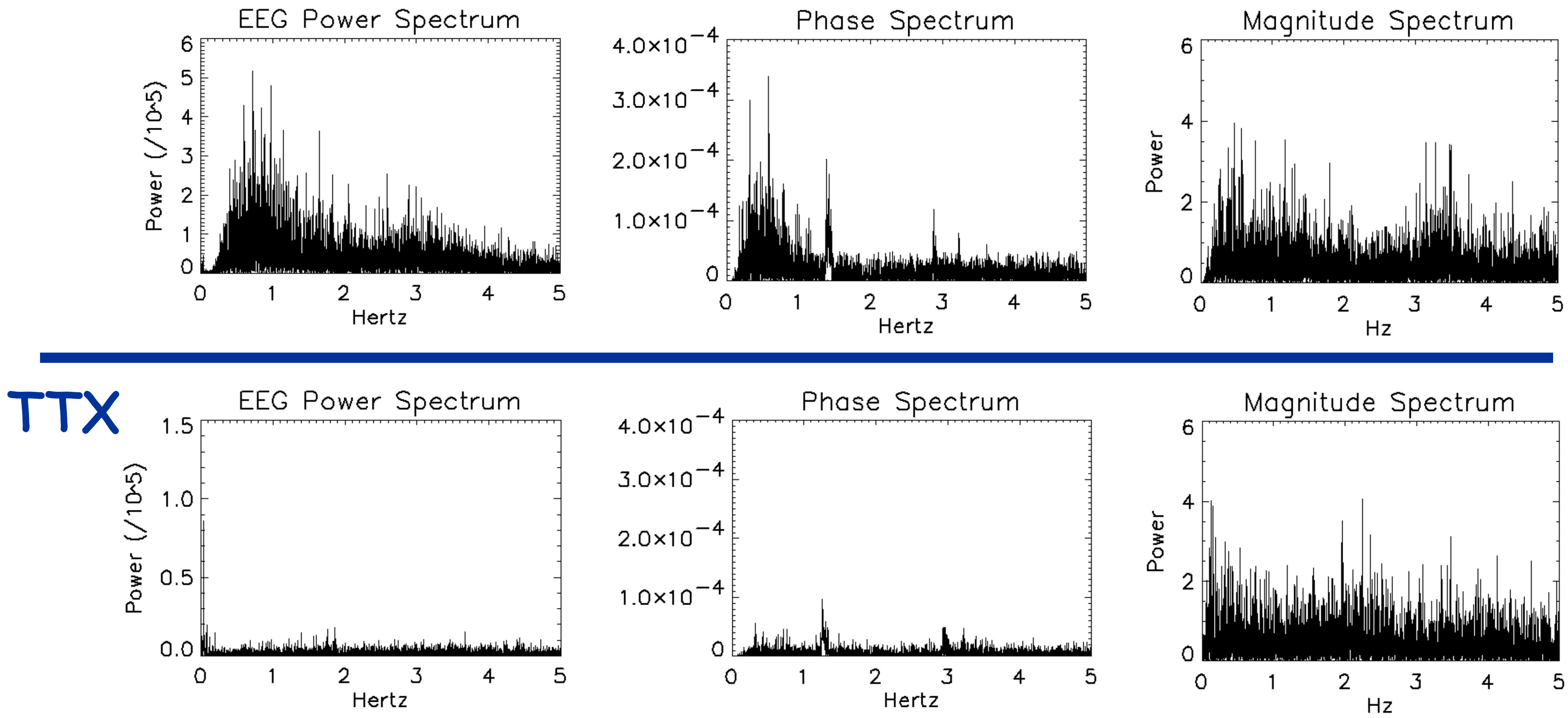
0.15Hz map



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



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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Sean Marrett	staff scientist
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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).