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

September, 1991

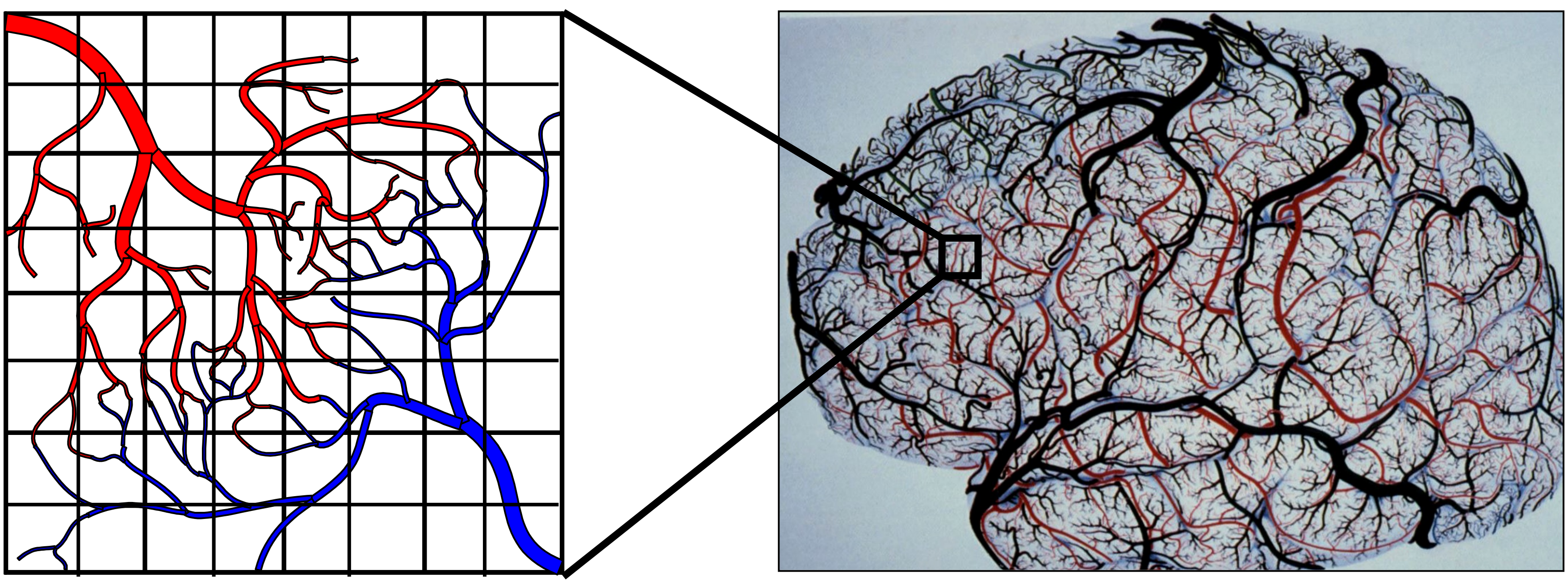
Neuronal Activation → Measured Signal

?

? Hemodynamics ?

?

Noise



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

1. Dynamics

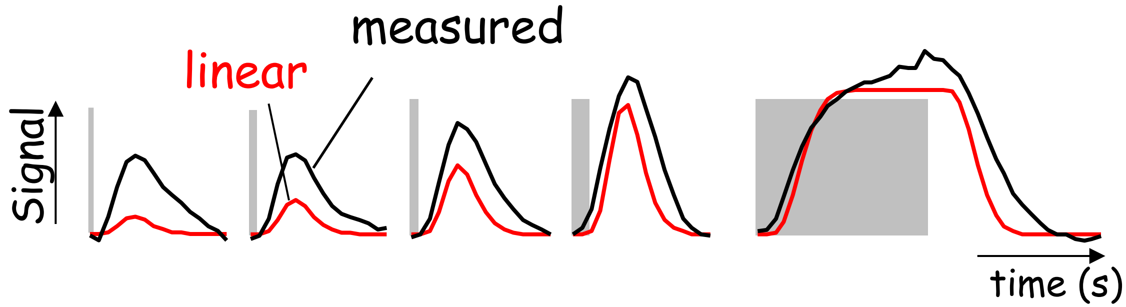
Motivation:

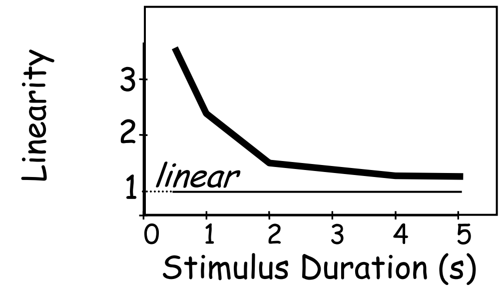
- To understand neuronal and non-neuronal influences on the fMRI signal.

Studies:

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

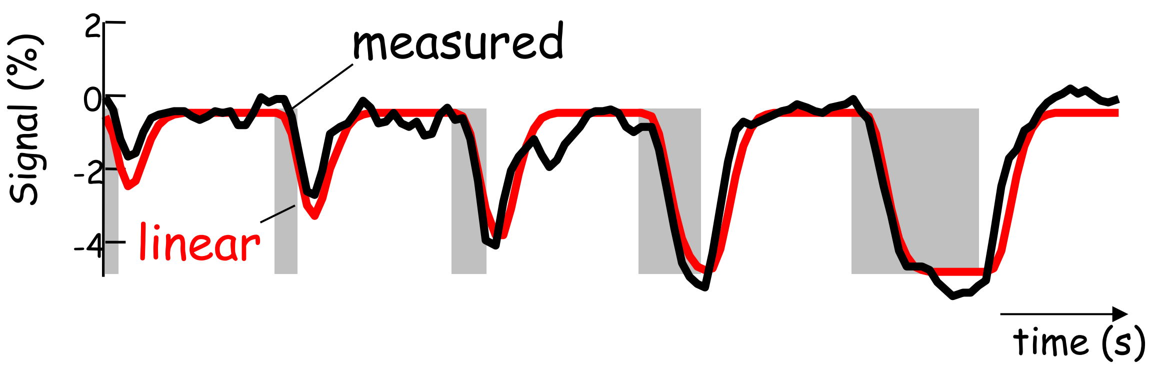
Brief “on” periods produce **larger** increases than expected.

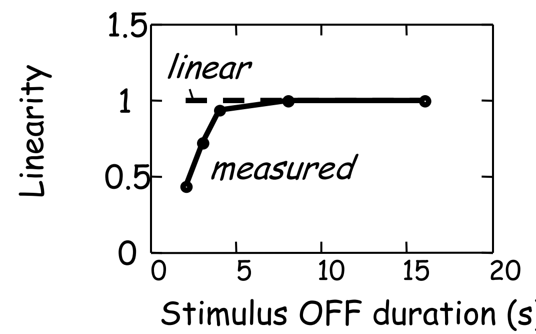




R. M. Birn, Z. Saad, P. A. Bandettini, NeuroImage, 14: 817-826, (2001)

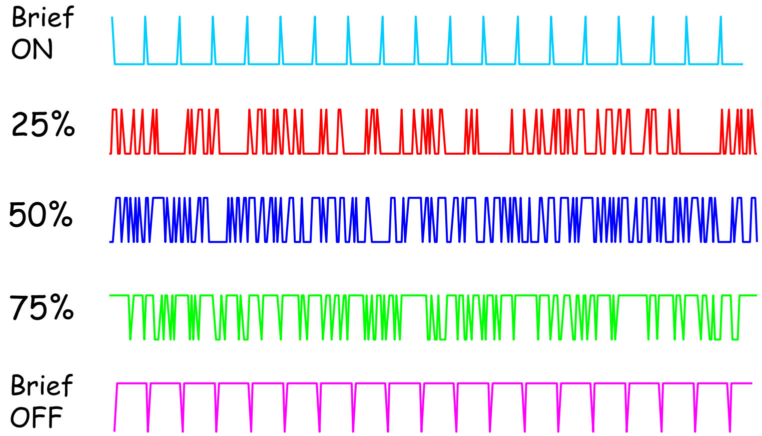
Brief “off” periods produce **smaller** decreases than expected.

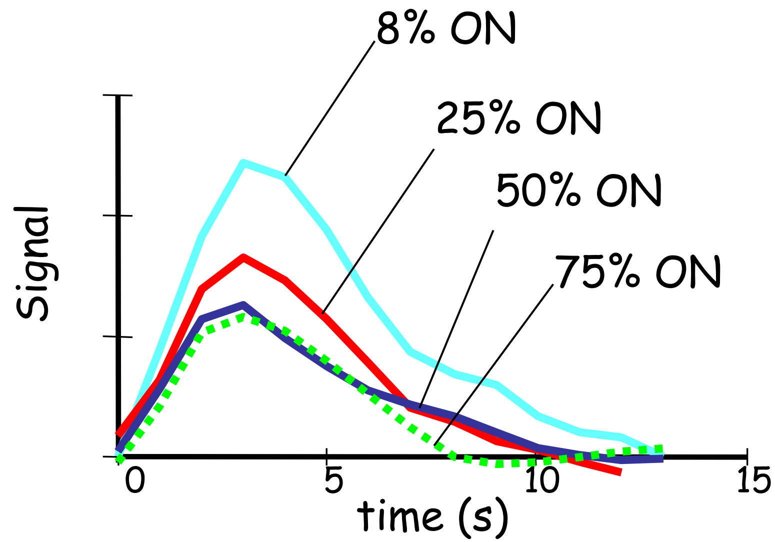




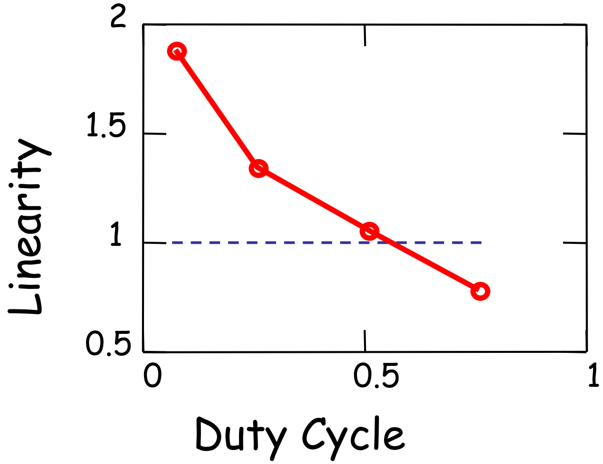
R.M. Birn, P. A. Bandettini, NeuroImage, 27, 70-82 (2005)

Varying the Duty Cycle



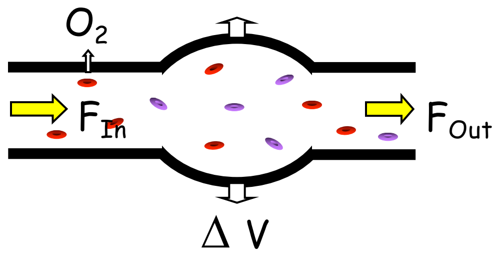


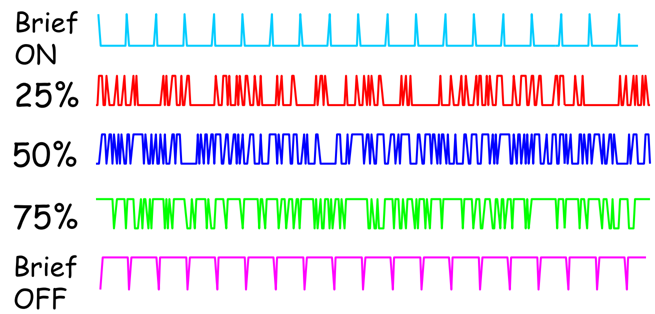
Deconvolved Response



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

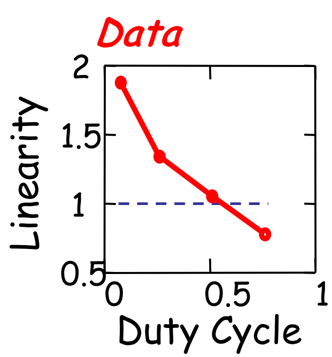
Simulation of Hemodynamic Mechanisms
(Balloon model)

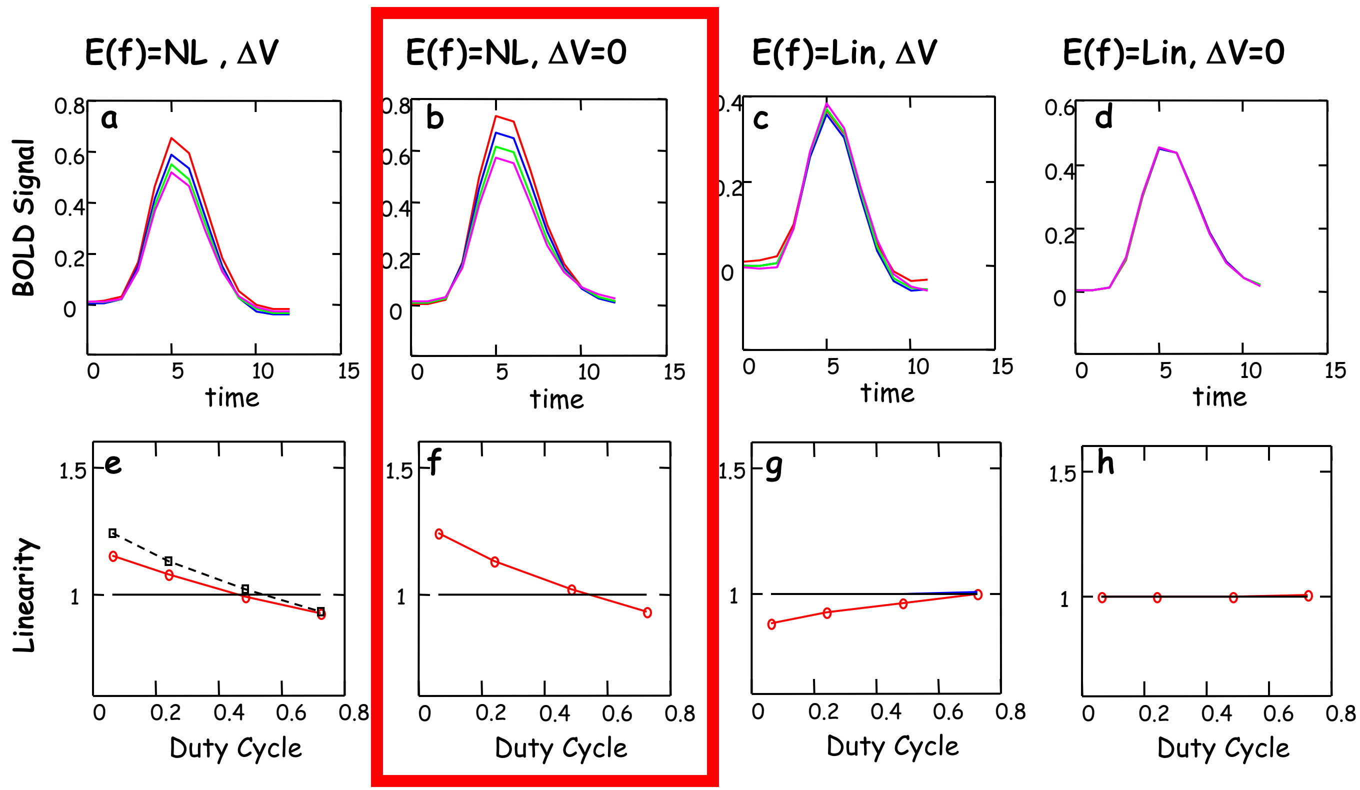




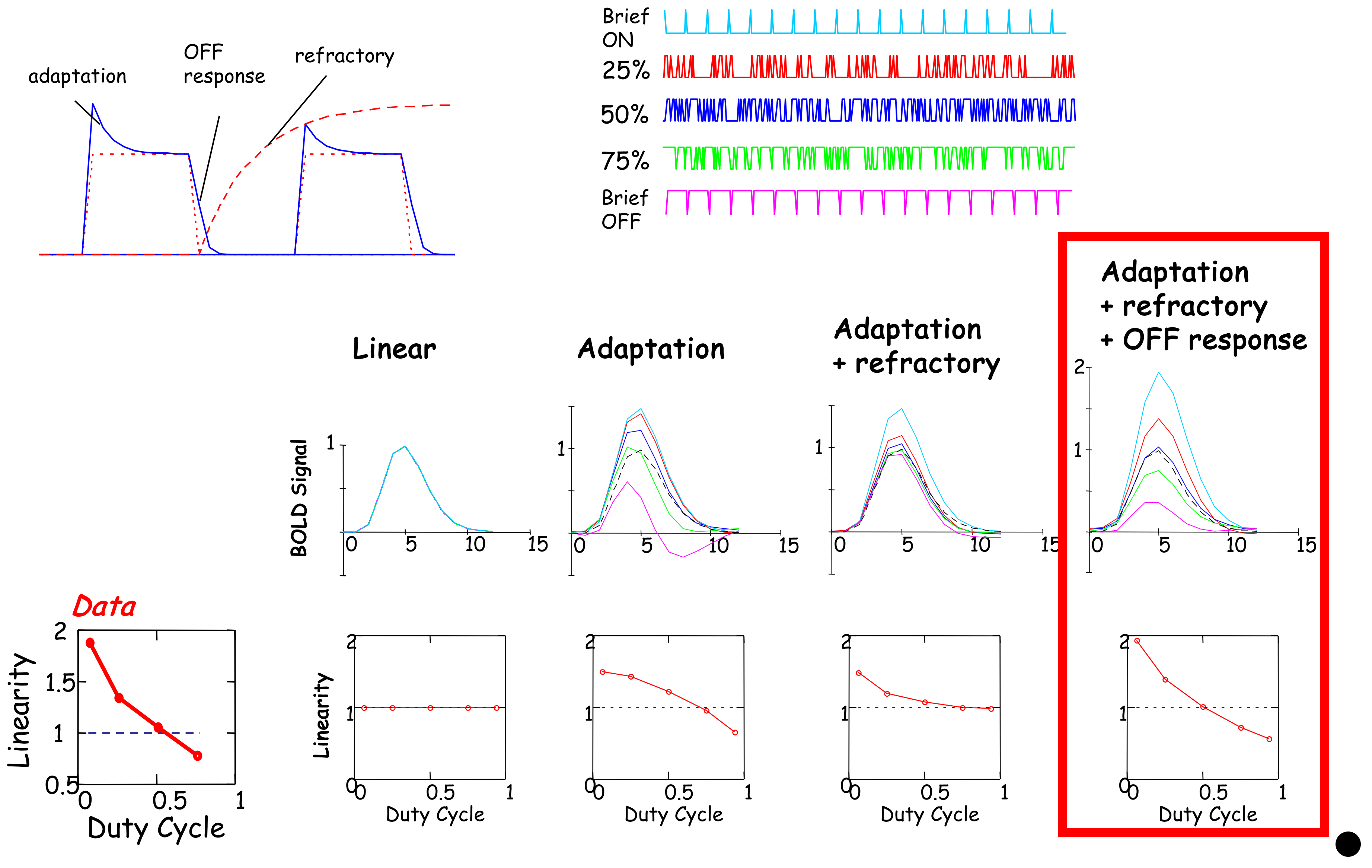
E(f) = oxygen extraction fraction

V = blood volume

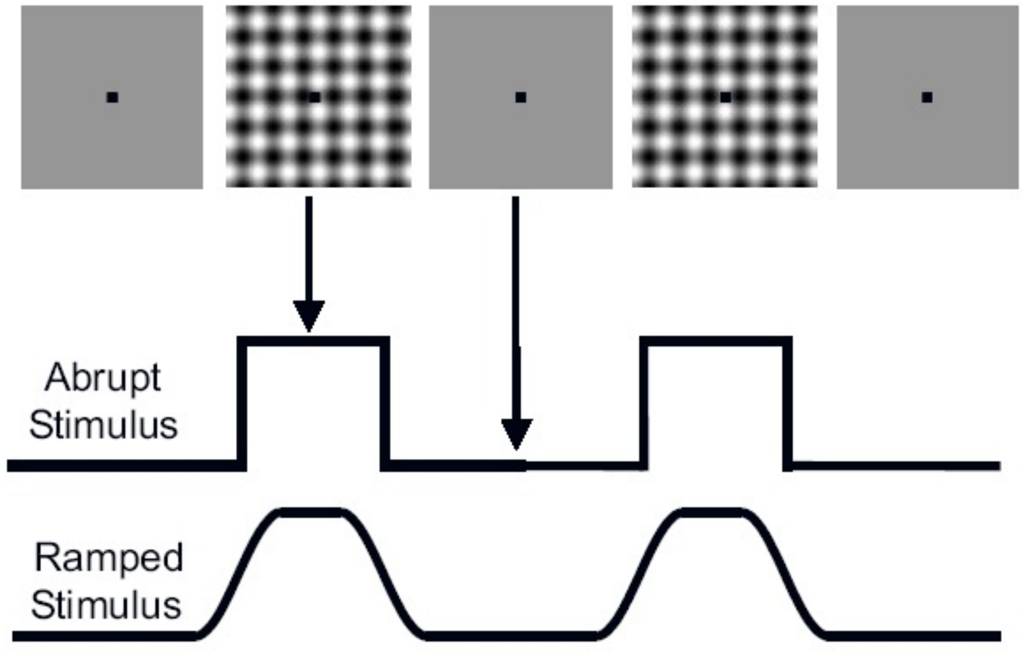


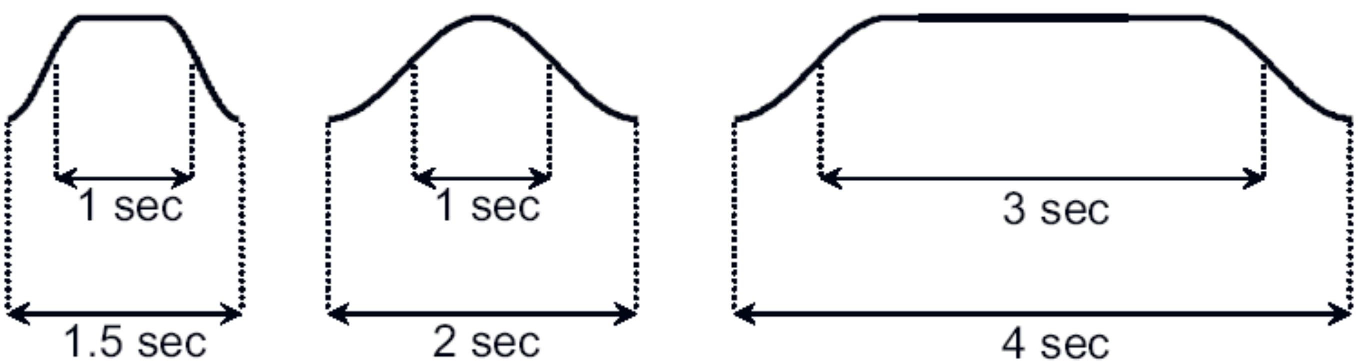


Simulation of Neuronal Mechanisms



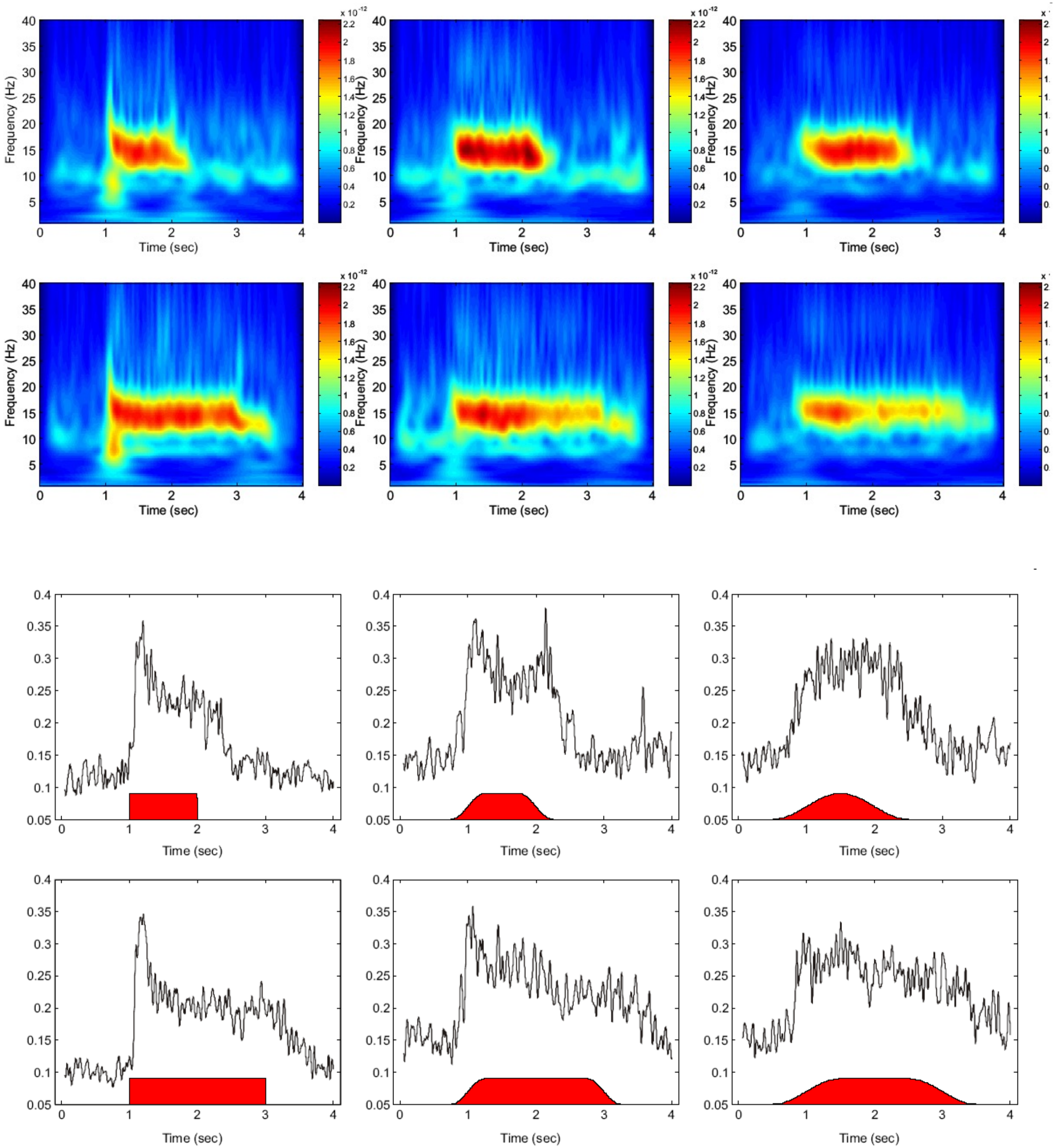
MEG & fMRI Linearity Comparison





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

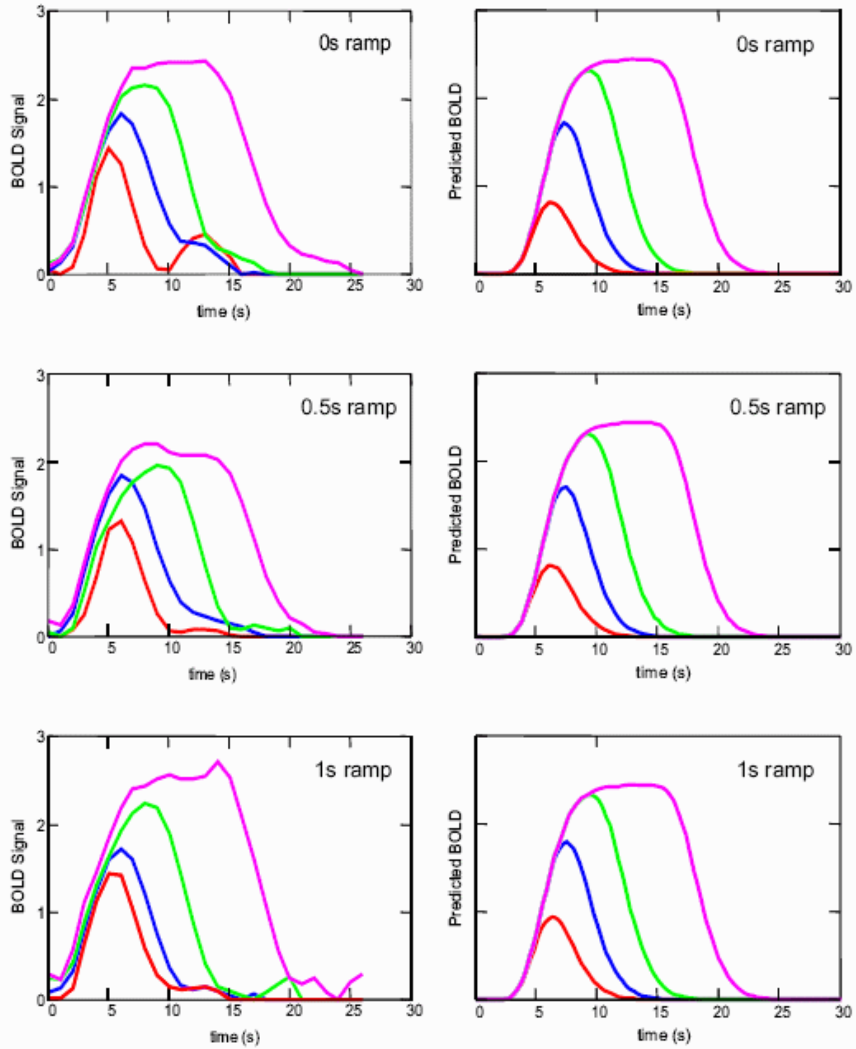
MEG Results



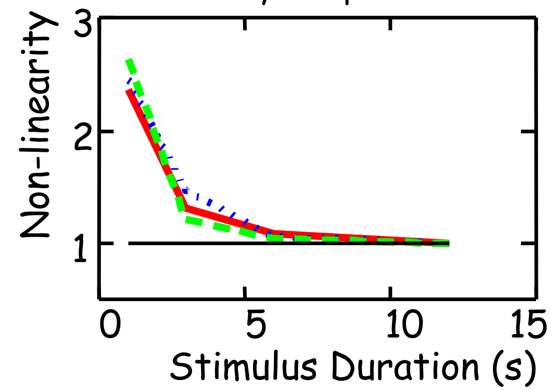
A. Tuan, R. M. Birn, P. A. Bandettini, G. M. Boynton, (submitted)

Measured and Predicted BOLD responses

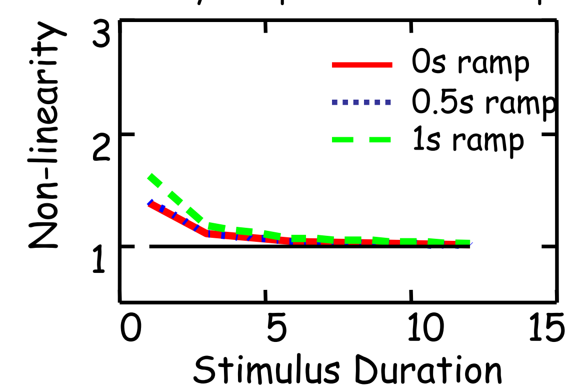
BOLD **MEG**



Non-linearity computed from BOLD

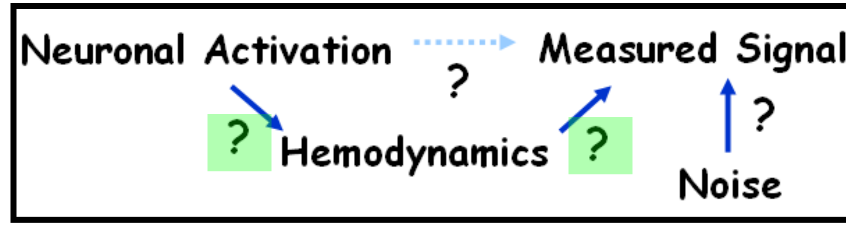


Non-linearity computed from MEG prediction



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

1. Dynamics



Conclusion:

- Nonlinearities are not fully explained by the Balloon model, nor are they fully explained by neuronal activity.

- "OFF" modulation sub-linearity suggests that blood volume change is not slower than flow change.

Future:

- Modulate neural activity or hemodynamic variables independently.

- Measure flow, volume to help constrain balloon model.

- Determine spatial and across-subject heterogeneity.

2. Fluctuations

Motivation:

- Applications of connectivity mapping (autism, schizophrenia, Alzheimer's, ADHD).

- 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.

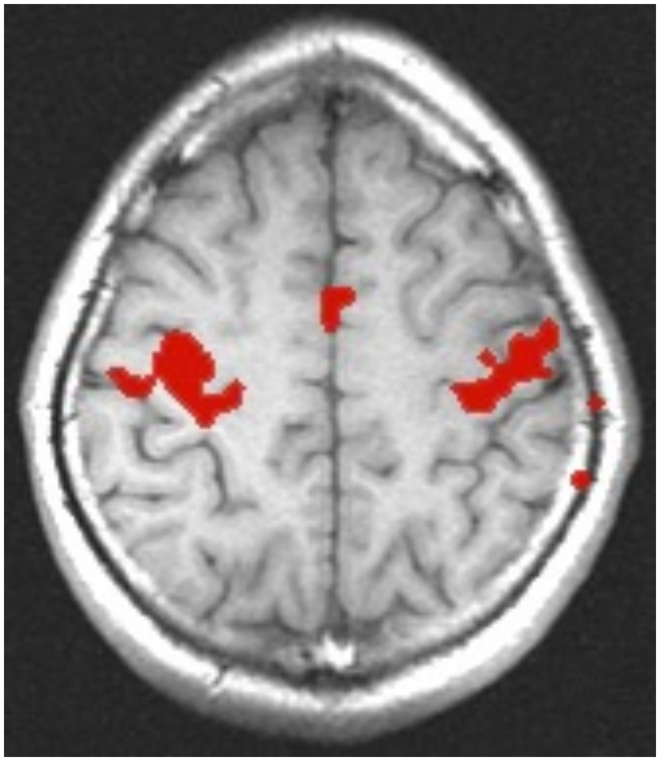
Studies:

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

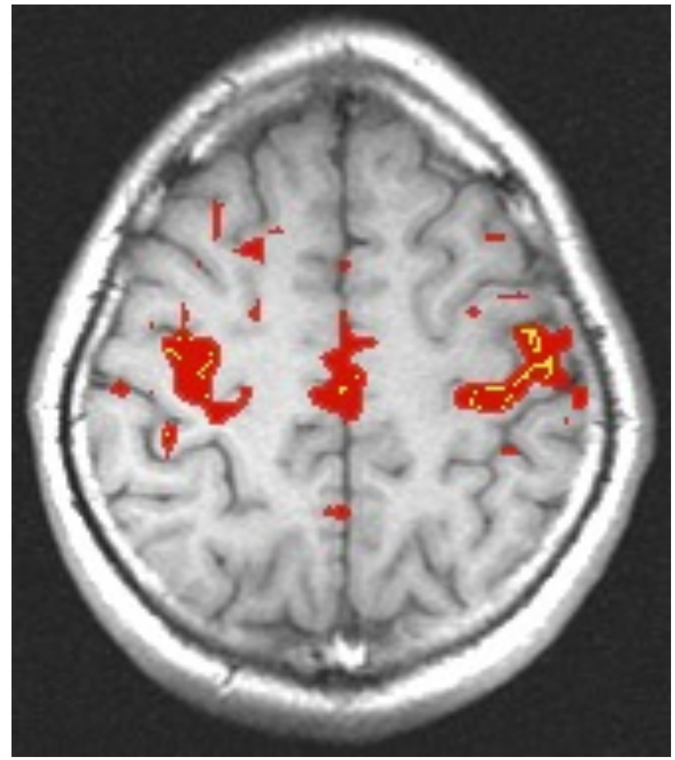
- The Respiration Response Function (RRF)

- FMRI Calibration using RRF

Resting State Correlations



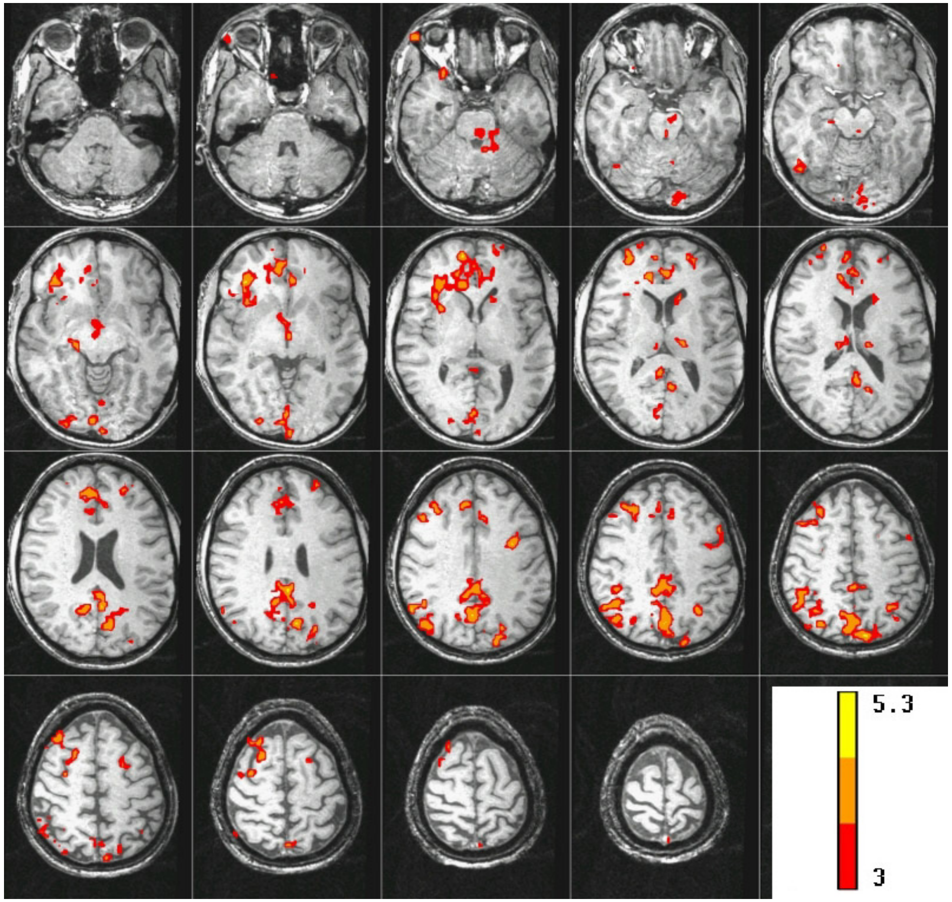
Activation:
correlation with reference function



Rest:
seed voxel in motor cortex

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

BOLD correlated with SCR during "Rest"

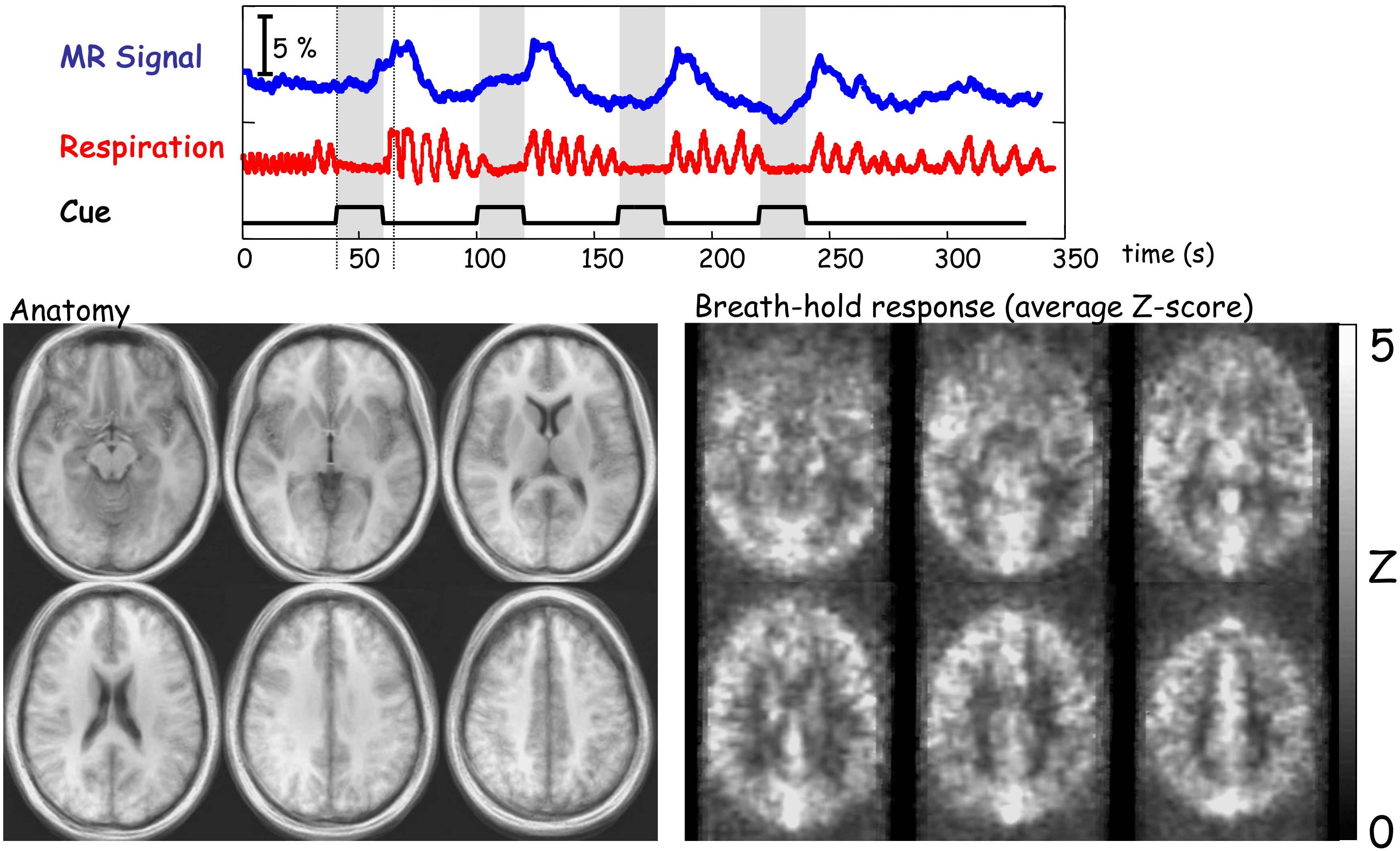


J. C. Patterson II, L. G. Ungerleider, and P. A Bandettini, *NeuroImage 17: 1787-1806, (2002).*

Sources of time series fluctuations:

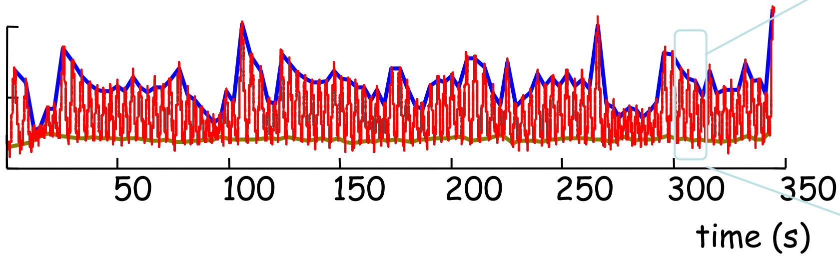
- Blood, brain and CSF pulsation
- Vasomotion
- Breathing cycle (B_0 shifts with lung expansion)
- Bulk motion
- Scanner instabilities
- Changes in blood CO_2 (changes in breathing)
- Spontaneous neuronal activity

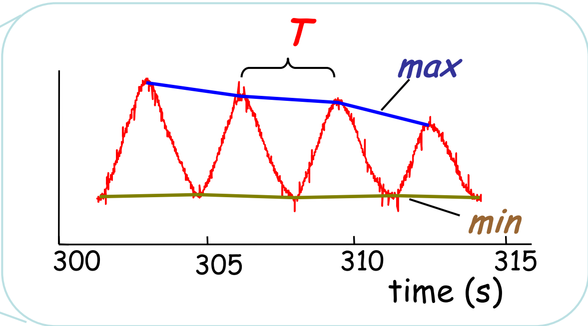
Breath-holding Group Maps (N = 7)



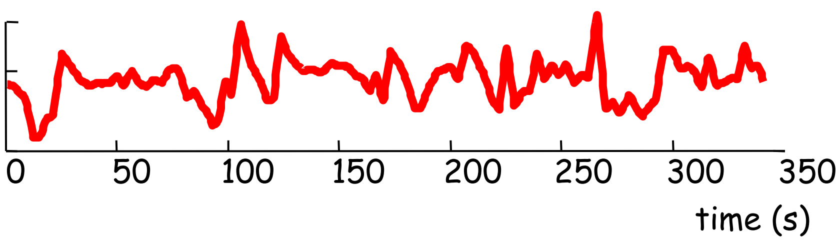
Estimating respiration volume changes

Respiration

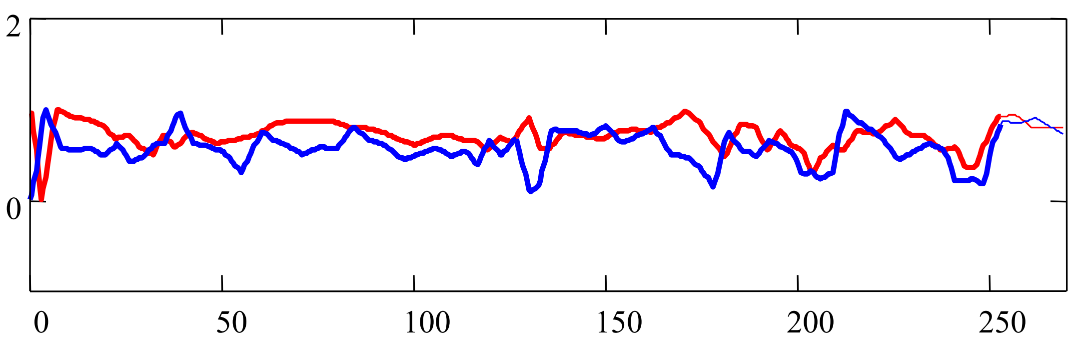


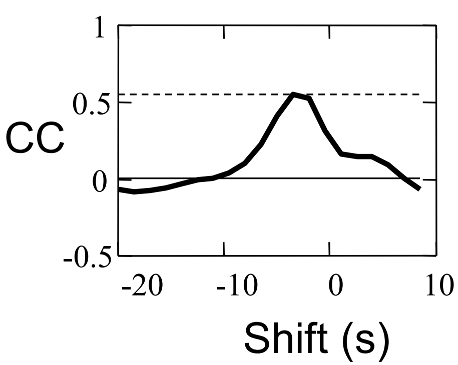


Respiration Volume / Time (RVT)



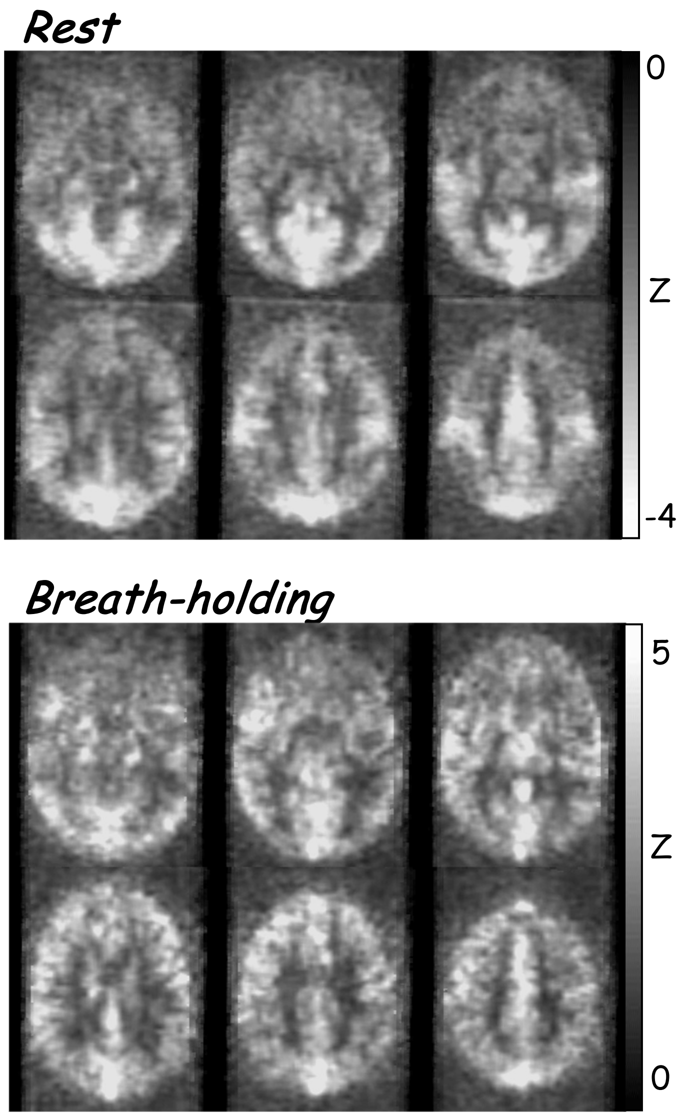
$$RVT = \frac{max - min}{T}$$

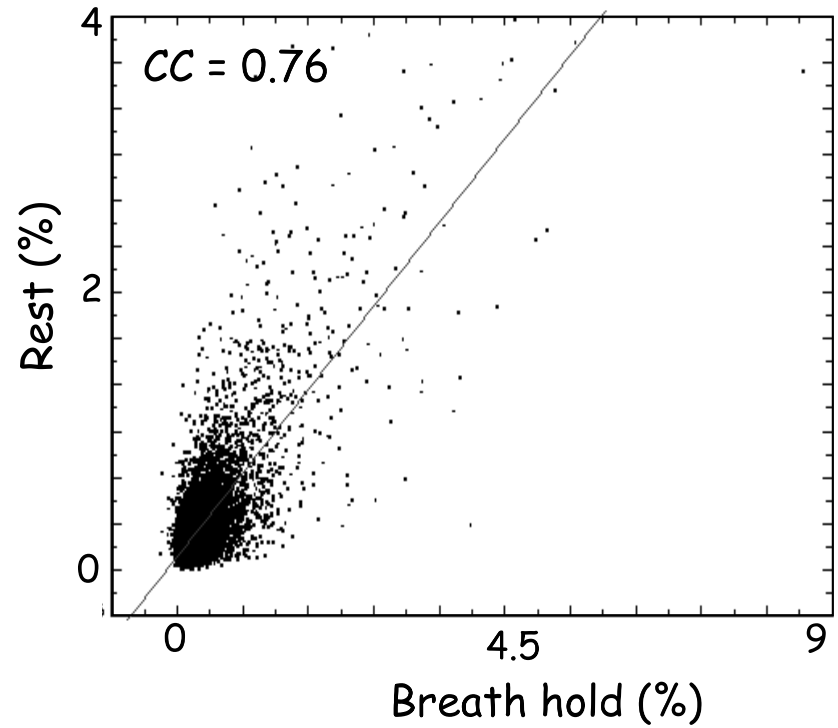




RVT precedes end tidal CO_2 by 5 sec.

Respiration induced signal changes

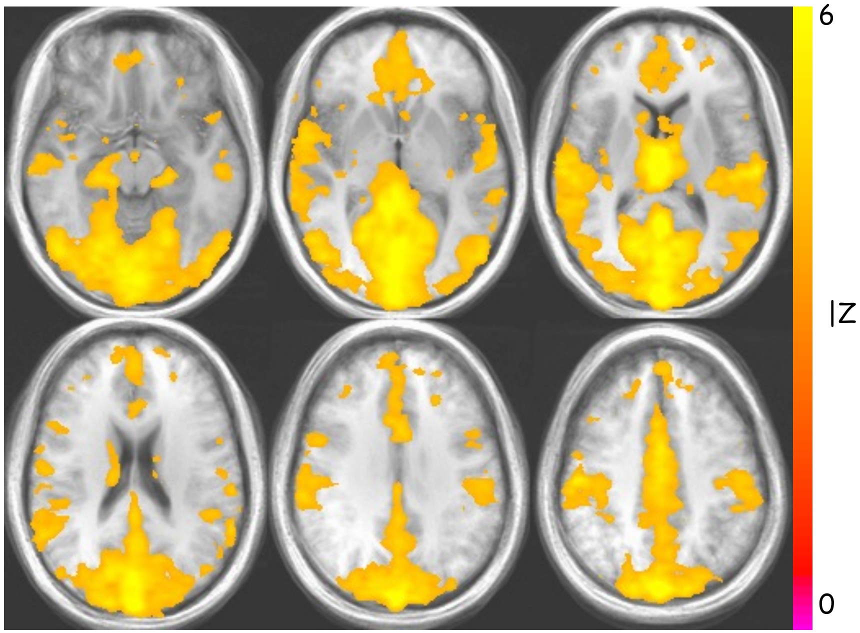




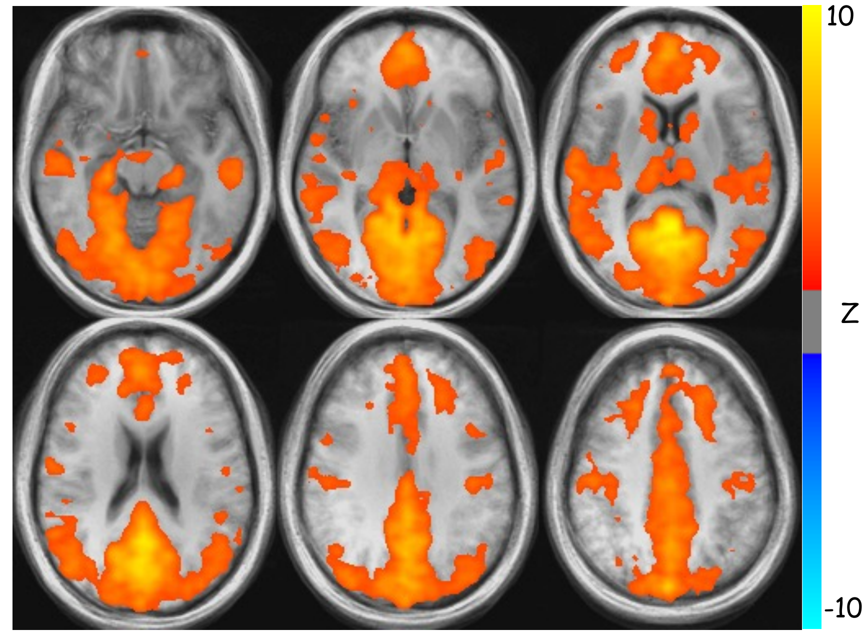
(N=7)

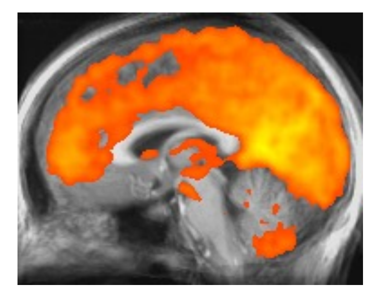
RVT Correlation Maps & Functional Connectivity Maps

Resting state correlation with RVT signal



Resting state correlation with signal from posterior cingulate

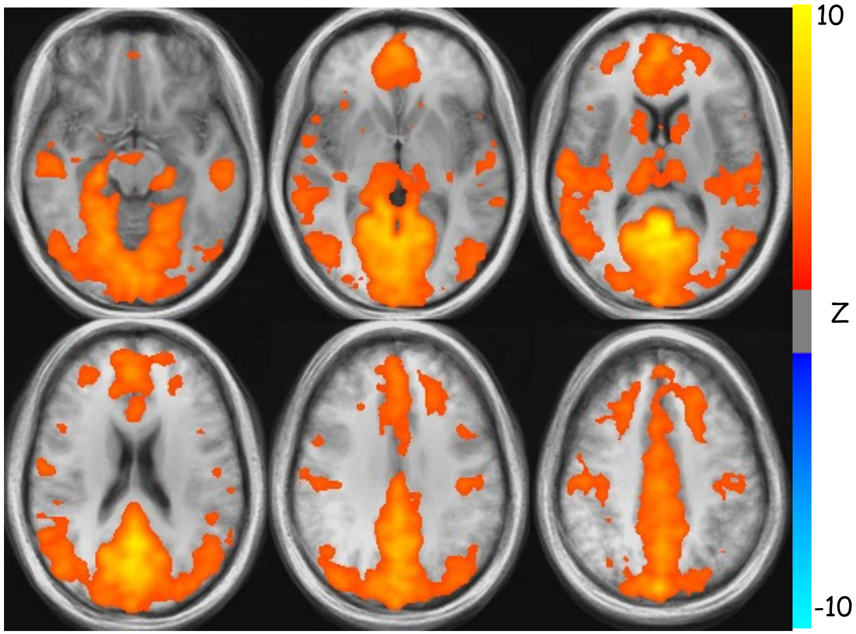




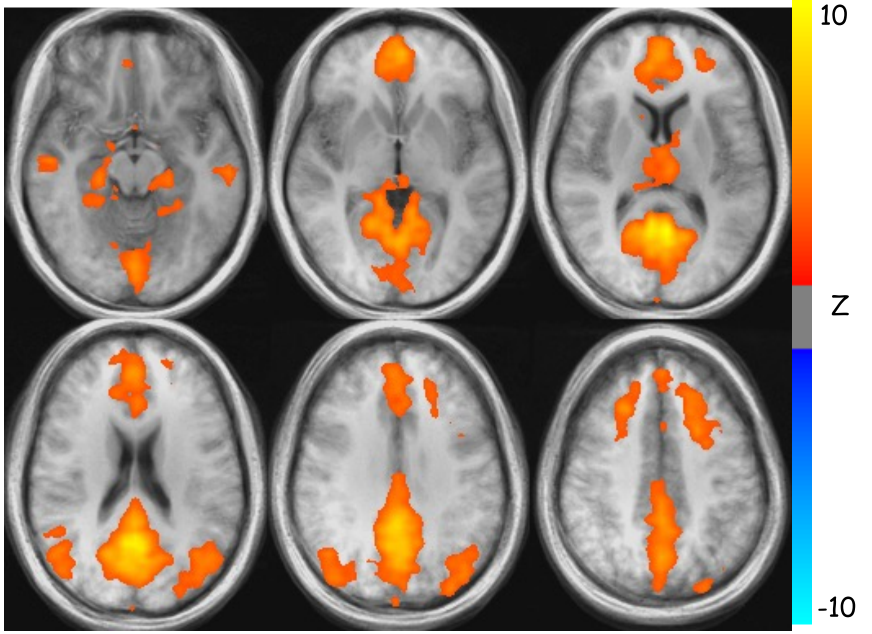
Group (n=10)

Effect of Respiration Rate Consistency on Resting Correlation Maps

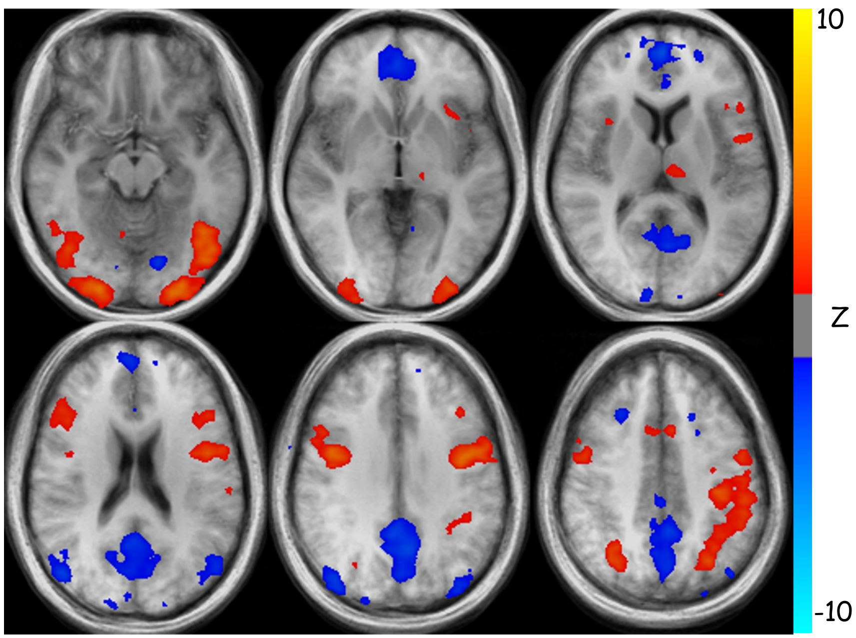
Spontaneously Varying Respiration Rate



Constant Respiration Rate



Lexical Decision Making Task

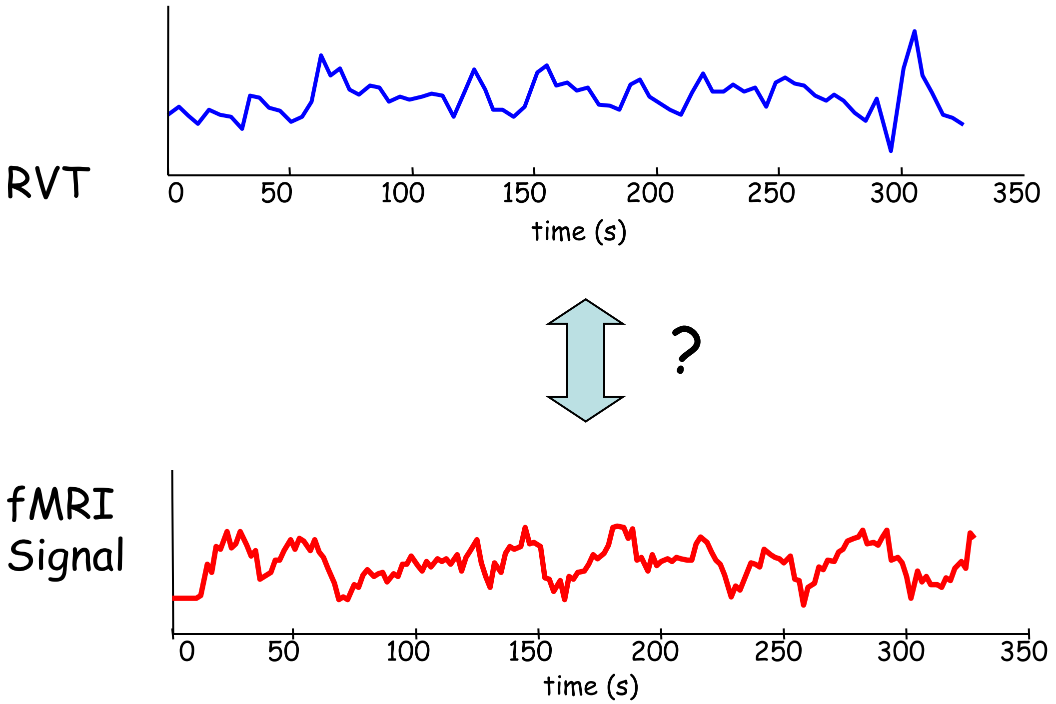


Blue: deactivated network

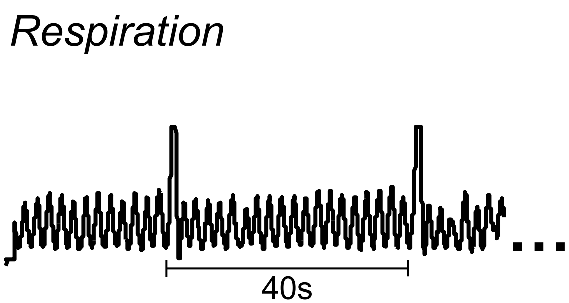
Group (n=10)

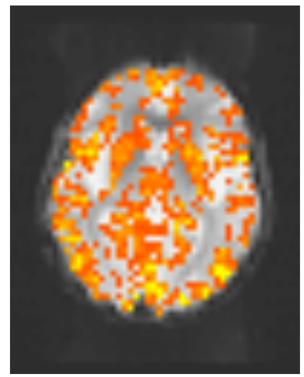
Respiration Changes vs. BOLD

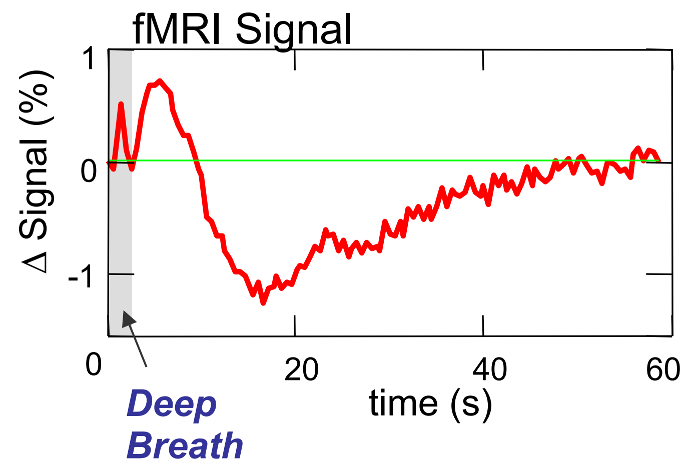
How are the BOLD changes related to respiration variations?

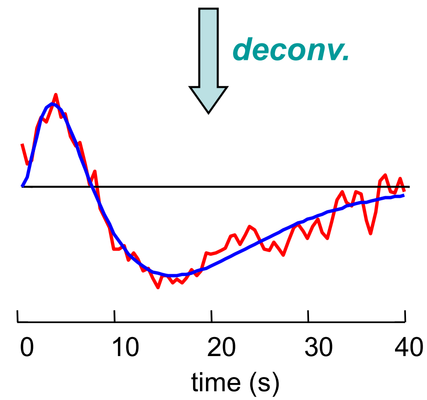


fMRI response to a single Deep Breath









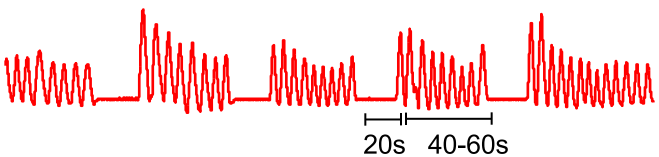
Respiration Response Function (**RRF**)

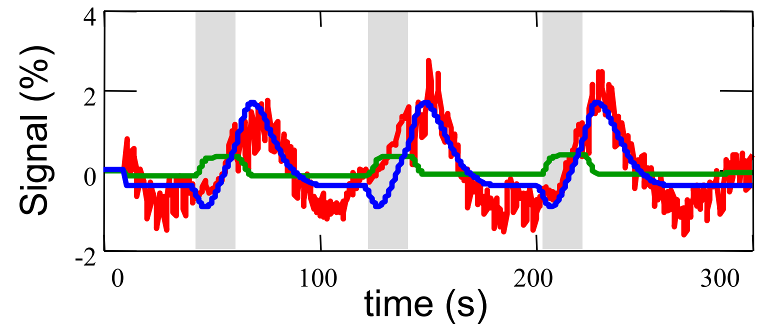
$$\mathrm{RRF}(t) = 0.6\, t^{2.1}\, e^{\frac{t}{1.6}} - 0.0023\, t^{3.54}\, e^{\frac{t}{4.25}}$$

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

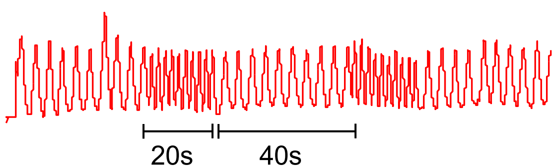
Respiration response function predicts BOLD signal associated with breathing changes better than activation response function.

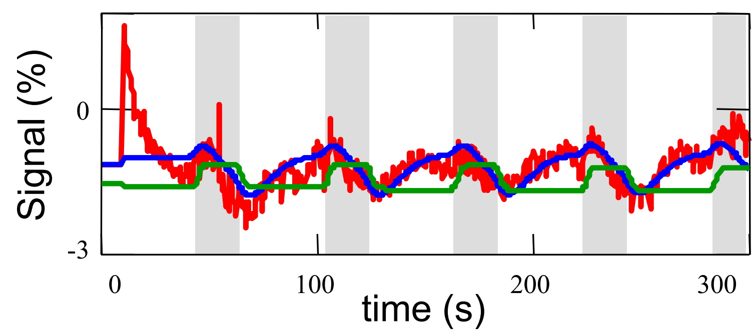
Breath-holding



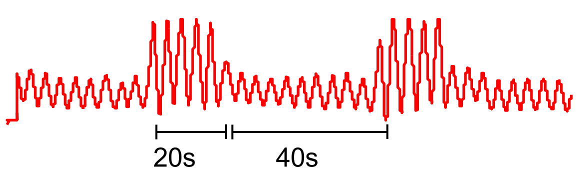


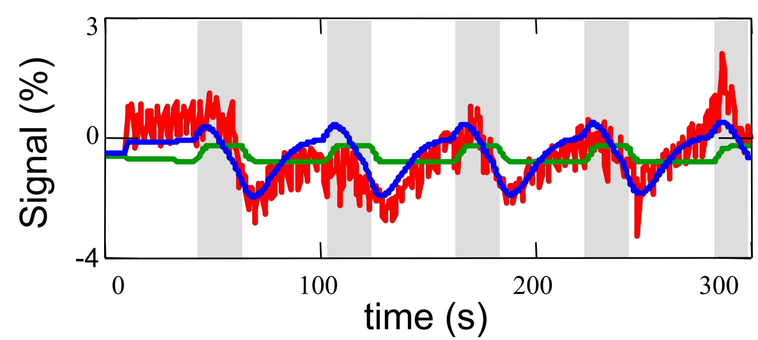
Rate Changes





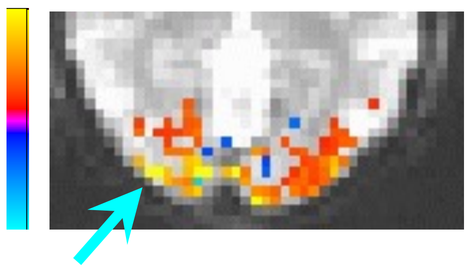
Depth Changes





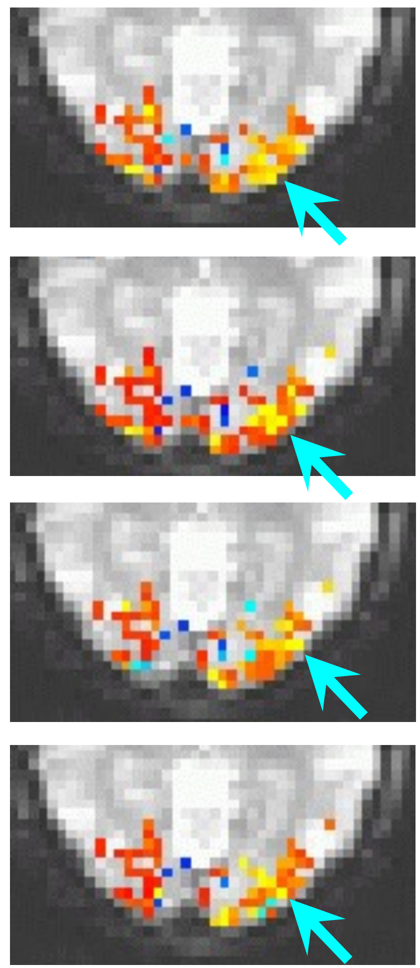
BOLD magnitude calibration

Before Calibration



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

After Calibration



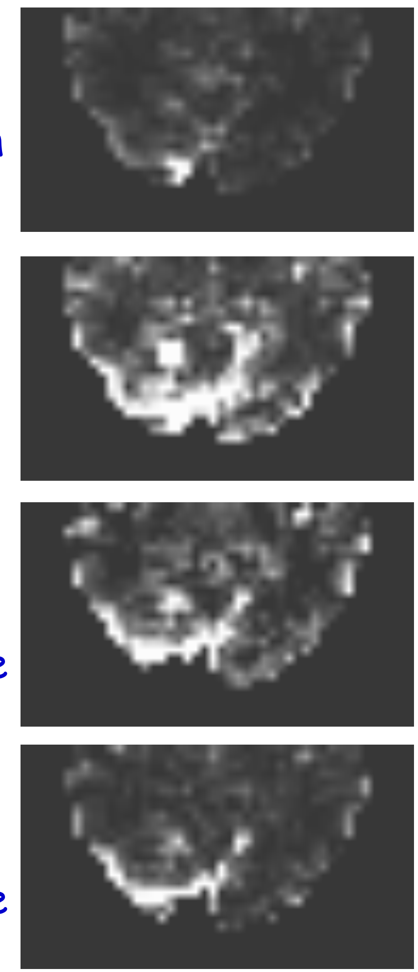
Respiration-induced ΔS

Breath Hold

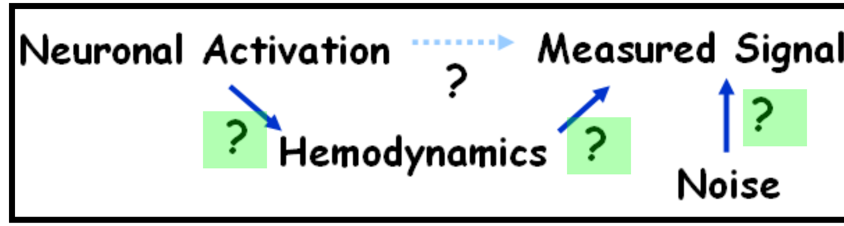
Rest

Depth Change

Rate Change



2. Fluctuations



Conclusion:

- RVT maps resemble connectivity maps.
- Constant breathing is effective in reducing fluctuations.
- Respiration Response Function is characterized.
- Breath hold, rate changes, depth changes, AND resting fluctuations can be used to calibrate BOLD magnitude.

Future:

- Test calibration effectiveness.
- Compare ICA derived maps before and after RVT regression or breathing rate controls.

3. Experimental Design

Motivation:

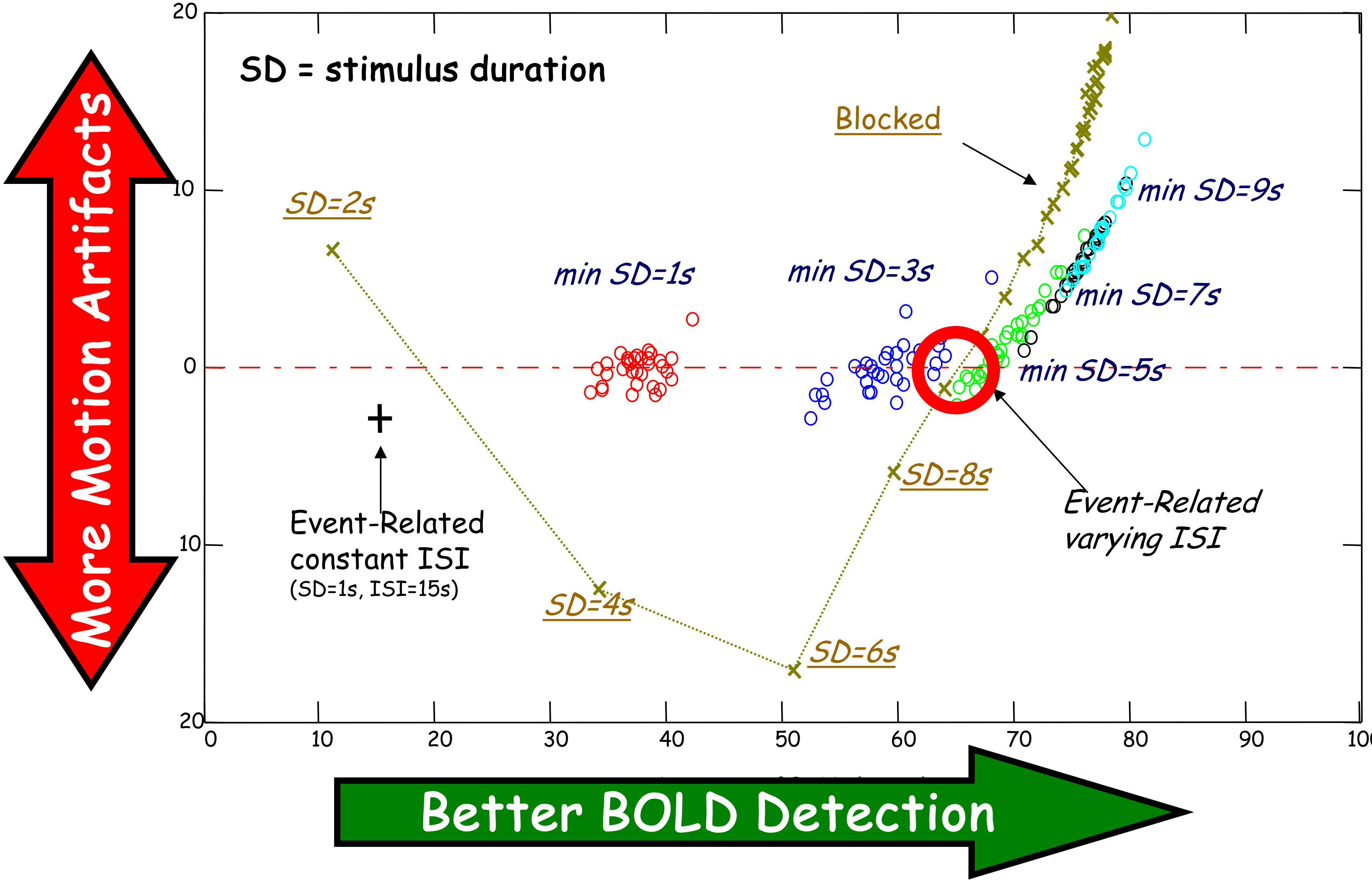
- Guides for *individual* subject scanning at the limits of detectability, resolution, available time, and subject performance.

Studies:

- Overt response timing

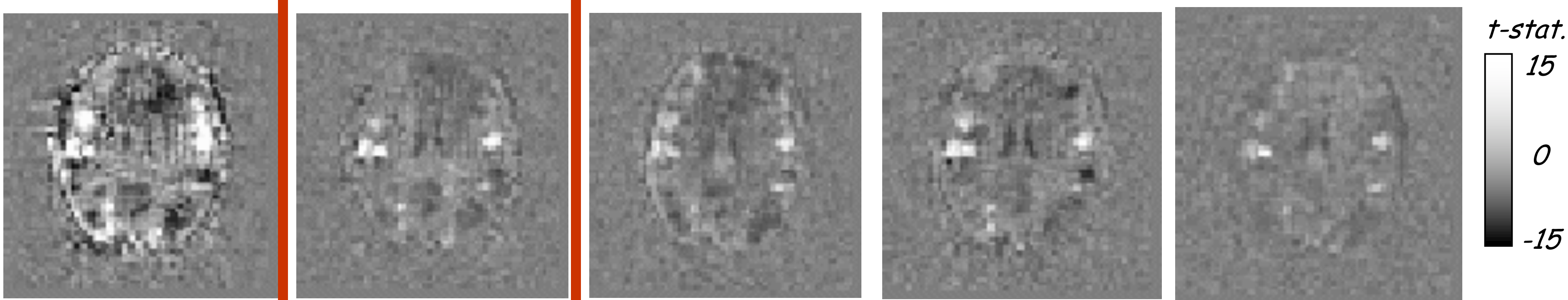
- Suggested resolution

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)

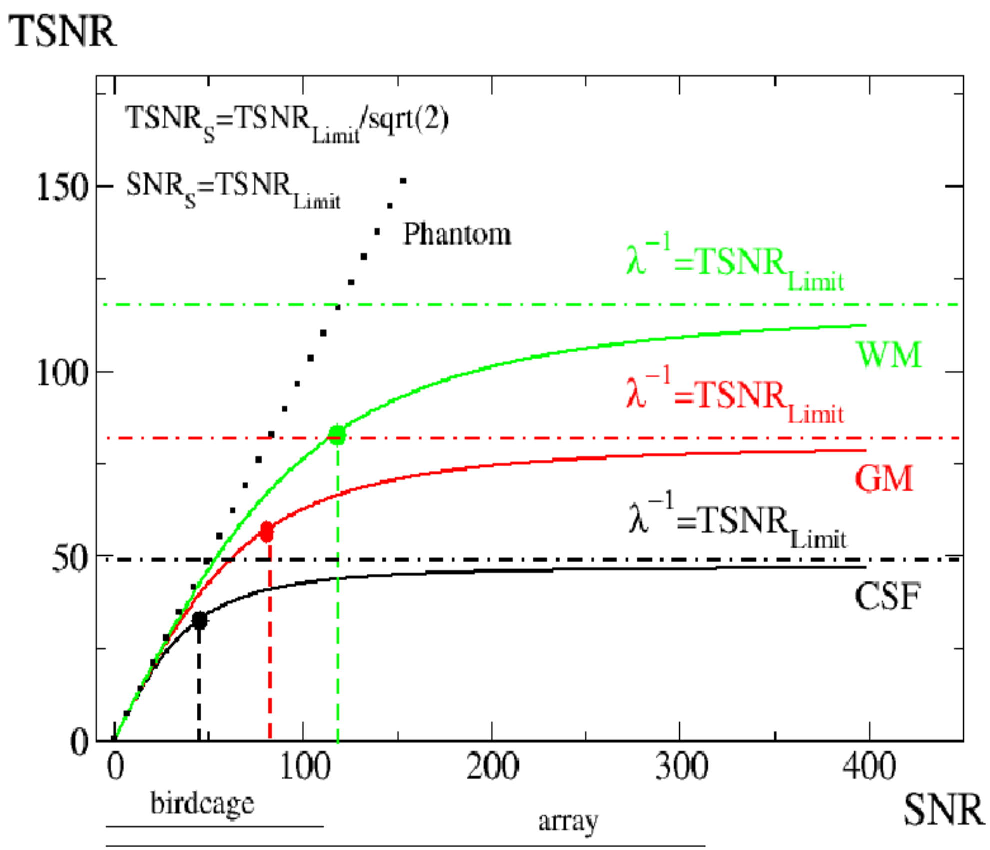
Event-related Varying ISI (1s min. SD)

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

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

Finding the "suggested voxel volume"

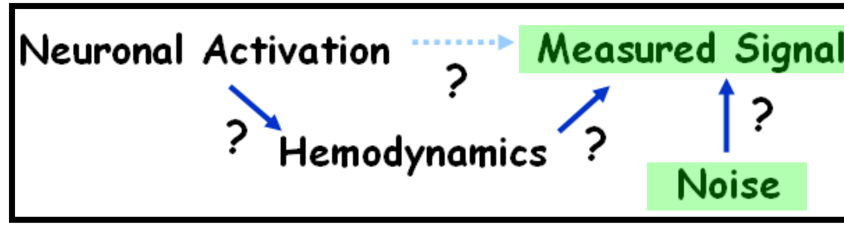
Temporal Signal to Noise Ratio (TSNR) vs. Signal to Noise Ratio (SNR)



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)

3. Experimental Design



Conclusion:

- Overt response paradigms are experimentally verified (blocked, 10 on/ 10 off is best).

- The "suggested voxel volume" concept shows the importance of TSNR in gray matter rather than SNR.

Future:

- Implement rapid "suggested voxel volume" calculation at scanner, based on TSNR measure.

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?

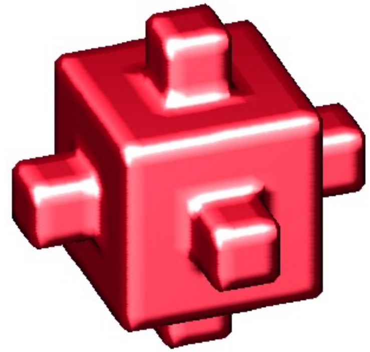
Study:

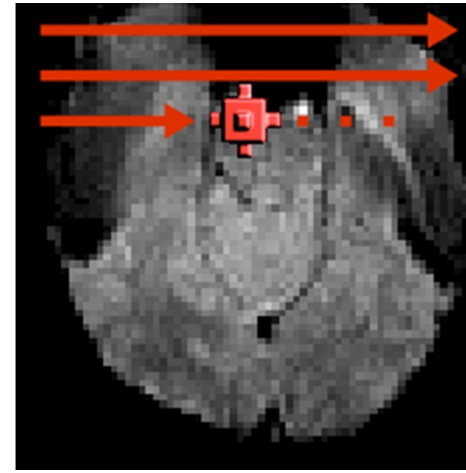
- Pattern-Information Mapping

- Dis-similarity matrix

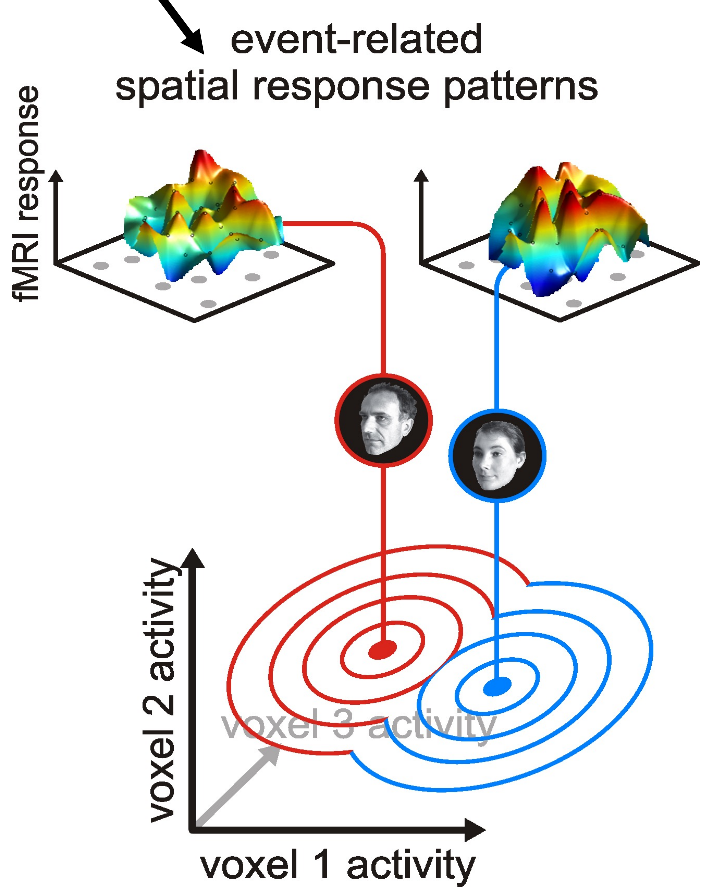
Pattern Information Mapping

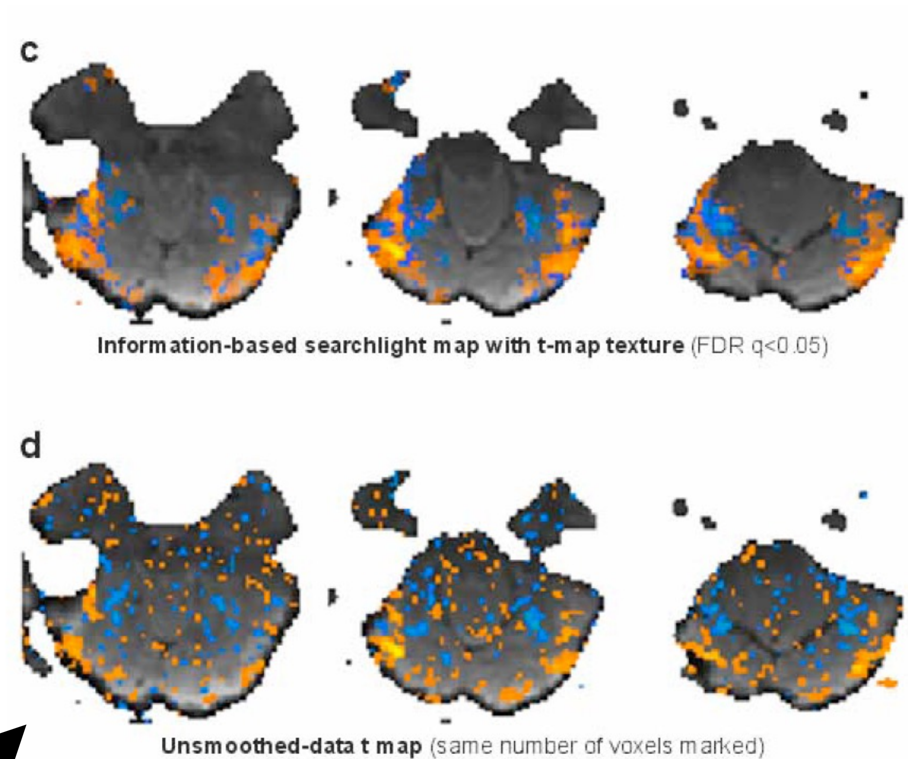
"searchlight" ROI





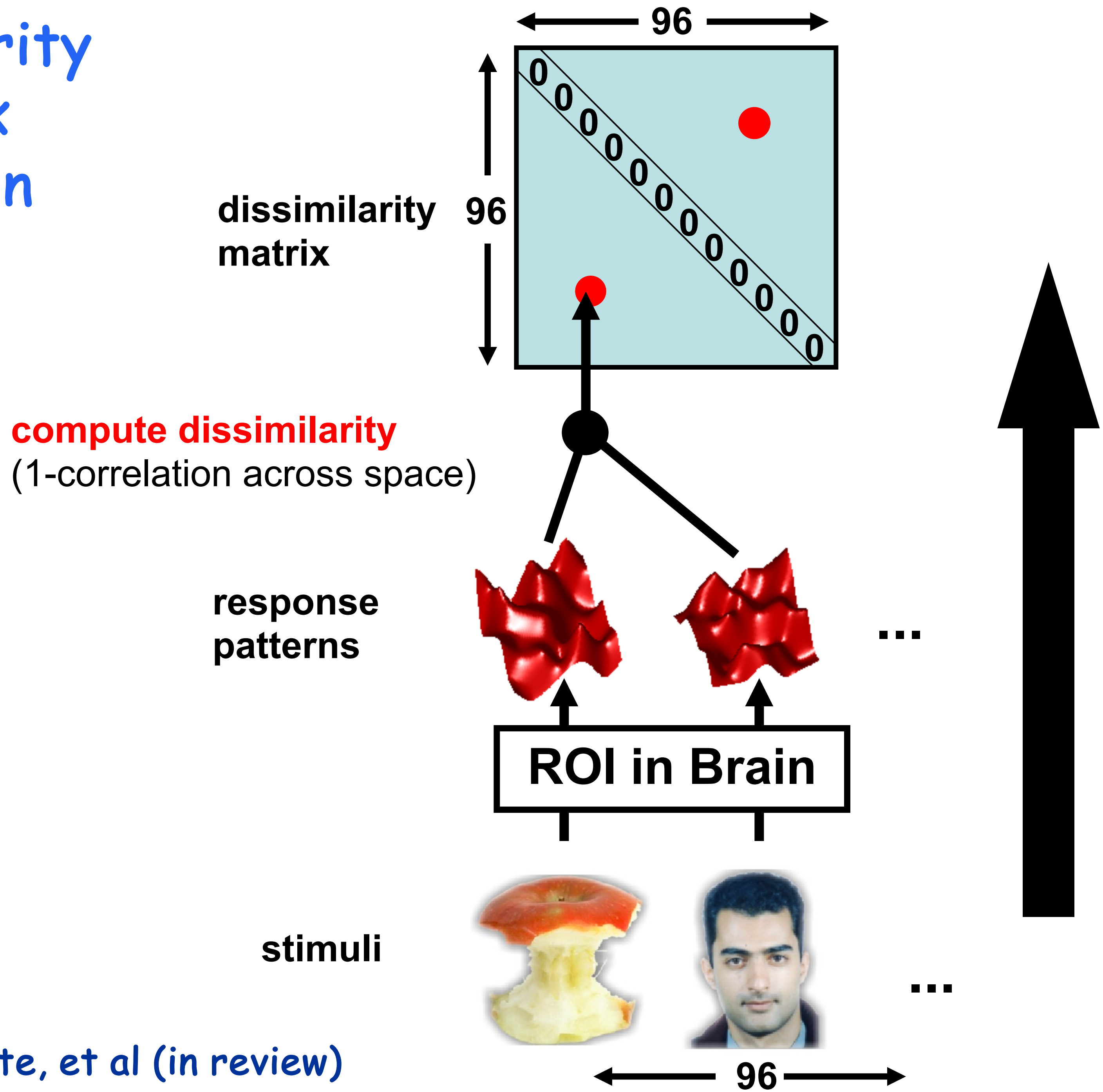
From fixed ROI





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

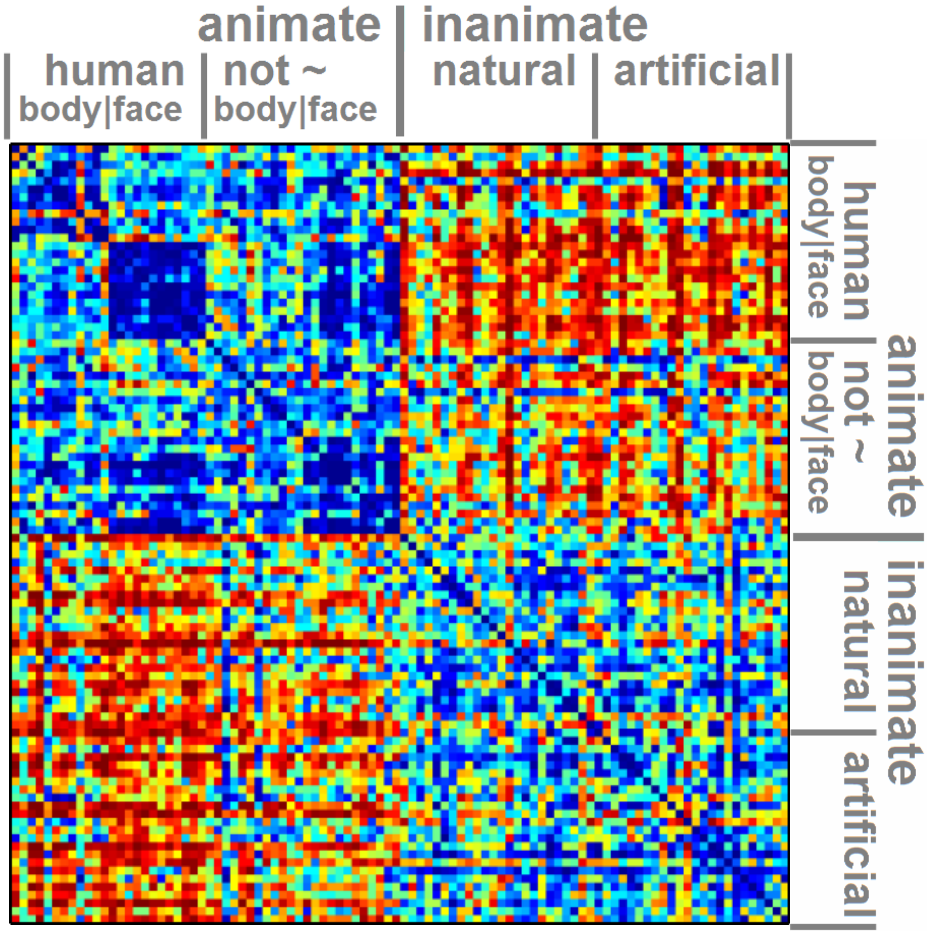
- fMRI in four subjects
  (repeated sessions,
  >12 runs per subject)
- "quick" event-related design
  (stimulus duration: 300ms,
  stimulus onset asynchrony: 4s)
- fixation task
  (with discrimination of fixation-point color changes)
- occipitotemporal measurement slab
  (5-cm thick)
- small voxels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

Monkey (Kiani et al. 2007)

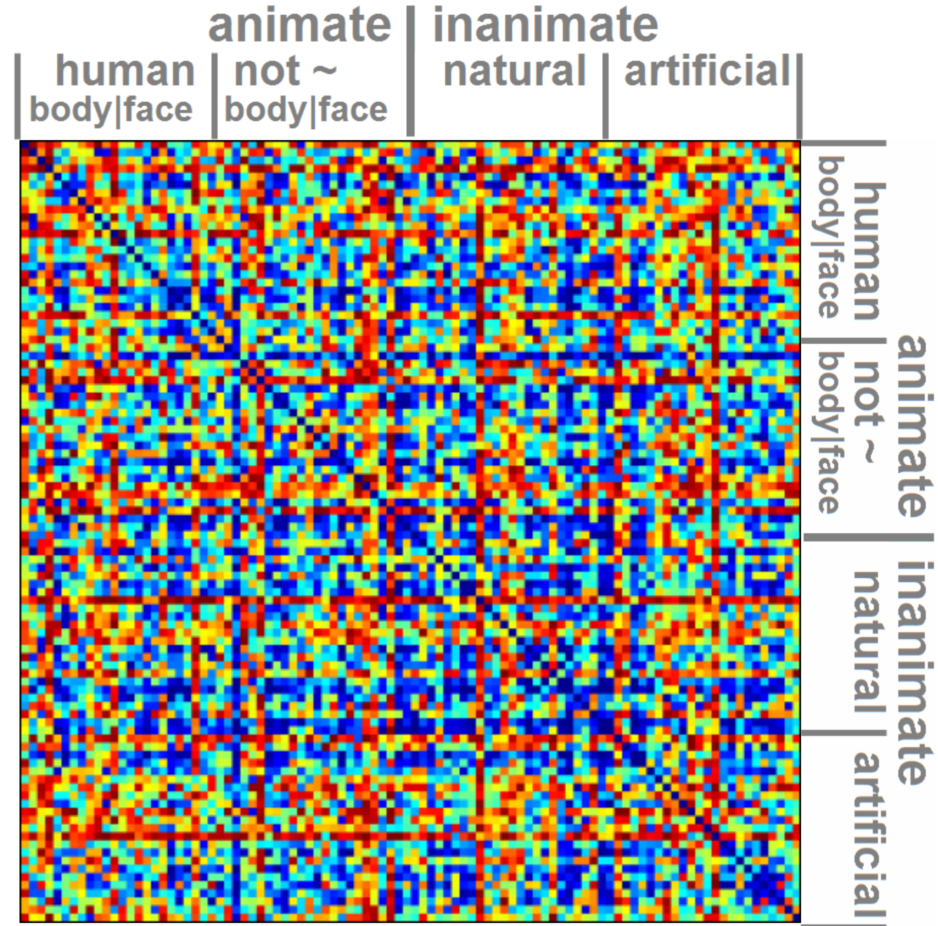
- single-cell recordings in two monkeys
- rapid serial presentation
  (stimulus duration: 105ms)
- fixation task
- electrodes in anterior IT
  (left in monkey 1, right in monkey 2)
- 674 cells total
- windowed spike count
  (140-ms window starting 71ms after stimulus onset)

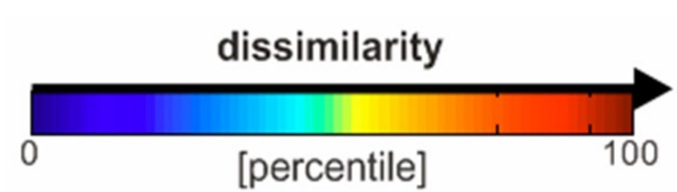
Visual Stimuli

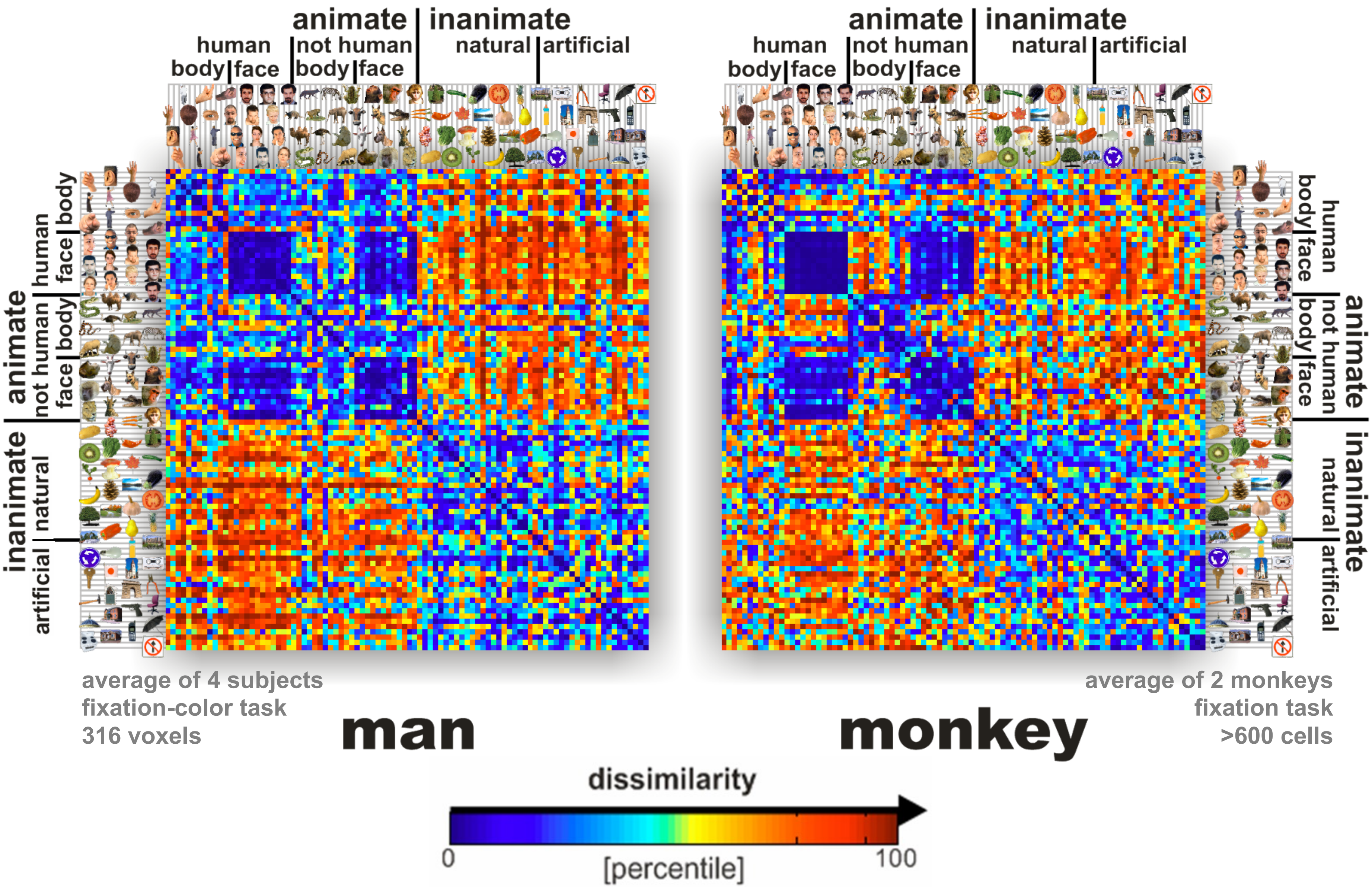
Human IT
(1000 visually most responsive voxels)



Human Early Visual Cortex
(1057 visually most responsive voxels)

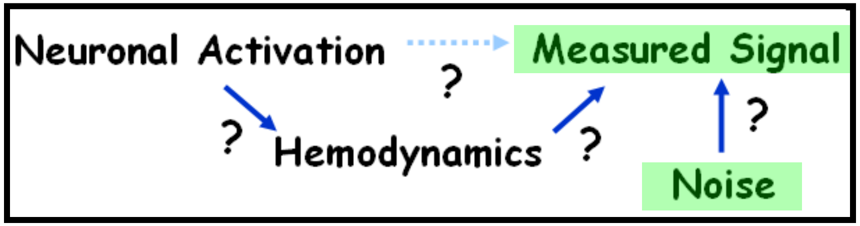






N. Kriegeskorte, et al (in review)

4. Pattern-Information Analysis



Conclusion:

•Useful for mapping and comparing voxel wise patterns that may be missed with classical approaches.

Future:

•Spatial scale/distribution of most informative patterns with learning, categorization?

•Careful comparisons to mapping approaches.

•High resolution, high field.

•

5. Neuronal Current MRI

Motivation:

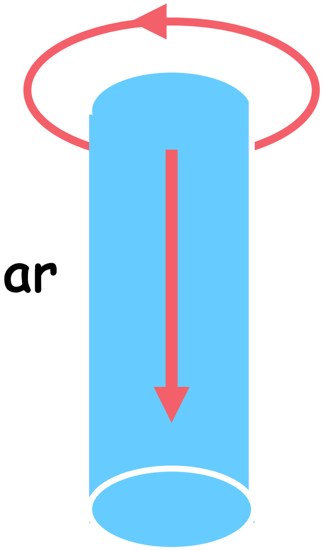
- Direct fMRI of neuronal activity.

Studies:

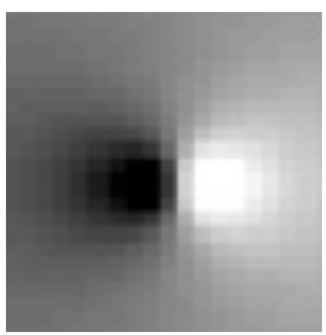
- Model
- Phantom Studies
- Cell Cultures at 7T and 3T

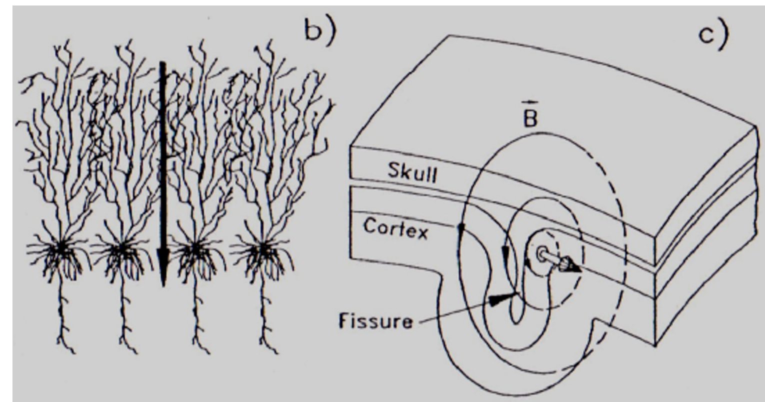
Magnetic Field

Intracellular Current



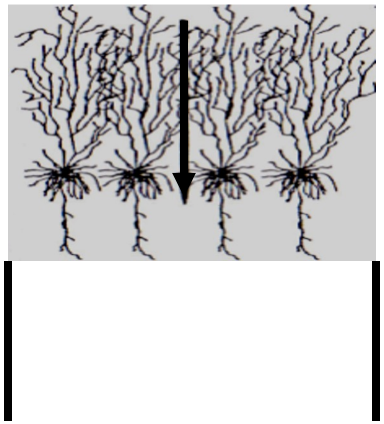
Surface Fields



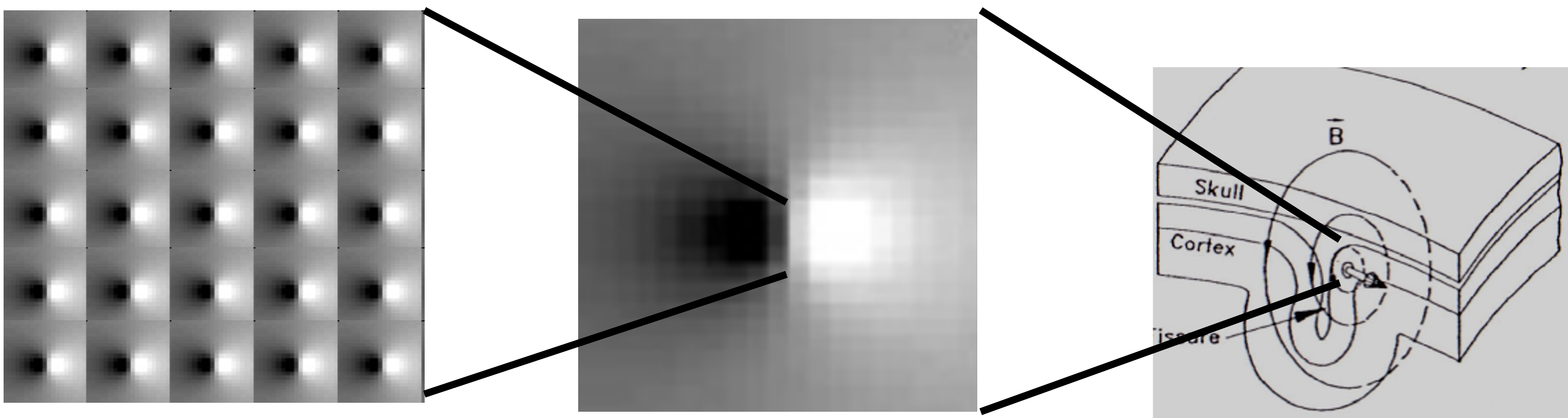


100 fT at on surface of skull

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



Surface Field Distribution Across Spatial Scales

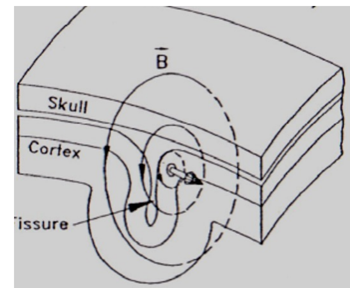


Adapted from: J.P. Wikswo Jr et al.

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

Magnetic field associated with a bundle of dendrites

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

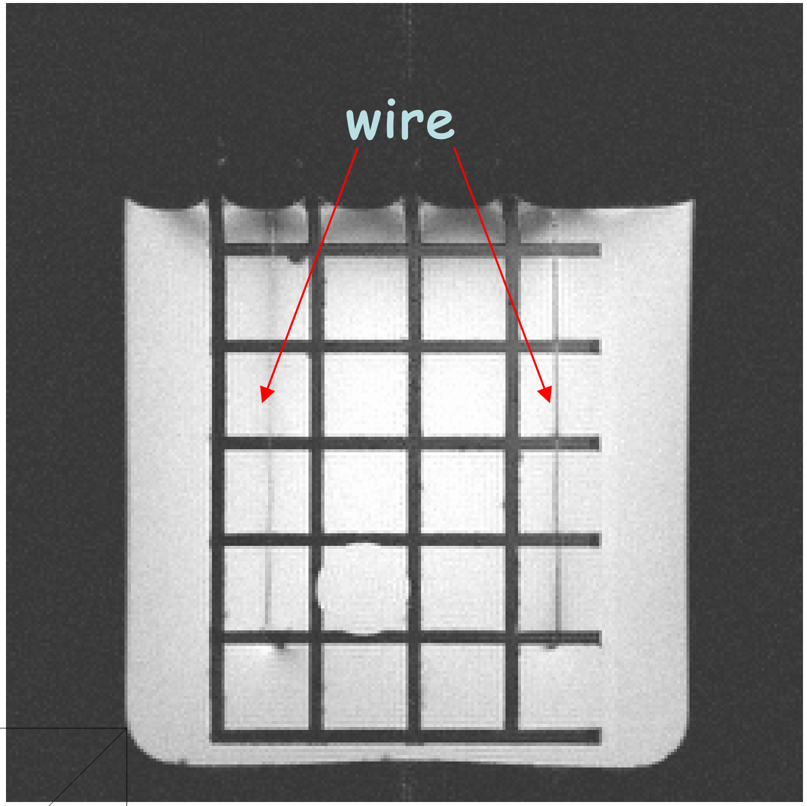


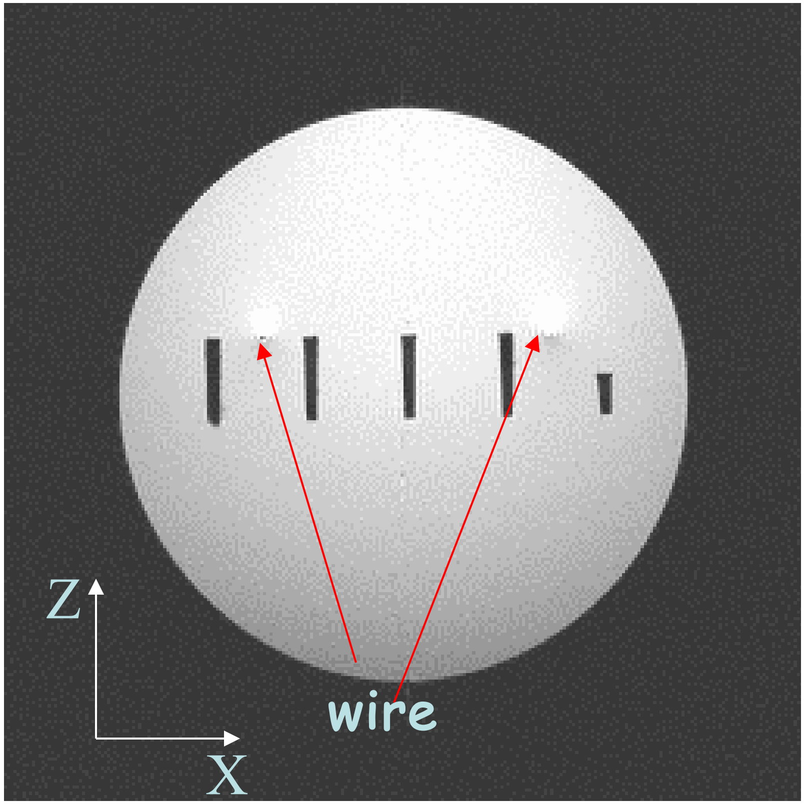
at least 50,000 neurons (0.002 fT (per dendrite) x 50,000 = 100 fT), must coherently act to generate such field. These bundles of neurons produce, within a typical voxel, 1 mm x 1 mm x 1 mm, a field of order:

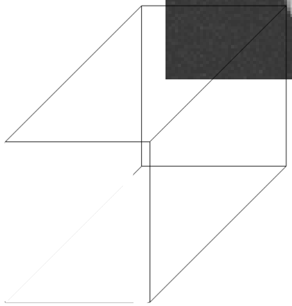
$$B_{MRI} = B_{MEG}\left(\frac{r_{MEG}}{r_{MRI}}\right)^2 = B_{MEG}\left(\frac{4\,cm}{0.1\,cm}\right)^2 = 1600\,B_{MEG}$$

$B_{MRI} \approx 0.2nT$

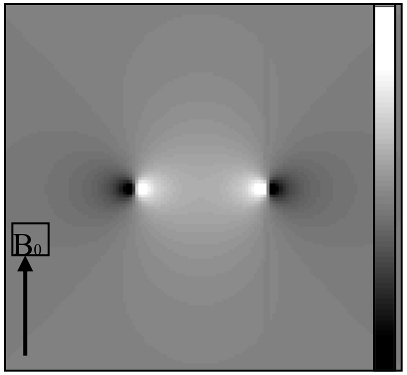
Current Phantom Experiment



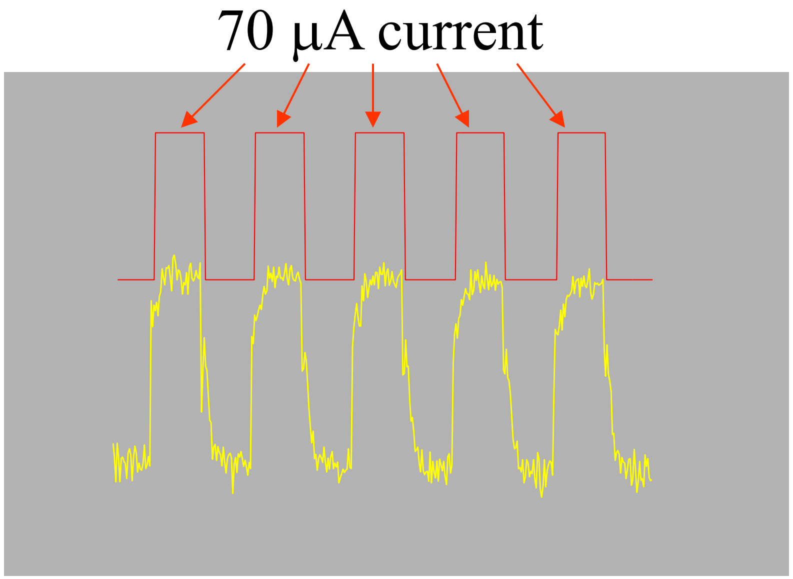




calculated B_c || B_0

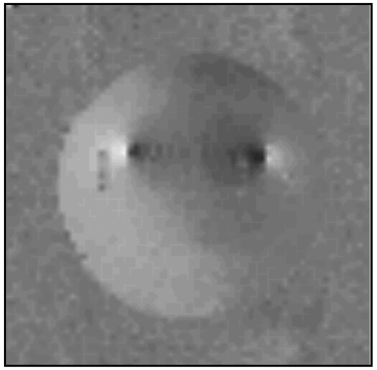


Measurement



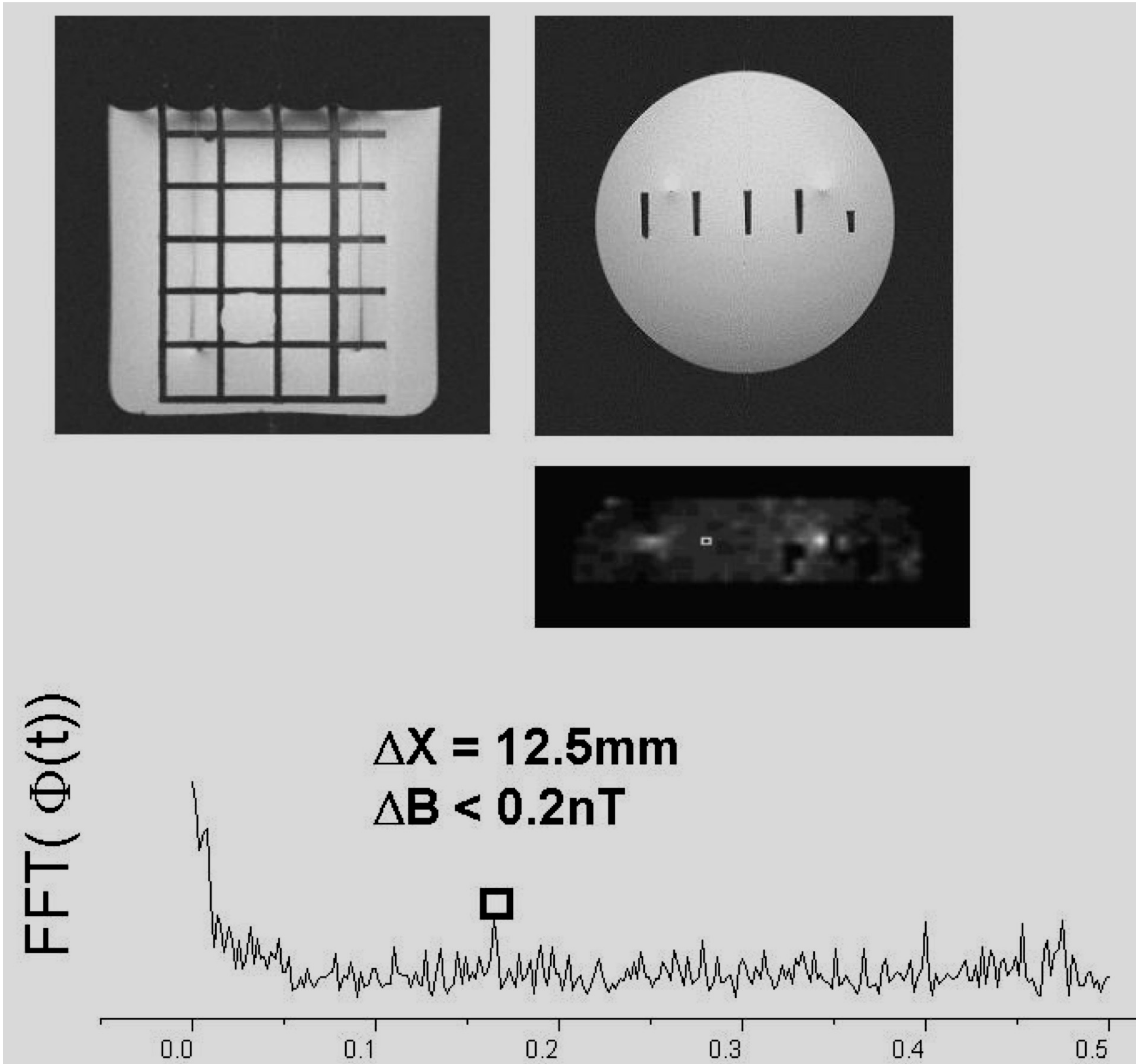
Single shot GE EPI

$\Delta\phi \cong 20^0$



Correlation image

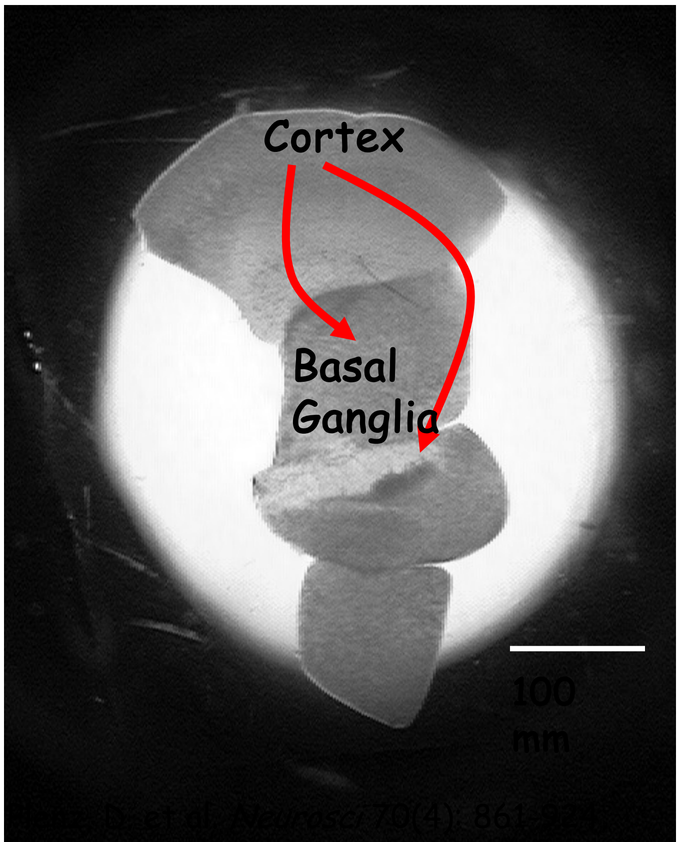
J. Bodurka, P. A. Bandettini. Magn. Reson. Med. 47: 1052-1058, (2002).



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



D. et al. *Neurosci* 70(4): 861-92
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

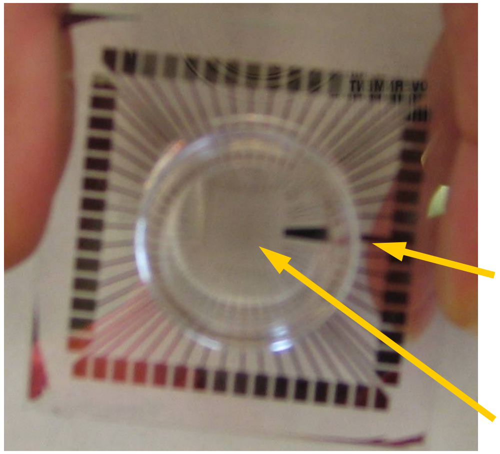
Culture Preparation

Multi-Electrode Arrays (MEA)

Multichannelsystems Germany 8x8 electrodes

0.8ml culture medium

Multi-Electrode Array

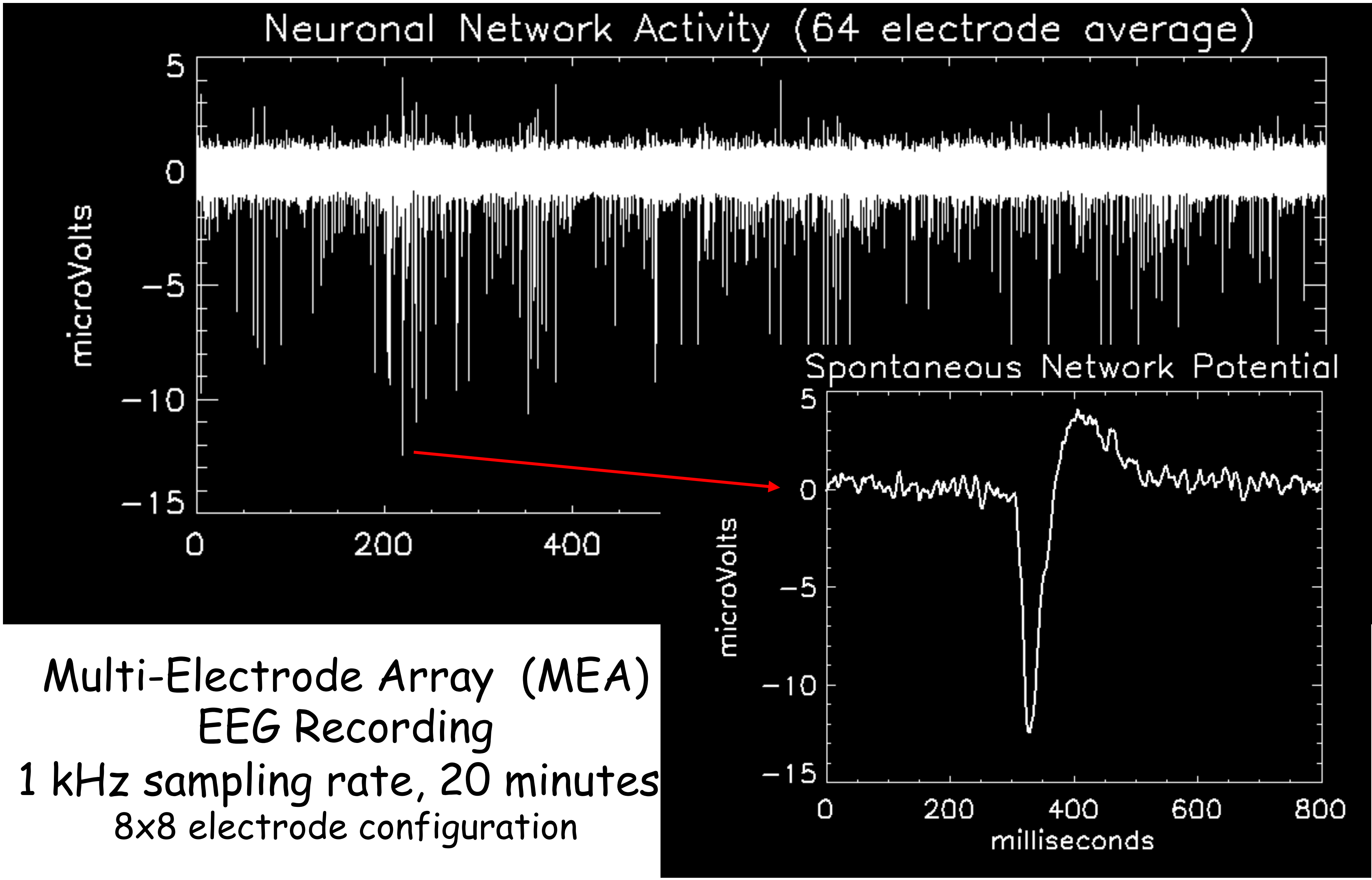


Reference electrode

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

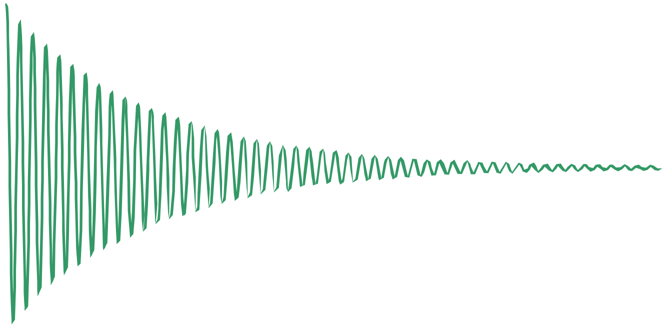
SE EPI image

- 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)

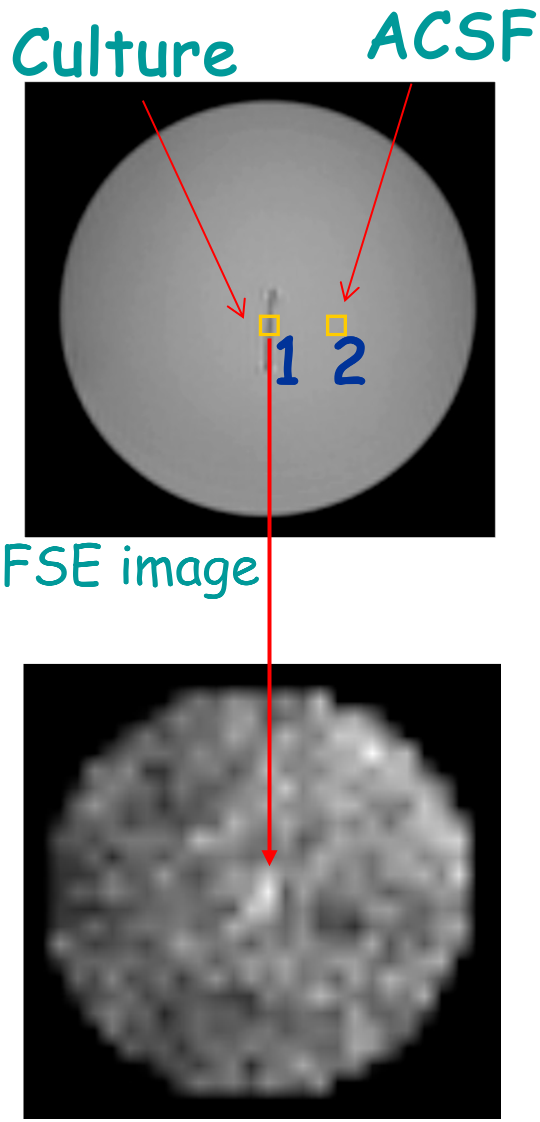
Six Experiments

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

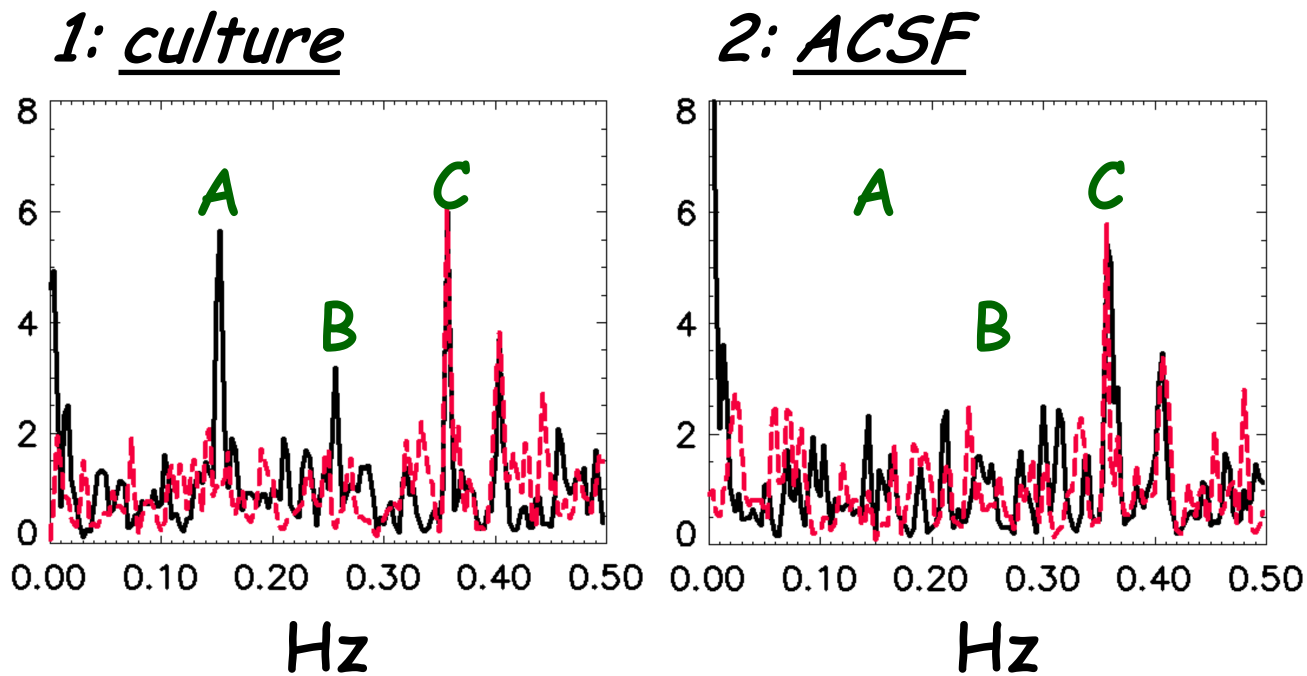
Inactive : ~17 min (10,000 images) neuronal activity terminated via TTX administration

Pre- and Post- MR scan electrical recordings

3 Tesla data



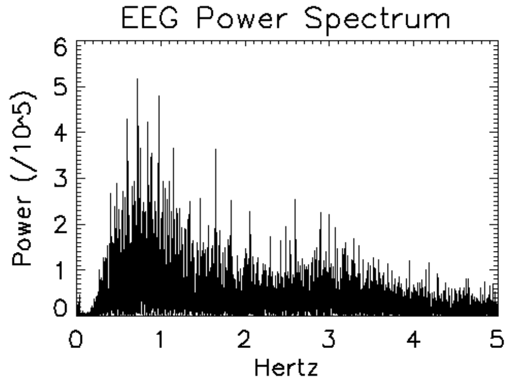
0.15Hz map

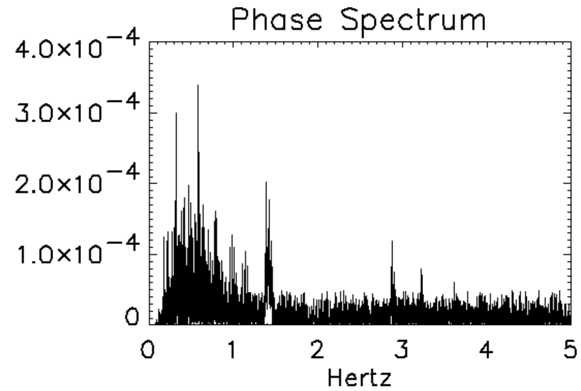


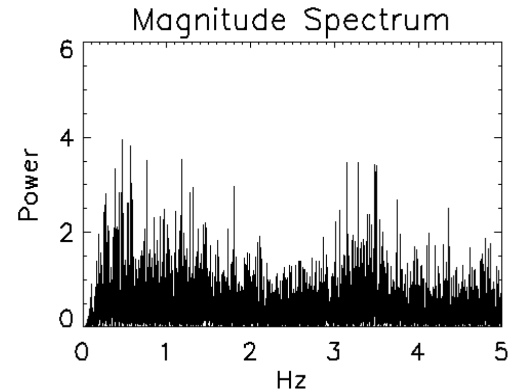
Active condition: black line
Inactive condition: red line

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

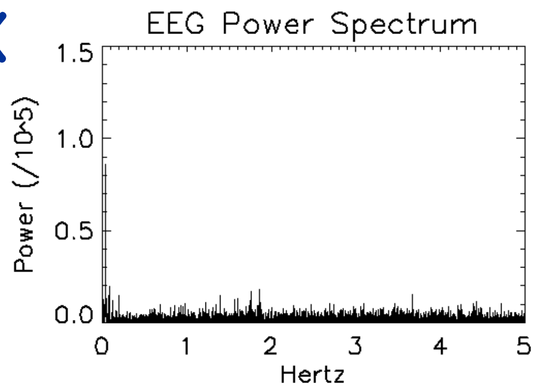
7 Tesla data

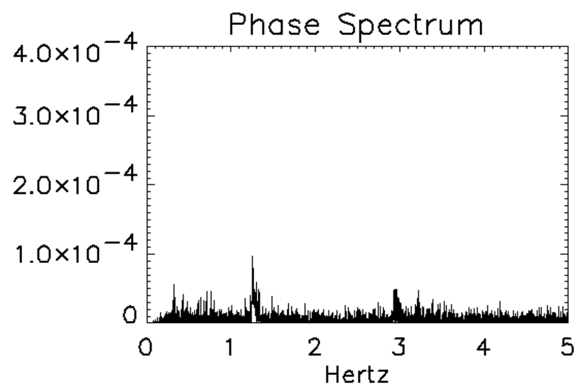


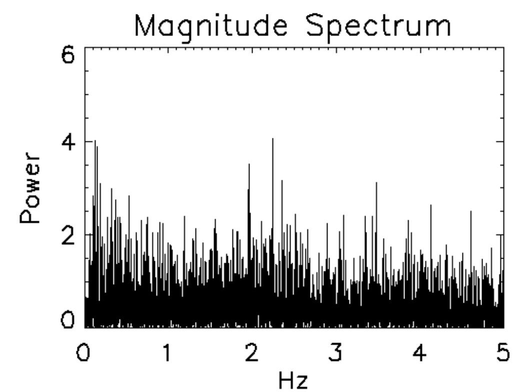




TTX







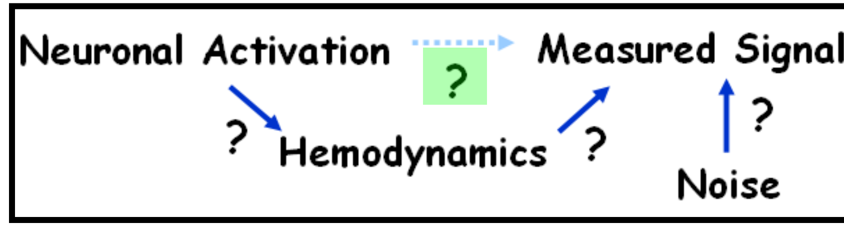
Power decrease between PRE & TTX EEG : ~ 81%

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).

5. Neuronal Current MRI



Conclusion:

- MR phase and magnitude of cell cultures was modulated by TTX administration – suggestive of neuronal currents (phase >> magnitude).

Future:

- Detection in humans: pulse-sequence based neuronal frequency tuning, multivariate processing strategies, matched filters, high field.

September, 1991

Section on Functional Imaging Methods

Rasmus Birn	staff scientist
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 Maieron	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).