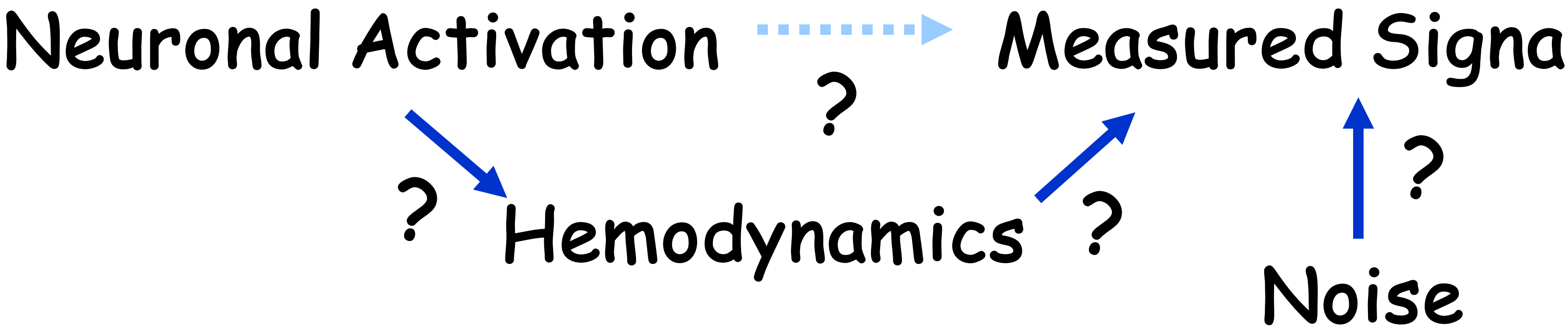
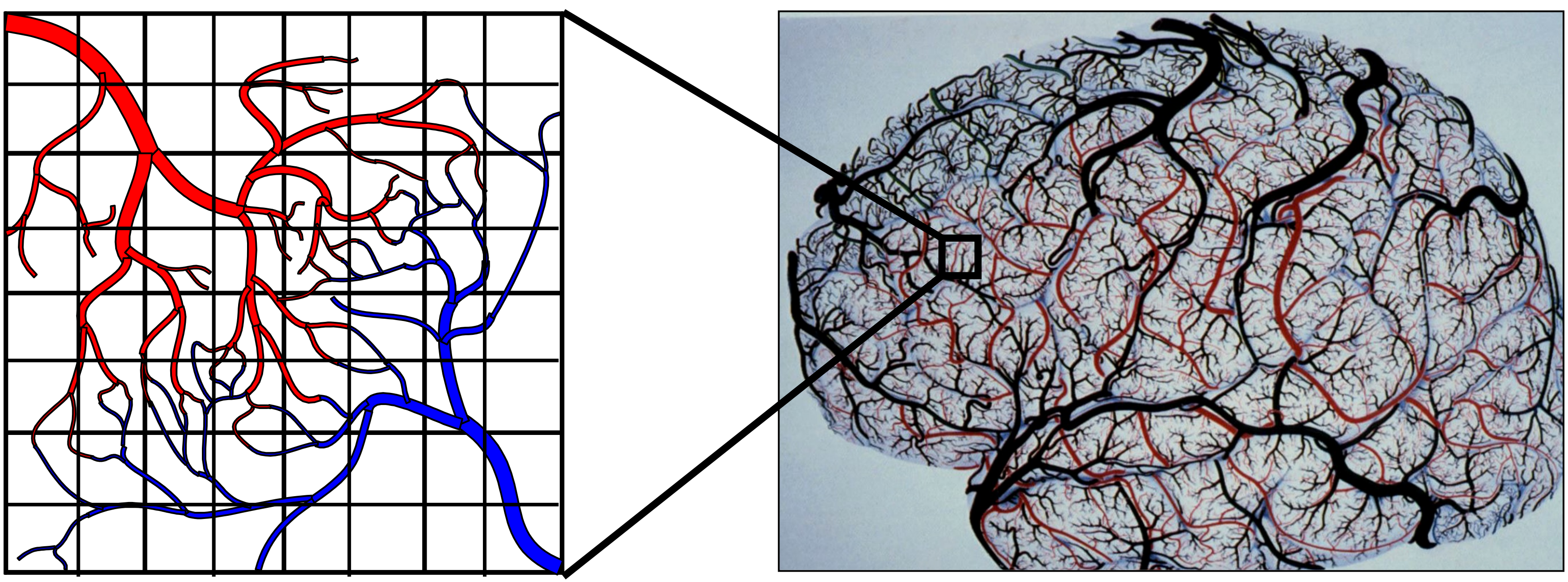
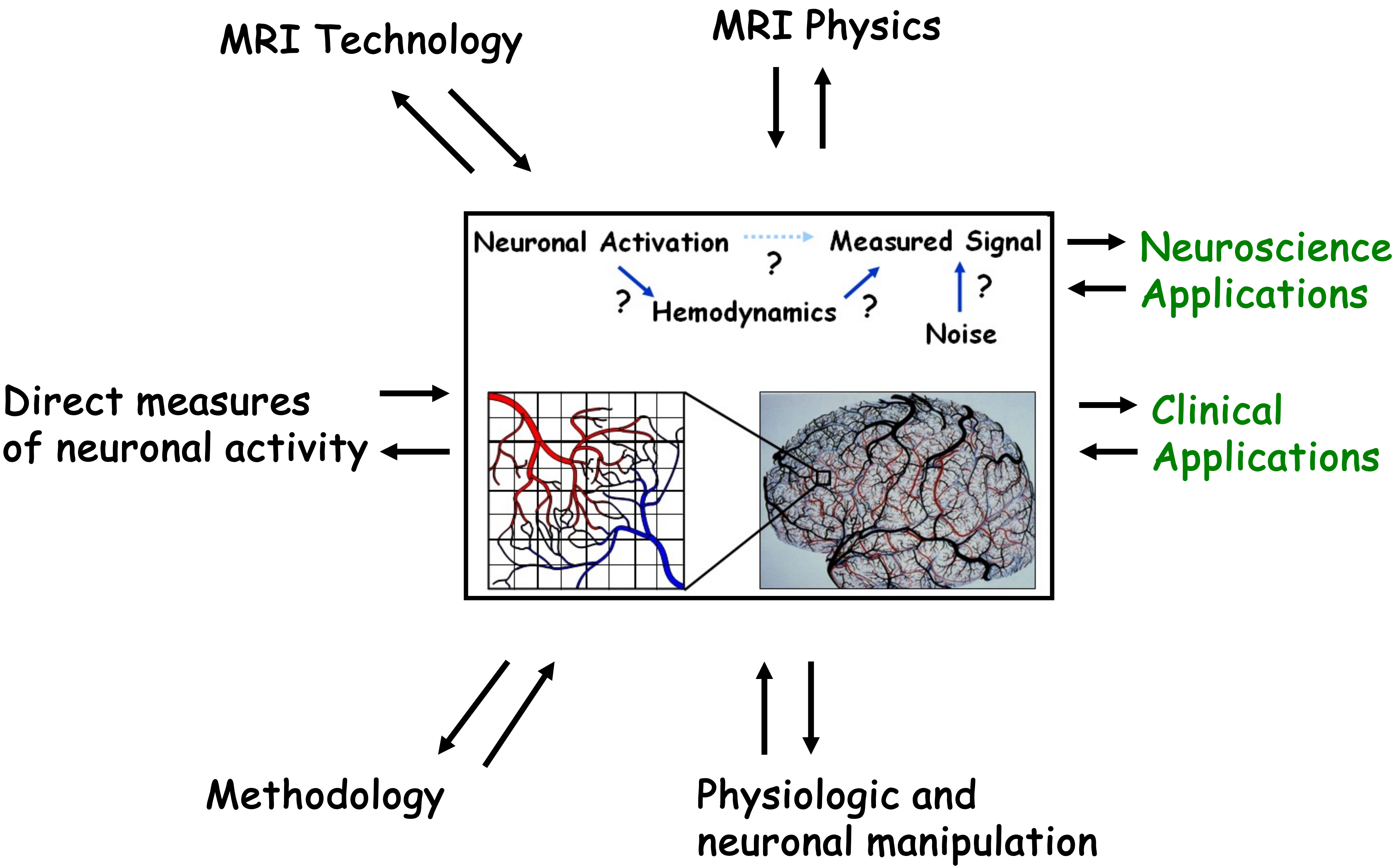
Section on Functional Imaging Methods

(May 2003- November 2007)

Peter A. Bandettini, Ph.D.


Neuronal Activation
Measured Signal
?
?
Hemodynamics
?
?
Noise




MRI Technology
MRI Physics
Neuronal Activation
?
Measured Signal
?
Hemodynamics
?
?
Noise
Neuroscience
Applications
Direct measures
of neuronal activity
Clinical
Applications
Methodology
Physiologic and
neuronal manipulation

1. Dynamics

2. Fluctuations

3. Exp. Design

4. Pattern Information

5. Neuronal Current MRI

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1. Dynamics

Motivation:

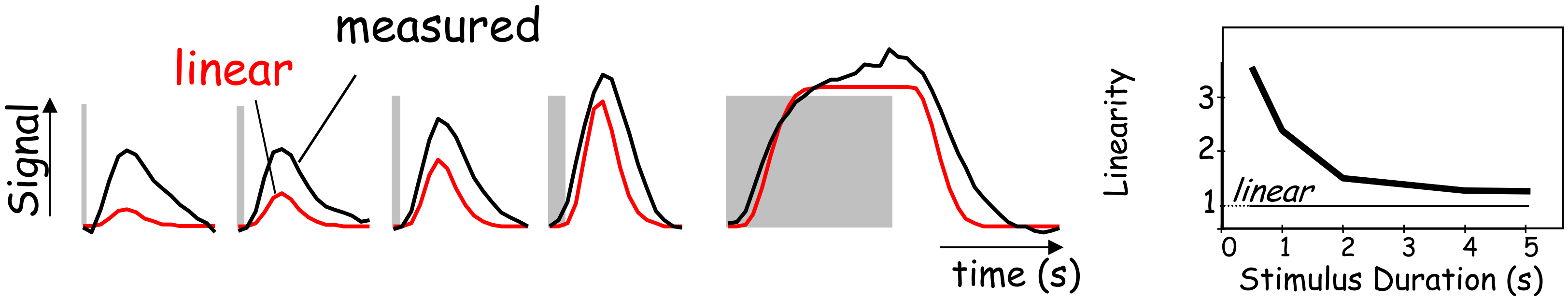
- To understand neuronal and non-neuronal influences on the fMRI signal.

Studies:

- Modulate “on” duration, “off” duration, and duty cycle of visual cortex activation.

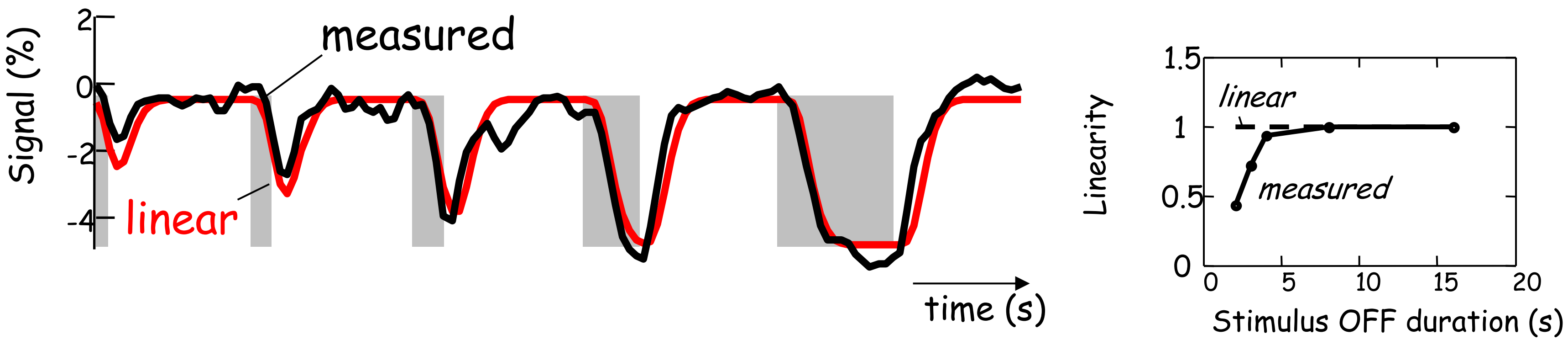
- Neuronal and Hemodynamic Modeling

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



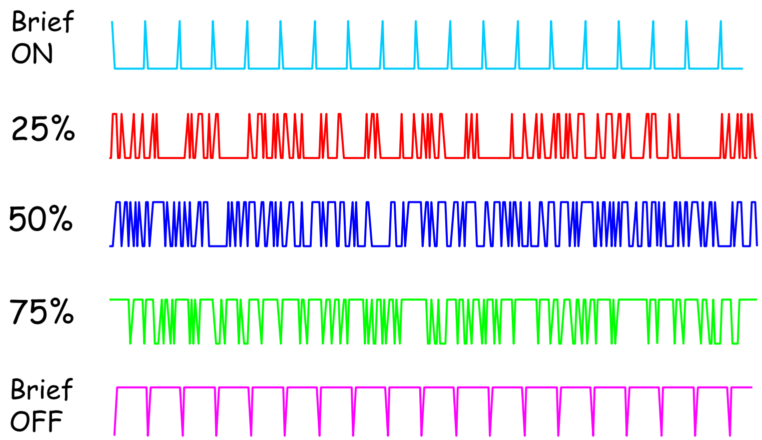
R. M. Birn, Z. Saad, P. A. Bandettini, NeuroImage, 14: 817-826, (2001)

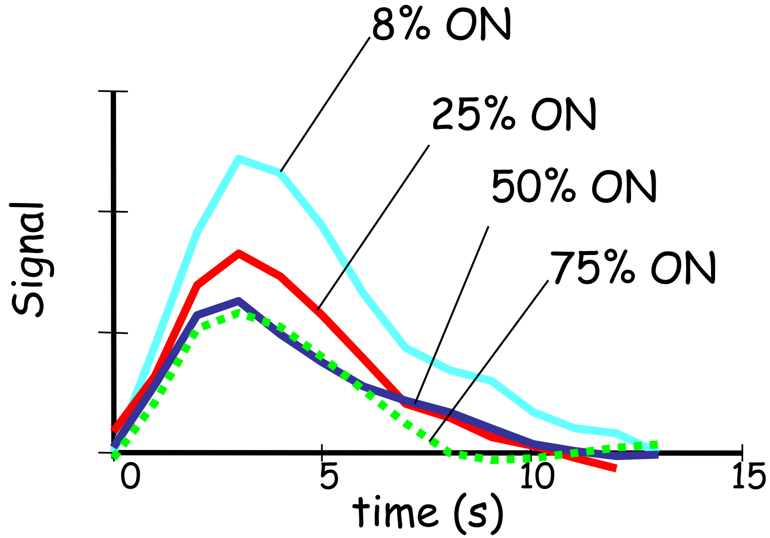
Brief "off" periods produce **smaller** decreases than expected.



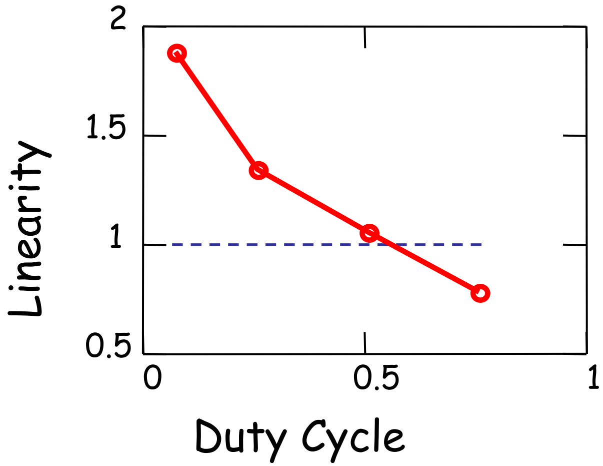
R.M. Birn, P. A. Bandettini, NeuroImage, 27, 70-82 (2005)

Varying the Duty Cycle



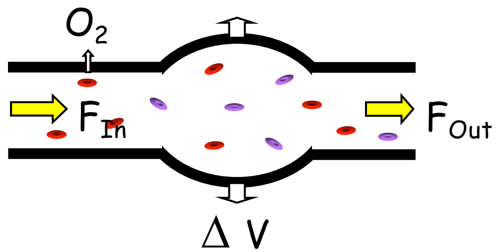


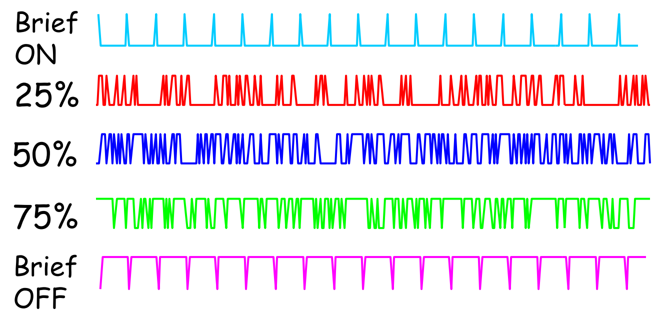
Deconvolved Response



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

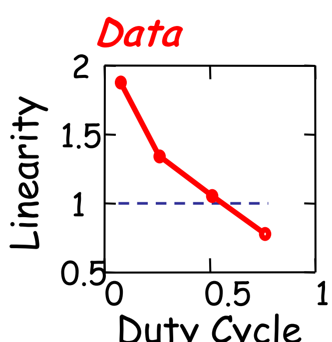
Simulation of Hemodynamic Mechanisms
(Balloon model)

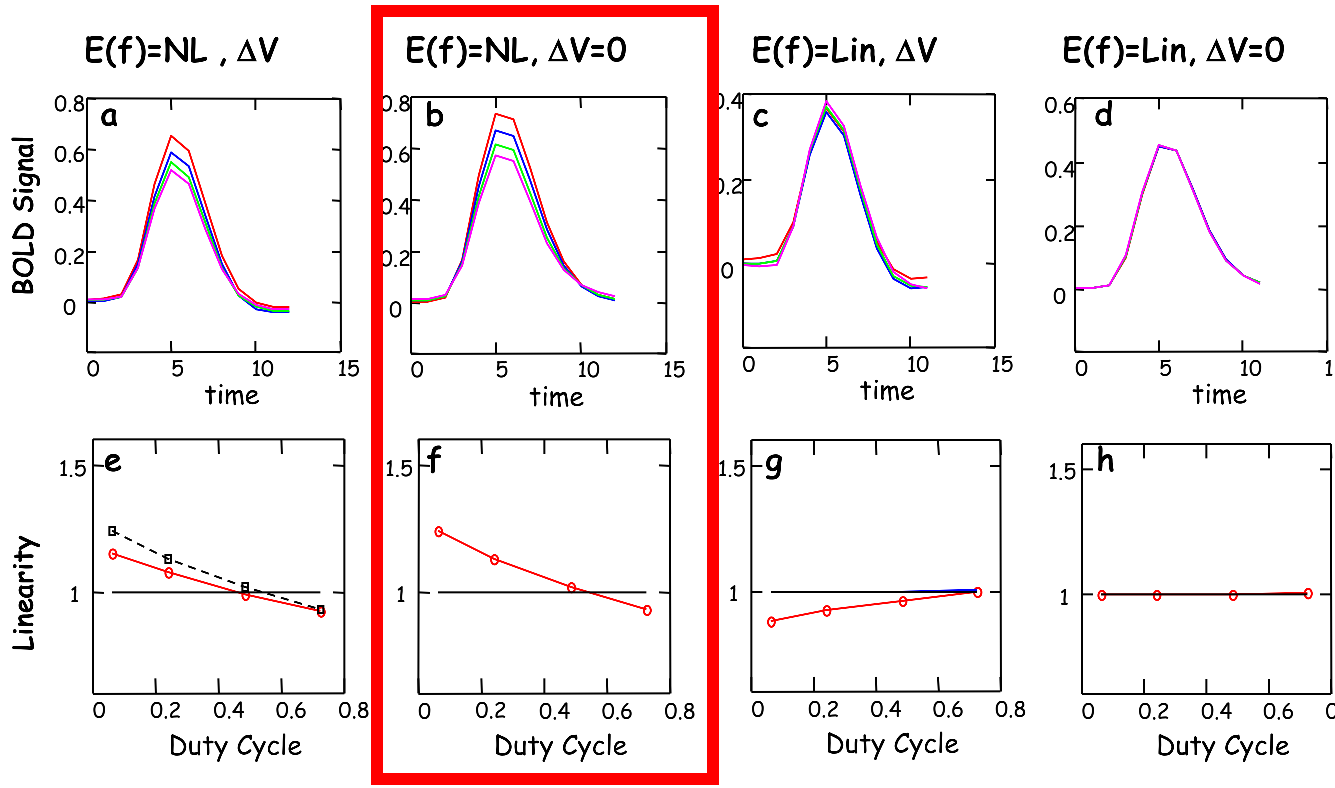




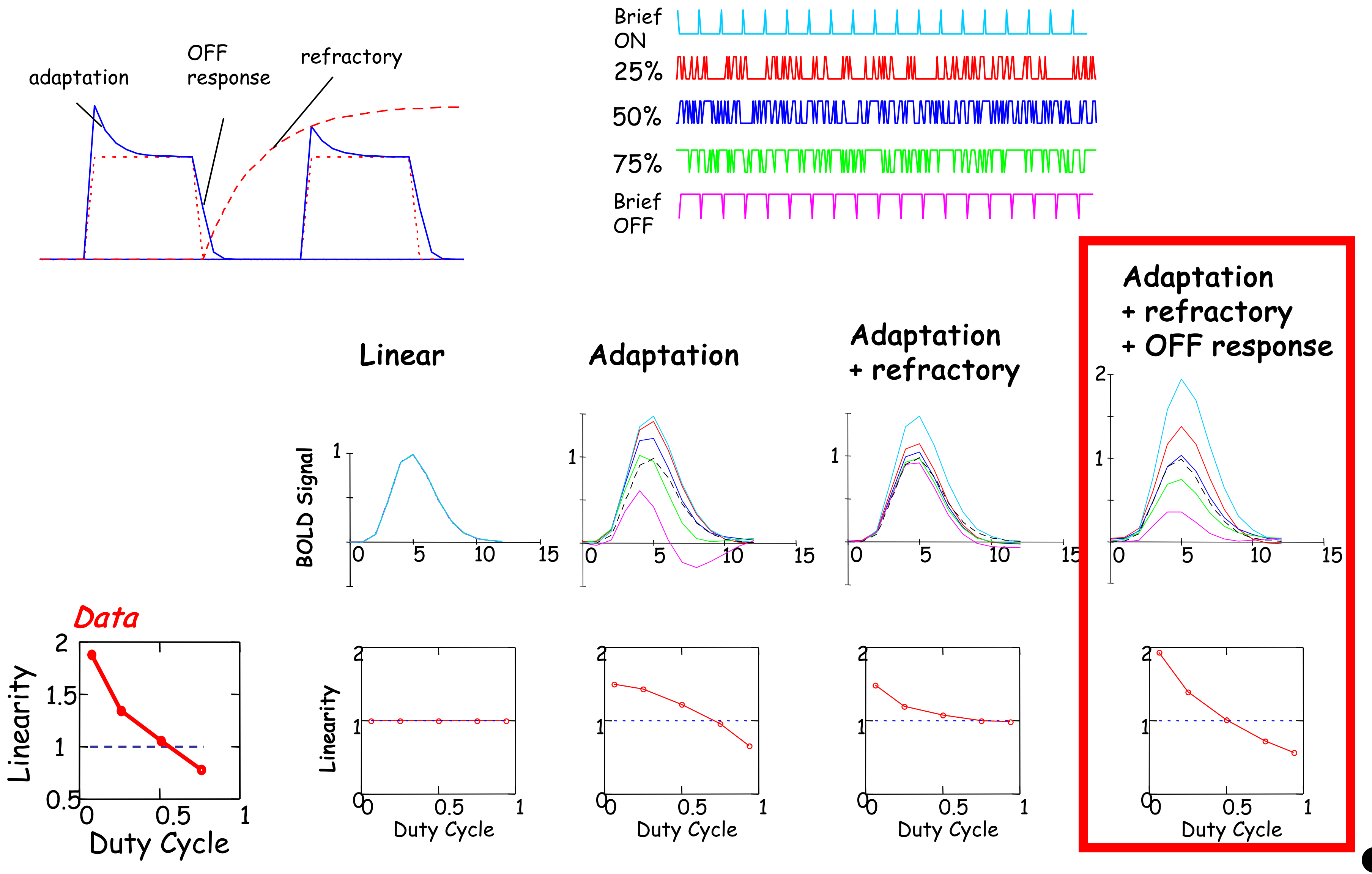
E(f) = oxygen extraction fraction

V = blood volume

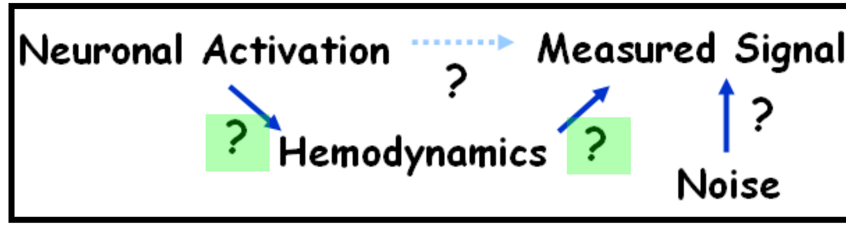




Simulation of Neuronal Mechanisms



1. Dynamics



Conclusion:

- Nonlinearities are not fully explained by the Balloon model.
- "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)

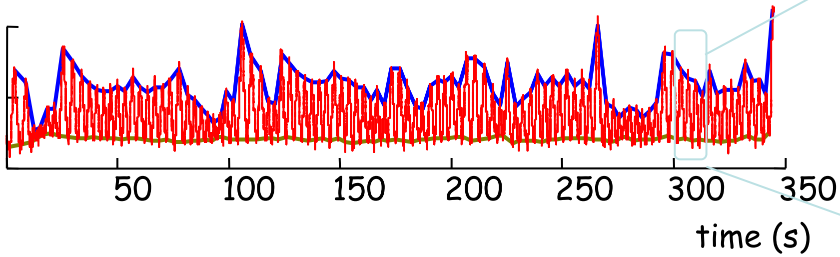
- FMRI Calibration using RRF

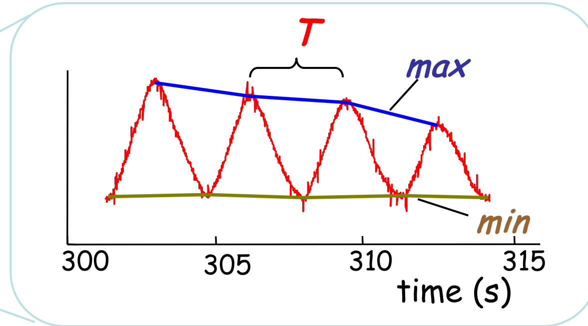
Sources of time series fluctuations:

- 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

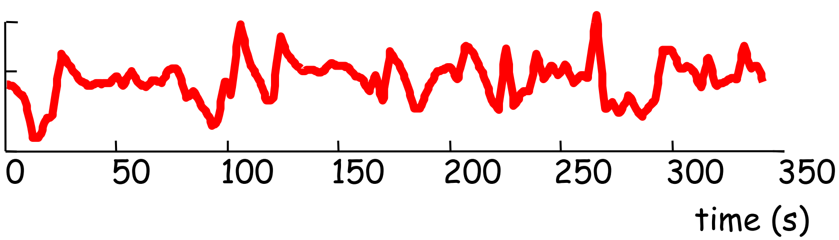
Estimating respiration volume changes

Respiration

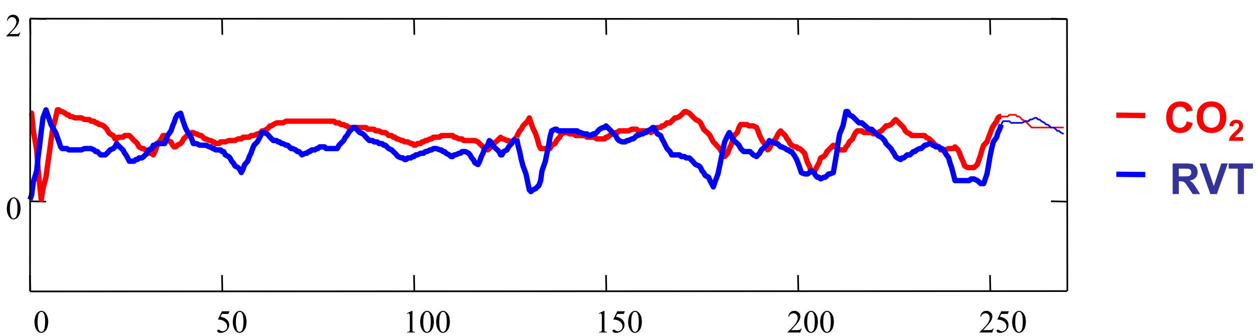


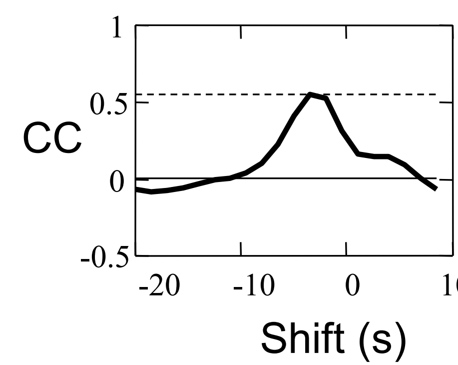


Respiration Volume / Time (RVT)



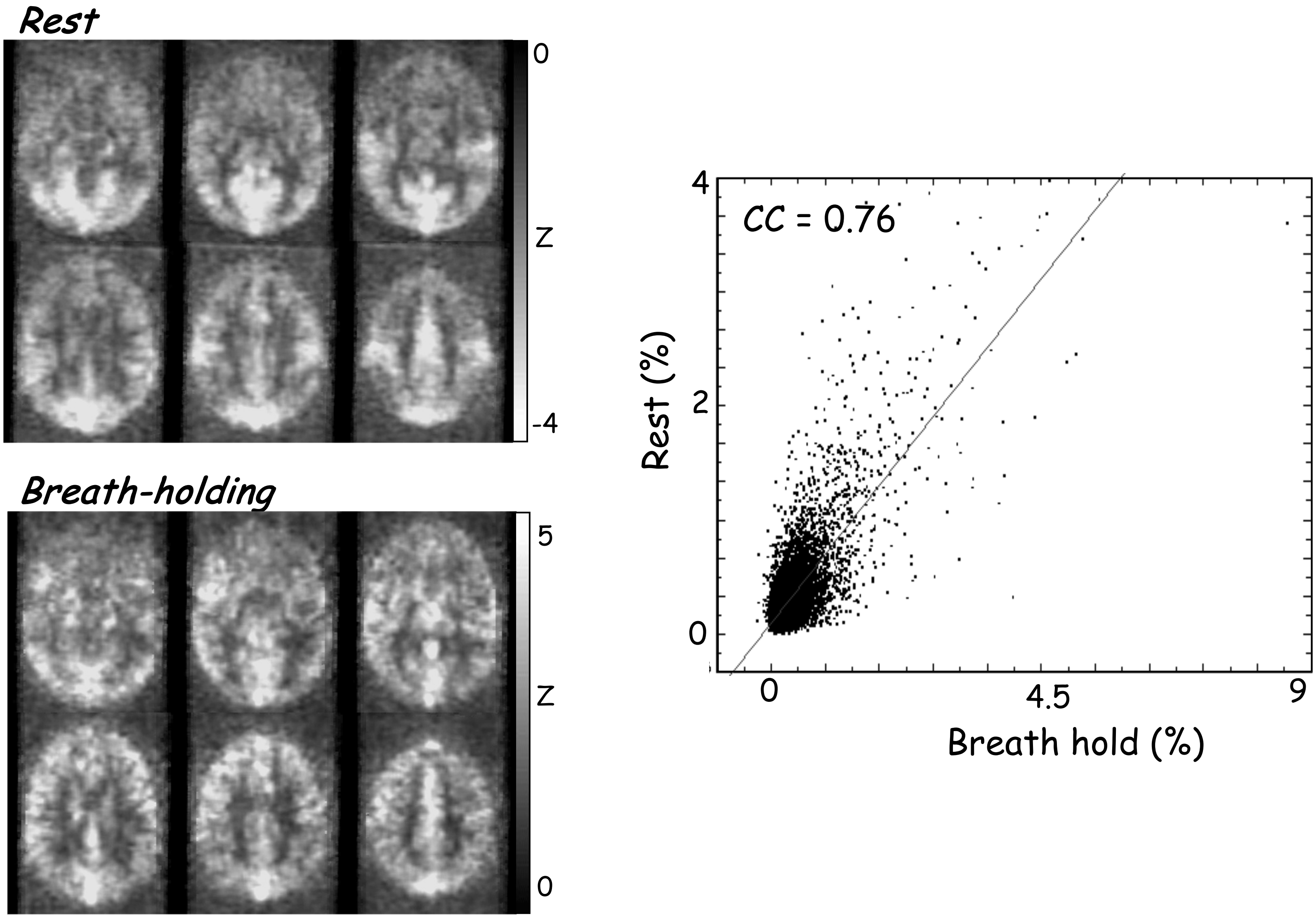
$$\mathrm{RVT} = \frac{\mathrm{max} - \mathrm{min}}{T}$$





RVT precedes end tidal CO_2 by 5 sec.

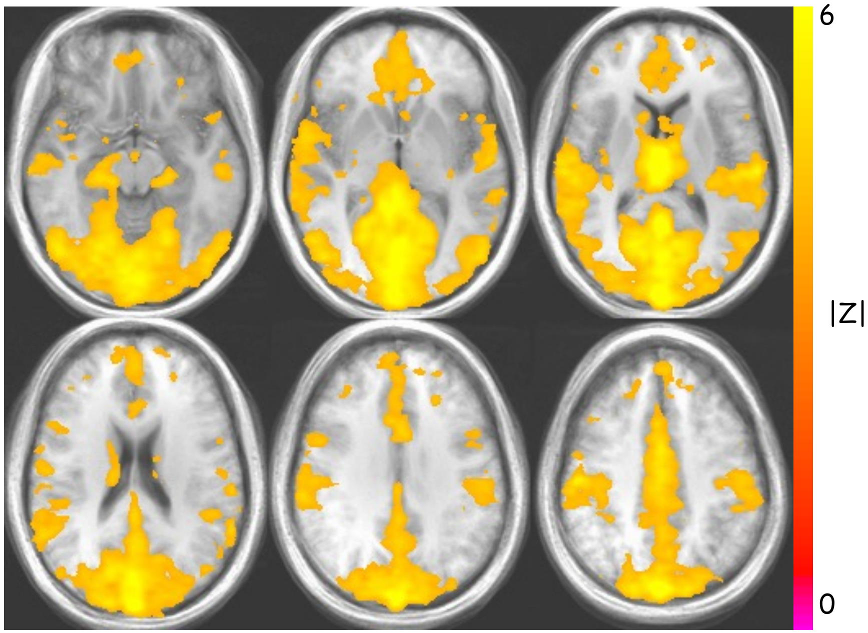
Respiration induced signal changes



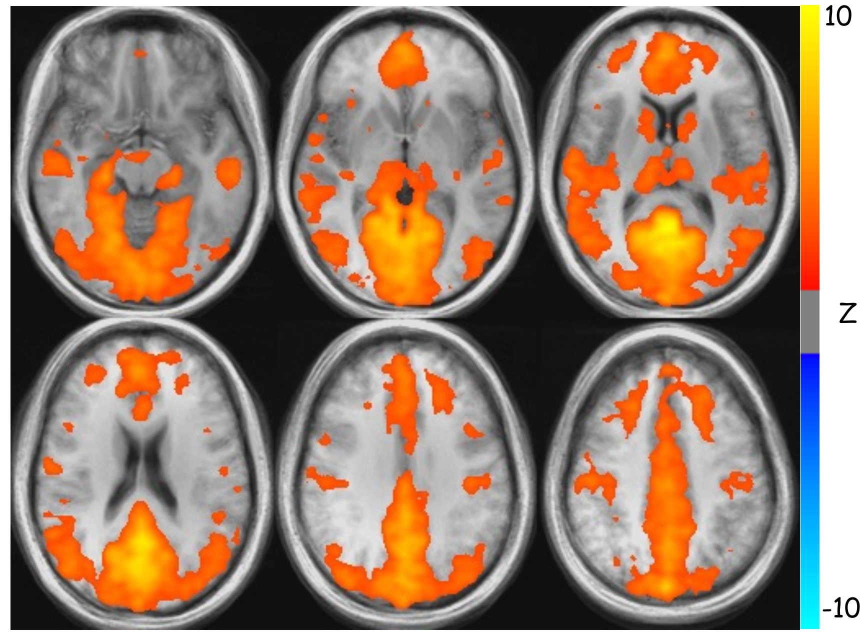
(N=7)

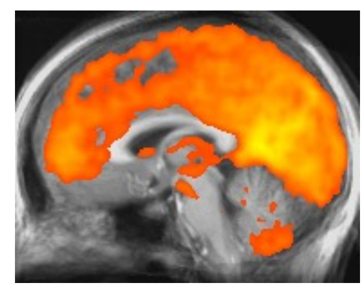
RVT Correlation Maps & Functional Connectivity Maps

Resting state correlation with RVT signal



Resting state correlation with signal from posterior cingulate

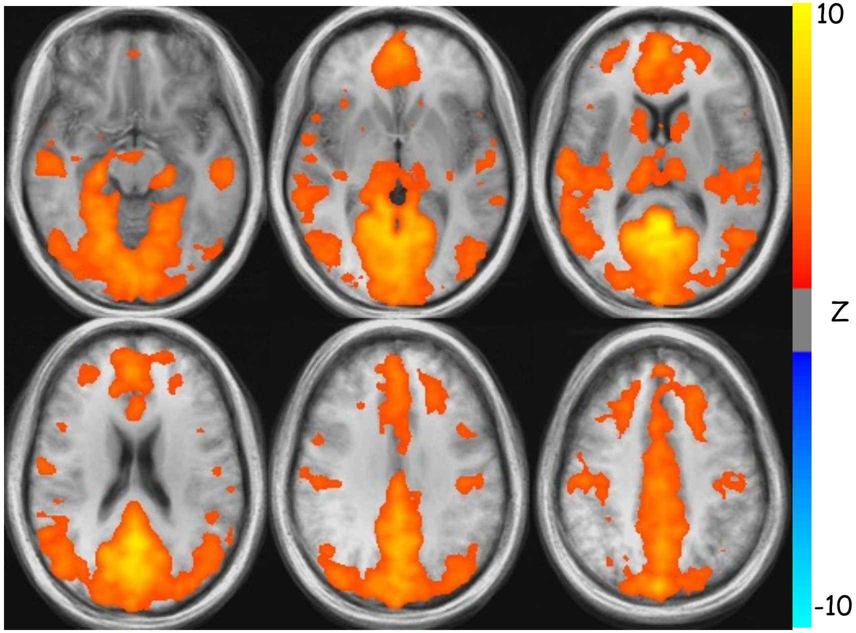




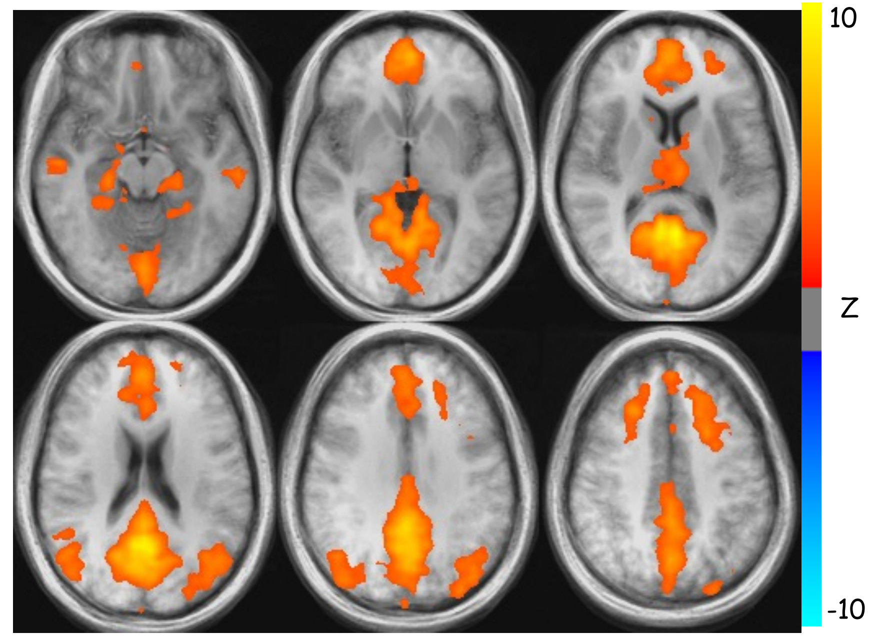
Group (n=10)

Effect of Respiration Rate Consistency on Resting Correlation Maps

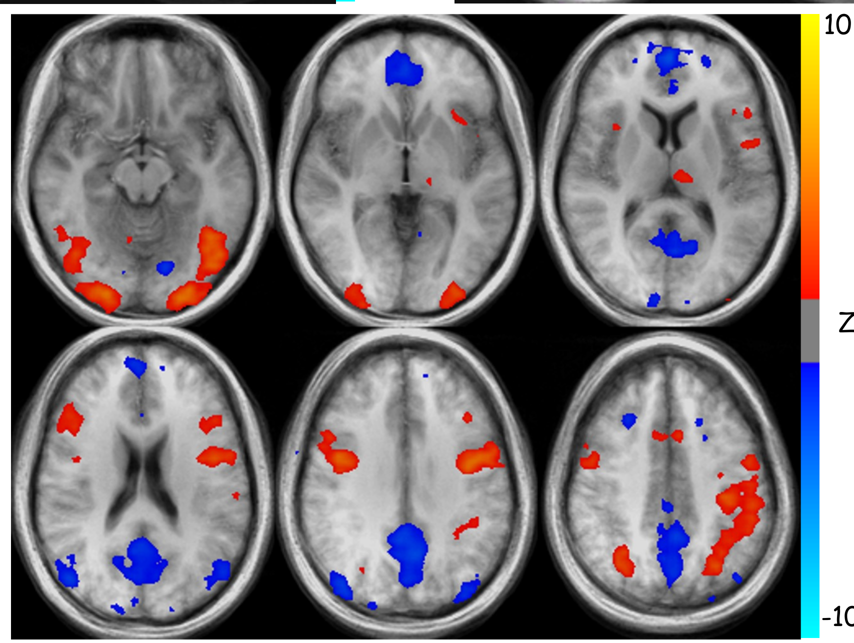
Spontaneously Varying Respiration Rate



Constant Respiration Rate



Lexical Decision Making Task

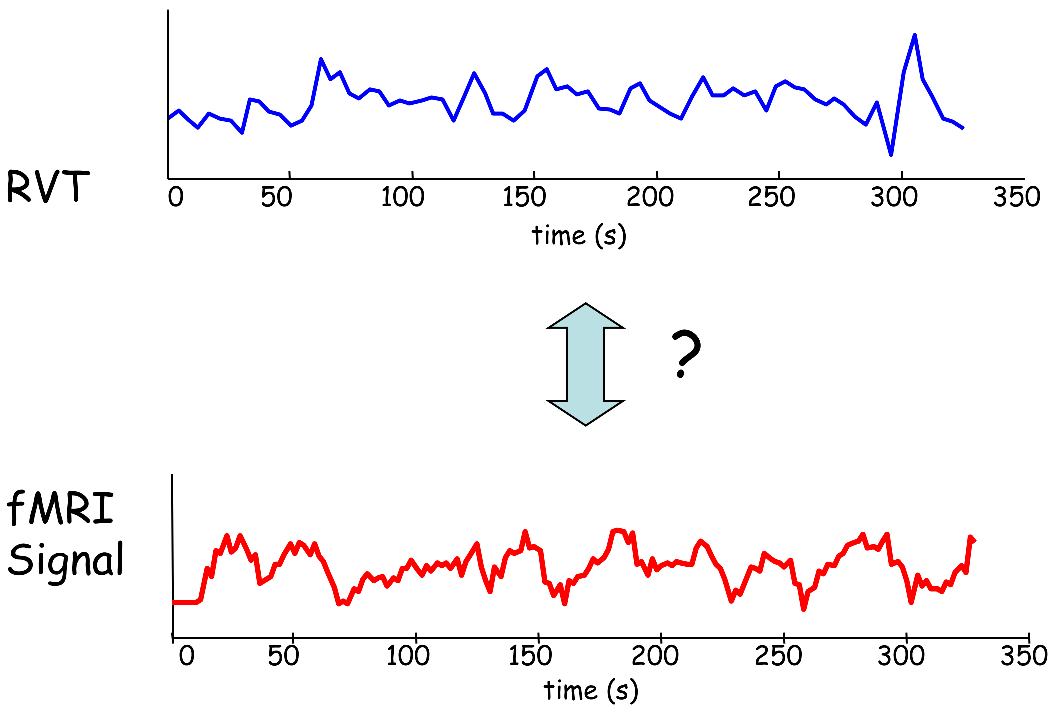


Blue: deactivated network

Group (n=10)

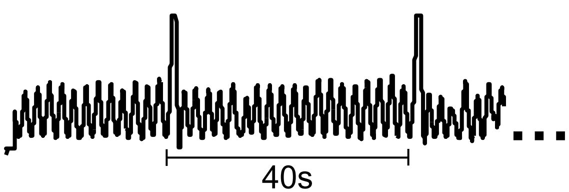
Respiration Changes vs. BOLD

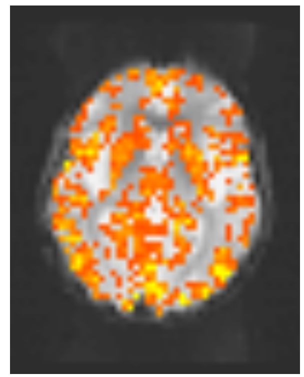
How are the BOLD changes related to respiration variations?

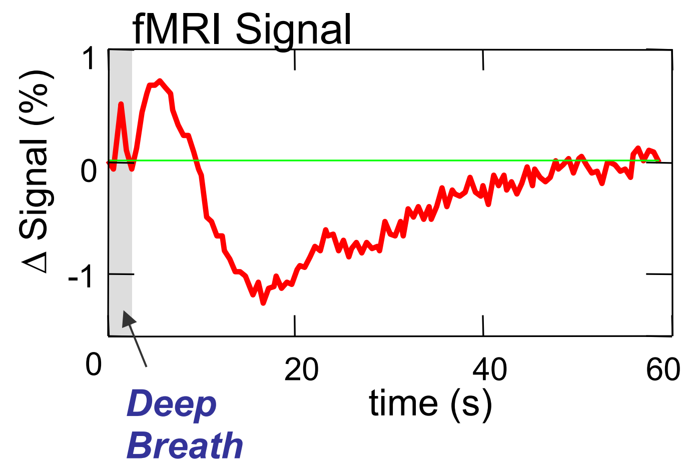


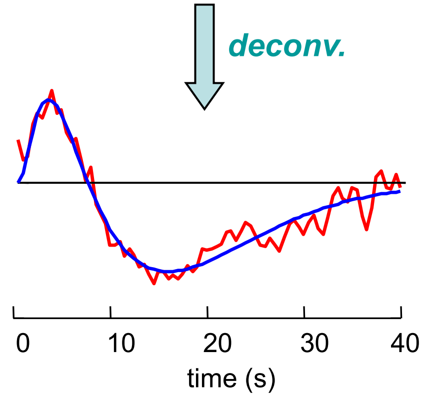
fMRI response to a single Deep Breath

Respiration









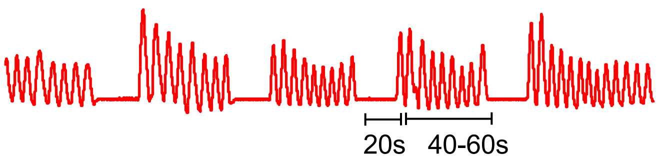
Respiration Response Function (**RRF**)

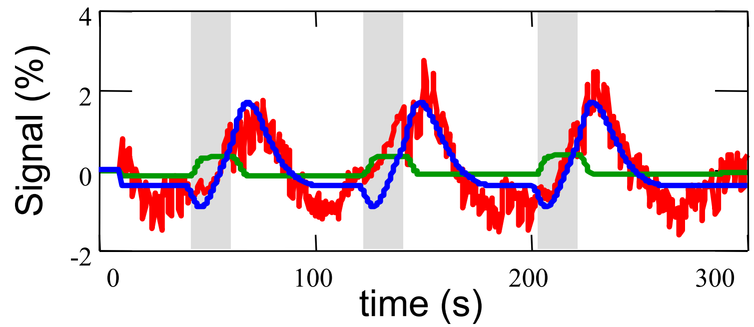
$$\mathrm{RRF}(t) = 0.6\ t^{2.1}\ e^{\frac{t}{1.6}} - 0.0023\ t^{3.54}\ e^{\frac{t}{4.25}}$$

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

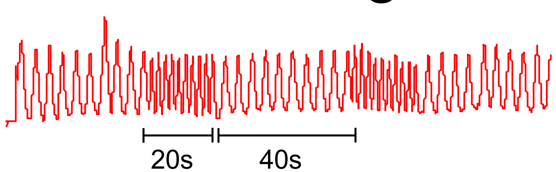
Respiration response function predicts BOLD signal associated with breathing changes better than **activation response function**.

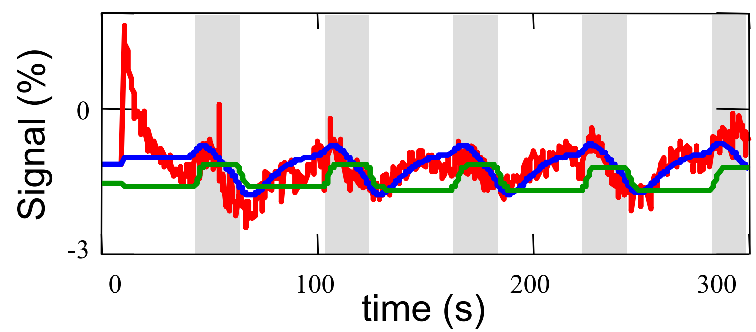
Breath-holding



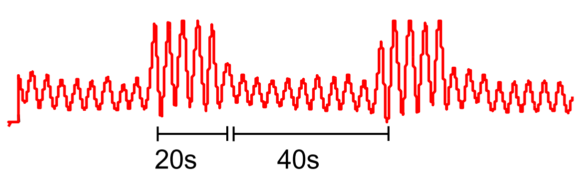


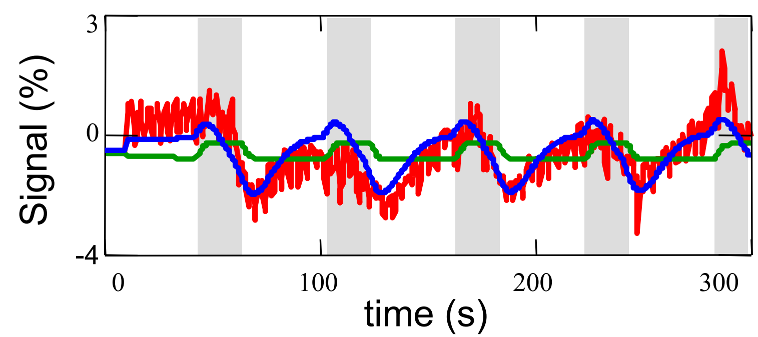
Rate Changes





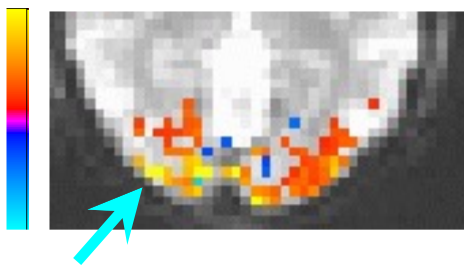
Depth Changes





BOLD magnitude calibration

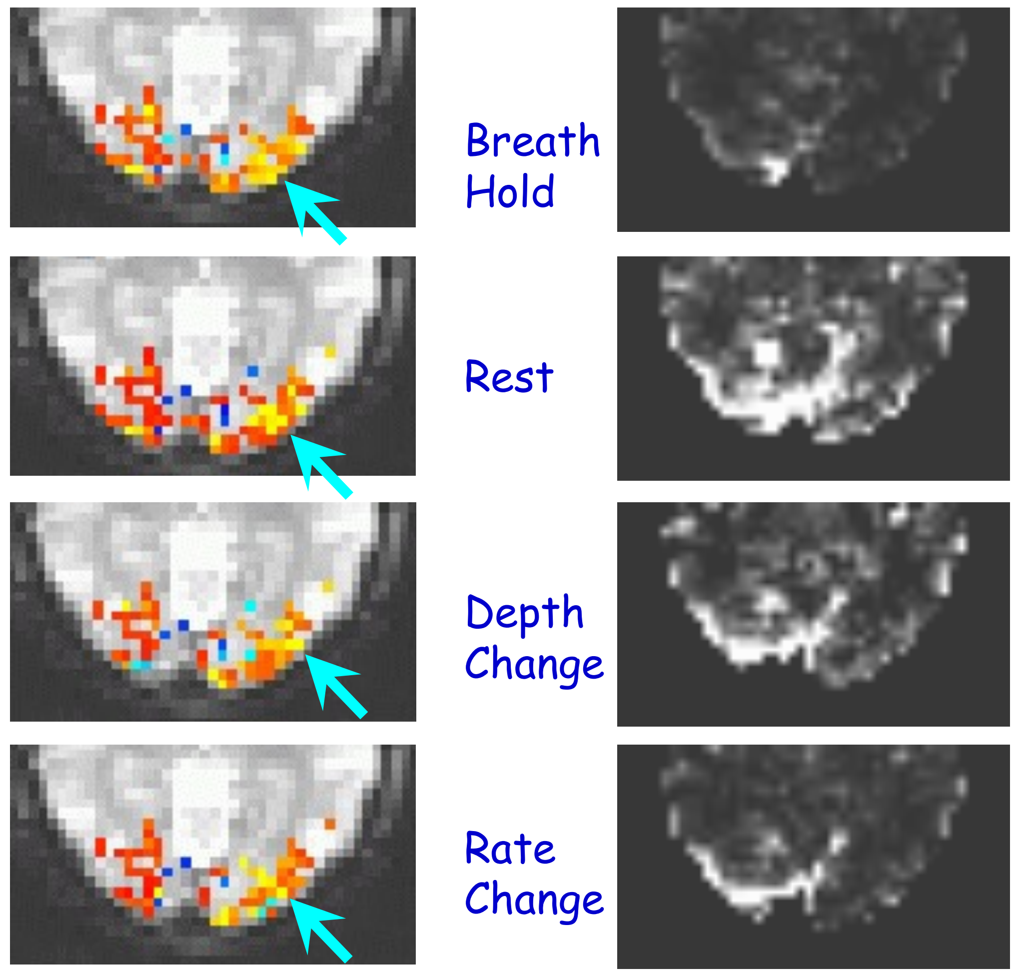
Before Calibration



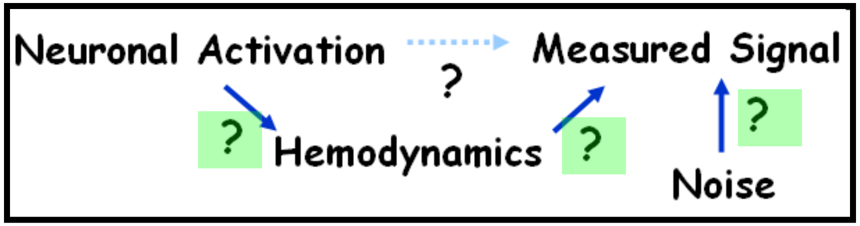
$$\mathrm{BOLD}_{calib} = \frac{\%\Delta S\ (\mathrm{BOLD})}{\%\Delta S\ (\mathrm{Resp})}$$

After Calibration

Respiration-induced ΔS



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:

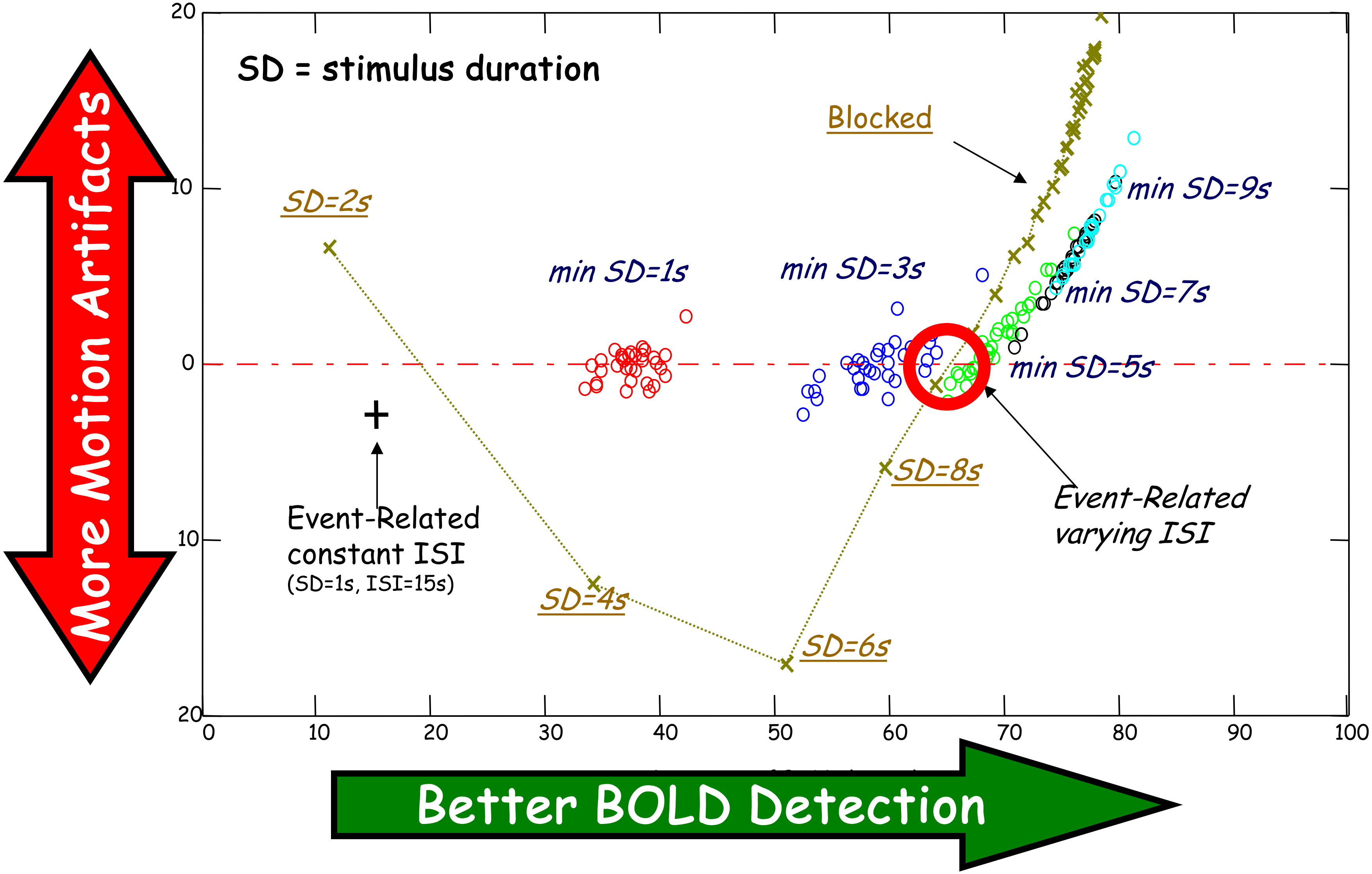
- Guides for *individual* subject scanning at the limits of detectability, resolution, available time, and subject performance.

Studies:

- Overt response timing

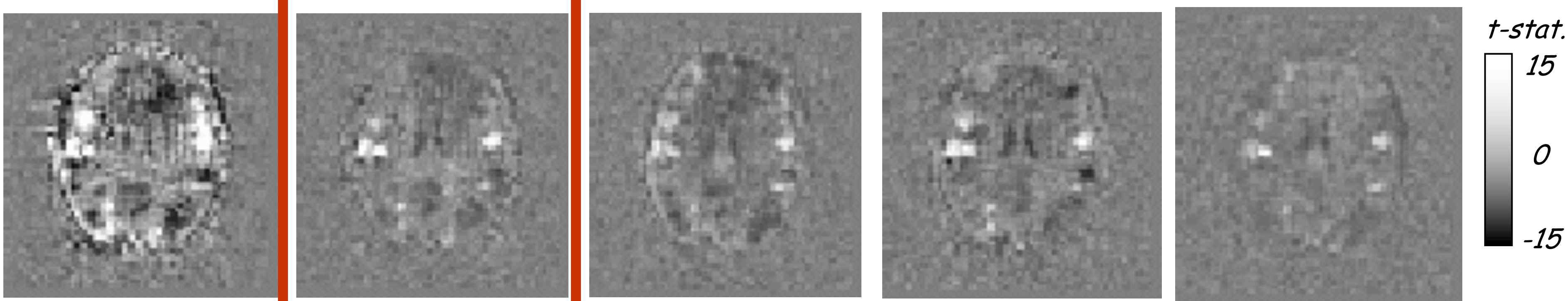
- Suggested resolution

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)

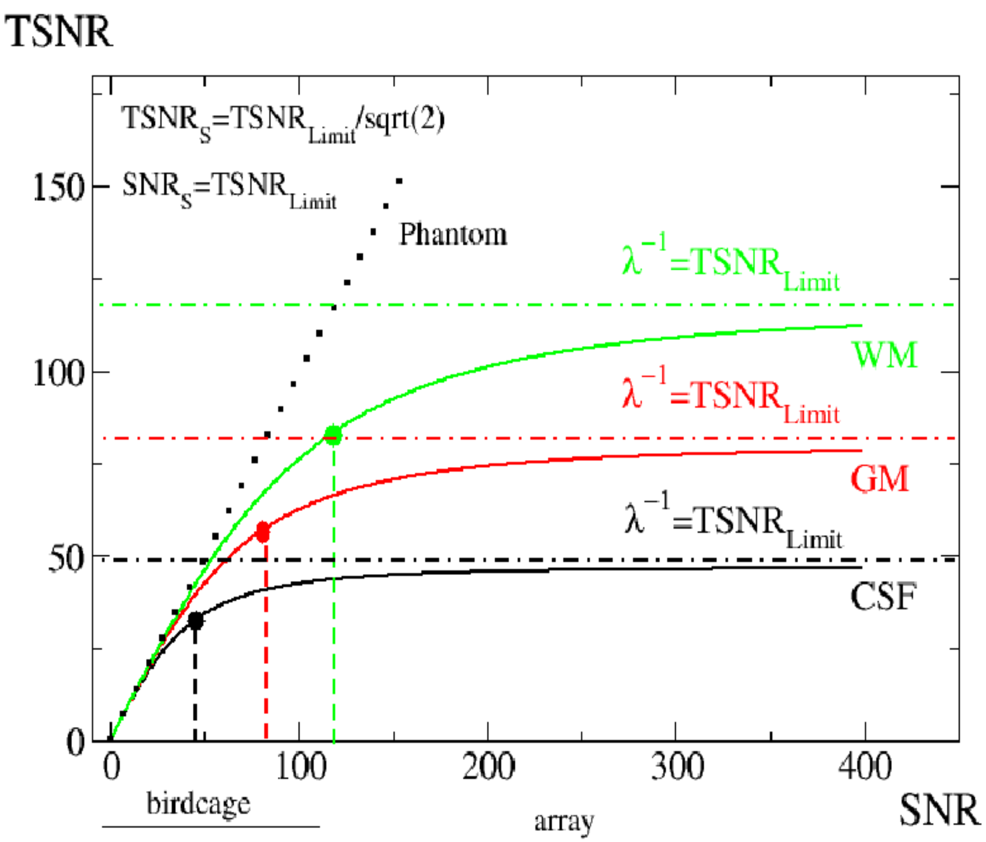
Event-related Varying ISI (1s min. SD)

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

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

Finding the "suggested voxel volume"

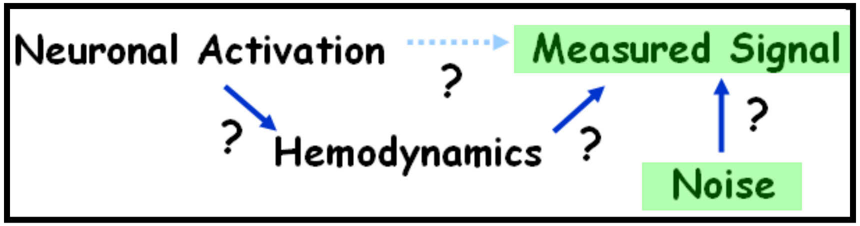
Temporal Signal to Noise Ratio (TSNR) vs. Signal to Noise Ratio (SNR)



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?

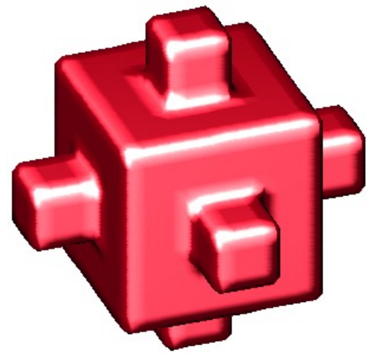
Study:

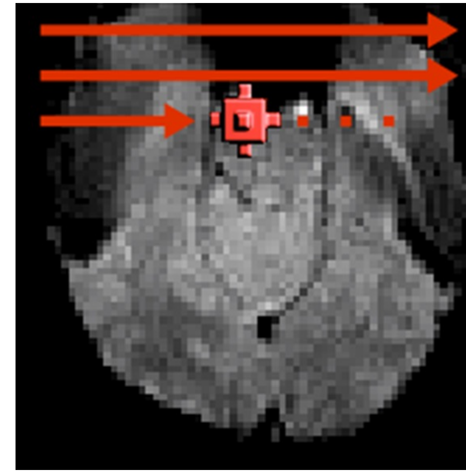
- Pattern-Information Mapping

- Dis-similarity matrix

Pattern Information Mapping

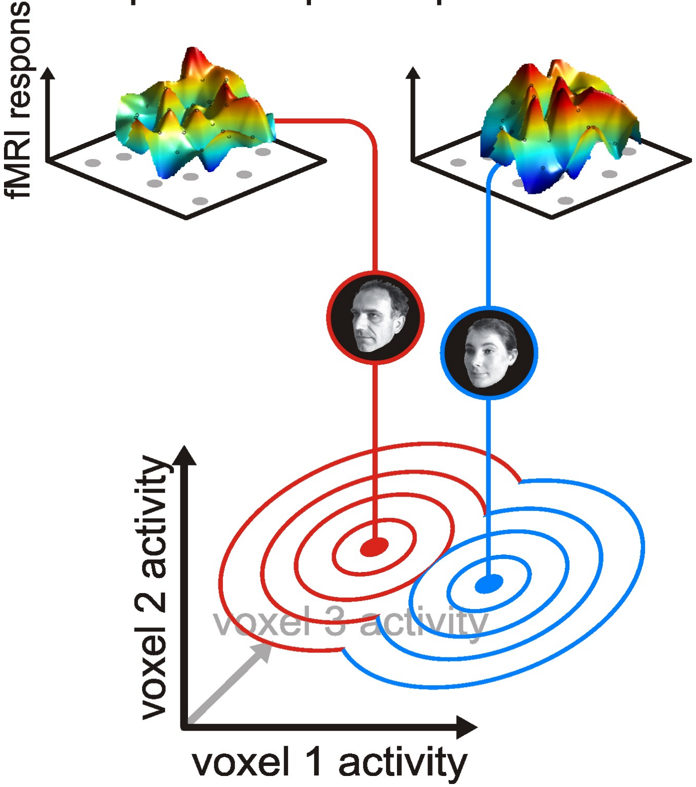
"searchlight" ROI

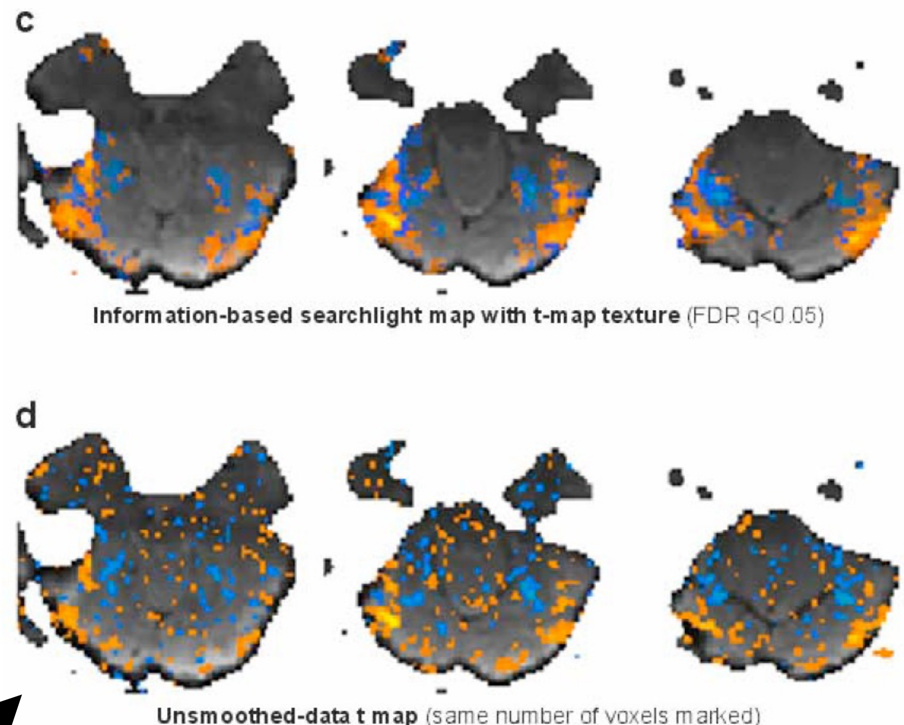




From fixed ROI

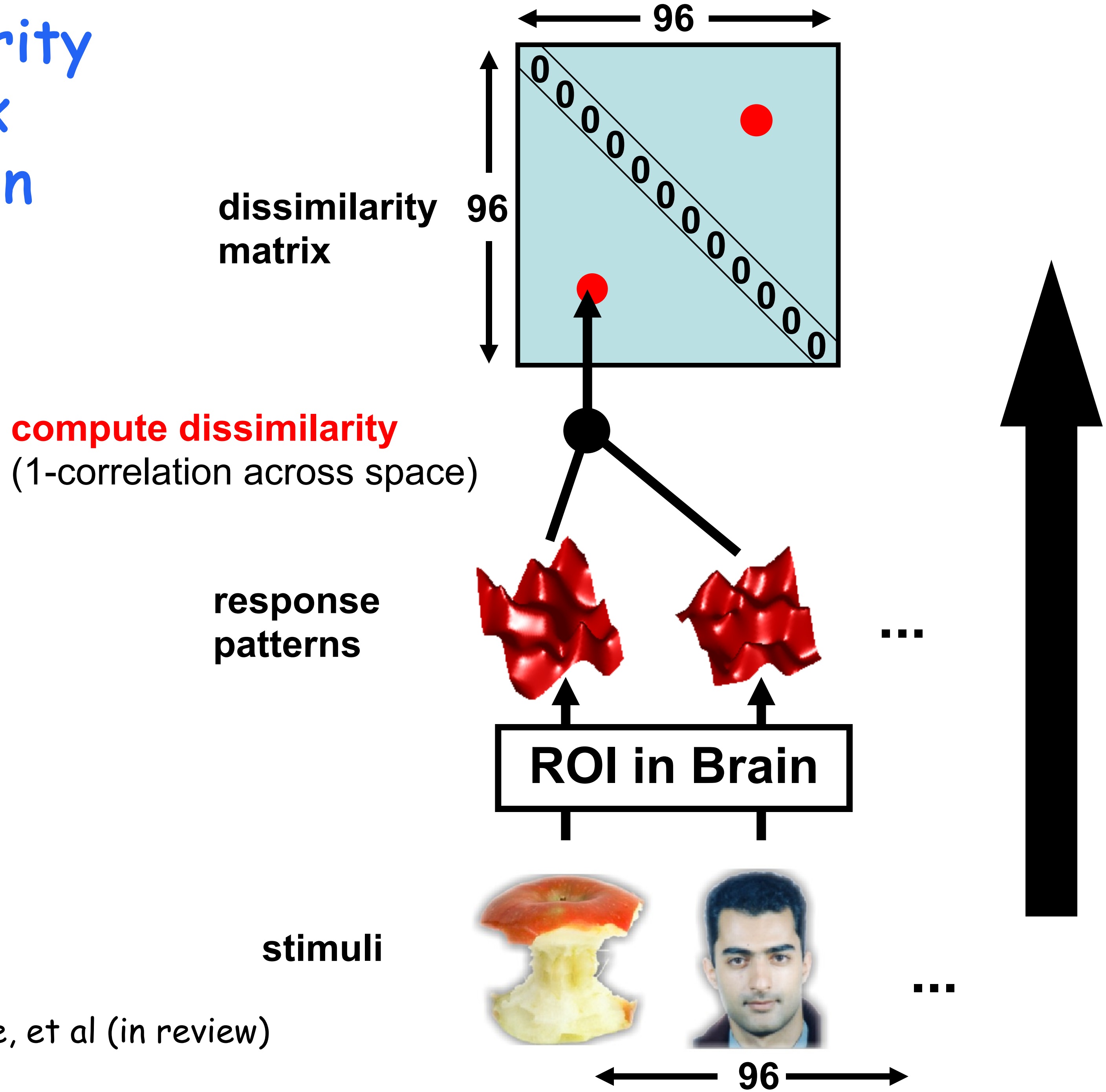
event-related
spatial response patterns





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

Dissimilarity Matrix Creation

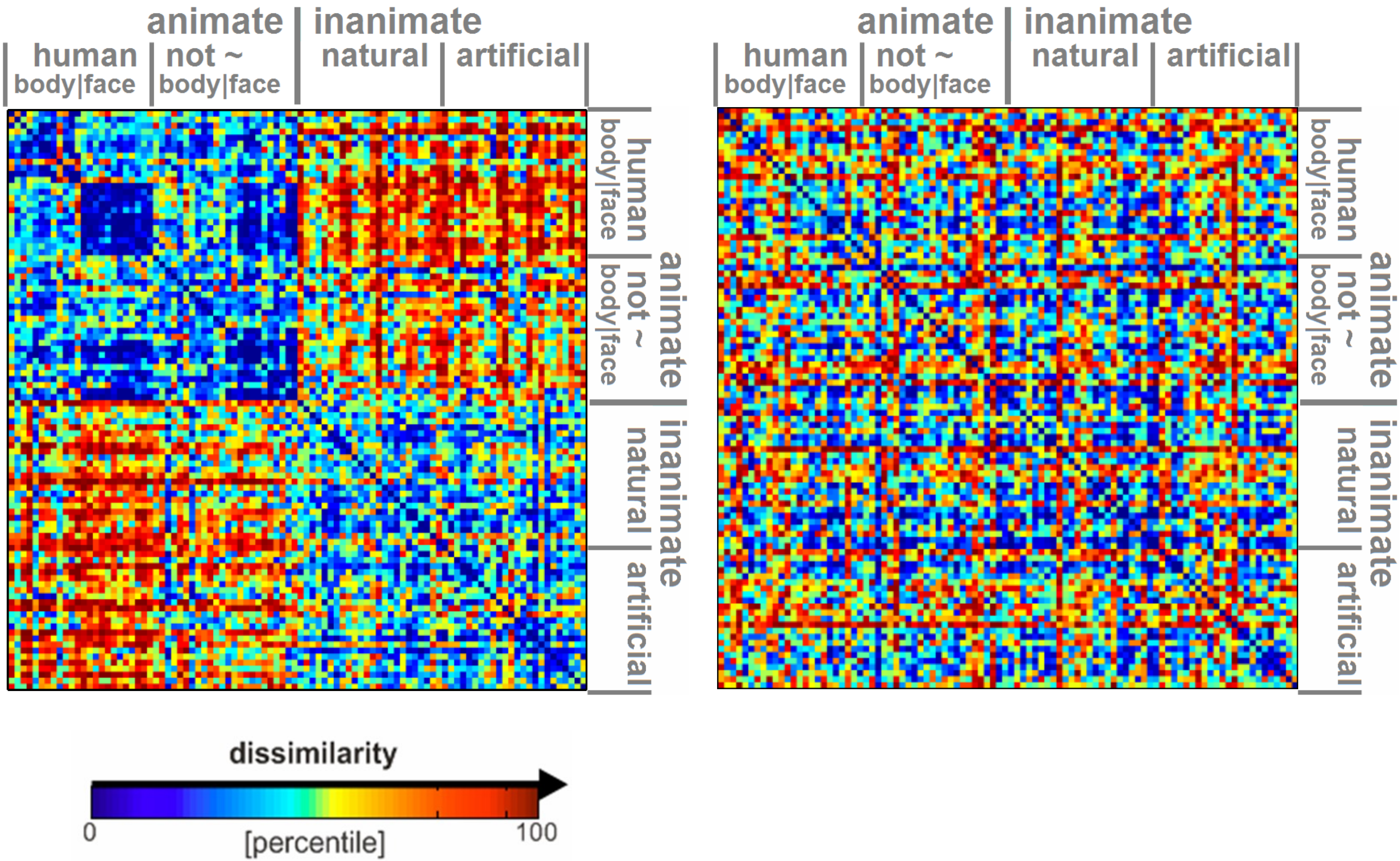


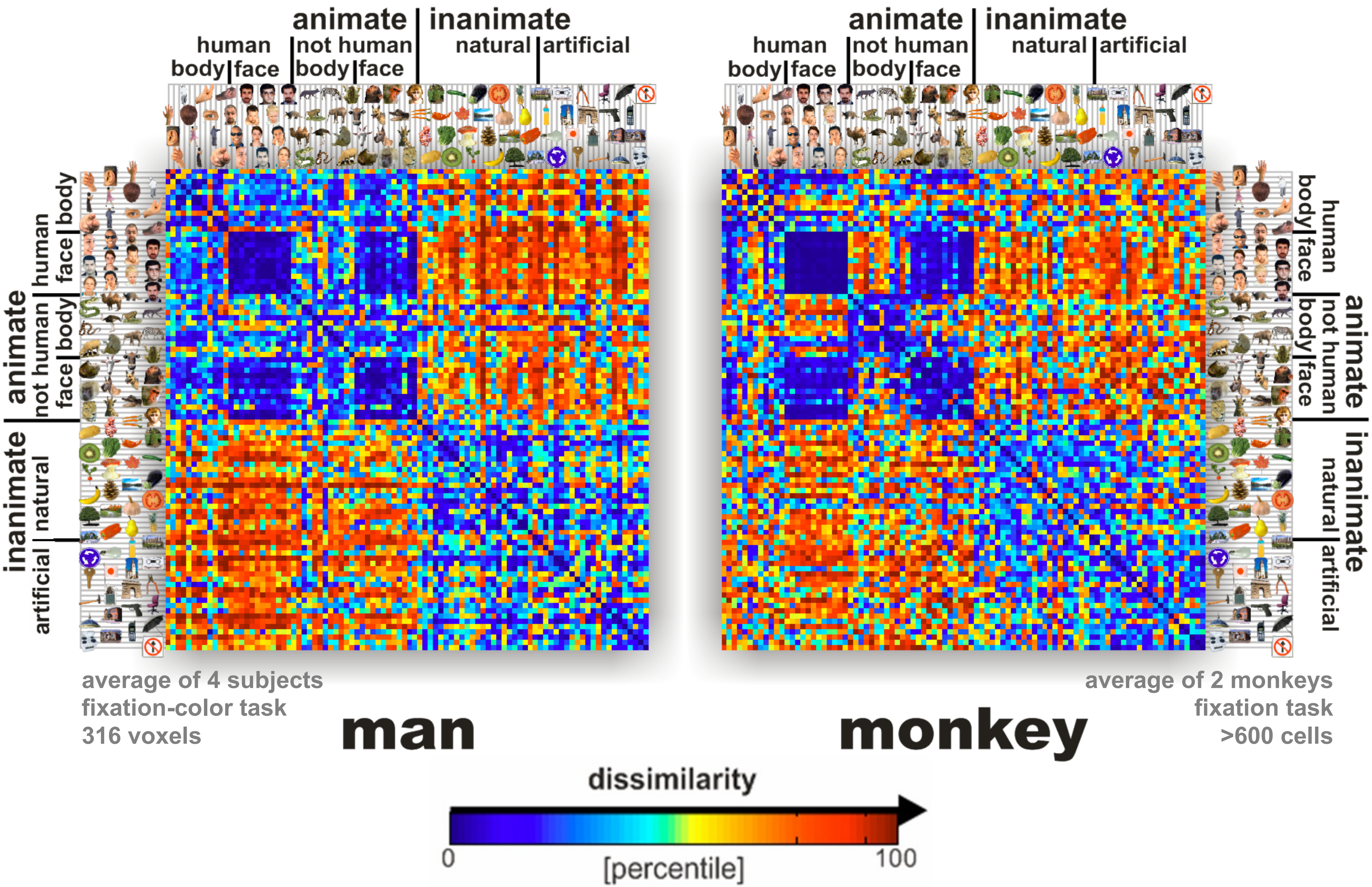
N. Kriegeskorte, et al (in review)

Visual Stimuli

Human IT
(1000 visually most responsive voxels)

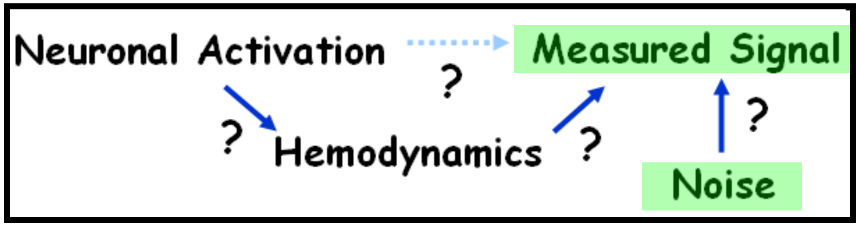
Human Early Visual Cortex
(1057 visually most responsive voxels)





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.

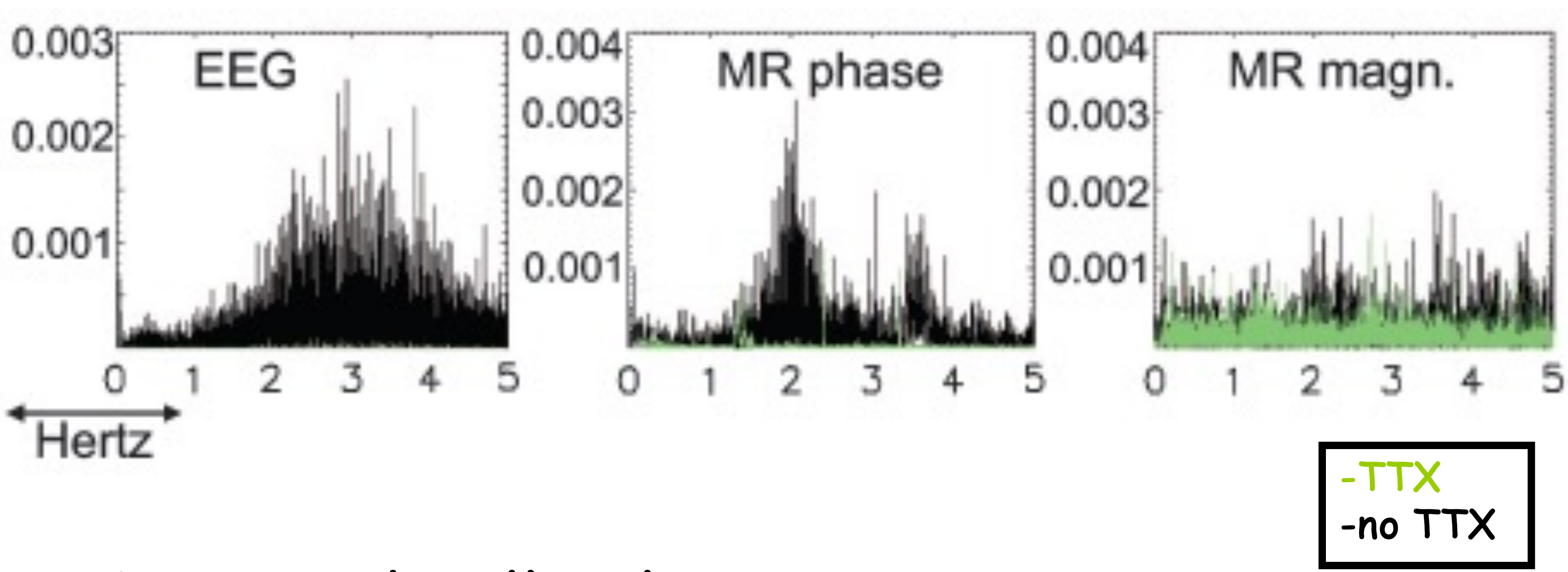
5. Neuronal Current MRI

Motivation:

- Direct fMRI of neuronal activity.

Studies:

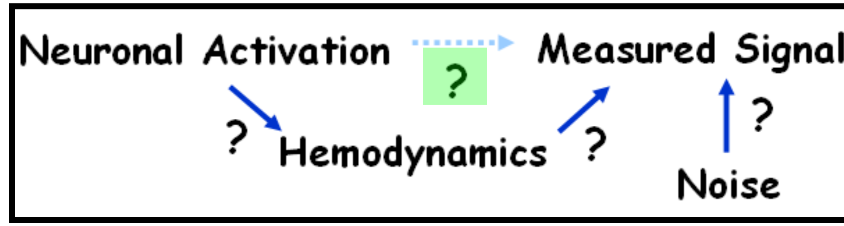
- 7T and 3T



Neuronal Cell Cultures at 7T

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

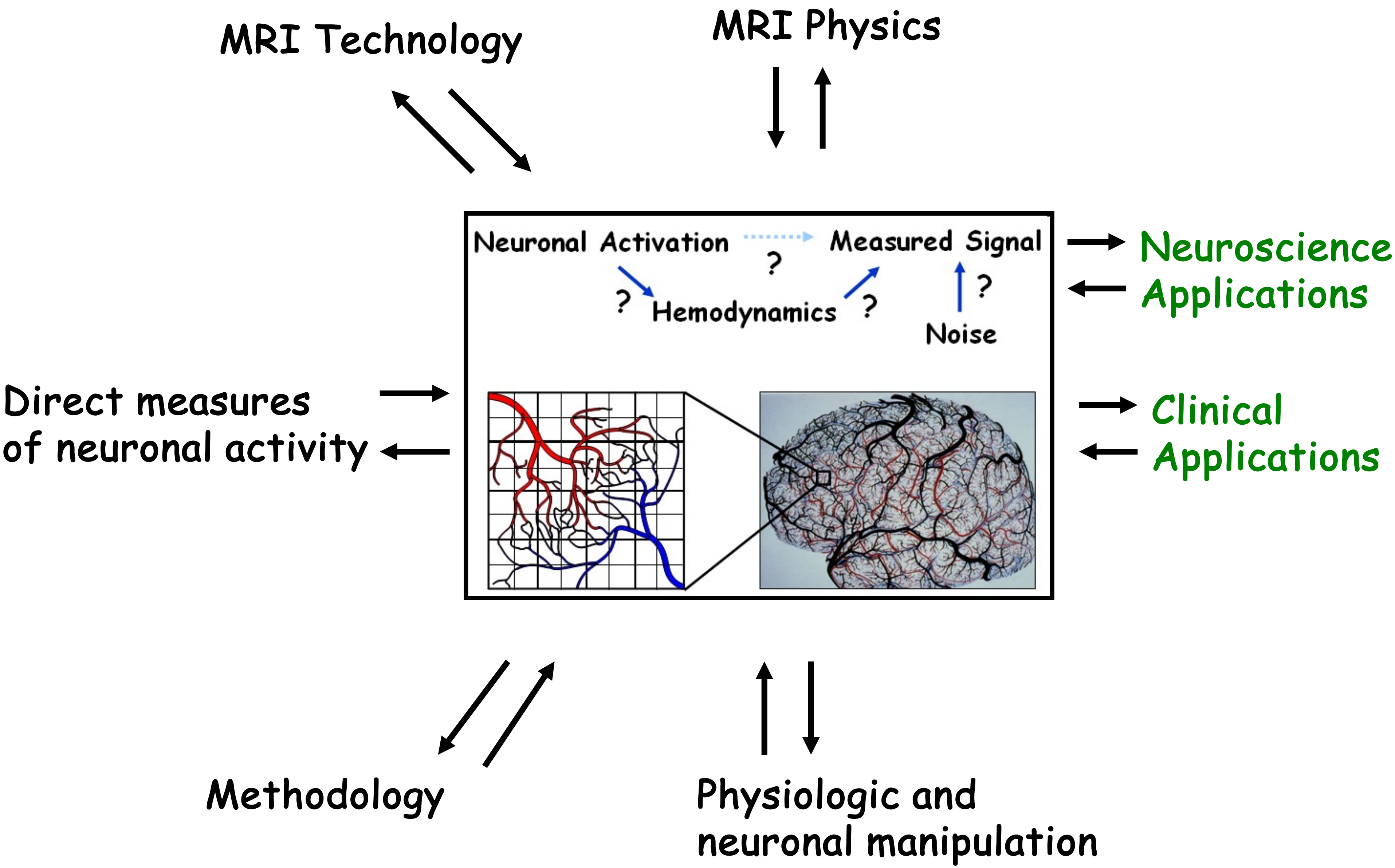


Conclusion:

- 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.


MRI Technology
MRI Physics
Neuronal Activation
?
Measured Signal
?
Hemodynamics
?
?
Noise
Neuroscience
Applications
Direct measures
of neuronal activity
Clinical
Applications
Methodology
Physiologic and
neuronal manipulation

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Interpretation

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Applications

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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).