

# fMRI Paradigm Designs and Processing Methods

**Peter A. Bandettini, Ph.D.**

**Section on Functional Imaging Methods  
Laboratory of Brain and Cognition**

<http://fim.nimh.nih.gov>

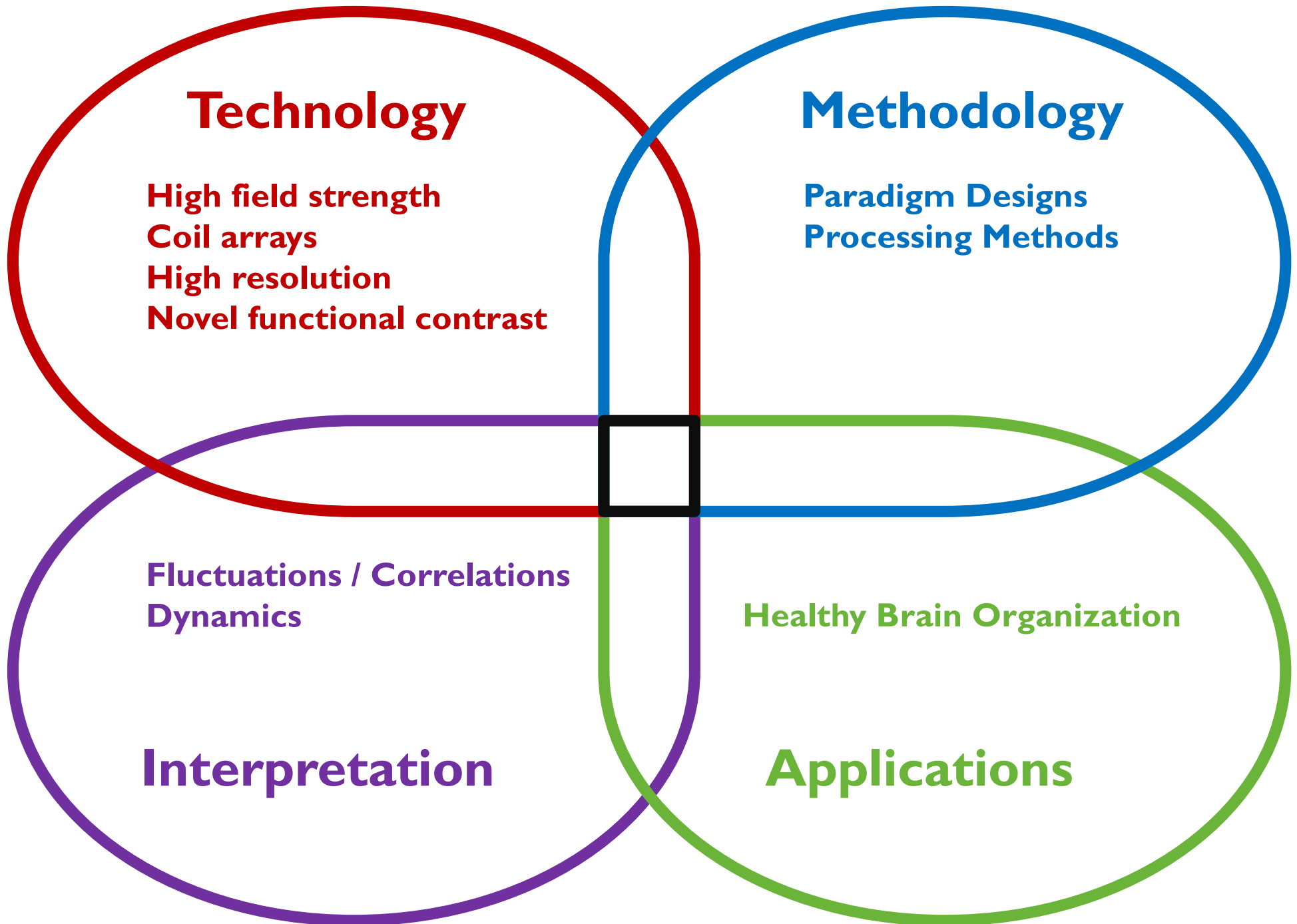
**&**

**Functional MRI Facility**

<http://fmrif.nimh.nih.gov>



## Focus of this lecture

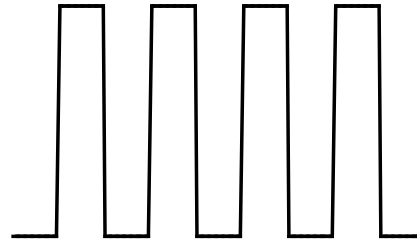


# **fMRI Paradigm Designs and Processing Strategies**

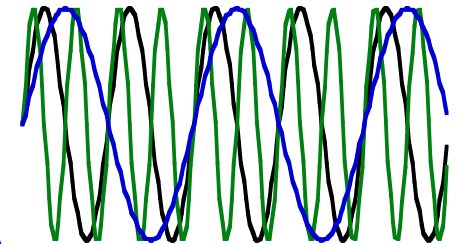
- 1. Neuronal Activation Input Strategies**
- 2. Resting State fMRI**
- 3. fMRI Decoding**

# Neuronal Activation Input Strategies

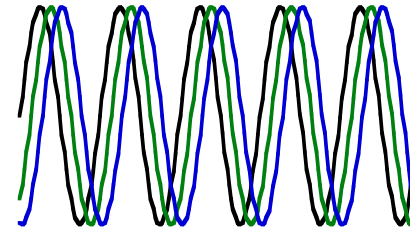
1. Block Design



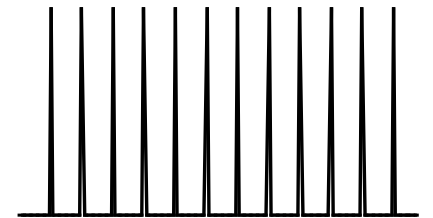
2. Frequency Encoding



3. Phase Encoding

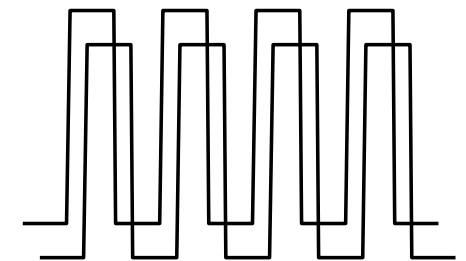


4. Event-Related



5. fMRI adaptation

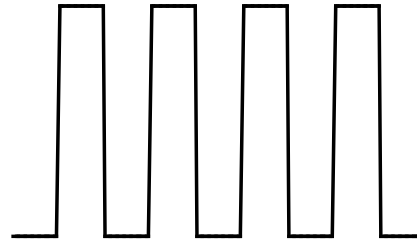
6. Orthogonal Block Design



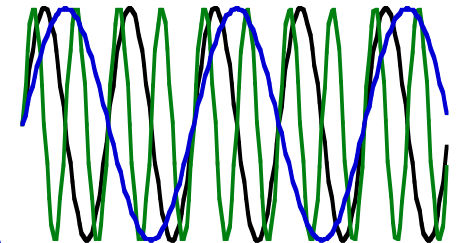
7. Free Behavior Design.

# Neuronal Activation Input Strategies

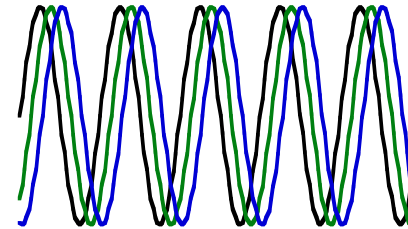
**1. Block Design**



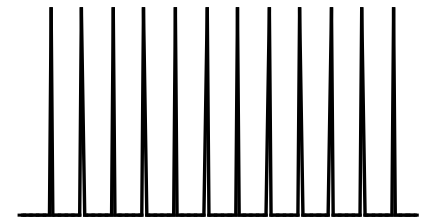
**2. Frequency Encoding**



**3. Phase Encoding**

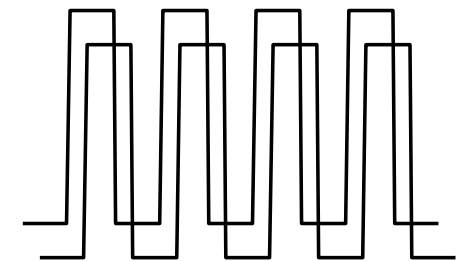


**4. Event-Related**

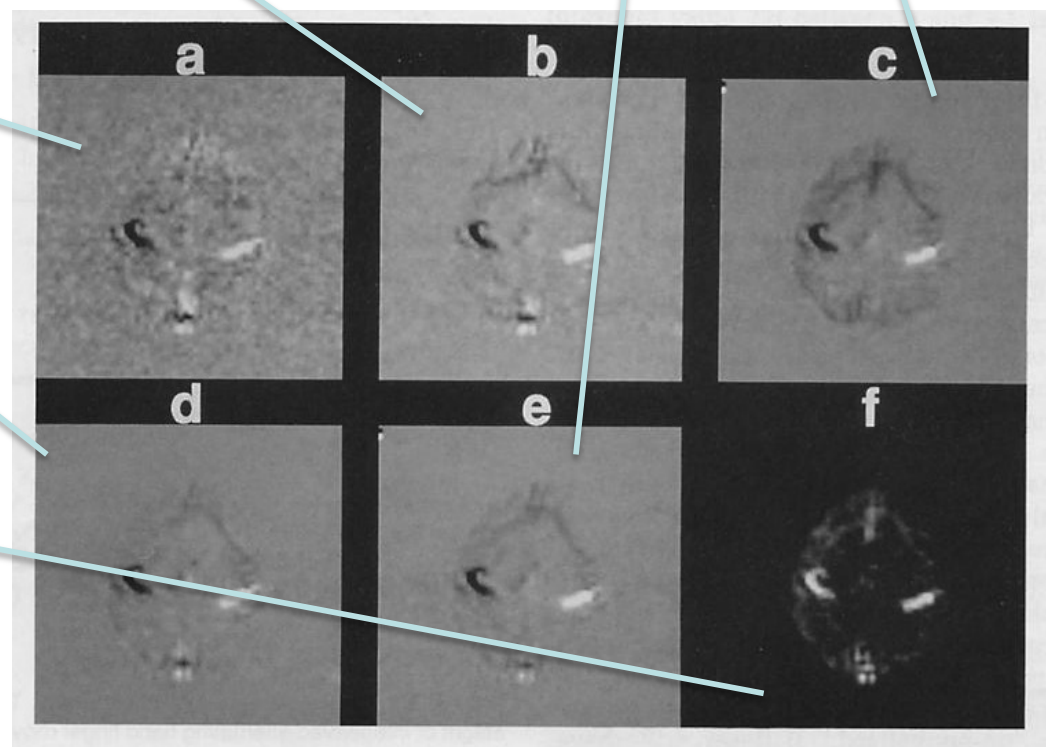
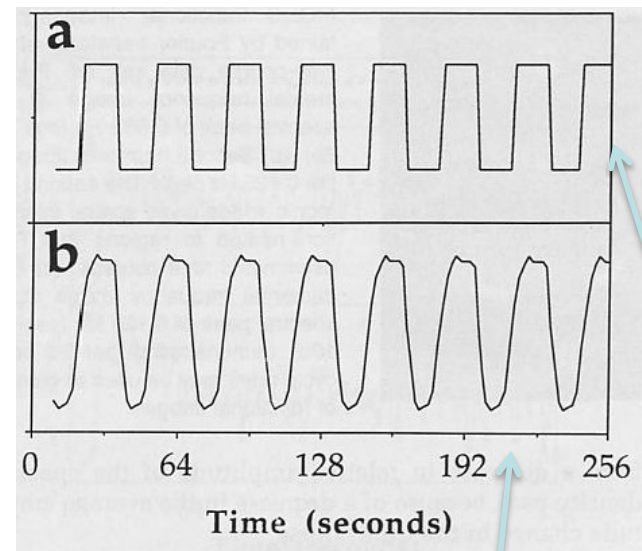
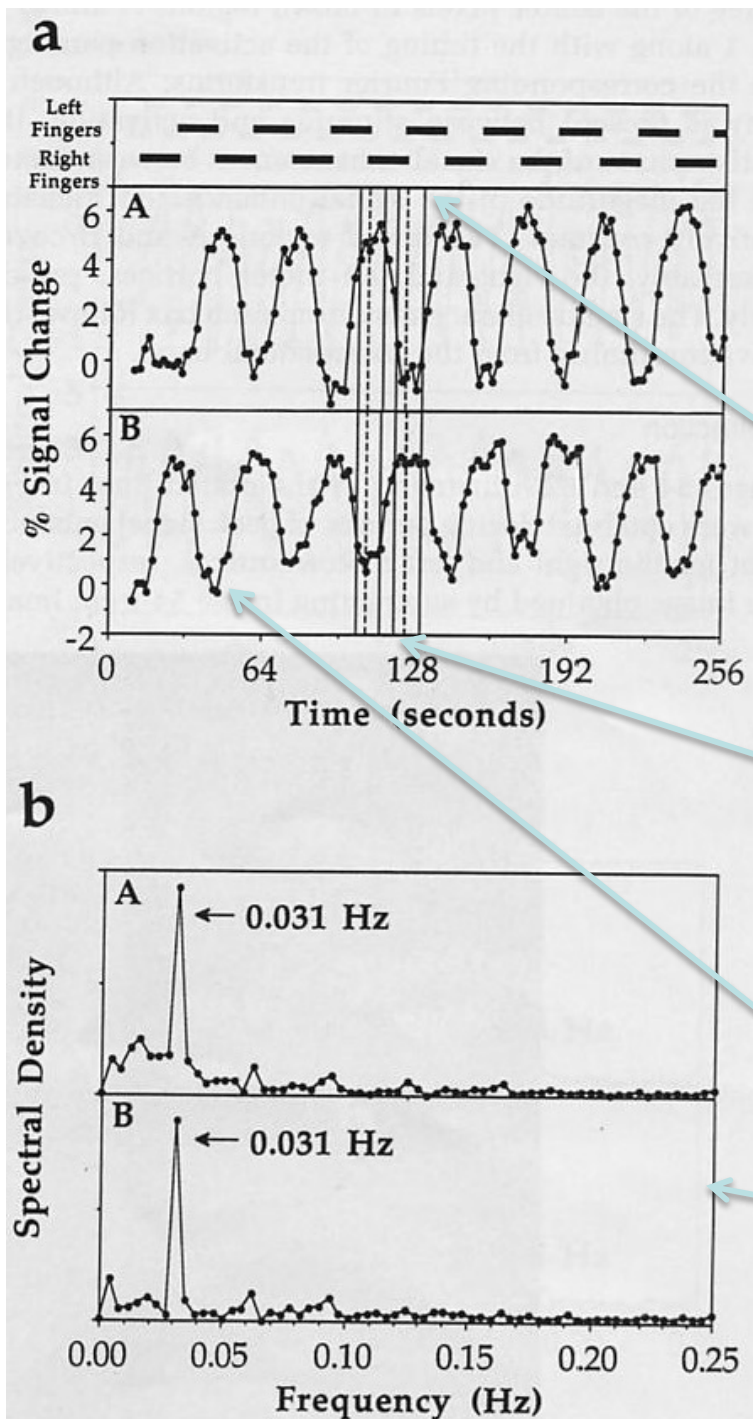


**5. fMRI adaptation**

**6. Orthogonal Block Design**

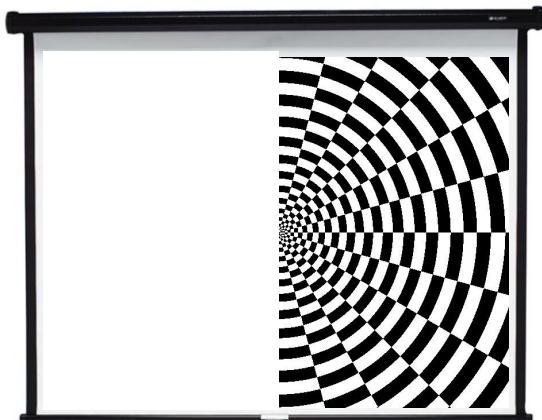


**7. Free Behavior Design.**

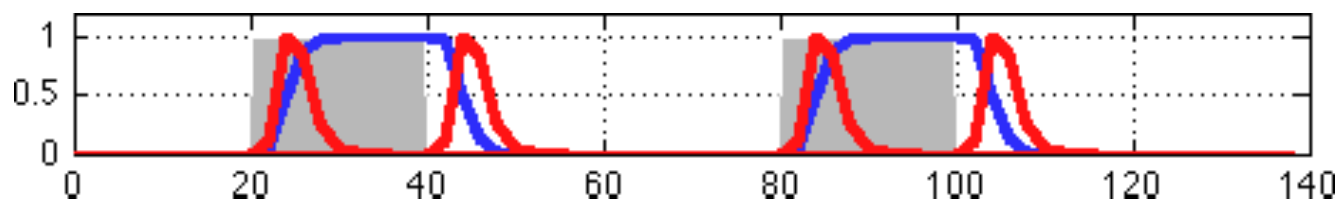


P. A. Bandettini, A. Jesmanowicz, E. C. Wong, J. S. Hyde, Processing strategies for time-course data sets in functional MRI of the human brain. *Magn. Reson. Med.* 30, 161-173 (1993).

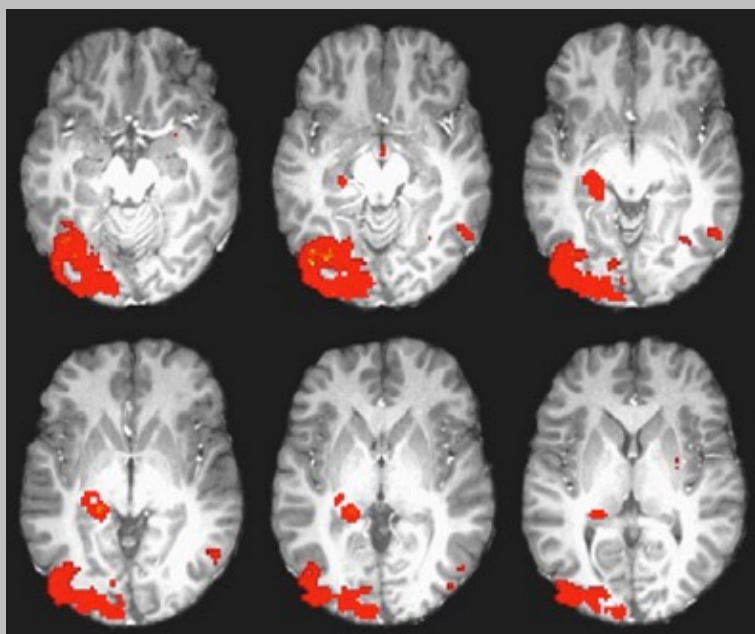
# Predictive Response Model effect on fMRI Results (III)



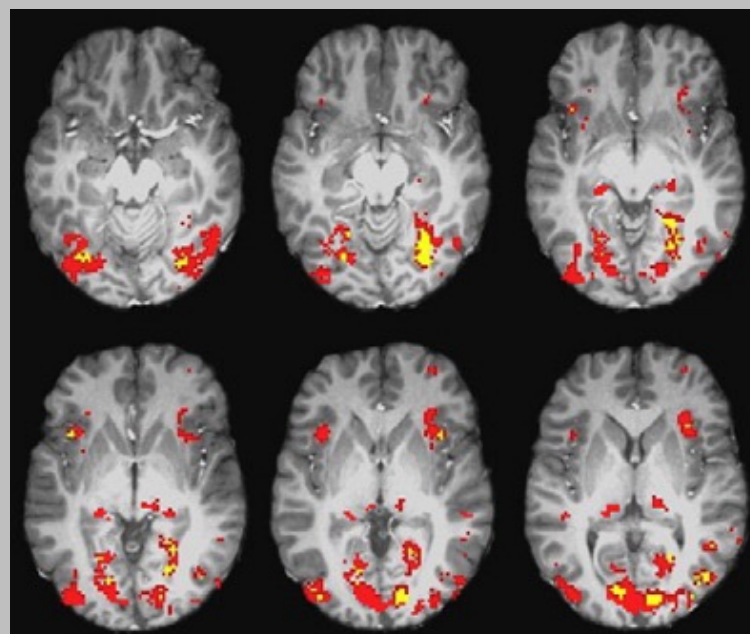
## BLOCK DESIGN & HEMIFIELD VISUAL STIMULATION



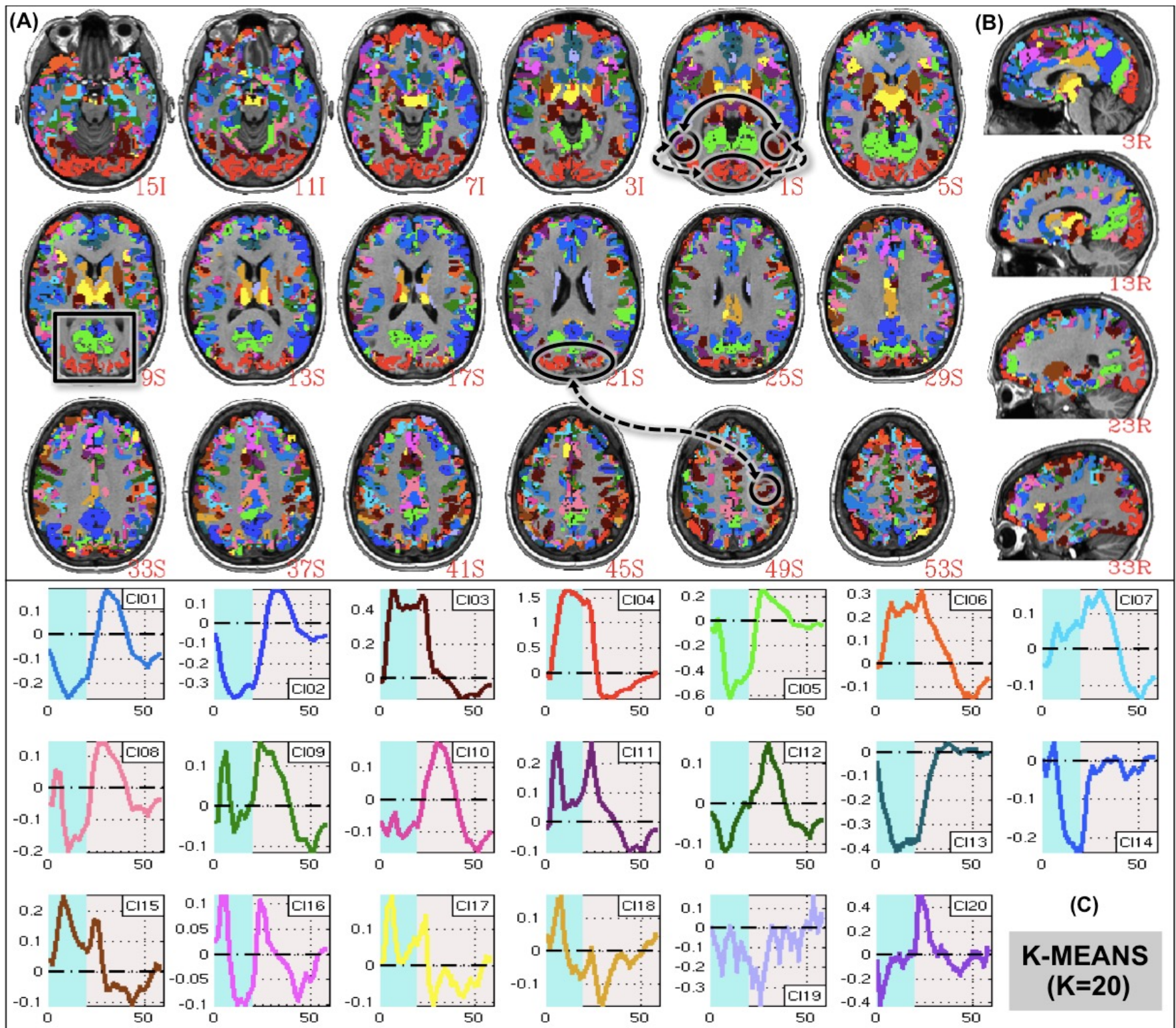
### SUSTAINED RESPONSE MODEL



### ONSET/OFFSET RESPONSE MODEL



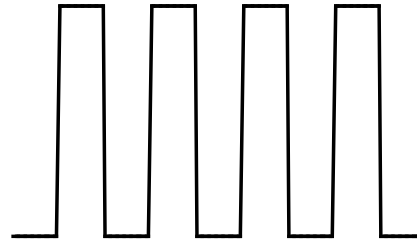
**DIFFERENT RESPONSE SHAPES ARE PRESENT ACROSS DIFFERENT REGIONS OF THE BRAIN FOR A SINGLE STIMULUS TYPE**



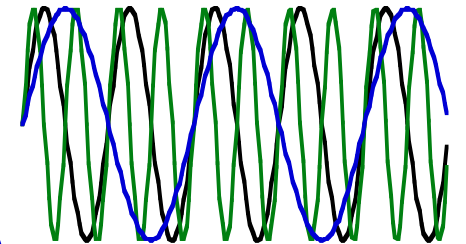


# Neuronal Activation Input Strategies

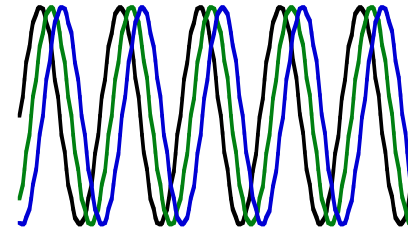
1. Block Design



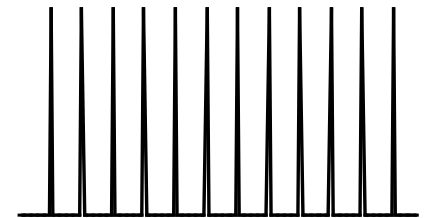
2. Frequency Encoding



3. Phase Encoding

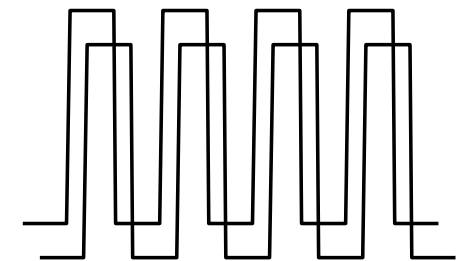


4. Event-Related

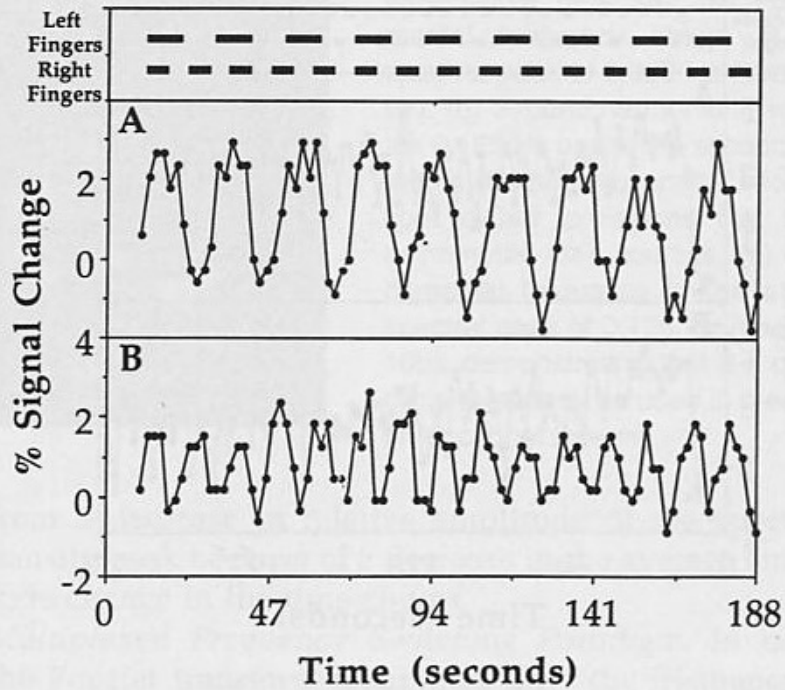


5. fMRI adaptation

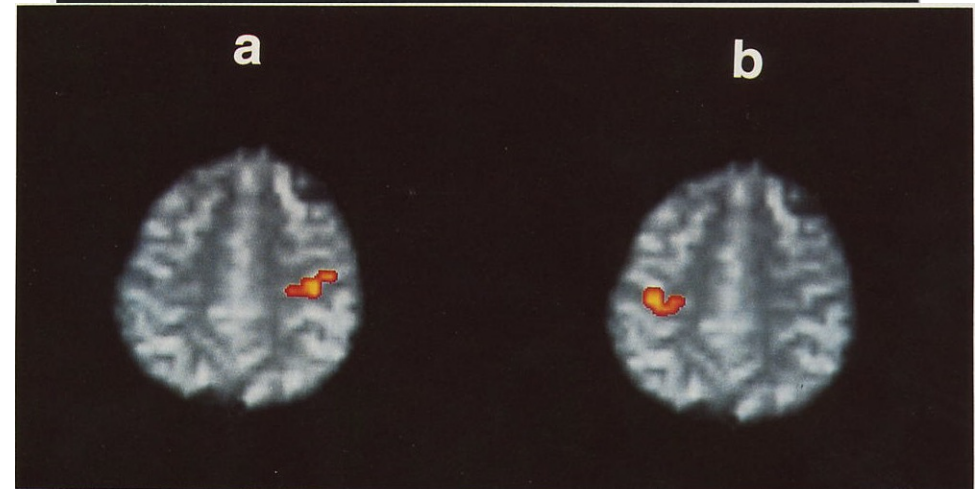
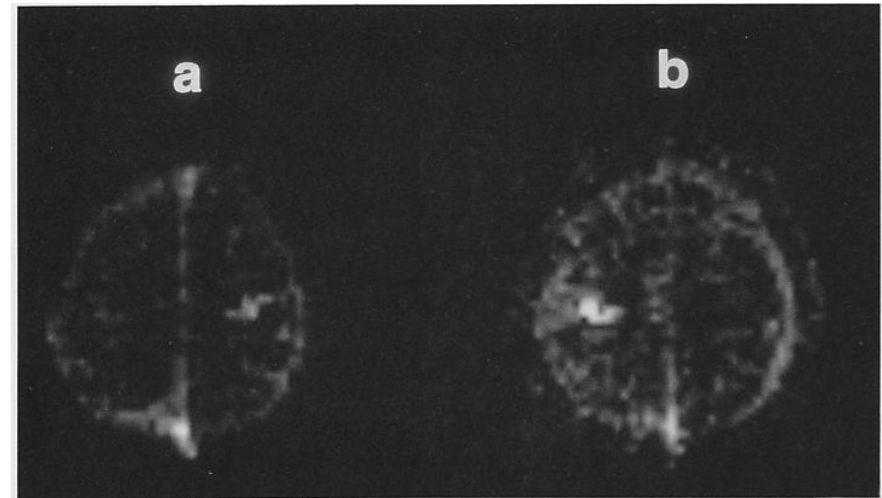
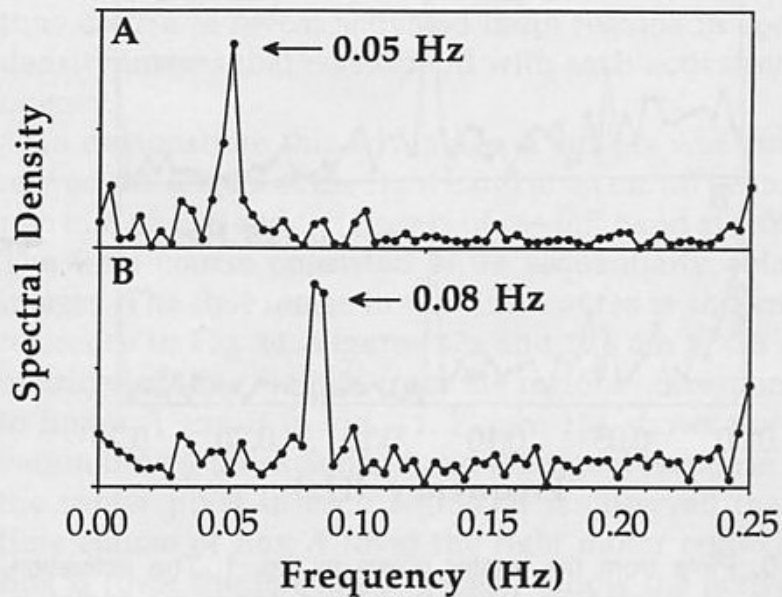
6. Orthogonal Block Design



7. Free Behavior Design.

**a**

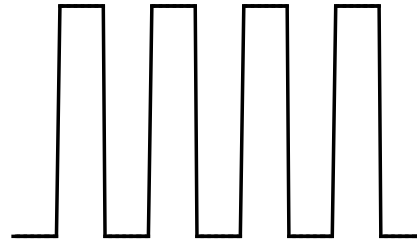
Tapping left and right fingers at two different “on/off” frequencies

**b**

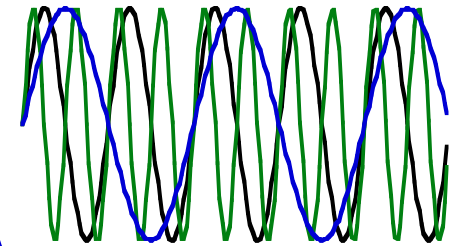
P. A. Bandettini, A. Jesmanowicz, E. C. Wong, J. S. Hyde, Processing strategies for time-course data sets in functional MRI of the human brain. *Magn. Reson. Med.* 30, 161-173 (1993).

# Neuronal Activation Input Strategies

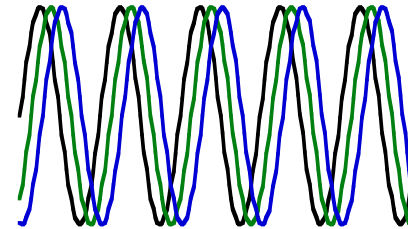
1. Block Design



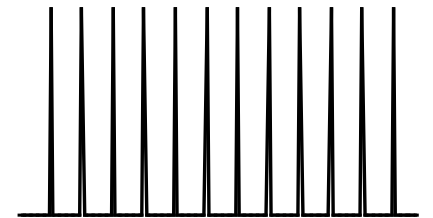
2. Frequency Encoding



3. Phase Encoding

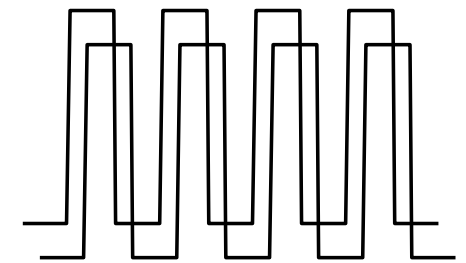


4. Event-Related

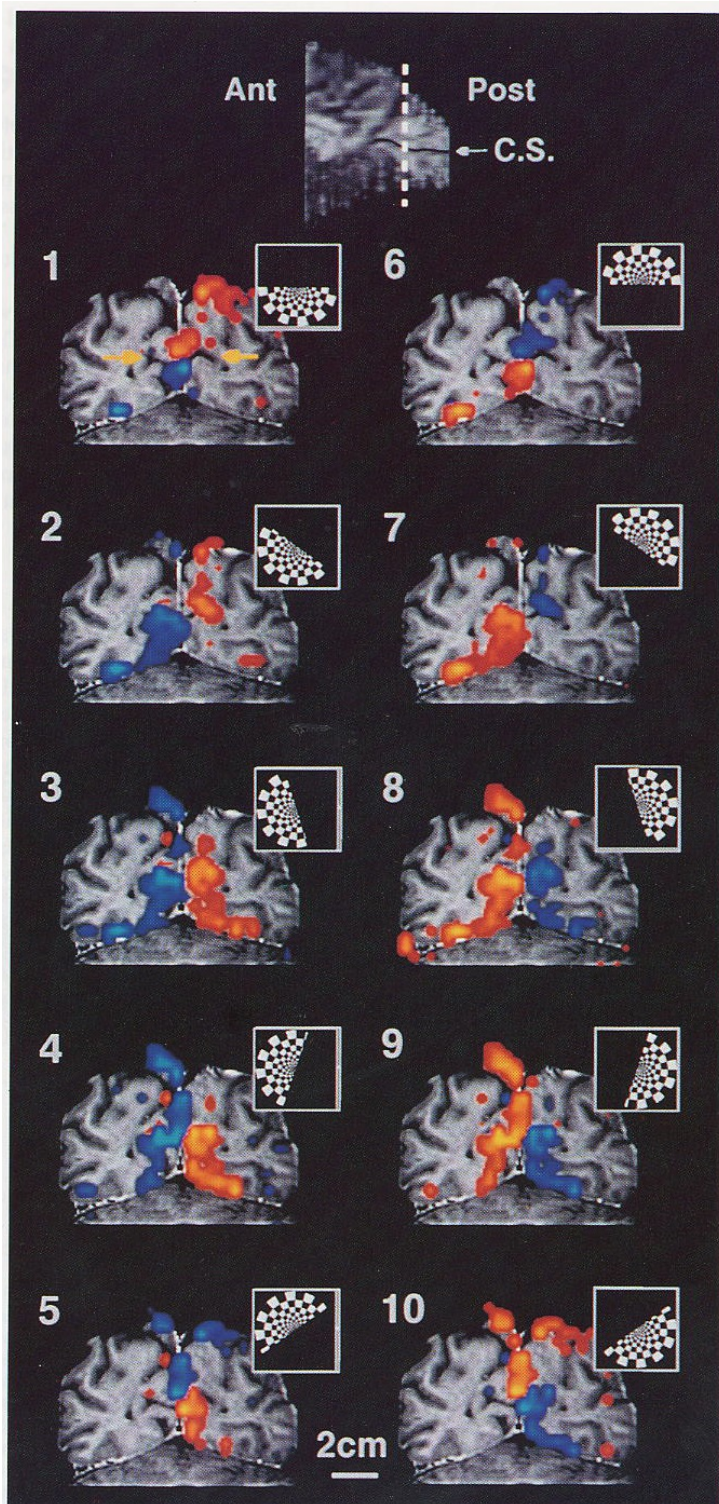


5. fMRI adaptation

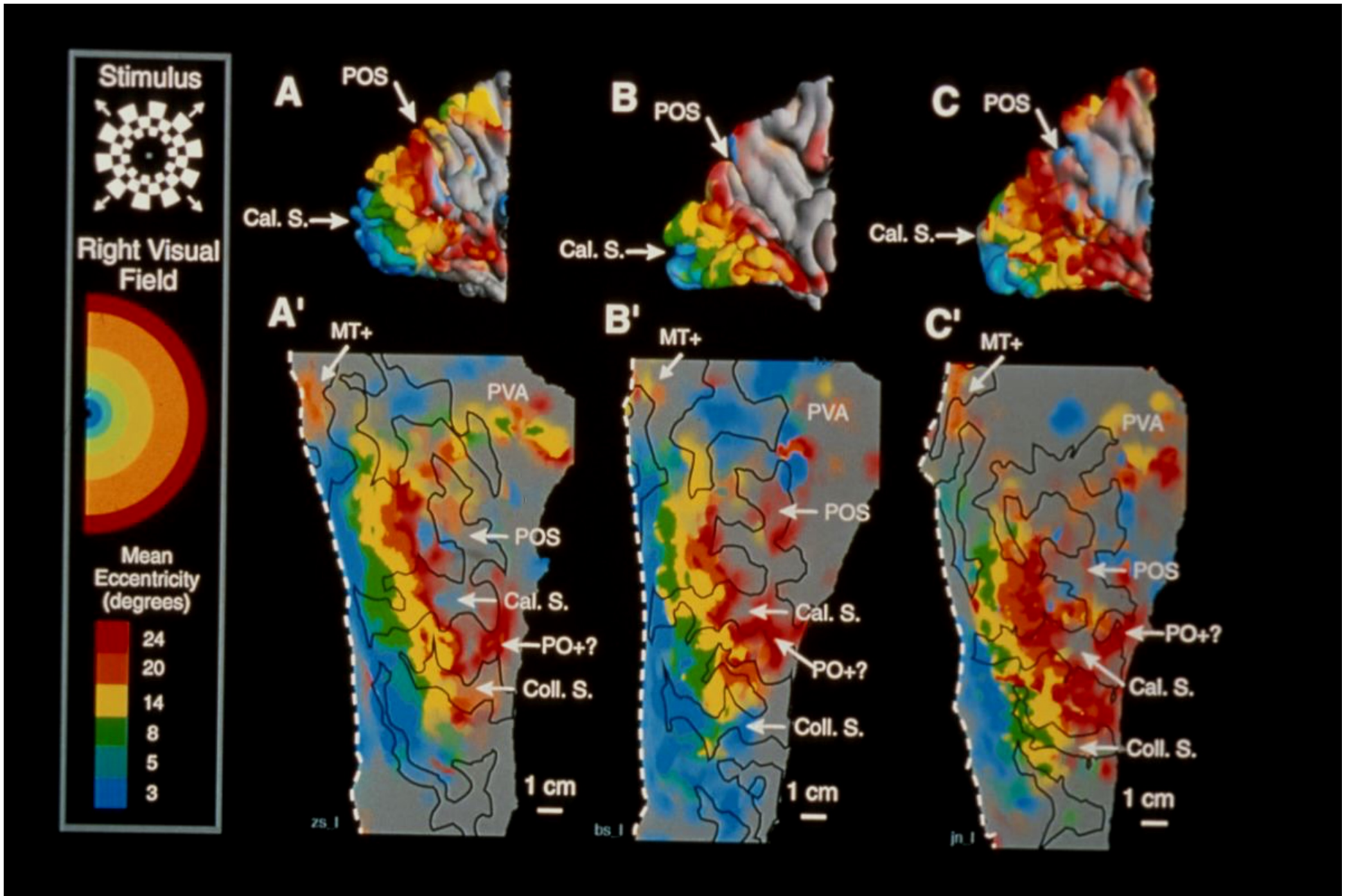
6. Orthogonal Block Design



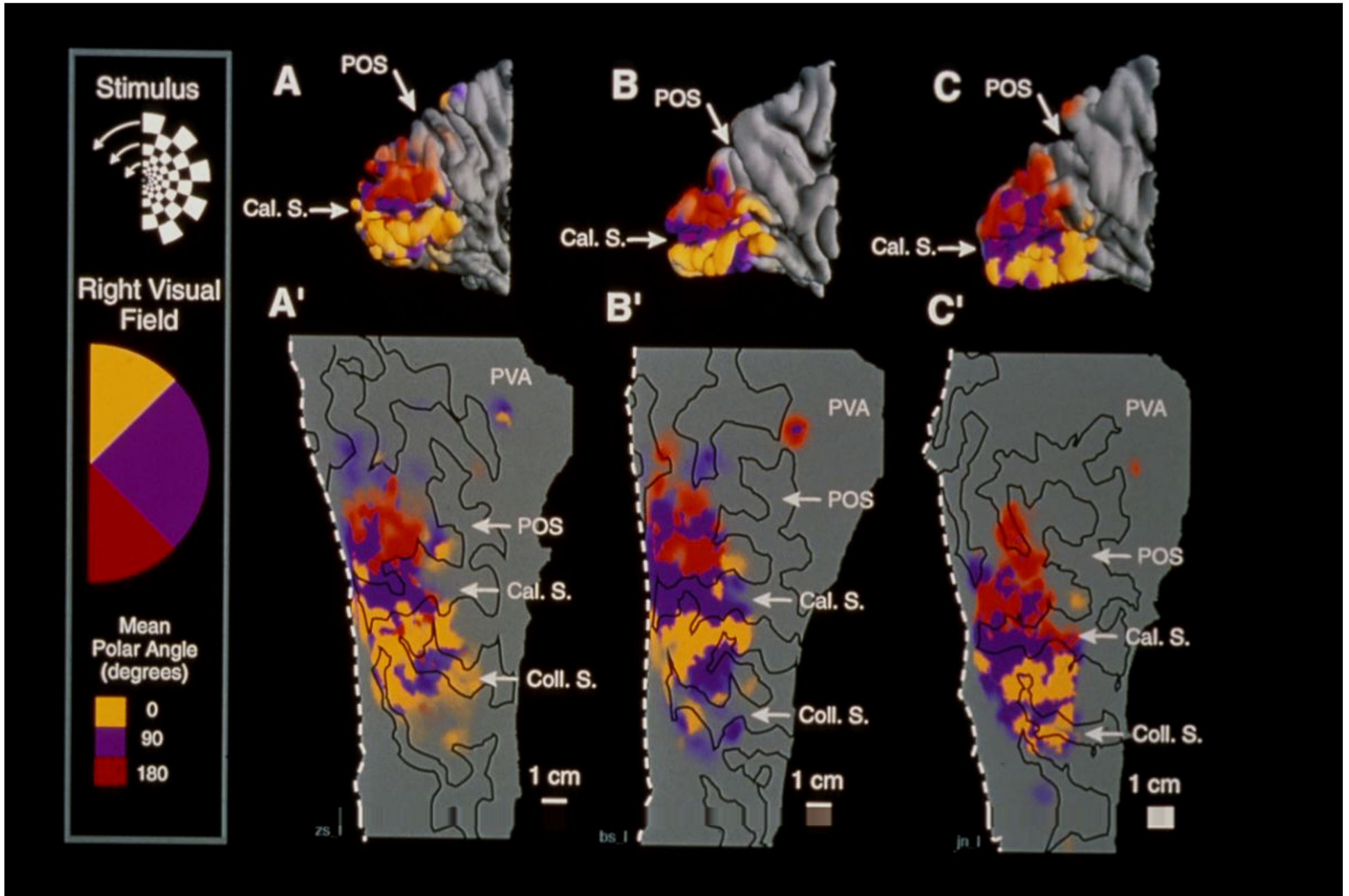
7. Free Behavior Design.



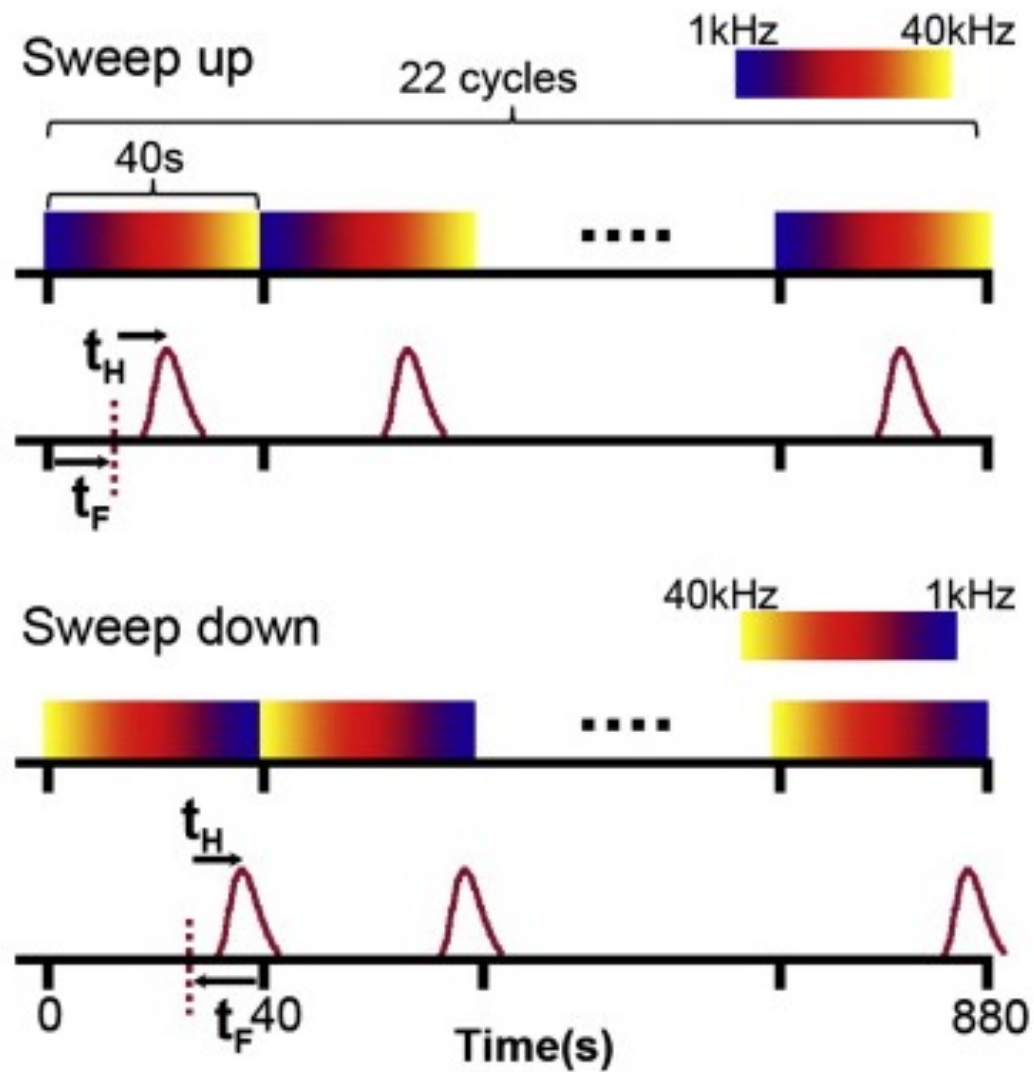
E. A. DeYoe, P. A. Bandettini, J. Nietz, D. Miller, P. Winas, Functional magnetic resonance imaging (fMRI) of the human brain. *J. Neuroscience Methods* 54, 171-187 (1994).



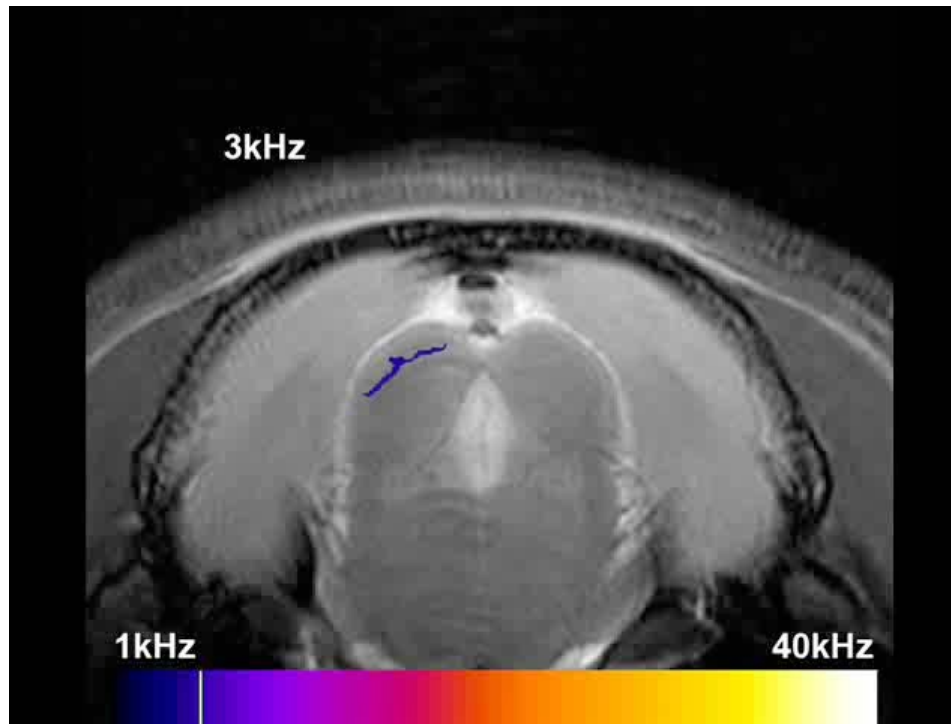
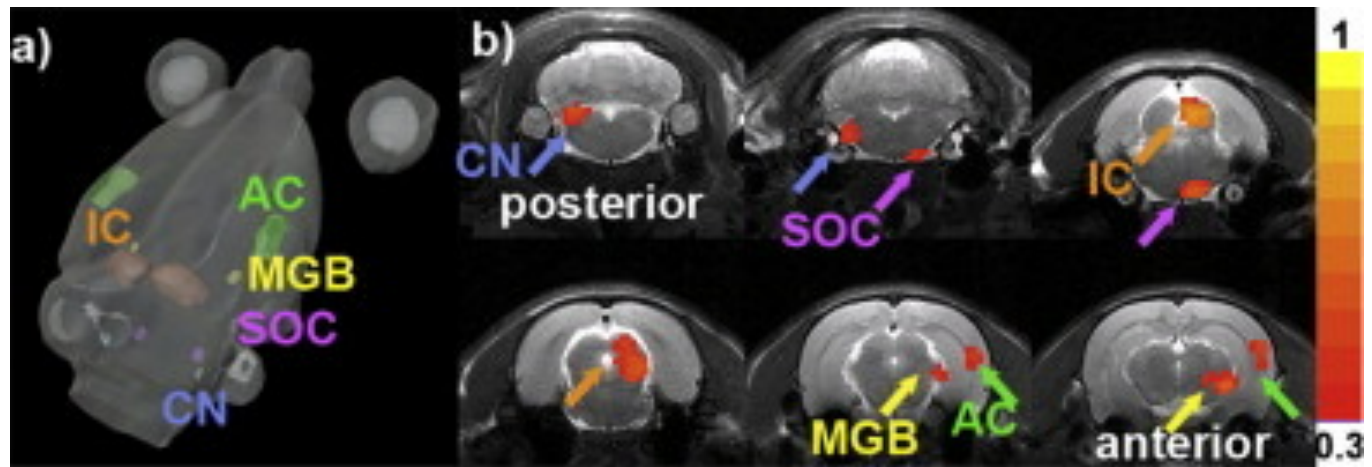
E. A. DeYoe, G. Carman, P. Bandettini, G. S., W. J., R. Cox, D. Miller, J. Neitz, Mapping striate and extrastriate visual areas in human cerebral cortex. *Proc. Nat'l. Acad. Sci.* 93, 2282-2386 (1996).



E. A. DeYoe, G. Carman, P. Bandettini, G. S., W. J., R. Cox, D. Miller, J. Neitz, Mapping striate and extrastriate visual areas in human cerebral cortex. *Proc. Nat'l. Acad. Sci.* 93, 2282-2386 (1996).



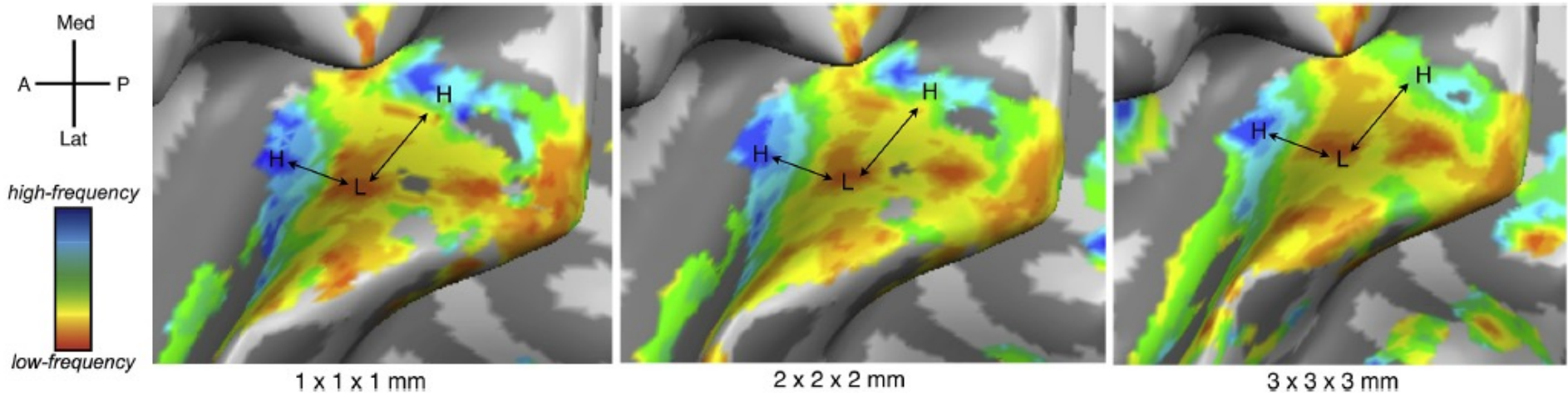
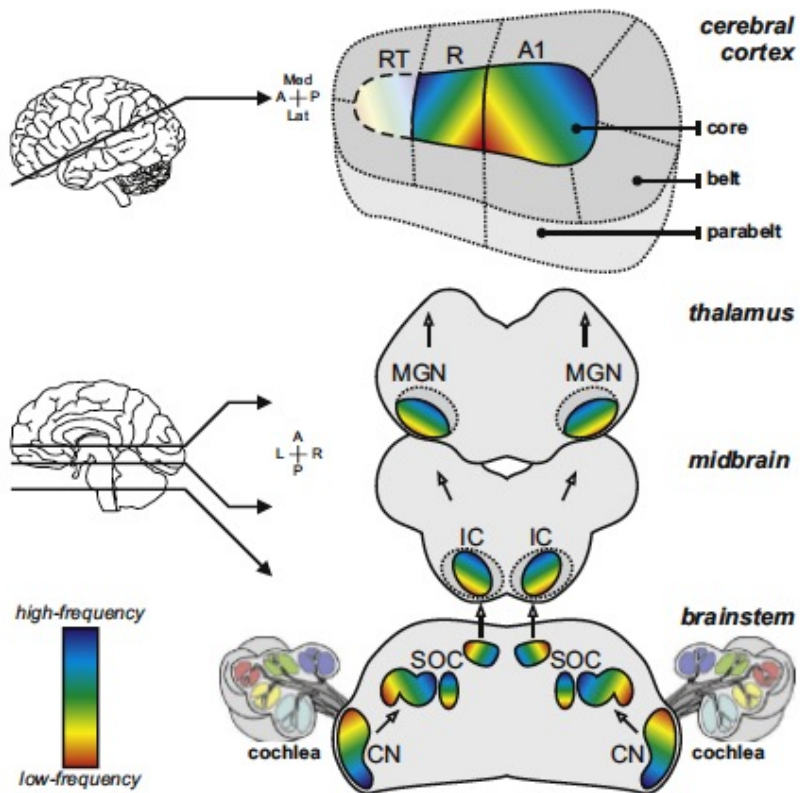
**High fidelity tonotopic mapping using swept source functional magnetic resonance imaging, MM Cheung et al. NeuroImage Volume 61, Issue 4, 16 July 2012, Pages 978-986**



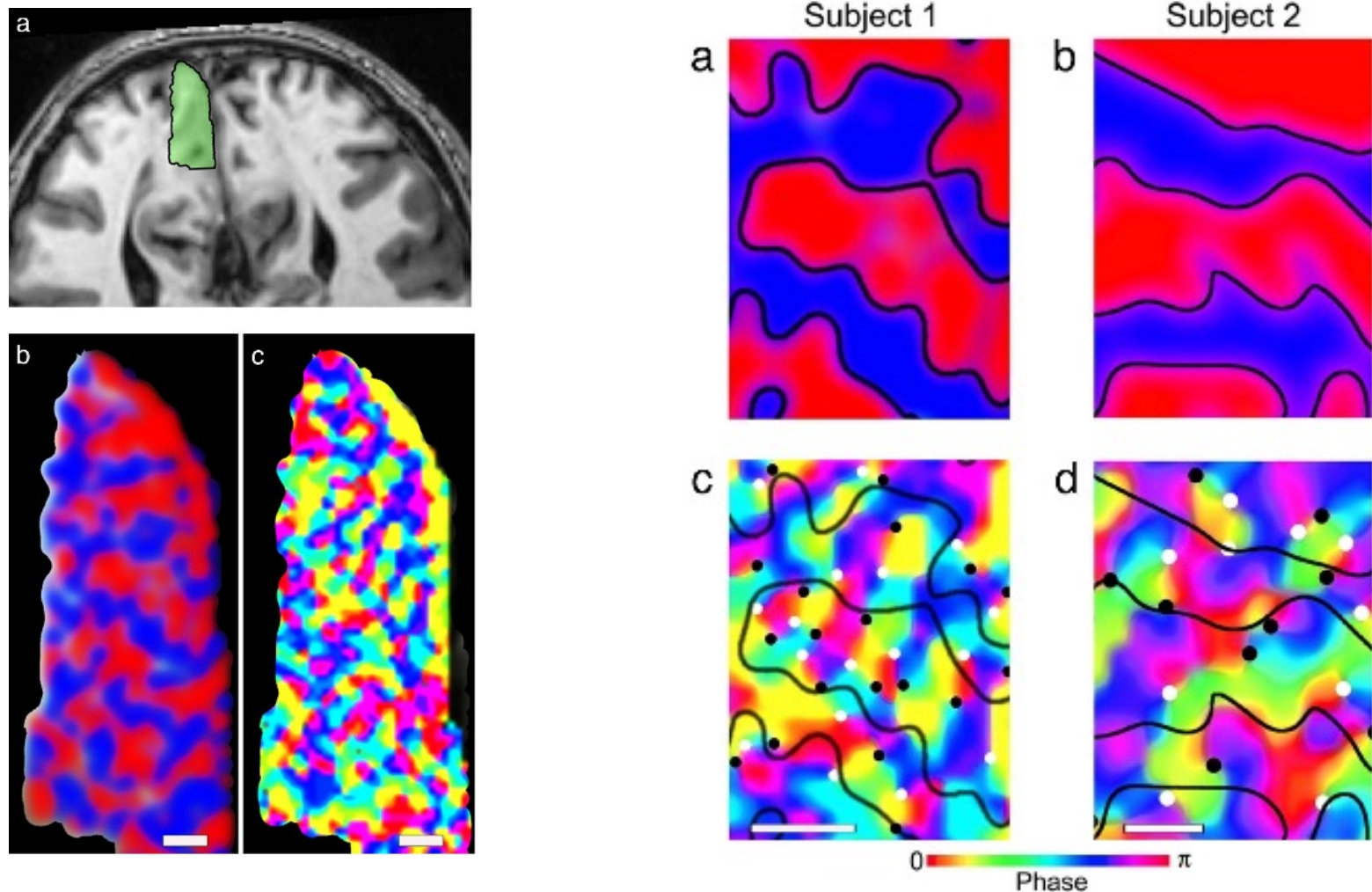
**High fidelity tonotopic mapping using swept source functional magnetic resonance imaging, MM Cheung et al. NeuroImage Volume 61, Issue 4, 16 July 2012, Pages 978-986**



Tonotopic mapping of human auditory cortex  
 Melissa Saenz, Dave R.M. Langers,  
 Hearing Research, 307, 42-52  
 (2014)

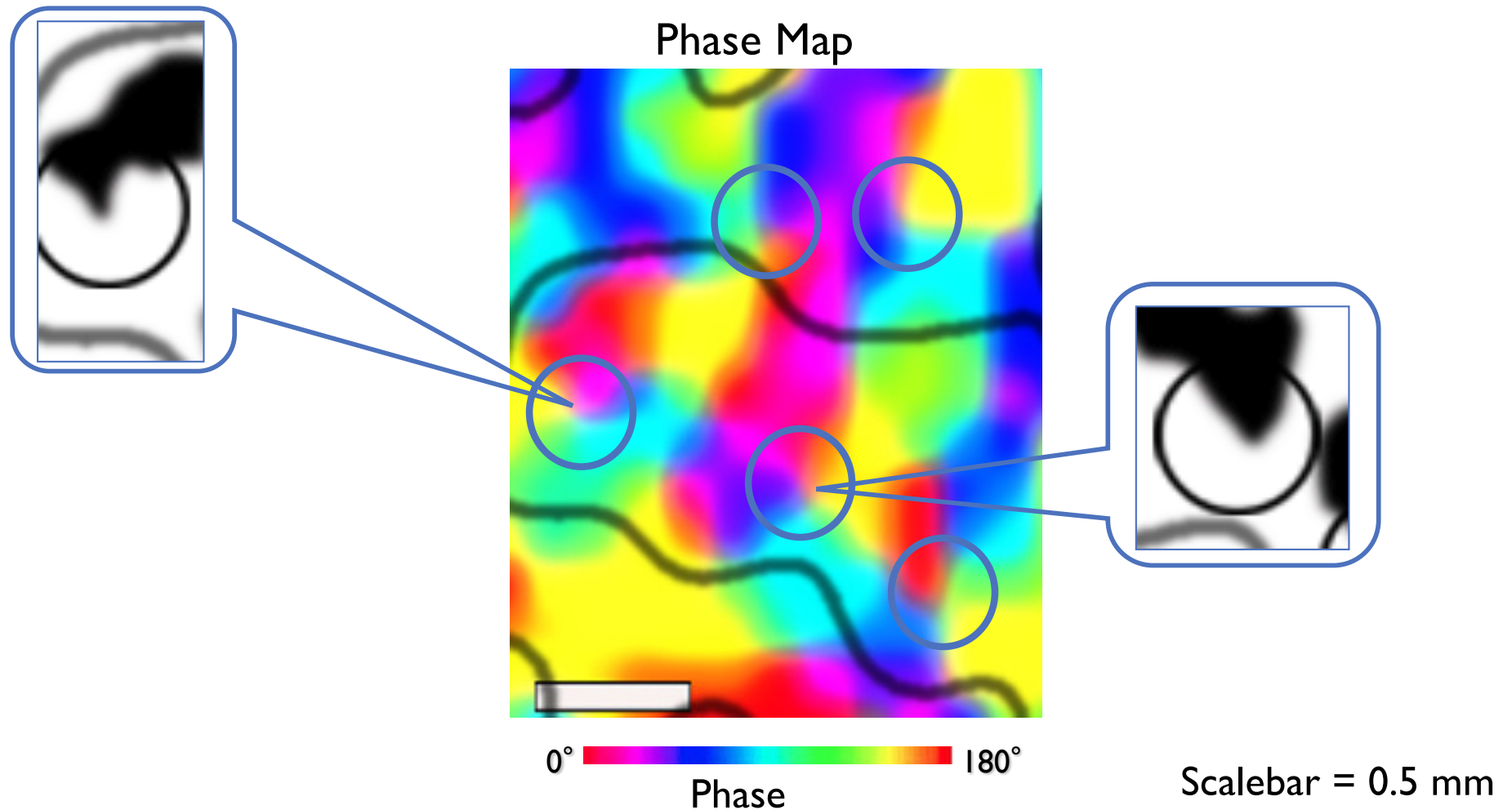


# Orientation Columns in Human VI as Revealed by fMRI at 7T



**High-field fMRI unveils orientation columns in humans,**  
E. Yacoub, N. Harel, K. Ugurbil, **PNAS**, vol 105, pp. 10607-10612

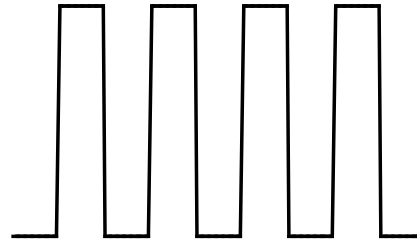
# Orientation Columns in Human VI as Revealed by fMRI at 7T



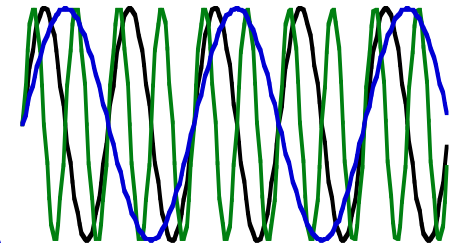
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# Neuronal Activation Input Strategies

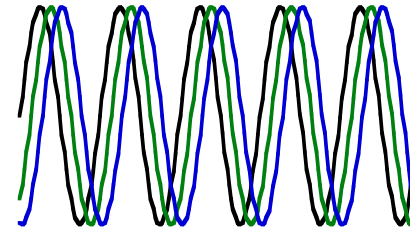
1. Block Design



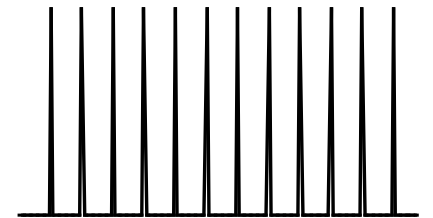
2. Frequency Encoding



3. Phase Encoding

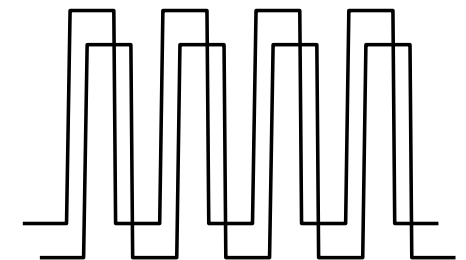


4. Event-Related



5. fMRI adaptation

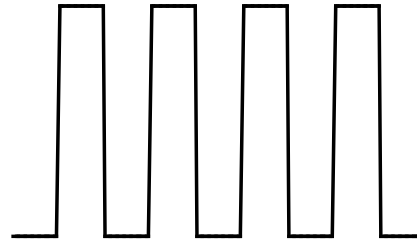
6. Orthogonal Block Design



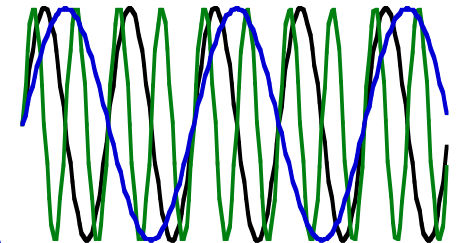
7. Free Behavior Design.

# Neuronal Activation Input Strategies

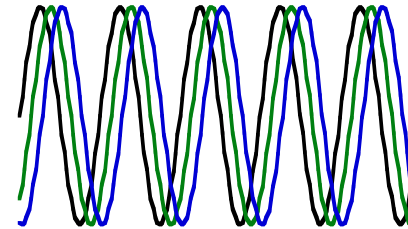
1. Block Design



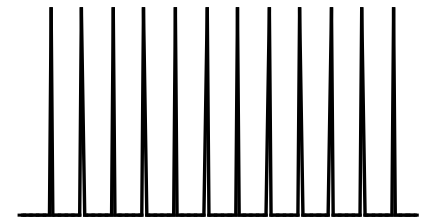
2. Frequency Encoding



3. Phase Encoding

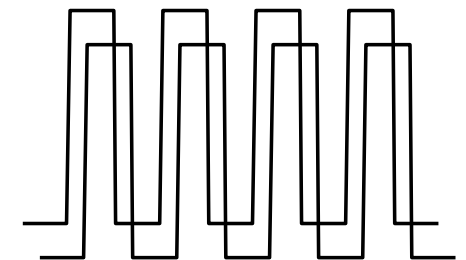


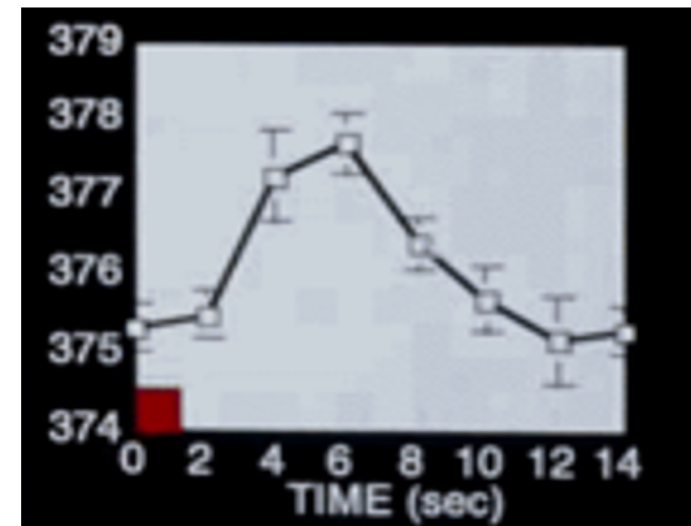
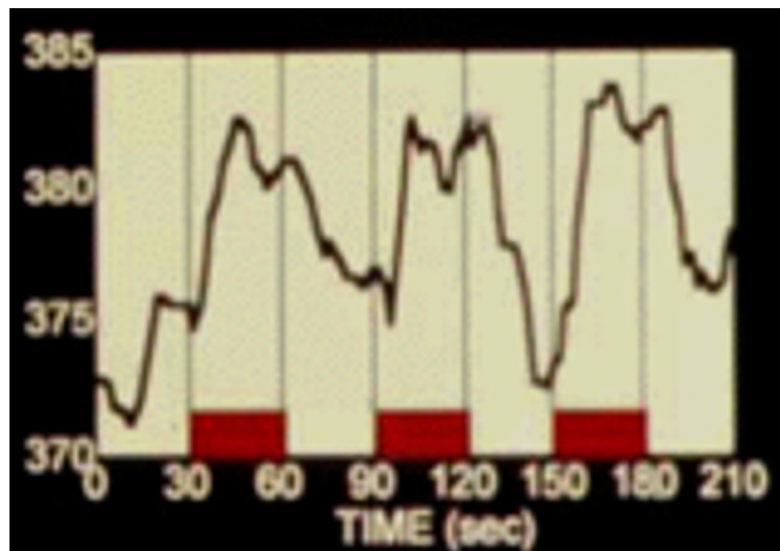
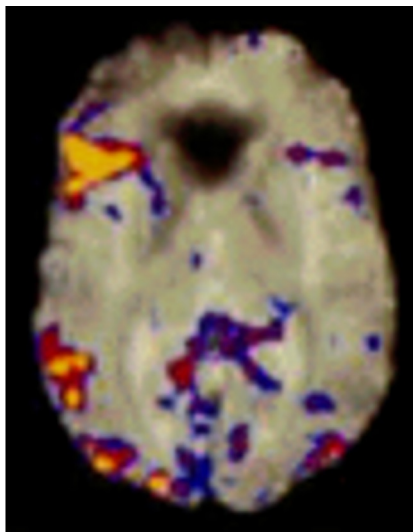
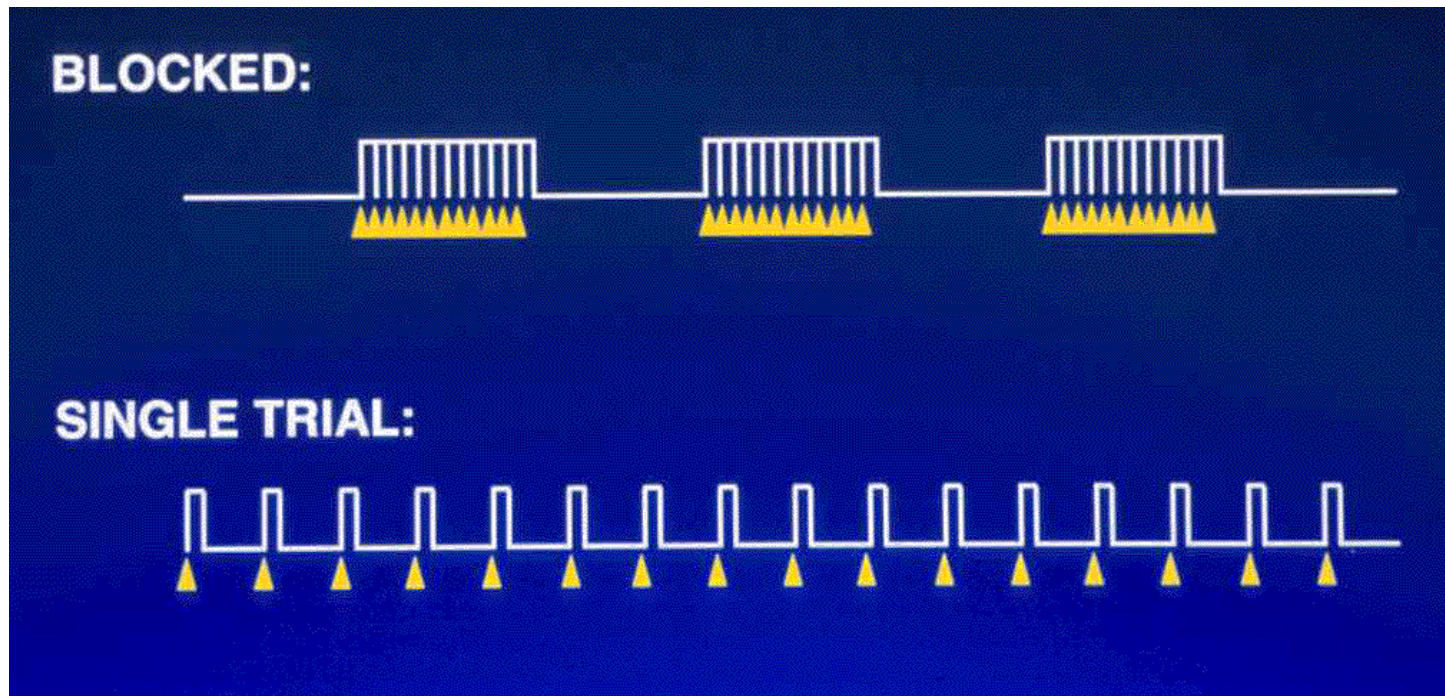
4. Event-Related



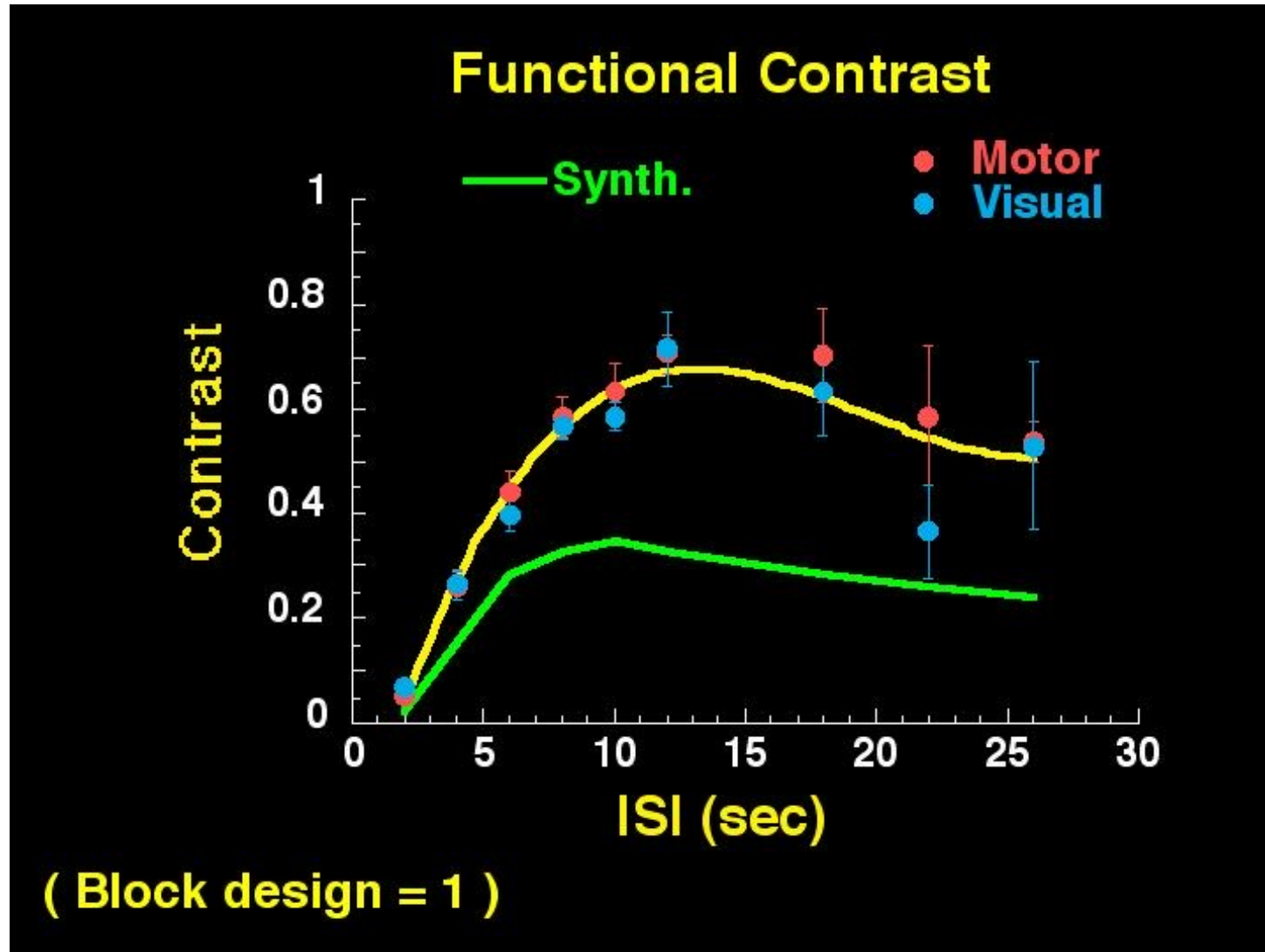
5. Orthogonal Block Design

6. Free Behavior Design.





R. L. Buckner, P. A. Bandettini, K. M. O'Craven, R. L. Savoy, S. E. Peterson, M. E. Raichle, T. L. Brady, B. R. Rosen, fMRI detection and time course of distributed cortical activations during single trials of a cognitive task. *Proc. Nat'l. Acad. Sci. USA* 93, 14878-14883 (1996).



P. A. Bandettini, R. W. Cox. Functional contrast in constant interstimulus interval event - related fMRI: theory and experiment. *Magn. Reson. Med.* 43: 540-548 (2000).

# Contrast to Noise Images

( ISI, SD )

20, 20

12, 2

10, 2

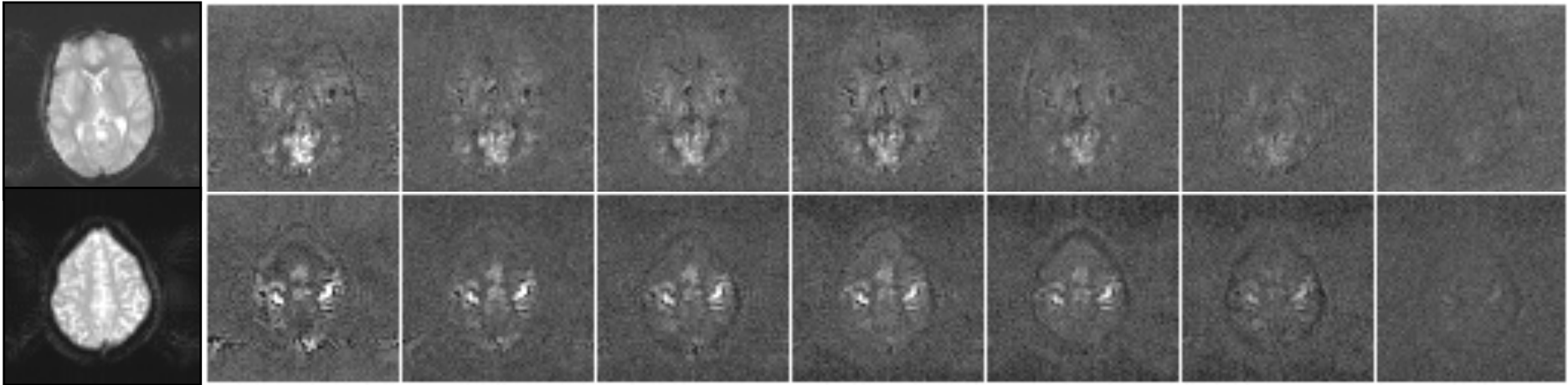
8, 2

6, 2

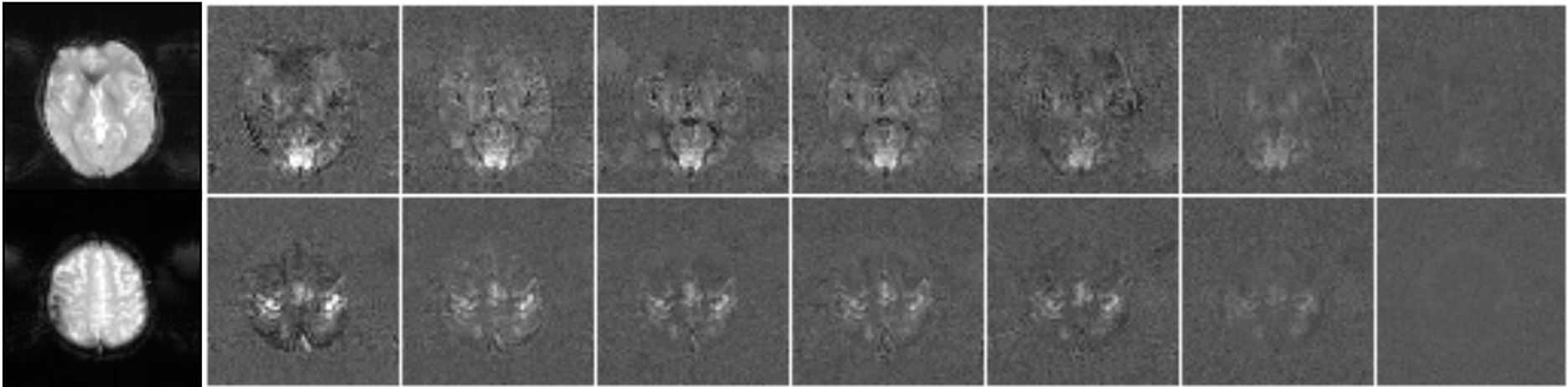
4, 2

2, 2

S1



S2



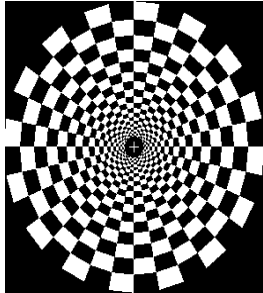
**P. A. Bandettini, R. W. Cox. Functional contrast in constant interstimulus interval event - related fMRI: theory and experiment. *Magn. Reson. Med.* 43: 540-548 (2000).**



## Selective Averaging of Rapidly Presented Individual Trials Using fMRI

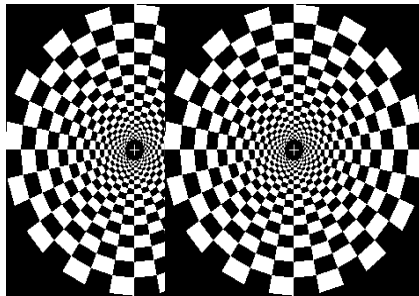
Anders M. Dale\* and Randy L. Buckner

*Massachusetts General Hospital Nuclear Magnetic Resonance Center and the Department of Radiology,  
Harvard Medical School, Boston, Massachusetts 02129*



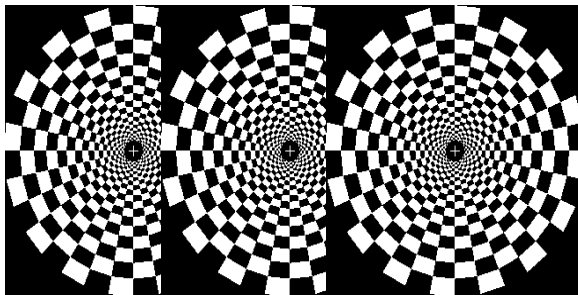
0 sec

20 sec



0 sec 2 sec

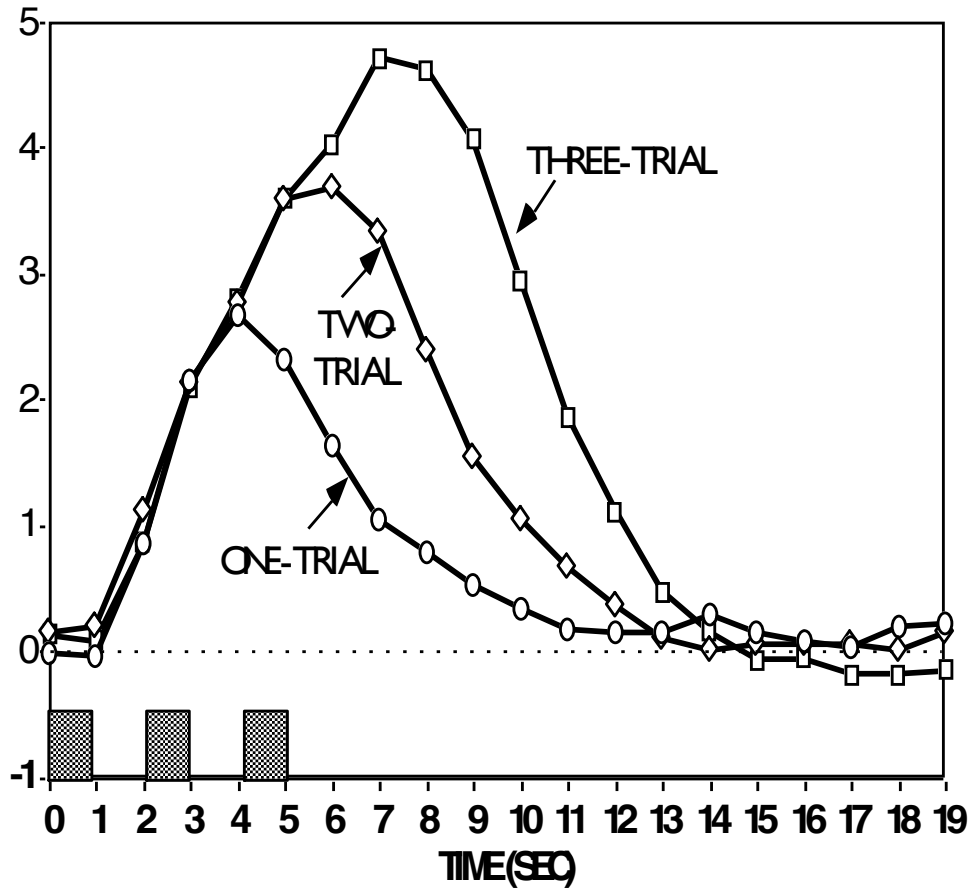
20 sec



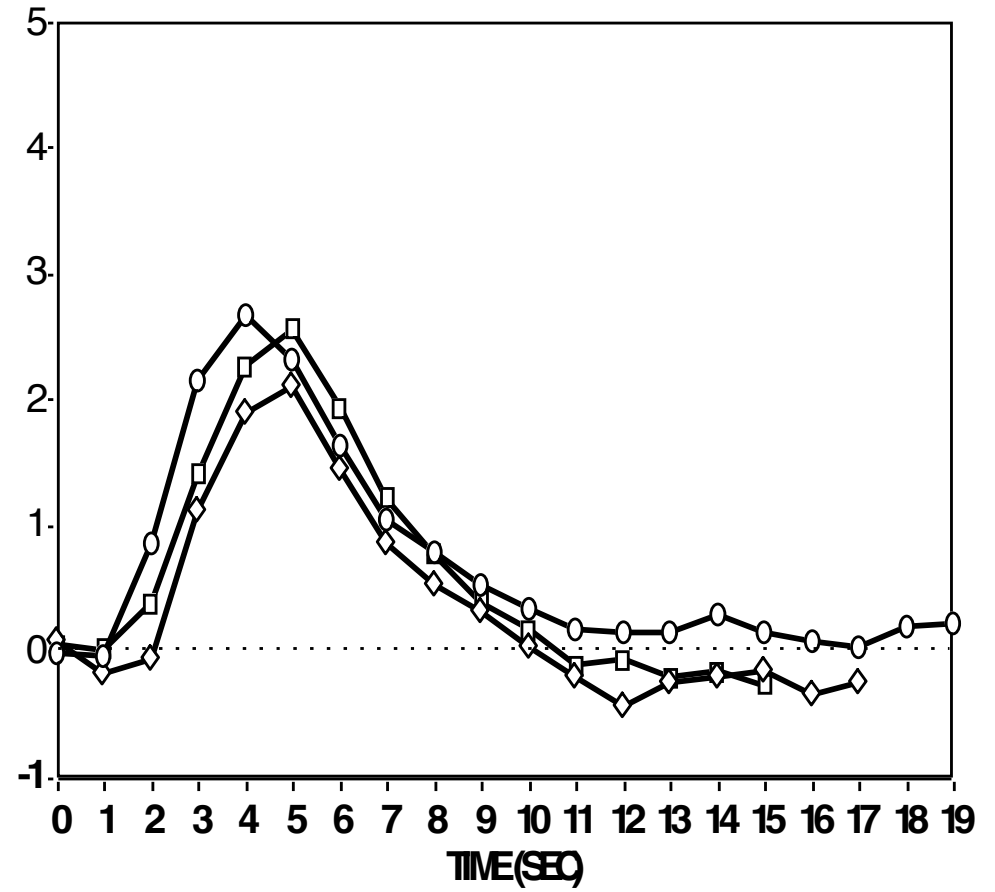
0 sec 2 sec 4 sec

20 sec

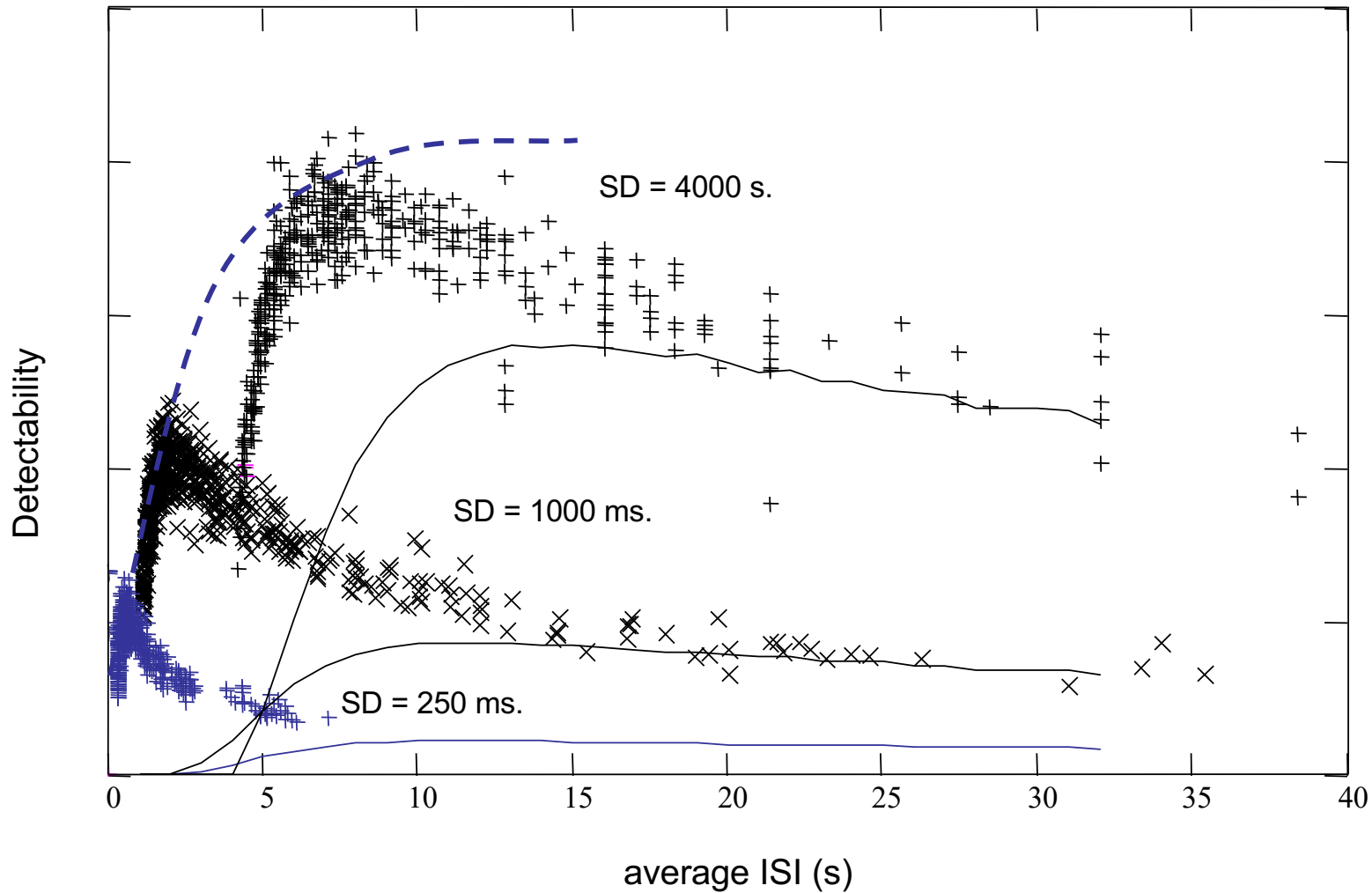
## RAW DATA



## ESTIMATED RESPONSES

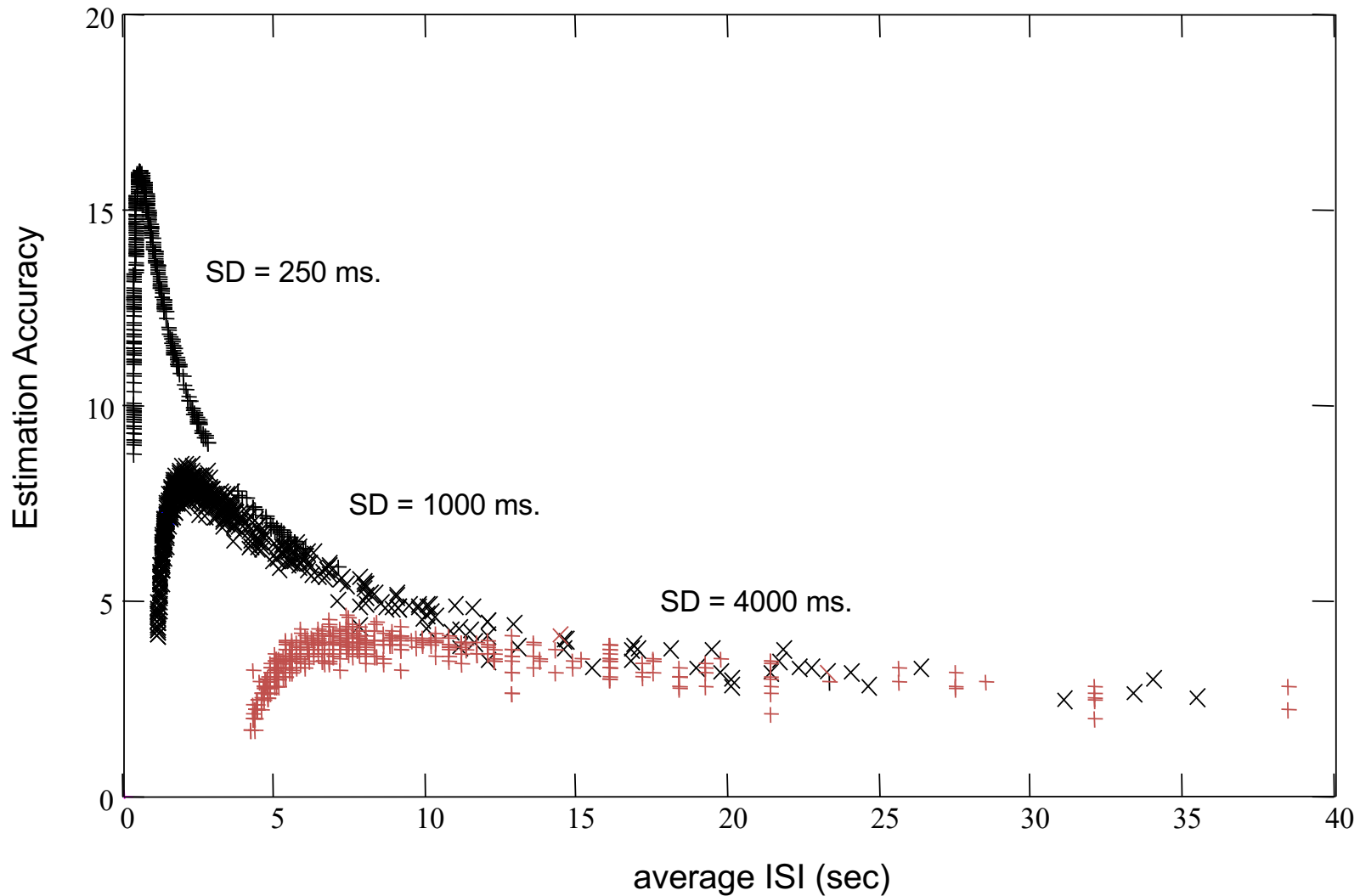


# Detectability vs. Average ISI



R. M. Birn, R. W. Cox, P. A. Bandettini, Detection versus estimation in Event-Related fMRI: choosing the optimal stimulus timing. *NeuroImage* 15: 262-264, (2002).

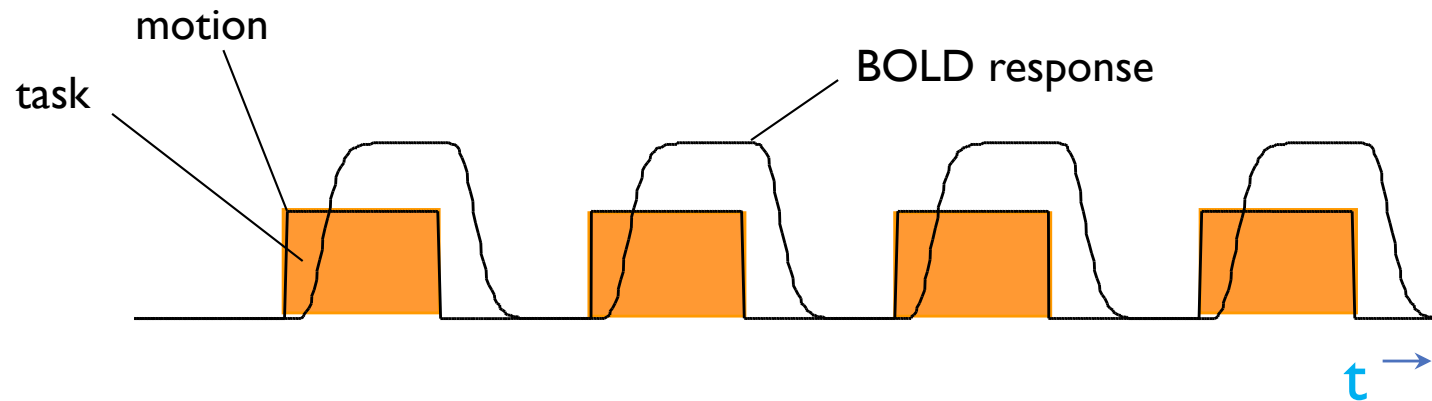
# Estimation accuracy vs. average ISI



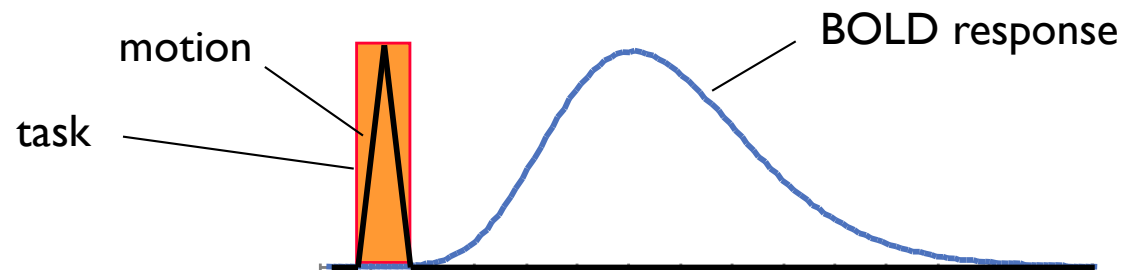
R. M. Birn, R. W. Cox, P. A. Bandettini, Detection versus estimation in Event-Related fMRI: choosing the optimal stimulus timing. *NeuroImage* 15: 262-264, (2002).

# fMRI during tasks that involve brief motion

## Blocked Design

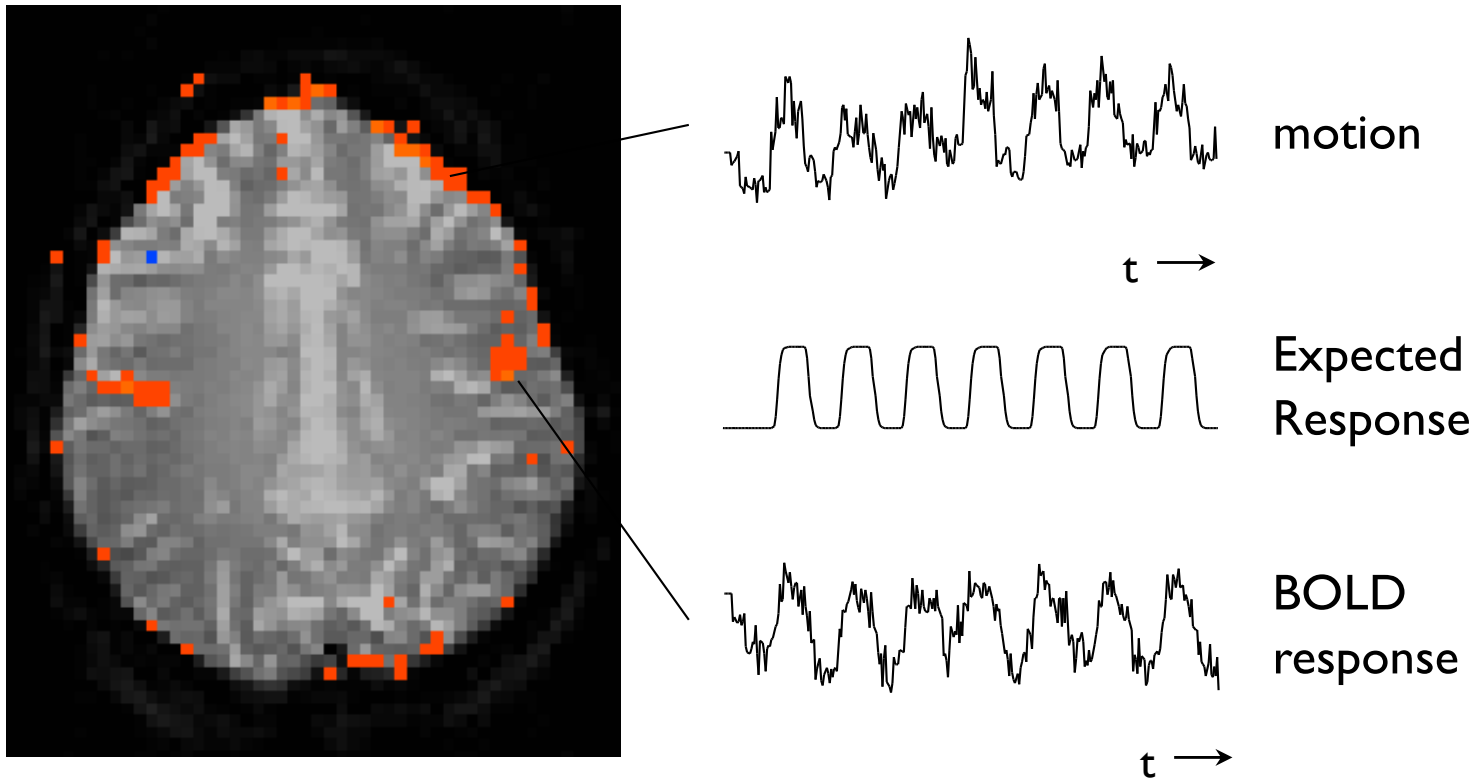


## Event-Related Design



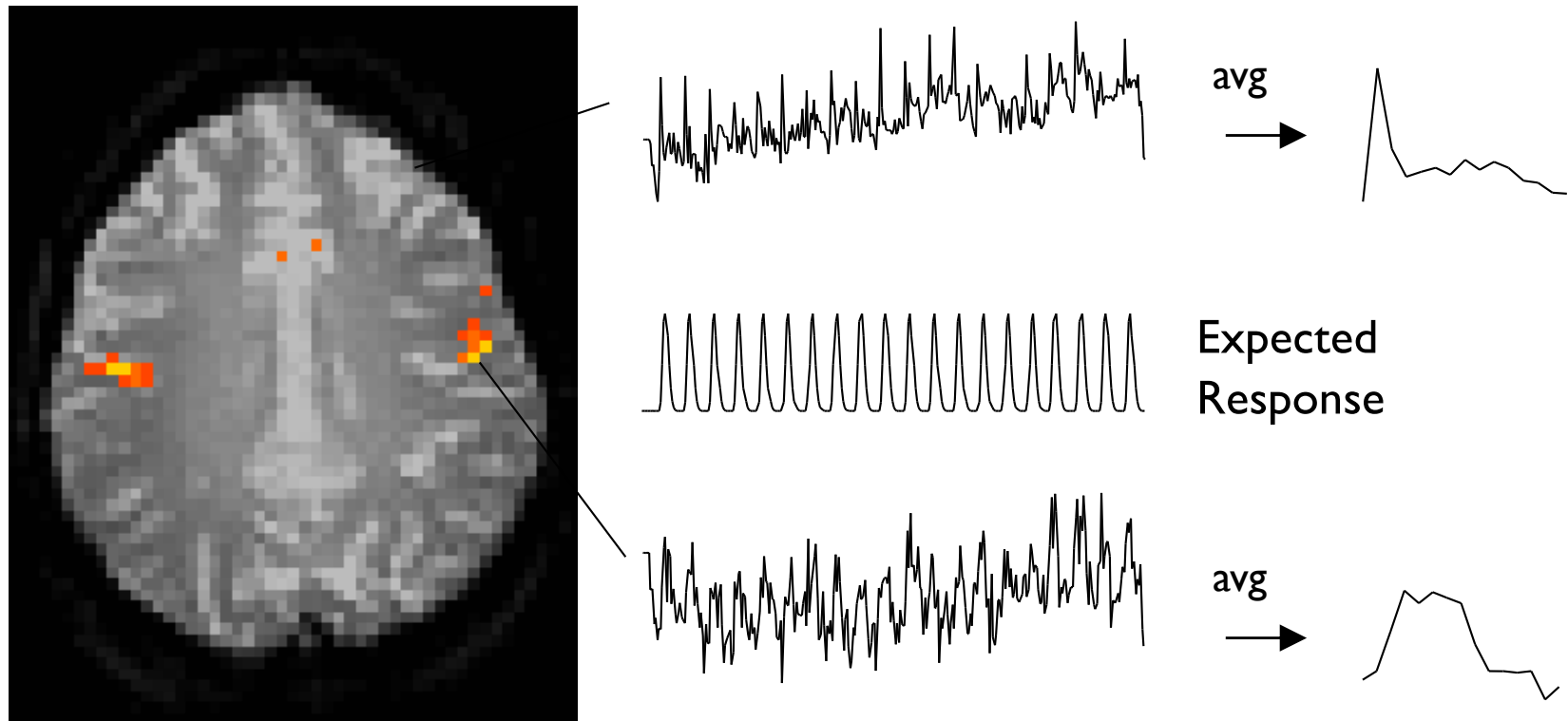
**R. M. Birn, P. A. Bandettini, R. W. Cox, R. Shaker, Event - related fMRI of tasks involving brief motion. *Human Brain Mapping* 7: 106-114 (1999).**

# Speaking - Blocked Trial



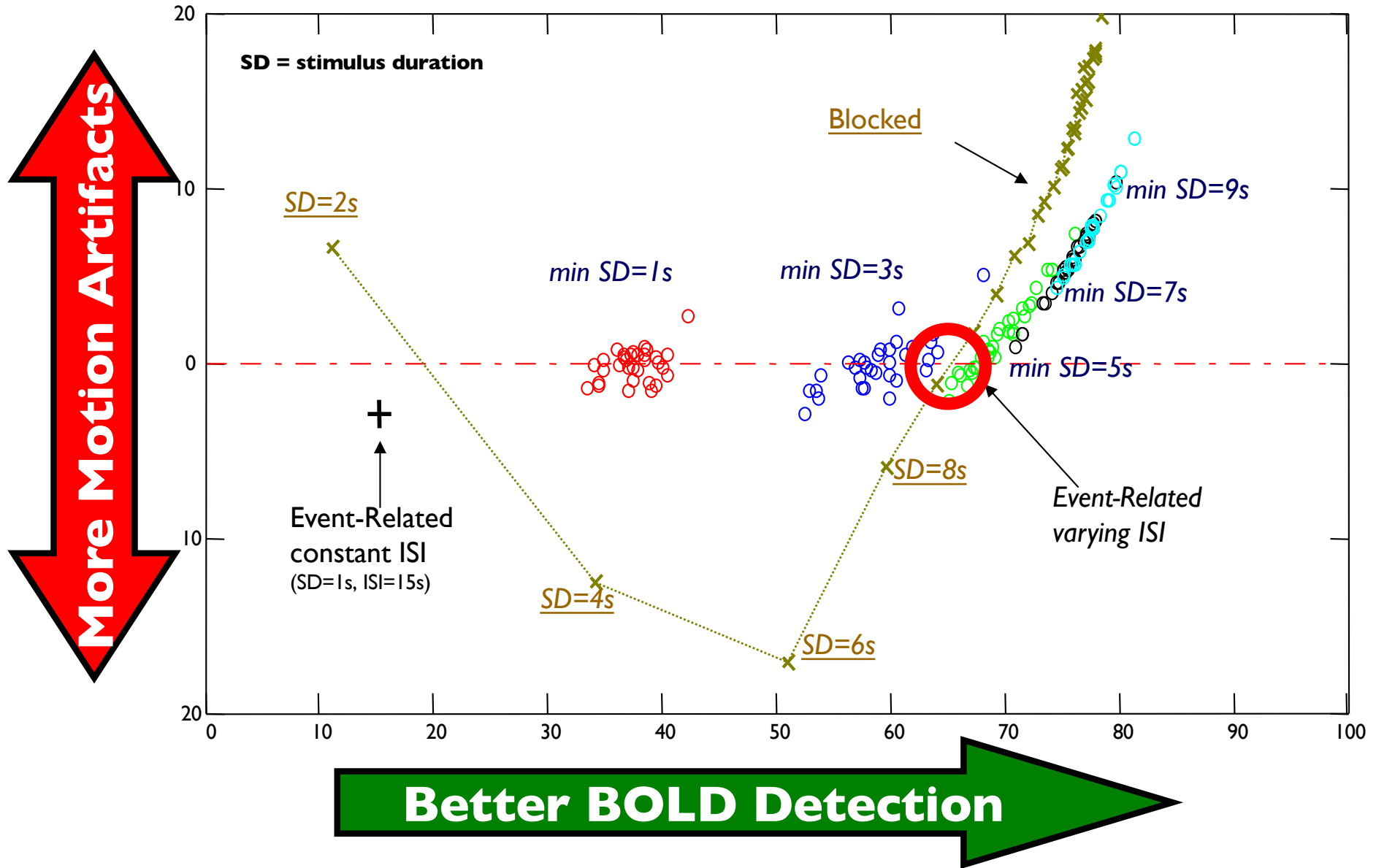
**R. M. Birn, P. A. Bandettini, R. W. Cox, R. Shaker, Event - related fMRI of tasks involving brief motion. *Human Brain Mapping* 7: 106-114 (1999).**

# Speaking - ER-fMRI



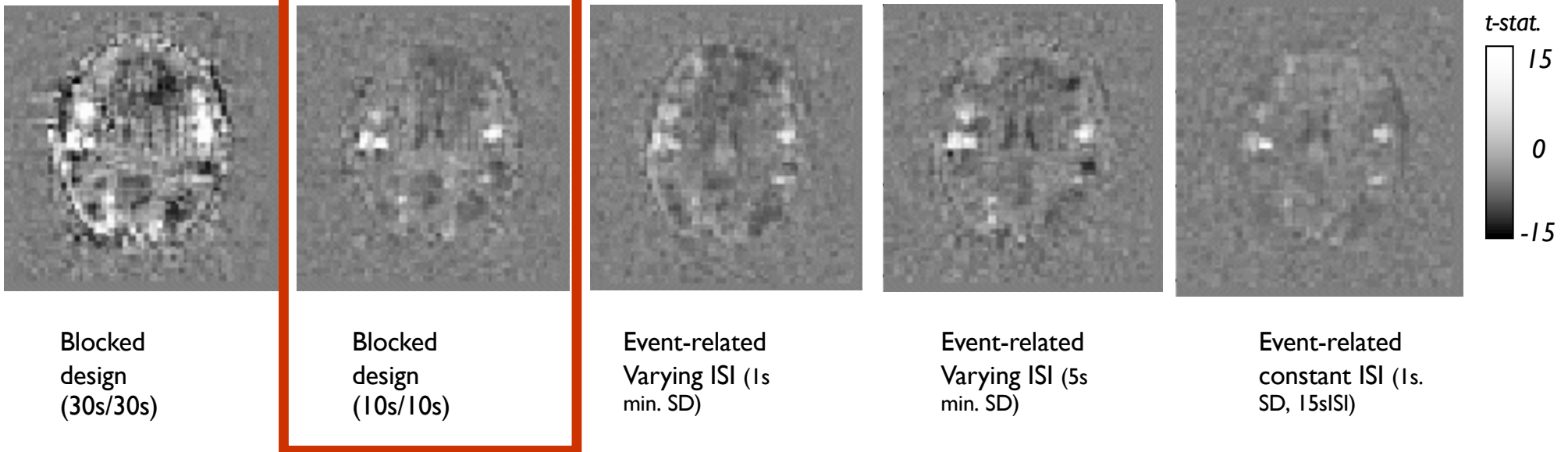
**R. M. Birn, P. A. Bandettini, R. W. Cox, R. Shaker, Event - related fMRI of tasks involving brief motion. *Human Brain Mapping* 7: 106-114 (1999).**

# Overt Responses - Simulations





# Overt Responses



Blocked design (30s/30s)

Blocked design (10s/10s)

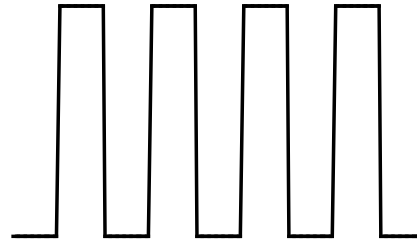
Event-related Varying ISI (1s min. SD)

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

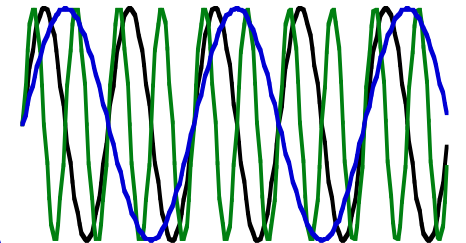
Event-related constant ISI (1s. SD, 15sISI)

# Neuronal Activation Input Strategies

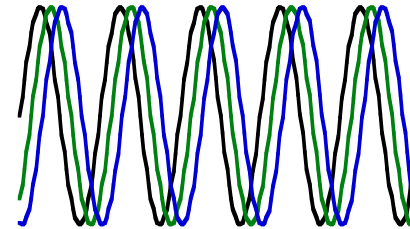
1. Block Design



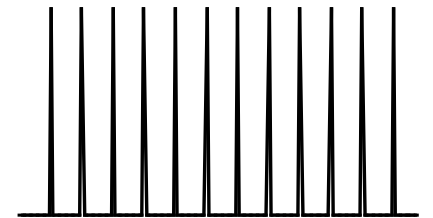
2. Frequency Encoding



3. Phase Encoding

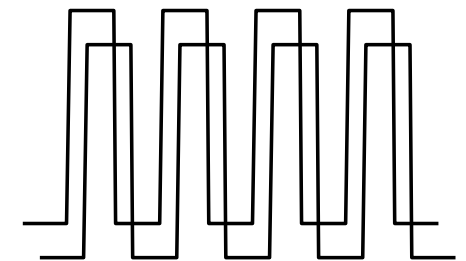


4. Event-Related



5. fMRI adaptation

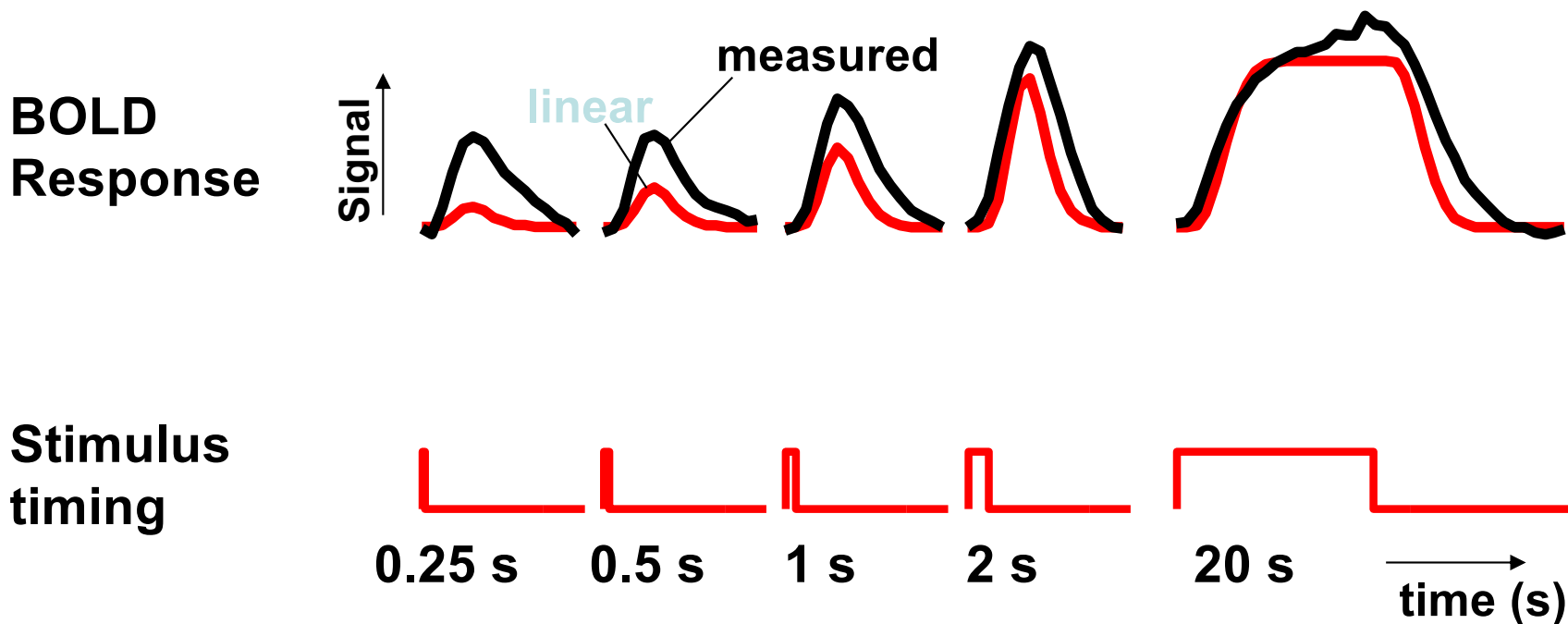
6. Orthogonal Block Design



7. Free Behavior Design.

# Dynamic Nonlinearity Assessment

## Different stimulus “ON” periods

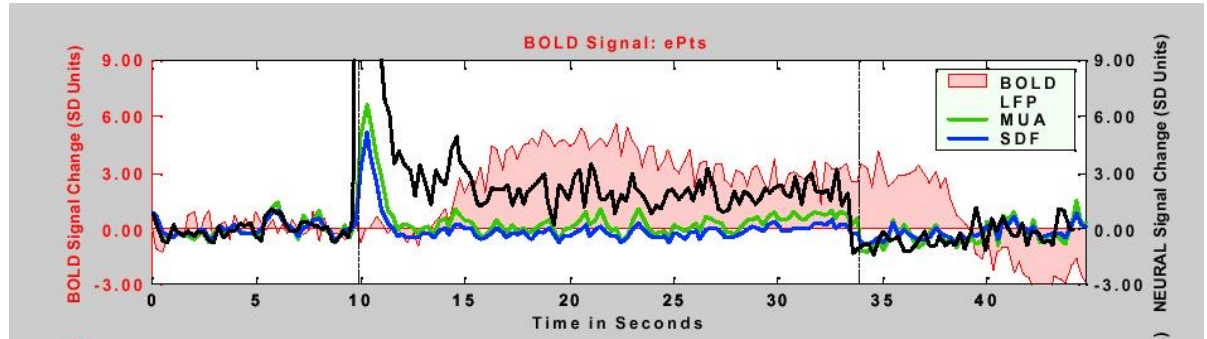


**Brief stimuli produce larger responses than expected**

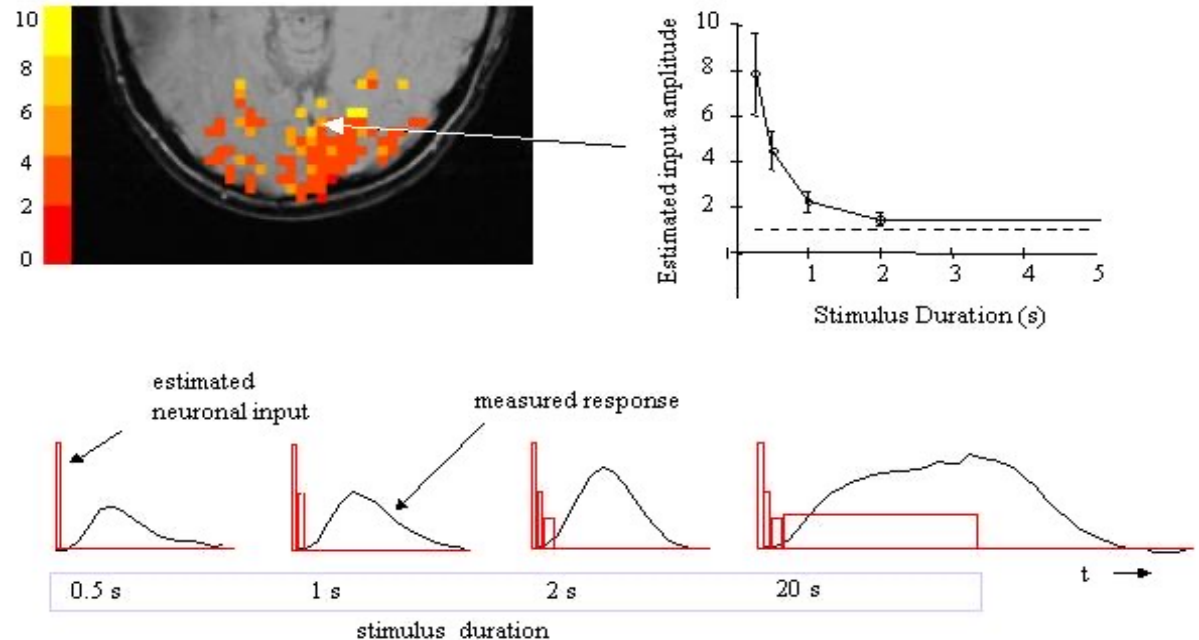
R. M. Birn, Z. Saad, P. A. Bandettini, (2001) “Spatial heterogeneity of the nonlinear dynamics in the fMRI BOLD response.” *NeuroImage*, 14: 817-826.

# BOLD Correlation with Neuronal Activity

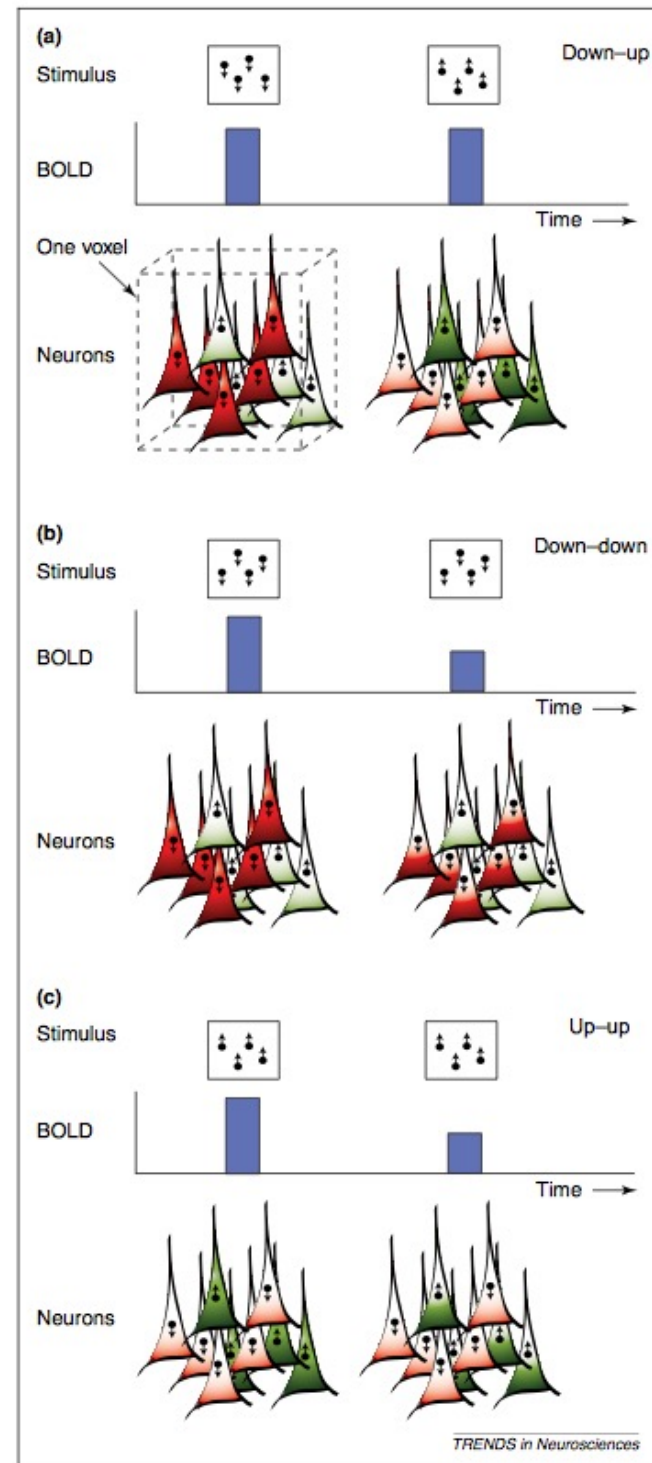
**Logothetis et al. (2001)**  
“Neurophysiological investigation  
of the basis of the fMRI signal”  
*Nature*, 412, 150-157.

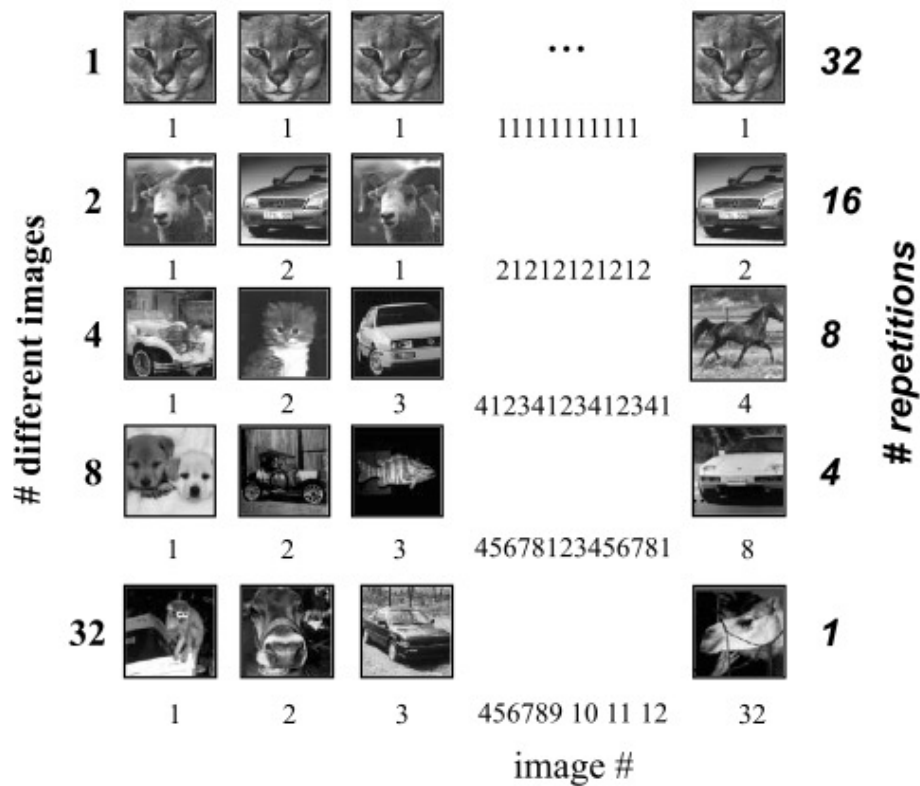


**P. A. Bandettini and L. G. Ungerleider, (2001)** “From neuron to BOLD: new connections.”  
*Nature Neuroscience*, 4: 864-866.

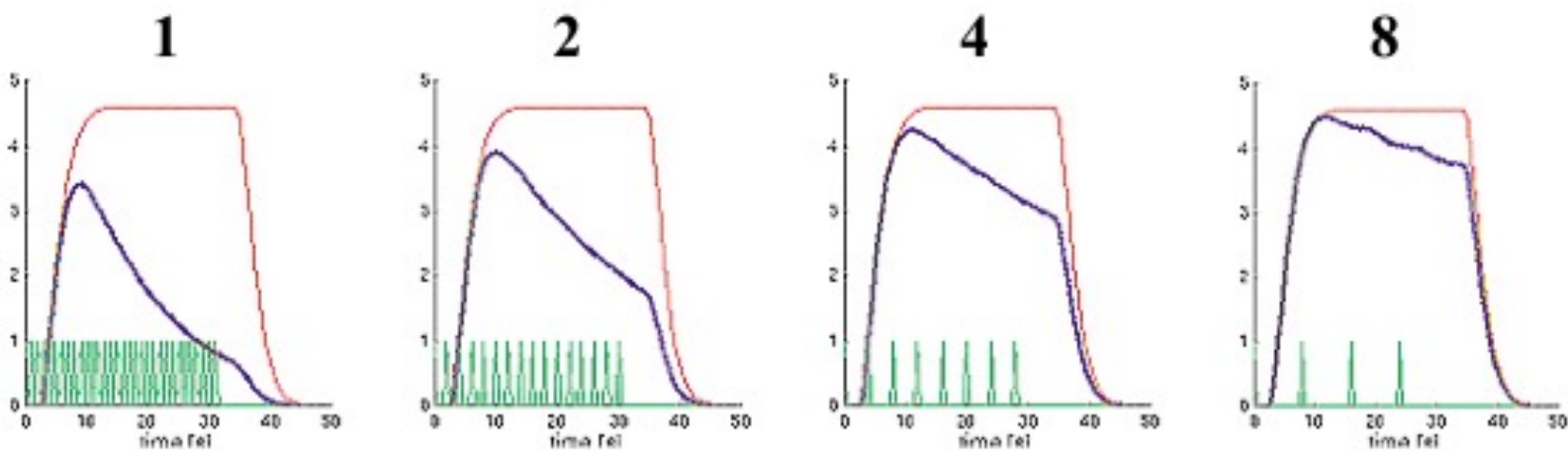


**Adaptation: from single cells to BOLD signals**, Bart Krekelberg, Geoffrey M. Boynton, and Richard J.A. van Wezel, Trends in Neurosciences, 29, 5, 2006



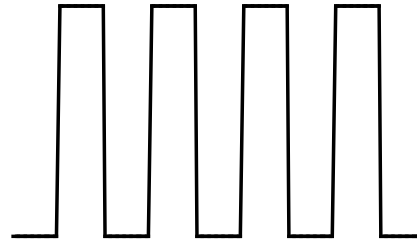


**fMRI-adaptation: a tool for studying the functional properties of human cortical neurons** Kalanit Grill-Spector, Rafael Malach, *Acta Psychologica*, 107 (2001), 293-321

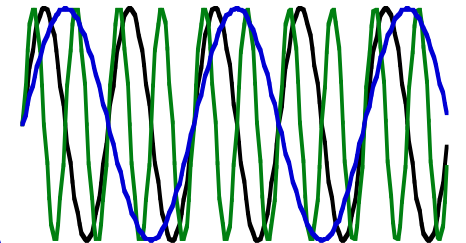


# Neuronal Activation Input Strategies

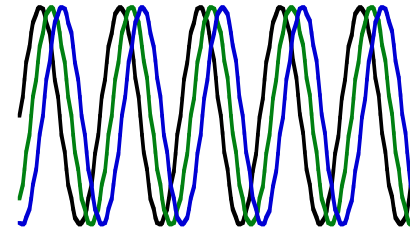
1. Block Design



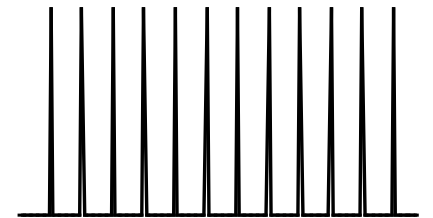
2. Frequency Encoding



3. Phase Encoding

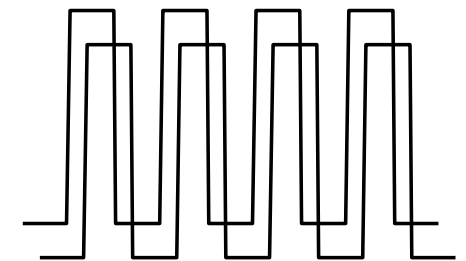


4. Event-Related



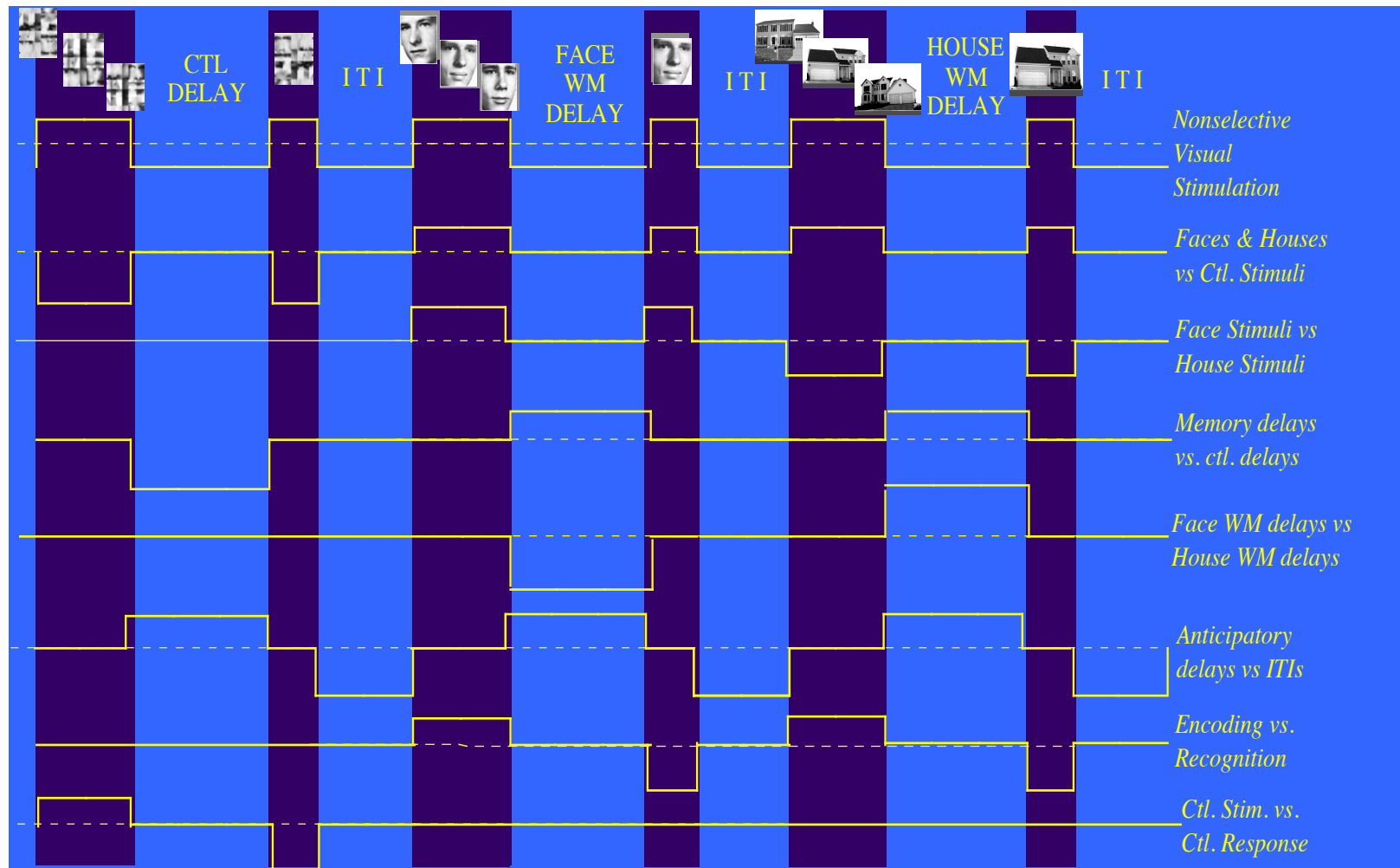
5. fMRI adaptation

6. Orthogonal Block Design



7. Free Behavior Design

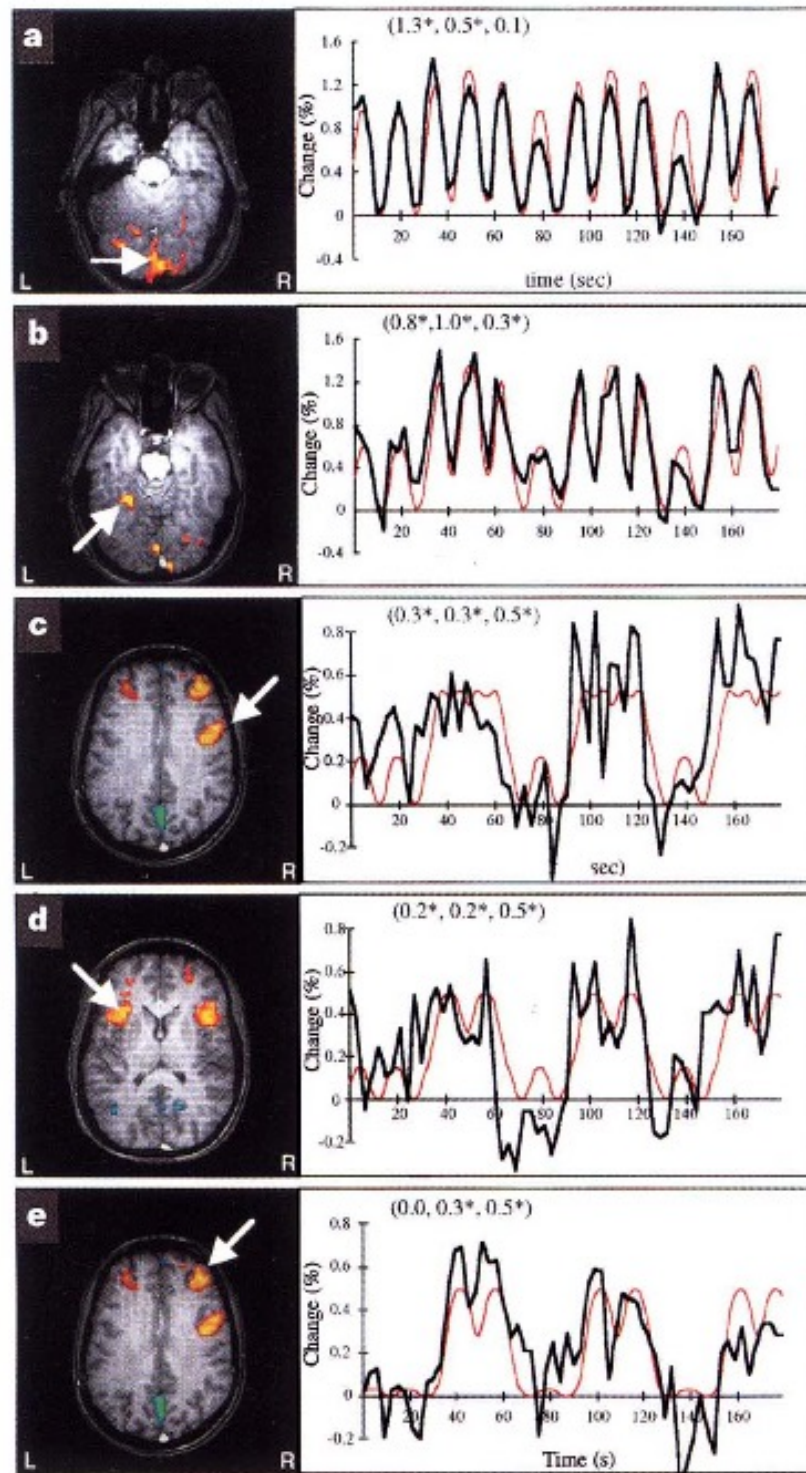
# Example of a Set of Orthogonal Contrasts for Multiple Regression



**Transient and Sustained activity in a distributed neural system for human working memory, S. M. Courtney, L. G. Ungerleider, K. Keil, J. V. Haxby, Nature, 386, pp. 608-611**

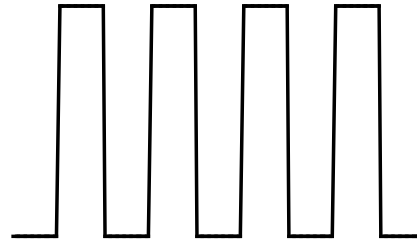


**Transient and Sustained activity in a distributed neural system for human working memory, S. M. Courtney, L. G. Ungerleider, K. Keil, J. V. Haxby, Nature, 386, pp. 608-611**

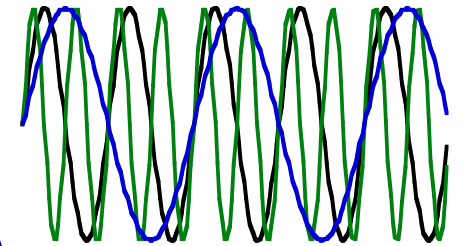


# Neuronal Activation Input Strategies

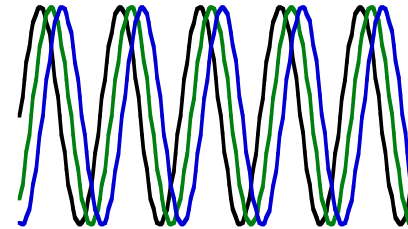
1. Block Design



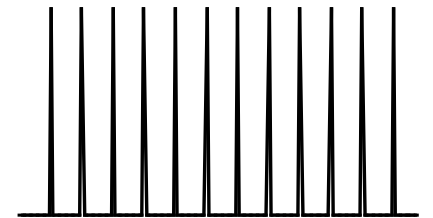
2. Frequency Encoding



3. Phase Encoding

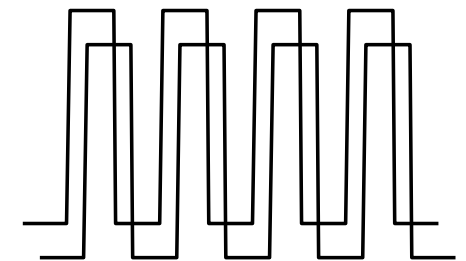


4. Event-Related



5. fMRI adaptation

6. Orthogonal Block Design



7. Free Behavior Design

**Free behavior or naturalistic or continuous stimuli**

**Maguire – navigation**

**U. Hasson – time reversal, cross subject**

**Gallant – semantic space multiple regression**

**DARPA competition – guess what's happening**

Category	Definition	Mean number of occurrences (SD)
Customer-driven Route Planning	Planning a route to a given destination	16.6 (1.8)
Subtypes: Initial plan	Planning from the initial request	6.8 (0.8)
Change in plan	Planning after an en route request from a customer to alter the destination	9.8 (1.0)
Spontaneous Route Planning	Further planning en route, independent of customers	34.3 (10.9)
Subtypes: Filling in	Planning the next stage of the journey	17.7 (6.6)
Re-planning	Altering the current plan to adapt to the environment	16.7 (5.7)
Action Planning	Planning future movements with the vehicle	45.8 (15.1)
Expectation Confirmation	Detecting the presence of an expected environmental feature	28.6 (9.9)
Expectation Violation	Detecting the absence of an expected environmental feature	31.6 (10.5)
Expectation	Looking out for the next expected environmental feature	24.5 (8.5)
Visual Inspection	Visual inspection of an environmental feature	36.0 (11.8)
Monitoring Traffic	Watching moving traffic in the environment	11.4 (5.9)
Coasting	Navigating automatically without any directed thoughts	25.8 (7.5)
Customers' Navigationally-Irrelevant Statements	Navigationally-irrelevant statements by customers, (a control for Customer-driven Route Planning)	6.6 (0.9)

**A**



**B**

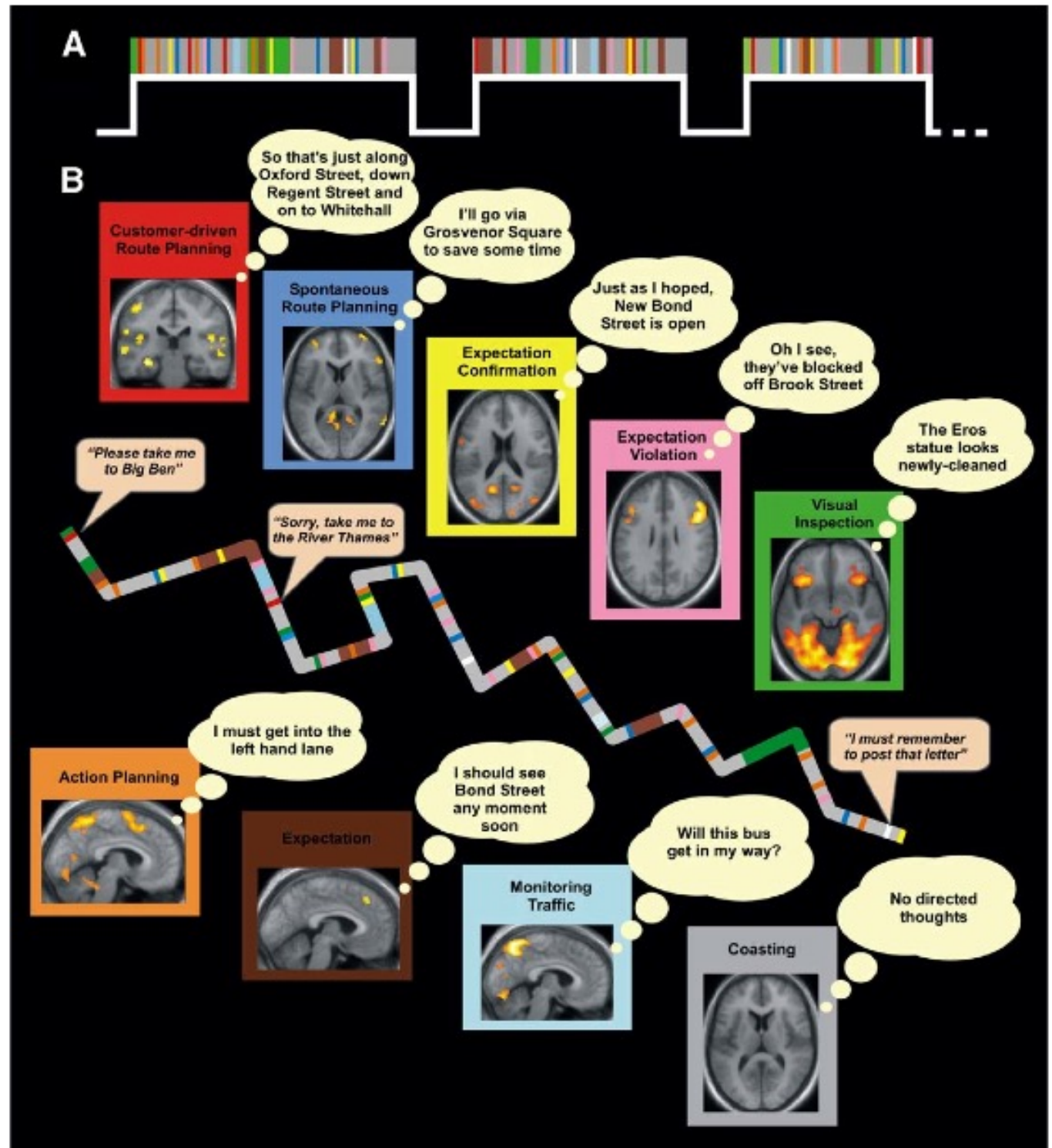


**C**



**Thoughts, behaviour, and brain dynamics during navigation in the real world.** Hugo J. Spiers and Eleanor A. Maguire, *NeuroImage*, 31 (2006), 1826-1840.

Thoughts, behaviour, and brain dynamics during navigation in the real world. Hugo J. Spiers and Eleanor A. Maguire, *NeuroImage*, 31 (2006), 1826-1840.



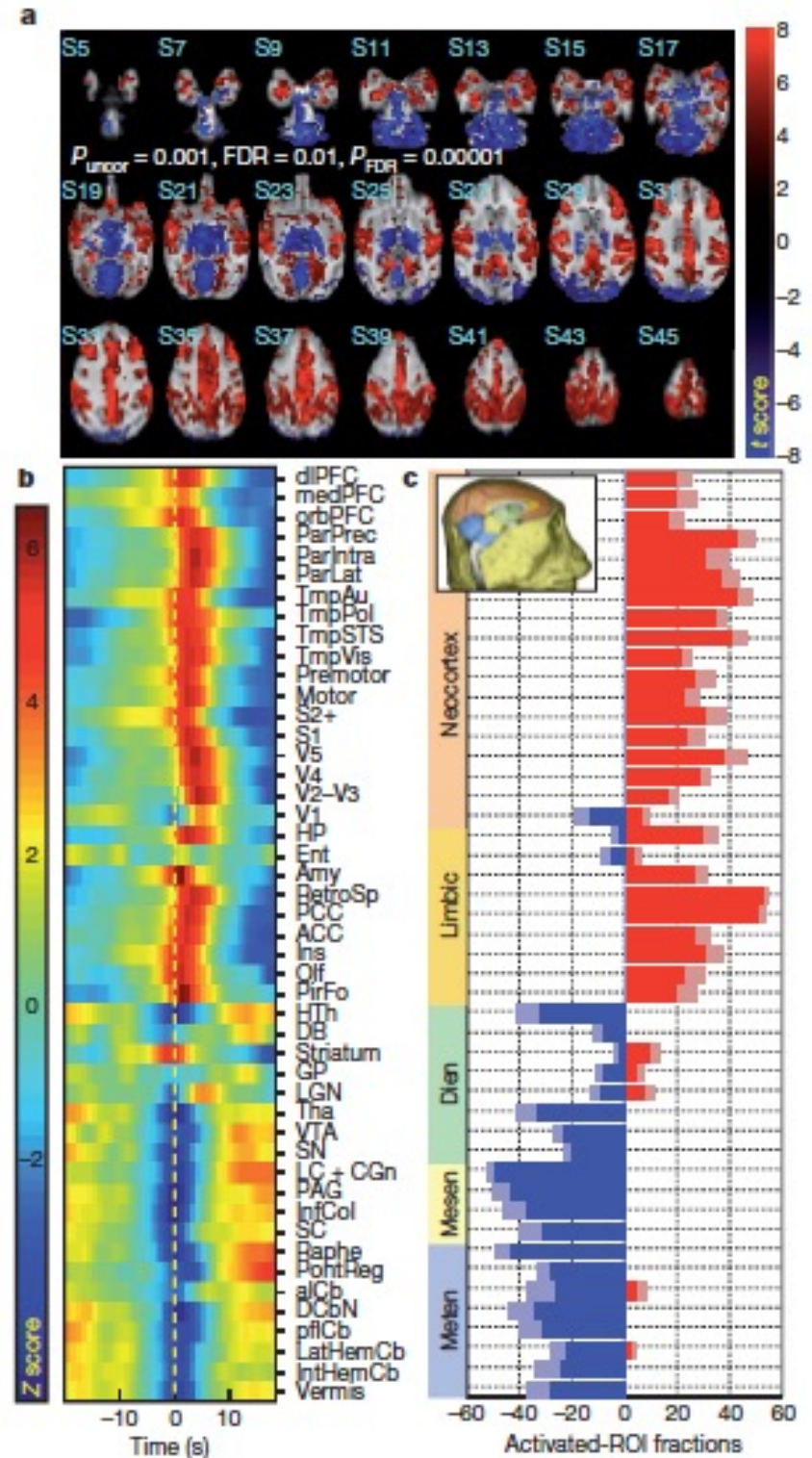
# Multi-modal integration

## Hippocampal–cortical interaction during periods of subcortical silence

N. K. Logothetis<sup>1,2</sup>, O. Eschenko<sup>1</sup>, Y. Murayama<sup>1</sup>, M. Augath<sup>1</sup>, T. Steudel<sup>1</sup>, H. C. Evrard<sup>1</sup>, M. Besserve<sup>1,3</sup> & A. Oeltermann<sup>1</sup>

By combining electrophysiological recordings in hippocampus with ripple-triggered functional magnetic resonance imaging, here we show that most of the cerebral cortex is selectively activated during the ripples, whereas most diencephalic, midbrain and brainstem regions are strongly and consistently inhibited

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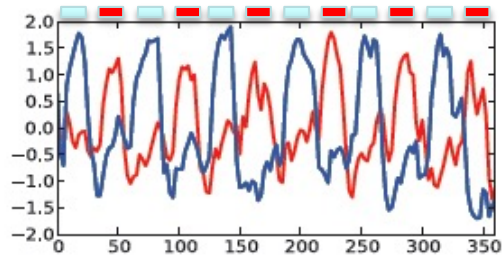
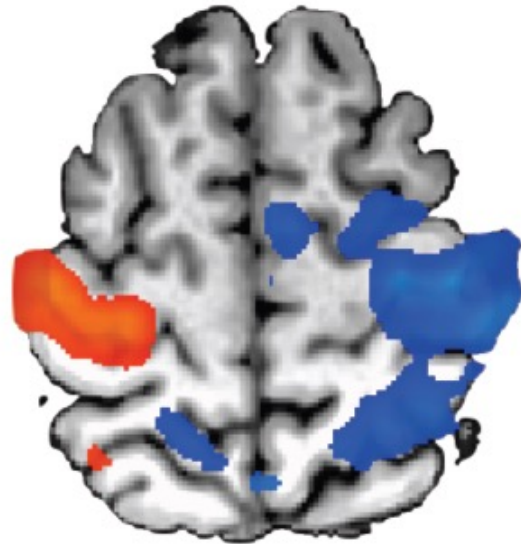


# **fMRI Paradigm Designs and Processing Strategies**

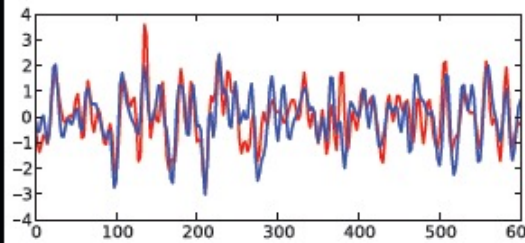
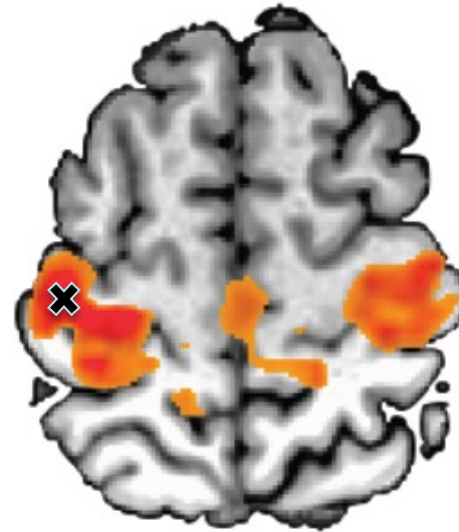
- 1. Neuronal Activation Input Strategies**
- 2. Resting State fMRI**
- 3. fMRI Decoding**

# Activation-based fMRI and “resting state” fMRI

**Task Activation**  
(Right vs. Left Hand Tapping)

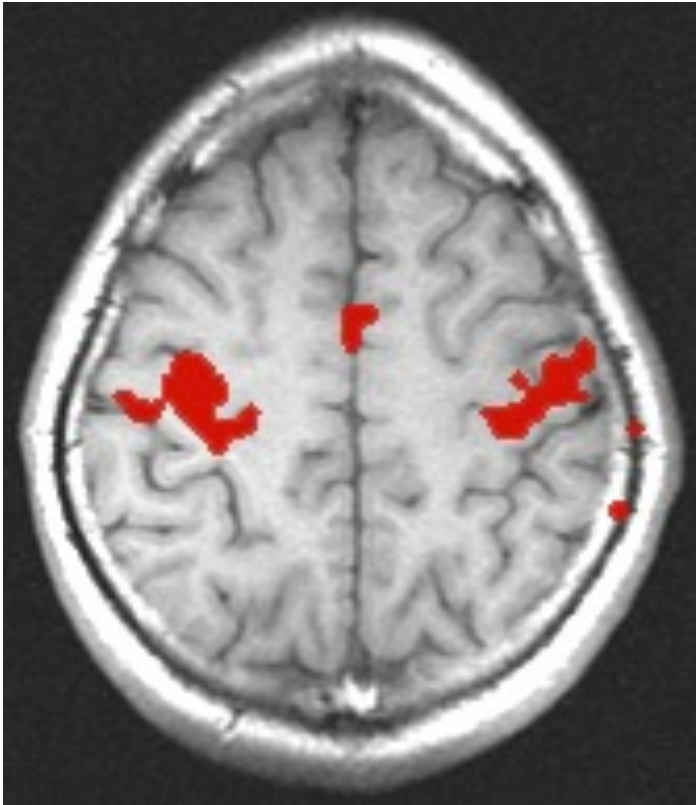


**Resting Correlation**  
(Right Hand Seed)

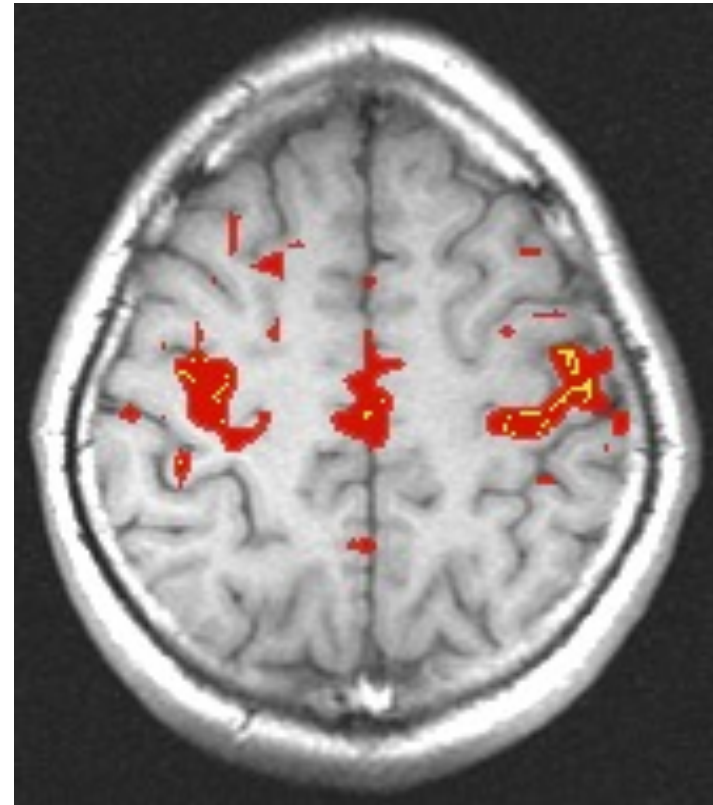




## Resting State Correlations



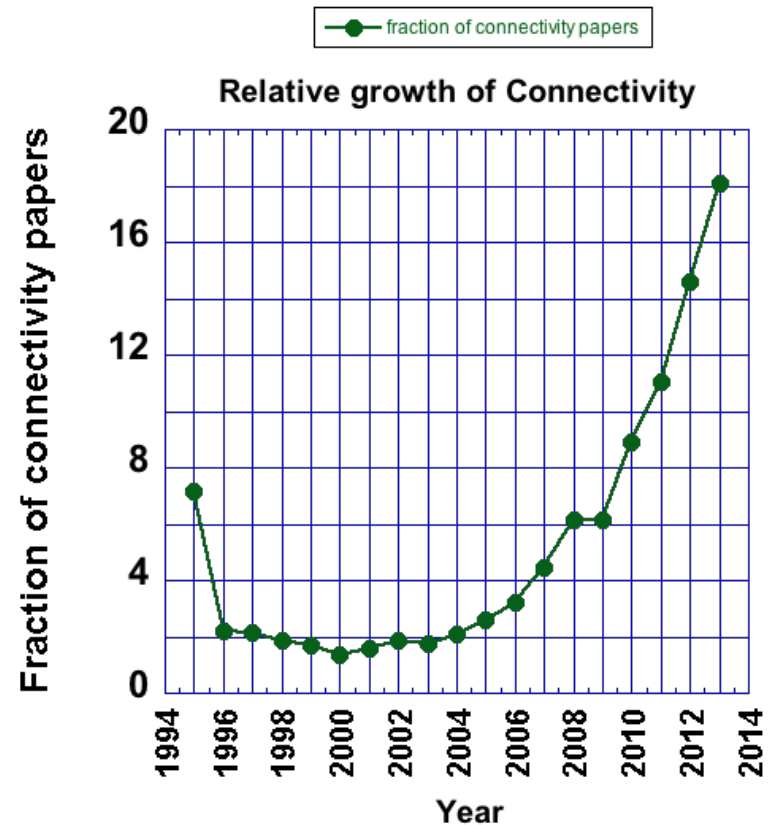
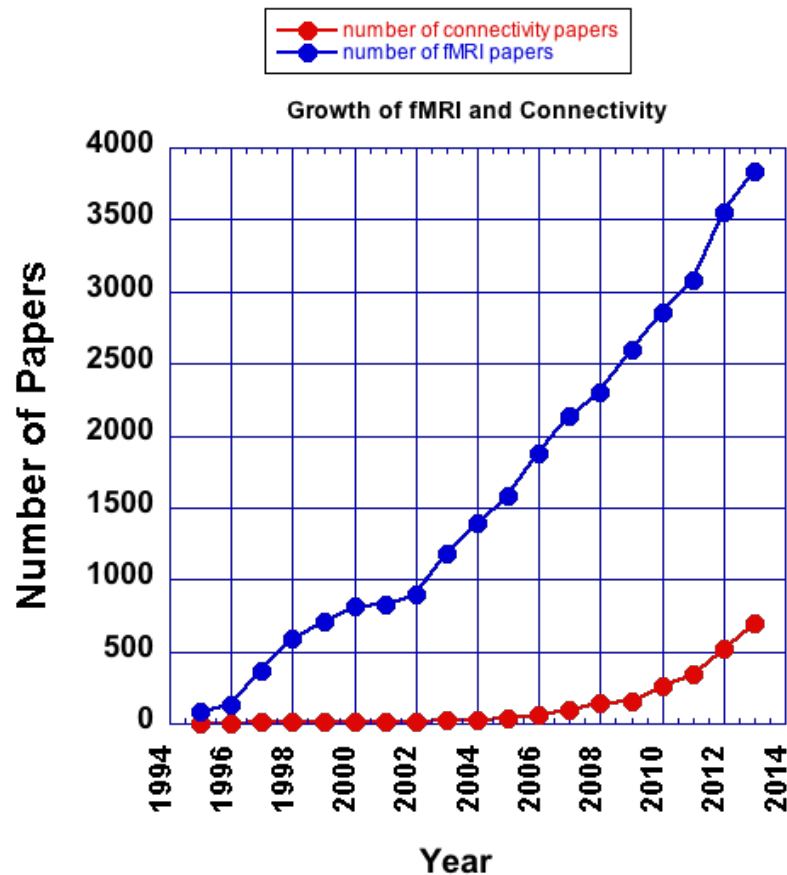
**Activation:**  
correlation with reference function



**Rest:**  
seed voxel in motor cortex

# Resting state fMRI: Why is this area important?

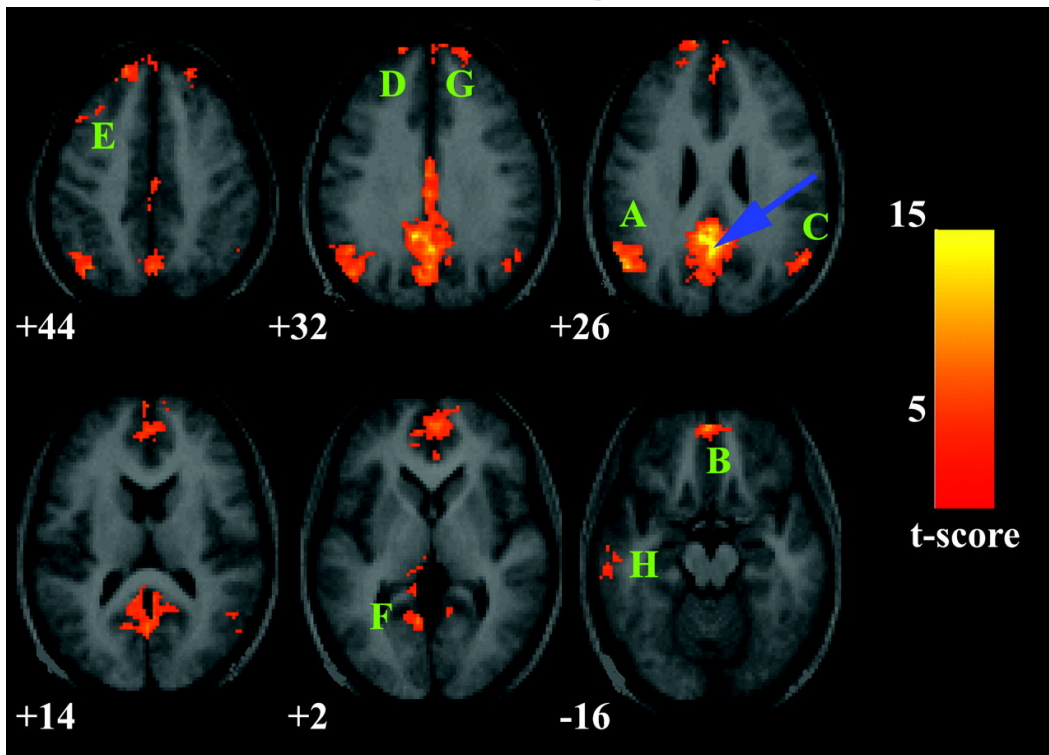
- The number of papers and applications has exploded.
- Neuronal, psychiatric, and developmental disorders may relate to altered connectivity.
- Methods are in their infancy, and rapidly evolving.
- Neuronal correlates of spontaneous fluctuations are not fully understood.



# ICA

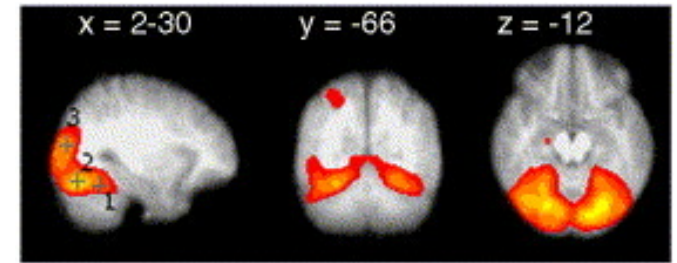
## Seed Voxel

### Seed Based Correlation from the Posterior Cingulate Cortex

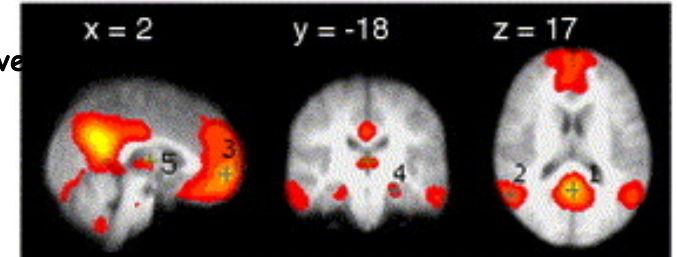


Greicius M D et al. PNAS 2003;100:253-258

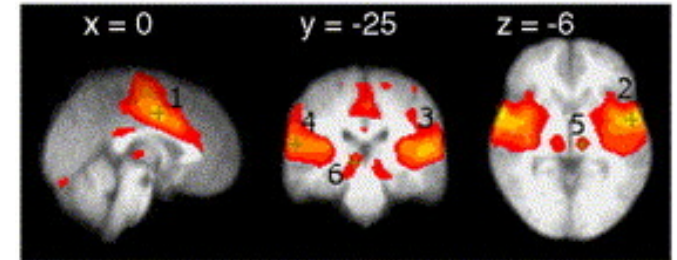
Visual



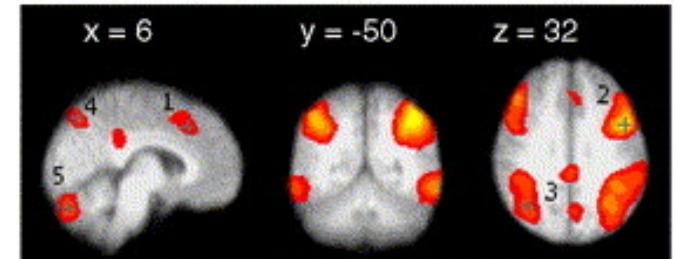
Visuospatial Executive



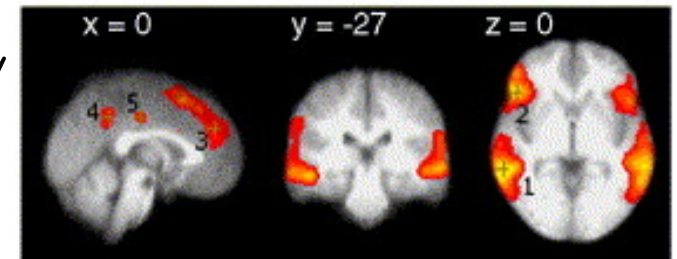
Sensory Auditory



Dorsal Pathway



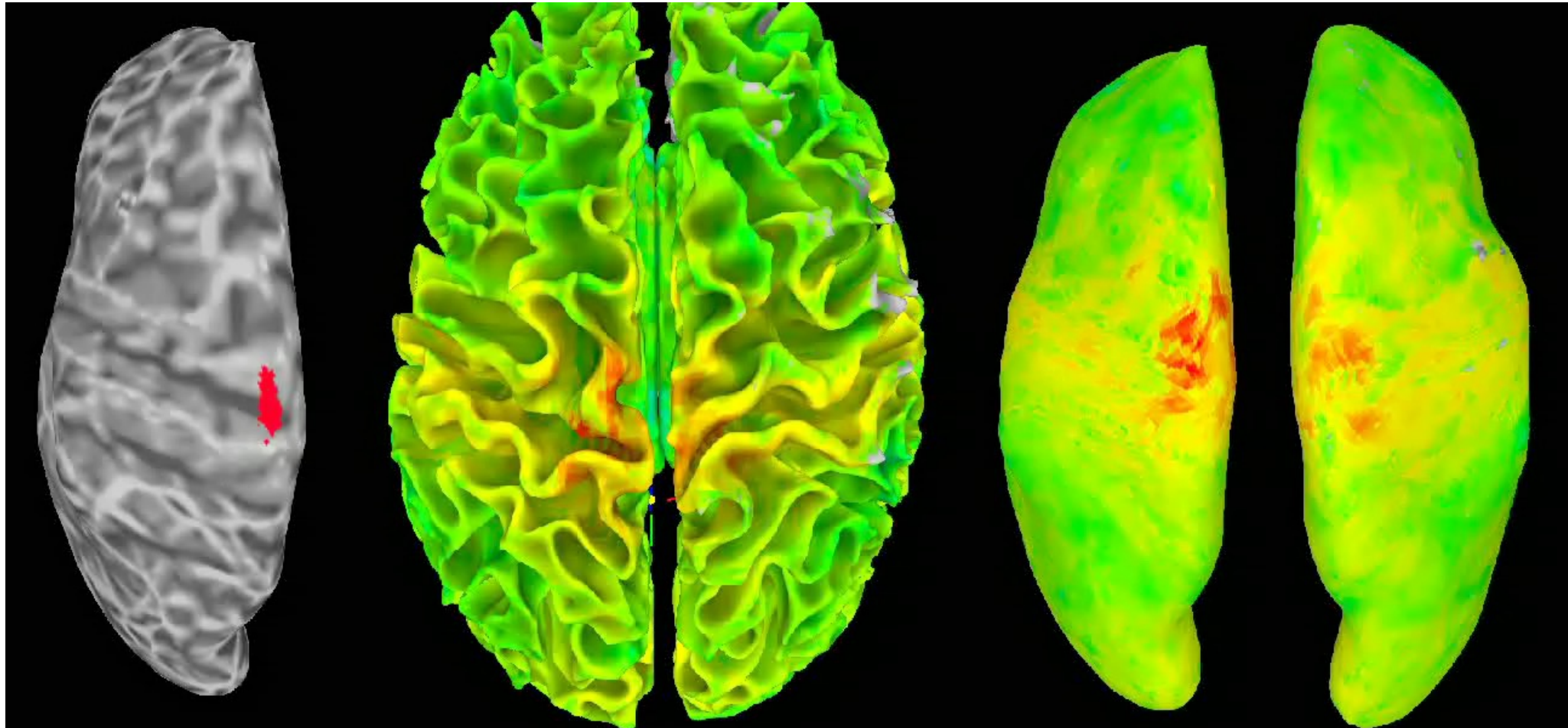
Ventral Pathway



De Luca, Neuroimage 27(4) 2000

# Sliding Seed Movies

Relative correlation strength pattern obtained with a systematically shifted seed region

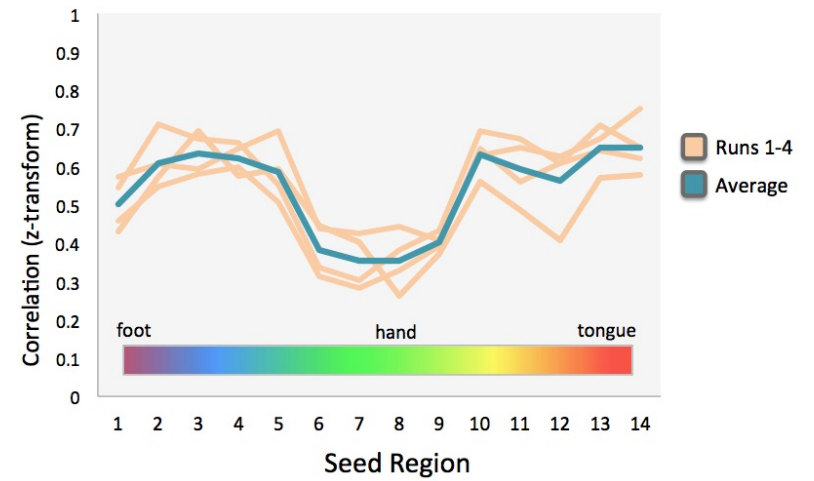
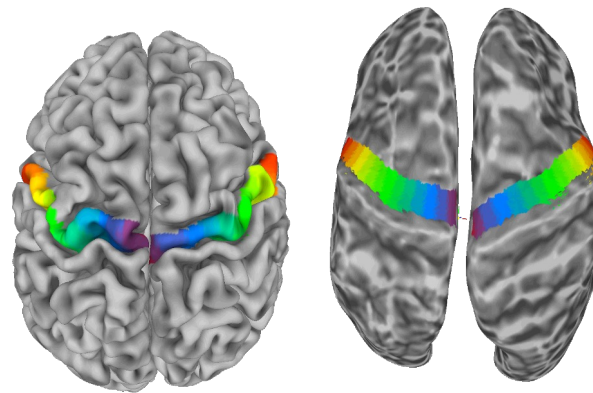
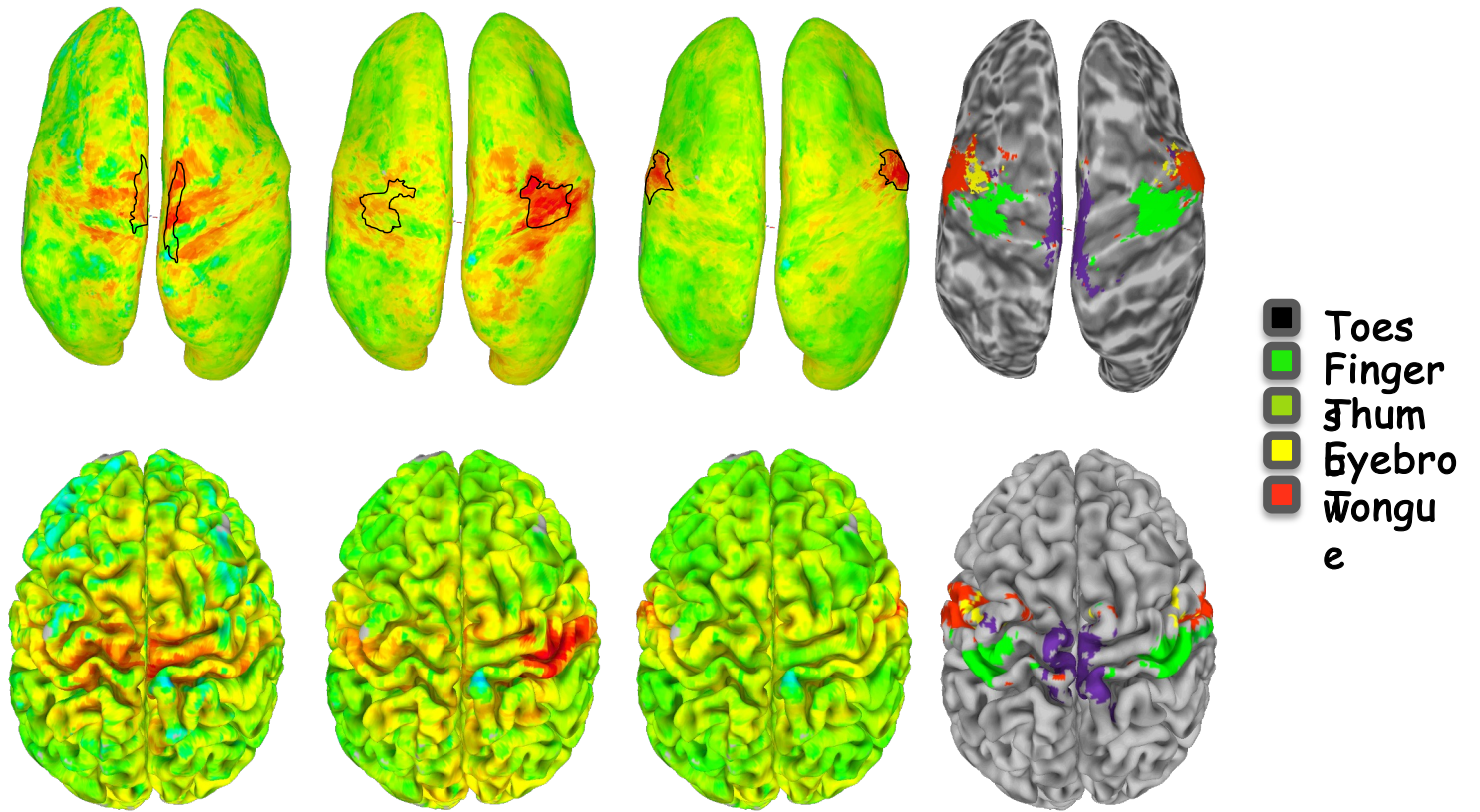


Seed 1

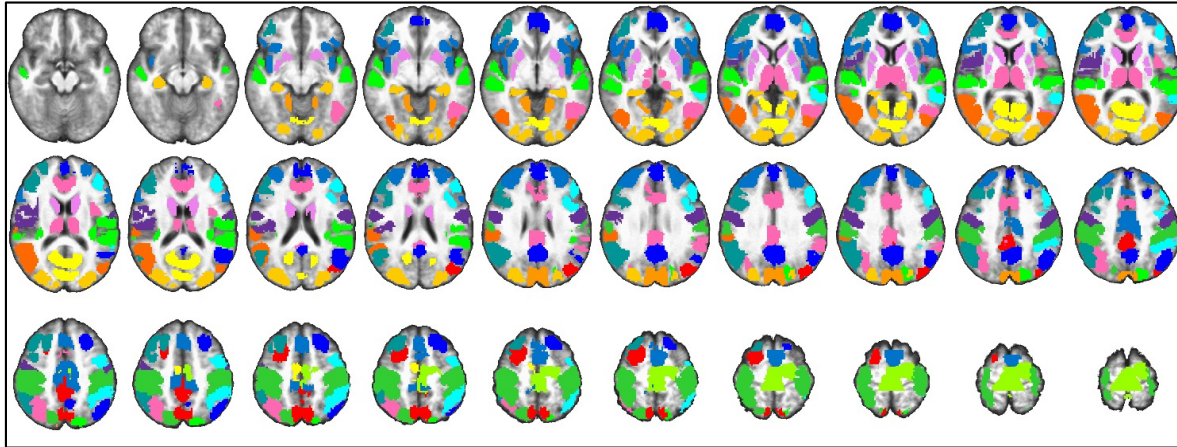
GM/WM Boundary

LH (seed hemi)

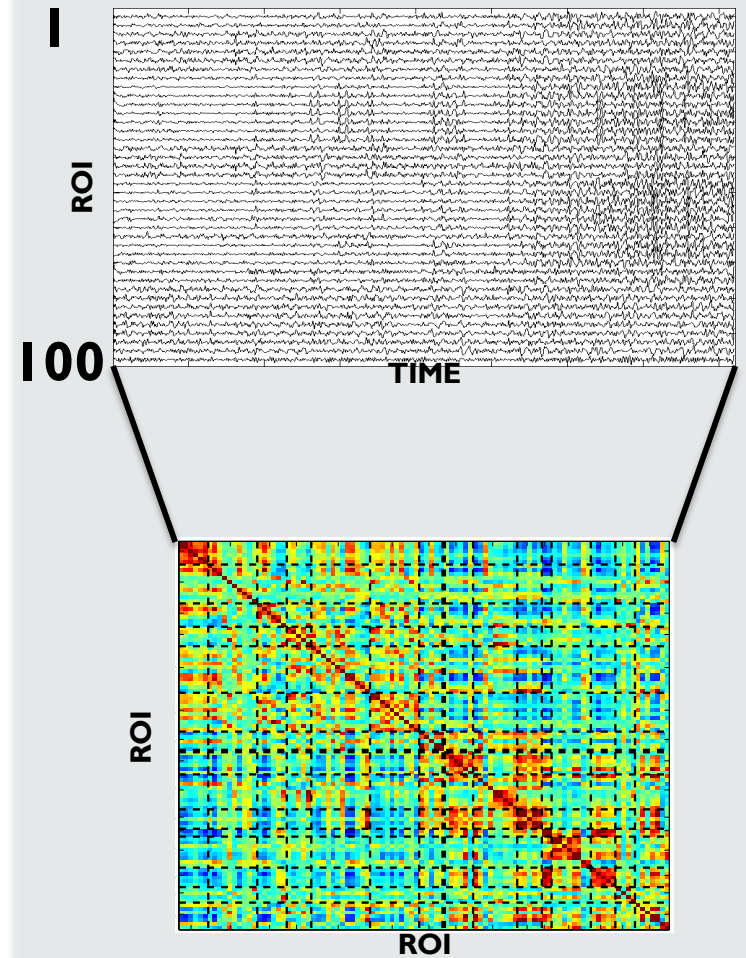
RH (contra hemi)



# Time Course Correlation Matrix



## PAIR-WISE TIME COURSE CORRELATION MATRIX





<http://www.nil.wustl.edu>





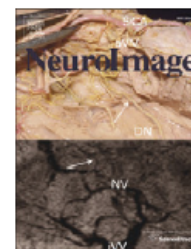


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journal homepage: [www.elsevier.com/locate/ynimg](http://www.elsevier.com/locate/ynimg)



## Differentiating BOLD and non-BOLD signals in fMRI time series using multi-echo EPI

Prantik Kundu<sup>a,c,\*</sup>, Souheil J. Inati<sup>b</sup>, Jennifer W. Evans<sup>a,d</sup>, Wen-Ming Luh<sup>b</sup>, Peter A. Bandettini<sup>a,b</sup>

<sup>a</sup> Section on Functional Imaging Methods, Laboratory of Brain and Cognition, National Institutes of Health, Bethesda, MD, 20892 USA

<sup>b</sup> Functional MRI Facility, National Institute of Mental Health, National Institutes of Health, Bethesda, MD, 20892 USA

<sup>c</sup> Department of Psychiatry, University of Cambridge, Addenbrooke's Hospital, Hills Road, Cambridge, CB2 2QQ UK

<sup>d</sup> Center for Neuroscience and Regenerative Medicine, Henry M. Jackson Foundation, Rockville, Maryland, 20852 USA

## Integrated strategy for improving functional connectivity mapping using multiecho fMRI

Prantik Kundu<sup>a,b,1</sup>, Noah D. Brenowitz<sup>a</sup>, Valerie Voon<sup>b</sup>, Yulia Worbe<sup>b</sup>, Petra E. Vértes<sup>b</sup>, Souheil J. Inati<sup>c</sup>, Ziad S. Saad<sup>d</sup>, Peter A. Bandettini<sup>a,c,2</sup>, and Edward T. Bullmore<sup>b,e,f,2</sup>

PNAS Vol 110, No 40, 16187-

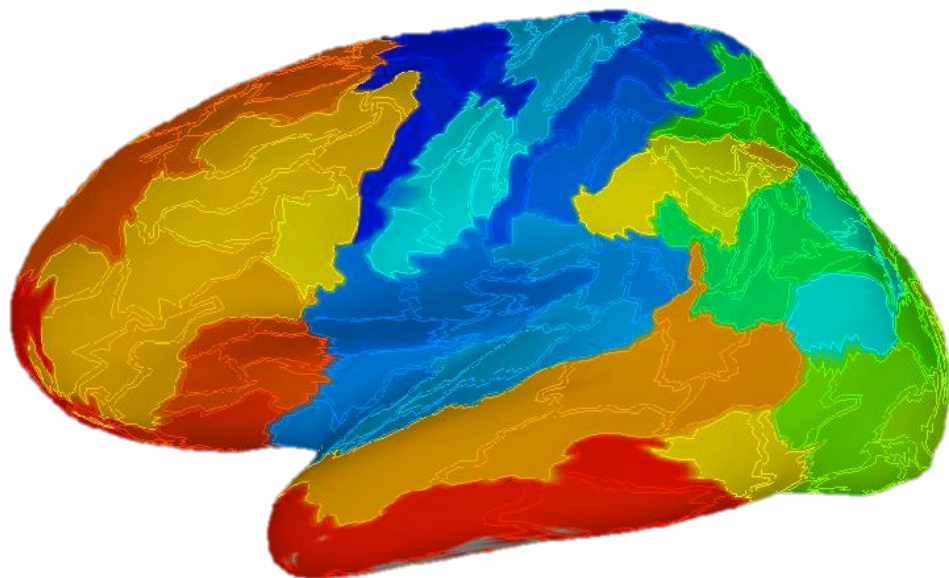
16192

<sup>a</sup>Section on Functional Imaging Methods, <sup>b</sup>Functional MRI Core Facility, and <sup>c</sup>Statistical and Scientific Computing Core, National Institute of Mental Health, Bethesda, MD 20814; <sup>d</sup>Behavioural and Clinical Neuroscience Institute, University of Cambridge, Cambridge CB2 1QP, United Kingdom; <sup>e</sup>National Institute of Health Research Cambridge Biomedical Research Centre, Cambridgeshire Peterborough National Health System Foundation Trust, Cambridge SW1A 2NS, United Kingdom; and <sup>f</sup>Clinical Unit Cambridge, GlaxoSmithKline, Cambridge CB2 0QQ, United Kingdom

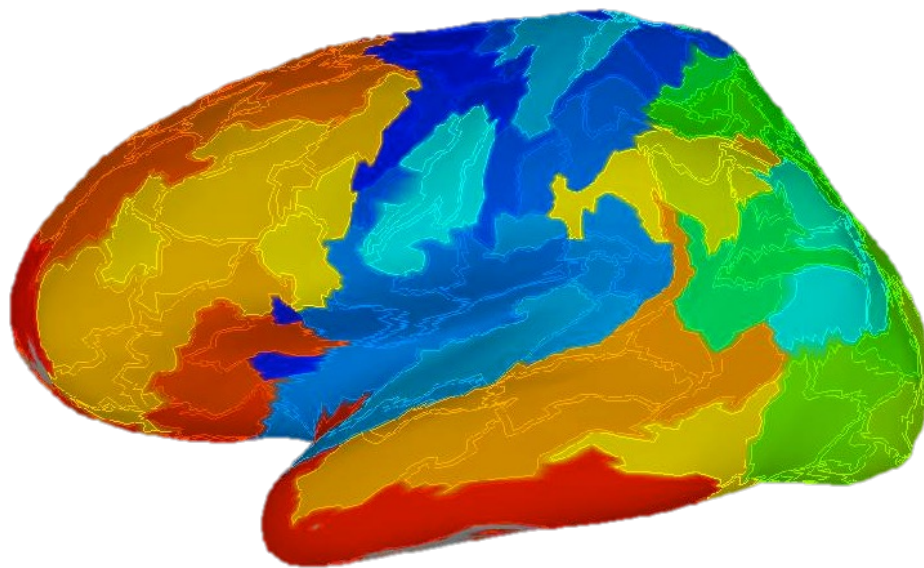
Edited by Marcus E. Raichle, Washington University in St. Louis, St. Louis, MO, and approved July 31, 2013 (received for review January 29, 2013)

Test-retest of **group** clustering at 350 clusters

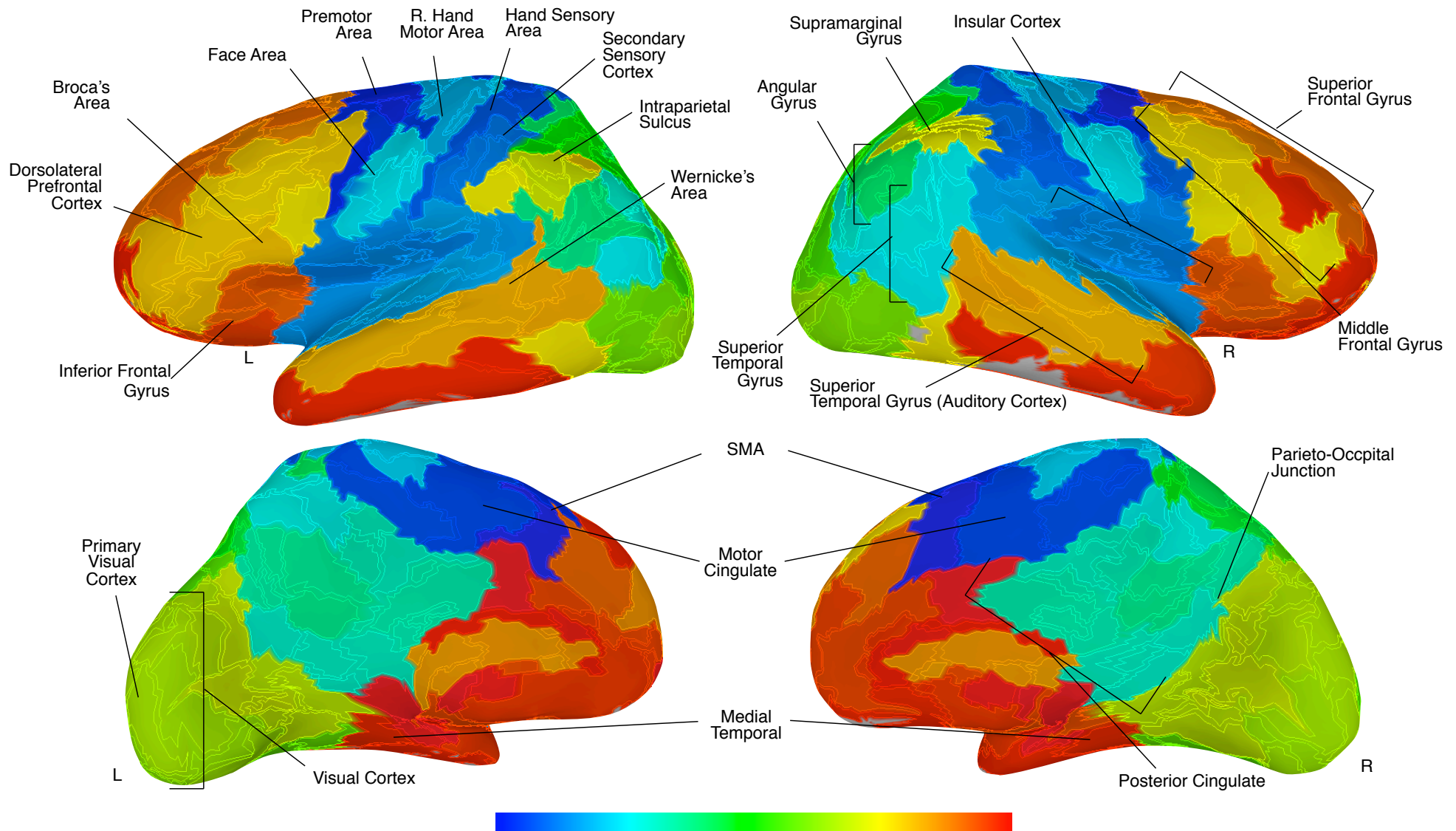
*Rest 1*

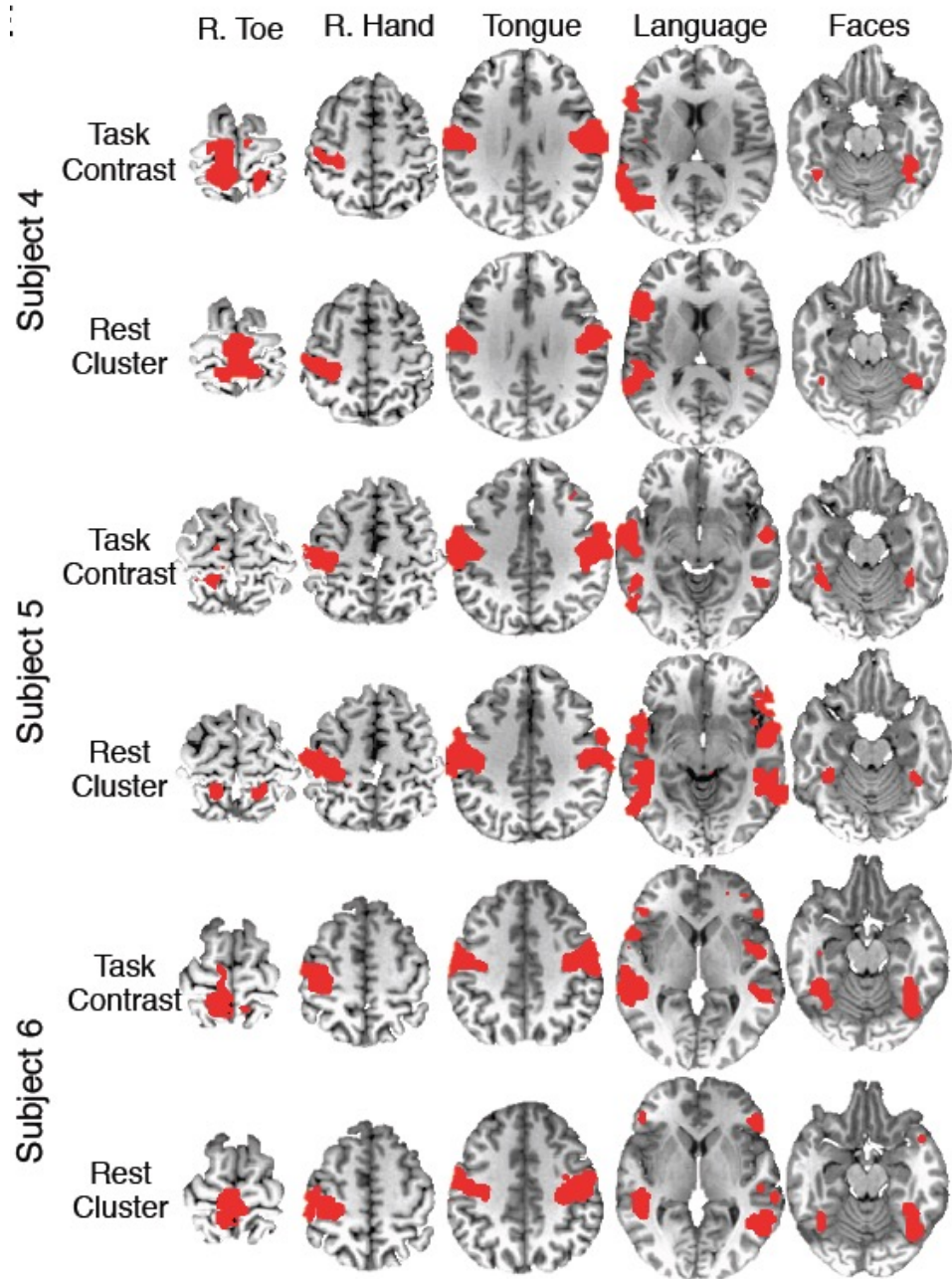
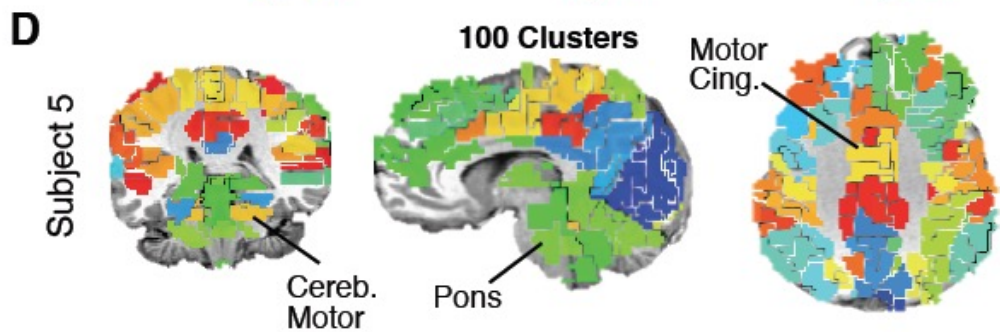
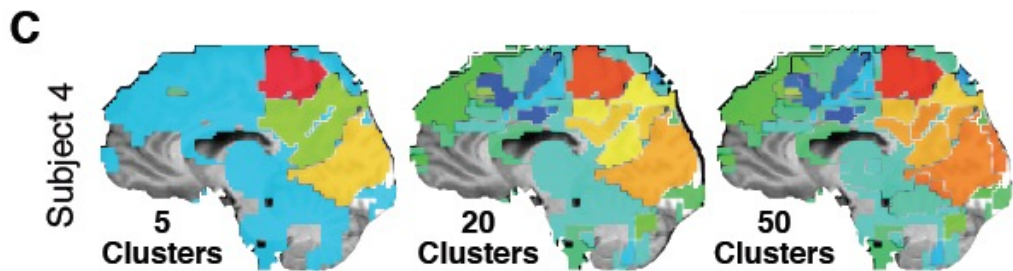


*Rest 2*  
(color matched to Rest 1)



# Clustering based on Resting State

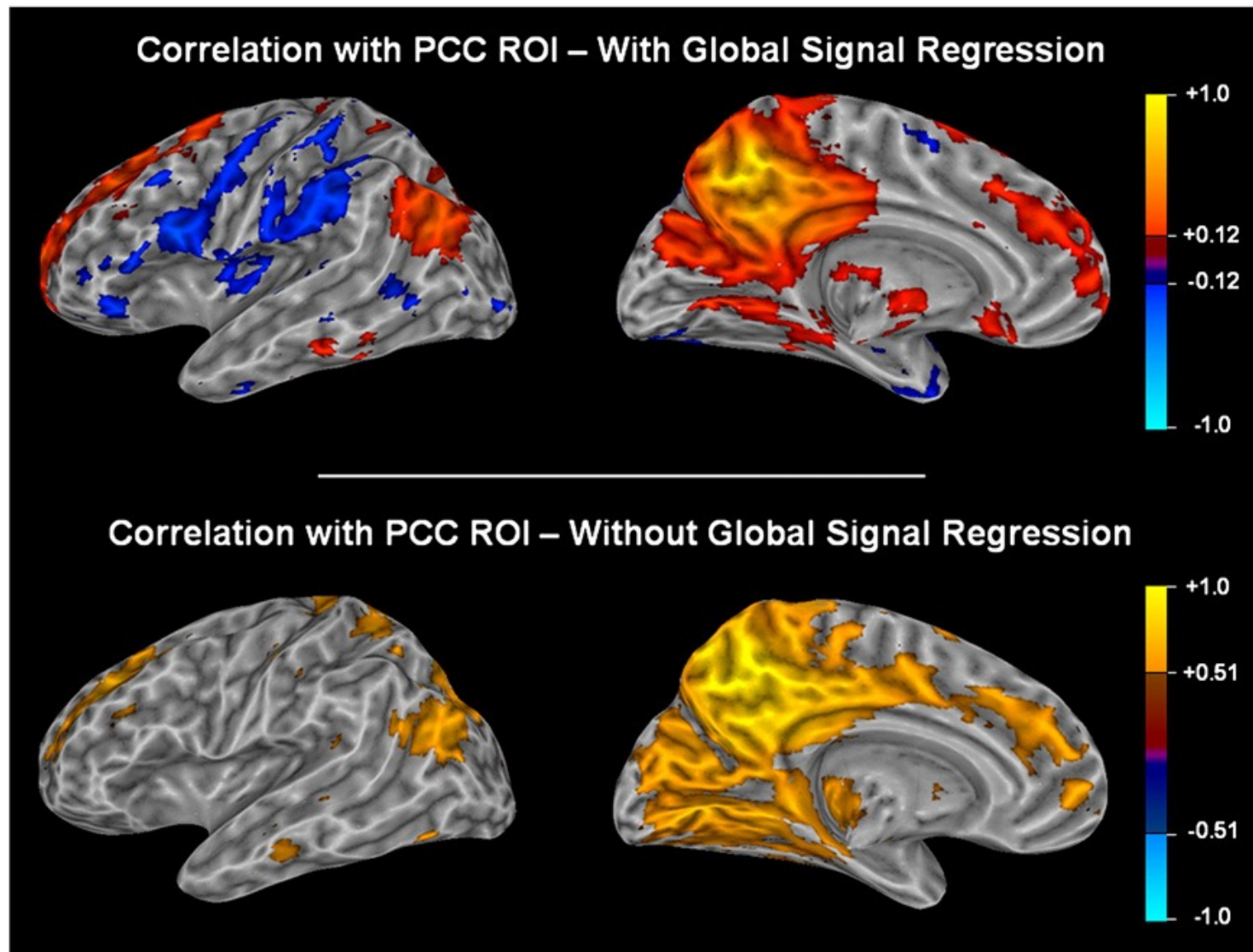




Two other issues with imaging resting state fluctuations:

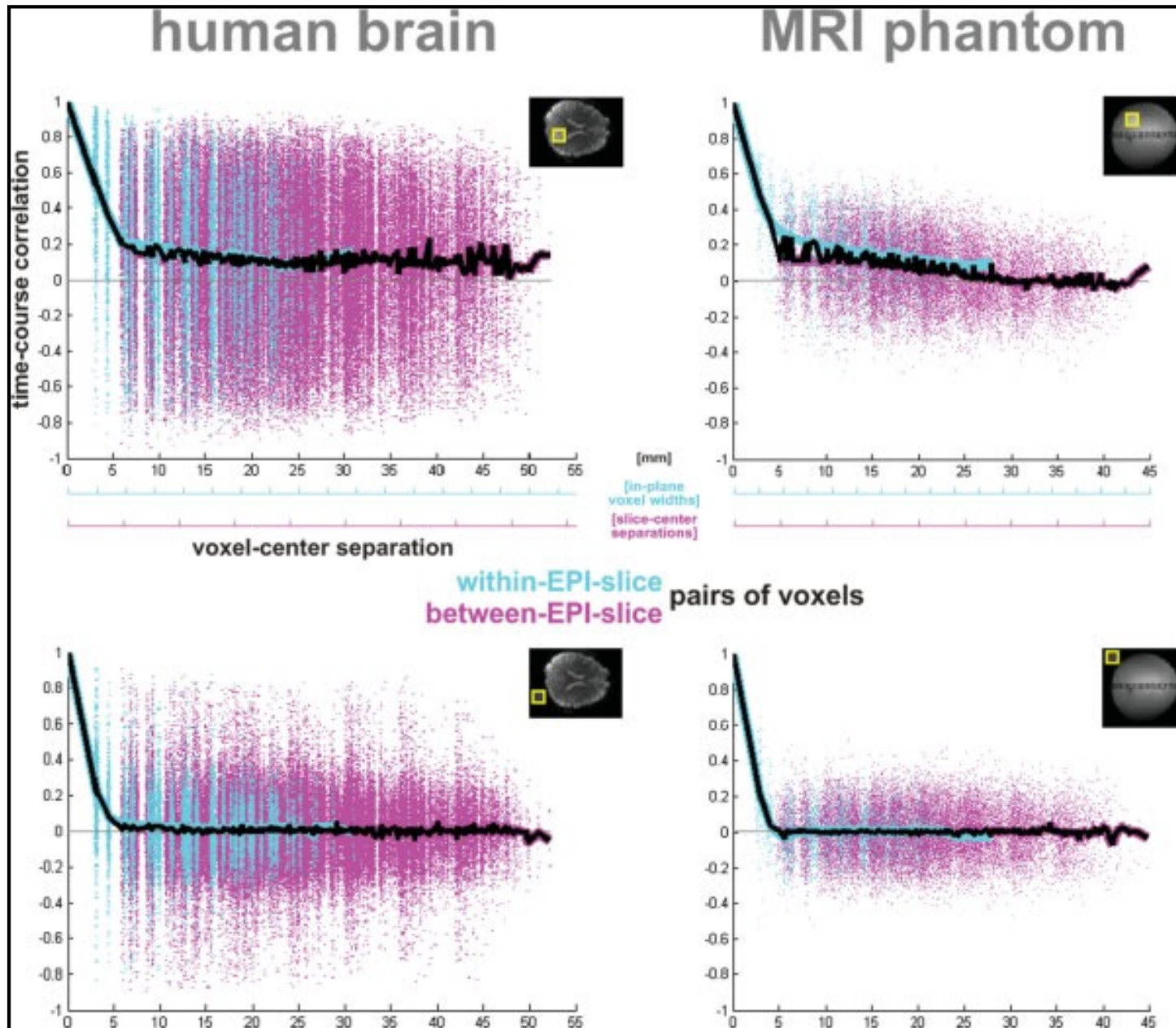
1. Global signal correction or not?
2. Short range correlations may be scanner-related.

# The issue of global signal regression



K. Murphy, R. M. Birn, D. A. Handwerker, T. B. Jones, P. A. Bandettini, *NeuroImage*, 44, 893-905 (2009)

The issue of correlation across voxels due scanner instabilities



N. Kriegeskorte, J. Bodurka, P. Bandettini, *International Journal of Imaging Systems and Technology*, 18 (5-6), 345-349 (2008)

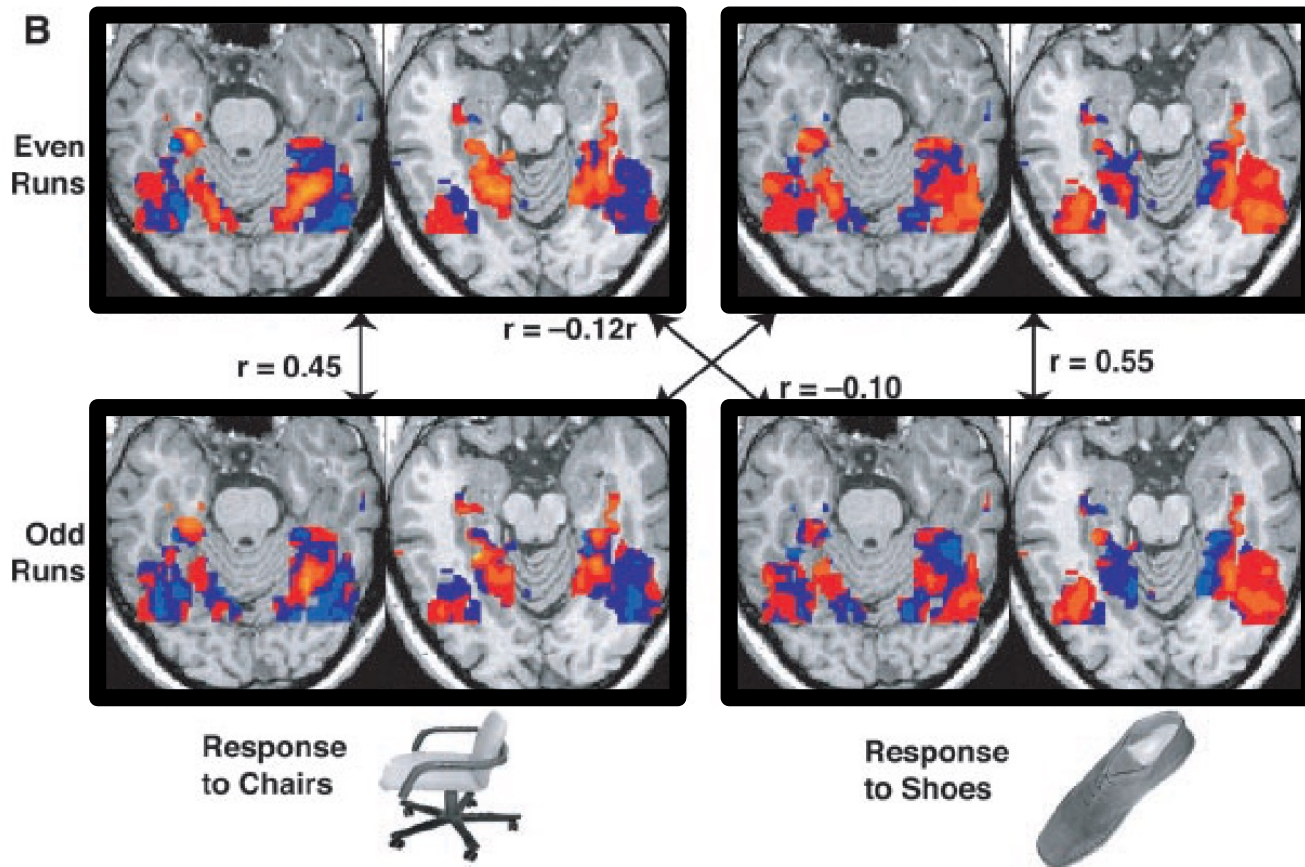
# **fMRI Paradigm Designs and Processing Strategies**

- 1. Neuronal Activation Input Strategies**
- 2. Resting State fMRI**
- 3. fMRI Decoding**



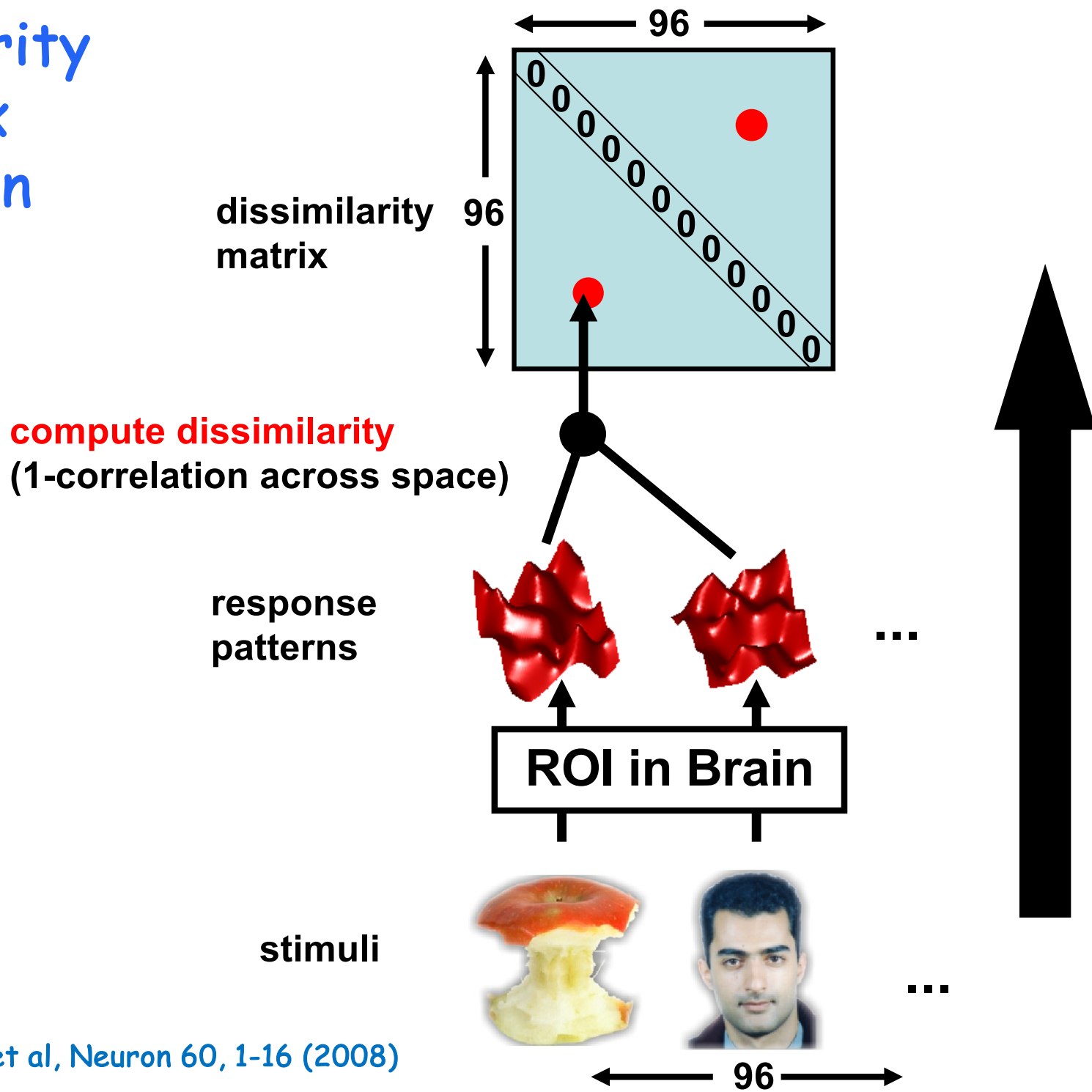
# Ventral temporal category representations

Object categories are associated with distributed representations in ventral temporal cortex



Haxby et al. Nature 2001

# Dissimilarity Matrix Creation

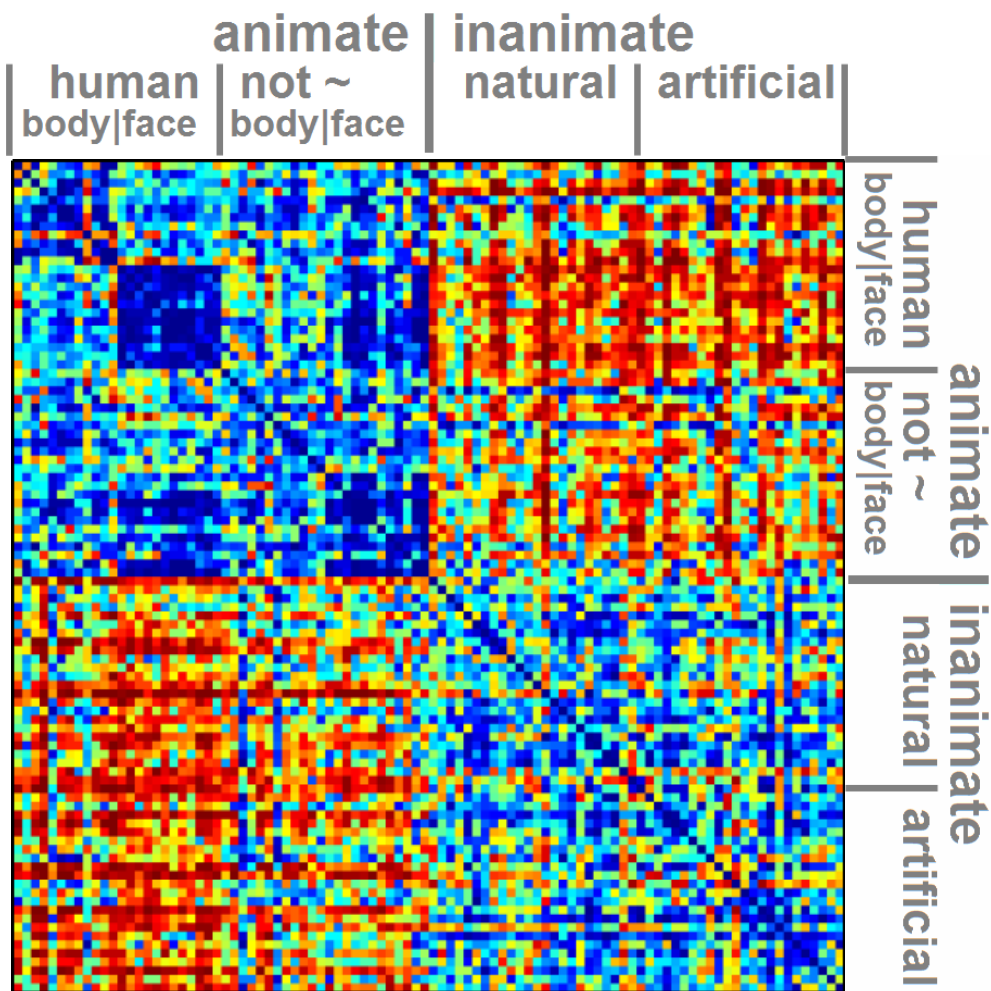


# Visual Stimuli



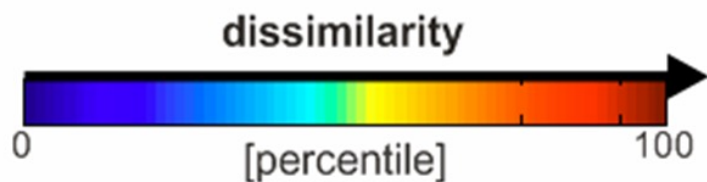
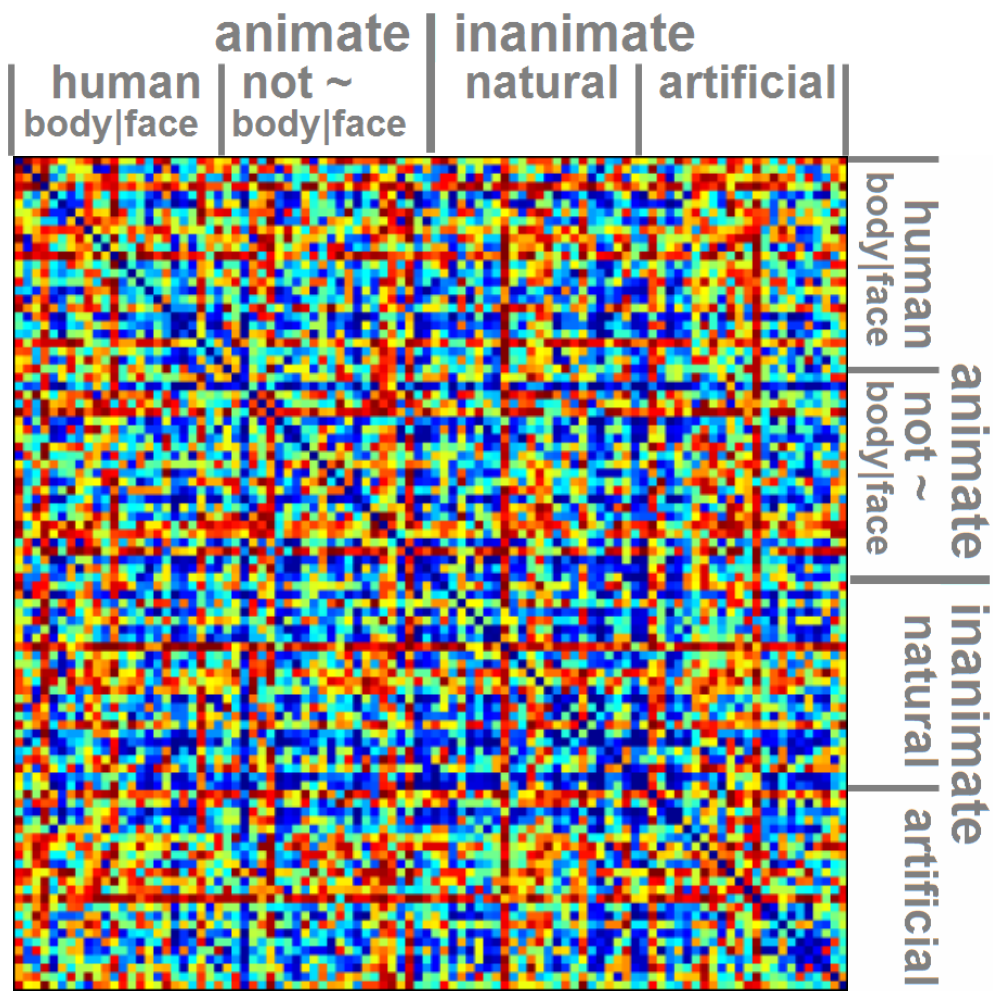
# Human IT

(1000 visually most responsive voxels)



# Human Early Visual Cortex

(1057 visually most responsive voxels)



# Monkey-Human Comparison Procedure

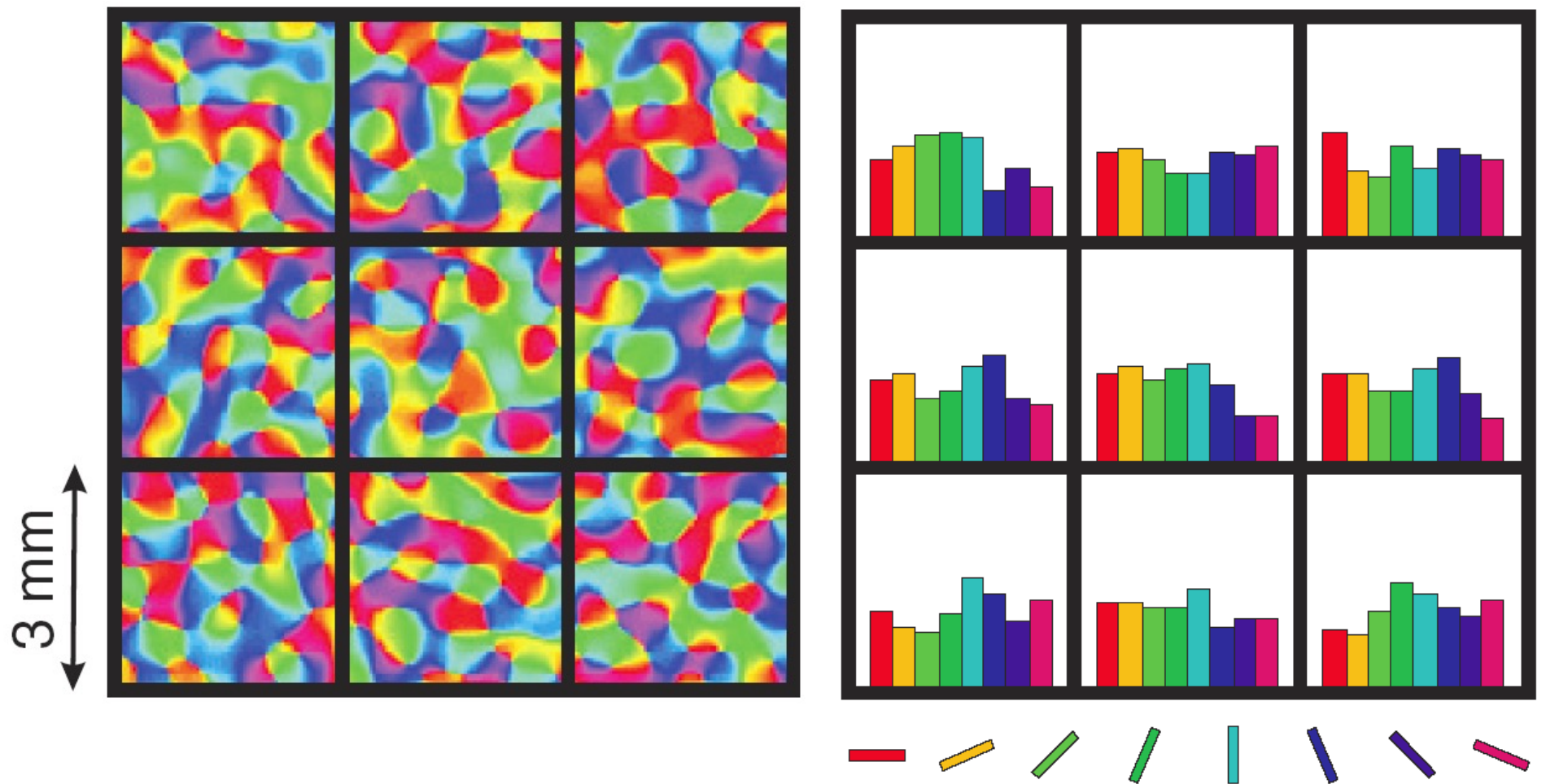
## Human

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

## Monkey (Kiani et al. 2007)

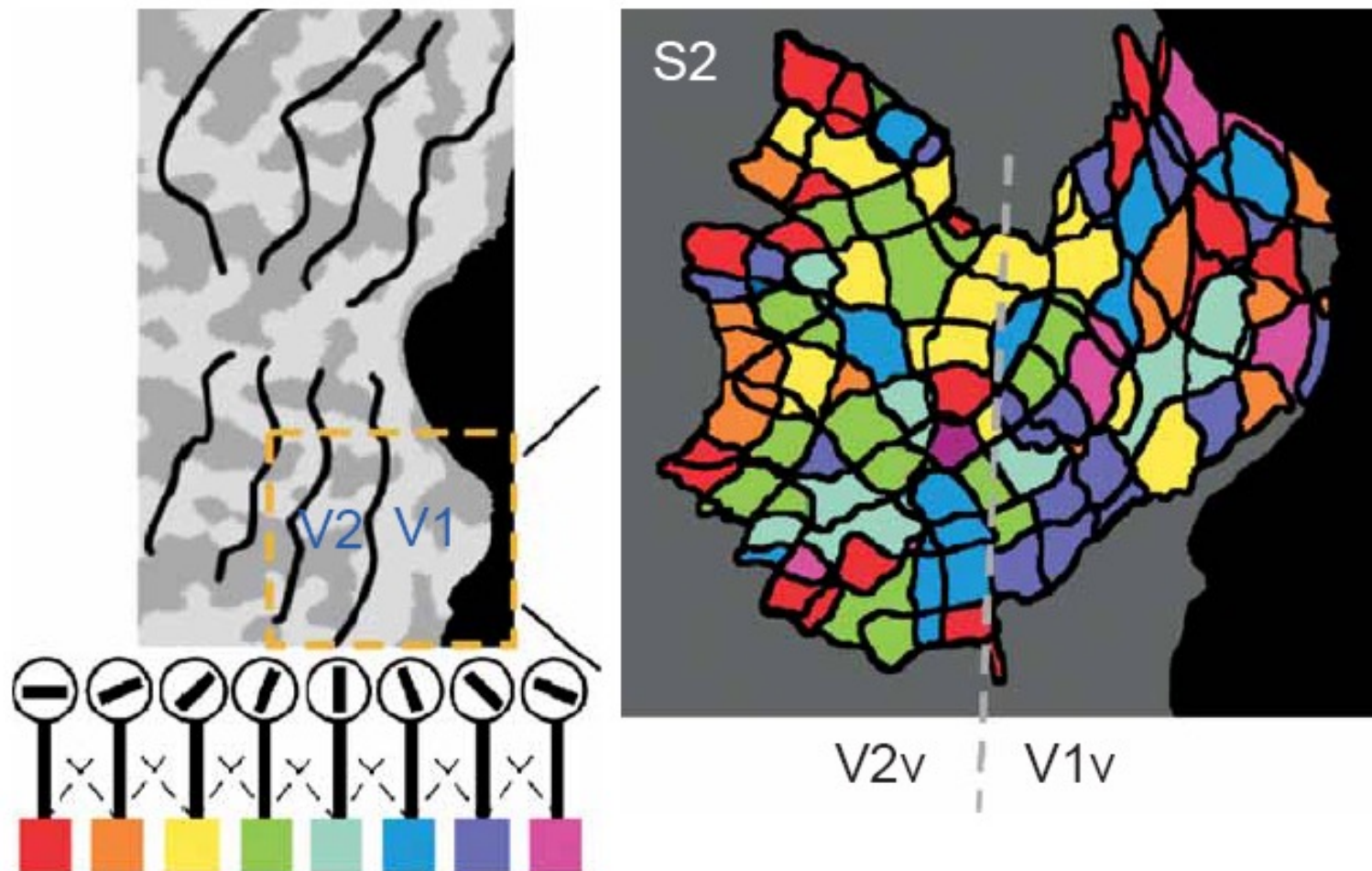
- single-cell recordings  
in two monkeys
- rapid serial presentation  
(stimulus duration: 105ms)
- fixation task
- electrodes in anterior IT  
(left in monkey 1, right in monkey 2)
- 674 cells total
- windowed spike count  
(140-ms window starting 71ms after  
stimulus onset)





Boynton (2005), News & Views on Kamitani & Tong (2005) and Haynes & Rees (2005)

# Lower spatial frequency clumping



Kamitani & Tong (2005)



# **fMRI Paradigm Designs and Processing Strategies**

- 1. Neuronal Activation Input Strategies**
- 2. Resting State fMRI**
- 3. fMRI Decoding**