

# fMRI Methods That Have Not Caught On

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**&**

**Functional MRI Facility**

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



Le Medecin guarissant Phantasie

Purgeant aussi Par drogues la folie



## Acquisition:

- **Spiral Scanning**
- Multi-Shot Spiral
- Multi-shot EPI
- Keyhole Imaging
- Partial k-space
- Echo-volume imaging
- 3D EPI
- Zoomed EPI
- Multiband excitation
- Low flip angle

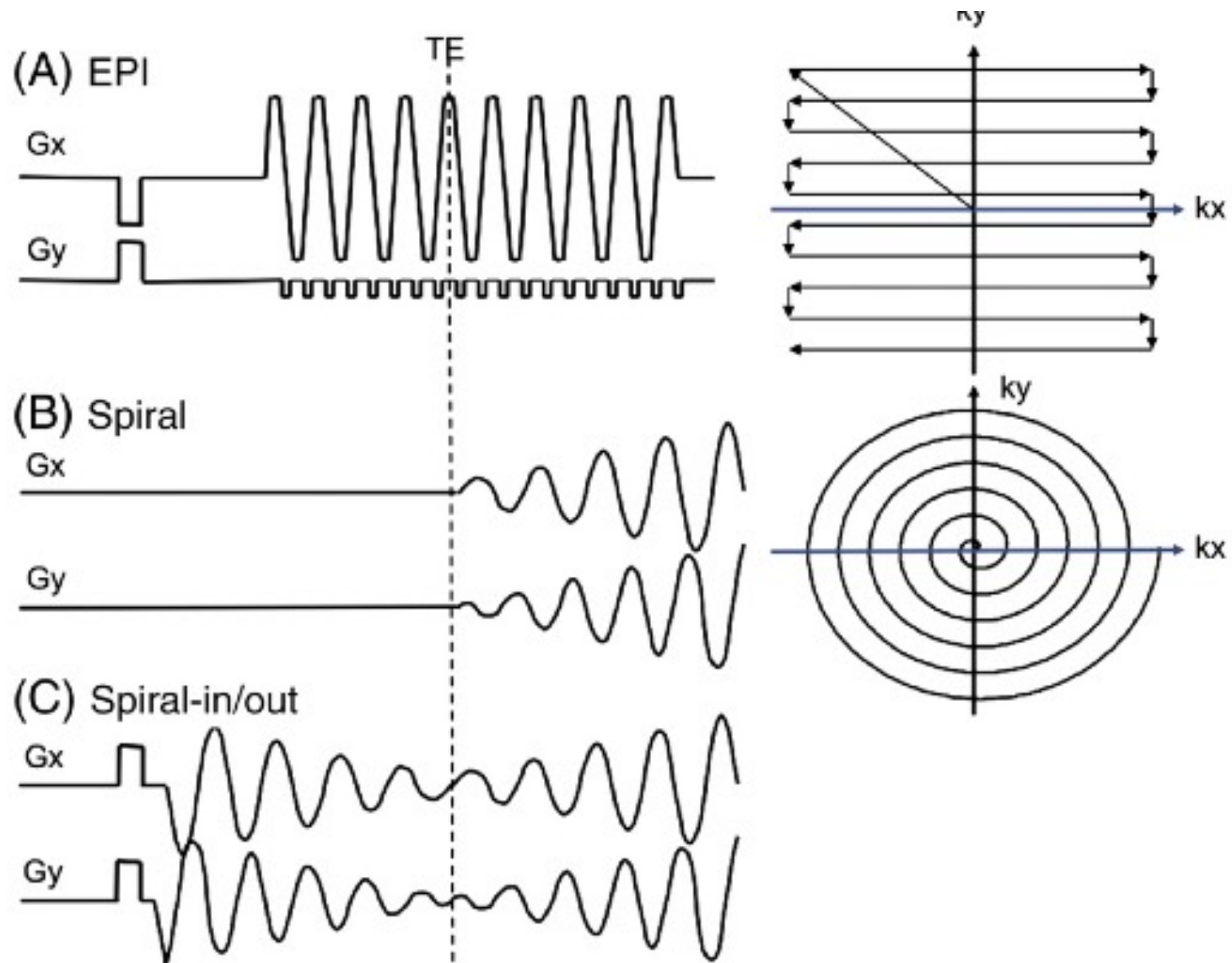
## Contrast Weighting

- Spin-echo
- Asymmetric Spin-Echo
- Arterial Spin Labeling
- VASO
- Low b Diffusion Weighting
- High b Diffusion Weighting
- Neuronal Current Imaging
- Multi-echo acquisition
- MRI time series phase information
- Steady State Free Precession
- Manganese contrast

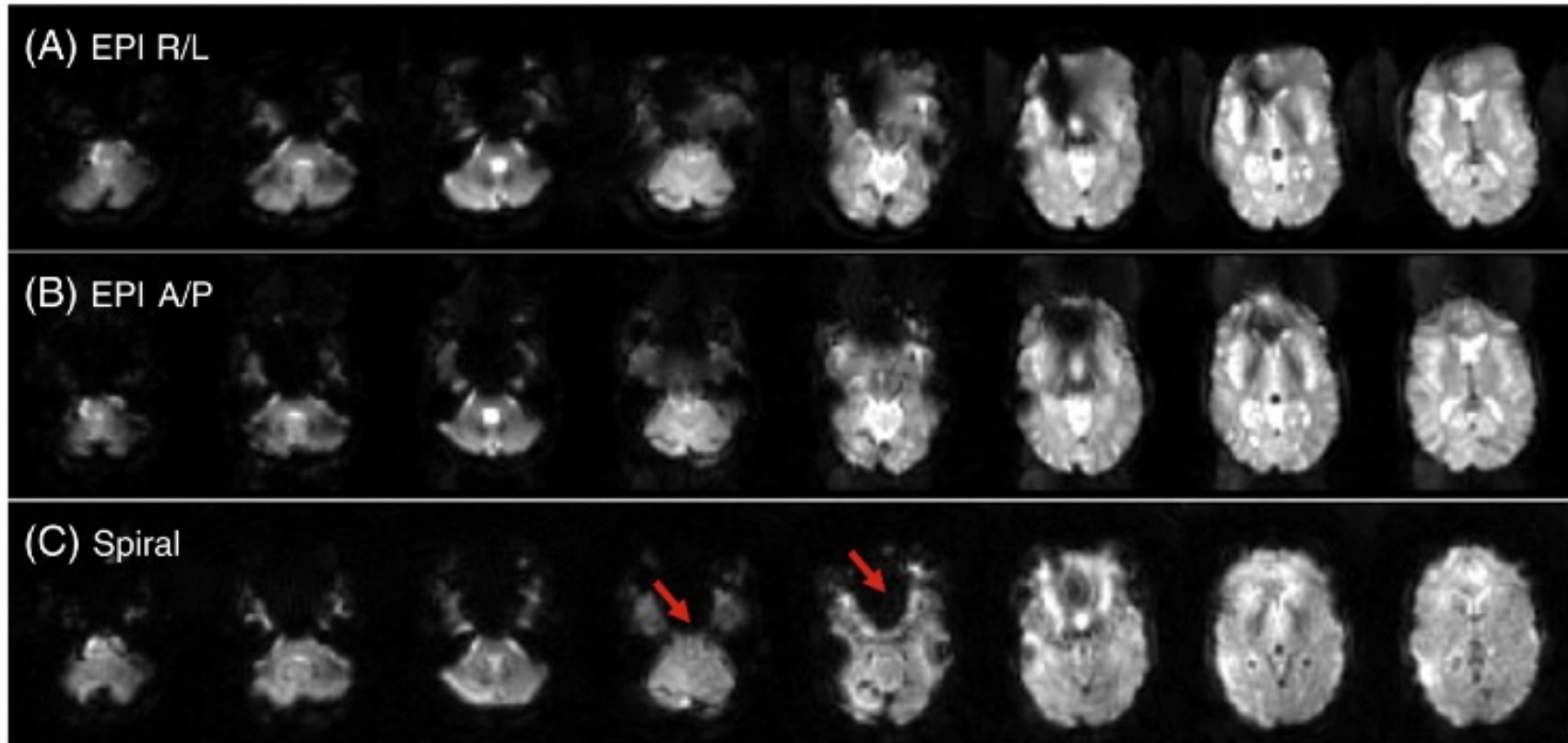
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- Gating and variable TR correction
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- large raw data databases

# Spiral Scanning

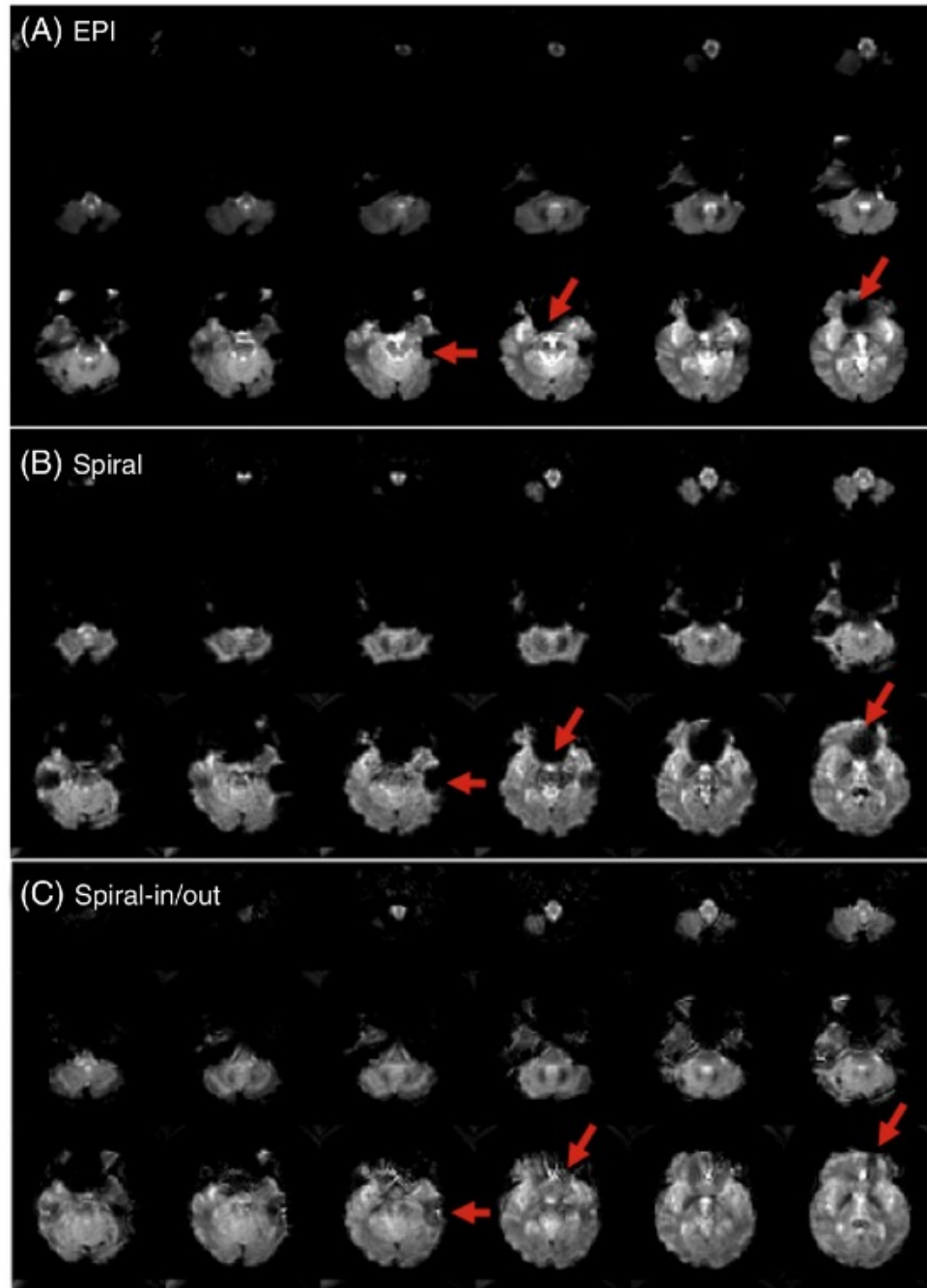


# Spiral Scanning



**Fig. 3.** EPI images with phase encoding direction R/L (A) or A/P (B). Susceptibility-induced field gradients (SFGs) cause geometric distortion along the phase encoding direction. With spiral (C), SFGs instead cause blurring. Note that there is increased signal in most slices with spiral, but loss in several slices (arrows).

# Spiral Scanning



G. Glover, NeuroImage 62, 706-12 (2012)

# Spiral Scanning

## Pros

- No distortion
- Minimal motion sensitivity
- Efficient

## Cons

- Blurring
- Pulsation effects are ripples  
(not lines as with EPI)
- Reconstruction requires regridding – slower.

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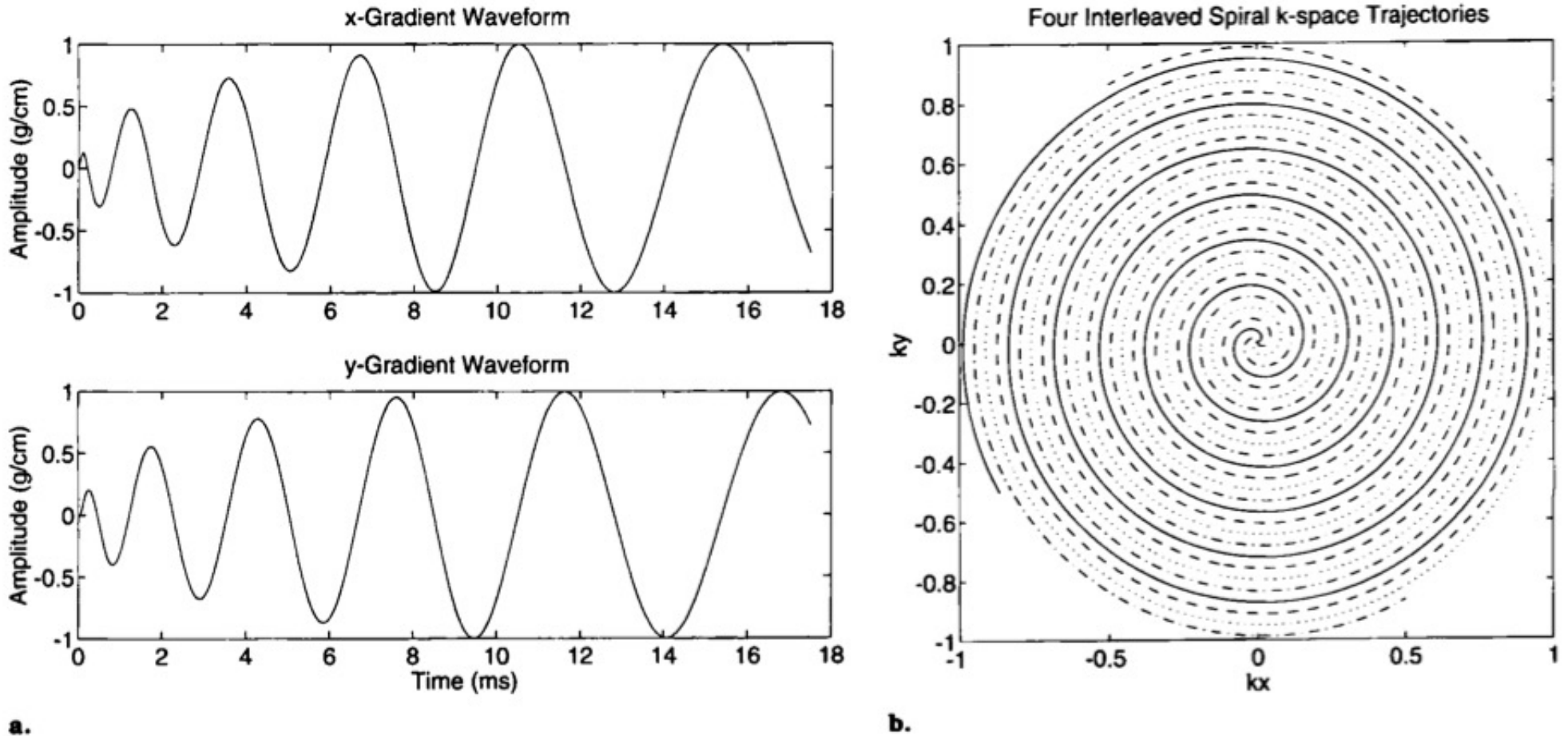
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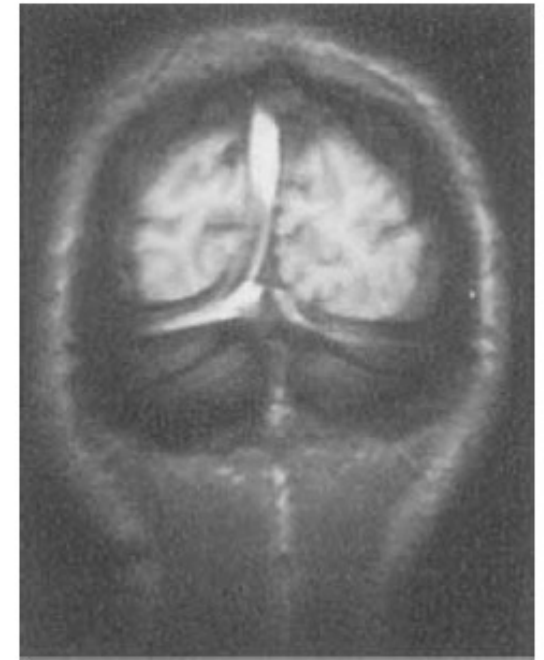
# Multi-Shot Spiral



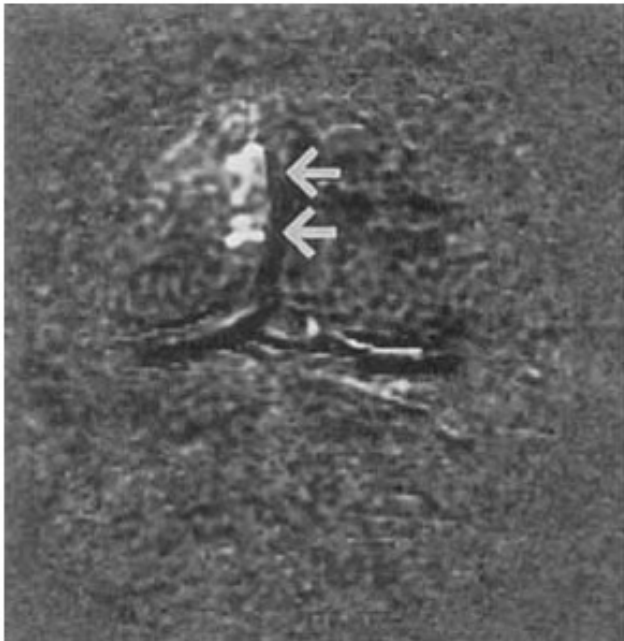
**a.** **Figure 2.** (a) Numerically designed gradient waveforms for spiral k-space trajectories and (b) four interleaved trajectories generated with these gradients.

For multi-shot EPI (another technique that has not caught on), Spiral works better than multi-shot standard rastering.

**Figure 3.** Activation in primary visual cortex with a single character in the visual field. **(a)** T1-weighted image of coronal section near occipital pole. **(b-d)** Average difference images obtained with **(b)** spiral k-space acquisition, **(c)** 2DFT with left-to-right phase encoding, and **(d)** 2DFT with superoinferior phase encoding. Ghosted images of the sagittal sinus are seen in **c** (arrow). The Table lists measurements of the area and degree of activation of the two regions of activation indicated by the arrows in **b**.



**a.**

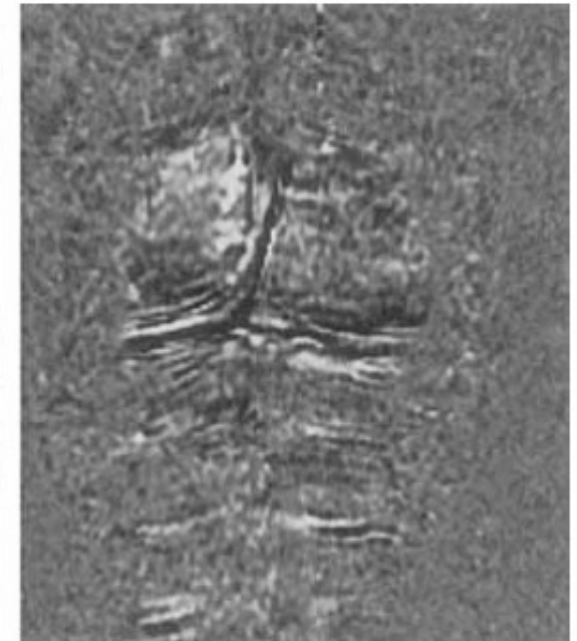


**b.**

Spiral

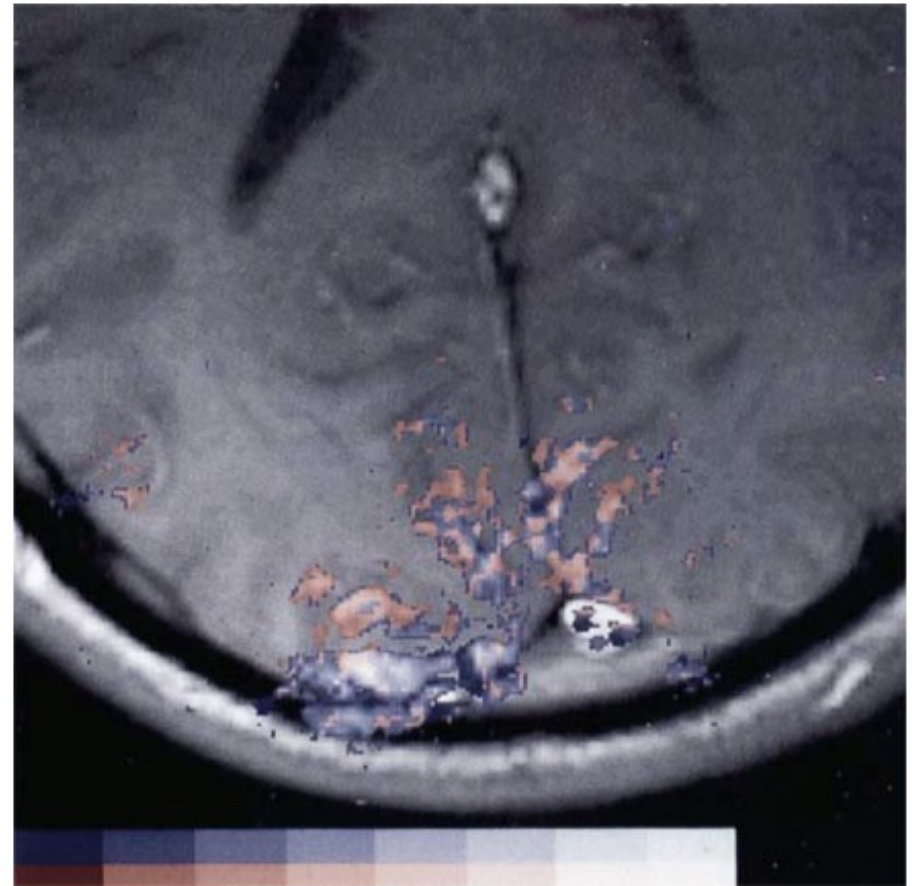
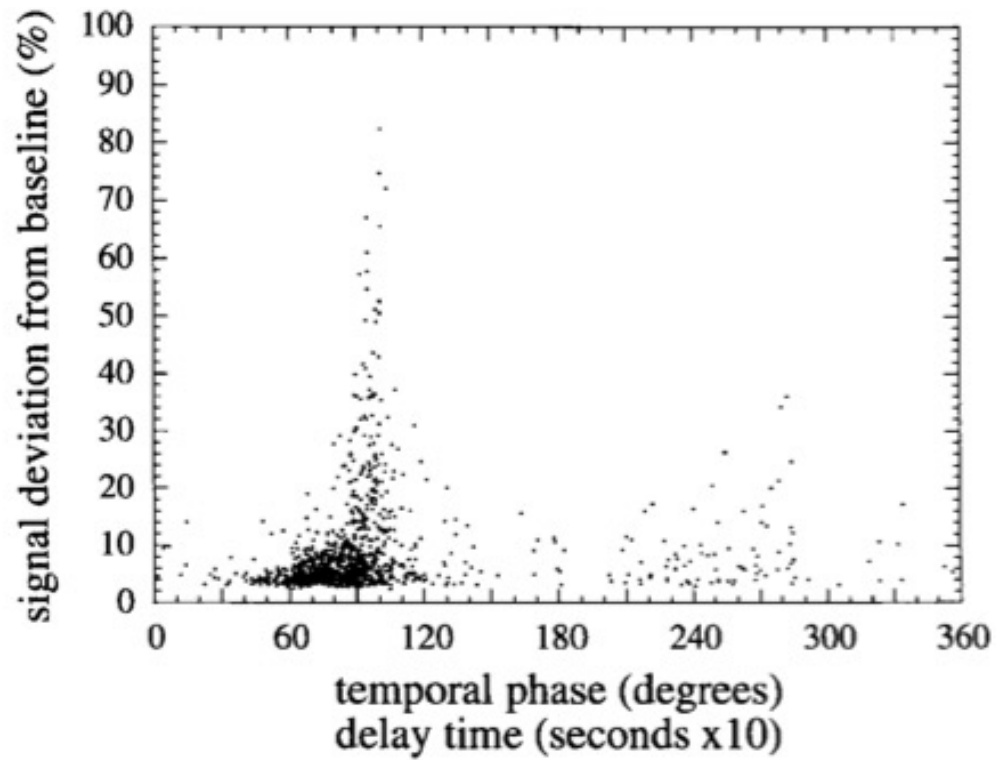


**c.**



**d.**

# Multi-Shot Spiral – latency mapping



A. Lee et al, MRM 33, 745-754 (1995)

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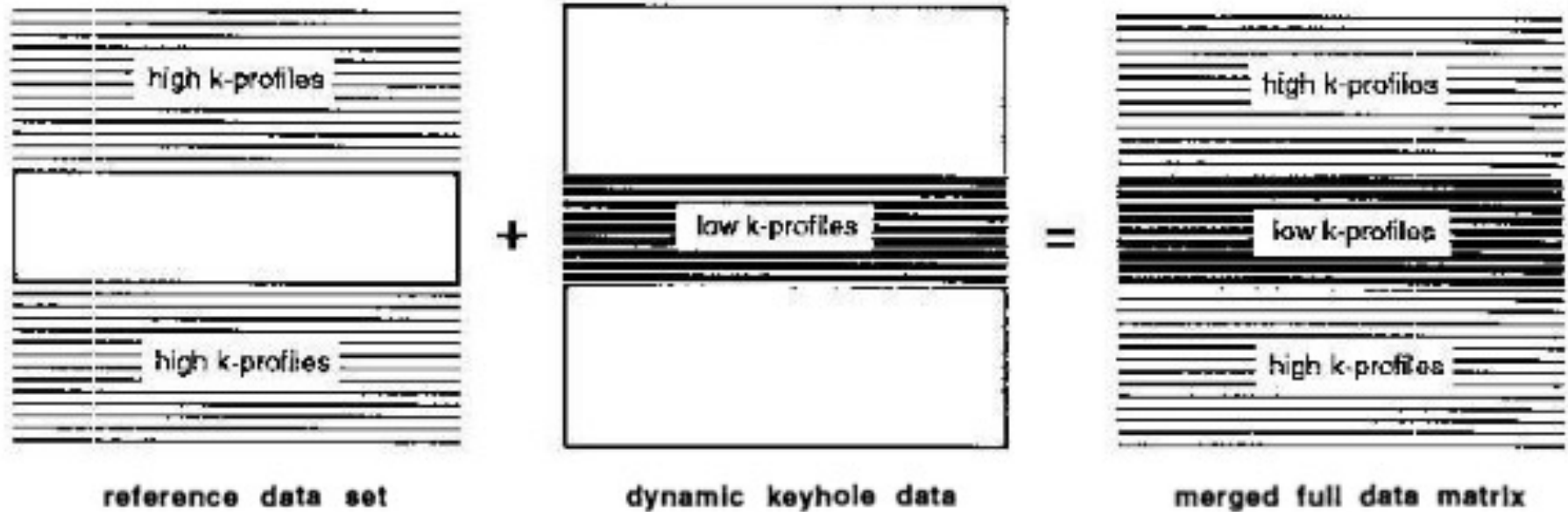
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# Keyhole imaging



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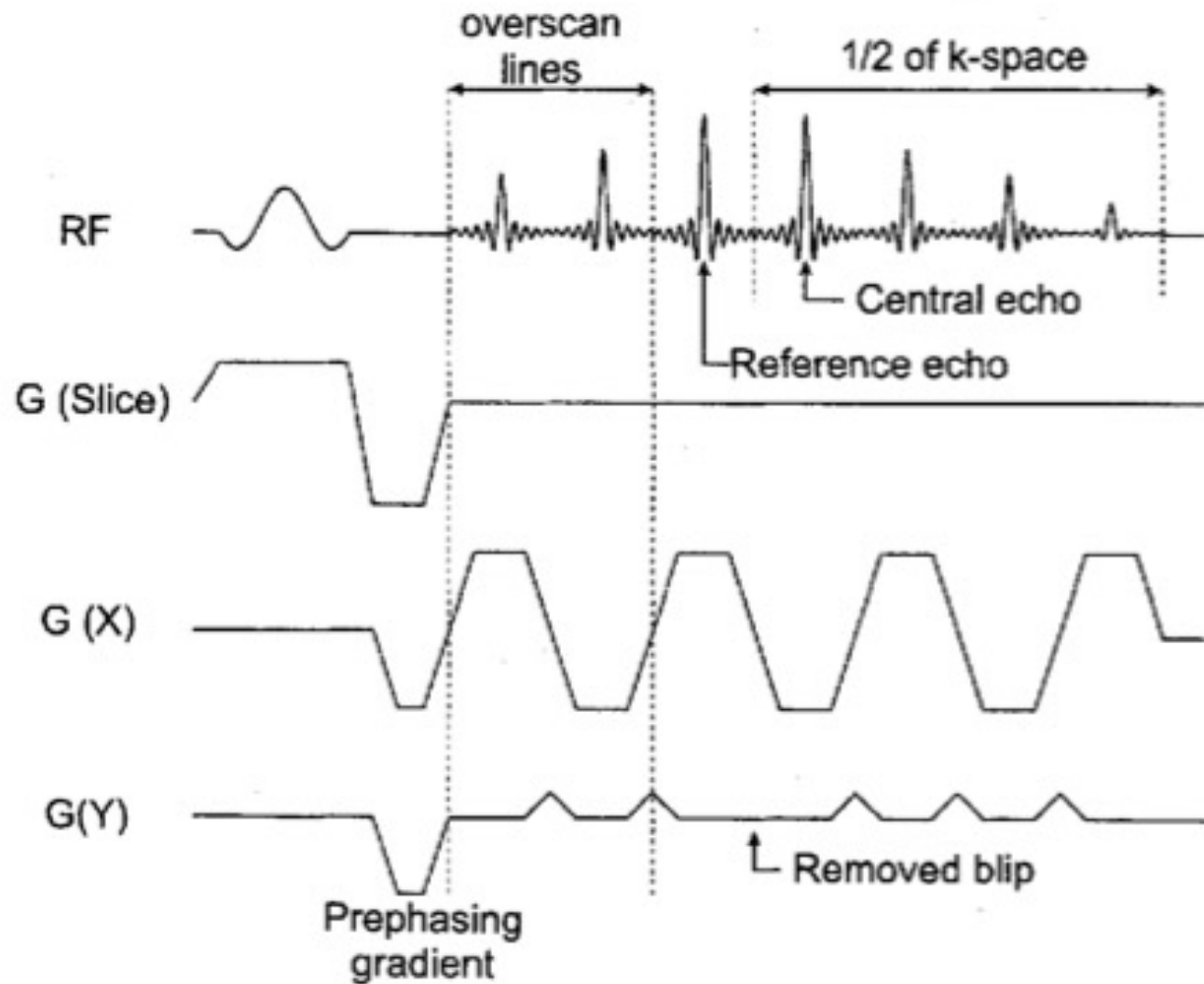
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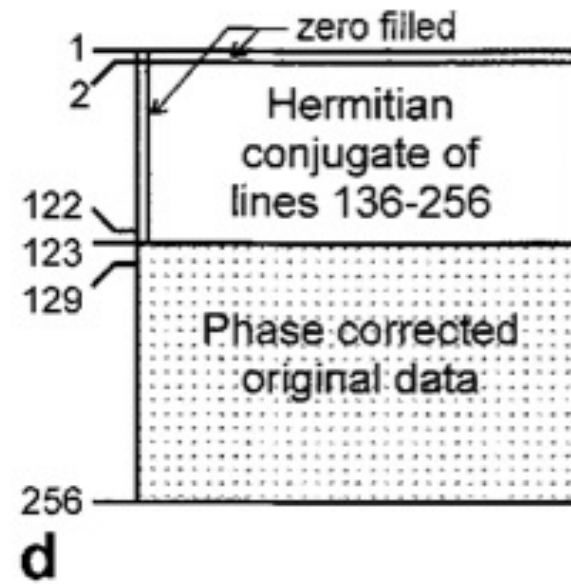
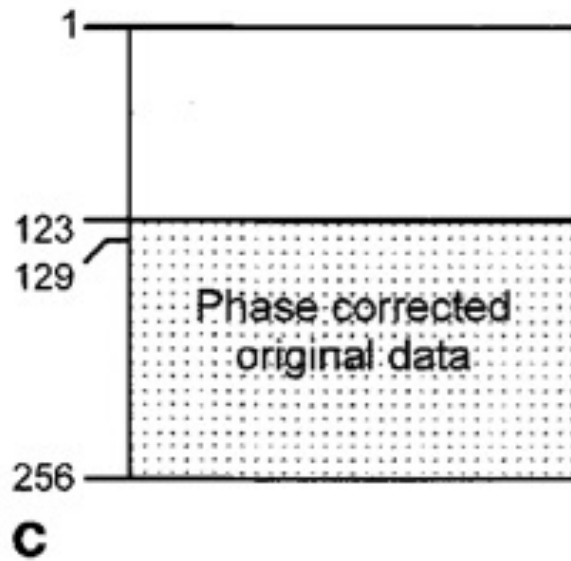
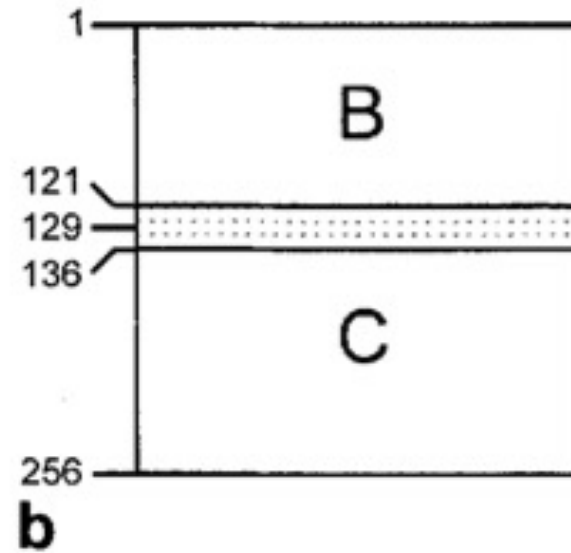
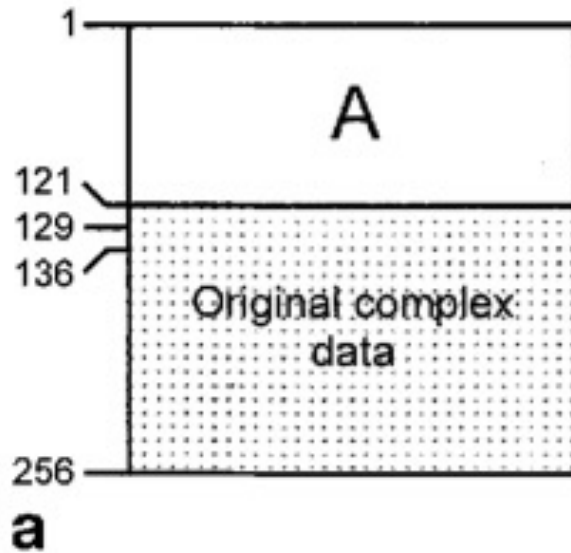
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# Partial k-space reconstruction



A. Jesmanowicz et al, MRM 40, 754-762 (1998)

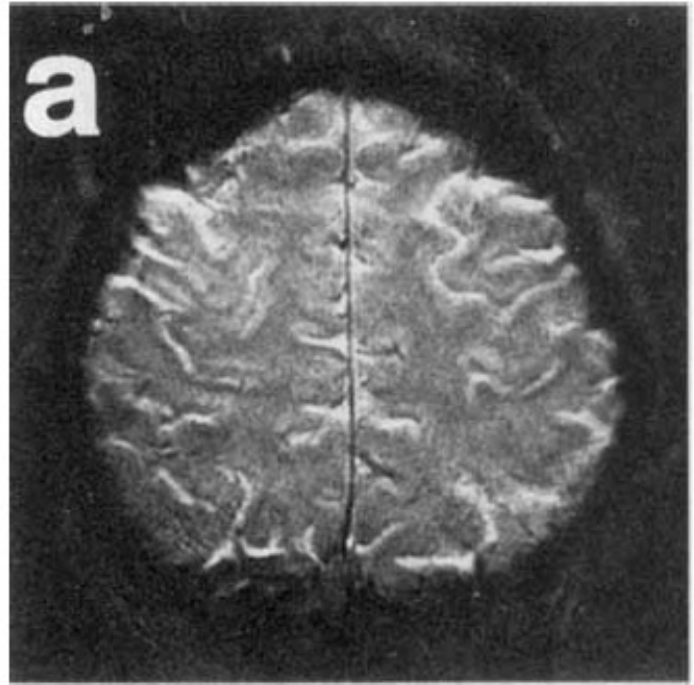
# Partial k-space reconstruction



A. Jesmanowicz et al, MRM 40, 754-762 (1998)



# Partial k-space reconstruction



Echo and Readout Times (ms)				
Resolution	TE		Readout time	
	Full <i>k</i> -space	Half <i>k</i> -space	Full <i>k</i> -space	Half <i>k</i> -space
64 × 64	23.0	9.2	37.4	23.6
128 × 128	66.4	12.6	123.8	70.1
192 × 192	134.4	16.1	259.4	141.1
256 × 256	226.9	19.5	444.1	236.7

A. Jesmanowicz et al, MRM 40, 754-762 (1998)

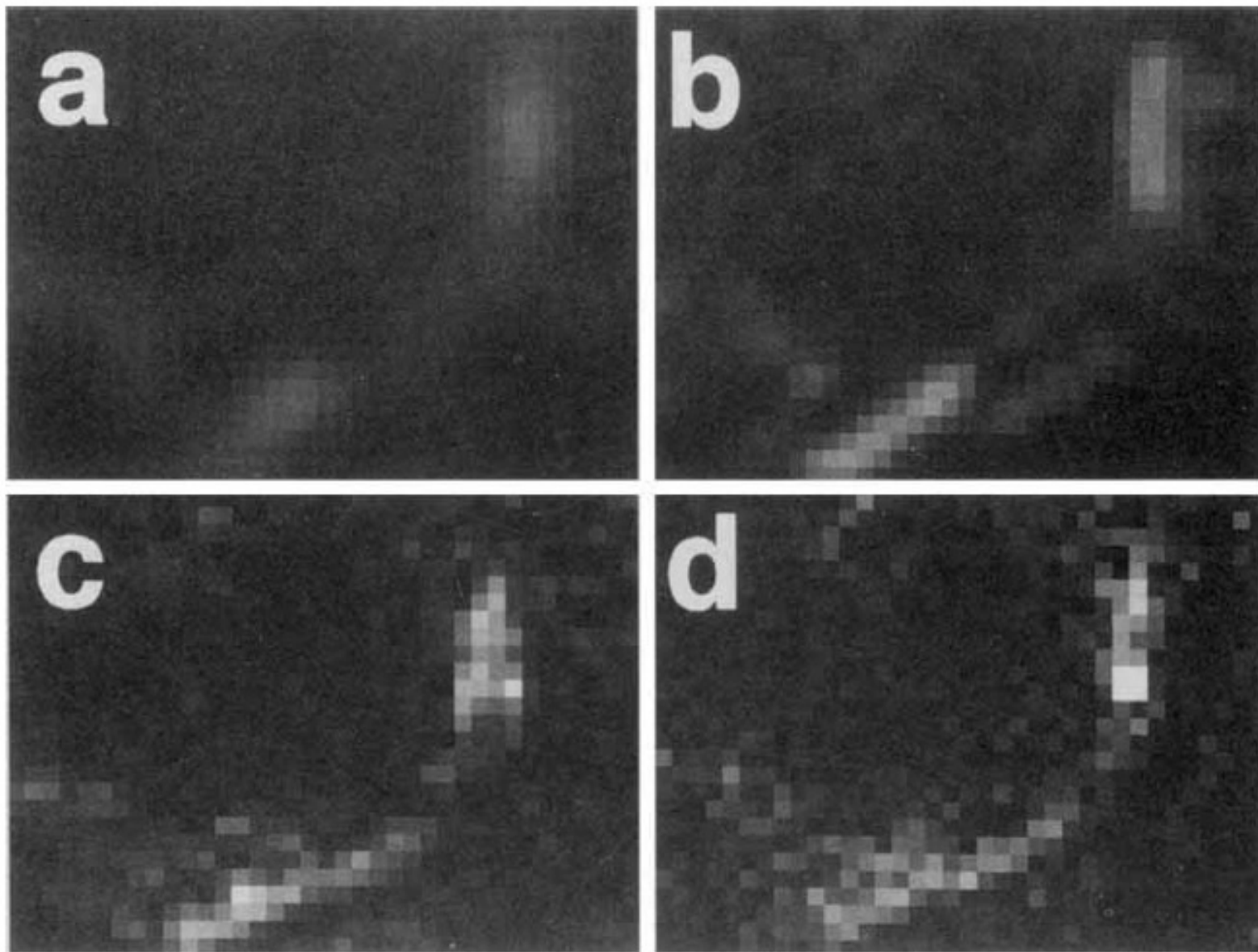


FIG. 9. Percent change maps of the right motor cortex. Slice width was 5 mm, and the FOV was 16 cm. Image matrix sizes and corresponding voxel sizes were: (a)  $64 \times 64$  and  $2.5 \text{ mm}^2$ ; (b)  $128 \times 128$  and  $1.25 \text{ mm}^2$ ; (c)  $192 \times 192$  and  $0.83 \text{ mm}^2$ ; (d)  $256 \times 256$  and  $0.62 \text{ mm}^2$ . TE was 20 ms for each image, and the bandwidth was 166.6 kHz. Partial  $k$ -space acquisition and conjugate synthesis reconstruction were used for all time series. TR = 1 s. Each time series consisted of 120 images. The bilateral finger-tapping paradigm was 30 s off, 20 s on, 20 s off, 20 s on, 30 s off. All the images were reconstructed onto a  $256 \times 256$  matrix.

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# Echo Volume Imaging

## *Echo-Volume Imaging*

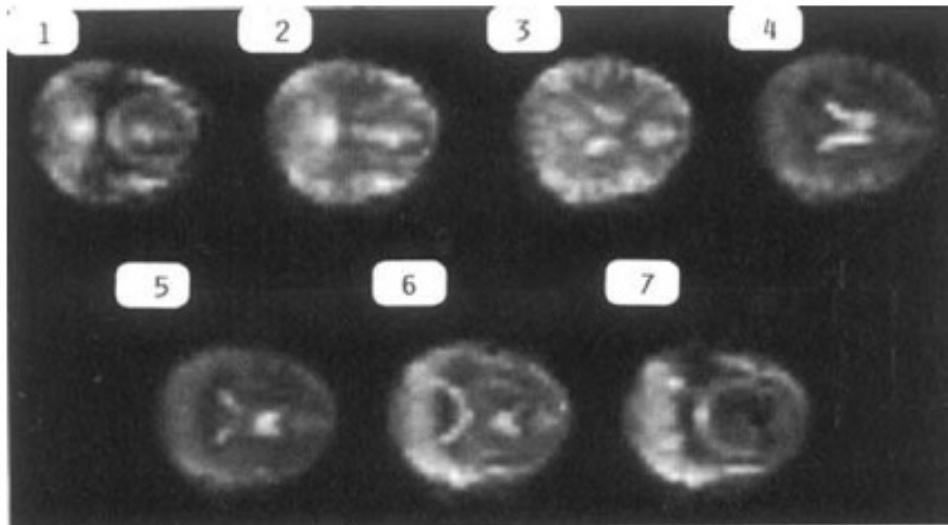
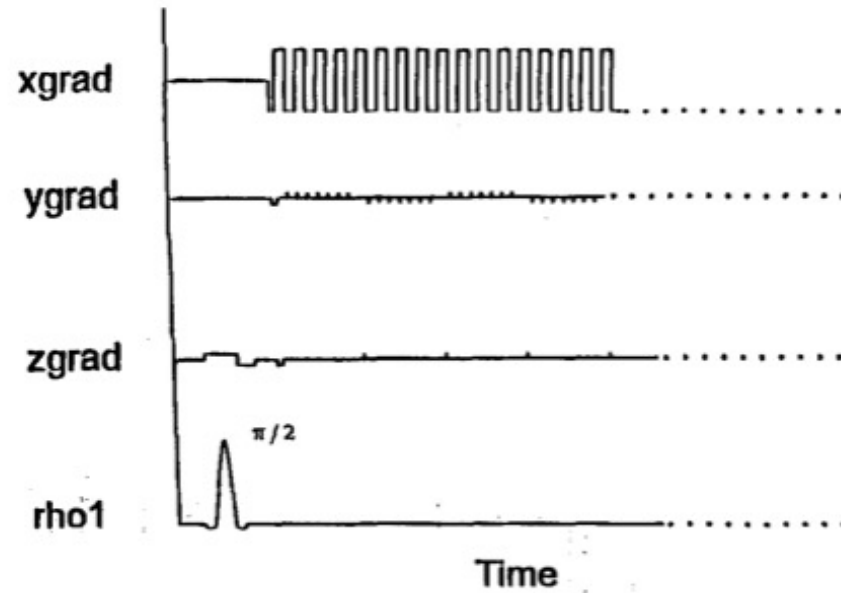


FIG. 3. Single-echo EVI human brain images. Images are taken with a FOV of  $24 \times 24 \times 3.5 \text{ cm}^3$  and matrix of  $32 \times 32 \times 7$ .

A. Song et al MRM, 32, 668-671 (1994)

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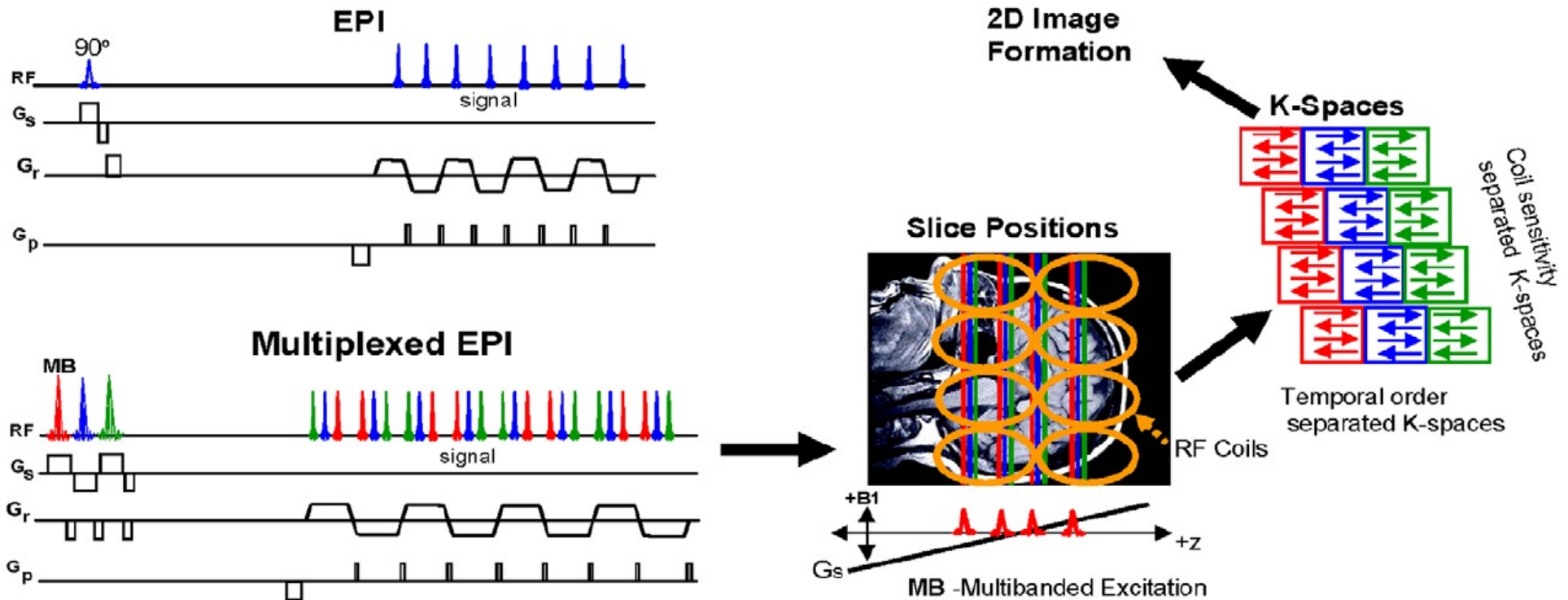
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# Multiband Excitation



Feinberg et al, PLoS one, 5, 12, e15710 (2010)

D. A. Feinberg and K. Setsompop, JMR, 229, 90-100, (2013)

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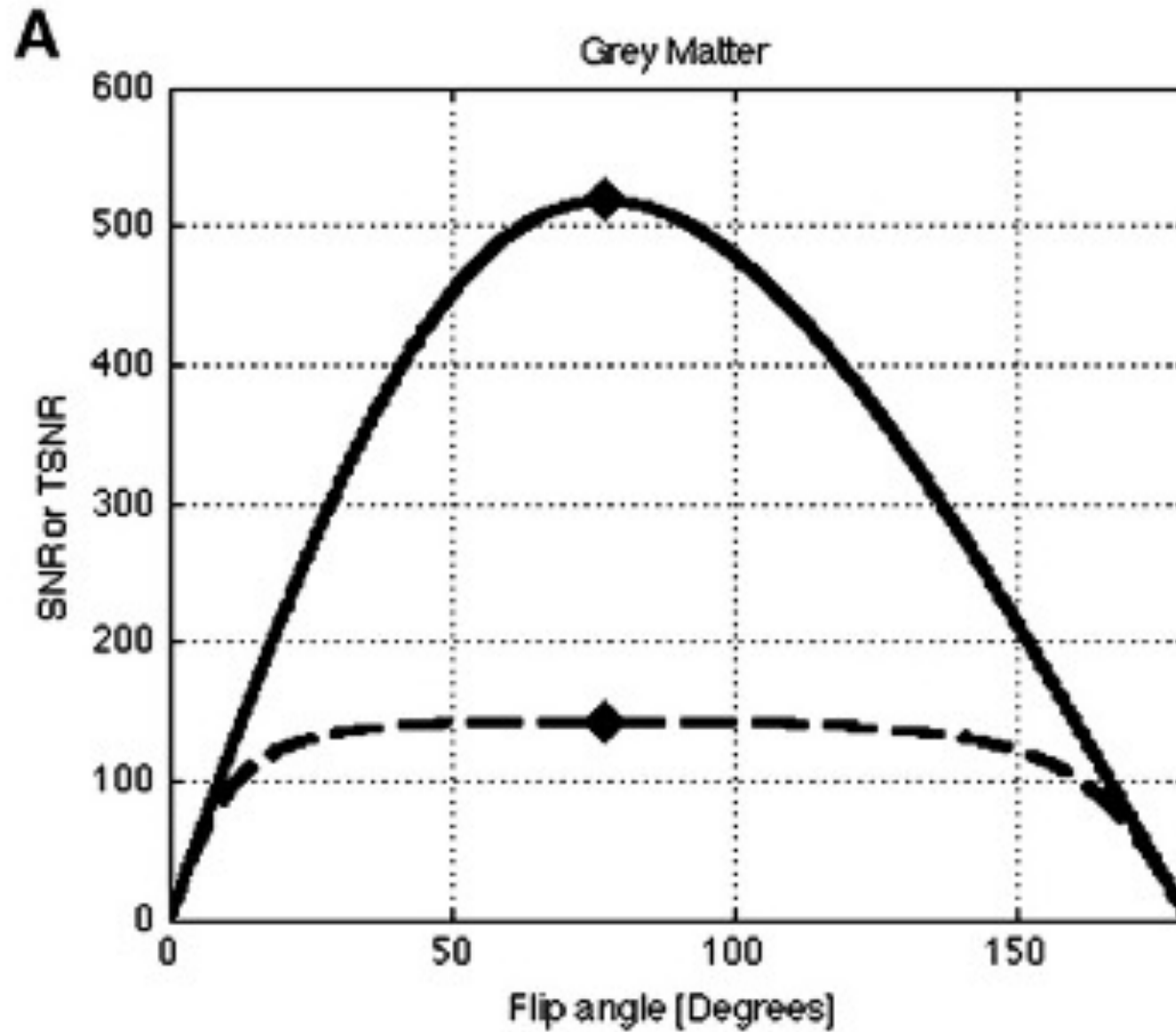
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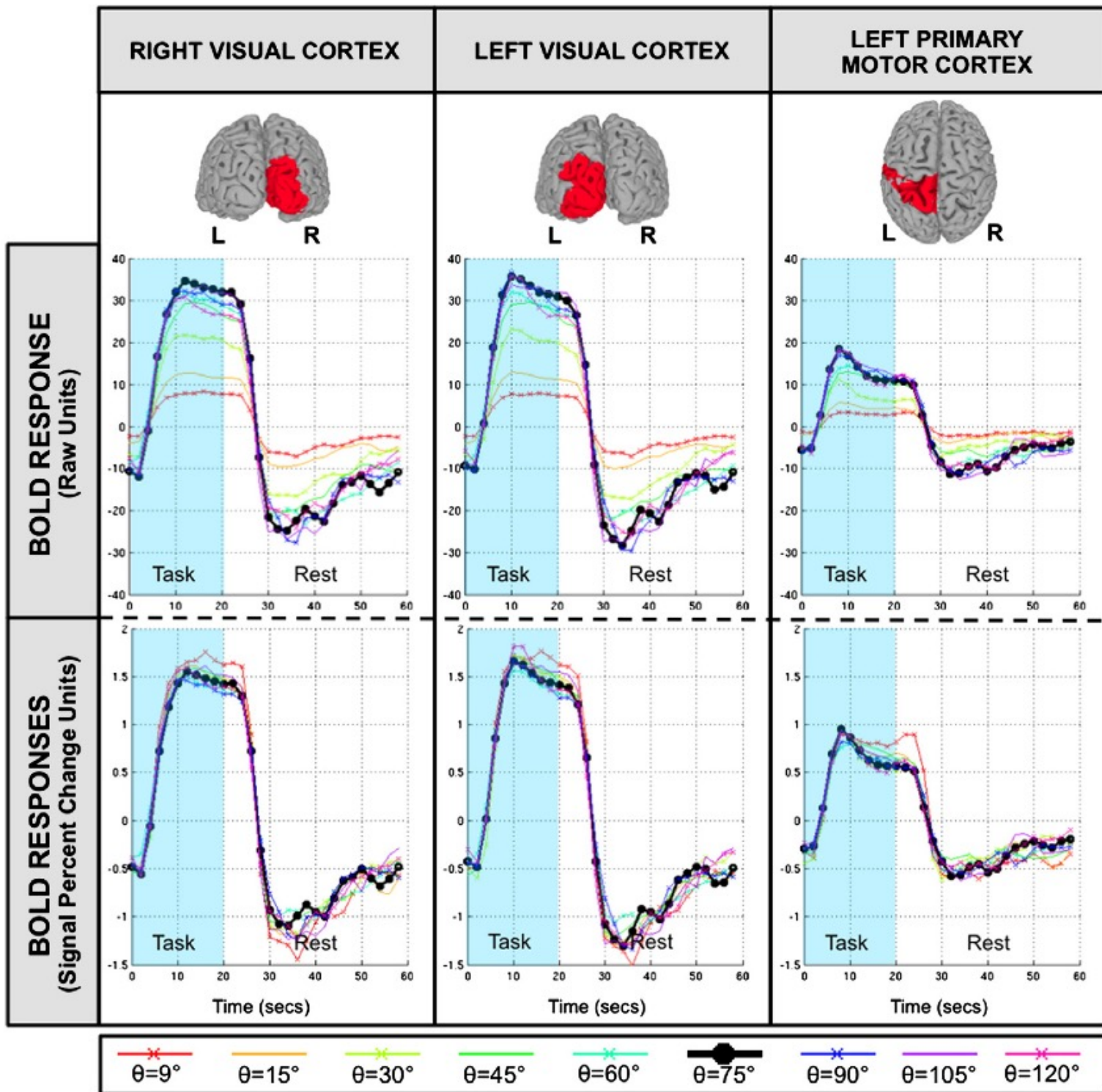
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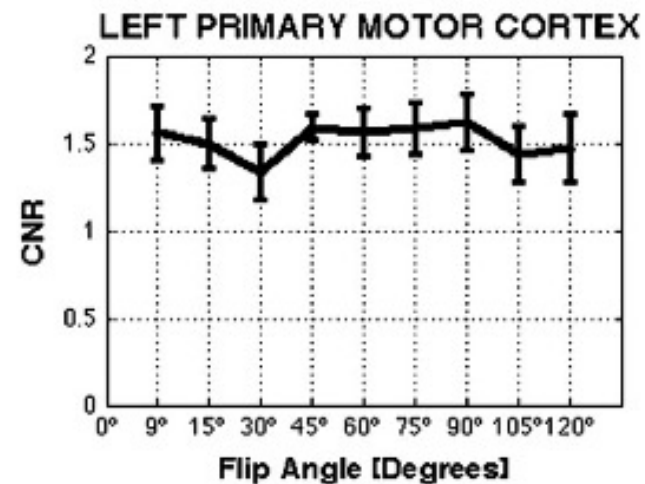
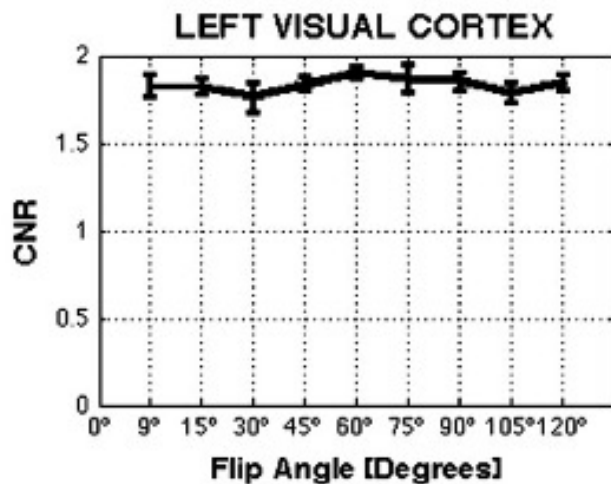
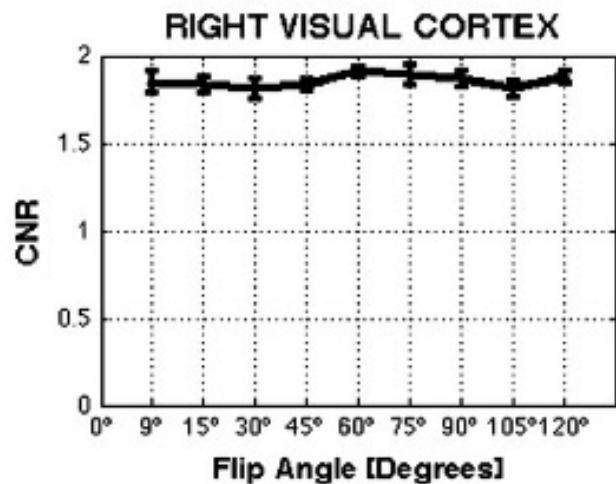
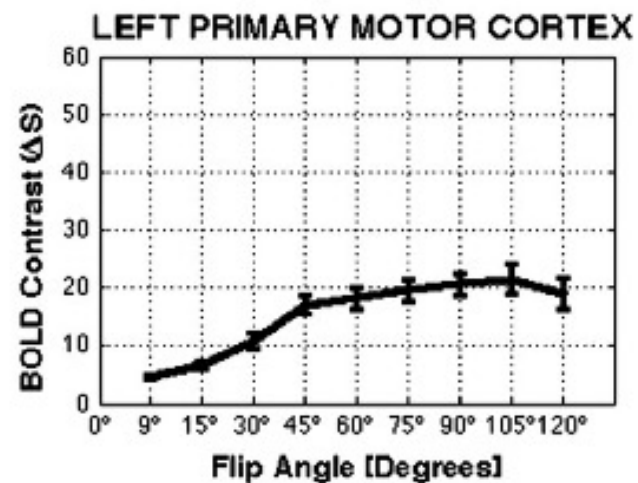
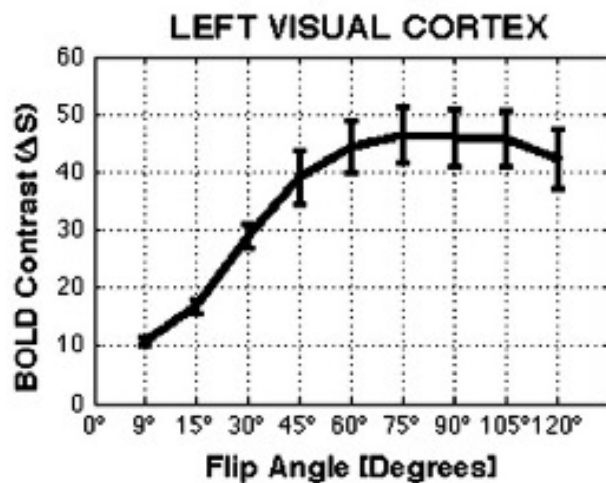
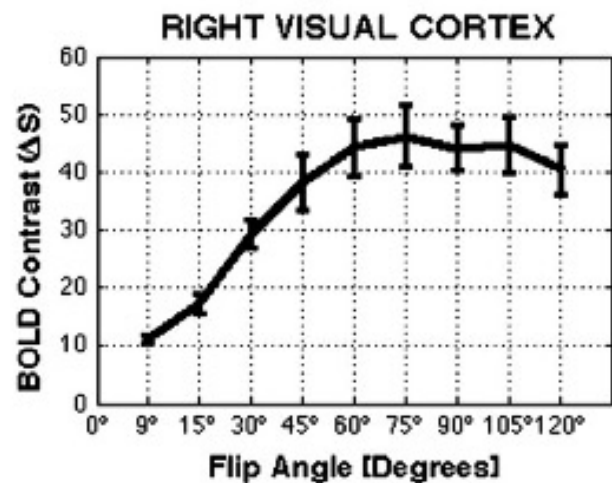
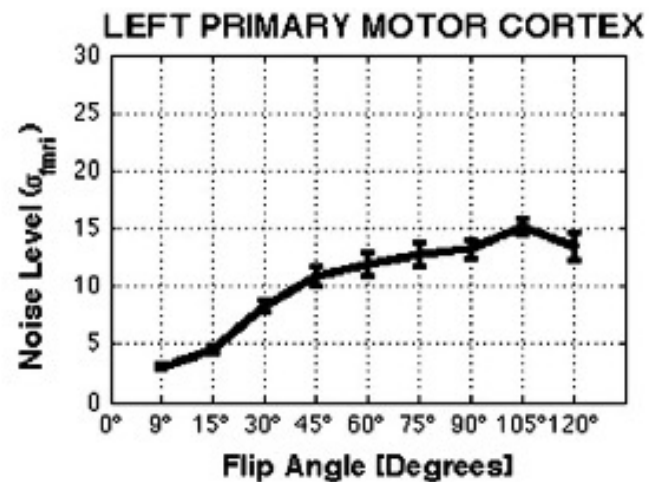
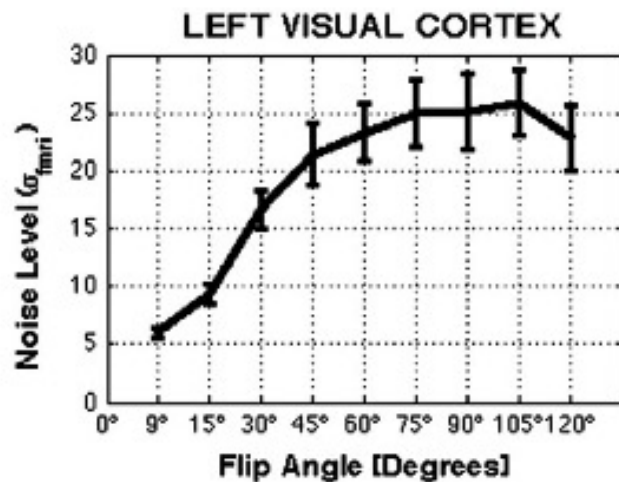
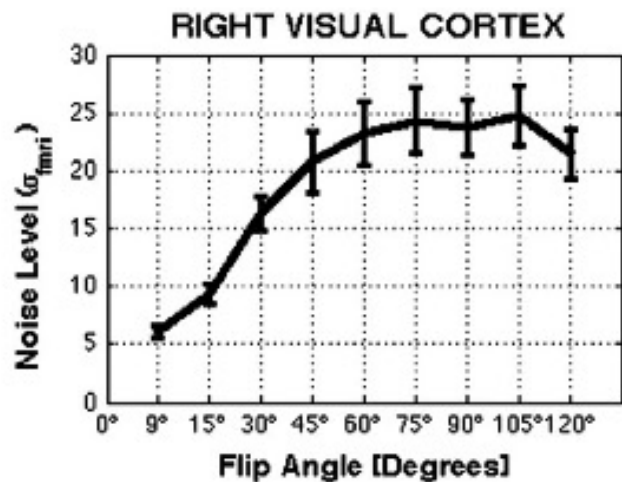
Low flip angle



J. Gonzalez-Castillo, et al., NeuroImage, 54, 2764-2778 (2011)









**Pros:**

reduced inflow

better slice profile

higher anatomical contrast for registration

**Cons:**

Only works when physiologic noise dominates

Resting state seems to have less clear advantages

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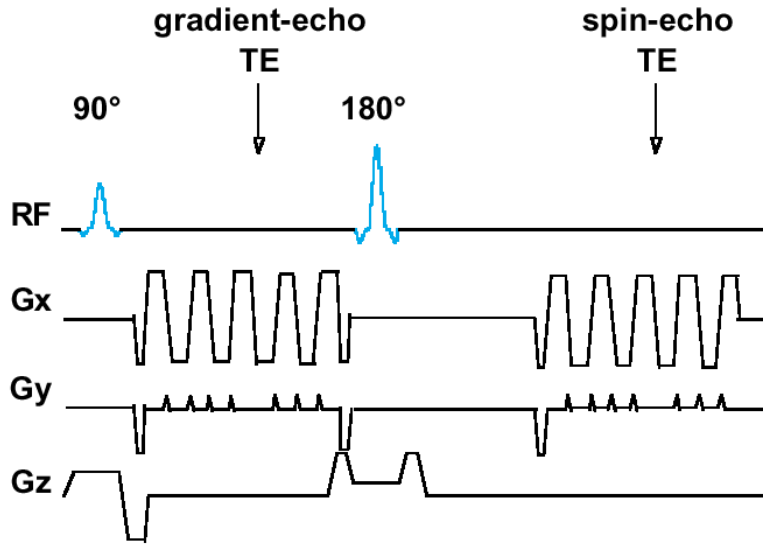
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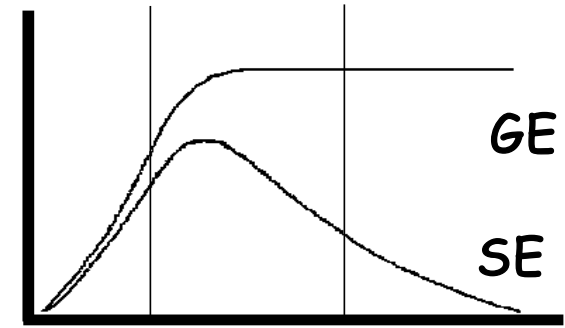
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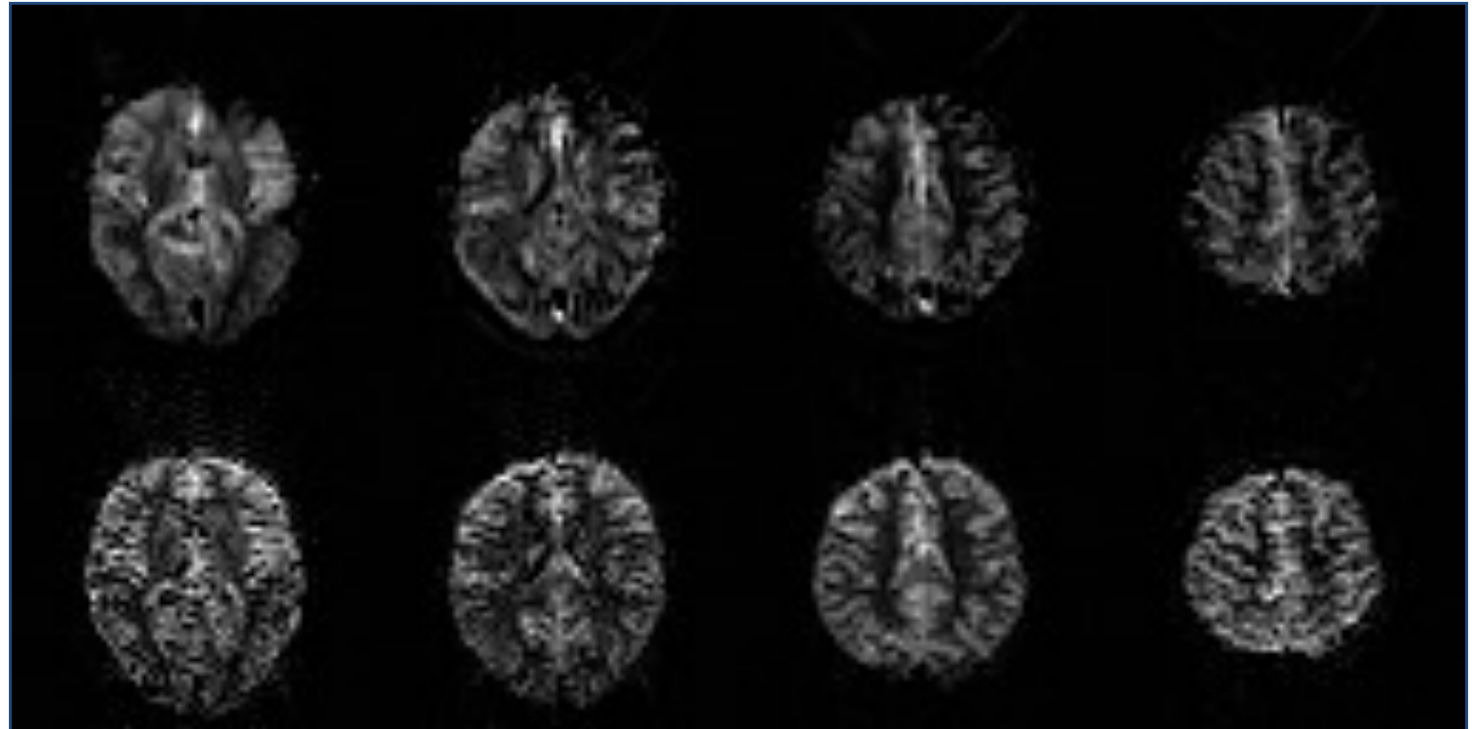
contrast



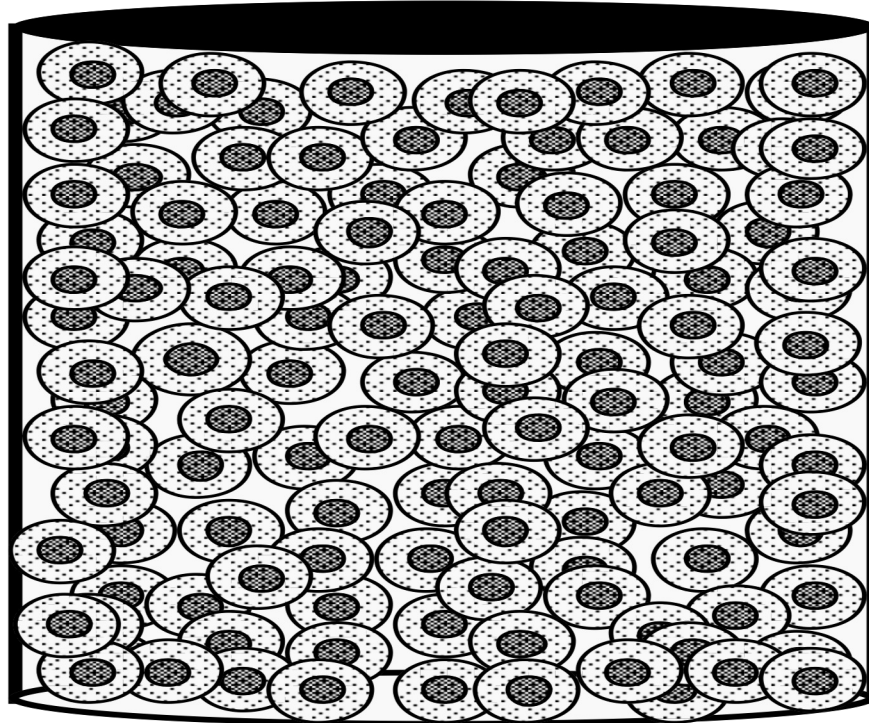
2.5 to 3 μm    3 to 15 μm    15 to ∞ μm  
compartment size

**GE**  
TE = 30 ms

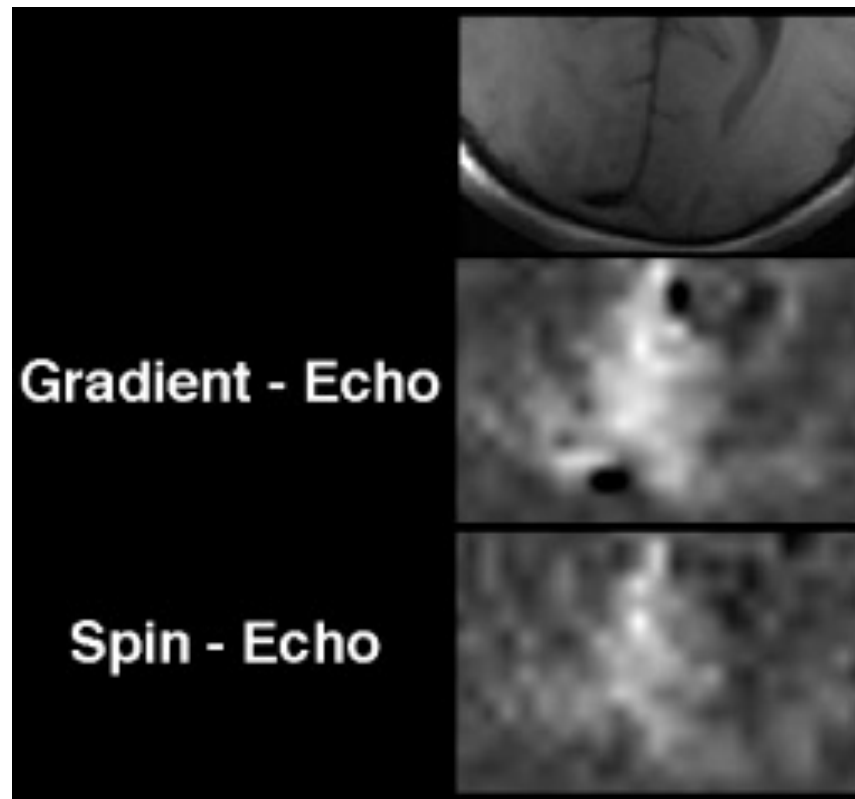
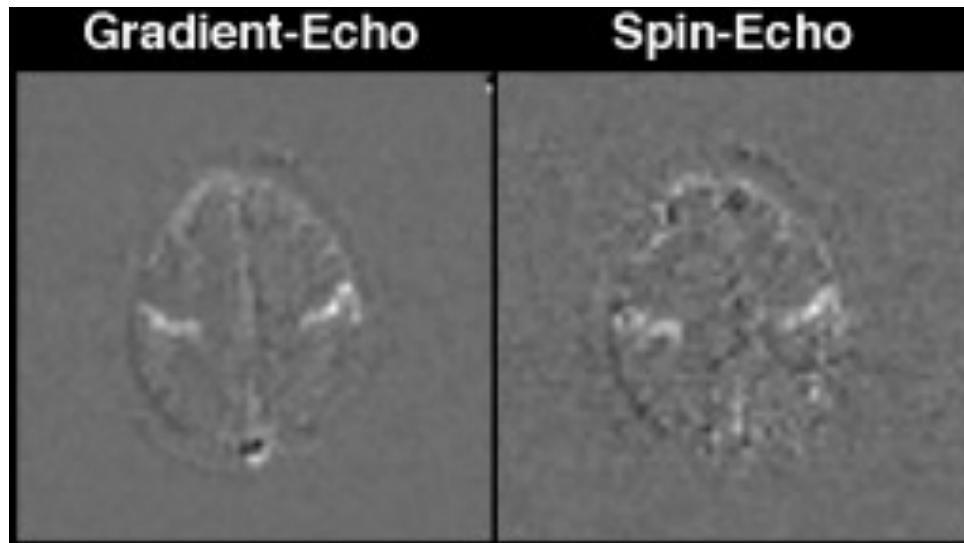
**SE**  
TE = 110 ms



# The Problem with Spin-Echo

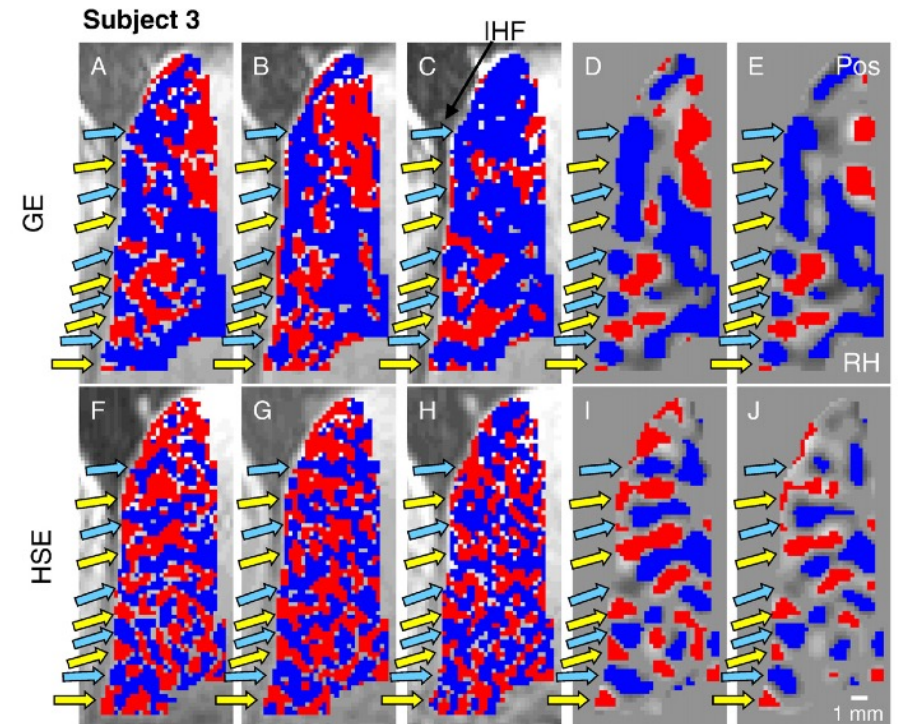
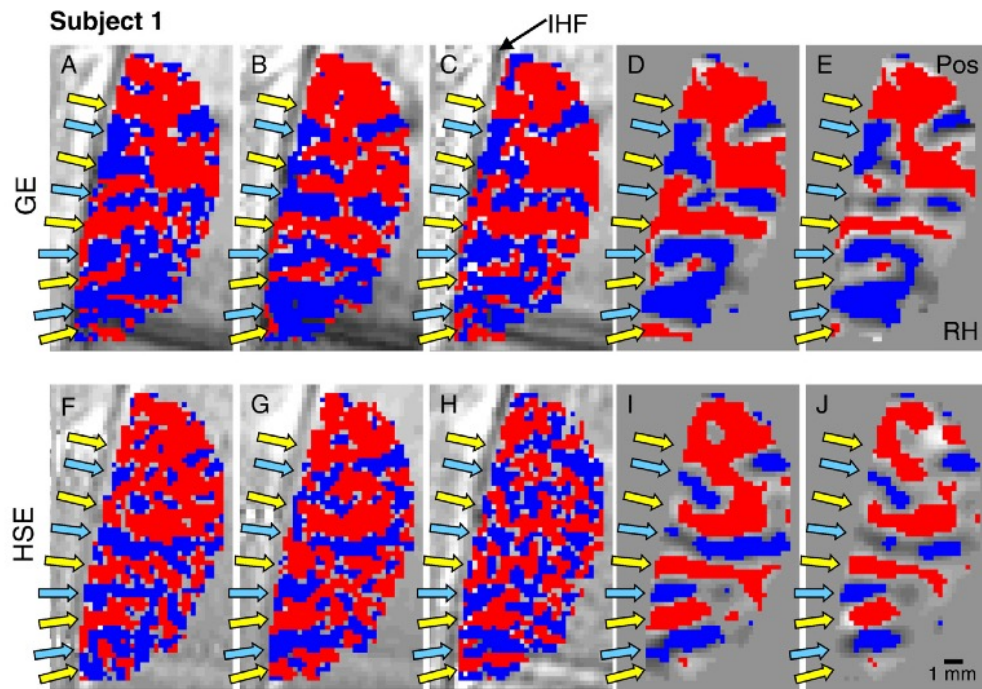


Spin-echo



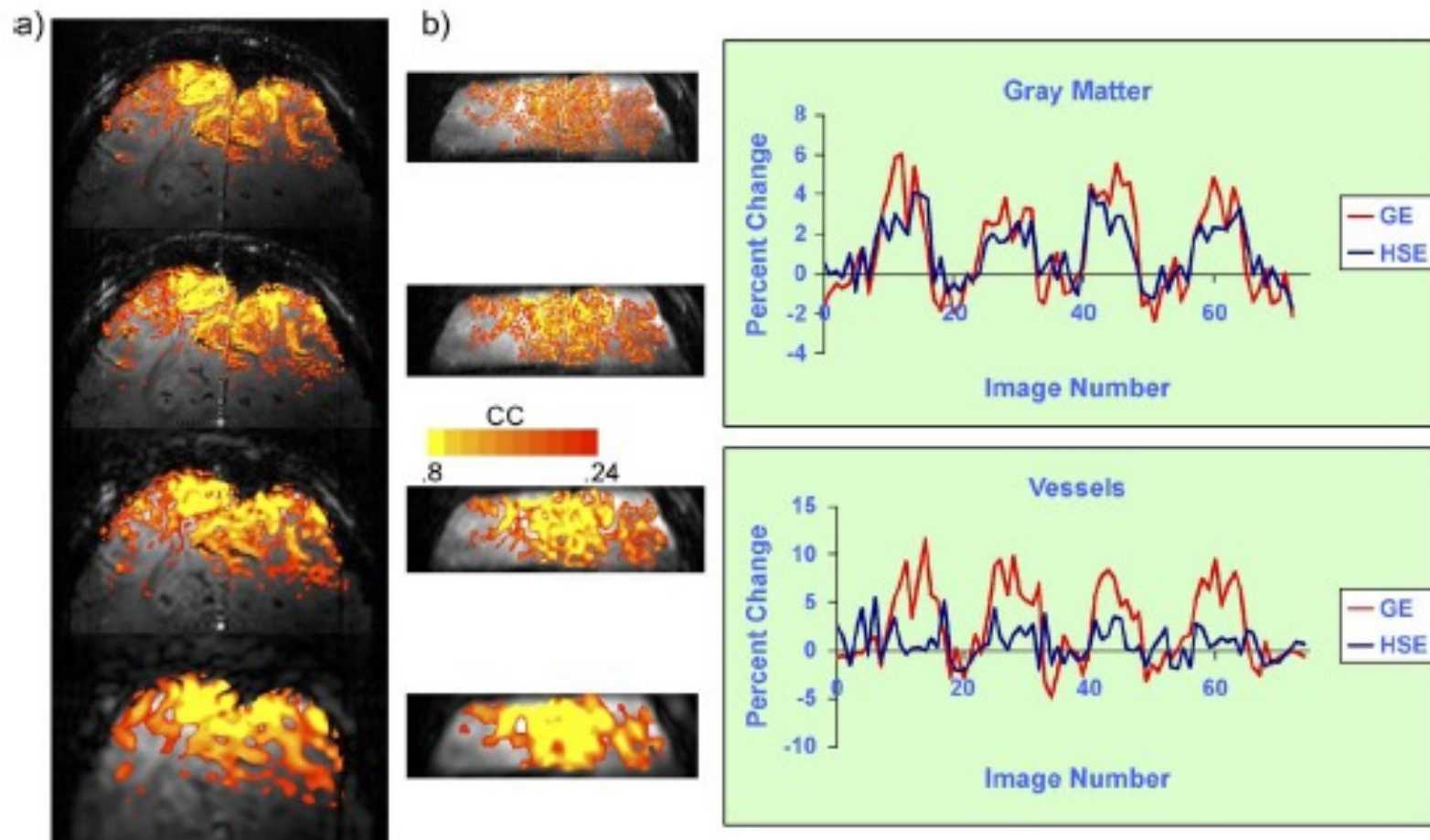


# Spin-echo



E. Yacoub, NeuroImage 37, 1161 – 1177 (2007)

# Spin-echo



Yacoub et al. NeuroImage 24 (3), pp. 738-750

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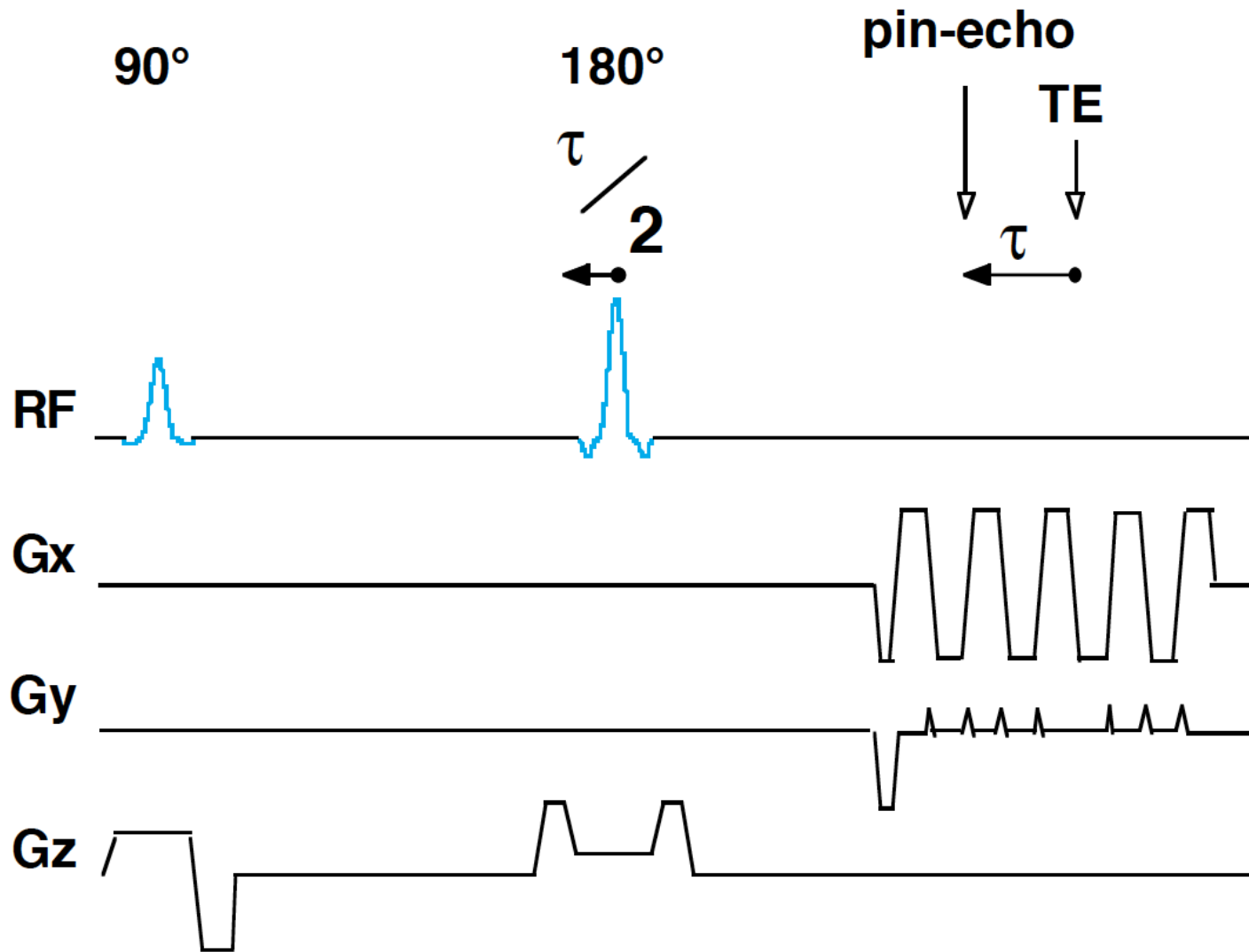
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# Assymmetric Spin-echo



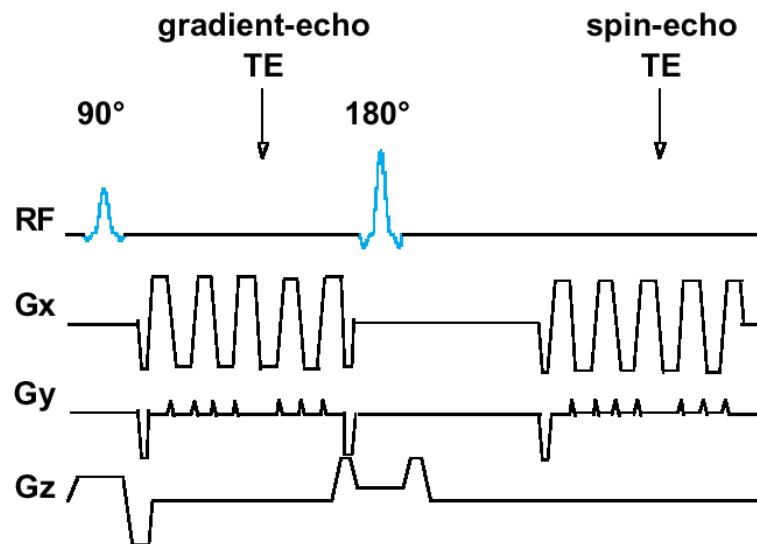
# Assymmetric Spin-echo

## Pros:

- The 180 pulse does not refocus rapidly flowing spins (reduces noise)
- T2\* weighting lower limit is not limited by readout window width
- Can add a gradient-echo EPI readout in first part of sequence.

## Cons:

- Takes about 60 ms longer, so reduces number of slices per TR.



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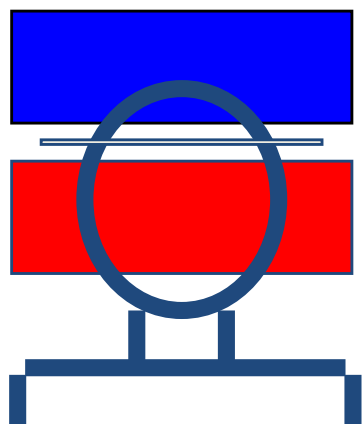
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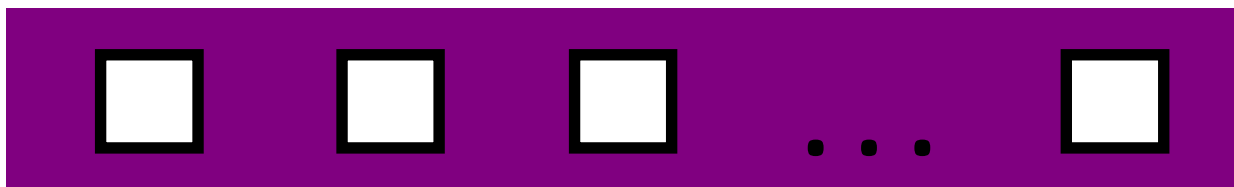
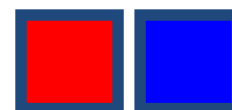
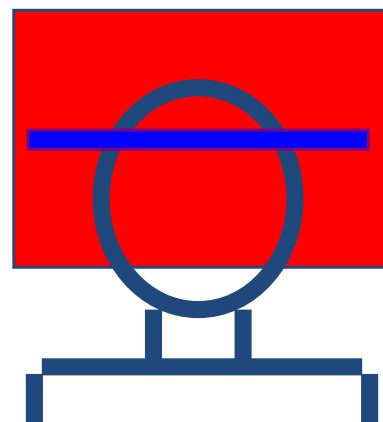
# Arterial Spin Labeling

## ASL

### EPISTAR

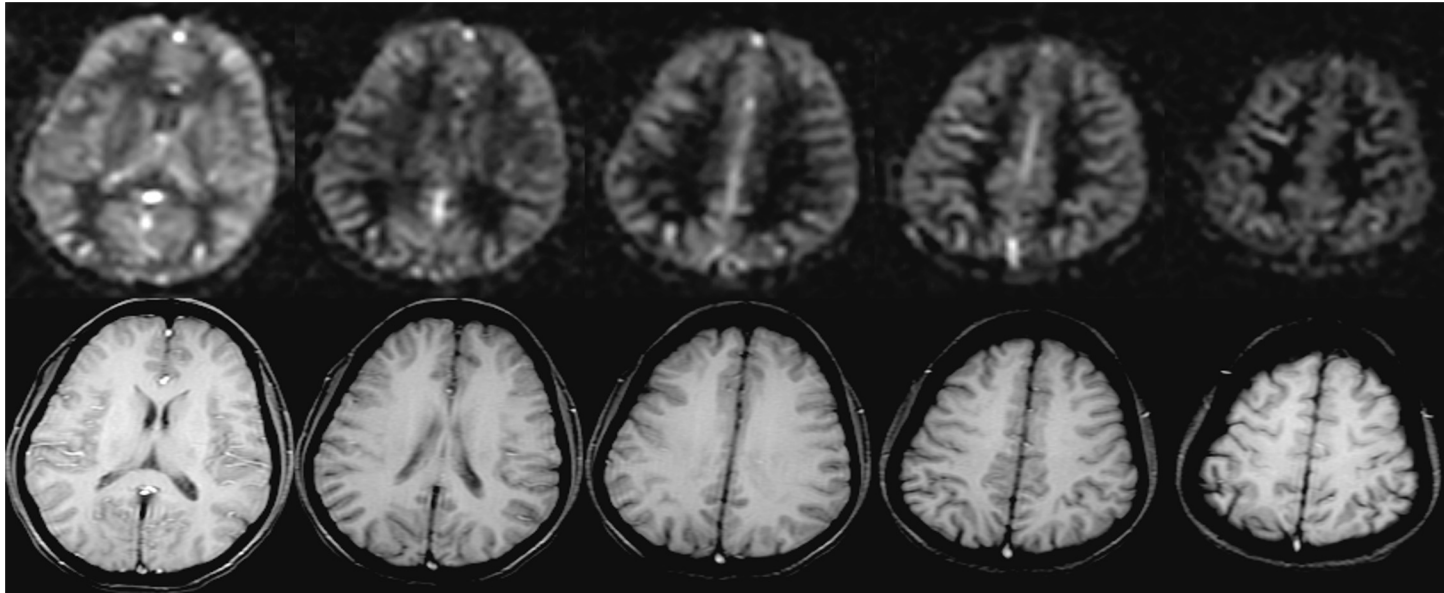


### FAIR



Perfusion  
Time Series

# Arterial Spin Labeling



Williams, D. S., Detre, J. A., Leigh, J. S. & Koretsky, A. S. (1992) "Magnetic resonance imaging of perfusion using spin-inversion of arterial water." *Proc. Natl. Acad. Sci. USA* 89, 212-216.

Edelman, R., Siewert, B. & Darby, D. (1994) "Qualitative mapping of cerebral blood flow and functional localization with echo planar MR imaging and signal targeting with alternating radiofrequency (EPISTAR)." *Radiology* 192, 1-8.

Kim, S.-G. (1995) "Quantification of relative cerebral blood flow change by flow-sensitive alternating inversion recovery (FAIR) technique: application to functional mapping." *Magn. Reson. Med.* 34, 293-301.

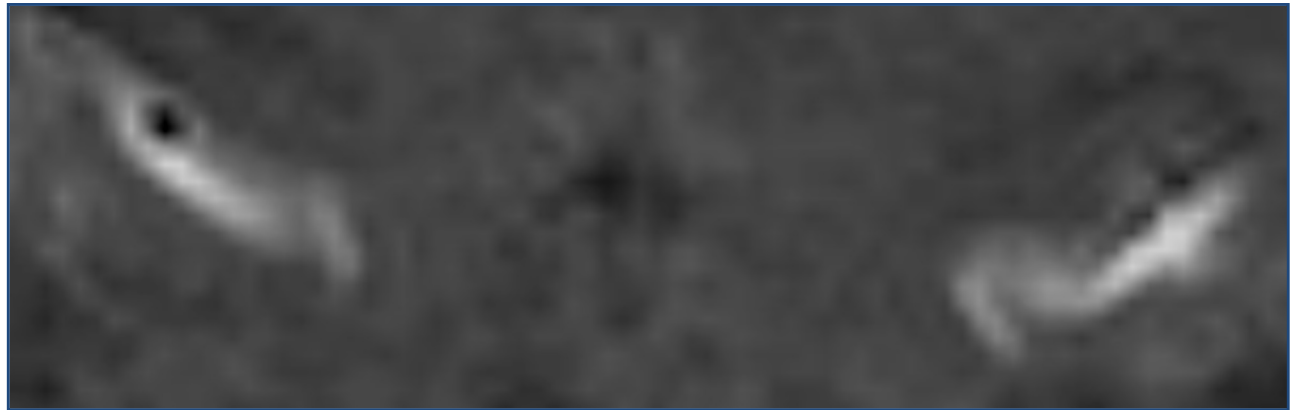
Kwong, K. K. et al. (1995) "MR perfusion studies with T1-weighted echo planar imaging." *Magn. Reson. Med.* 34, 878-887.



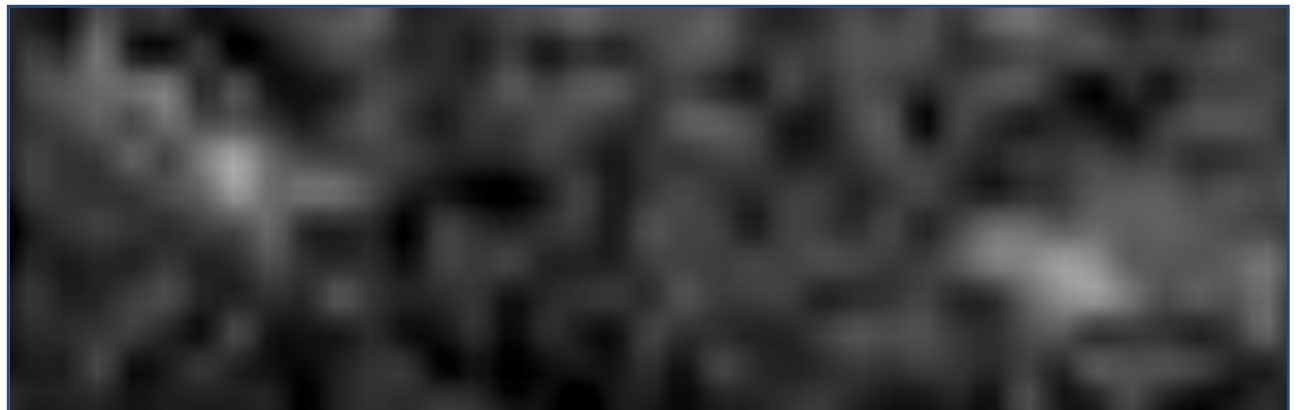
# Anatomy



# BOLD



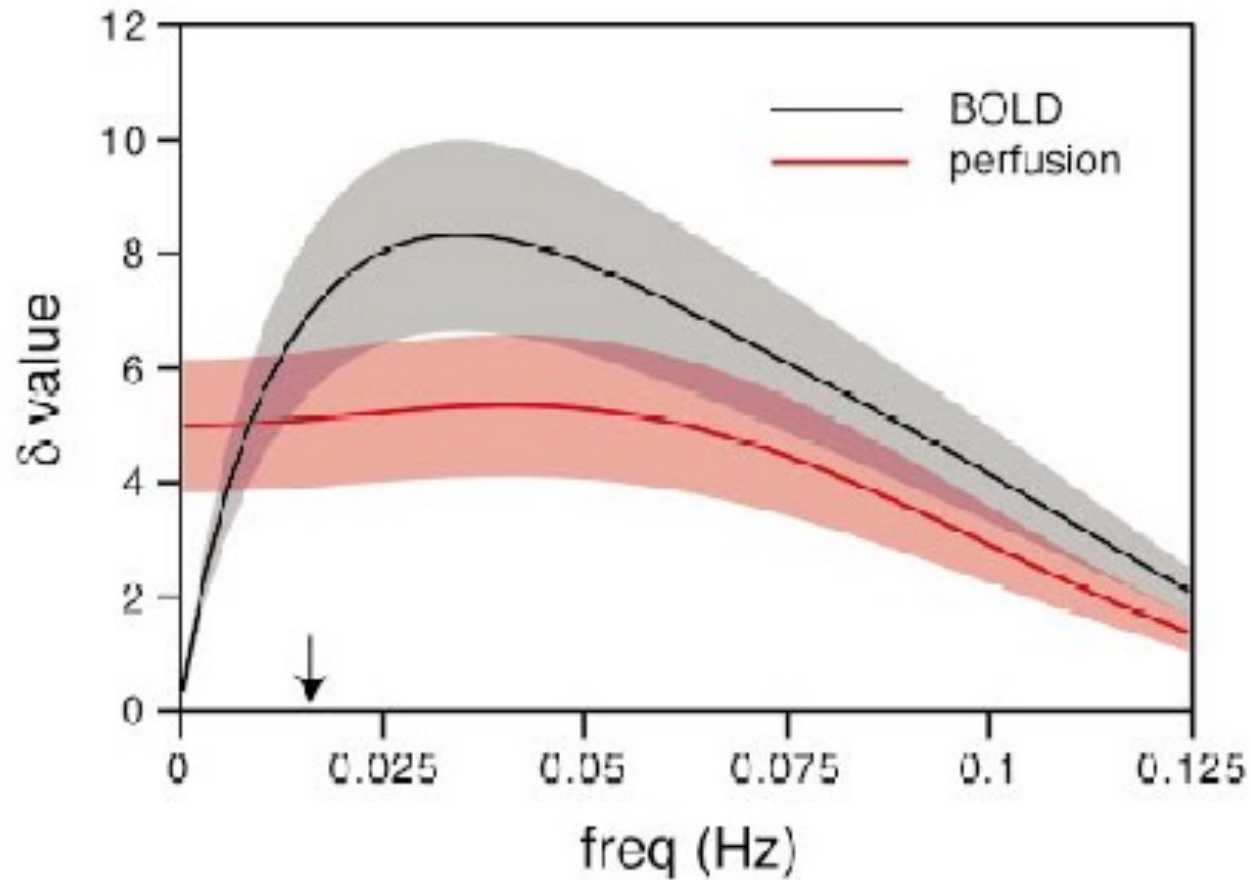
# Perfusion



P. A. Bandettini, E. C. Wong, Magnetic resonance imaging of human brain function: principles, practicalities, and possibilities, *in* "Neurosurgery Clinics of North America: Functional Imaging" (M. Haglund, Ed.), p.345-371, W. B. Saunders Co., 1997.

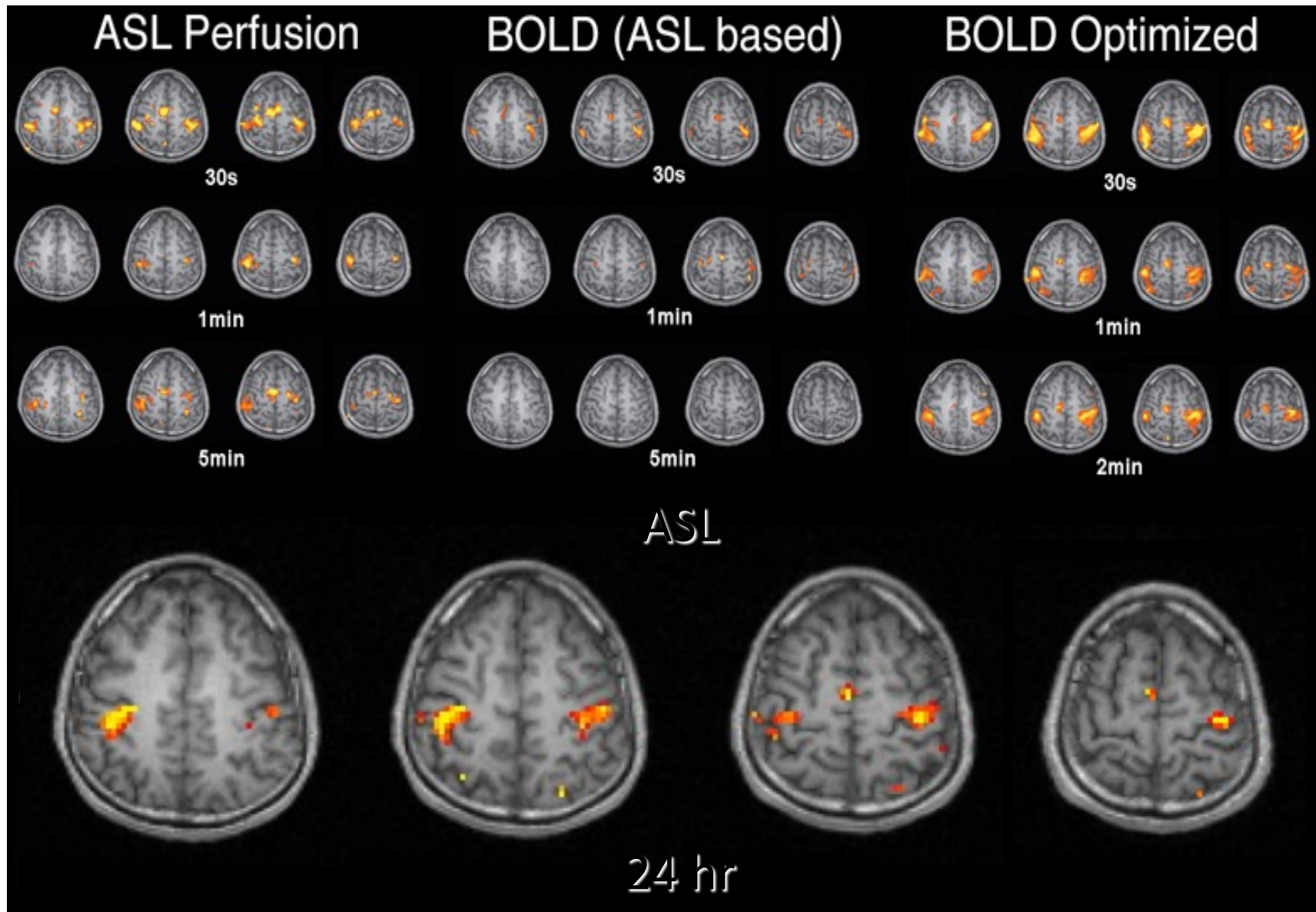
# Arterial Spin Labeling

Better than BOLD for long duration activation...



GK Aguirre et al, (2002) NeuroImage 15 (3): 488-500

# Perfusion vs. BOLD: Low Task Frequency



# Arterial Spin Labeling

## Pros:

- Potentially quantitative
- Localized to capillary effects
- Stable over time
- Allows baseline comparisons

## Cons:

- Slow (Prep times are up to 2 sec)
- Limited spatial coverage of the slab
- Low temporal SNR

## Acquisition:

- Spiral Scanning
- Multi-Shot Spiral
- Multi-shot EPI
- Keyhole Imaging
- Partial k-space
- Echo-volume imaging
- 3D EPI
- Zoomed EPI
- Multiband excitation
- Low flip angle

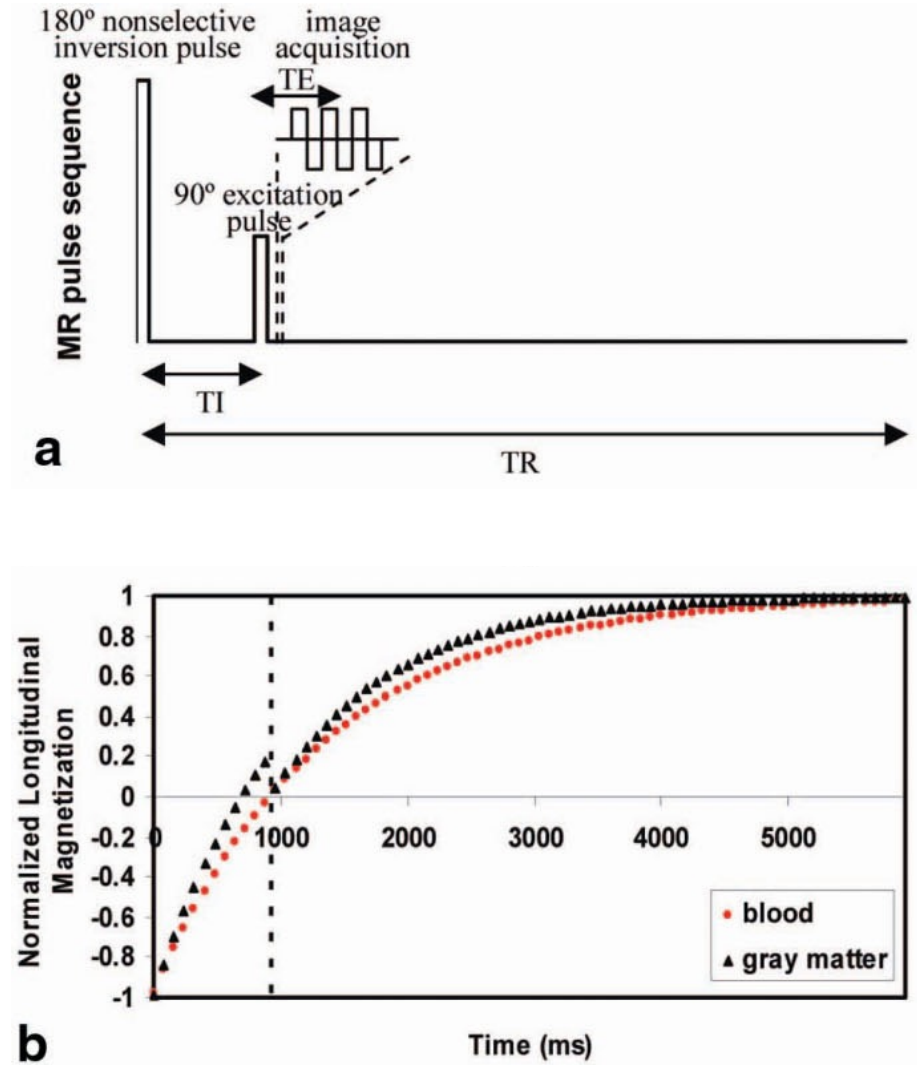
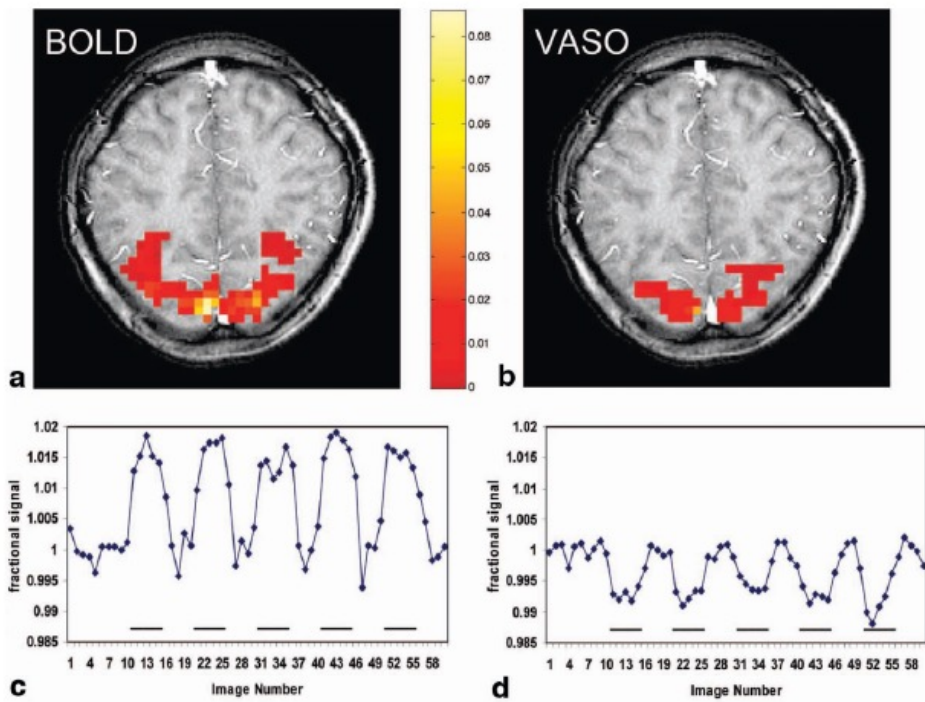
## Contrast Weighting

- Spin-echo
- Asymmetric Spin-Echo
- Arterial Spin Labeling
- **VASO**
- Low b Diffusion Weighting
- High b Diffusion Weighting
- Neuronal Current Imaging
- Multi-echo acquisition
- MRI time series phase information
- Steady State Free Precession
- Manganese contrast

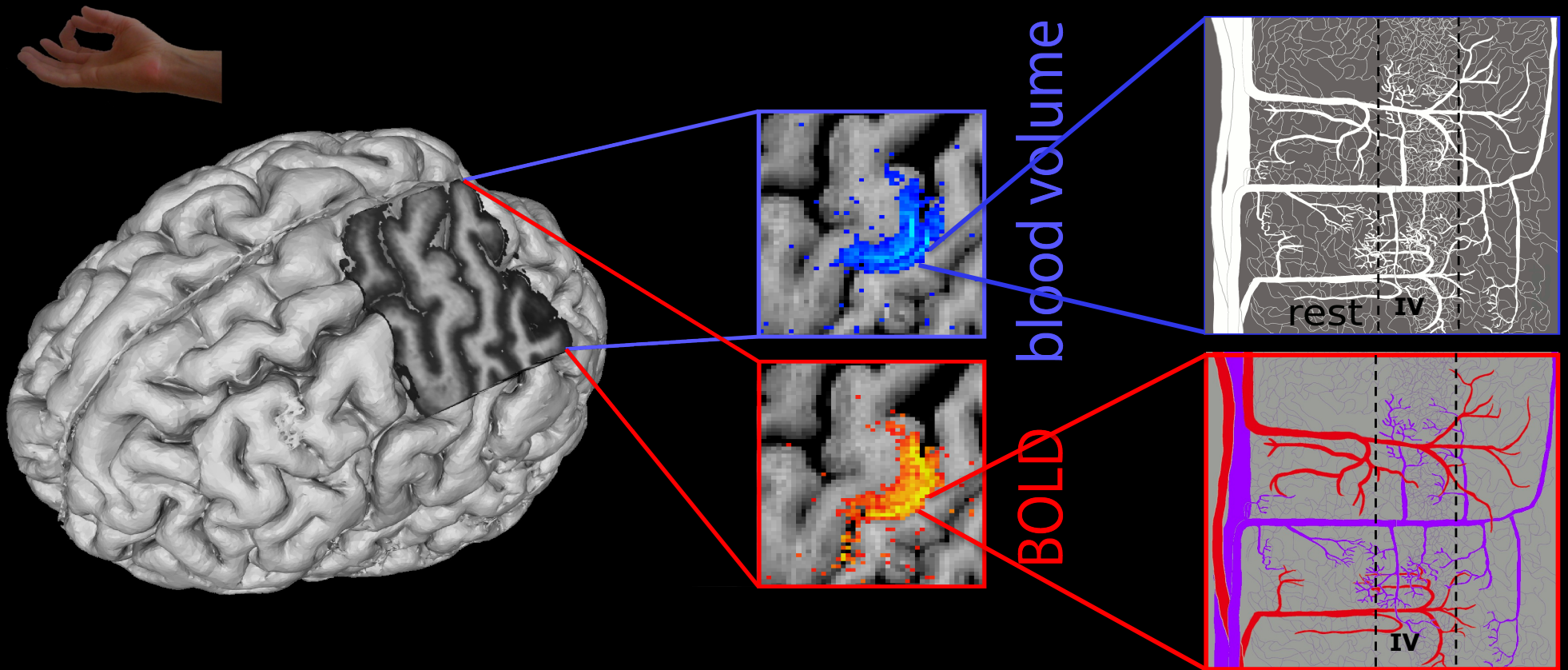
## Processing:

- Gating and variable TR correction
- event-related optimizing for response characterization rather than mapping
- calibration or global stressors
- vessel identification and masking  
(standard deviation, dark dots, latency...)
- noise regression from regions in brain  
(sagittal sinus, etc..)
- Modeling also the transients.
- Phase shifting reference functions
- latency mapping/modulation
- SE/GE ratios for localization
- large raw data databases

# VASO



# Local specificity of fMRI



## Acquisition:

- Spiral Scanning
- Multi-Shot Spiral
- Multi-shot EPI
- Keyhole Imaging
- Partial k-space
- Echo-volume imaging
- 3D EPI
- Zoomed EPI
- Multiband excitation
- Low flip angle

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- Spin-echo
- Asymmetric Spin-Echo
- Arterial Spin Labeling
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- **Low b Diffusion Weighting**
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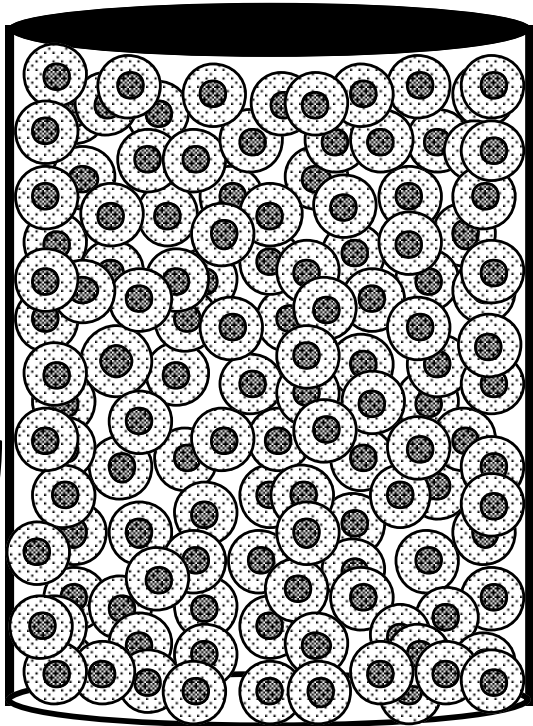
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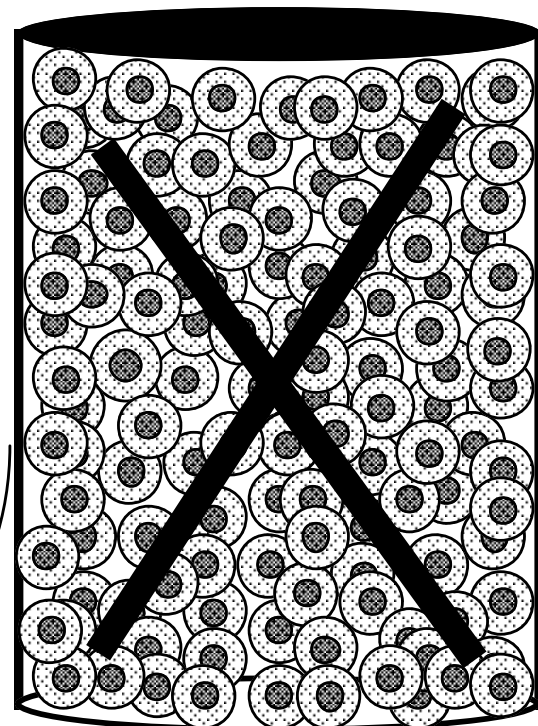


# Low b Diffusion Weighting

**no diffusion weighting**



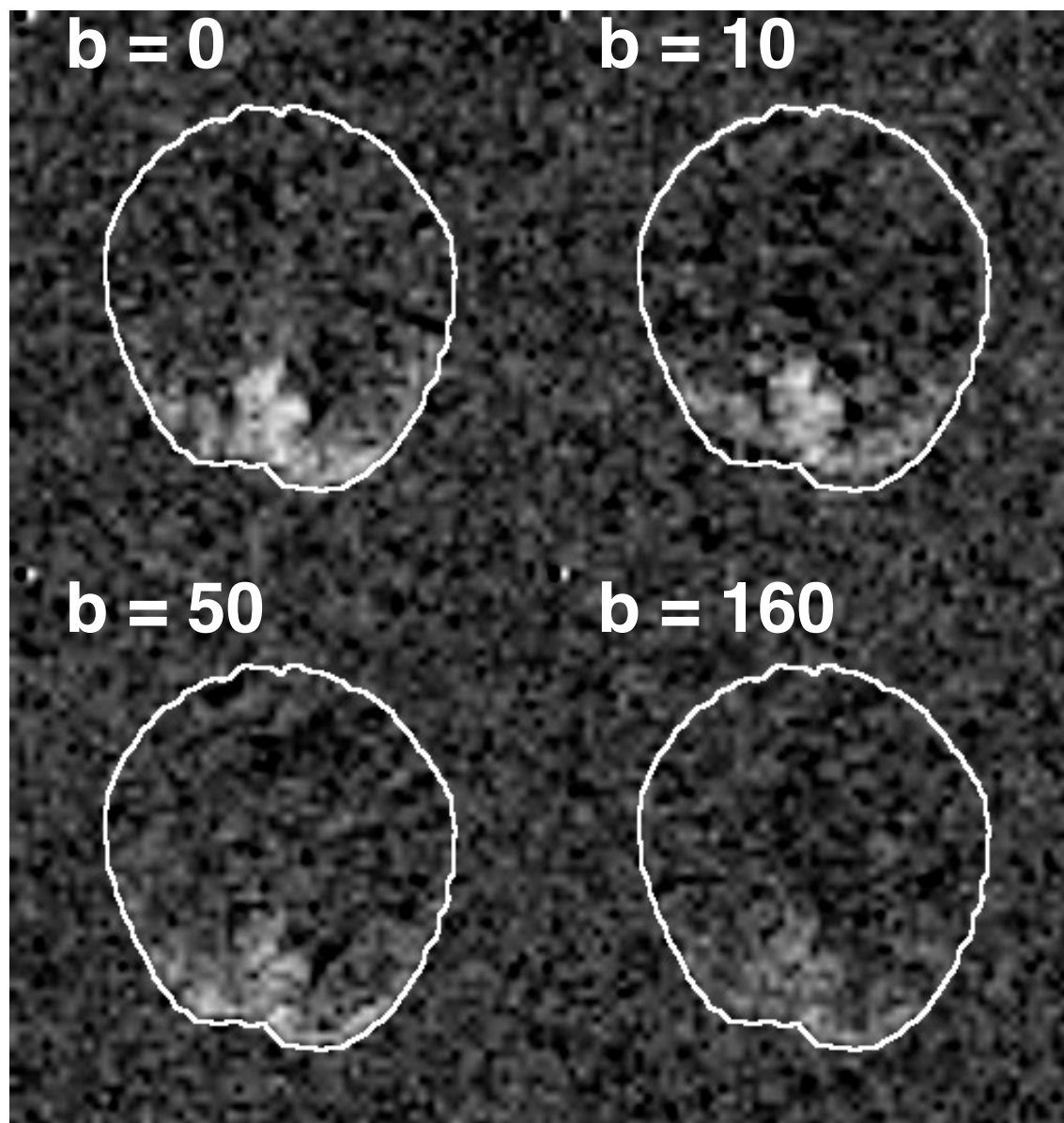
**diffusion weighting**



J. L. Boxerman, et al. MRM, 34, 4-10, (1995)

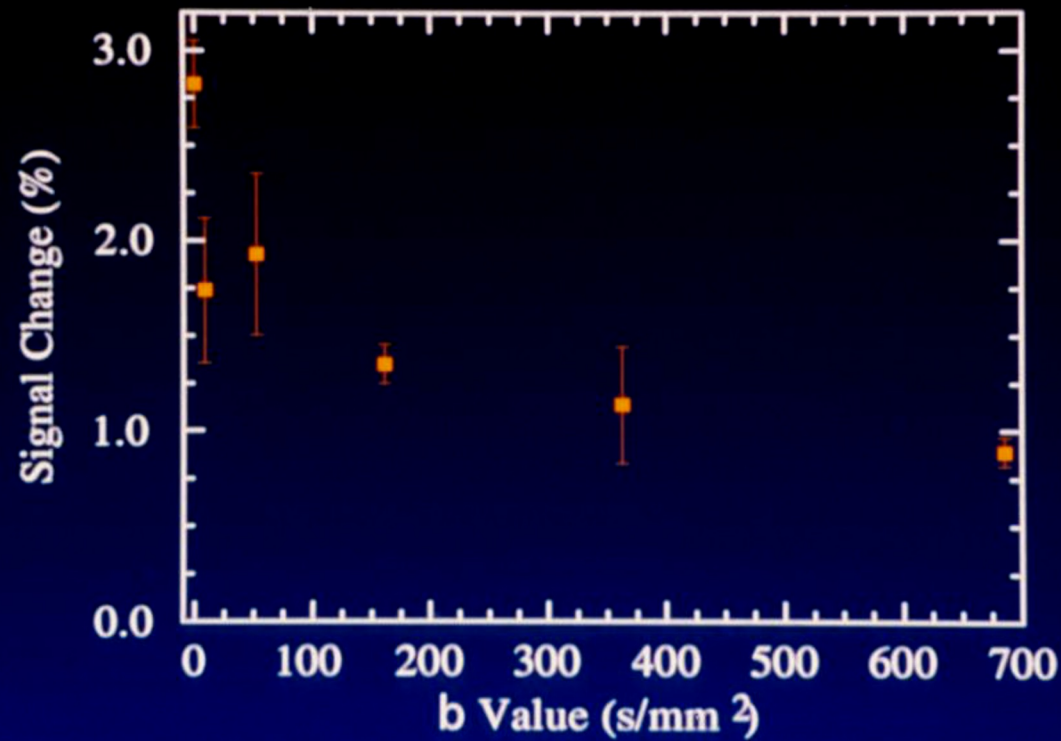
A. W. Song, et al. MRM, 35, 155-158 (1996)

## Low b Diffusion Weighting



# Low b Diffusion Weighting

## Summary of Diffusion-Weighted fMRI Data



## **Pros:**

- Remove intravascular signal (i.e. most of large vessel signal)

## **Cons:**

- Gradient-echo still sensitive to extravascular large vessels.
- Diffusion weighting and Spin-echo leaves one with no functional signal

## Acquisition:

- Spiral Scanning
- Multi-Shot Spiral
- Multi-shot EPI
- Keyhole Imaging
- Partial k-space
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- Zoomed EPI
- Multiband excitation
- Low flip angle

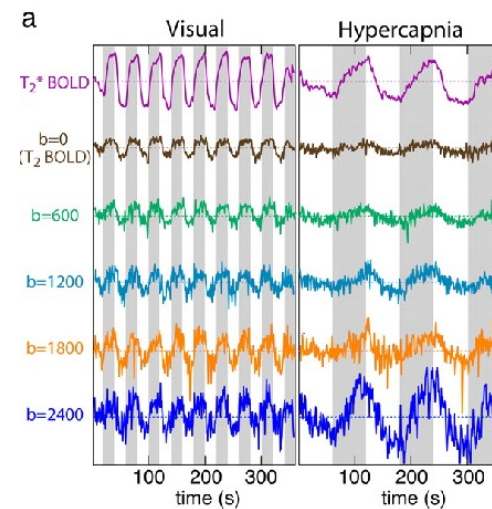
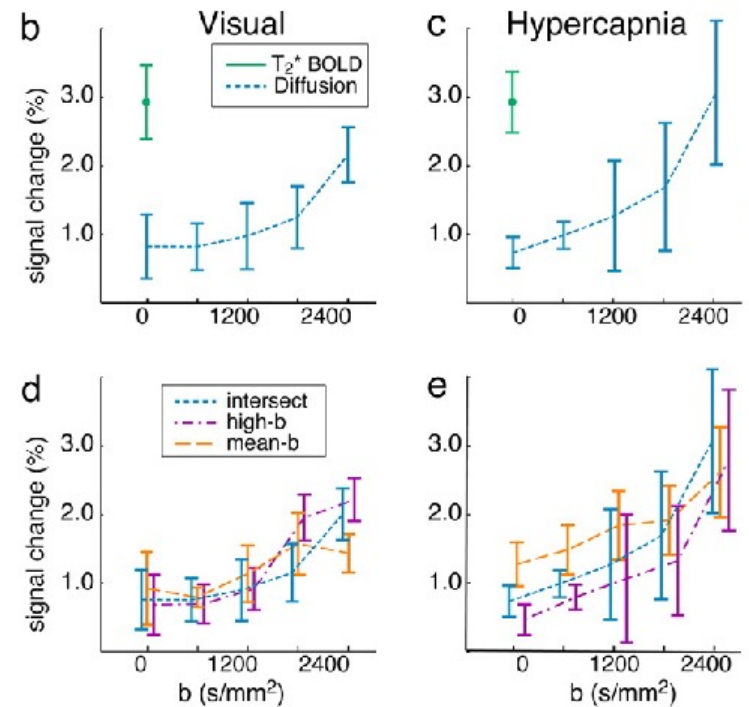
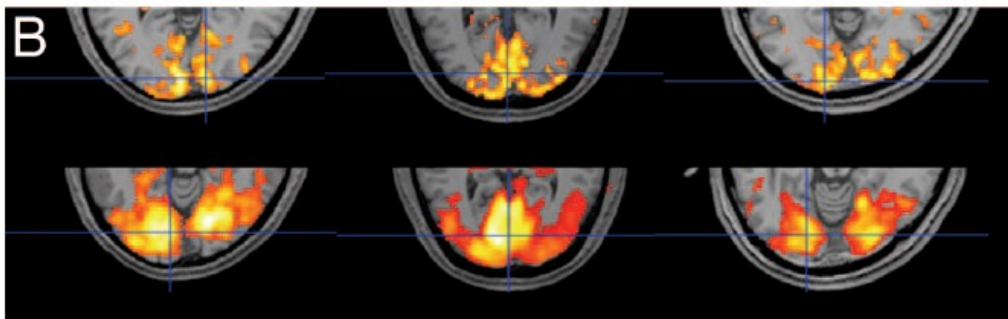
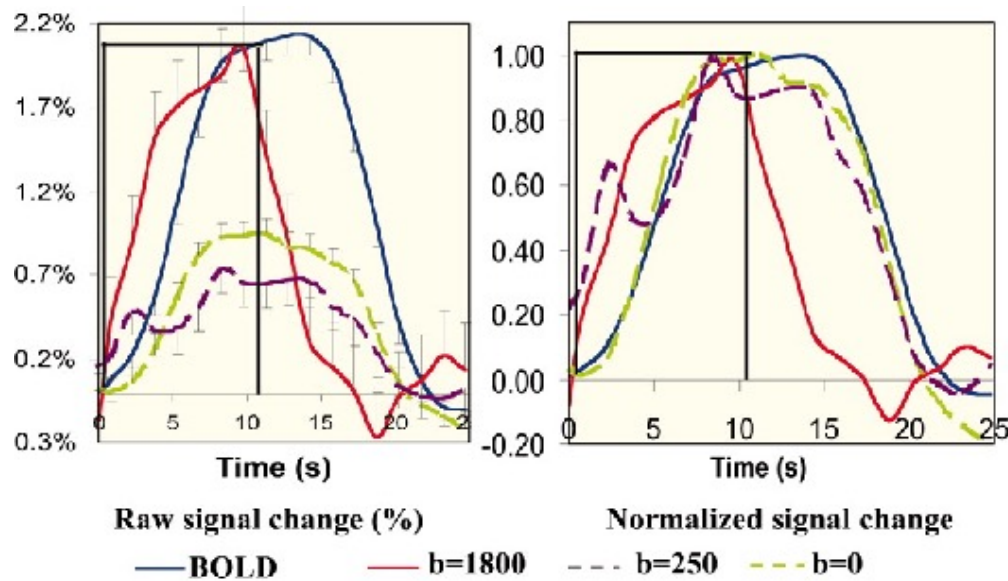
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- VASO
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- **High b Diffusion Weighting**
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- latency mapping/modulation
- SE/GE ratios for localization
- large raw data databases

# High b Diffusion Weighting



D. Le Bihan, et al Proceedings of the National Academy of Sciences of the United States of America 103 (21), pp. 8263-8268

K. Miller, et al Proceedings of the National Academy of Sciences of the United States of America 104 (52), pp. 20967-20972

## Acquisition:

- Spiral Scanning
- Multi-Shot Spiral
- Multi-shot EPI
- Keyhole Imaging
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- 3D EPI
- Zoomed EPI
- Multiband excitation
- Low flip angle

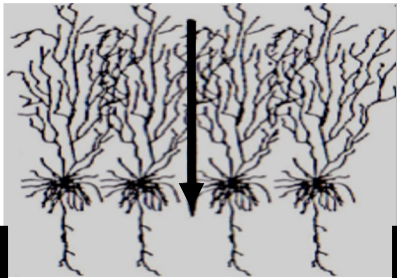
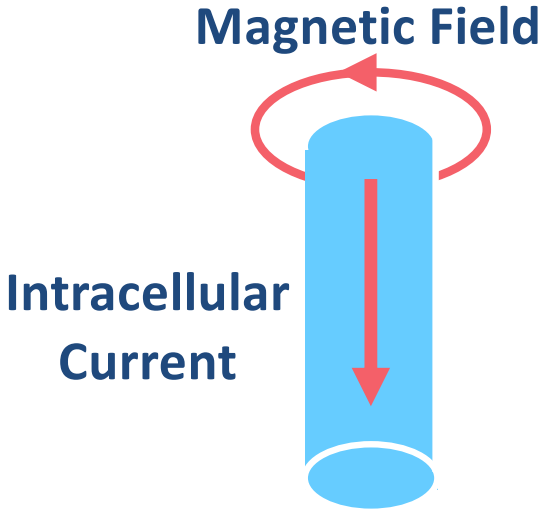
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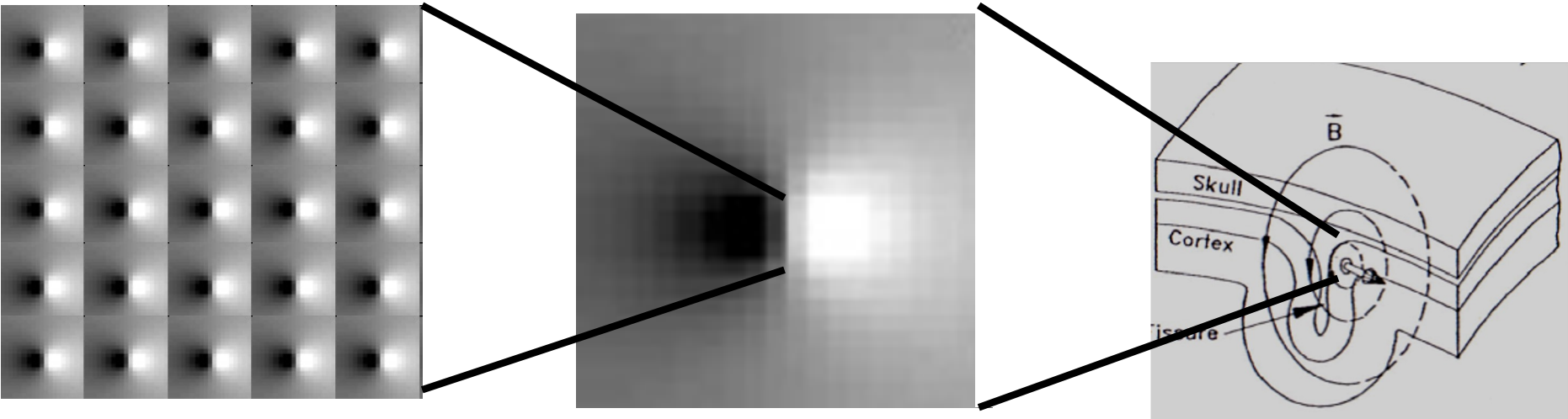
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# Neuronal Current Imaging



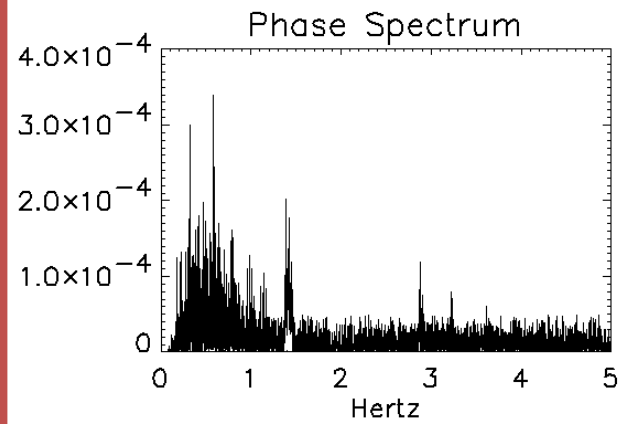
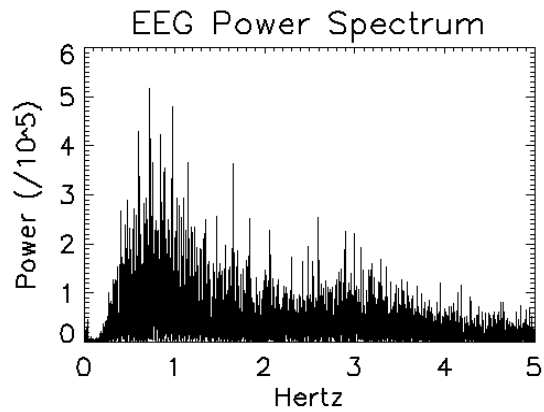
## Surface Field Distribution Across Spatial Scales



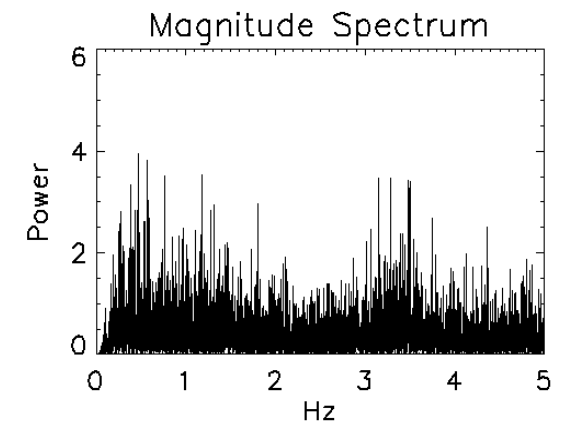
Adapted from: J.P. Wikswo Jr et al. *J Clin Neurophy* 8(2): 170-188, 1991



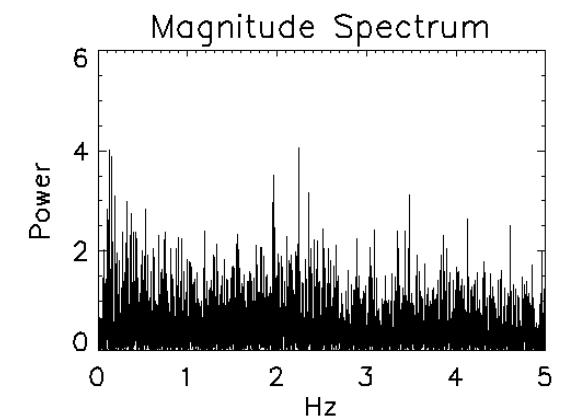
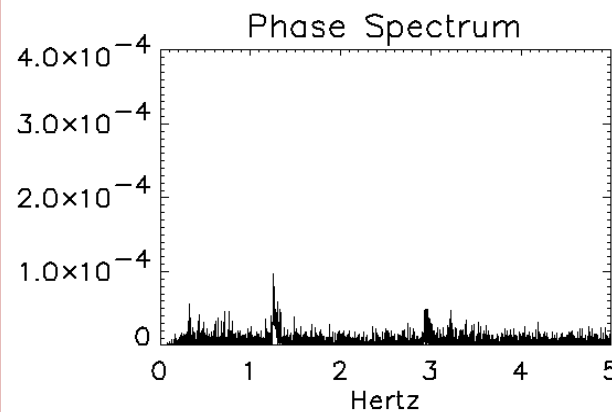
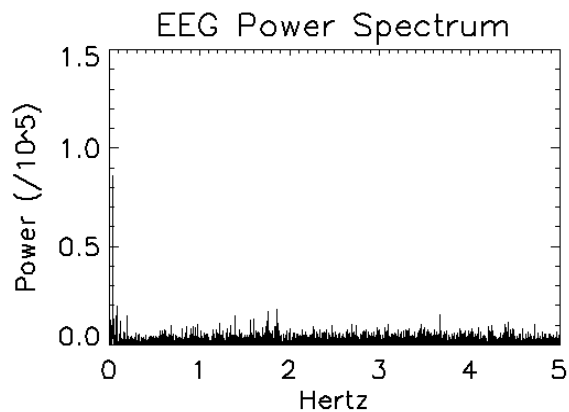
# EEG



# MR (7T)



# 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).

## Acquisition:

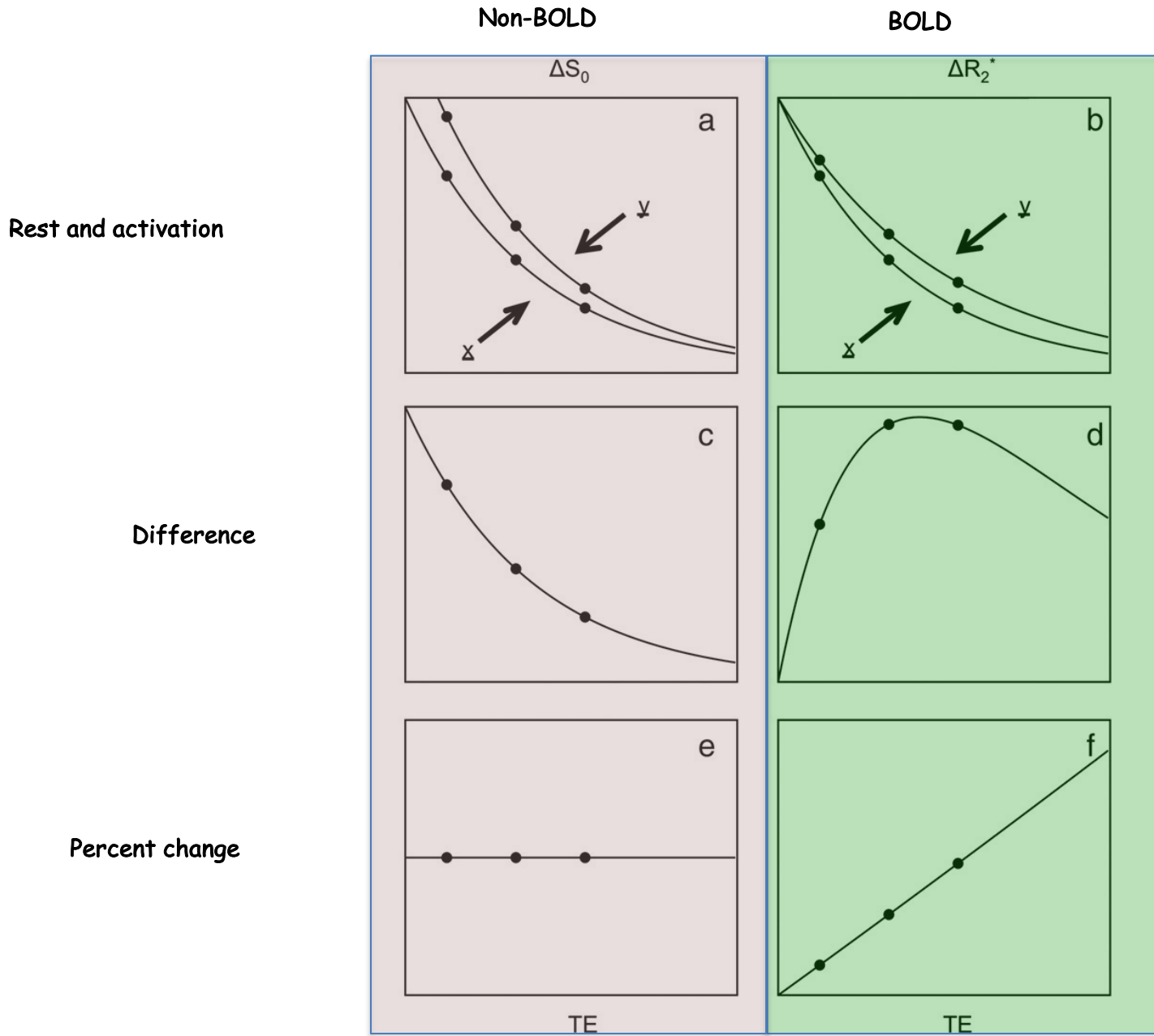
- Spiral Scanning
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- Multi-shot EPI
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# Resting multi-echo time course data

Two typical ICA Components

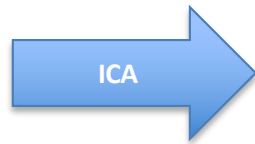
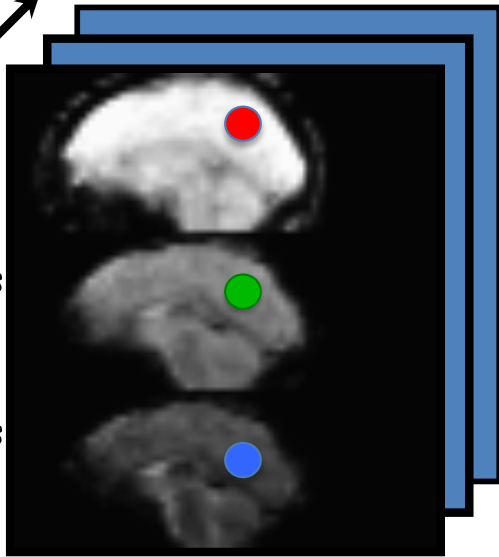
time ↑

14ms

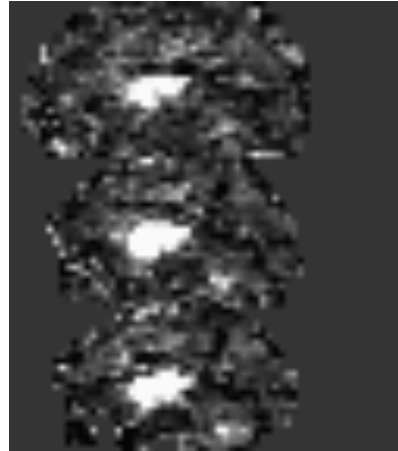
37ms

60ms

TE



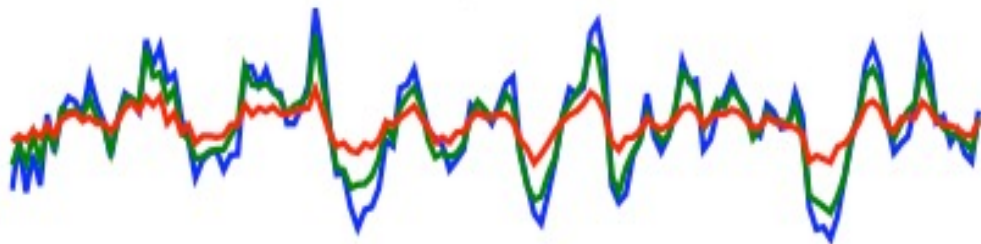
Putamen



Default Mode Network

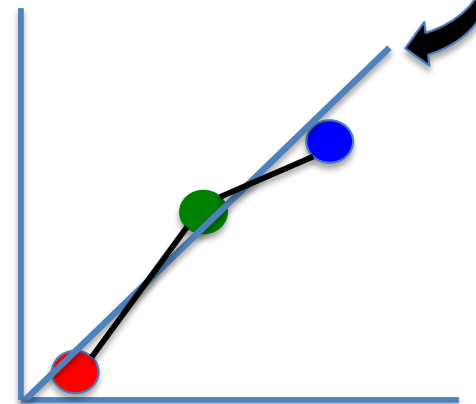


time courses ↓



% Signal Change

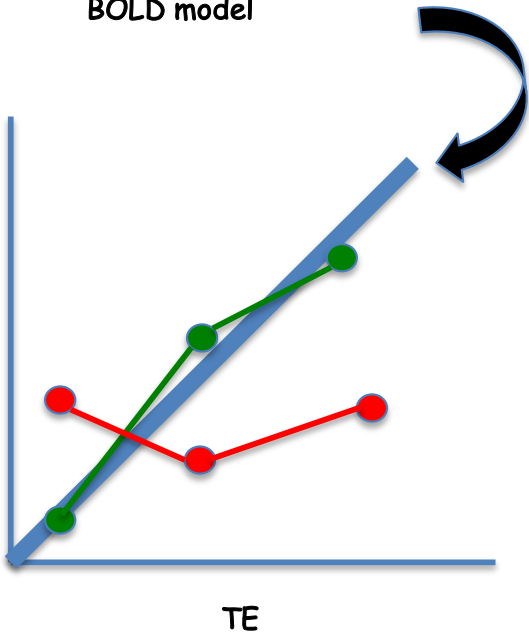
BOLD model



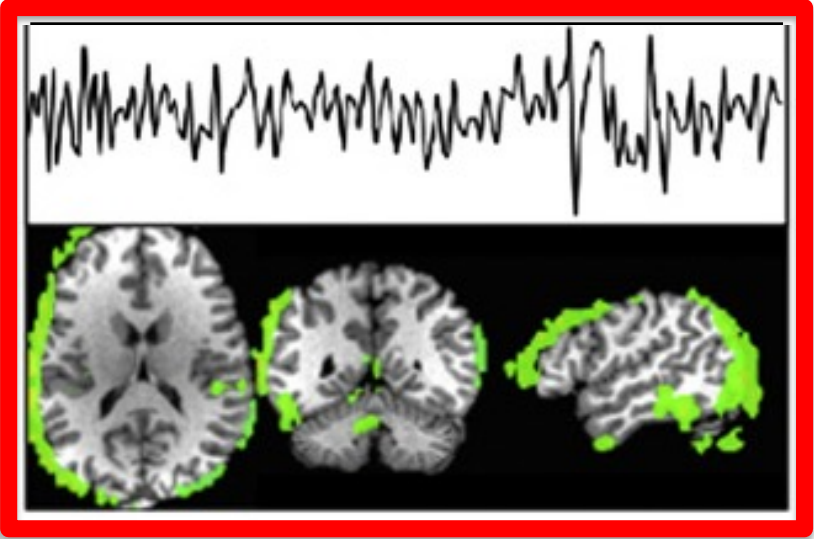
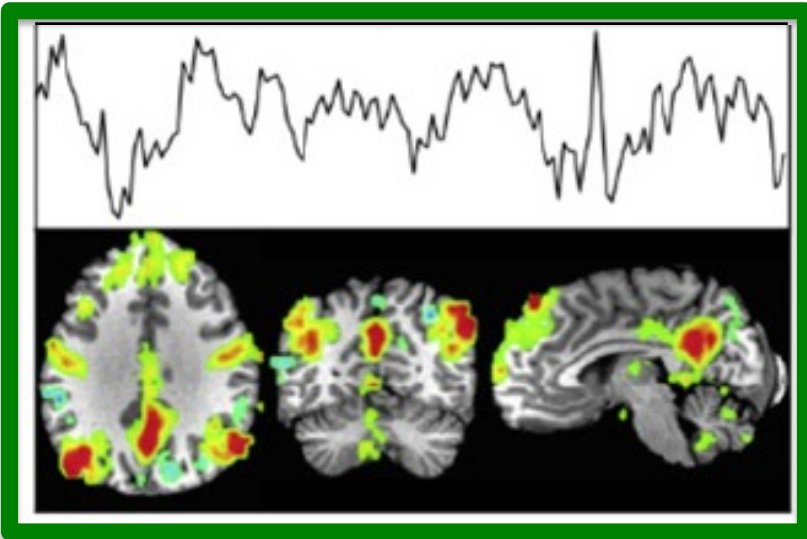
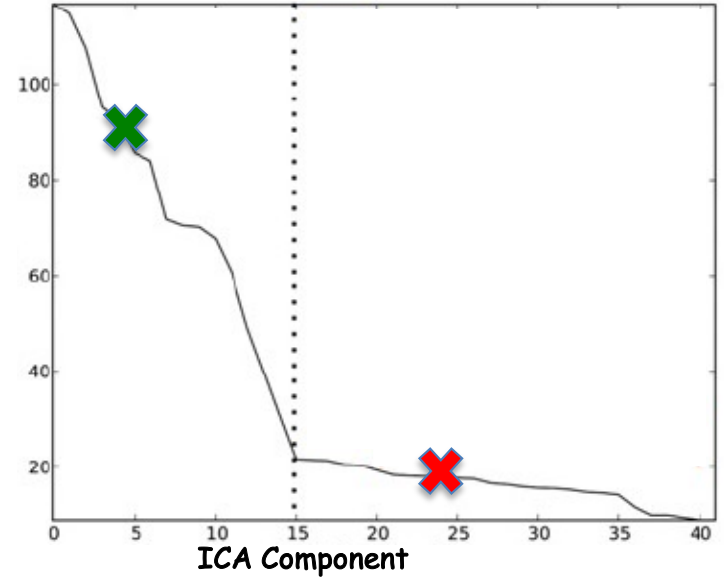
TE

BOLD model

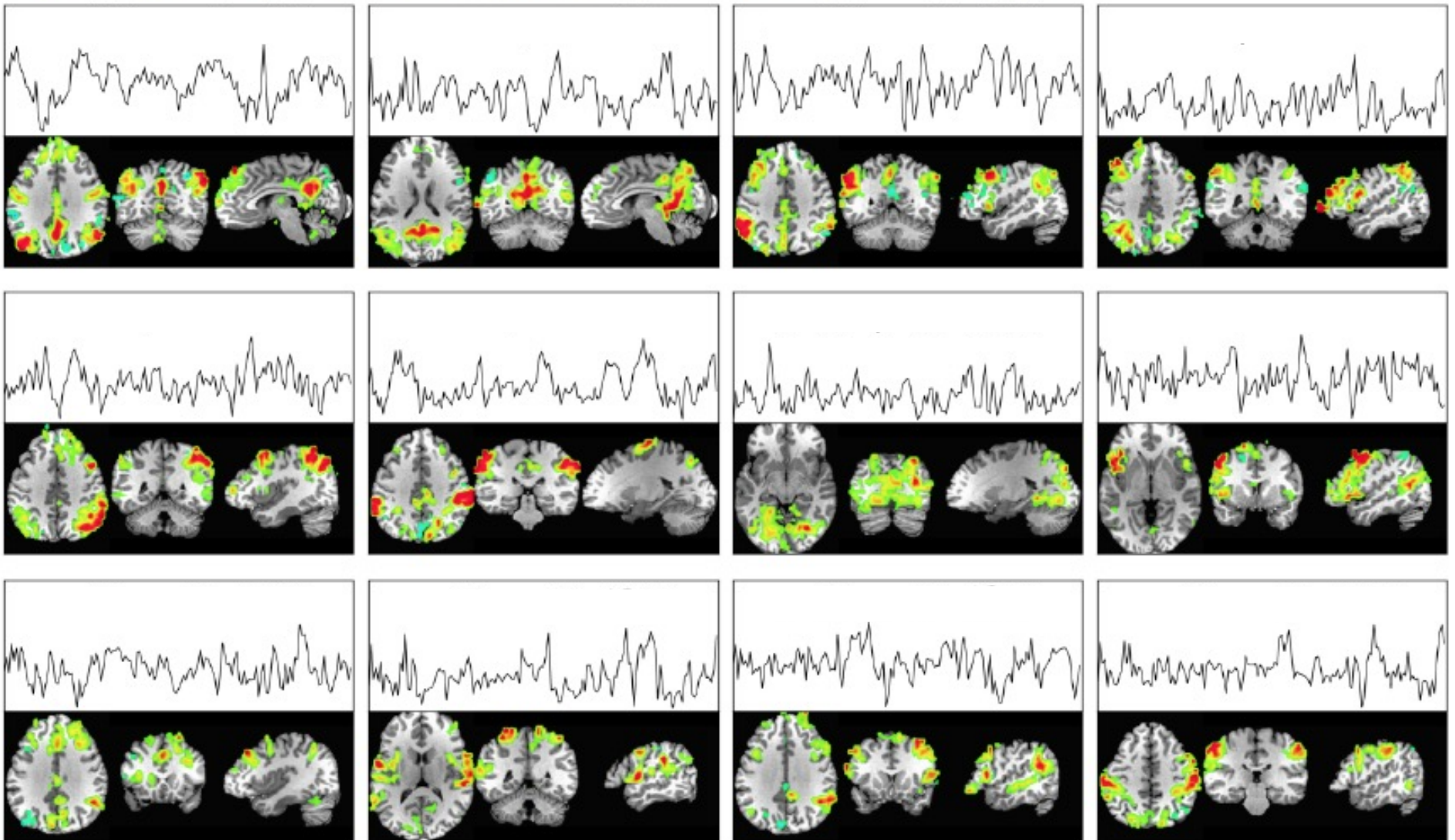
% Signal Change



Goodness of fit to BOLD model

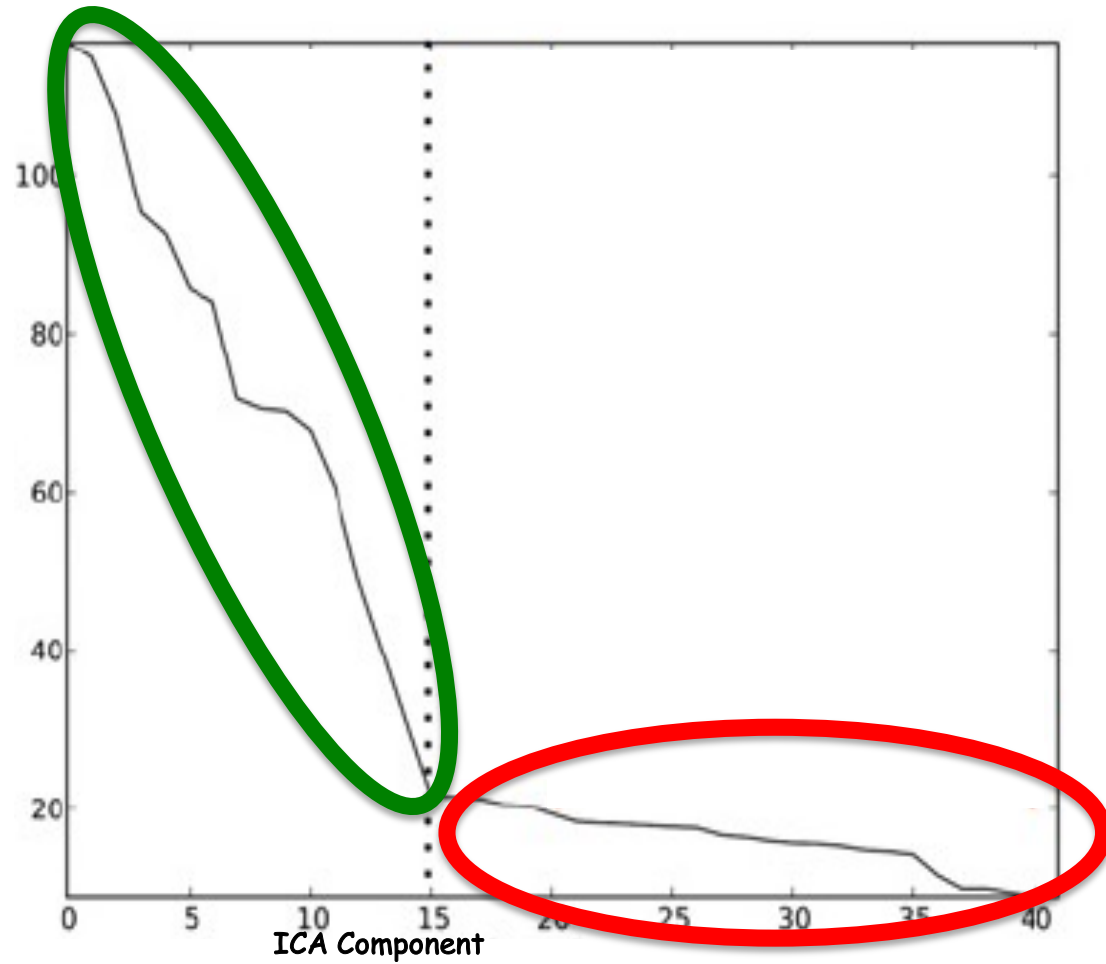


# Automatic Selection of BOLD Component Map:

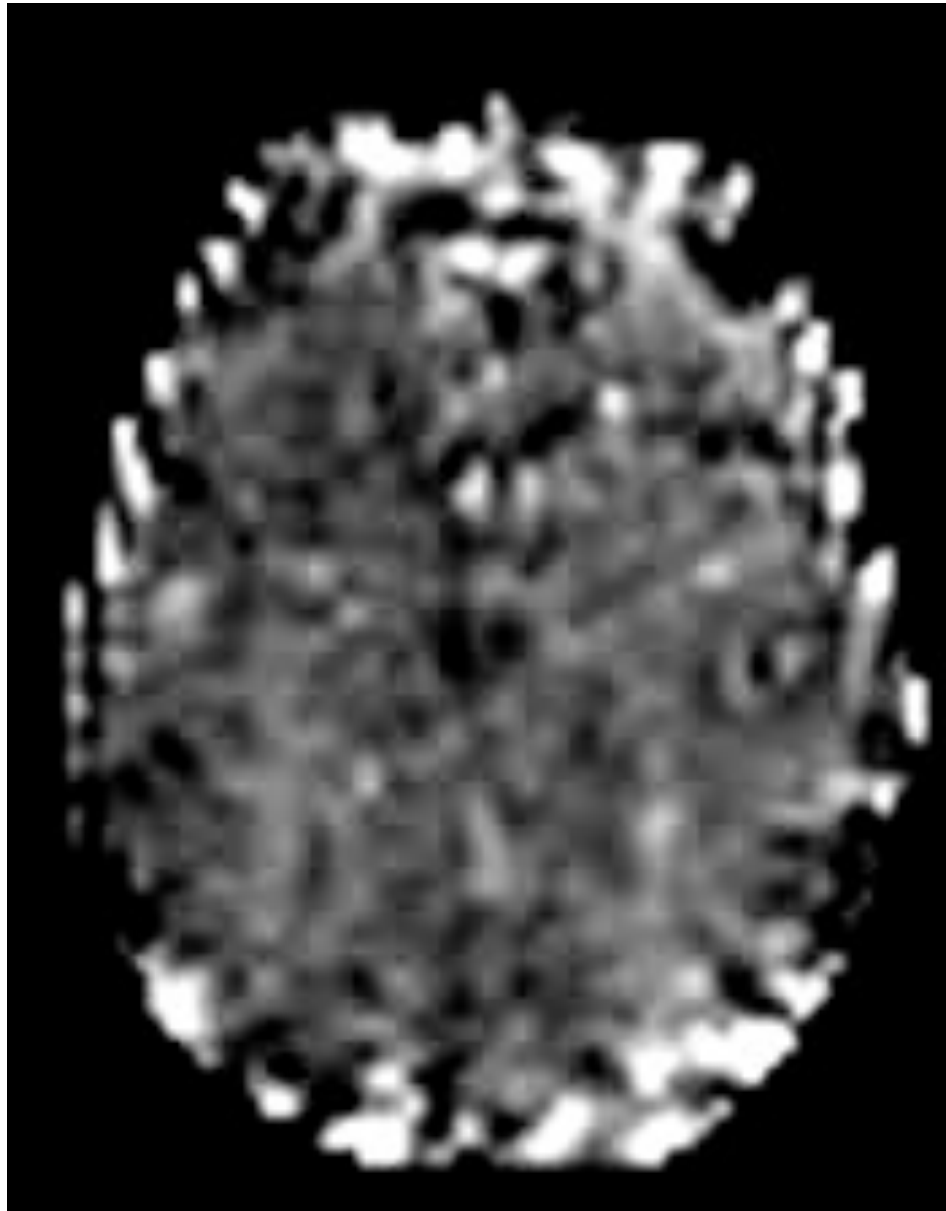


Clustering is extremely robust on small groups and on individuals when using multi-echo selected BOLD Components.

Goodness of fit to BOLD model

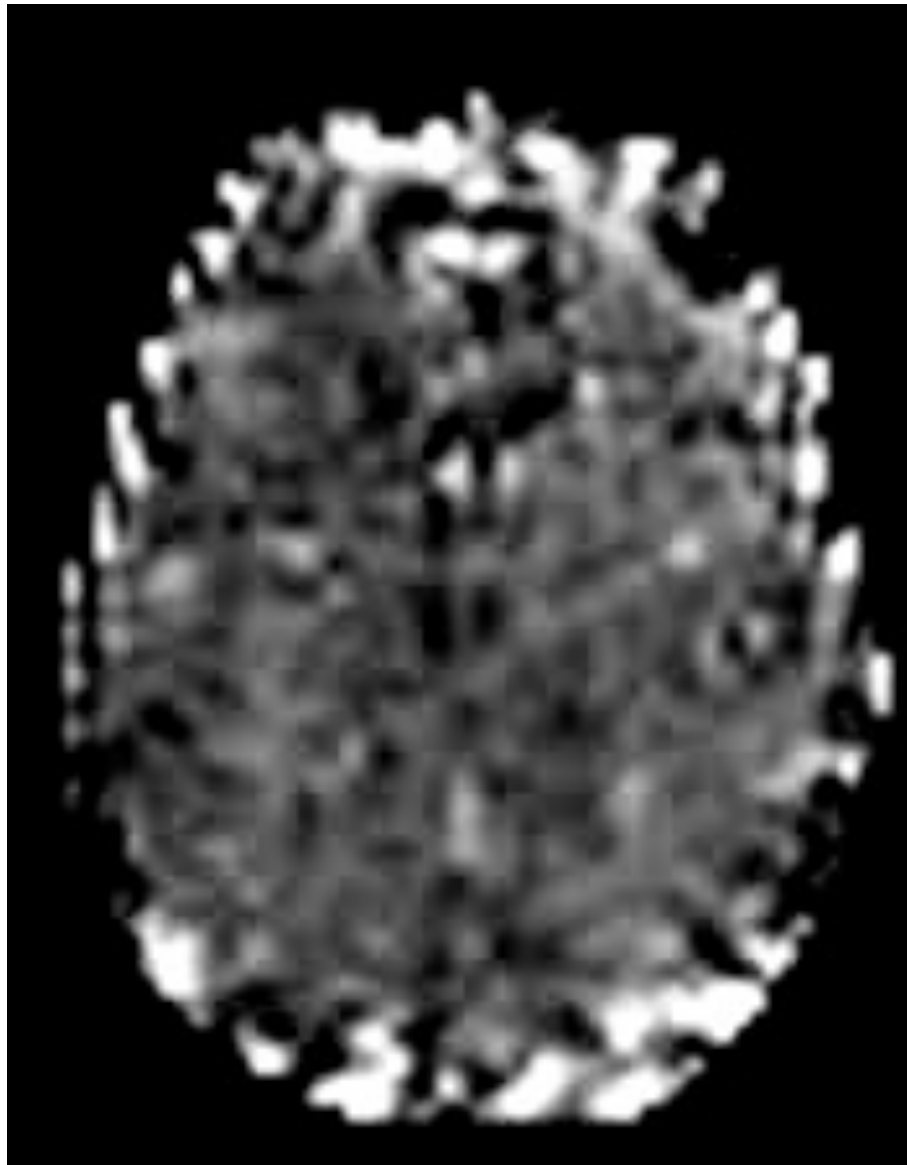


## Typical raw time series signal

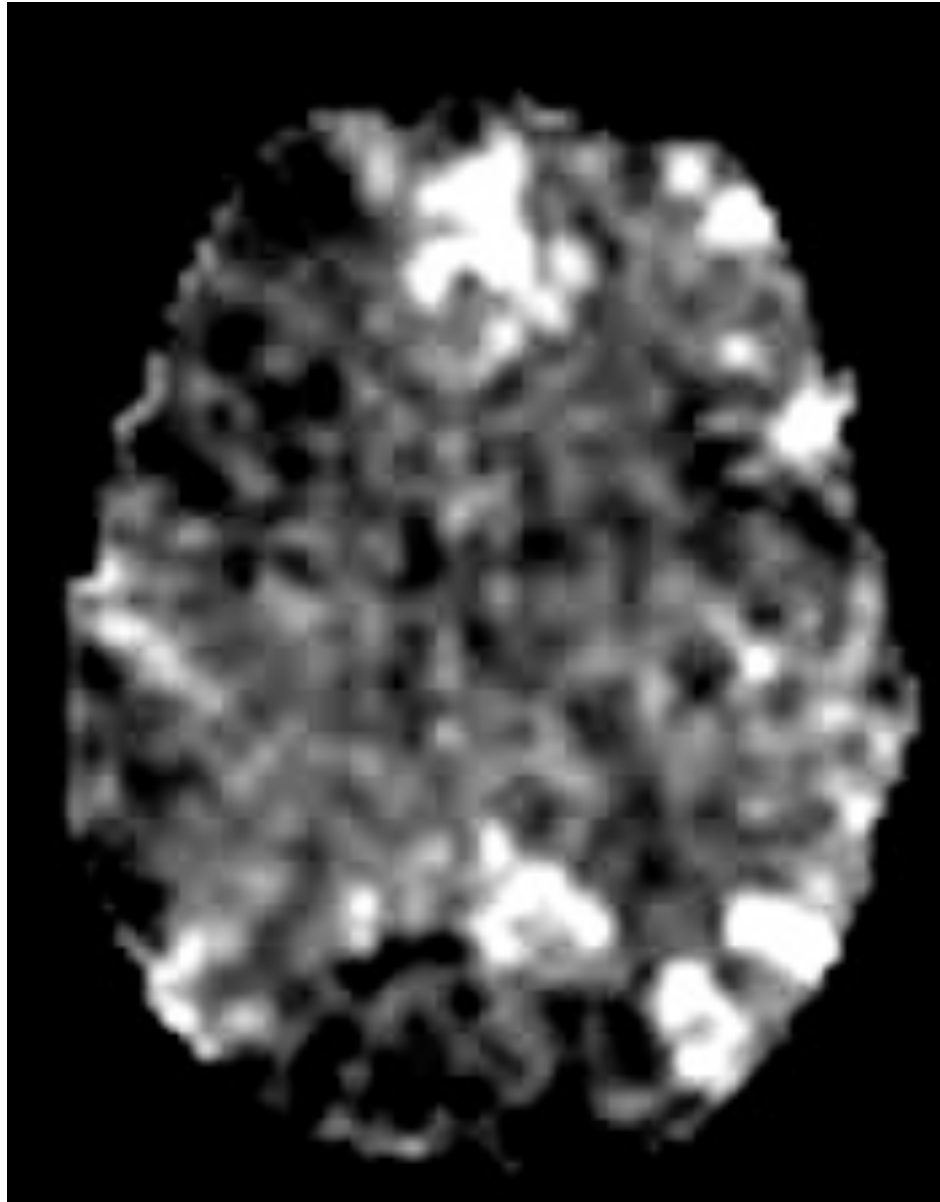




**Non-BOLD fluctuations...what is regressed out.**



**After non-BOLD noise is regressed out...this is what remains**



## Acquisition:

- Spiral Scanning
- Multi-Shot Spiral
- Multi-shot EPI
- Keyhole Imaging
- Partial k-space
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- 3D EPI
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- Multiband excitation
- Low flip angle

## Contrast Weighting

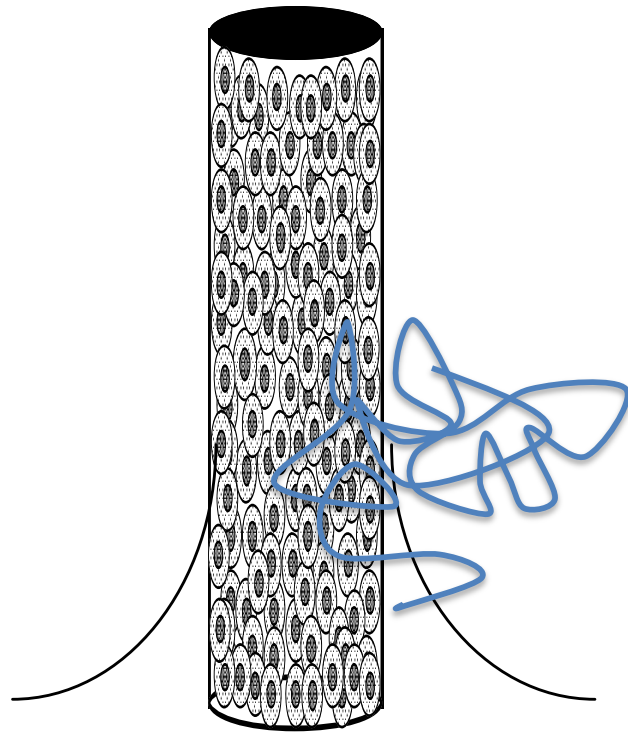
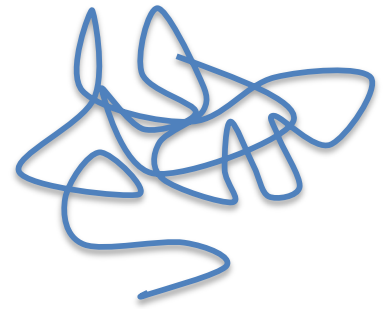
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- Multi-echo acquisition
- **MRI time series phase information**
- Steady State Free Precession
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## Processing:

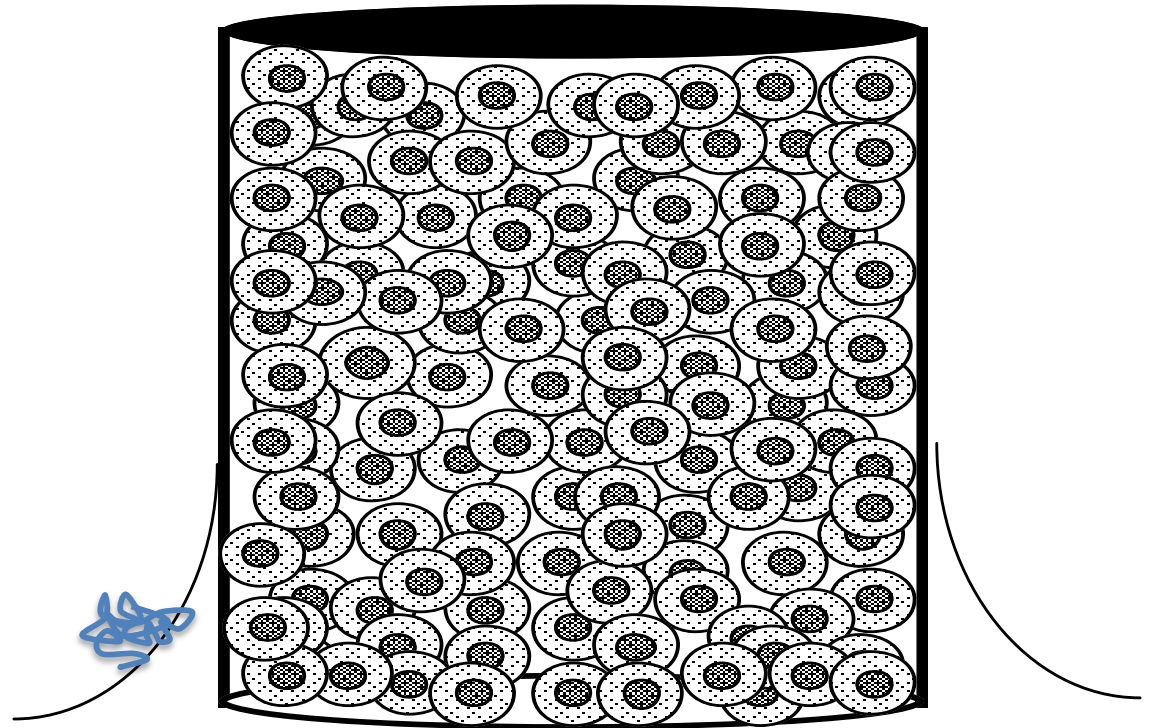
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# MRI time series phase information

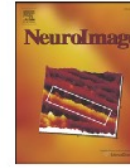
Diffusing spin



$\delta\text{phase} = 0$   
 $\delta\text{magnitude} = 1$



$\delta\text{phase} = 1$   
 $\delta\text{magnitude} = 1$



## Technical Note

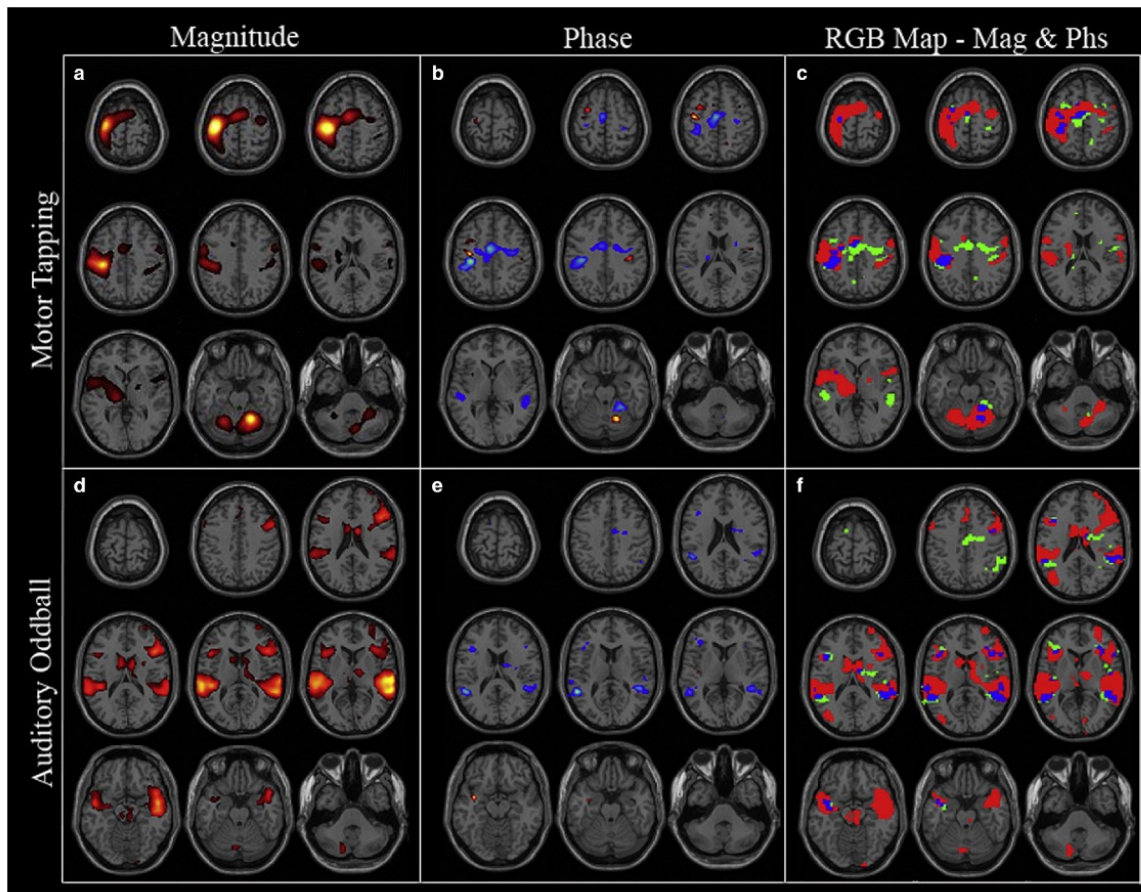
## Changes in fMRI magnitude data and phase data observed in block-design and event-related tasks

Sunil Kumar Arja<sup>a,b,\*</sup>, Zhaomei Feng<sup>a,b</sup>, Zikuan Chen<sup>a</sup>, Arvind Caprihan<sup>a</sup>, Kent A. Kiehl<sup>a</sup>, Tülay Adali<sup>c</sup>, Vince D. Calhoun<sup>a,b</sup>

<sup>a</sup> The Mind Research Network, 1101 Yale Blvd NE, Albuquerque, NM 87131, USA

<sup>b</sup> Department of ECE, University of New Mexico, Albuquerque, NM, USA

<sup>c</sup> Department of CSEE, University of Maryland, Baltimore County, Baltimore, MD, USA



Red = mag  
Green = mag+phase  
Blue = phase

## Acquisition:

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# Gating and variable TR correction

◆ Human Brain Mapping 6:33–41(1998) ◆

## Imaging Subcortical Auditory Activity in Humans

**A.R. Guimaraes,<sup>1,2\*</sup> J.R. Melcher,<sup>3</sup> T.M. Talavage,<sup>2,3</sup> J.R. Baker,<sup>1,2</sup> P. Ledden,<sup>1</sup>  
B.R. Rosen,<sup>1,2</sup> N.Y.S. Kiang,<sup>2-4</sup> B.C. Fullerton,<sup>2,3</sup> and R.M. Weisskoff<sup>1,2</sup>**

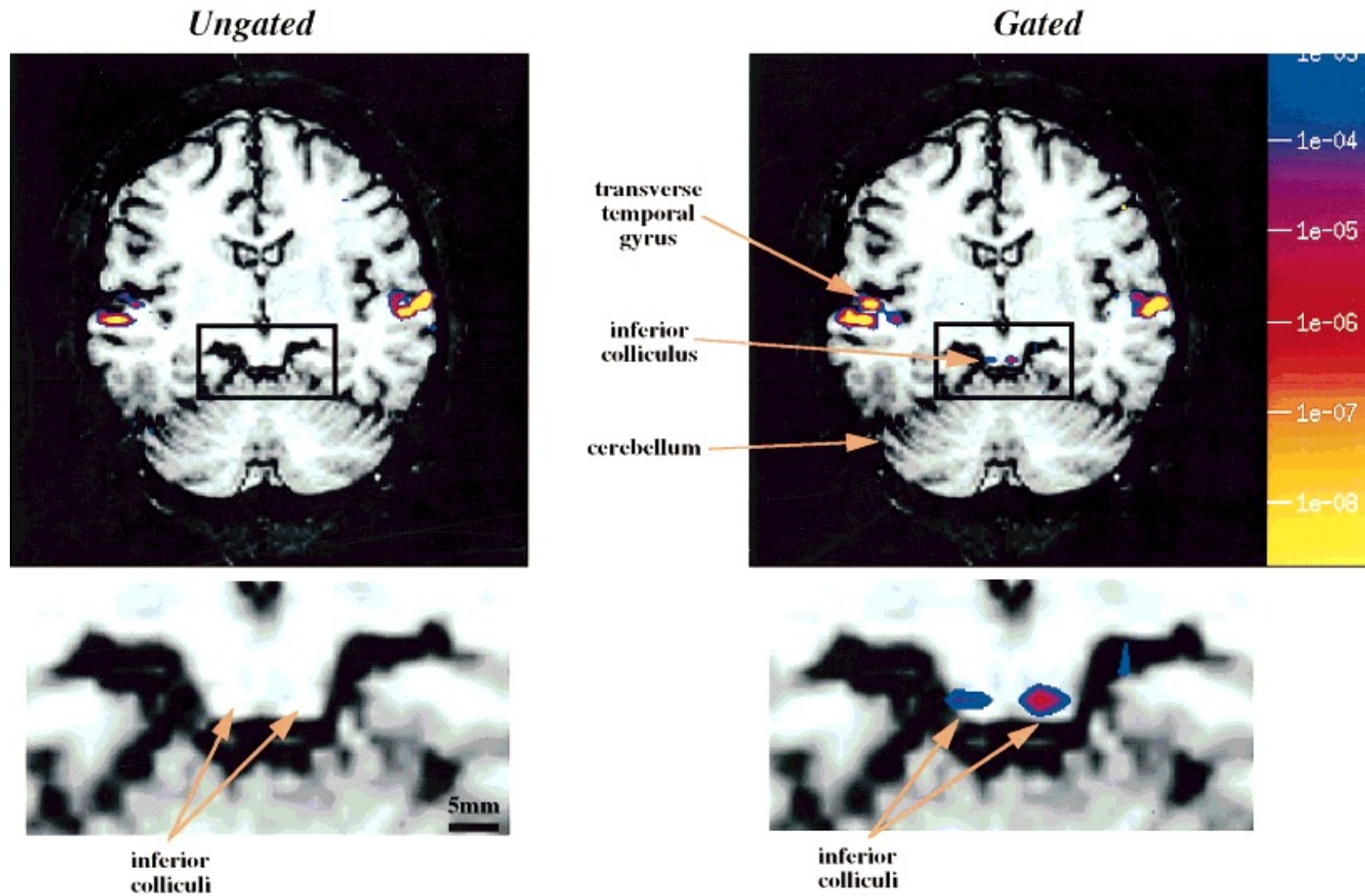
<sup>1</sup>*MGH-NMR Center, Department of Radiology, Massachusetts General Hospital,  
Charlestown, Massachusetts 02129*

<sup>2</sup>*Harvard-Massachusetts Institute of Technology Division of Health, Sciences and Technology,  
Cambridge, Massachusetts 02139*

<sup>3</sup>*Eaton-Peabody Laboratory, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts*

<sup>4</sup>*Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology,  
Cambridge, Massachusetts 02139*

# Gating and variable TR correction



A. R. Guimaraes et al., Human Brain Mapping 6, 33-41 (1998)



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# Event-related optimizing for response characterization rather than mapping

NeuroImage 15, 252–264 (2002)

doi:10.1006/nimg.2001.0964, available online at <http://www.idealibrary.com> on 

## RAPID COMMUNICATION

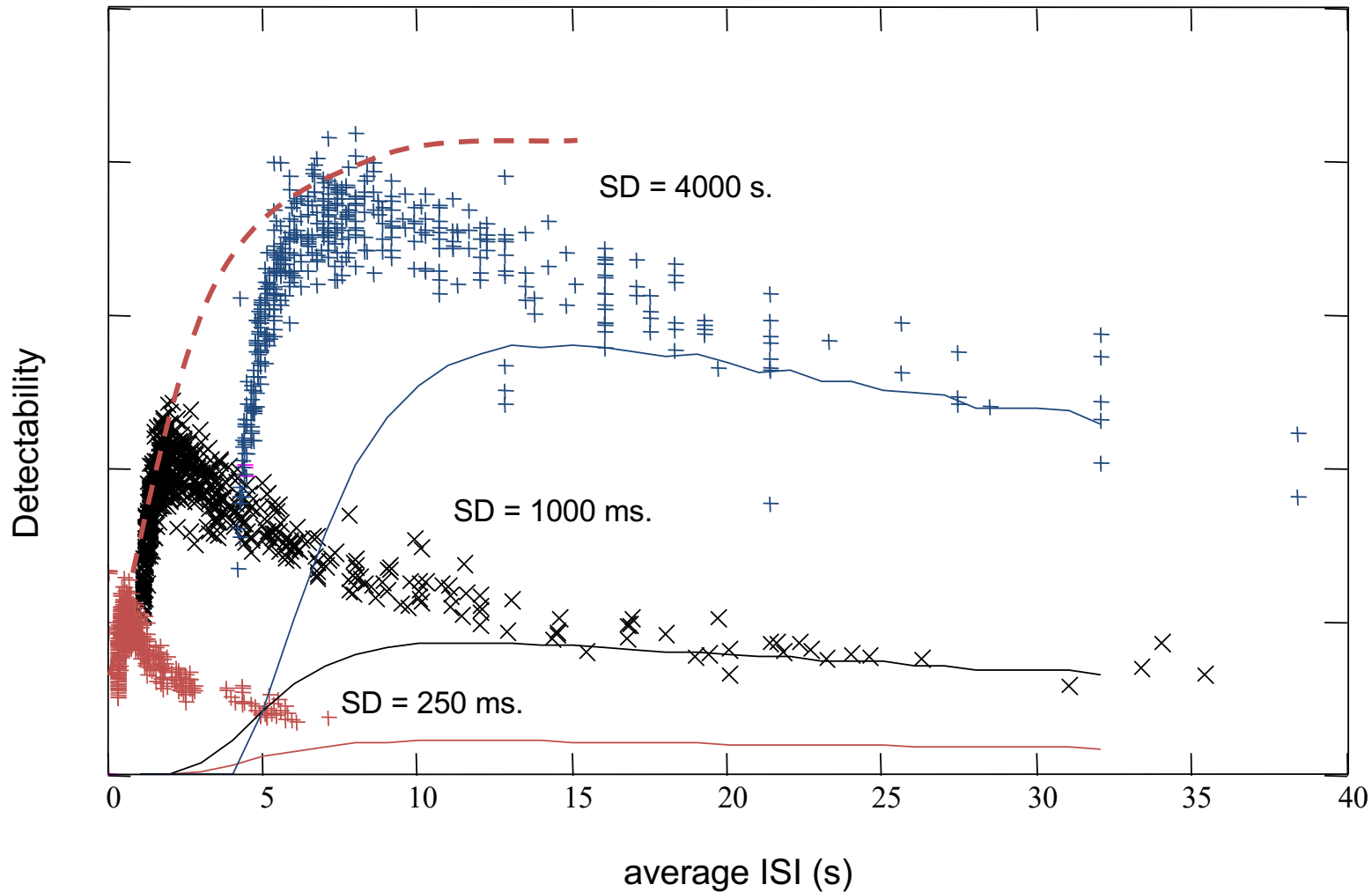
### Detection versus Estimation in Event-Related fMRI: Choosing the Optimal Stimulus Timing

Rasmus M. Birn, Robert W. Cox,\* and Peter A. Bandettini

*3T Functional Neuroimaging Core, National Institute of Mental Health, and \*Scientific and Statistical Computing Core,  
National Institute of Mental Health, Bethesda, Maryland*

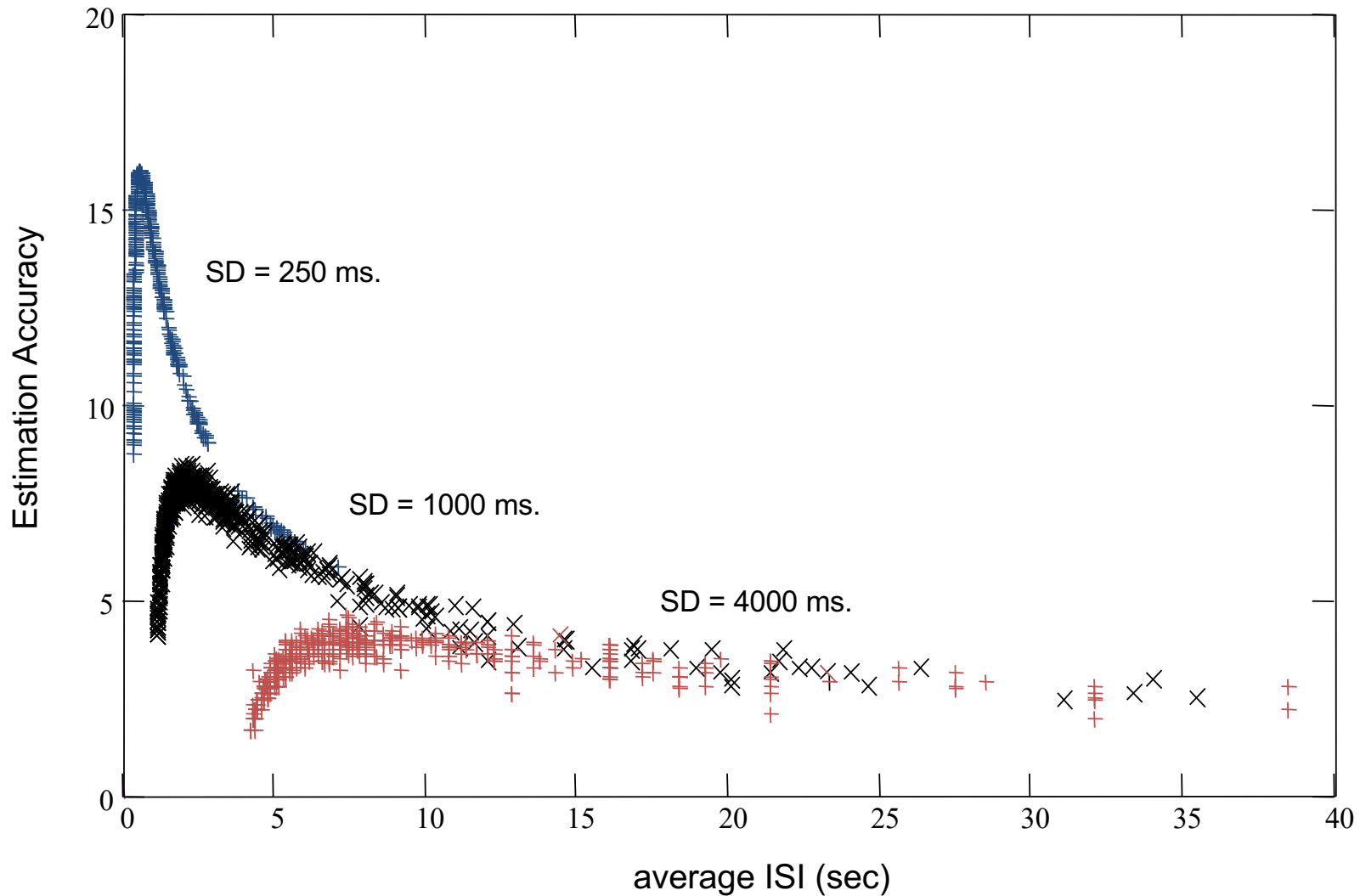
Received December 28, 2000

# 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).

## Acquisition:

- Spiral Scanning
- Multi-Shot Spiral
- Multi-shot EPI
- Keyhole Imaging
- Partial k-space
- Echo-volume imaging
- 3D EPI
- Zoomed EPI
- Multiband excitation
- Low flip angle

## Contrast Weighting

- Spin-echo
- Asymmetric Spin-Echo
- Arterial Spin Labeling
- VASO
- Low b Diffusion Weighting
- High b Diffusion Weighting
- Neuronal Current Imaging
- Multi-echo acquisition
- MRI time series phase information
- Steady State Free Precession
- Manganese contrast

## Processing:

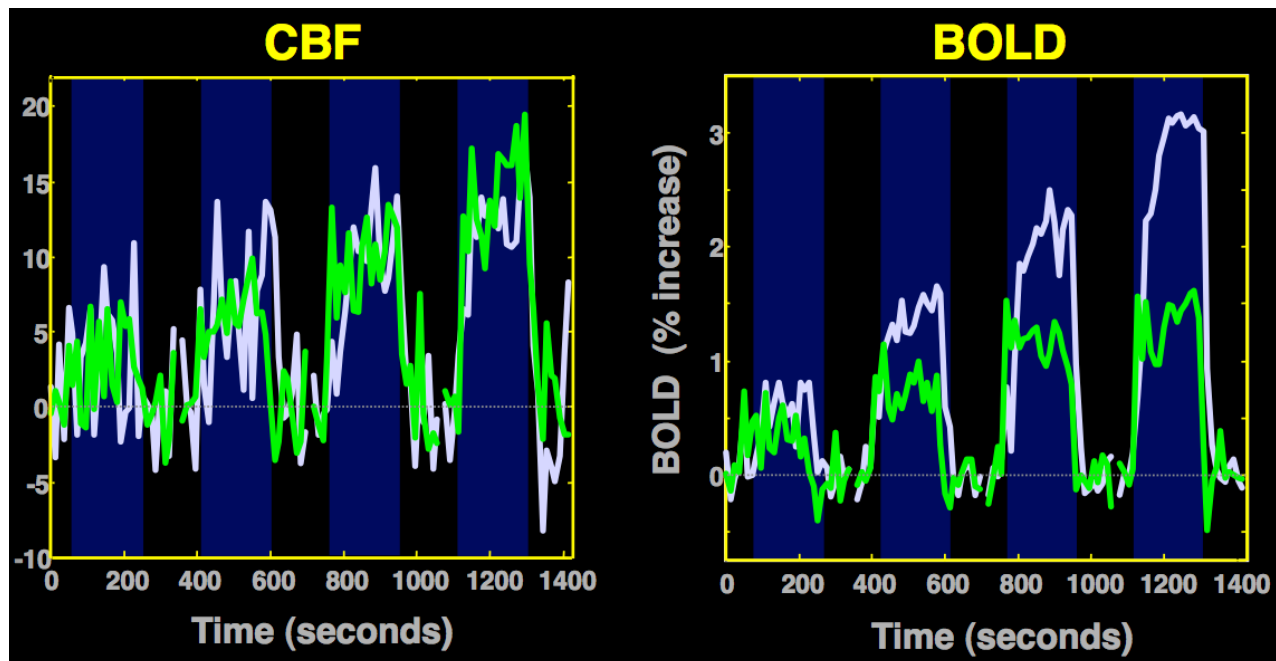
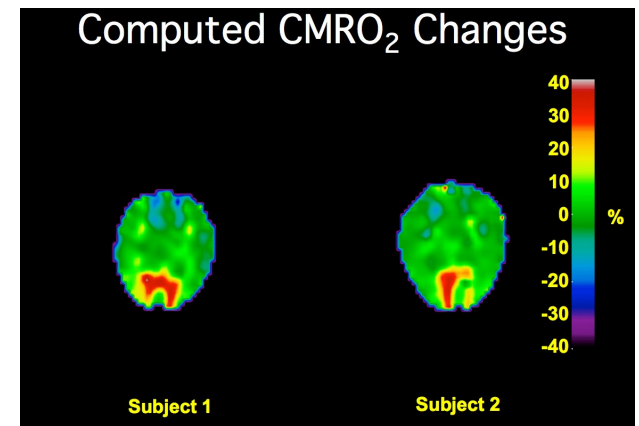
- Gating and variable TR correction
- event-related optimizing for response characterization rather than mapping
- **calibration or global stressors**
- vessel identification and masking  
(standard deviation, dark dots, latency...)
- noise regression from regions in brain  
(sagittal sinus, etc..)
- Modeling also the transients.
- Phase shifting reference functions
- latency mapping/modulation
- SE/GE ratios for localization
- large raw data databases

# Calibration and Global Stressors

## Activation-induced $CMRO_2$ changes

- requires a global hemodynamic stress
- assumption is that  $CMRO_2$  unchanged with global stress
- requires simultaneous flow and BOLD collection

R. D. Hoge, et al, PNAS 96: 9403-9408, 1999



*Visual = green*  
*Hypercapnia = white*

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## Vessel identification and masking

- dark dots
- percent signal change upper limit
- standard deviation of phase and magnitude
- hemodynamic latency

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Pros:

Will remove larger veins and perhaps some temporal and spatial variability

Cons:

Take a bit of extra processing

At low resolution, we like veins as they amplify the signal.



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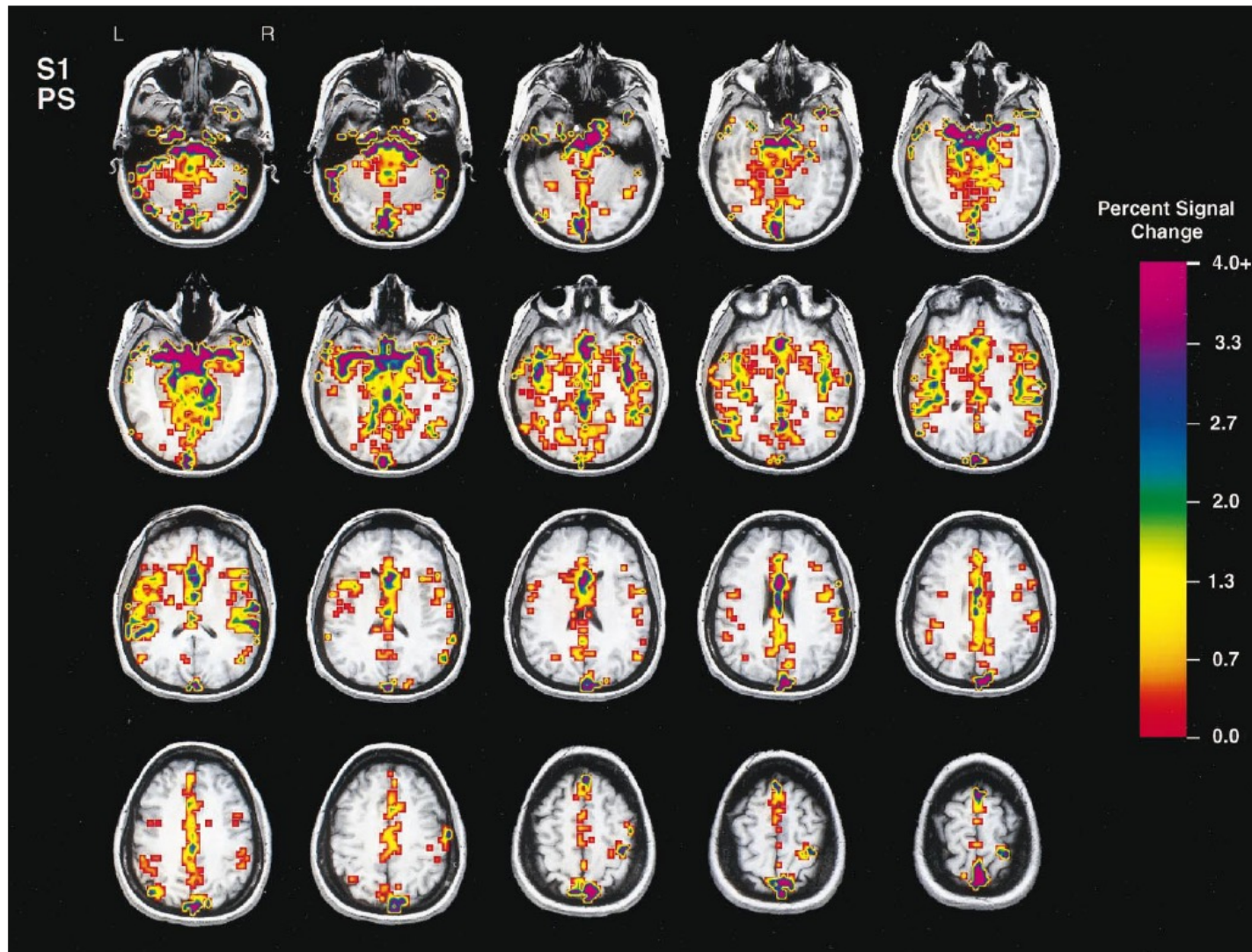
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# Data – based Cardiac Noise Removal



Dagli, et al. NeuroImage, 9, 407-415 (1999)

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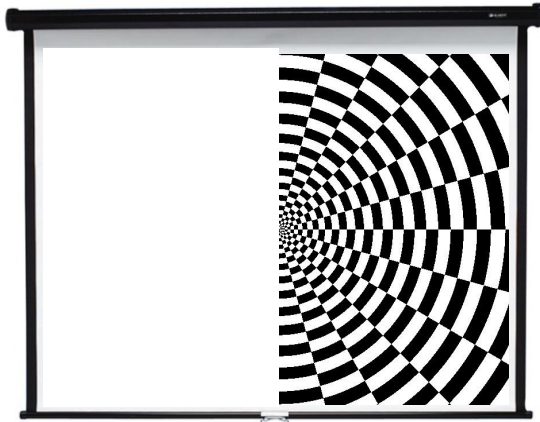
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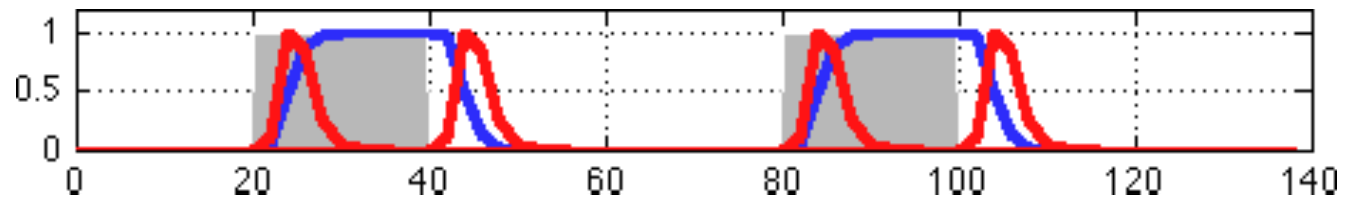
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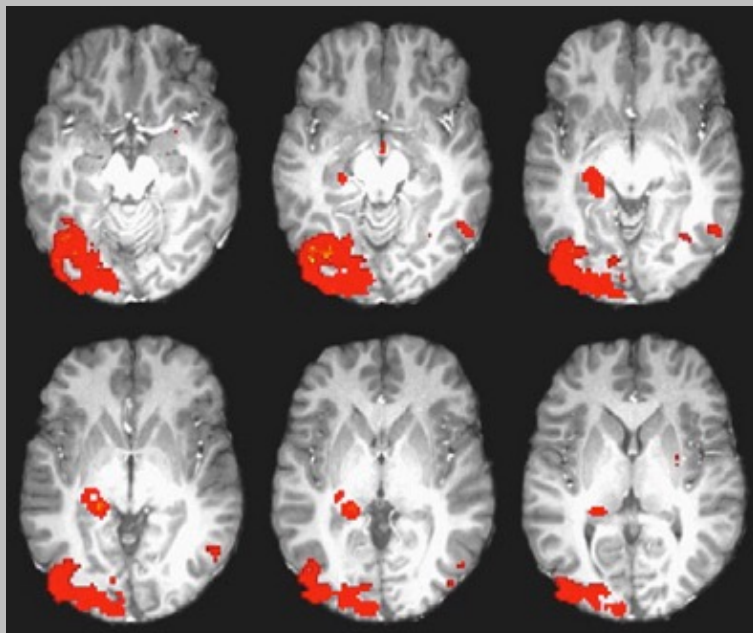
Using transients as regressors also.



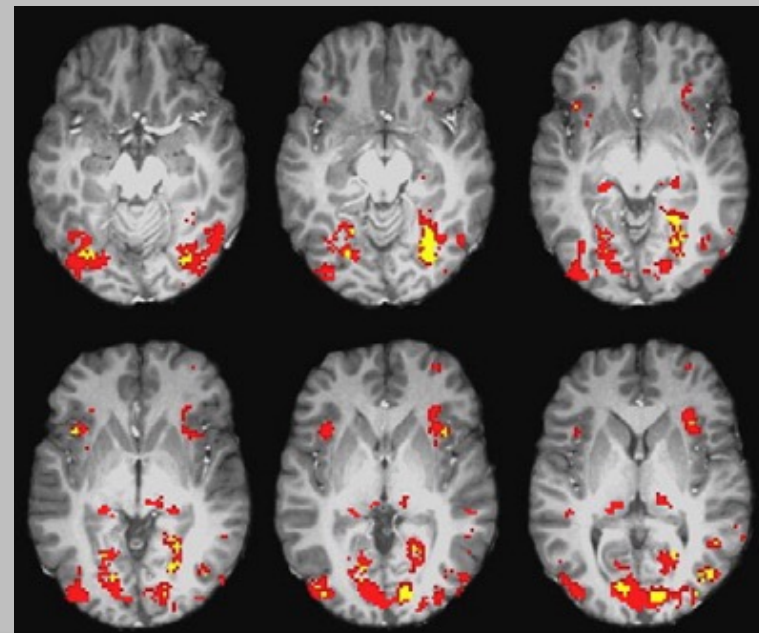
BLOCK DESIGN & HEMIFIELD VISUAL STIMULATION



SUSTAINED RESPONSE MODEL



ONSET/OFFSET RESPONSE MODEL



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

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