

# The Biggest Unknowns in Functional MRI

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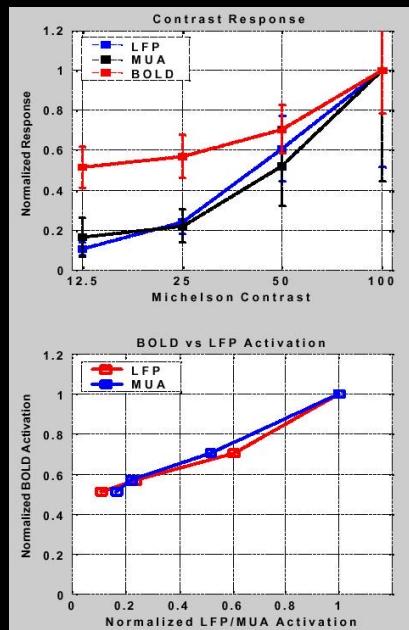


# The Biggest Unknowns in Functional MRI

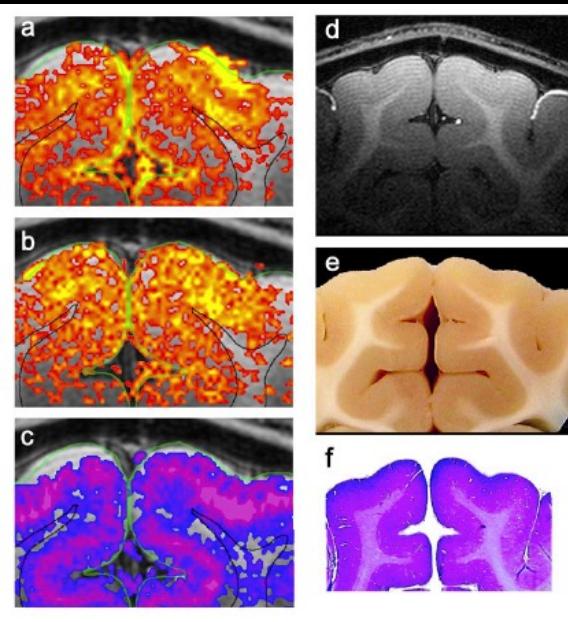
1. Relationship between neuronal activity and BOLD contrast?
2. Source of BOLD dynamic characteristics?
3. Sources of variability?
4. What's really in the noise?
5. What's "resting" state?
6. Other sources of functional contrast?
7. Ultimate temporal resolution?
8. Ultimate spatial resolution?
9. Ultimate clinical utility?
10. Best display methods?
11. Best processing methods?
12. Optimal Field Strength?

# Relationship between neuronal activity and BOLD contrast?

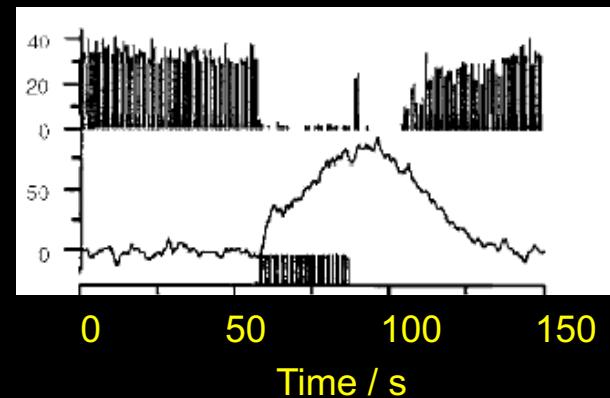
## Magnitude



## Location



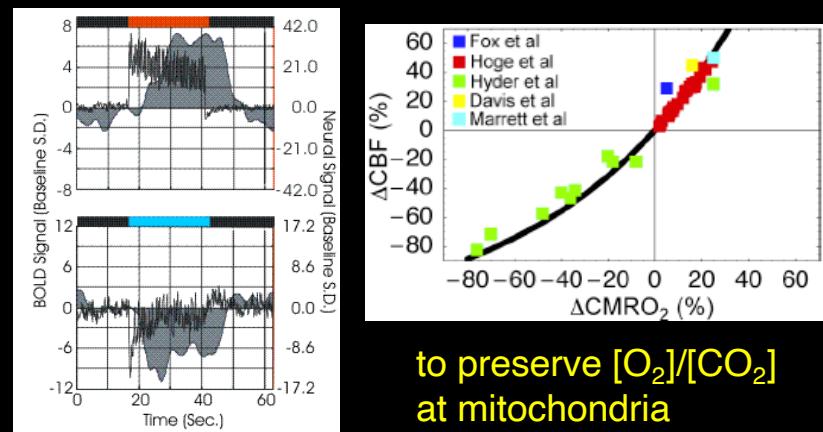
## Inhibition



Mathiesen, et al (1998), J Physiol 512.2:555-566

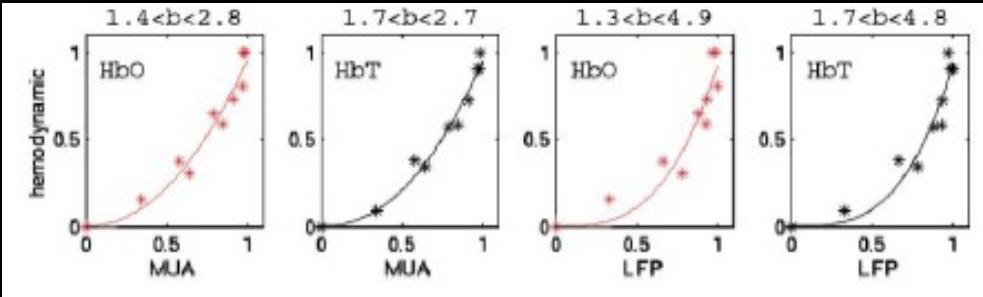
## Neg. BOLD

## Why?



to preserve  $[O_2]/[CO_2]$   
at mitochondria

Logothetis et al. (2001) Nature, 412, 150-157 Harel et al. (2004) ISMRM, 200

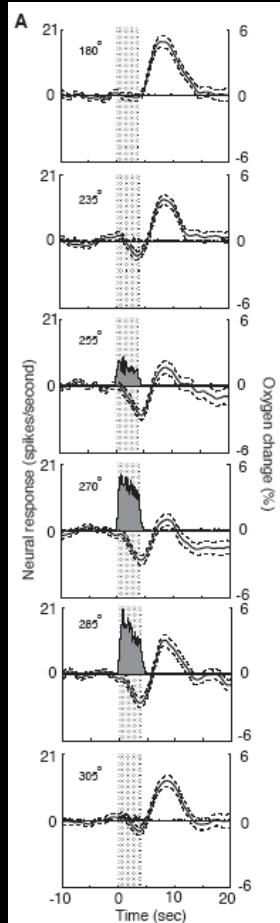


Devor et al. (2001) Neuron, 39, 353-359

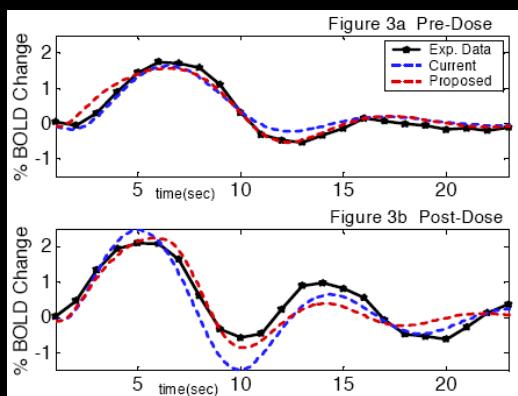
Schmucl et al. (2003) OHBM, 308

Buxton (2004) ISMRM, 273

# Source of BOLD Characteristics?

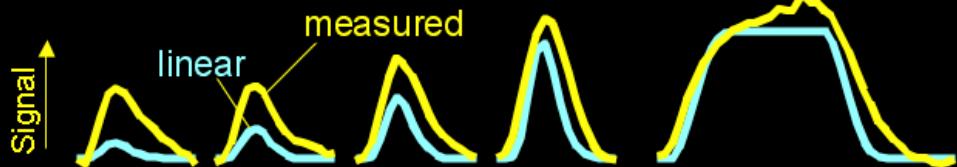


Yacoub, et al (1999), MRM 41, 1088-1092

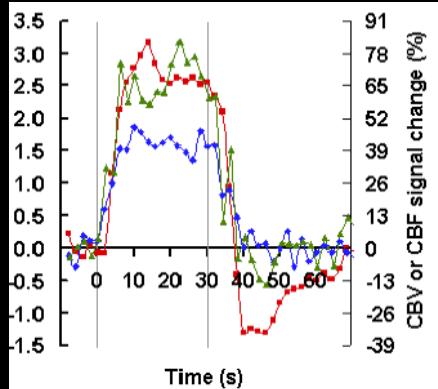


Behzadi, et al (2004), ISMRM 279

Thompson, et al (2003), Science 299, 1070-1072

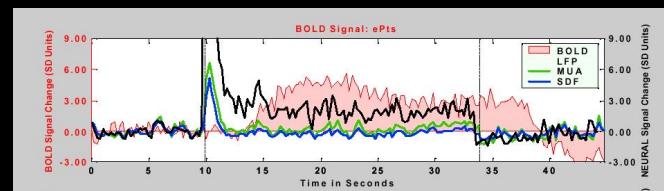
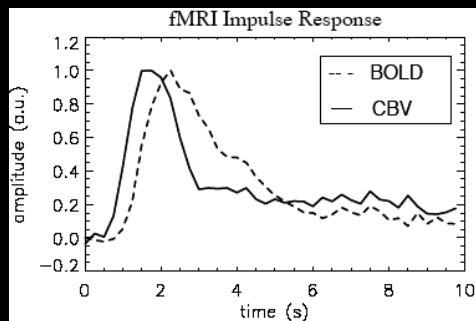


R. M. Birn, (2001) NeuroImage, 14: 817-826.

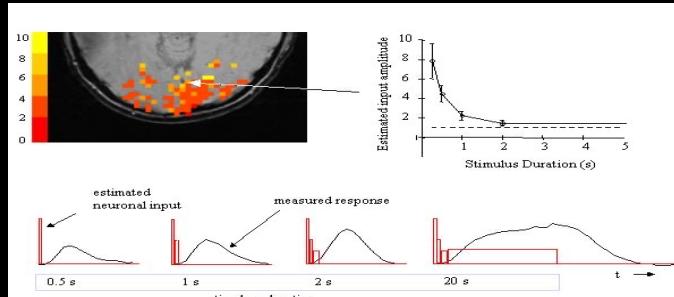


Lu, et al (2004), ISMRM 271

Silva, et al (2004), ISMRM 277

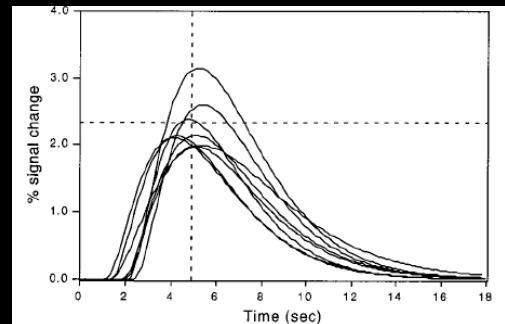


Logothetis et al. (2001) Nature, 412, 150-157.

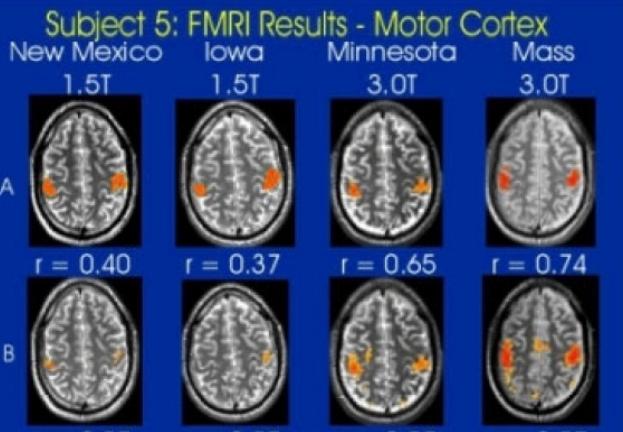


P. A. Bandettini et al, (2001) Nature Neuroscience, 4: 864-866.

# Sources of variability?

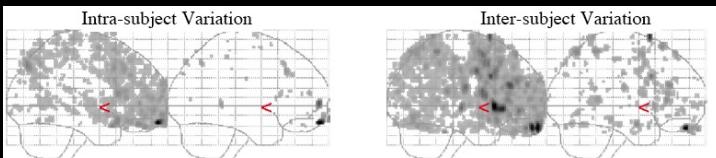


Miezin, et al (2000), NeuroImage 11, 735-759

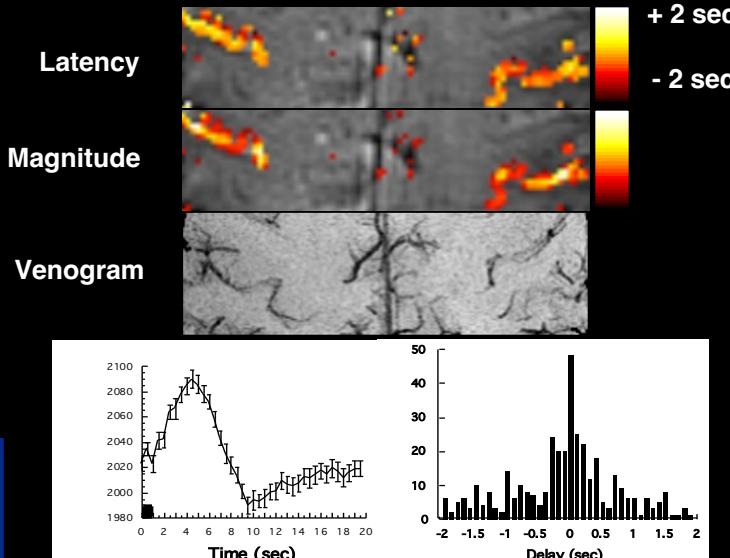


F. BIRN project

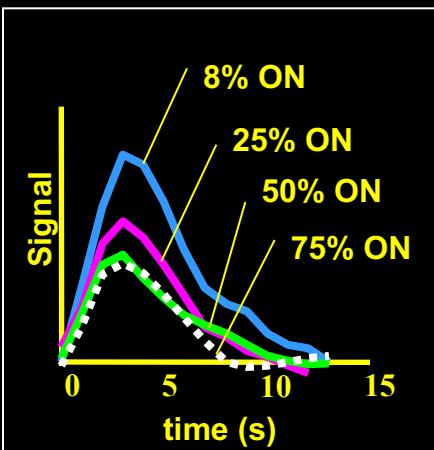
L. Friedman, et al (2004), ISMRM 489



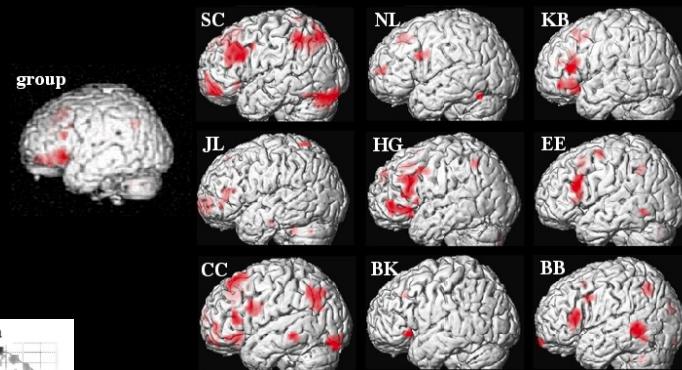
T.E. Lund, et al (2004), ISMRM 497<sup>a</sup>



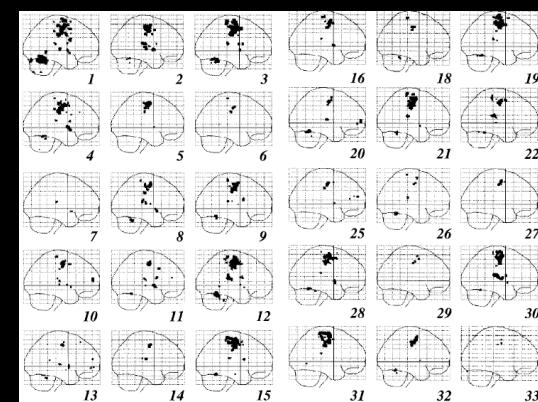
P. A. Bandettini, (1999) "Functional MRI" 205-220.



R. Birn, et al (2001), OHBM 971

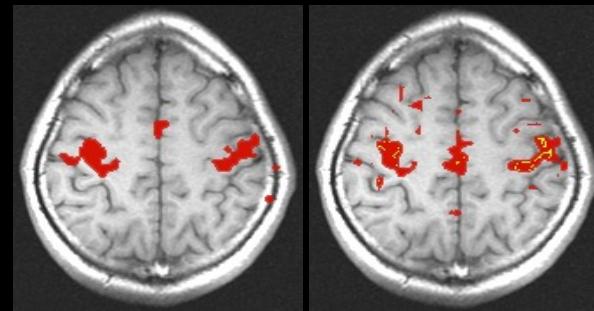
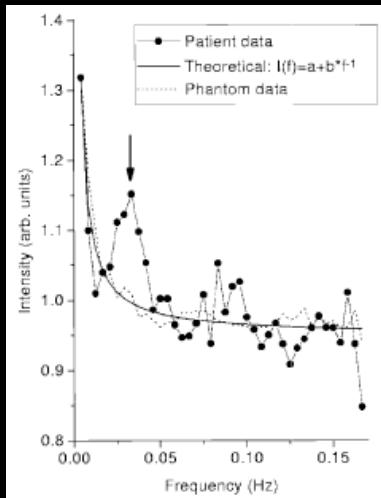


Courtesy, Mike Miler, UC Santa Barbara and Jack Van Horn, fMRI Data Center, Dartmouth

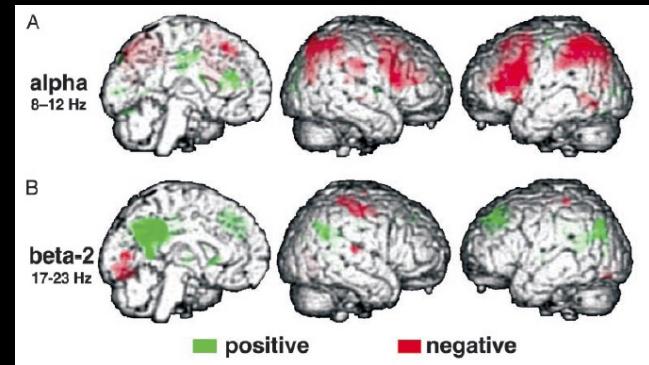
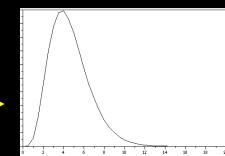
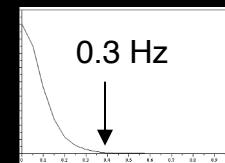


McGonigle, et al (2000), NeuroImage 11, 708-734

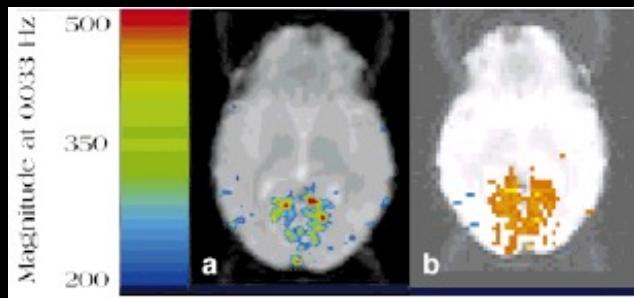
# What's really in the noise?



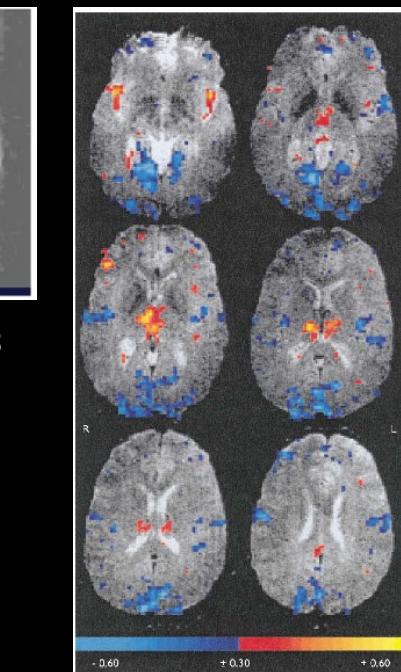
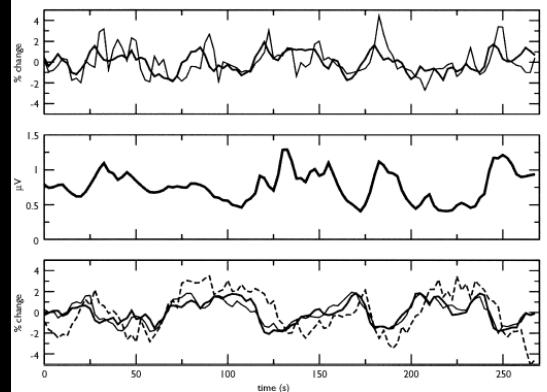
Biswal, et al (1995), MRM 34, 537-541



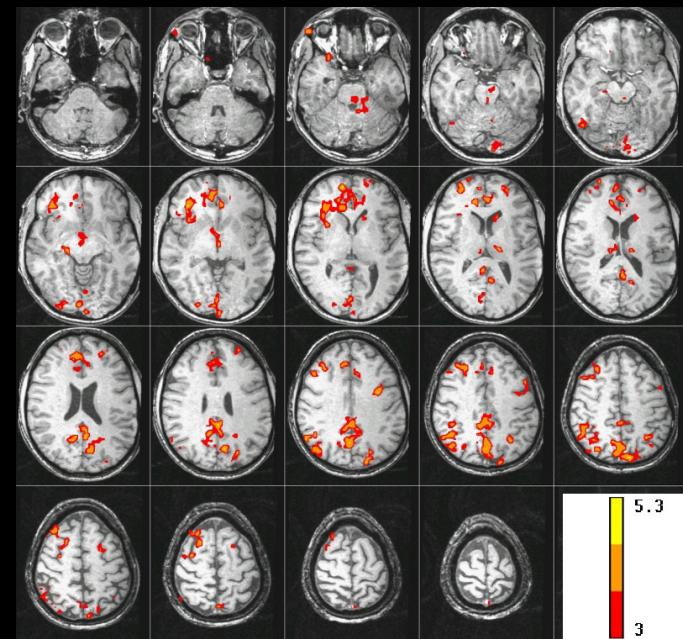
Laufs, et al (1995), PNAS 100 (19), 11053=11058



Kiviniemi, et al (2000), MRM 44, 373-378

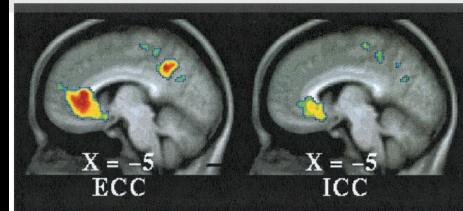


Goldman, et al (2002), Neuroreport

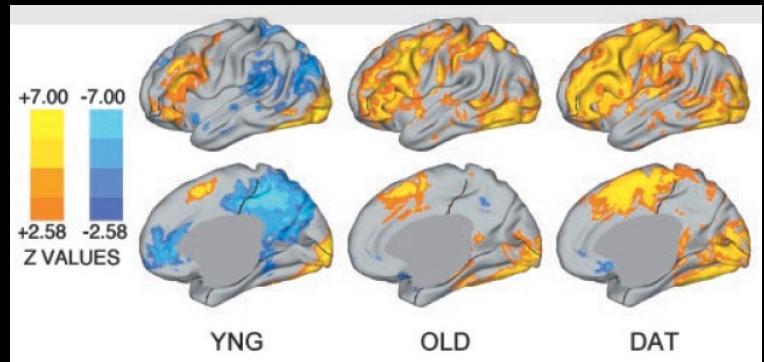


Patterson, et al (2002), NeuroImage 17, 1787-1806

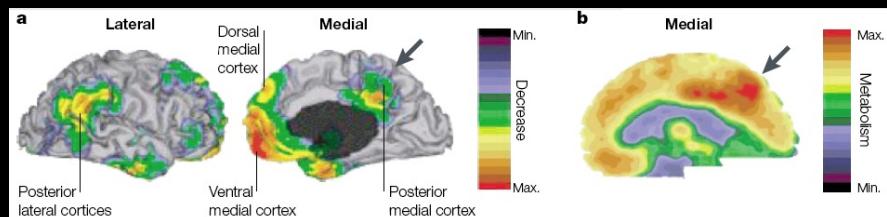
# What is “resting” state?



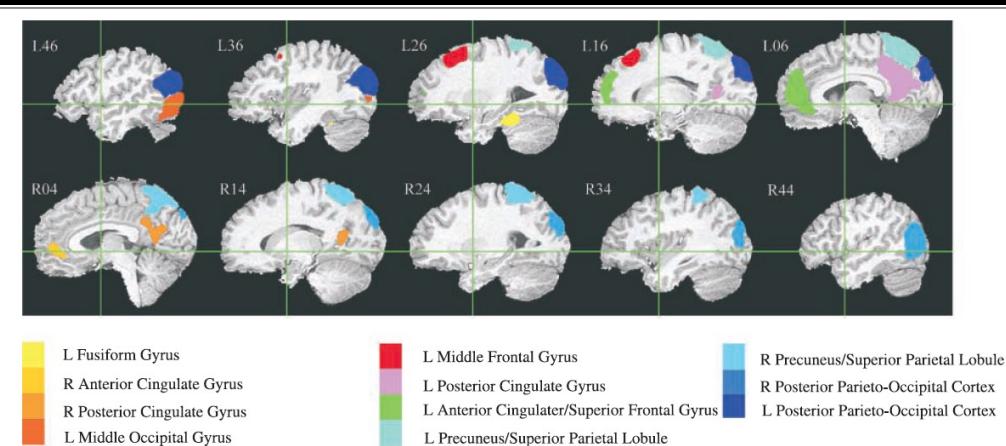
Gusnard, et al (2001), PNAS 98 (7), 4259-4264



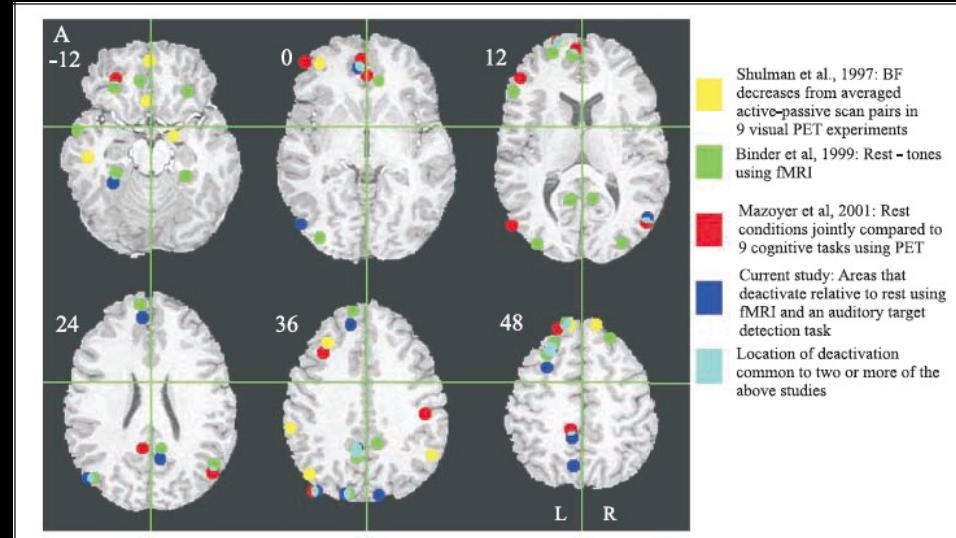
Lustig, et al (2003), PNAS 100 (19), 14504-14509



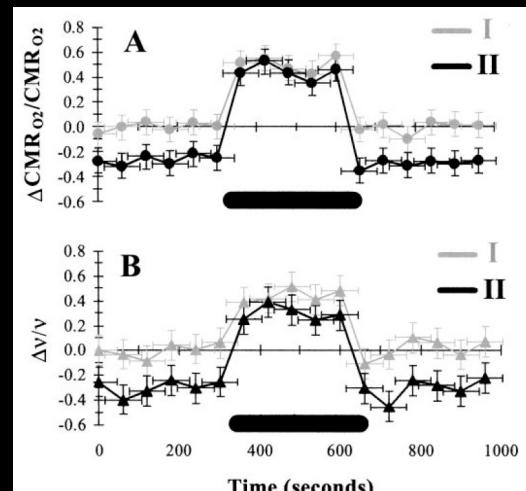
Gusnard, et al (2001), Nature Reviews Neuroscience (2), 685-694



McKiernan, et al (2003), Journ. of Cog. Neurosci. 15 (3), 394-408

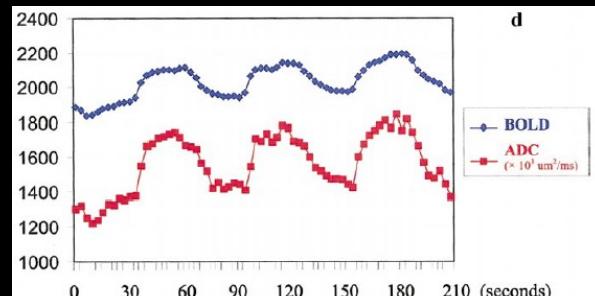
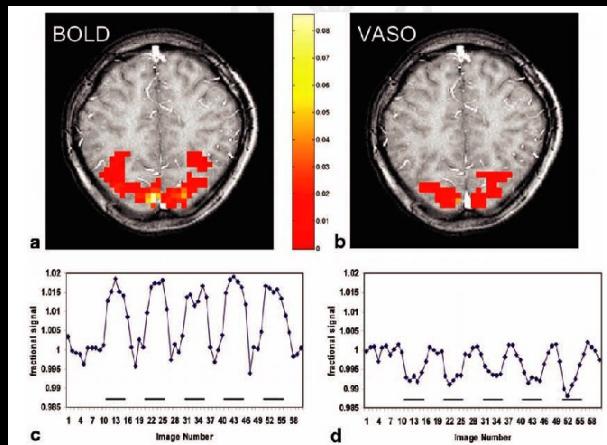


McKiernan, et al (2003), Journ. of Cog. Neurosci. 15 (3), 394-408

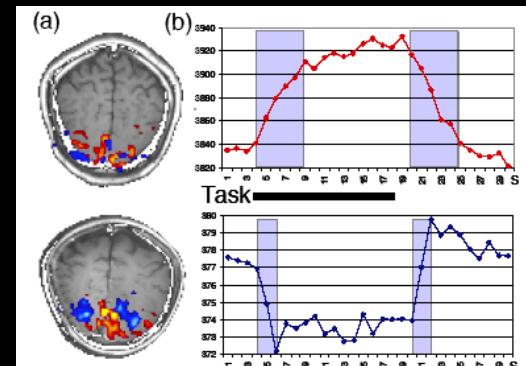


Hyder, et al (2002), PNAS 99 (16), 10771-10776

# Other sources of functional contrast?

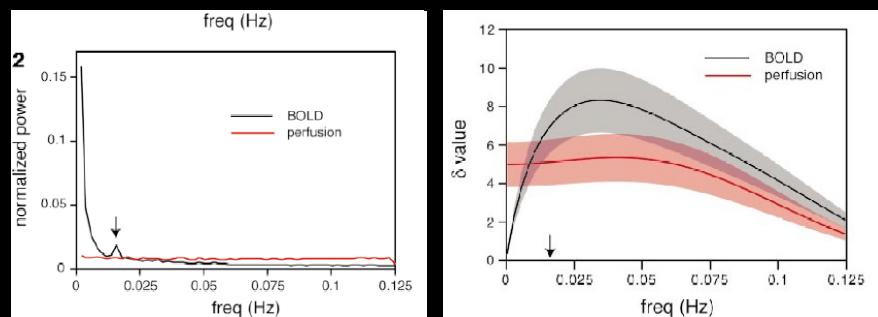


A. Song, et al (2002), NeuroImage 17, 742-750

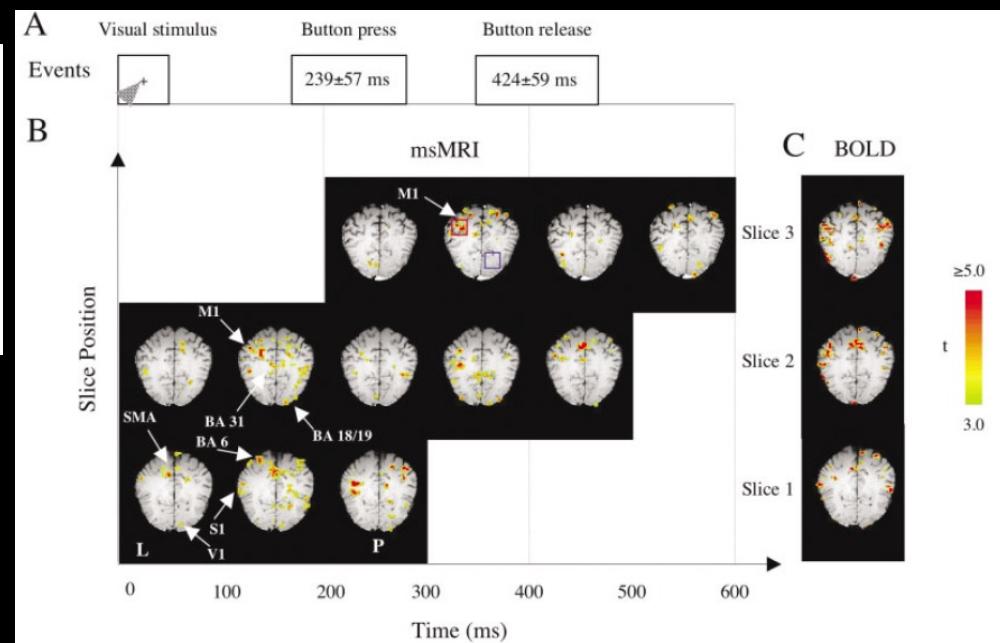
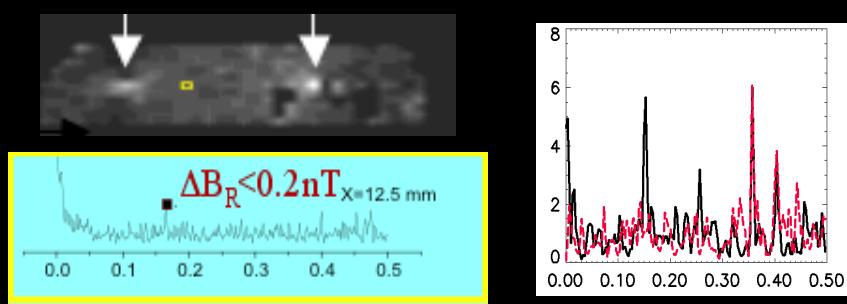


A. Song, et al (2004), ISMRM 1063

Lu, et al (2003) MRM 50 (2): 263-274

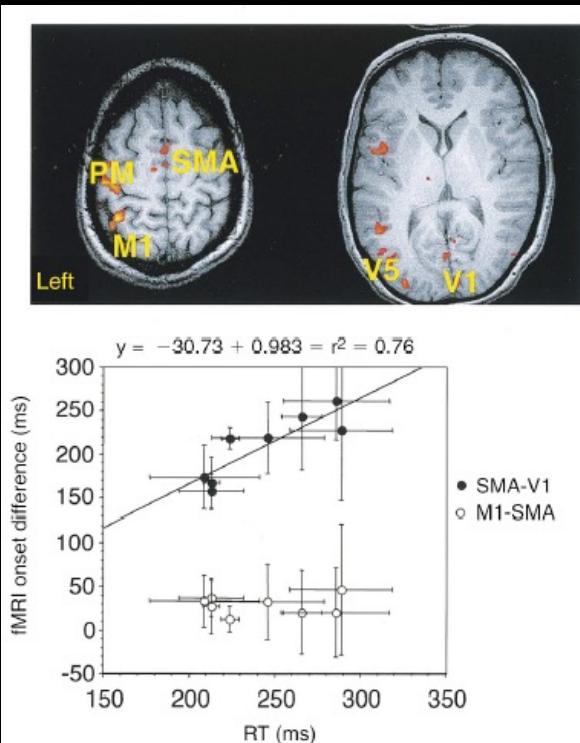
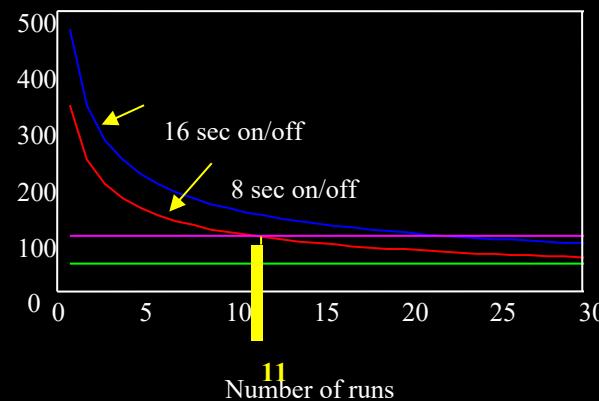


GK Aguirre et al, (2002) NeuroImage 15 (3): 488-500



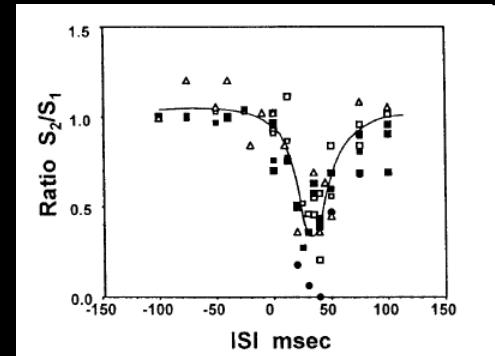
J. Xiong, et al. (2003) HBM, 20: 41-49.

# Ultimate temporal resolution?



Menon, et al (2000), TICS 3 (6) 207-215

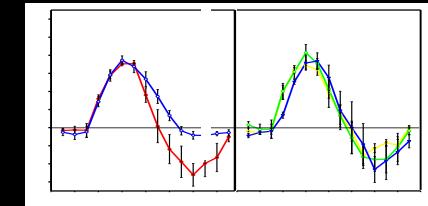
Smallest latency  
Variation Detectable  
(ms) ( $p < 0.001$ )



Ogawa, et al (2000), PNAS 97 (20) 11026–11031

Temporal resolution factors	Values for each factor
Fastest image acquisition rate	≈ 64 images/s
Minimum time for signal to significantly deviate from baseline	≈ 3 s
Fastest on-off rate in which amplitude is not compromised	≈ 8 s on, 8 s off
Fastest on-off rate in which hemodynamic response keeps up	≈ 2 s on, 2 s off
Minimum activation duration	≈ 30 ms (no limit determined yet, but the response behaves similarly below 500 ms)
Standard deviation of baseline signal	≈ 1% (less if physiological fluctuations and system instabilities are filtered out)
Standard deviation of onset time estimation	≈ 450 ms
Standard deviation of return to baseline time estimation	≈ 1250 ms
Standard deviation of entire on-off response time estimation	≈ 650 ms
Range of latencies over space	± 2.5 s

Word vs. Non-word  
**0°, 60°, 120° Rotation**



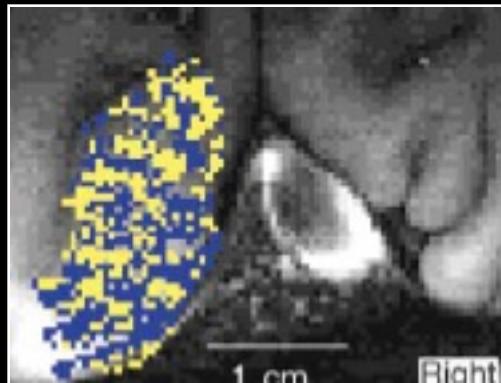
P. A. Bandettini, (1999) "Functional MRI" 205-220.

Bellgowan, et al (2003), PNAS 100, 15820–15283

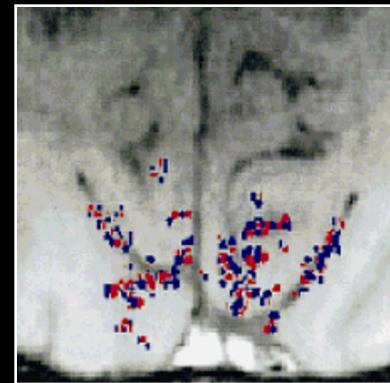
## Ultimate spatial resolution?

Resolving columns with single shot EPI is a goal..

0.47 x 0.47 in plane resolution



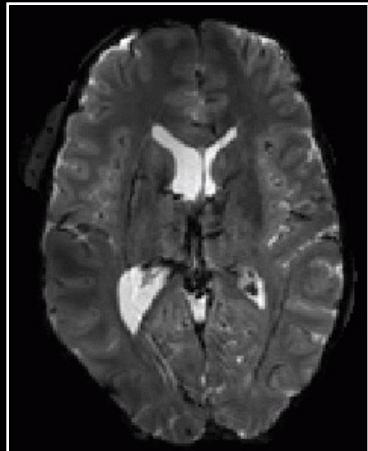
0.54 x 0.54 in plane resolution



Multi-shot with  
navigator pulse

Cheng, et al. (2001) Neuron, 32:359-374

Menon et al, (1999) MRM 41 (2): 230-235



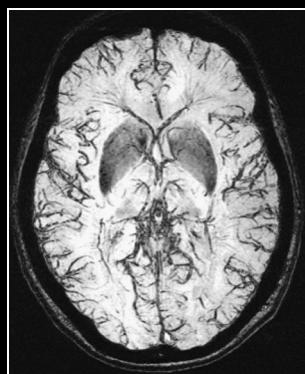
...using SENSE, 32 channels, 7T,  
and perhaps partial k-space we might get to  $0.5 \text{ mm}^3$

3T single-shot SENSE EPI using 16-channels:  $1.25 \times 1.25 \times 2 \text{ mm}$

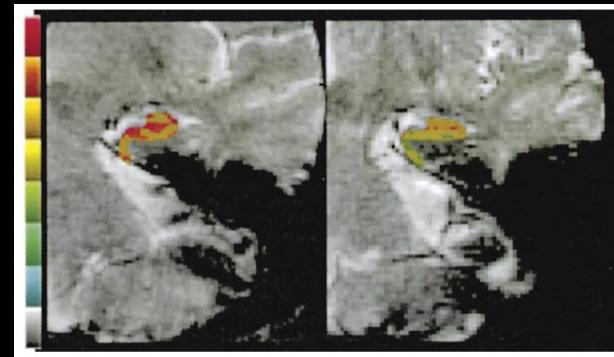
# Ultimate clinical utility?

Needs:

- Real time feedback
- Characterization of confounding effects
- Robust yet incisive set of probe tasks
- Baseline information?



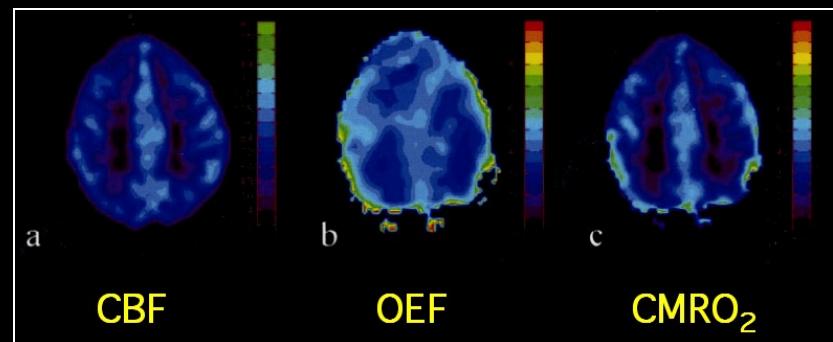
Bove-Bettis, et al (2004), SMRT



Small, et al (2001), Neuron 28:853-664



Bartha, et al (2002), MRM 47:742-750



An, et al (2001), NMR in Biomedicine 14:441-447

Best processing methods?

fMRI data, and noise is time and space varying in predictable and unpredictable ways over several temporal and spatial scales...

Signal and noise models...

Model free, open ended, methods?

Classification methods?

Multivariate methods?

Connectivity (across time and space scales?)

## Best display methods?

To convey:

- collapsed multidimensional data
- sense of data quality

Surface

Glass brain

ROI

Time courses

Example slices

Connectivity maps?

“Quality” index?

# Optimal Field Strength?

## Utility vs. Difficulty

Both depend on the specific needs

...needs tend to increase with better technology



# Functional Imaging Methods Unit &



## Functional MRI Facility

### Computer Specialist:

Adam Thomas

### Scanning Technologists:

Karen Bove-Bettis

Paula Rowser

Alda Ottley

Ellen Condon

### Staff Scientists:

Sean Marrett

Jerzy Bodurka

Frank Ye

Wen-Ming Luh

Rasmus Birn

### Program Assistant:

Kay Kuhns

### Post Docs:

Hauke Heekeren

David Knight

Anthony Boemio

Niko Kriegeskorte

### Graduate Student:

Natalia Petridou