# The Biggest Unknowns in Functional MRI

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# The Biggest Unknowns in Functional MRI

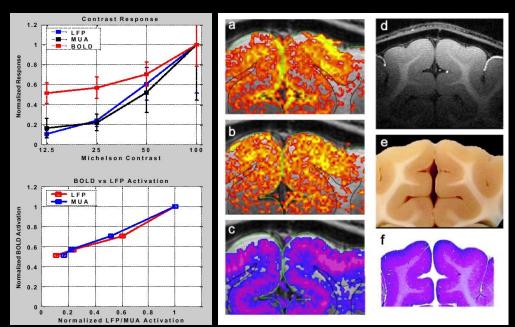
- 1. Relationship between neuronal activity and BOLD contrast?
- 2. Source of BOLD dynamic characteristics?
- 3. Sources of variability?
- 4. What's really in the noise?
- 5. What's "resting" state?
- 6. Other sources of functional contrast?
- 7. Ultimate temporal resolution?
- 8. Ultimate spatial resolution?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

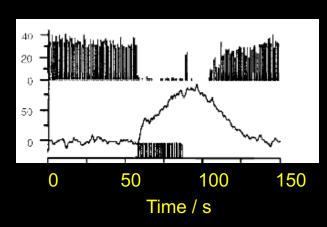
#### Relationship between neuronal activity and BOLD contrast?



#### Location

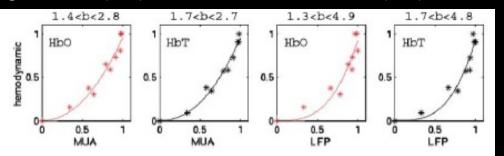
#### Inhibition



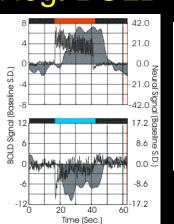


Mathiesen, et al (1998), J Physiol 512.2:555-566

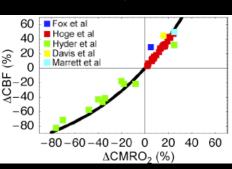
#### Logothetis et al. (2001) Nature, 412, 150-157 Harel et al. (2004) ISMRM, 200



# Neg. BOLD



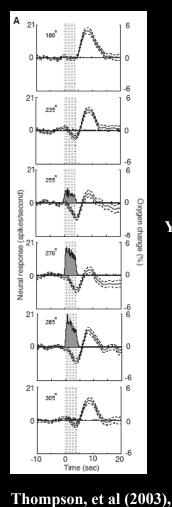
# Why?

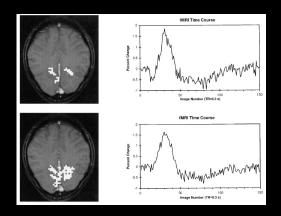


to preserve [O<sub>2</sub>]/[CO<sub>2</sub>] at mitochondria

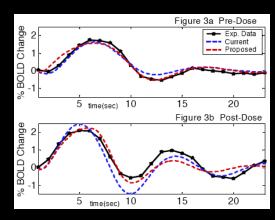
**Buxton (2004) ISMRM, 273** 

#### Source of BOLD Characteristics?

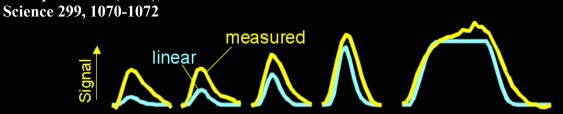




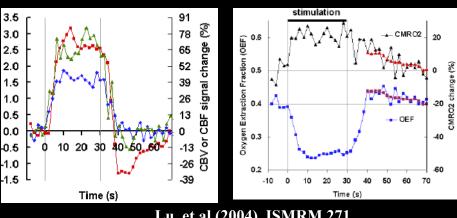
Yacoub, et al (1999), MRM 41, 1088-1092



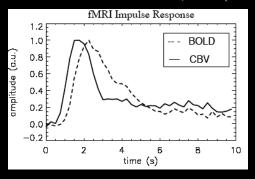
Behzadi, et al (2004), ISMRM 279



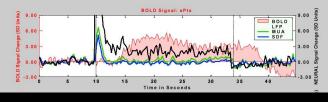
R. M. Birn, (2001) NeuroImage, 14: 817-826.



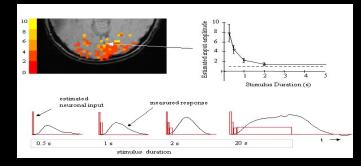
Lu, et al (2004), ISMRM 271



Silva, et al (2004), ISMRM 277

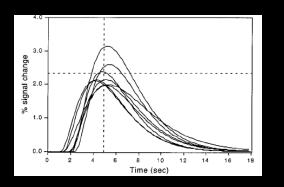


Logothetis et al. (2001) Nature, 412, 150-157.

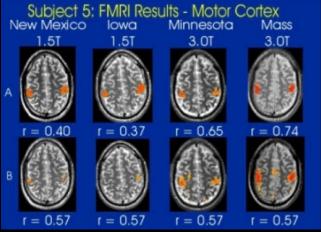


P. A. Bandettini et al, (2001) Nature Neuroscience, 4: 864-866.

#### Sources of variability?

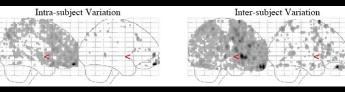


Miezin, et al (2000), NeuroImage 11, 735-759



F. BIRN project

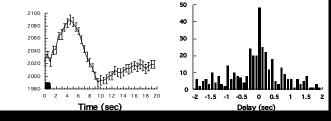
L. Friedman, et al (2004), ISMRM 489



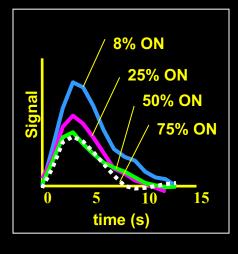
Latency + 2 sec

Magnitude

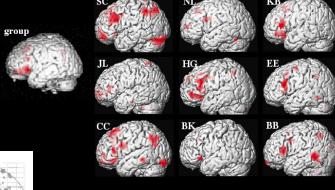
Venogram



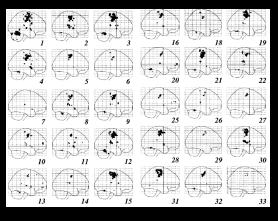
P. A. Bandettini, (1999) "Functional MRI" 205-220.



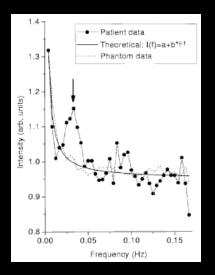
R. Birn, et al (2001), OHBM 971

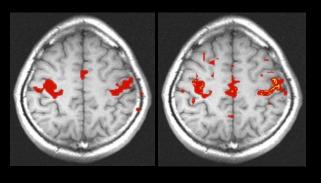


Courtesy, Mike Miler, UC Santa Barbara and Jack Van Horn, fMRI Data Center, Dartmouth



#### What's really in the noise?





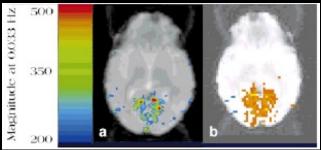
A alpha 8-12 Hz

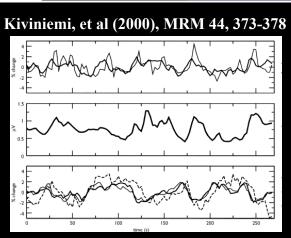
B beta-2 17-23 Hz

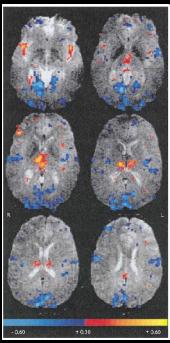
positive ■ negative

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

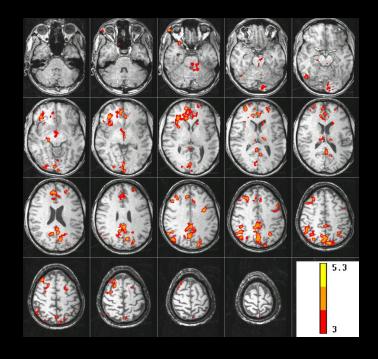
Laufs, et al (1995), PNAS 100 (19), 11053=11058





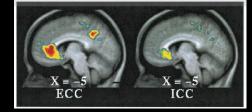


Goldman, et al (2002), Neuroreport

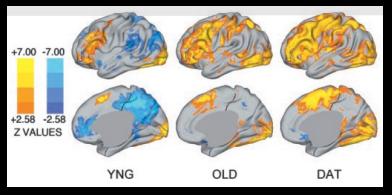


Patterson, et al (2002), NeuroImage 17, 1787-1806

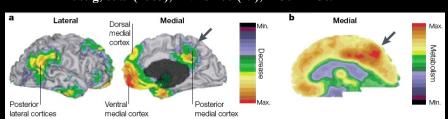
#### What is "resting" state?



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



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

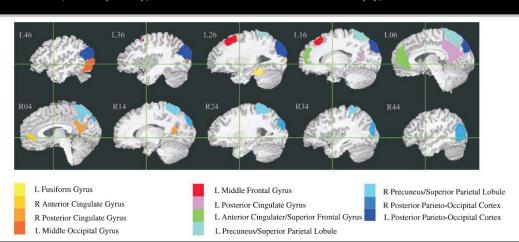


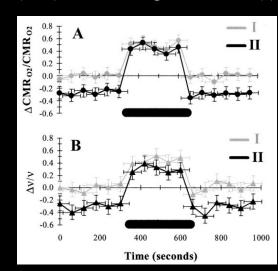
Shulman et al., 1997: BF
decreases from averaged
active-passive scan pairs in
9 visual PET experiments
Binder et al, 1999: Rest - tones
using fMRI

Mazoyer et al, 2001: Rest
conditions jointly compared to
9 cognitive tasks using PET
Current study: Areas that
deactivate relative to rest using
fMRI and an auditory target
detection task
Location of deactivation
common to two or more of the
above studies

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

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

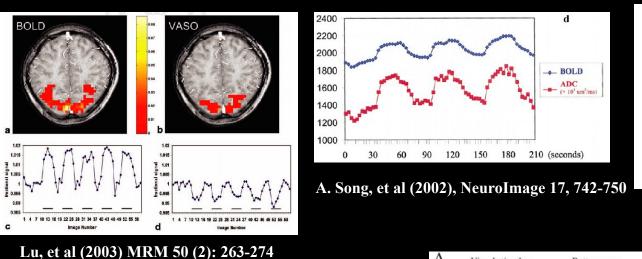


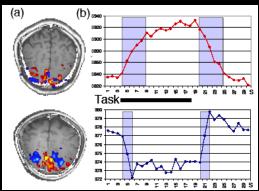


Hyder, et al (2002), PNAS 99 (16), 10771-10776

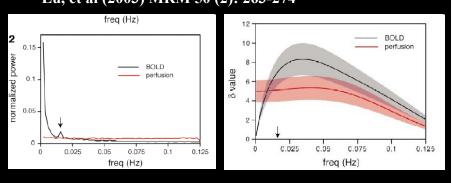
McKiernan, et al (2003), Journ. of Cog. Neurosci. 15 (3), 394-408

#### Other sources of functional contrast?

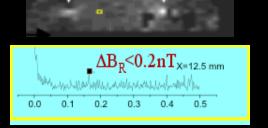


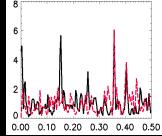


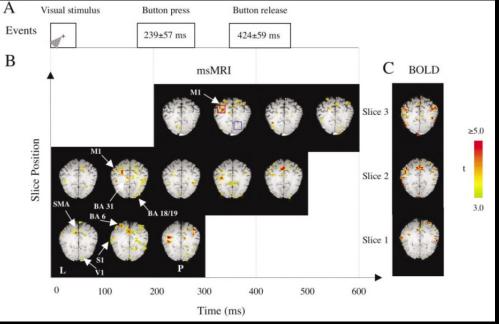
A. Song, et al (2004), ISMRM 1063



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



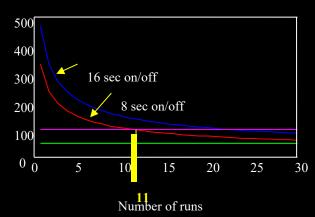




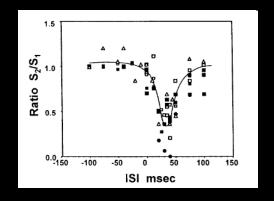
J. Xiong, et al. (2003) HBM, 20: 41-49.

J. Bodurka, et al (2002). MRM 47: 1052-1058. Petridou, et al (2003), OHBM

#### Ultimate temporal resolution?



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

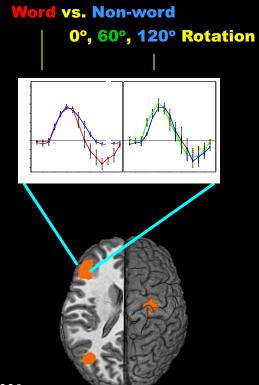


Ogawa, et al (2000), PNAS 97 (20)11026-11031

L	.eft		A		が下ノルー		
fMRI onset difference (ms)	300 <sub>T</sub>	y = -30.73	3 + 0.983 =	$= r^2 = 0.7$	6		
	250		. 15				
	200	Īi	•	- 1			
	150		<del>-</del>			SMA-V1 M1-SMA	
	100						
	50	I					
	0	Ĭĵ	, t	-			
	-50			Ţ1			
	15	0 200	250	300	350		
	RT (ms)						

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

	Ogawa,
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 deter- mined yet, but the response behaves similarly below 500 ms)
Standard deviation of baseline signal	~1% (less if physiologi- cal 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	≈650 ms
Range of latencies over space	± 2.5 s



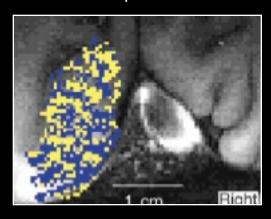
P. A. Bandettini, (1999) "Functional MRI" 205-220.

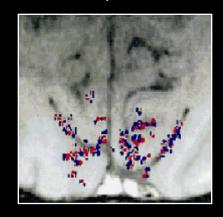
#### Ultimate spatial resolution?

# 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

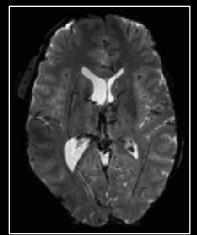




Multi-shot with navigator pulse

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 mm<sup>3</sup>

3T single-shot SENSE EPI using 16-channels:1.25x1.25x2mm

#### Ultimate clinical utility?

#### Needs:

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

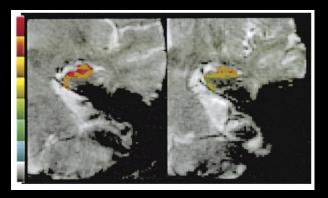




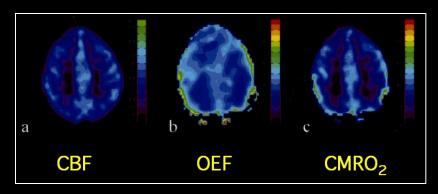
Bove-Bettis, et al (2004), SMRT



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



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



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