The Biggest Unknowns in Functional MRI

Peter A. Bandettini, Ph.D

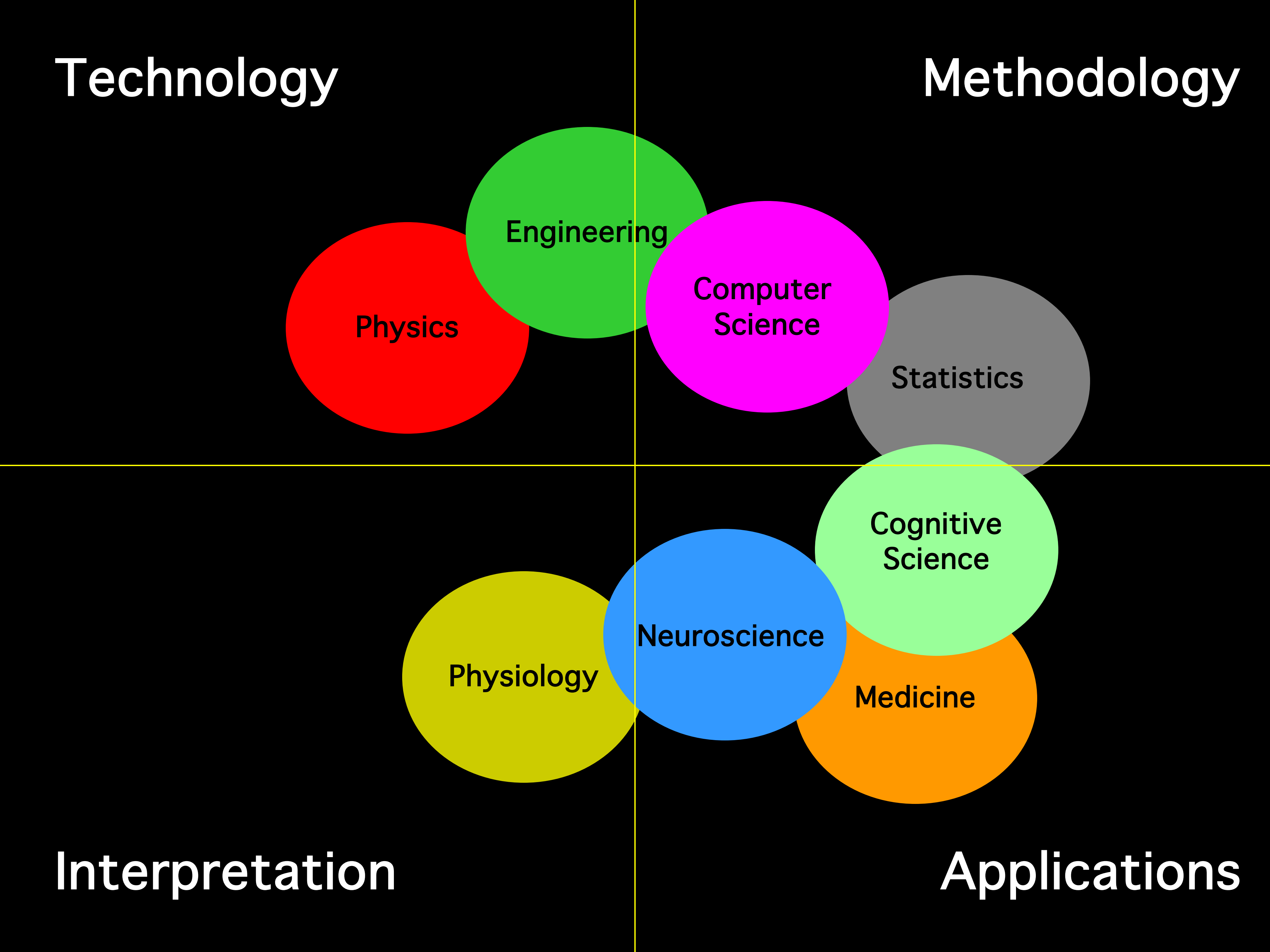
Unit on Functional Imaging Methods
&
Functional MRI Facility

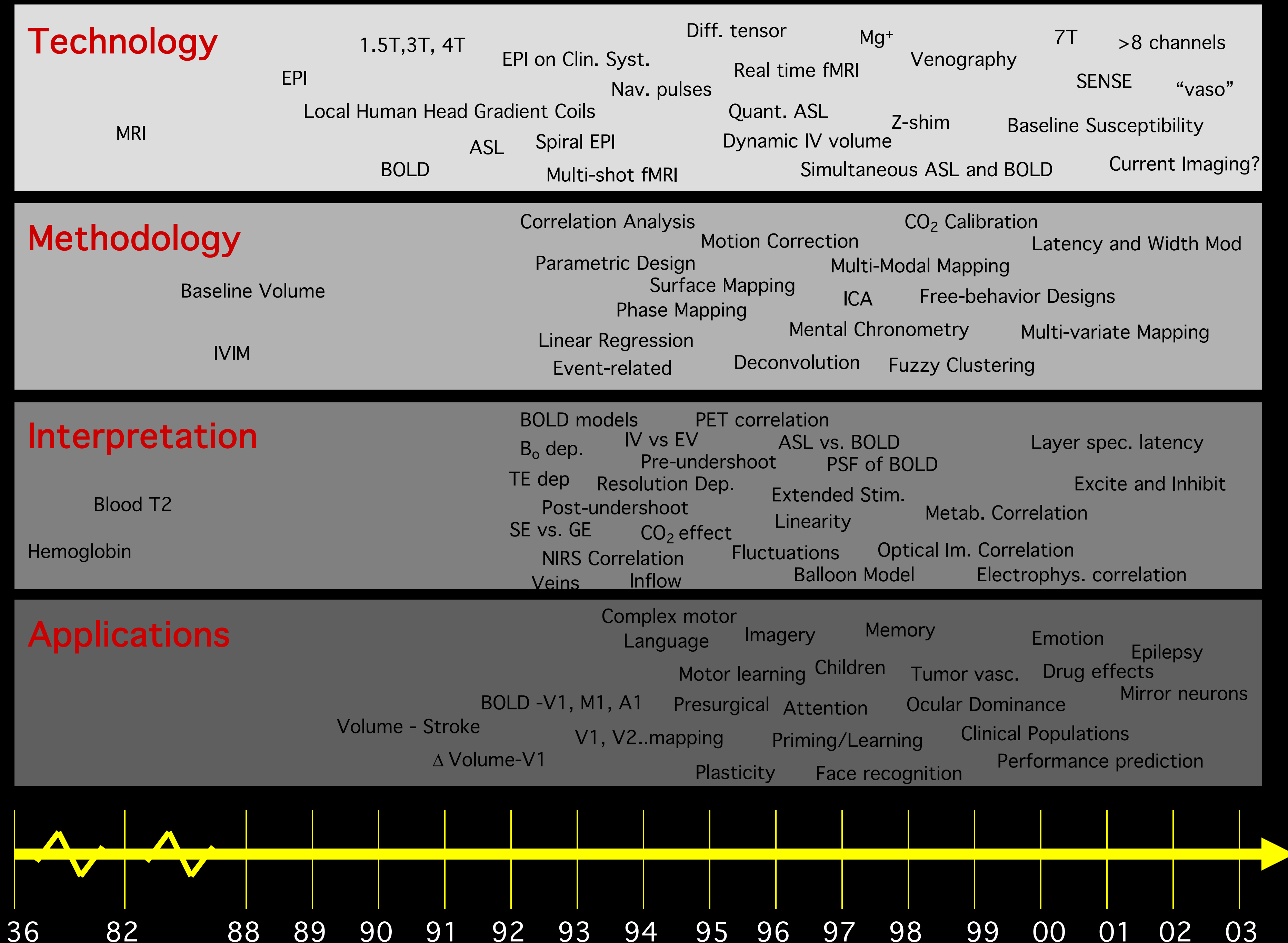
Laboratory of Brain and Cognition
National Institute of Mental Health

National Institute of Mental Health

fim.nimh.nih.gov

fmrif.nimh.nih.gov


Technology
Methodology
Engineering
Physics
Computer Science
Statistics
Cognitive Science
Neuroscience
Physiology
Medicine
Interpretation
Applications


Technology
1.5T,3T, 4T
Diff. tensor
Mg+
7T
>8 channels
EPI on Clin. Syst.
Venography
Real time fMRI
EPI
SENSE
"vaso"
Nav. pulses
Local Human Head Gradient Coils
Quant. ASL
Z-shim
Baseline Susceptibility
MRI
ASL
Spiral EPI
Dynamic IV volume
BOLD
Simultaneous ASL and BOLD
Current Imaging?
Multi-shot fMRI
Methodology
Correlation Analysis
CO2 Calibration
Motion Correction
Latency and Width Mod
Parametric Design
Multi-Modal Mapping
Baseline Volume
Surface Mapping
ICA
Free-behavior Designs
Phase Mapping
Mental Chronometry
Multi-variate Mapping
Linear Regression
IVIM
Deconvolution
Fuzzy Clustering
Event-related
Interpretation
BOLD models
PET correlation
Bo dep.
IV vs EV
ASL vs. BOLD
Layer spec. latency
Pre-undershoot
PSF of BOLD
TE dep
Resolution Dep.
Excite and Inhibit
Extended Stim.
Blood T2
Post-undershoot
Metab. Correlation
SE vs. GE
Linearity
CO2 effect
Hemoglobin
Fluctuations
Optical Im. Correlation
NIRS Correlation
Balloon Model
Electrophys. correlation
Veins
Inflow
Applications
Complex motor
Imagery
Memory
Language
Emotion
Epilepsy
Children
Motor learning
Tumor vasc.
Drug effects
Mirror neurons
BOLD -V1, M1, A1
Presurgical
Attention
Ocular Dominance
Volume - Stroke
V1, V2..mapping
Priming/Learning
Clinical Populations
Δ Volume-V1
Performance prediction
Plasticity
Face recognition
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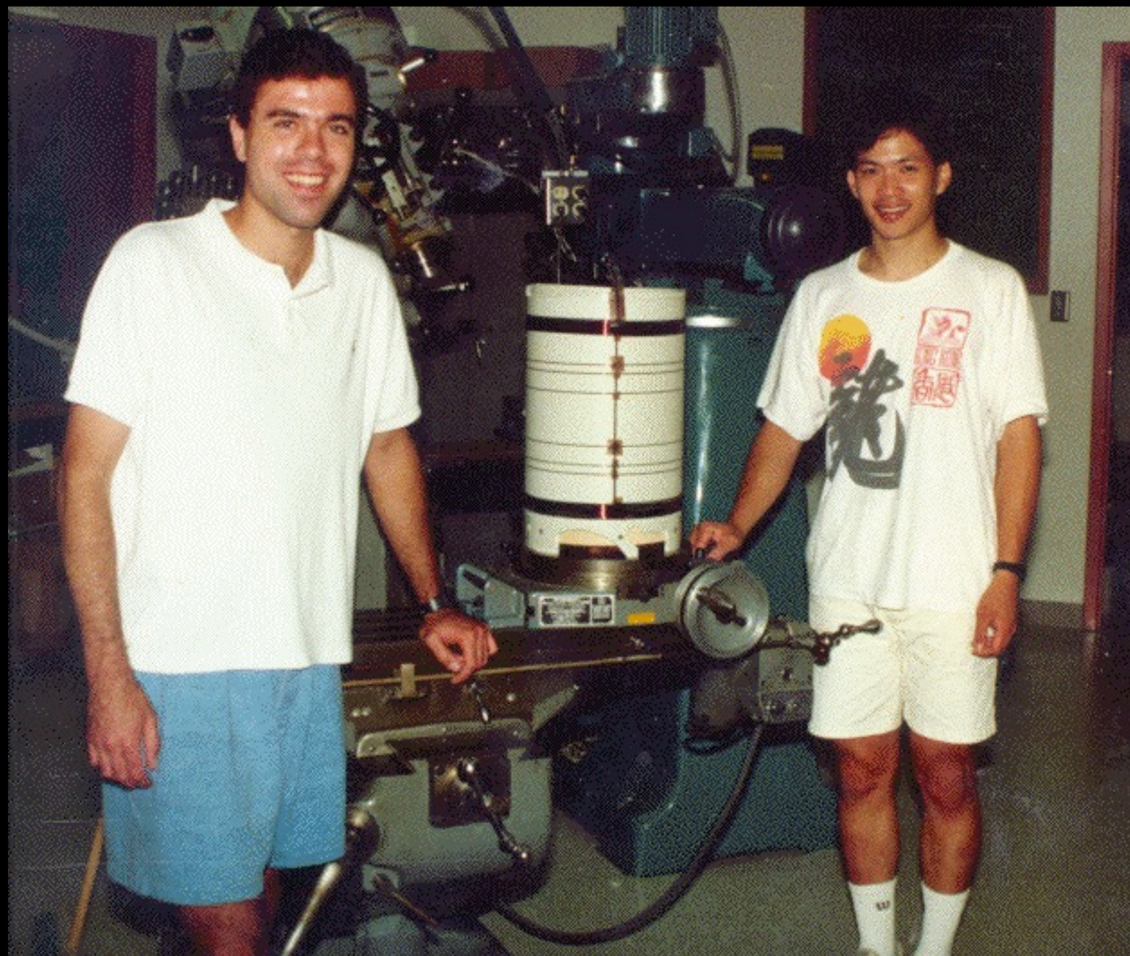
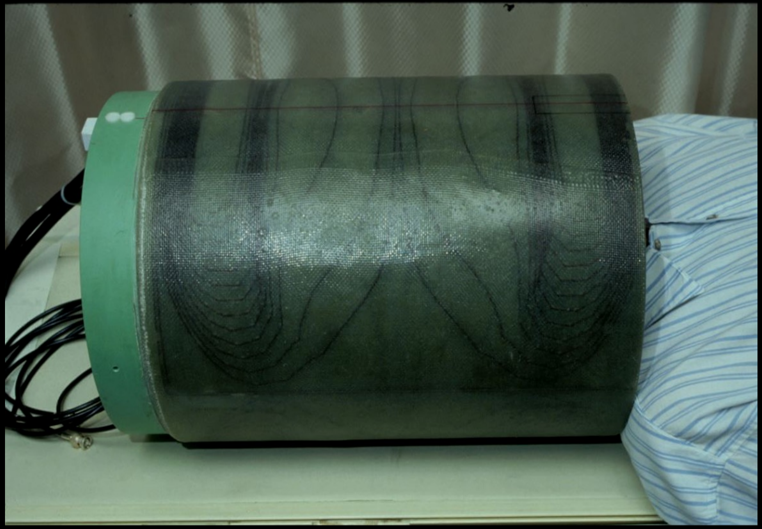


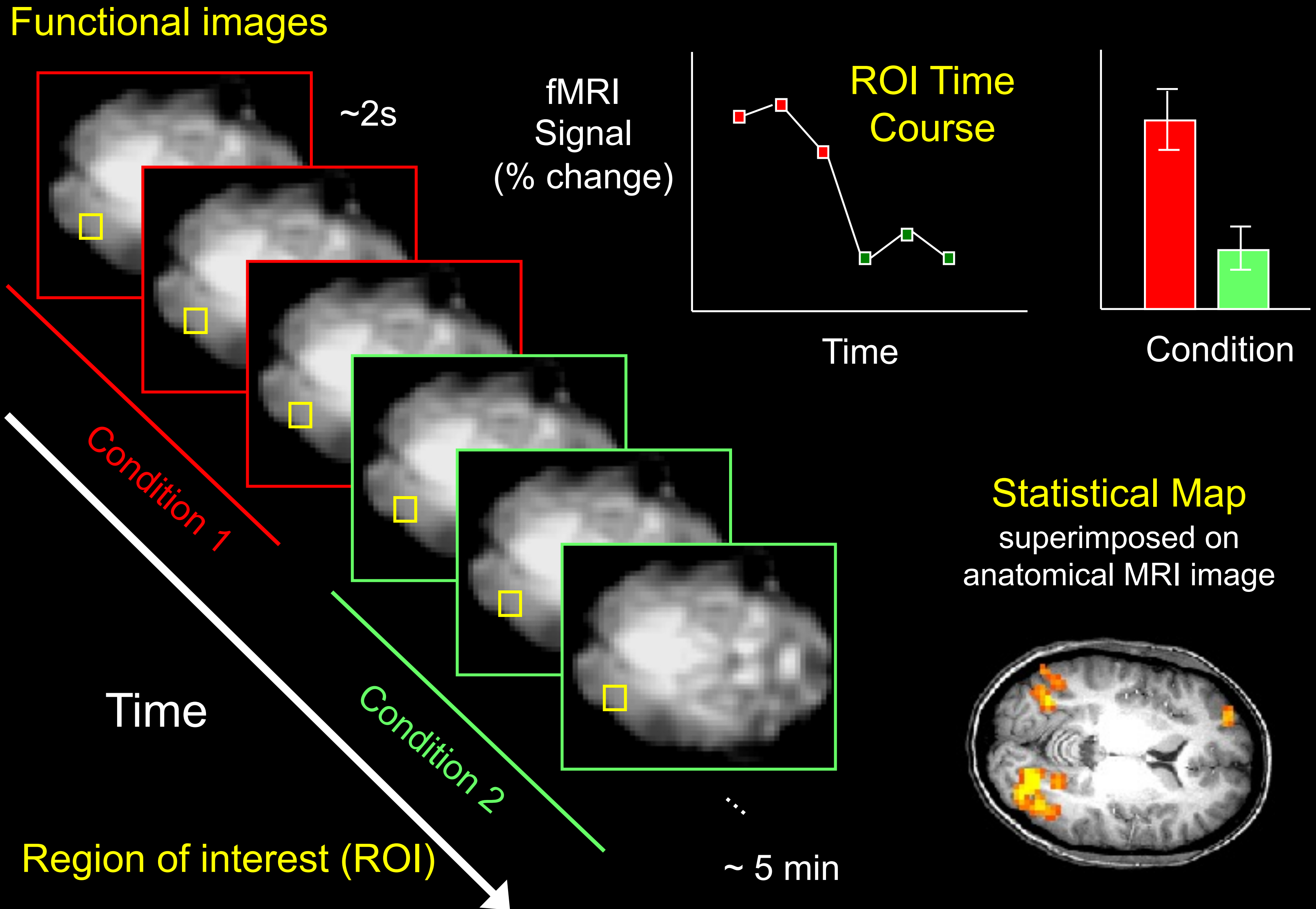
1991-1992

1992-1999



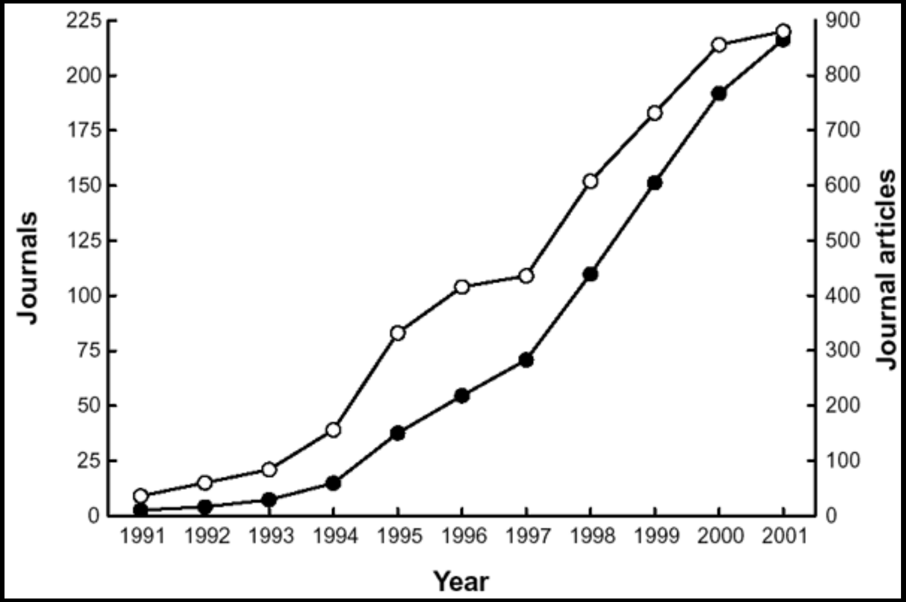
General Electric 3 Tesla Scanner

Activation Statistics

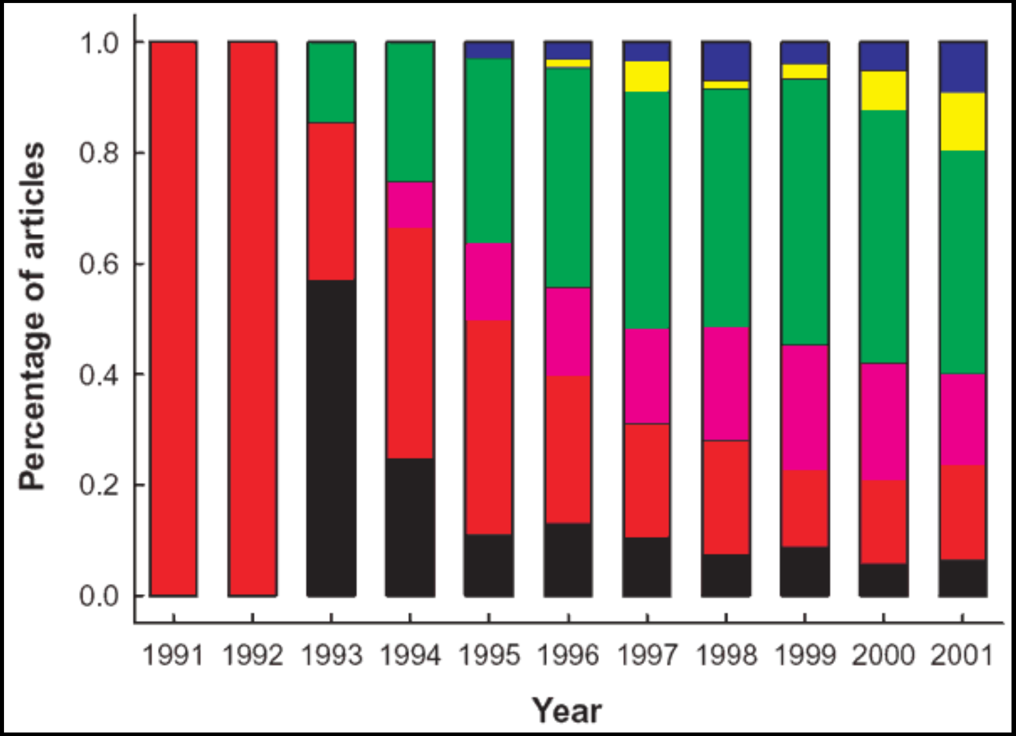


Courtesy, Robert Cox, Scientific and Statistical Computing Core Facility, NIMH

J. Illes, M. P. Kirschen,
J. D. E. Gabrielli,
Nature Neuroscience,
6 (3)m p.205



Motor (black)
Primary Sensory (red)
Integrative Sensory (violet)
Basic Cognition (green)
High-Order Cognition (yellow)
Emotion (blue)



Uses

Understanding normal brain organization and changes

-networks involved with specific tasks (low to high level processing)
-changes over time (seconds to years)
-correlates of behavior (response accuracy, performance changes...)

Clinical research

-correlates of specifically activated networks to clinical populations
-presurgical mapping

Future Uses

Complementary use for clinical diagnosis

-utilization of clinical research results
-prediction of pathology

Clinical treatment and assessment

-drug, therapy, rehabilitation, biofeedback
-epileptic foci mapping
-drug effects

Non clinical uses

-complementary use with behavioral, anatomical, other modality results
-lie detection
-prediction of behavior tendencies
-brain/computer interface

Most fMRI studies since 1992:

Minimum necessary:

- Whole Brain EPI
- Field strength of 1.5T or greater
- Basic stimulus delivery and feedback
- Software for image transfer, analysis, and display

Typical advanced features:

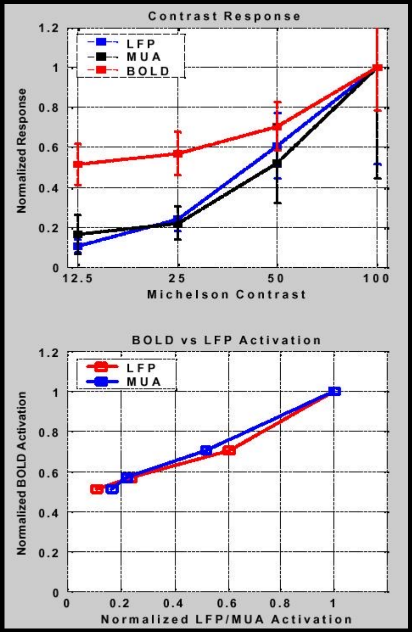
- Higher resolution whole brain EPI, spiral, or multi-shot
- Field strength of 3T to 7T
- Quadrature and Surface coils (single, multiple)
- Susceptibility correction
- ASL
- Multiple subject interface devices, including EEG, SCR, eye position.
- Multi-subject analysis, more rigorous statistics, more sophisticated display methods, exploratory analysis

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?

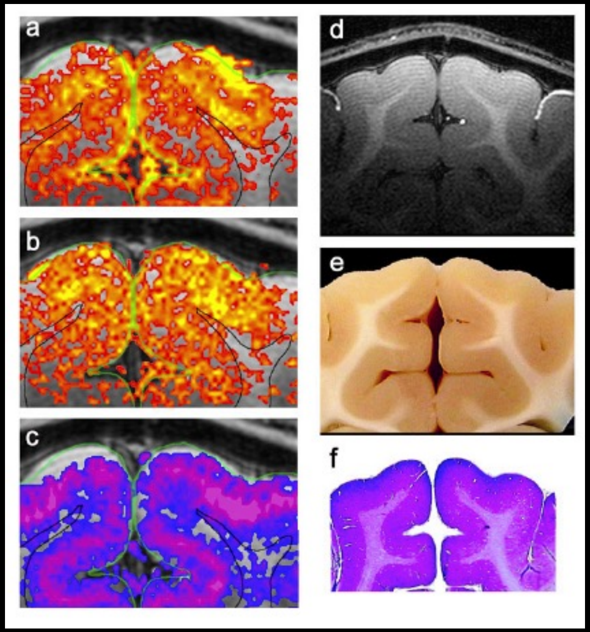
Relationship between neuronal activity and BOLD contrast?

Magnitude



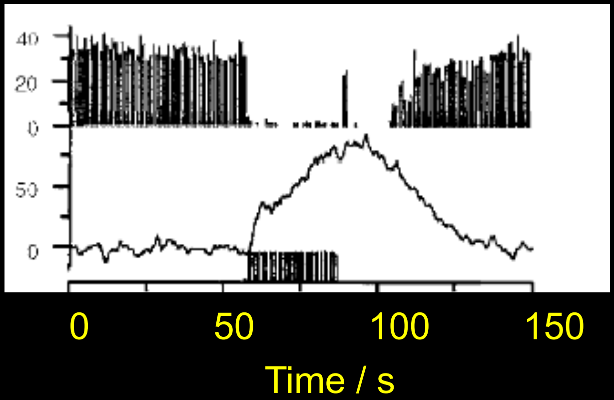
Logothetis et al. (2001) Nature, 412, 150-157

Location

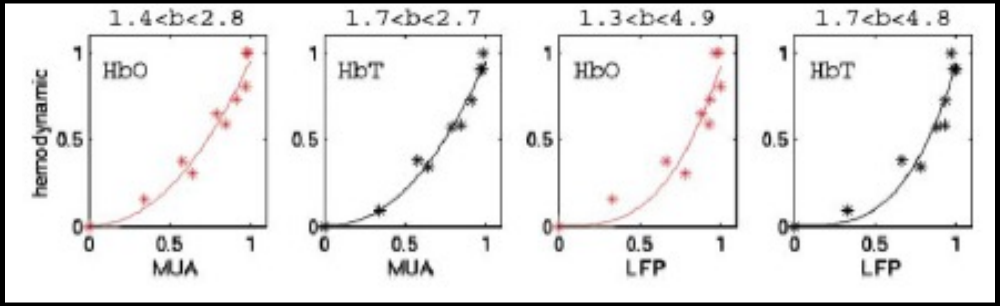


Harel et al. (2004) ISMRM, 200

Inhibition

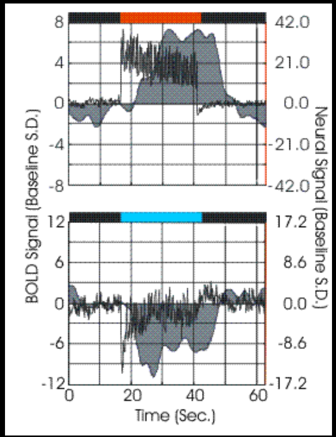


Mathiesen, et al (1998), J Physiol 512.2:555-566



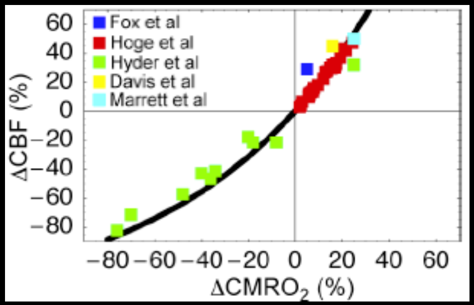
Devor et al. (2001) Neuron, 39, 353-359

Neg. BOLD



Schmuel et al. (2003) OHBM, 308

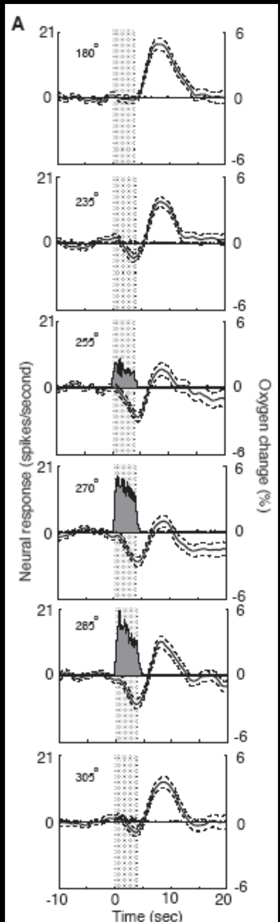
Why?



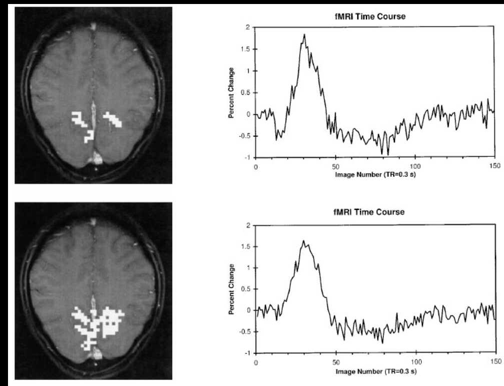
to preserve $[O_2]/[CO_2]$ at mitochondria

Buxton (2004) ISMRM, 273

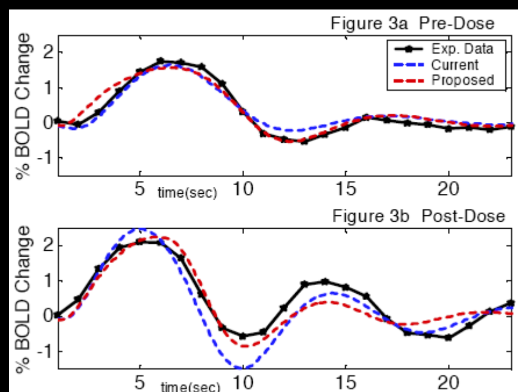
Source of BOLD Characteristics?



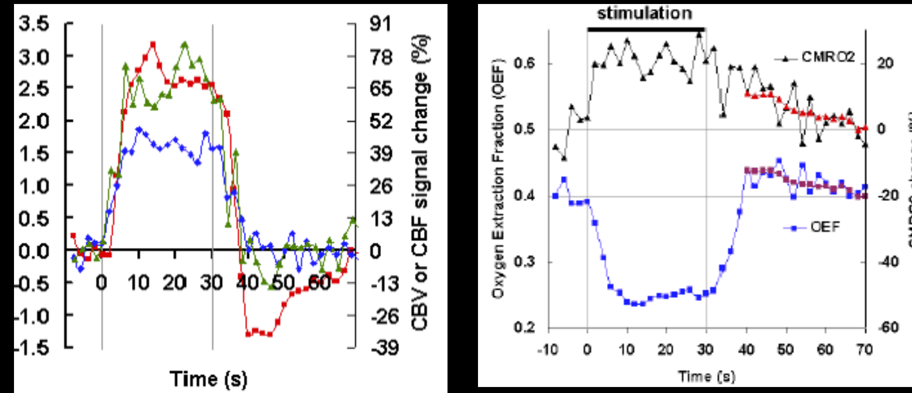
Thompson, et al (2003), Science 299, 1070-1072



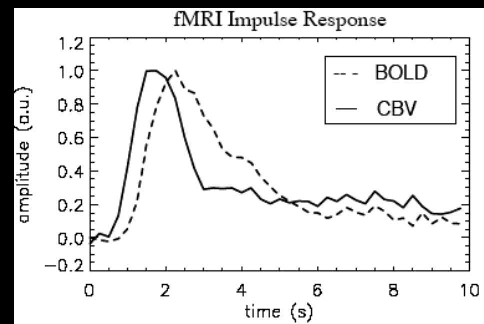
Yacoub, et al (1999), MRM 41, 1088-1092



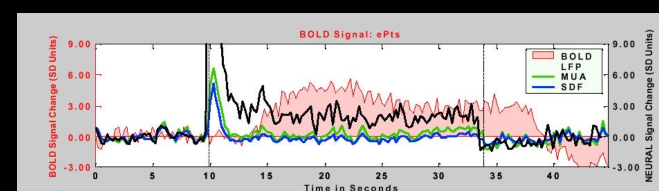
Behzadi, et al (2004), ISMRM 279



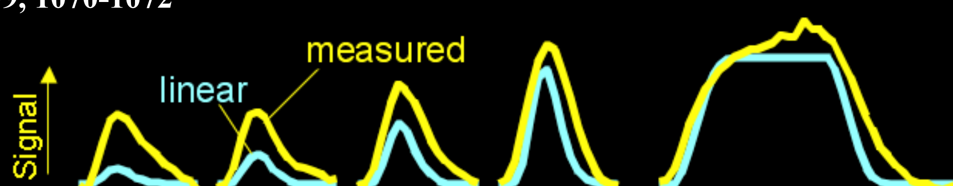
Lu, et al (2004), ISMRM 271



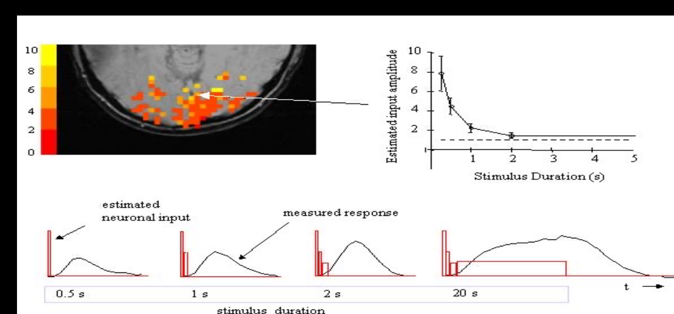
Silva, et al (2004), ISMRM 277



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

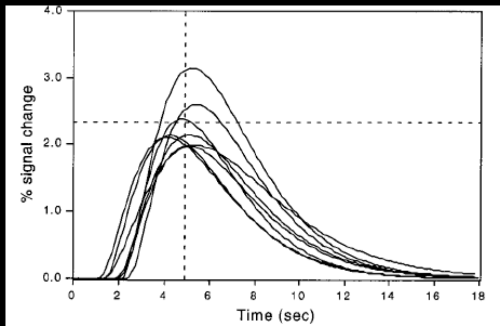


R. M. Birn, (2001) NeuroImage, 14: 817-826.

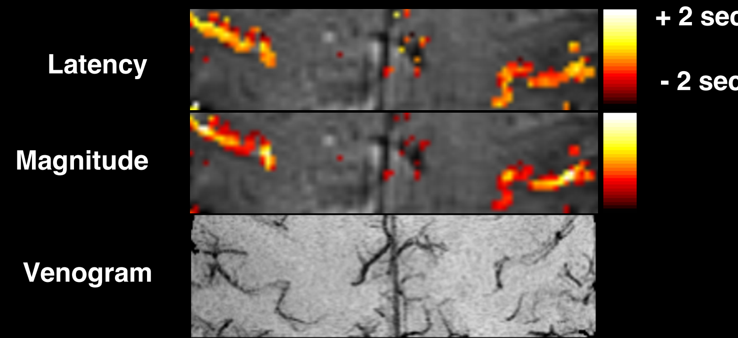


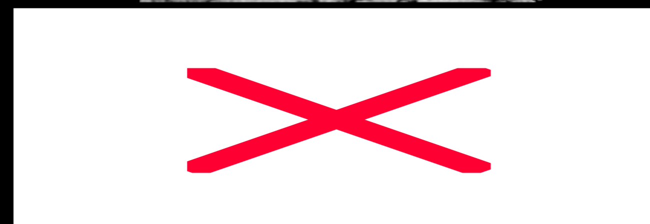
P. A. Bandettini et al, (2001) Nature Neuroscience, 4: 864-866.

Sources of variability?

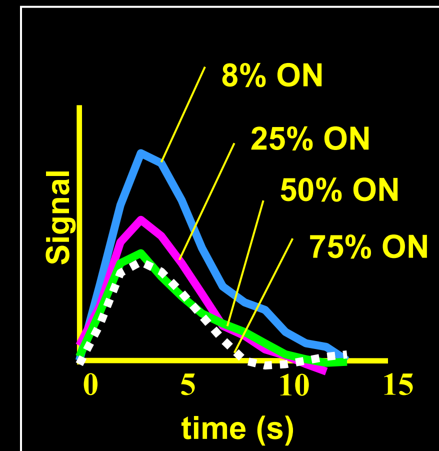


Miezin, et al (2000), NeuroImage 11, 735-759

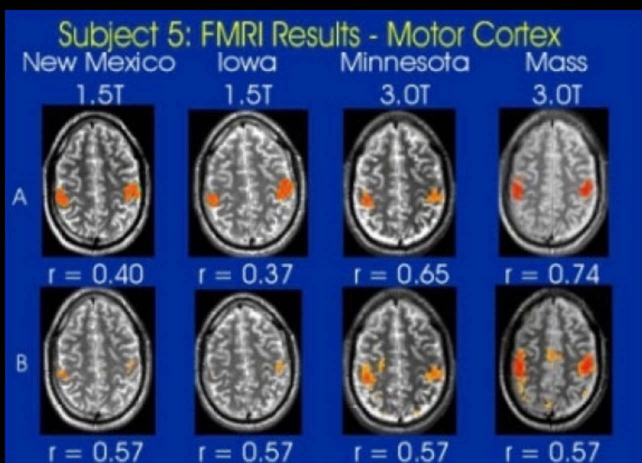




P. A. Bandettini, (1999) "Functional MRI" 205-220.

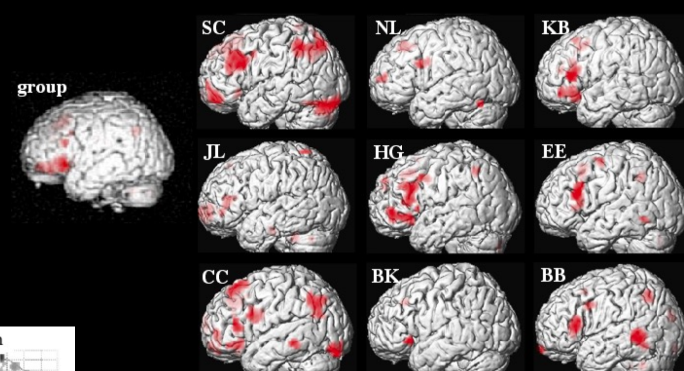


R. Birn, et al (2001), OHBM 971

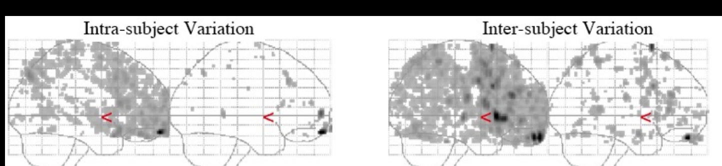


F. BIRN project

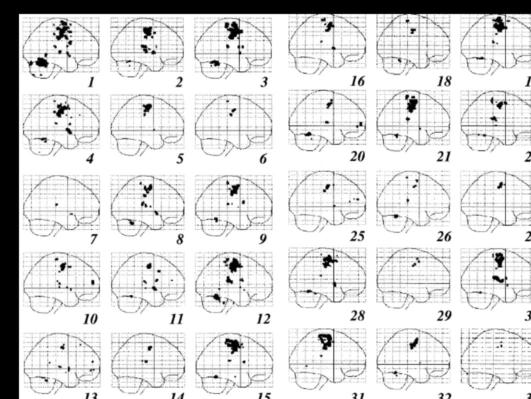
L. Friedman, et al (2004), ISMRM 489



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

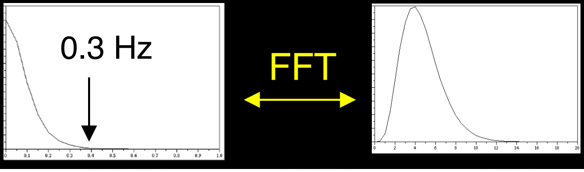


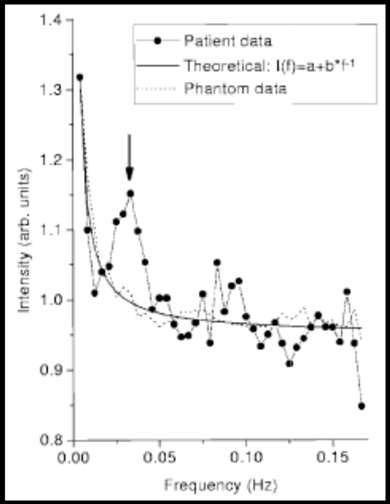
T.E. Lund, et al (2004), ISMRM 497å

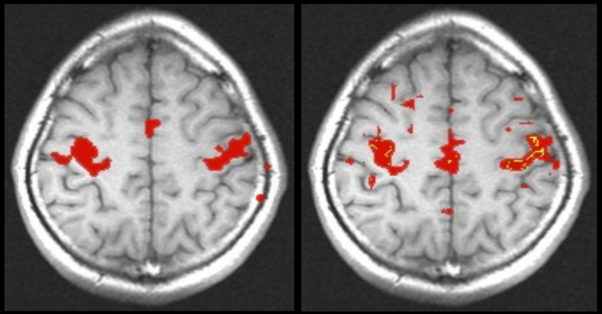


McGonigle, et al (2000), NeuroImage 11, 708-734

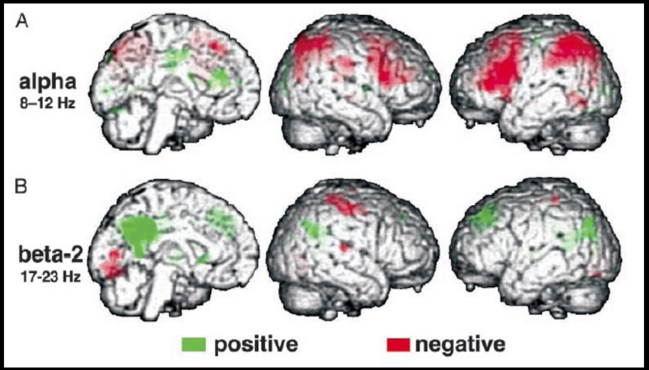
What's really in the noise?



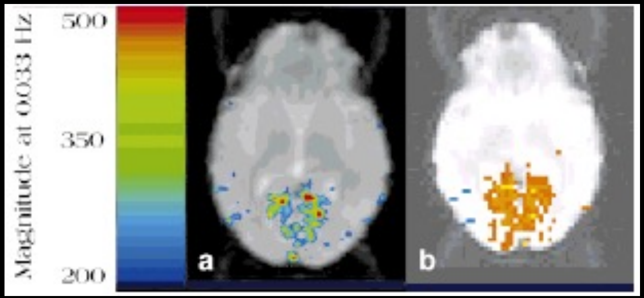




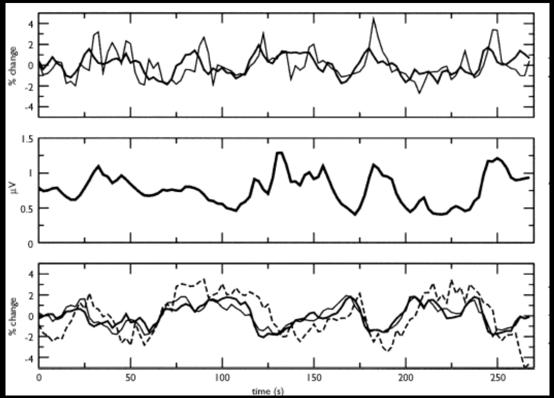
Biswal, et al (1995), MRM 34, 537-541

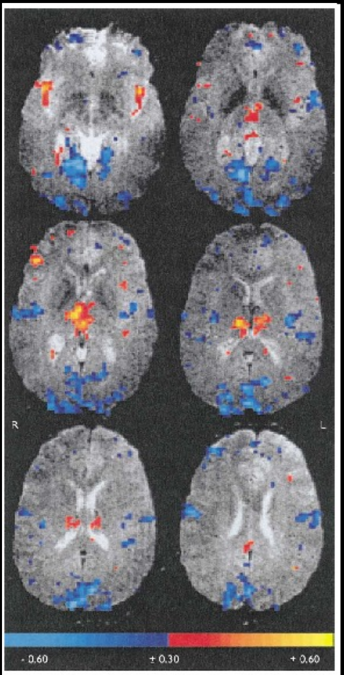


Laufs, et al (1995), PNAS 100 (19), 11053=11058

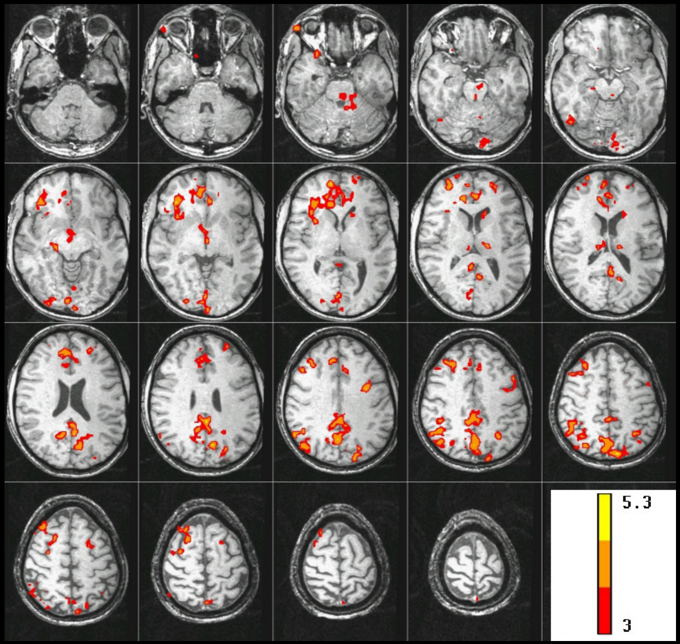


Kiviniemi, et al (2000), MRM 44, 373-378



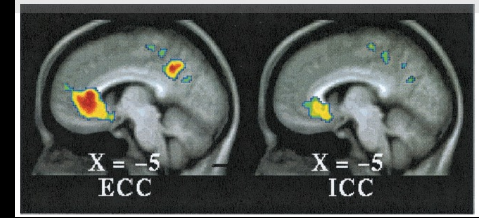


Goldman, et al (2002), Neuroreport

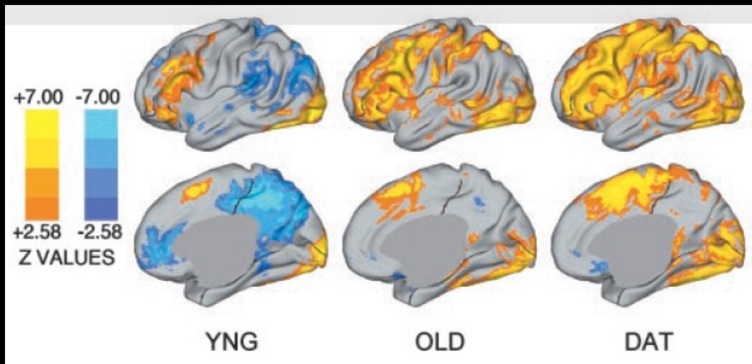


Patterson, et al (2002), NeuroImage 17, 1787-1806

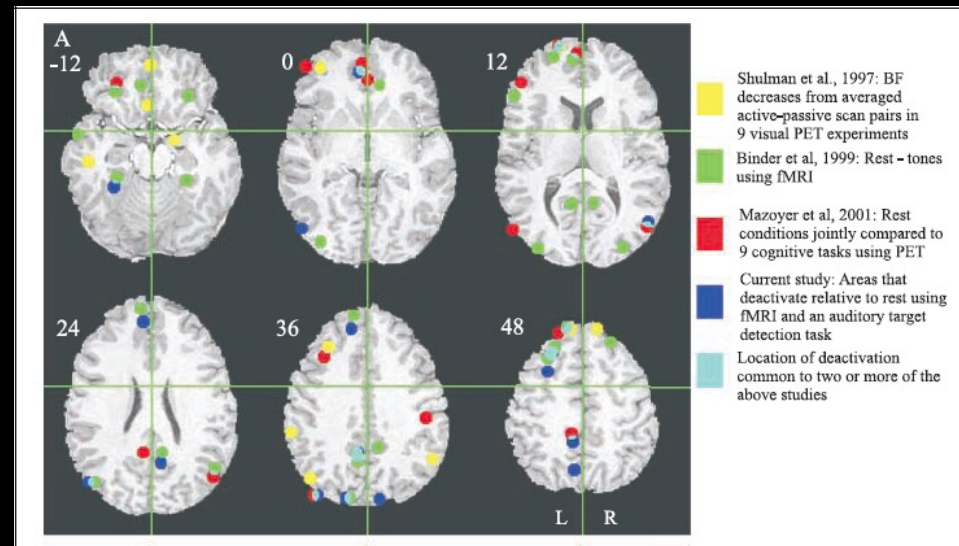
What is “resting” state?



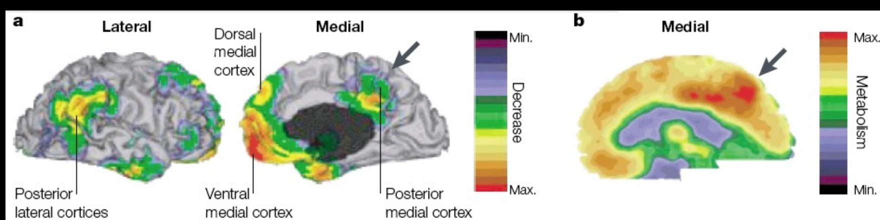
Gusnard, et al (2001), PNAS 98 (7), 4259-4264



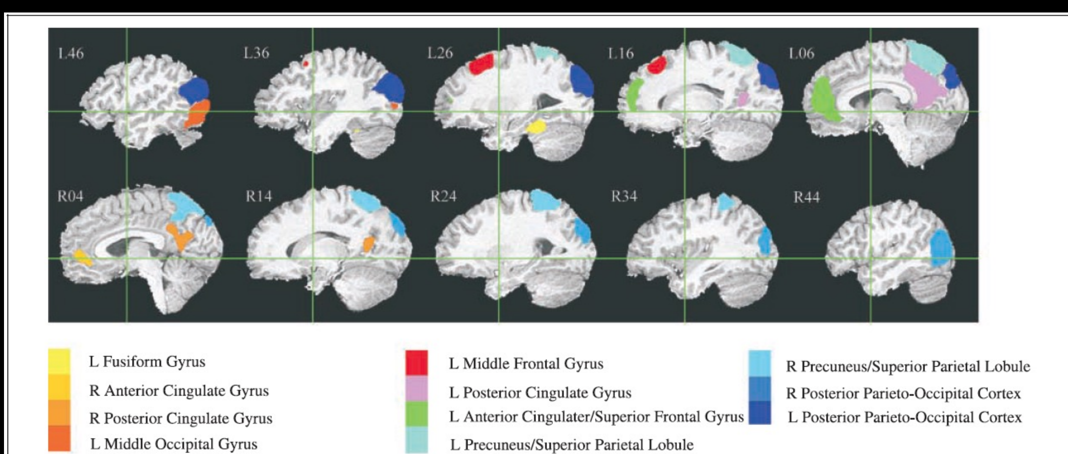
Lustig, et al (2003), PNAS 100 (19), 14504-14509



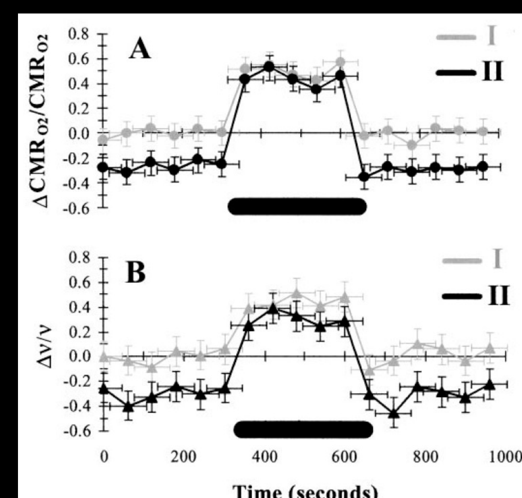
McKiernan, et al (2003), Journ. of Cog. Neurosci. 15 (3), 394-408



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

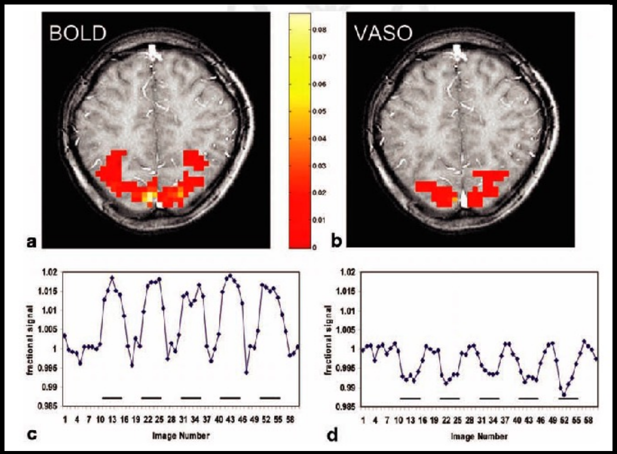


McKiernan, et al (2003), Journ. of Cog. Neurosci. 15 (3), 394-408

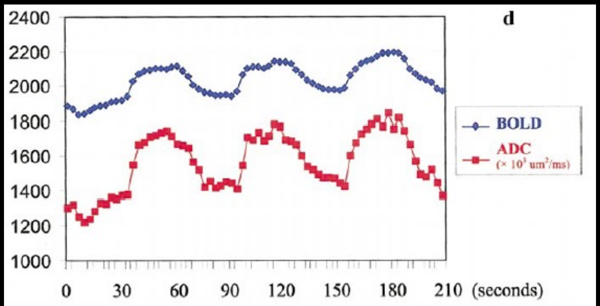


Hyder, et al (2002), PNAS 99 (16), 10771-10776

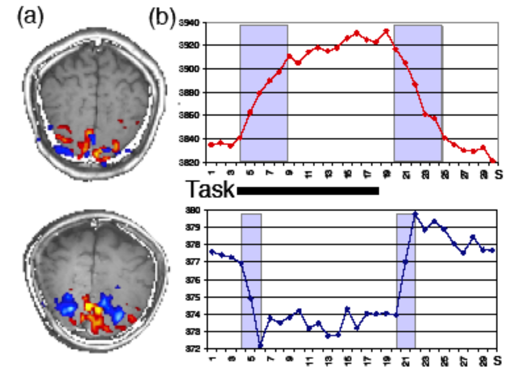
Other sources of functional contrast?



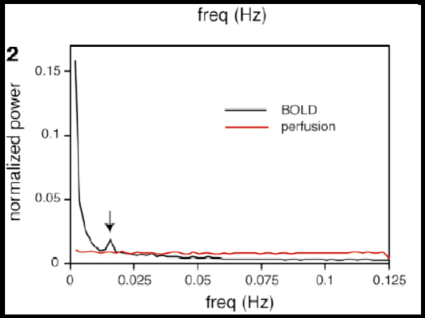
Lu, et al (2003) MRM 50 (2): 263-274

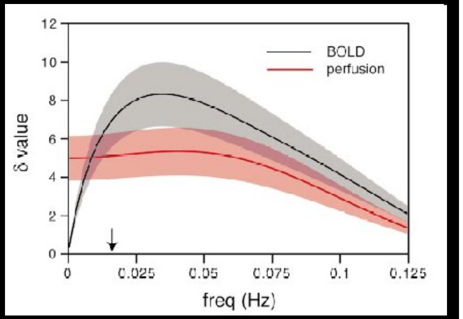


A. Song, et al (2002), NeuroImage 17, 742-750

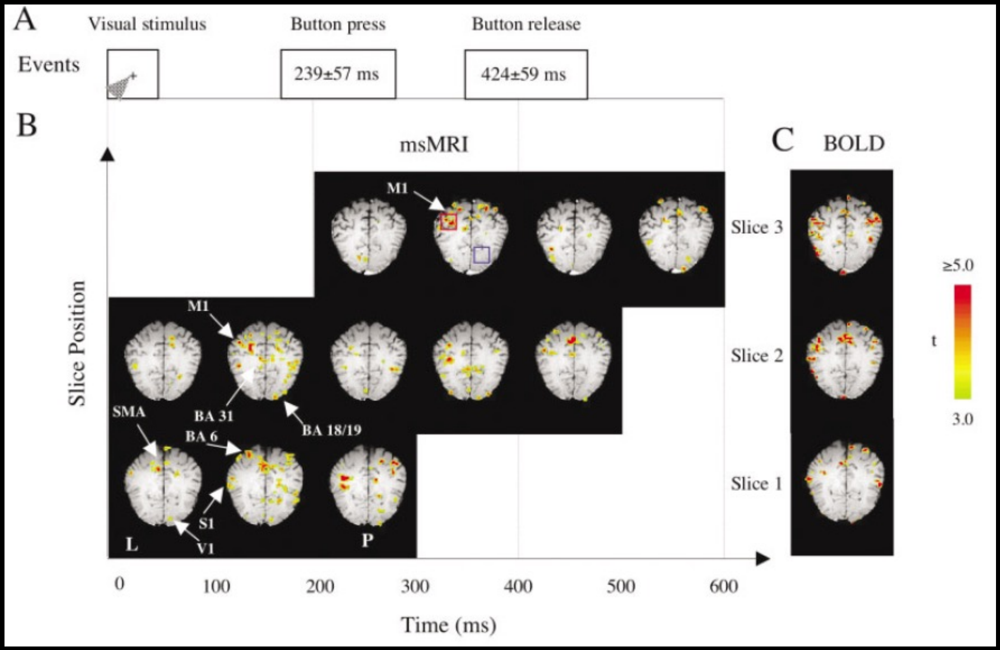


A. Song, et al (2004), ISMRM 1063

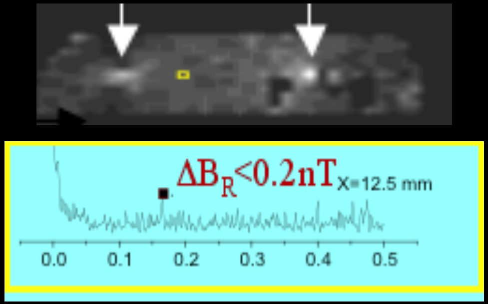


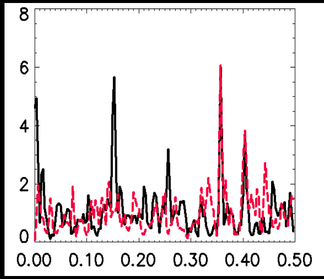


GK Aguirre et al, (2002) NeuroImage 15 (3): 488-500



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

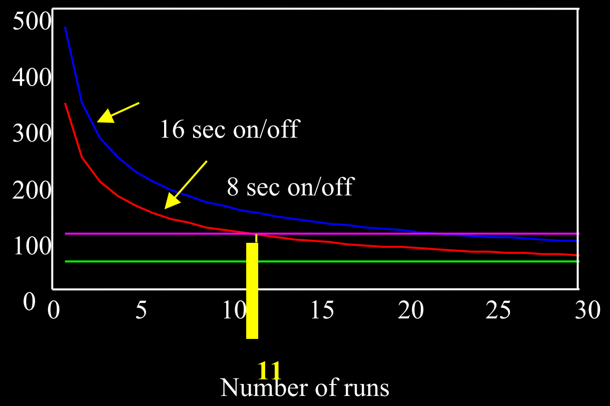




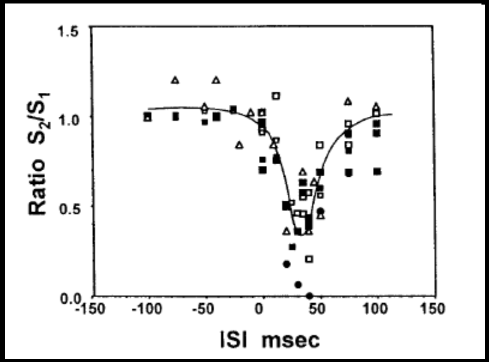
J. Bodurka, et al (2002). MRM 47: 1052-1058.

Petridou, et al (2003), OHBM

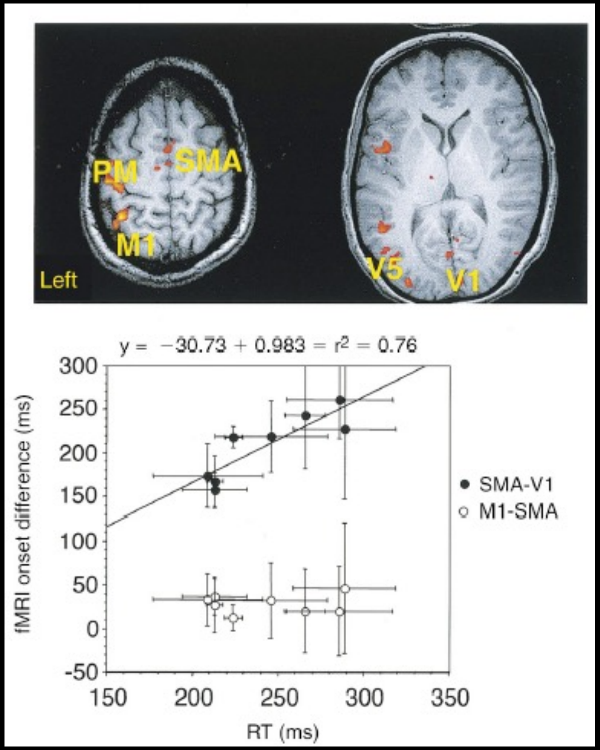
Ultimate temporal resolution?



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



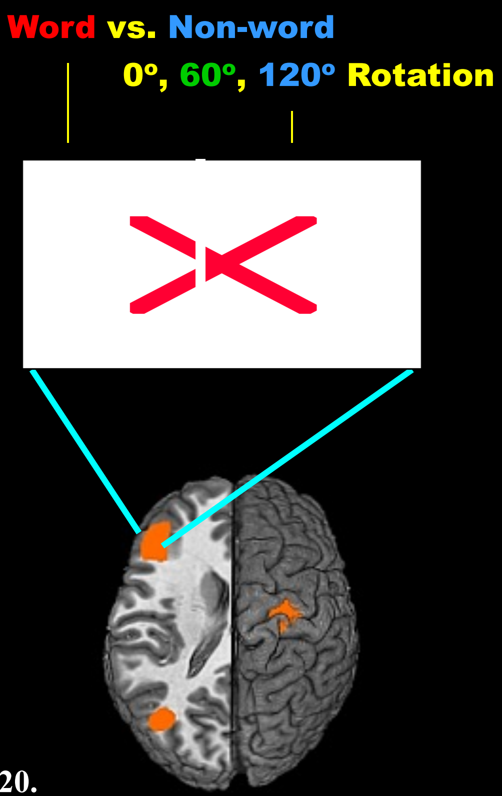
Ogawa, et al (2000), PNAS 97 (20)11026–11031



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

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

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

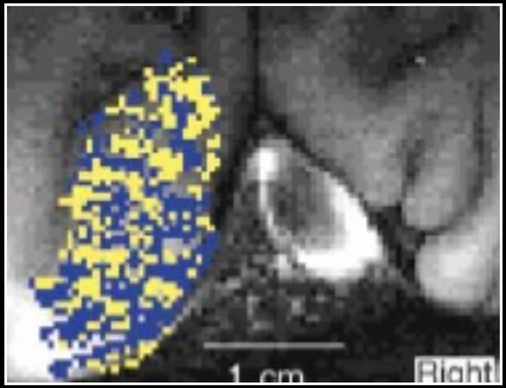


Bellgowan, et al (2003), PNAS 100, 15820–15283

Ultimate spatial resolution?

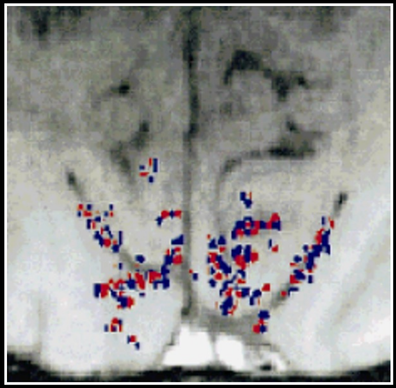
Resolving columns with single shot EPI is a goal..

0.47 x 0.47 in plane resolution



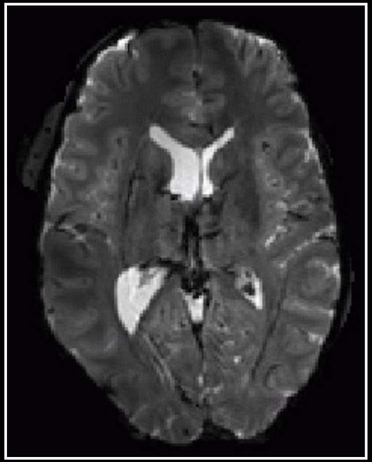
Cheng, et al. (2001) Neuron,32:359-374

0.54 x 0.54 in plane resolution



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

Multi-shot with navigator pulse



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

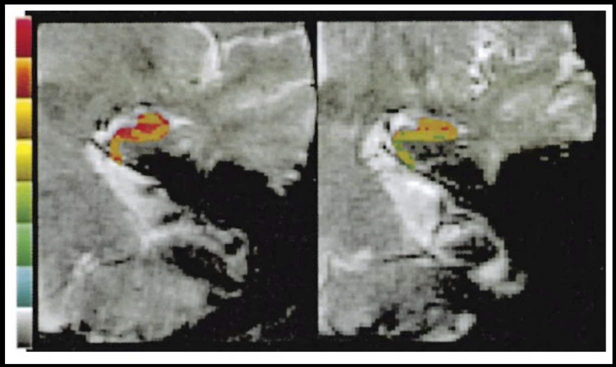
…using SENSE, 32 channels, 7T,
and perhaps partial k-space we might get to 0.5 mm^3

Ultimate clinical utility?

Needs:

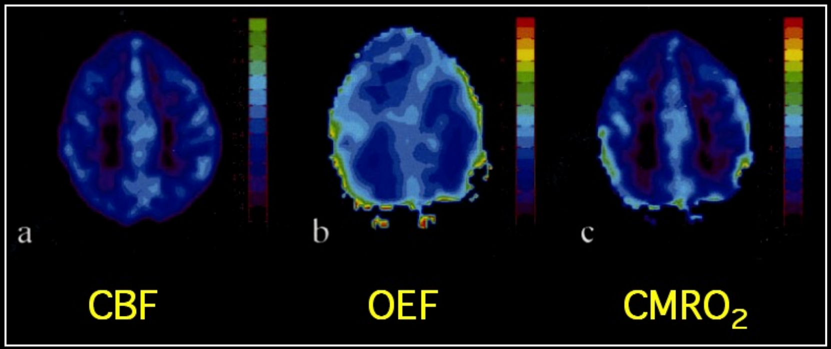
- Real time feedback
- Characterization of confounding effects
- Robust yet incisive set of probe tasks
- Baseline information?

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

fim.nimh.nih.gov

fmrif.nimh.nih.gov

Computer Specialist:
Adam Thomas

Staff Scientists:
Sean Marrett
Jerzy Bodurka
Frank Ye
Wen-Ming Luh
Rasmus Birn

Post Docs:
Hauke Heekeren
David Knight
Anthony Boemio
Niko Kriegeskorte

Scanning Technologists:
Karen Bove-Bettis
Paula Rowser
Alda Ottley
Ellen Condon

Program Assistant:
Kay Kuhns

Graduate Student:
Natalia Petridou