# A Closer Look at BOLD Fluctuations, Decreases, and Increases

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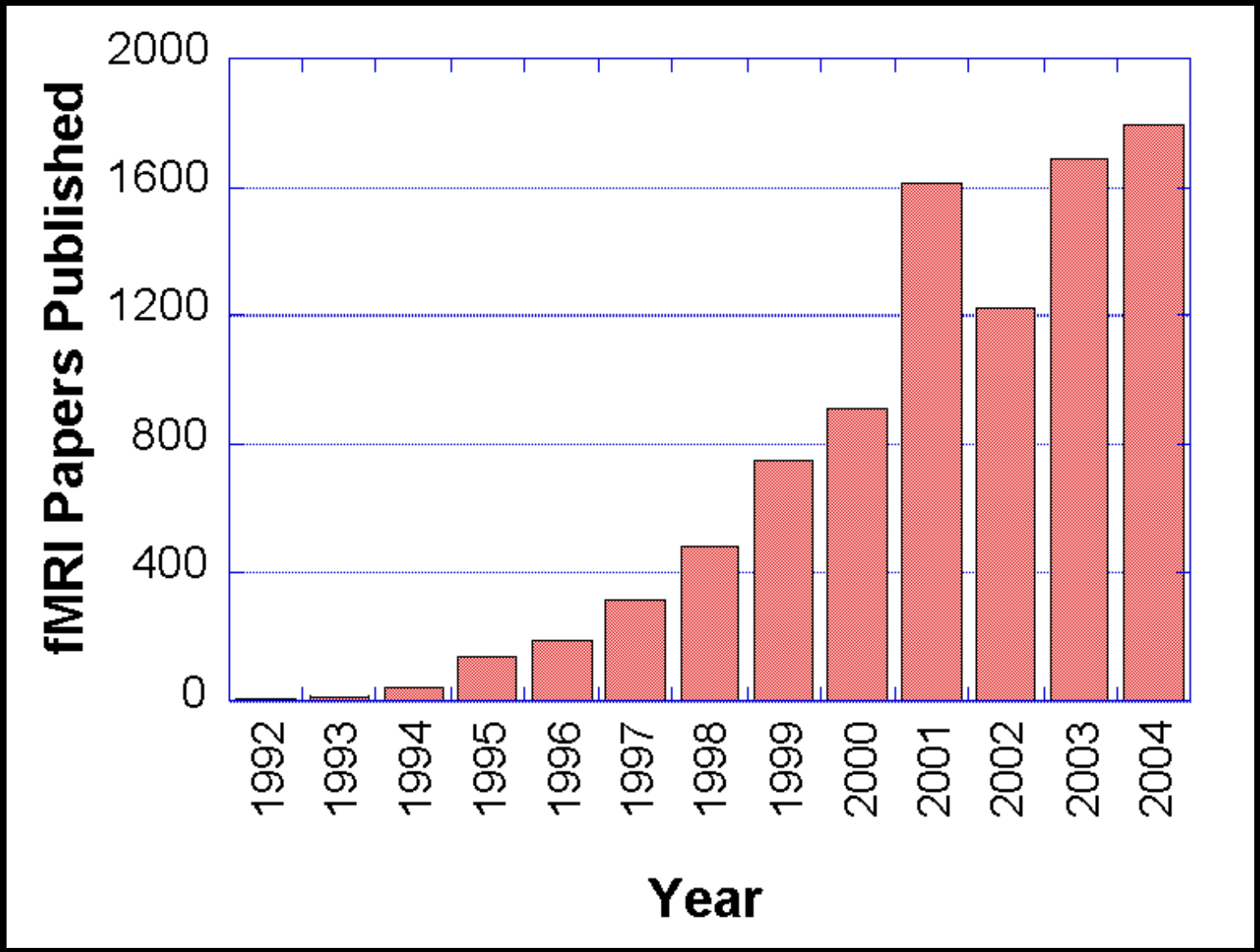
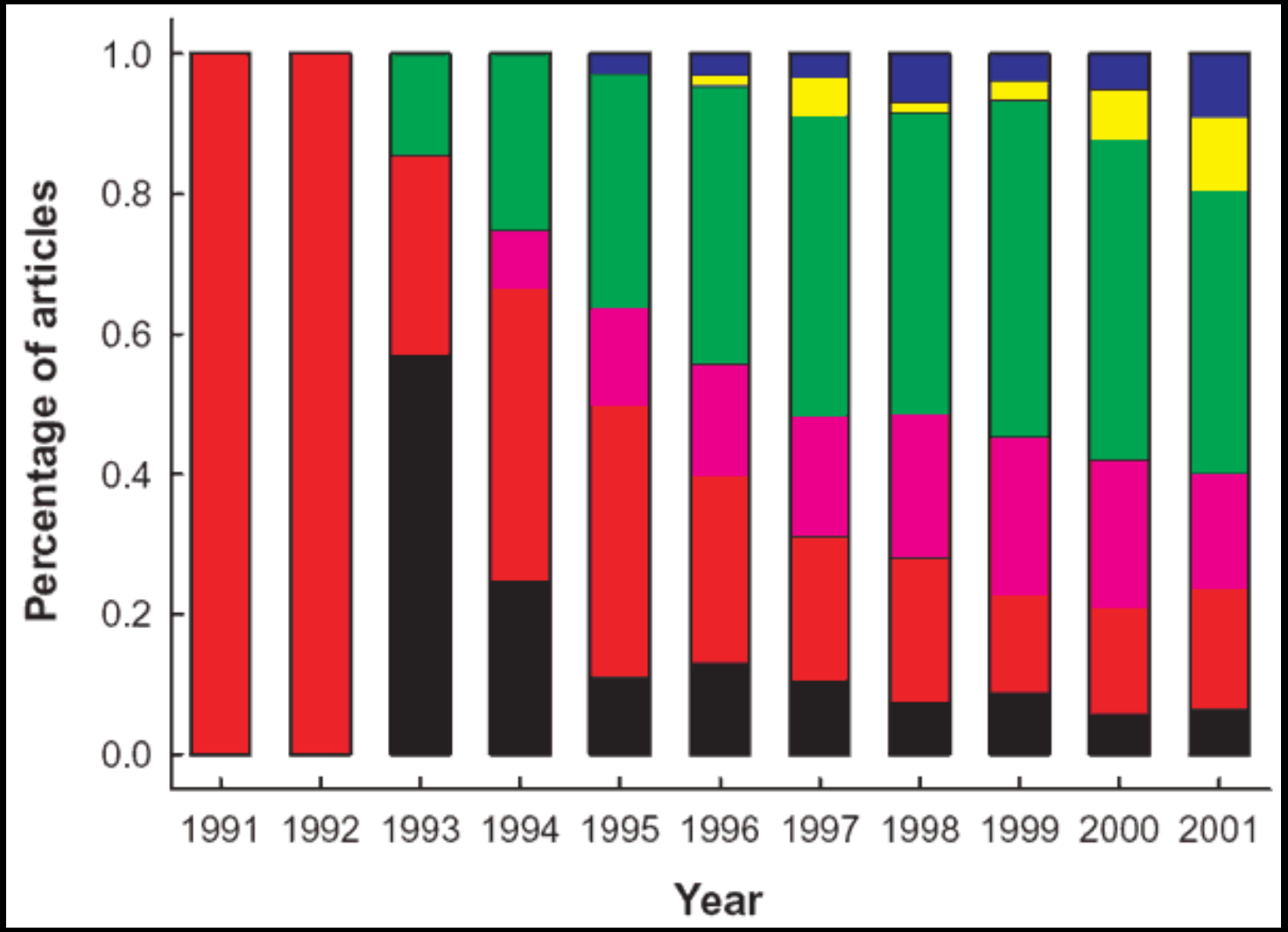

fMRI Papers Published
2000
1600
1200
800
400
0
1992
1993
1994
1995
1996
1997
1998
1999
2000
2001
2002
2003
2004
Year

# Many remaining unknowns

- Relationship between neuronal activity and BOLD contrast?
- Sources of BOLD variability?
- Information content / artifact in time series fluctuations?
- Source of BOLD timing and dynamics?
- Sources of BOLD signal decreases?
- Other sources of functional contrast?
- Temporal resolution?
- Spatial resolution?
- Clinical utility?
- Best processing and display strategies?
- Best paradigm designs strategies?
- Optimal field strength?
- Applications..??

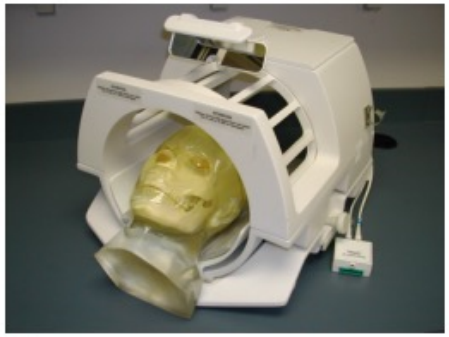



Motor (black)
Primary Sensory (red)
Integrative Sensory (violet)
Basic Cognition (green)
High-Order Cognition (yellow)
Emotion (blue)

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

# 16 channel parallel receiver coil

A



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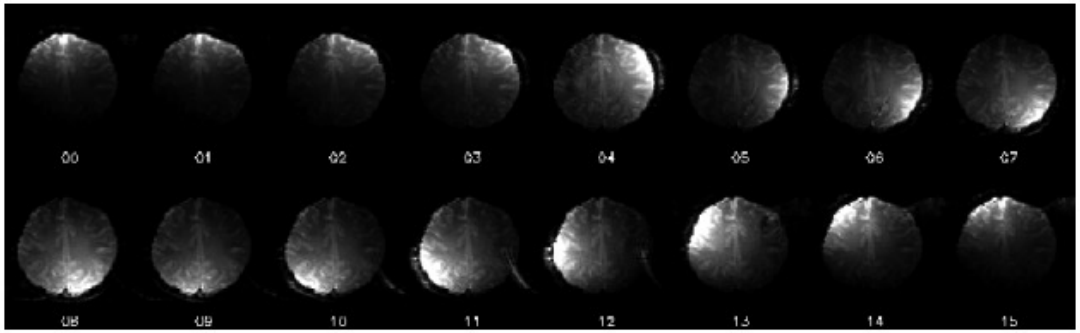
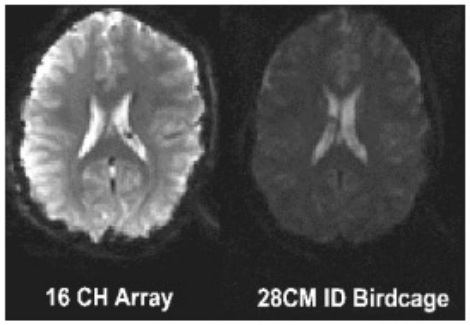
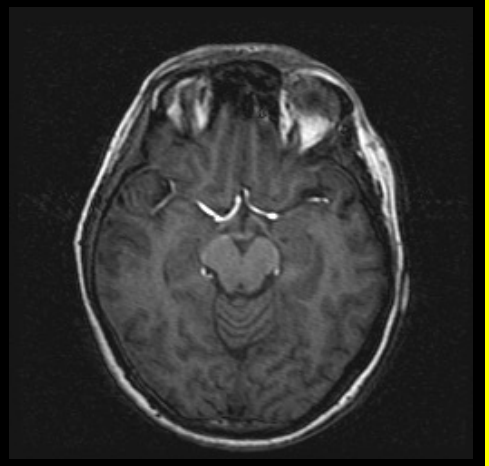



C

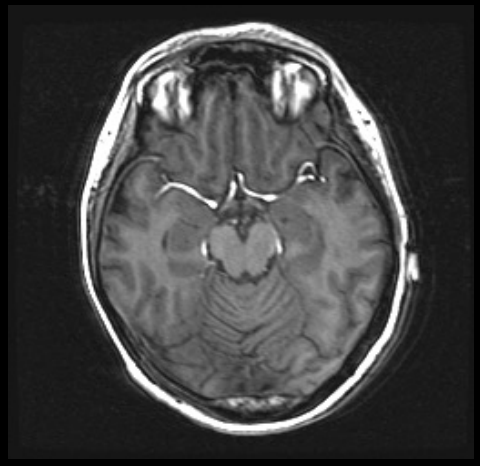



D

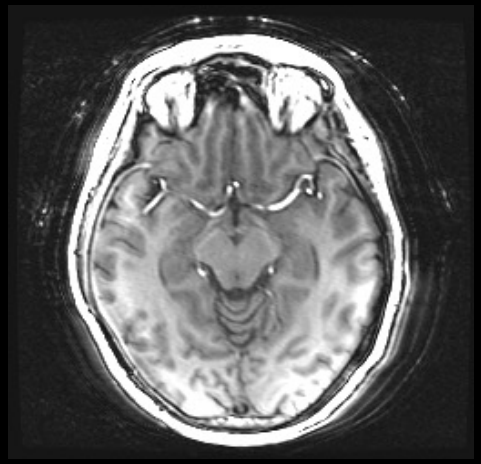
# 8 channel parallel receiver coil



GE birdcage

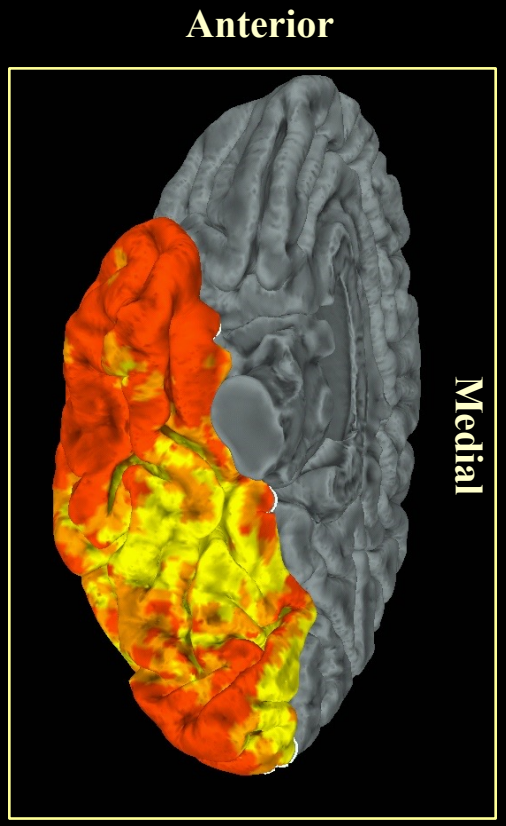


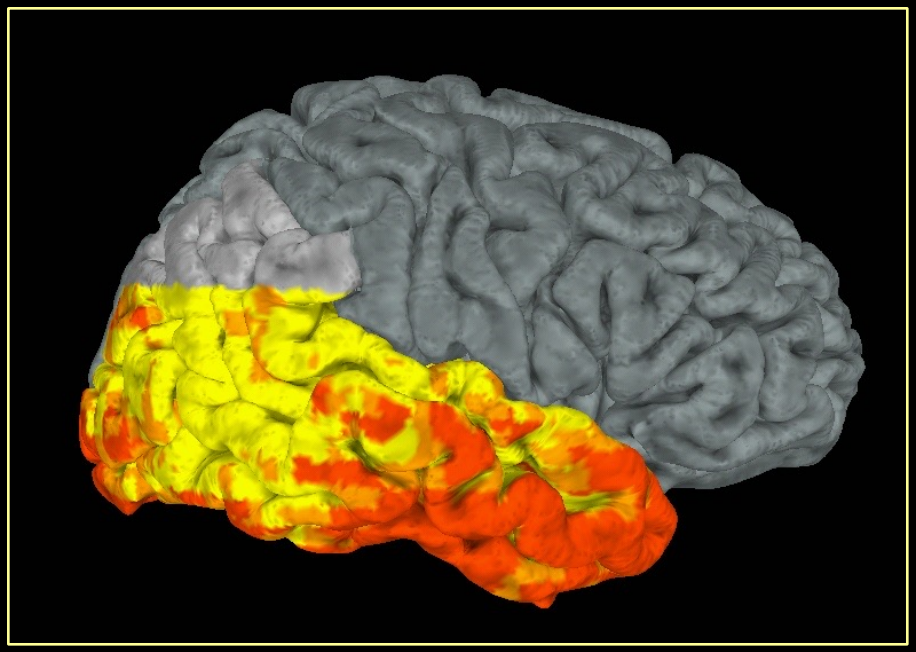
GE 8 channel coil



Nova 8 channel coil

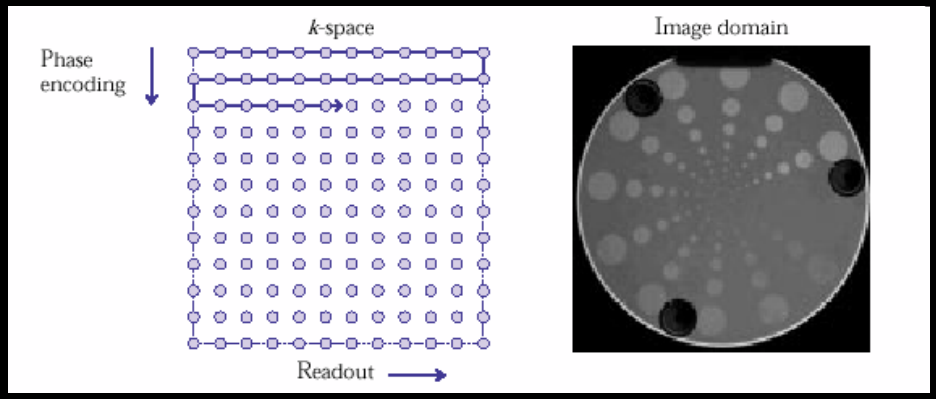
# Average Temporal Signal-to-Noise ratio Comparison Between Coils

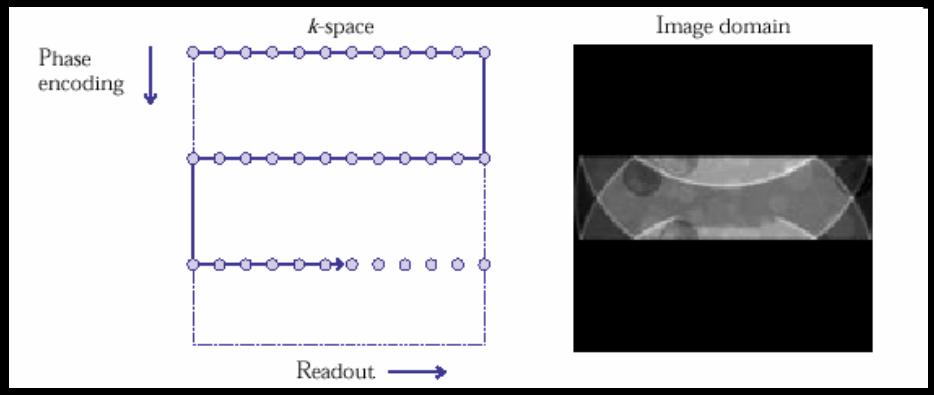


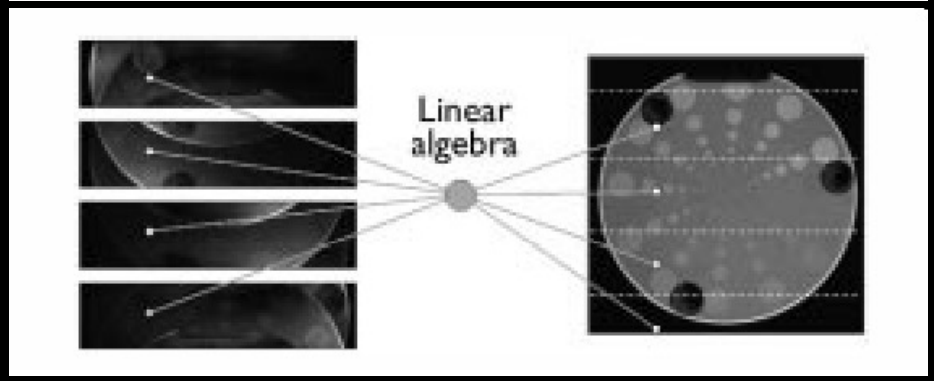



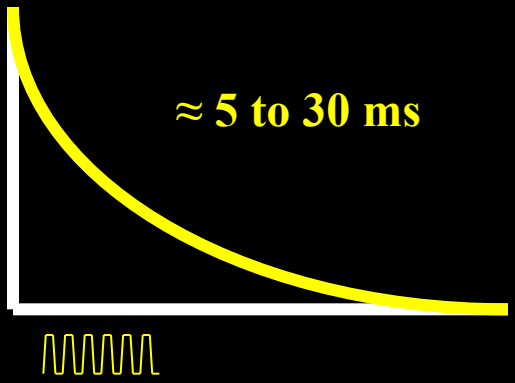
150% 100% 50% 16 Element Array > GE coil

# Sensitivity Encoding (SENSE) Imaging



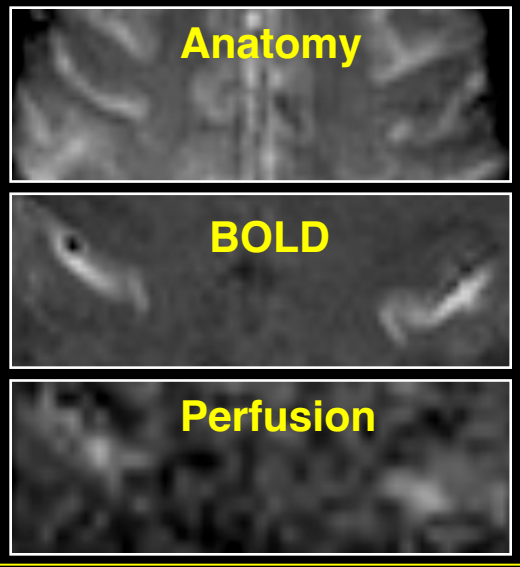



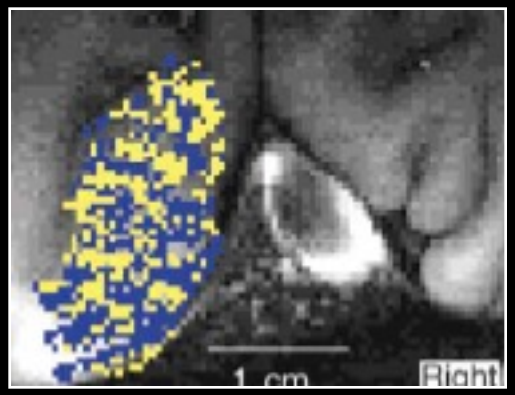

3T single-shot SENSE EPI using 16 channels:1.25x1.25x2mm

Pruessmann, et al.

# Spatial Resolution




0.47 x 0.47 in plane resolution

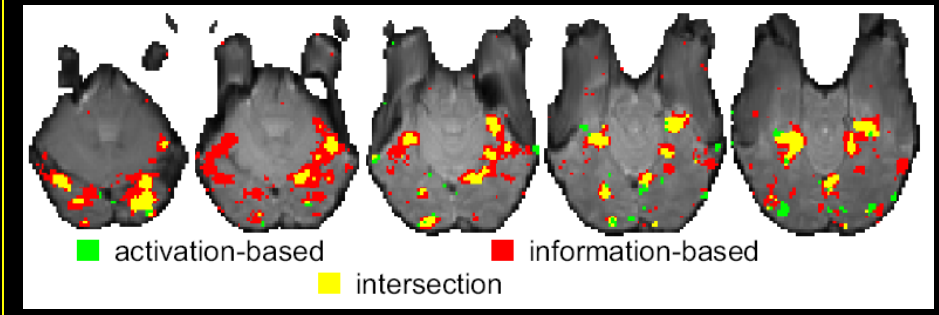


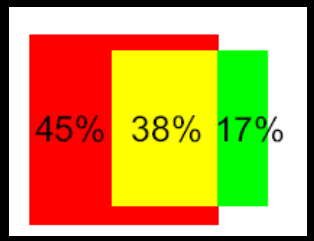

Cheng, et al. (2001) Neuron,32:359-374

***Activation-based*** **mapping: data smoothing**
(classical approach)

***Information-based*** **mapping: local multivariate analysis**

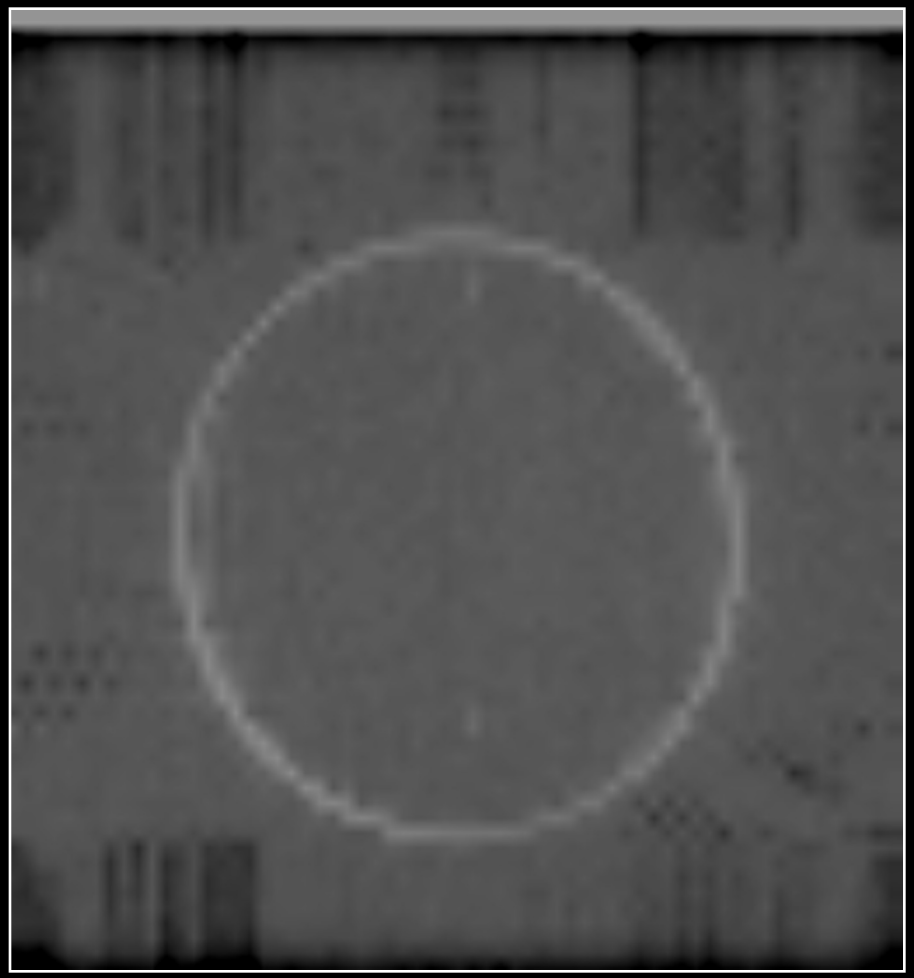
volume scanned with MANCOVA searchlight→



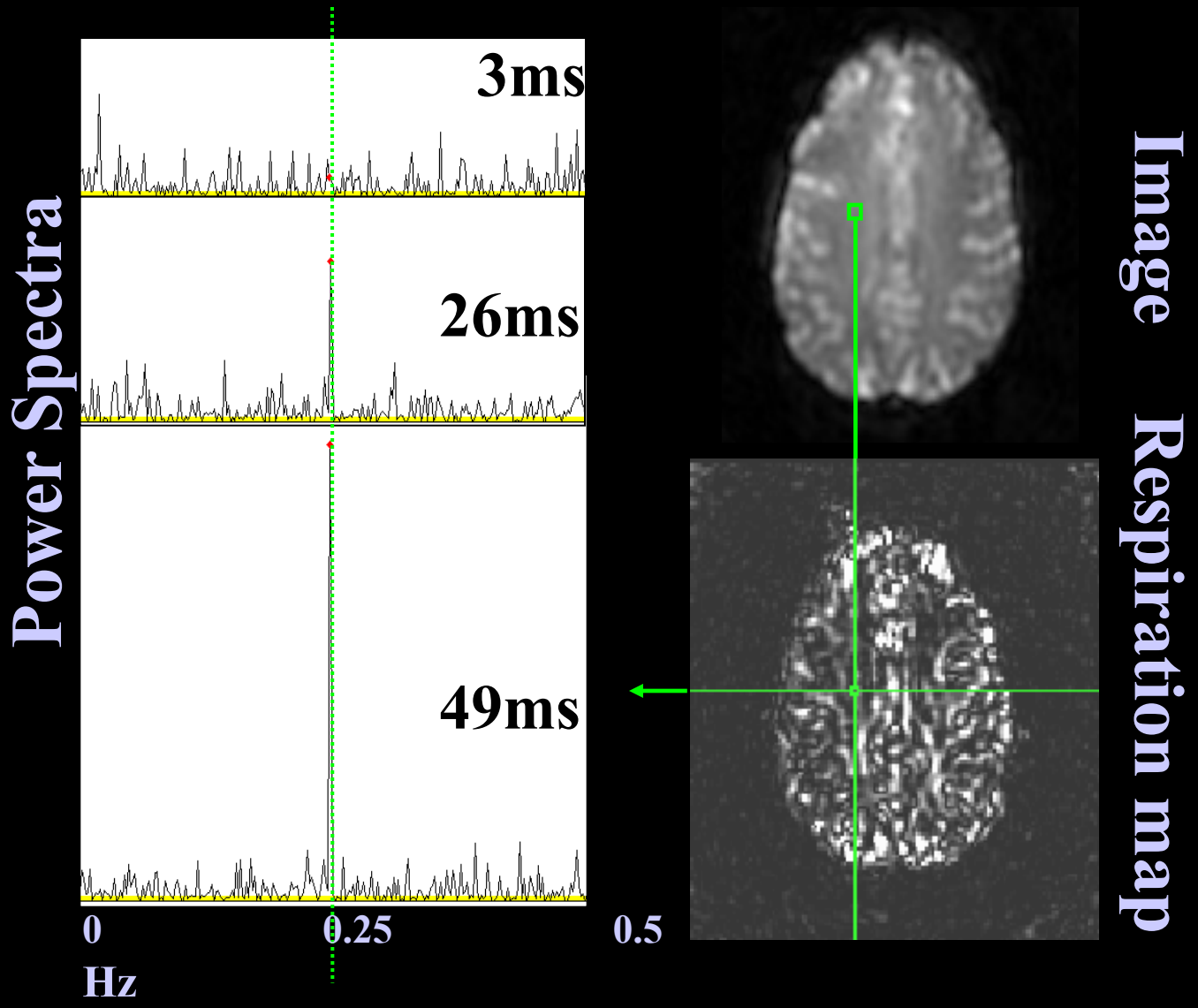




voxel sets

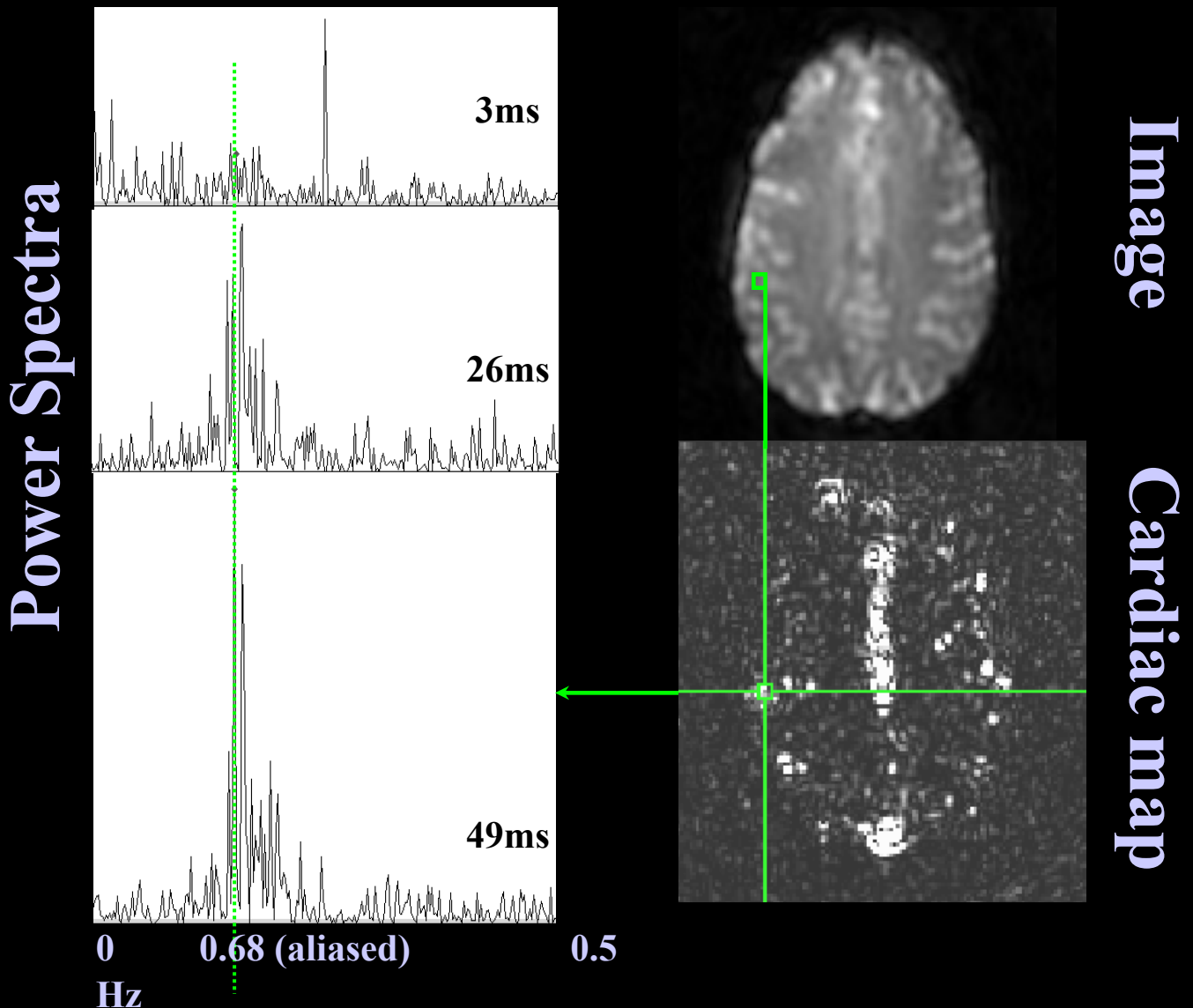
# Fluctuations

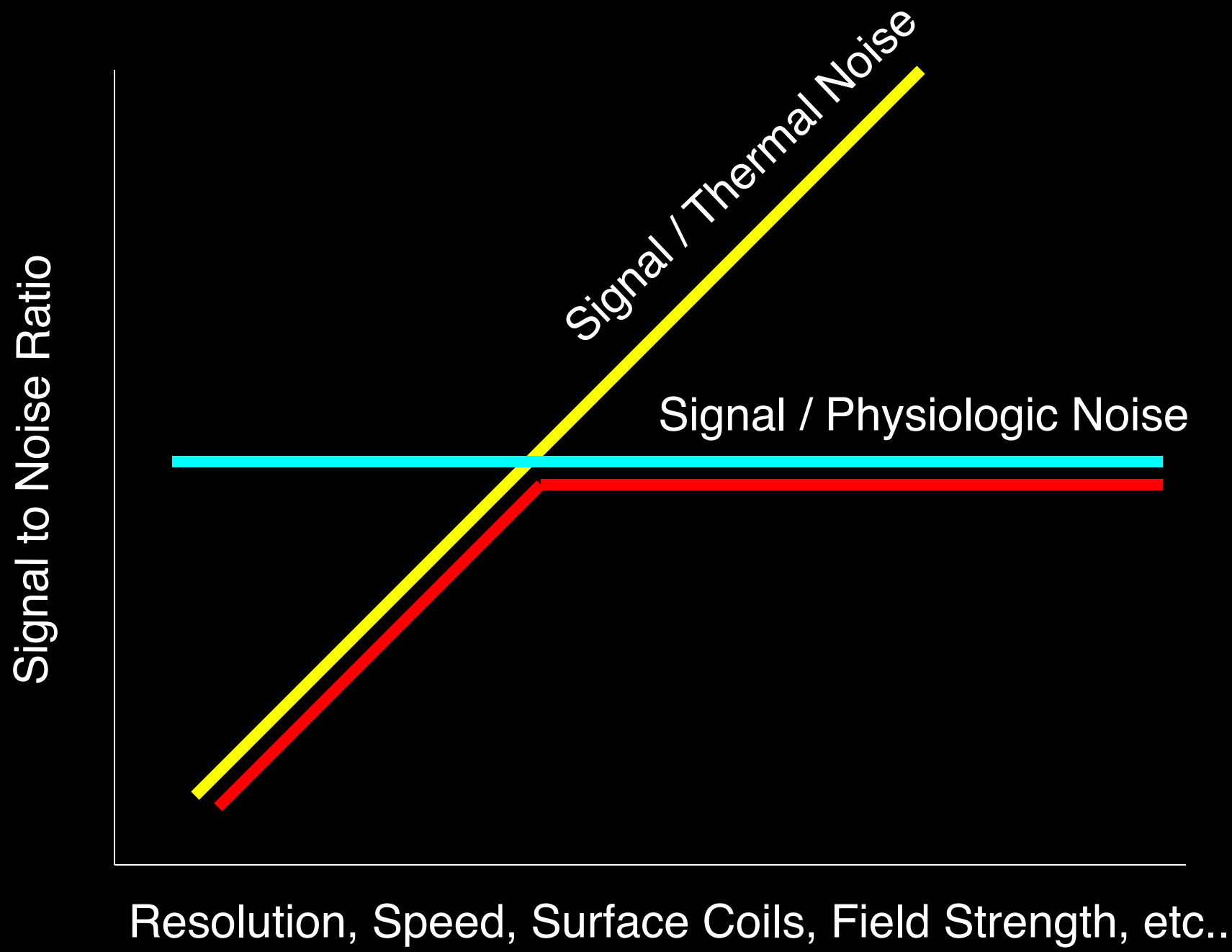


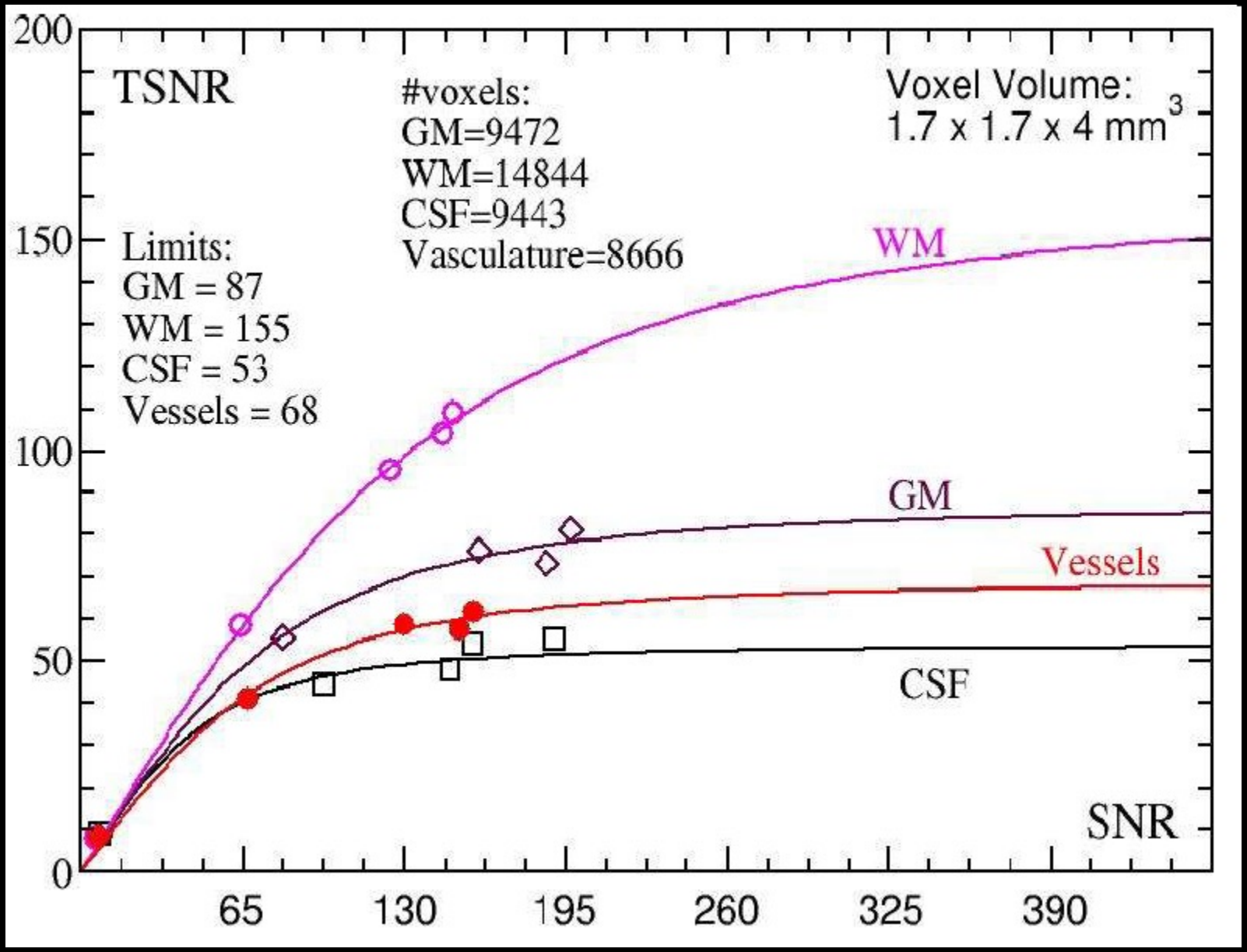
# Respiration Effects



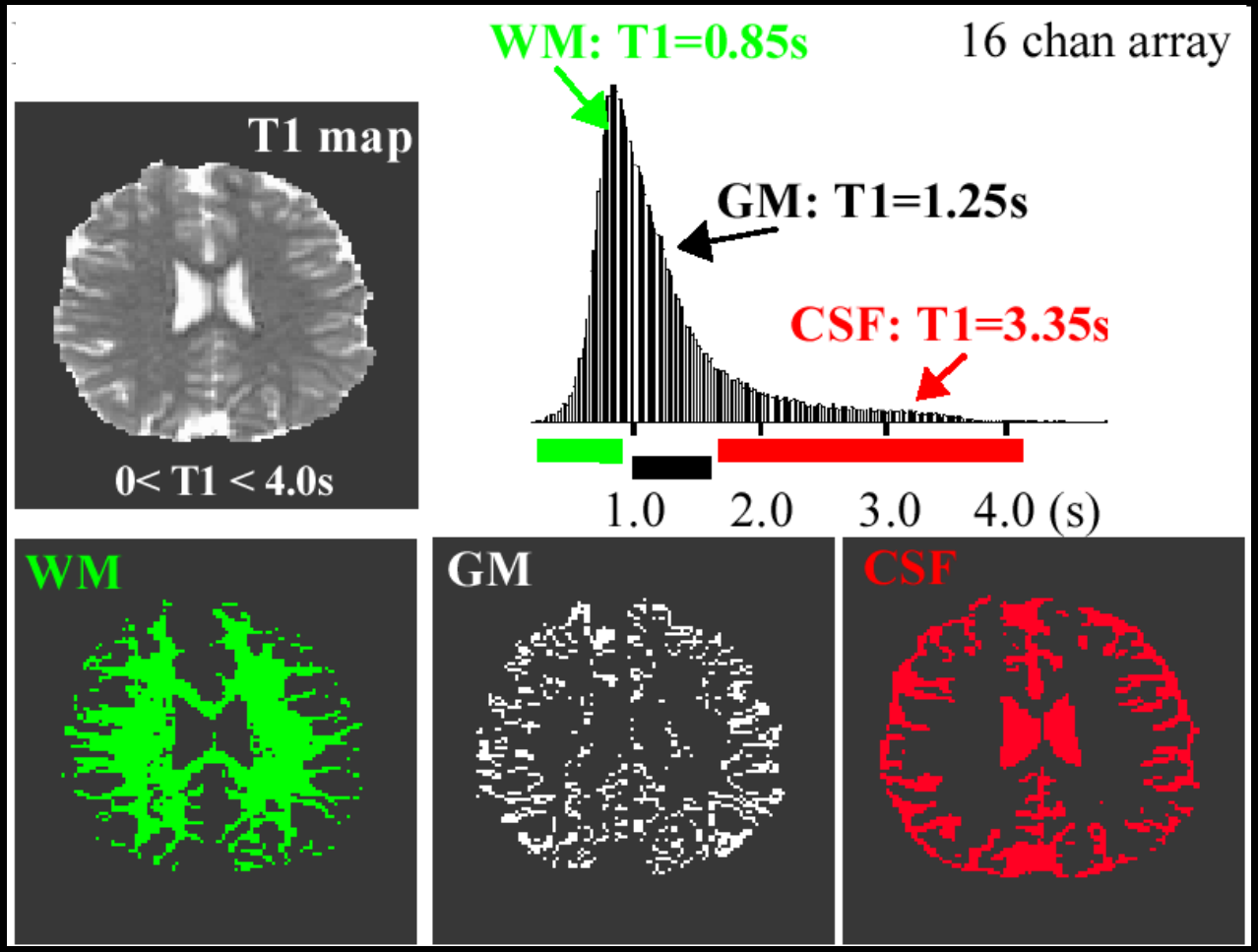
# Cardiac Effects



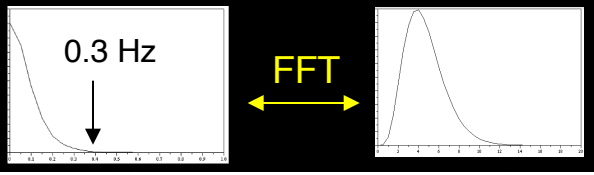

Signal / Thermal Noise
Signal / Physiologic Noise
Signal to Noise Ratio
Resolution, Speed, Surface Coils, Field Strength, etc..

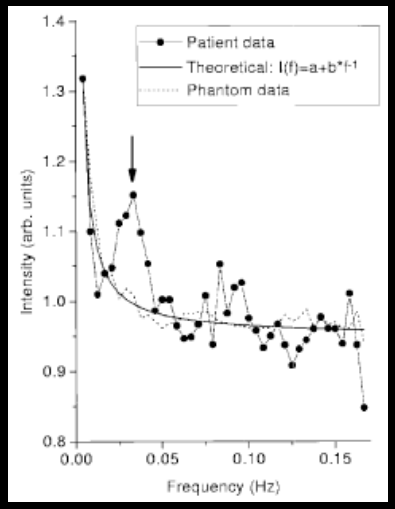

TSNR
#voxels:
GM=9472
WM=14844
CSF=9443
Vasculature=8666
Voxel Volume:
1.7 x 1.7 x 4 mm3
Limits:
GM = 87
WM = 155
CSF = 53
Vessels = 68
WM
GM
Vessels
CSF
SNR
200
150
100
50
0
65
130
195
260
325
390

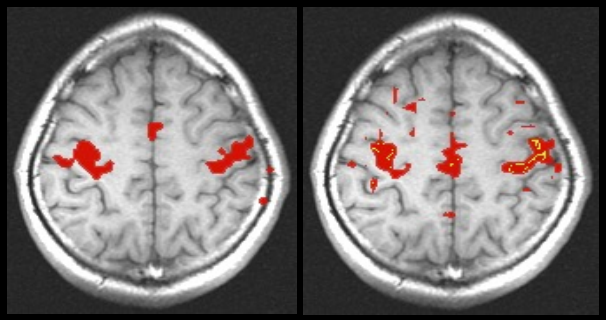
# Segmentation using EPI Transient



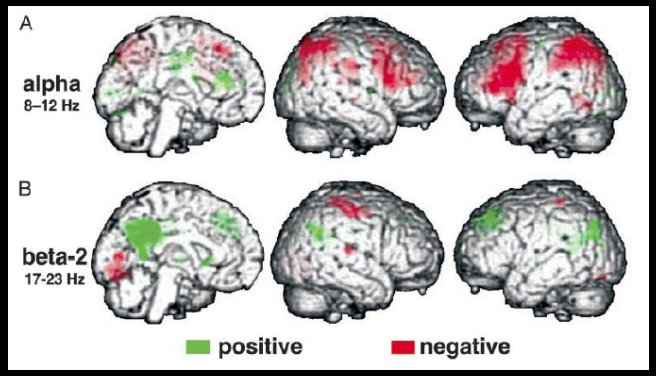
# Interesting Fluctuations



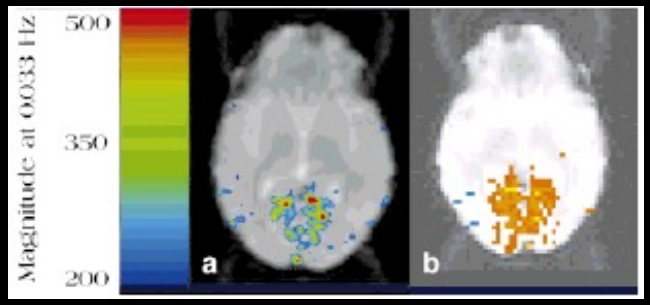



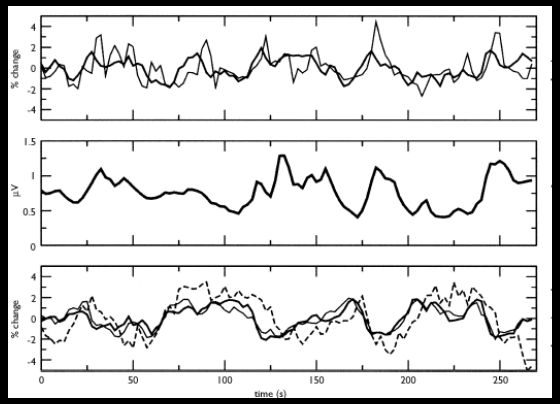
Biswal, et al (1995), MRM 34, 537-541

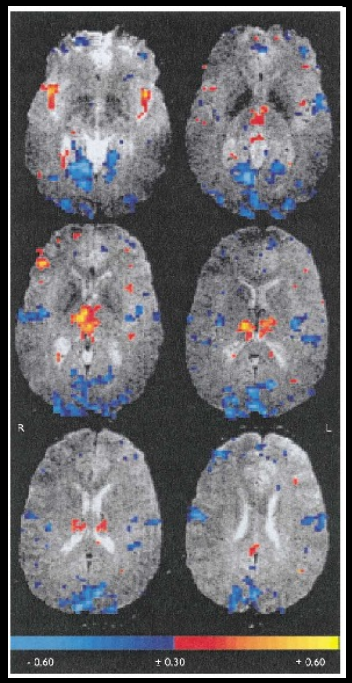



Laufs, et al (1995), PNAS 100 (19), 11053=11058

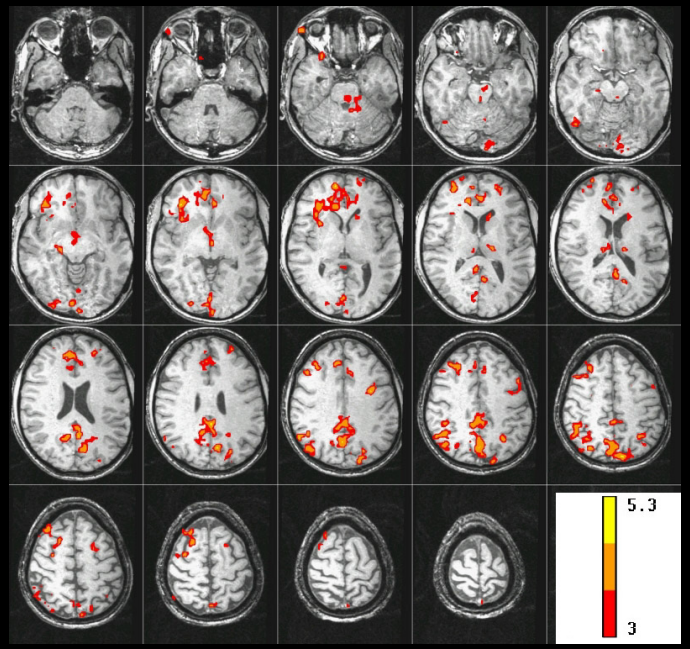



Kiviniemi, et al (2000), MRM 44, 373-378



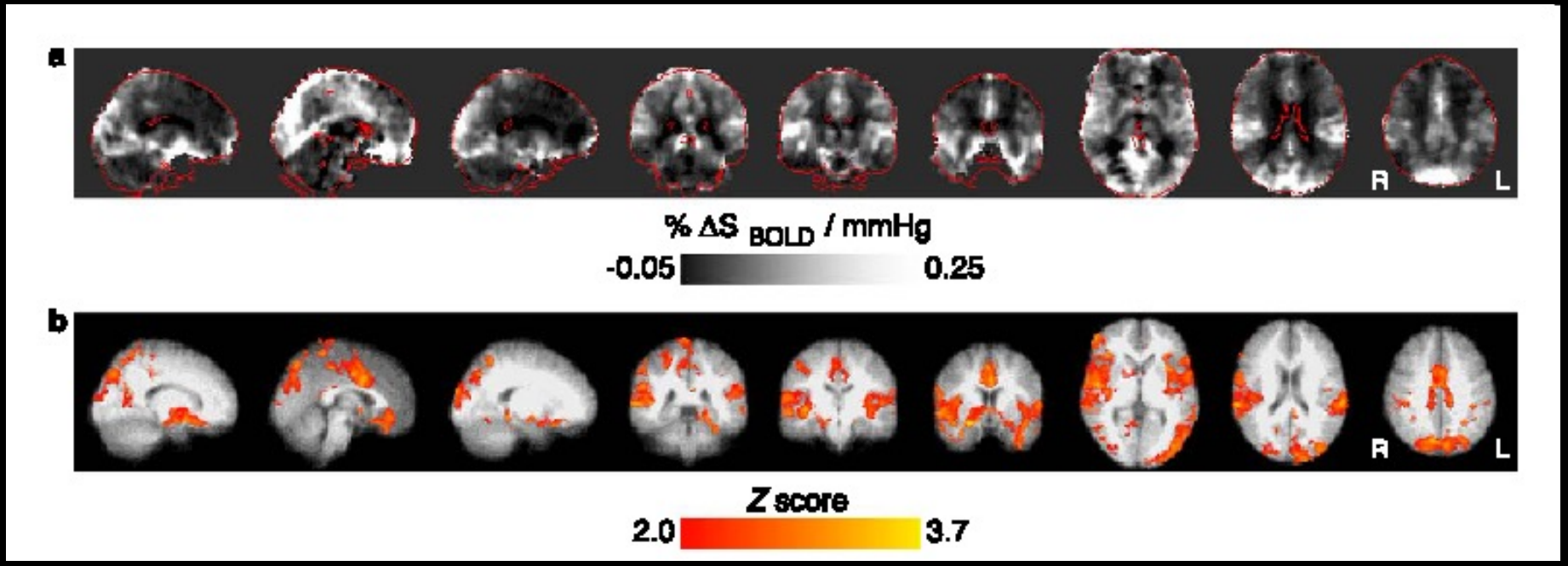

Goldman, et al (2002), Neuroreport




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

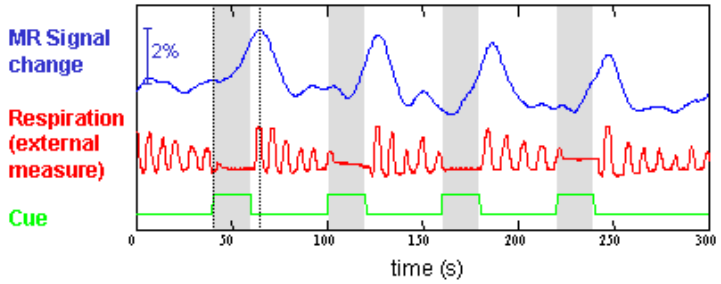
# Respiration fluctuations revisited...

Correlation with spontaneous changes in end tidal $CO_2$

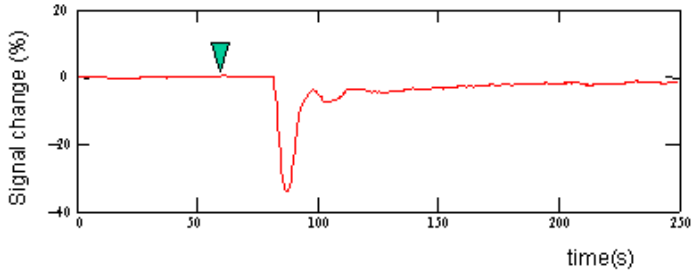



R. G. Wise, et al, NeuroImage 21 (2004), 1652-1664

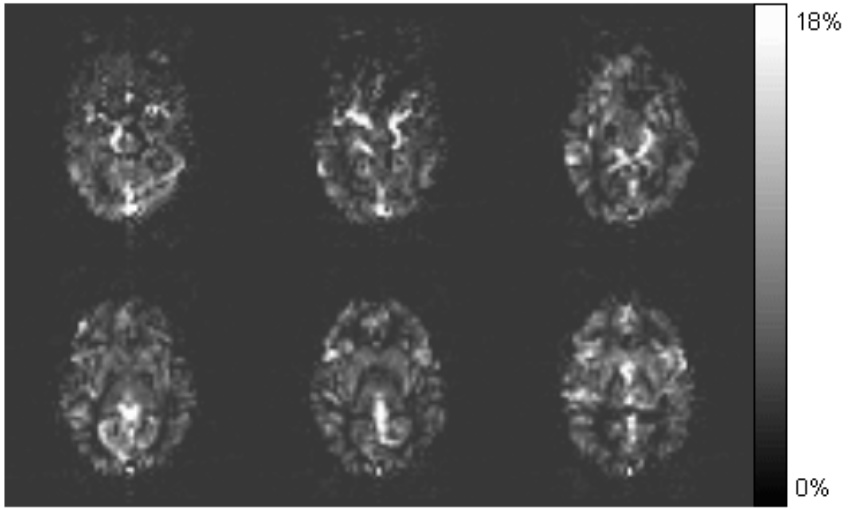
## Breath-Holding



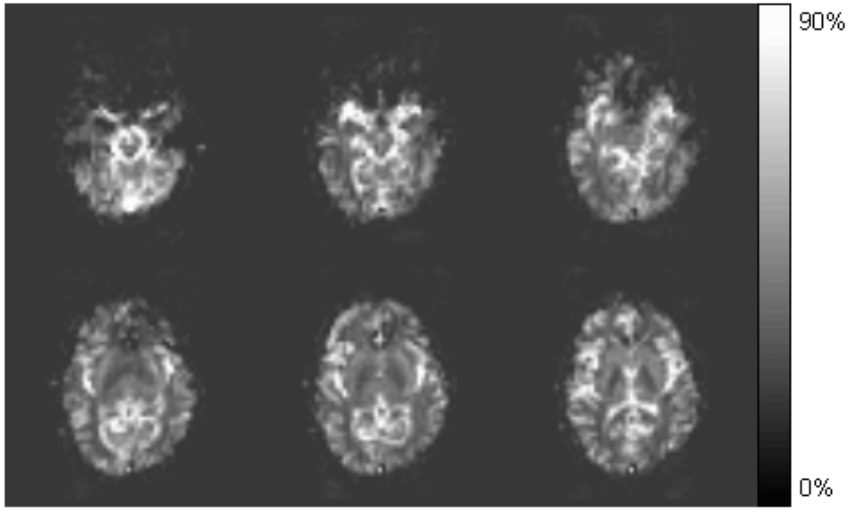

## Gd-DTPA




BOLD Signal change resulting from breath holding

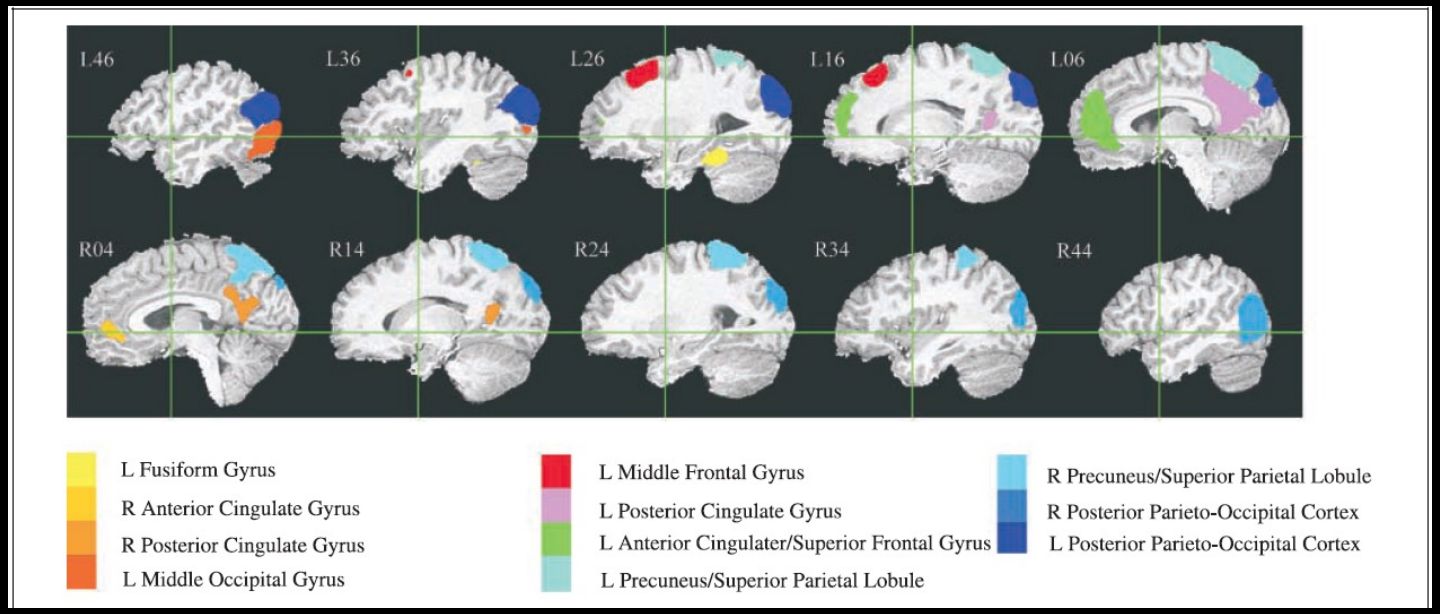


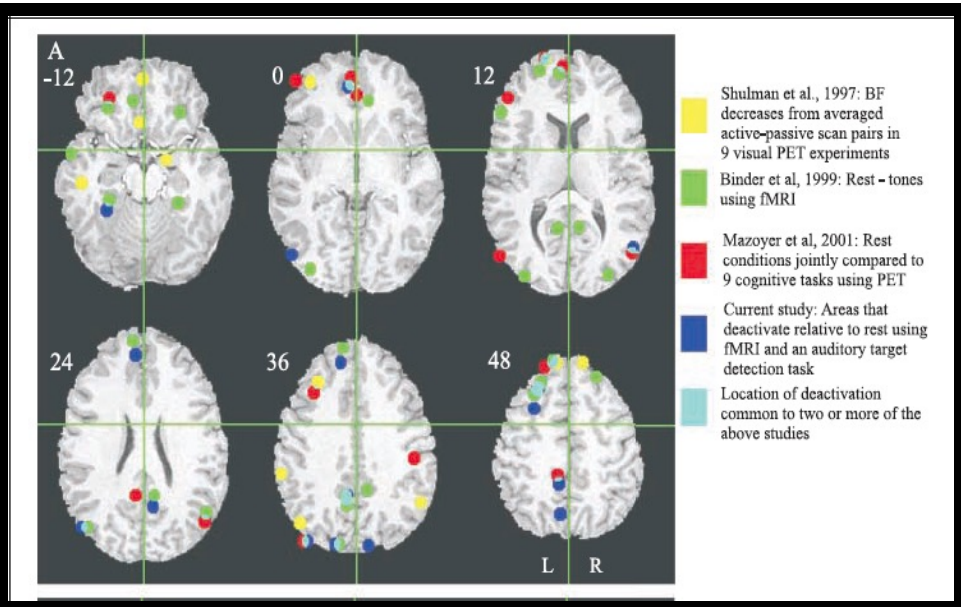

Signal change resulting bolus injection of Gd-DTPA




Note that although there are many similarities in the signal change amplitudes resulting from breath holding and exogenous contrast agent, there are several regions showing differences potentially indicating different contributions from arteries and veins.

# Regions showing decreases during cognitive tasks



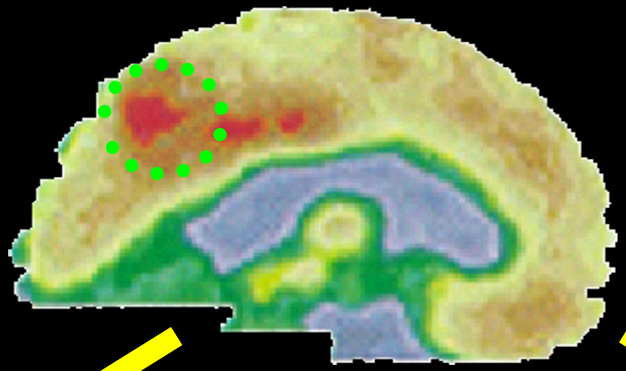




**McKiernan, et al (2003), Journ. of Cog. Neurosci. 15 (3), 394-408**

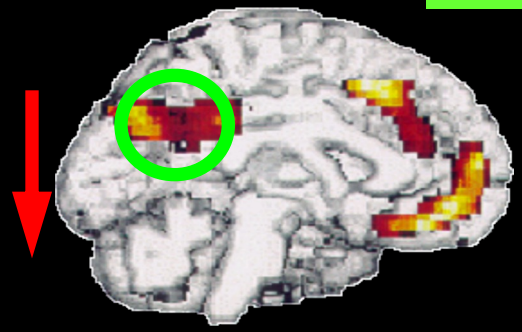
strongly reduced vigilance: ⟷

# rest

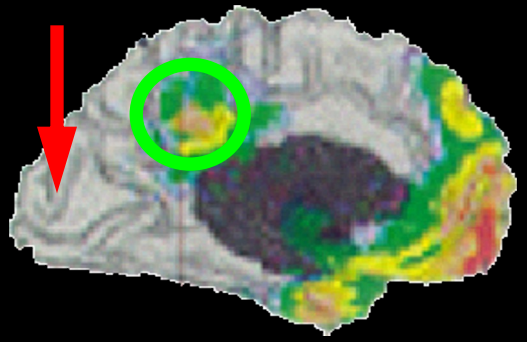
⟷ perception + action



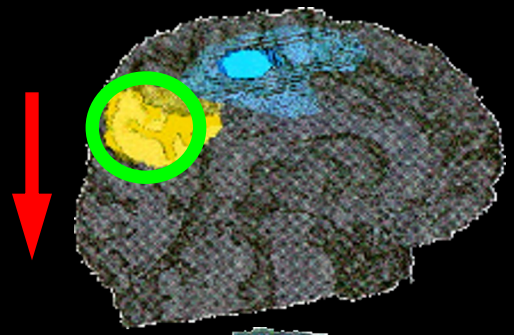
sleep



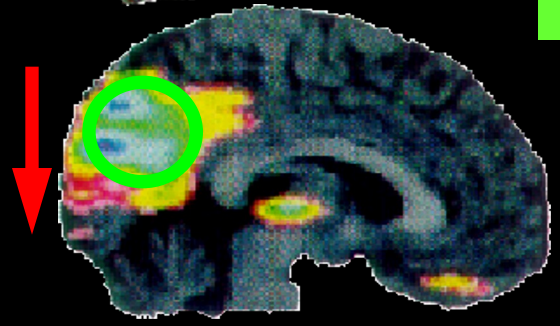
tasks



## “default mode”



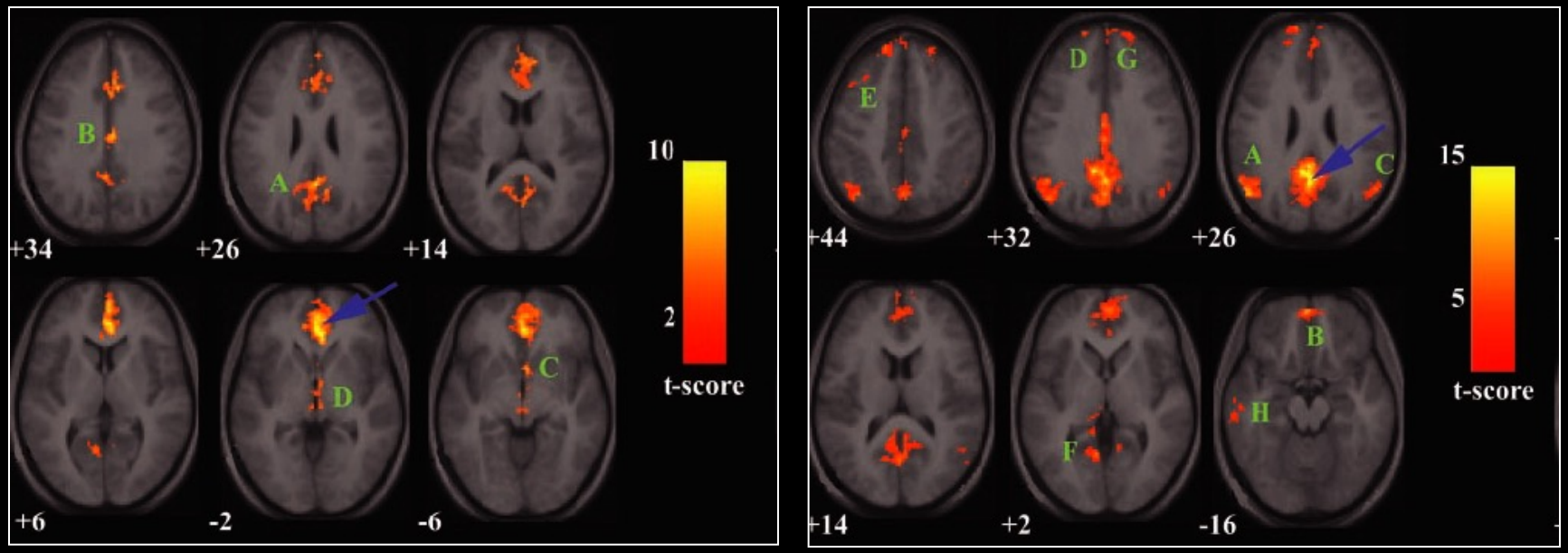
vegetative state



general anaesthesia

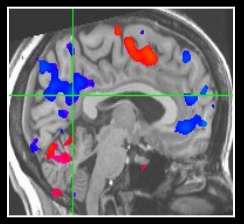
*(Gusnard and Raichle 2001)*

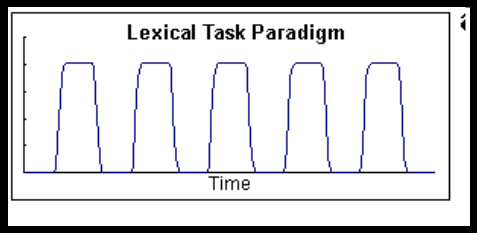
# Spatial correlation of decreased signal change regions with regions showing resting state corrrelated fluctuations?

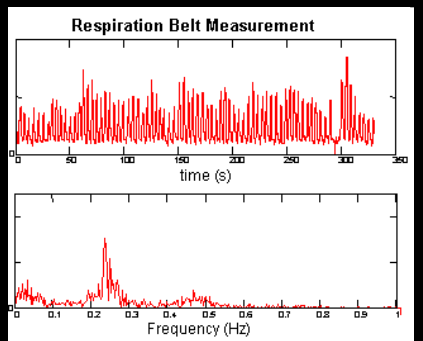



Greicius, et al (2003), PNAS 100 (1), 253-258

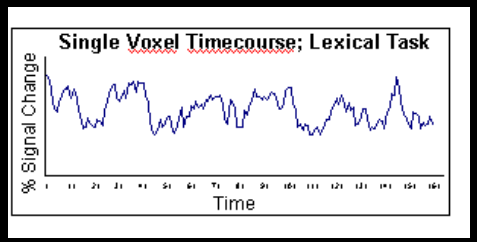
Lexical Task



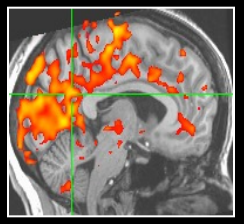


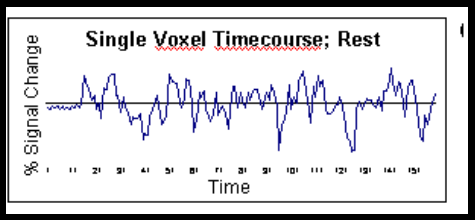




ROI

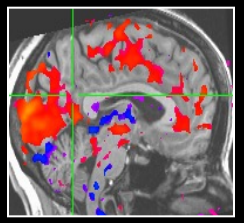


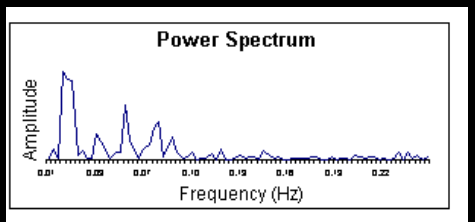

Functional Connectivity: Rest

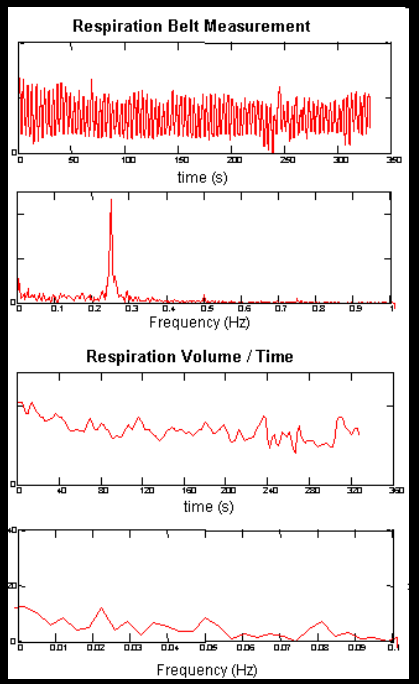




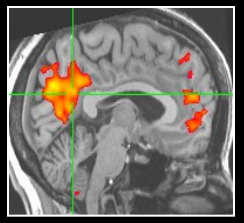

Correlation with Respiration Vol./Time

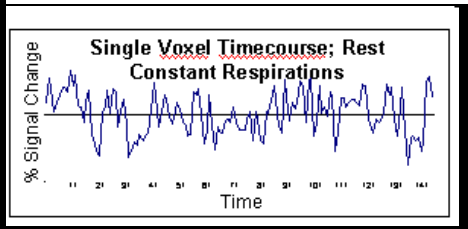




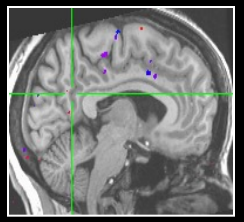



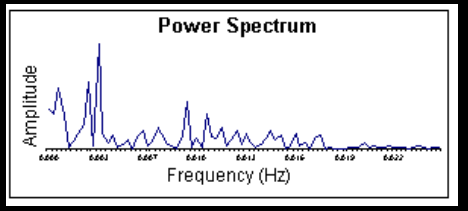

Functional Connectivity: Constant Resp.



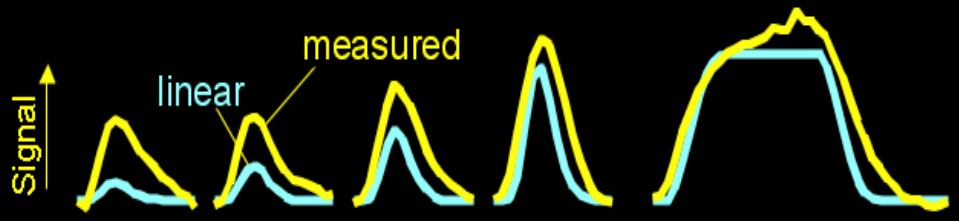



Correlation with Respiration Vol./Time: Constant Resp.

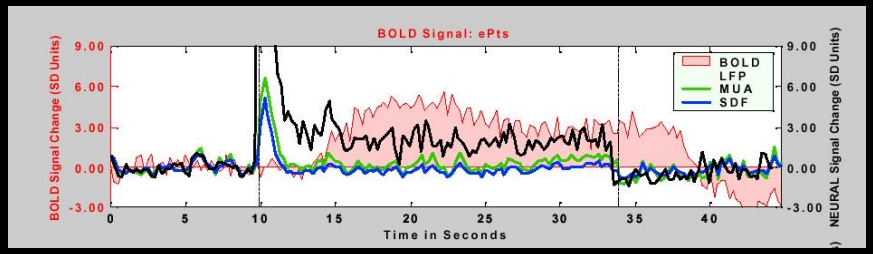




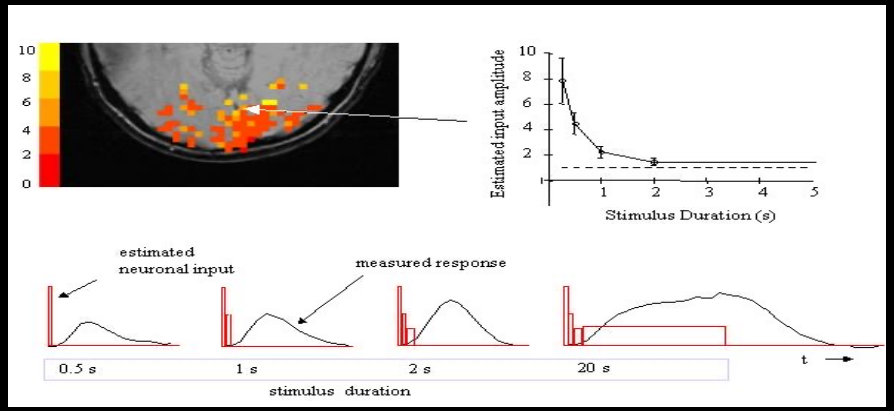
# Increases: linearity




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

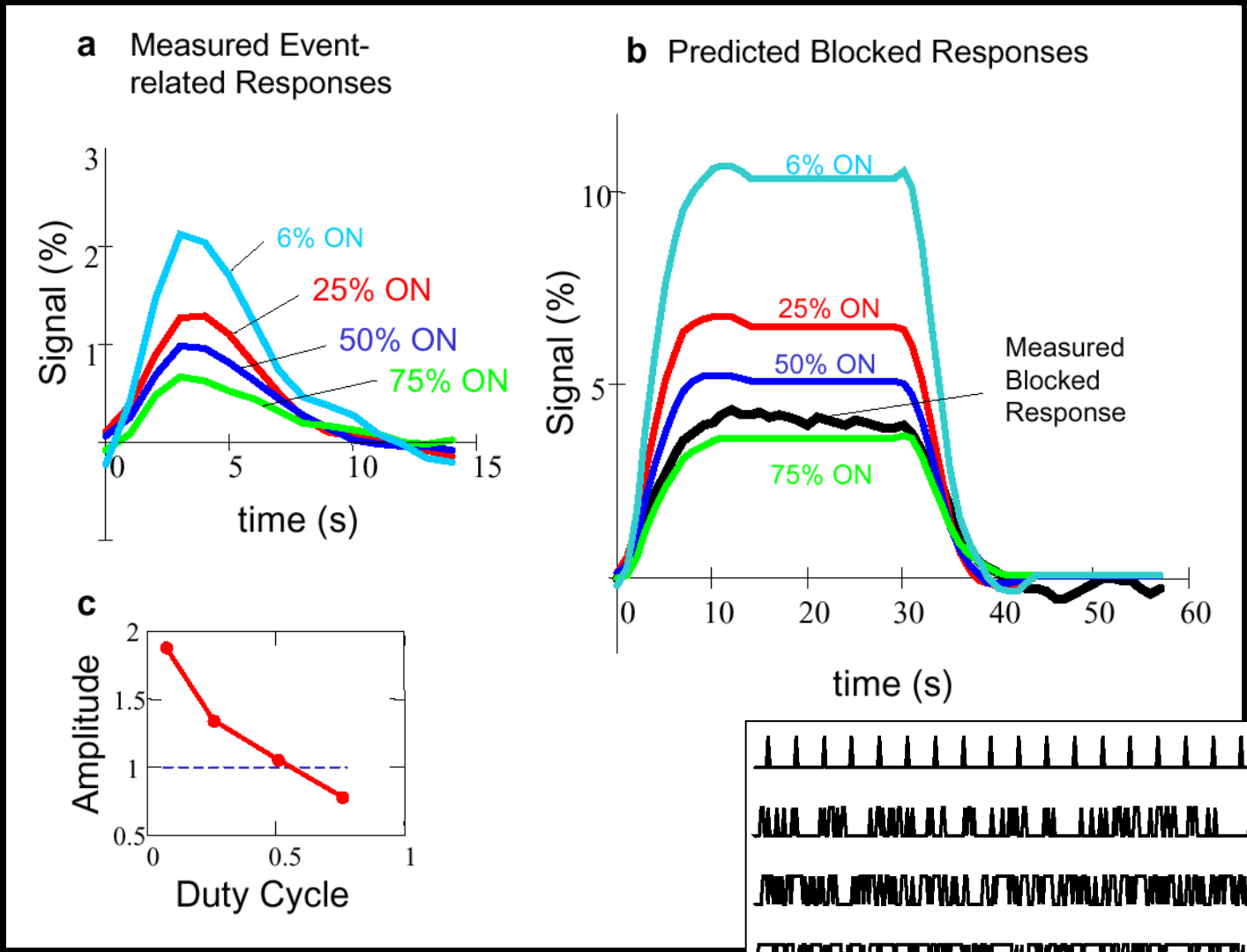



Logothetis et al. (2001) Nature, 412, 150-157.



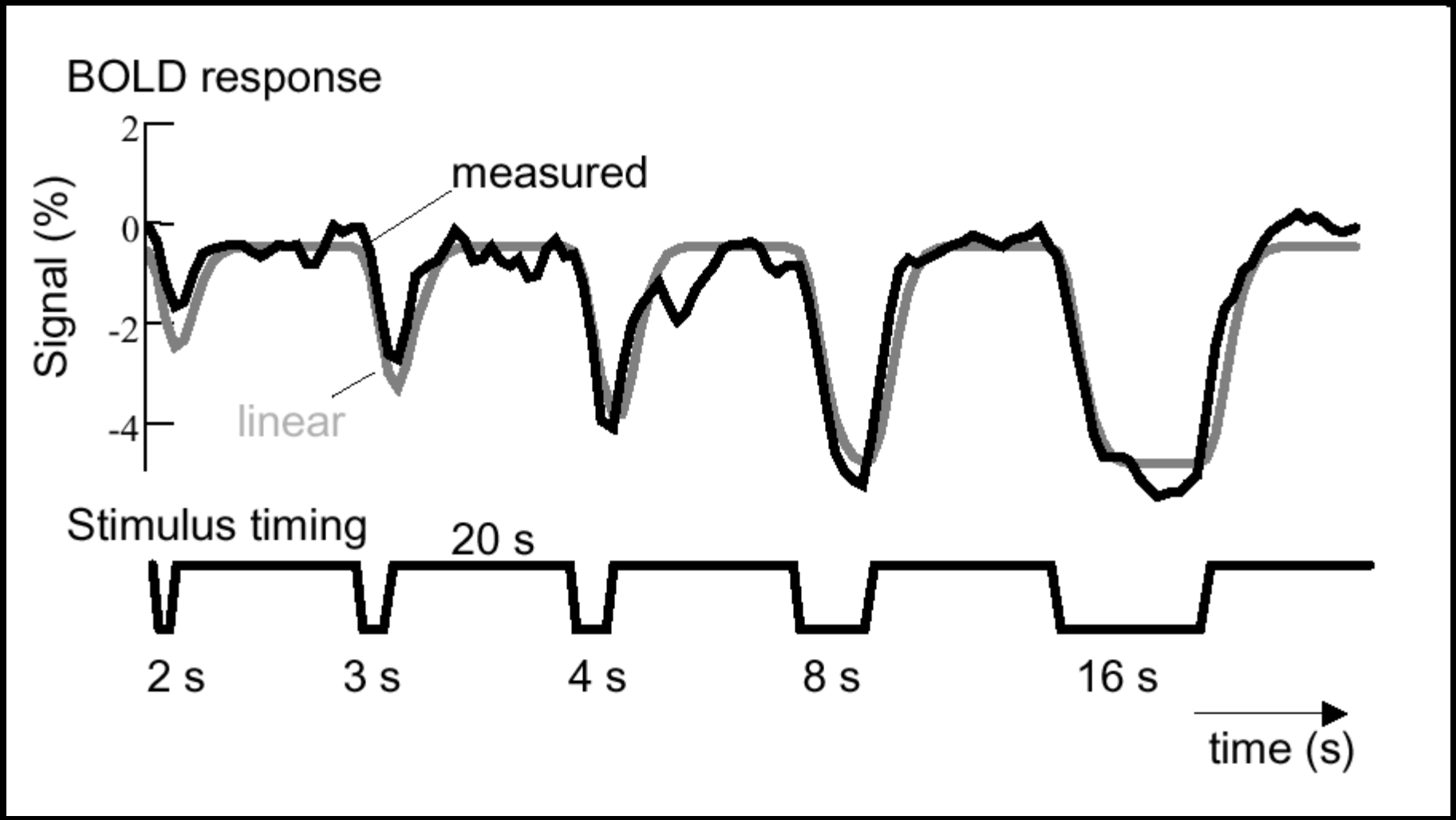

P. A. Bandettini et al, (2001) Nature Neuroscience, 4: 864-866.

# Increases: duty cycle

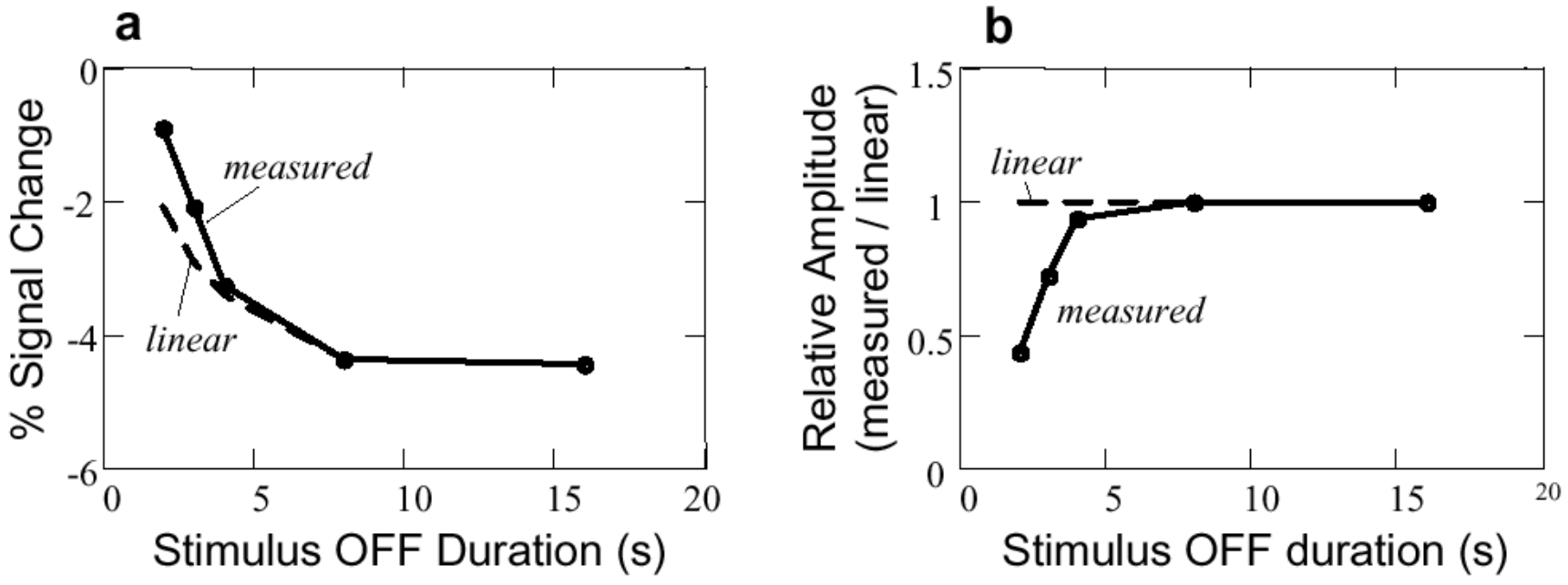



R.M. Birn, P. A. Bandettini. *NeuroImage*, *(in press)*

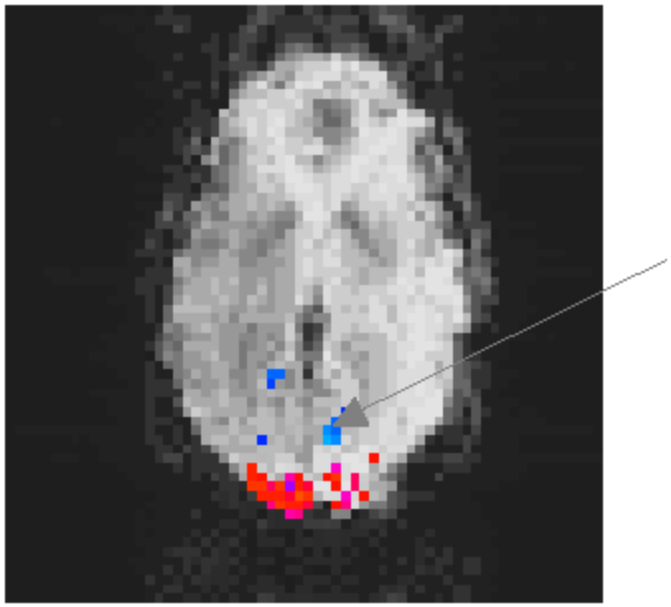
# Decreases: linearity

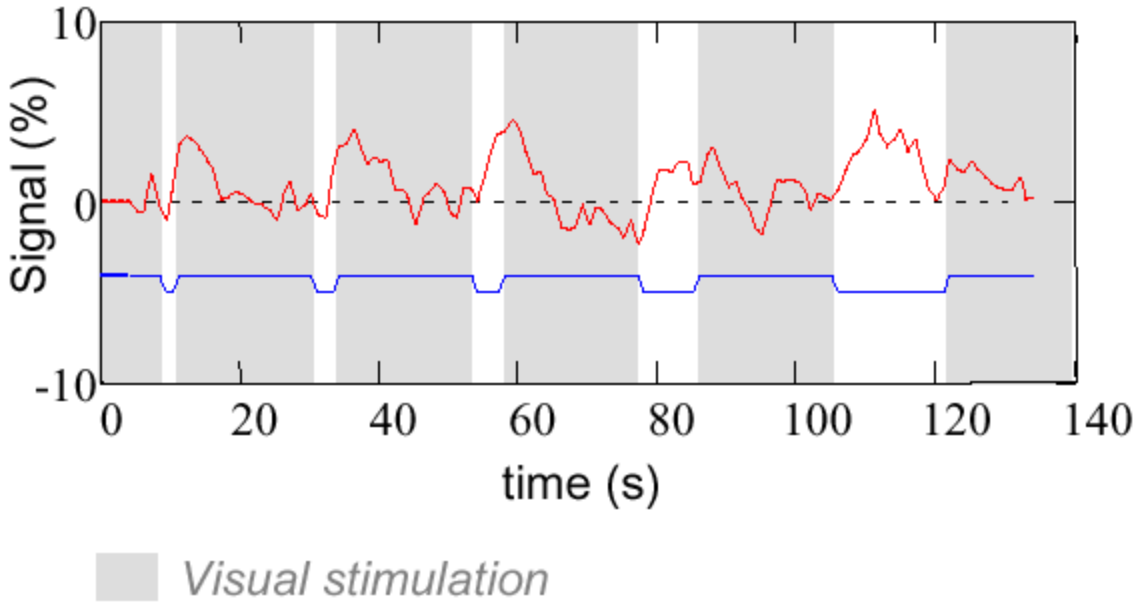



R.M. Birn, P. A. Bandettini. *NeuroImage*, *(in press)*

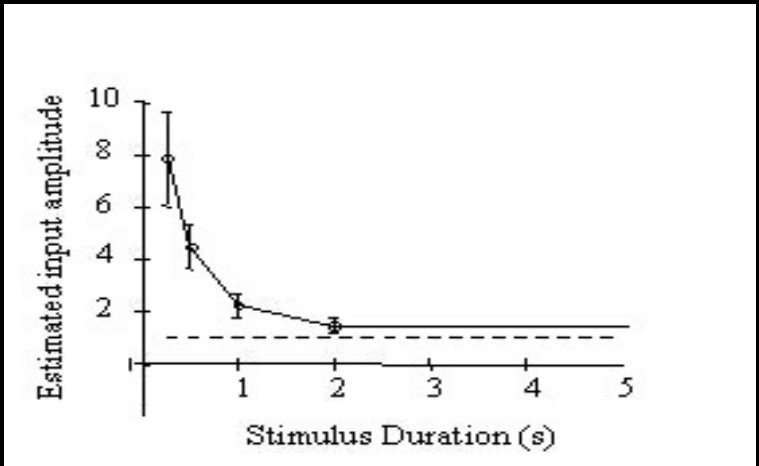

a
0
-2
-4
-6
% Signal Change
measured
linear
0
5
10
15
20
Stimulus OFF Duration (s)
b
1.5
1
0.5
0
Relative Amplitude
(measured / linear)
linear
measured
0
5
10
15
20
Stimulus OFF duration (s)

# We also see increases during stimulus cessation...

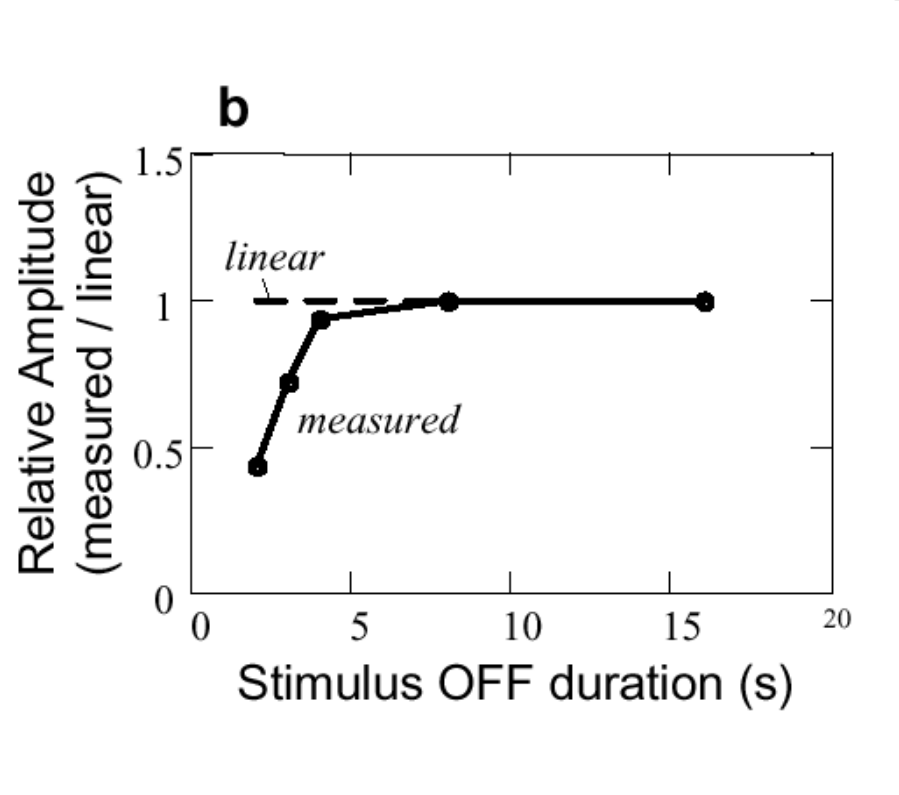




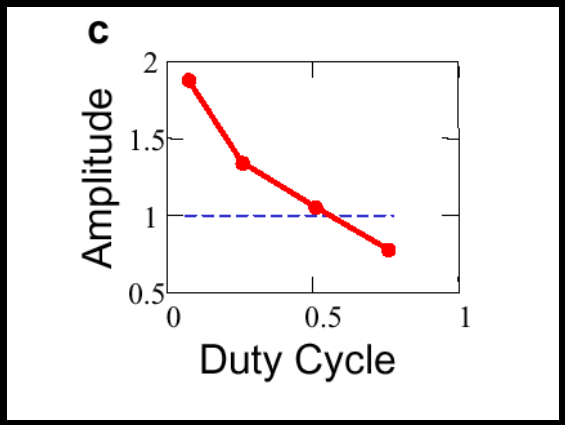
Increase: duration on




Decrease: duration off



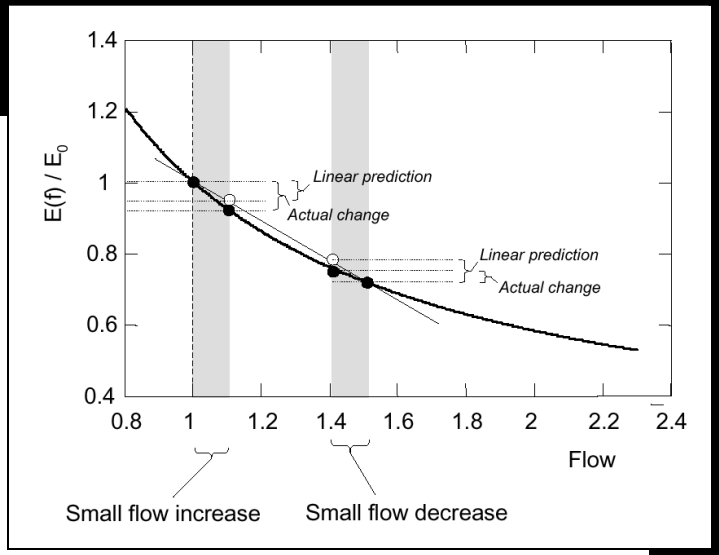

Increase: duty cycle

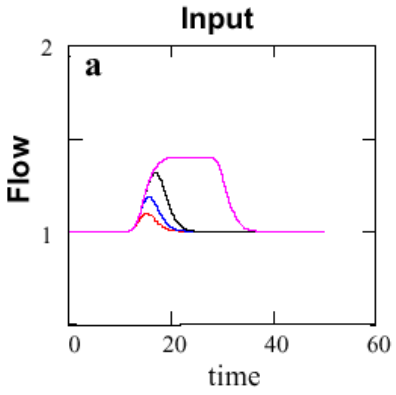


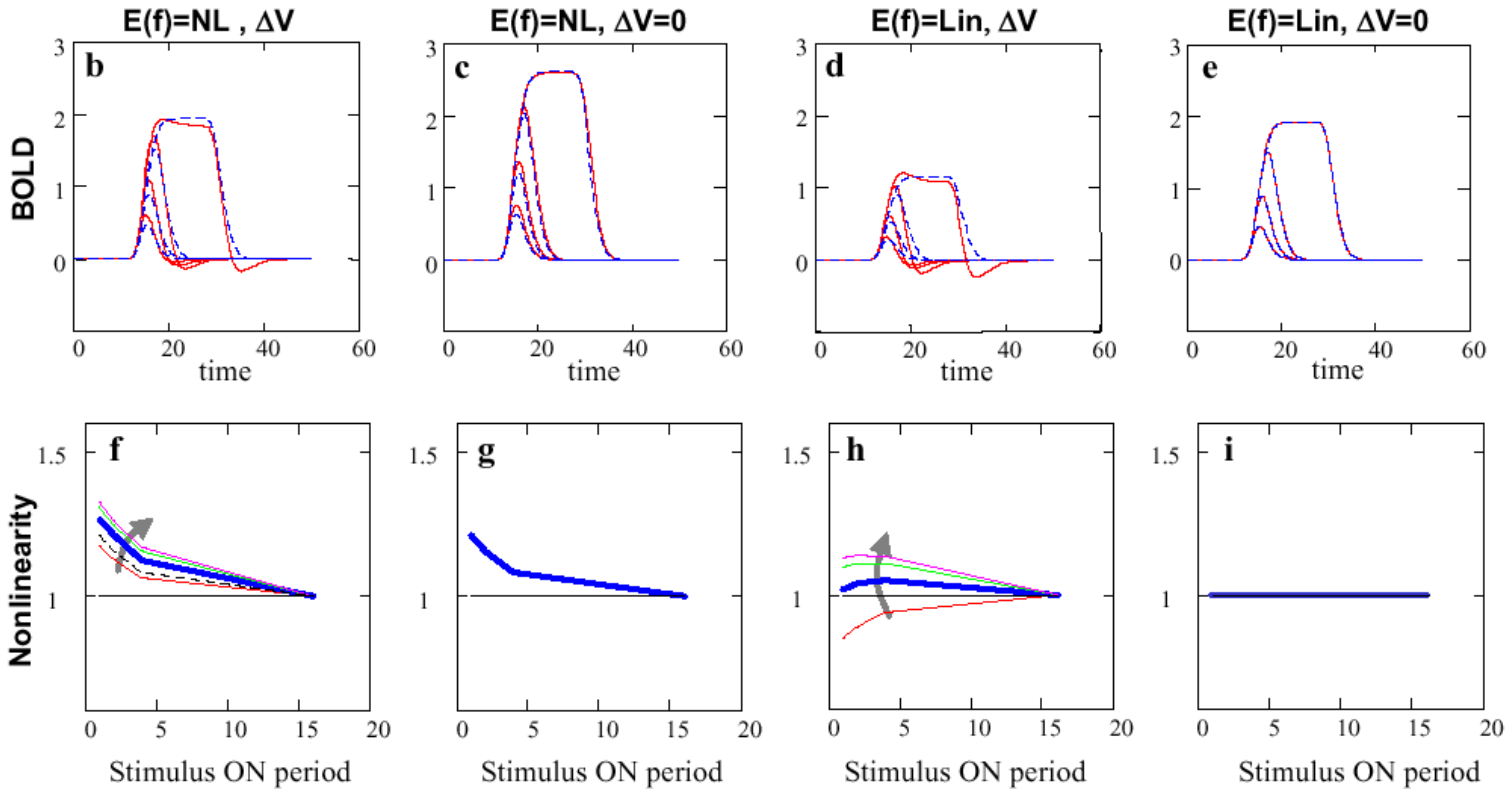
# Balloon Model Parameters

| Parameter | Description | Default Value | Range Evaluated |
|---|---|---|---|
| $E_0$ | *Resting oxygen extraction fraction* | 0.4 | 0.3 – 0.6 |
| $v_0$ | *Resting blood volume fraction* | 0.03 | 0.03 – 0.18 |
| $f_0$ | *Resting relative blood flow* | 0.01 $s^{-1}$ | 0.01 s – 0.16 s |
| $\Delta f$ | *Fractional blood flow change* | 0.4 | – |
| $\alpha$ | *Steady-state flow-volume relationship* | 0.4 | 0.25 – 1.0 |
| $\tau_{MTT}$ | *Blood mean transit time ($v_0/f_0$)* | 3 s | 1.1 s – 18 s |
| $\tau_+$ | *Viscoelastic time constant (inflation)* | 20 s | 10 s – 40 s |
| $\tau_-$ | *Viscoelastic time constant (deflation)* | 20 s | 10 s – 40 s |
| $a_1$ | *Weight for deoxyHb change* | 3.7 | 2.8 – 5.6 |
| $a_2$ | *Weight for blood volume change* | 1.1 | 0.7 – 1.9 |

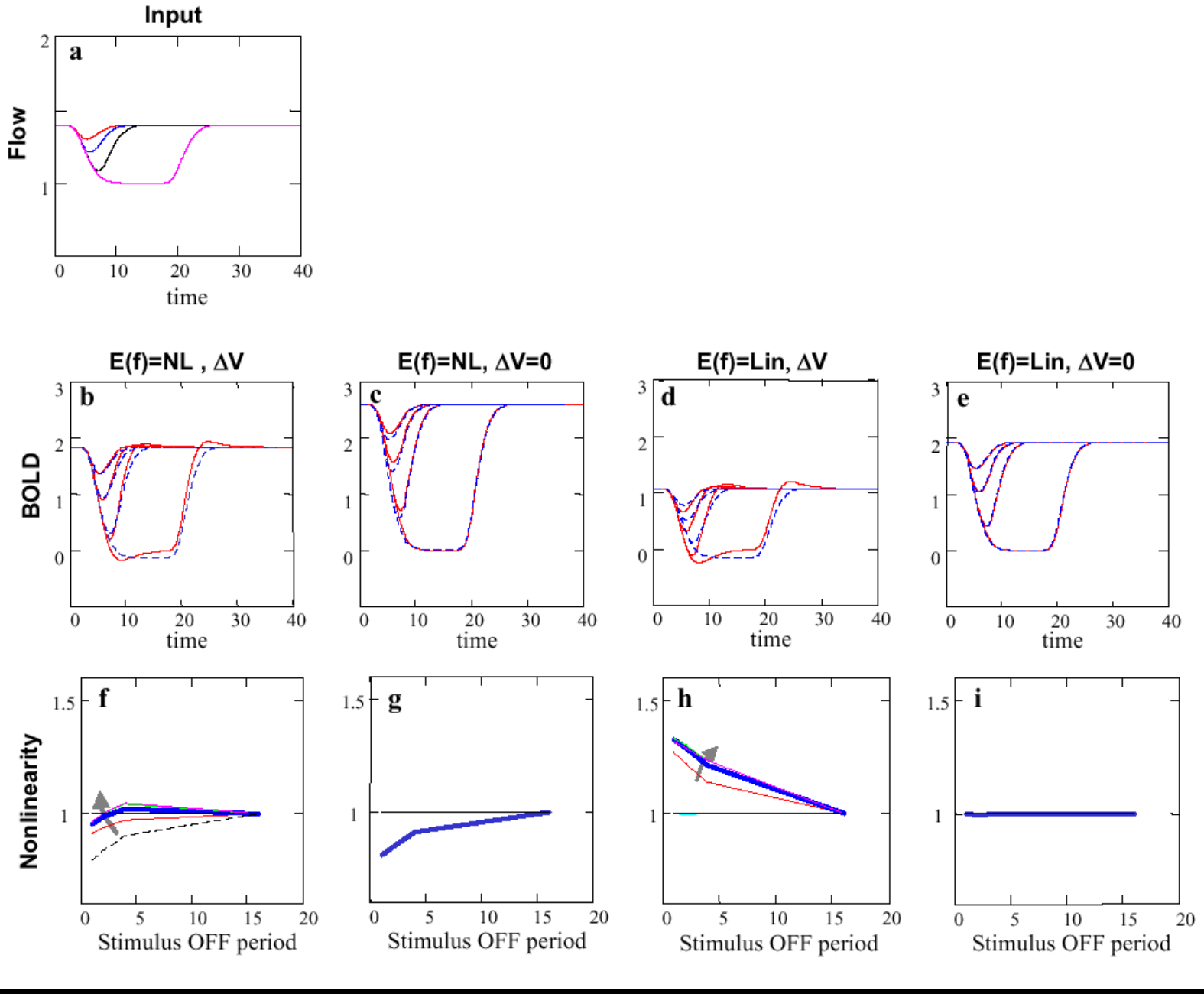
# “on” Linearity



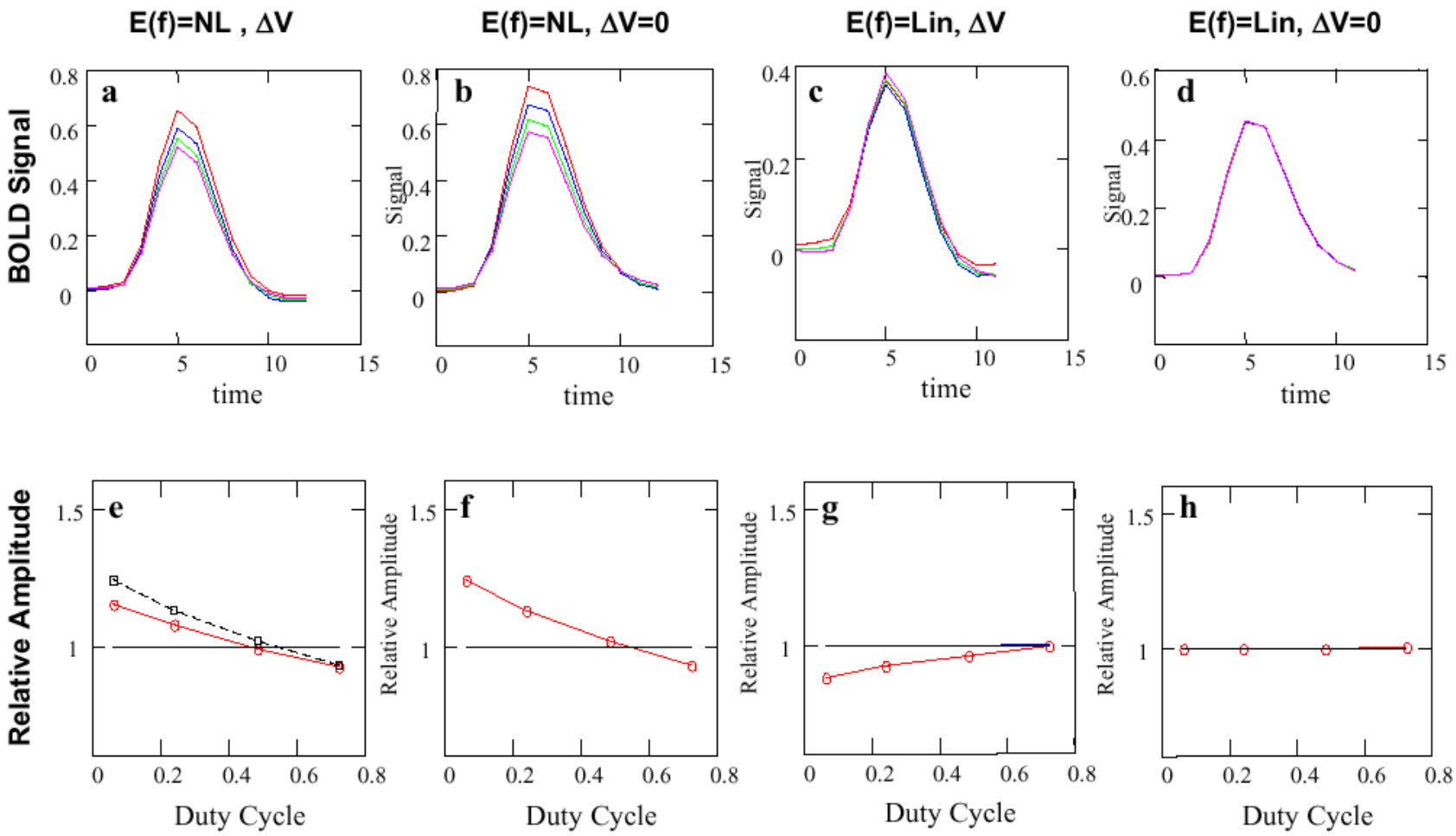



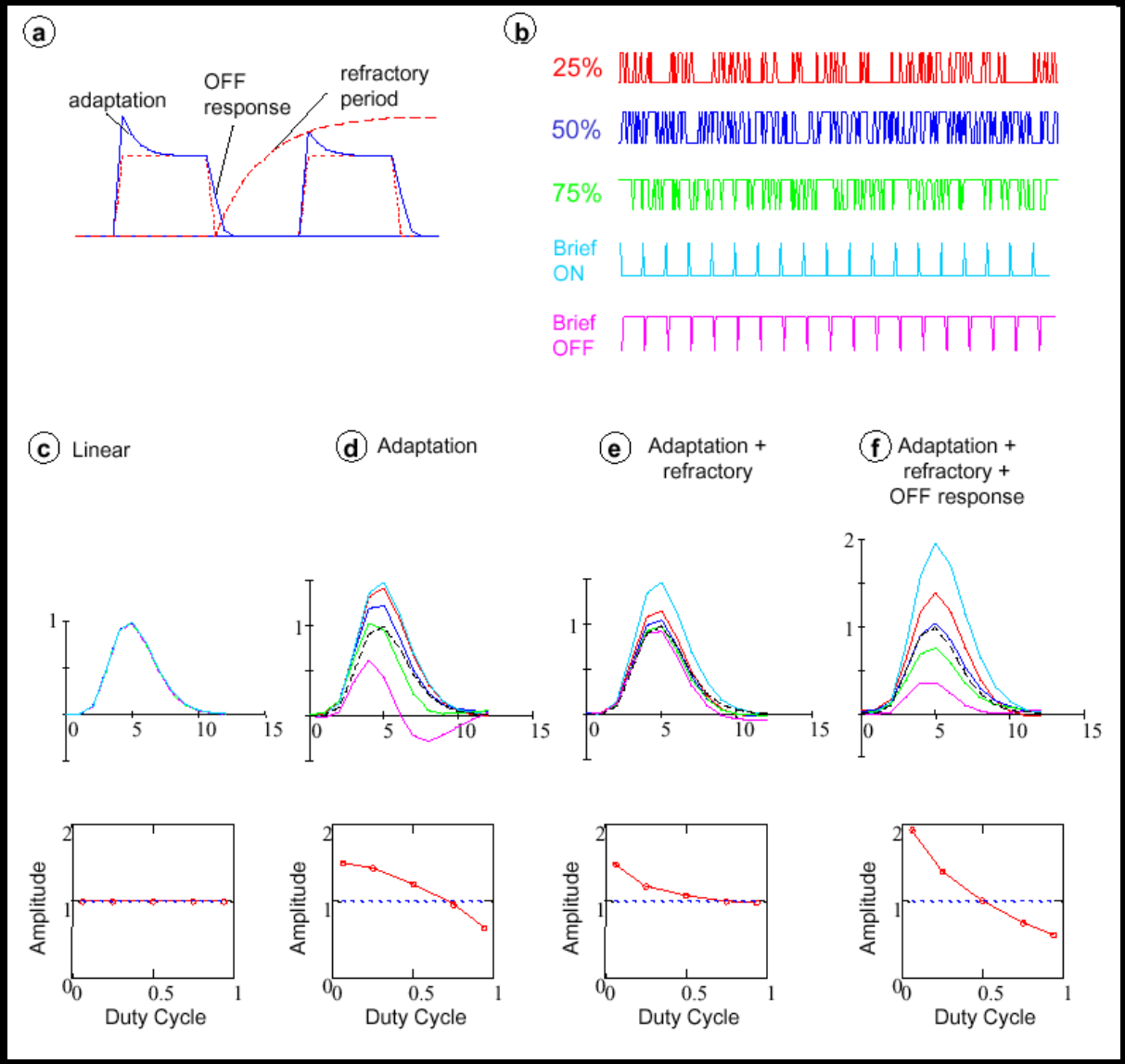
# “off” linearity



# Duty Cycle


E(f)=NL , ΔV
E(f)=NL, ΔV=0
E(f)=Lin, ΔV
E(f)=Lin, ΔV=0
BOLD Signal
Signal
time
Relative Amplitude
Duty Cycle
a
b
c
d
e
f
g
h

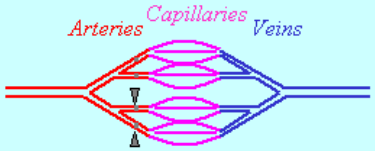
# Neuronal effects to explain duty cycle effects

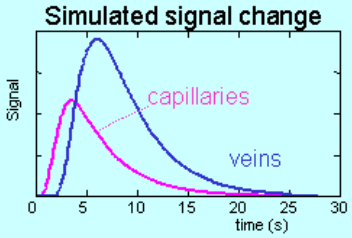


# Temporal Resolution: potential calibration

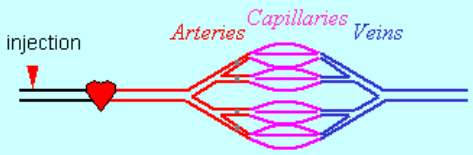
Signal origins and simulated signal changes

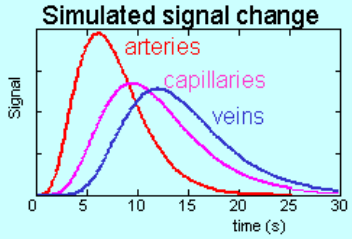
**BOLD** (brief neuronal activation)




**Gd-DTPA** (bolus of contrast agent)

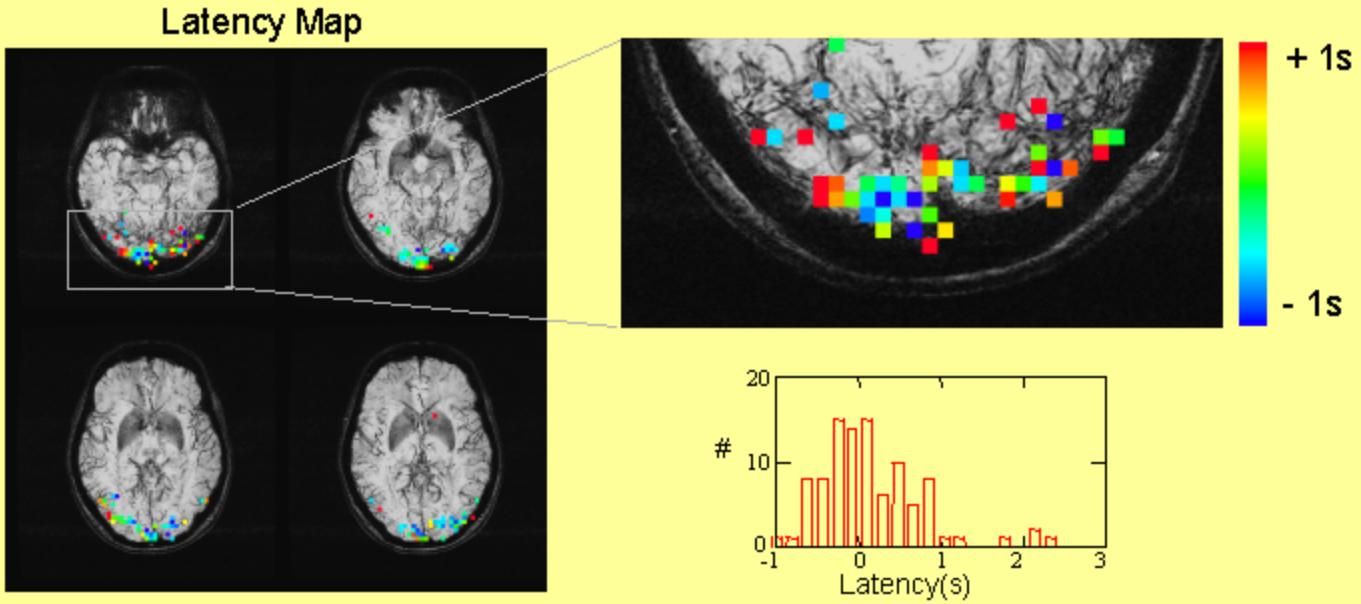



*A voxel can contain a mixture of arteries, capillaries, and veins*

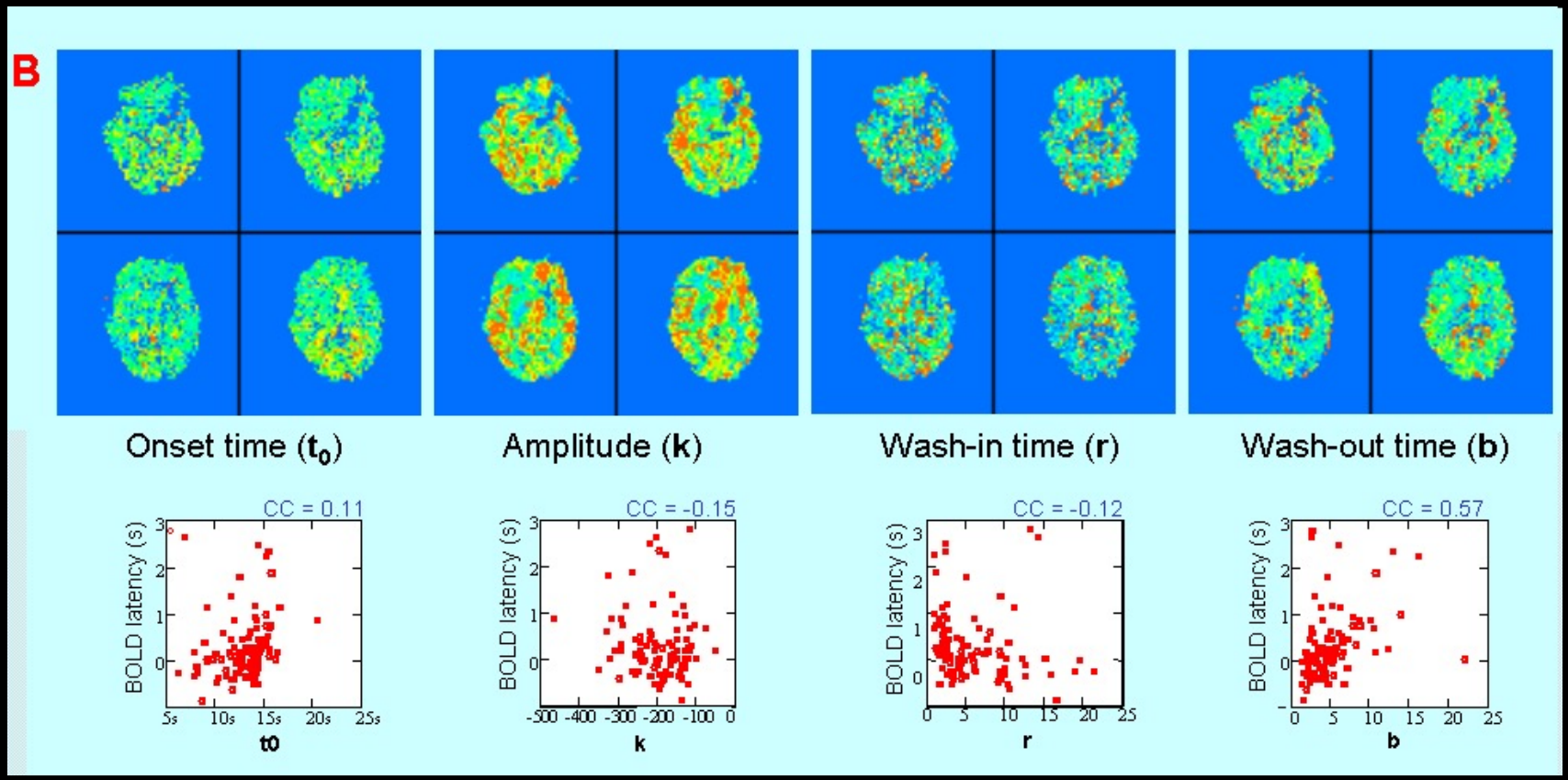
- The latency of BOLD response depends on the vessels between the arteriolar sphincters and the voxel of interest.
- The dynamics of the Gd-DTPA bolus induced signal change depends on the vessels between the site of injection and the voxel of interest.
- Previous calibration studies have focused on the onset latency of the Gd-DTPA induced signal decrease (2).
  - This time constant is influenced by variations in the arrival time of the bolus from the site of the injection to the arteriolar sphincters
- We hypothesize that the wash-out time of the Gd-DTPA bolus is more reflective of the time for blood to travel from the arterioles through capillaries and veins, and is therefore more predictive of BOLD onset time and duration

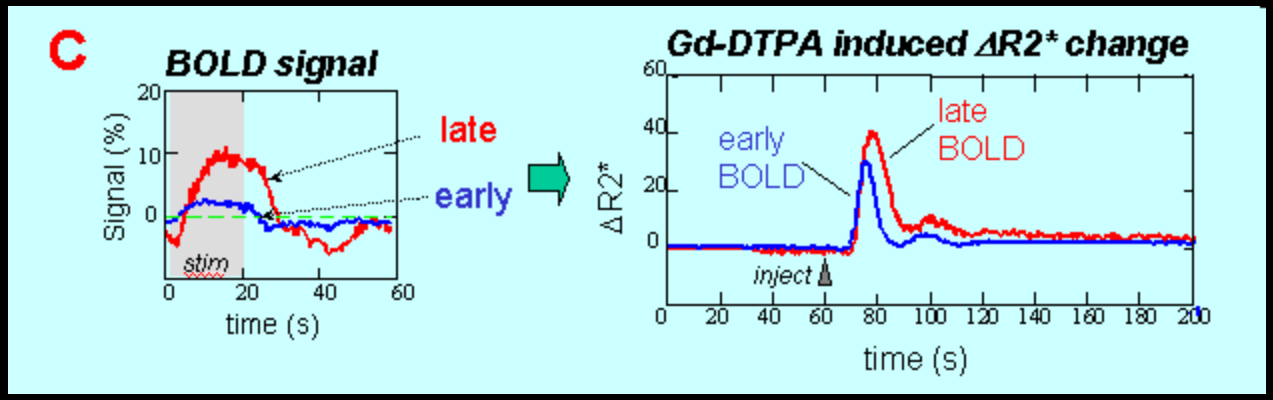
1. **Latency of fMRI BOLD response varies by several seconds across regions of the brain**




These latency variations, likely the result of BOLD signals arising from different vessels (capillaries, venules, or veins), dominate any underlying neuronal timing differences (1).

2. **Can we correct for hemodynamic variations in the latency estimate by using a separate measure of vascular dynamics – the signal changes from a bolus of contrast agent?**


B
Onset time ($t_0$)
Amplitude (k)
Wash-in time (r)
Wash-out time (b)
CC = 0.11
CC = -0.15
CC = -0.12
CC = 0.57
BOLD latency (s)
t0
k
r
b


C
BOLD signal
Signal (%)
time (s)
stim
late
early
Gd-DTPA induced ΔR2* change
ΔR2*
early BOLD
late BOLD
inject
time (s)

1. In general, the latency of BOLD response is correlated with the washout time of Gd-DTPA bolus.

2. This correlation is not strong enough to correct the large spatial variations in BOLD response latency.

3. Future improvements include:

    a. More accurate modeling of BOLD and Gd-DTPA bolus signal changes.

    b. Finding ways to separate arterial and venous contributions.

# Many remaining unknowns

- Relationship between neuronal activity and BOLD contrast?
- Sources of BOLD variability?
- Information content / artifact in time series fluctuations?
- Source of BOLD timing and dynamics?
- Sources of BOLD signal decreases?
- Other sources of functional contrast?
- Temporal resolution?
- Spatial resolution?
- Clinical utility?
- Best processing and display strategies?
- Best paradigm designs strategies?
- Optimal field strength?
- Applications..??