I have no conflicts to disclose with regard to this presentation.

What is known and what is not about BOLD mechanisms and sources of fMRI signals

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Controversies Regarding fMRI Contrast

1. The Undershoots (pre and post)
2. Negative Signal Change
3. Relationship to neuronal activity
4. Linearity
5. Fluctuations
6. Effects of Pathology / Medication
7. Other controversial contrast mechanisms:
    a. T2 contrast – Spin-echo
    b. Blood Volume (VASO)
    c. Diffusion
    d. Neuronal Current

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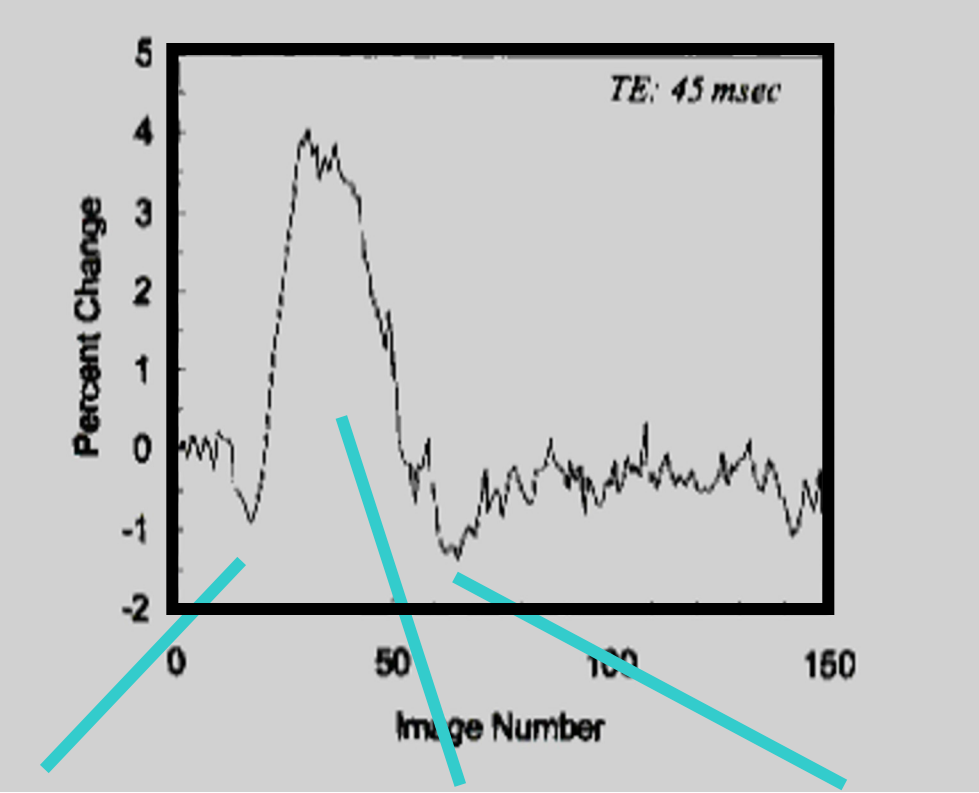
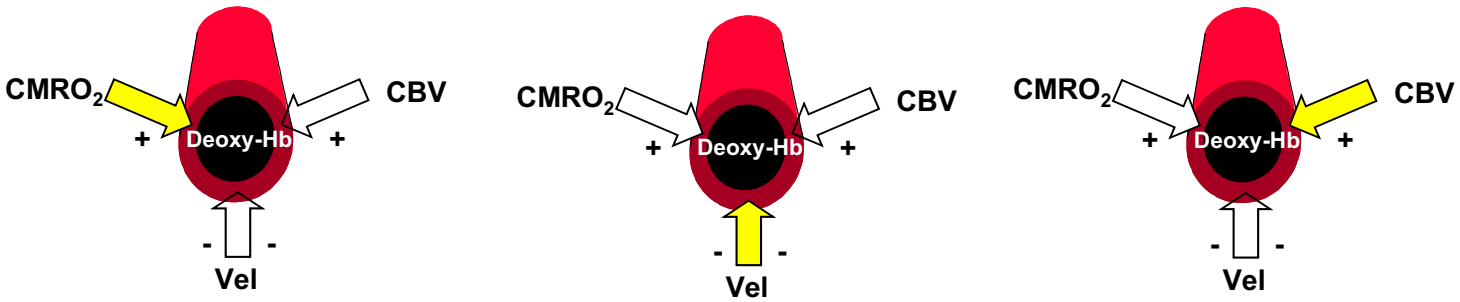
The Undershoots



Yacoub E, Le TH, Ugurbil K, Hu X (1999) Magn Res Med 41(3):436-41



Courtesy of Arno Villringer

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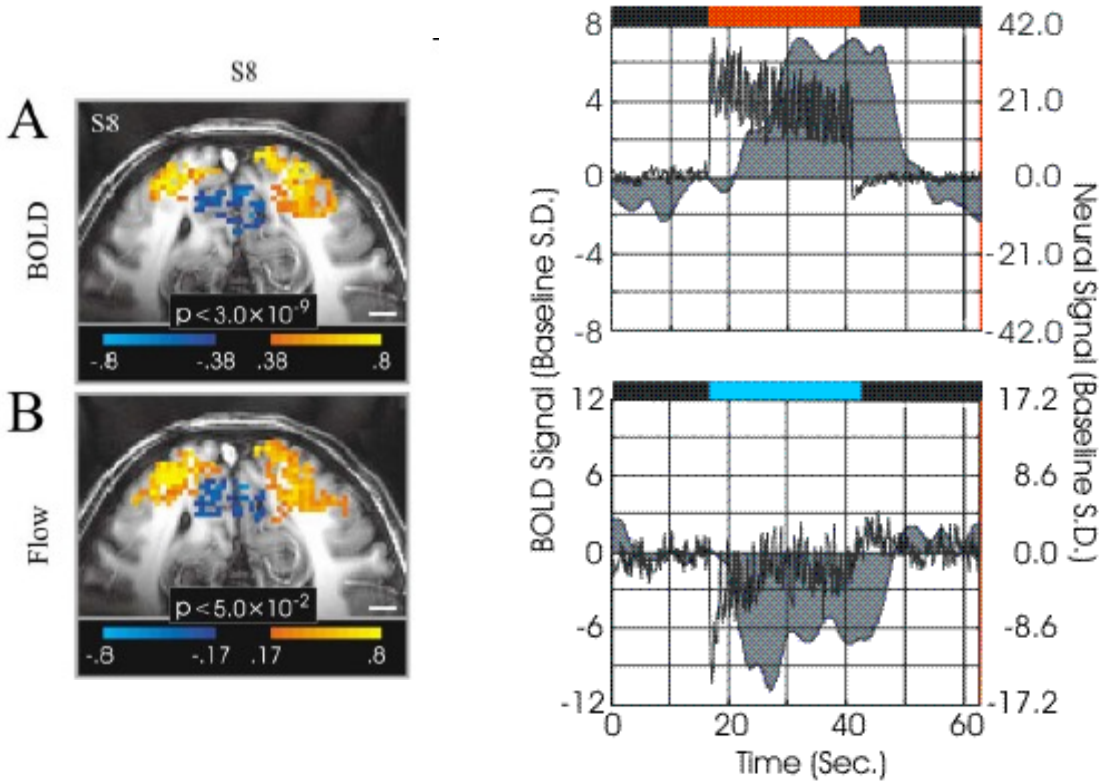
Negative Signal Change

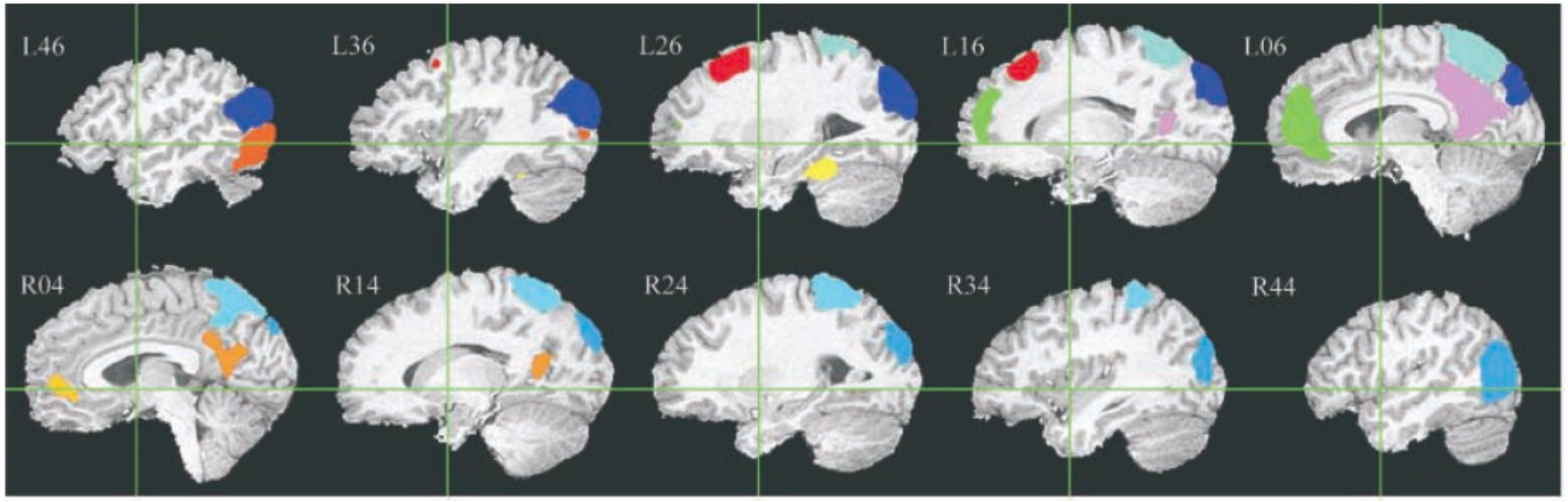
Neg. BOLD



Schmuel et al. (2002) Neuron, Vol. 36, 1195–1210

Negative Signal Change

Regions showing negative signal changes during cognitive tasks



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

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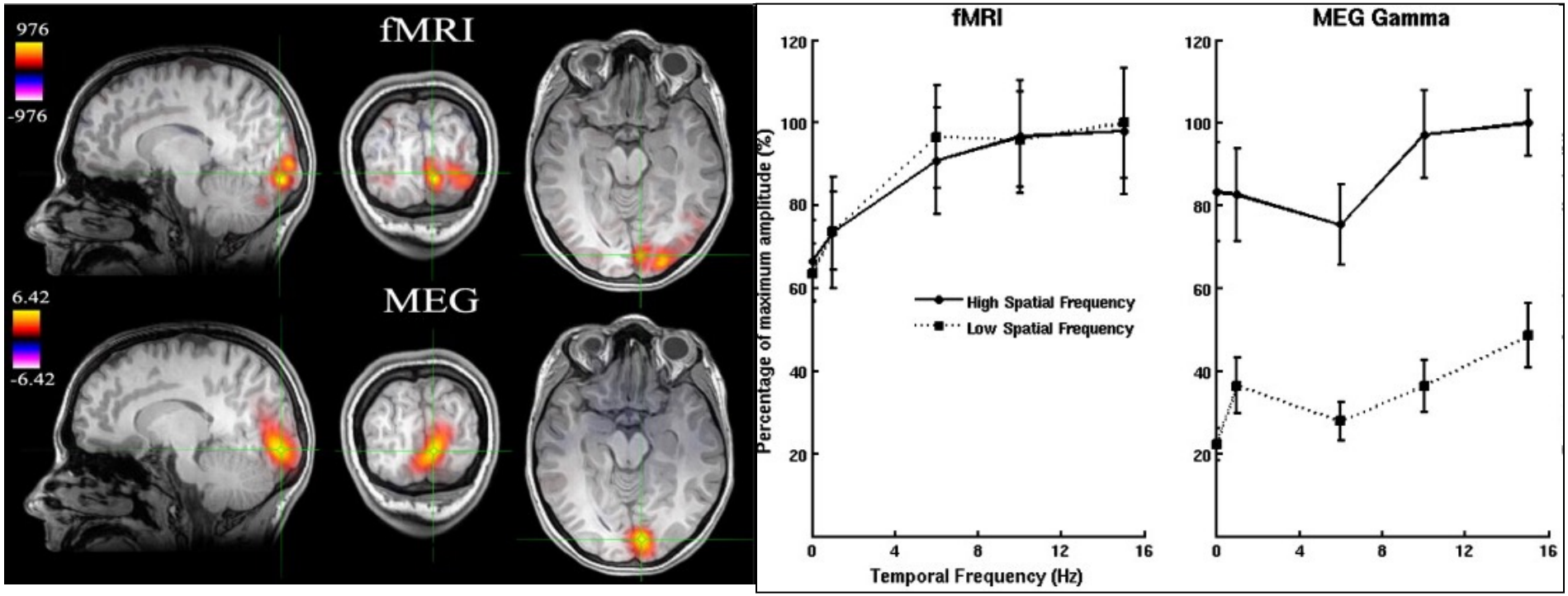
Relationship to Neuronal Activity



Muthukumaraswamy, S. D., Singh, K. D. (2008)
NeuroImage 40 (4), pp. 1552-1560

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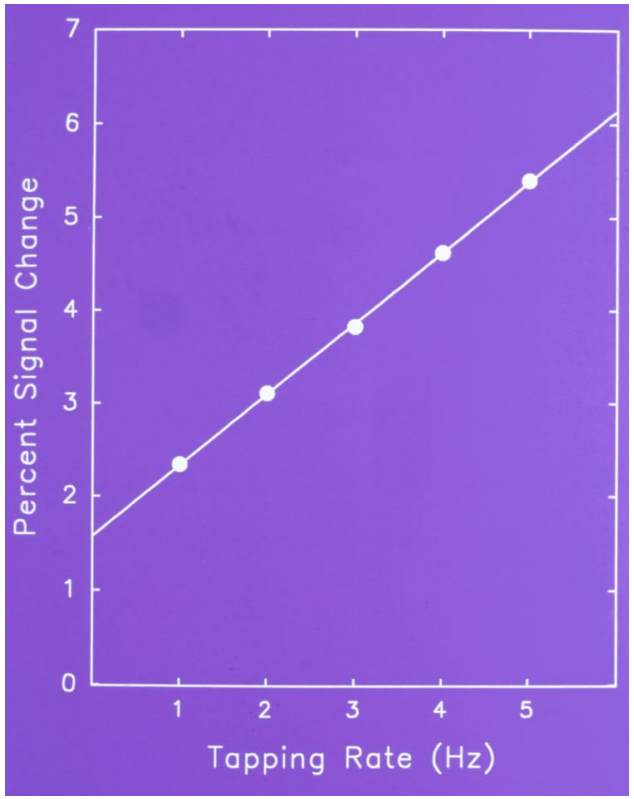
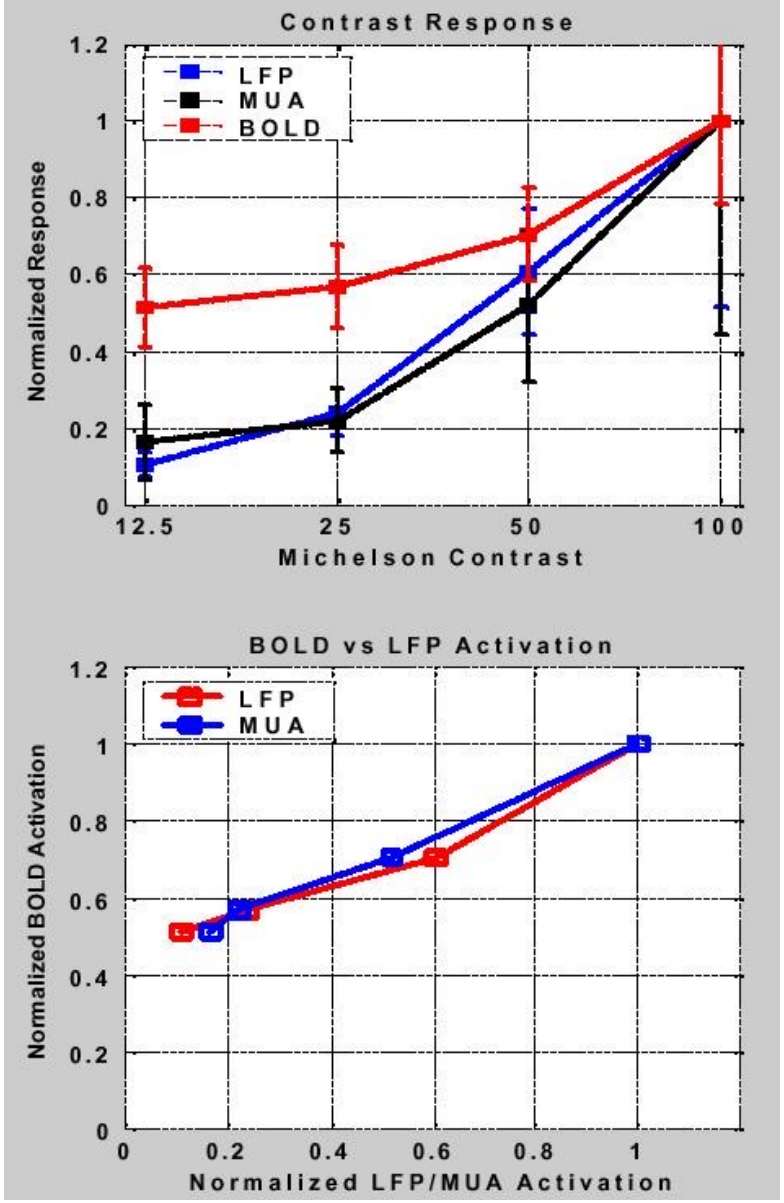
Linearity



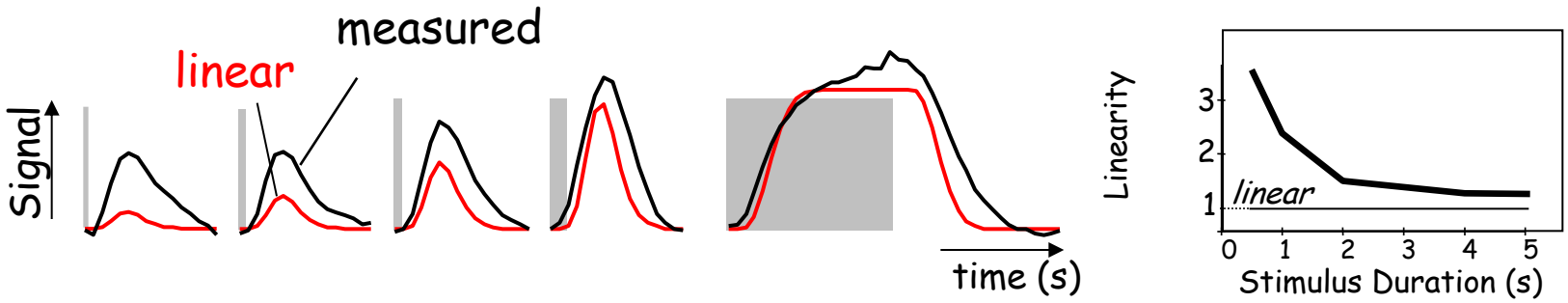
S. M. Rao et al, (1996) "Relationship between finger movement rate and functional magnetic resonance signal change in human primary motor cortex." *J. Cereb. Blood Flow and Met.* 16, 1250-1254.



Logothetis et al. (2001) "Neurophysiological investigation of the basis of the fMRI signal" Nature, 412, 150-157

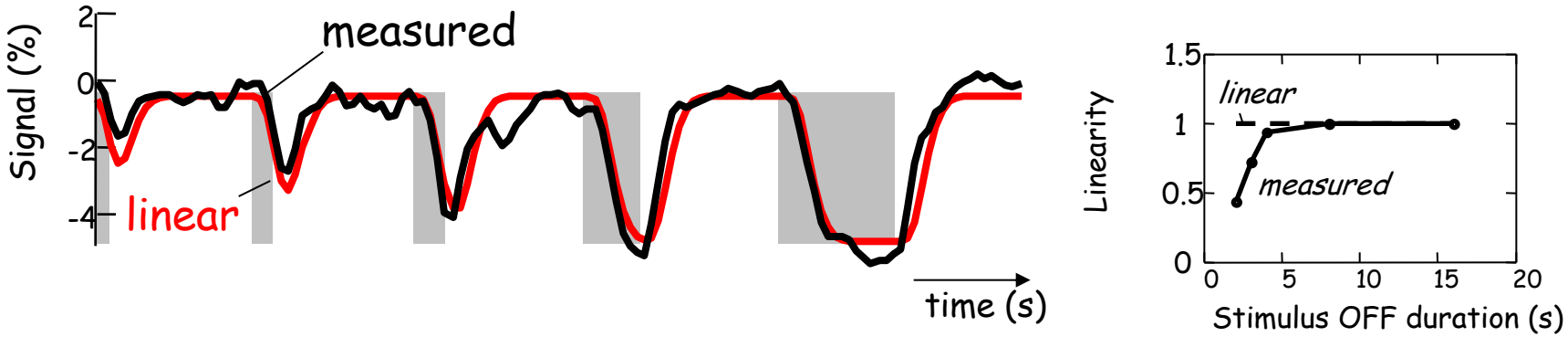
Linearity

Brief "on" periods produce larger increases than expected.



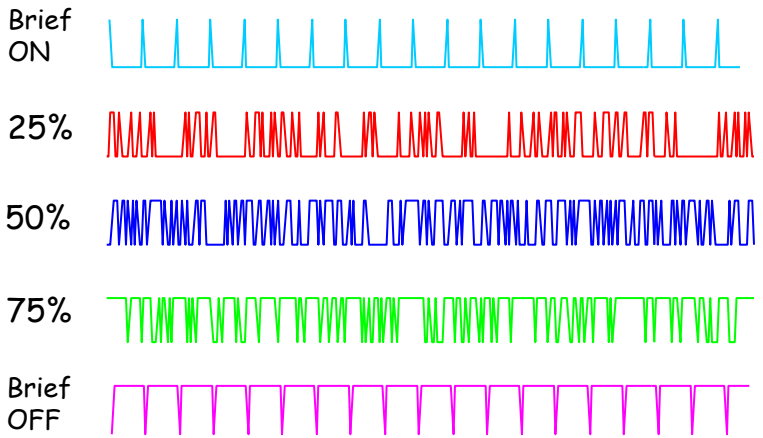
R. M. Birn, Z. Saad, P. A. Bandettini, NeuroImage, 14: 817-826, (2001)

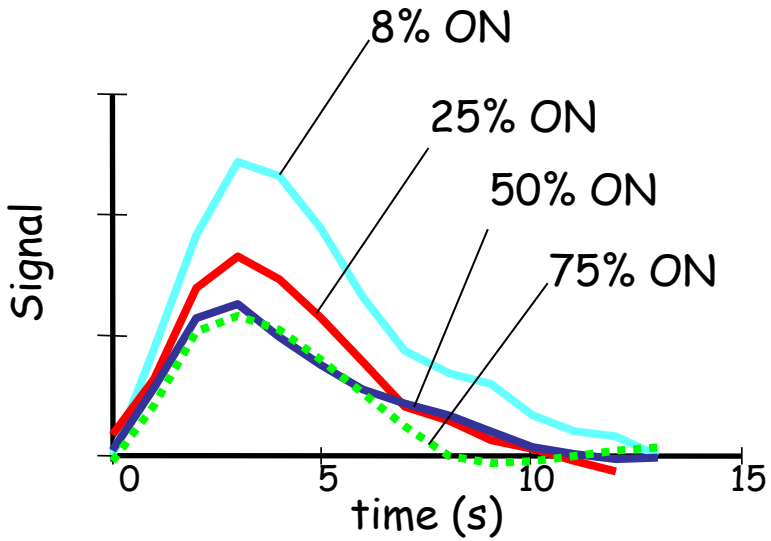
Brief "off" periods produce smaller decreases than expected.



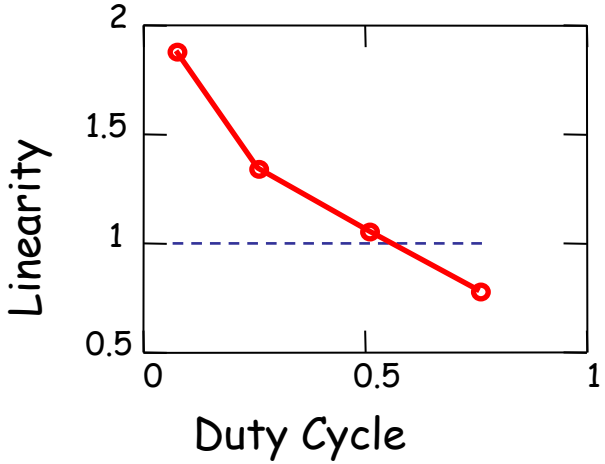
R.M. Birn, P. A. Bandettini, NeuroImage, 27, 70-82 (2005)

Varying the Duty Cycle



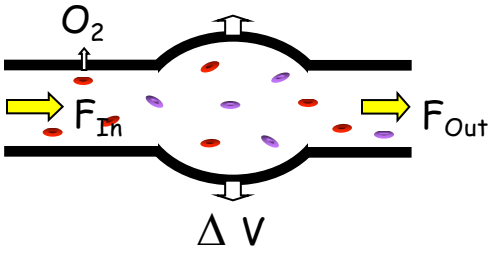


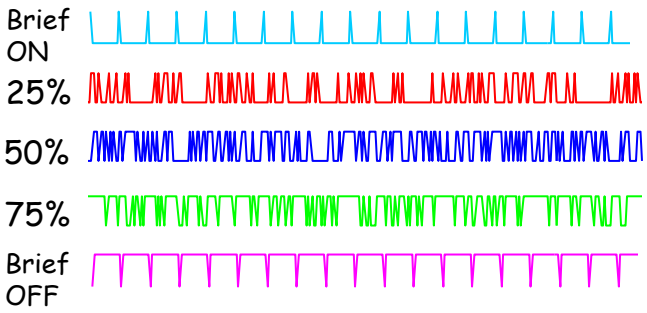
Deconvolved Response



R.M. Birn, P. A. Bandettini, *NeuroImage*, 27, 70-82 (2005)

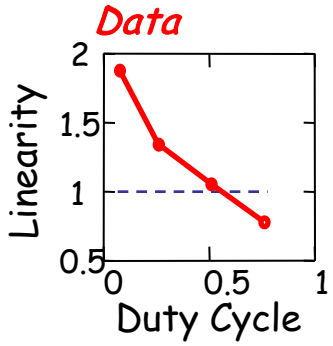
Simulation of Hemodynamic Mechanisms *(Balloon model)*

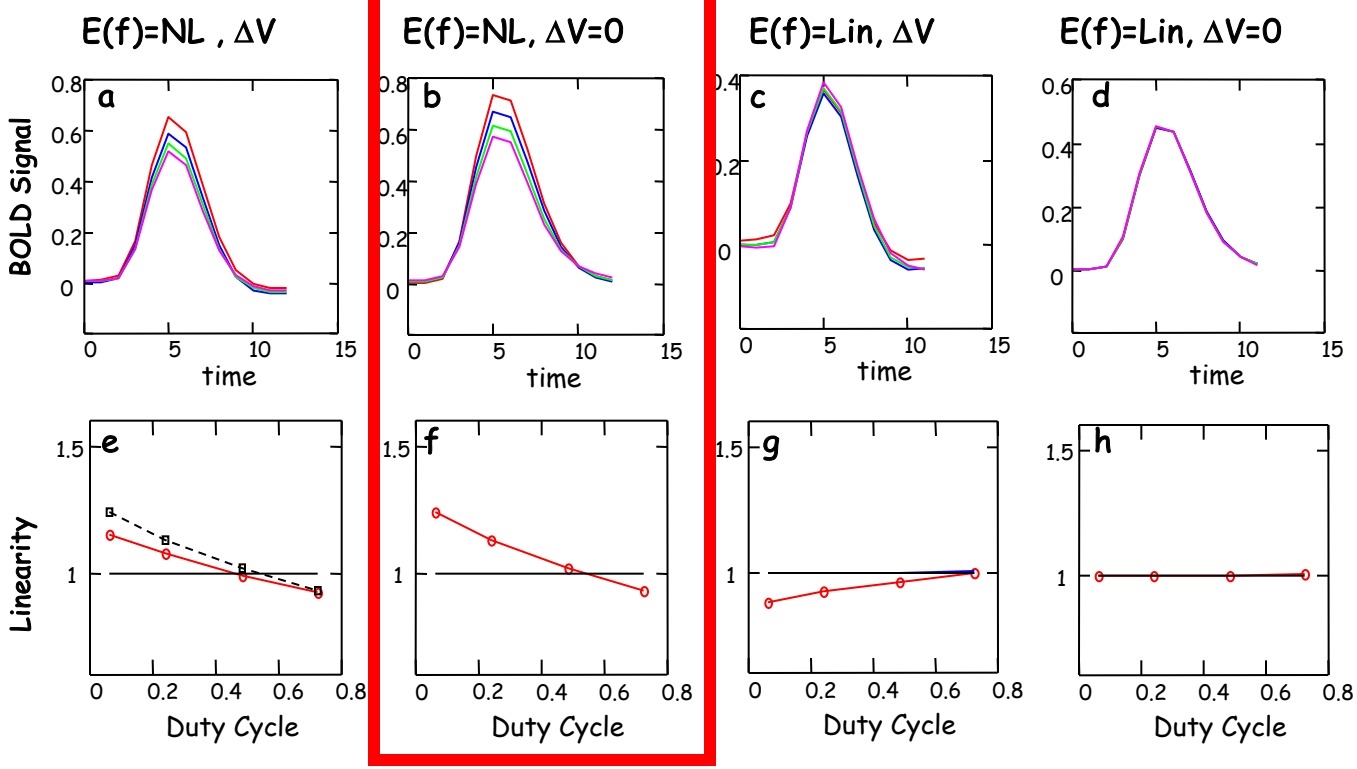




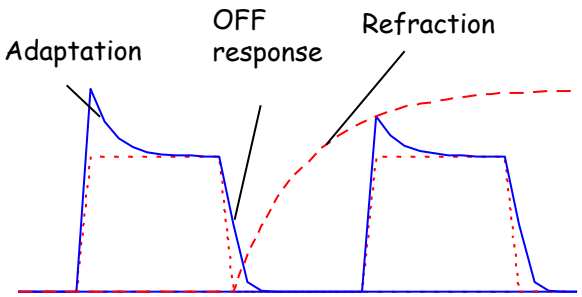
E(f) = oxygen extraction fraction

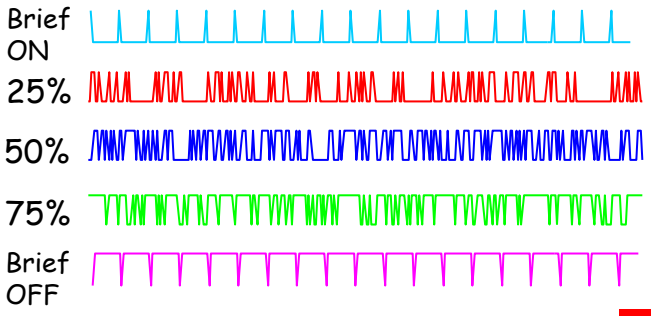
V = blood volume

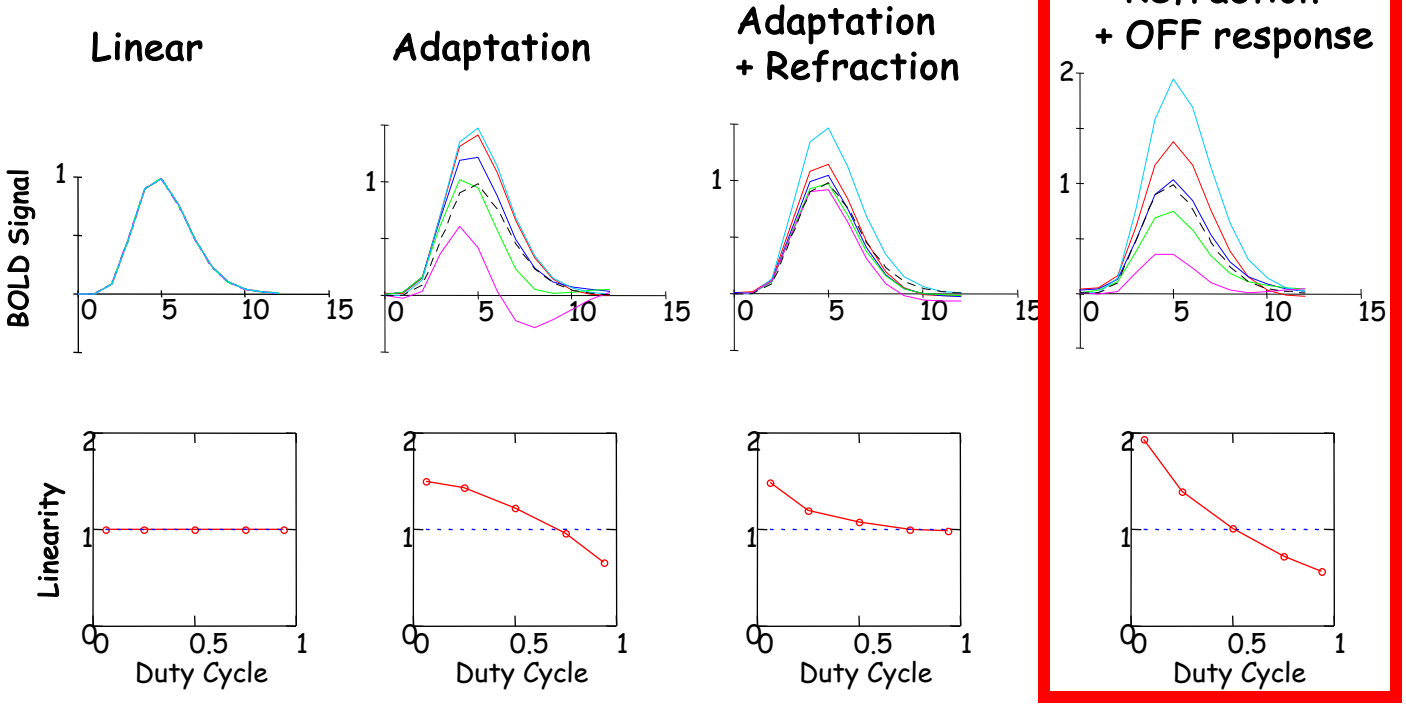




Simulation of Neuronal Mechanisms







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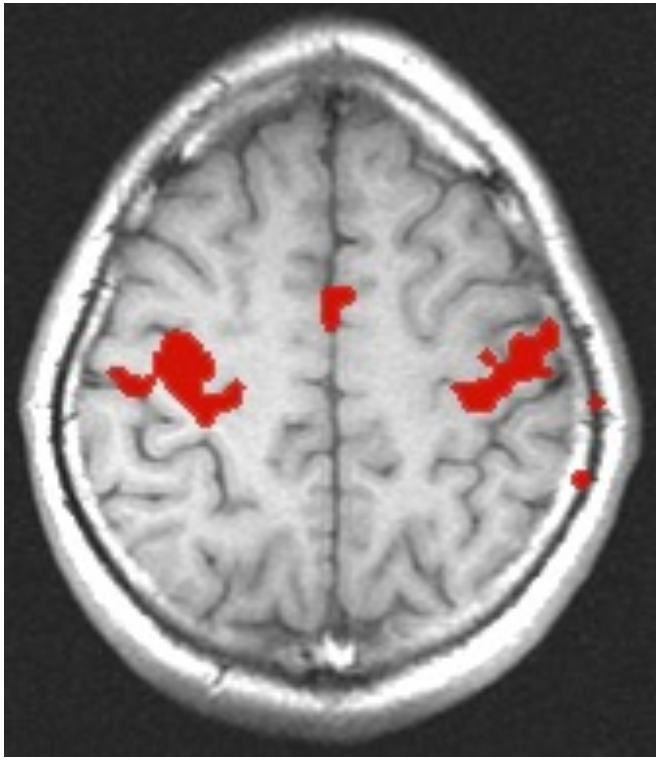
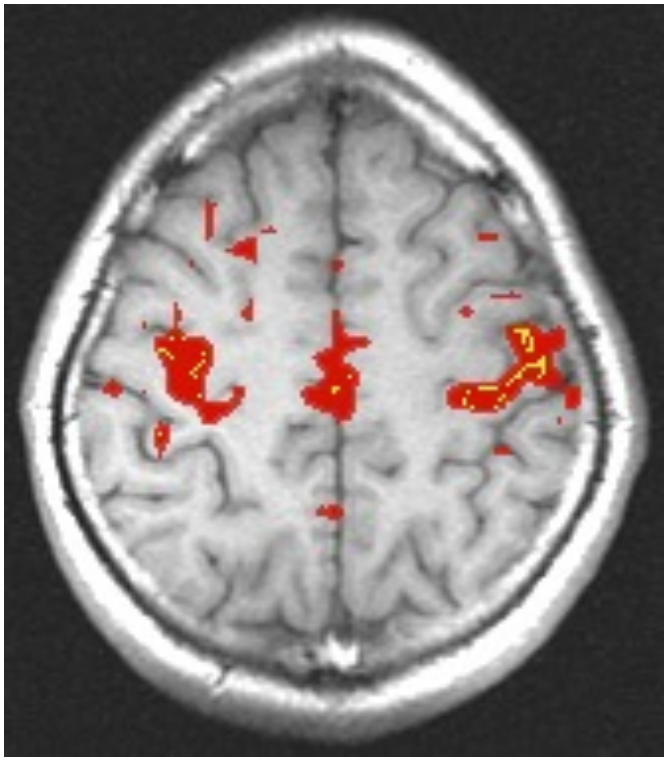
Fluctuations

Resting State Correlations



Activation:
correlation with reference function



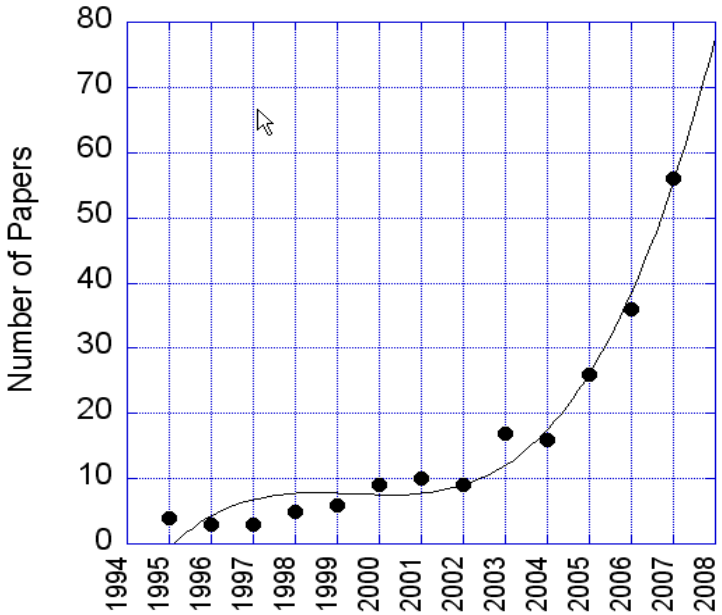
Rest:
seed voxel in motor cortex

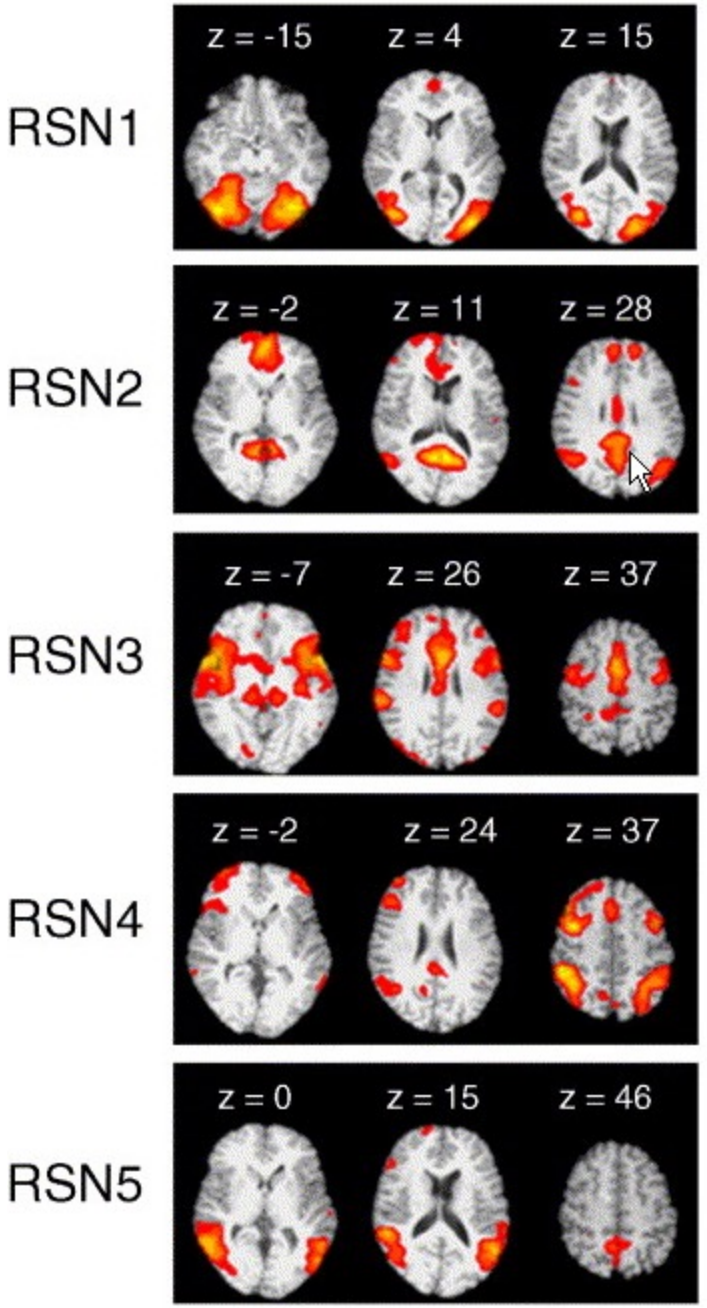
B. Biswal *et al.*, MRM, 34:537 (1995)

Fluctuations

Resting state networks identified with ICA

M. DeLuca, C.F. Beckmann, N. De Stefano, P.M. Matthews, S.M. Smith, fMRI resting state networks define distinct modes of long-distance interactions in the human brain. NeuroImage, 29, 1359-1367



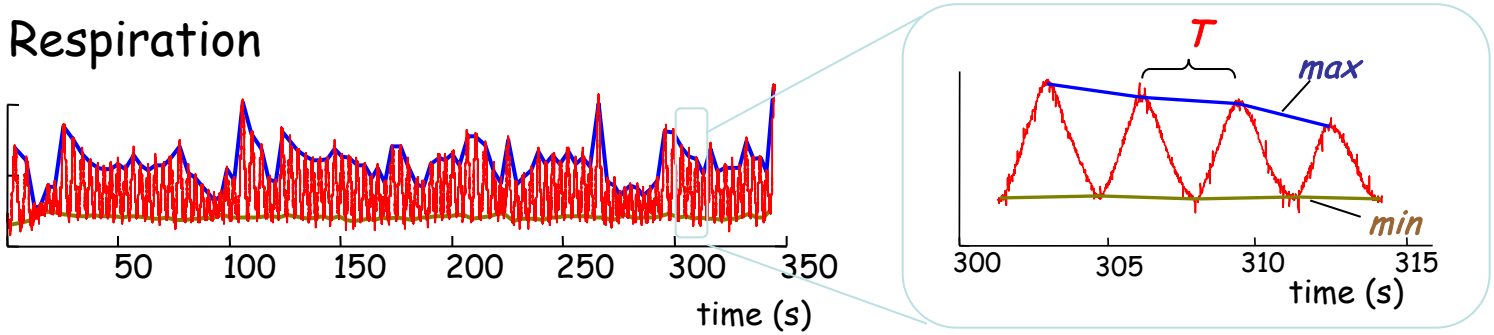


Fluctuations

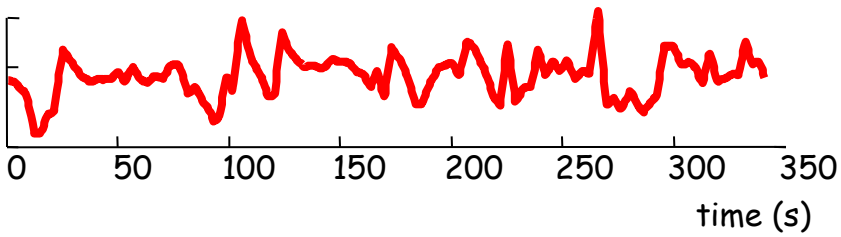
Sources of time series fluctuations:

- Blood, brain and CSF pulsation
- Vasomotion
- Breathing cycle (B_0 shifts with lung expansion)
- Bulk motion
- Scanner instabilities
- Changes in blood CO_2 (changes in breathing)
- Spontaneous neuronal activity

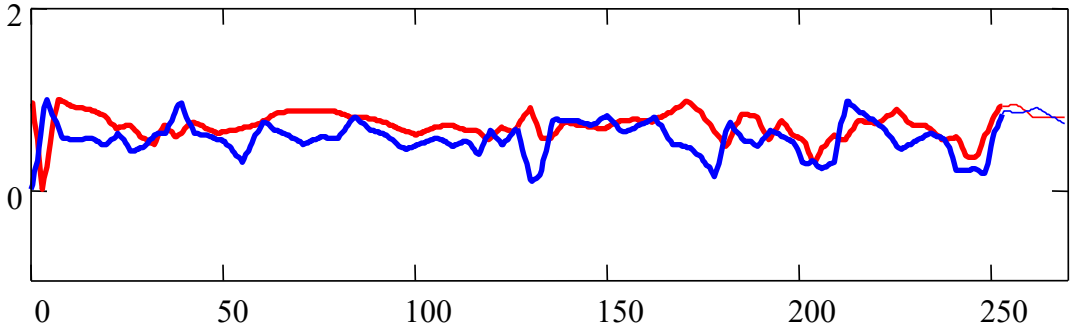
Estimating respiration volume changes



Respiration Volume / Time (RVT)

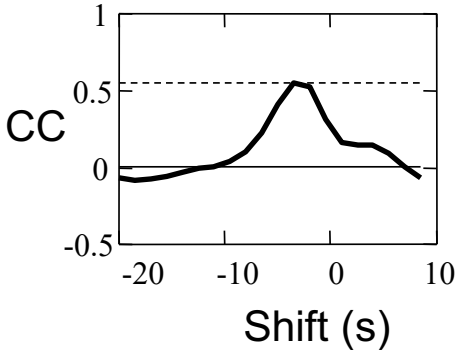


$$RVT = \frac{max - min}{T}$$



CO_2

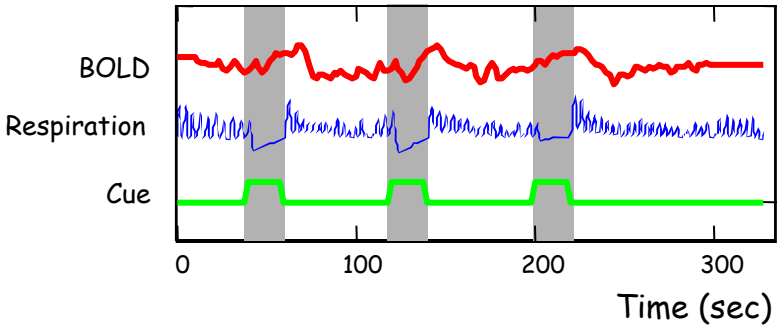
RVT



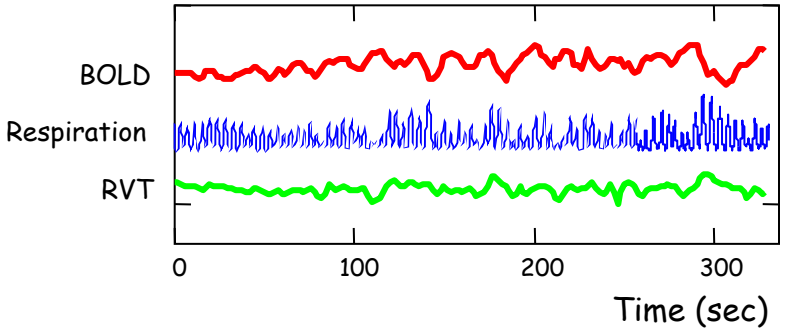
RVT precedes end tidal CO_2 by 5 sec.

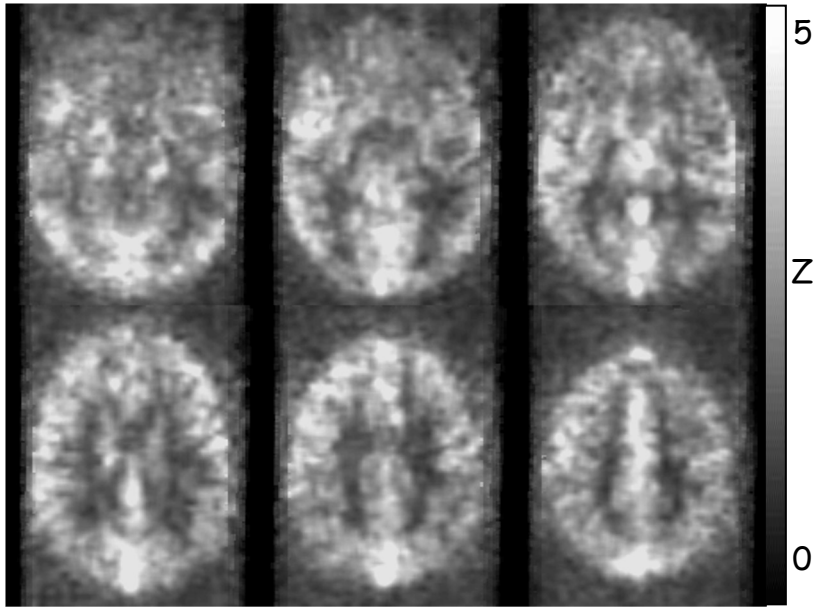
Respiration induced signal changes

Breath-holding

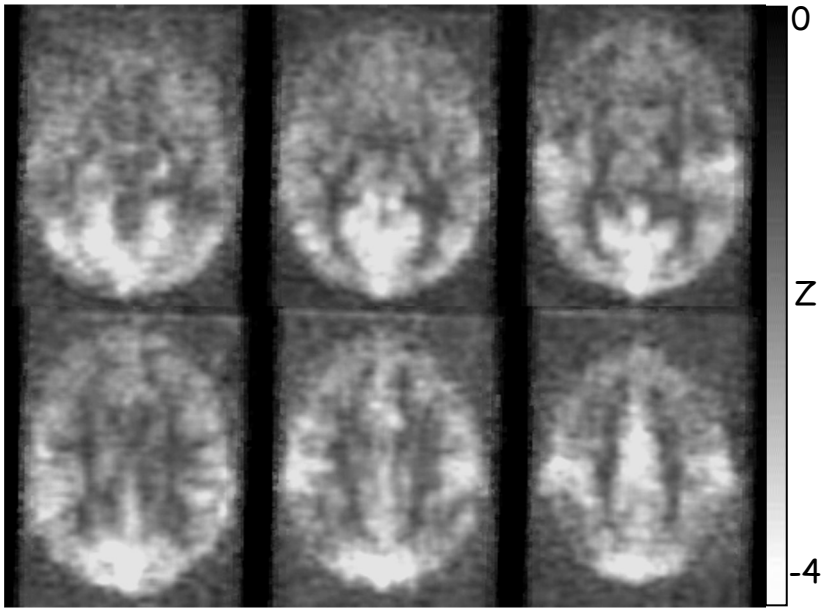


Rest





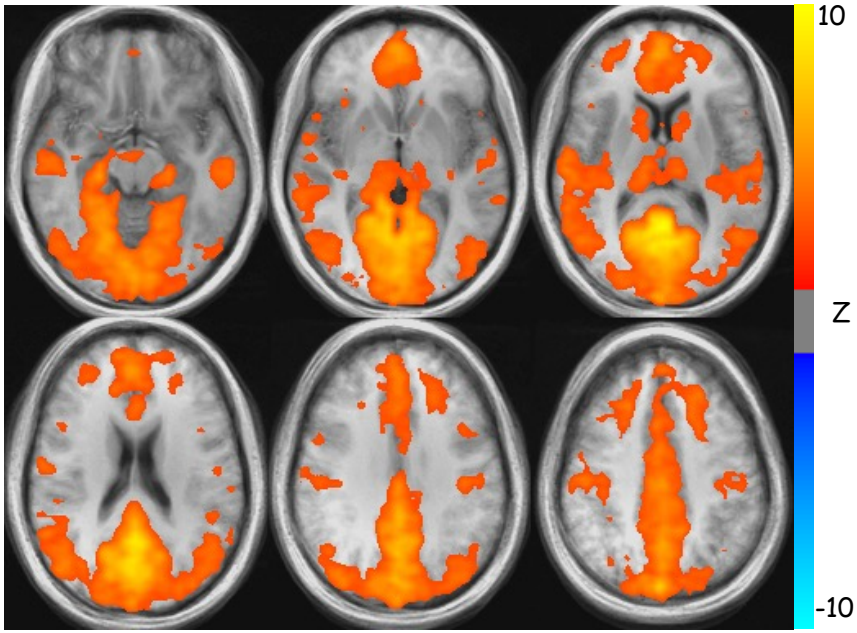
(N=7)



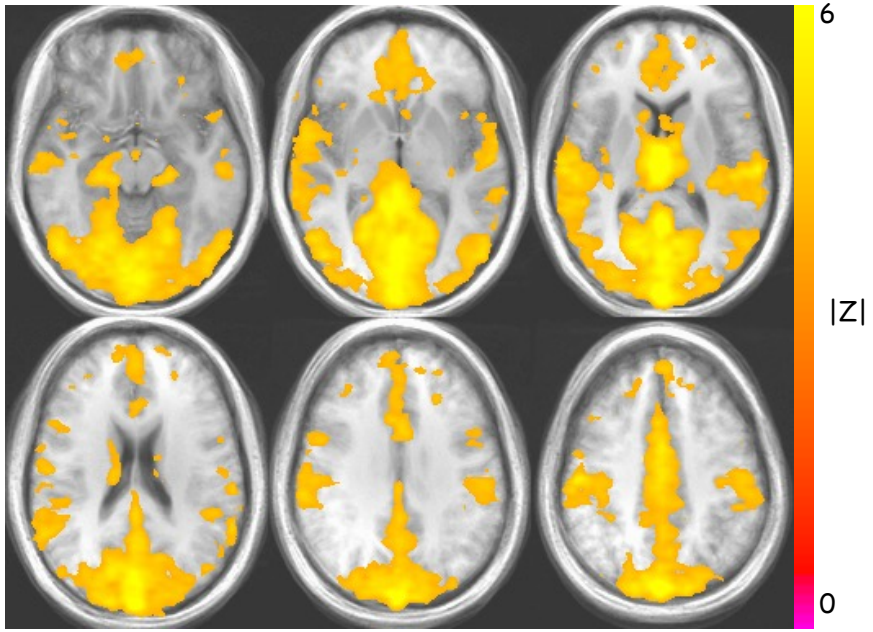
R.M. Birn, J. A. Diamond, M. A. Smith, P. A. Bandettini, *NeuroImage*, 31, 1536-1548 (2006)

RVT Correlation Maps & Functional Connectivity Maps

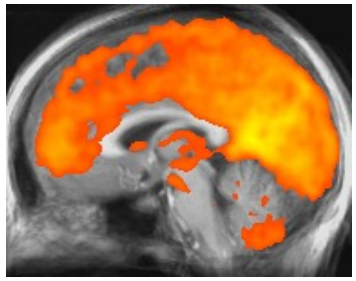
Resting state correlation with signal from posterior cingulate



Resting state correlation with RVT signal



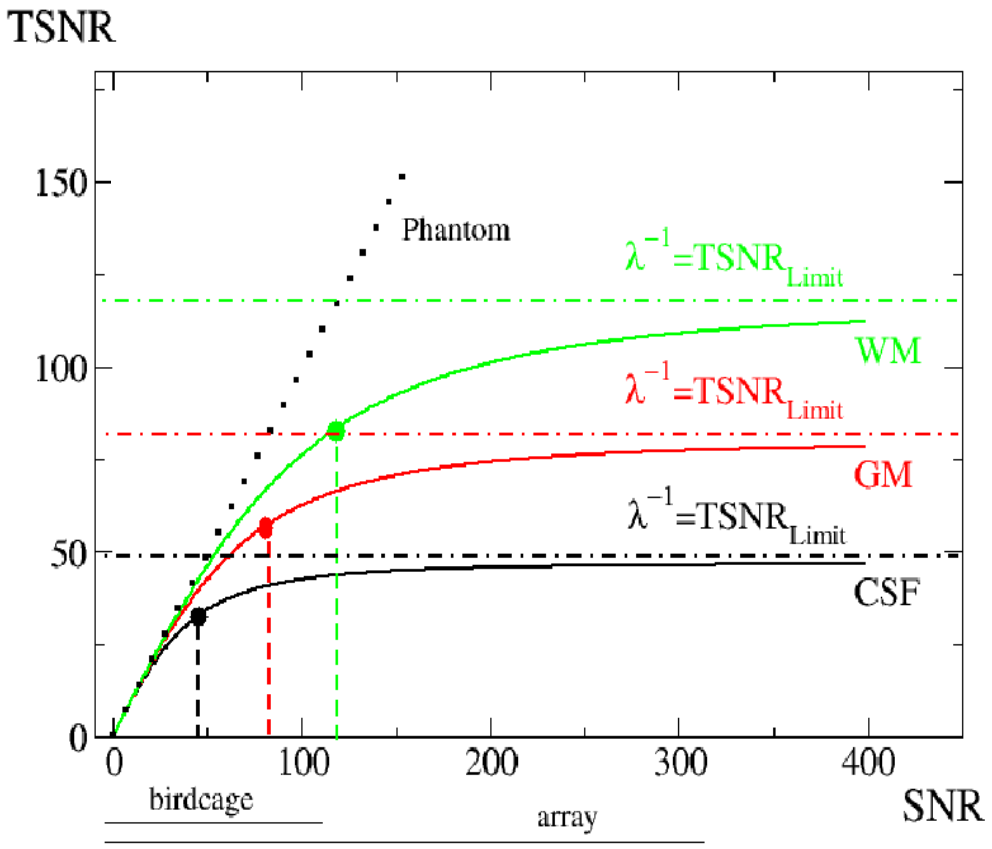
Group (n=10)



R.M. Birn, J. A. Diamond, M. A. Smith, P. A. Bandettini, *NeuroImage*, 31, 1536-1548 (2006)

Fluctuations

Temporal Signal to Noise Ratio (TSNR) vs. Signal to Noise Ratio (SNR)



J. Bodurka, F. Ye, N Petridou, K. Murphy, P. A. Bandettini, *NeuroImage*, 34, 542-549 (2007)

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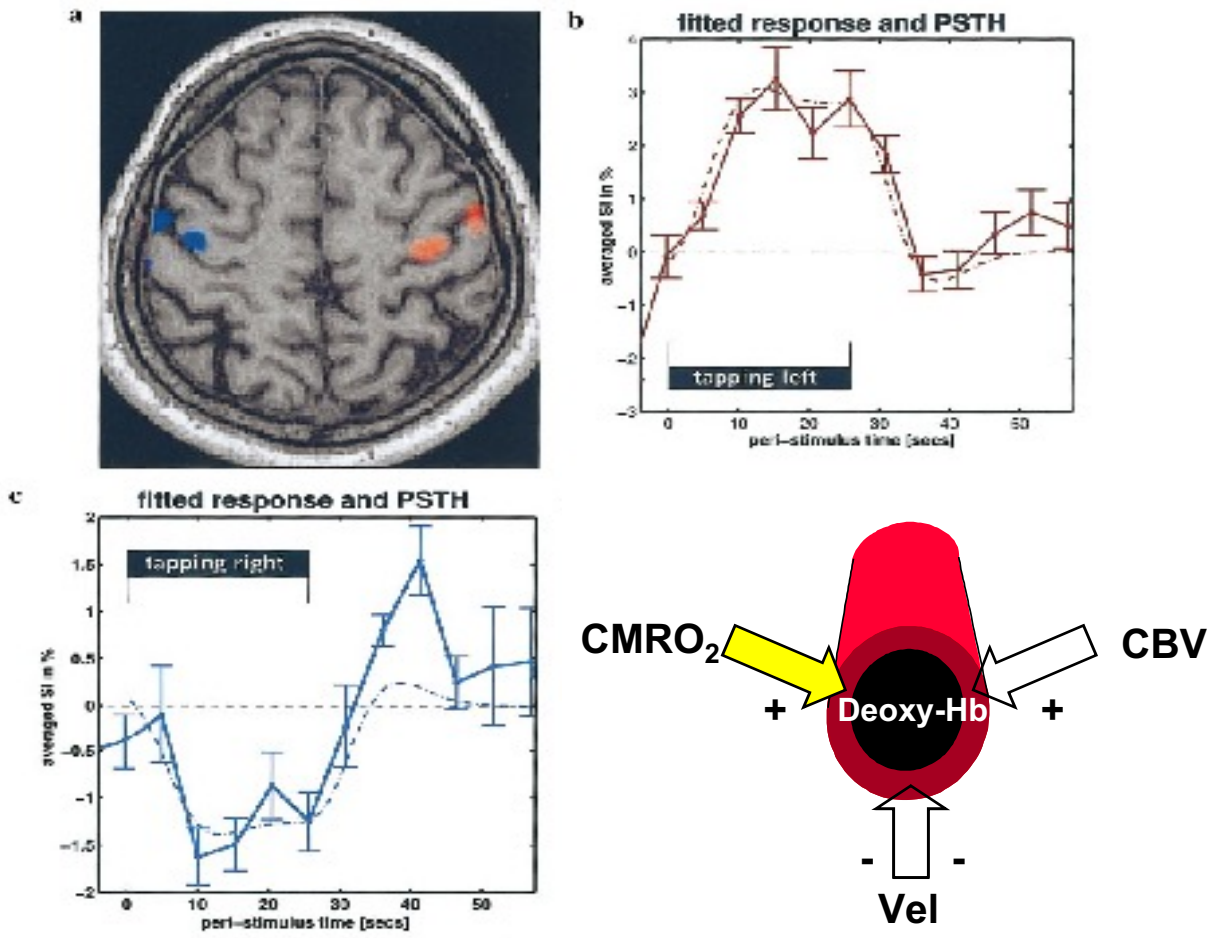
Effects of Pathology / Medication

Negative BOLD in carotid artery disease



Röther et al. NeuroImage 2002

Courtesy of Arno Villringer

Effects of Pathology / Medication

Altered neurovascular coupling: Pathology, drugs

Pathologic state / Drug	Reference
Carotid occlusion	Röther et al. 2002
Transient global ischemia	Schmitz et al. 1998
Penumbra of cerebral ischemia	Mies et al. 1993, Wolf et al. 1997
Subarachnoid hemorrhage	Dreier et al. 2000
Trauma	Richards et al. 2001
Epilepsy	Fink et al. 1996, Brühl et al. 1998, von Pannwitz et al. 2002
Alzheimer´s disease	Hock et al. 1996, Niwa et al. 2000
Theophylline	Ko et al. 1990, Dirnagl et al. 1994
Scopolamine	Tsukada et al. 1998

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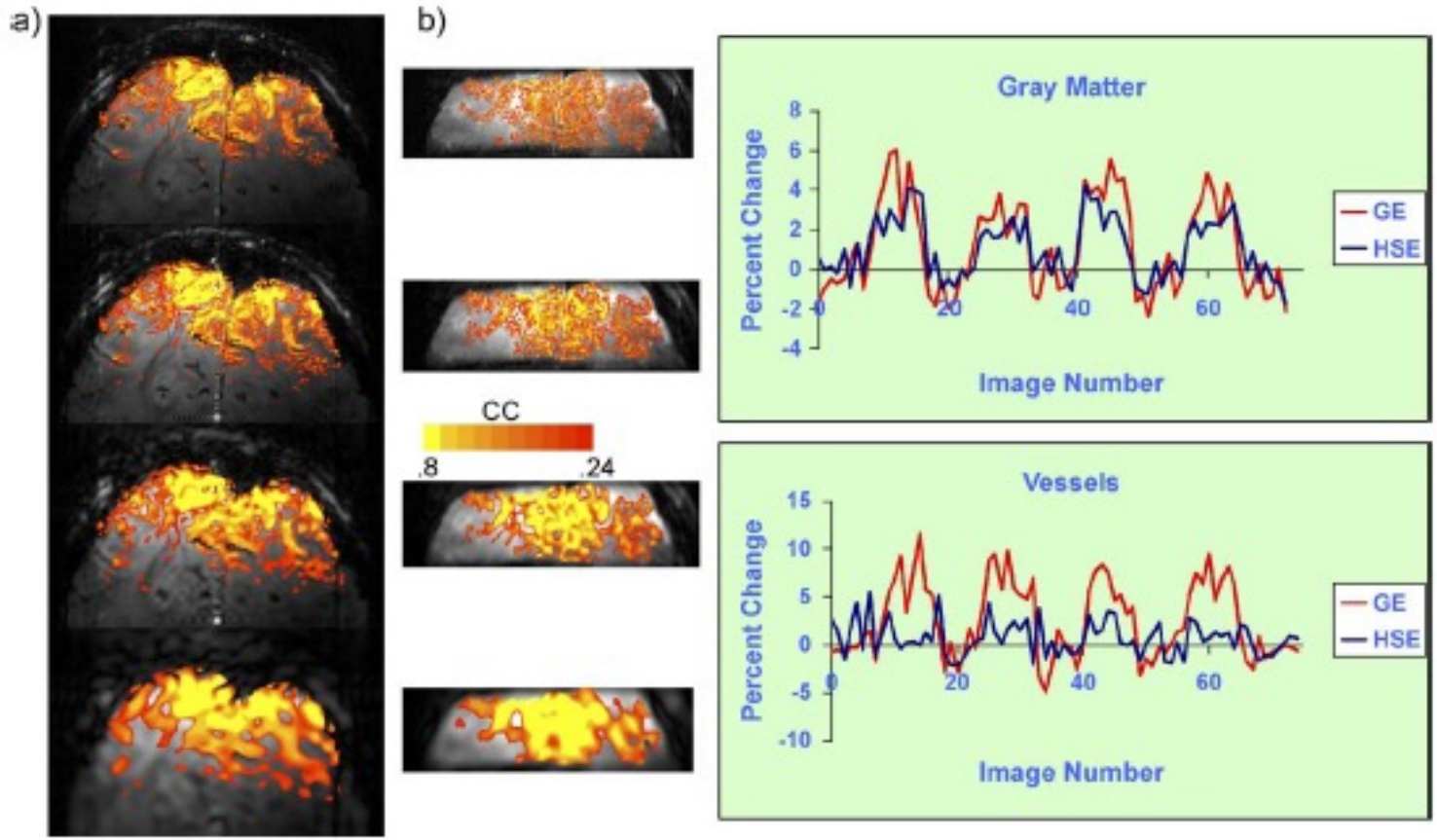

Yacoub et al. NeuroImage 24 (3), pp. 738-750

Other controversial contrast mechanisms:

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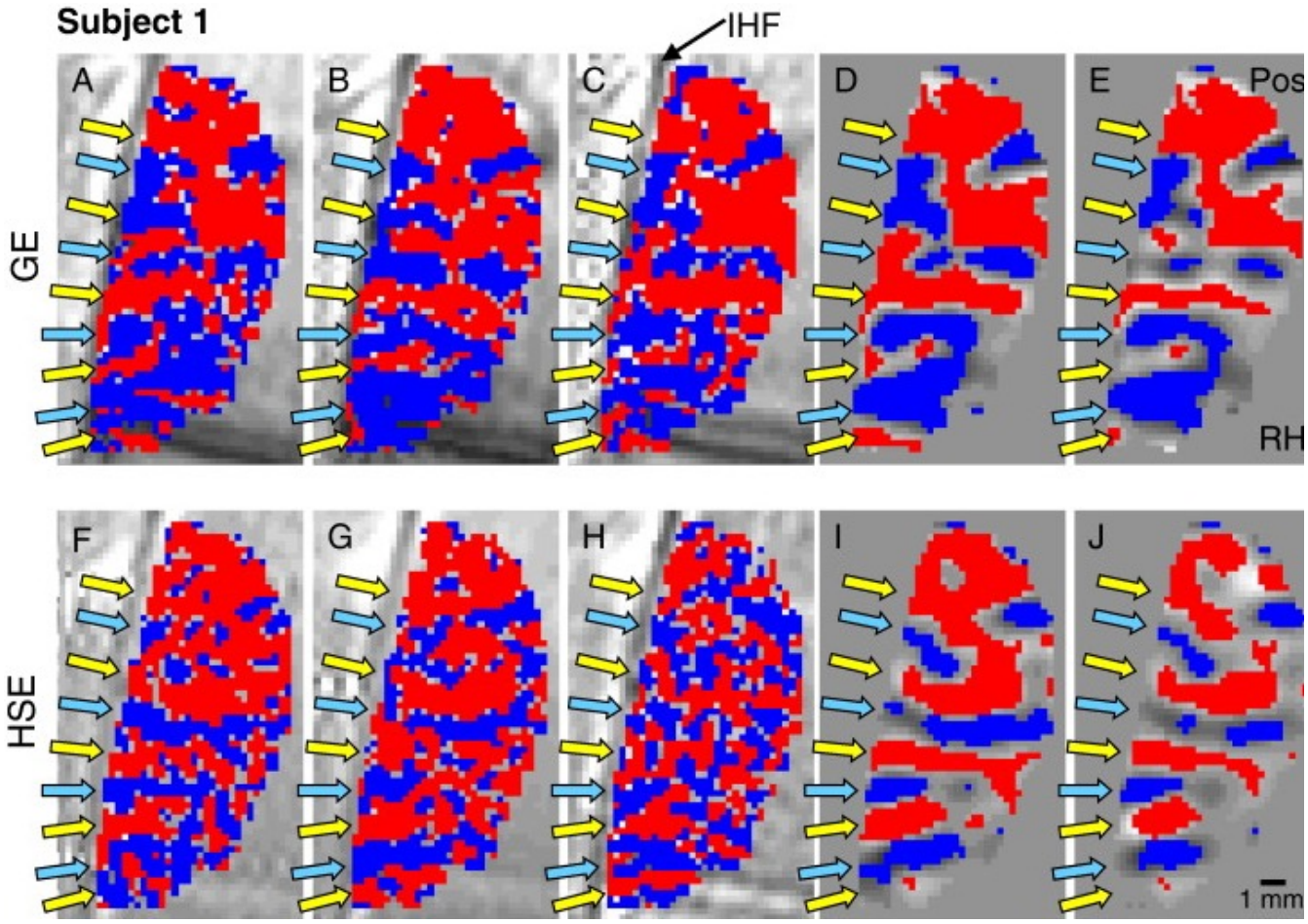

Yacoub et al. NeuroImage 37 (4), pp. 1161-1177

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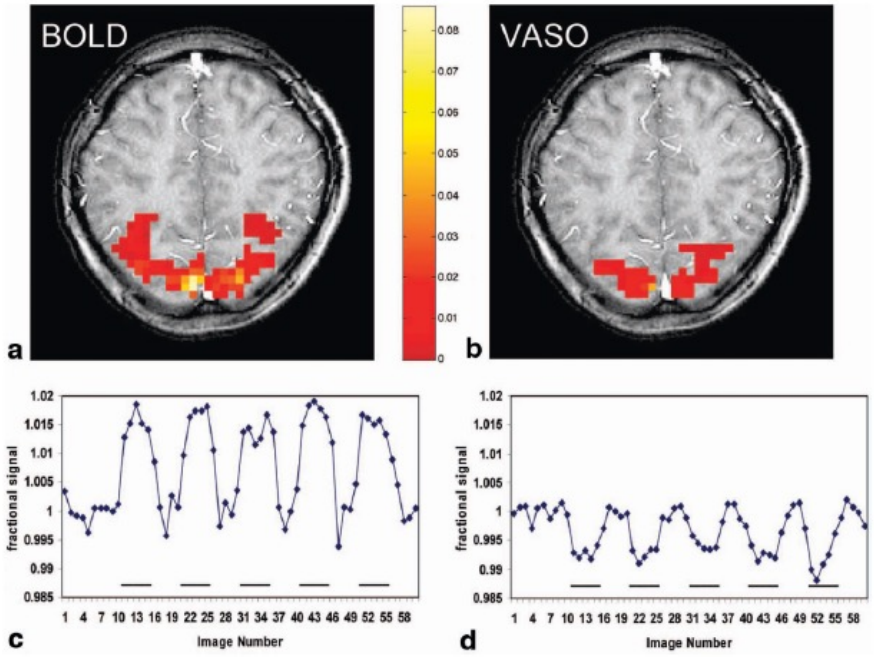

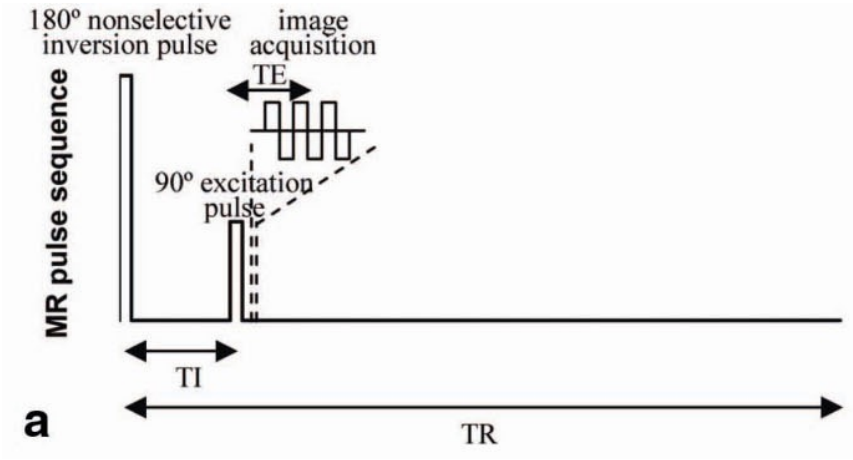

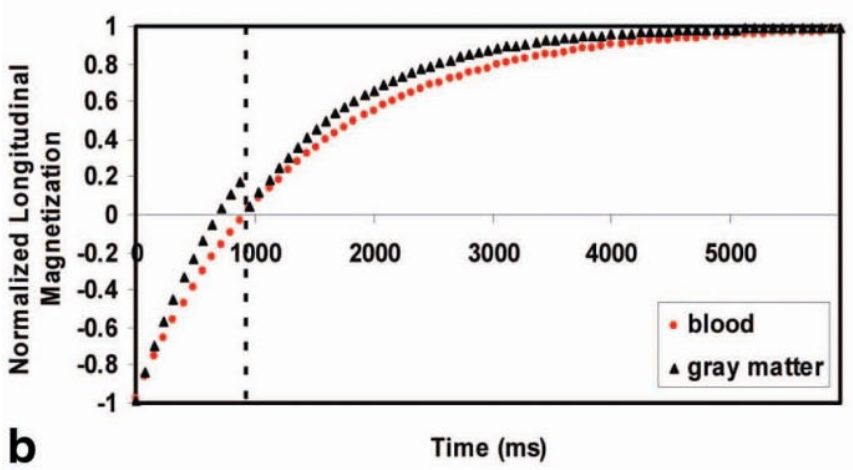

H. Lu et al. Magnetic Resonance in Medicine 50 (2), pp. 263-274

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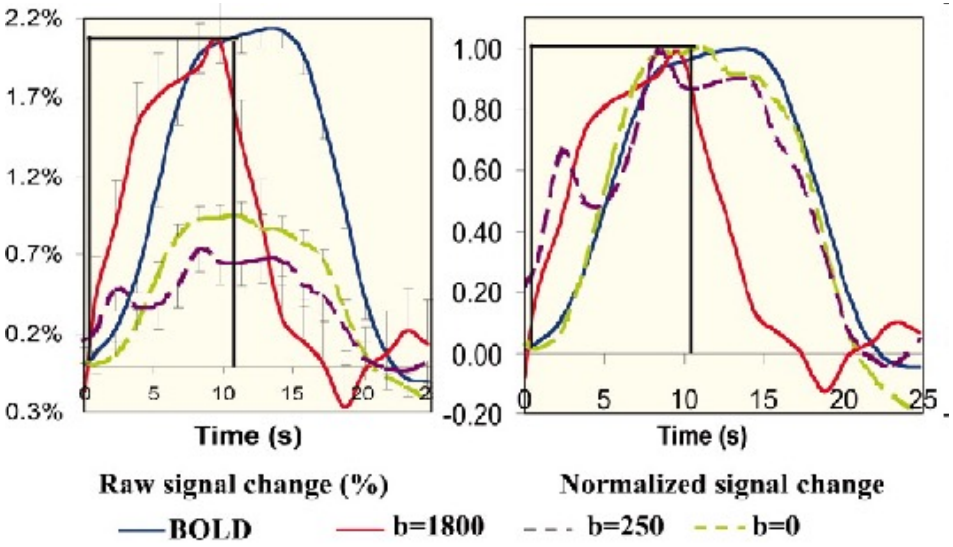

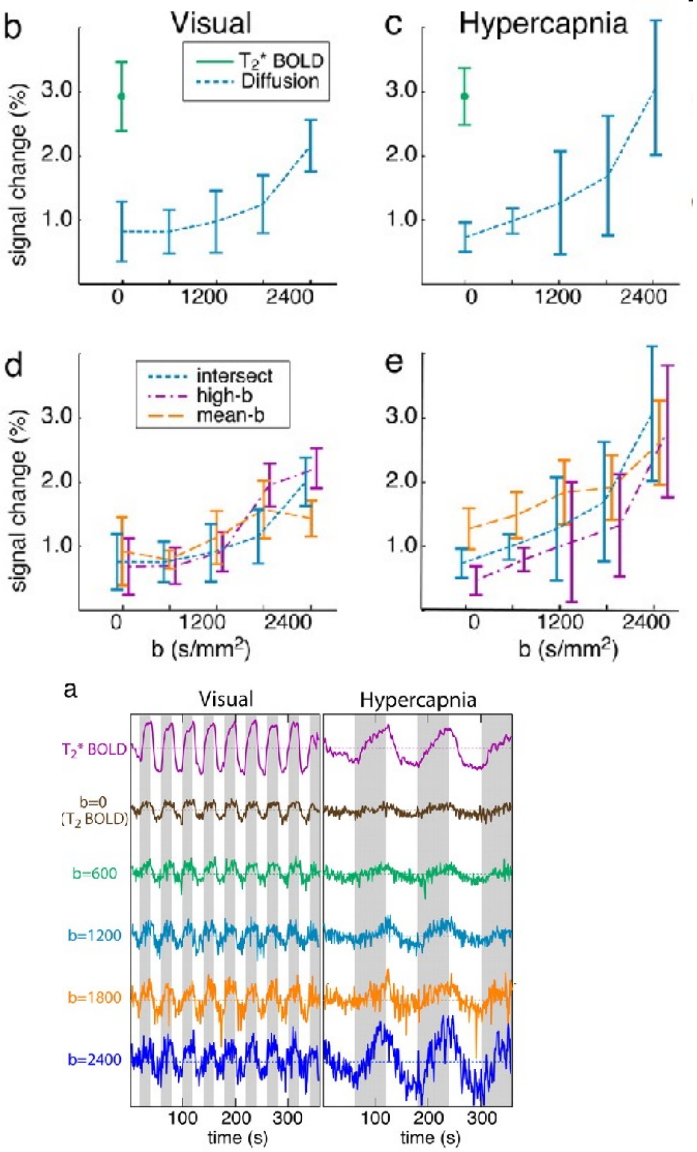

D. Le Bihan, et al Proceedings of the National Academy of Sciences of the United States of America 103 (21), pp. 8263-8268

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

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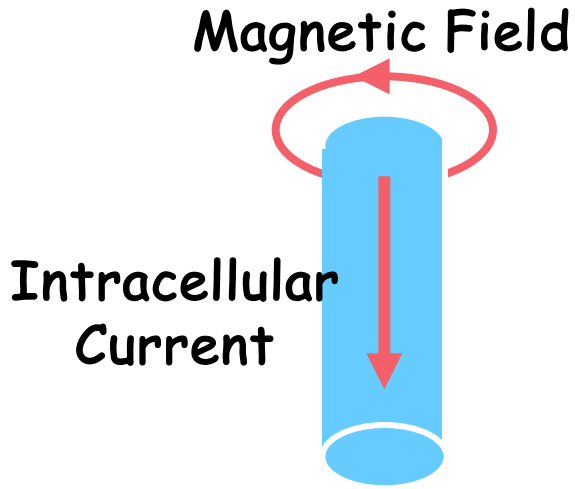
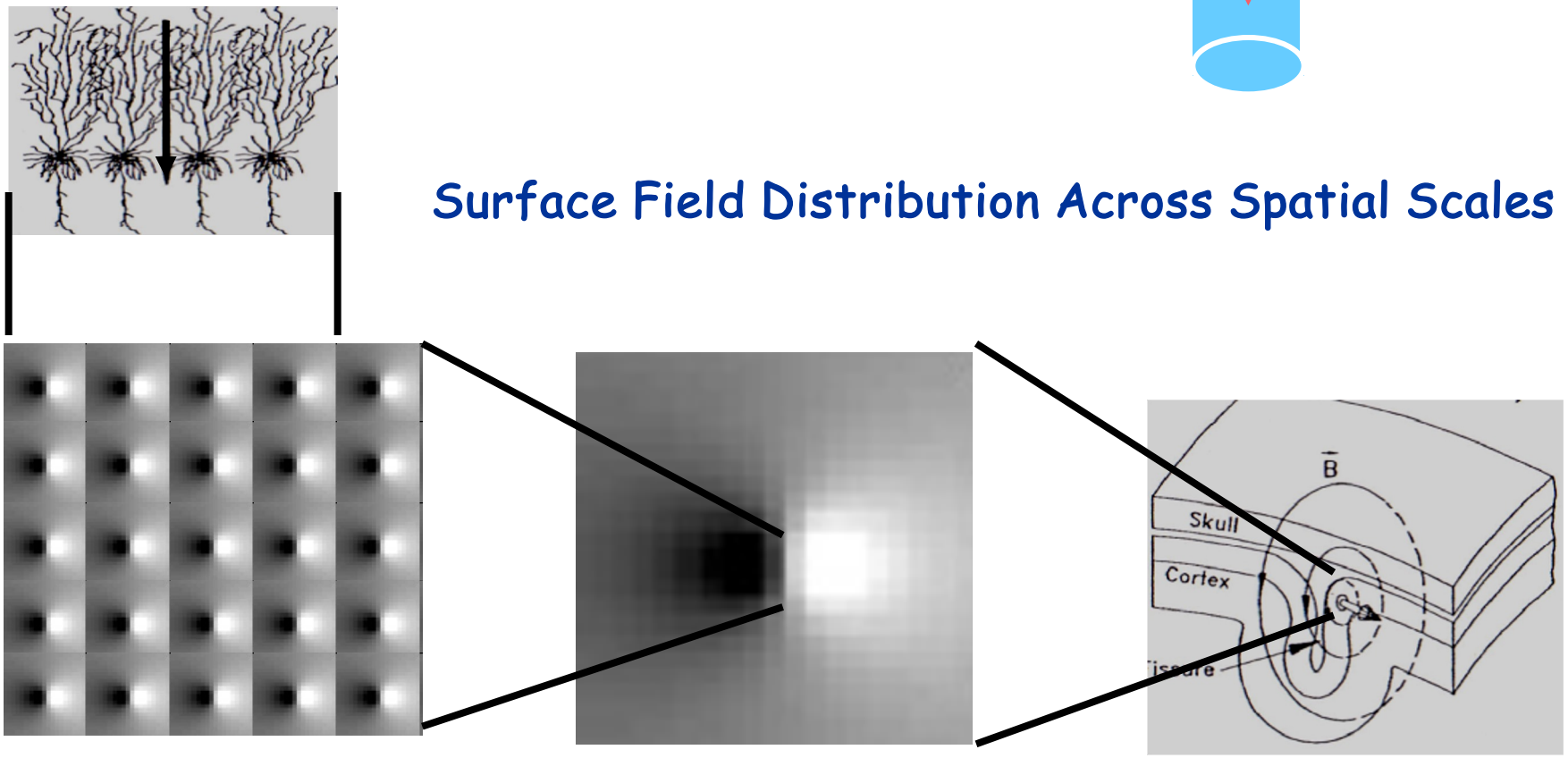
c. Diffusion
d. Neuronal Current



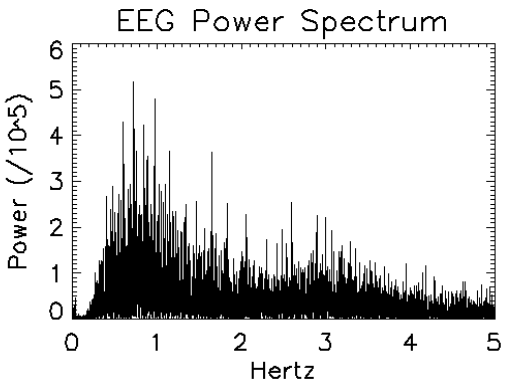


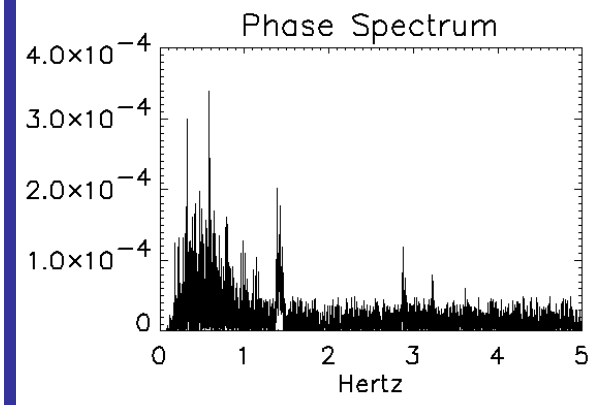
Surface Field Distribution Across Spatial Scales

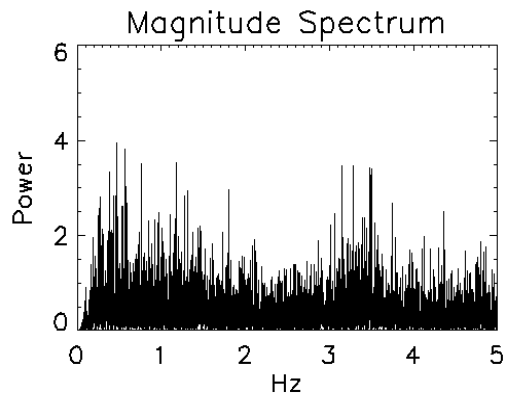
Adapted from: J.P. Wikswo Jr et al. *J Clin Neurophy* 8(2): 170-188, 1991

EEG

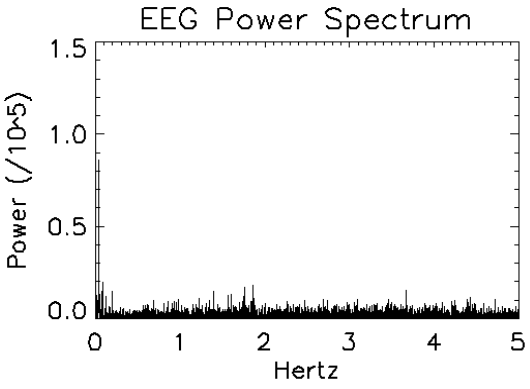
MR (7T)

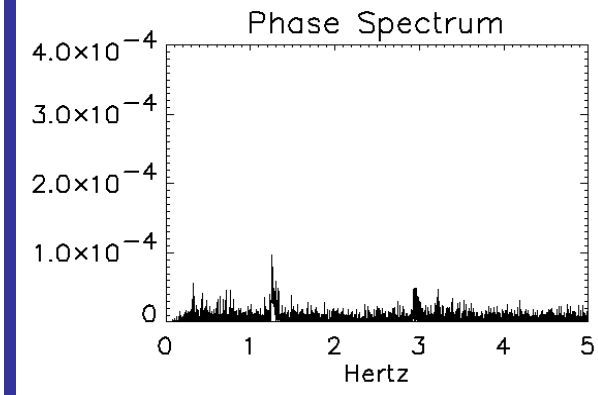


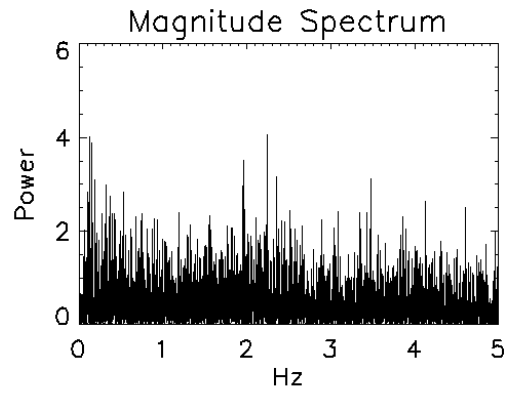




TTX







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).

Controversies Regarding fMRI Contrast

1. The Undershoots (pre and post)
2. Negative Signal Change
3. Relationship to neuronal activity
4. Linearity
5. Fluctuations
6. Effects of Pathology / Medication
7. Other controversial contrast mechanisms:
   a. T2 contrast – Spin-echo
   b. Blood Volume (VASO)
   c. Diffusion
   d. Neuronal Current

Close to being figured out

Not close to being figured out

Very far from being figured out