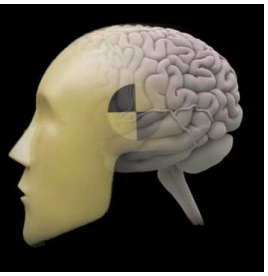
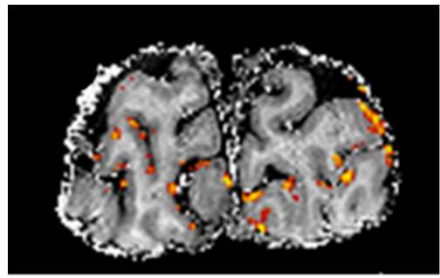


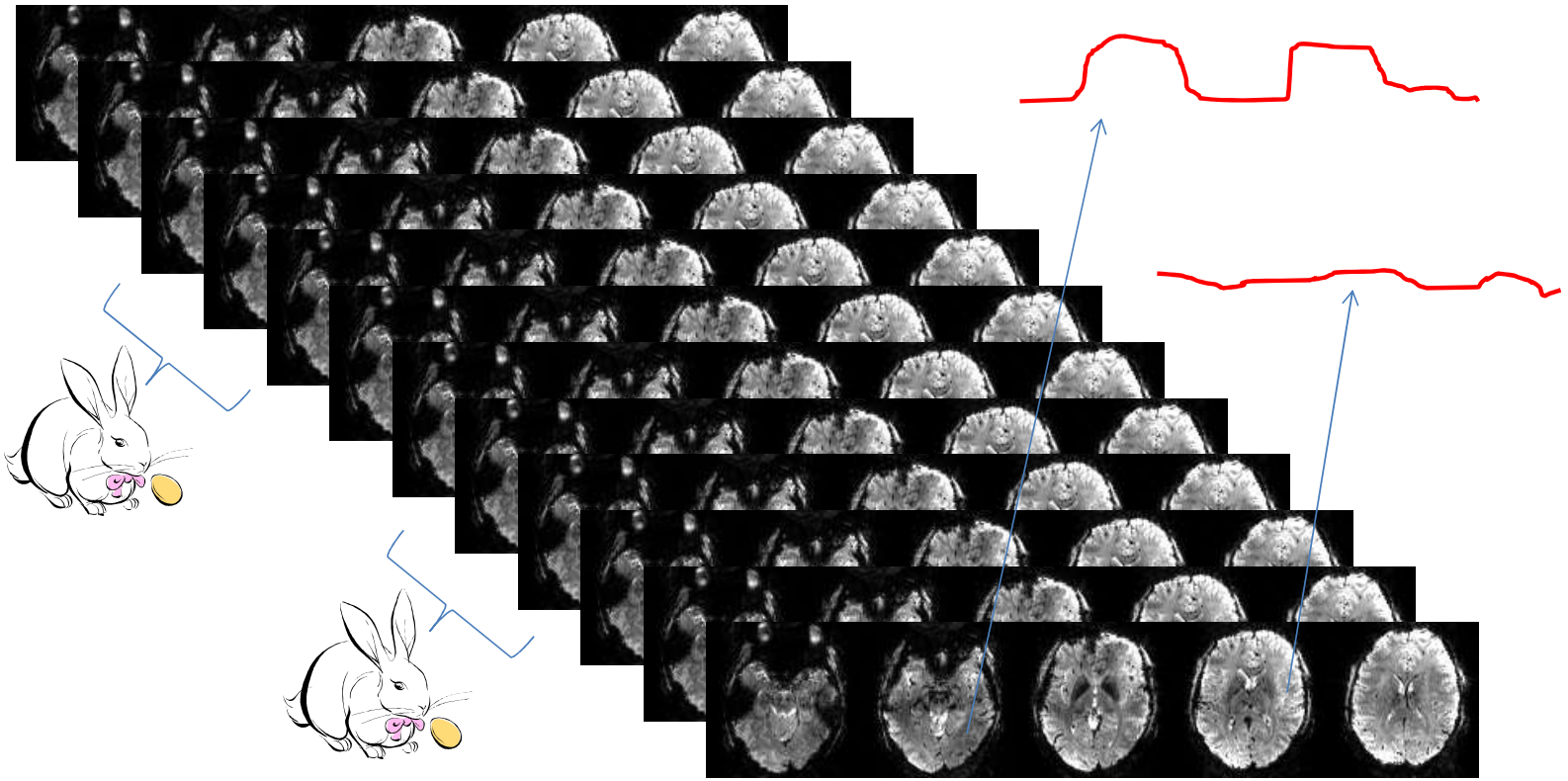
http://www.fmri4newbies.com/
How Neurons Become BOLD
Jody Culham



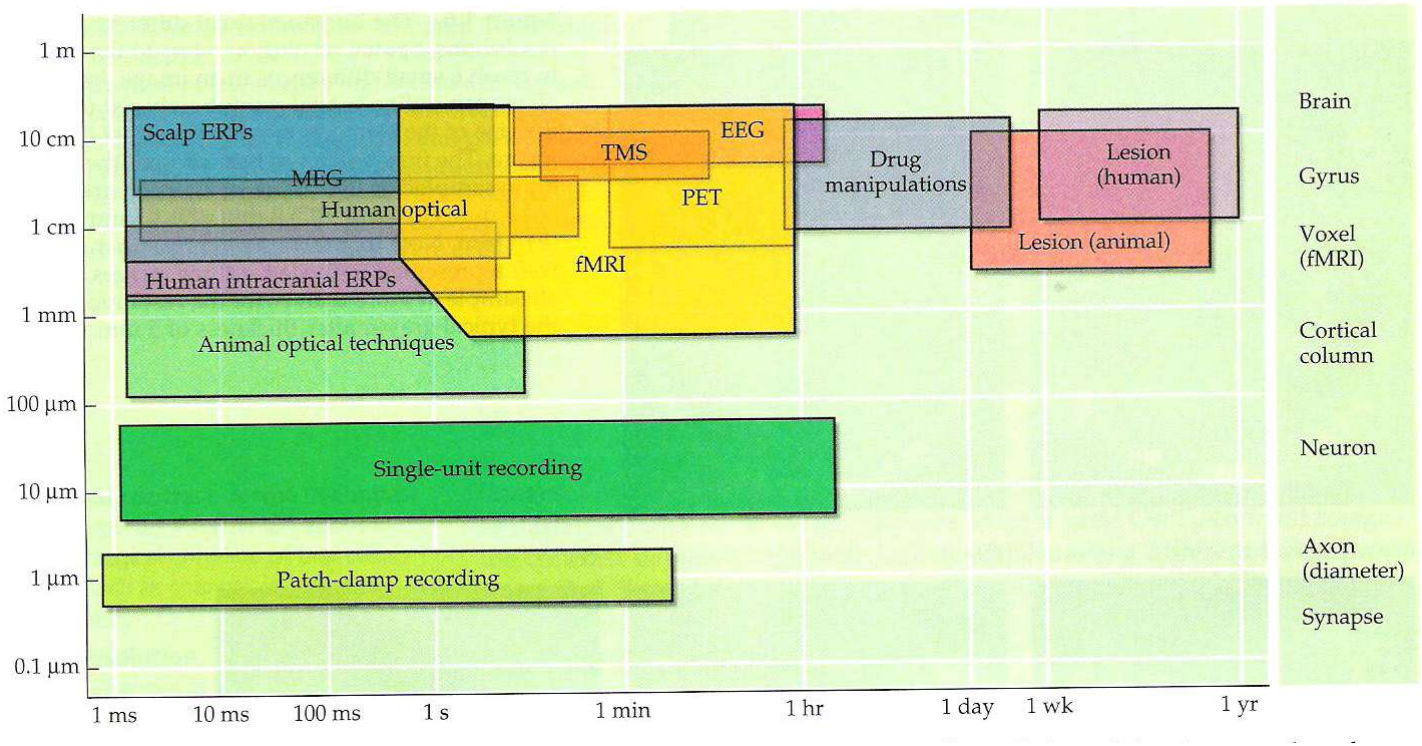
Functional Magnetic Resonance Imaging

Wietske van der Zwaag

timecourses

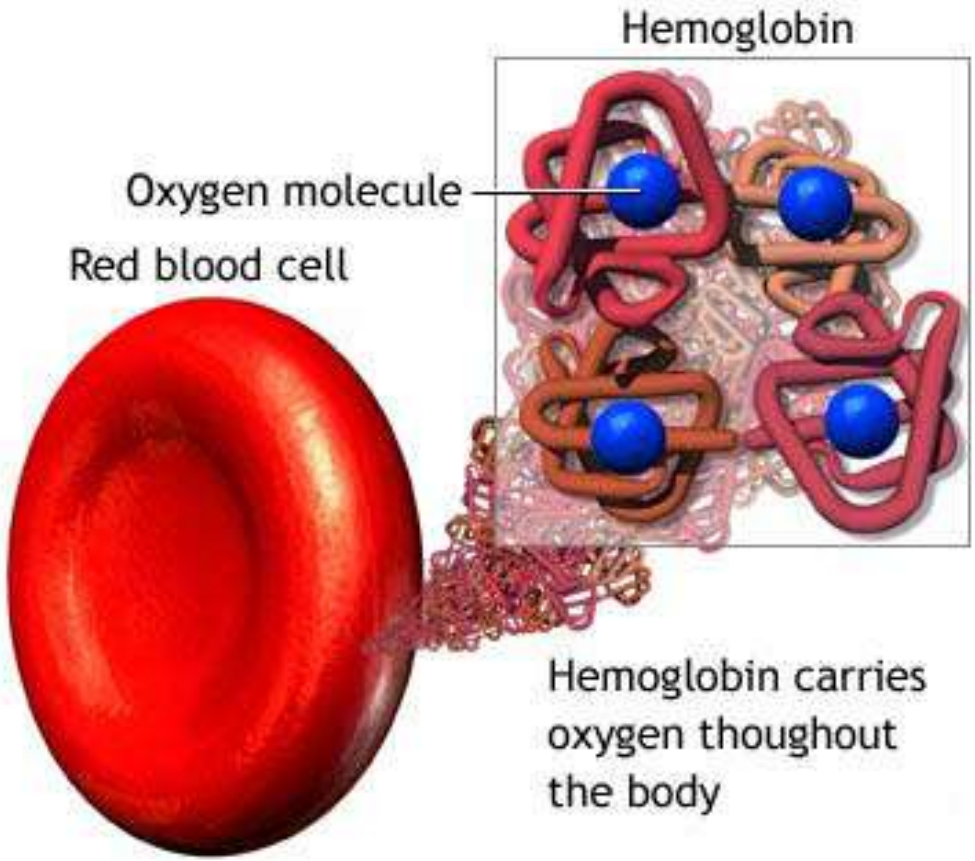


fMRI in the Big Picture



Section 1: The BOLD Signal

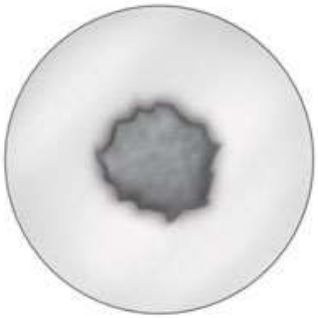
Hemoglobin (Hb)



Deoxygenated Blood → Signal Loss

Oxygenated blood?

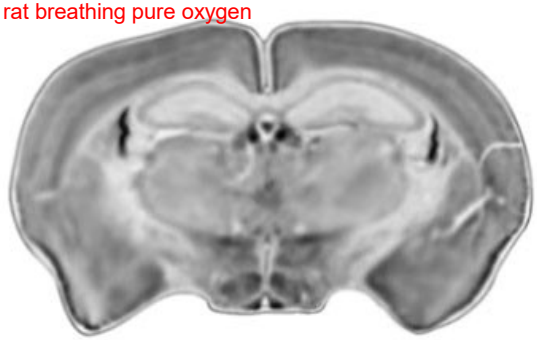
- Diamagnetic
- Does not distort magnetic field
- No signal loss



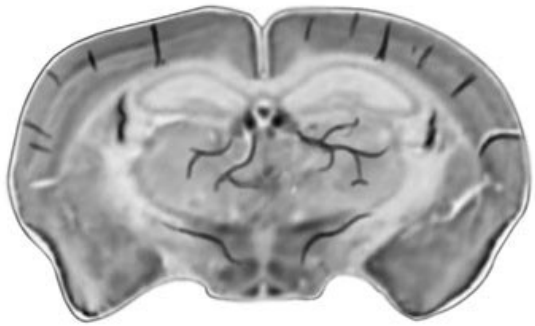
Deoxygenated blood

- Paramagnetic
- Distorts surrounding magnetic field
- Signal loss

rat breathing pure oxygen



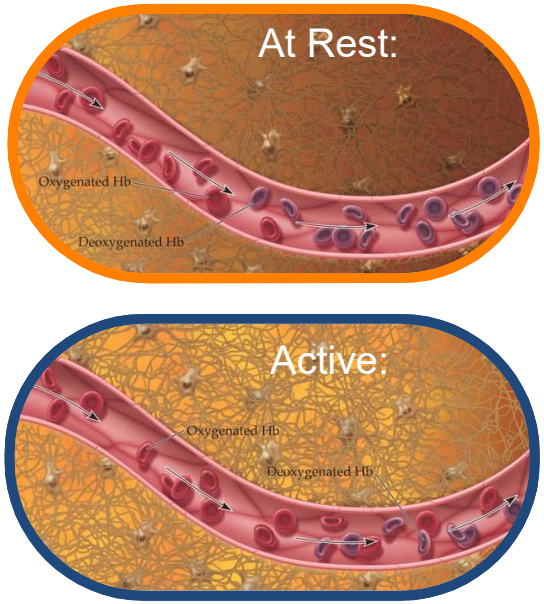
rat breathing normal air (less than pure oxygen)

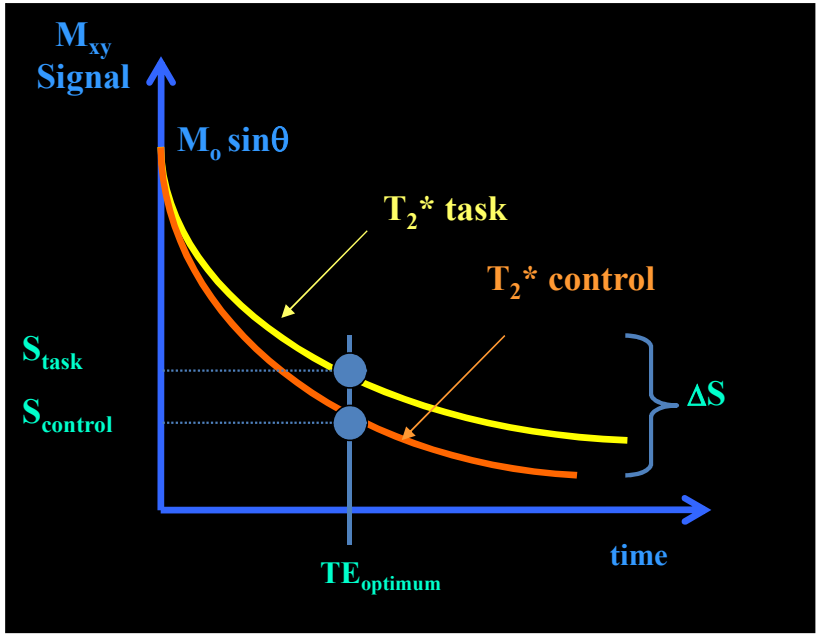


Huettel, Song & McCarthy, 2004, Functional Magnetic Resonance Imaging
based on two papers from Ogawa et al., 1990, both in MRM

BOLD signal

- neural activity ➔ ↑ blood flow ➔ ↑ oxyhemoglobin ➔ ↑ T2* ➔ ↑ MR signal

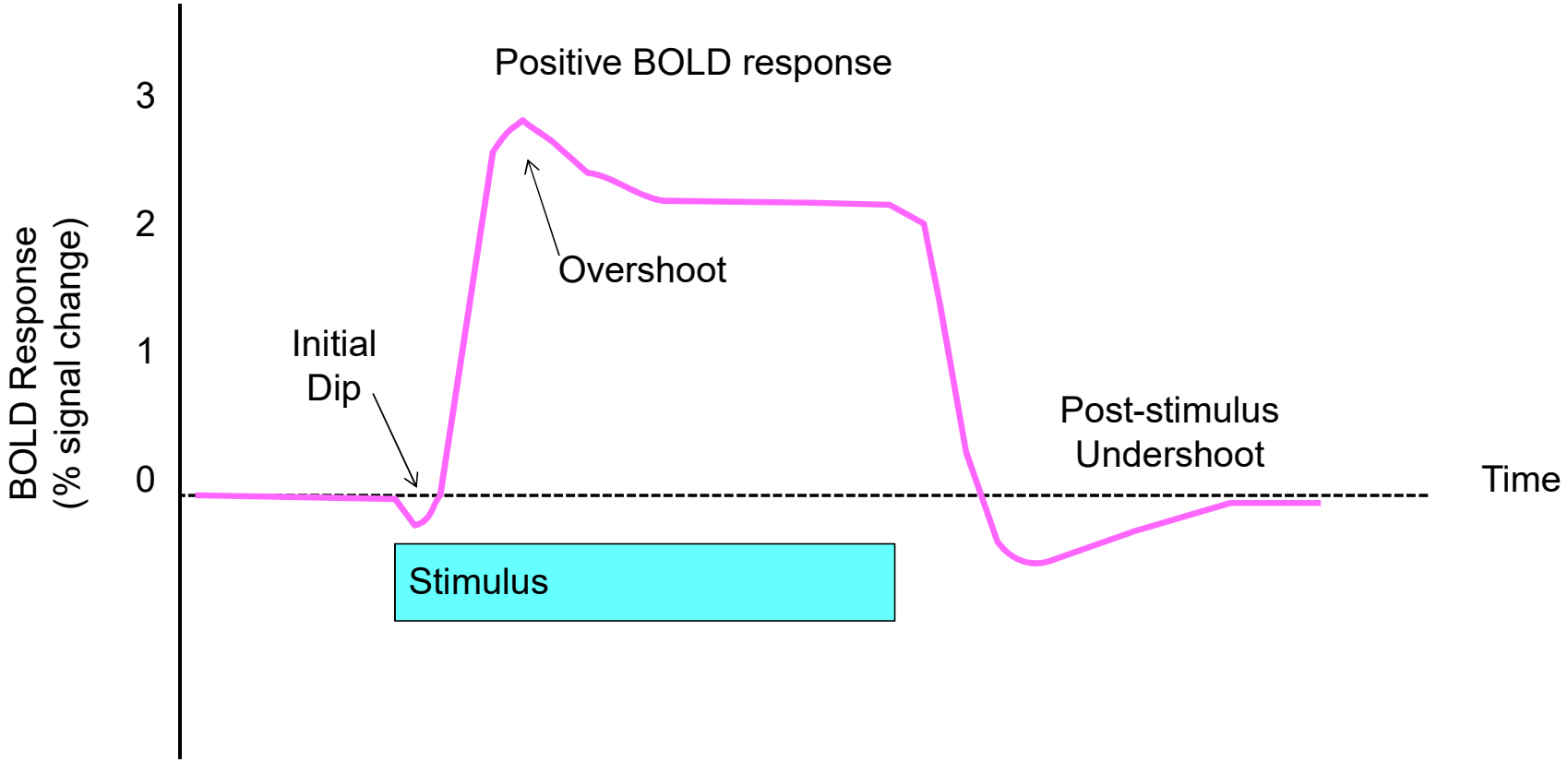




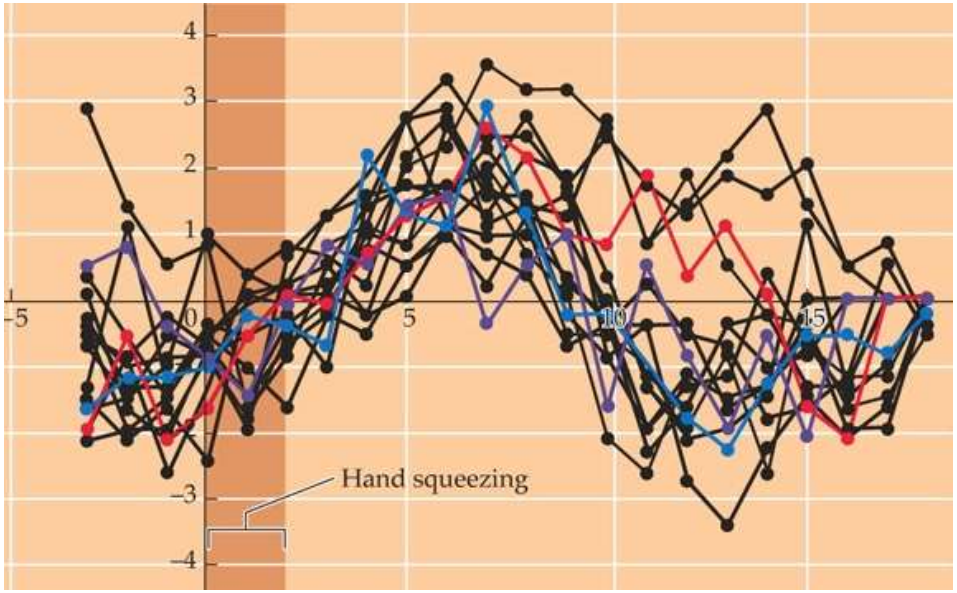
Images: Jorge Jovicich

BOLD Time Course

- Blood Oxygenation Level-Dependent Signal



Trial-to-Trial Variability

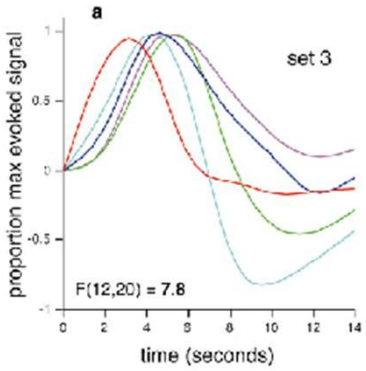


Huettel, Song & McCarthy, 2004,
Functional Magnetic Resonance Imaging

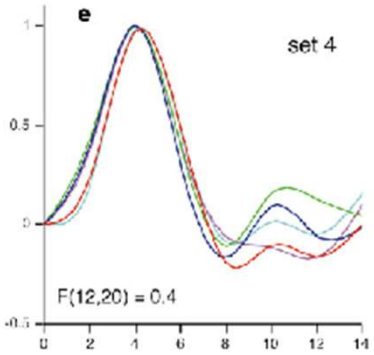
Variability of HRF Between Subjects

HRF shows considerable variability between subjects

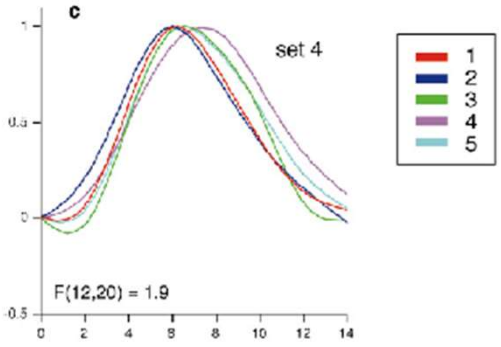
Within subjects, responses are more consistent, although there is still some variability between sessions



different subjects



same subject, same session

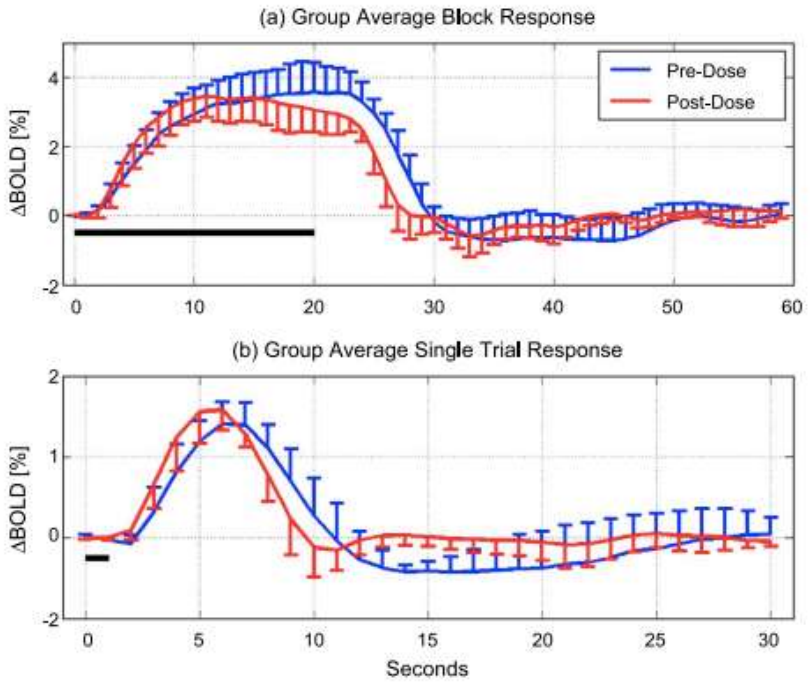


same subject, different session

Aguirre, Zarahn & D'Esposito, 1998

Factors that affect HRF

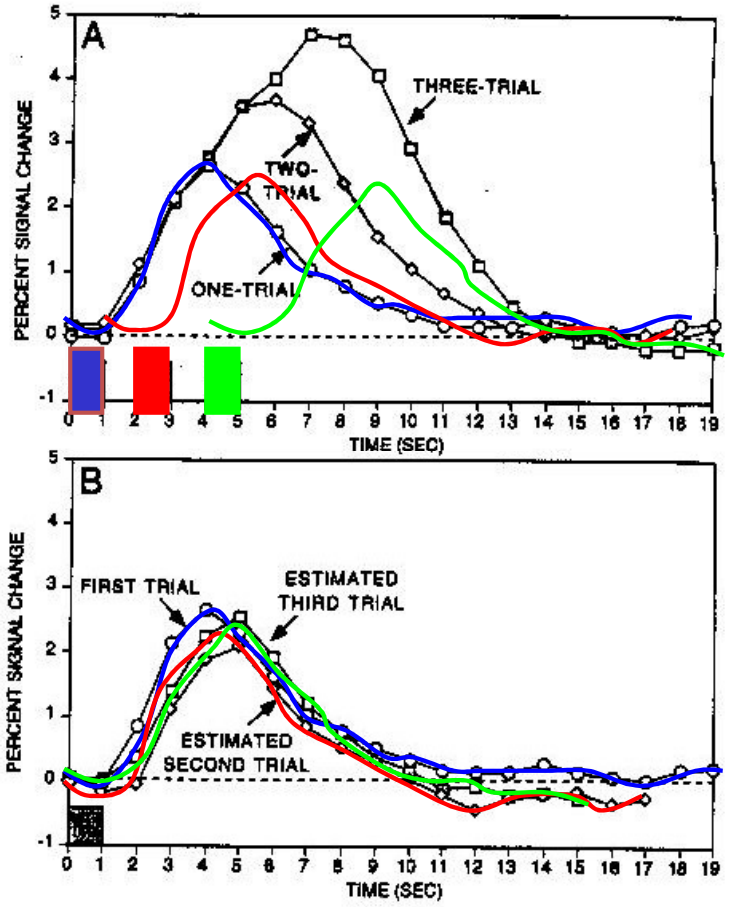
- drugs: alcohol, caffeine
- digestion: fat consumption
- aging
- disease: dementia



Effect of caffeine
Liu et al, 2004, NeuroImage

Handwerker et al. 2012, NeuroImage

Linearity of BOLD response



Linearity:
"Do things add up?"

red = 2 - 1

green = 3 - 2

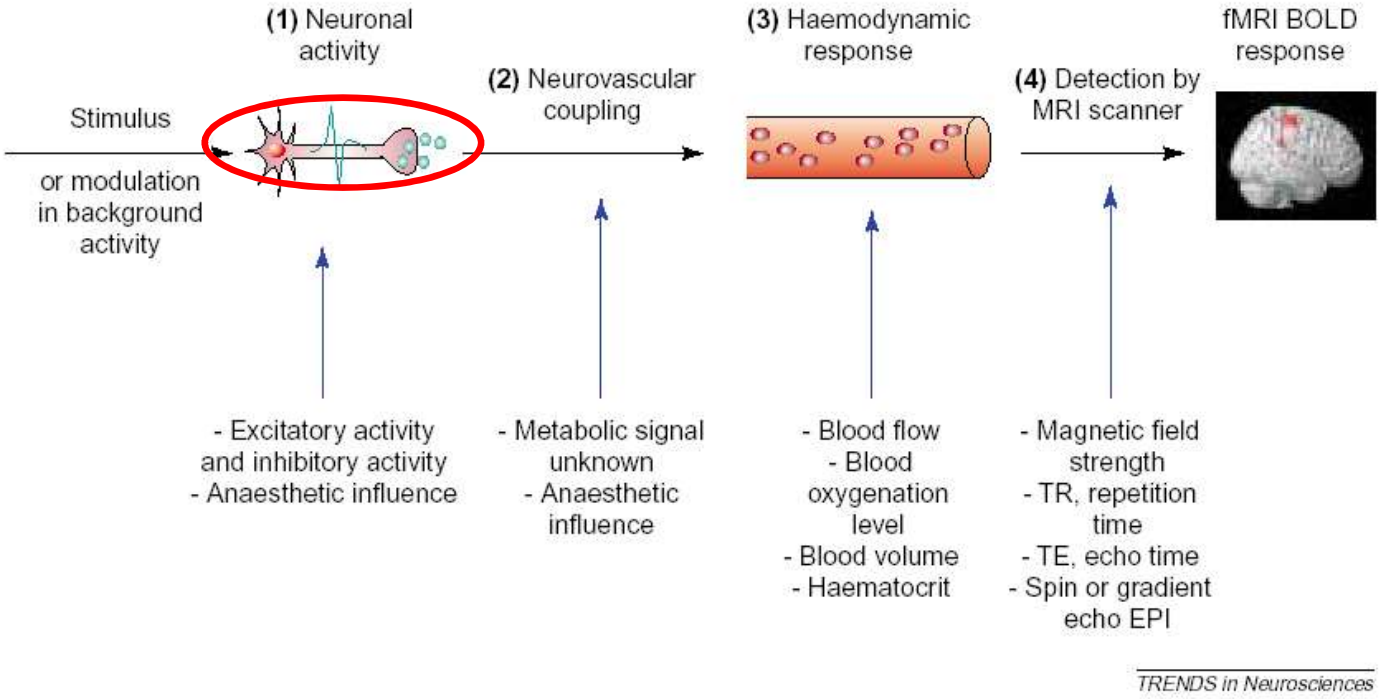
Sync each trial response to start of trial

Not quite linear but good enough!

Dale & Buckner, 1997

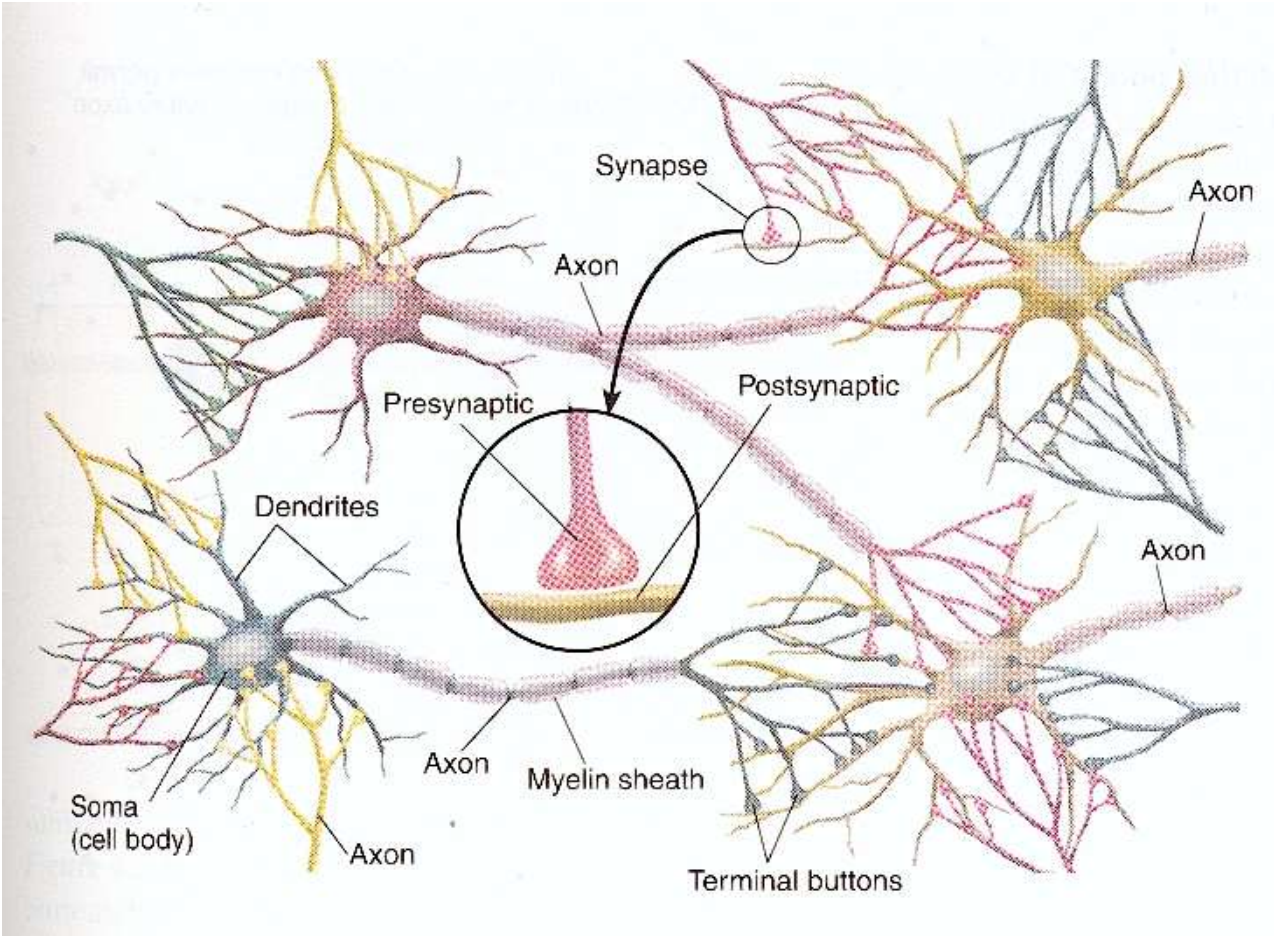
Section 2: From Neurons to BOLD

Stimulus to BOLD



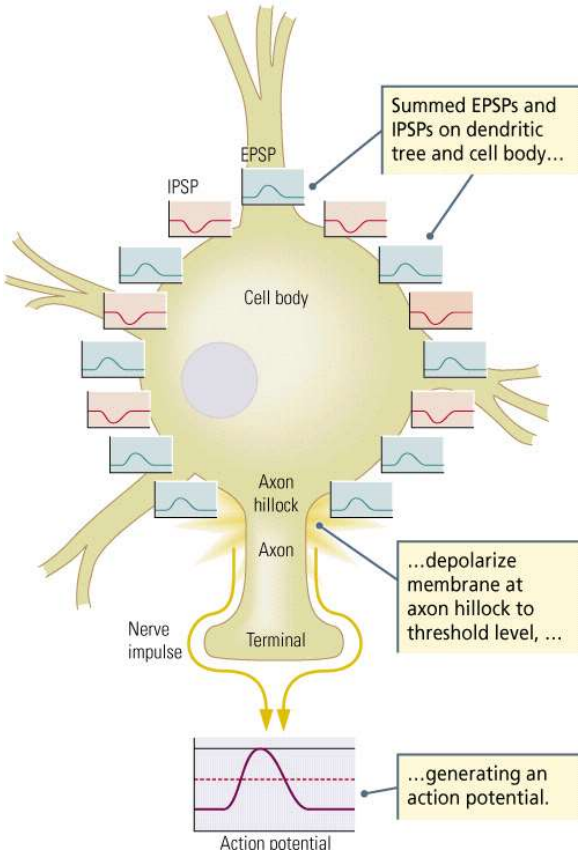
Arthurs & Boniface, 2002, *Trends in Neurosciences*

Neural Networks

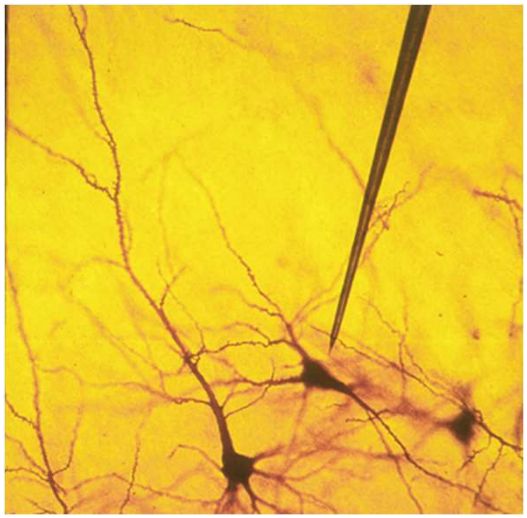


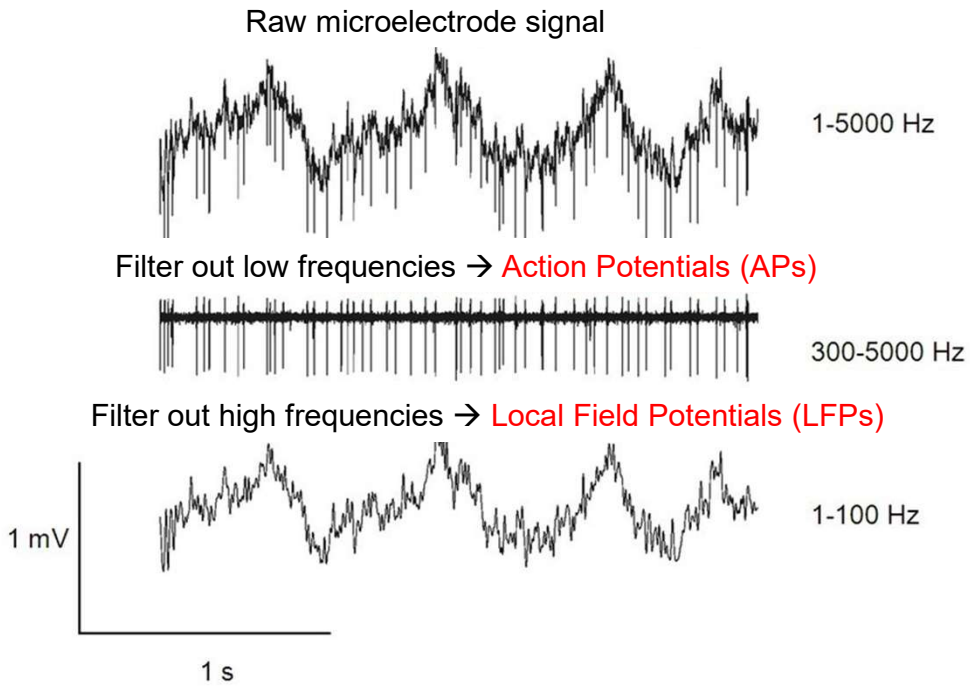
Post-Synaptic Potentials

- The inputs to a neuron (post-synaptic potentials) increase (excitatory PSPs) or decrease (inhibitory PSPs) the membrane voltage
- If the summed PSPs at the axon hillock push the voltage above the threshold, the neuron will fire an action potential



What does electrophysiology measure?





http://www.cin.uni-tuebingen.de/research/methods-in-neuroscience/networks.php

BOLD Correlations

Local Field Potentials (LFP)

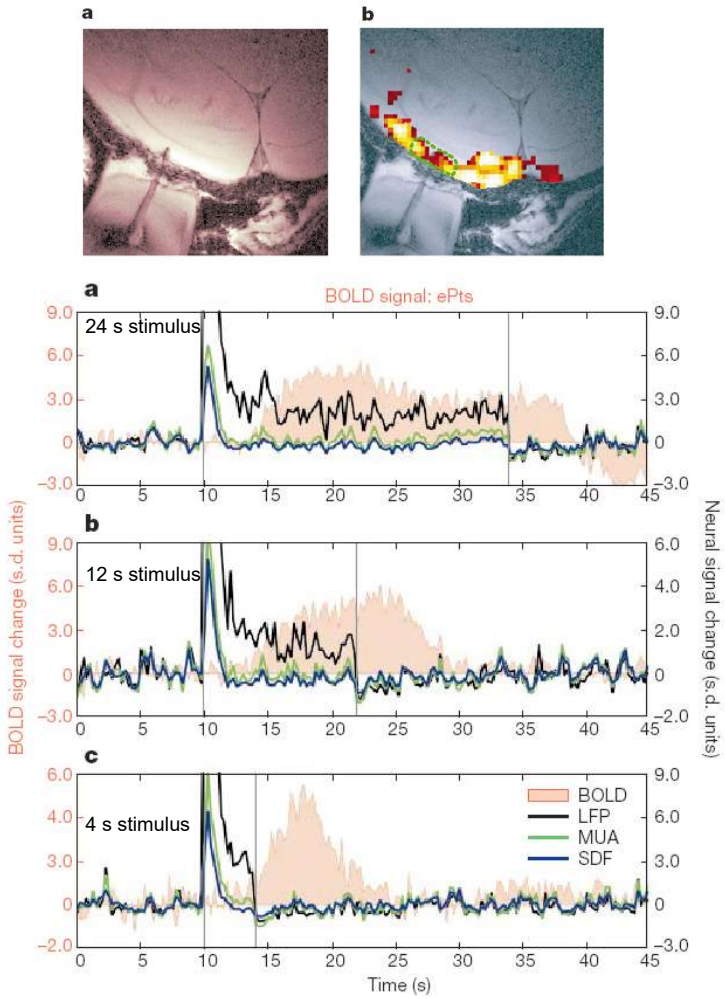
- reflect post-synaptic potentials
- similar to what EEG (ERPs) and MEG measure

Multi-Unit Activity (MUA)

- reflects action potentials
- similar to what most electrophysiology measures

Logothetis et al. (2001)

- combined BOLD fMRI and electrophysiological recordings
- found that **BOLD** activity is more closely related to **LFPs** than MUA

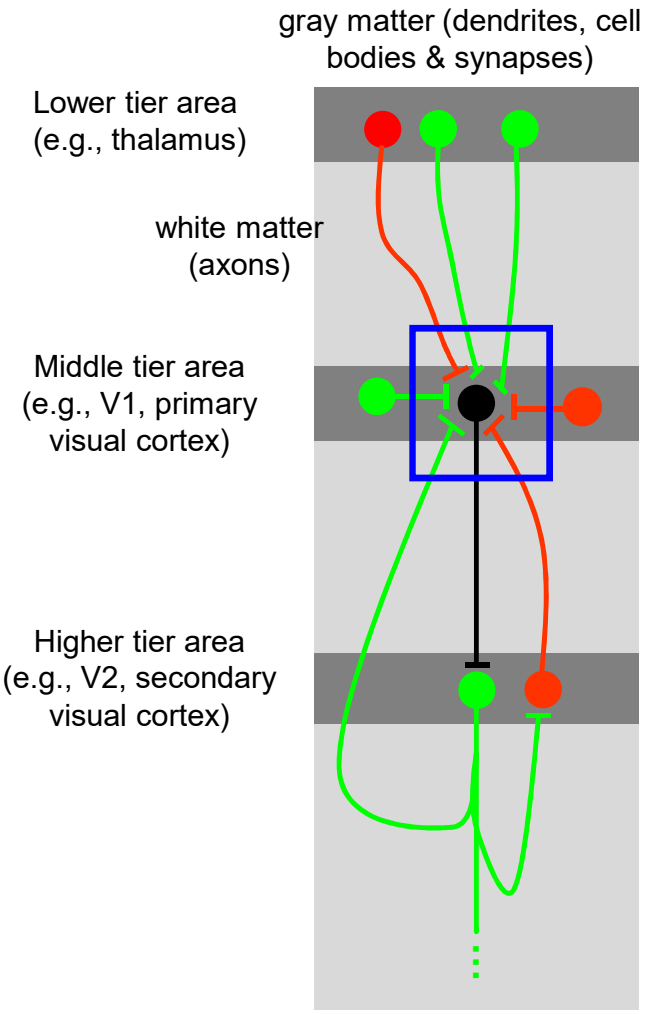


Logothetis et al., 2001, Nature

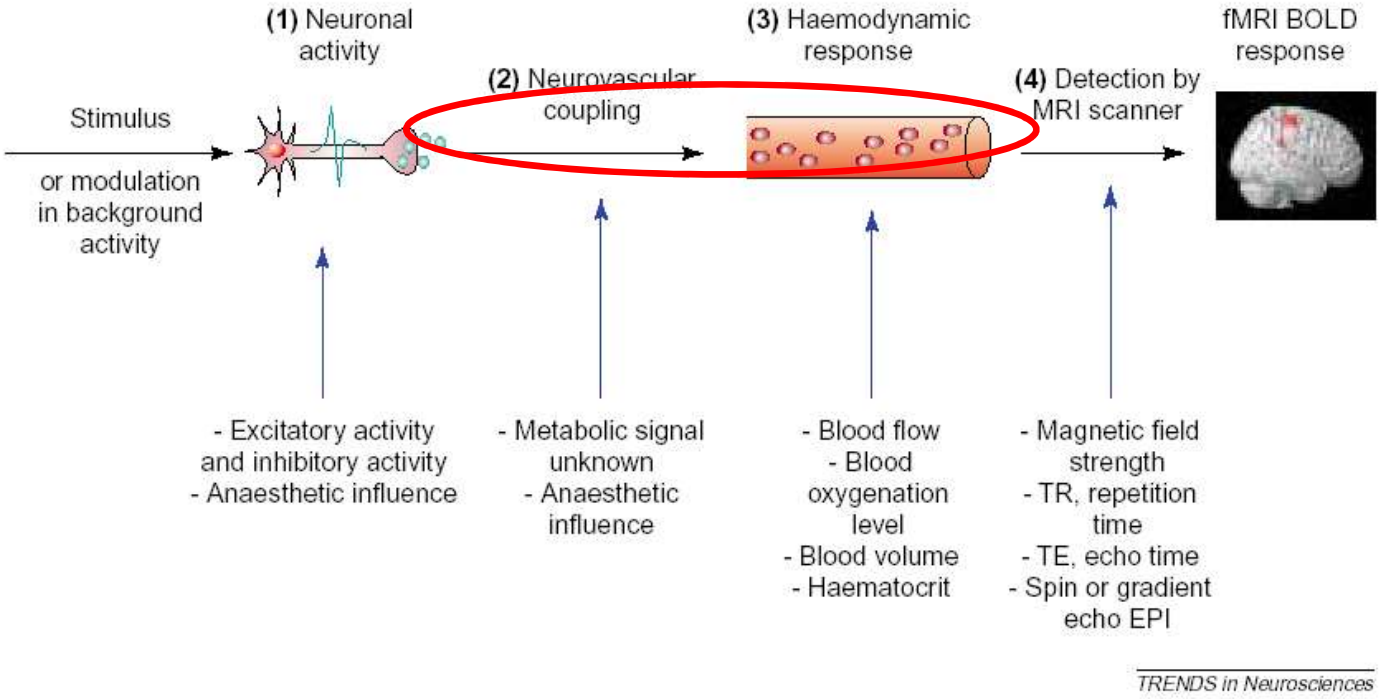
Even simple circuits aren't simple

Will BOLD activation from the blue voxel reflect:

- output of the black neuron (action potentials)?
- excitatory input (green synapses)?
- inhibitory input (red synapses)?
- inputs from the same layer (which constitute ~80% of synapses)?
- feedforward projections (from lower-tier areas)?
- feedback projections (from higher-tier areas)?

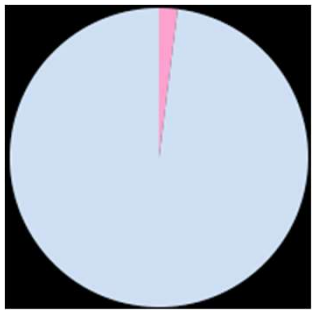


Stimulus to BOLD

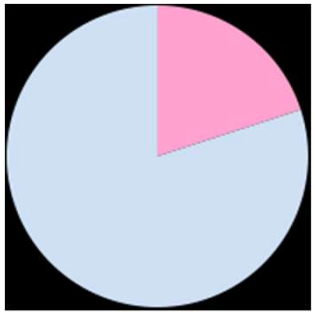


Arthurs & Boniface, 2002, *Trends in Neurosciences*

Brain and Blood

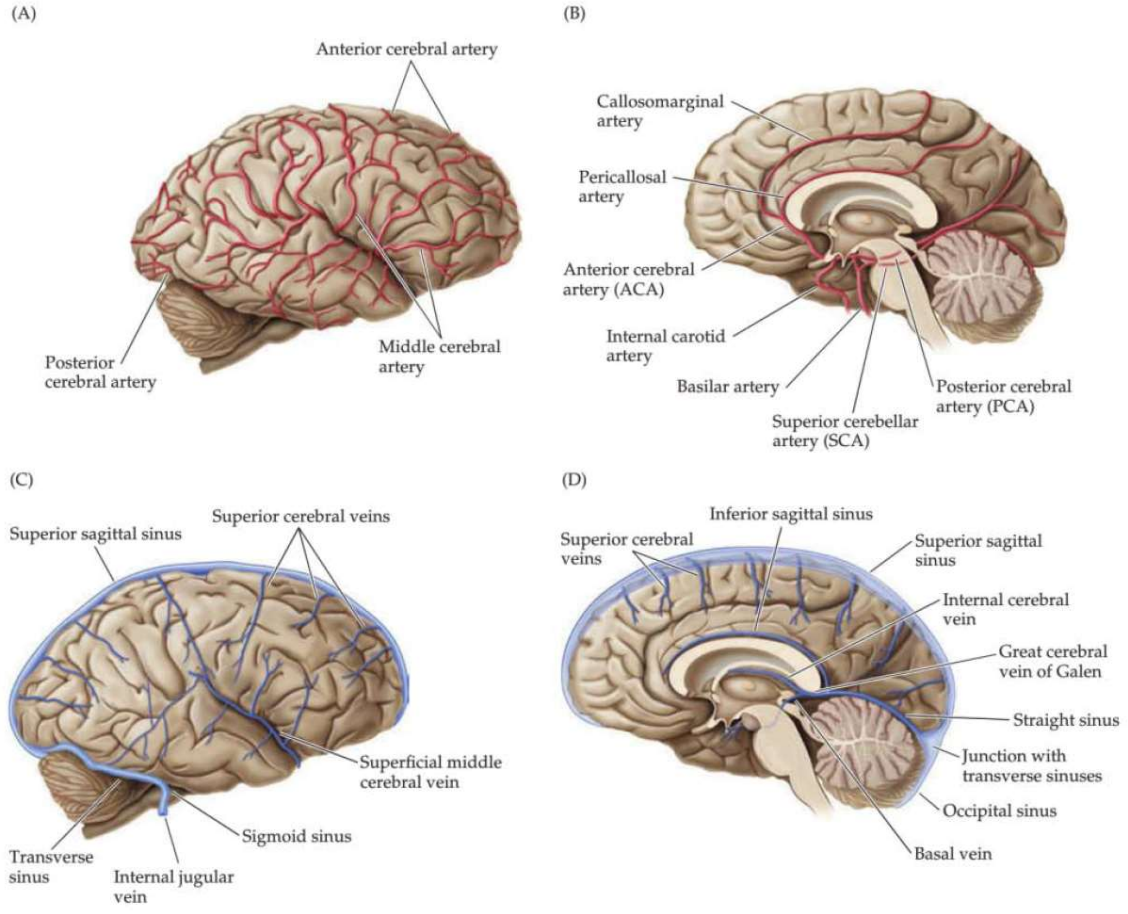


The brain is ~2% of the body by weight

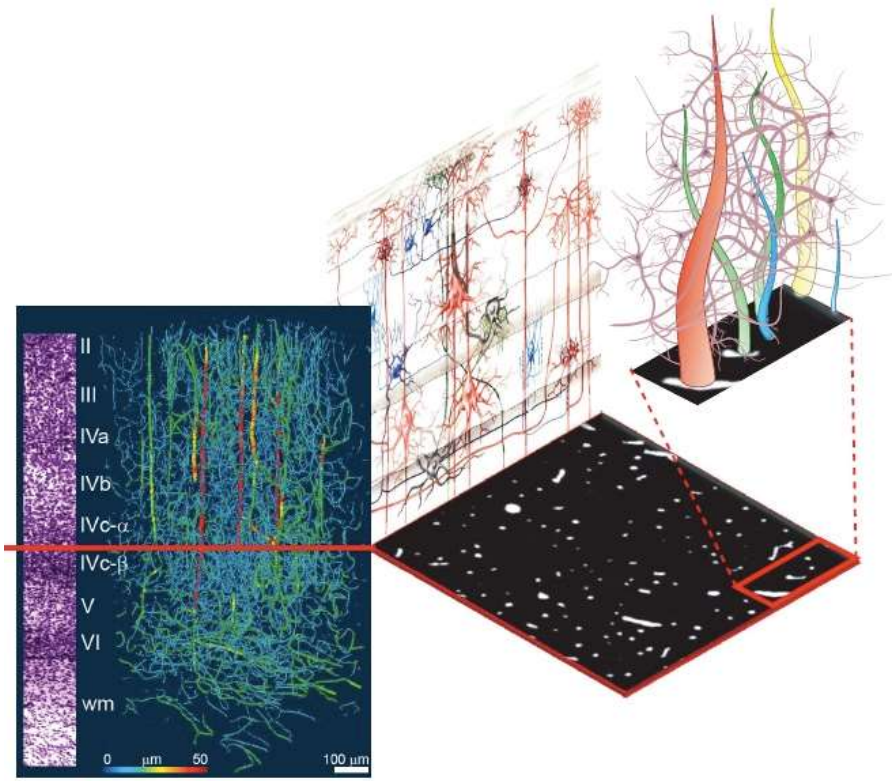


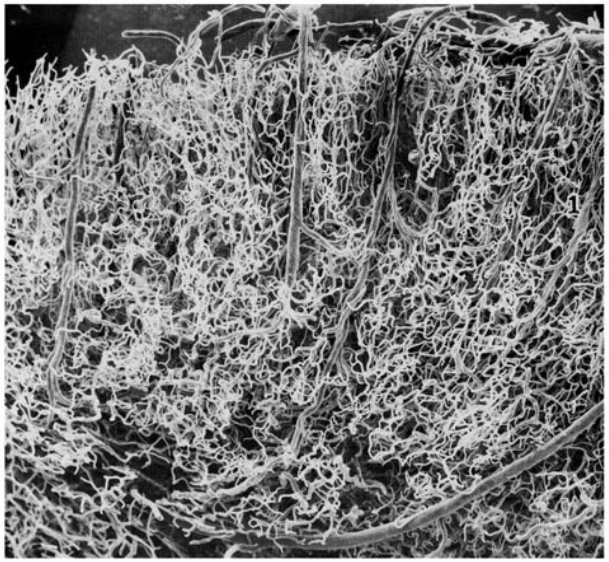
…but it uses about 20% of the body's oxygen supply and 20-25% of its glucose supply

Vascular system



Contents of a Voxel

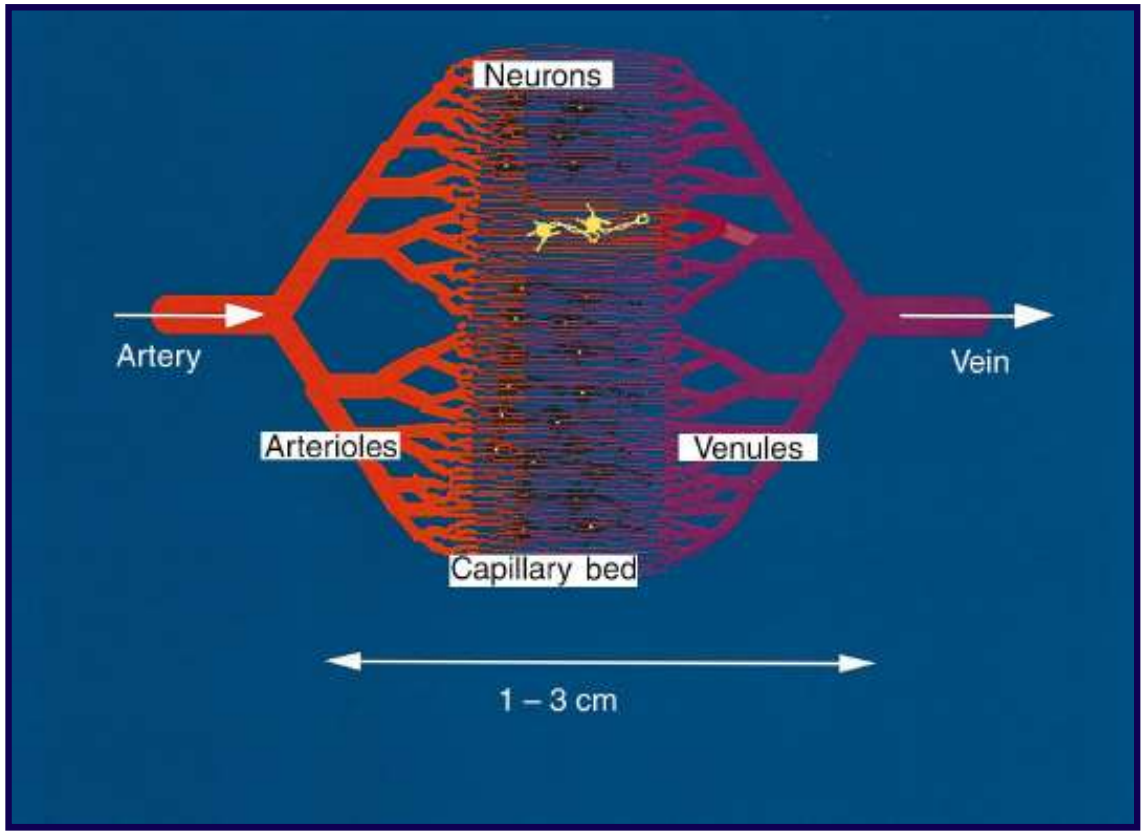




Capillary beds within the cortex

Logothetis, 2008, Nature
Duvernoy, Delon & Vannson, 1981, Brain Research Bulletin

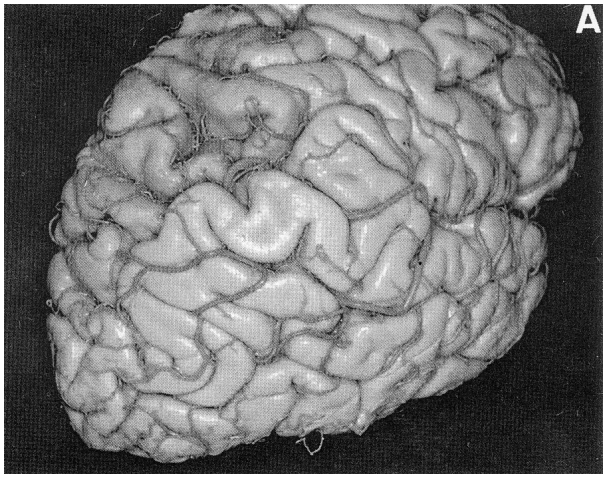
Vasculature: Brain vs. Vein



Menon & Kim, TICS

“Brain vs. Vein”

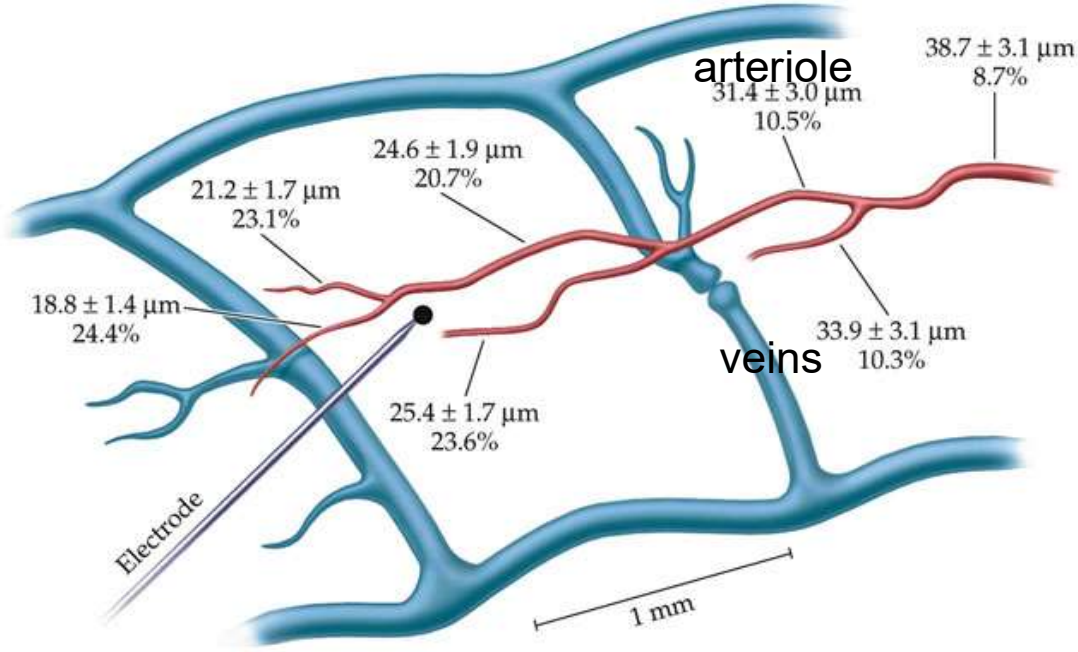
- large vessels produce BOLD activation further from the true site of activation than small vessels
- large vessels line the sulci and make it hard to tell which bank of a sulcus the activity arises from
- % signal change in large vessels can be considerably higher than in small vessels (e.g., 10% vs. 2%)
- activation in large vessels occurs up to 1 s later than in small ones



Ono et al., 1990, Atlas of the Cerebral Sulci

Upstream Effects

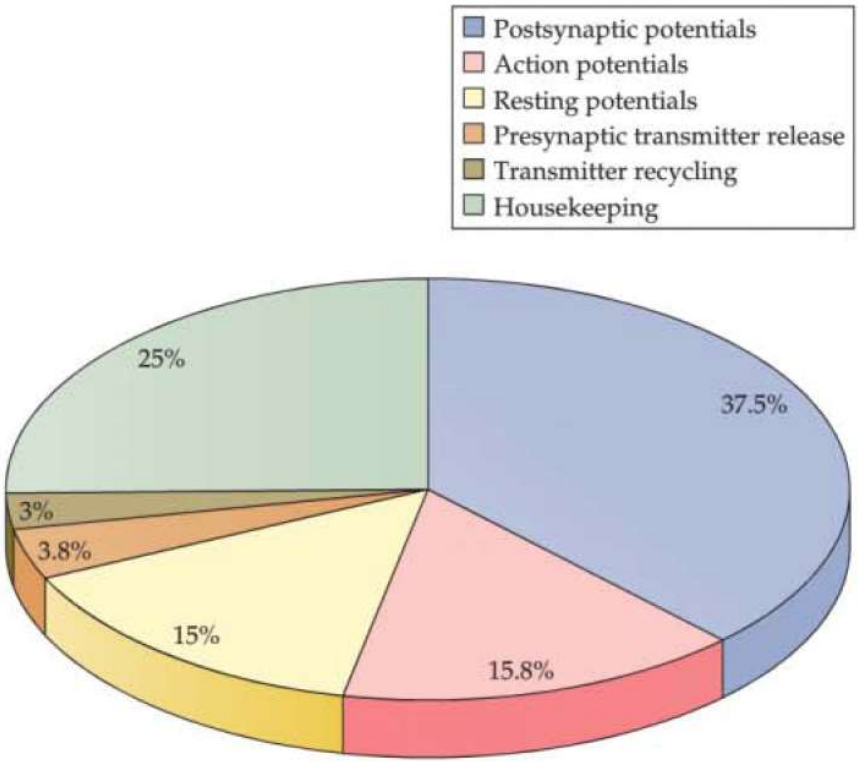
- biggest changes in arteriole dilation occurred near stimulation; however, effects could also be observed several mm upstream



***Functional Magnetic Resonance Imaging 2e*, Figure 6.16**

Huettel, et al., 2nd ed.

Energy Budget

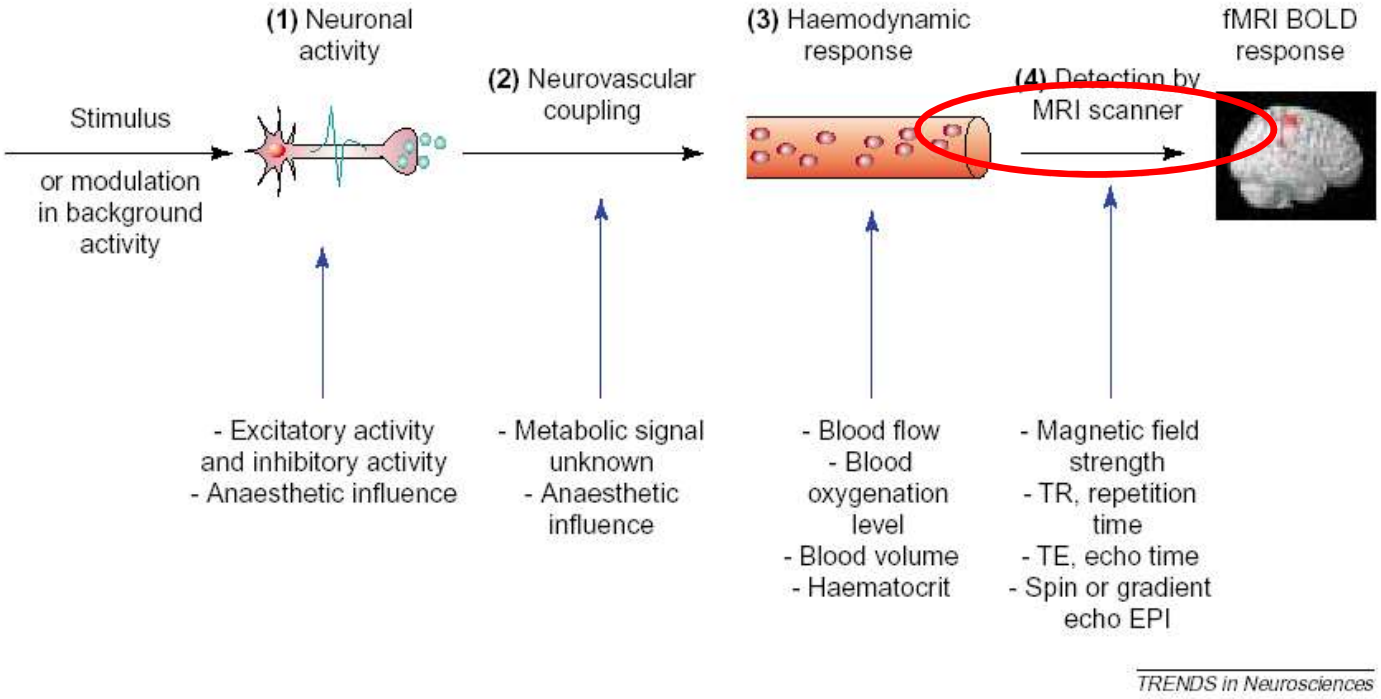


Huettel, Song & McCarthy, Functional Magnetic Resonance Imaging, 3rd ed.

What about inhibitory synapses?

- GABA = inhibitory neurotransmitter
- less metabolically demanding than excitatory (glutamatergic) activity
- GABA can be taken up presynaptically rather than recycled through astrocytes
- Therefore, neurotransmission at inhibitory synapses likely influences the BOLD signal less than at excitatory synapses

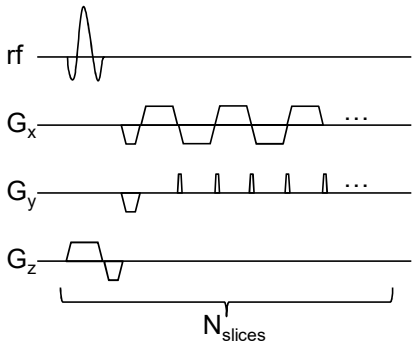
Stimulus to BOLD



Arthurs & Boniface, 2002, *Trends in Neurosciences*

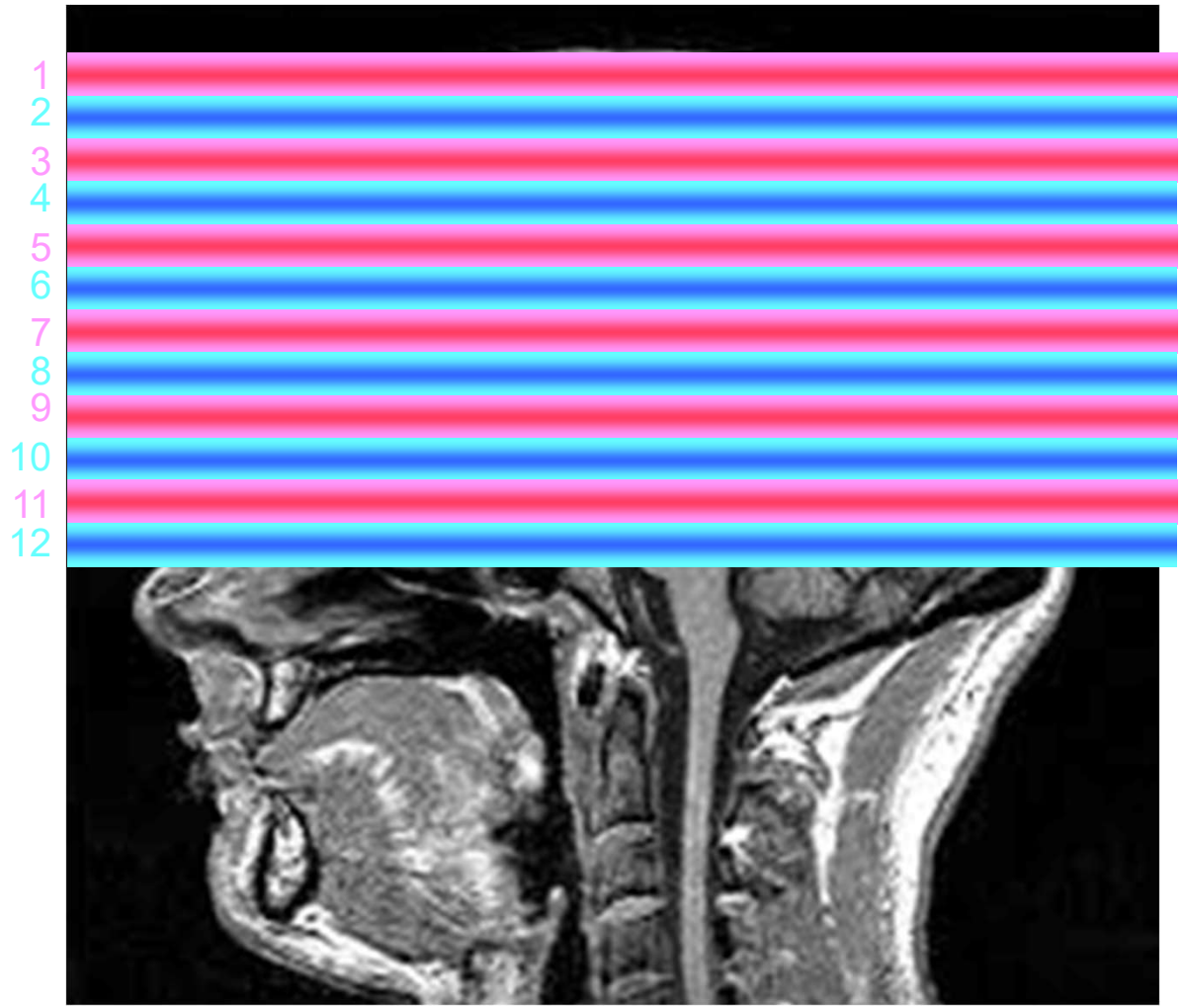
2D-EPI

- Efficient sequence with long gradient readouts
- Advantages:
  - Fast (compared to anatomical scanning).
  - Naturally BOLD weighted.
- Disadvantages:
  - Acquiring many slices is quite slow compared to the BOLD response.
  - Distortions
  - Through-slice dephasing

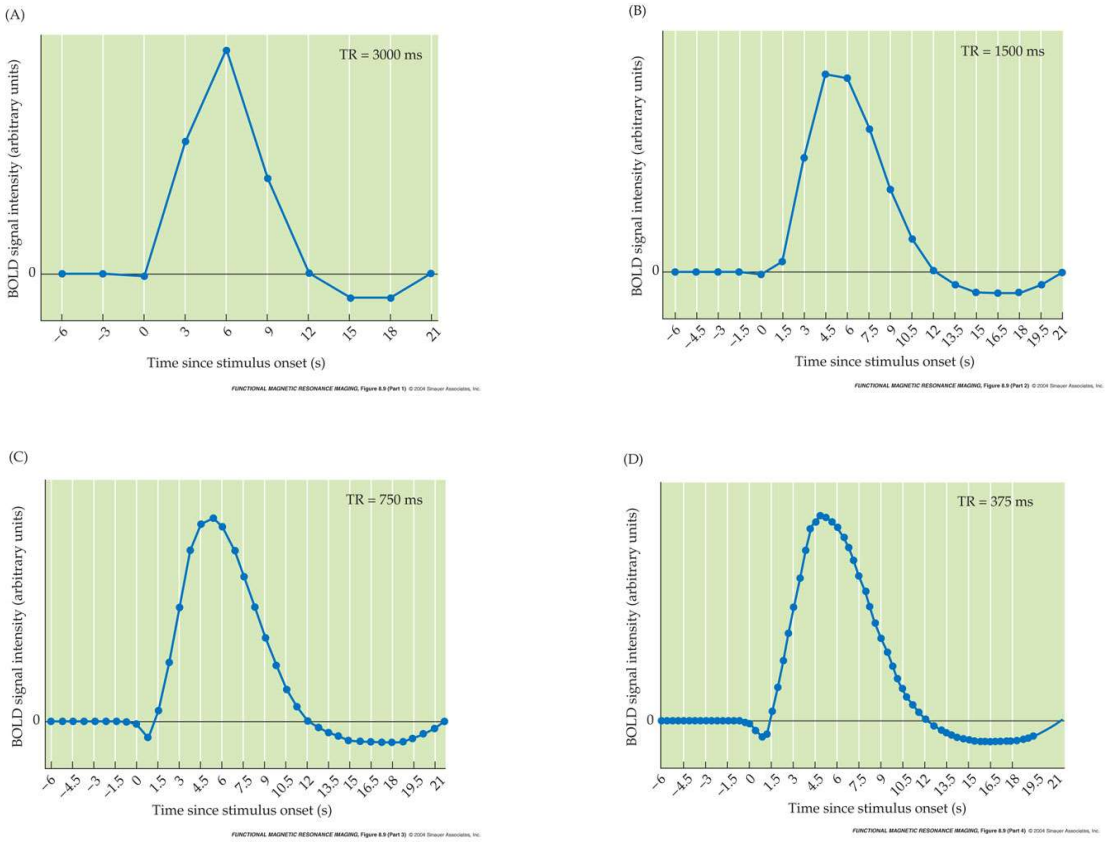


1 slice in TR/N_{slices}

Typical slice acquisition order



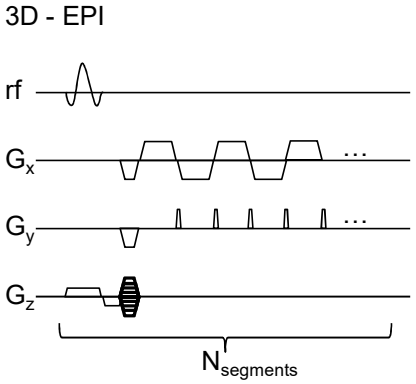
Sampling Rate



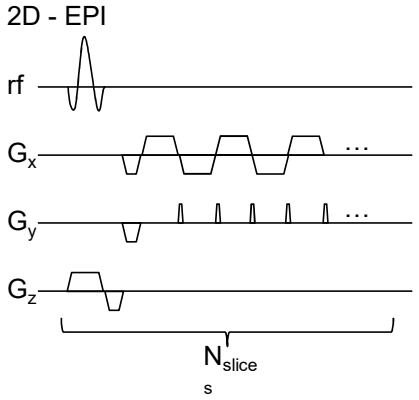
Huettel, Song & McCarthy, 2004, Functional Magnetic Resonance Imaging

3D-EPI

- Efficient sequence with long gradient readouts
- Third dimension in k-space sampled with phase-encoding steps
- TR ≠ volume acquisition time
- Much smaller α



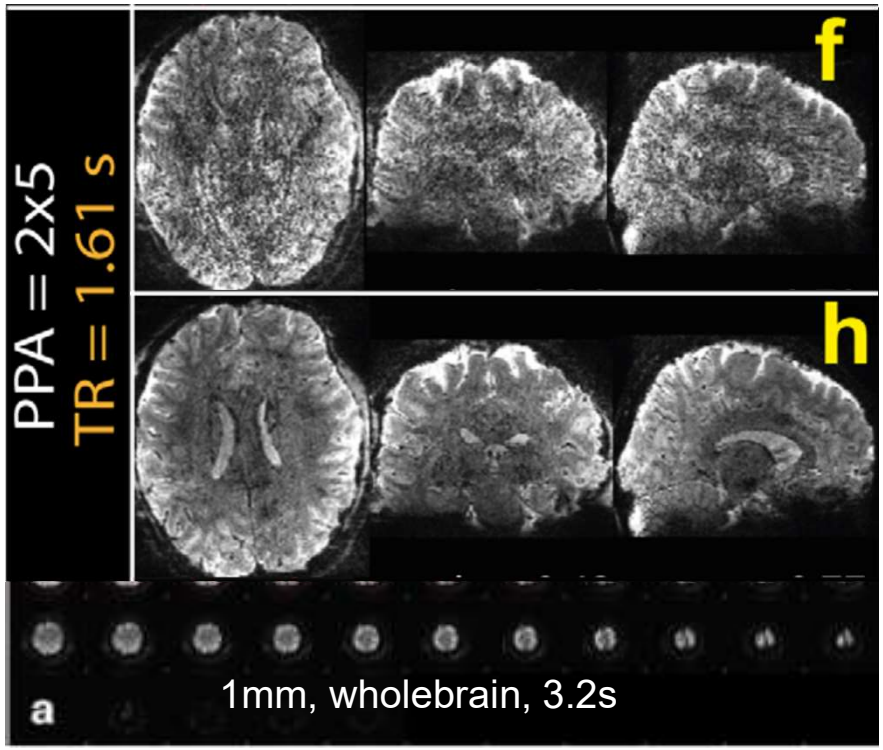
1 segment per TR



1 slice in TR/N_{slices}

3D-EPI undersampling

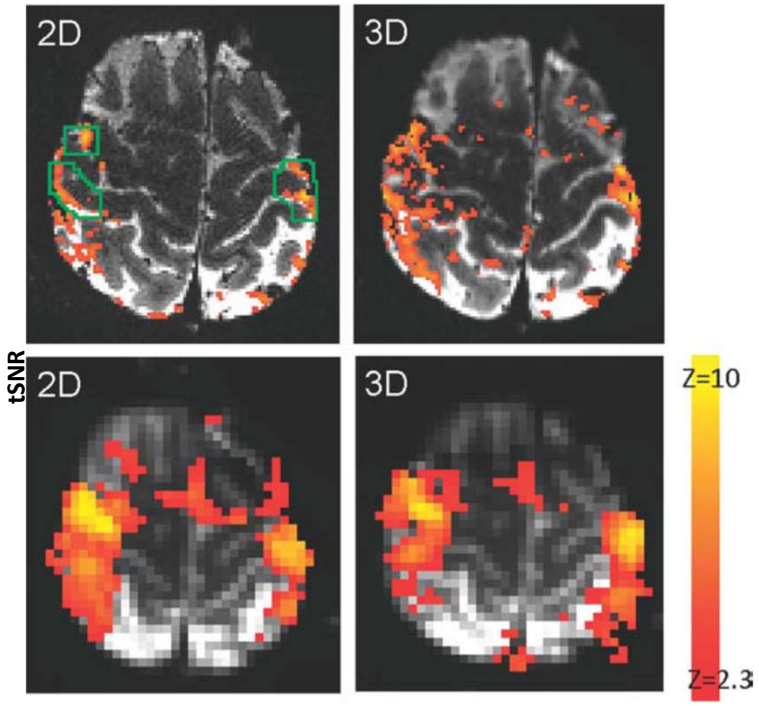
- 2 phase-encoding directions = 2 undersampling directions[1]
- Undersampling in the slice-direction significantly speeds up volume acquisitions
- CAIPIRINHA can further improve parallel imaging[2]



[1]Poser et al, 2010, Neuroimage [2]Narsude et al, 2016, MRM

3D-EPI SNR

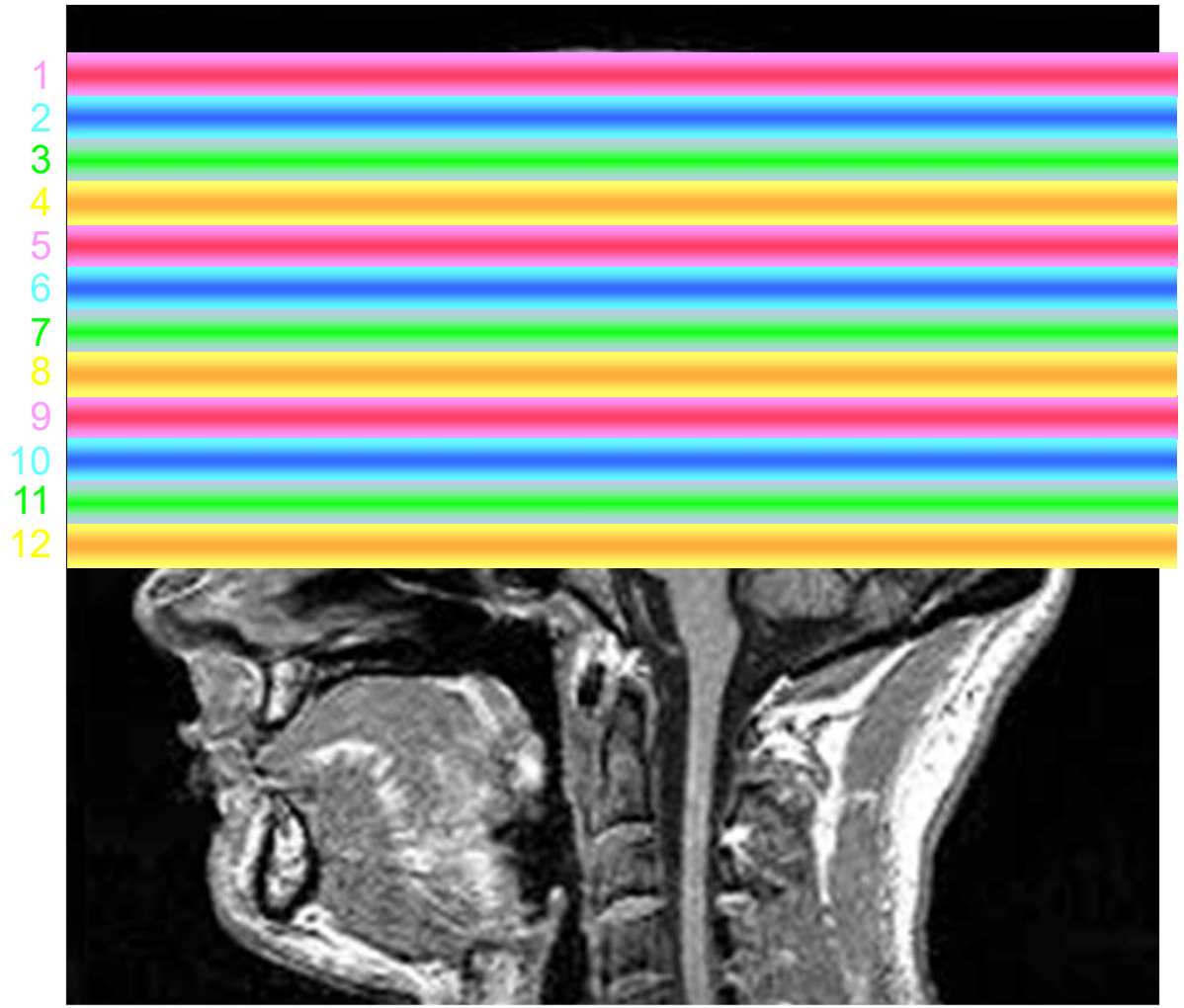
- The **image SNR** of 3D-EPI is **higher** than for 2D-EPI
- The **temporal** stability is strongly affected by **physiological noise**



$$tSNR = SNR_0 / (1 + \lambda^2 * SNR_0^2)^{1/2}$$

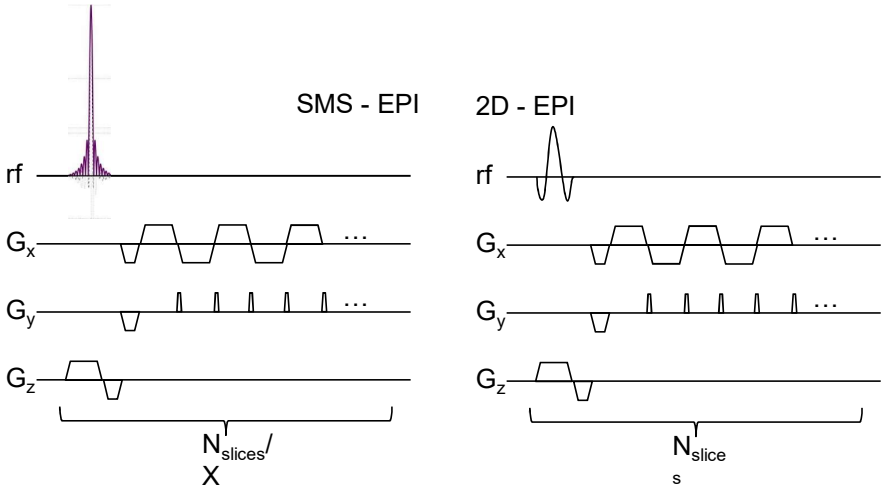
[1]Krüger et al, 2001, MRM [2]van der Zwaag et al, 2012, MRM

Multiband Imaging



Multiband / SMS

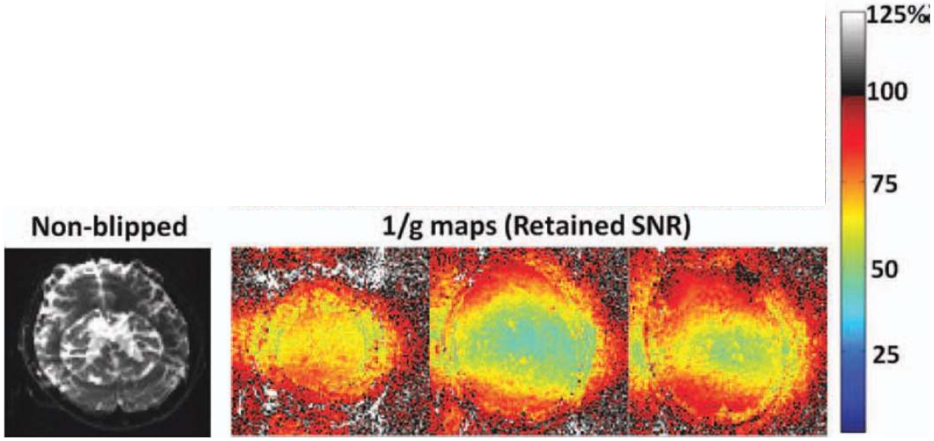
- Pulse replacement by multi-band rf-pulse
- More complicated profile means higher peak power or more SAR[1]
- Shorter TR means smaller optimal flip angle, lower SAR

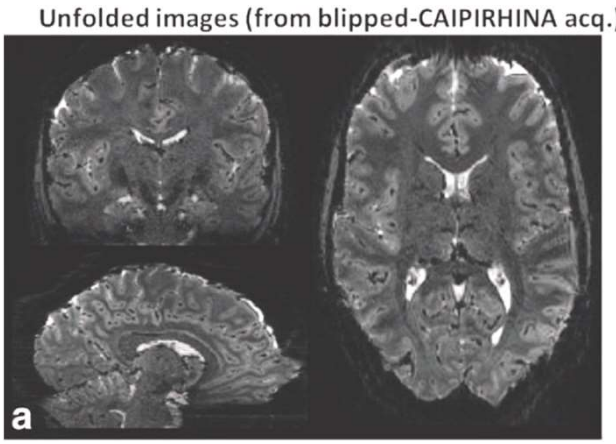


[1]Auerbach et al, MRM 2013

Multiband / SMS undersampling

- Simultaneous excitation means signal from different slices needs to be disentangled
- Improved unfolding by shifting the slices within the image FOV to reduce overlap[1]



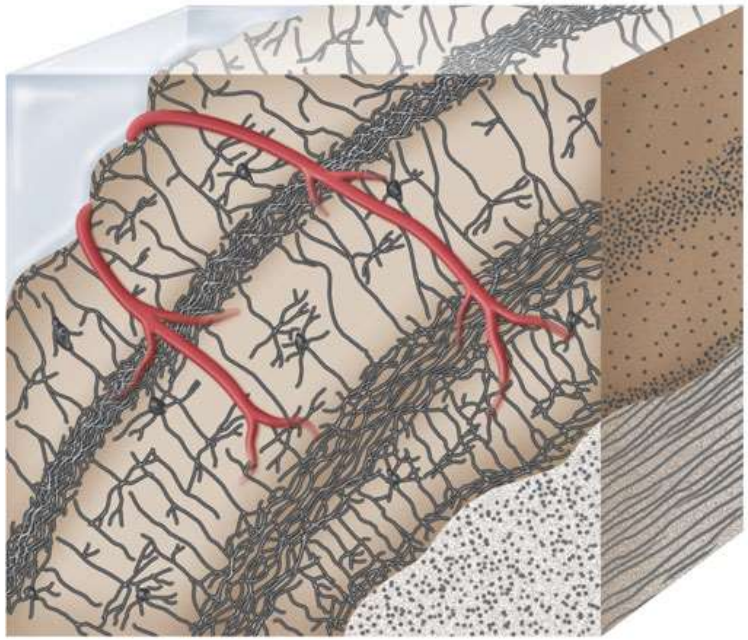


1-mm, 3x2 accelerated images, TR=2.88s

[1]Setsompop et al, 2012, MRM

Spatial resolution

- The fMRI signal occurs in gray matter (where the synapses and dendrites are) and downstream (in the veins)
- If your voxel includes white matter (where the axons are), fluid, or space outside the brain, you effectively water down your signal



FUNCTIONAL MAGNETIC RESONANCE IMAGING, Figure 8.3 © 2004 Sinauer Associates, Inc.

[fMRI for Dummies]

What limits spatial resolution

- Hardware
  - Large matrix sizes require strong gradients
- Noise
  - smaller voxels have lower SNR
- Minimum TE
  - Optimum BOLD contrast is obtained at TE≈T2*
- Head motion
  - the smaller your voxels, the more contamination head motion induces
- Temporal resolution
  - the smaller your voxels, the longer it takes to acquire the same volume
- Vasculature
  - depends on pulse sequence (GE/SE)

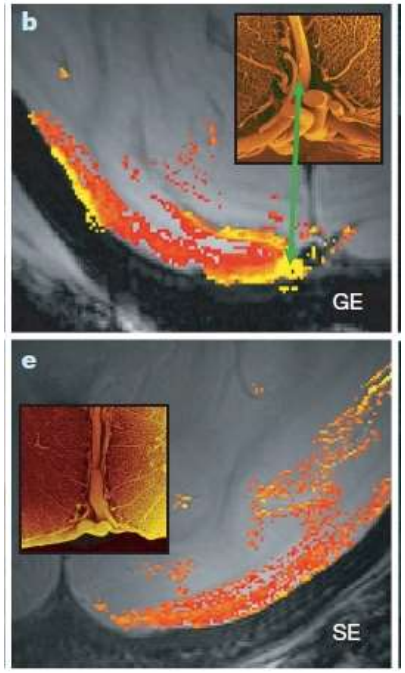
Gradient Echo vs. Spin Echo

Gradient Echo

- high SNR
- strong contribution of vessels

Spin Echo

- lower SNR
- weaker contribution of vessels



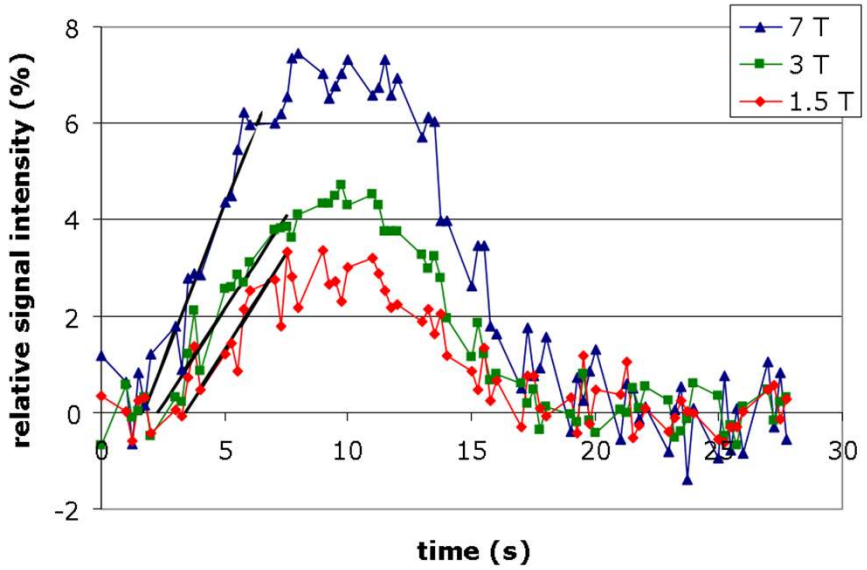
Logothetis, 2008, Nature

Field strength (7T vs 3T)

PROS	CHALLENGES
Higher SNR$\propto B_0^{1\text{-}1.5}$	
Increased susceptibility related contrast	More susceptibility induced distortion (EPI)
Longer T_1 (T_1 contrast and perfusion)	Longer T_1 (slower imaging)
	B_1 inhomogeneity, high SAR
Increased T_2 contrast	Shorter T_2 (less time to image)
Increased T_2^* /BOLD contrast	Shorter T_2^* (less time to image)
Increase in BOLD specificity	

increased BOLD signal

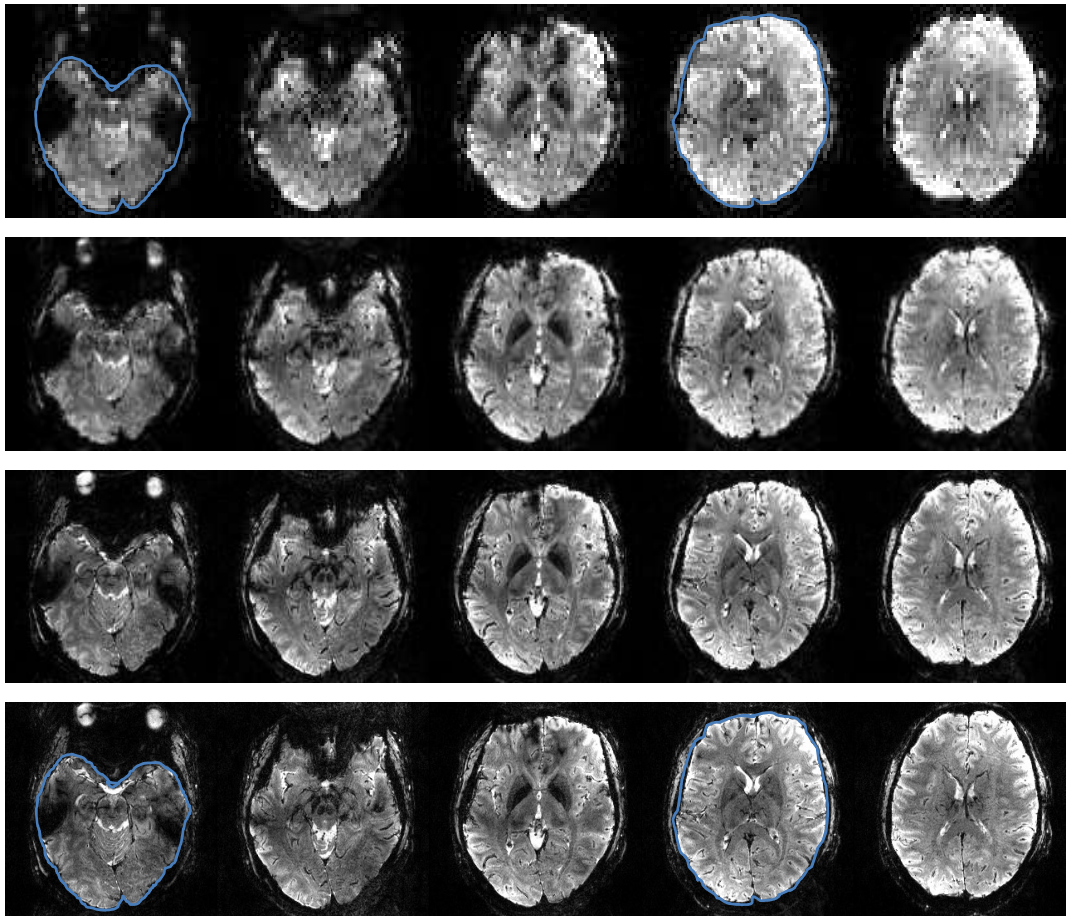
- Motor task, 3 B_0's
- Same subject
- fixed ROI
- timecourses TE≈T_2^*



[1]van der Zwaag et al (2009) Neuroimage

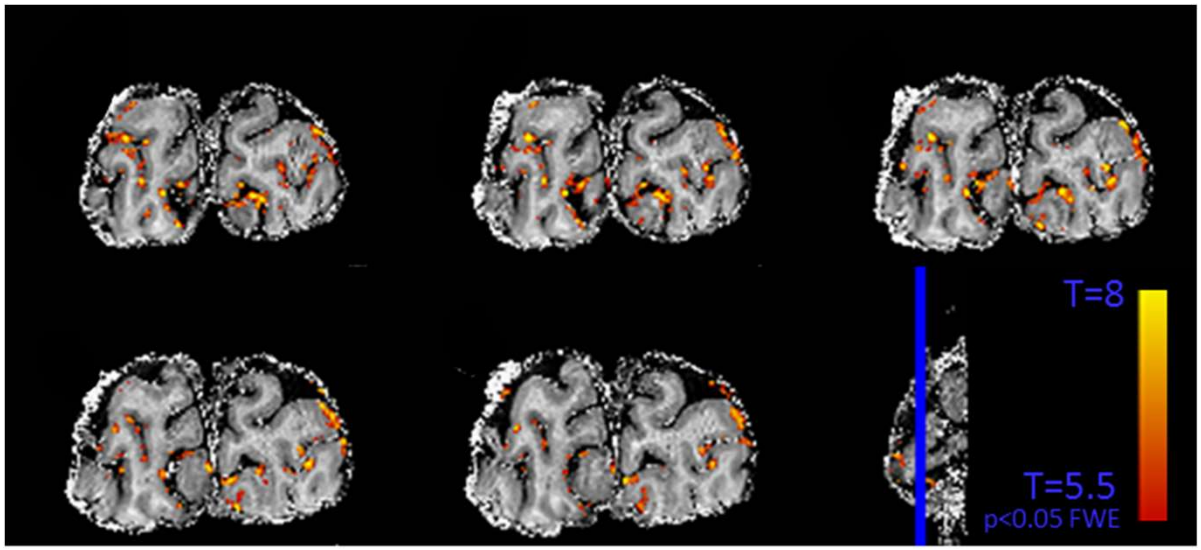
Susceptibility-induced dephasing

- 3*3*2 mm :
- 2*2*2 mm :
- 1.2*1.2*2 mm :
- 0.8*0.8*2 mm :

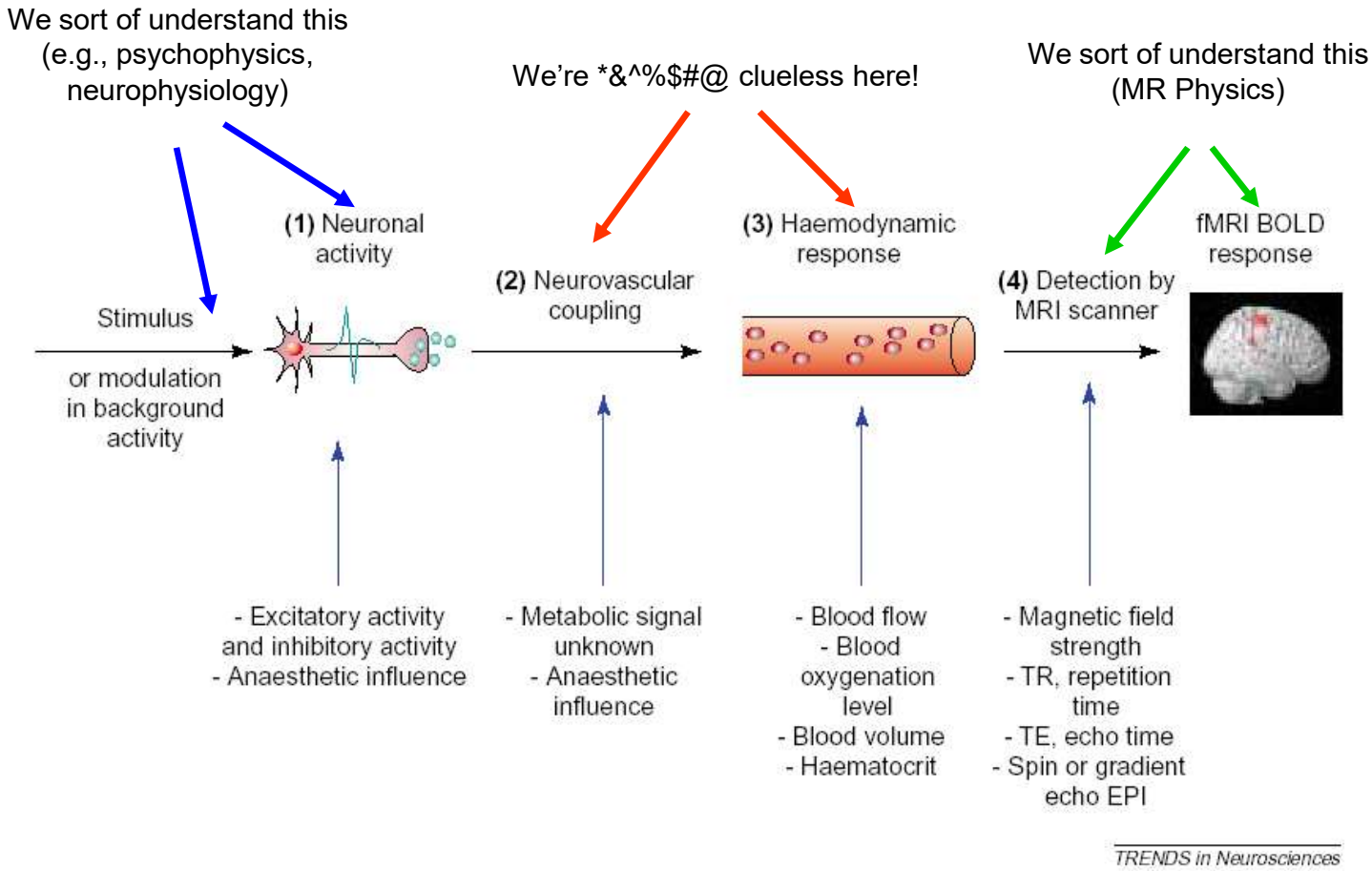


0.7 mm^3 voxels, visual cortex

- 7T acquisition, 4 minutes functional run
- Background T_1-weighted EPI ($T_1$23DEPI)
- Visual stimulus, partial brain coverage, 0.7mm, 4s TR



The Concise Summary



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Questions?