Basic tradeoffs and constraints in fMRI methodology and applications

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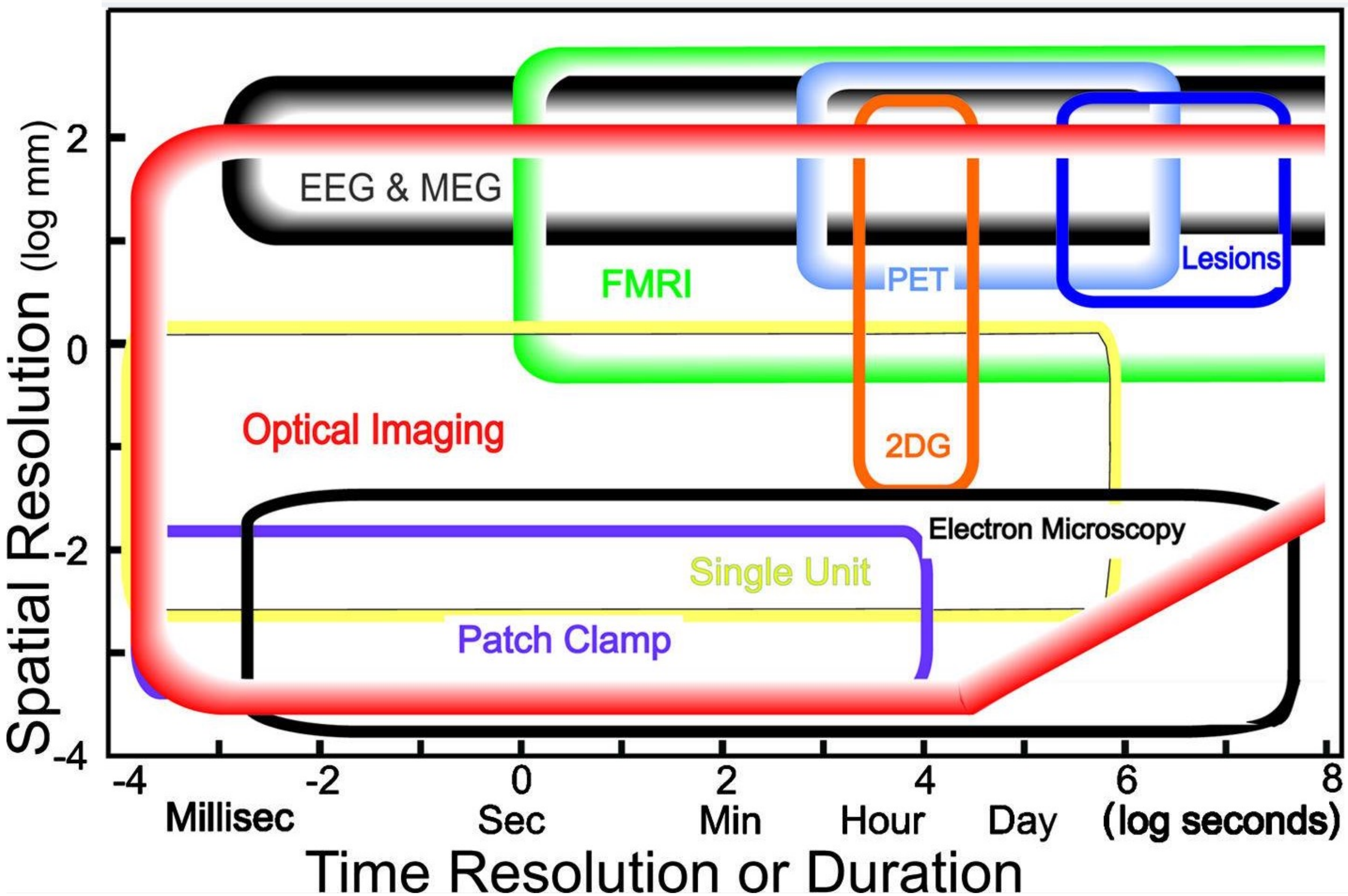
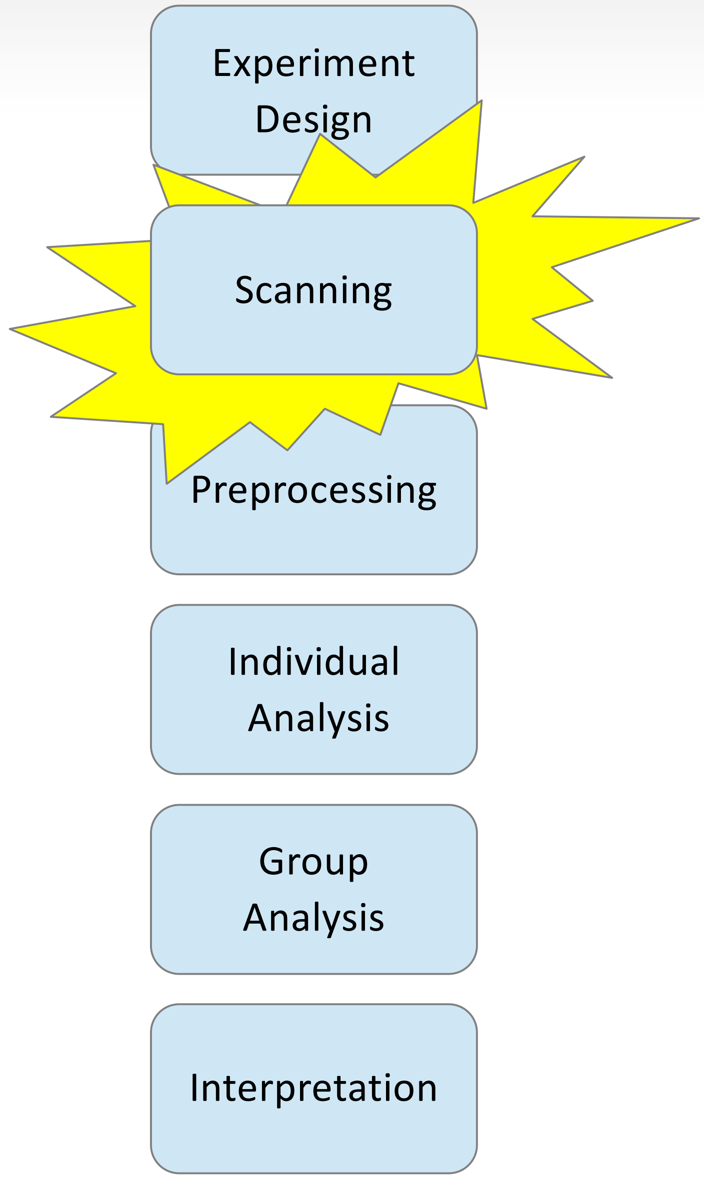
fMRI in temporal – spatial perspective



Grinvald A. PNAS (2005)

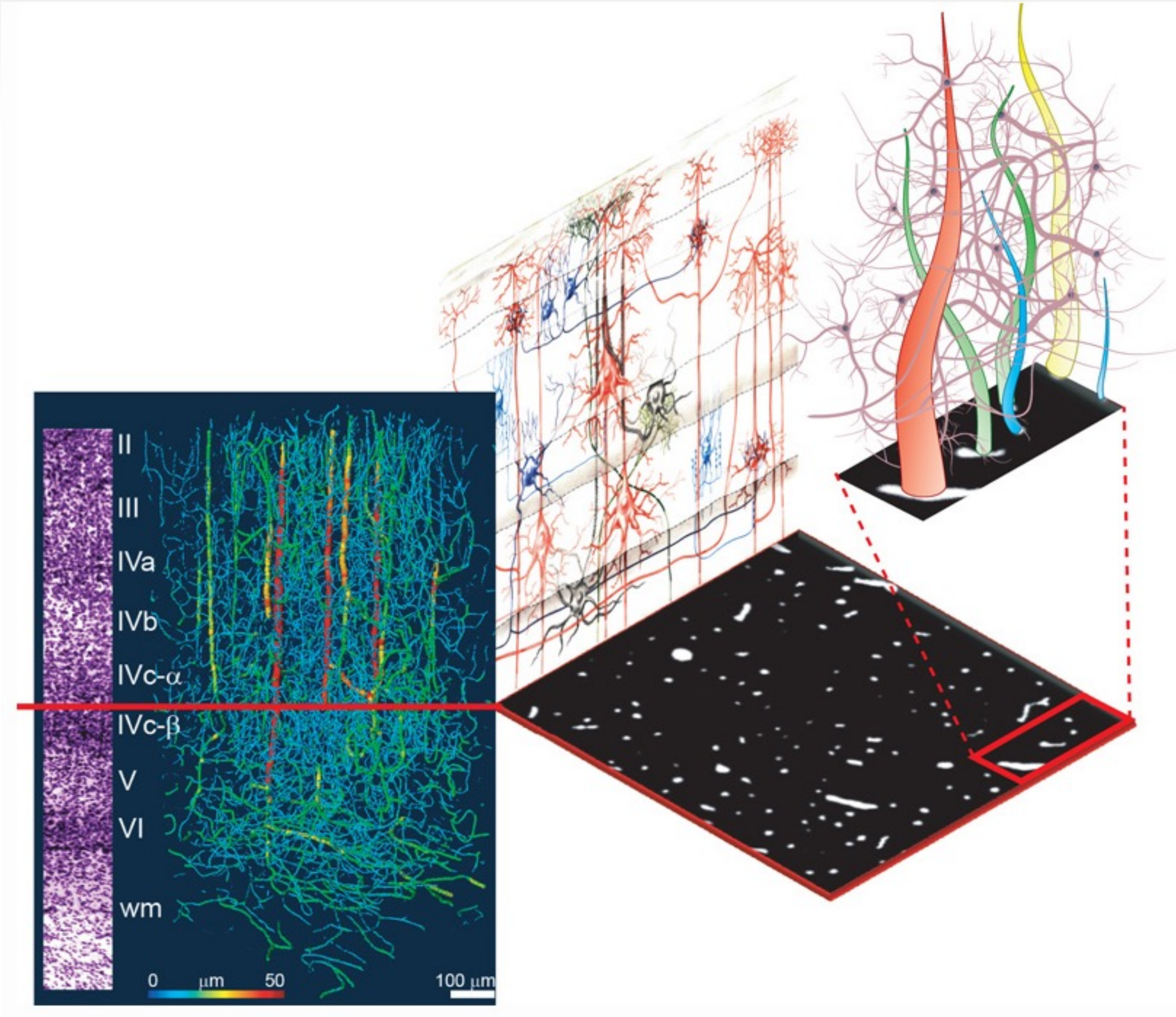
fMRI data pipeline



Outline

- Limitations based on the biophysical constraints
  - voxel contents
  - neurovascular coupling
  - hemodynamic response
- Limitations based on imaging constraints
  - Space – time tradeoffs (optimal voxel size)
  - Pulse sequence contrasts
- Summary

What's in a voxel?



- Neurons
- Synapses
- Axons
- Dendrites

- Vasculature
- Capillaries
- Aterioles/venules
- Arteries/Veins

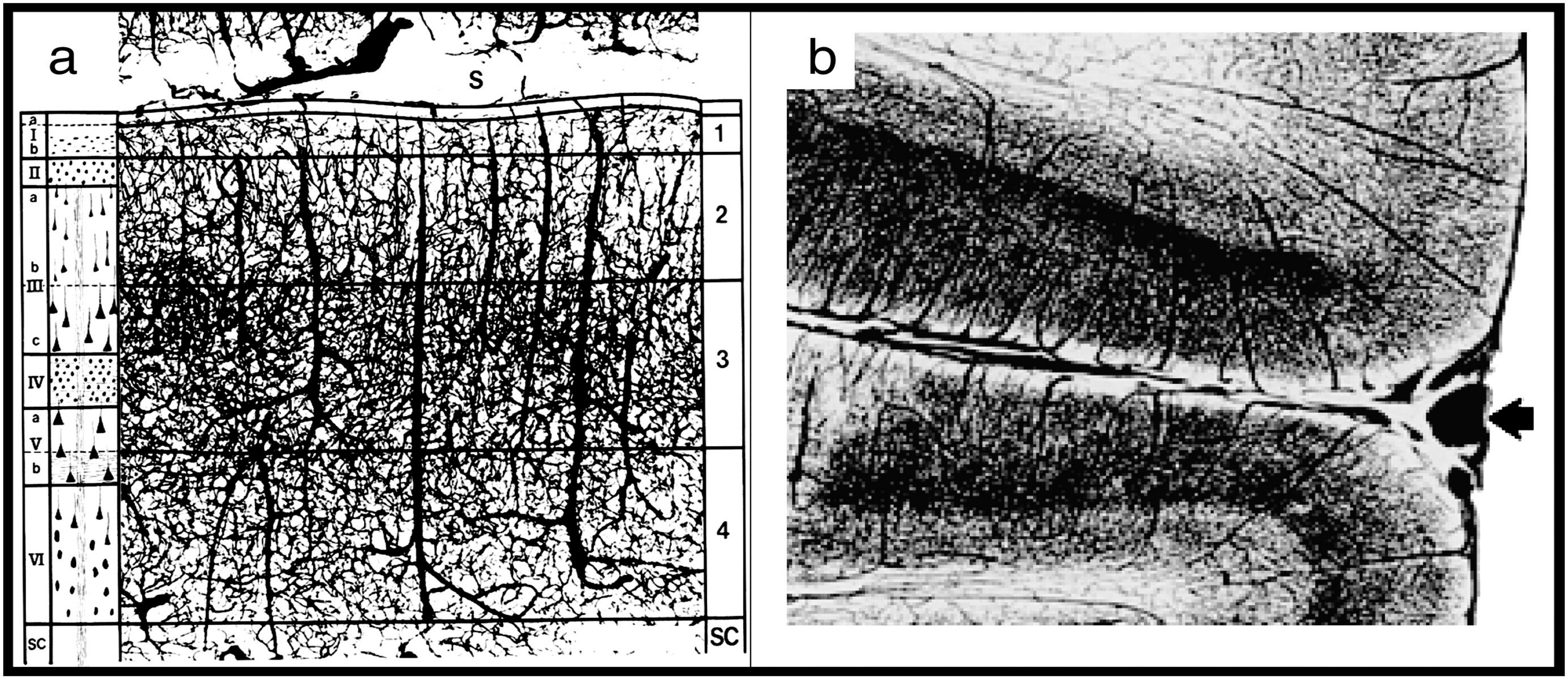
Logothetis NK, Nature (2008)

Average size of fMRI voxels

- In plane resolution of 9-16 mm^2 (3x3, 4x4)
- Slice thickness 5-7 mm
- Average voxel size: 55 mm^3

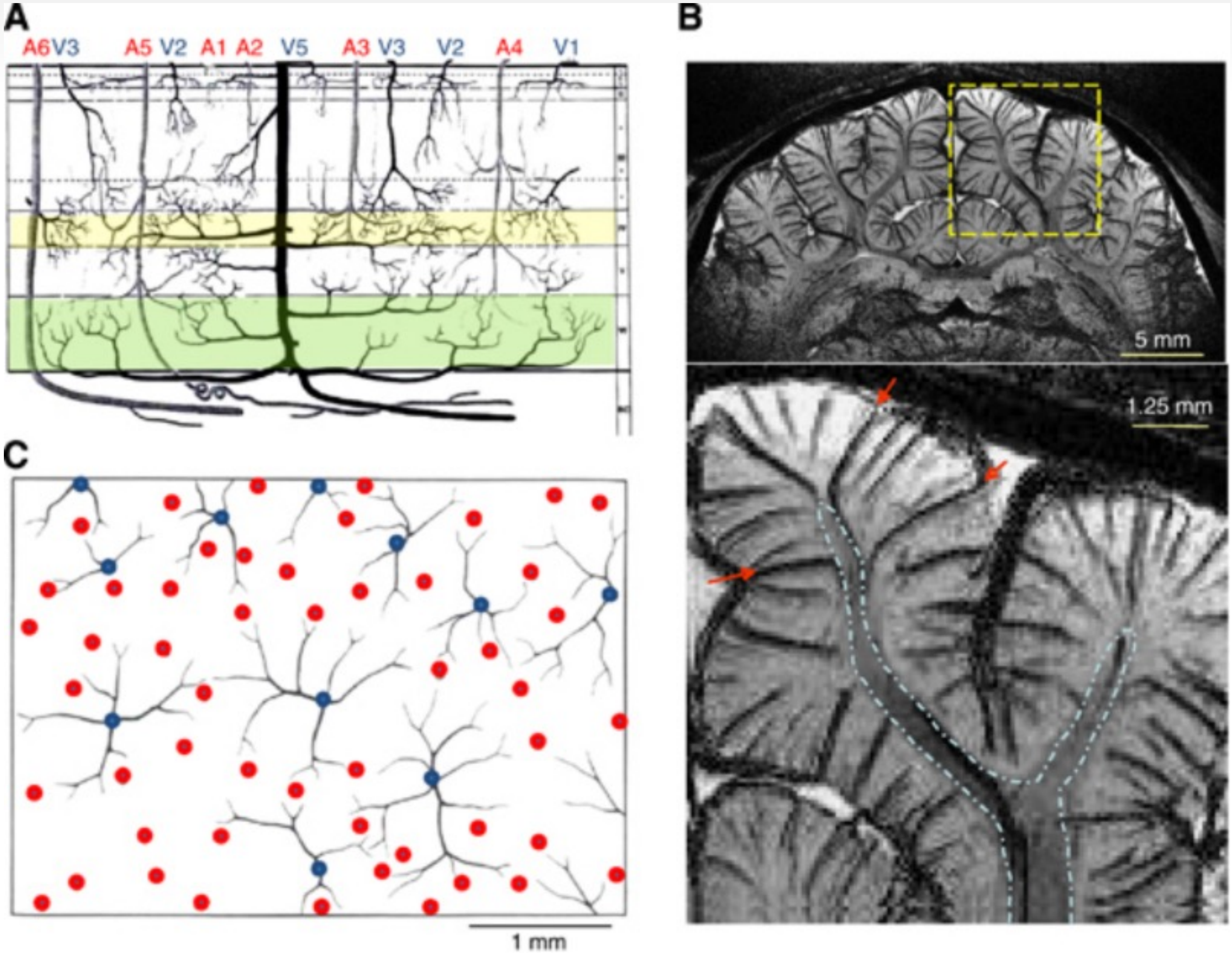
- 5.5 million neurons
- 2.2-5.5 10^{10} synapses
- 22 km of dendrites
- 220 km of axons

And vasculature ...

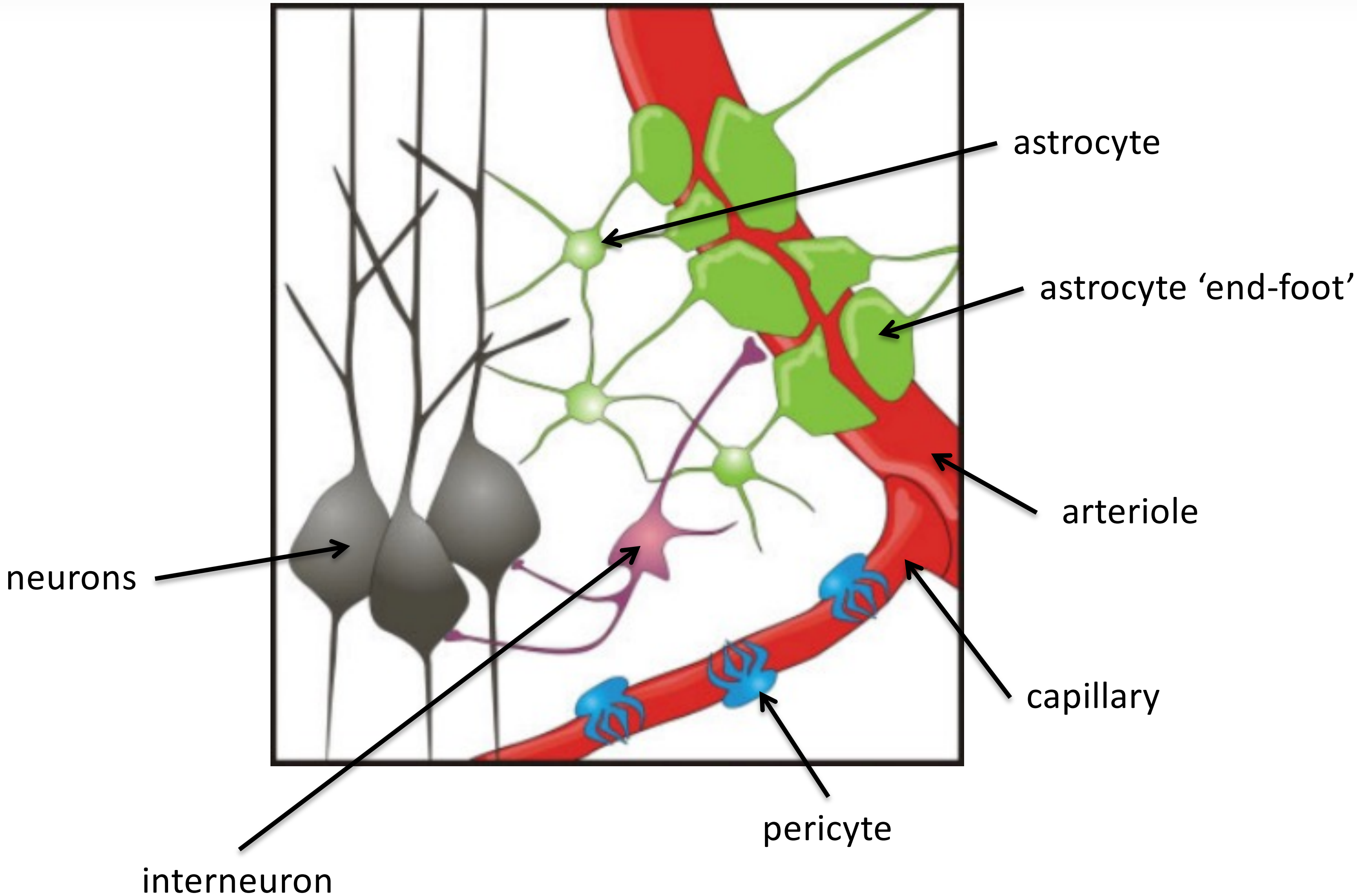


Duvernoy, Brain Res. Bull. (1981)

Spatial inhomogeneity of vasculature

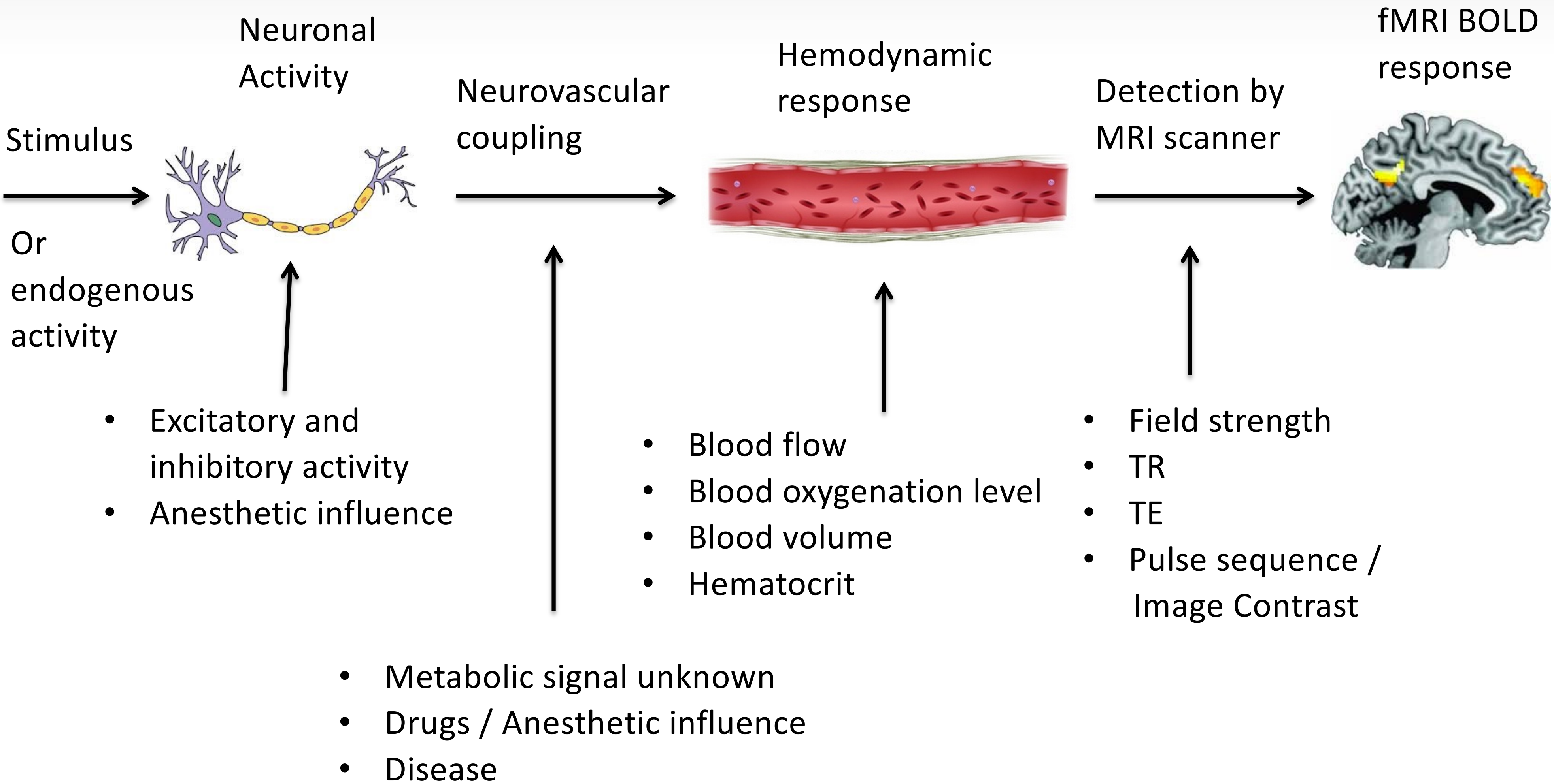


Neurovascular coupling



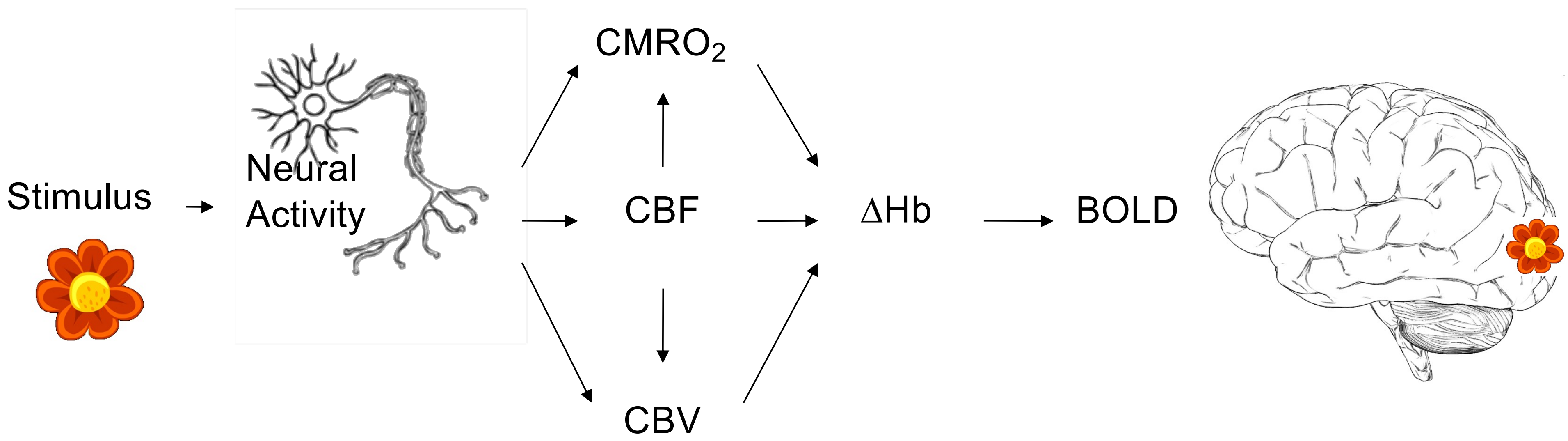
http://orion.bme.columbia.edu/~hillman/Brain_Imaging.html

Hemodynamic response and BOLD signals



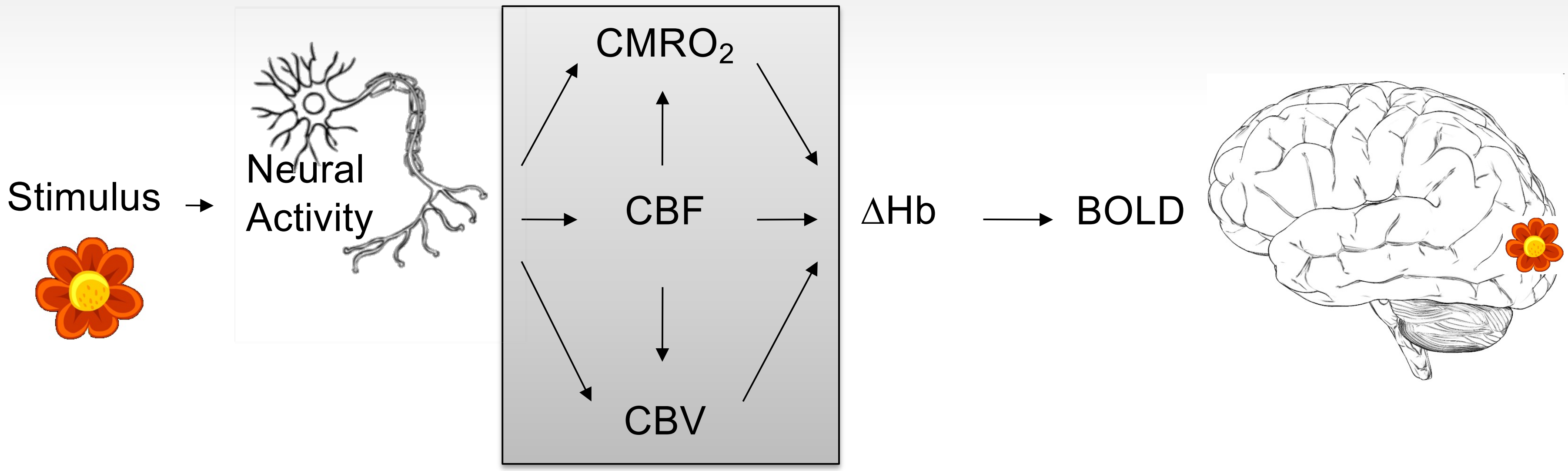
Modified from Arthurs and Boniface, Trends in Neuroscience, 2002

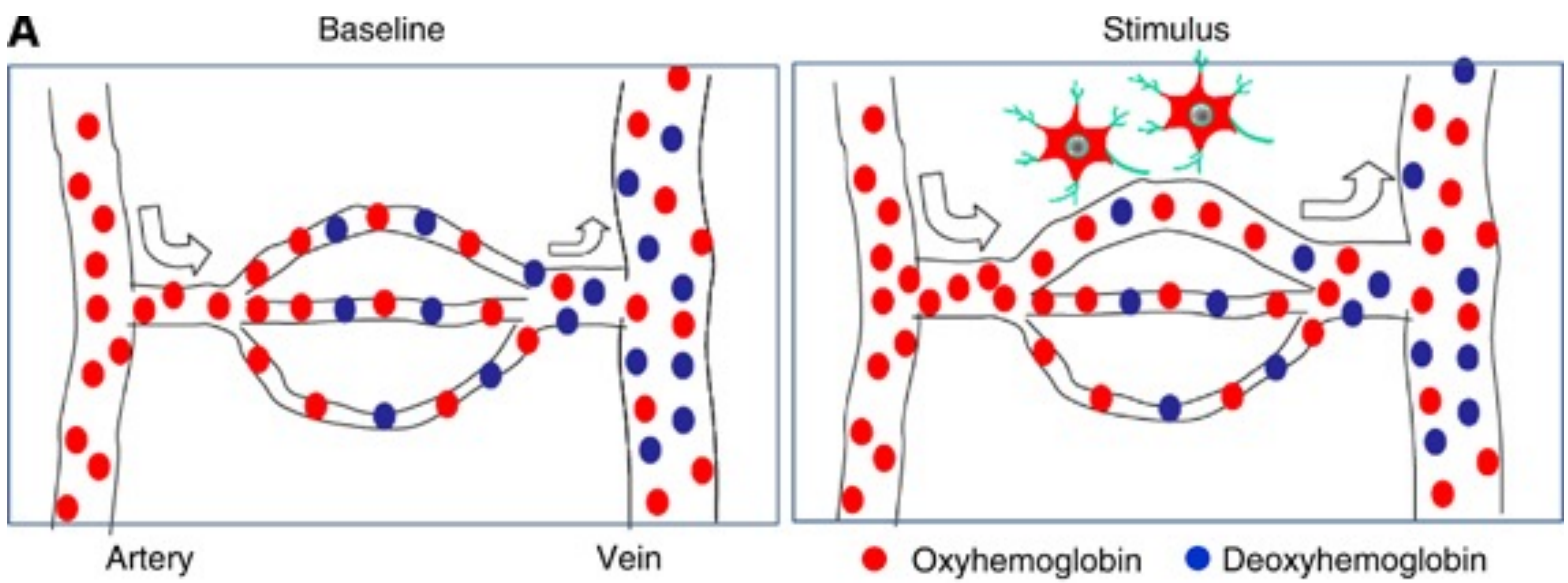
Signal components of the BOLD effect



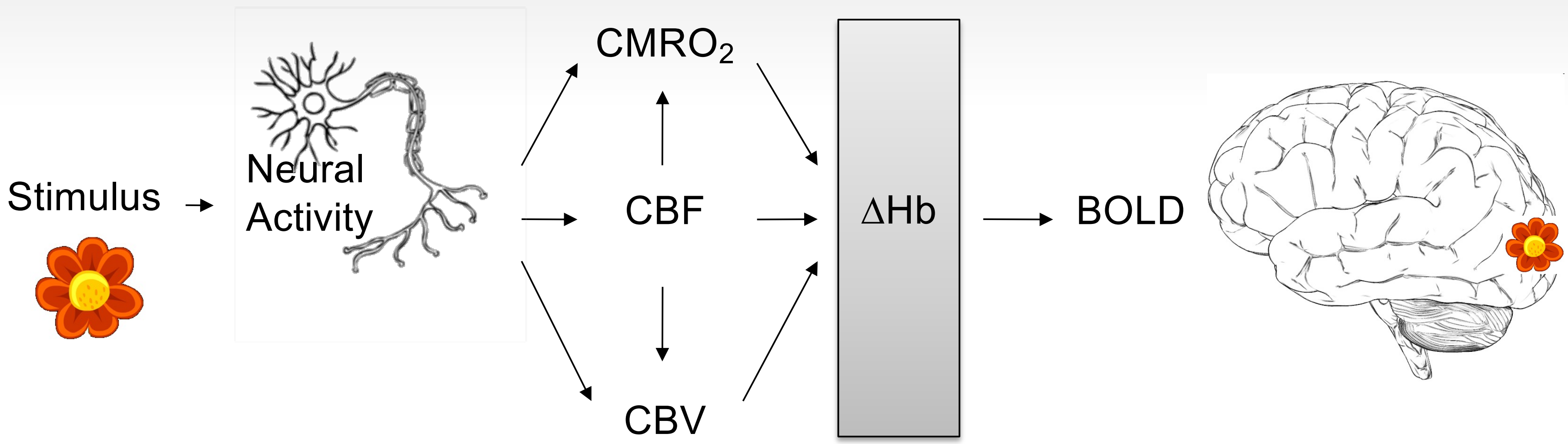
$CMRO_2$ – metabolic oxygen uptake
CBF – Cerebral Blood Flow
CBV – Cerebral Blood Volume
Hb – Haemoglobin
BOLD – Blood Oxygenation Level Dependent effect

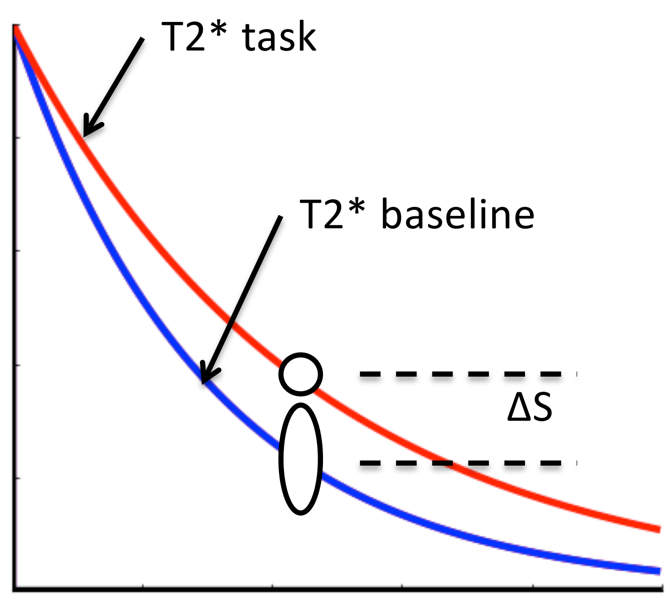
Signal localization of the BOLD effect





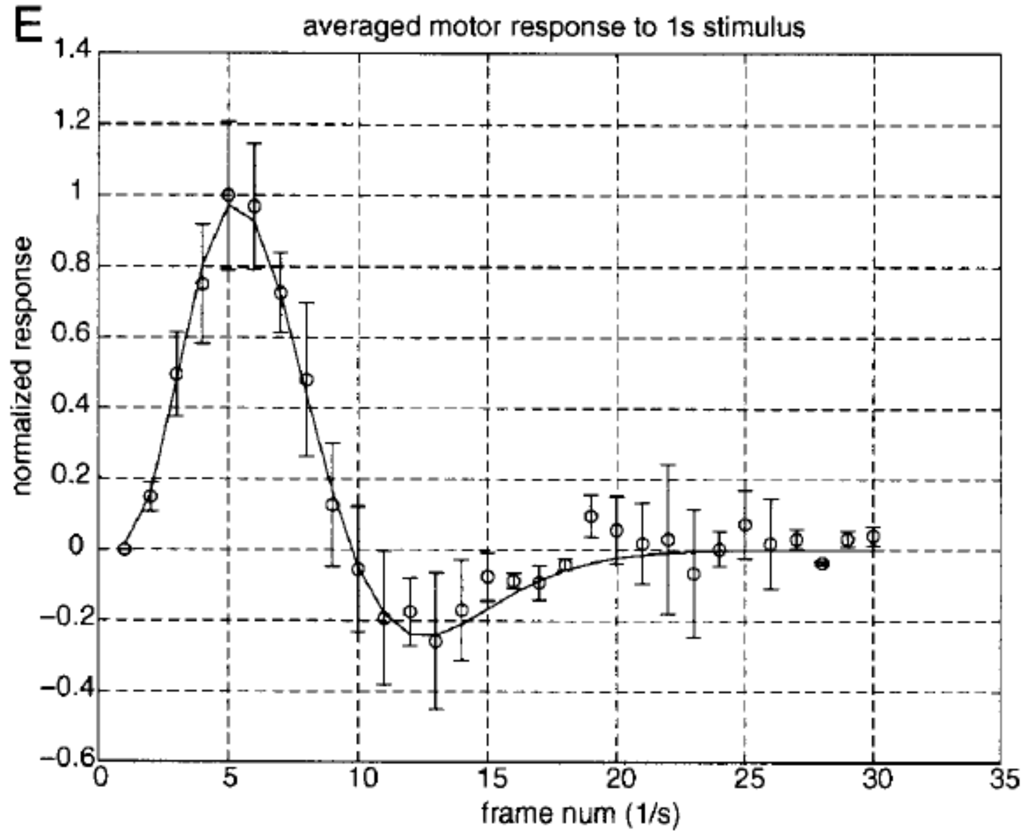
Contrast Mechanisms





Hemodynamic Response speed

- Slow response, delayed 4-6 s, lasts ~ 4-6 s, returns to baseline much later
- Post and pre stimulus undershoot, vascular variation



Glover, GH Neuroimage (1999)

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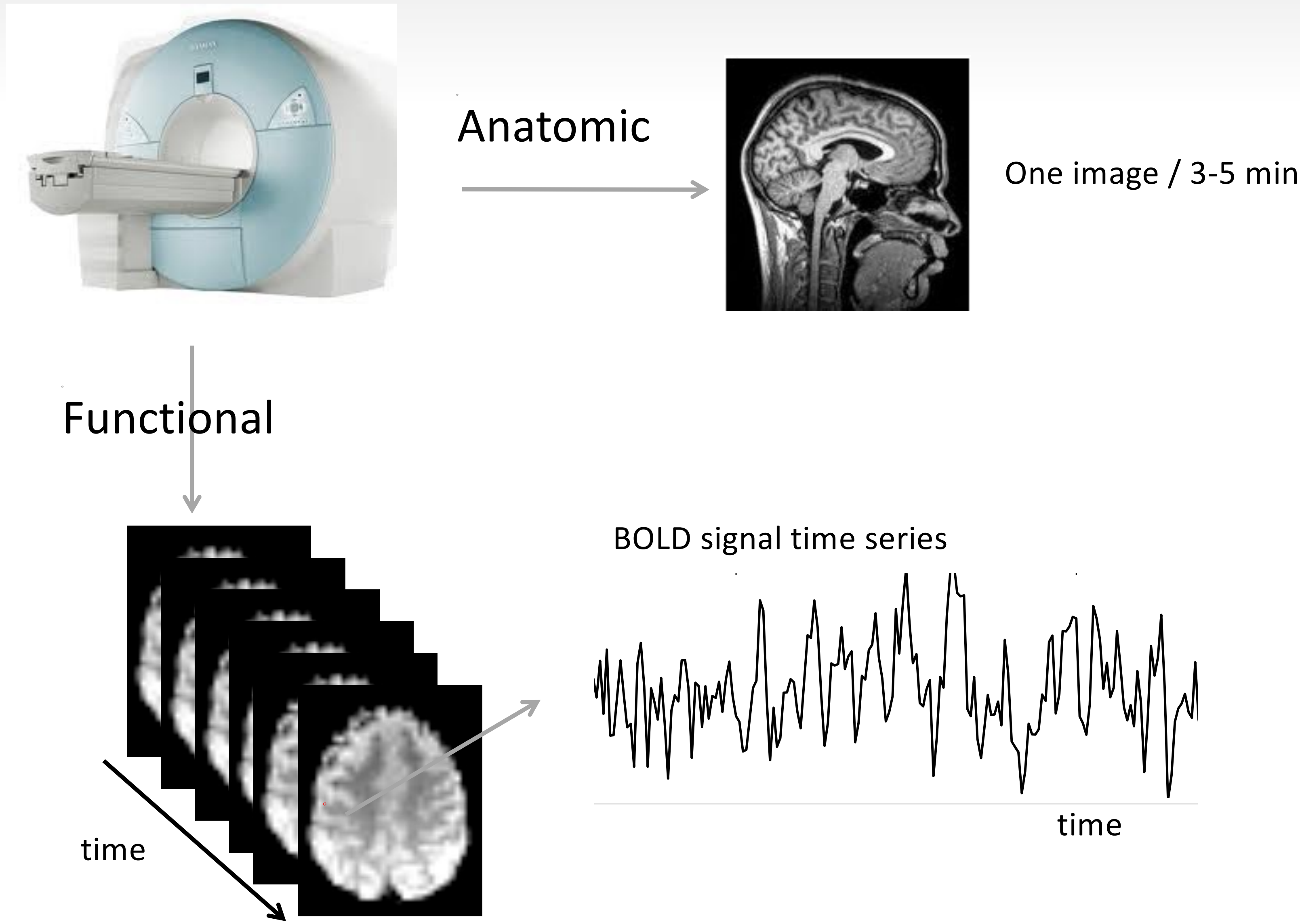
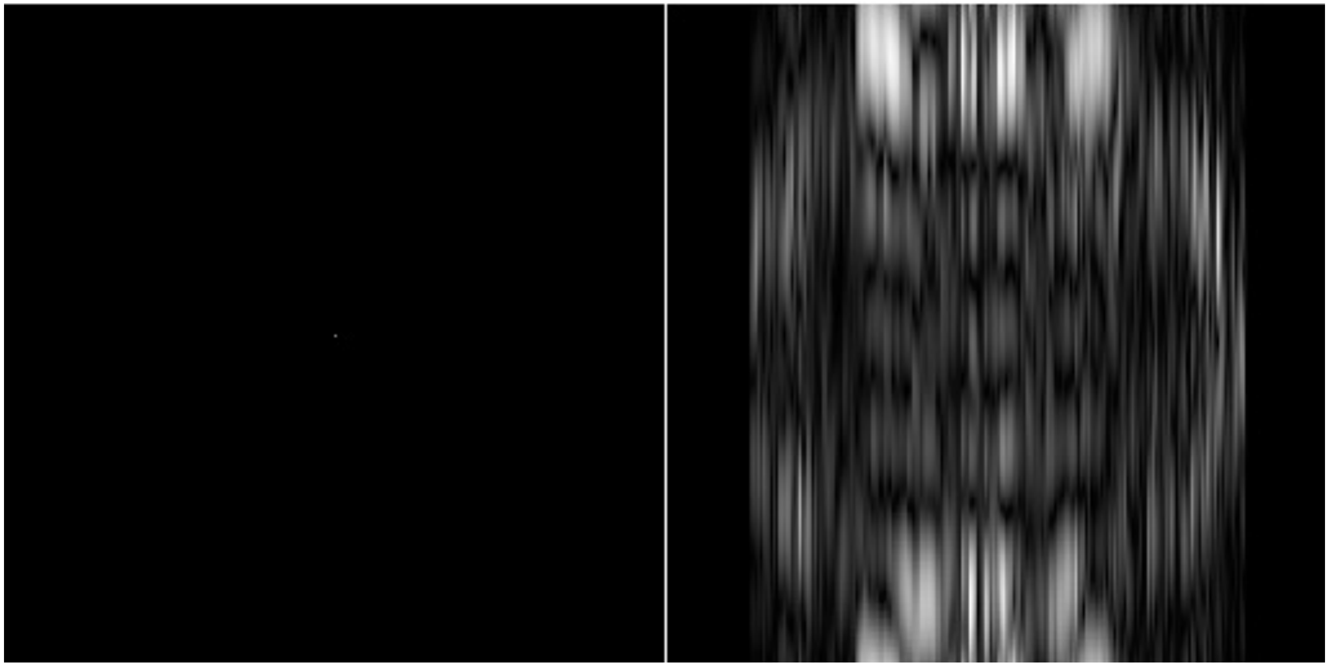
fMRI acquisition

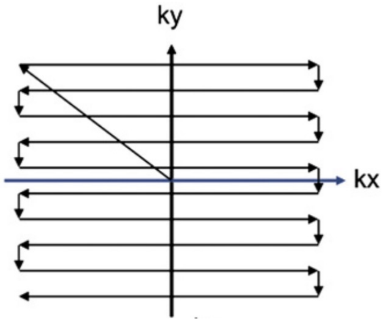


One image / 2 s for 5 min

Courtesy of Catie Chang NINDS

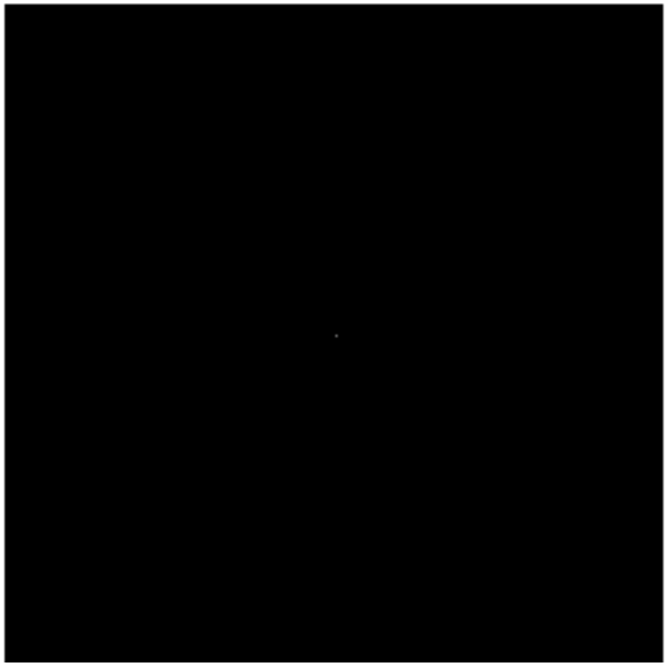
Filling k-space, one line at a time

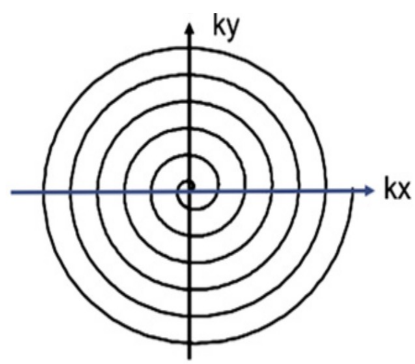




Courtesy of Nick Bock, McMaster

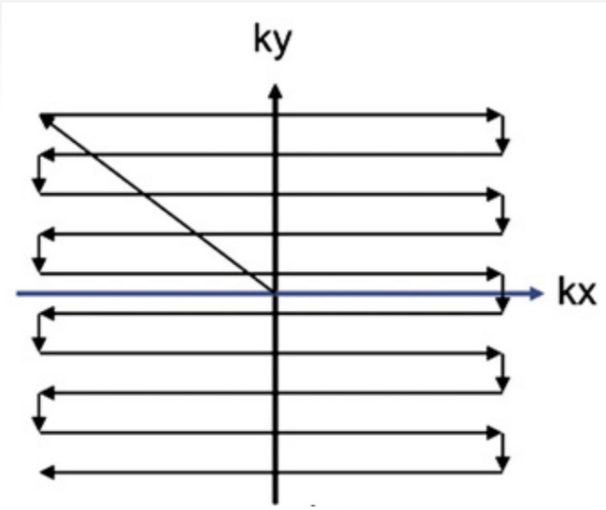
Filling k-space, center out



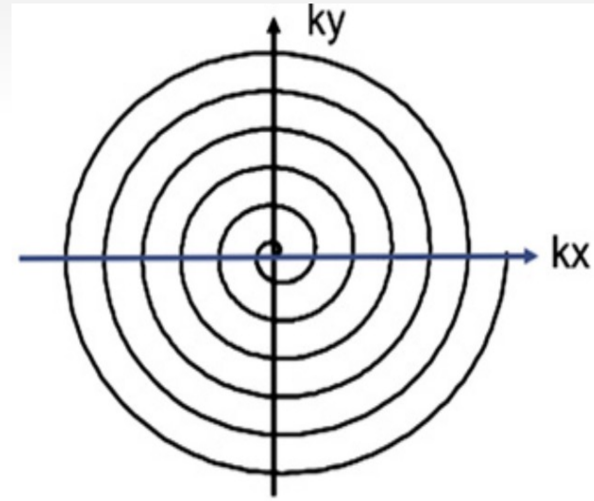


Courtesy of Nick Bock, McMaster

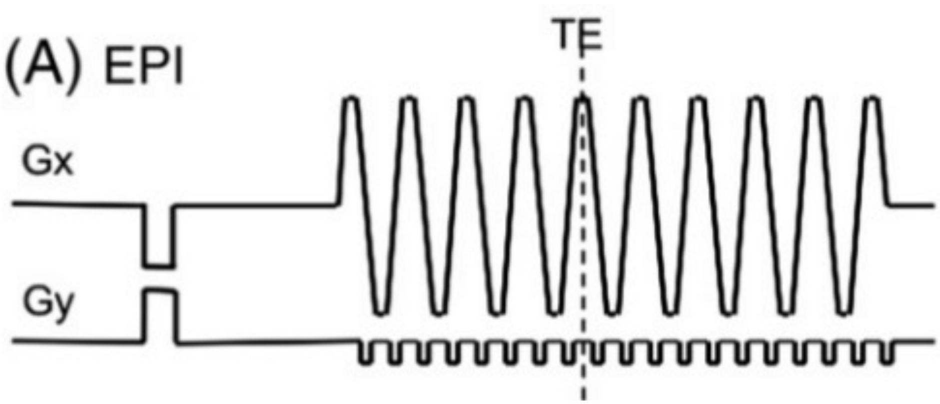
Standard pulse sequences

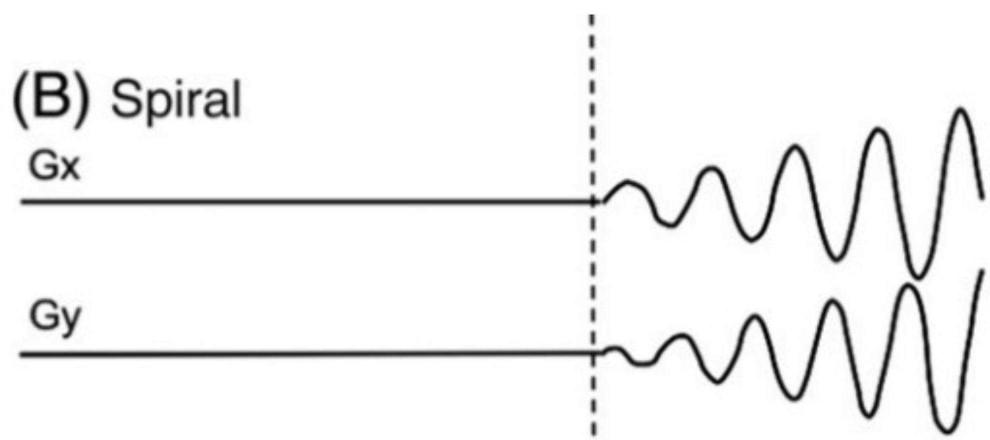


EPI



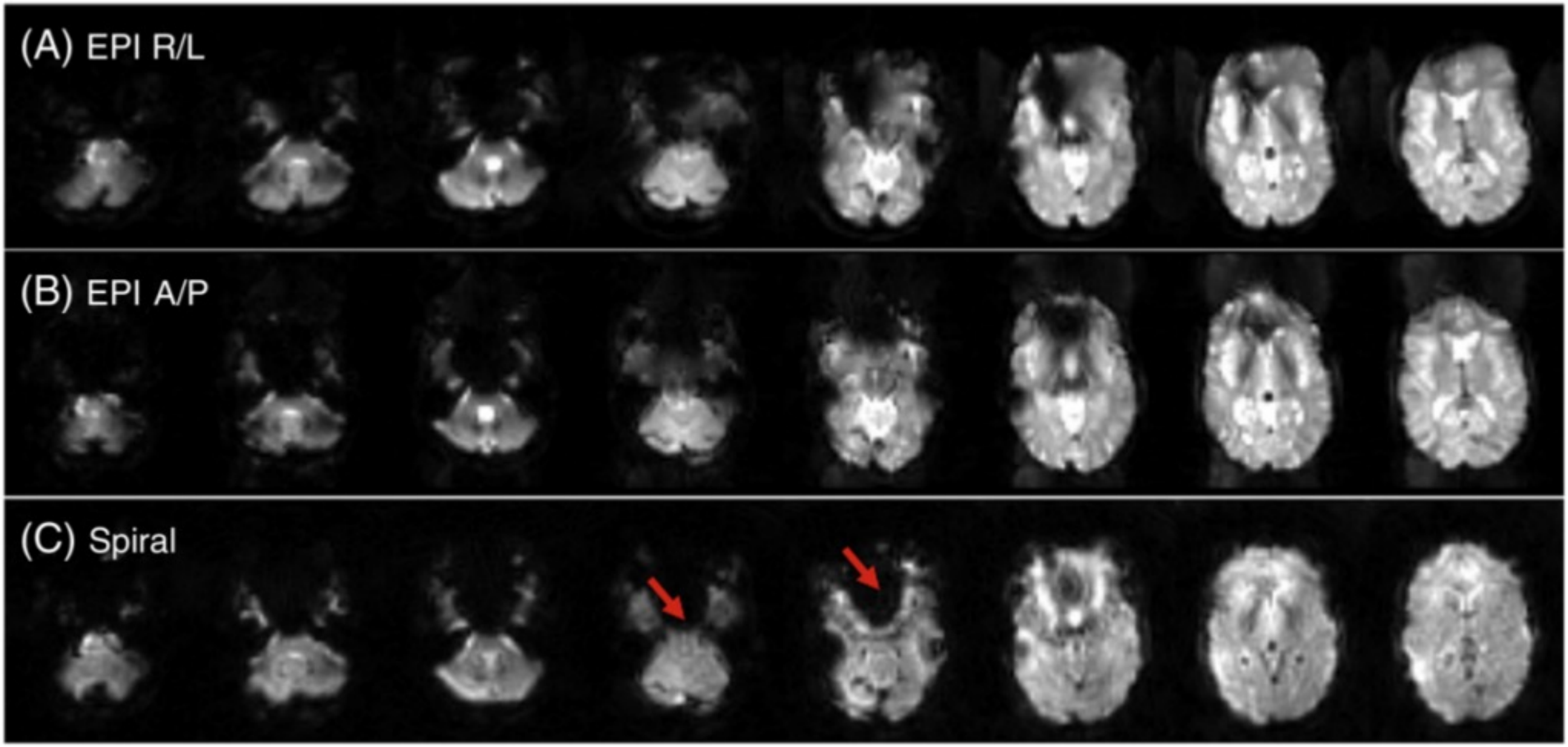
Spiral





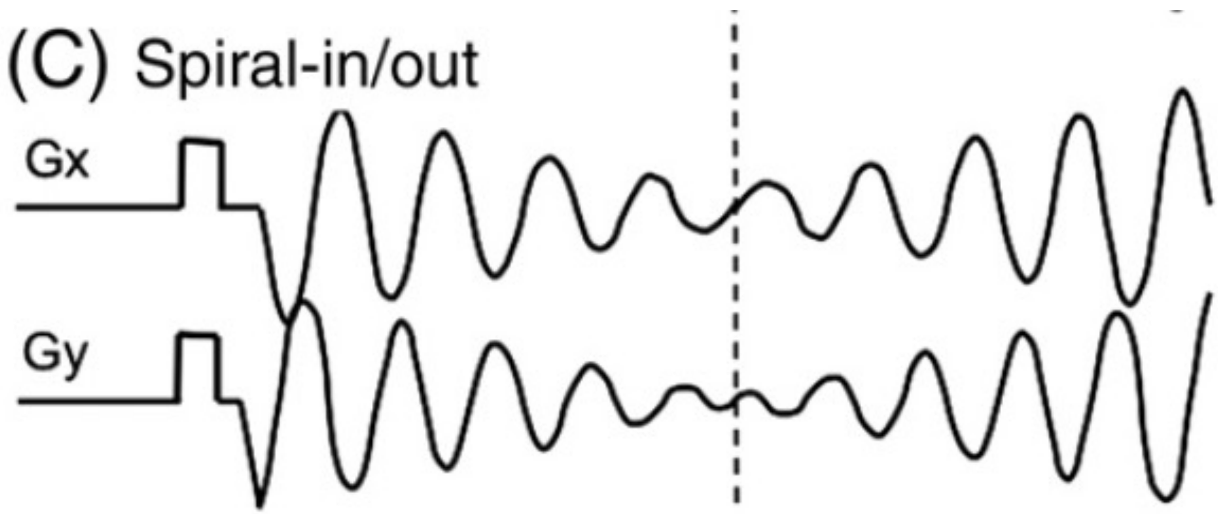
Glover, Neuroimage (2012)

Example EPI/Spiral images … susceptibility



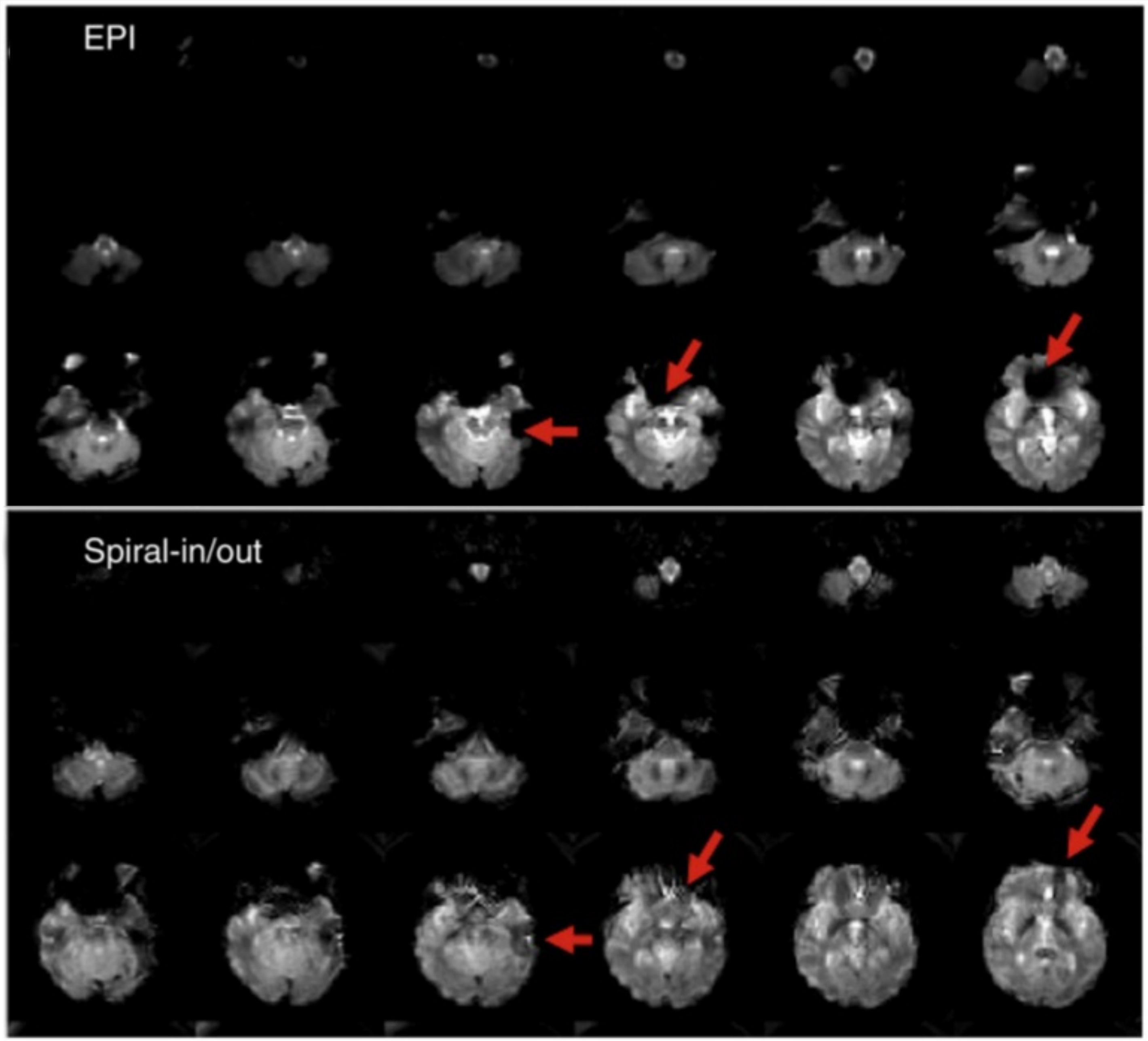
Glover, Neuroimage (2012)

Spiral in/out



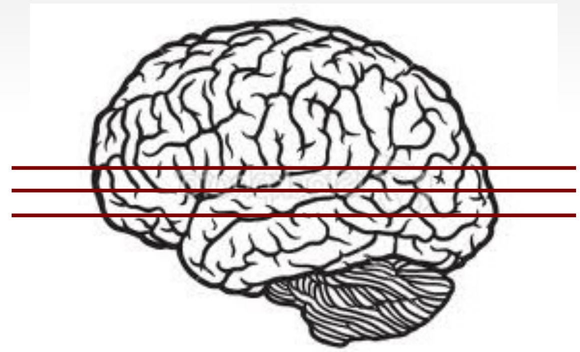
Glover, Neuroimage (2012)

Susceptibility reduction



Glover, Neuroimage (2012)

Whole brain vs. Partial coverage



Increasing **number** of slices:
- Decreased temporal **or**
- Decreased in-plane resolution

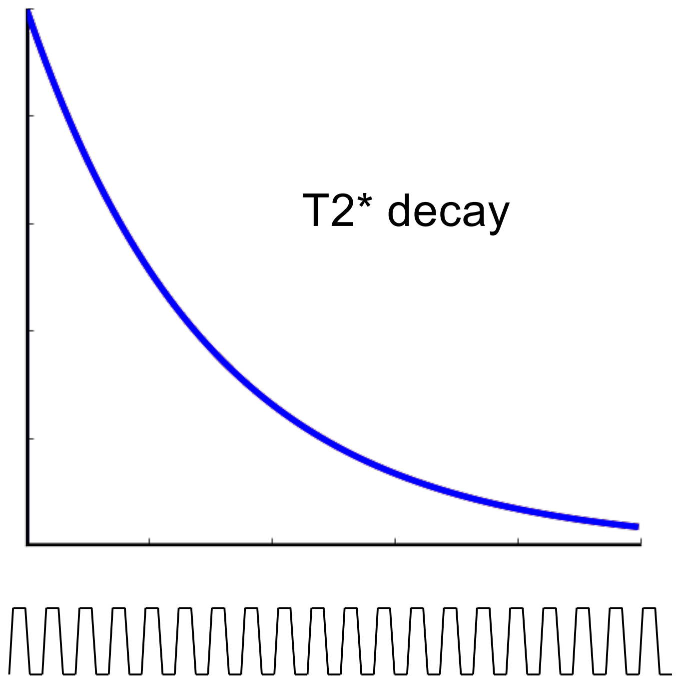
Increasing slice **thickness**:
- Increased partial voluming
- Increased susceptibility artifacts

Useful for:
- cognitive studies
- resting state

- Thinner slices for short TRs
- Increased in-plane resolution
- shorter TR

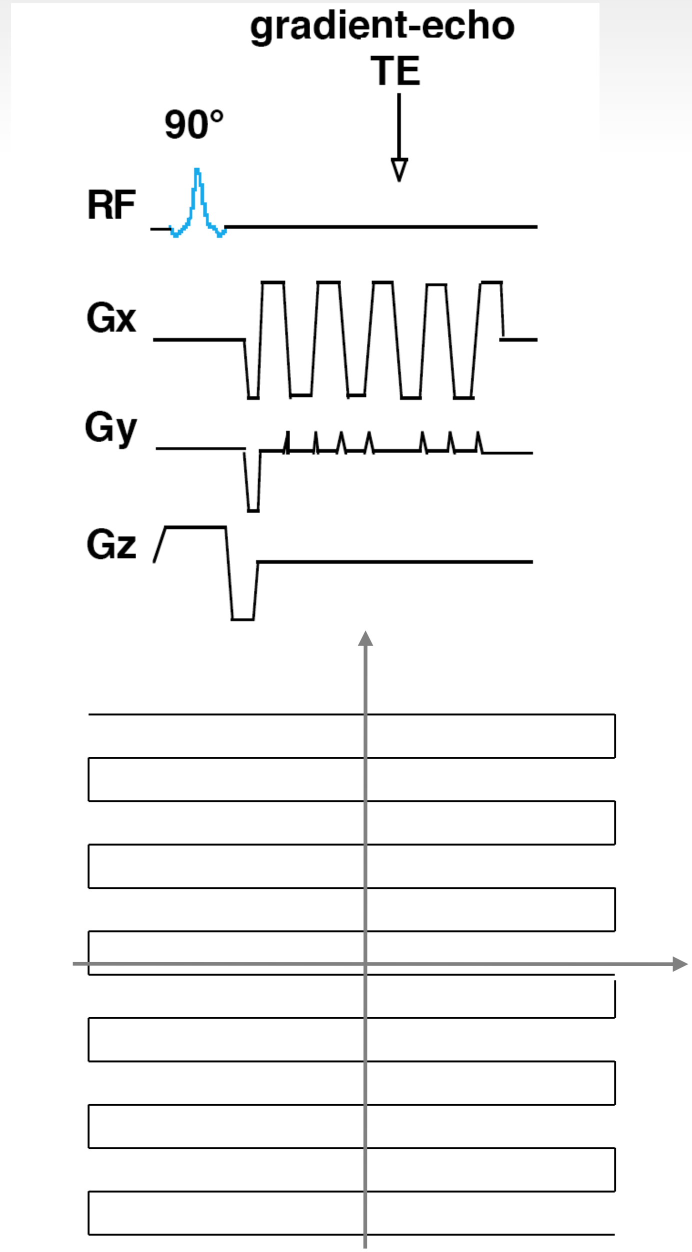
Useful for:
- Specific ROIs

Single shot EPI



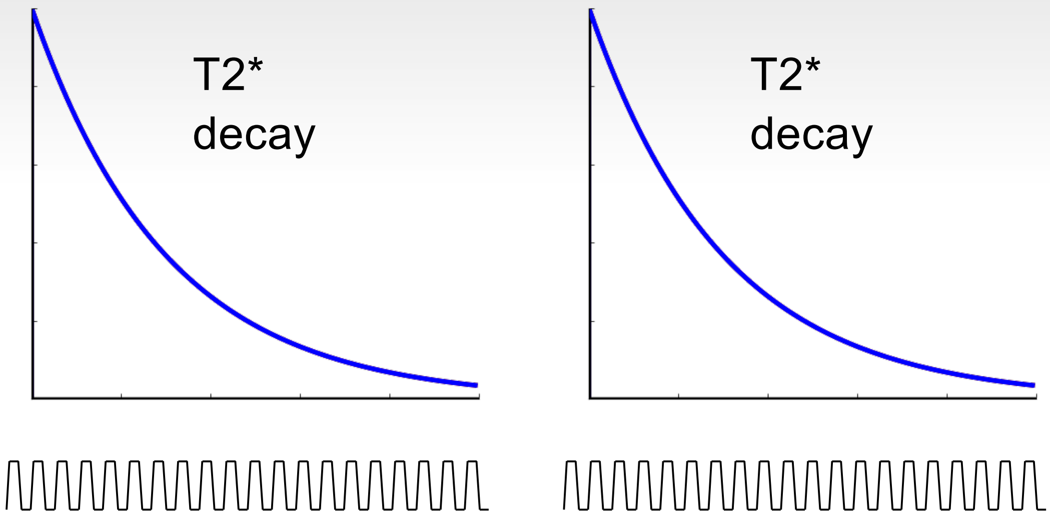
EPI readout window

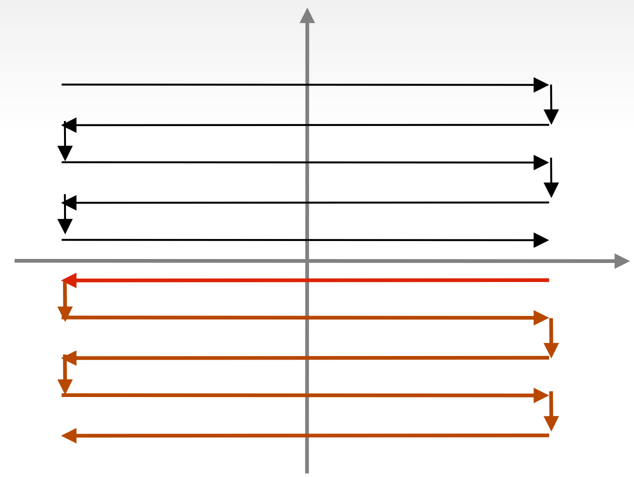
≈ **20 to 40** ms



Courtesy of Peter Bandettini

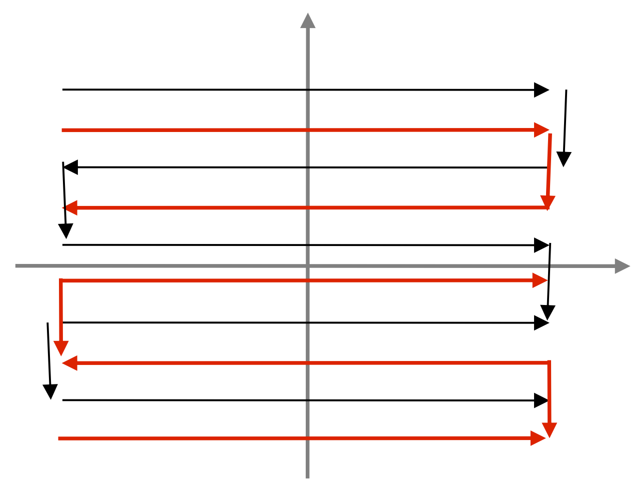
Multi-shot EPI





Shot 1

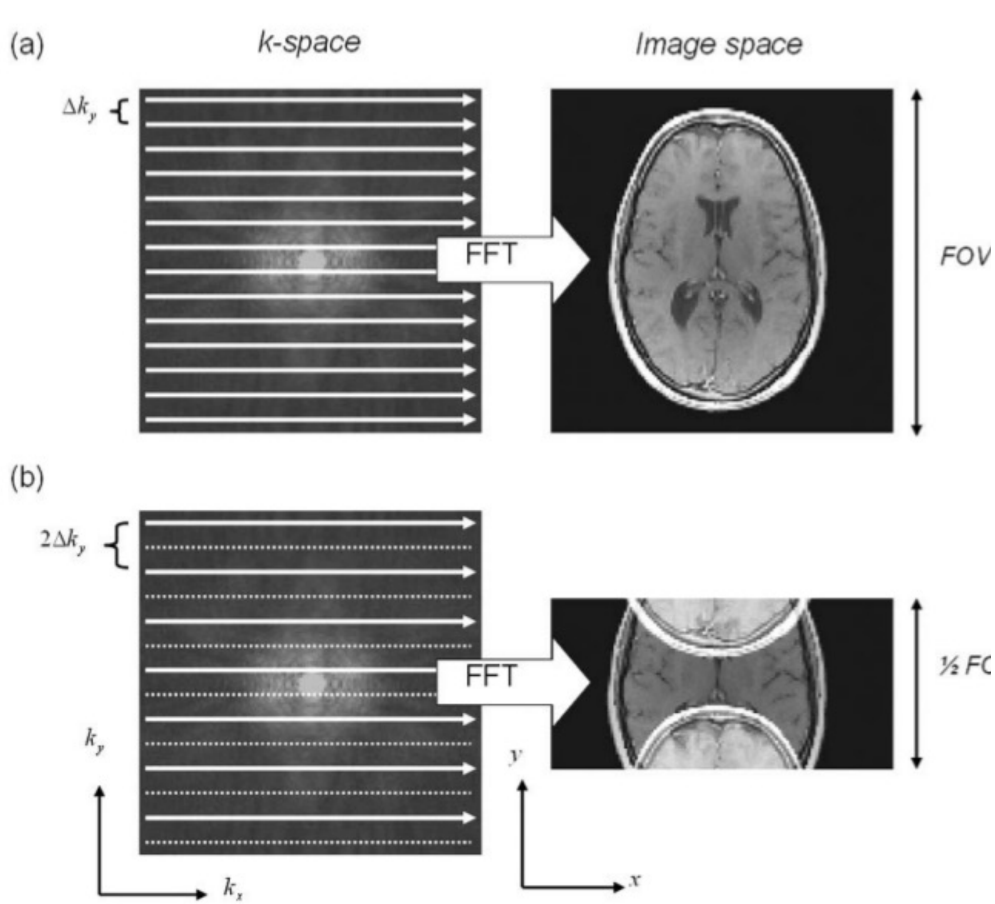
Shot 2

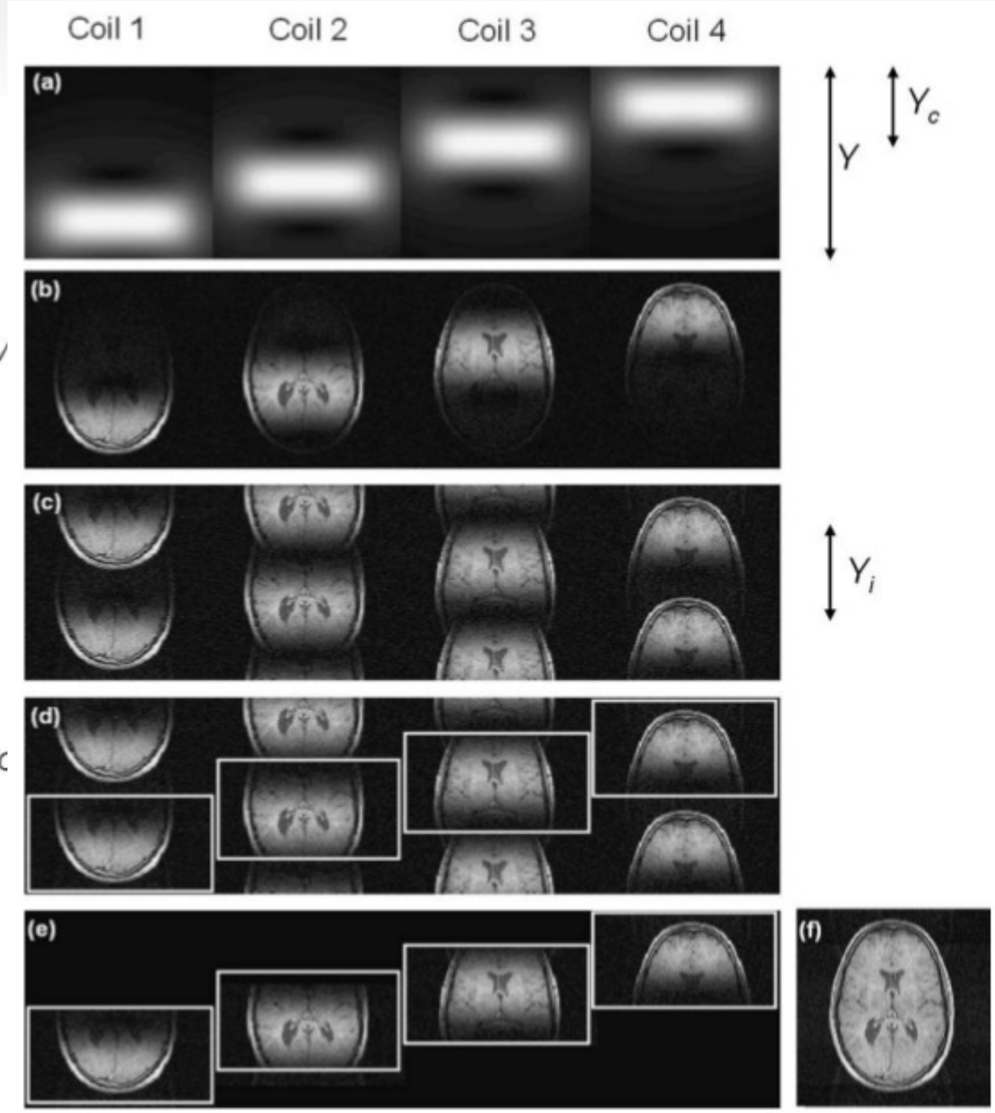


- All lines acquired in a single "shot" with one RF pulse
  - Pros: Fast
  - Cons: Long readout => distortions

- Split the acquisition into parts
  - Pros: acquire higher resolution
  - Cons: phase errors, ghosting, requires more time

Acceleration: SENSE/GRAPPA

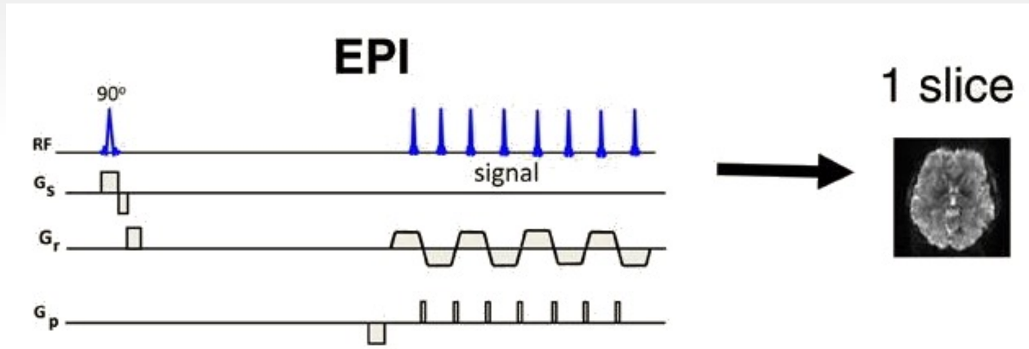


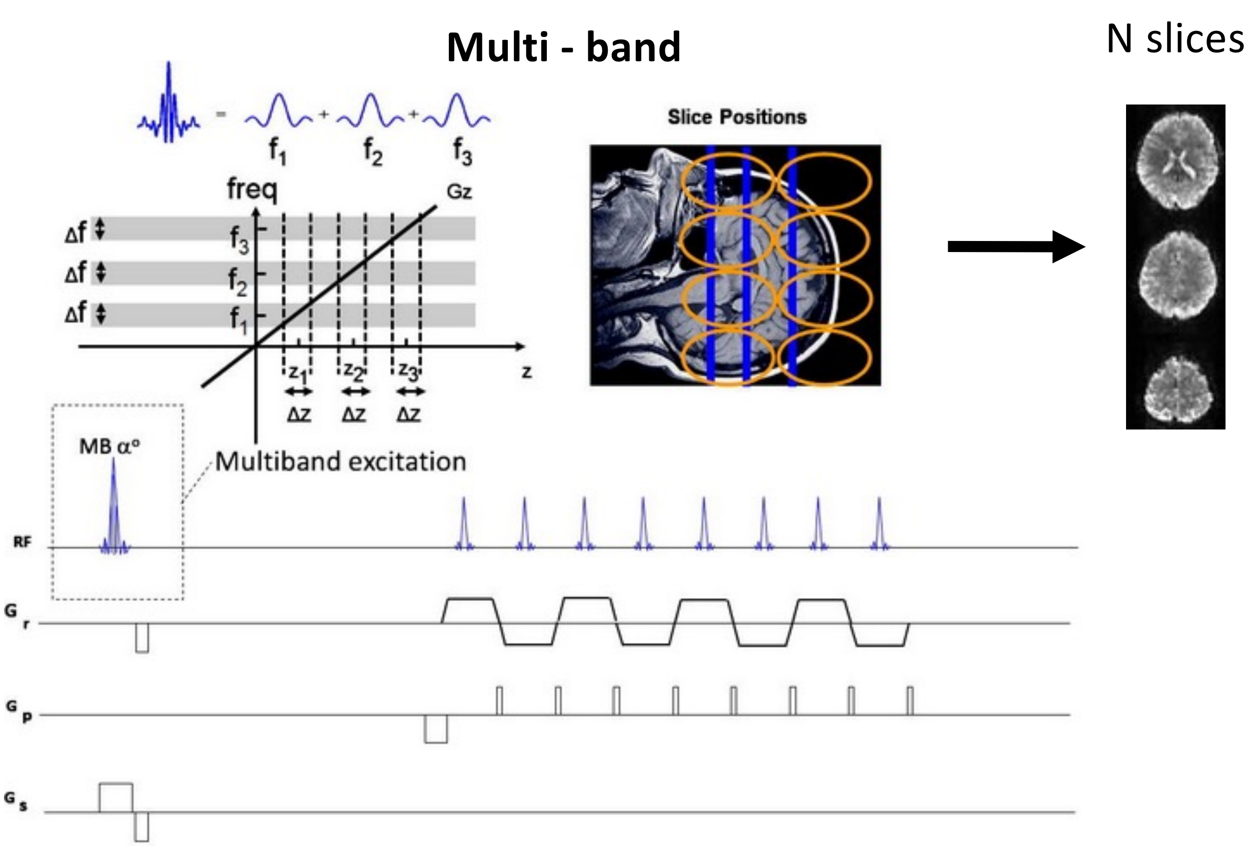


- Undersample k-space by accleration factor n
-reconstruct either in k-space (GRAPPA) or image space (SENSE)
- maximum acceleration limited by number of coils and SNR reduction

Blaimer M. et al Top Magn Reson Imaging. (2004)

Multi-slice or mutli-band excitation



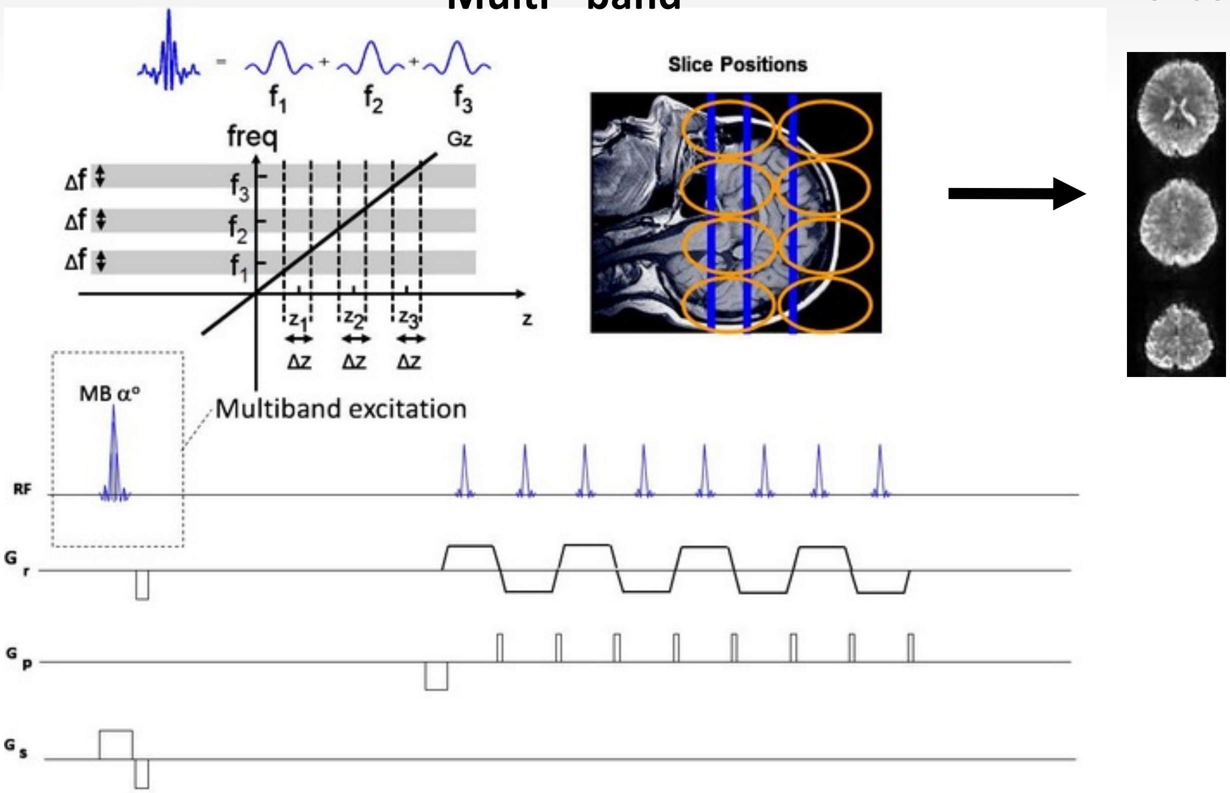


Feinberg DA and Setsompop K. Journal of Magnetic Resonance (2013)

Multi-slice or mutli-band excitation

Multi - band

N slices



- excites multiple slices at once,
- uses coil sensitivity profiles to unmix the images
- sub TR whole brain images are achievable
- loss in SNR
- long reconstruction times

Feinberg DA and Setsompop K. Journal of Magnetic Resonance (2013)

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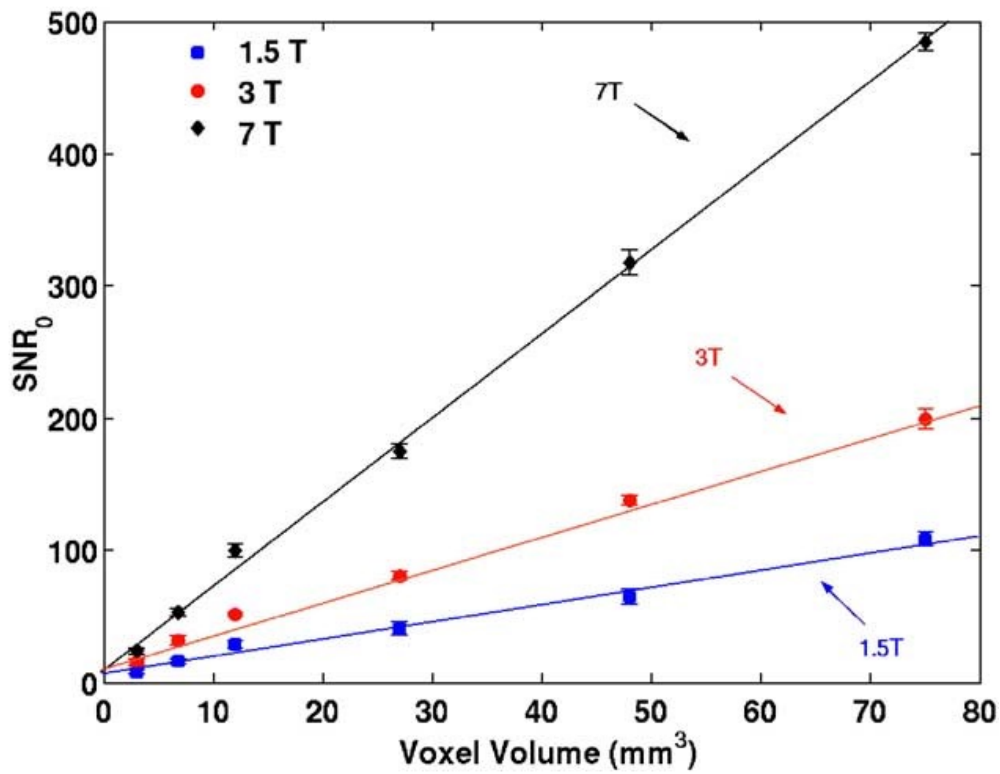
Voxel size

- In going smaller voxel size is primarily limited by SNR
-smaller is usually desirable to reduce partial volume effects, physiological noise

- -Voxel SNR is given by

$$SNR \propto p^2 w \sqrt{T_{acq} N}$$

- Where p is the voxel size, w is the slice thickness, T is the acquisition time, and N is the number of time frames
- T acq is about 20-30ms for single shot EPI.

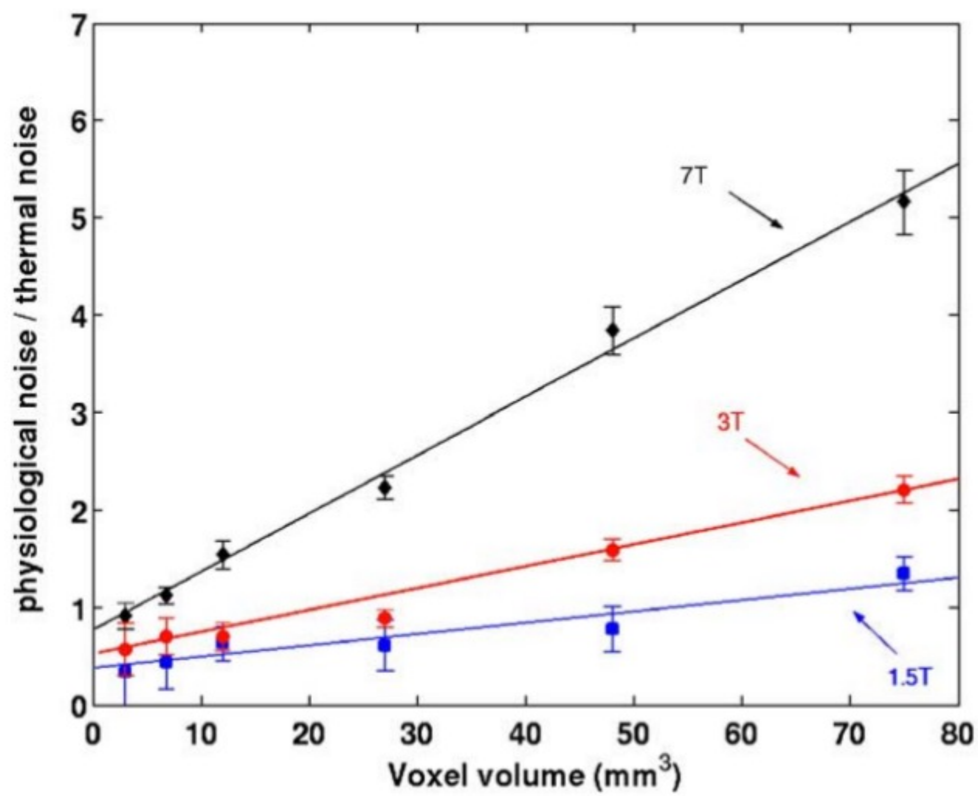


Triantafyllou et al, Neuroimage (2005)

Field Strength

•Pros
•- Higher SNR (1.6 times at 7t v 4t)
• => potential increased resolution / specificity

•Cons
•-shorter T2*
•=> faster readout/ acceleration ne
•-long TR
•=>longer repetition time to get sig
•-larger field perturbations/ inhom
• -SAR limitations

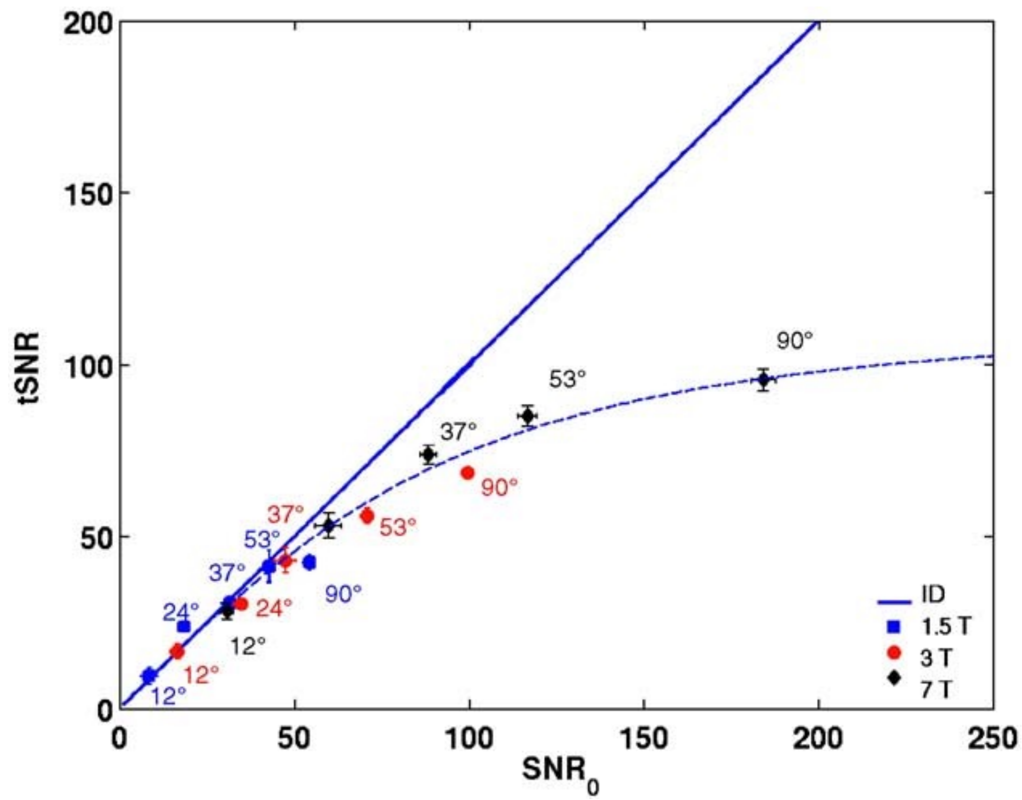


What is the optimal voxel size?

- Need to take into account noise fluctuations over time
- Thermal sources, physiological noise

- TSNR is the ratio over the average voxel time course signal over the time course standard deviation.

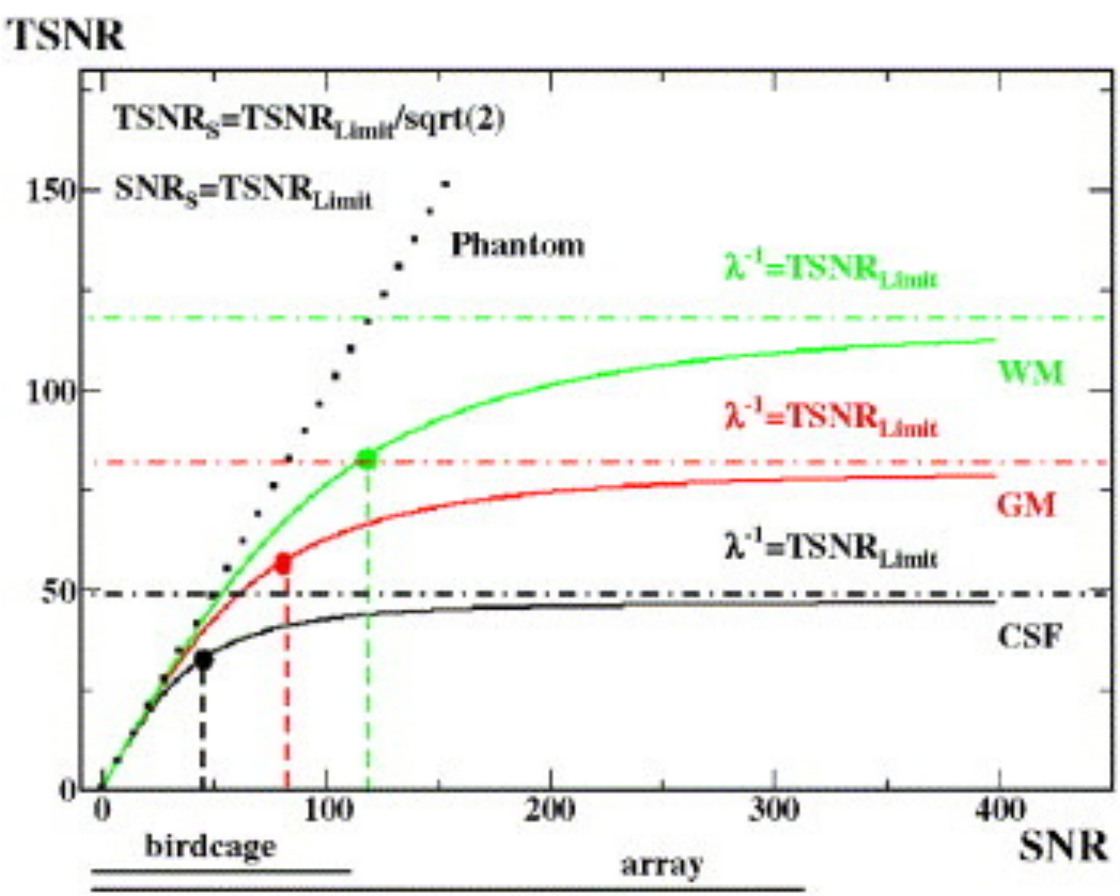
- TSNR has a nonlinear relation with image SNR



Triantafyllou et al, Neuroimage (2005)

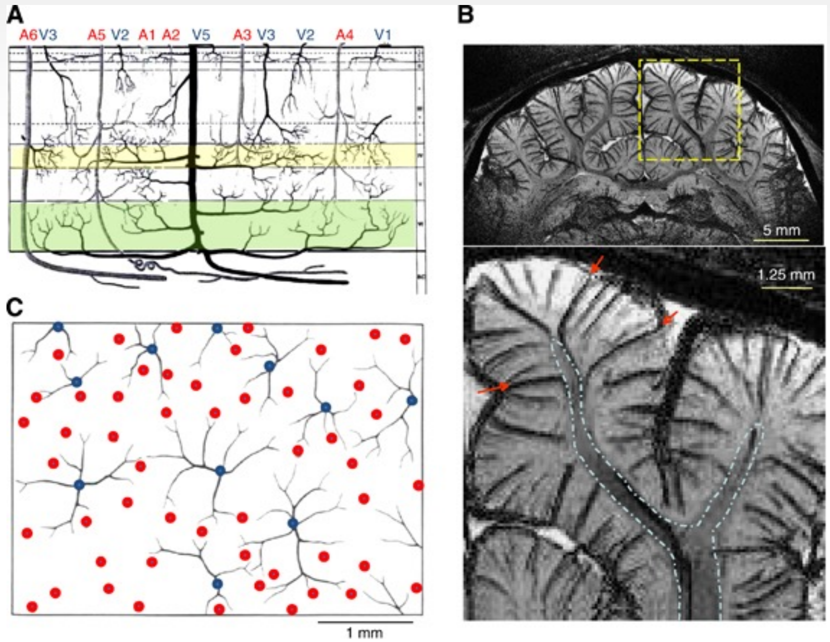
Optimal voxel size?

Has been suggested as a guide to choosing voxel size given a particular image SNR
Based on tissue types and imaging parameters



J. Bodurka, et al., NeuroImage, (2007)

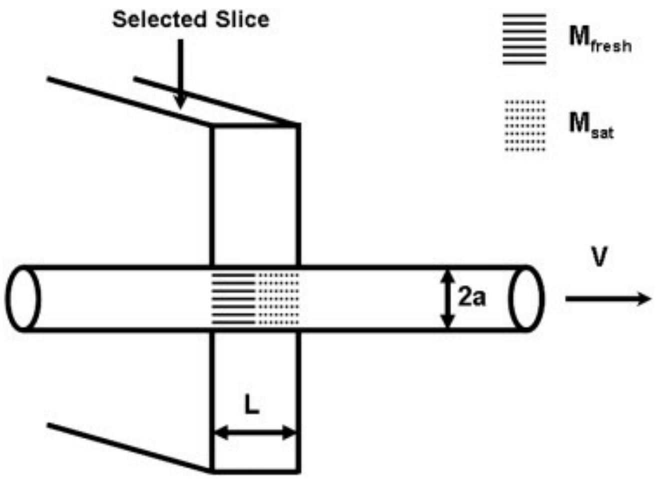
What's the effective spatial resolution?



- imaging limit ~0.5 mm, easily 2mm, standard 3 ish mm
- hemodynamic PSF 3.5 mm (Engel, 1997)
- higher at 7T ~2.3 mm
- smoothing improves reproducibility, alignment between subjects ~10mm (Strother 2005)

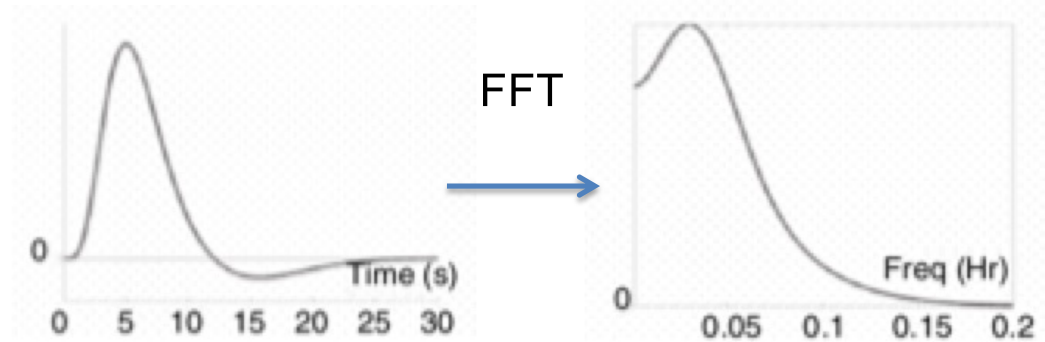
Optimal TR?

- Inflow effects affect TRs < 1s



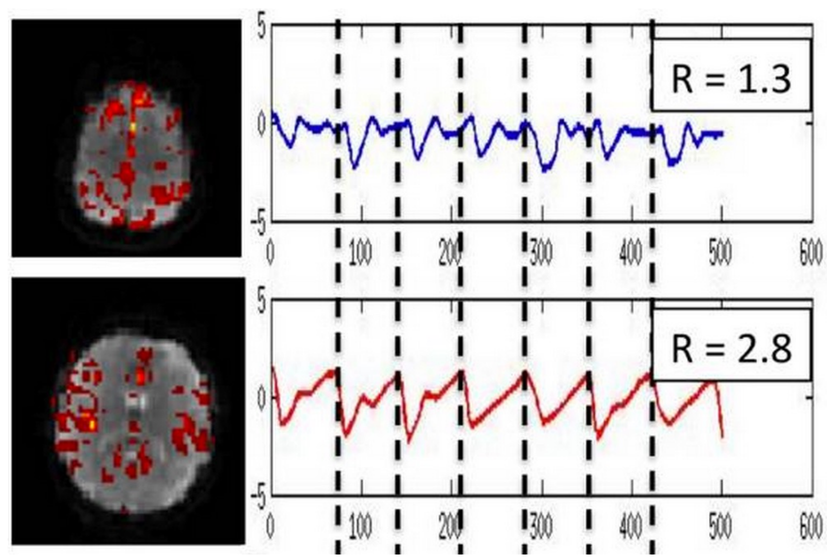
Gao Je et al., NeuroImage, Volume 62, Issue 2, 2012, 1035 - 1039

- HRF is a low pass filter



Henson, 2007; http://imaging.mrc-cbu.cam.ac.uk/imaging/DesignEfficiency

- Sampling of physiological noise (no aliasing)



Posse et al. Front Hum Neurosci. 2013; 7: 479.

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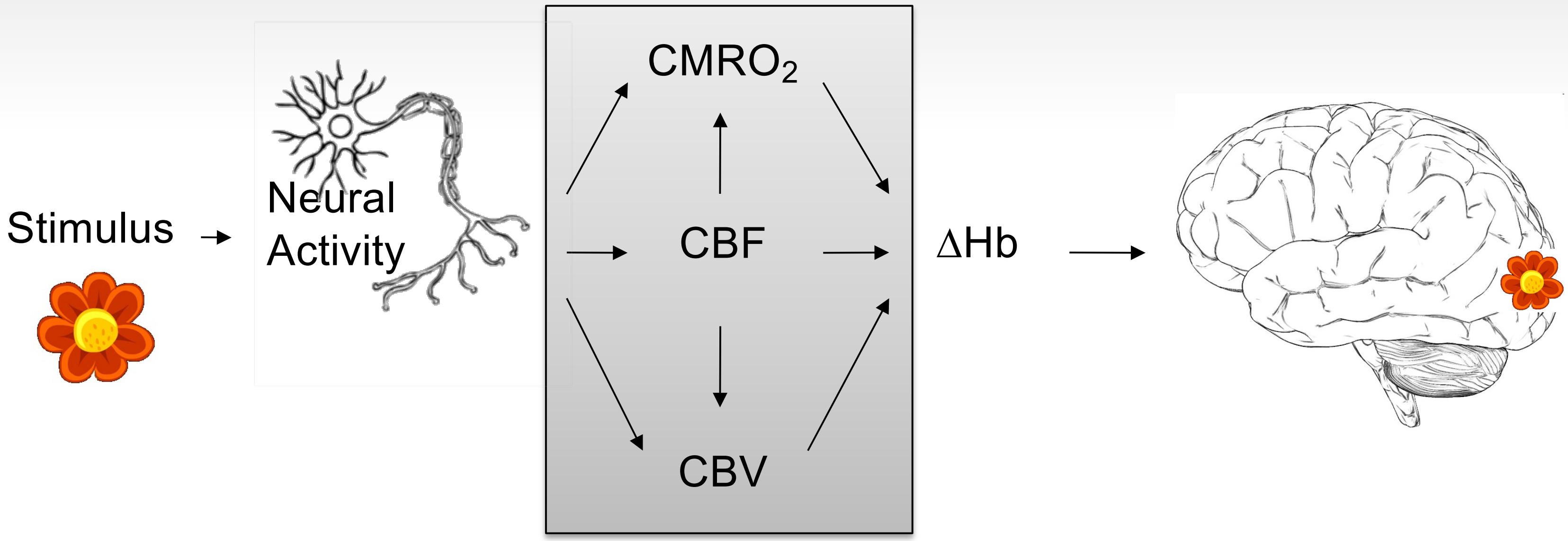
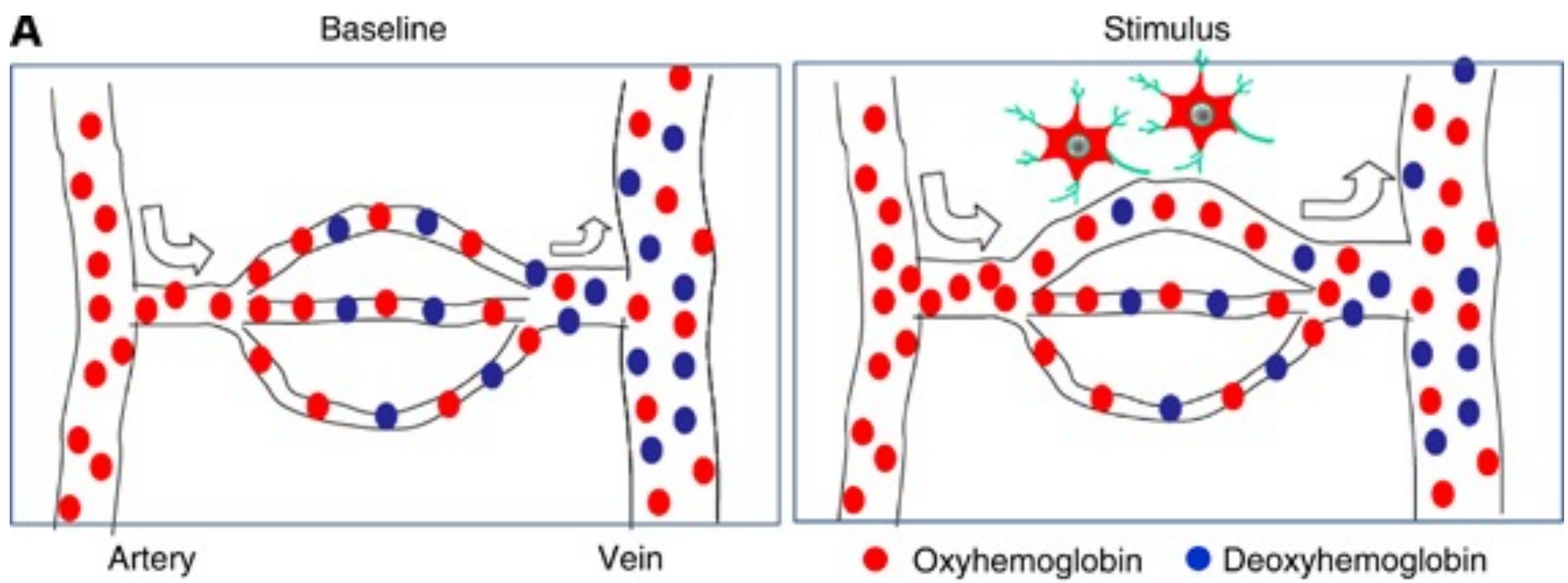
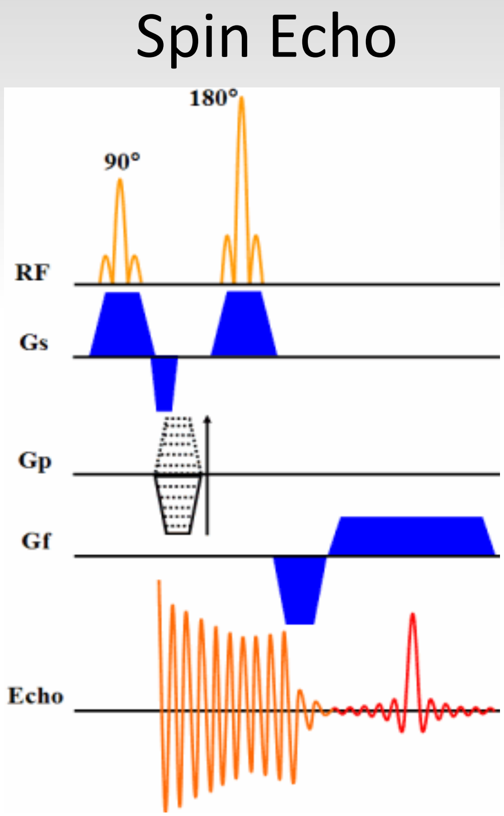
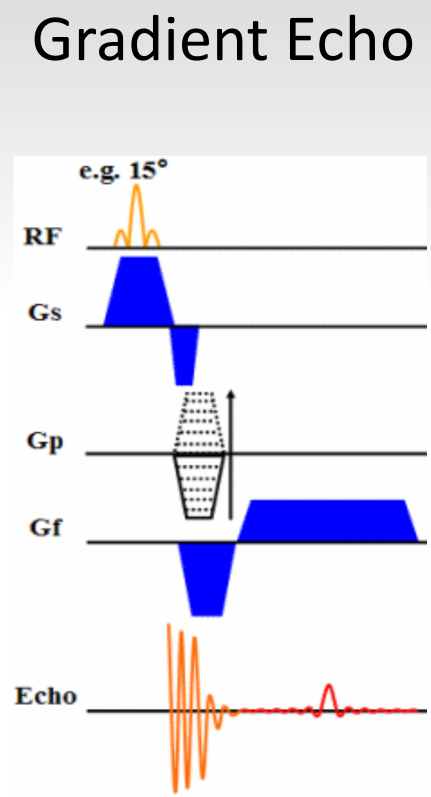
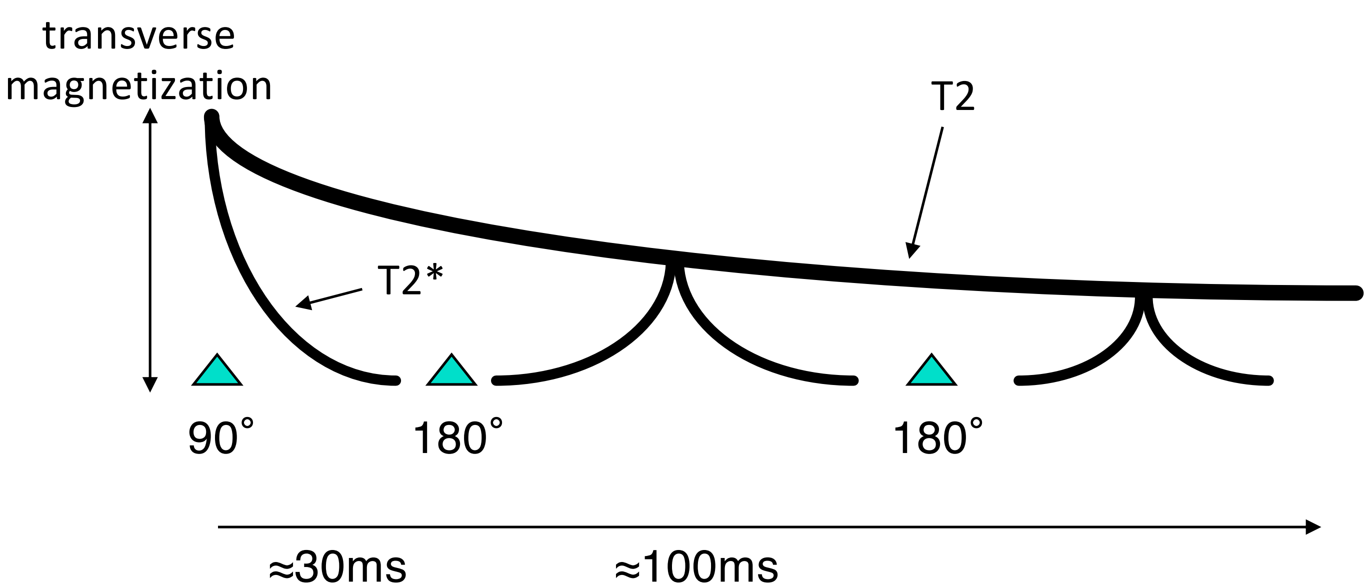
Contrast Mechanisms





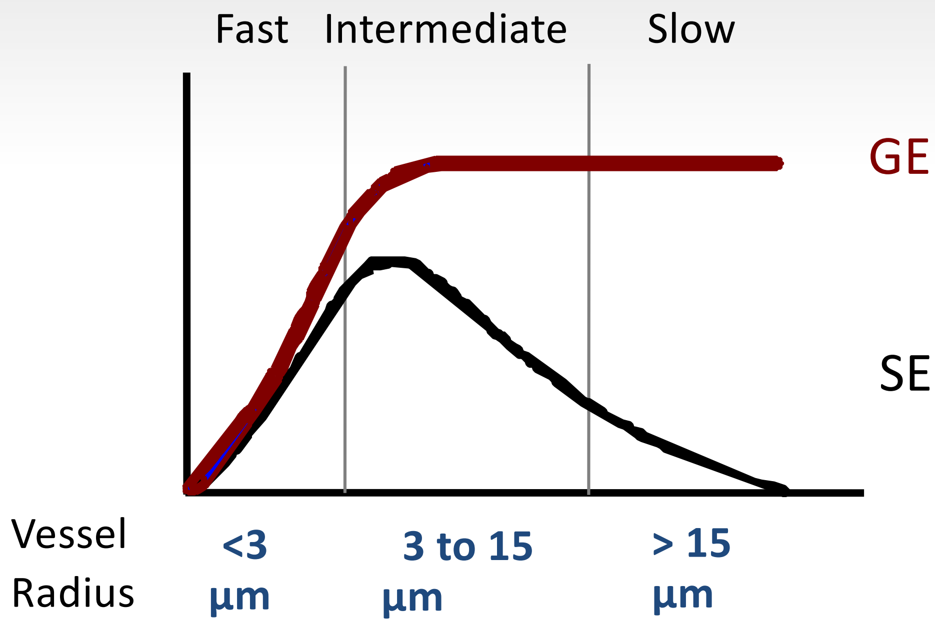




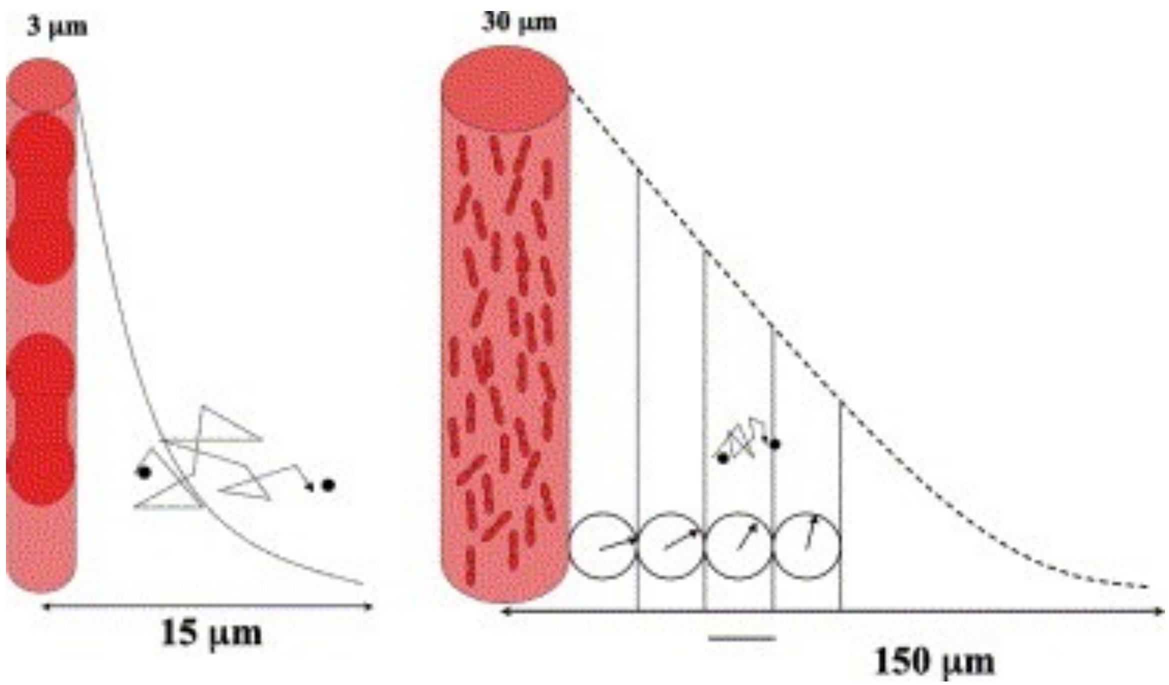


revisemri.com

Increased specificity with SE

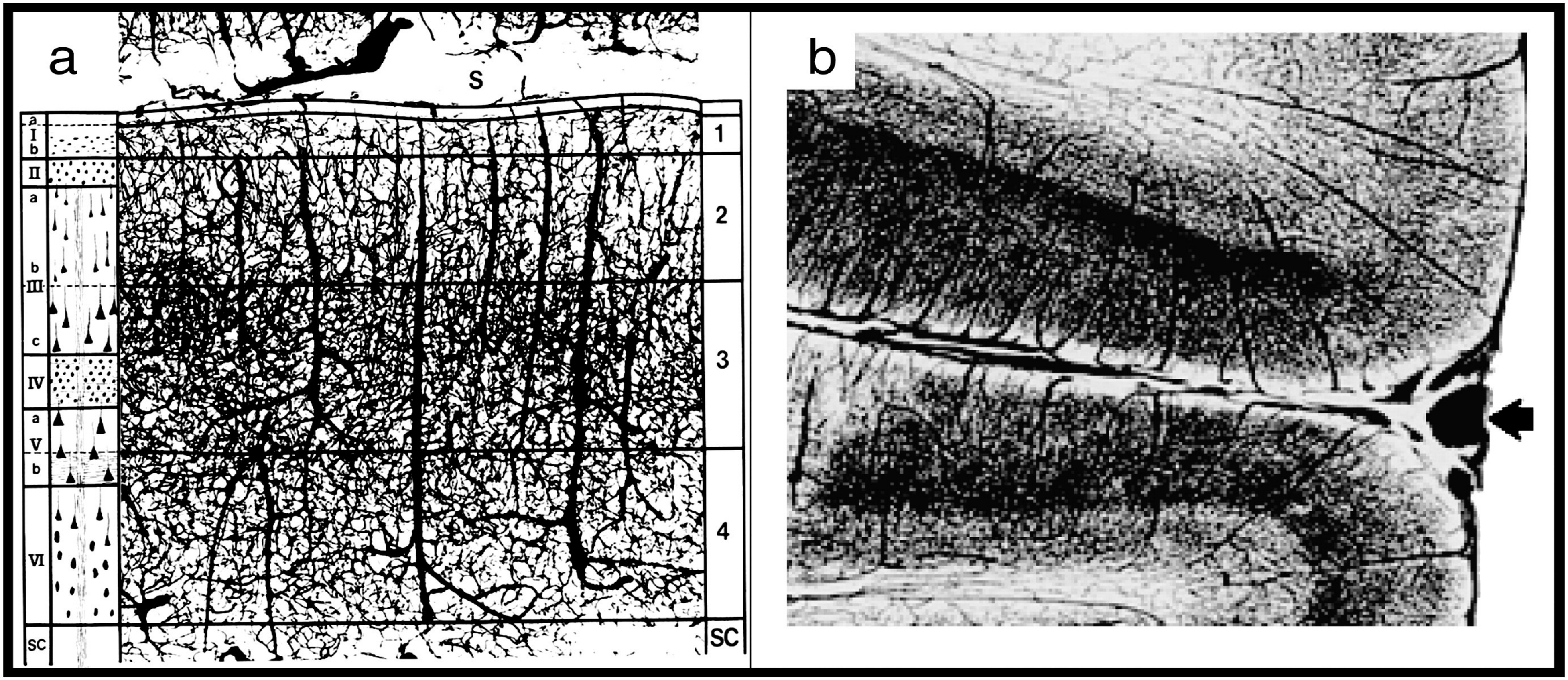


Courtesy of Peter Bandettini

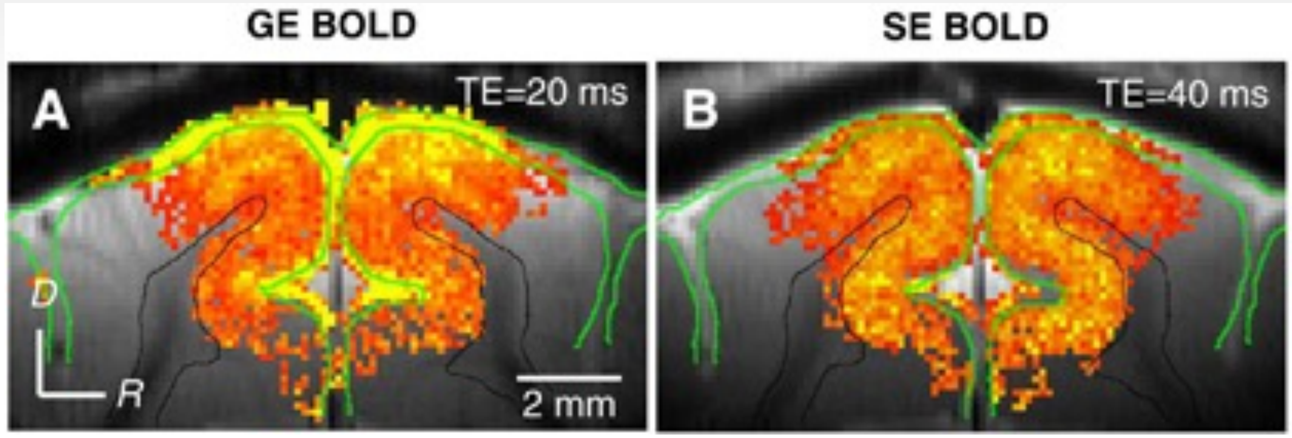


Kim, Methods (2003)

Vasculature density



Duvernoy, Brain Res. Bull. (1981)



- GE BOLD fMRI (A) has the highest percent signal change at the cortical surface, where large pial vessels are located (green contours)
- Large vessel contributions are suppressed in SE BOLD

Kim SG Journal of Cerebral Blood Flow & Metabolism (2012)

Spin echo summary

Pros

- Increased specificity

(esp at high fields where IV signal is low)

- Less sensitive to rapidly flowing blood
- Less signal dropout.

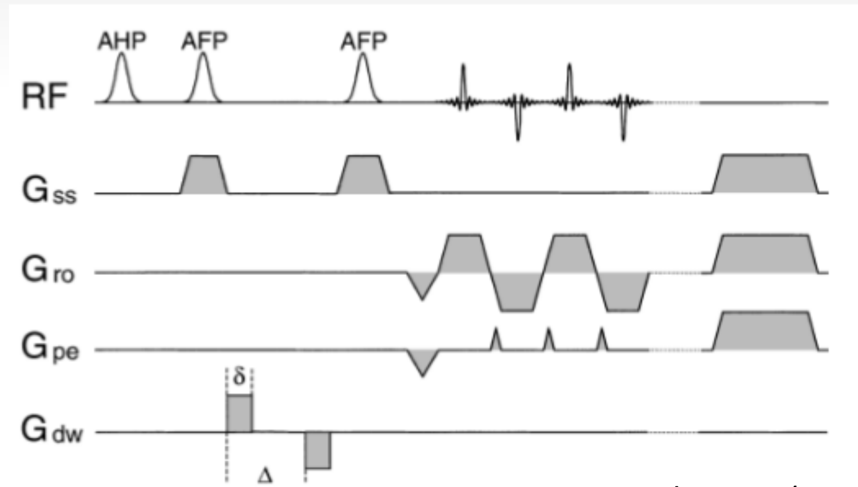
Cons

- Fewer slices per TR
- Lower fCNR by x 2 to 4.
- Acquisition window still T2*
- Very large IV signal still present at most field strengths.

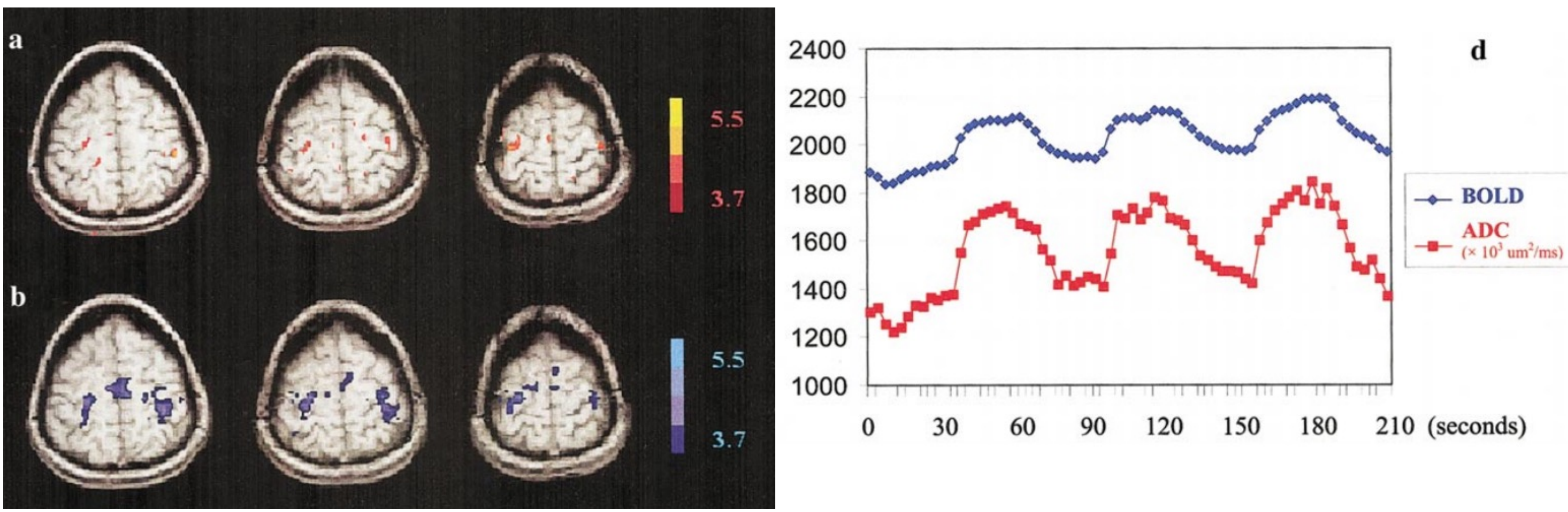
Courtesy of Peter Bandettini

Diffusion weighted fMRI

- Add diffusion gradients to increase the spatial specificity of the fMRI signal
- Attenuates signal from the larger vessels (faster moving flow) reducing the contribution from distant neural sources
- Intravascular incoherent motion weighted
- Potentially sensitive to cell swelling

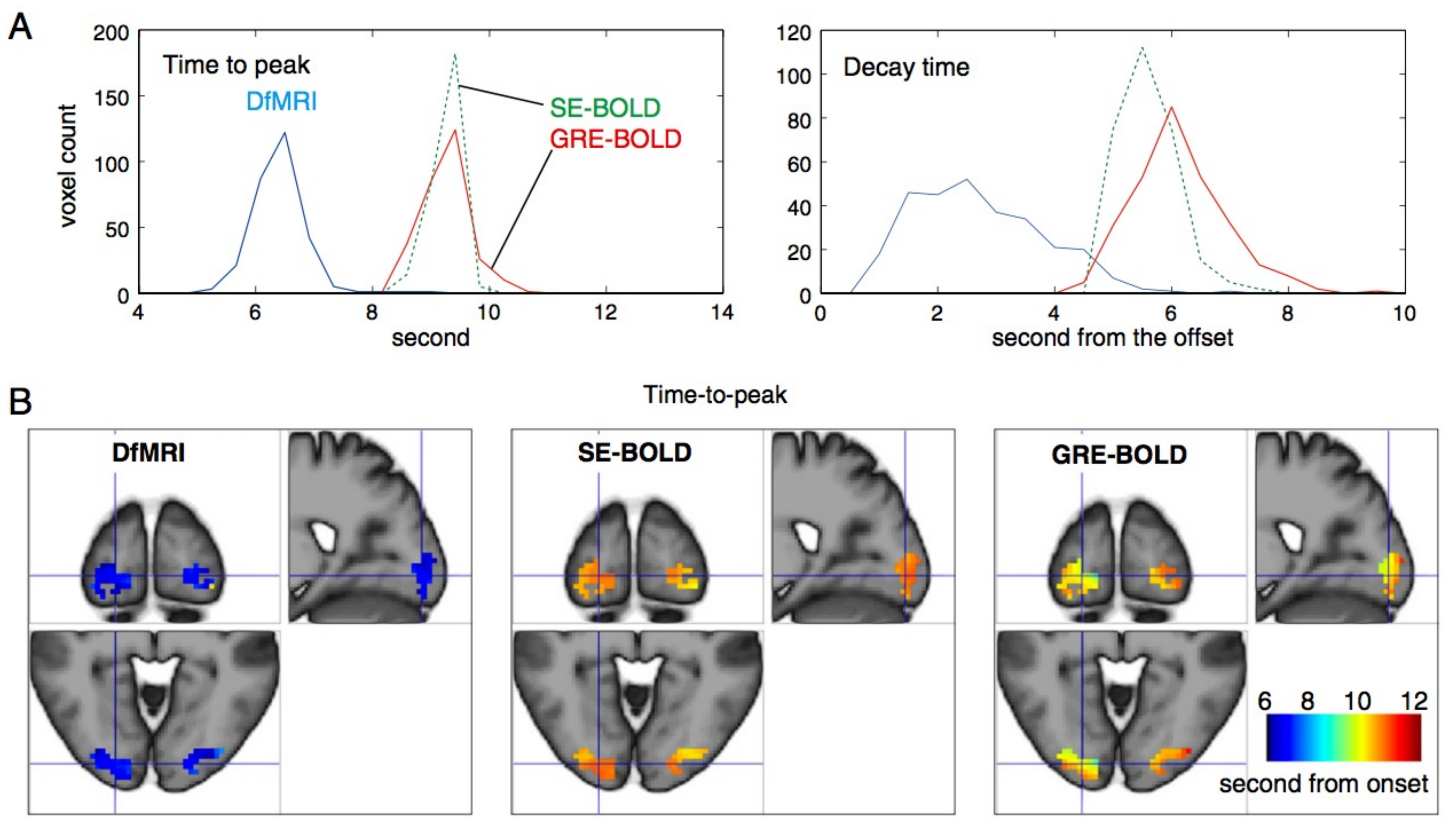


Lee SP et al, MRM (1999)



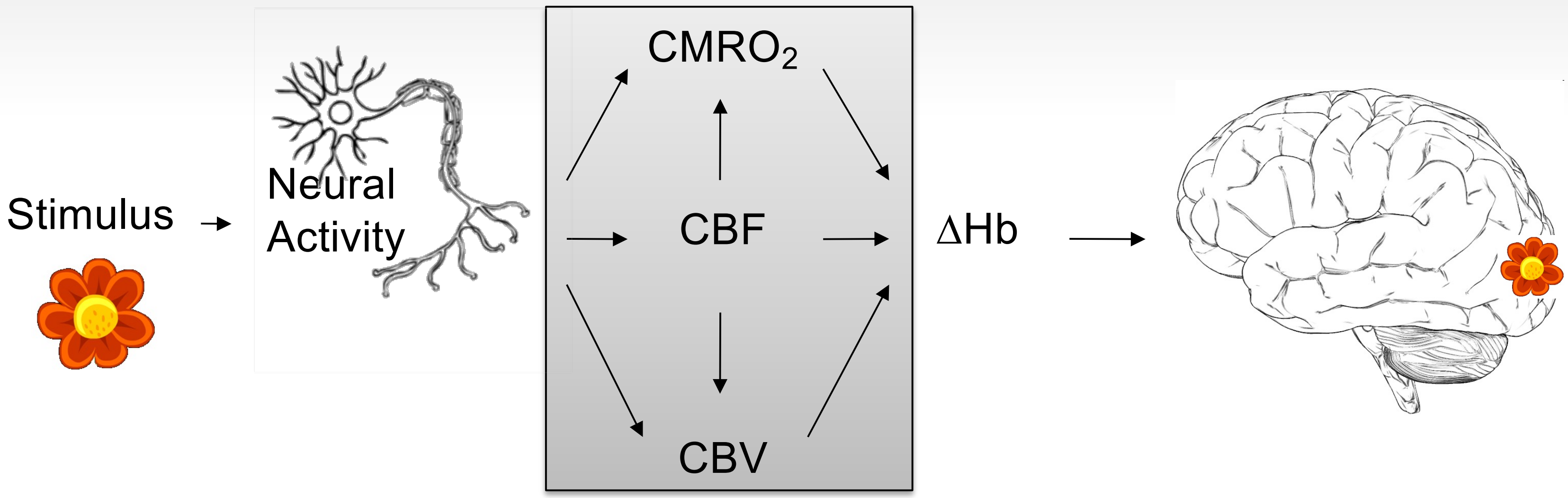
Song et al, NeuroImage 17, 742–750 (2002)

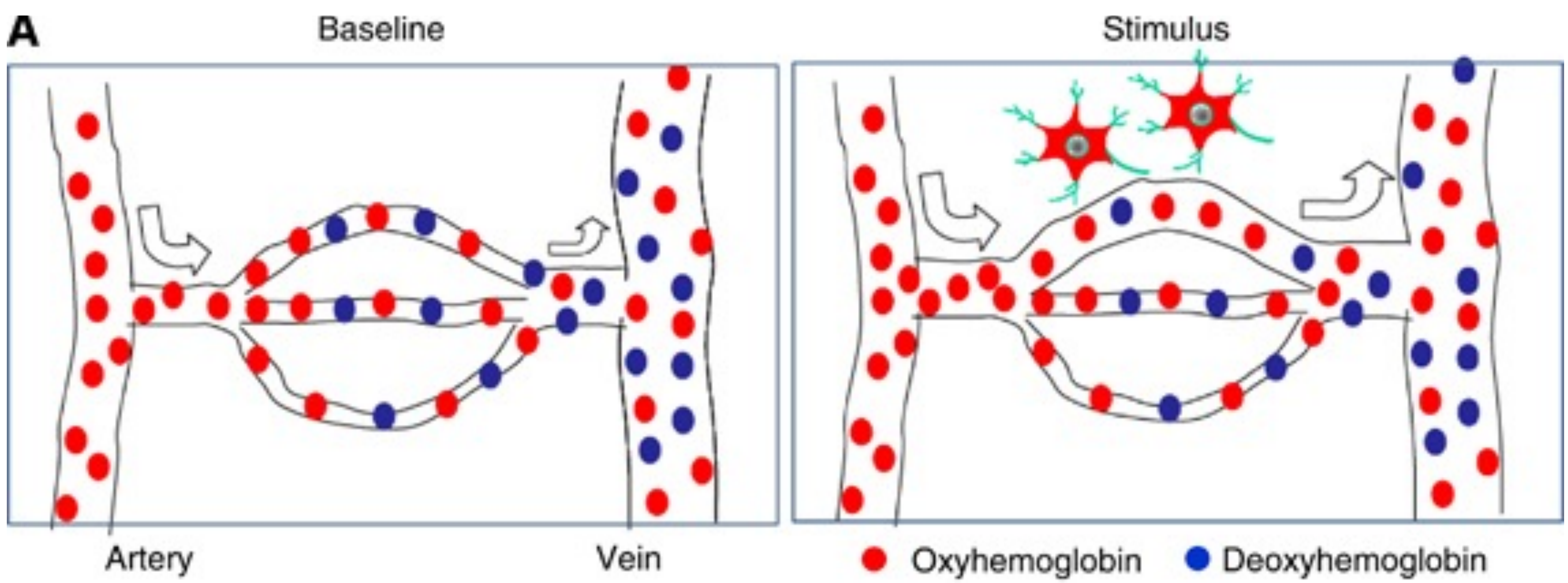
Faster response than SE/GE BOLD



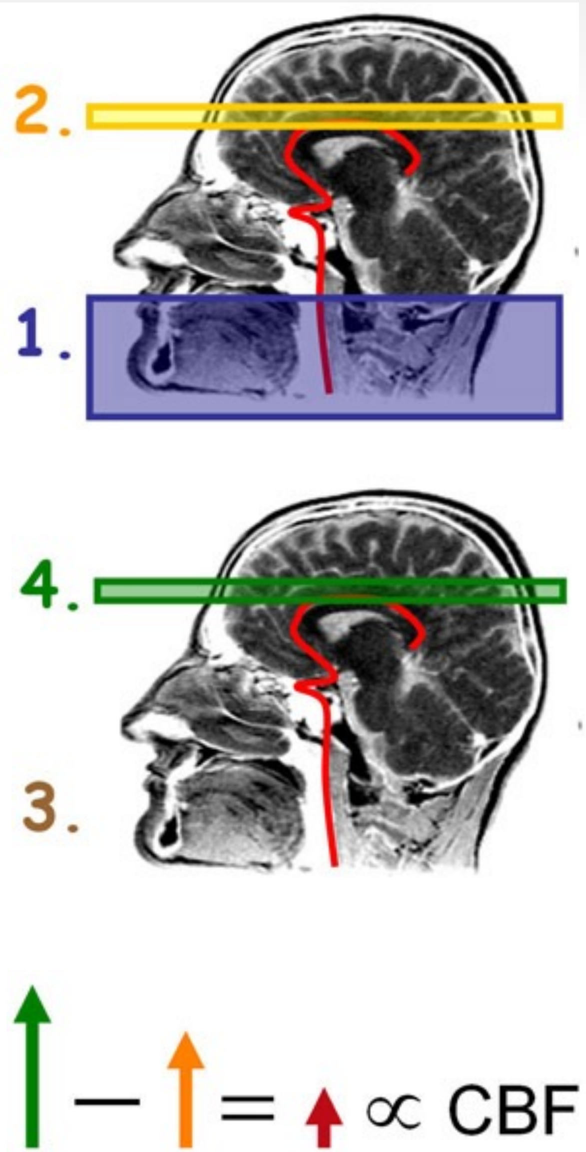
T. Aso et al. NeuroImage 67 (2013) 25–32

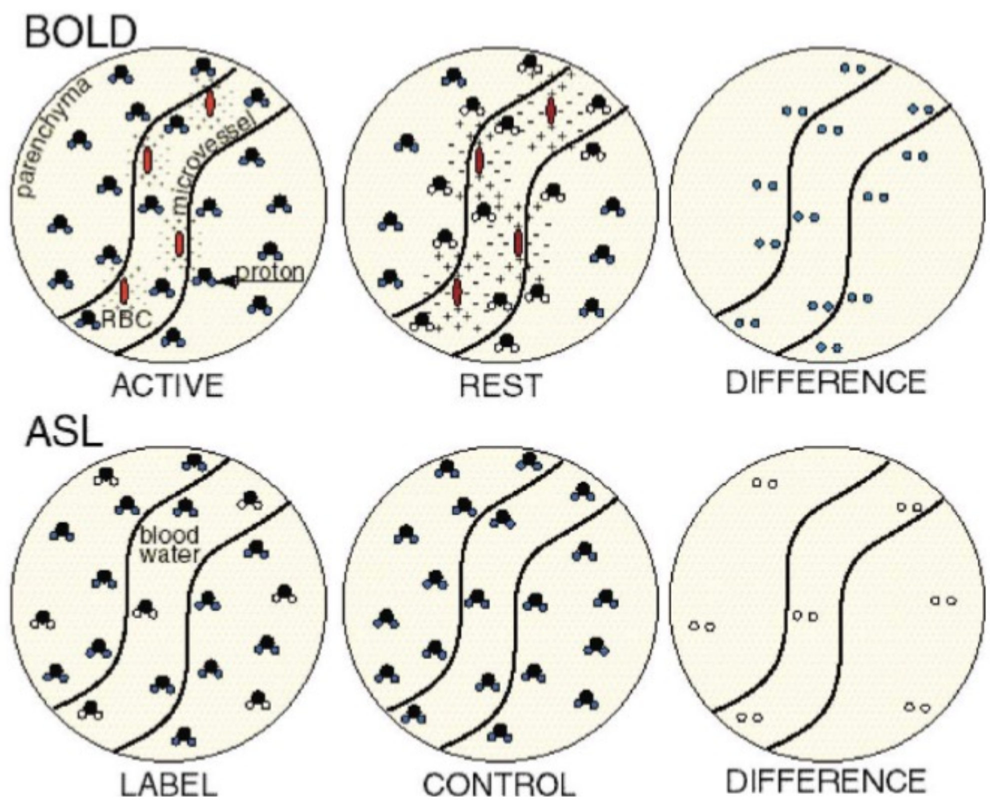
Contrast Mechanisms





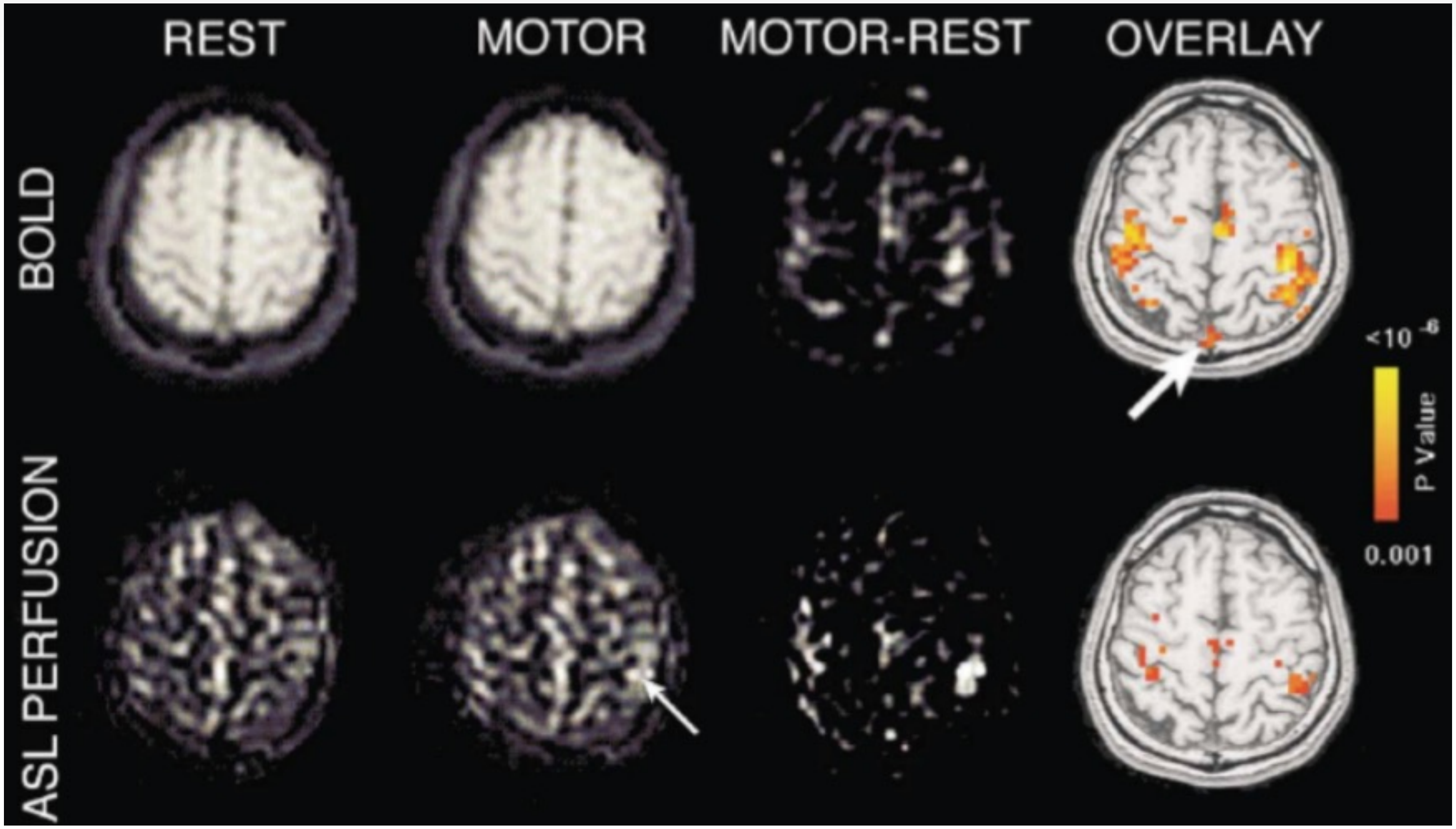
ASL vs. BOLD





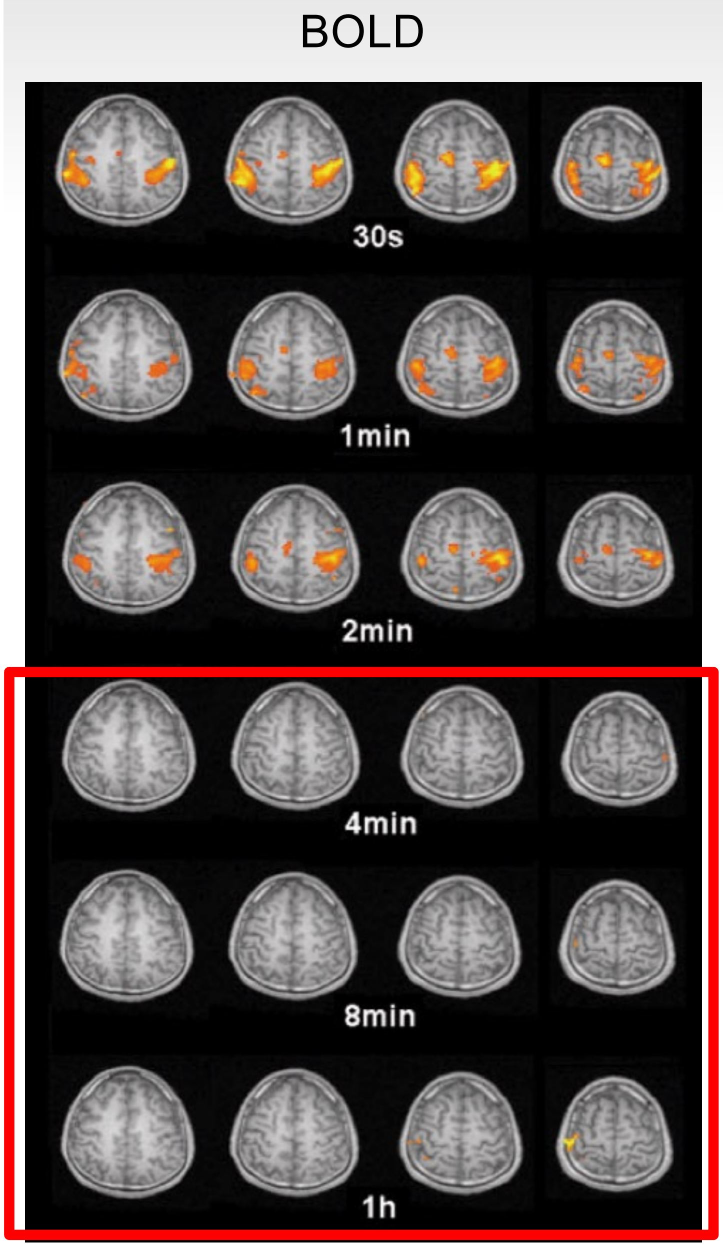
http://fmri.research.umich.edu/research/main_topics/asl.php

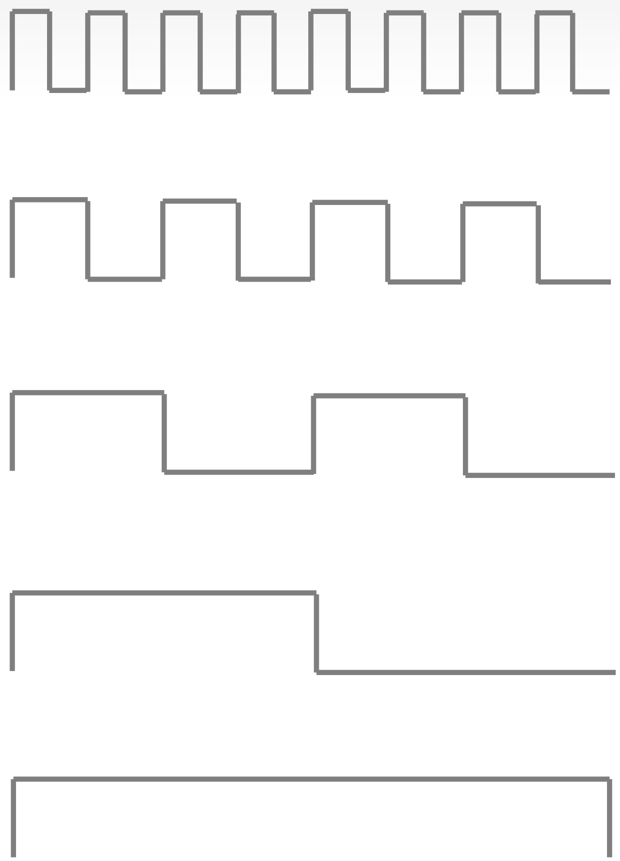
Detre JA et al., Clinical Neurophysiology (2002)

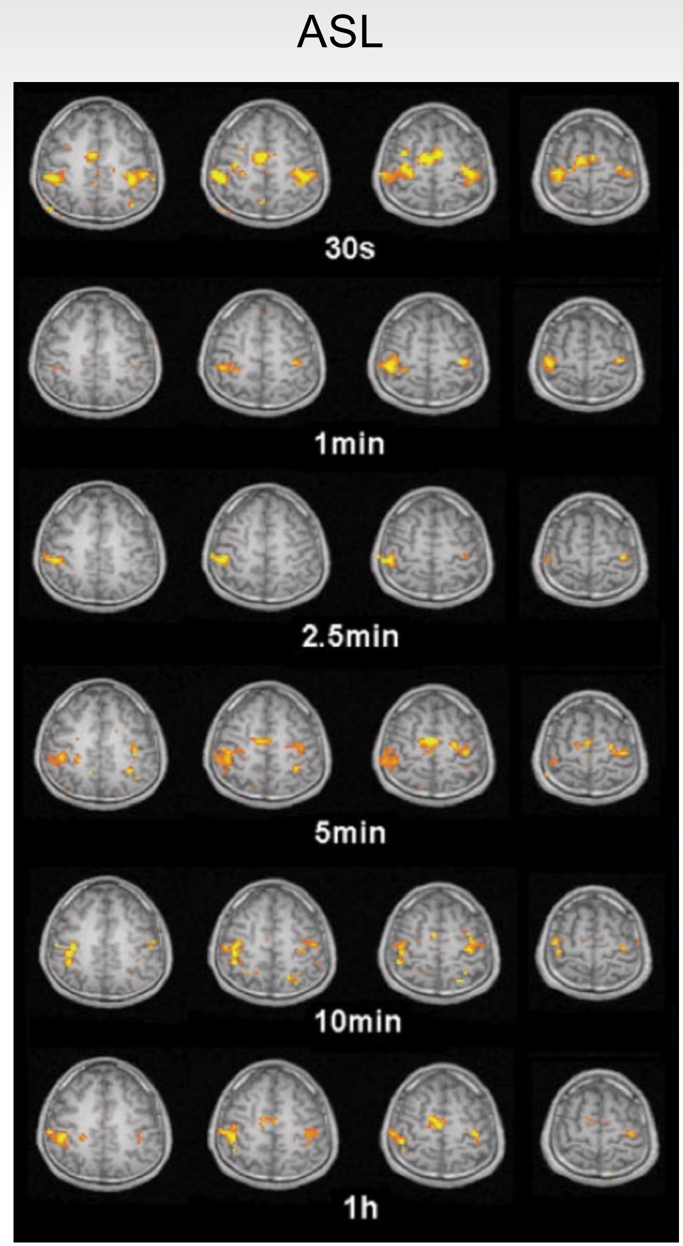


Detre JA et al., Clinical Neurophysiology (2002)

The trouble with slow stimuli







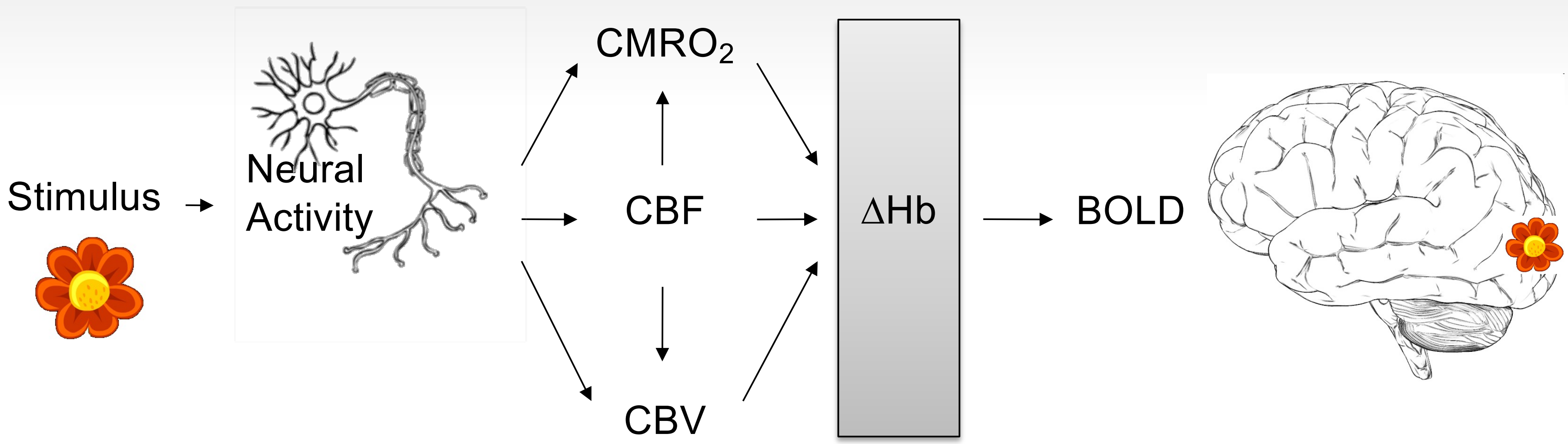
- BOLD has greater signal strength
- ASL has greater sensitivity for long duration stimuli

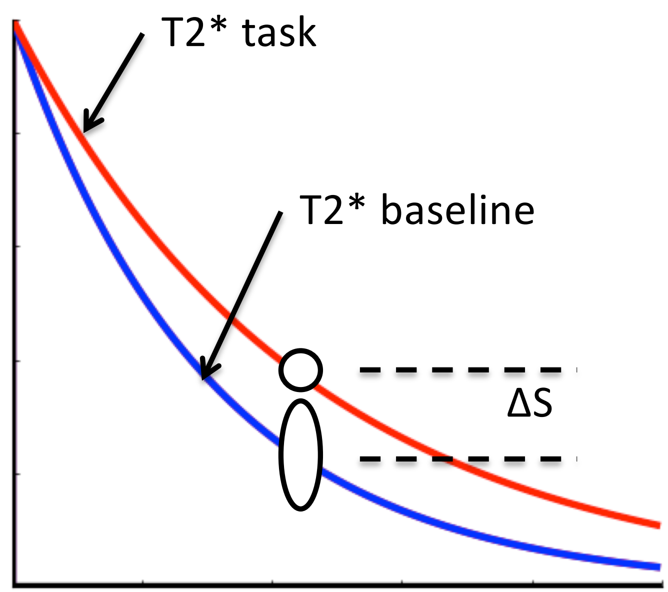
ASL vs. BOLD

	BOLD	ASL
Signal Mechanism	Blood flow, Blood volume, Oxygenation consumption	Blood flow
Contrast parameter	T2*	T1
Spatial specificity	Venules and draining veins	Capillaries, arterioles
Typical signal change	0.5-5 %	< 1 %
Imaging methods	Gradient-echo, spin-echo	Spin-echo
Sample rate (TR)	1-3 s per image	< 3-8s per perfusion image
Optimal task frequency (block design)	0.01 – 0.06 Hz (100 s - 16 s)	< 0.01 Hz
Intersubject variability	High	Low
Imaging coverage	Whole brain	Most of brain cortex
Major artifacts	Susceptibility, motion, baseline drift	Vascular artifact
Relative CNR	> 2 high task frequency < 0.5 low task frequency	1

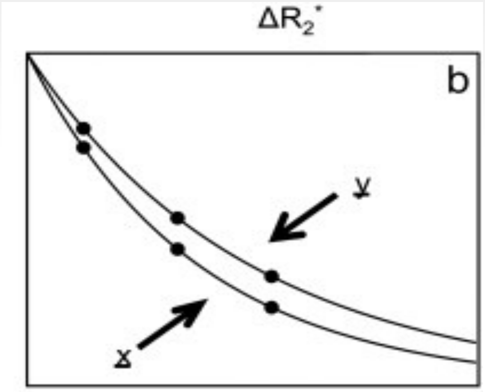
Detre JA et al., Clinical Neurophysiology (2002)

Contrast Mechanisms





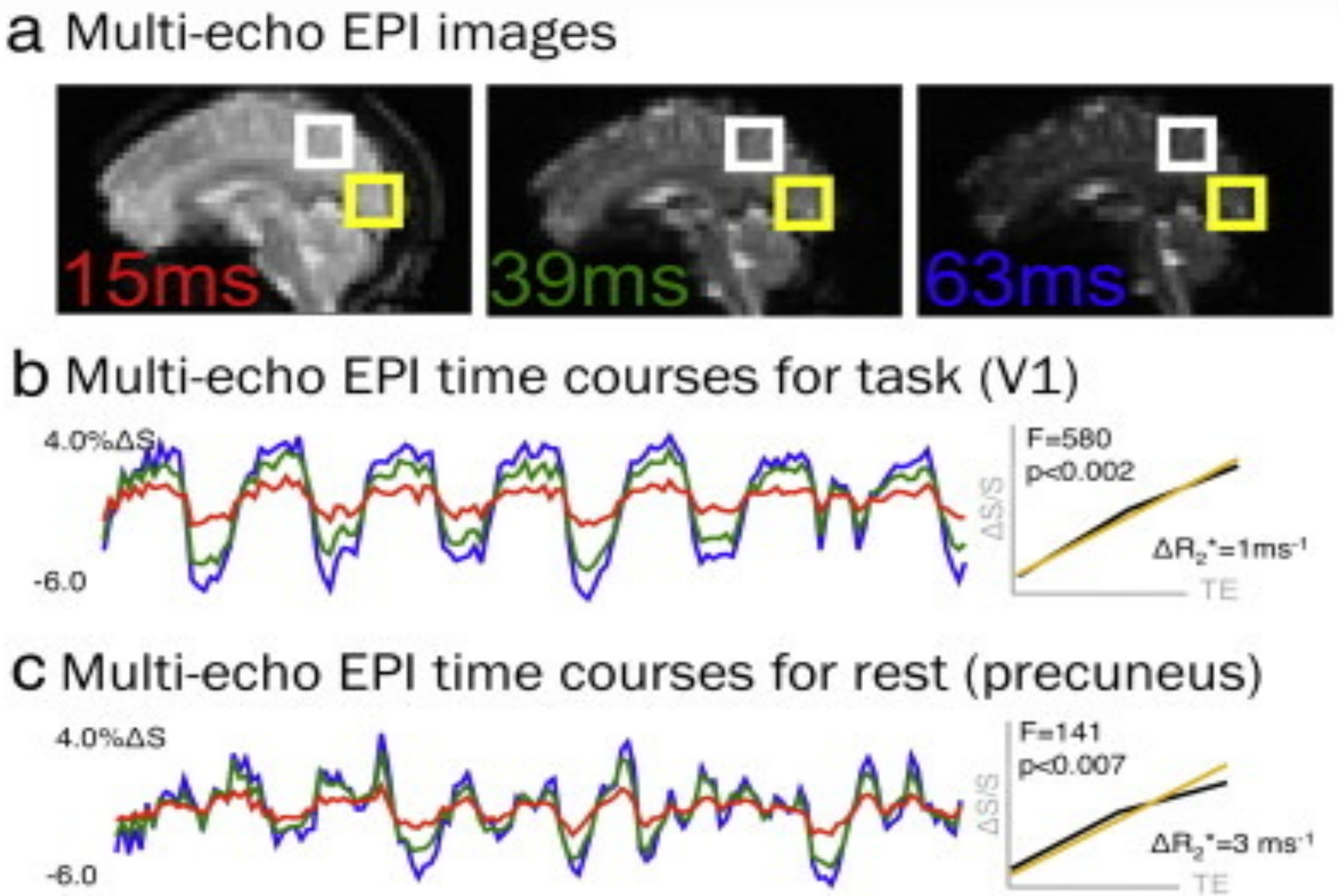
Separating BOLD from non-BOLD



- The BOLD signal is TE dependent
- Non-BOLD signals do not scale with TE

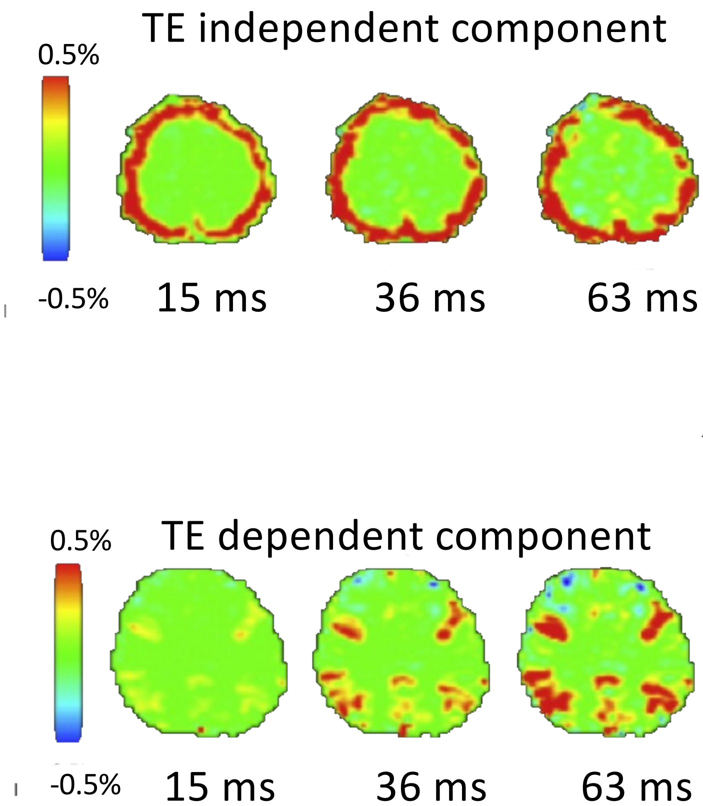
- Measuring several TEs enables the separation of non-BOLD artifacts from the data

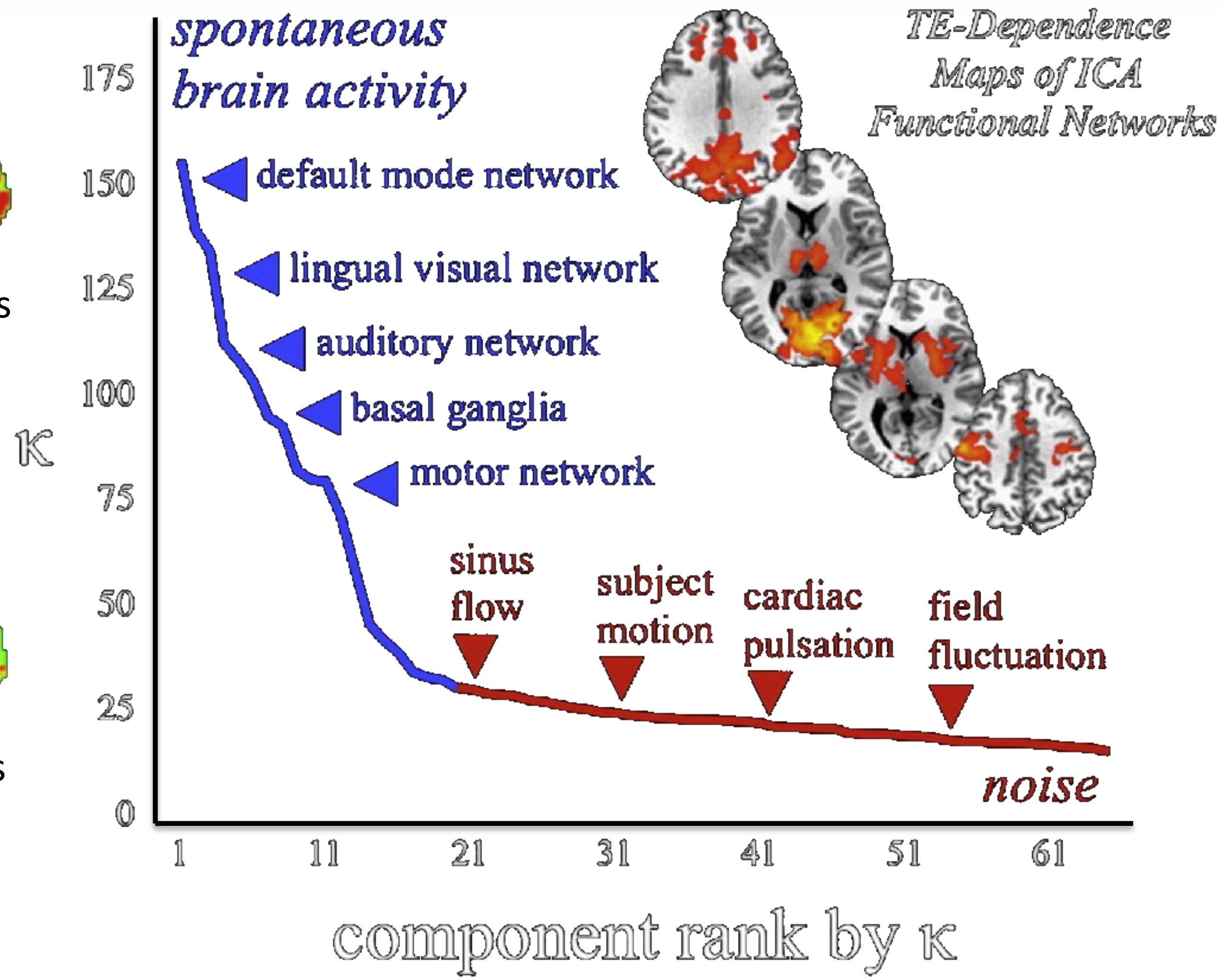
Signal scaling



Kundu, P,l (2012) NeuroImage Vol 60, Iss 3 2012 1759 - 1770

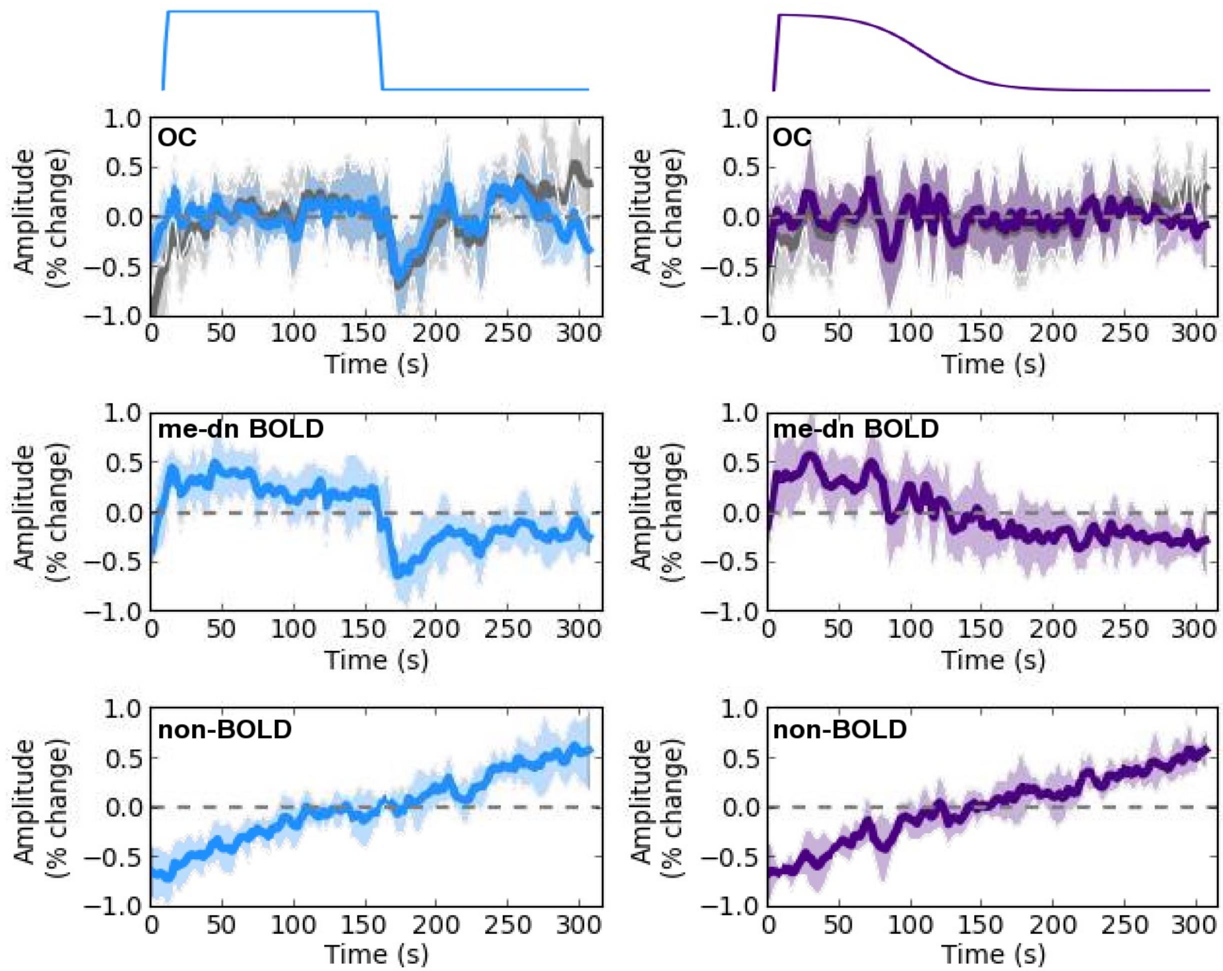
Multi-echo Component selection





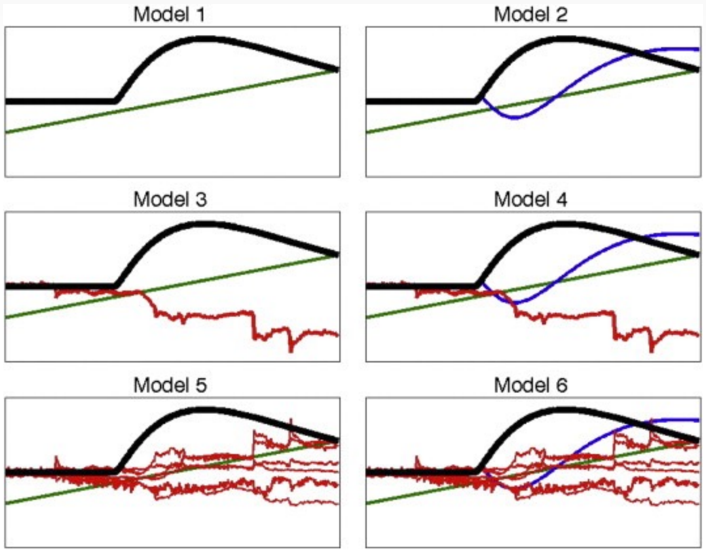
Detection of slow BOLD signals with ME

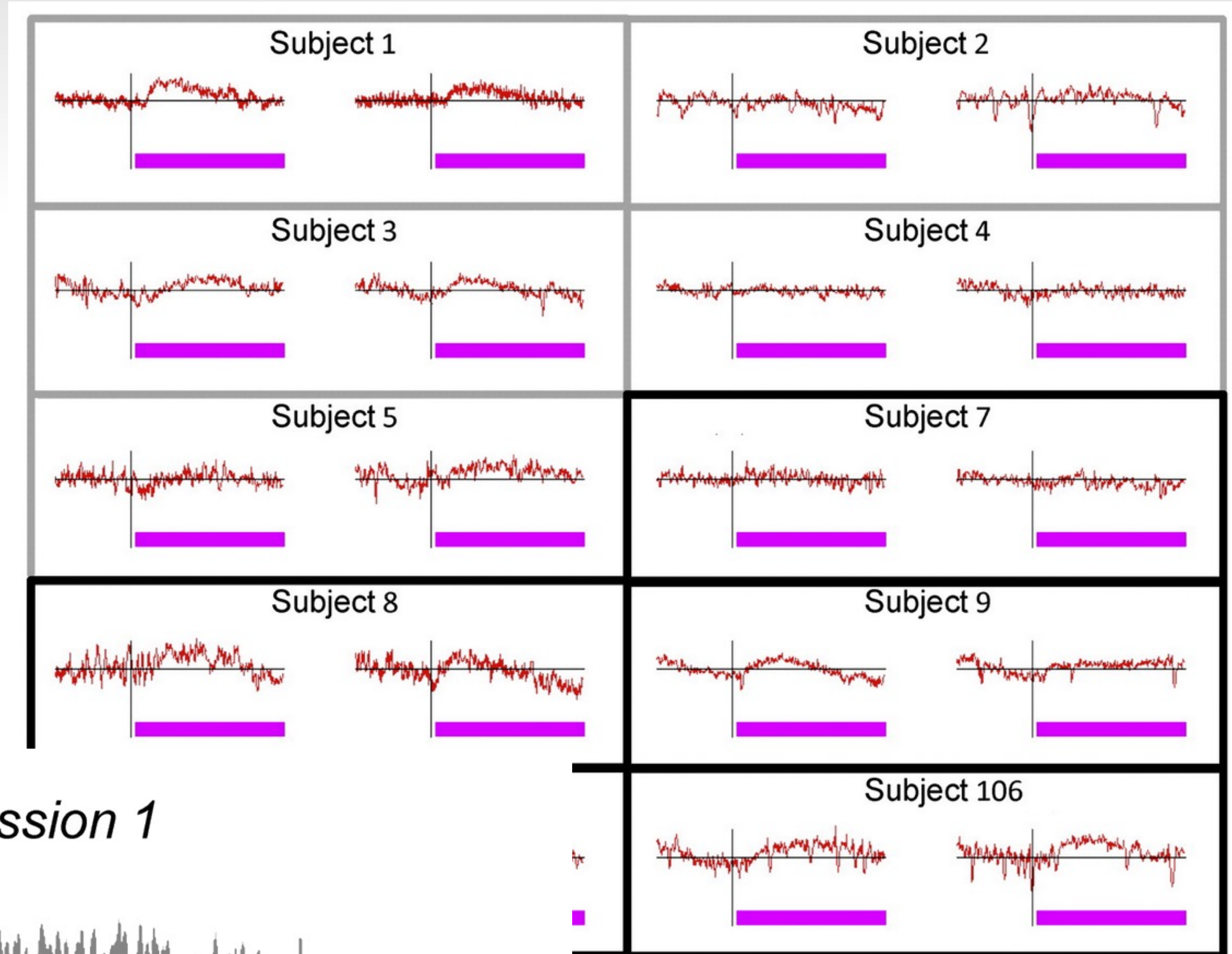
- Group average timeseries taken over voxels in V1 for a visual block and ramp contrast task
- The thick line is the mean and the shading is the standard error.

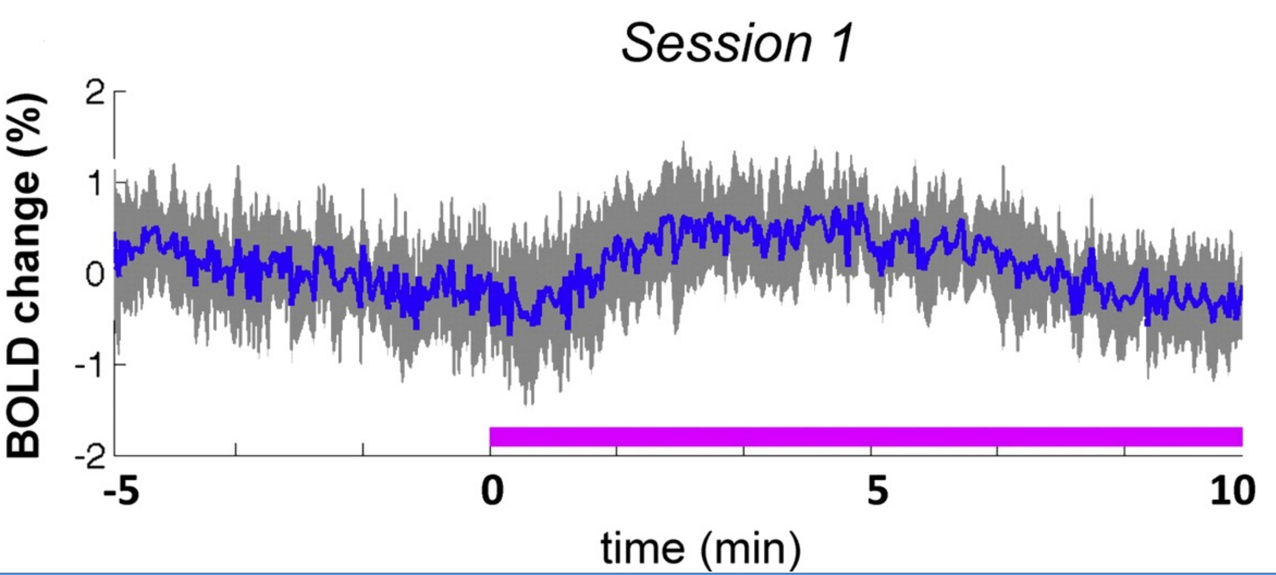


- The block is visible but not the ramp in the OC or standard data
- Both tasks are clear in the me-dn BOLD data
- The scanner specific drift is visible in the non-BOLD data
- It effectively cancels the ramp in the OC data

Response to ketamine infusion.





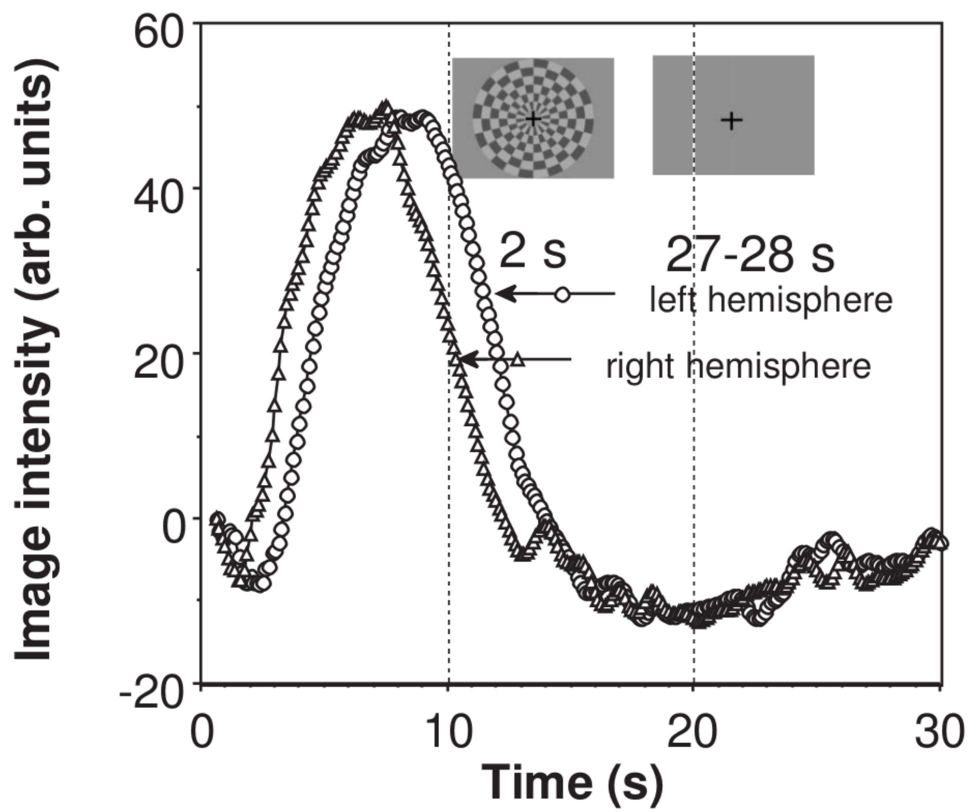


Outline

- Limitations based on the biophysical constraints
  - voxel contents
  - neurovascular coupling
  - hemodynamic response
- Limitations based on imaging constraints
  - Space – time tradeoffs (optimal voxel size)
  - Pulse sequence contrasts
- **Summary**

Temporal limits

- Create a functional image within 2s for more robust activation or in less than 1s using acceleration
- Limited by filtering lag of hemodynamic response function 4-6 s
- Can detect differences in the onset of hemodynamic responses down to 100 ms using paradigm manipulations
- Long (> 2 min) duration stimuli are hampered by baseline changes but can be measured using ME acquisitions



Menon and Kim, Biochem. Cell Biol. 1998

Spatial limitations

• At 3 T : ~ 1.5 mm^3 resolution

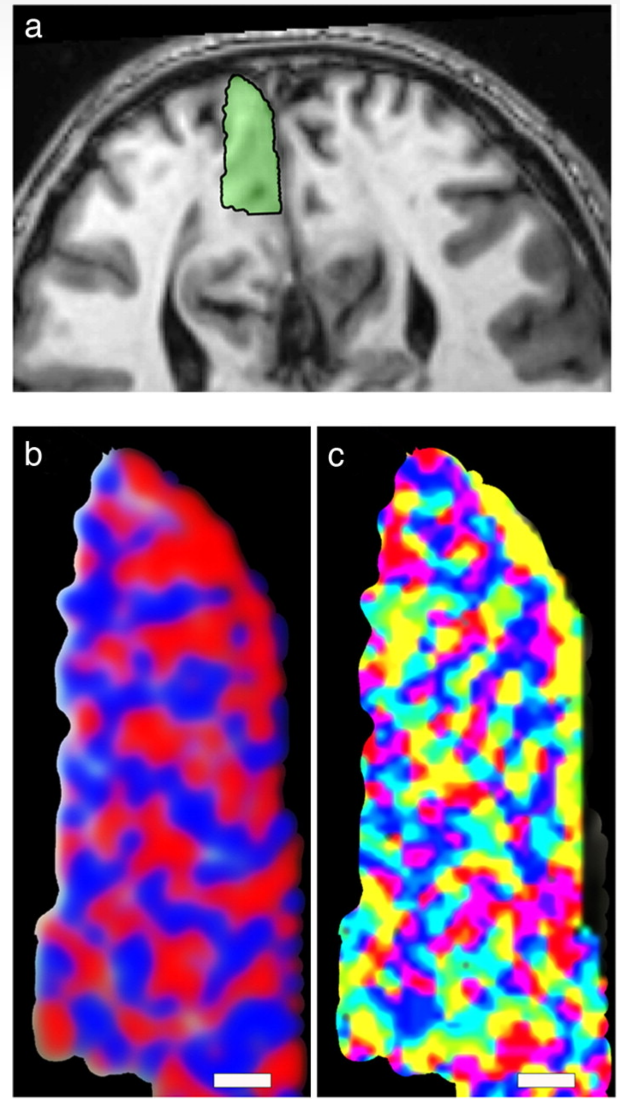
The functional point spread function is about 3.5 mm.

• At 7 T, ~ 0.5 mm^3 resolution

- The functional point spread function can be has high as 1.5 mm.

• At 7 T, using spin-echo sequences, the smallest resolved functional unit was orientation columns (on the order of 0.5-mm width).

• Practically limited by smoothing kernels, template alignment in group studies.



Yacoub E et al. PNAS 2008;105:10607-10612

Summary

- Technical / hardware abilities are rapidly approaching the temporal and spatial resolution of the functional response
- Limitation with fMRI now lie in the origins of the signal

Acknowledgements

Thanks to:

Catie Chang
Peter Bandettini