Tradeoffs in fMRI acquisition

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Experimental Therapeutics and Pathophysiology Branch
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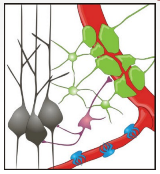
fMRI summer course
08Jun16

National Institute
of Mental Health

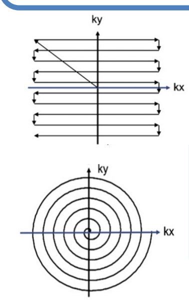
Outline

Introduction



- Voxel contents
- neurovascular coupling
- hemodynamic response
- MR signal basics
- BOLD signal basics

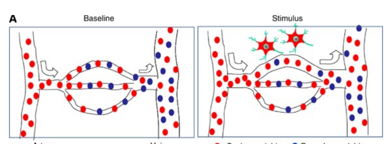
MR acquisition Basics

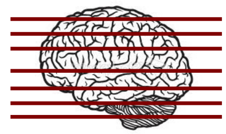


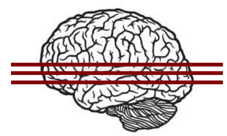
- K-space
- EPI
- Spiral
- TR/TE

Functional Contrast

- BOLD
  - Gradient-echo
  - Spin-echo
  - Multi-echo
- Perfusion
- Diffusion
- VASO







Spatial/Temporal resolution

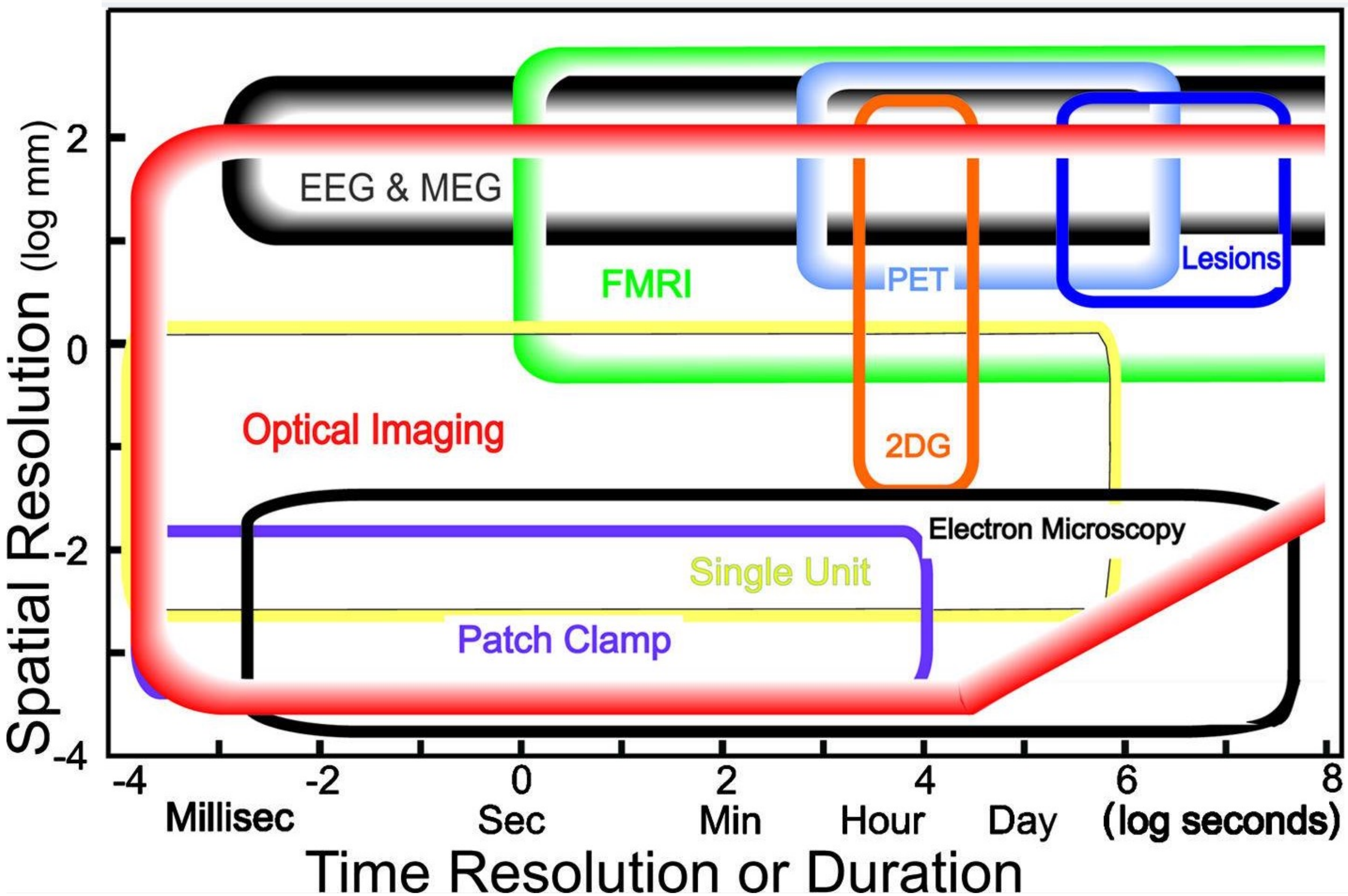
Imaging Factors

- Field strength 3T, 7T
- <u>Acceleration:</u>
- k-space: Single/multi-shot EPI
- In-plane: SENSE (ASSET)
  GRAPPA (iPAT)
- Multi-slice

Biological factors

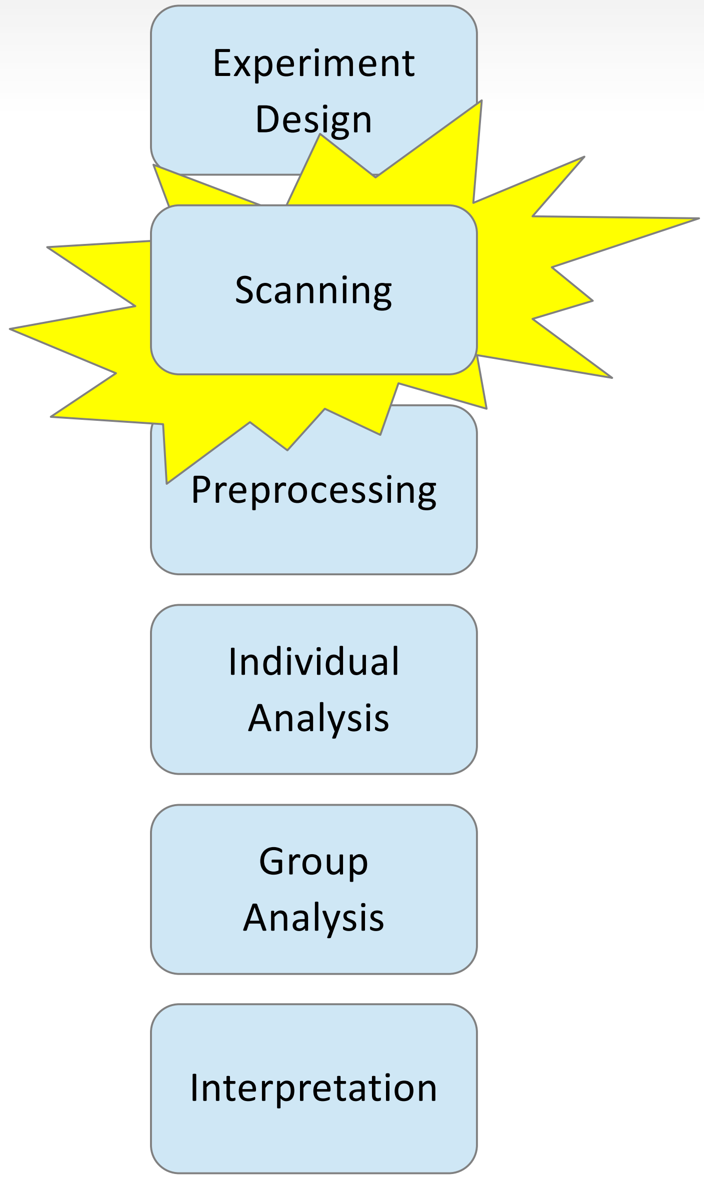
- Veins/capillaries
- Physiological noise

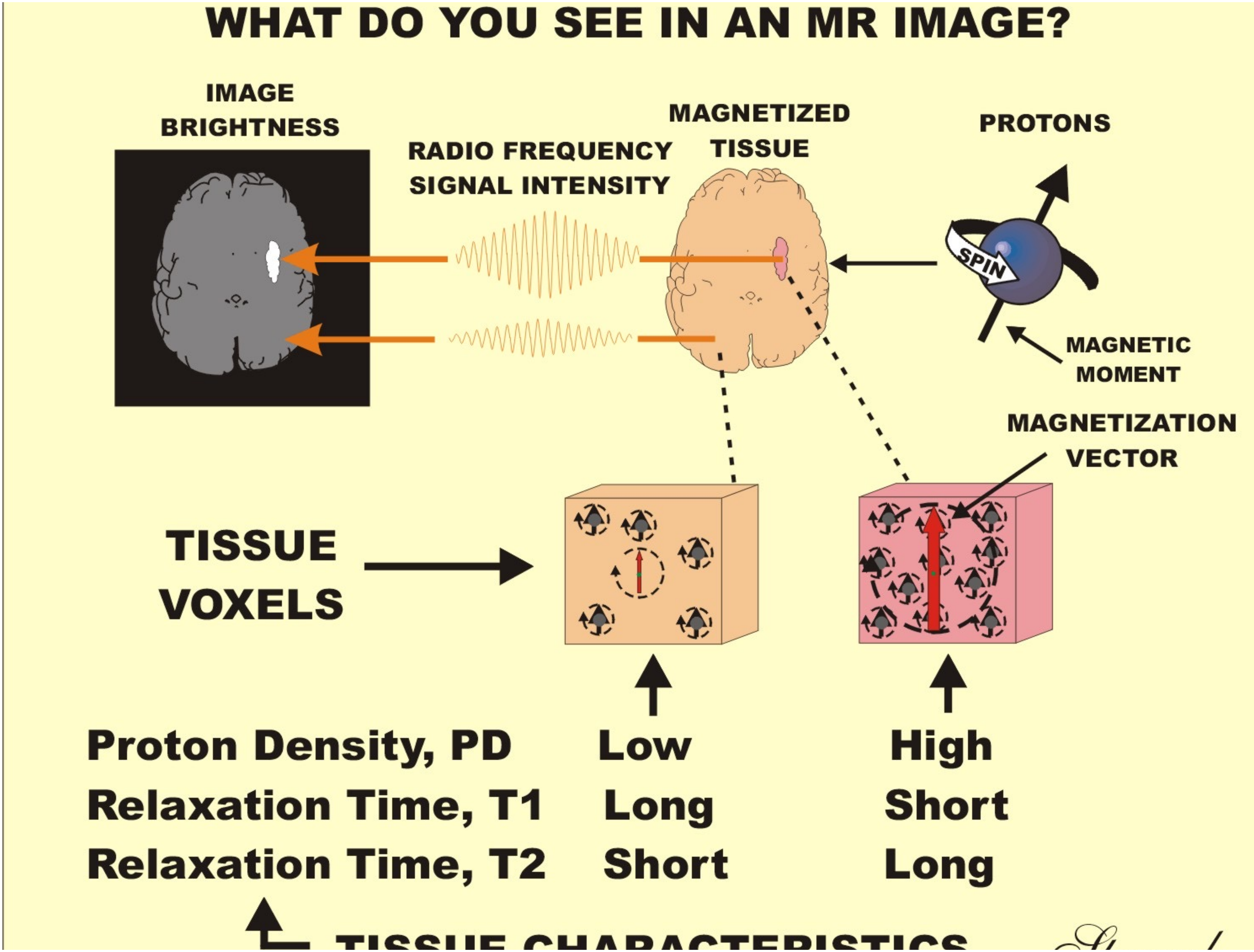
fMRI in temporal – spatial perspective

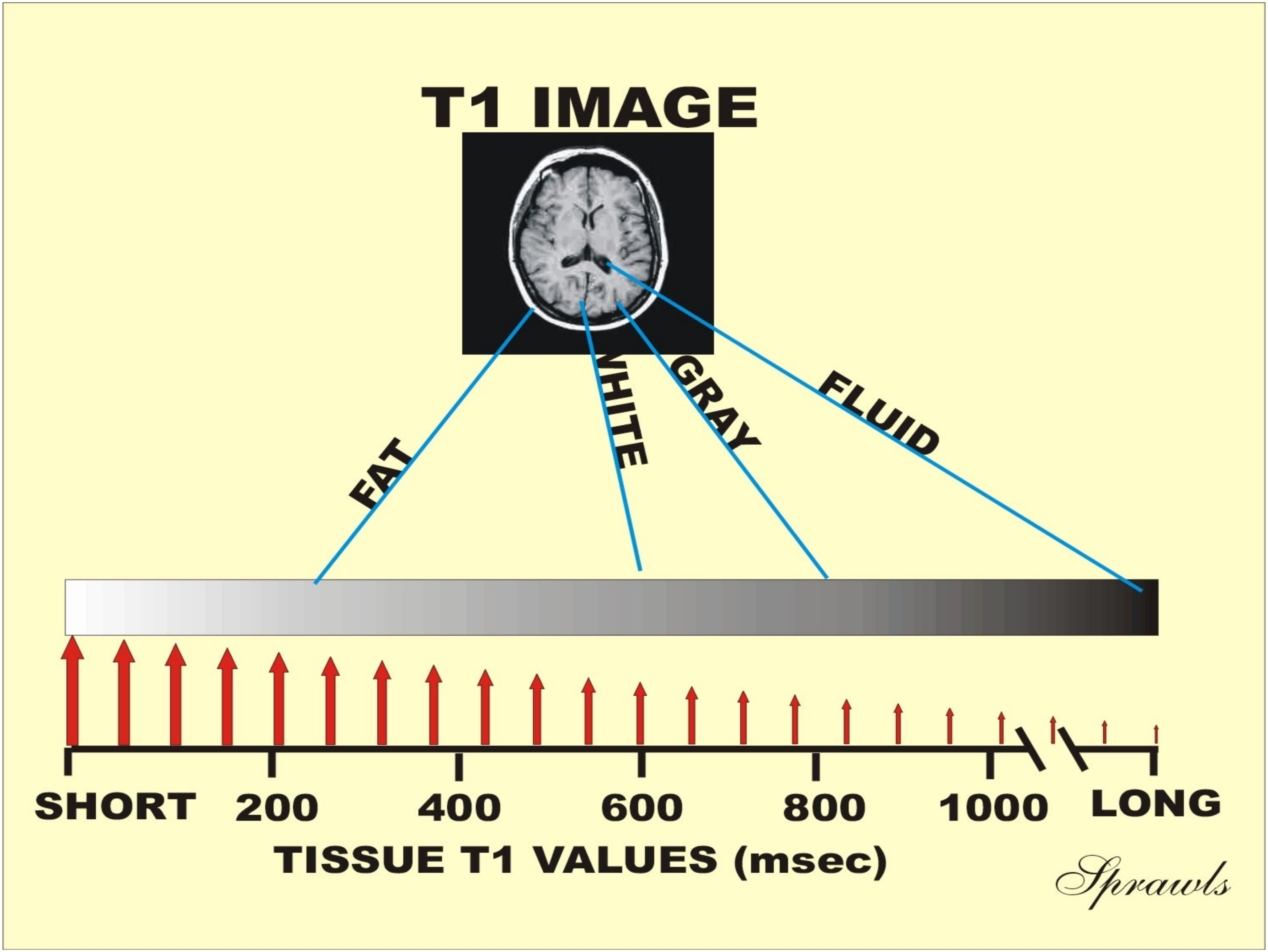


Grinvald A. PNAS (2005)

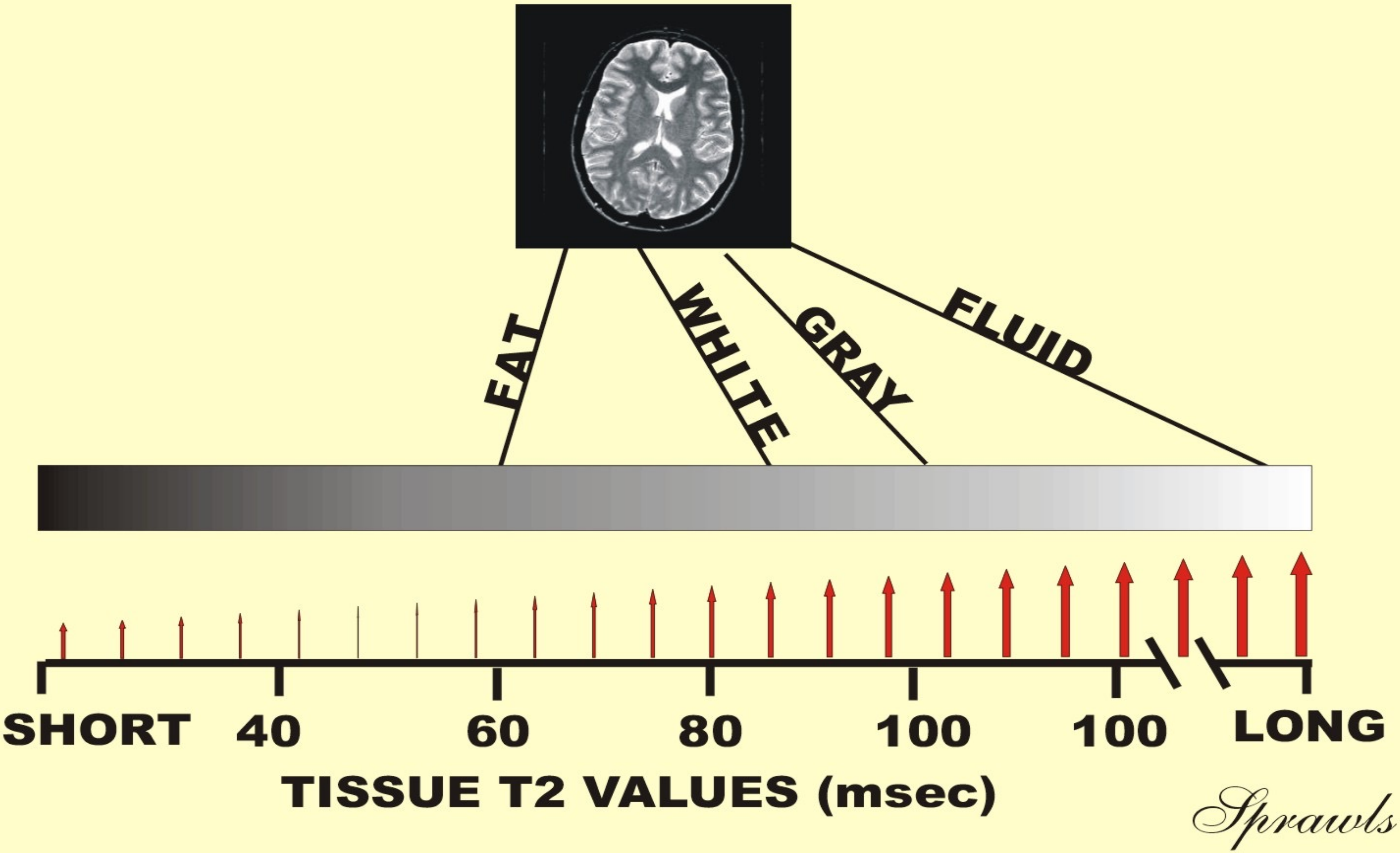
fMRI data pipeline



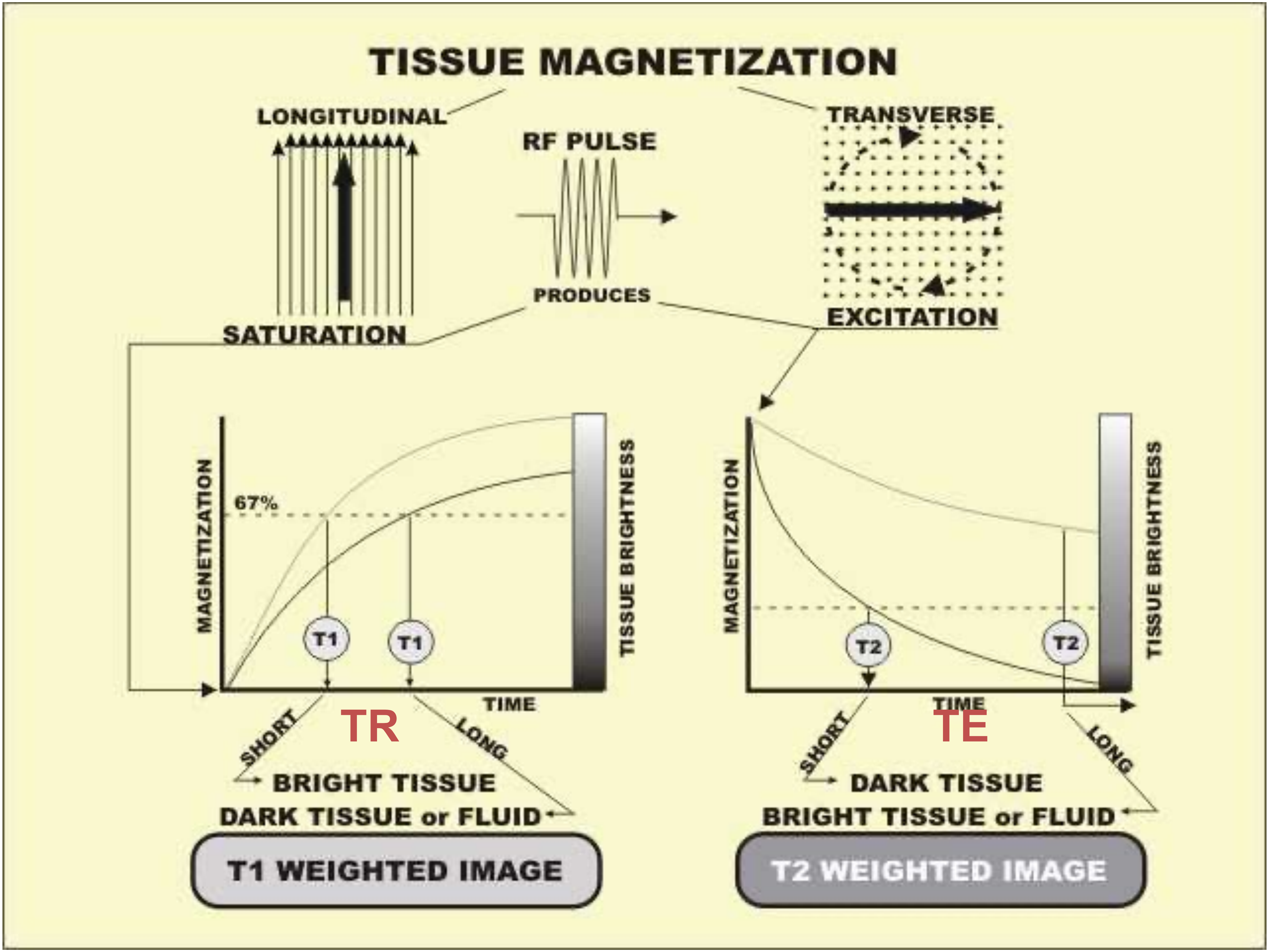

WHAT DO YOU SEE IN AN MR IMAGE?
IMAGE BRIGHTNESS
RADIO FREQUENCY SIGNAL INTENSITY
MAGNETIZED TISSUE
PROTONS
SPIN
MAGNETIC MOMENT
MAGNETIZATION VECTOR
TISSUE VOXELS
Proton Density, PD Low High
Relaxation Time, T1 Long Short
Relaxation Time, T2 Short Long
TISSUE CHARACTERISTICS


T1 IMAGE
FAT
WHITE
GRAY
FLUID
SHORT
200
400
600
800
1000
LONG
TISSUE T1 VALUES (msec)
Sprawls

T2 IMAGE

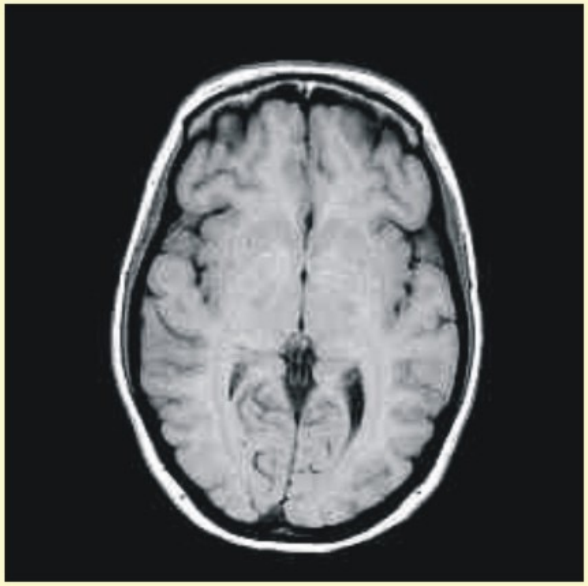


FAT
WHITE
GRAY
FLUID
SHORT
40
60
80
100
100
LONG
TISSUE T2 VALUES (msec)
Sprawls

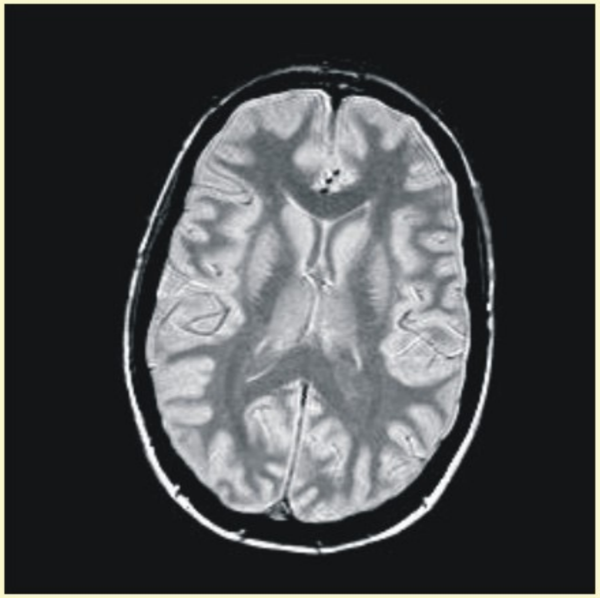

TISSUE MAGNETIZATION
LONGITUDINAL
RF PULSE
TRANSVERSE
PRODUCES
SATURATION
EXCITATION
MAGNETIZATION
67%
T1
T1
TISSUE BRIGHTNESS
TIME
TR
SHORT
LONG
BRIGHT TISSUE
DARK TISSUE or FLUID
T1 WEIGHTED IMAGE
MAGNETIZATION
T2
T2
TISSUE BRIGHTNESS
TIME
TE
SHORT
LONG
DARK TISSUE
BRIGHT TISSUE or FLUID
T2 WEIGHTED IMAGE

MAGNETIC RESONANCE IMAGE

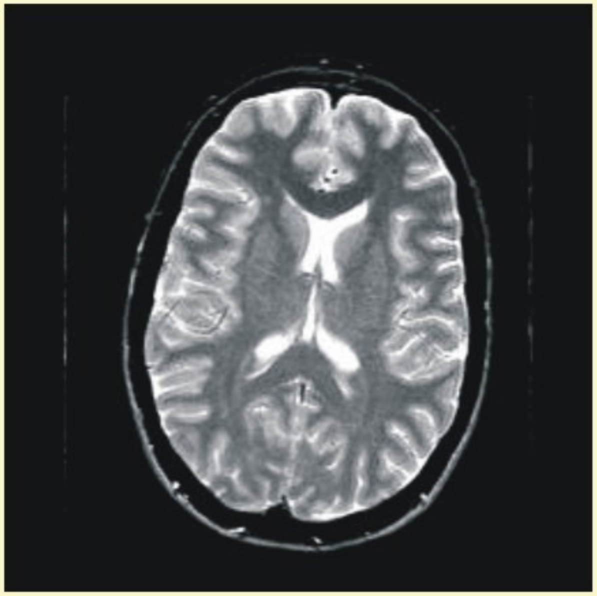
(WHAT DO YOU SEE?)



T1



PROTON DENSITY

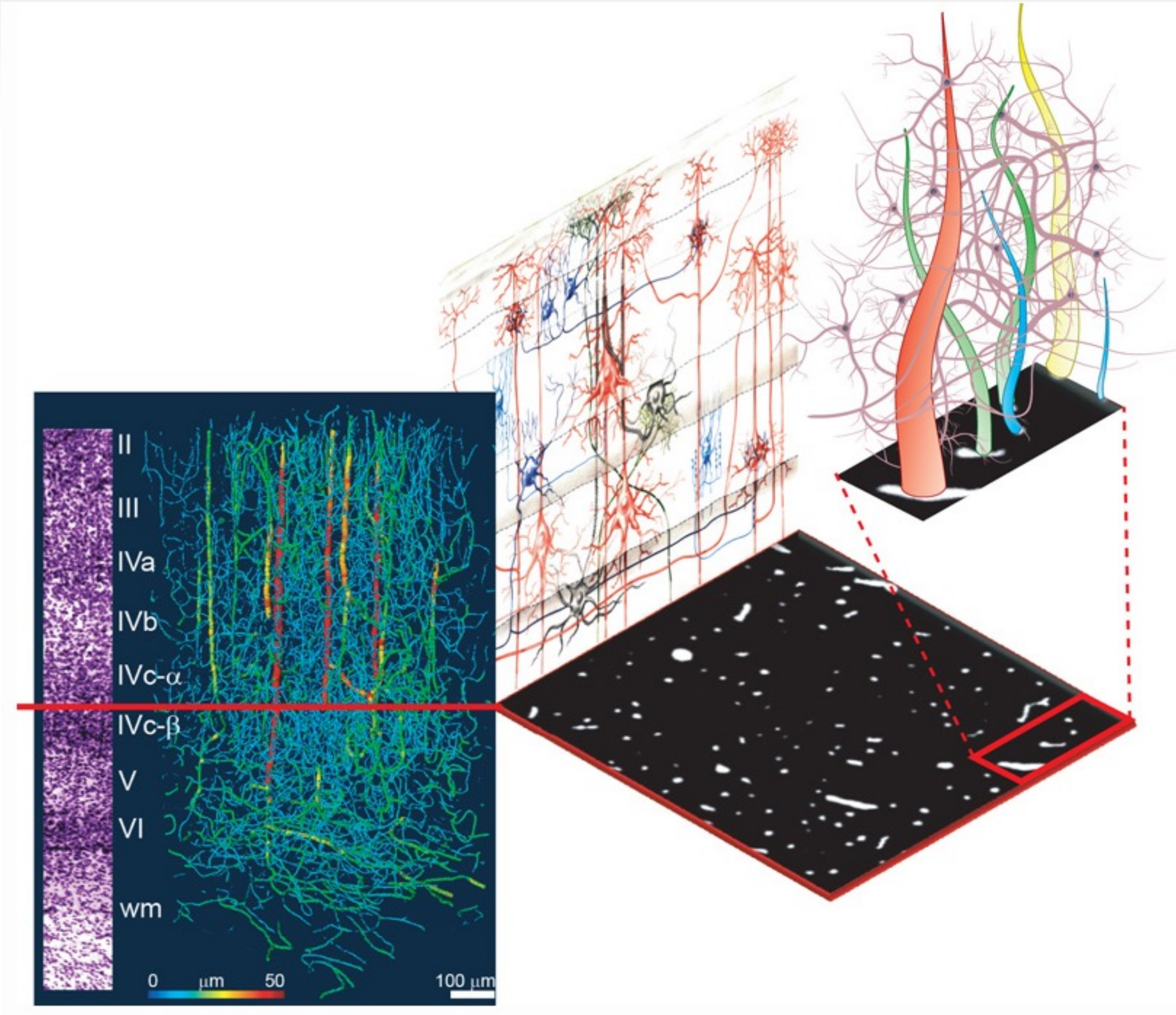


T2

TISSUE CHARACTERISTICS

Sprawls

What's in a voxel?



- Neurons
- Synapses
- Axons
- Dendrites

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

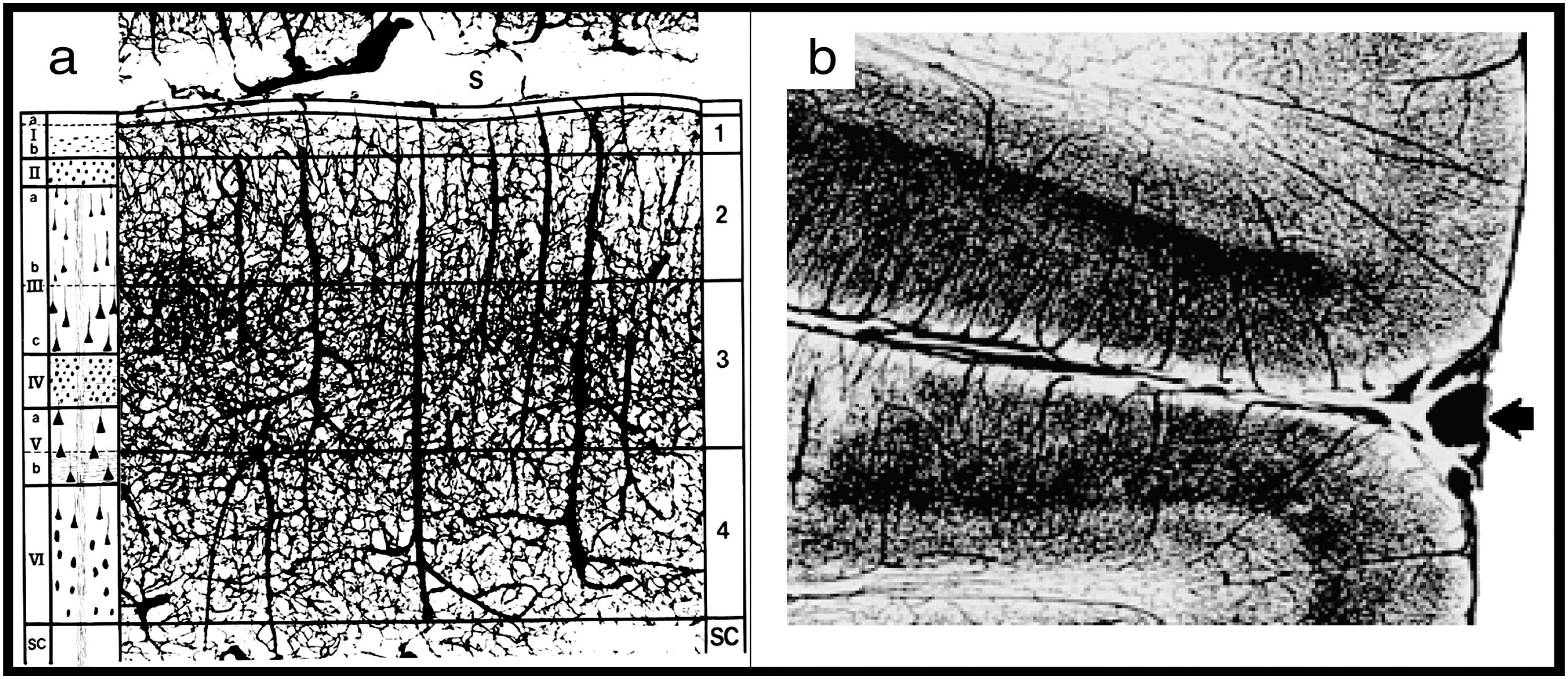
Logothetis NK, Nature (2008)

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

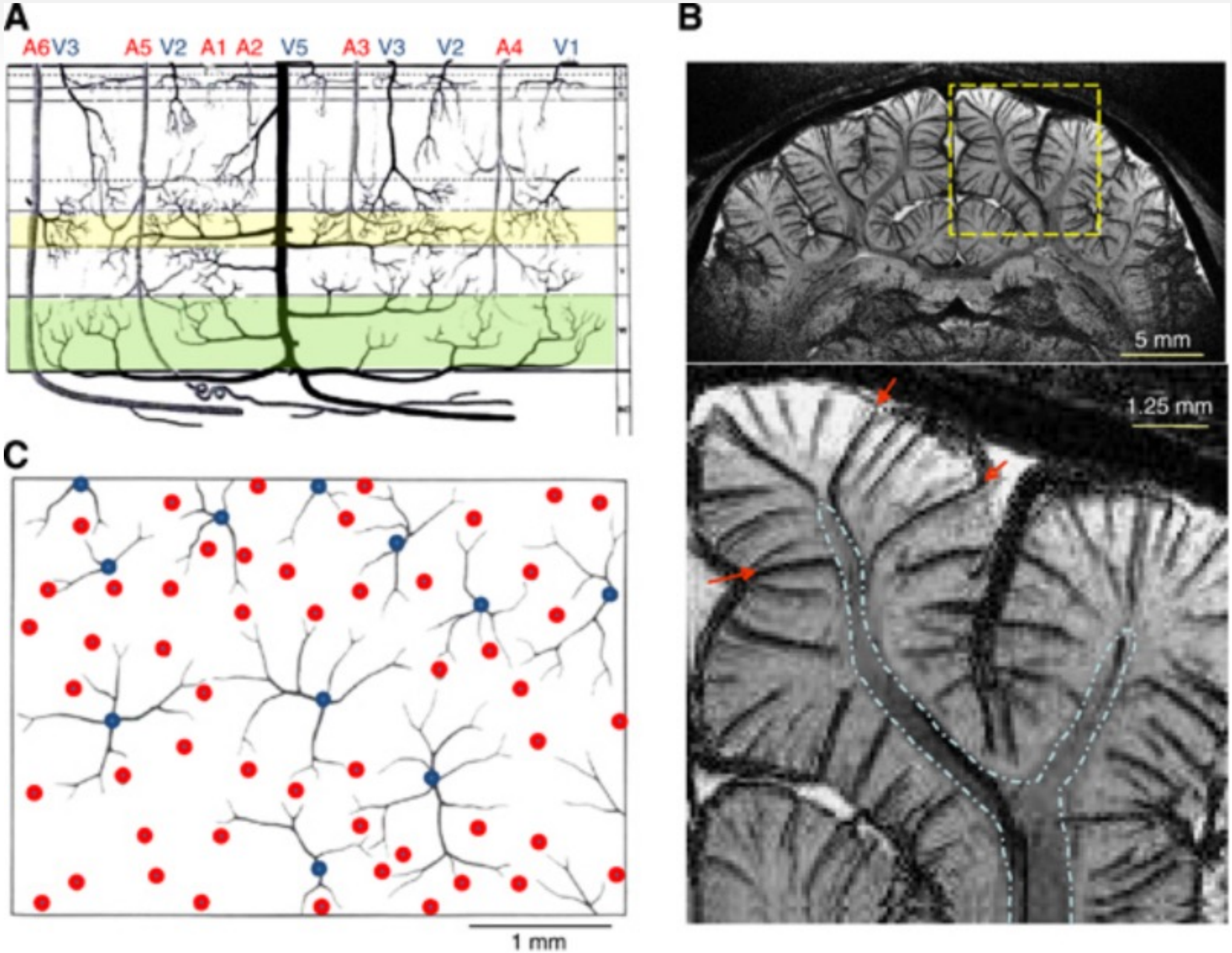
- 5.5 million neurons
- 2.2-5.5 10^{10} synapses
- 22 km of dendrites
- 220 km of axons

And vasculature ...

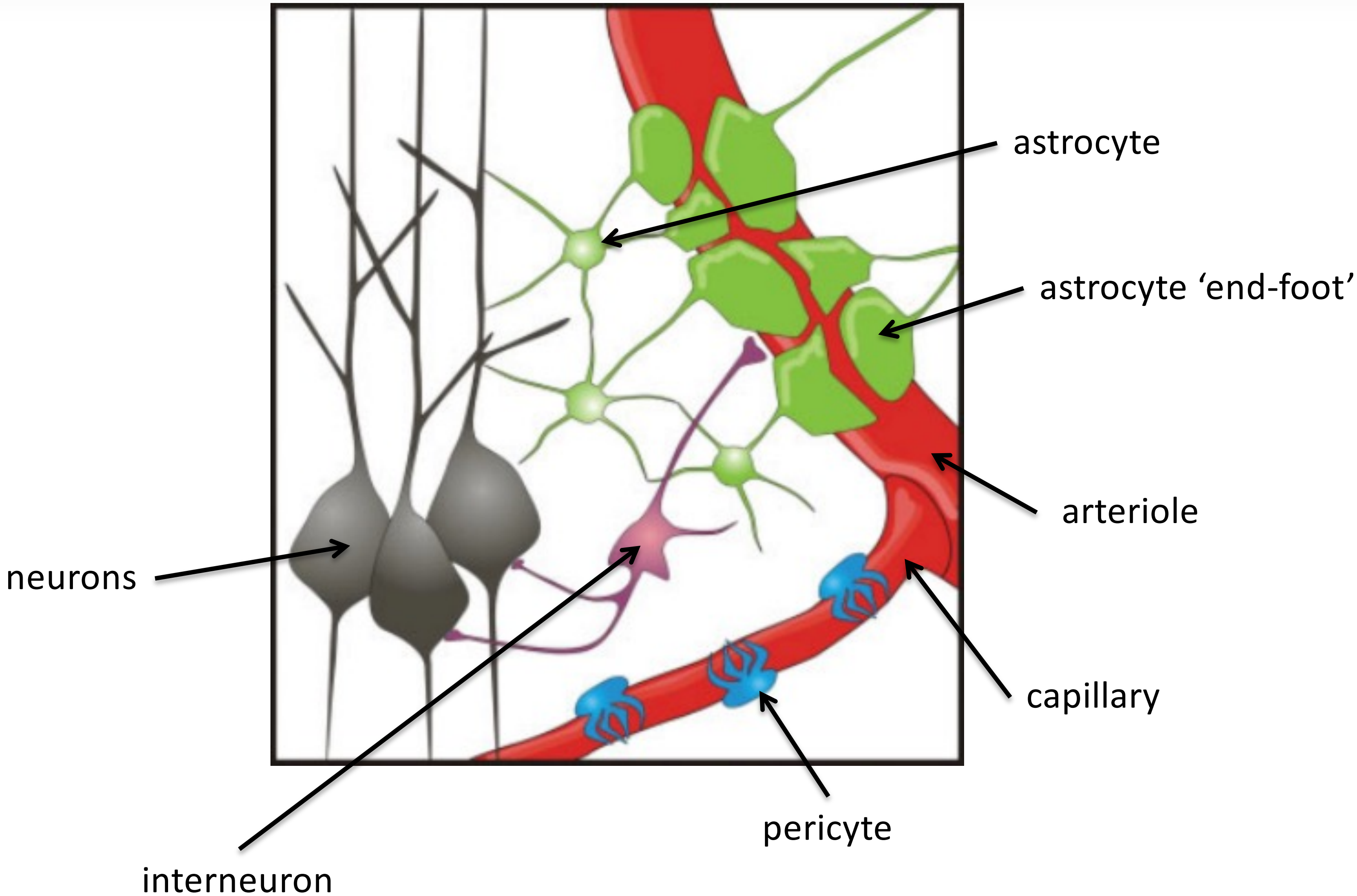


Duvernoy, Brain Res. Bull. (1981)

Spatial inhomogeneity of vasculature



Neurovascular coupling



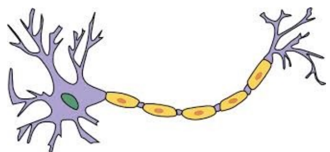
http://orion.bme.columbia.edu/~hillman/Brain_Imaging.html

Hemodynamic response and BOLD signals

Stimulus

Or endogenous activity

Neuronal Activity

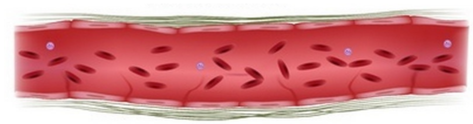


- Excitatory and inhibitory activity
- Anesthetic influence

Neurovascular coupling

- Metabolic signal unknown
- Drugs / Anesthetic influence
- Disease

Hemodynamic response

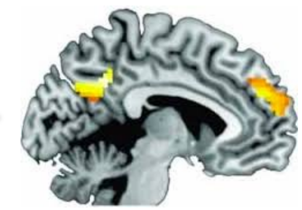


- Blood flow
- Blood oxygenation level
- Blood volume
- Hematocrit

Detection by MRI scanner

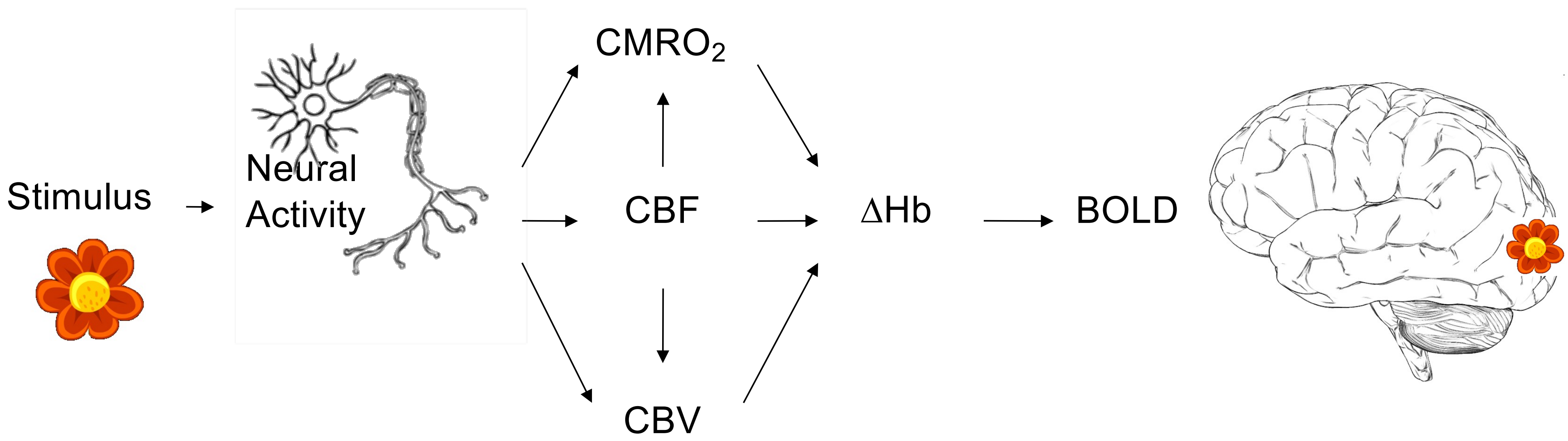
- Field strength
- TR
- TE
- Pulse sequence / Image Contrast

fMRI BOLD response



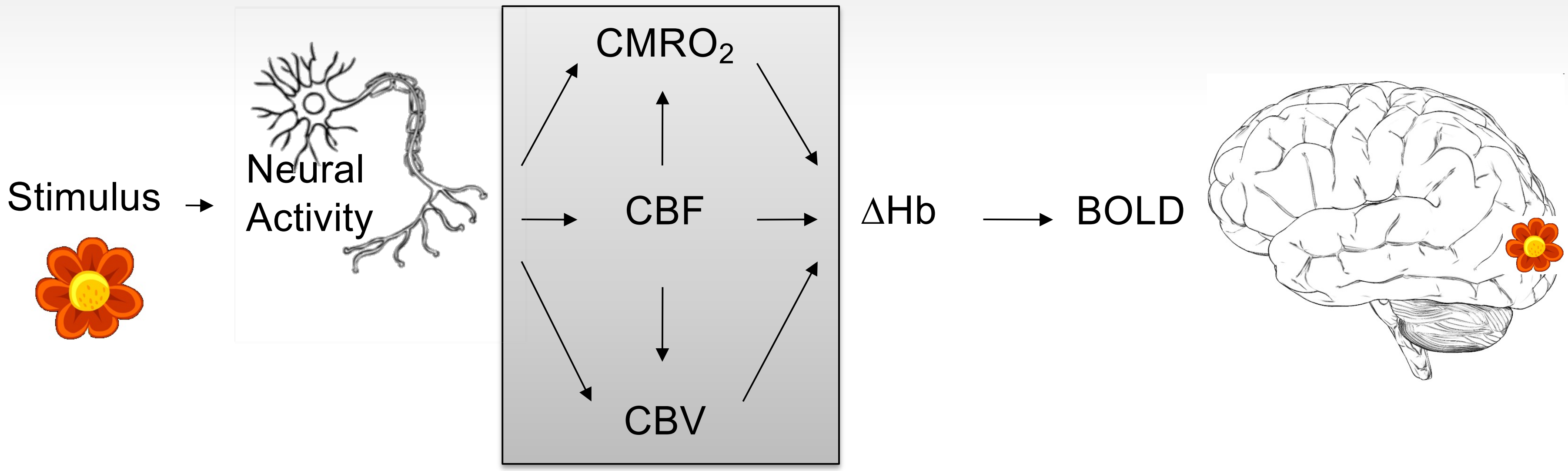
Modified from Arthurs and Boniface, Trends in Neuroscience, 2002

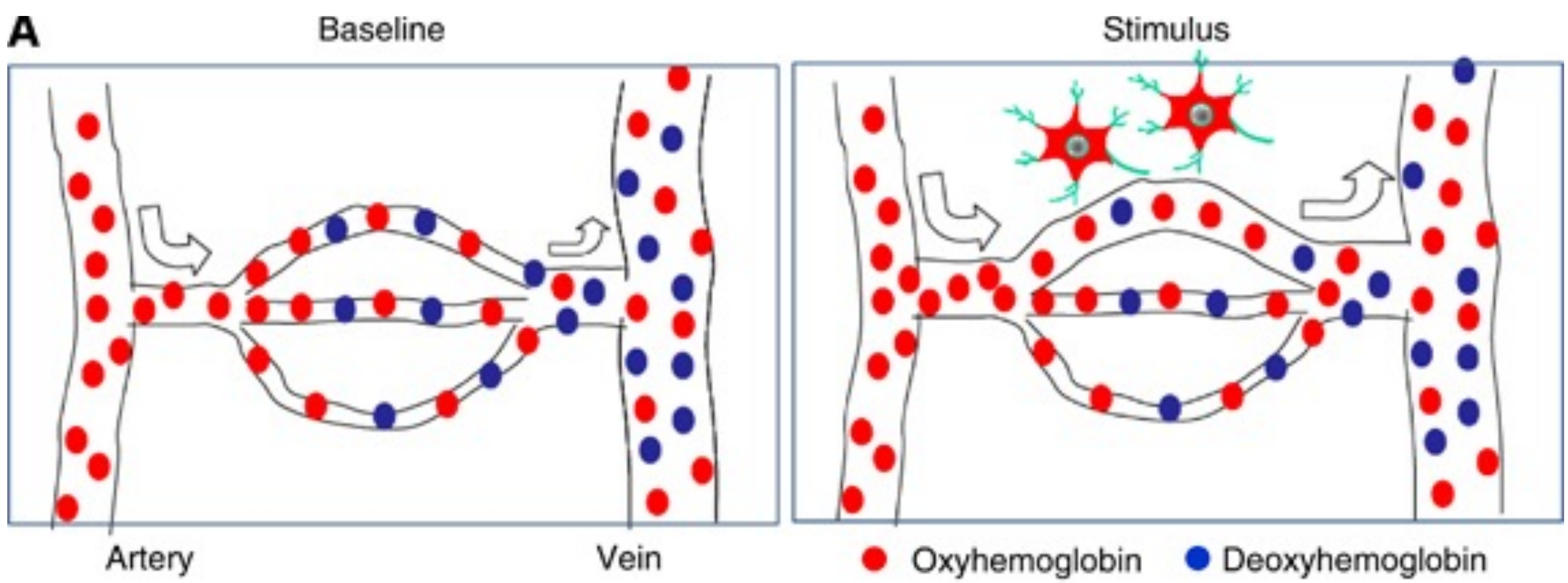
Signal components of the BOLD effect



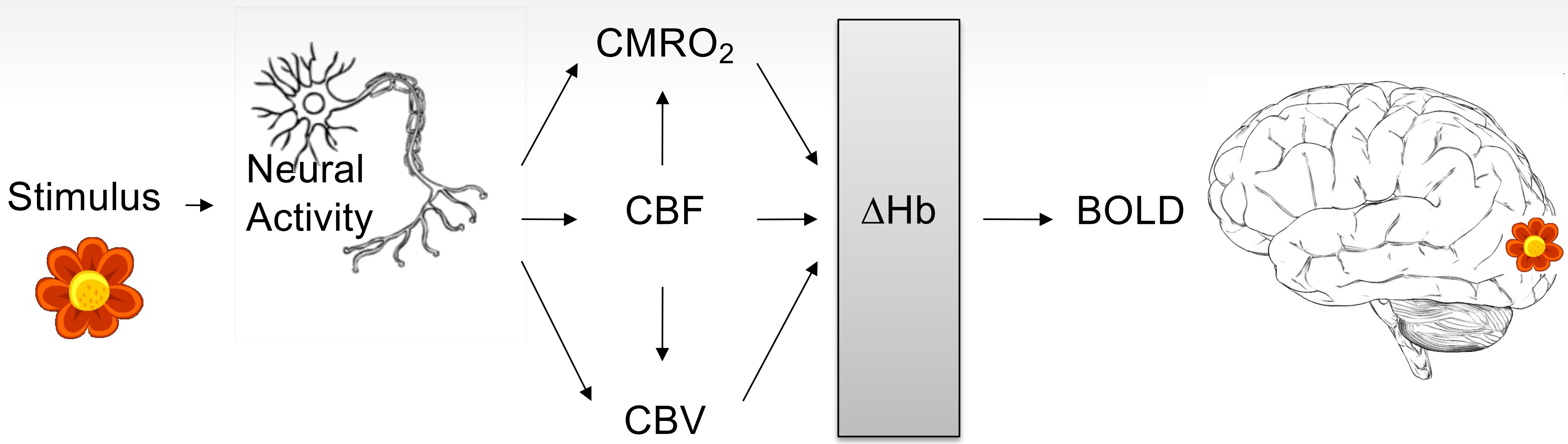
$CMRO_2$ – metabolic oxygen uptake
CBF – Cerebral Blood Flow
CBV – Cerebral Blood Volume
Hb – Haemoglobin
BOLD – Blood Oxygenation Level Dependent effect

Signal localization of the BOLD effect



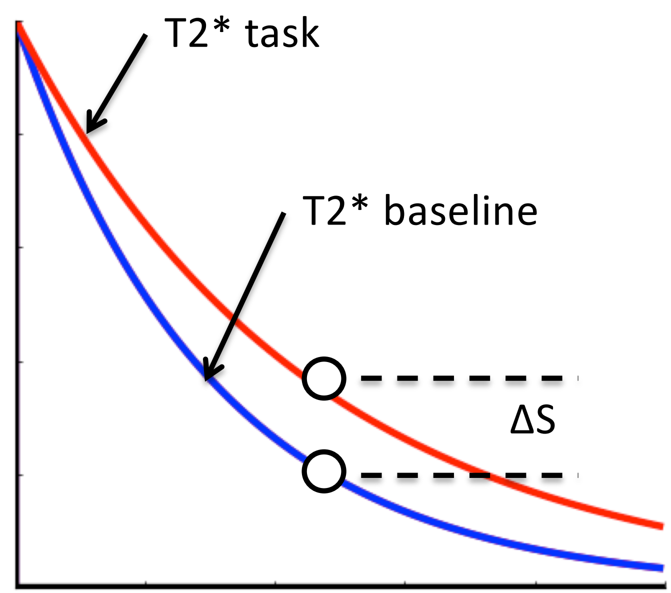


Contrast Mechanisms



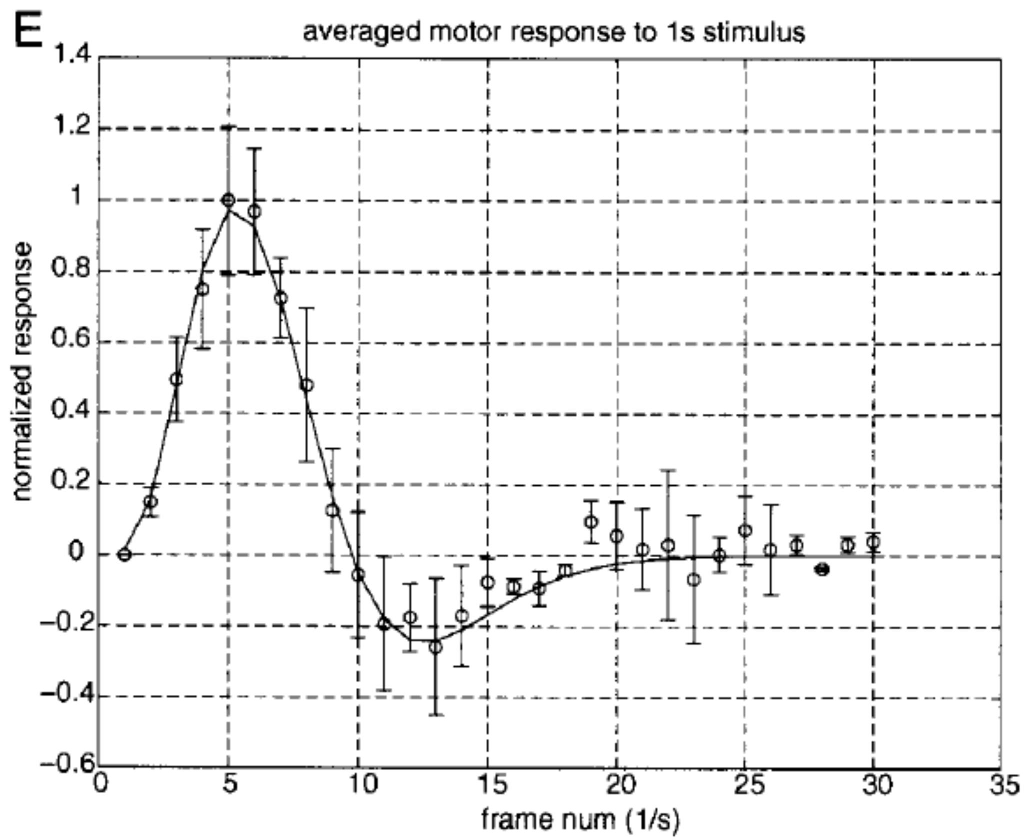
T2* is the "observed" or "effective" T2

* can come from:
- inhomogeneities in the main magnetic field
- susceptibility-induced field distortions produced by the tissue
  => BOLD contrast



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)

Outline

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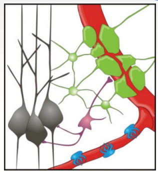

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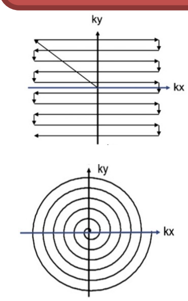

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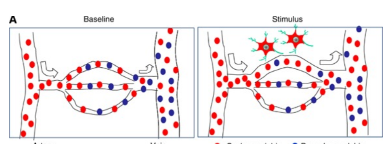
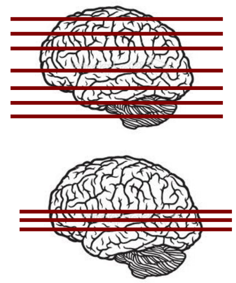
Perfusion   Diffusion   VASO





Spatial/Temporal resolution

Imaging Factors

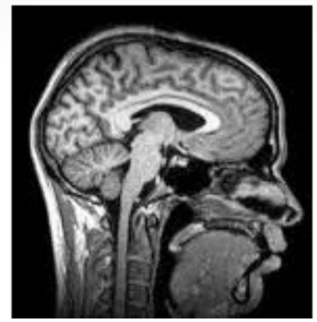
- Field strength 3T, 7T
- Acceleration:
- k-space: Single/multi-shot EPI
- In-plane: SENSE (ASSET)
  GRAPPA (iPAT)
- Multi-slice

Biological factors

- Veins/capillaries
- Physiological noise

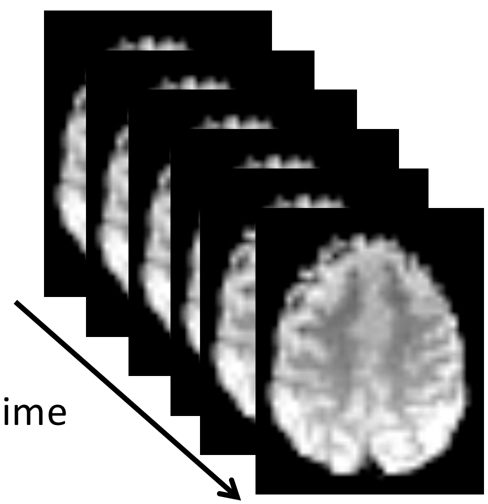
fMRI acquisition

Anatomical



One image / 3-5 min

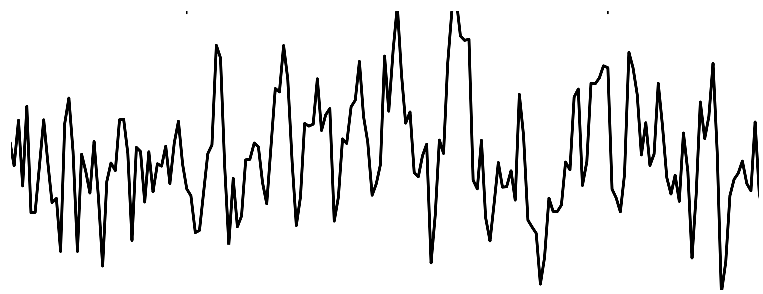
Functional



time

One image / 2 s for 5 min

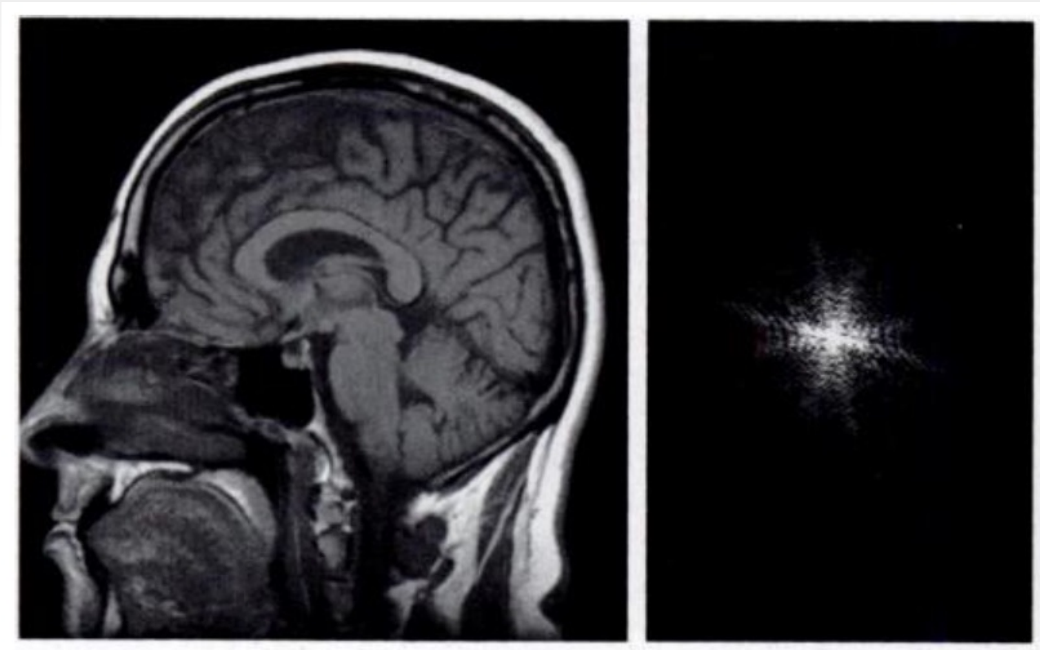
BOLD signal time series

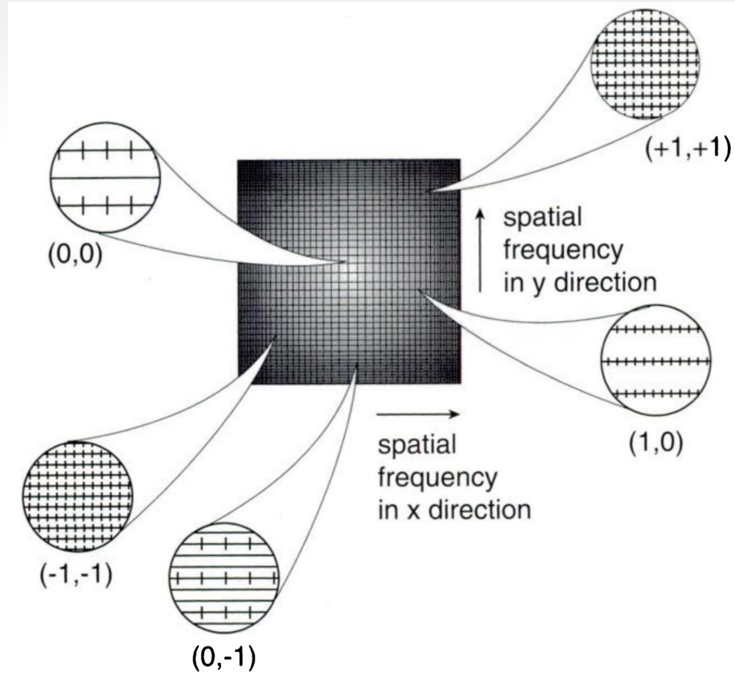


time

Courtesy of Catie Chang NINDS

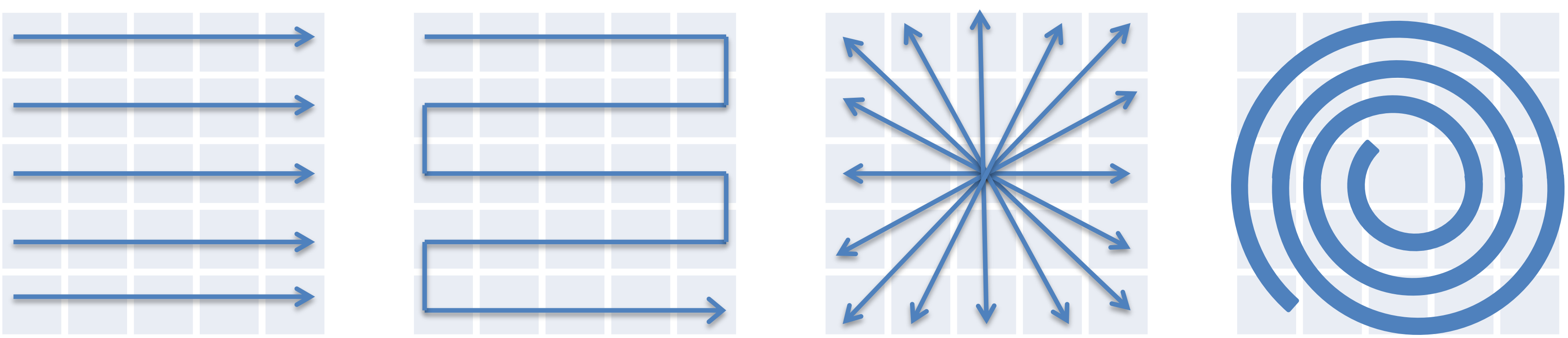
K-space, briefly



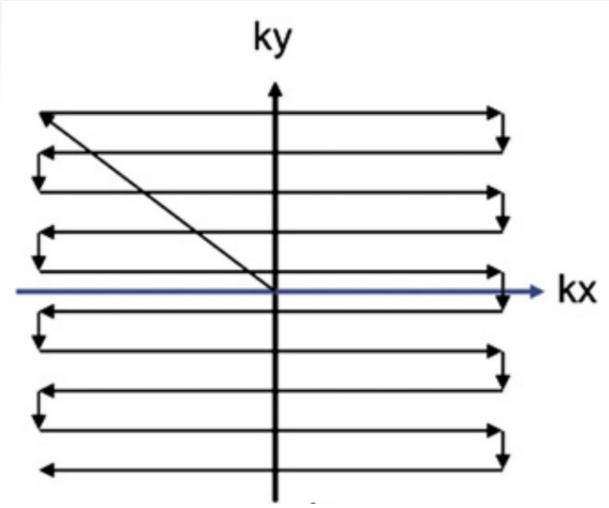


Mezrich,R. Radiology. 1995 May;195(2):297-315.

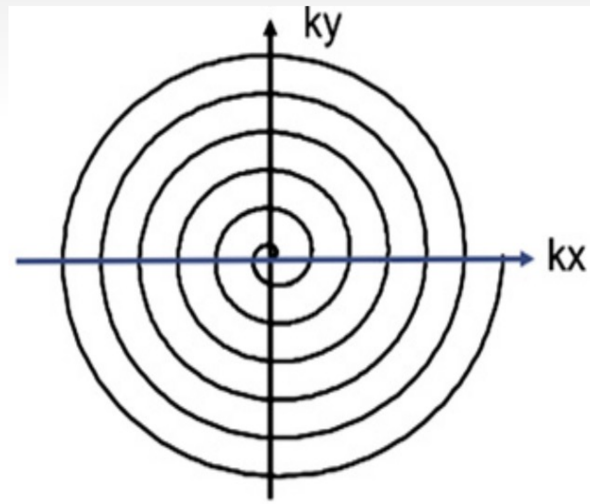
Ways of filling k-space:



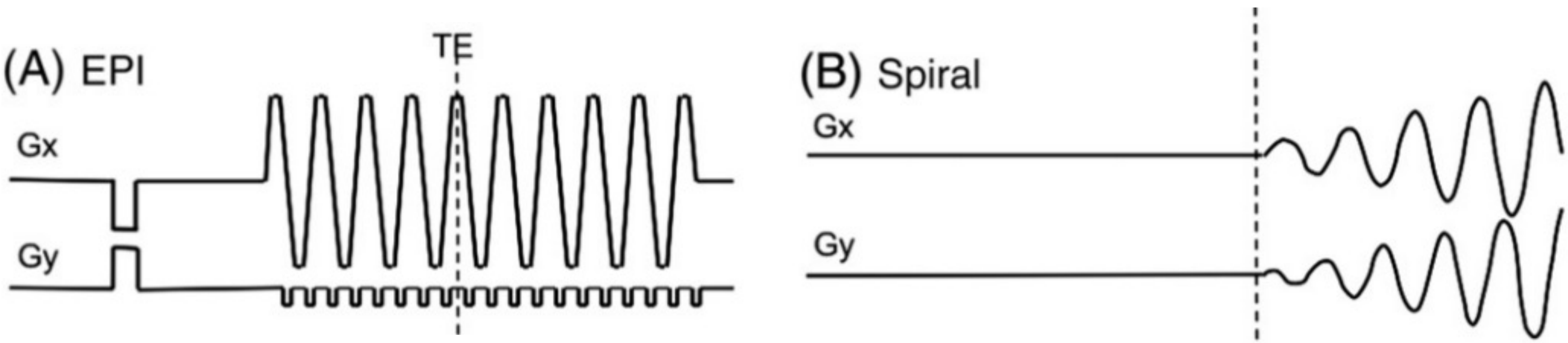
Standard pulse sequences



EPI

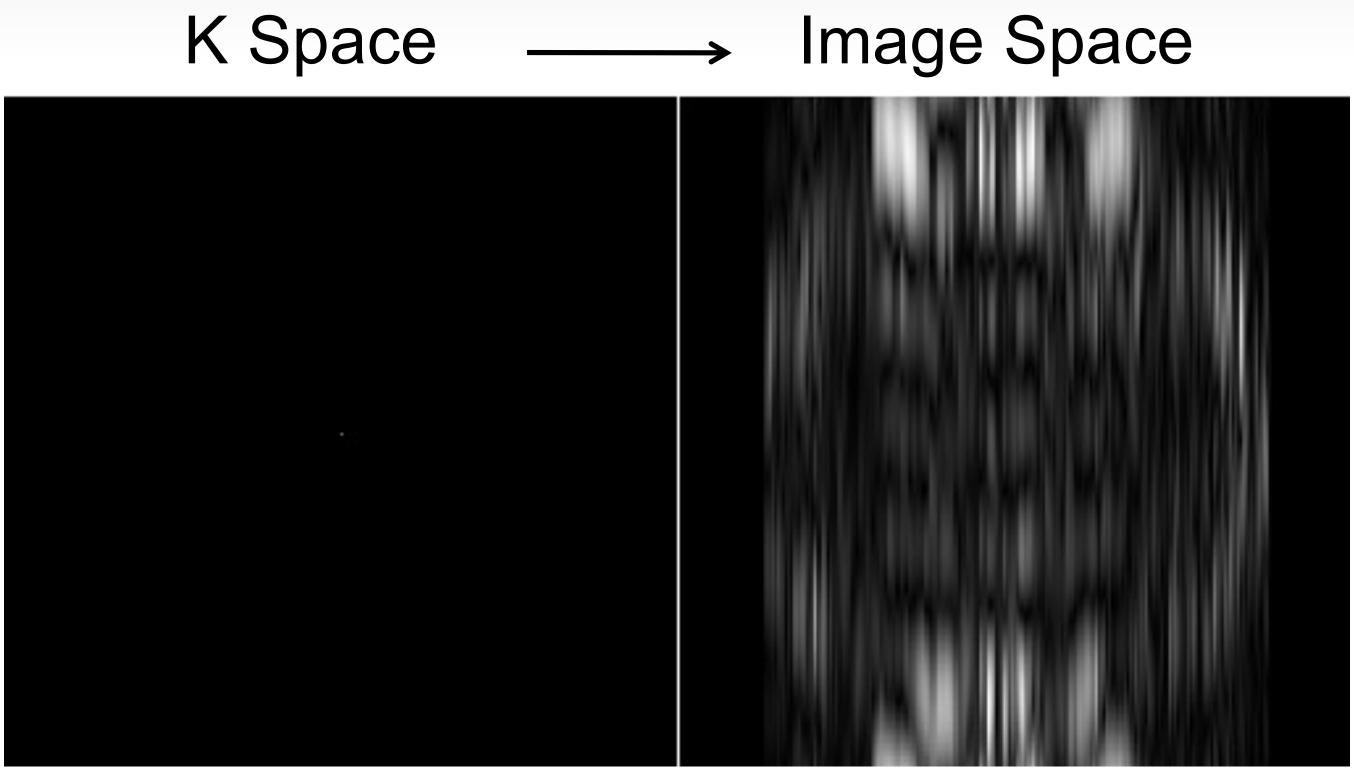


Spiral

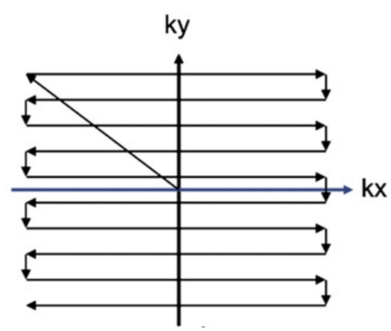


Glover, Neuroimage (2012)

Filling k-space, one line at a time



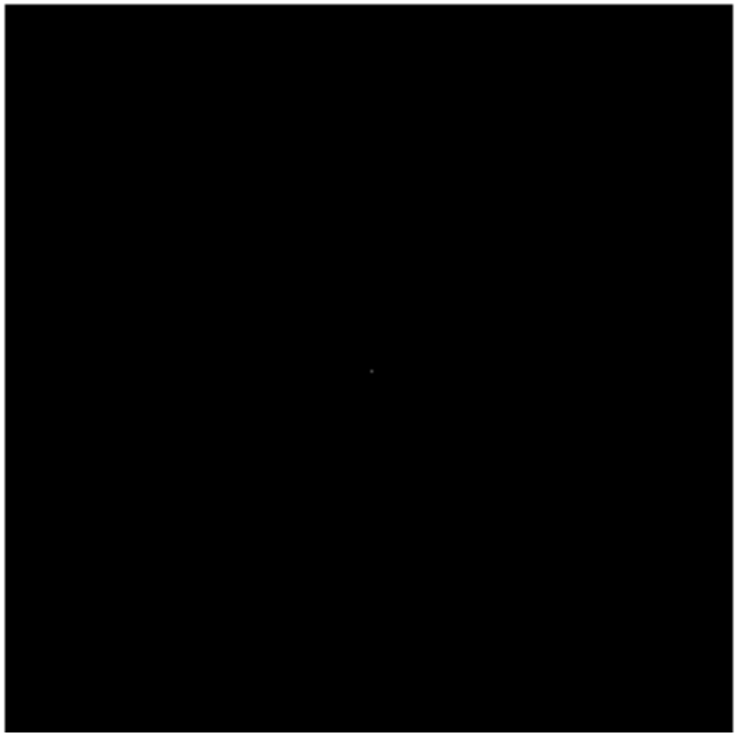
Movie

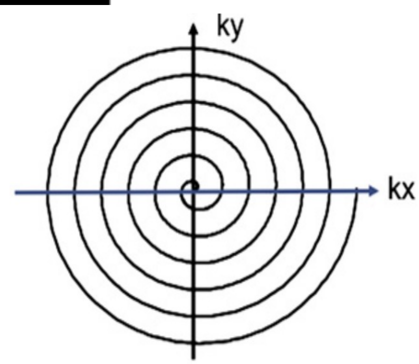


Courtesy of Nick Bock, McMaster

Filling k-space, center out

KSpace ⟶ Image Space

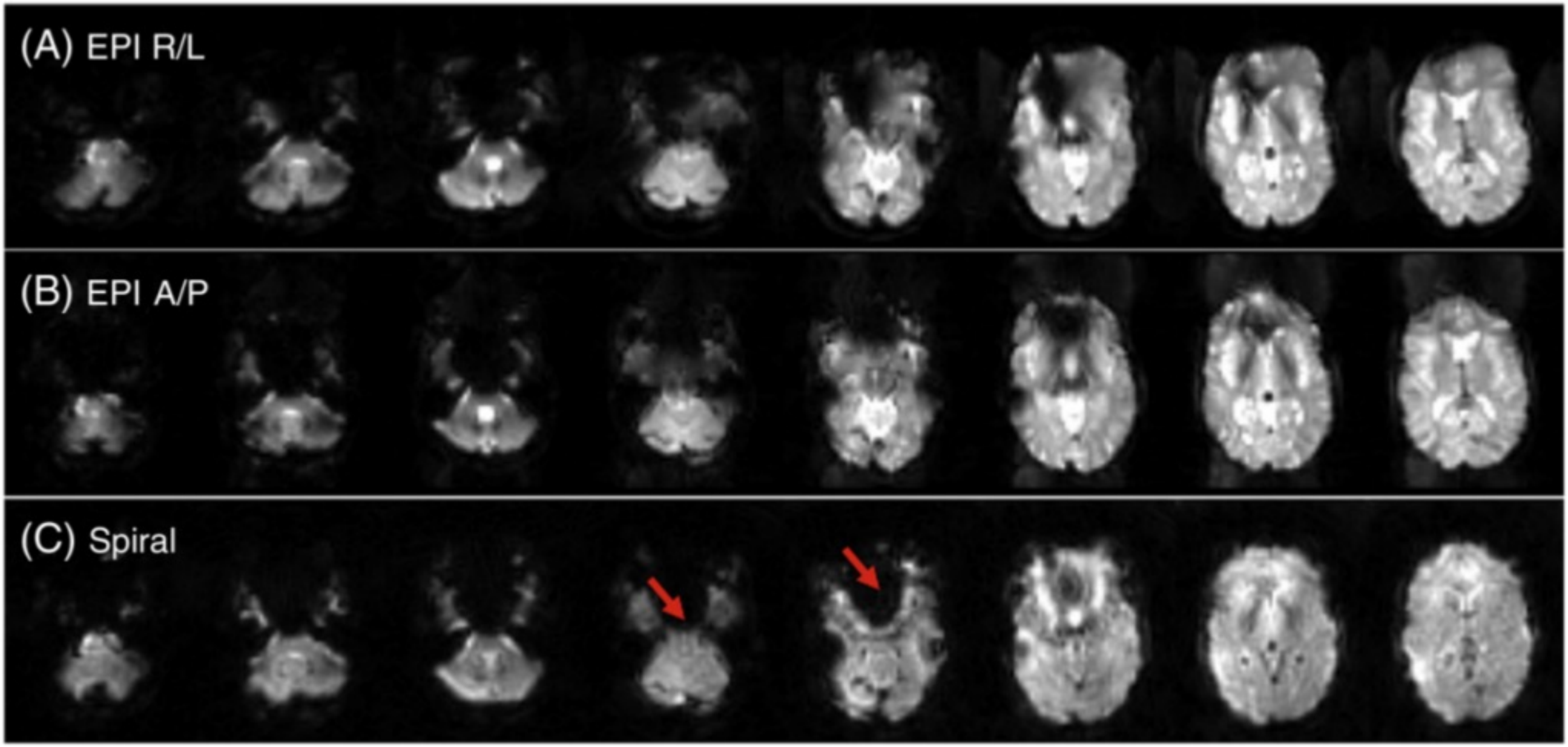




Movie

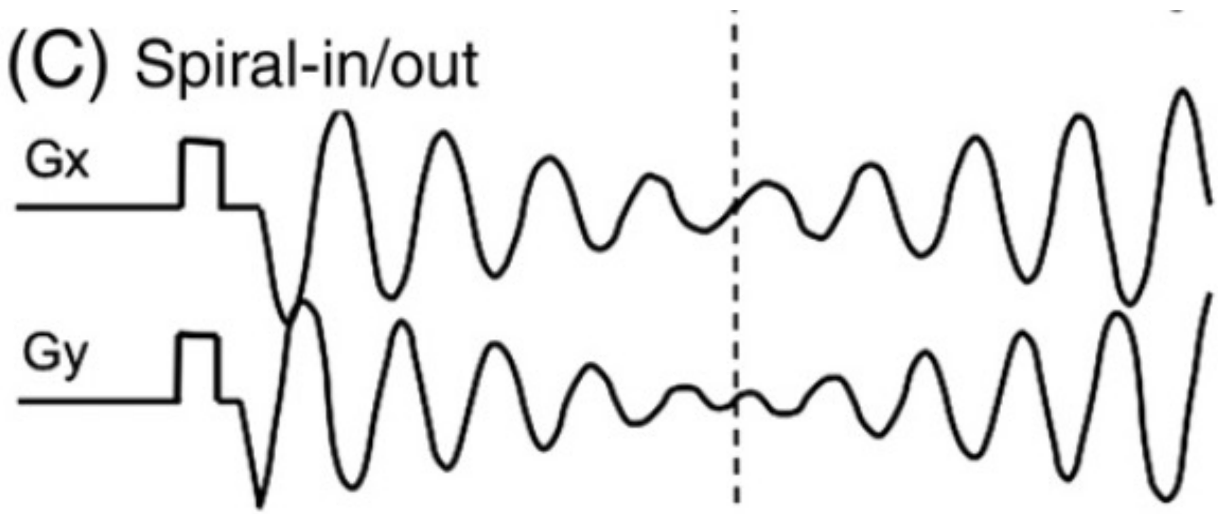
Courtesy of Nick Bock, McMaster

Example EPI/Spiral images … susceptibility



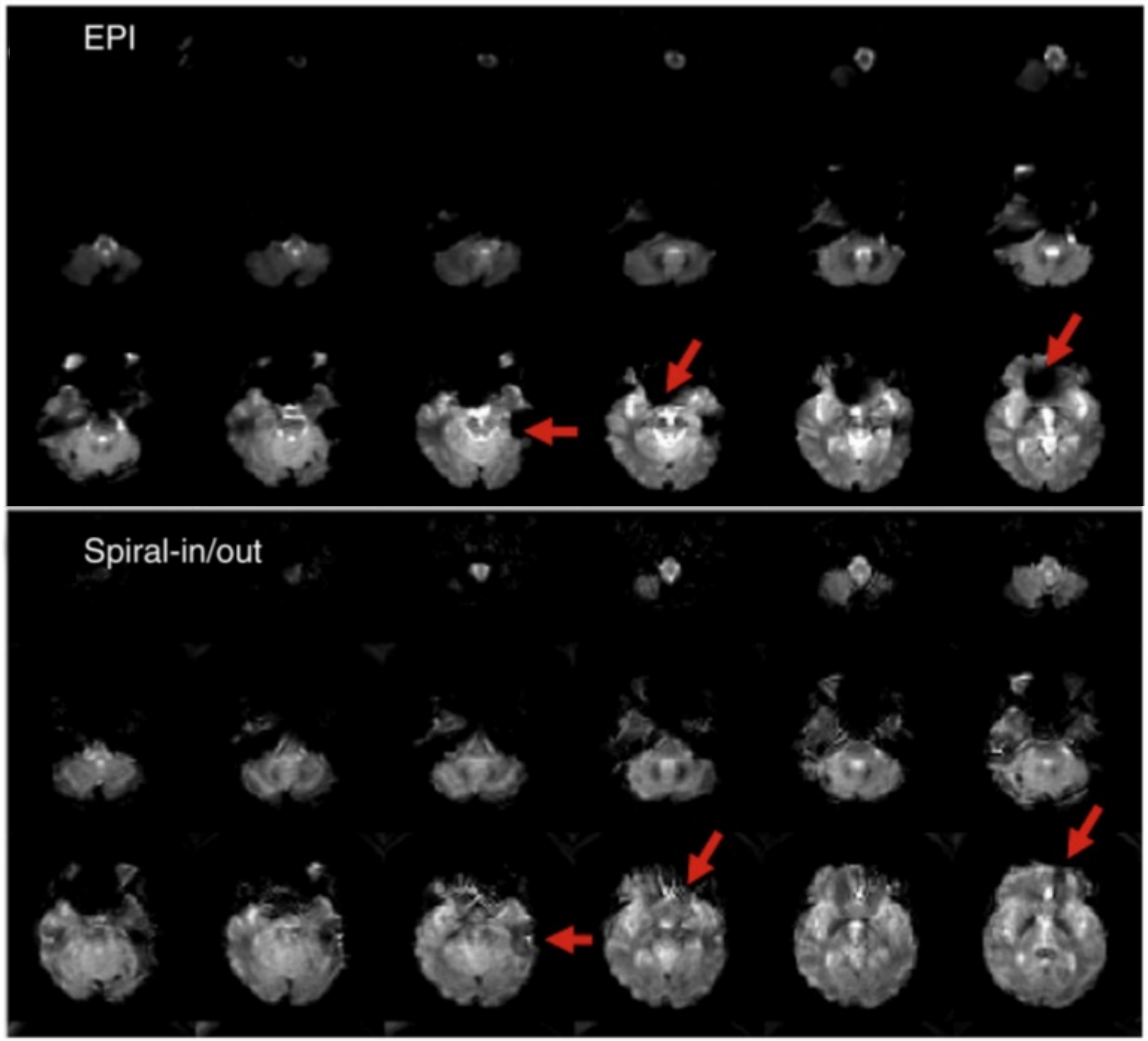
Glover, Neuroimage (2012)

Spiral in/out



Glover, Neuroimage (2012)

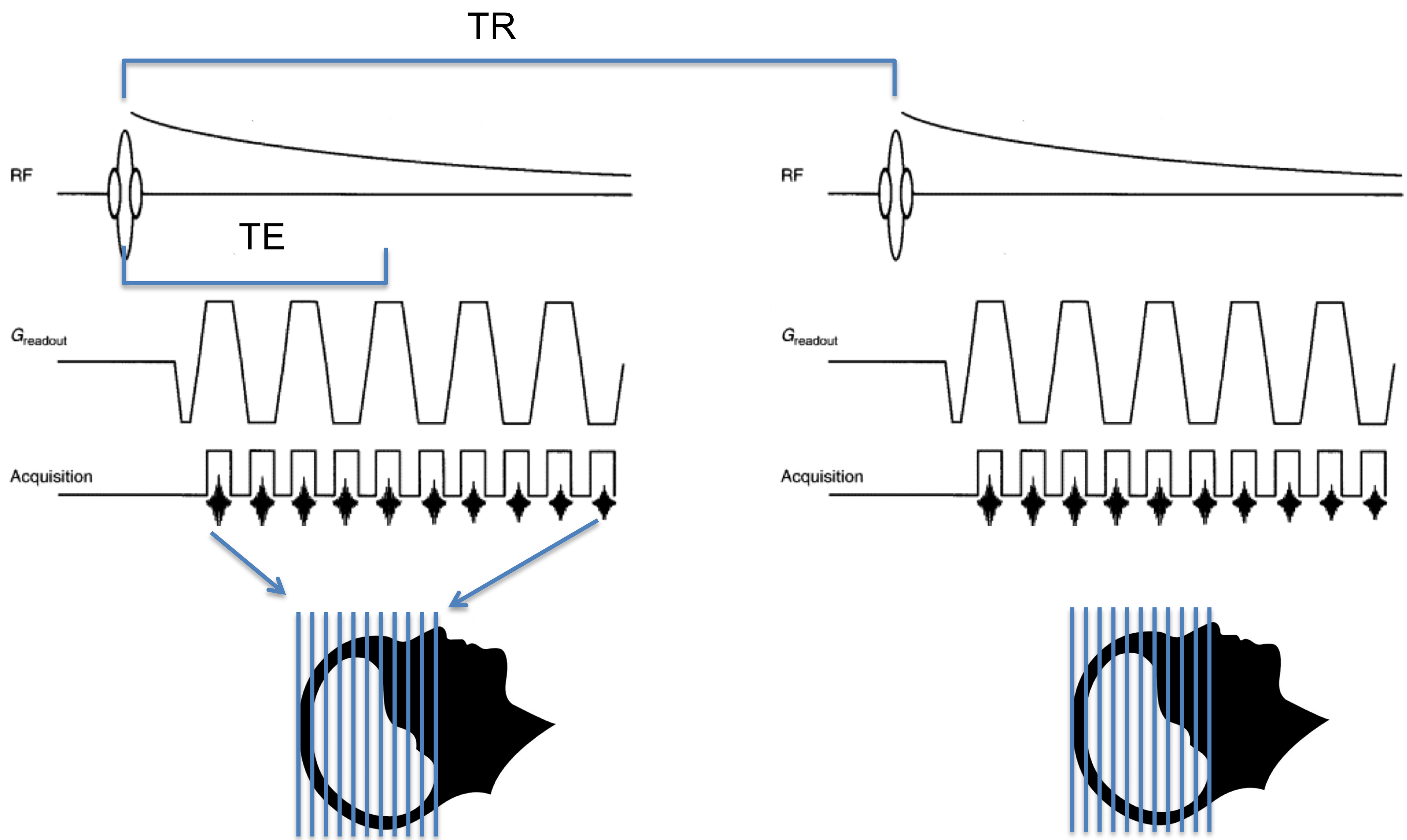
Susceptibility reduction



Glover, Neuroimage (2012)

Image acquisition basics

- Can acquire data for a limited time due to signal decay



Bernstein M. et al. Handbook of MRI Pulse Sequences, 2004, 702–801

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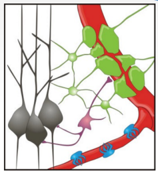

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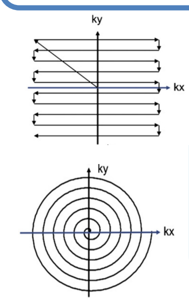

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Gradient-echo
Spin-echo
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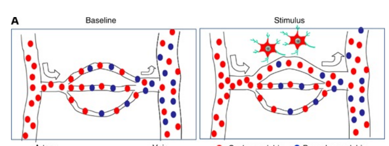
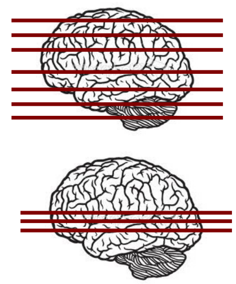
Perfusion   Diffusion   VASO





Spatial/Temporal resolution

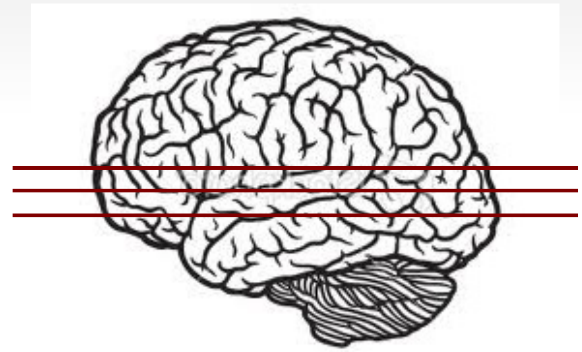
Imaging Factors

- Field strength 3T, 7T
- Voxel size, TR, TE
- Acceleration:
- k-space: Single/multi-shot EPI
- In-plane: SENSE (ASSET)
  GRAPPA (iPAT)
- Multi-slice

Biological factors

- Veins/capillaries
- Physiological noise

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:

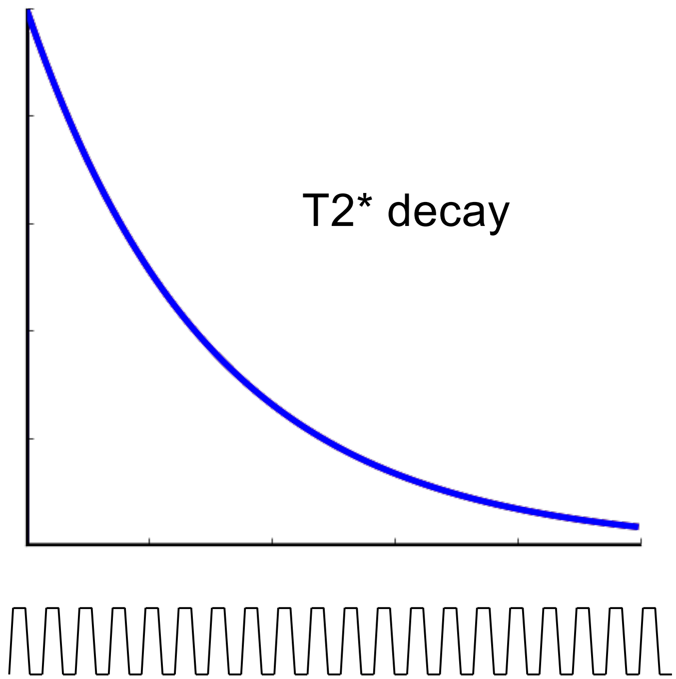
- cognitive studies
- resting state

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

Useful for:

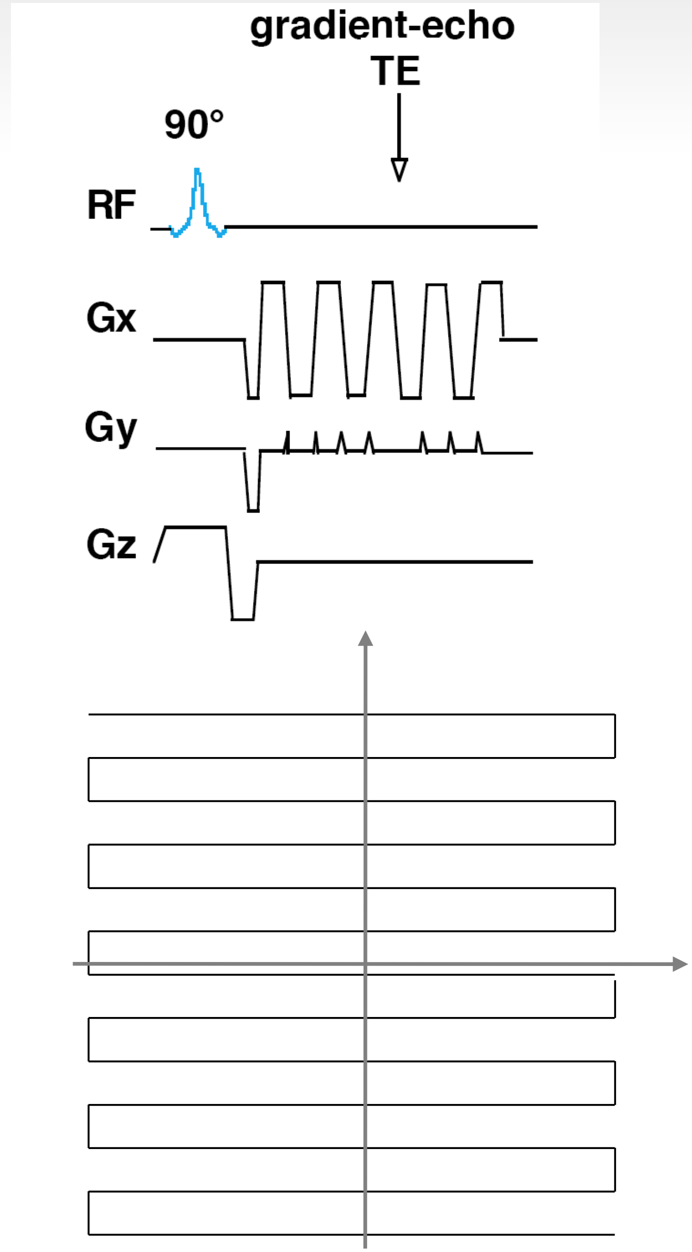
- Specific ROIs

Single shot EPI



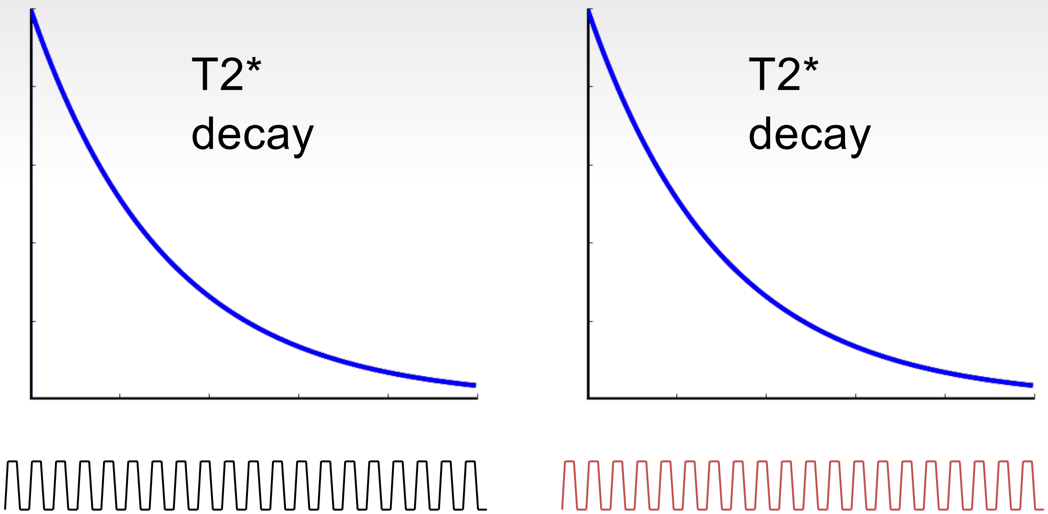
EPI readout window

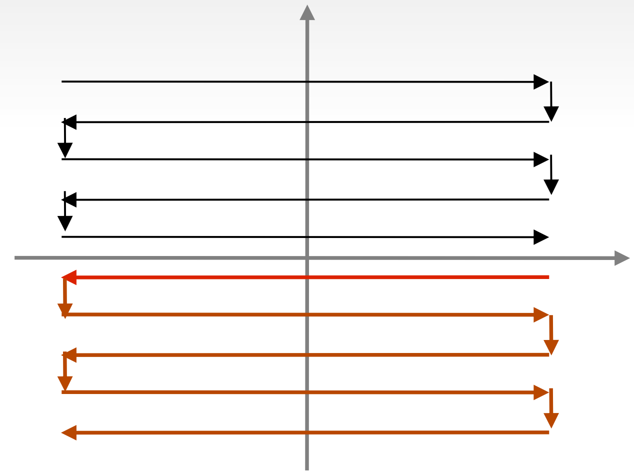
≈ **20 to 40** ms



Courtesy of Peter Bandettini

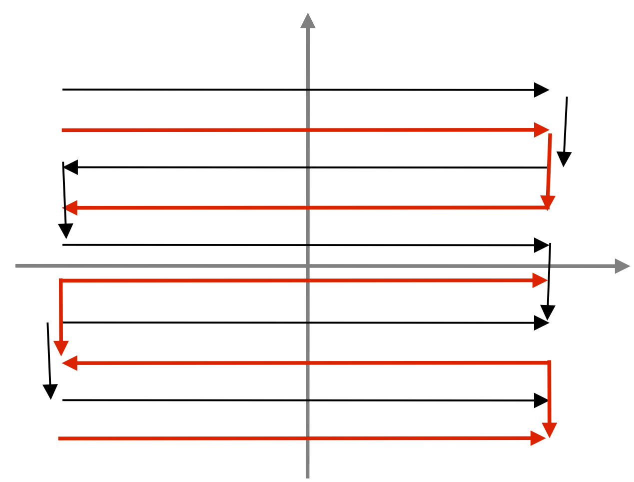
Multi-shot EPI (partial k-space)





Shot 1

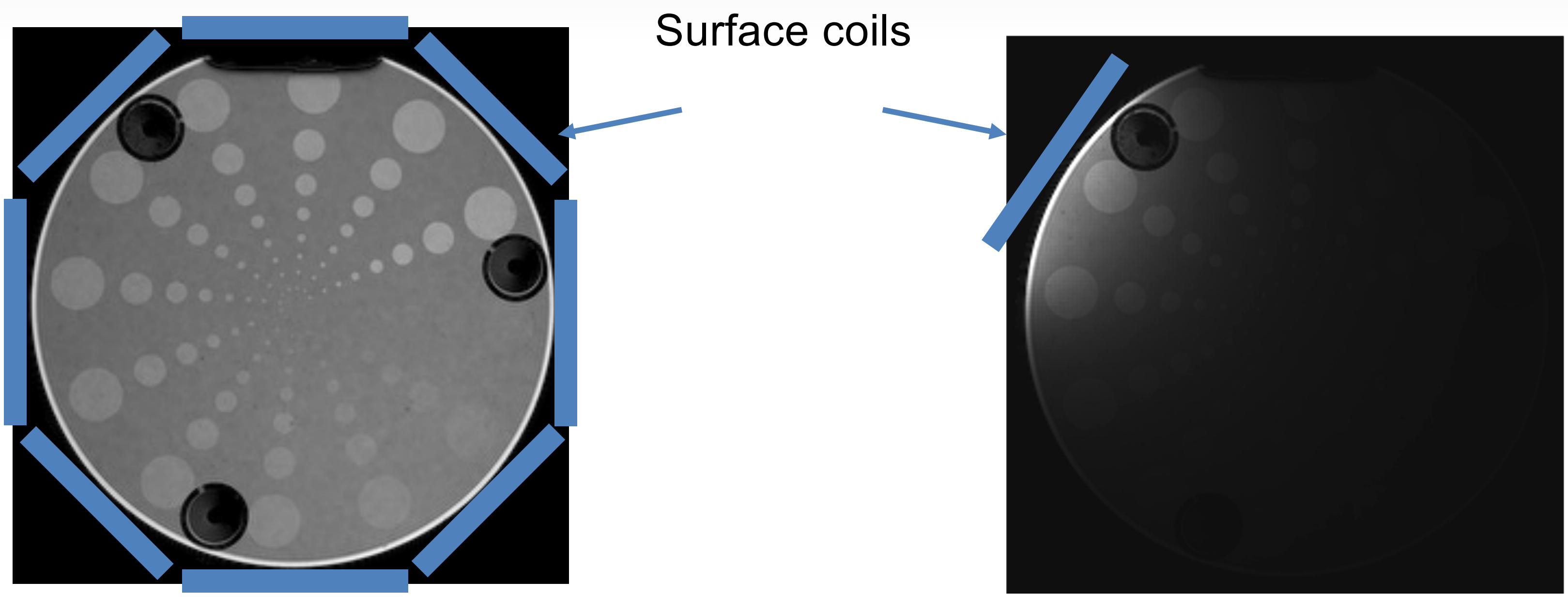
Shot 2



- 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

Parallel imaging

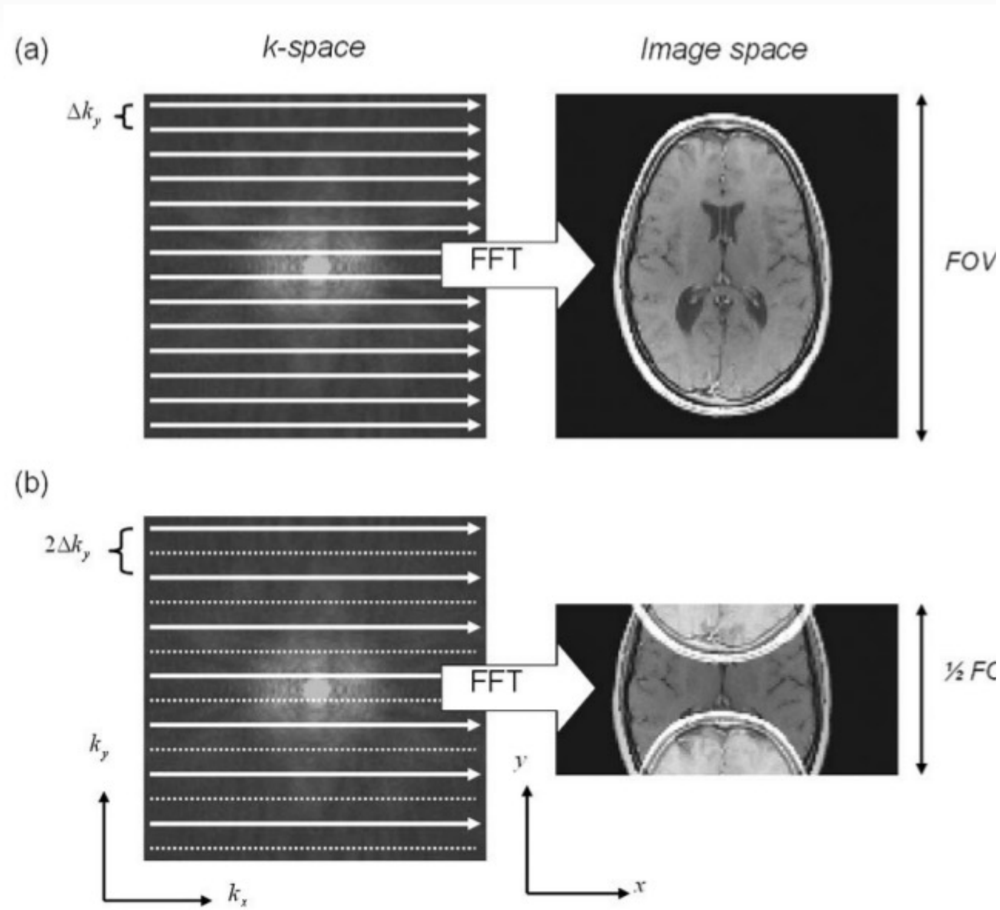
(SENSE, SMASH, GRAPPA, iPAT, etc)

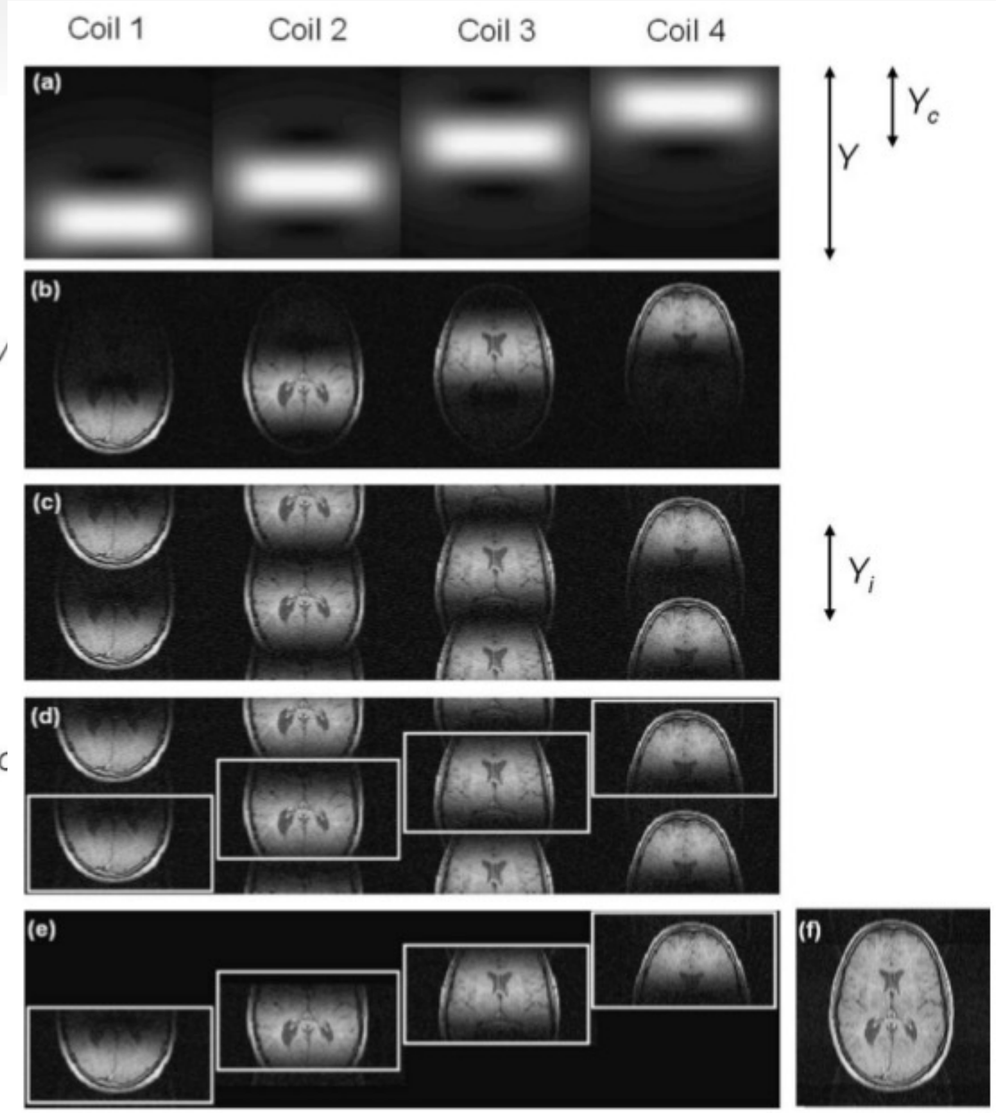


Multi-channel coils: Array of RF receive coils
Each coil is sensitive to a subset of the object
Coil sensitivity to encode additional information
Can "leave out" large parts of k-space (more than 1/2!)

Miller K. MRI image formation (ppt), http://users.fmrib.ox.ac.uk/~karla/teaching/image_formation.ppt

Acceleration: SENSE/GRAPPA

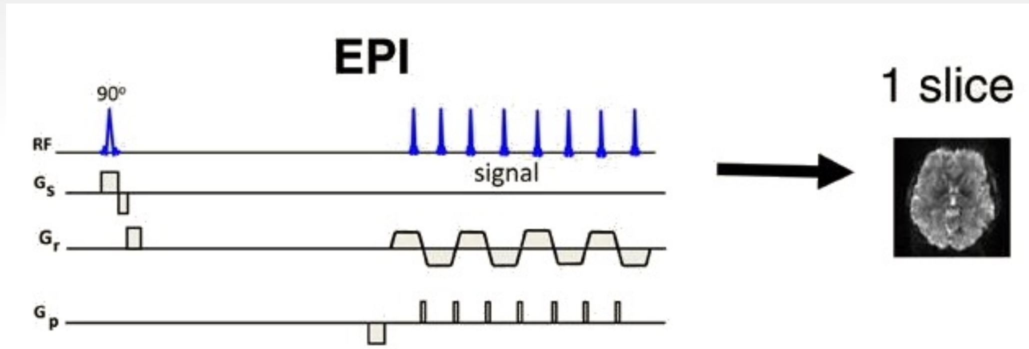




- Undersample k-space by accleration factor n
-reconstruct either in k-space (GRAPPA) or image space (SENSE)
- maximum acceleration limited by number of coils and SNR reduction

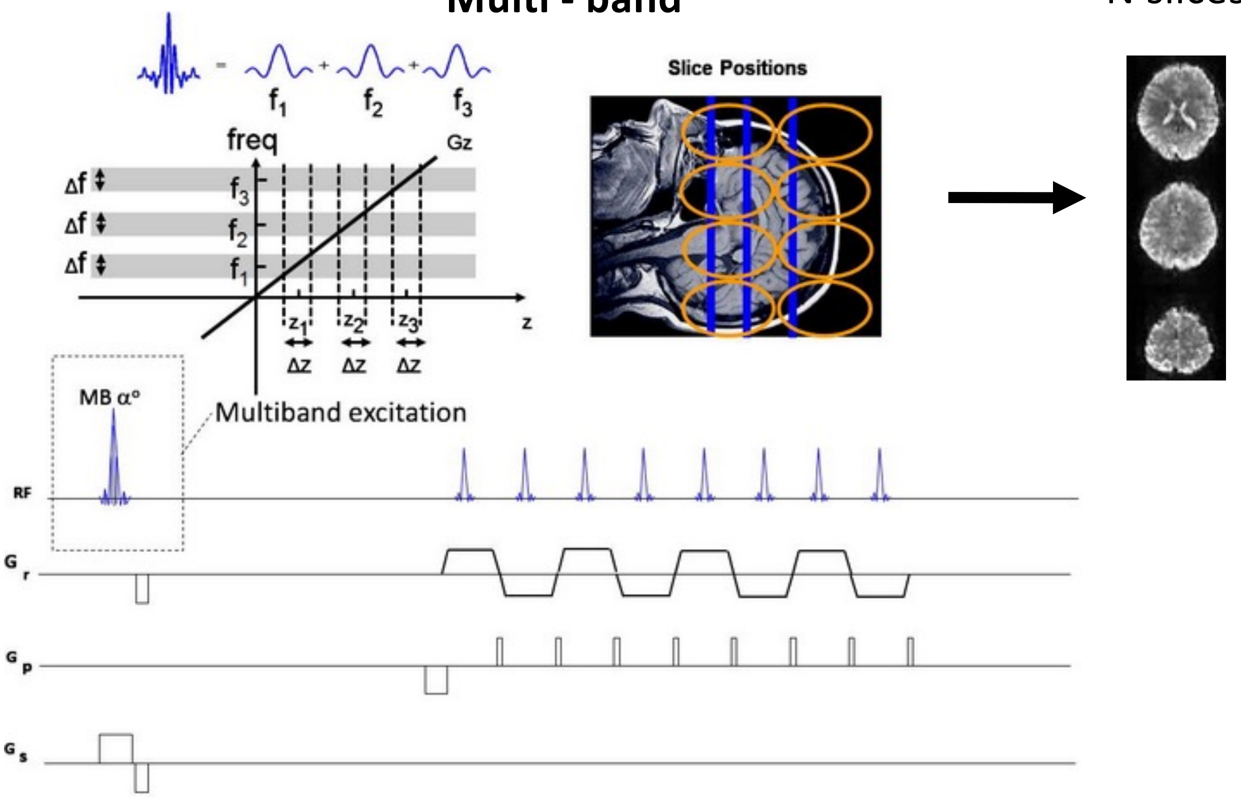
Blaimer M. et al Top Magn Reson Imaging. (2004)

Multi-slice or mutli-band excitation



Multi - band

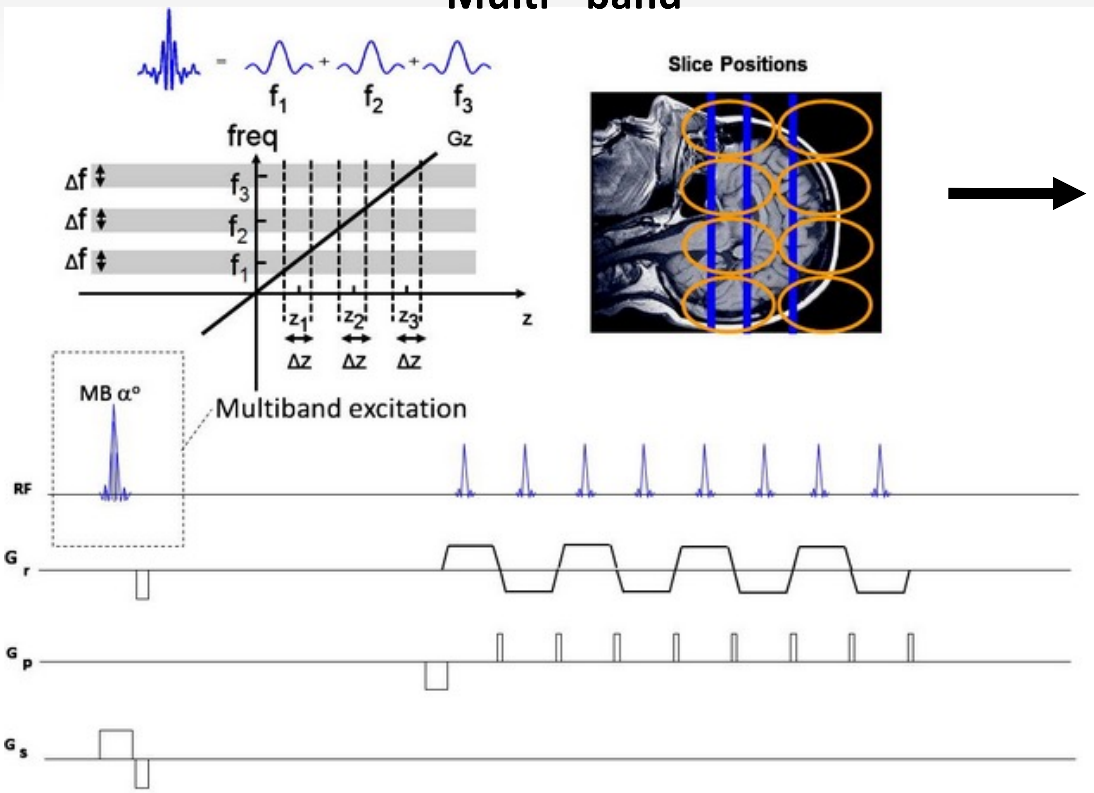
N slices



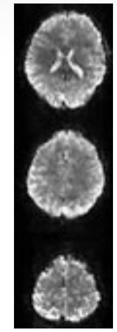
Feinberg DA and Setsompop K. Journal of Magnetic Resonance (2013)

Multi-slice or mutli-band excitation

Multi - band



N slices

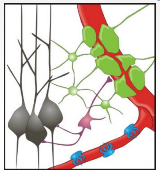


- excites multiple slices at once,
- uses coil sensitivity profiles to unmix the images
- sub TR whole brain images are achievable
- loss in SNR
- long reconstruction times

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

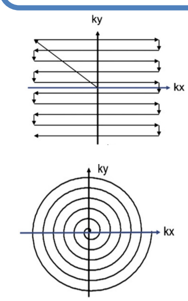
Outline

Introduction



- Voxel contents
- neurovascular coupling
- hemodynamic response
- MR signal basics
- BOLD signal basics

MR acquisition Basics

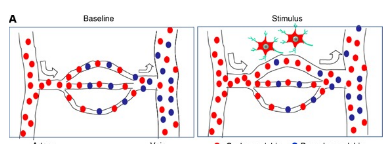


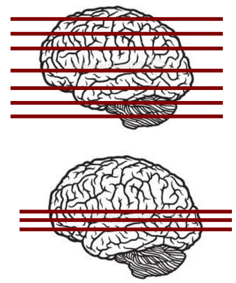
- K-space
- EPI
- Spiral
- TR/TE

Functional Contrast

BOLD
Gradient-echo
Spin-echo
Multi-echo

Perfusion Diffusion VASO





Spatial/Temporal resolution

Imaging Factors

Field strength 3T, 7T
Acceleration:
k-space: Single/multi-shot EPI
In-plane: SENSE (ASSET)
GRAPPA (iPAT)
Multi-slice

Biological factors

Veins/capillaries
Physiological noise

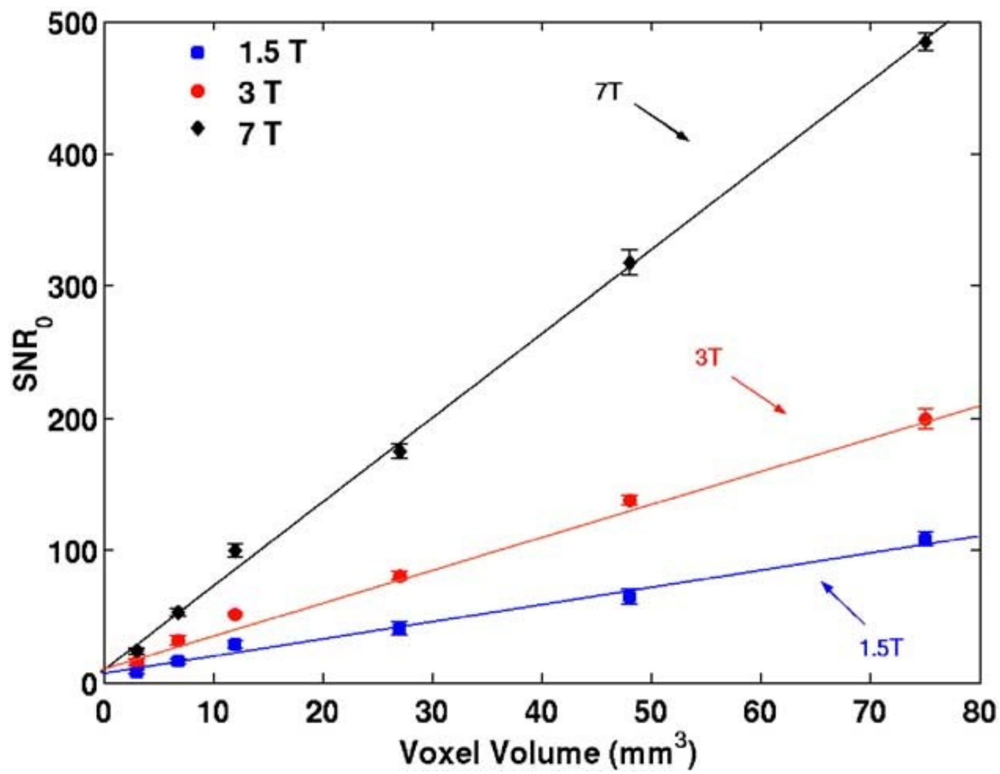
Voxel size

- 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)

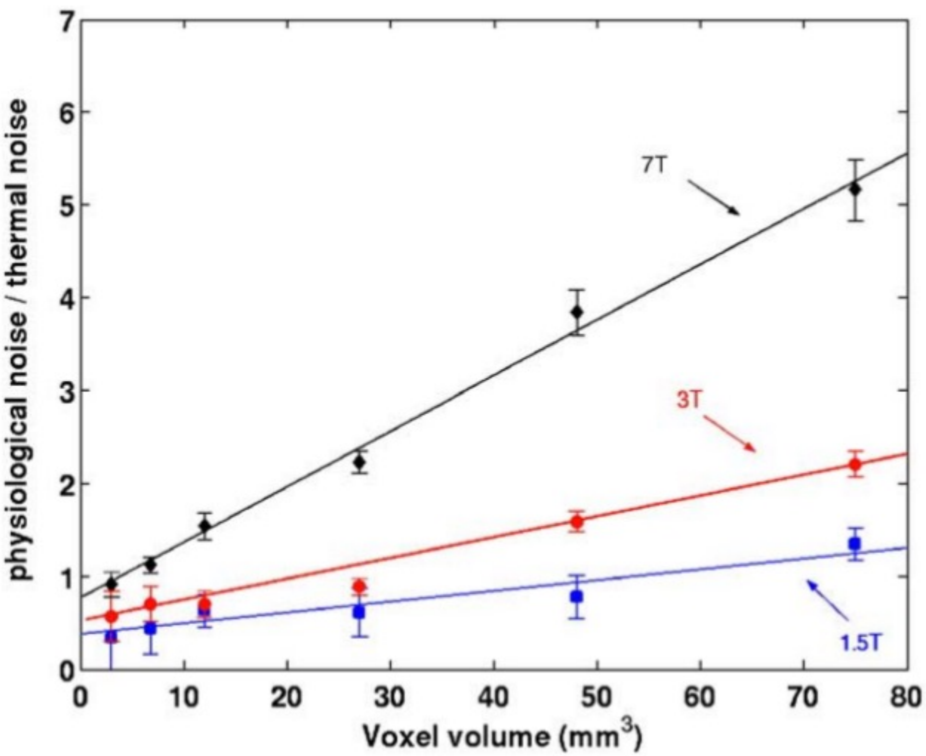
Field Strength

Pros

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

Cons

-shorter T2*
=> faster readout/ acceleration needed
-longer T1
=>longer repetition time to get signal
-larger field perturbations and
 inhomogeneities
 -SAR limitations

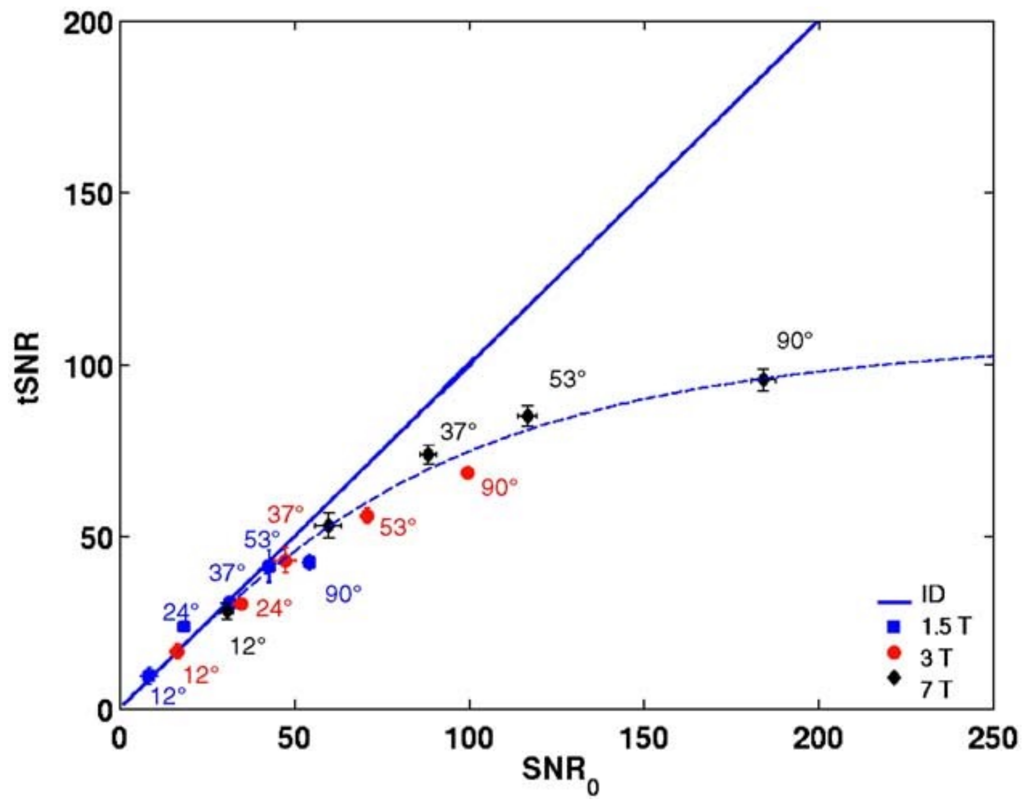


What is the optimal voxel size?

- 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

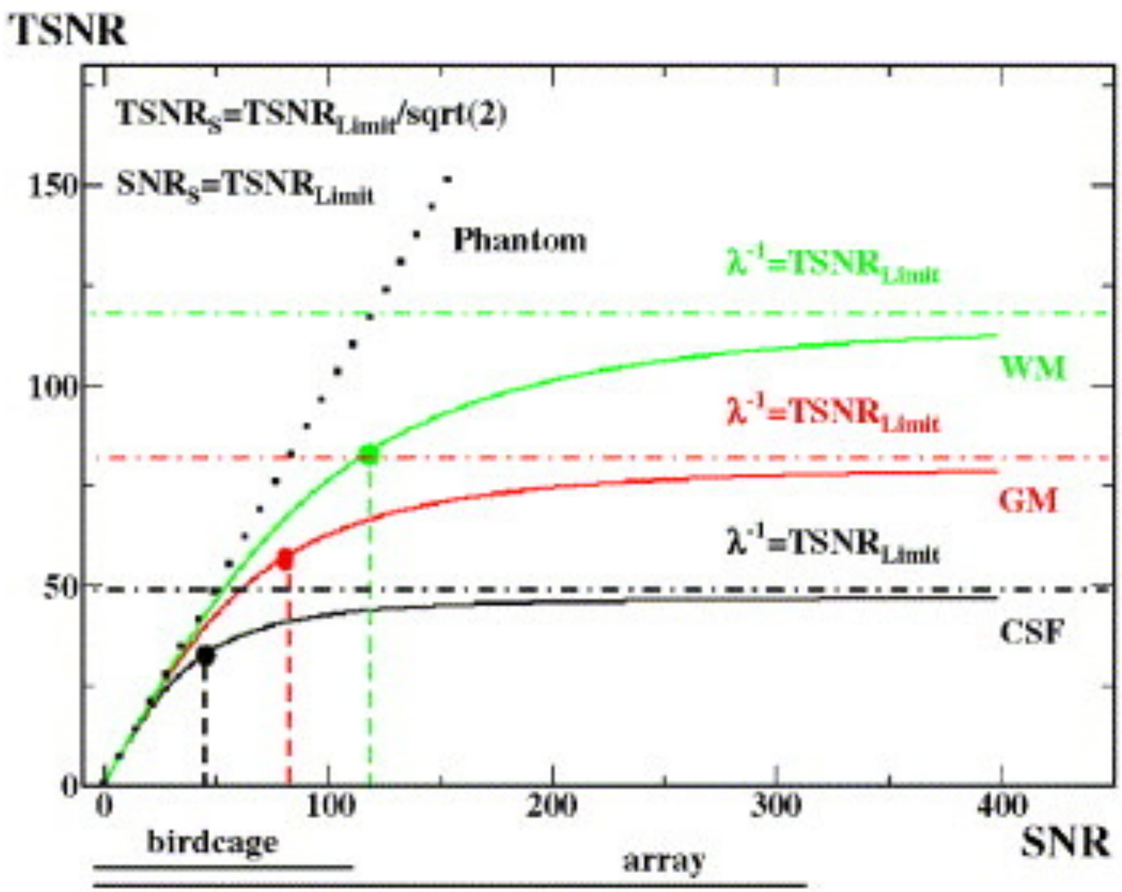


Triantafyllou et al, Neuroimage (2005)

Optimal voxel size?

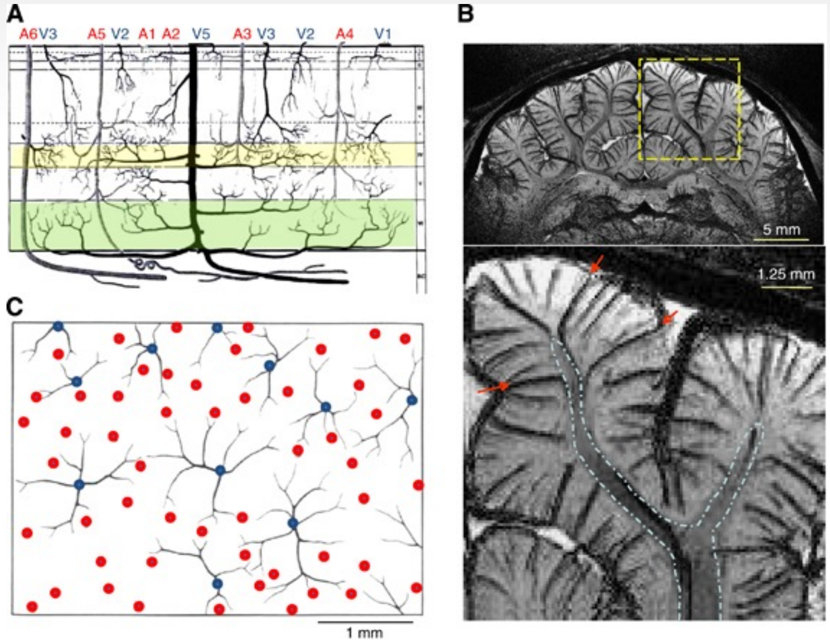
$$\sigma_{thermal} = \sigma_{physio}$$

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



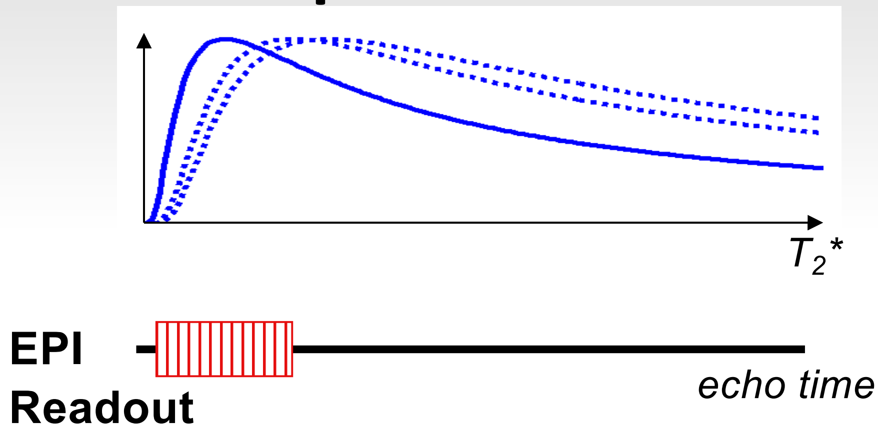
J. Bodurka, et al., NeuroImage, (2007)

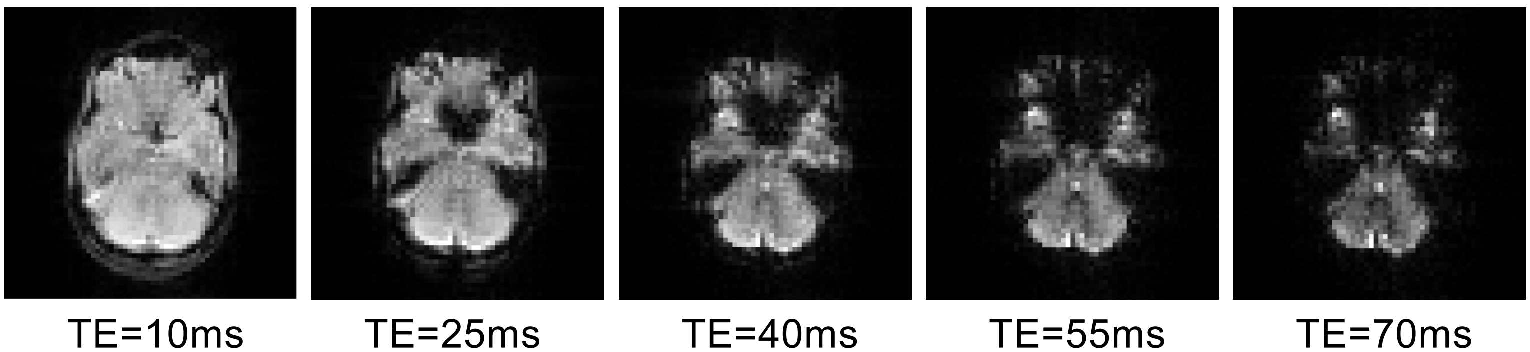
What's the effective spatial resolution?



- 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 TE



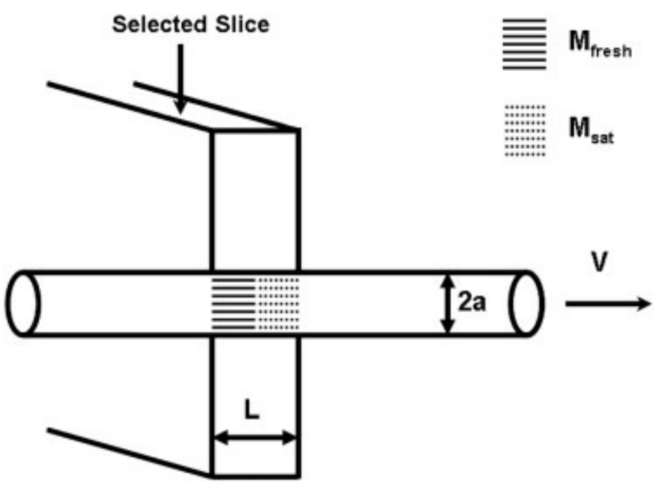


- Maximize BOLD signal where TE = T2*
- BUT: T2* varies across the brain => no ideal TE
- A shorter TE is typically chosen as compromise.
- This reduces BOLD sensitivity everywhere else

Modified from Ben Poser, Maastrict

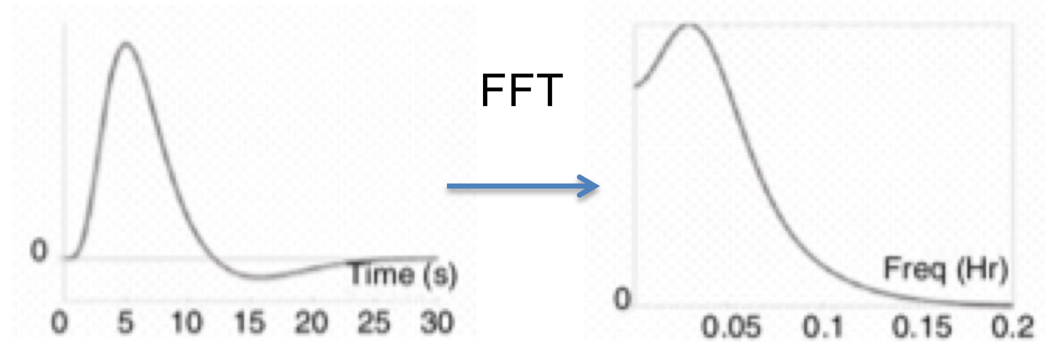
Optimal TR?

- Inflow effects affect TRs < 1s



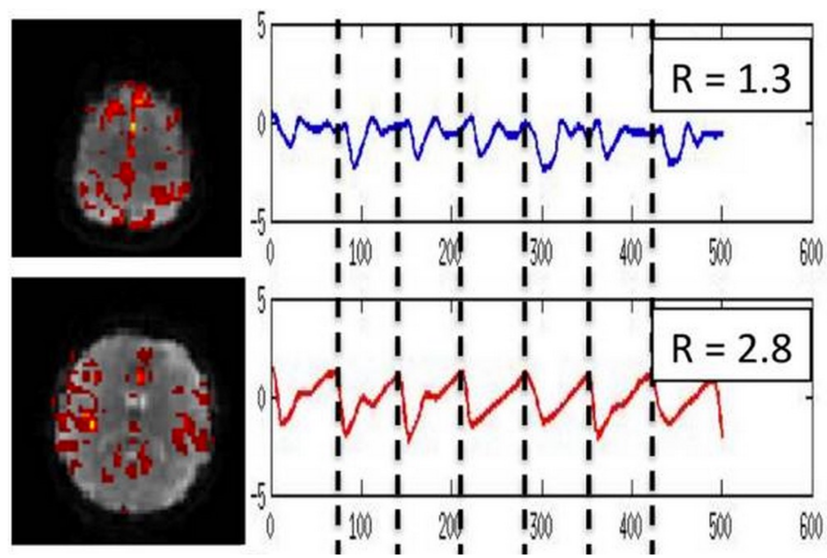
Gao Je et al., NeuroImage, Volume 62, Issue 2, 2012, 1035 - 1039

- HRF is a low pass filter



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

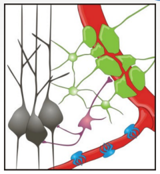
- Sampling of physiological noise (no aliasing)



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

Outline

Introduction



Voxel contents
neurovascular coupling
hemodynamic response
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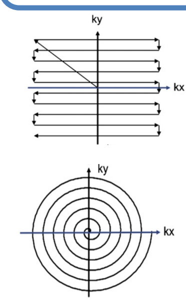
BOLD signal basics

MR acquisition Basics

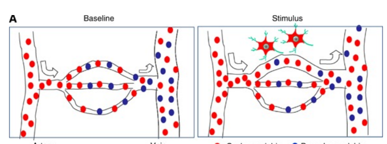


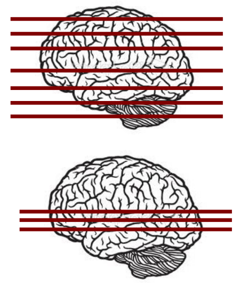
K-space
EPI
Spiral
TR/TE

Functional Contrast

BOLD
Gradient-echo
Spin-echo
Multi-echo

Perfusion Diffusion VASO





Spatial/Temporal resolution

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<u>Acceleration:</u>
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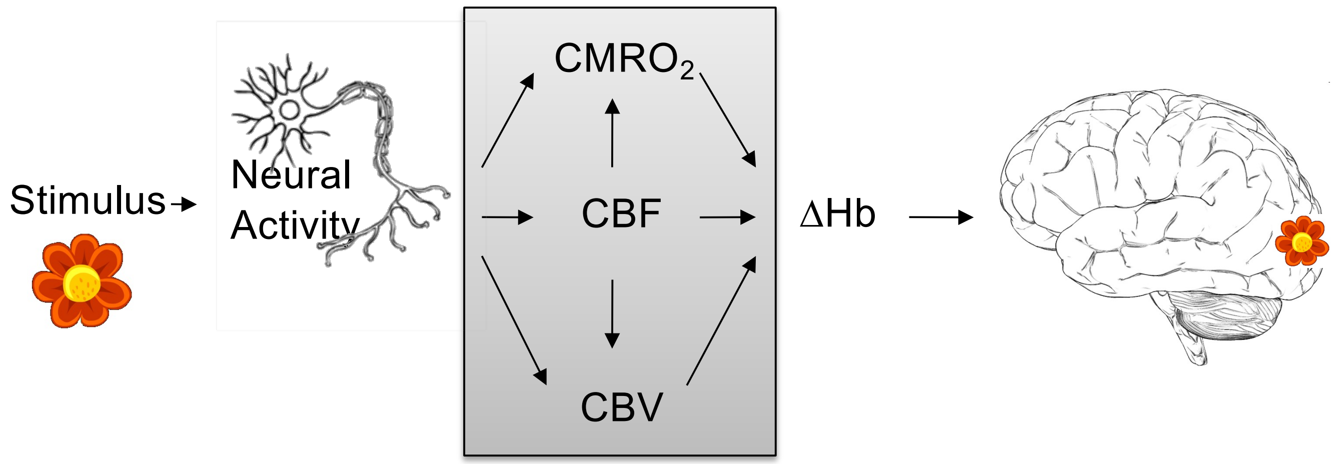
In-plane: SENSE (ASSET)
GRAPPA (iPAT)
Multi-slice

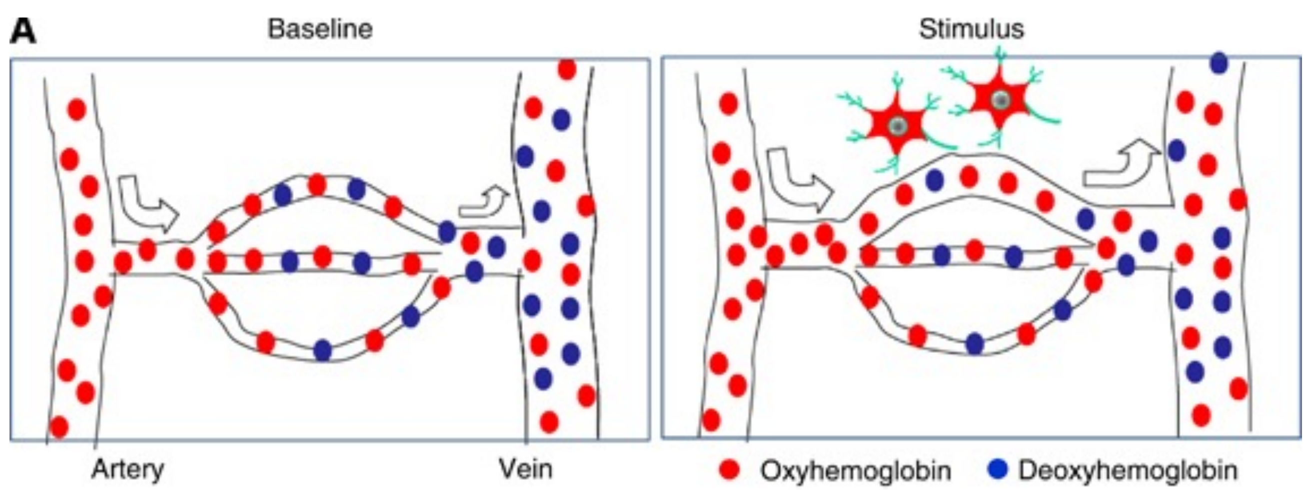
Biological factors

Veins/capillaries
Physiological noise

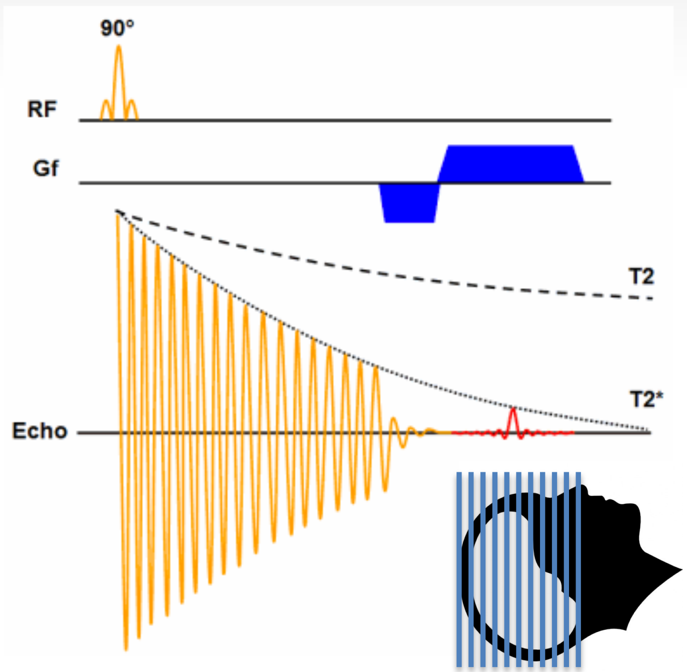
Contrast Mechanisms

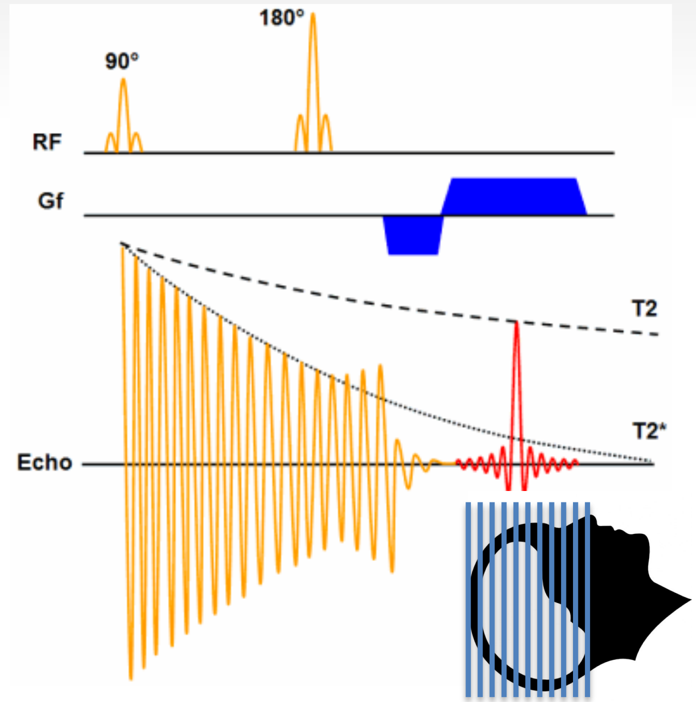
Spin-echo: Reduce the influence of veins





Gradient Echo (GE) | Spin Echo (SE)

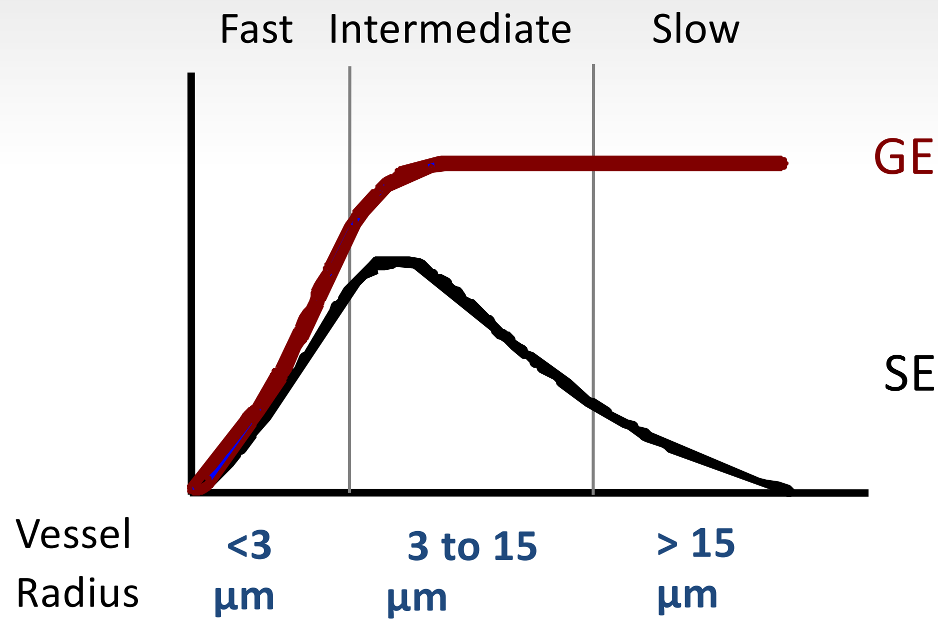




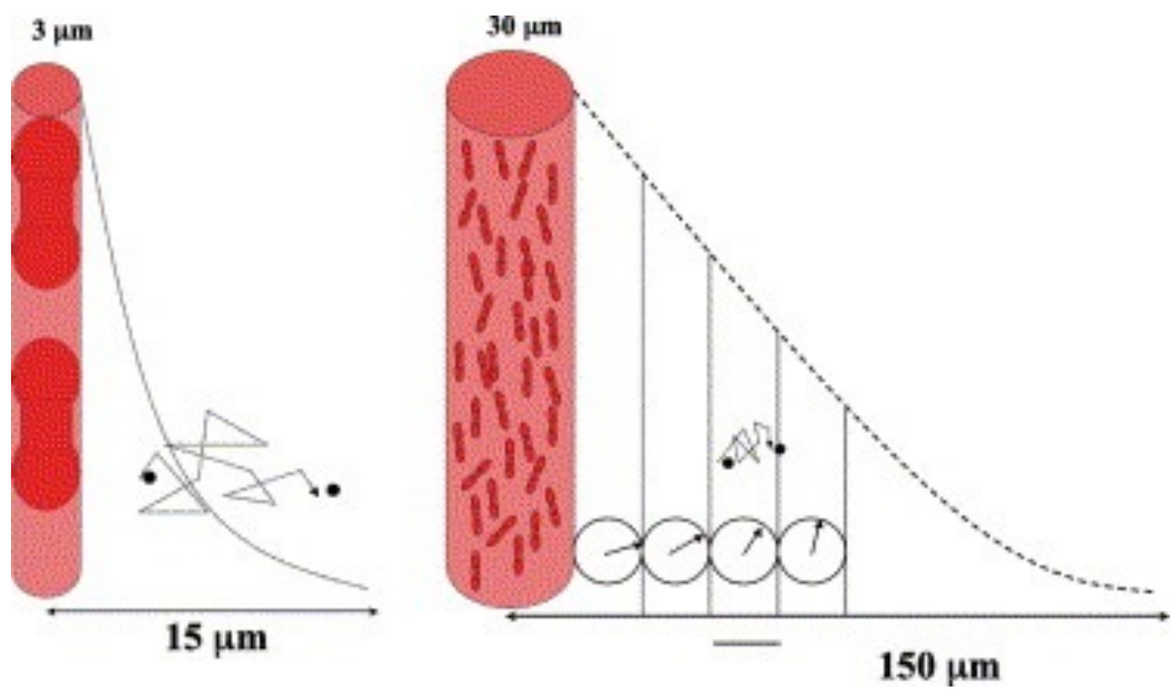
- Add a 'refocusing pulse' to get T2 contrast
- Reduced number of slices per TR
- Increased specificity, but still have intravascular signal at lower field strengths
- Less sensitive to rapidly flowing blood
- Less signal dropout
- Reduced contrast-to-noise ratio

Adapted from revisemri.com

Increased specificity with SE

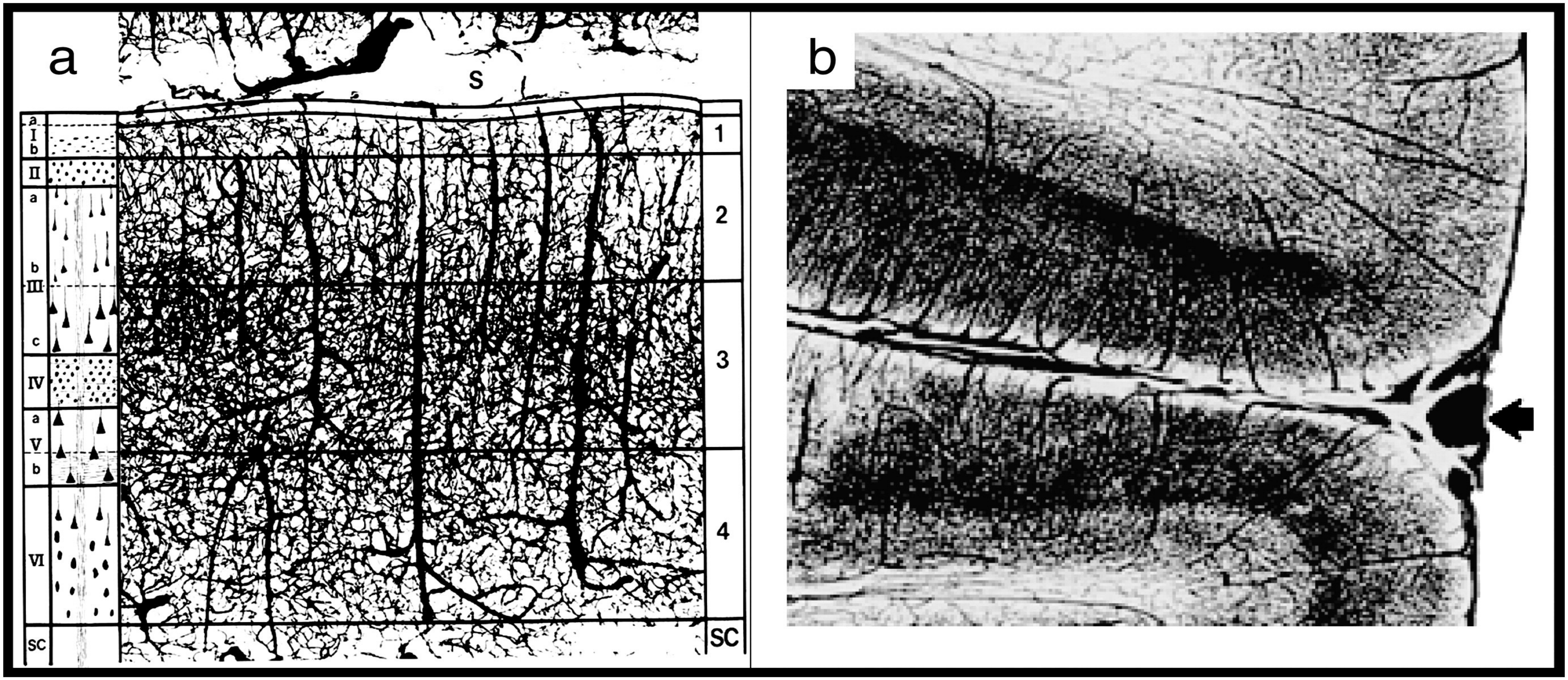


Courtesy of Peter Bandettini

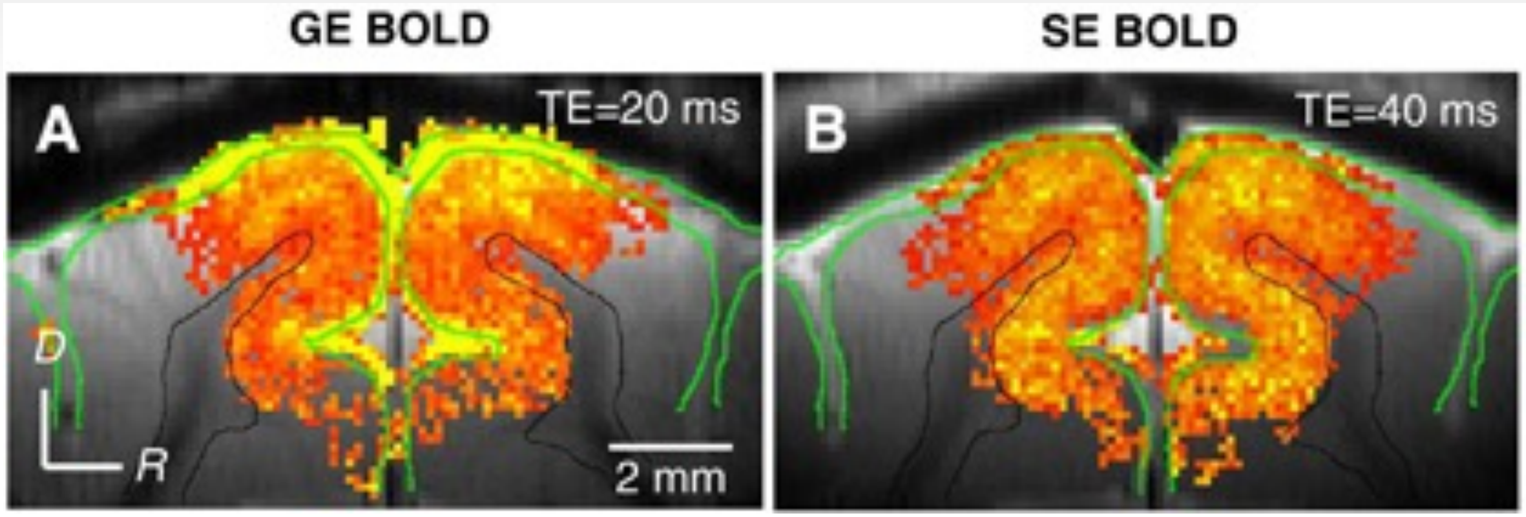


Kim, Methods (2003)

Vasculature density



Duvernoy, Brain Res. Bull. (1981)

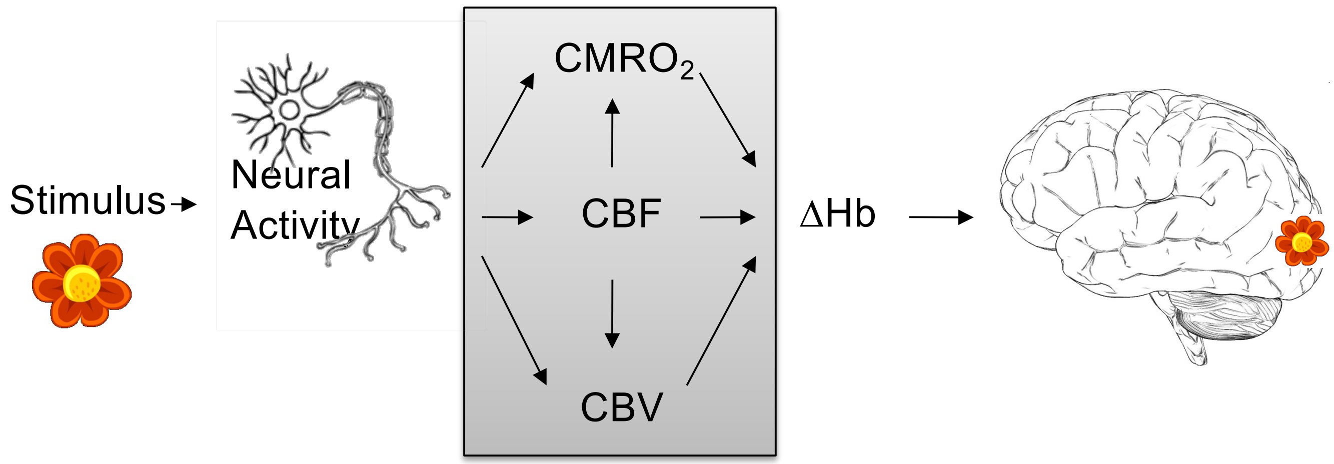


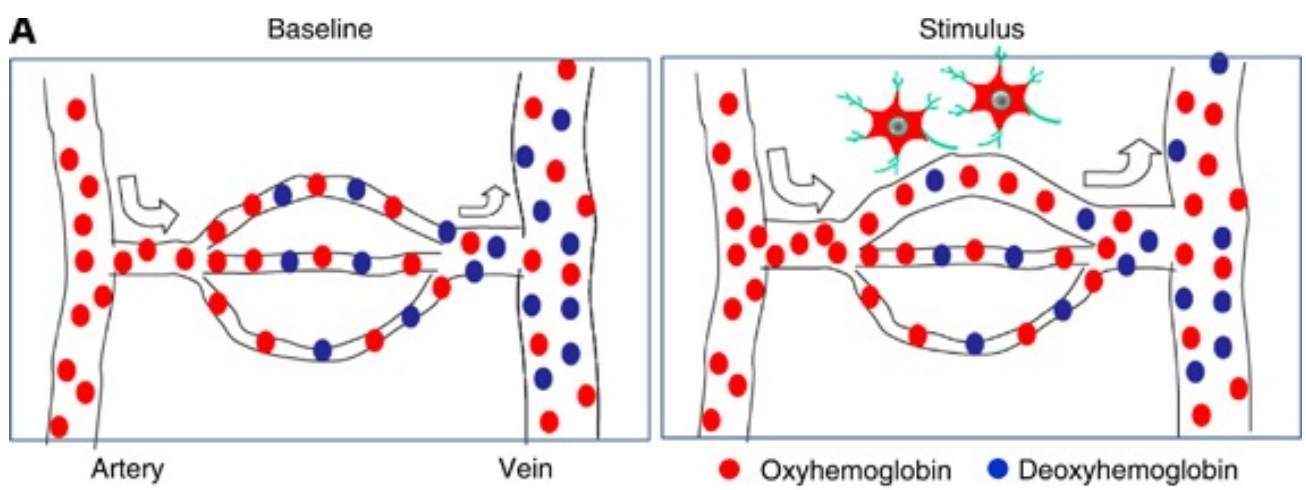
- GE BOLD fMRI (A) has the highest percent signal change at the cortical surface, where large pial vessels are located (green contours)
- Large vessel contributions are suppressed in SE BOLD

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

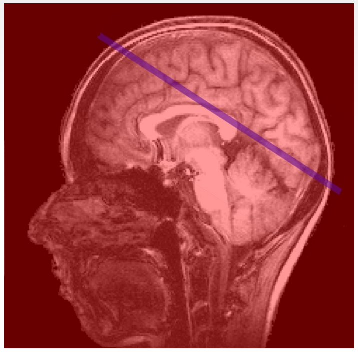
Contrast Mechanisms

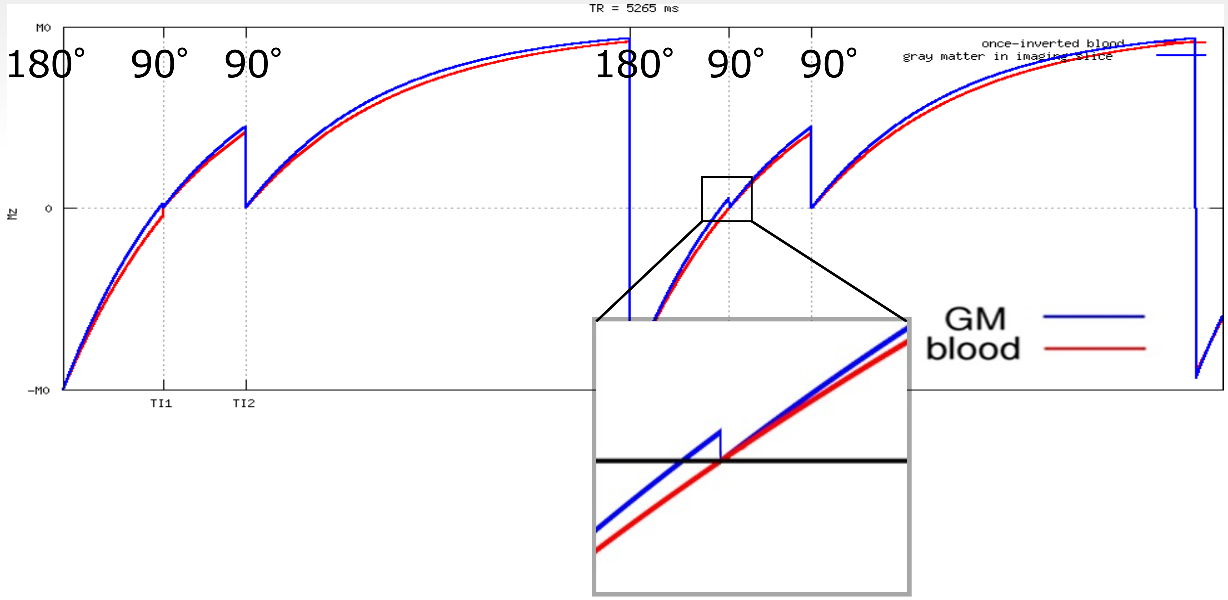
VASO: Null the blood signal





VASO





- single-slice method
- based on blood nulling in an inversion-recovery sequence
  - Grey matter is also saturated => smaller SNR
- VASO is a negative contrast

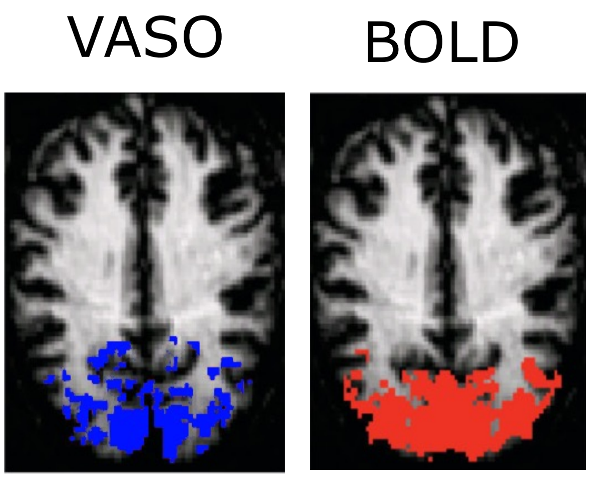


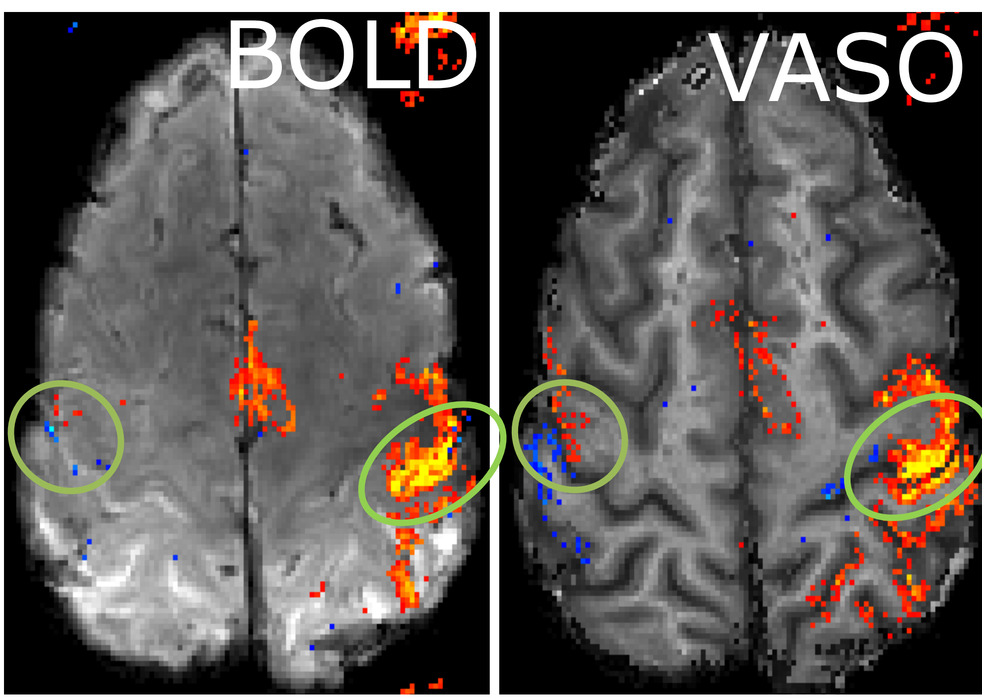
Figure from [Lu et al., 2014, NMR Biomed]

Courtesy of Laurentius Huber, SFIM, NIMH

Advantages of VASO

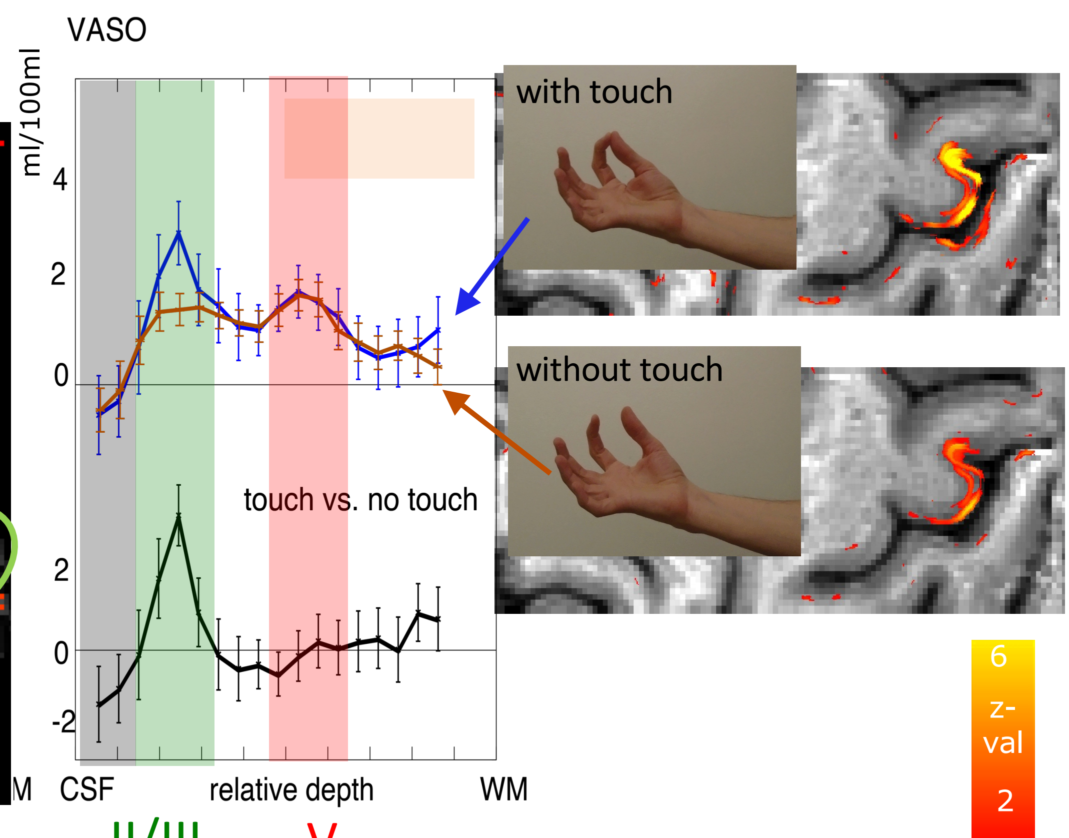
Negative BOLD (inhibition):

- VASO is quantitative compared to BOLD
- VASO is not contaminated from large veins



Layer-dependent fMRI:

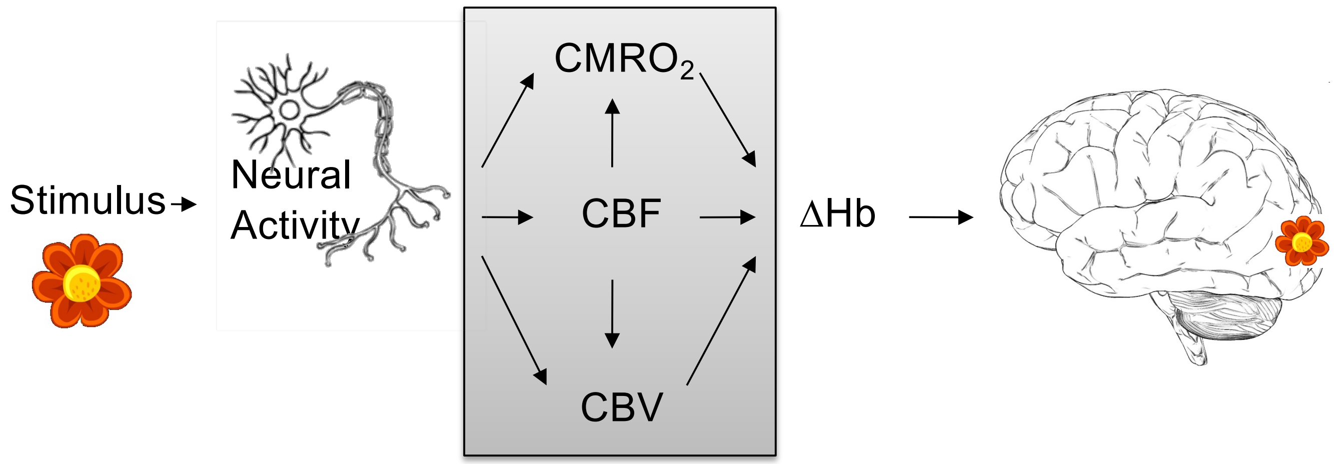
to distinguish between feed-forward
and feedback activity.

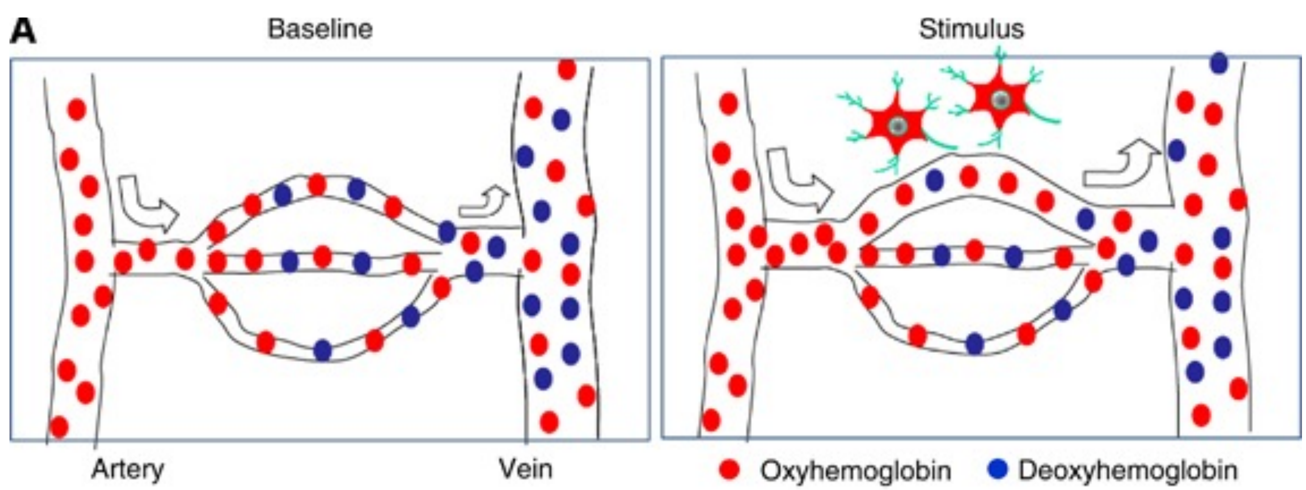


Courtesy of Laurentius Huber, SFIM, NIMH

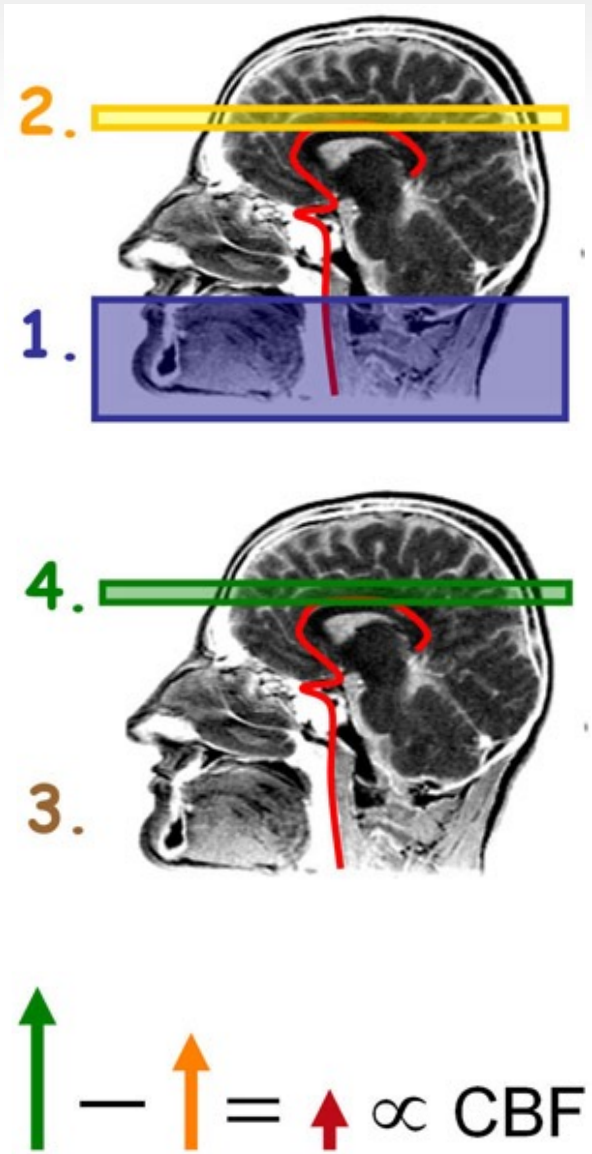
Contrast Mechanisms

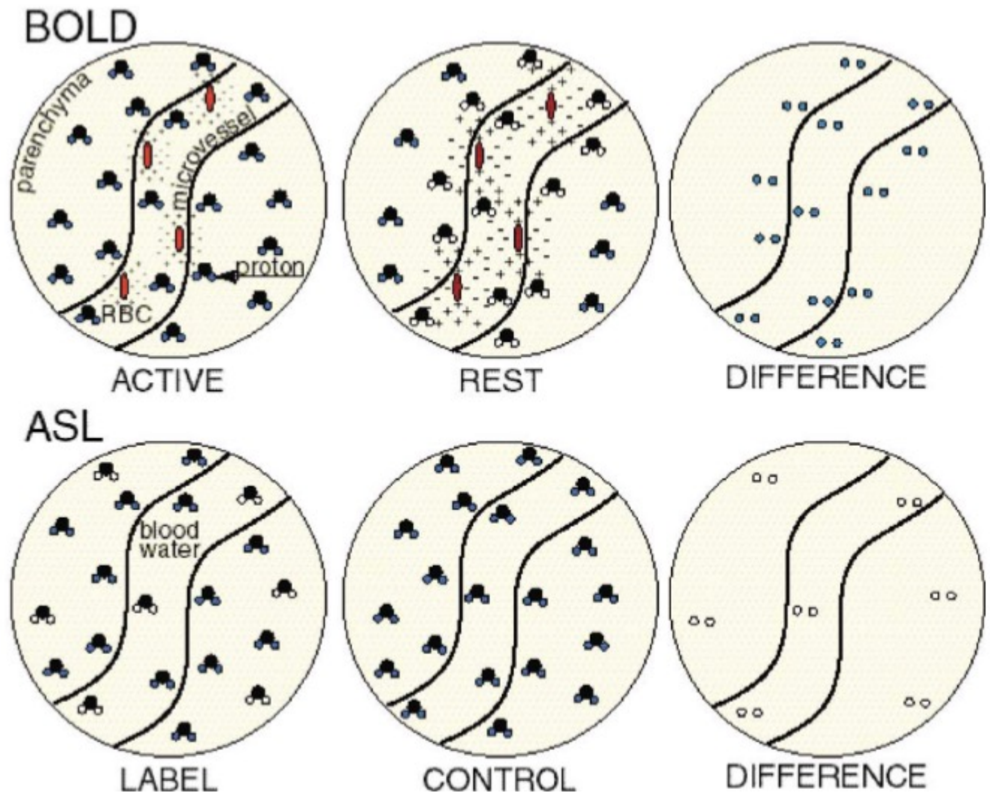
ASL: tag the blood signal





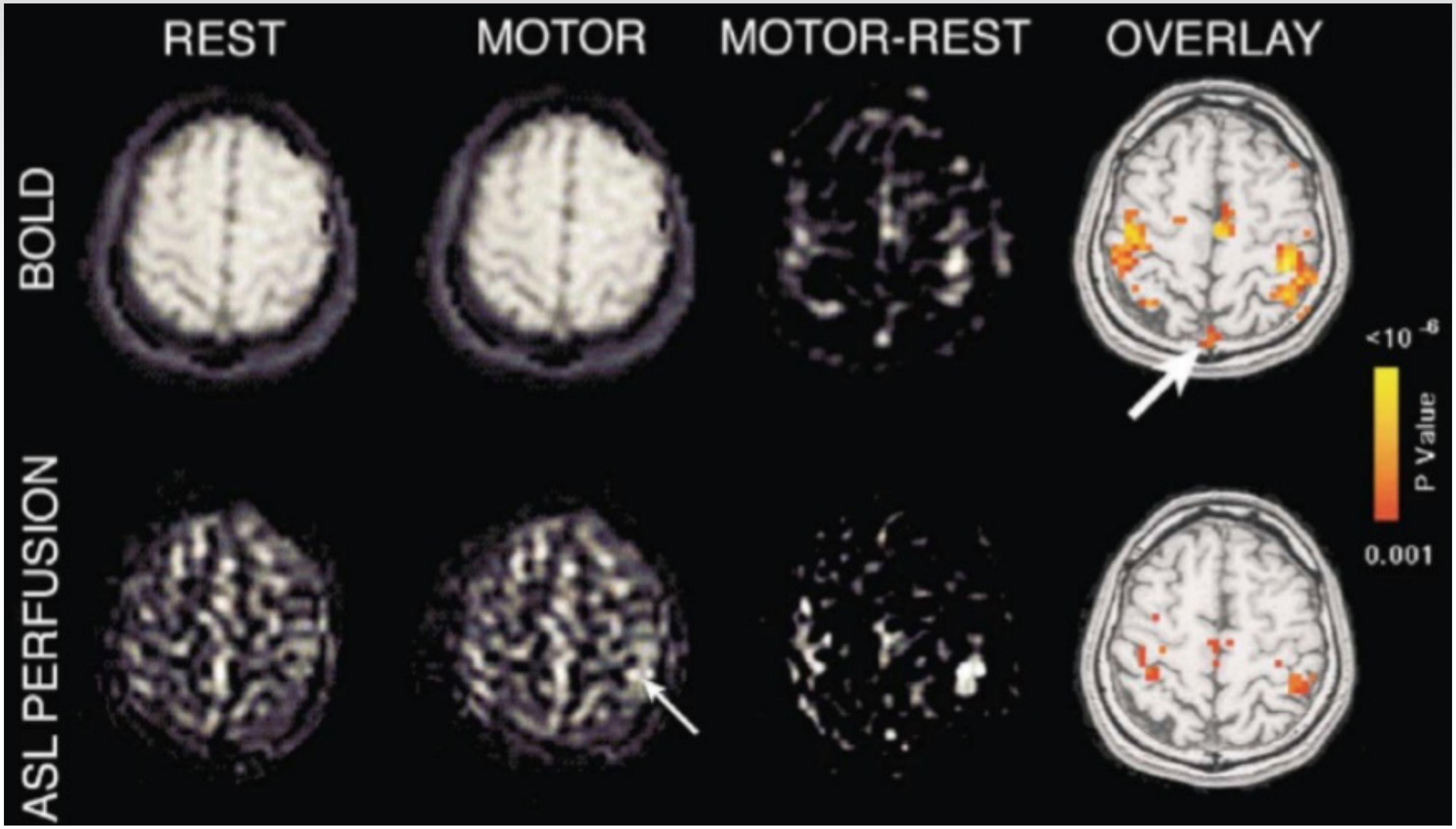
ASL vs. BOLD





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

Detre JA et al., Clinical Neurophysiology (2002)

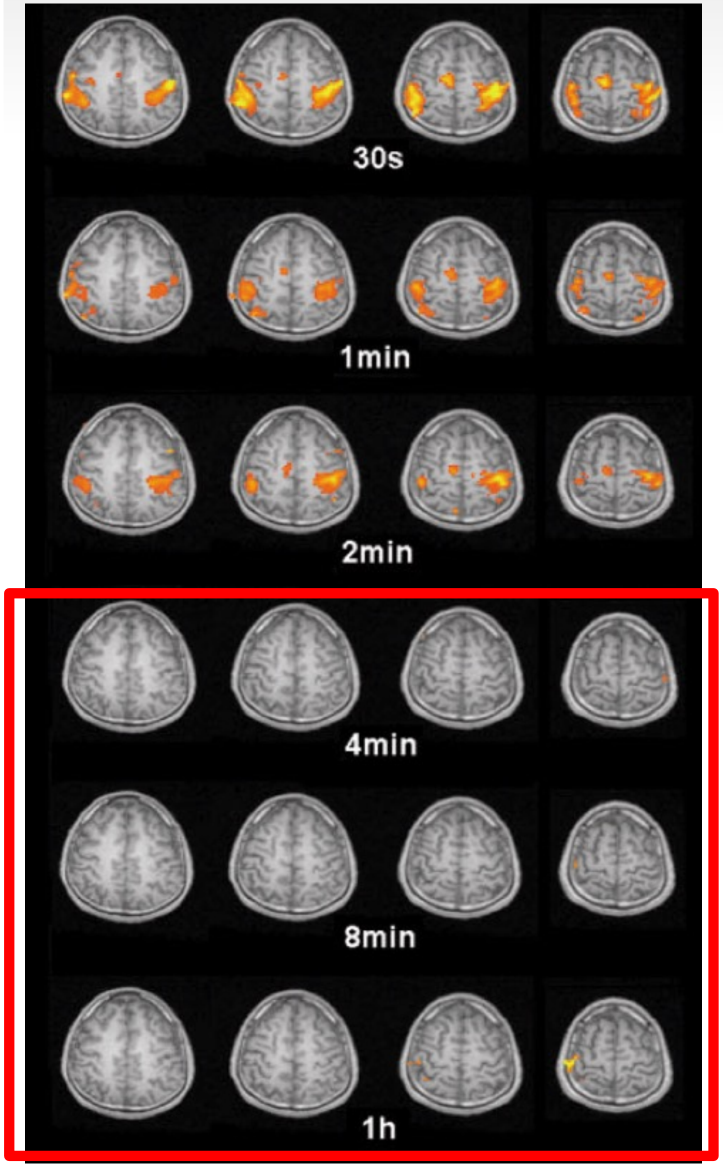


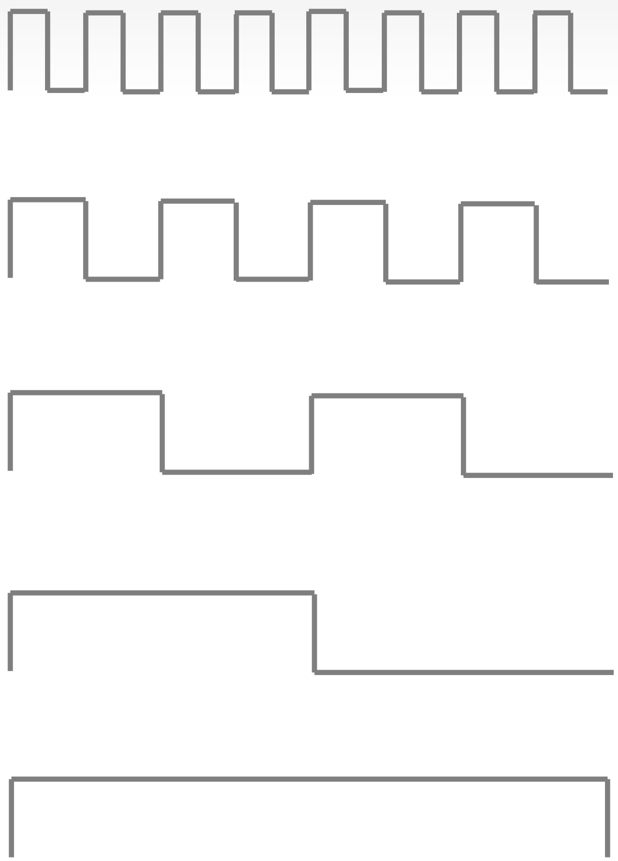
- Tagged blood is T1 contrast
- Signal is from arterioles and capillaries
- Longer TR, lower signal
- Lower inter-subject variability
- Insensitive to drift artifact

Detre JA et al., Clinical Neurophysiology (2002)

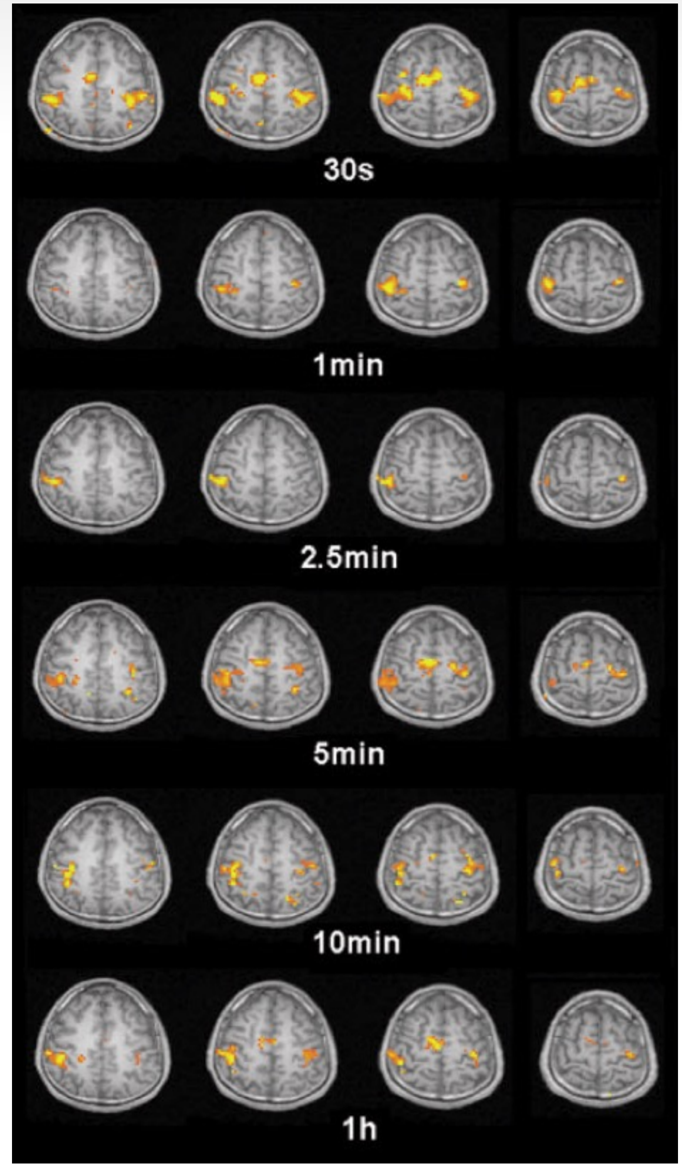
The trouble with slow stimuli

BOLD





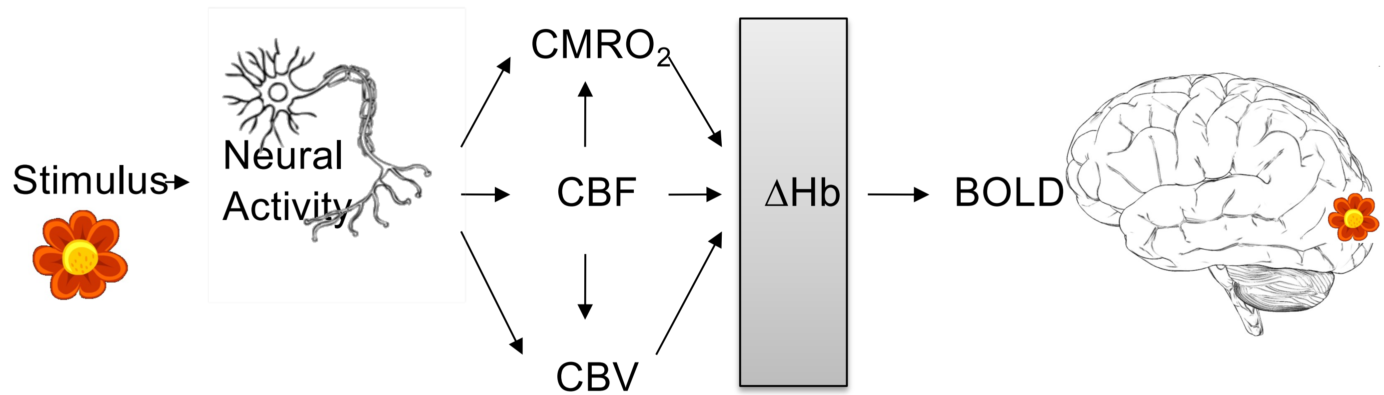
ASL



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

Contrast Mechanisms

multi-echo: measure at more than one point

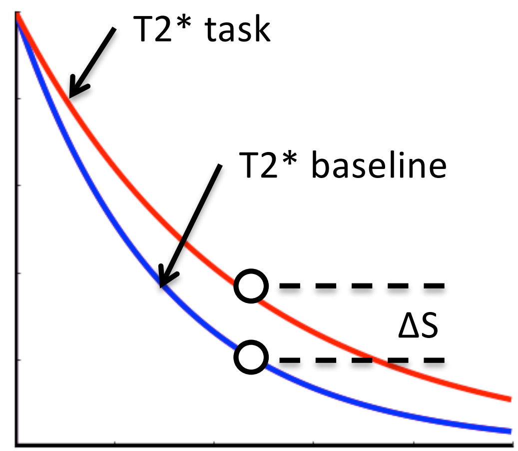


T2* is the "observed" or "effective" T2

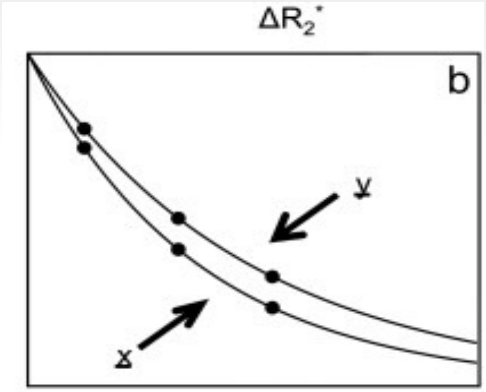
Can come from:

- inhomogeneities in the main magnetic field.
- susceptibility-induced field distortions produced by the tissue

=> BOLD contrast



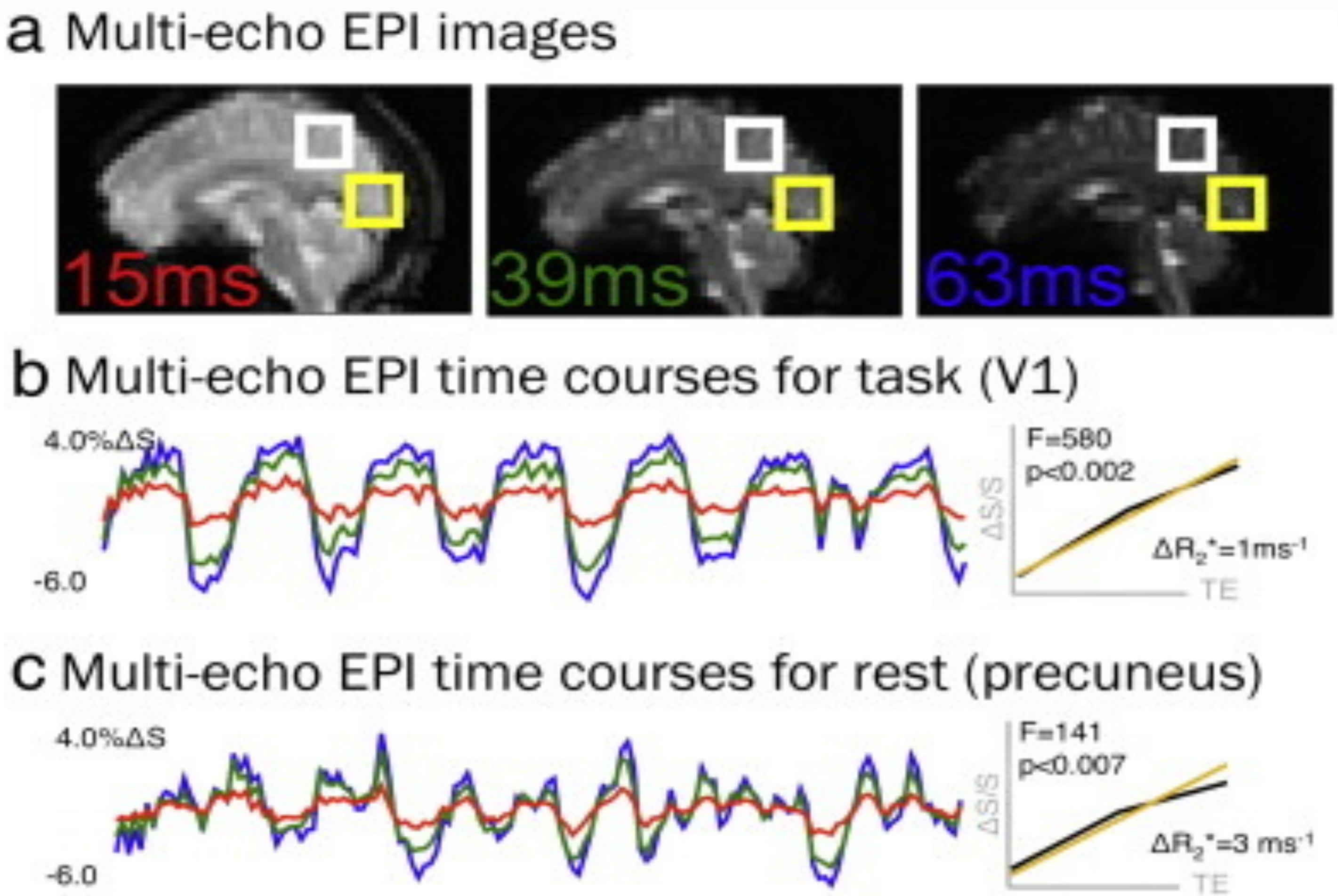
Separating BOLD from non-BOLD



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

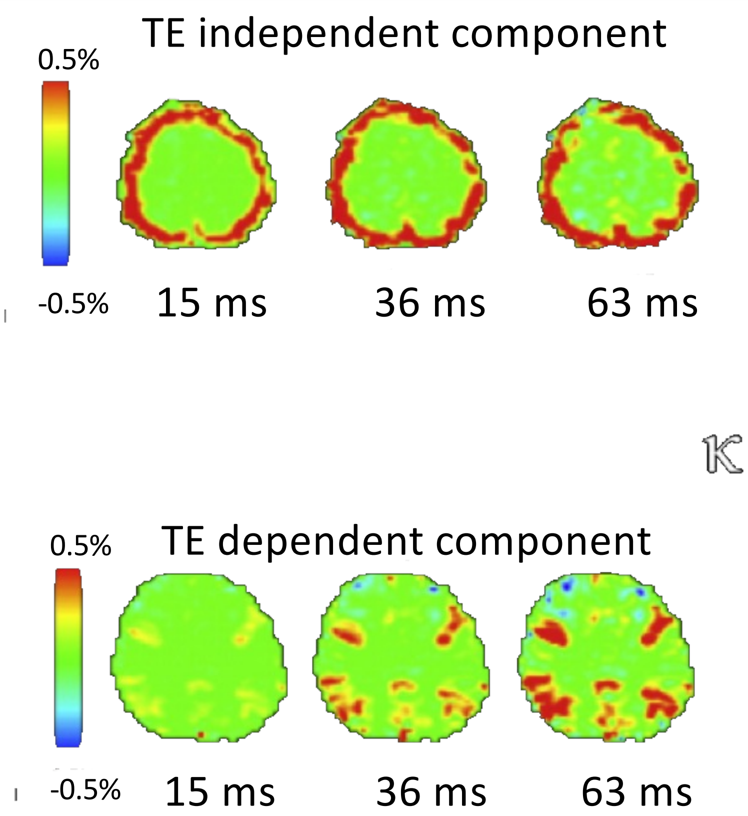
- Measuring several TEs enables the separation of non-BOLD artifacts from the data

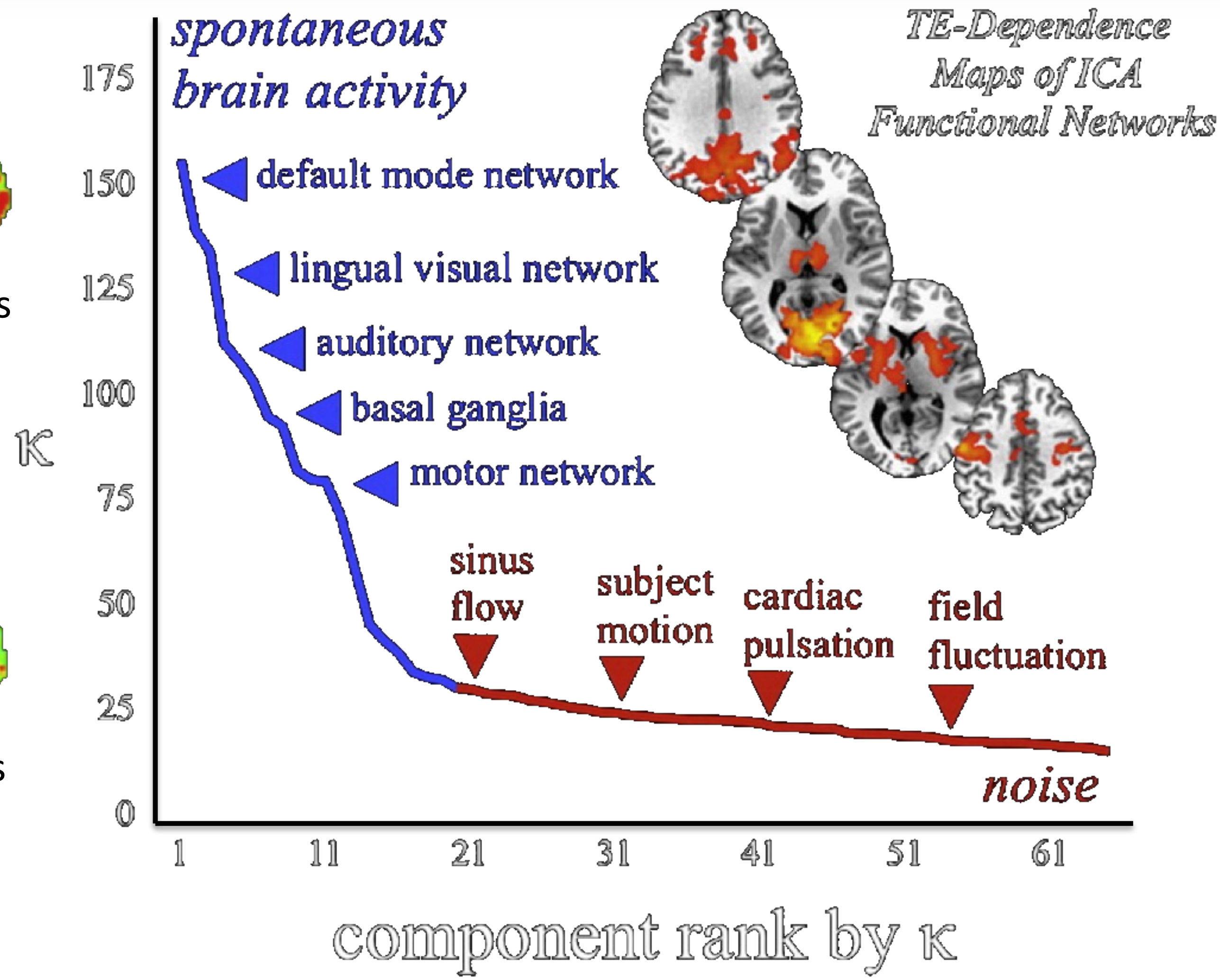
Signal scaling



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

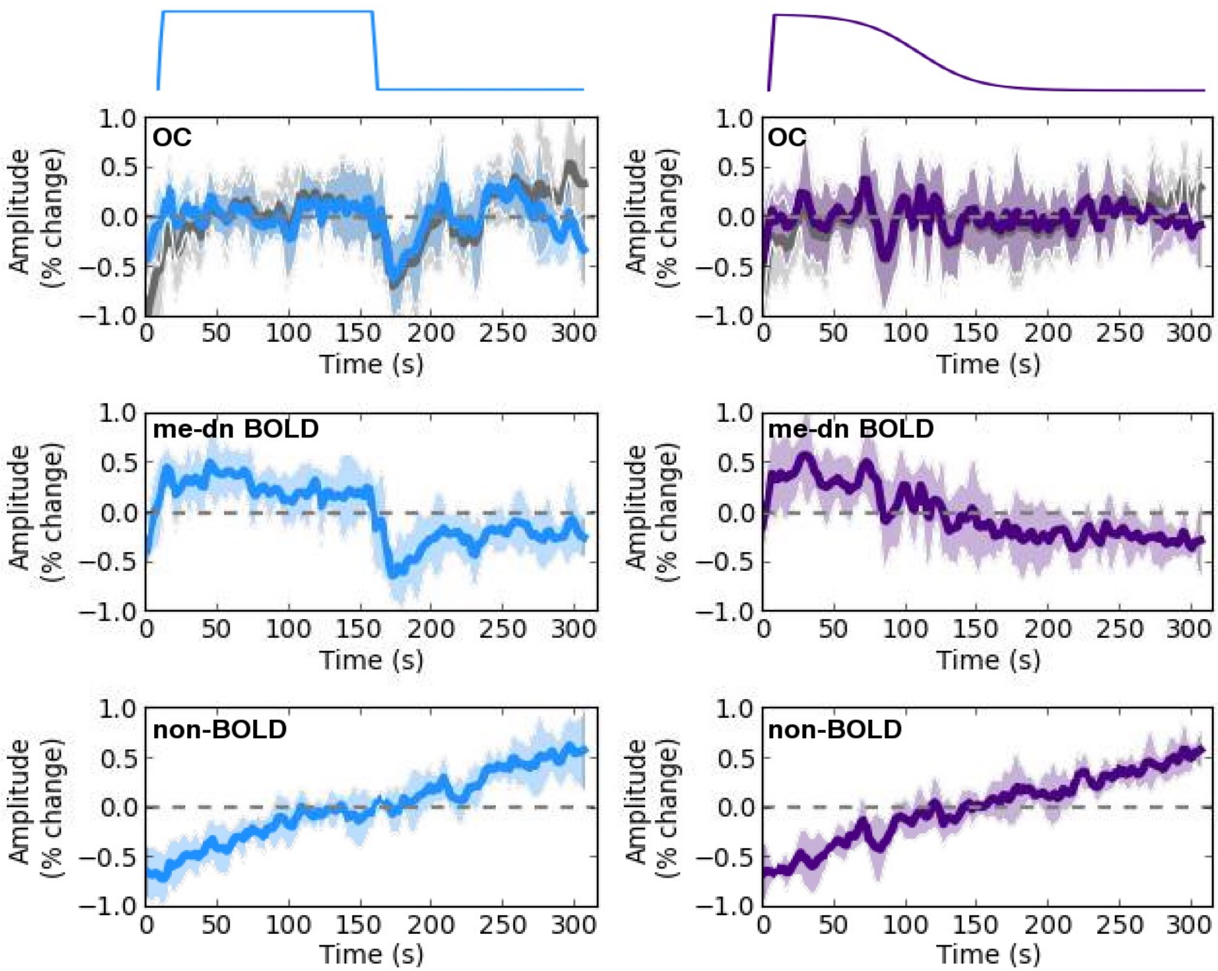
Multi-echo Component selection





Detection of slow BOLD signals with ME

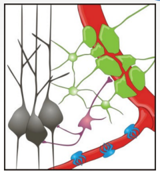
- Group average timeseries taken over voxels in V1 for a visual block and ramp contrast task
- The thick line is the mean and the shading is the standard error.



- 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

Outline

Introduction



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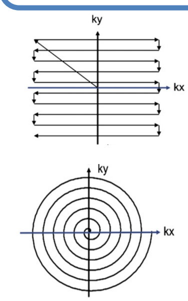
- BOLD signal basics

MR acquisition Basics

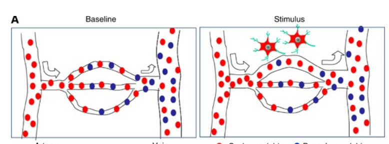


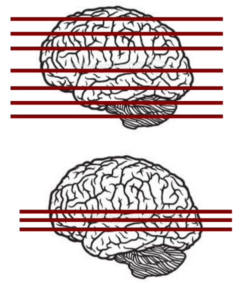
- K-space
- EPI
- Spiral
- TR/TE

Functional Contrast

- BOLD
- Gradient-echo
- Spin-echo
- Multi-echo

Perfusion Diffusion VASO





Spatial/Temporal resolution

Imaging Factors

- Field strength 3T, 7T
- <u>Acceleration:</u>
- k-space: Single/multi-shot EPI
- In-plane: SENSE (ASSET)
  GRAPPA (iPAT)
- Multi-slice

Biological factors

- Veins/capillaries
- Physiological noise

Summary

- BOLD is oxygen level dependent contrast indirectly related to neural activity
- spatial/temporal resolution and contrast tradeoffs
- ways to optimize acquisitions for specific applications
- appreciation of various contrast choices

- 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

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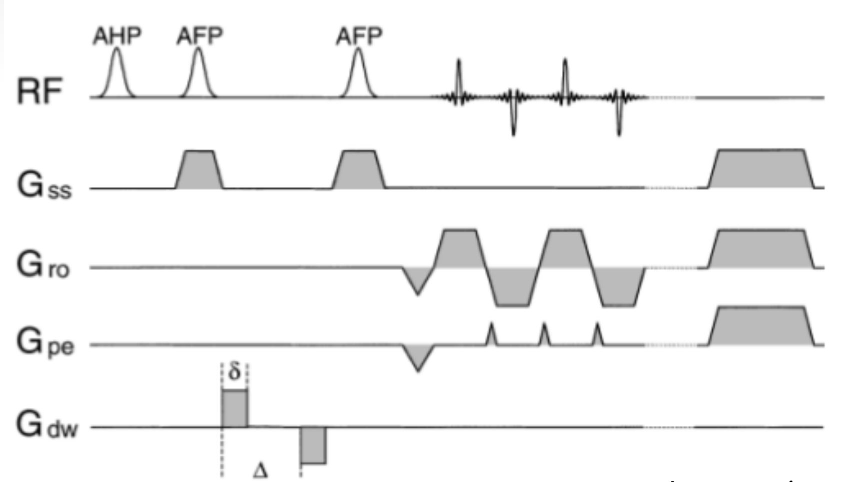
ASL vs. BOLD

	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

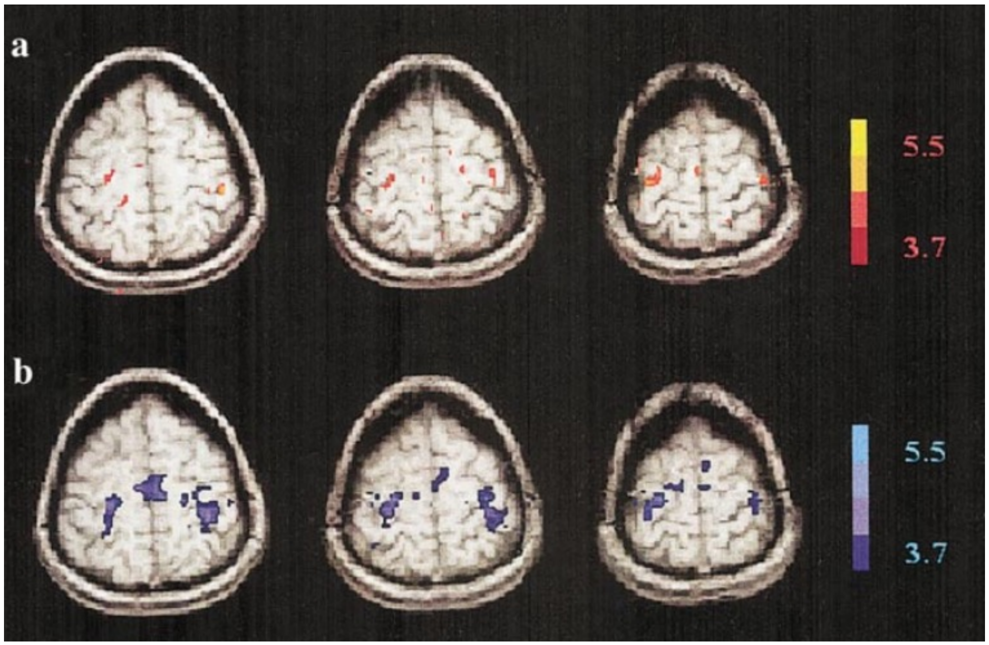
Detre JA et al., Clinical Neurophysiology (2002)

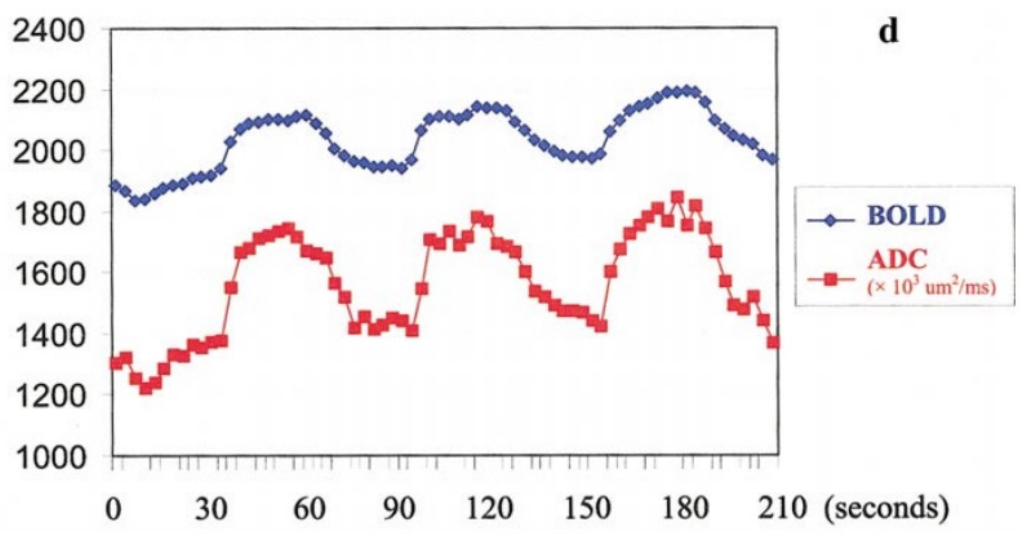
Diffusion weighted fMRI

- 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



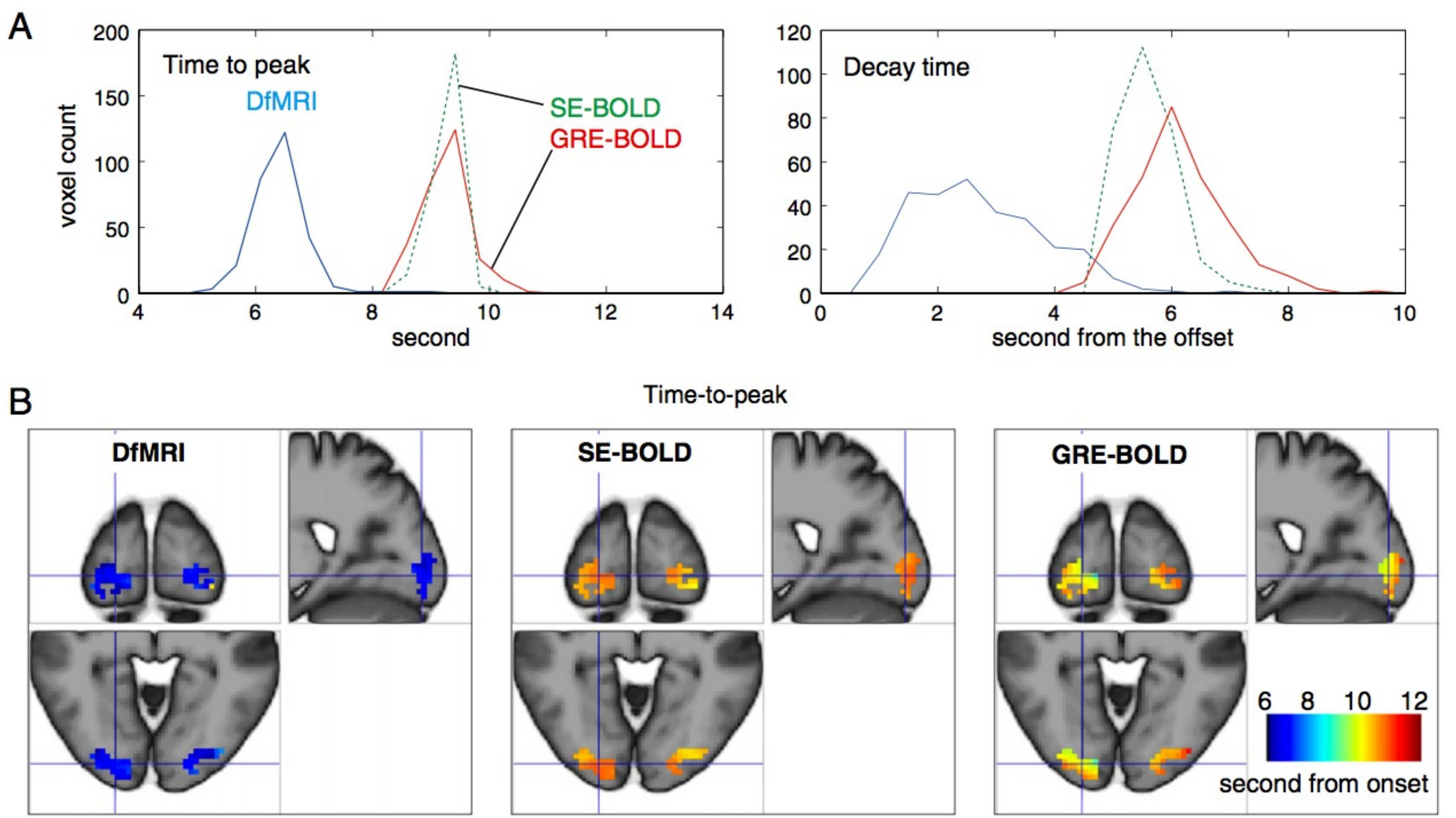
Lee SP et al, MRM (1999)





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

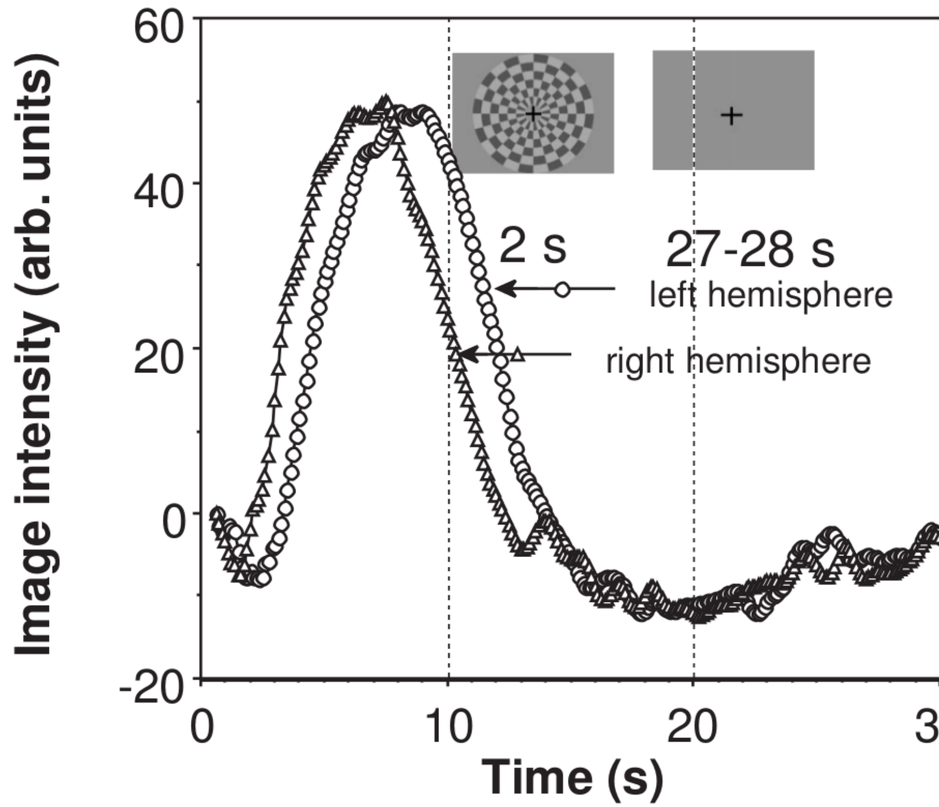
Faster response than SE/GE BOLD



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

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

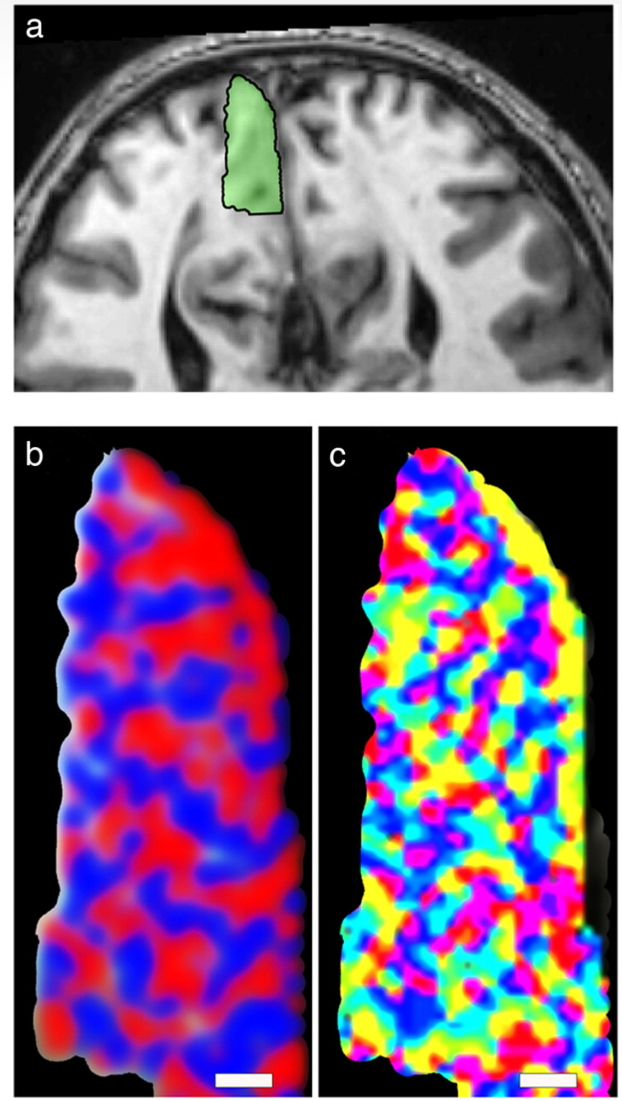
- At 3 T : ~ 1.5 mm^3 resolution

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.

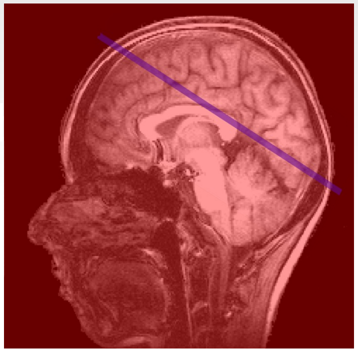
- At 7 T, using spin-echo sequences, the smallest resolved functional unit was orientation columns (on the order of 0.5-mm width).
- Practically limited by smoothing kernels, template alignment in group studies.

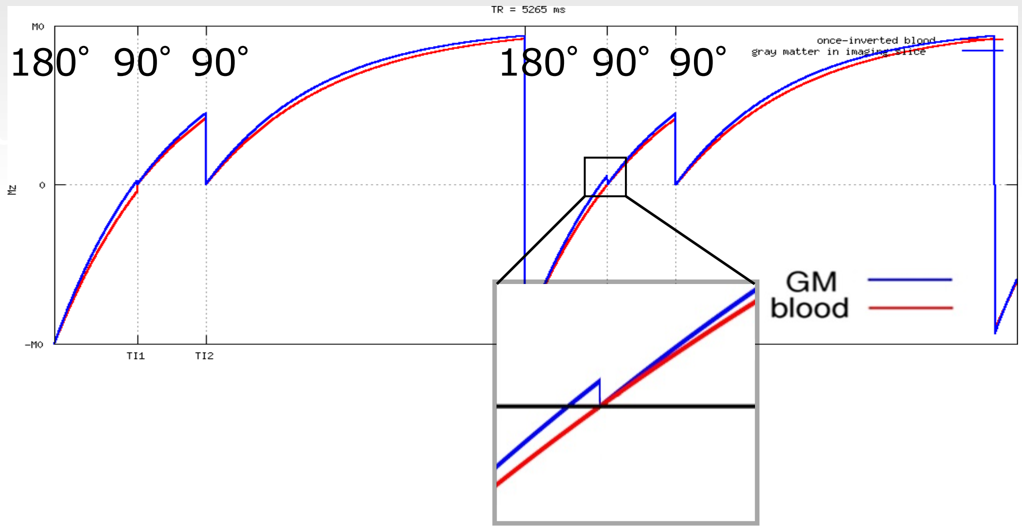


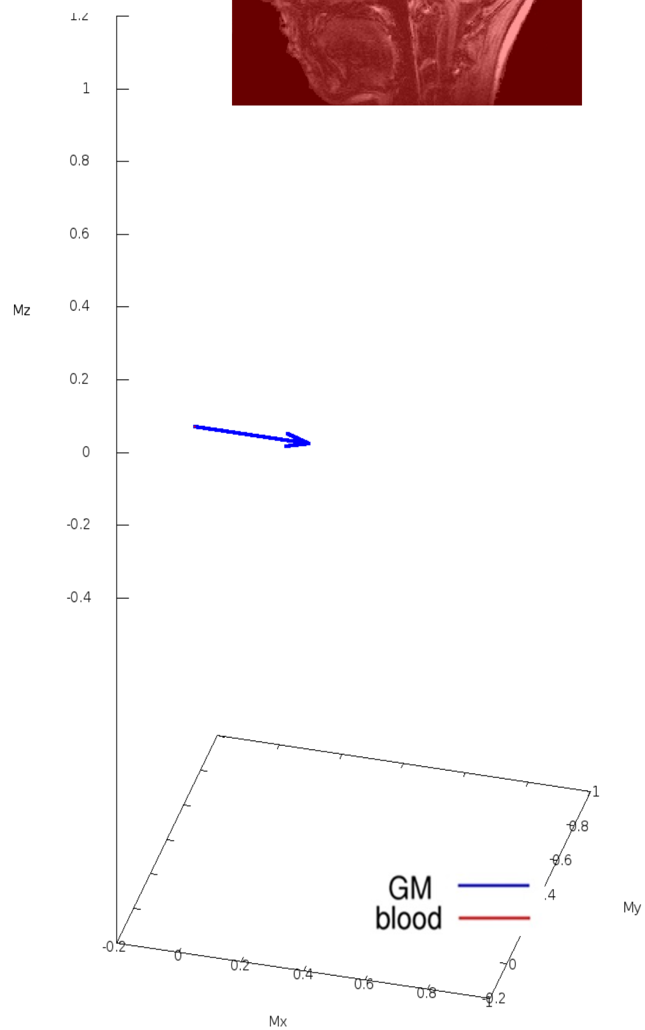
Yacoub E et al. PNAS 2008;105:10607-10612

Sequence	TR	Spatial coverage	Advantages	Disdvantages
EPI (single shot)	2s	3.5	Fast,	Signal drop out
Spiral	2s		Efficient gradient use	Blurry artefacts
Gradient echo (GE)			+CNR	
Contrasts				
Spin Echo (SE,EPI)			+spatial resolution	
Diffusion				
ASL				slow
VASO				
SSFP				
Acceleration				
EPI multi-shot				
SENSE/GRAPPA/SMASH/HASTE				
Multi-slice				

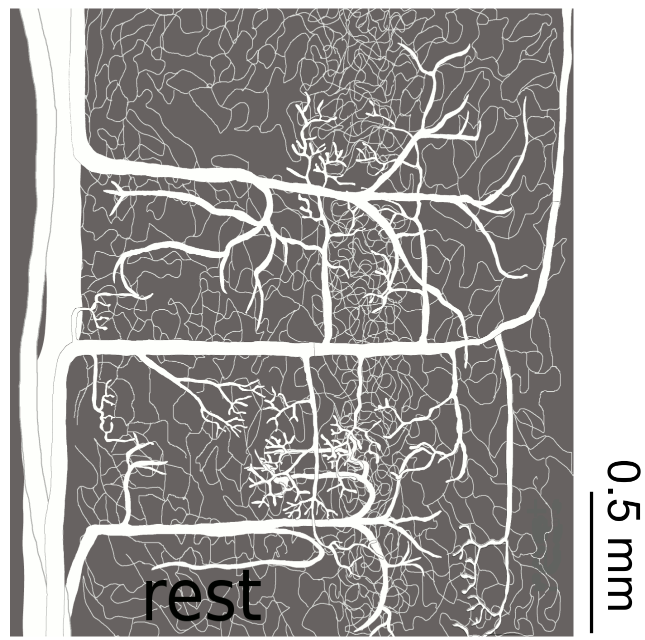
CBV contrast in Vascular Space Occupancy (VASO)







[Lu et al., MRM, 2003]



drawn based on [Duvernoy et al., 1981, Brain Research]