Basics of fMRI Part 1
Brain Activation, What can be Measured with MRI, and a dive into BOLD contrast and acquisition

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FMRIF

The Brain at “Baseline”

- CBF (cerebral blood flow): ~0.5 ml blood / g tissue / min
- CBV (cerebral blood volume): ~4% of tissue volume
- $CMRO_2$ (O_2 metabolic rate): ~1.6 μmol O_2 / g / min
- O_2 extraction fraction, E: ~40% (fraction of arterial O_2 extracted across the capillary bed)
- Arterial O_2 concentration: ~8 μmol O_2 / ml blood
- Firing rate 0.1 – 1Hz (population average)

Resting Membrane Potential: -70mV

Inside: high K+, low Na+, other negatively charged proteins and organic anions.

Outside: high Na+, low K+, and Cl-

K+ diffusing out (down concentration gradient but against electrical force)

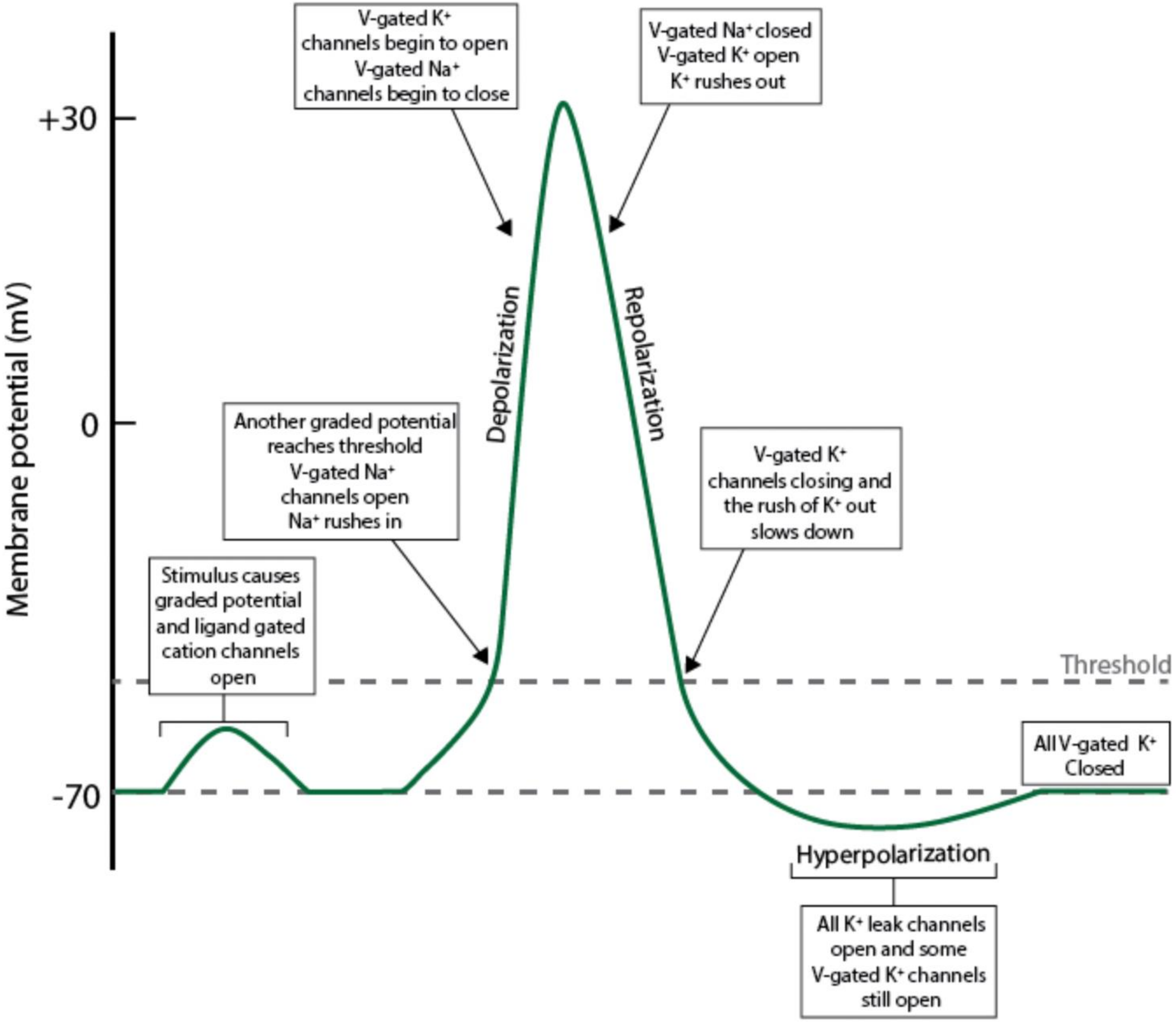
Sodium-Potassium Pump:

Moves 3 Na+ and 2K+ in for each ATP

What Accompanies Brain Activation?

Neuron

- **Action Potential:**
  - Neuron receives excitatory input (synaptic current) enough to reach -55mV:
  - Na+ channels open, Na+ rushes into the cell down electrochemical gradient.
  - Membrane potential increases to +60mV
  - Voltage gated Na+ channels inactivate, voltage gated K+ channels open, K+ flows down concentration gradient, carrying positive charge outward, making inside more negative again – transiently hyperpolarizing cell to -80mV
  - K+ channels close and Na+/K+ pump starts and K+ begins diffusing out again.



What Accompanies Brain Activation?

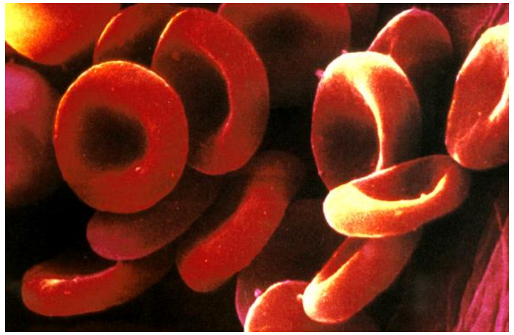
Spiking and Local Field Potentials

- **Spiking (output of individual neurons)**
  - Spiking rate ↑ **5–50** spikes/s (typically transient, falling to near baseline quickly)
  - Population-average (column, layer or region) ↑ **2–10 x**. (other regions show decrease)
- **Local Field Potentials (reflects synaptic and membrane currents, network synchrony)**
  - Low Frequency (<10Hz, Delta/Theta): Slow cortical and hippocampal rhythms, phase modulates spiking and power reflects brain state (i.e. sleep, navigation).
  - Alpha (8-12Hz) ↓ **10-50%** Inhibitory rhythm, modulates excitability and information flow.
  - Beta (13-30 Hz) ↓ **10-50%** Motor control/inhibition. Transient bursts reflect mesoscopic dynamics.
  - Gamma (30-80Hz) ↑ **20-100%** Attention/binding/working memory/perceptual processing. Tracks spiking.
  - High Frequency/hippocampal ripples (150-200 Hz): Memory replay and consolidation.
- **LFP captures population level oscillations in synaptic and subthreshold activity while spiking sits on top of it and is modulated by these rhythms.**

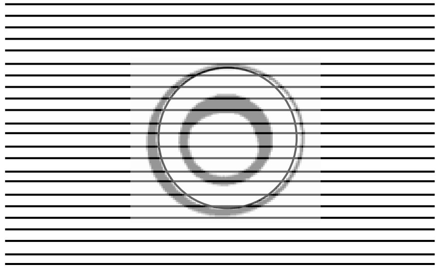
What Accompanies Brain Activation?
Metabolic, Hemodynamic, and Other Measurables

Effect	Increase	Decrease	Underlying Mechanism	Magnetic Resonance Measure	Relative Detectability
Deoxyhemoglobin		10 - 30%	Oxygen Delivery Exceeds Metabolic Need	Blood Oxygen Sensitive Dependent Contrast (BOLD)	100
CBF	30-50%		Vasodilatation & Capillary Perfusion	Arterial Spin Labelling (ASL)	25*
CBV	10-15%		Dilatation & Capillary Recruitment	Vascular Space Occupancy (VASO)	25
Middle cerebral artery (MCA) flow velocity	10-15%		Global autoregulation	Phase Contrast or Inflow Sensitive MRI	10
CMRO2	10-15%		Oxidative metabolism	Ratio of change in CBF/BOLD, calibrated by global stress of change in CBF/BOLD	10
Venous Oxygen Saturation	10-15%		Decresed oxygen extraction fraction	Possible T1 change in blood & tissue (Zero-TE sequences)	8
Glucose		5-12%	Increased Glucose metabolism	1H MRS	5
Lactate	10-30%		Increased glycolysis in Astrocytes	1H MRS	5
Glutamate (excitatory neurotrasmitter)	2-5%			1H MRS	5
GABA (inhibitory neurotrasmitter)	occasionally	5-10%		1H MRS	4
Cerebral Spinal Fluid (CSF) volume	small		displacement by increase blood volume	T1-wieghting	2
Cerebral Spinal Fluid (CSF) flow	small		displacement by increase blood volume	Phase Contrast MRI, T1-weighting	2
Elasticity Change	6-10%		increased blood volume	MR Elastography	2
Na+ moves intracellularly			Action potential	Na+ fMRI	1
Aspartate		3-4%		1H-MRI	1
Creatine Kinase (CK)	30%			31P magnetization transfer MRS	1
Nicotinamide adenine dinucleotide (NAD)		reduced NAD+	electron shuttle in glycolosys	31P MRS and 1H MRS	1
Temperature	0.1 degree Celsius			MR Phase or Diffusion Coefficient	0.5
Cell Swelling	3%		Ion flux draws water into neuons	Decrease in Diffusion Coefficient	0.5
Neuronal Currents?	transient/small		Dendritic currents with spiking	MR magntude or phase	0.01?

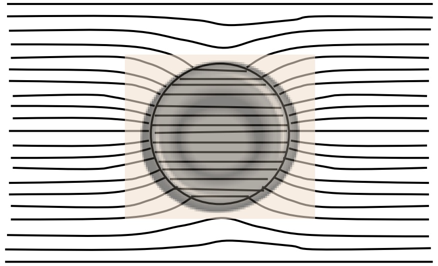
Blood Oxygenation



oxygenated

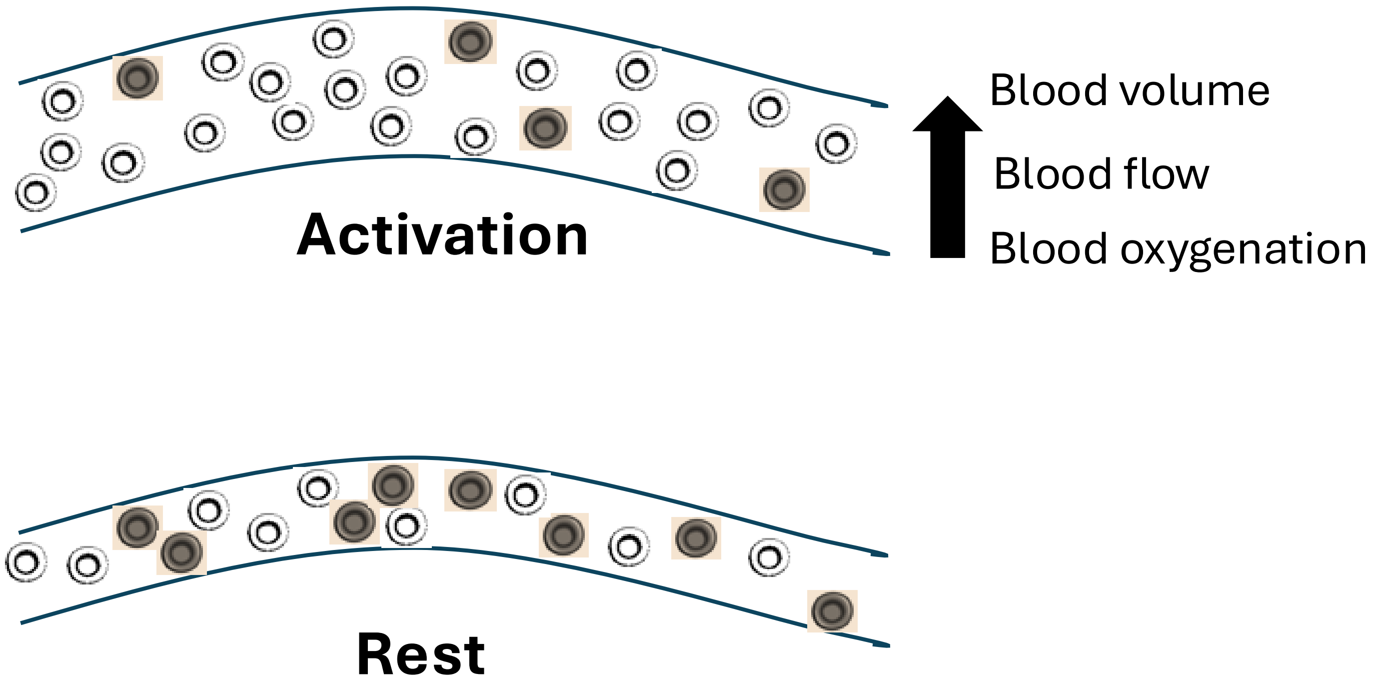


deoxygenated



Deoxy-hemoglobin: *distorts field, short T2*, **low signal***

Oxy-hemoglobin: *no distortions, longer T2*, **higher signal***



The Cascade of Events

Cerebral Tissue Activation

↓

Local Vasodilatation

↓

Increase in Cerebral Blood Flow and Volume → **Oxygen Delivery Exceeds Metabolic Need**

↓

Increase in Capillary and Venous Blood Oxygenation

↓

Decrease in Deoxy-hemoglobin

Deoxy-hemoglobin:	***paramagnetic***
Oxy-hemoglobin:	***diamagnetic***

↓

Decrease in susceptibility-related intravoxel dephasing → **Increase in T2 and T2***

↓

Local Signal Increase in T2 and T2* - weighted sequences

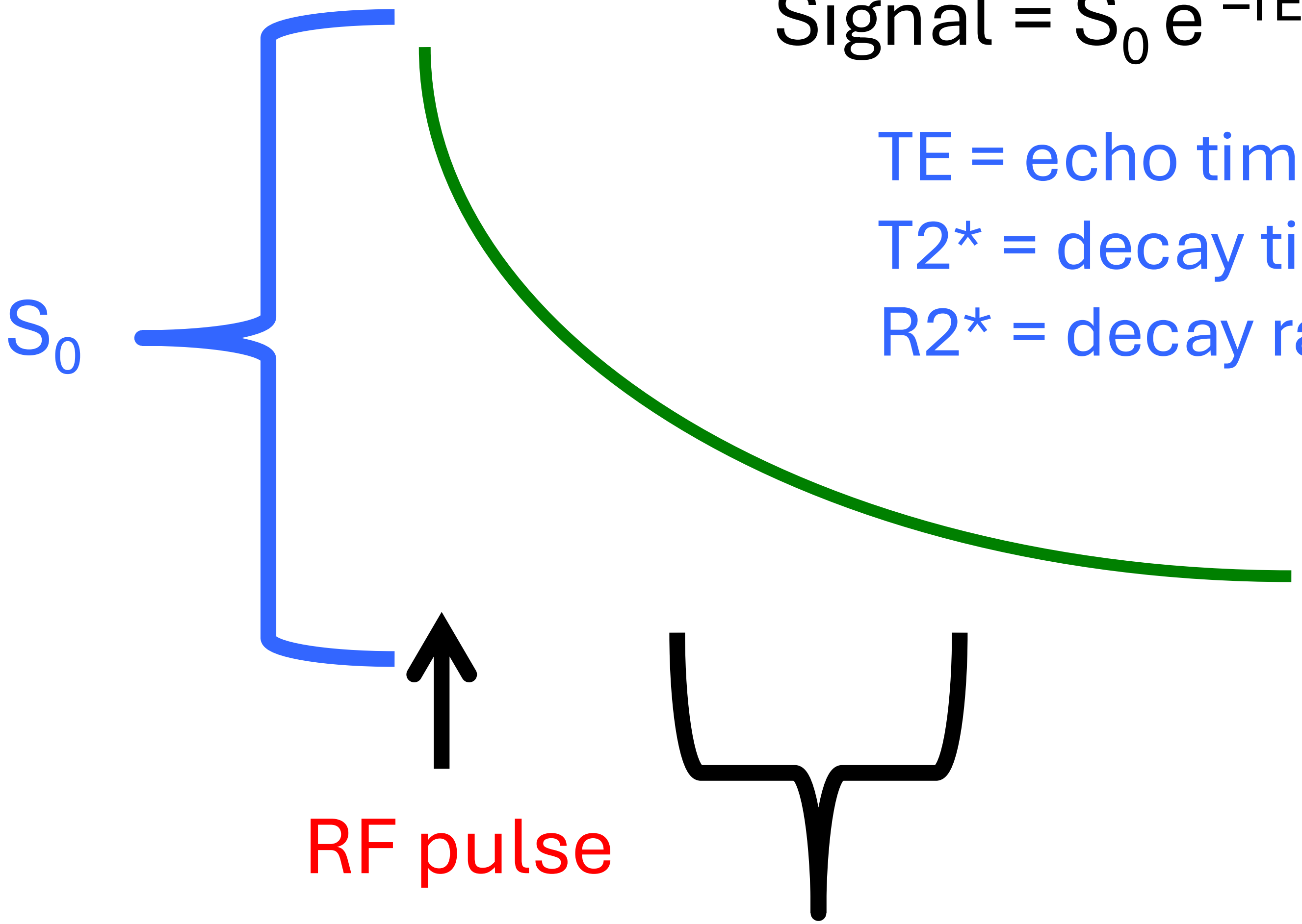
Gradient-Echo Acquisition

$$\text{Signal} = S_0\, e^{-TE/T2^*}$$

TE = echo time (pulse sequence parameter)

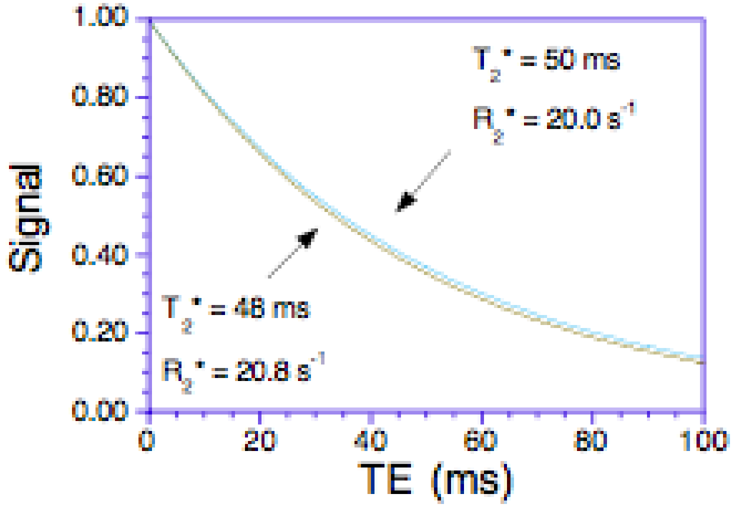
T2* = decay time (tissue property)

R2* = decay rate = 1/T2*

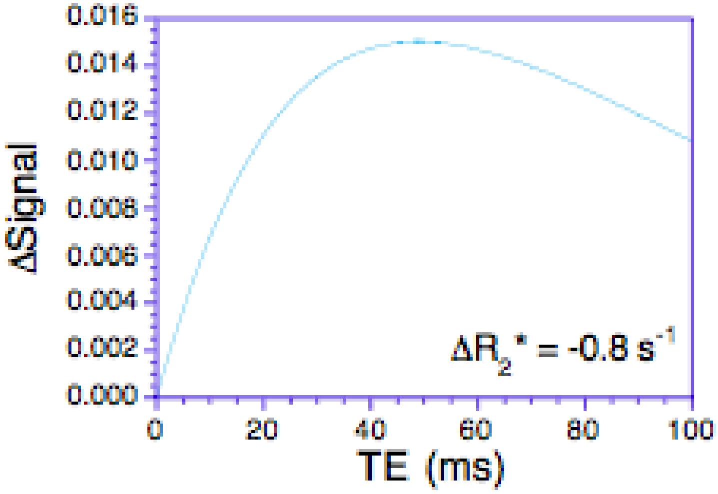


Data collection or “Readout Window”

TE dependence: Contrast vs Percent Change

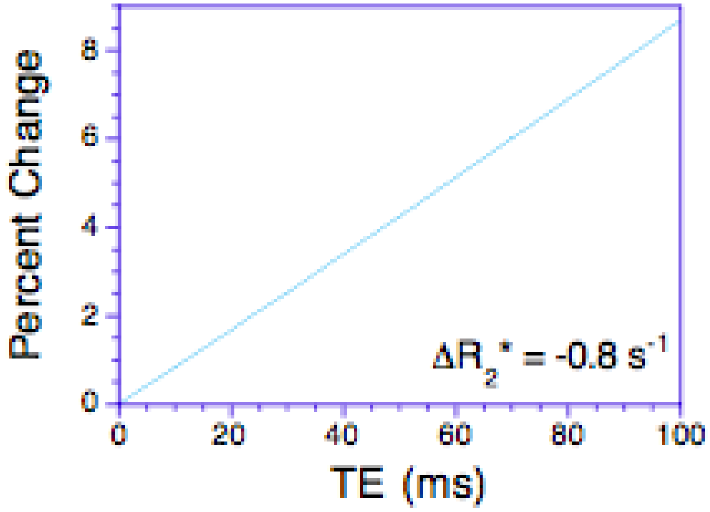


Functional Contrast



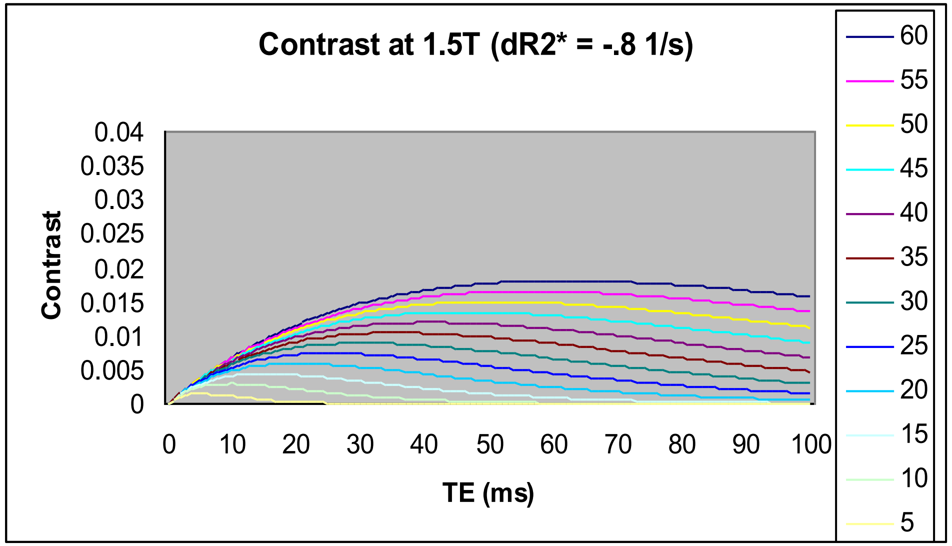
Optimal TE = T2*

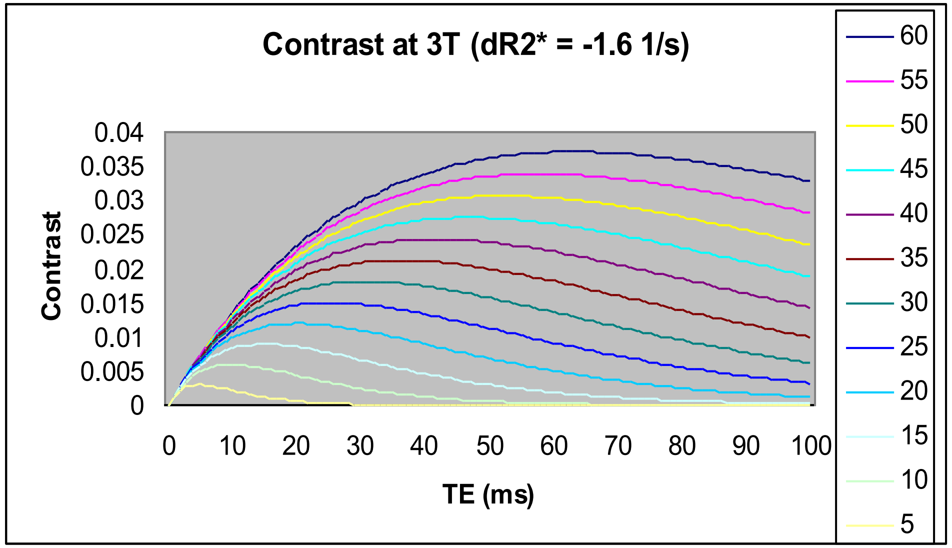
Percent Signal Change



Field Strength and Echo Time Effects on Contrast

Contrast gain with field strength is slightly offset by field-dependent decrease in baseline T2*





SNR ⬆

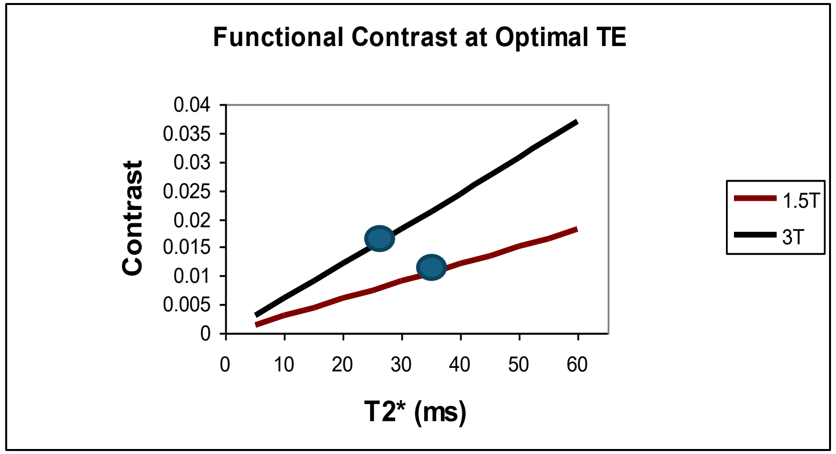
%change ⬆

Physio noise ⬆

CNR ⬆ (depends on physio/thermal)

Off-resonance artifacts ⬆

RF power deposition ⬆



Single Shot Imaging

Advantages of Single Shot Imaging

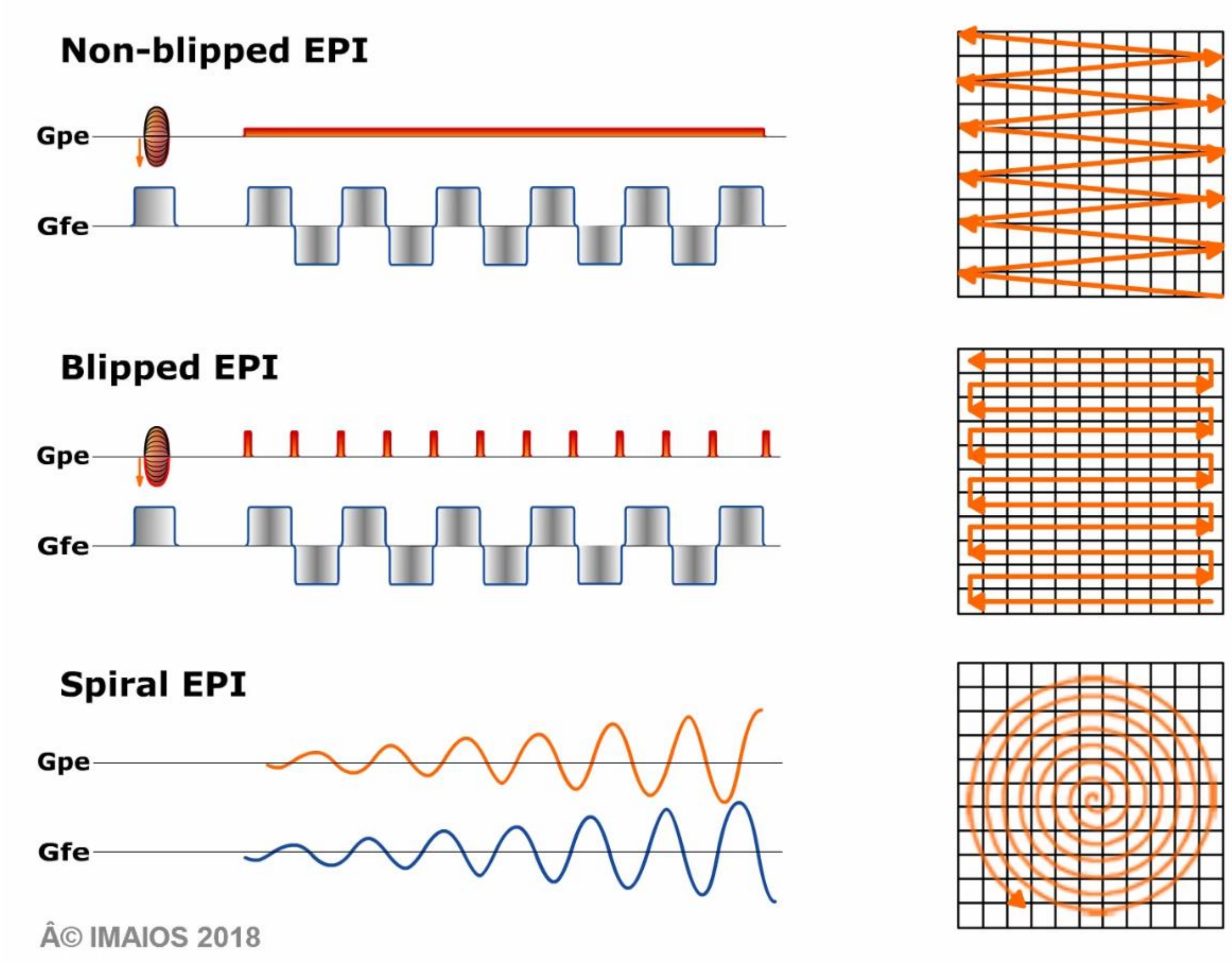
Freezes physiological processes during image acquisition, minimizing non-repeatable artifacts.

Allows short between image time, for time series acquisition.

Disadvantages of Single Shot Imaging

Warping, Distortion
Harder to obtain high resolution but possible (parallel imaging, RF sensitivity encoding)

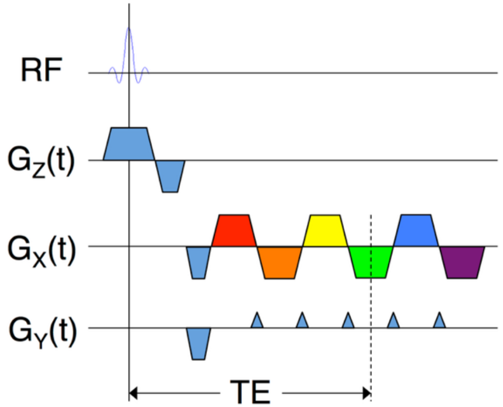
Used for high resolution: hybrid methods (few-shot) approaches, parallel imaging and (RF) sensitivity encoding, and 3D imaging approaches.

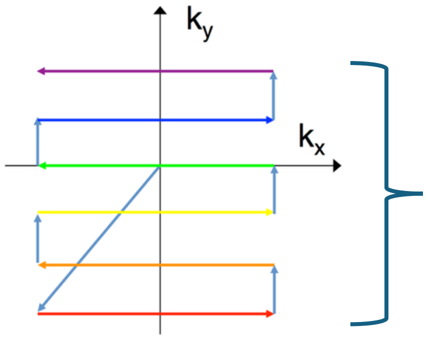


Readout Direction Effects

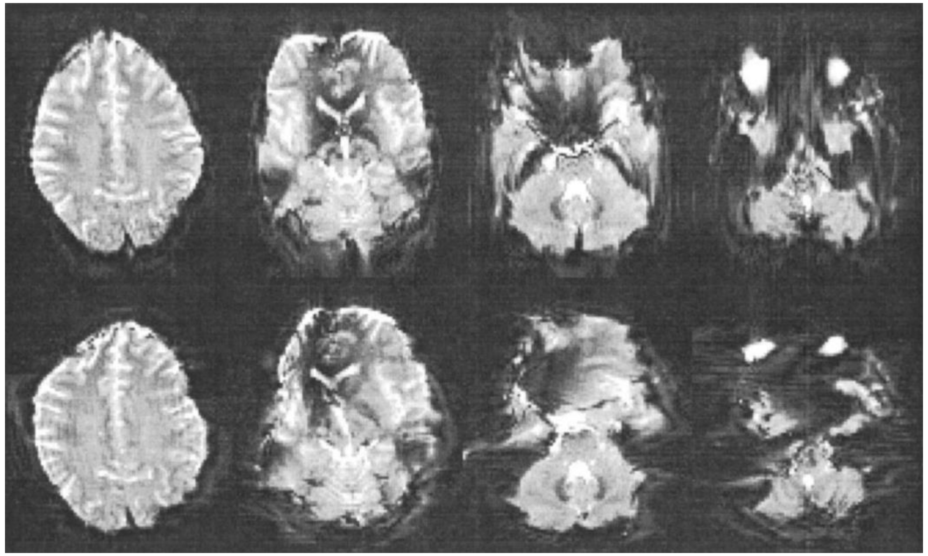
Echo Planar Imaging

0.25ms





30ms



Ky in AP direction

Ky in LR direction

Kybic, Jan et al, IEEE Trans. Med. Imaging, 2000

Echo Planar Imaging

Ky is long
Kx is short

Warping:

Determined by length and direction of readout window as well as field strength.

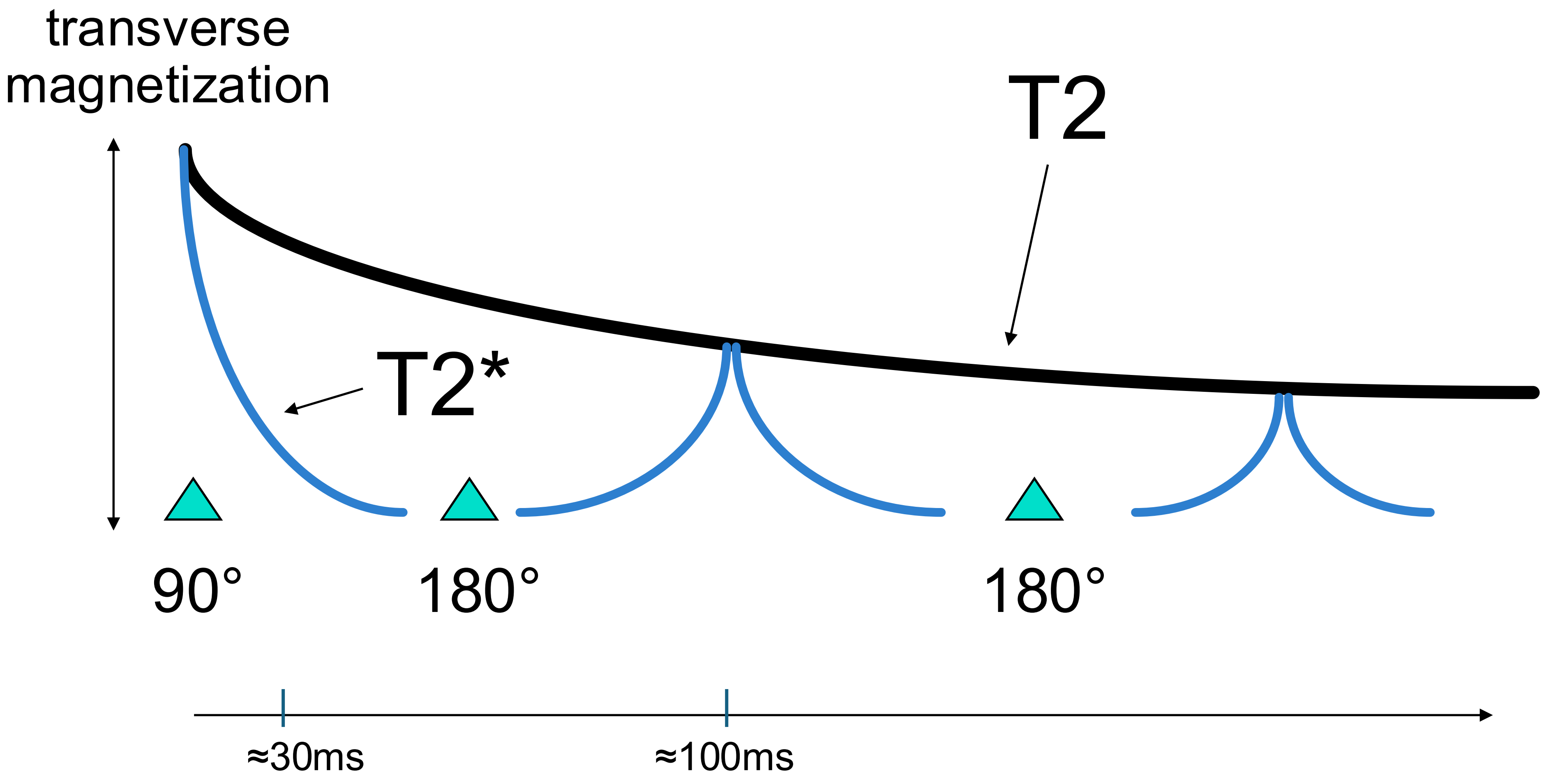
Dropout:

Determined by voxel size and field strength.

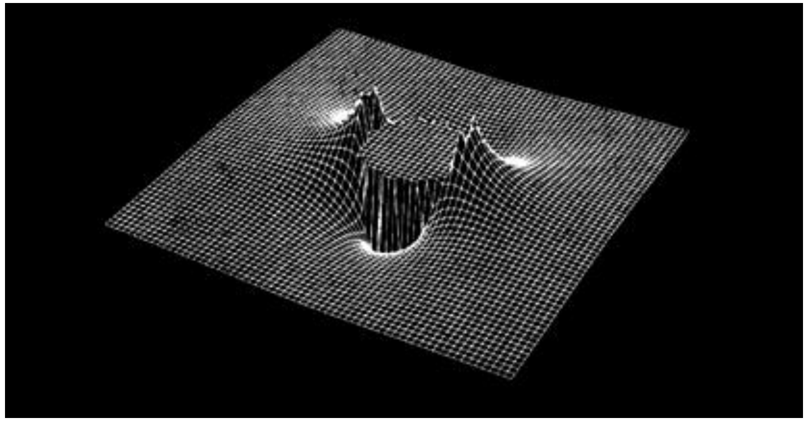
For Standard multi-shot structural imaging

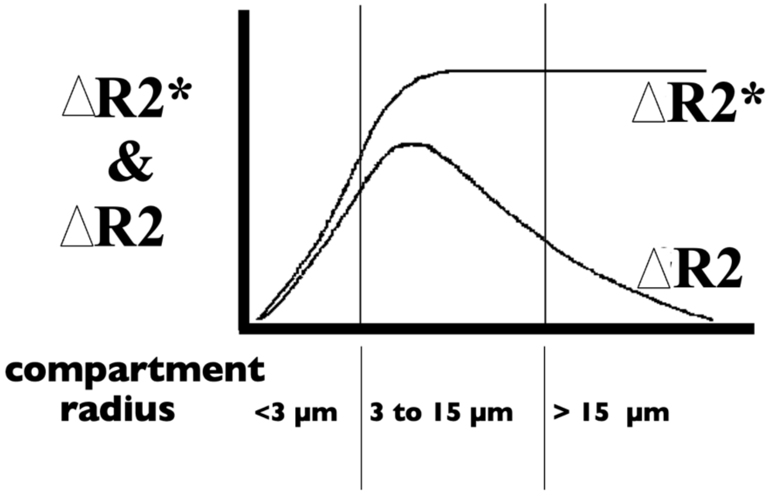
Ky is infinitely short
Kx is short

Spin Echo vs. Gradient Echo

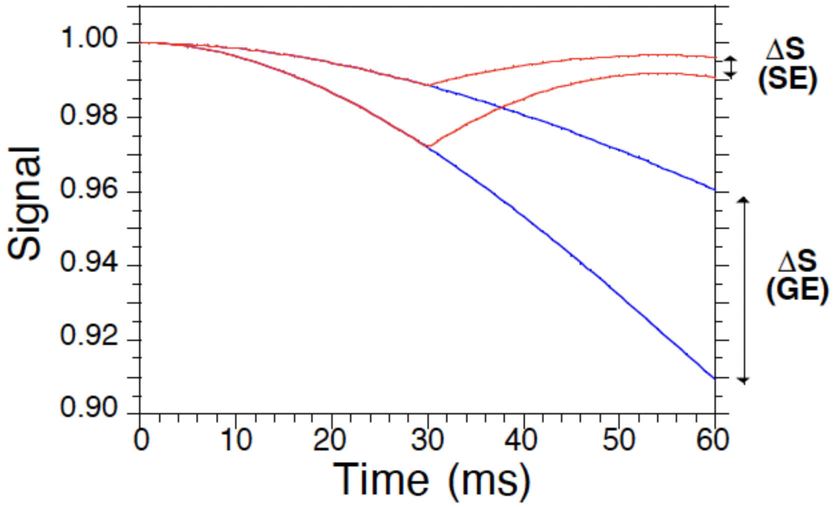


Spin Echo vs. Gradient Echo

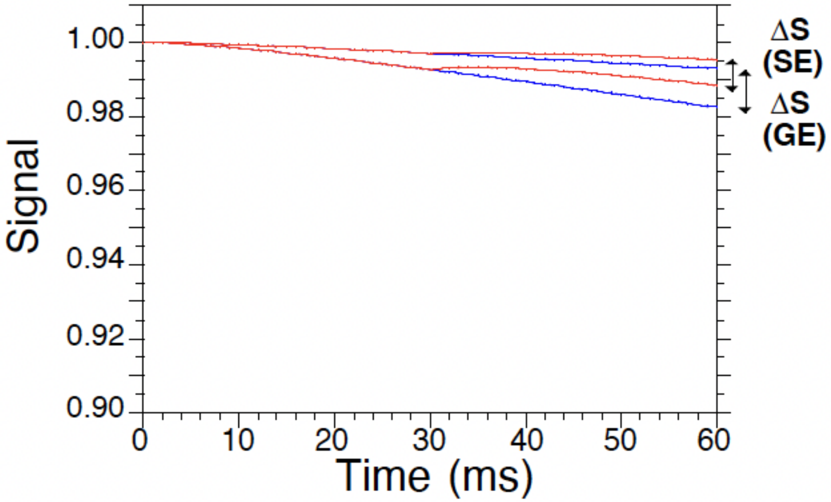




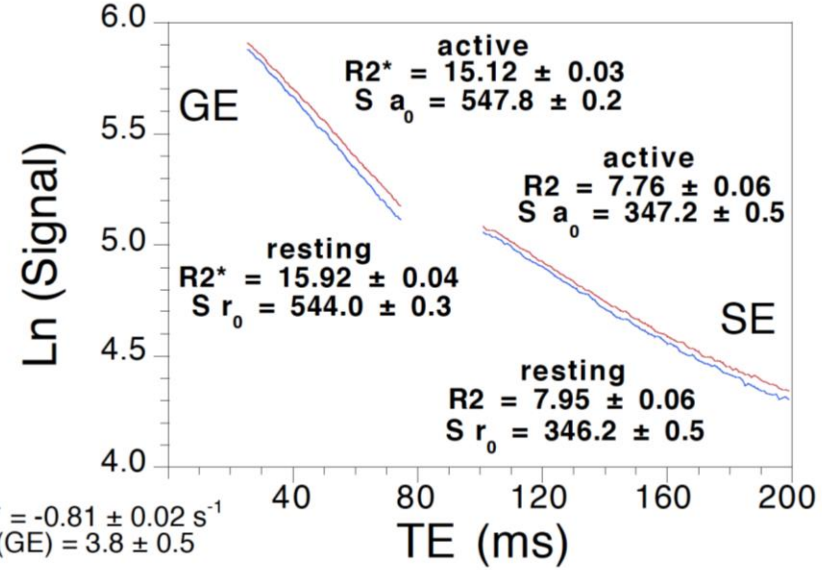
Large Vessels



Small Vessels

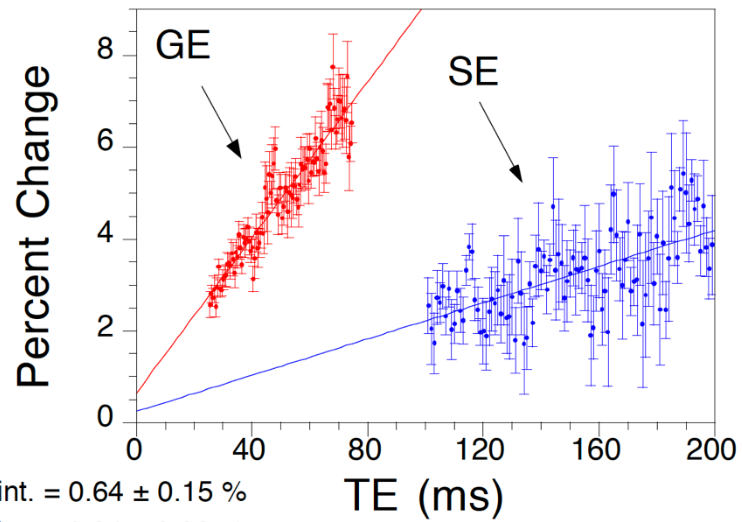


Spin Echo vs. Gradient Echo

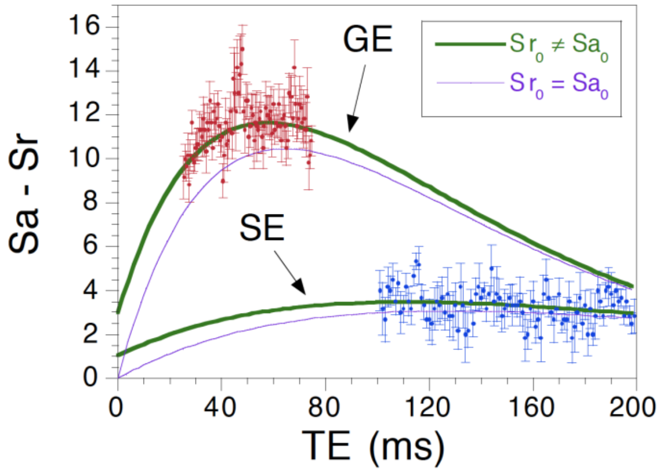


$\Delta R2^* = -0.81 \pm 0.02\ s^{-1}$
ΔS_0 (GE) = 3.8 ± 0.5

$\Delta R2 = -0.19 \pm 0.02\ s^{-1}$
ΔS_0 (SE) = 1.0 ± 1.0

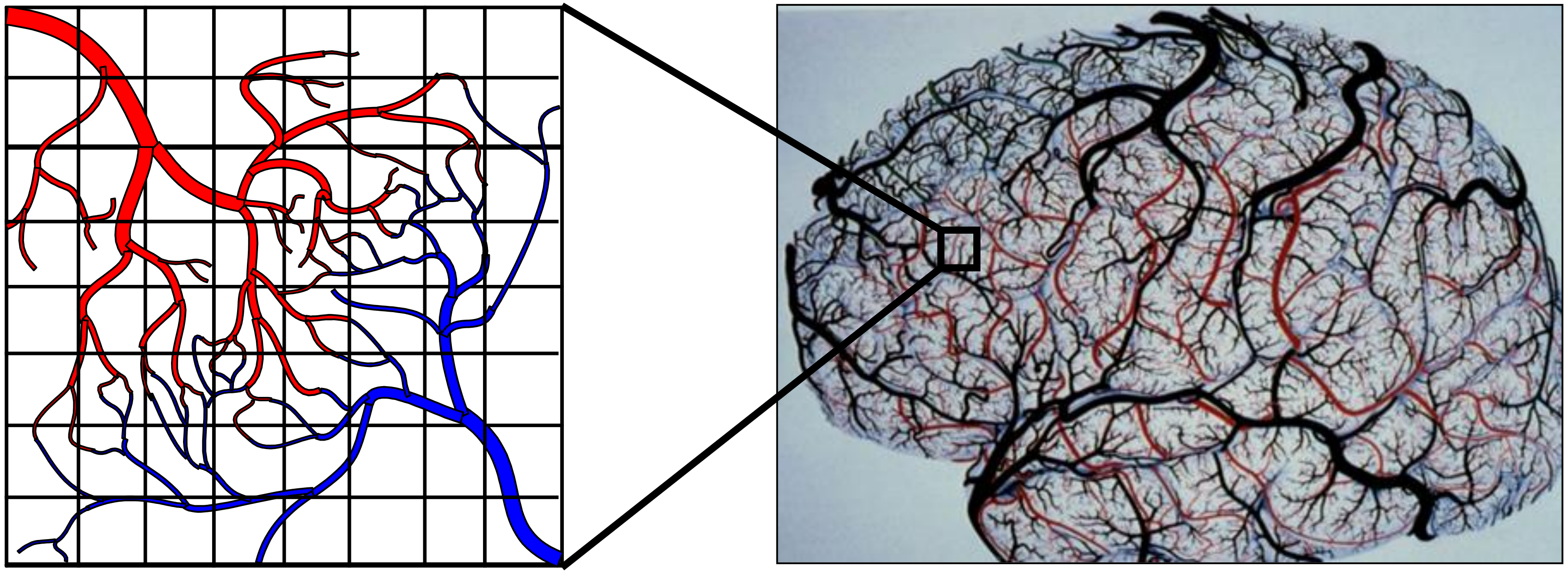


GE int. = 0.64 ± 0.15 %
SE int. = 0.24 ± 0.38 %



Why big veins are a problem...

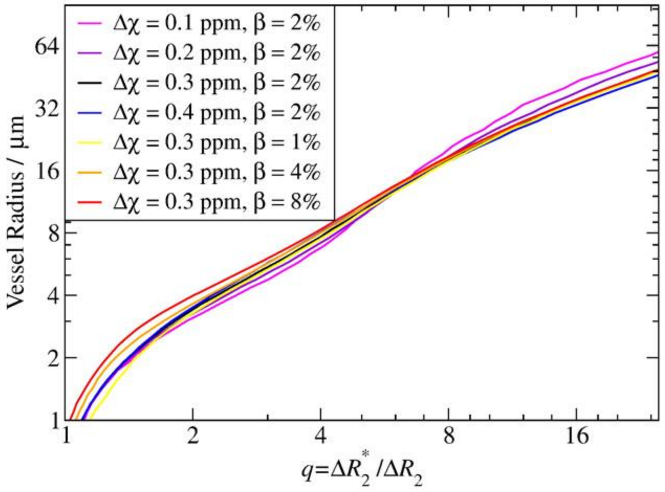
BOLD signal is most influenced by the fraction of venous blood in each voxel.

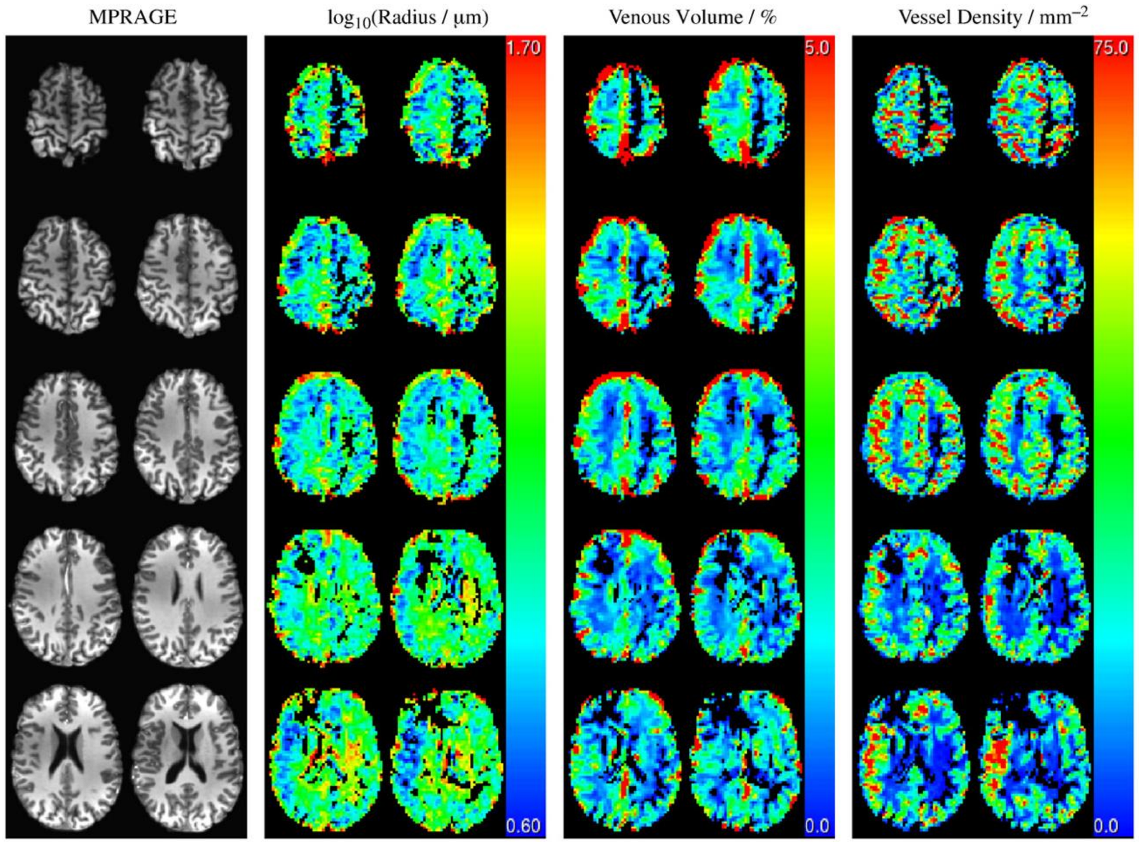


*V*essel Parameter Mapping using SE and GE with Hypercapnia

-SE/GE ratio -> vessel radius

-GE signal change with global stress
-> blood volume





T. H. Jochimsen, et al. NeuroImage, 51: 765-774 (2010)

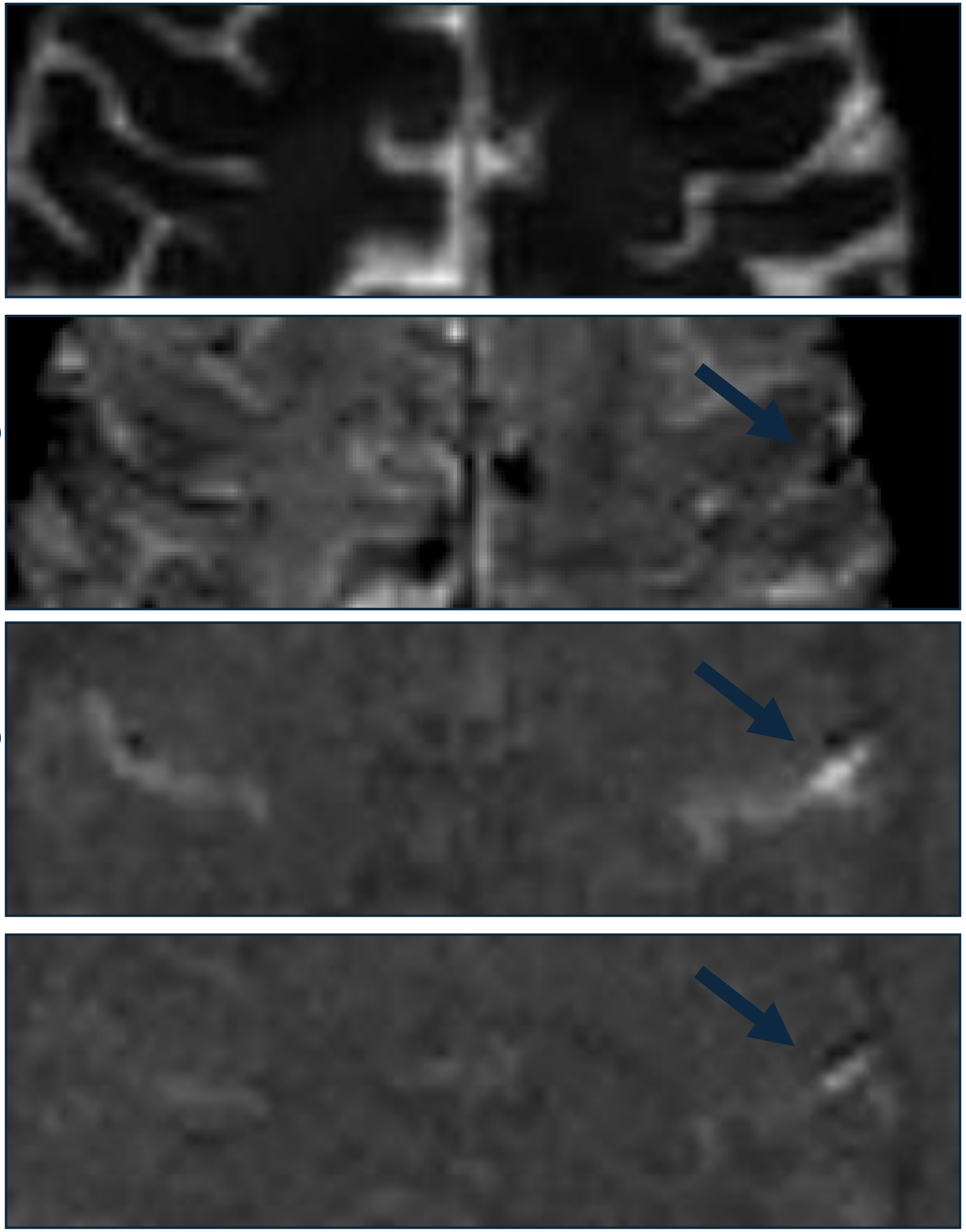
Vein Effects

Spin-Echo
TE = 105 ms
TR = ∞

Gradient-Echo
TE = 50 ms

Gradient-Echo
functional
TE = 50 ms

Spin-Echo
functional
TE = 105 ms



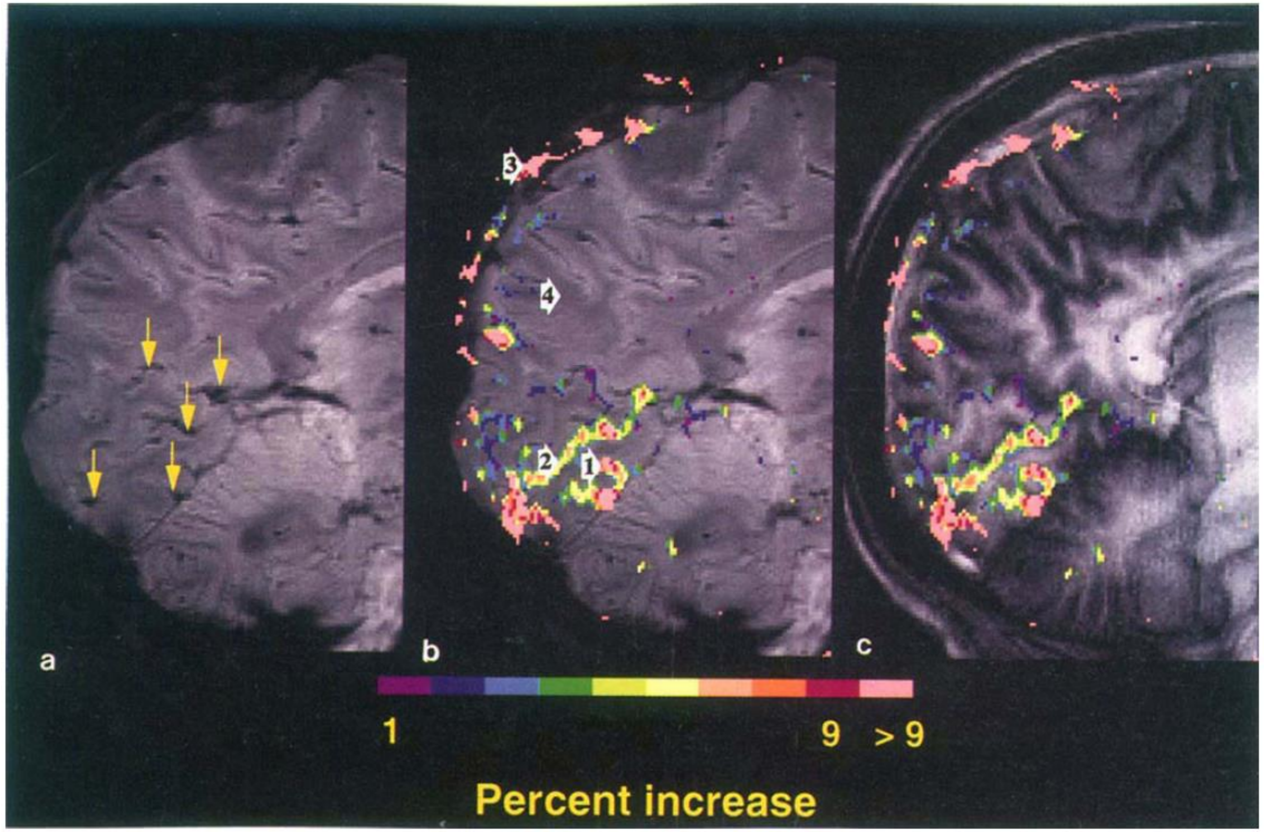
3T

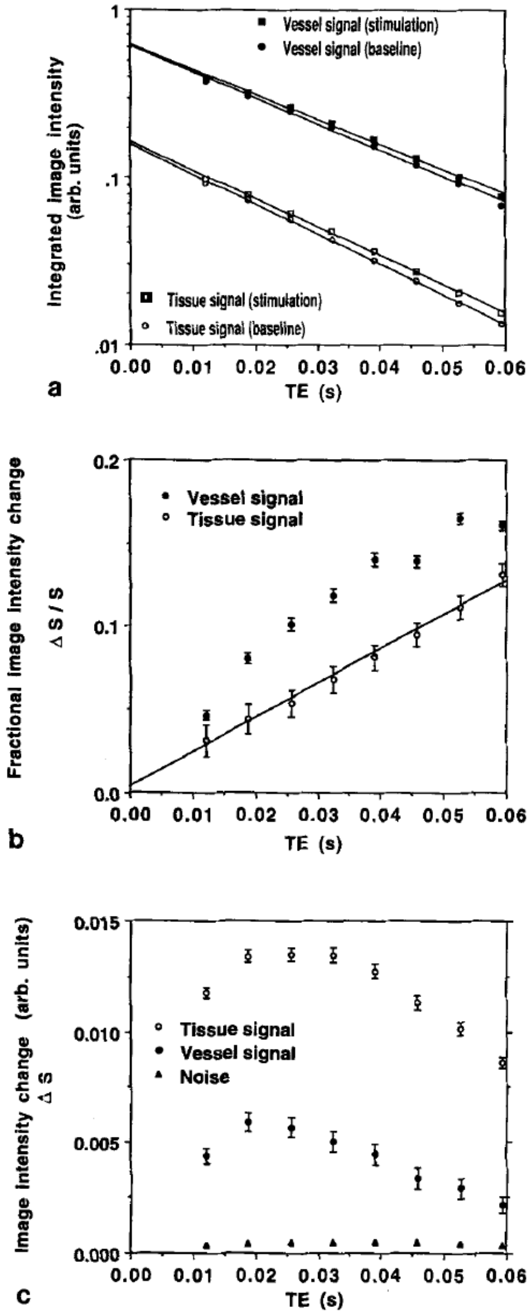
Vein Effects

MRM 30:380-386 (1993)

4 Tesla Gradient Recalled Echo Characteristics of Photic Stimulation-Induced Signal Changes in the Human Primary Visual Cortex

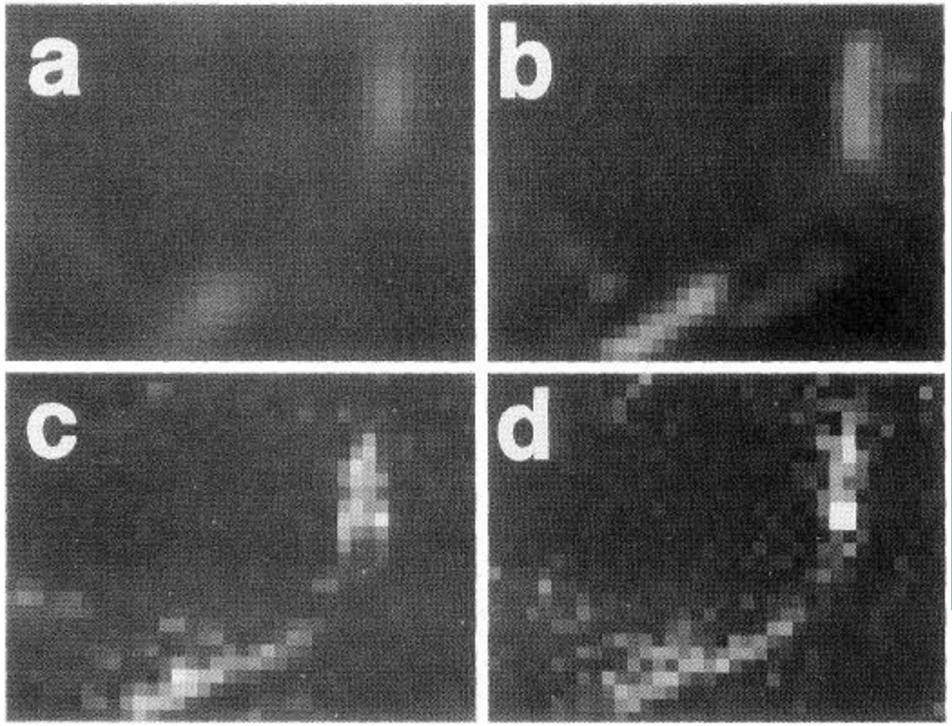
Ravi S. Menon, Seiji Ogawa, David W. Tank, Kâmil Uğurbil





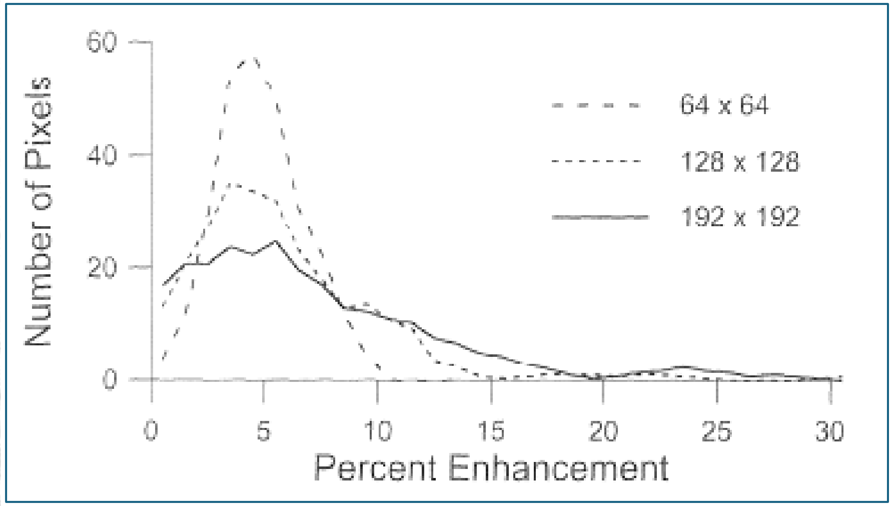
Imaging Resolution Effects

2.5mm^2 1.25mm^2



0.83 mm^2 0.62 mm^2

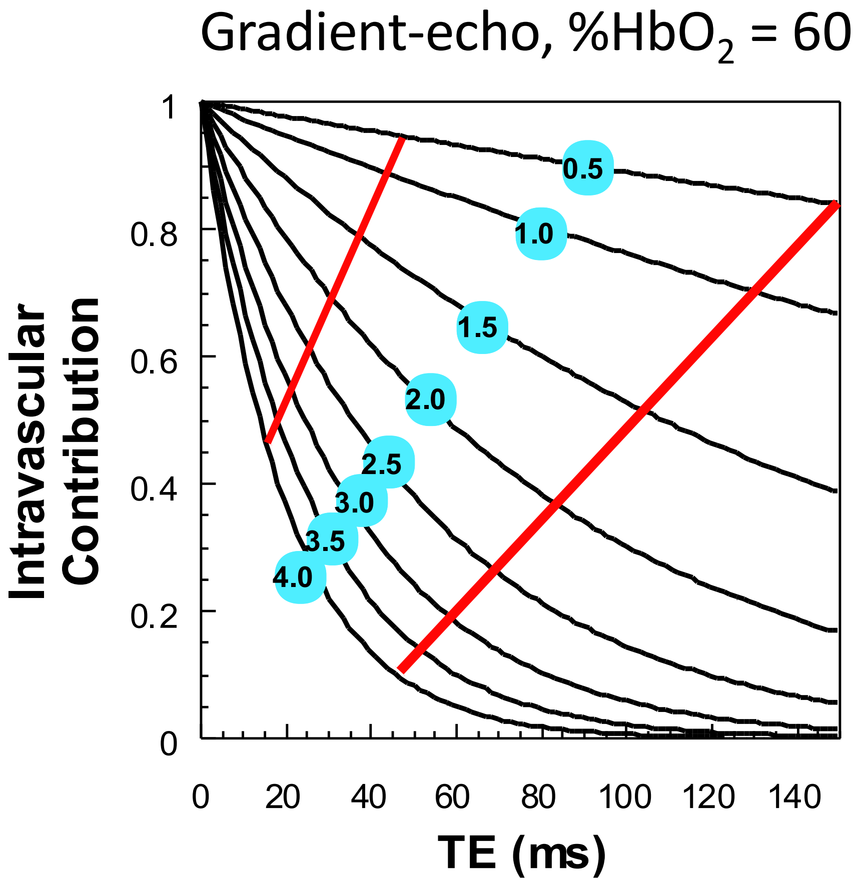
Large Vessel effect enhanced with High Resolution

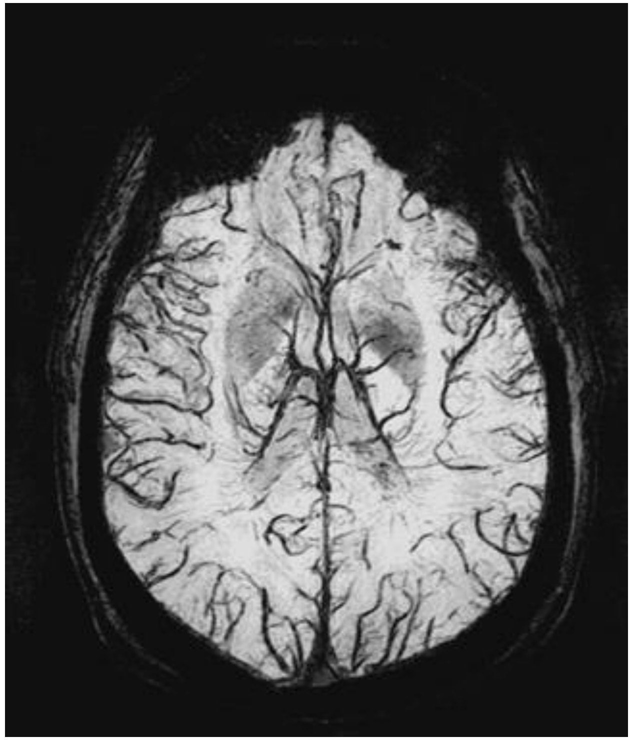


A. Jesmanowicz, P. A. Bandettini, J. S. Hyde, Single shot half k-space high resolution EPI for fMRI at 3T. Magn. Reson. Med. 40, 754-762 (1998).

Field strength dependence of intravascular signal.

The reason veins are dark at high field





Source of most contrast in venograms..

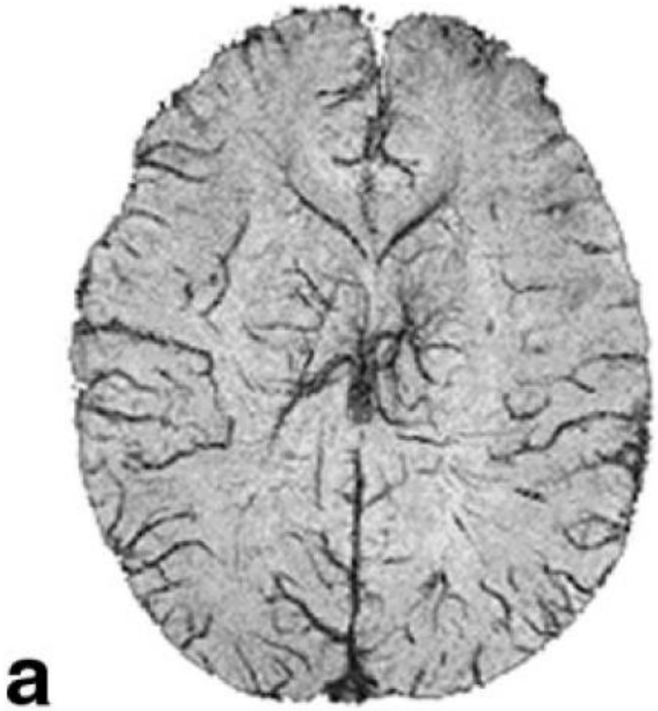
Magnetic Resonance in Medicine 52:612–618 (2004)

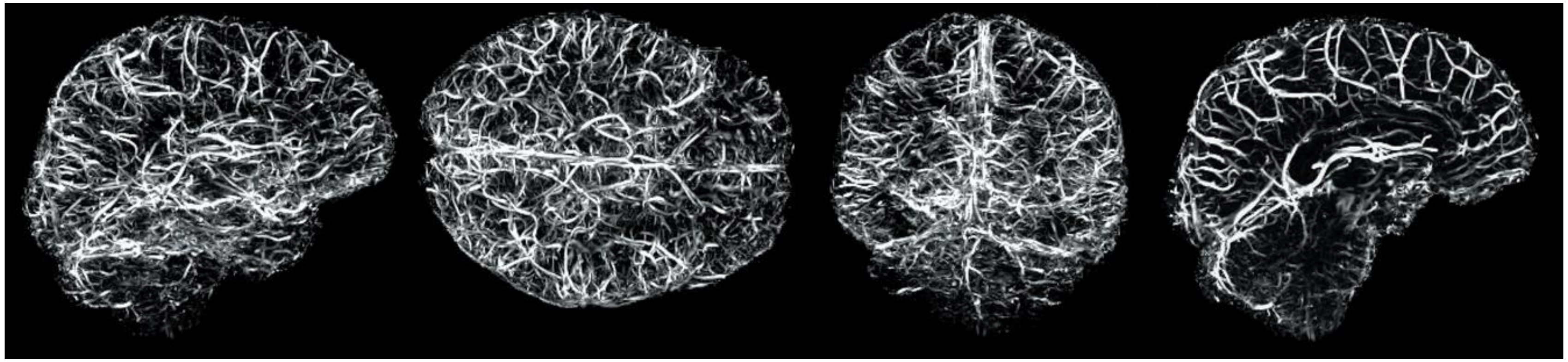
Susceptibility Weighted Imaging (SWI)

E. Mark Haacke,[1-4*] Yingbiao Xu,[1,2] Yu-Chung N. Cheng,[1] and Jürgen R. Reichenbach[5]

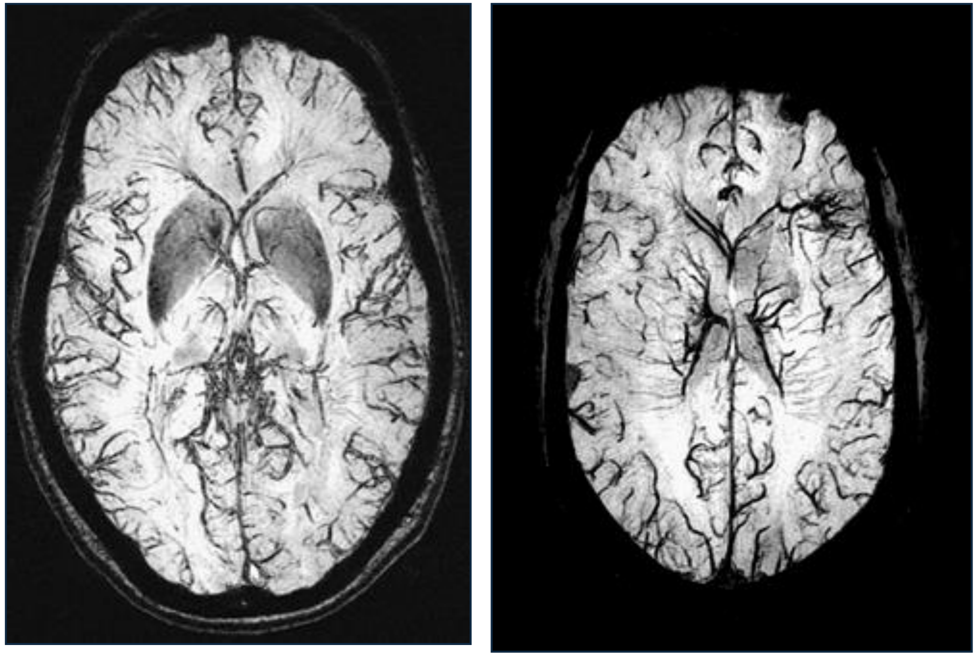
Blood Oxygenation

Venography



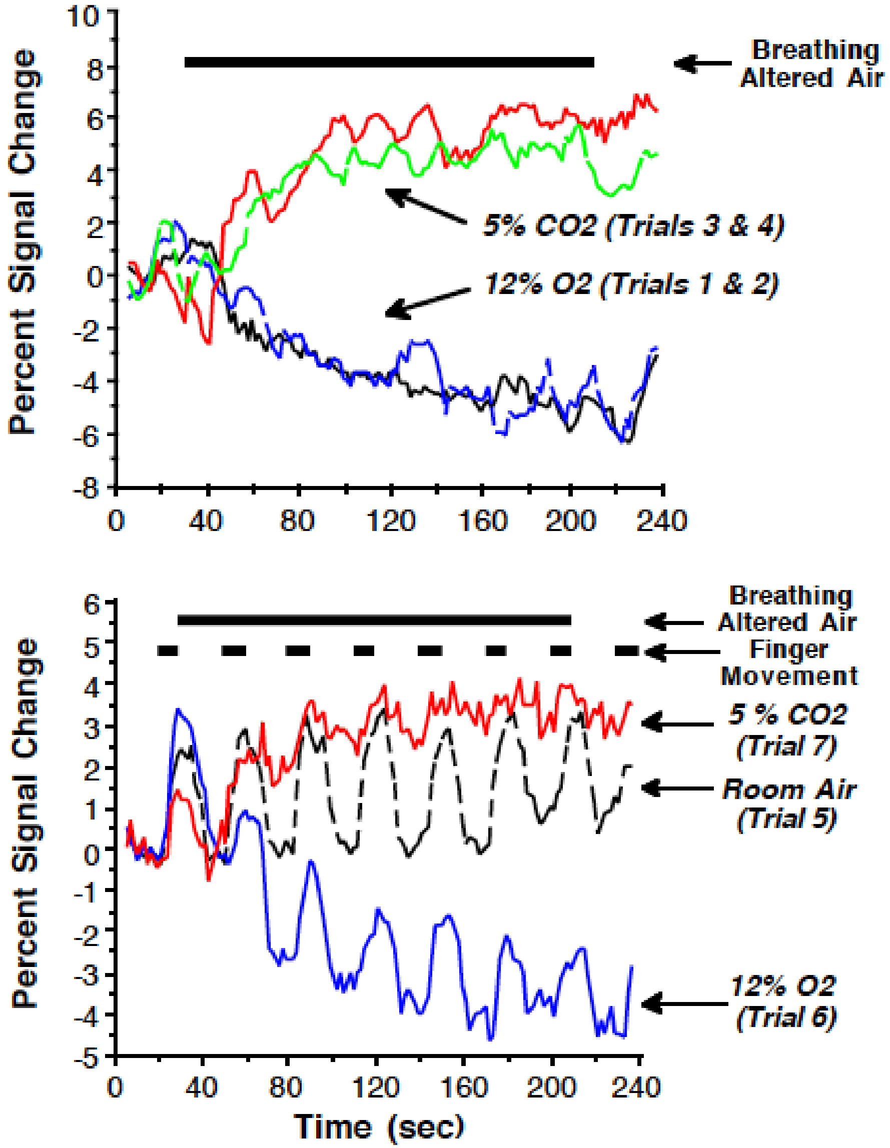


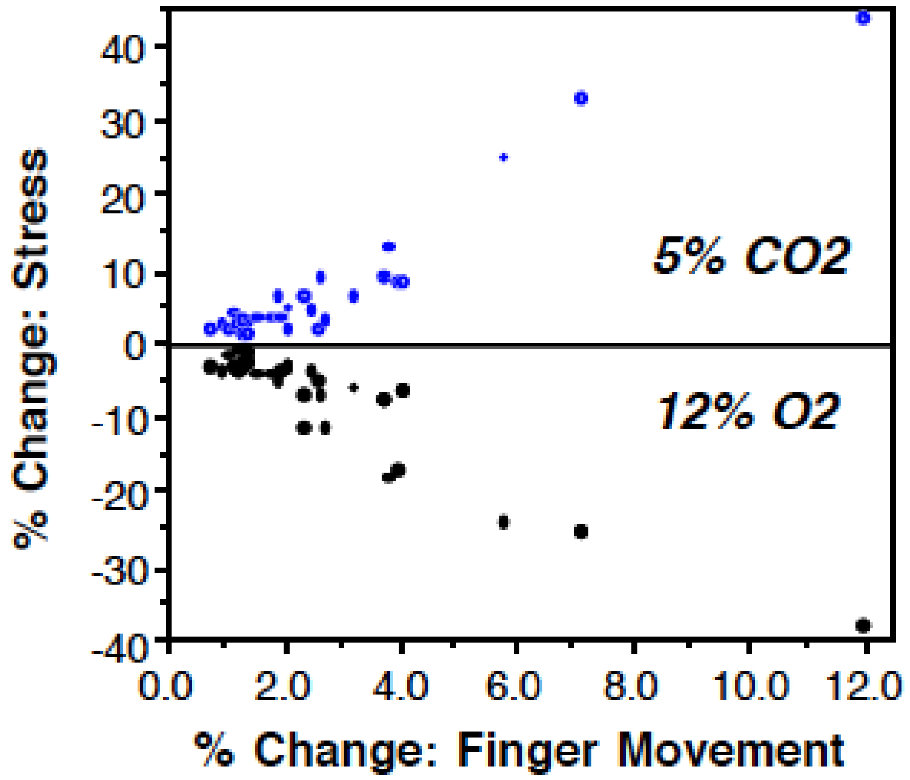
Norris and Barth
7T Hahn Institute



Bove-Bettis, et al (2004), SMRT

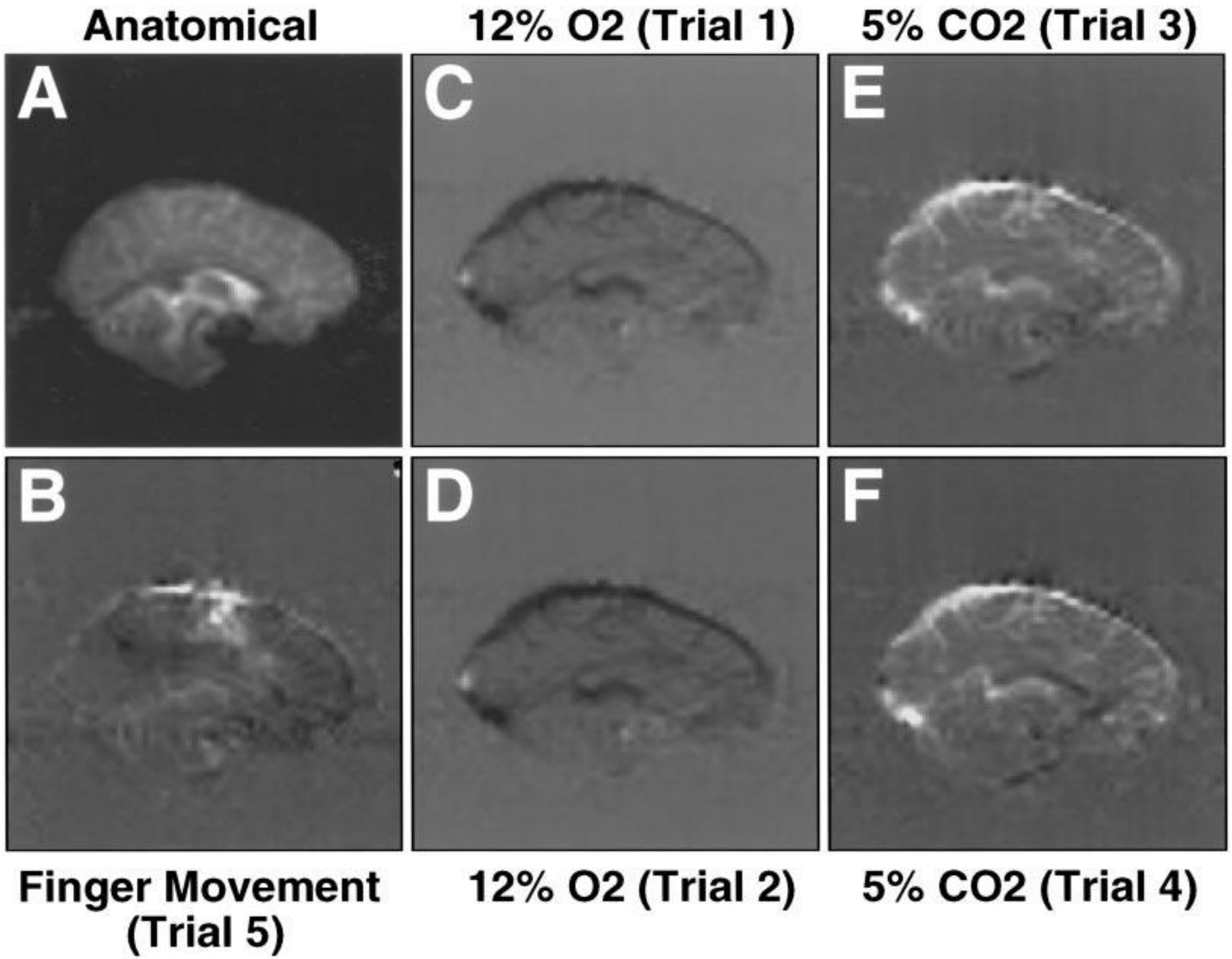
Global Stress Effects: CO_2 and O_2





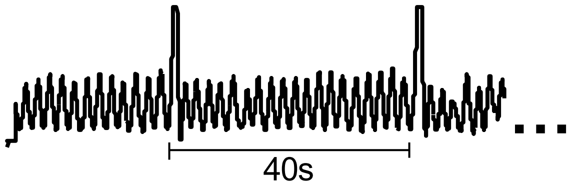
Bandettini et al. NMR in Biomedicine 1997

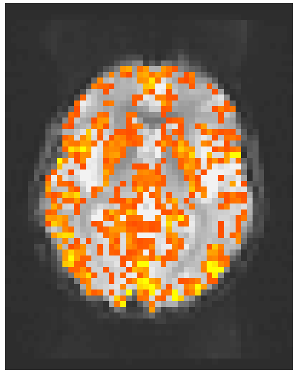
Mapping Global Stress Effects



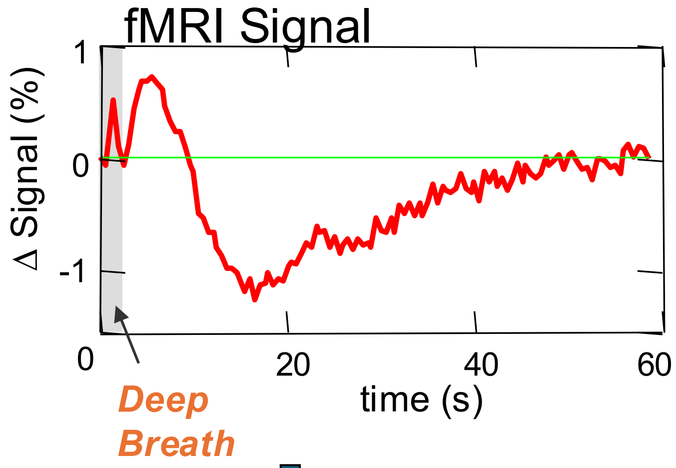
Effects of Breathing
The Respiration Response Function

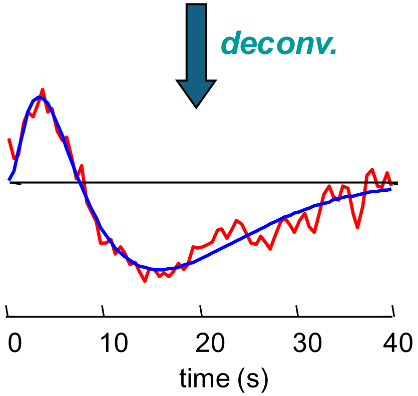
Respiration





fMRI response to a single Deep Breath





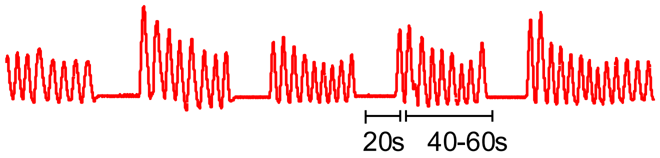
Respiration Response Function (**RRF**)

$$RRF(t) = 0.6\, t^{2.1} e^{-\frac{t}{1.6}} - 0.0023\, t^{3.54} e^{-\frac{t}{4.25}}$$

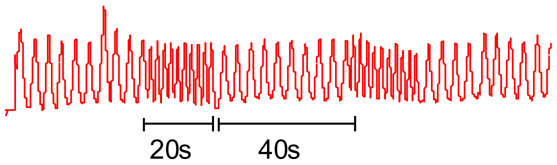
R.M. Birn, M. A. Smith, T. B. Jones, P. A. Bandettini, *NeuroImage*, 40, 644-654. (2008)

Respiration Effects

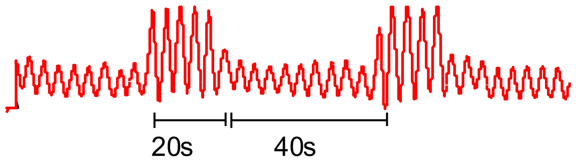
Breath-holding

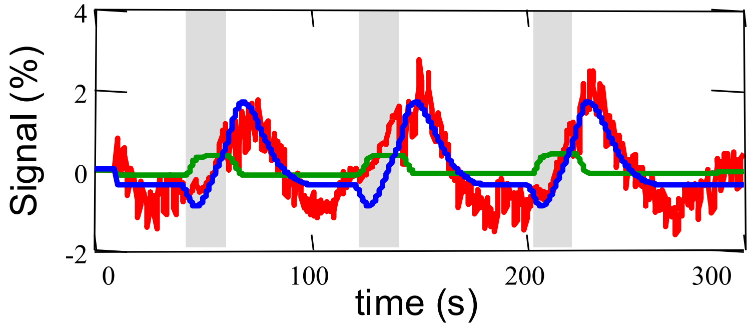


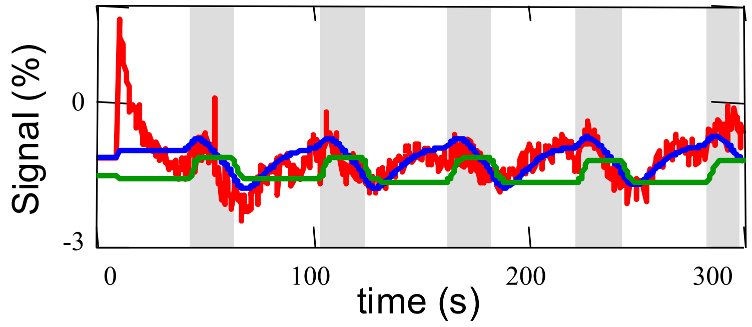
Rate Changes

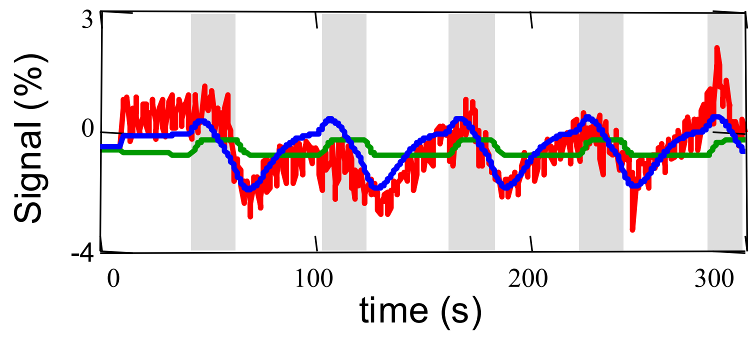


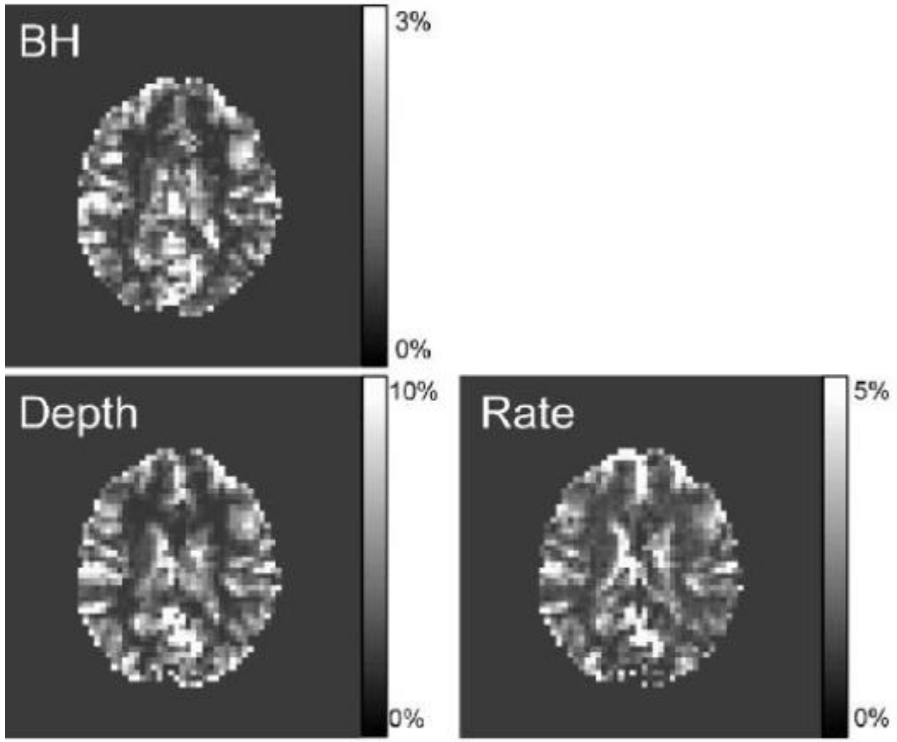
Depth Changes







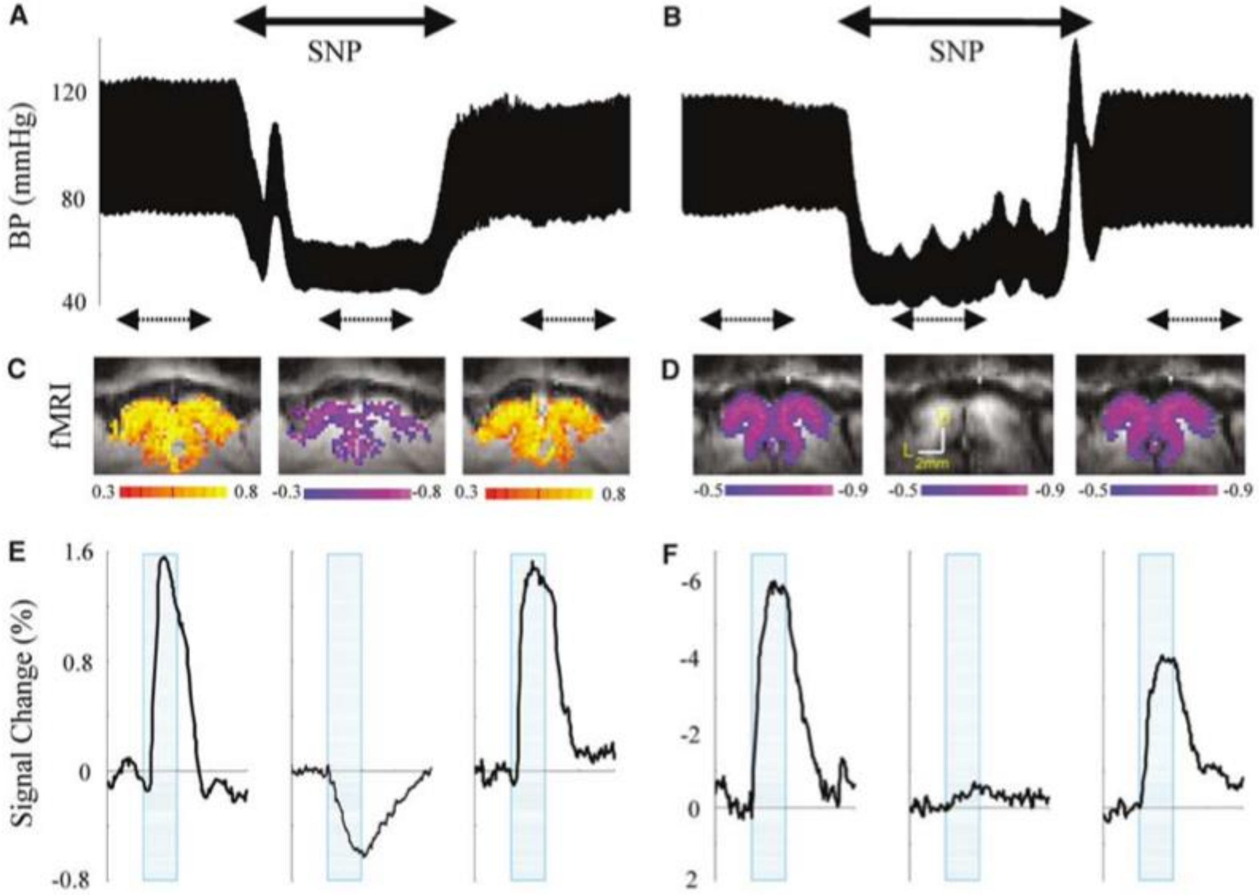




R.M. Birn, M. A. Smith, T. B. Jones, P. A. Bandettini, *NeuroImage*, 40, 644-654. (2008)

Effects of Extreme Blood Pressure Changes

Sodium Nitroprusside



BOLD **Blood Volume**

Nagaoka, et al. JCBFM 2006