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BOLD contrast and its measurement

Rexford Newbould

Background NMR Terminology

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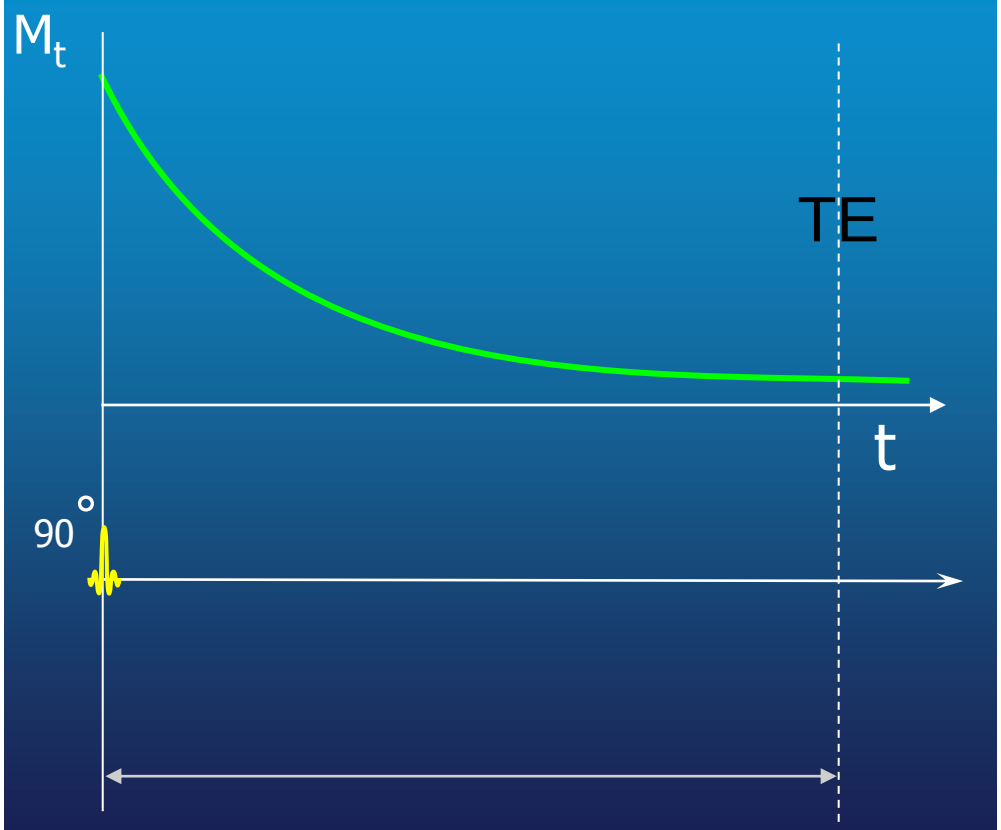
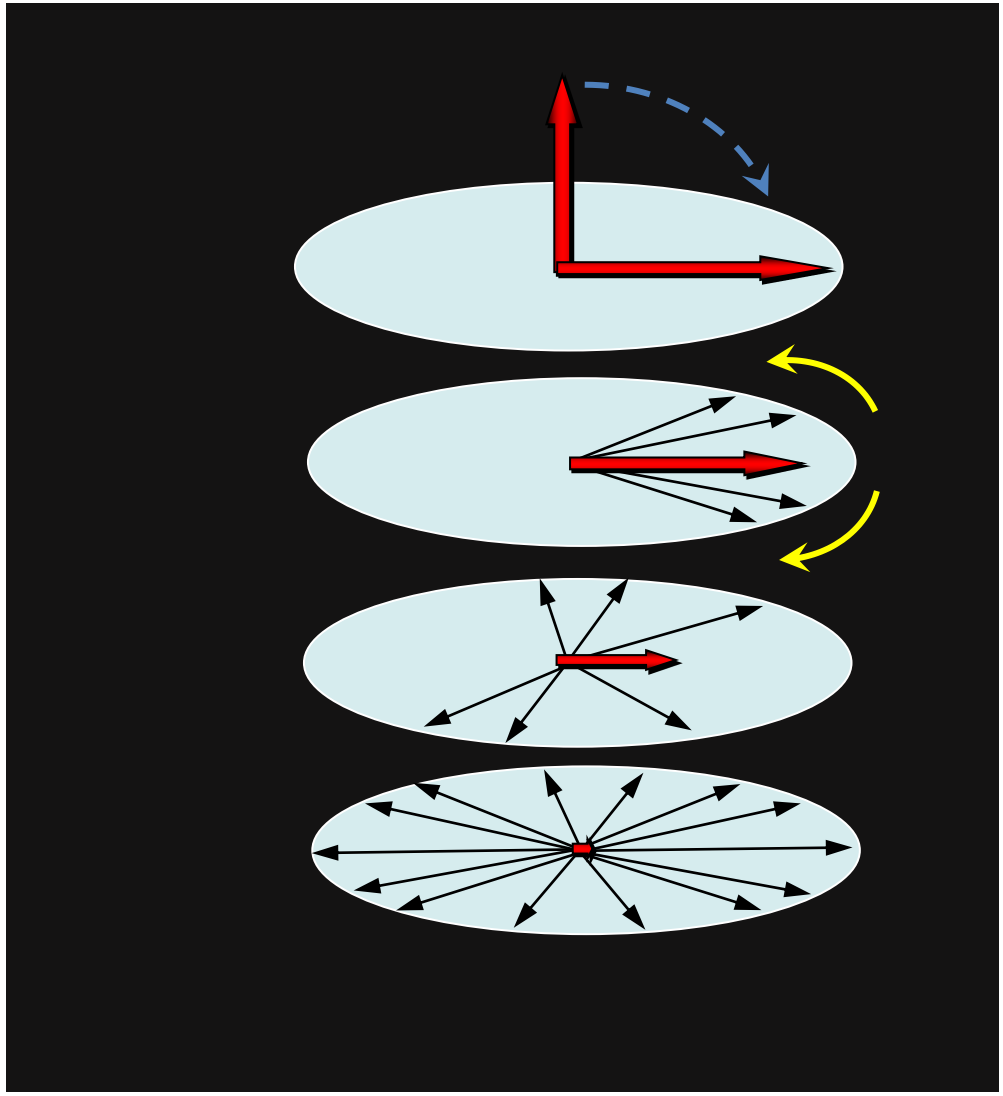
- Spins (protons)
- T1, T2
- Echo Time (TE)
- 90º, 180º RF Pulse

- Gradient Echo
- Spin Echo
- K-space
- Voxel

Gradient Echoes (T2*)

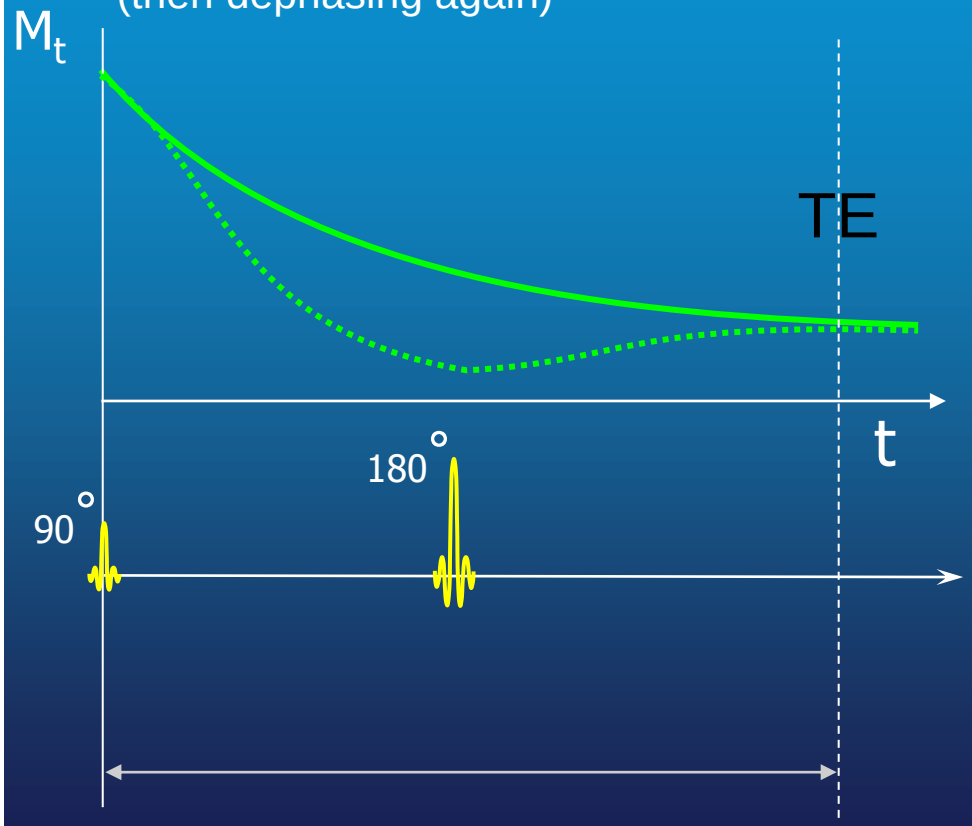
- Pulse-acquire experiment.

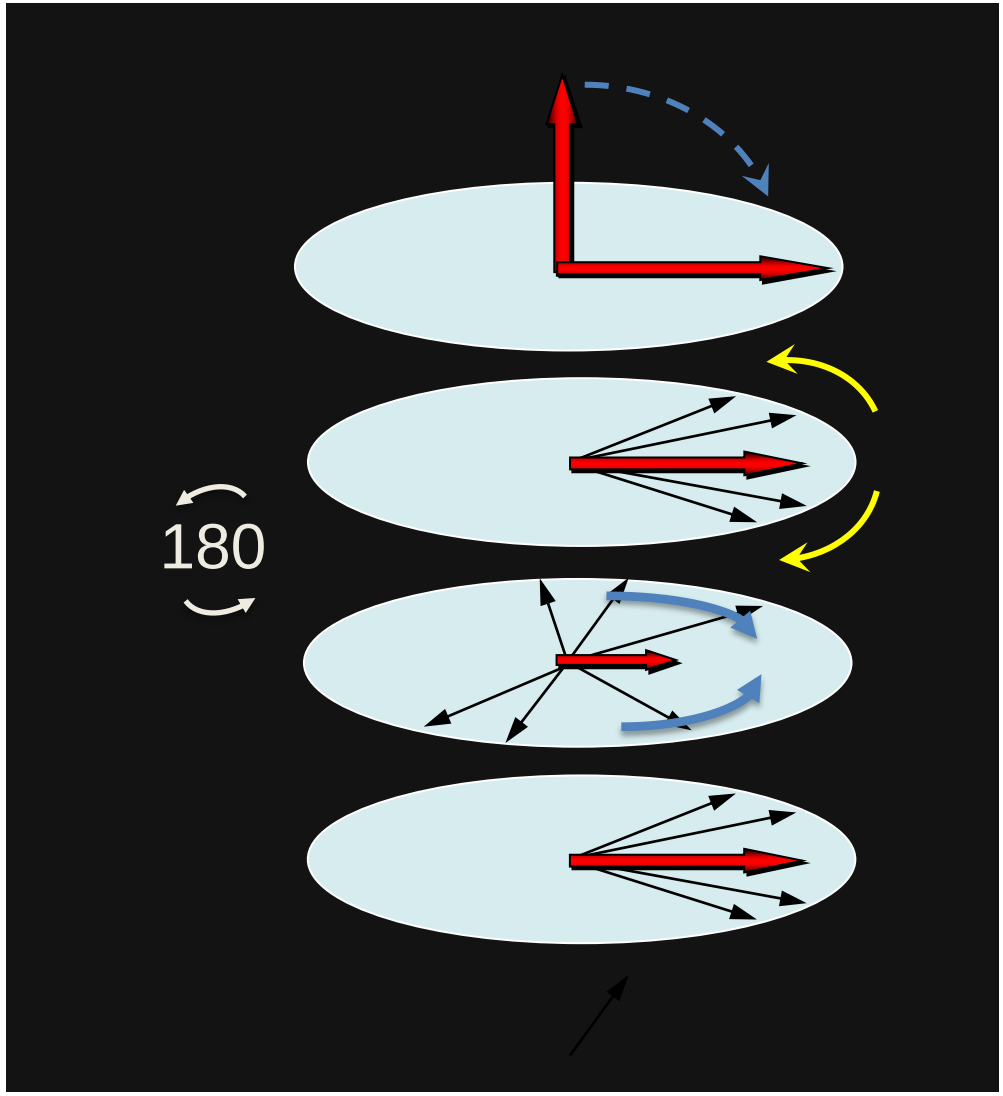




Spin Echoes (T2)

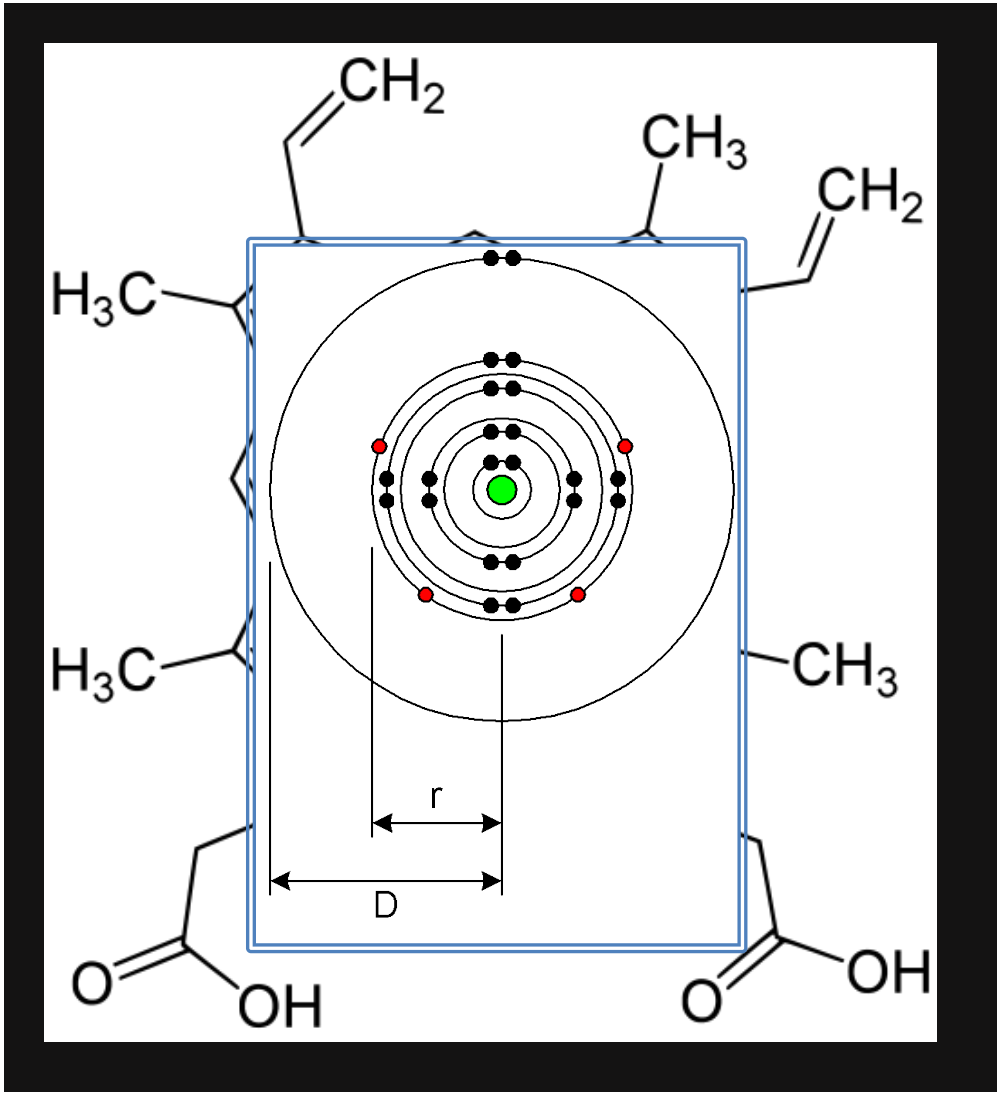
- Use a 180° pulse to flip dephased spins.
- Some dephasing now rephases until TE (then dephasing again)





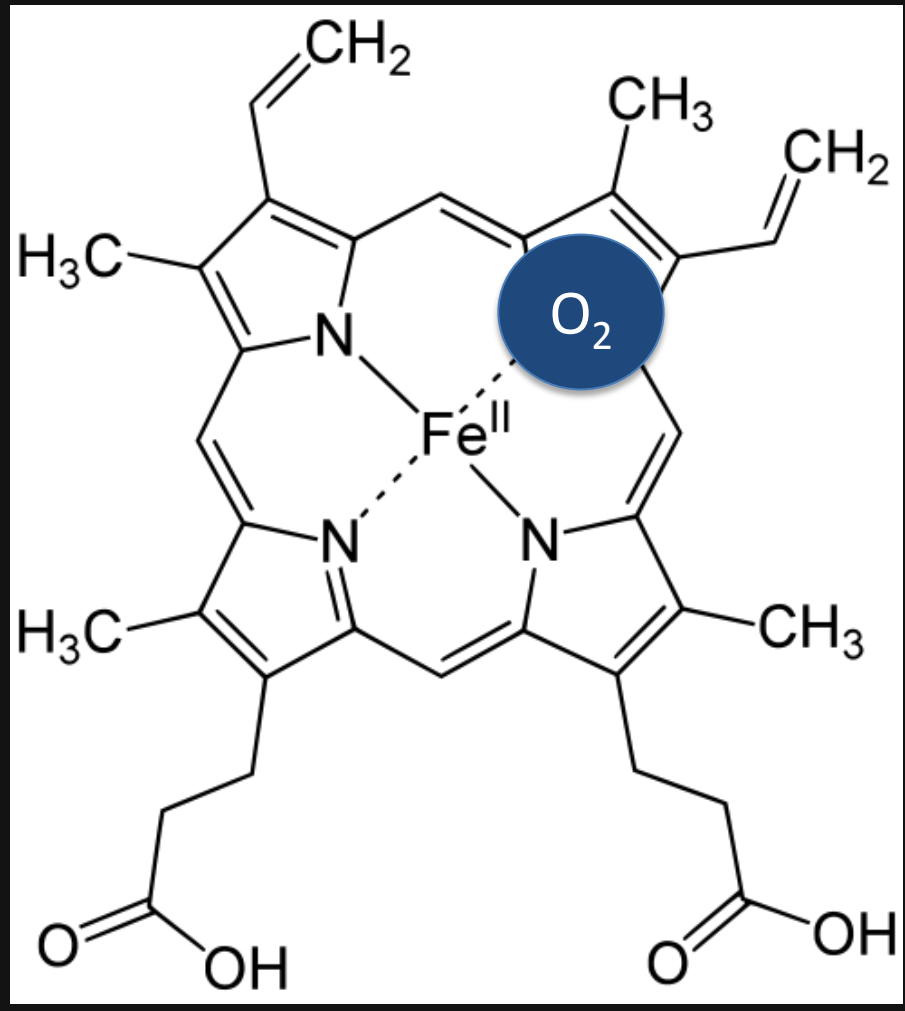
(Deoxy-) Haemoglobin

- Haemoglobin contains 4 sub-groups
  - Each subgroup contains an iron atom (Fe)
- Electrons have spin
  - Paired electrons have opposite spins
  - An unpaired electron results in an orbital magnetic moment.
  - Fe → 4 unpaired electrons
- Deoxy-haemoglobin
  - Fe results in a paramagnetic effect on our imaging spins
  - Paramagnetic = increased magnetic field
  - Magnetic susceptibility (χ) is higher for Deoxy-Hb than for surrounding tissue



(Oxy-) Haemoglobin

- Haemoglobin contains 4 sub-groups
  - Each subgroup contains an iron atom (Fe)
- Electrons have spin
  - Paired electrons have opposite spins
  - An unpaired electron results in an orbital magnetic moment.
  - Fe → 4 unpaired electrons
- Oxyhaemoglobin
  - Oxygen is strongly electronegative
  - Fe-O_2 complex is not paramagnetic but diamagnetic
  - Diamagnetic = weakens magnetic field
  - Surrounding tissue water spins also diamagnetic.
  - Magnetic susceptibility (χ) is similar for both



Previous Talk in 1 Slide

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- Increased metabolic demand from neuronal activity:
  - blood flow ↑ ~30%
  - 0_2 consumption ↑ ~10%
  - Blood volume ↑ ~5-30%
- Results in:
  - ↑ Oxy-Hb
  - ↓ Deoxy-Hb
  - Reduces the $\Delta\chi$ between blood and brain tissue
  - Changes amount of MR Signal acquired

Now: How can NMR measure these changes?

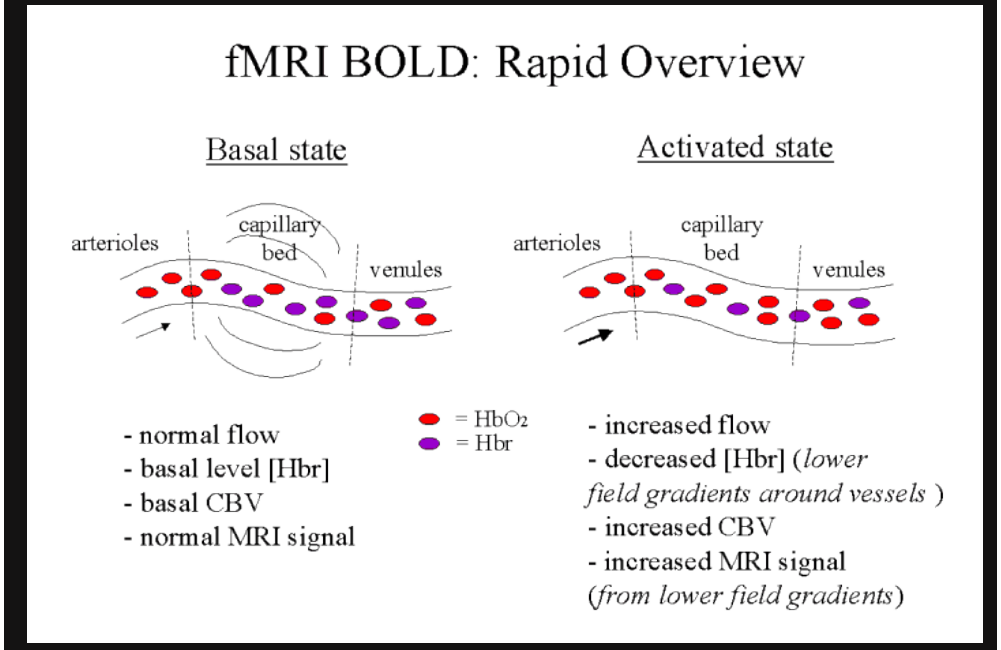
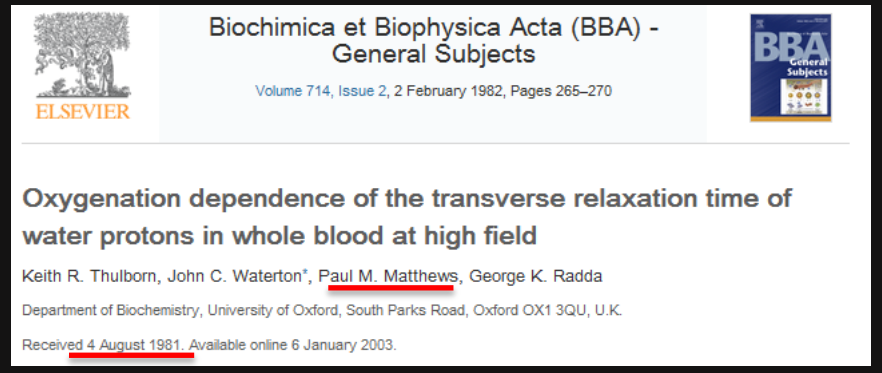


Image from P Jezzard / I Tracey

Paramagnetic Effects (RBC)

- Deoxy-Hb
  - Paramagnetic heme-iron
  - Efficient relaxation mechanism
  - Highly localized effect
    - $1/d^6$
    - Water Spins unable to approach
    - Little T1 effect (unless Hb breaks down)
- Compartmentalization in RBCs
  - Red blood cells have ~$1x10^9$ Fe's
  - If Deoxy, local magnetic field higher inside RBC's than outside in the plasma
  - Affects T2/T2* in the plasma
    - Hold on for 3 more slides
  - Effect is small in BOLD in the brain
    - CBV = 2-4%

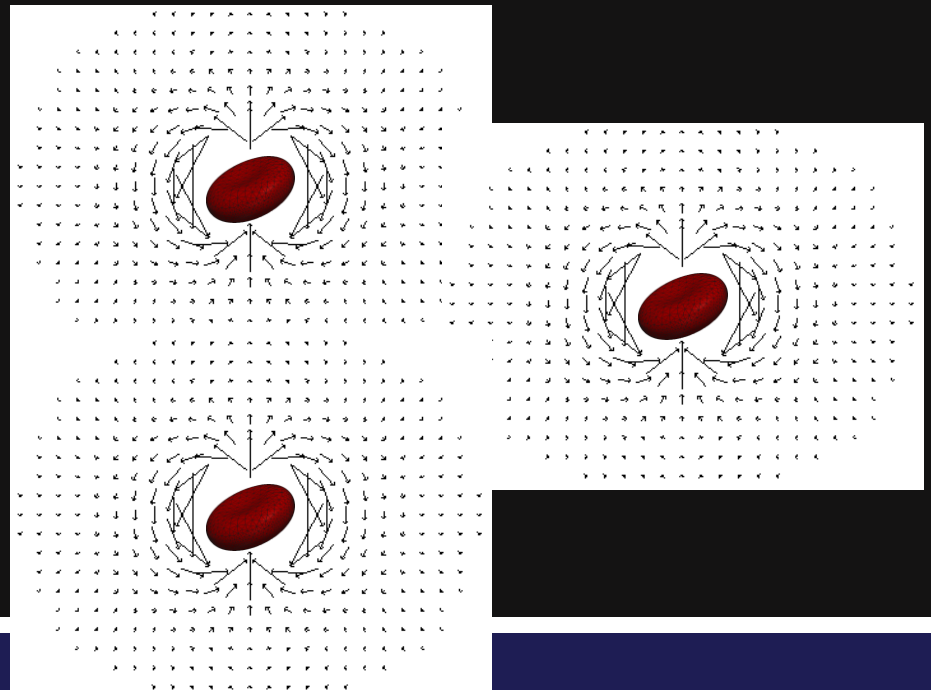

Biochimica et Biophysica Acta (BBA) - General Subjects
Volume 714, Issue 2, 2 February 1982, Pages 265–270

Oxygenation dependence of the transverse relaxation time of water protons in whole blood at high field

Keith R. Thulborn, John C. Waterton*, Paul M. Matthews, George K. Radda

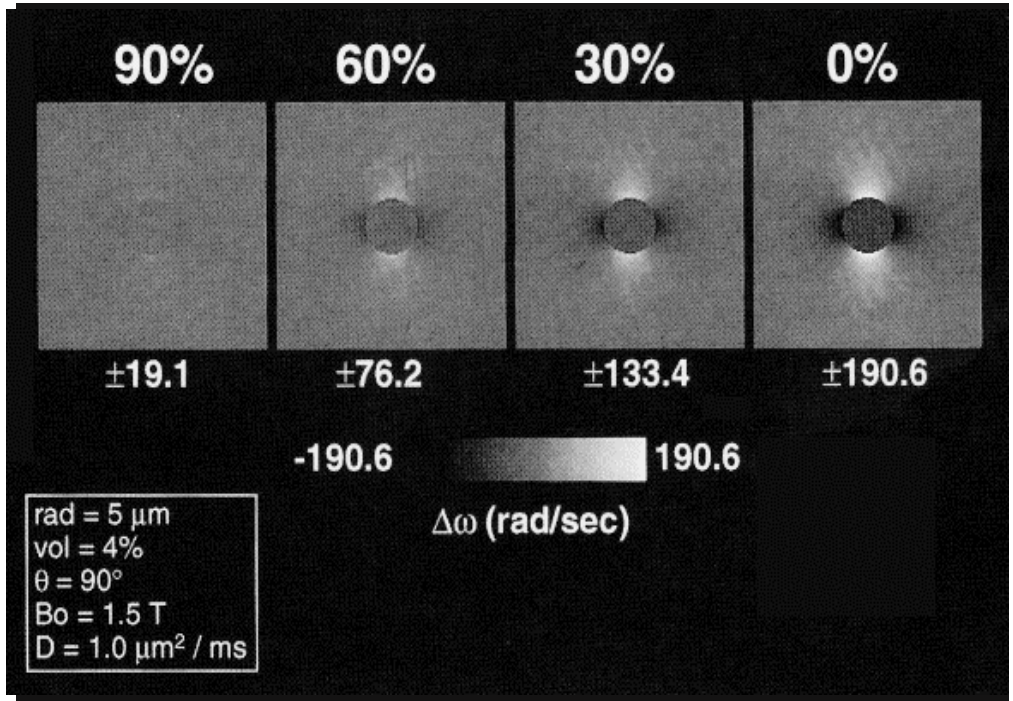
Department of Biochemistry, University of Oxford, South Parks Road, Oxford OX1 3QU, U.K.

Received 4 August 1981. Available online 6 January 2003.



Paramagnetic Effect (Vessel)

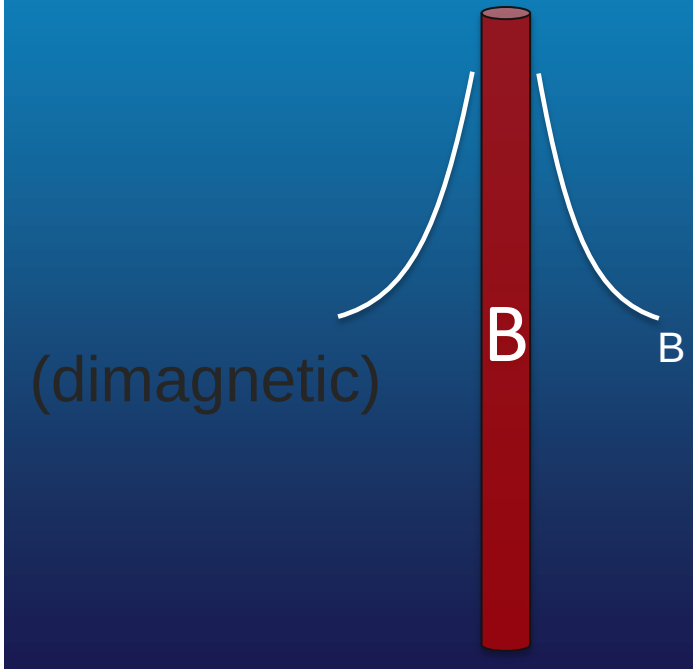
- Compartmentalization happens at the vessel level as well
  - Blood is 40-45% RBC's
  - De-Oxy: Magnetic Field is greater in vessel than outside
  - Oxy: Magnetic Field is similar to outside
- Affects T2 and T2* in tissue outside of the vessels
  - Hold on for 2 more slides
- The effect of vessels' magnetic fields on the tissue is the majority of the BOLD effect.
- CBV changes with activity; minor countereffect.

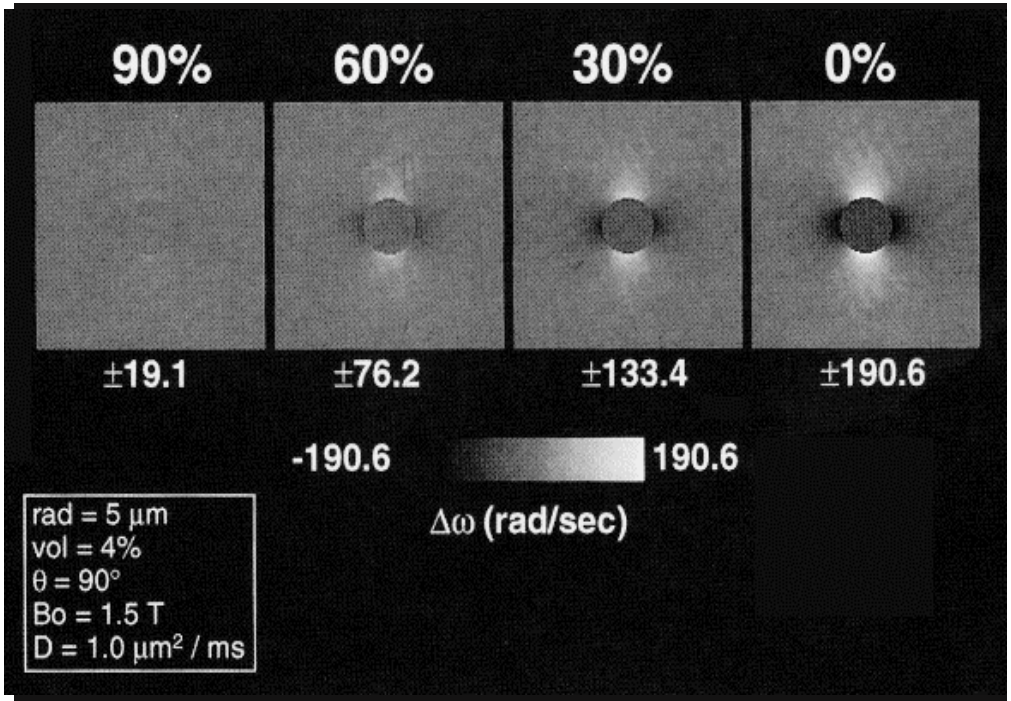


Bandettini/Wong, Intl Jnl of Imaging Systems and Technology (6), 2-3, 133–152, 1995

Local Magnetic Gradients

- Presence of paramagnetic Fe's changes local B field
- Maxwell dictates no step-changes in B field
  - Field must vary smoothly with distance: Magnetic Field Gradients
- For vessels, on the order of the diameter

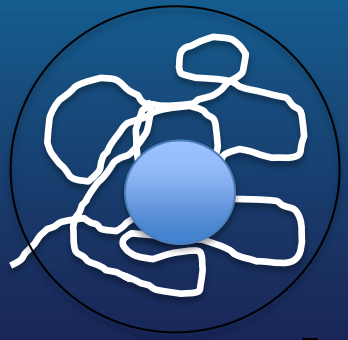




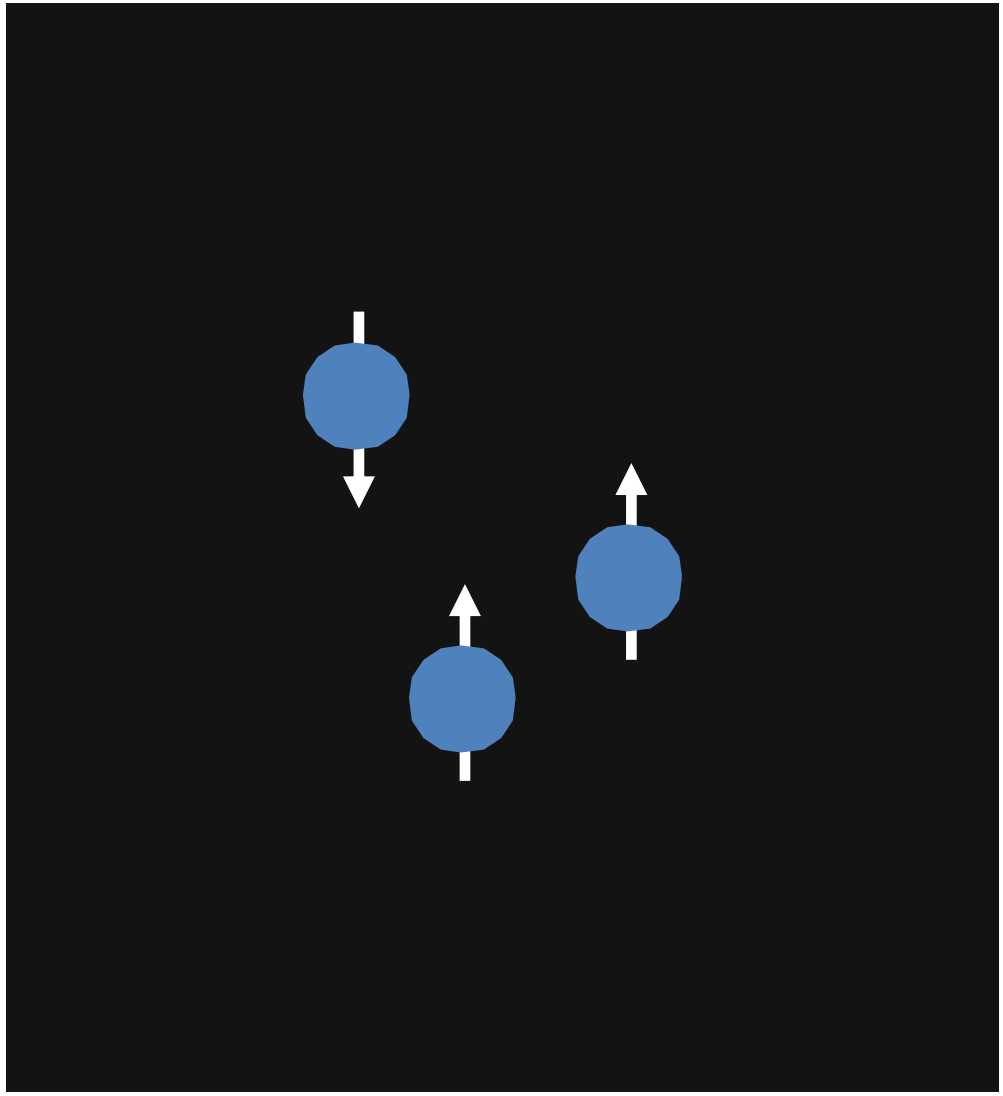
Bandettini/Wong, Intl Jnl of Imaging Systems and Technology (6), 2-3, 133–152, 1995

Diffusion of Spins

- Thermal energy of particles induces a random motion
- Distance travelled is characterized by radius.
  - Defines the sphere in which we will find the spin
  - Radius of sphere is proportional to sqrt(time) and the diffusion coefficient, D
  - For free water molecules, D = 3 x 10^{-3} mm^2 / s at 37° C.
- For fMRI timings, distance is on the order of 10µm

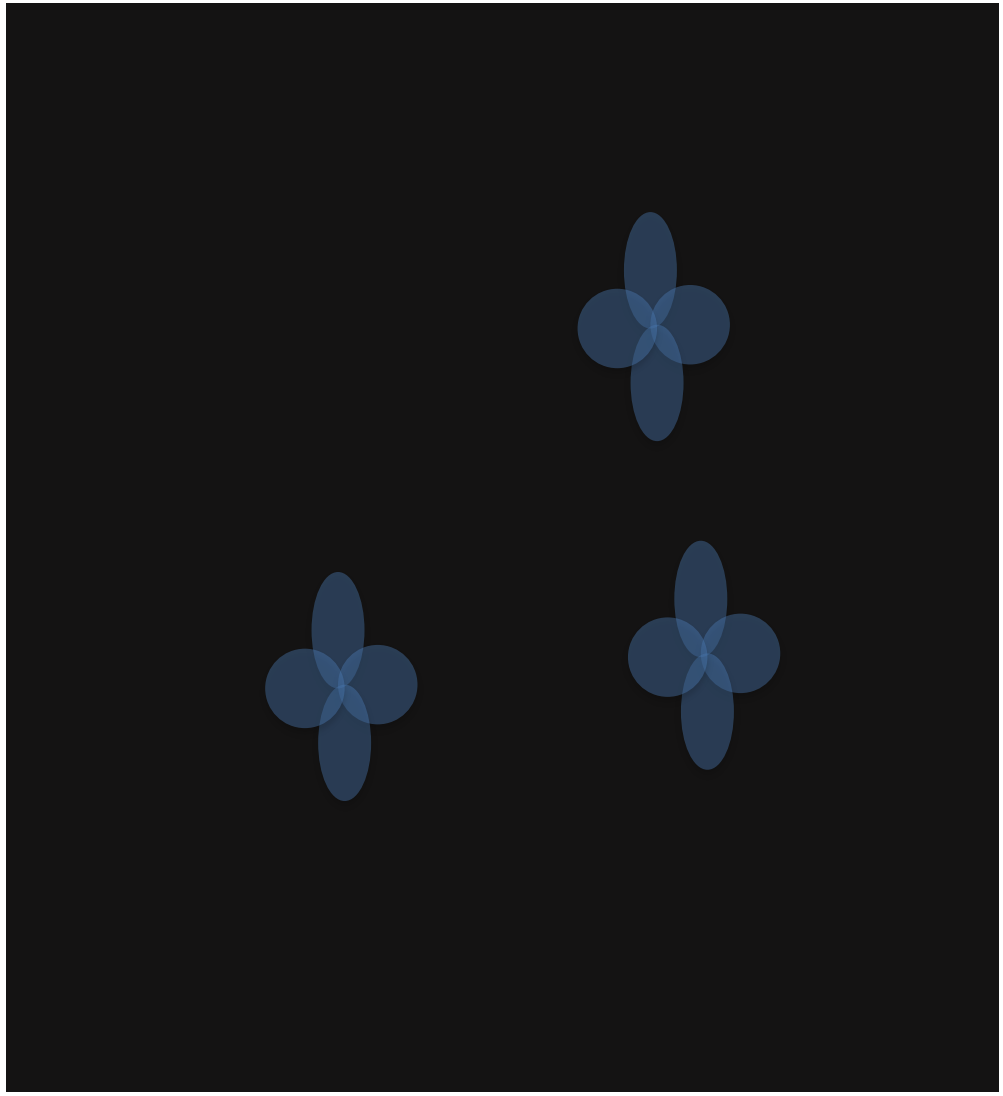


$$l = \sqrt{2Dt}$$



Effects of Microscopic Field Gradients

- Microscopic = on the order of nm
- Random interactions with other magnetic moments
  - Spin-nucleus and spin-electron interactions.
- Interactions induce relaxation of the spin systems
  - Stimulated, not spontaneous
- Give rise to T2 and T1 relaxation mechanisms
  - Signal loss cannot be recovered
- Dependent on the local chemical environment



Effects of Short-Mesoscopic Field Gradients

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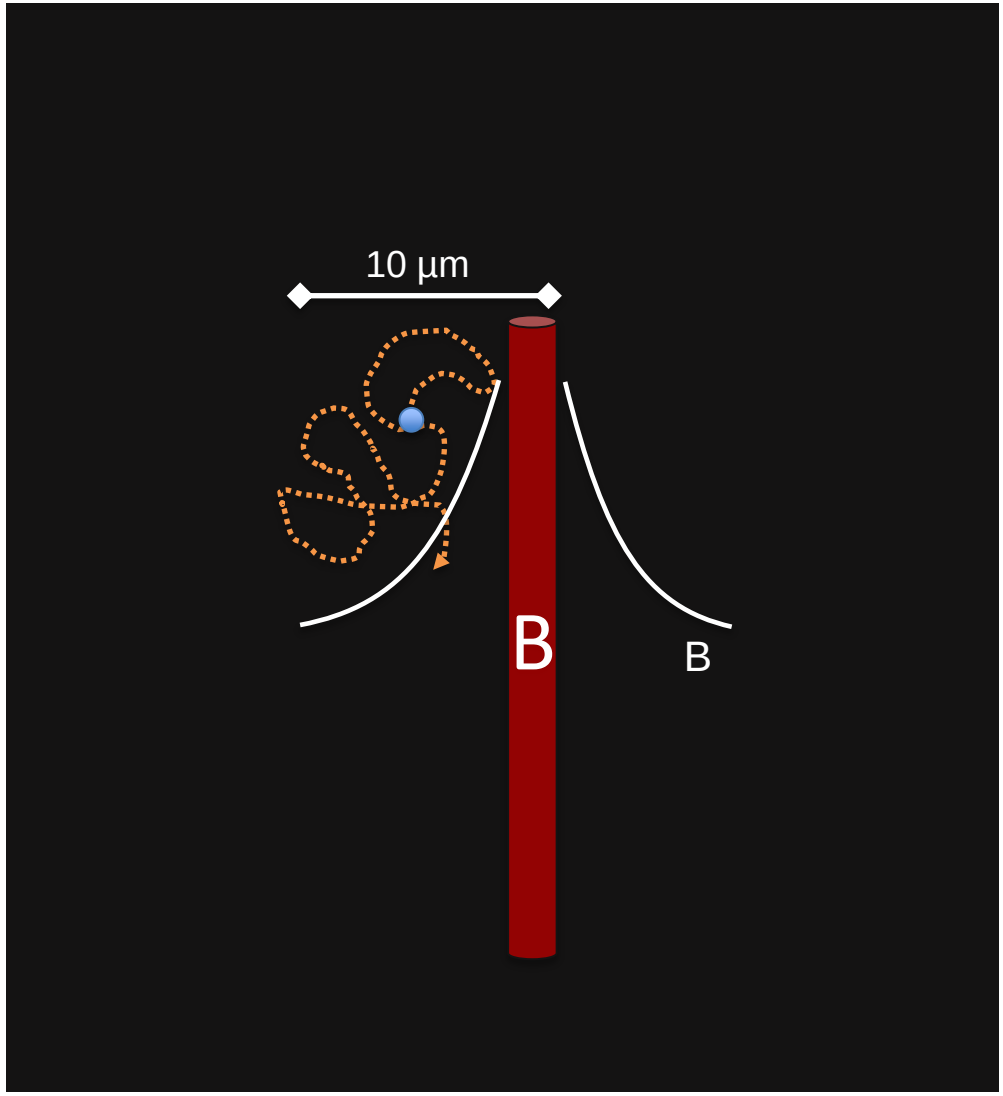
- Specific to inhomogenous tissue.
- Capillaries on order of 3-5um
- Experience a variety of magnetic fields
  - Varies the precessional frequency with time
  - Results in accrual of phase
- Diffusion results in random accruals
  - Can't be refocused by 180° pulse
- In a voxel, many randomly oriented capillaries
  - Length >> diameter
  - Often modelled as randomly oriented infinitely long cylinders.
- Adds to the T2 effect seen.



Effects of Long-Mesoscopic Field Gradients

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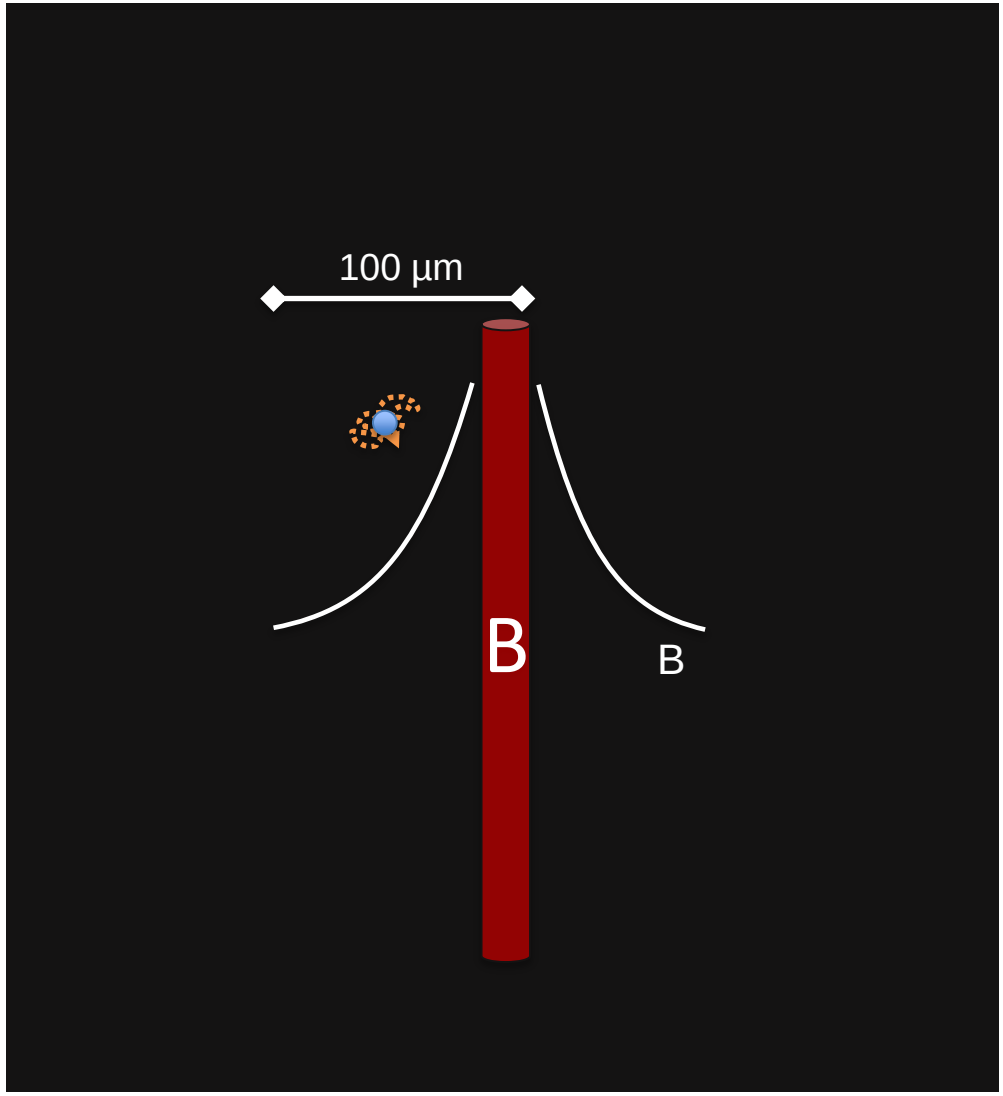
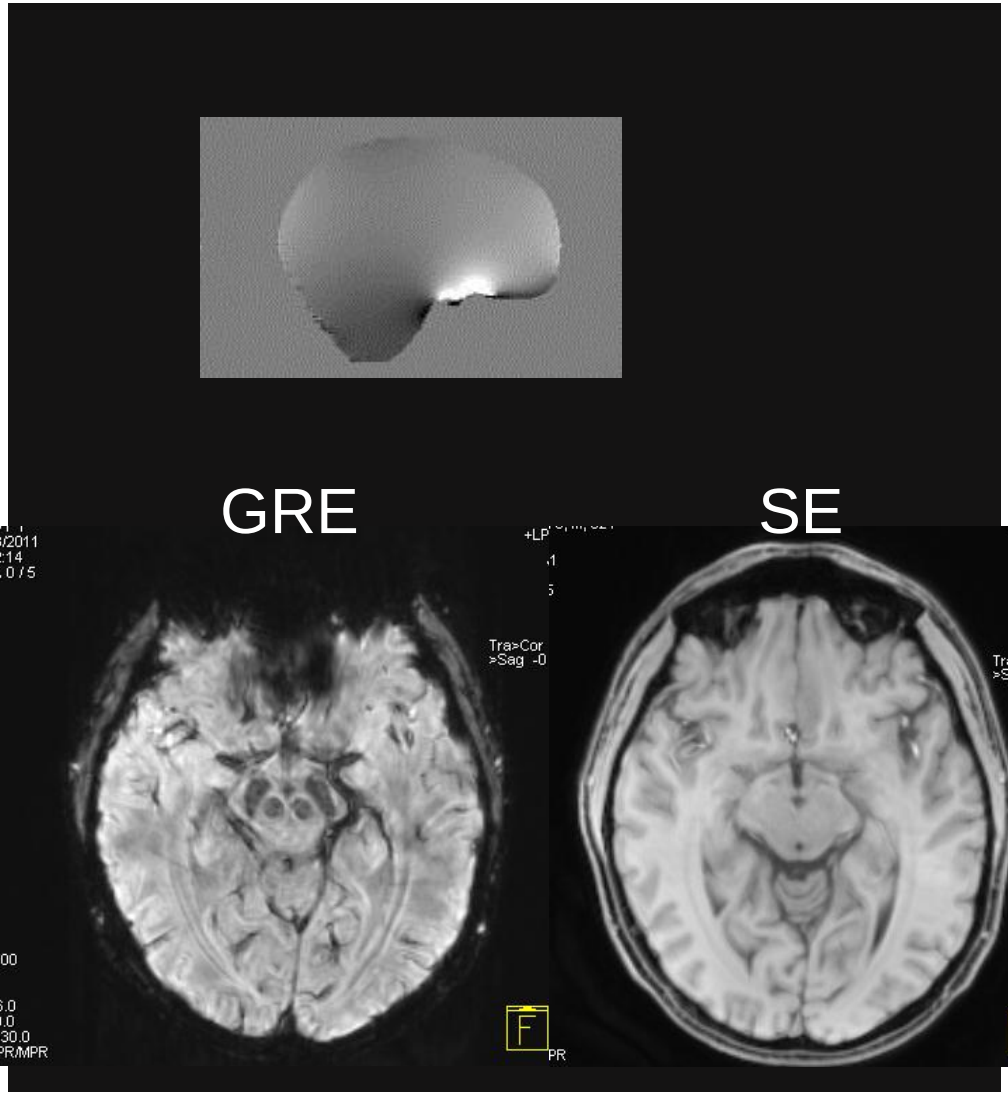
- Arterioles, Venules, etc: 10-50um in radius
- Mid-range vessels: 100-500um in radius
  - Smaller than but approaching voxel size
- Still ~10um diffusion
  - Diffusion distance is small compared to field gradient
  - Spin experience an approximately static magnetic field
  - Magnetic field is not identical to main magnetic field
- 180° pulse can refocus phase accrual from the presence of a field gradient on this order
- GRE = signal loss
- SE = no signal loss
- Contributes to R2' (dephasing that could be refocused)
  - R2* = R2 + R2'
  - R2 = 1/T2 R2*=1/T2* R2=1/T2'



Effects of Macroscopic Field Gradients

- Larger than voxel size (cm scale)
- Usually not physiologically interesting
  - Air->Tissue Interfaces
  - Imperfections in Main Magnetic Field
- 180º pulse can refocus phase accrual from the presence of a field gradient on this order
- GRE = signal loss
- SE = no signal loss
- Contributes to R2' (dephasing that could be refocused)
  - R2* = R2 + R2'

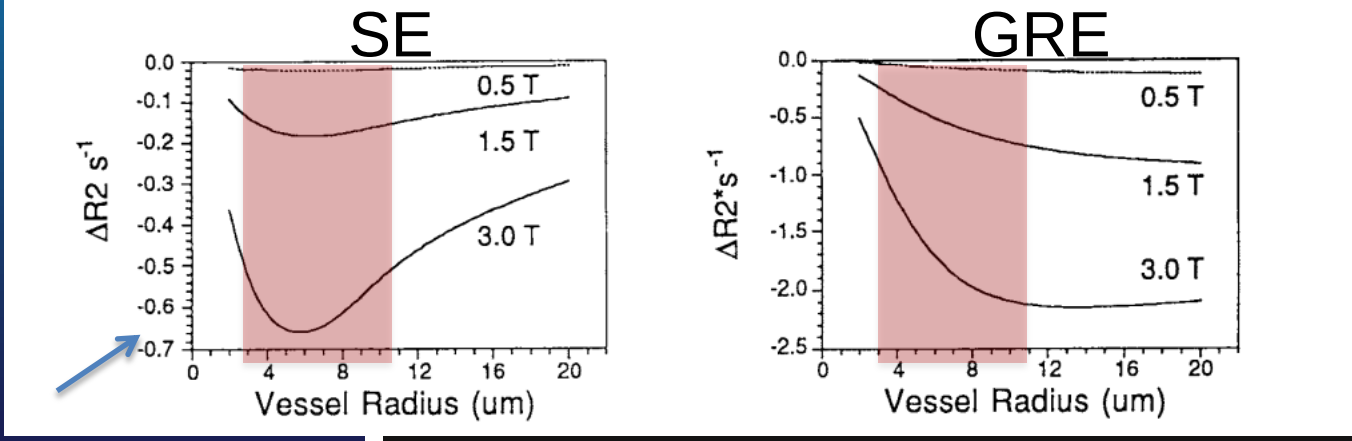


Spin Echo vs Gradient Echo

- Sensitive to:

	Spin Echo	Gradient Echo
Micro	Y	Y
Meso (short)	Y	Y
Meso (long)	N	Y
Macro	N	Y

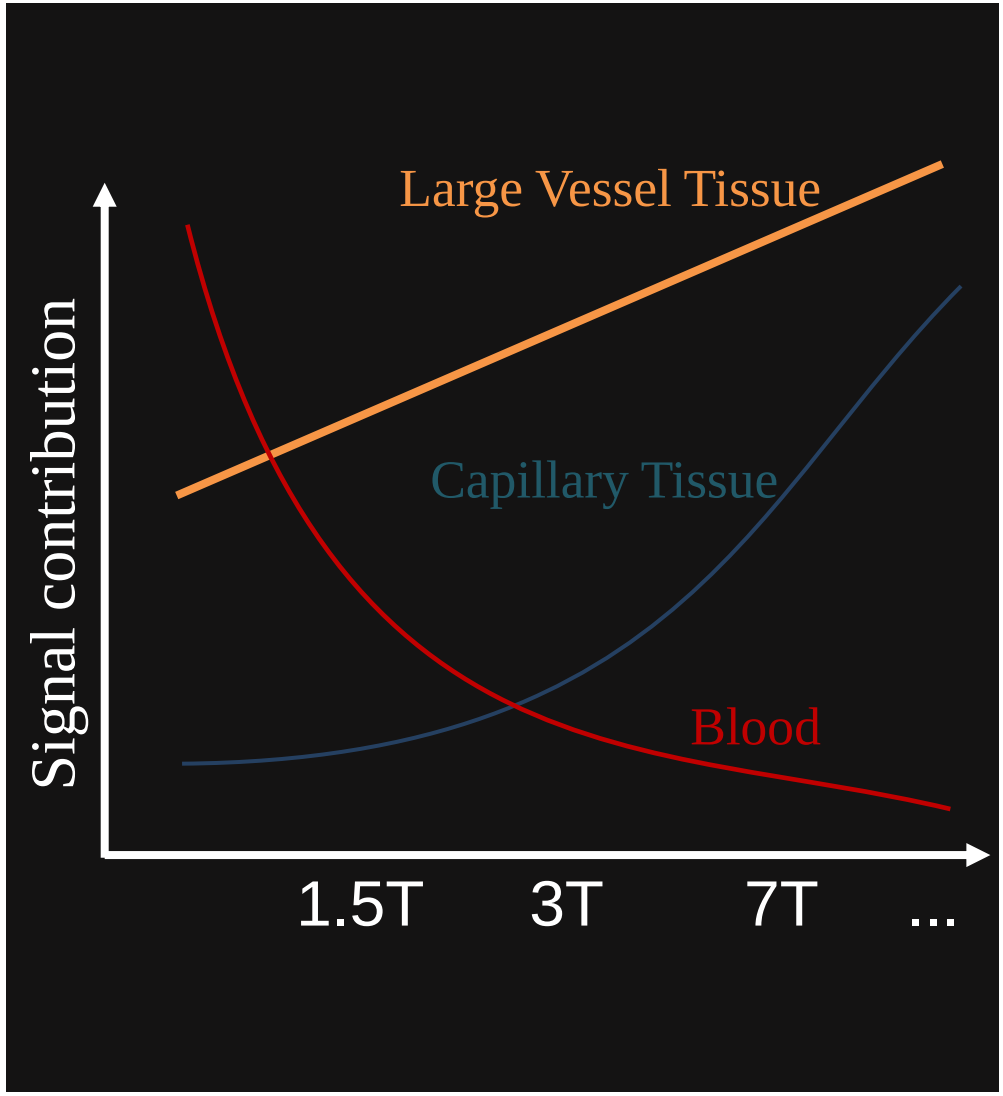
- Most interested in capillaries



Bandettini/Wor g, Intl Jnl of Imaging Systems and Technology (6), 2-3, 133–152, 1995

High Field ~~Concerns~~Benefits

- At increased fields, the signal change due to BOLD increases
- At increased fields, the proportion of signal from large vessels increases.
- BOLD is already weighted towards venous side
  - More Deoxy
- GRE is already weighted towards large vessels



High Field (or short TE) ~~Concerns~~Benefits

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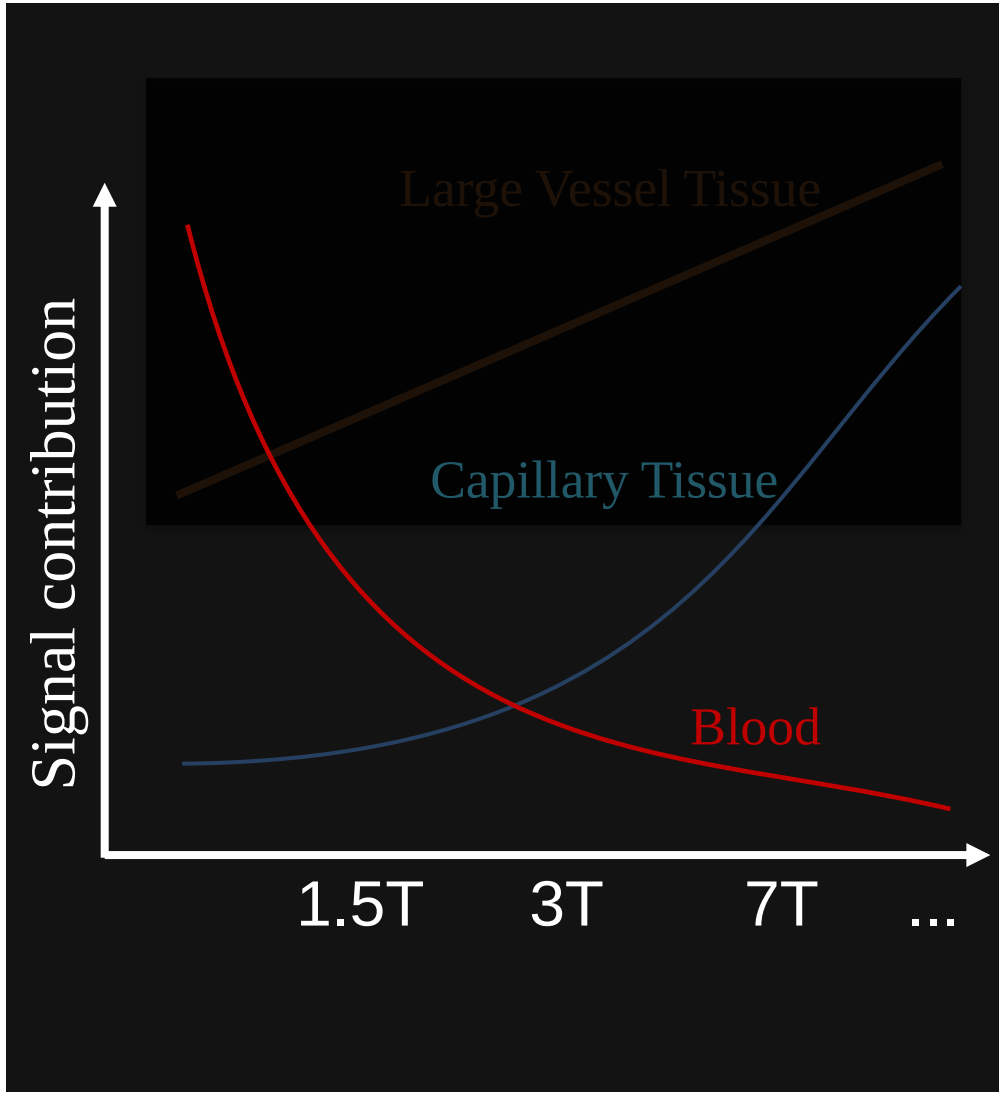
- Spin-echo has stronger advantages at higher fields.
- Insensitive to large vessels
- BOLD change due to small vessels increases
  - Less CNR penalty with SE

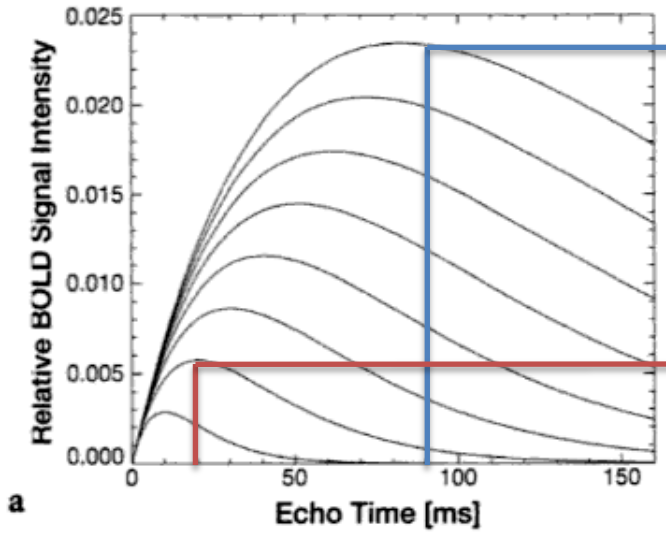


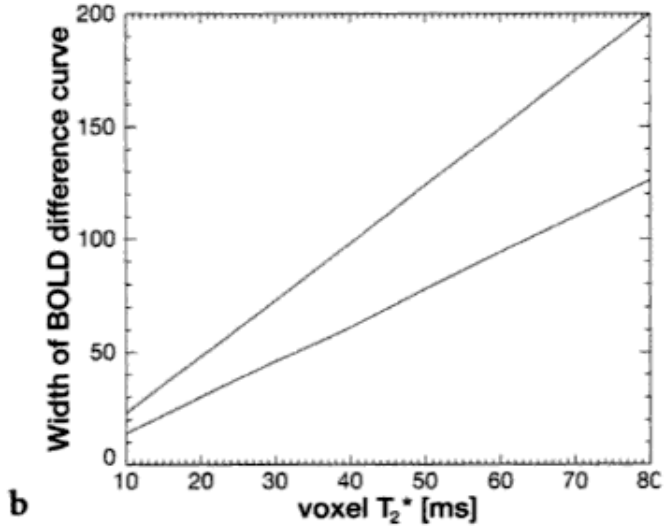
Practical Concerns – How long to wait

- The echo time (TE) is the time between excitation and acquisition of the signal.

$$TE_{opt} = \frac{\ln(R_2^{rest}) - \ln(R_2^{act})}{R_2^{rest} - R_2^{act}} \approx \frac{1}{R_2^{rest}}$$

- Acquire at TE = Underlying T2*
- Commonly:
  - ~40ms at 1.5T, ~30ms at 3T for GRE
    - Shorter at higher fields
  - ~70-80ms for SE
    - Less data per unit time





From: **Functional MRI** By Chrit T. W. Moonen, P. A. Bandettini

High Field (or short TE) ~~Concerns~~Benefits

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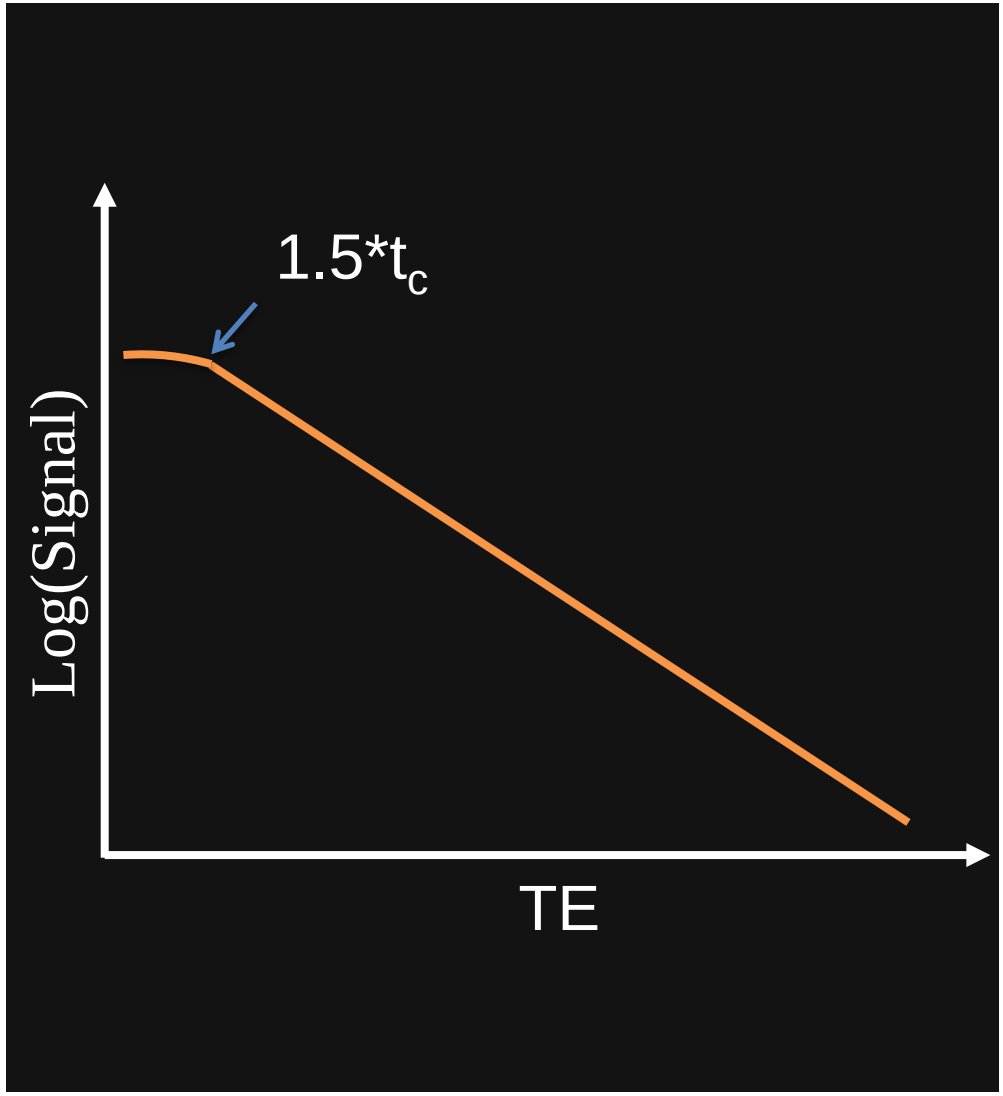
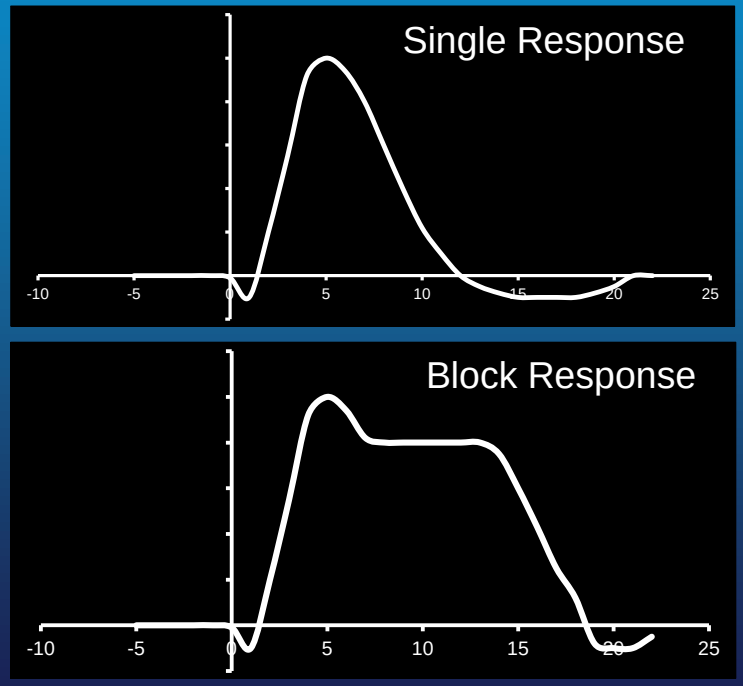
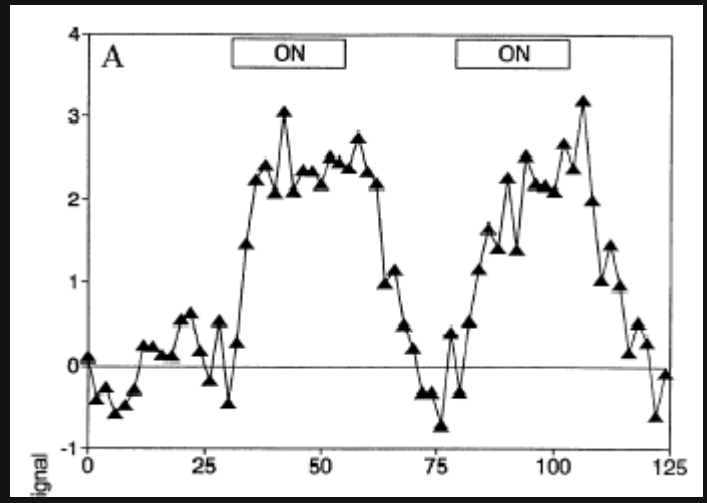
- Static Dephasing Regime
  - Static dephasing is the phase dispersion effect of spatially varying magnetic fields without the averaging effects of diffusion.
  - Diffusion of spins takes time
  - At higher fields, the static dephasing effect is stronger.
- Time taken to diffuse through mesoscopic (vessel) gradients (t_D) is α radius^2/4D ~ 5ms in capillaries.
- The characteristic time (t_c) of static dephasing:
  - At 1.5T, t_c is ~20ms
  - At 9.4T (FZJ), t_c is ~3ms
  - At 11T (UM), t_c is ~2ms
- If $t_c << t_D$, in the static dephasing regime.
- Before TE >1.5*t_c the signal is NOT proportional to exp(-TE/T2*), the measured T2* is a function of TE
- GRE only

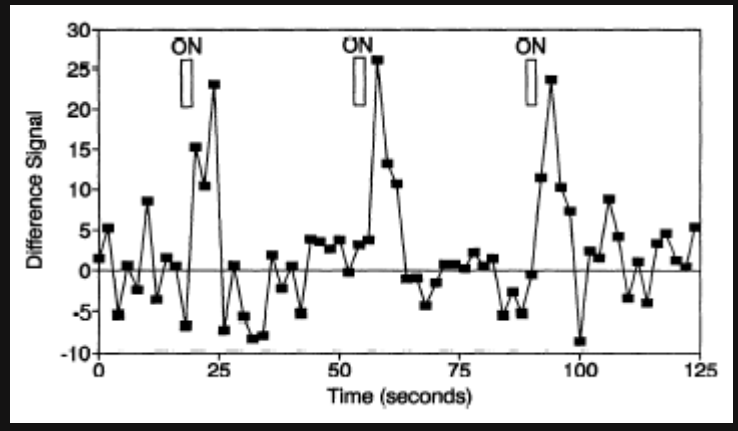


Temporal Resolution

- Each stimulating event has a response in the vascular network with a shape called the HRF
- HRF lasts about 15 seconds
- Multiple events together in time linearly add their HRF's



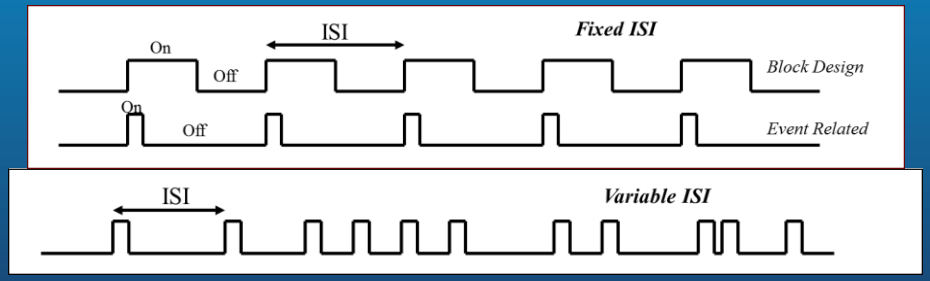




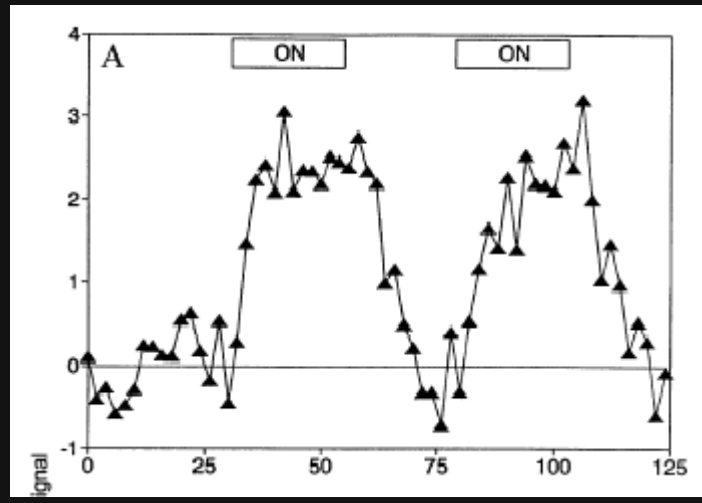
Blamire, *Proc. Natl Acad. Sci. USA* **89**,11069–11073 (1992)

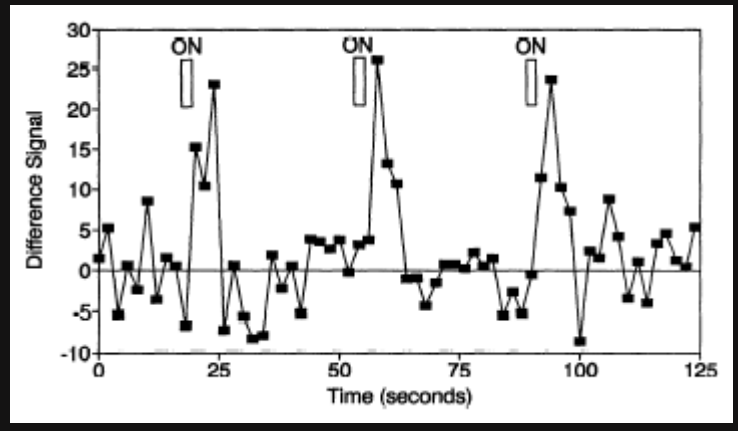
Temporal Resolution

- For best statistics, want several-many points to sample each stimulus response
- Stimuli that are too long have drawbacks:
  - Less definition of the response (weaker stats)
  - Want good definition of both active/rest states
  - Brain loses focus
- Inter-stimulus-intervals (ISI) of 15-45s are common



- Want to cover most (all) of the brain several to many time in ~15s
- Need rapid readouts that can give you a volume every 2-3s!

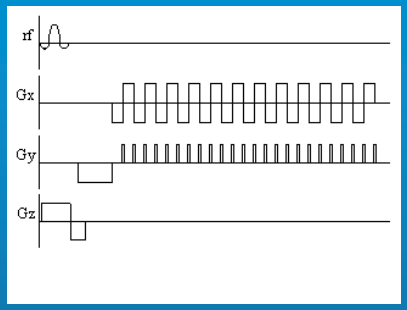




Blamire, *Proc. Natl Acad. Sci. USA* **89**,11069–11073 (1992)

Rapid Readout - EPI

- Echo-planar imaging forms an entire image from as little as a single excitation

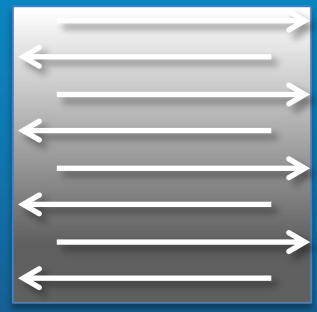


K-space

- Modern MR scanners are well-tuned for EPI, but some niggles remain
  - Heavy gradient use: generates heat in gradients, can change magnetic field
  - Scanners (esp high field ones) tend to exhibit drift of the field through time

Common EPI issues:

- Odd-even readout mismatch (Nyquist or FOV/2 ghosting)



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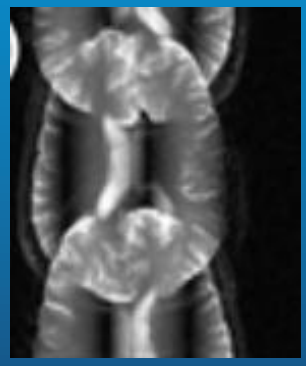

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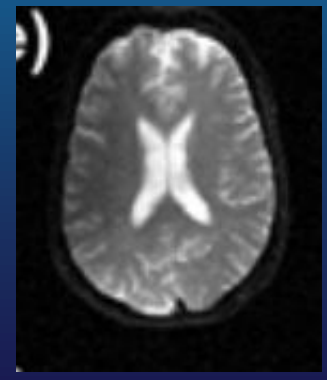

Susceptibility Dropouts (GRE-EPI)

- Macroscopic field gradients as discussed previously
- Air is paramagnetic
- Tissue is diamagnetic
  - Field gradient from air-filled sinuses several cm into the tissue
  - Phase dispersion in the Z-direction
  - Slices sum up those phases
- Large dropout regions above sinuses (OFC) and auditory canals (temporal lobes)
  - Short TE (but less BOLD)
  - Thin slices (but less SNR)
  - Z-shim (but hurt sensitivity in other areas)

Susceptibility Distortions

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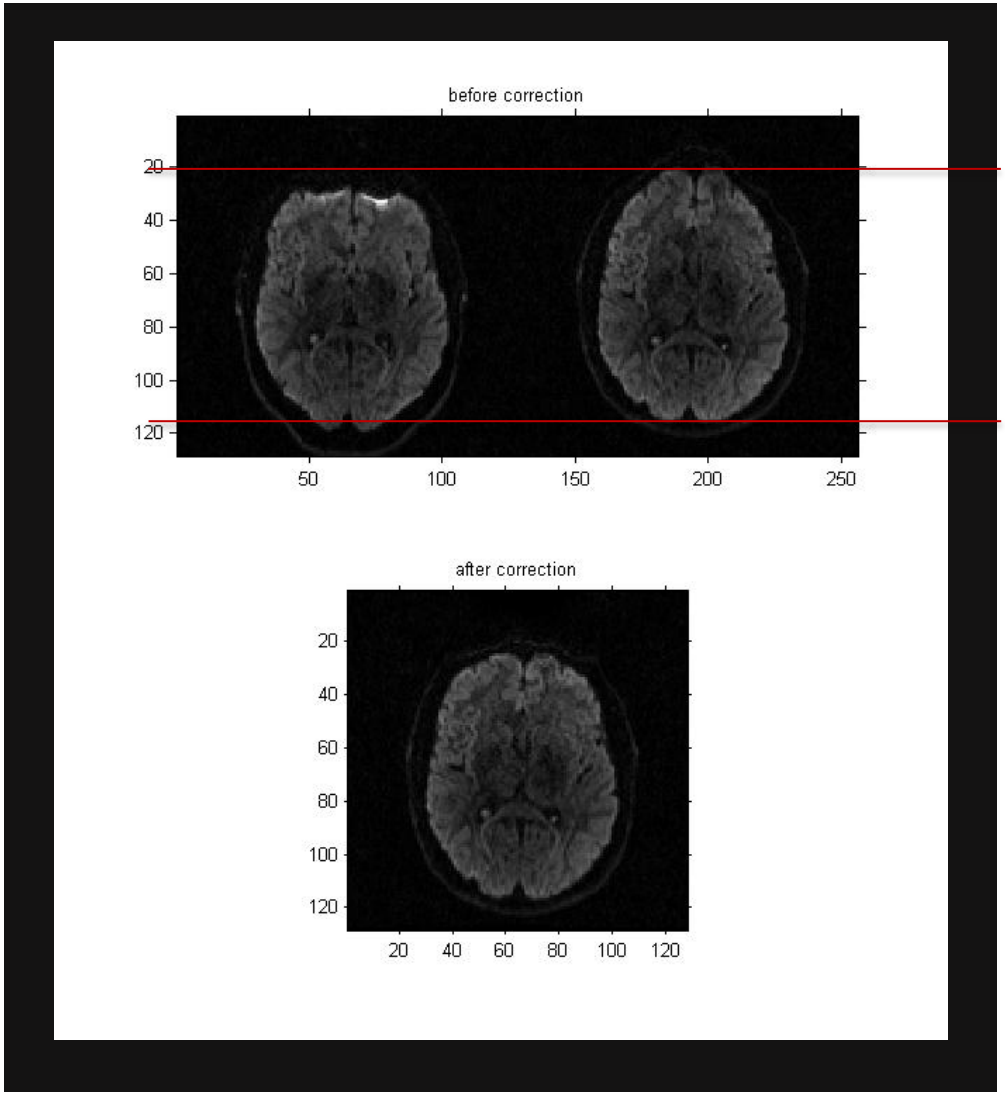
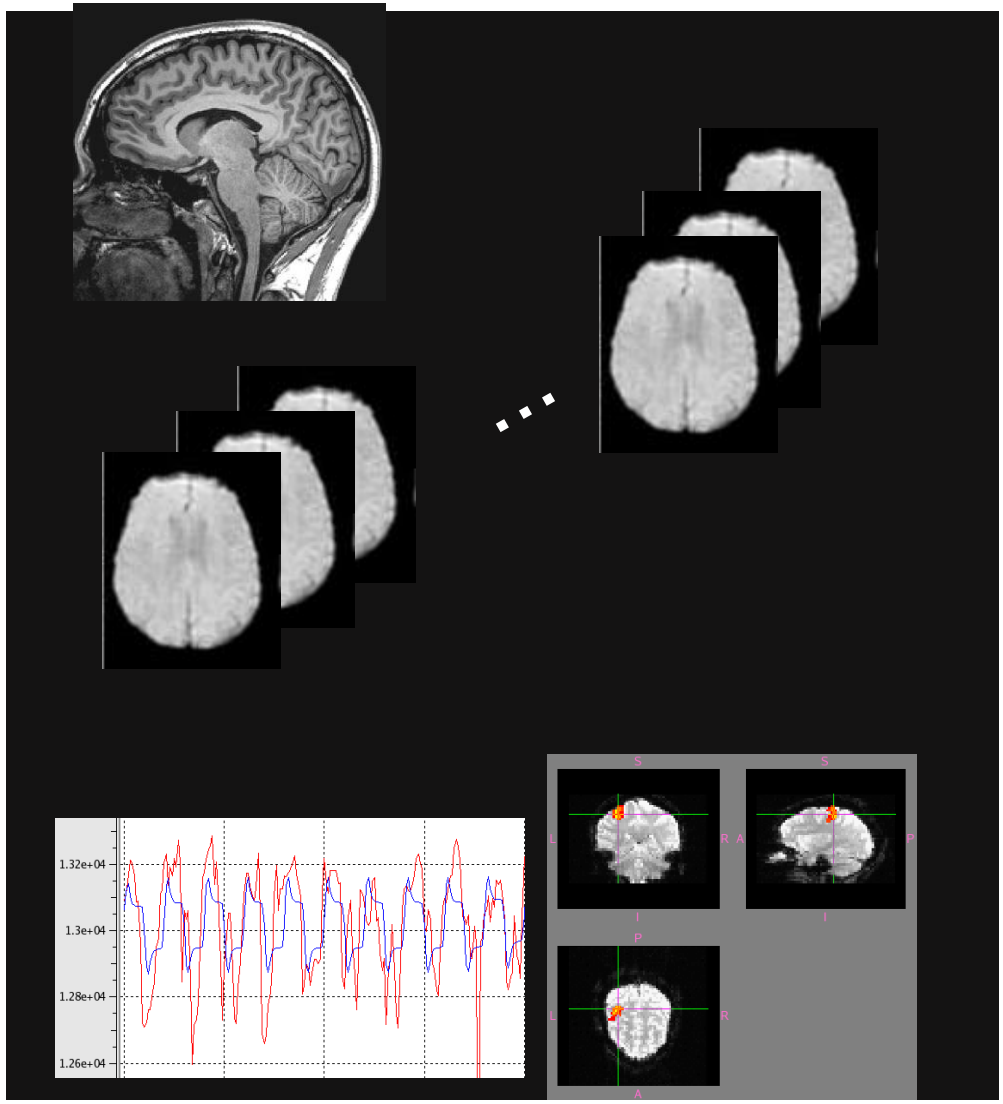
- Both SE and GRE EPI
- EPI-based readouts on inhomogenous areas
  - Global inhomogeneities: Shift, Stretch entire image
  - Focal areas can move many voxels, pile up
- Acquire a map of the magnetic field
  - Can unwarp global shifts
  - Can’t unwarp strong focal shifts
- Acquire two images with reversed phase encoding
  - Warps are opposite in each image
  - Can unwarp global and moderate focal areas



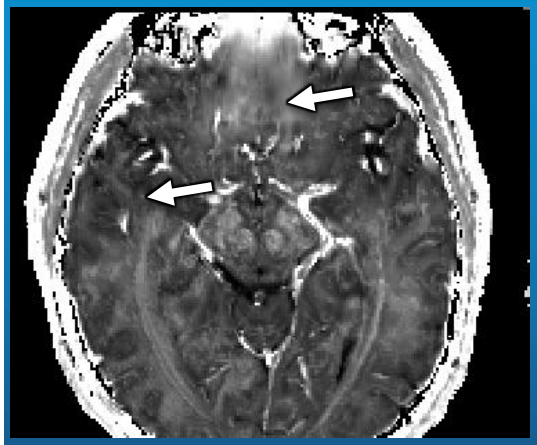
Common BOLD-sensitive experiment

- Most processing streams use a T1w structural image for underlays, regions of interest, etc.
- Often also acquire a field map
- 98% of fMRI out there uses GRE-EPI
  - Given TE_{opt} of 30 or 40ms
  - Spatial coverage of ~30 slices per TR
  - Repeat every TR (2-3s)
  - Acquire for ~10 minutes (6K-9K images, 200-300 volumes) in a mixture of rest and active states
- Correlate a voxel's timecourse over the experiment with predicted BOLD response
  - HRF * Stimulus pattern

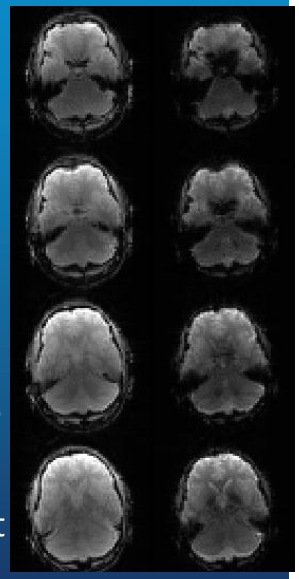


Multi-GRE-EPI

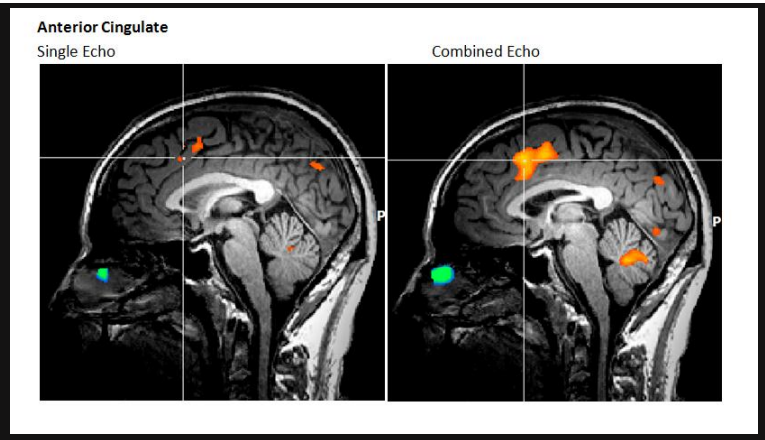
- Optimal TE = T2*
  - But T2* varies throughout the brain!
  - BOLD sensitivity is high when TE > T2*

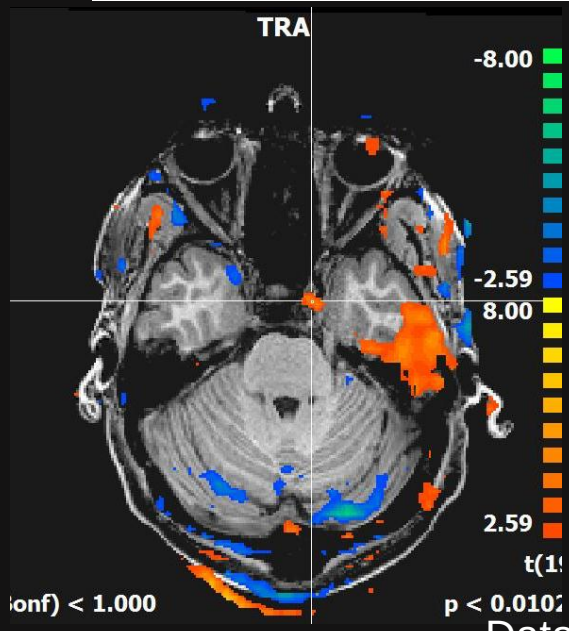


13ms 31ms



- Can acquire multiple GREs per acq.
- Combine by SNR-weighting
  - Closest to underlying T2* is most heavily weighted in the sum





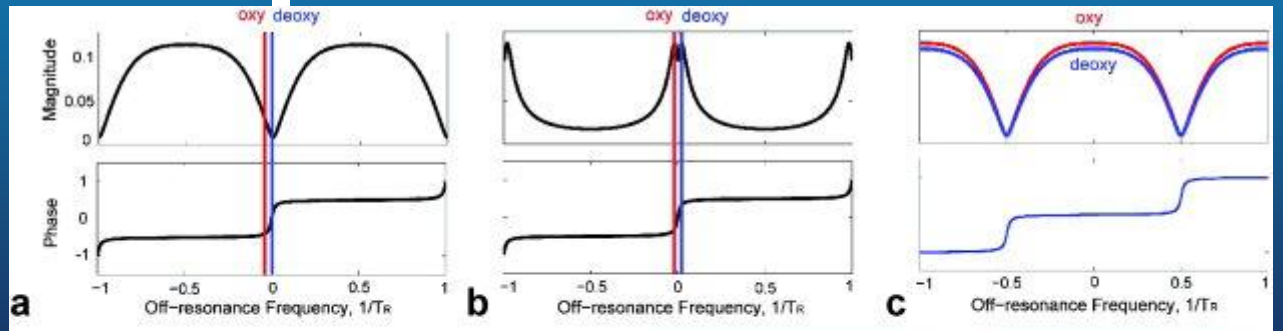
Data from M. Wall, UCL

fSSFP

- SSFP is a very rapid steady-state acquisition method
- Magnitude and Phase measured depends on acq. parameters, and on off-resonance
- 3 methods for BOLD sensitivity:
  - Tailor acq to give strong mag change over small freq shift btw oxy and deoxy (Scheffler 2001)
  - Tailor acq to give strong phase change over small freq shift btw oxy and deoxy (K Miller / fMRIB)
  - Tailor acq to give T2* contrast

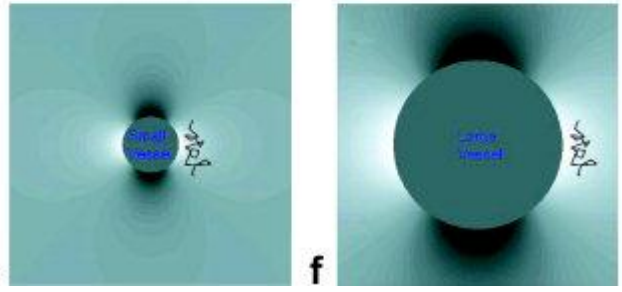
BOLD contrast *probably* most similar to SE-EPI

Utility may lie in very high field fMRI and fMRI in places GRE-EPI gives little coherent signal



	Transition-Band SSFP	Passband SSFP
Deoxy-hemoglobin	Resonant Frequency Shift	Apparent T_2 Relaxation Change
SSFP Imaging	Resonant Frequency Sensitive Magnitude and Phase	T_2 Sensitive Magnitude Profile

d



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imanova
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Questions / Comments ?