Basis of BOLD functional imaging contrast

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Blood
Oxygenation
Level
Dependant

BOLD Can see change in T2* image due to hemodynamic response associated with neuronal activation.

Ogawa et al.

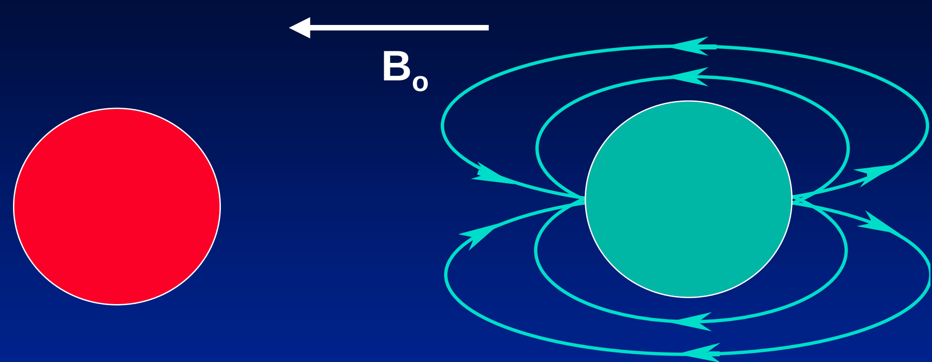
Basis of fMRI

Qualitative Changes during activation

Observation of Hemodynamic Changes

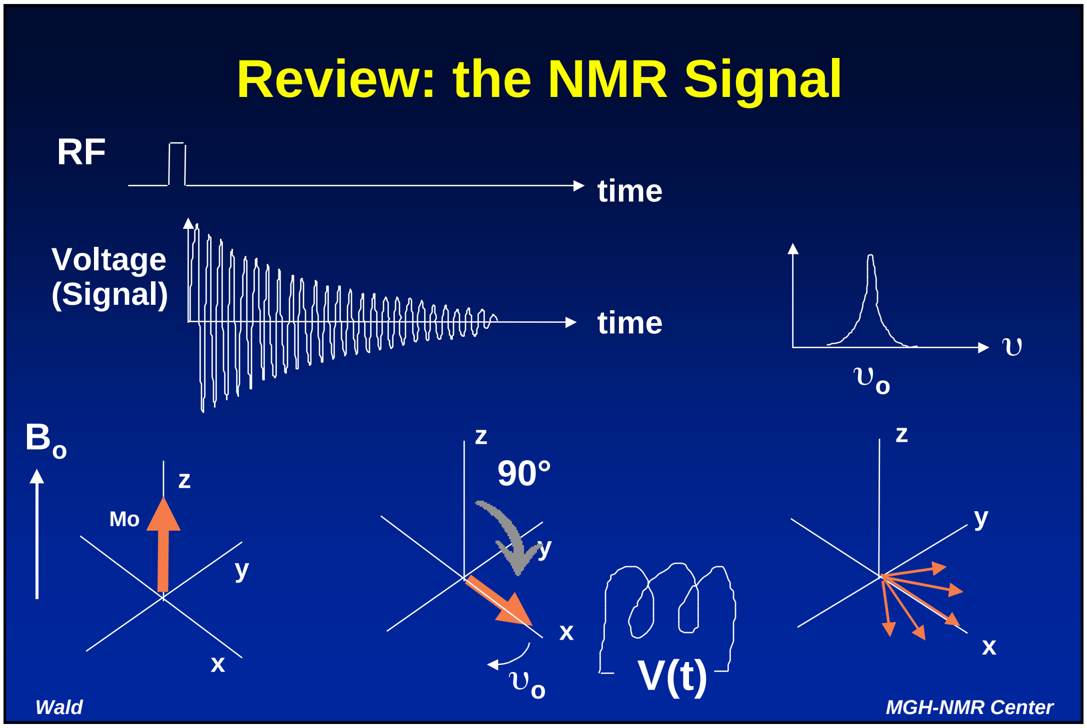
- Direct Flow effects
- Blood Oxygenation effects

Field Homogeneity and Oxygen State



Oxygenated Red Cell

de-Oxygenated Red Cell


Review: the NMR Signal
RF
time
Voltage
(Signal)
time
υ
υo
Bo
Mo
z
y
x
z
90°
y
x
υo
V(t)
z
y
x
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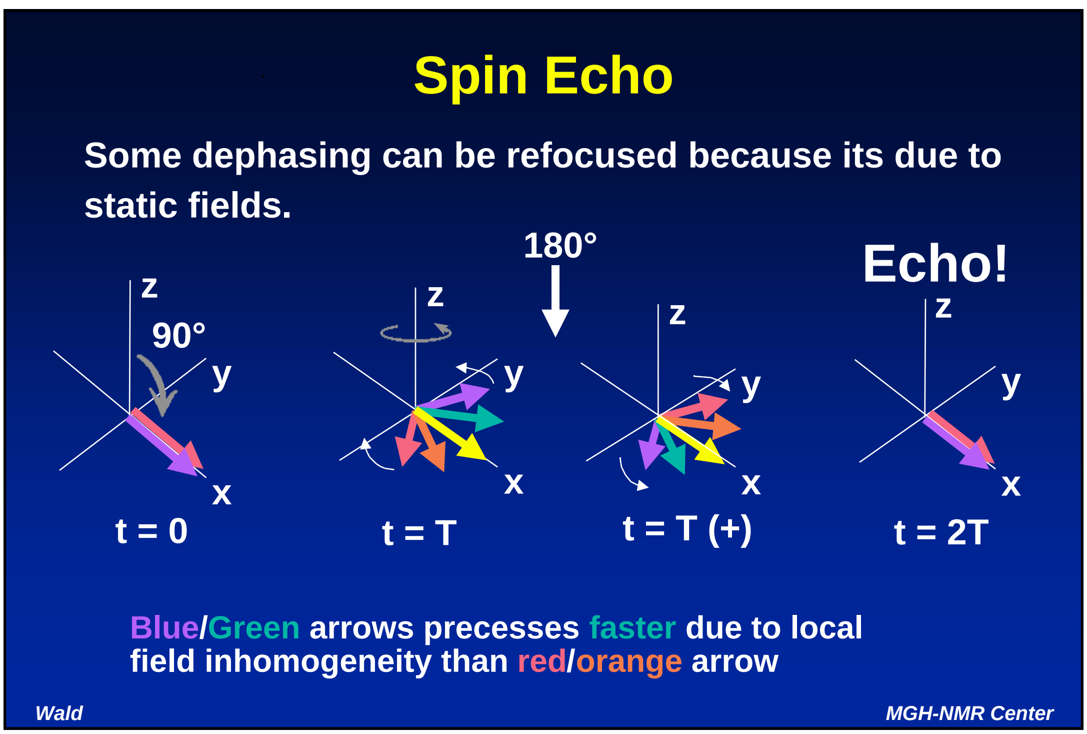
Spin Echo
Some dephasing can be refocused because its due to static fields.
180°
Echo!
z
90°
y
x
t = 0
z
y
x
t = T
z
y
x
t = T (+)
z
y
x
t = 2T
Blue/Green arrows precesses faster due to local field inhomogeneity than red/orange arrow
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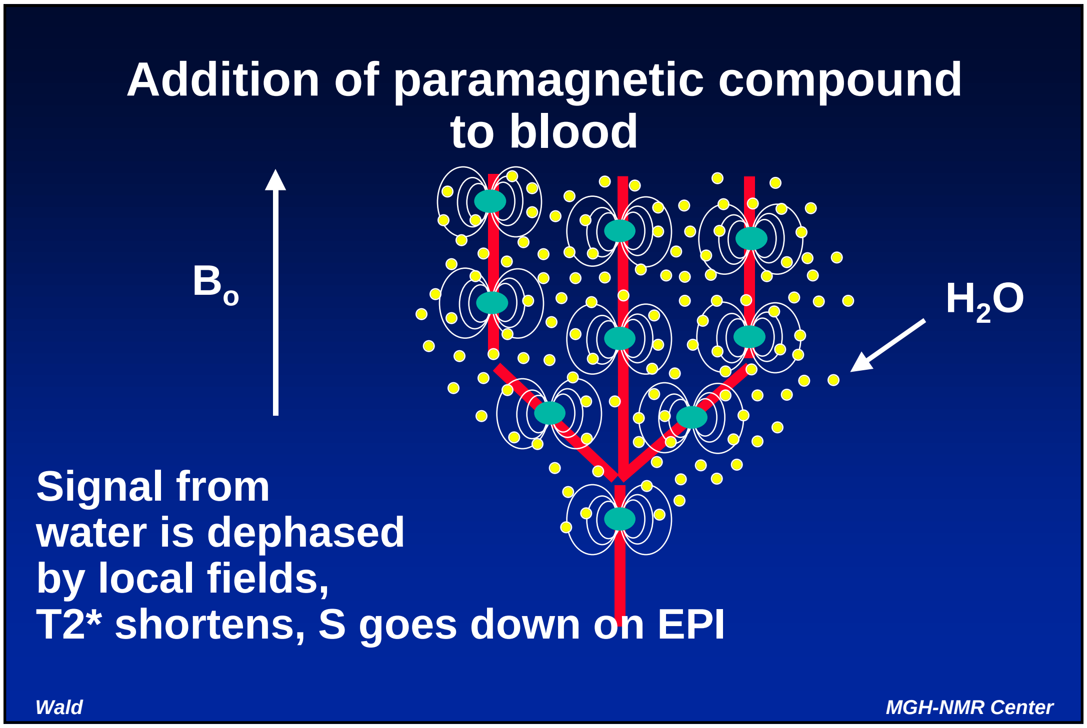
Addition of paramagnetic compound to blood
B$_o$
H$_2$O
Signal from
water is dephased
by local fields,
T2* shortens, S goes down on EPI
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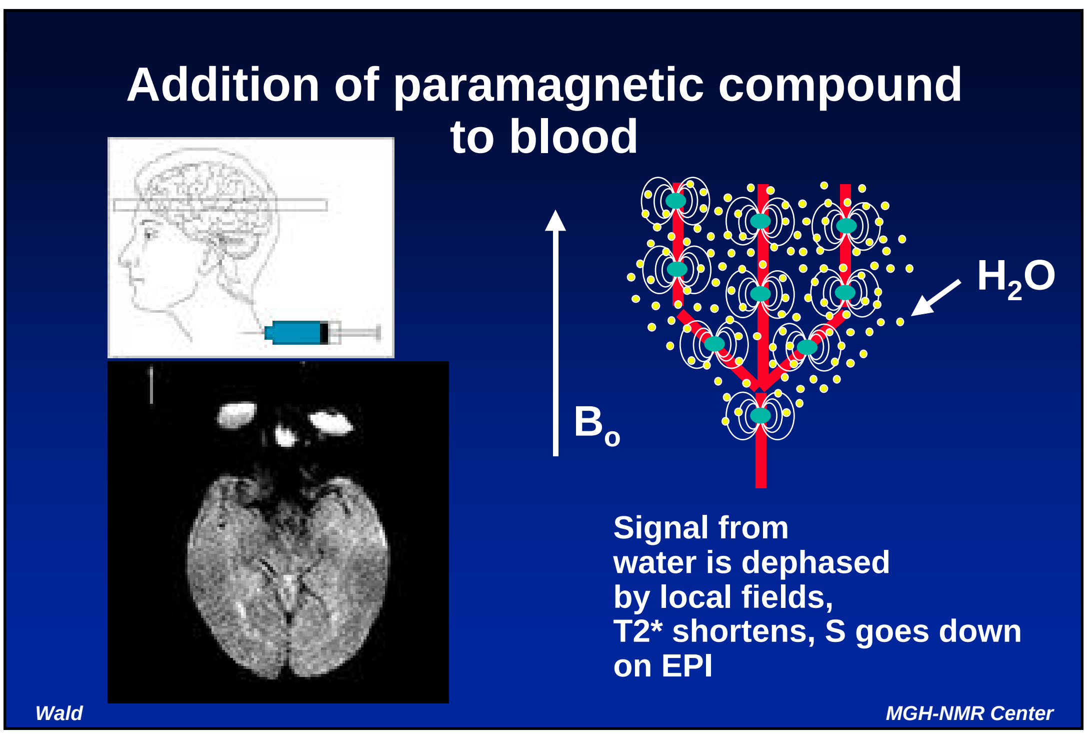
Addition of paramagnetic compound to blood
B$_o$
H$_2$O
Signal from
water is dephased
by local fields,
T2* shortens, S goes down
on EPI
Wald
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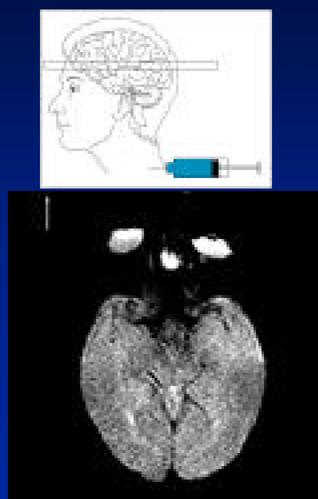
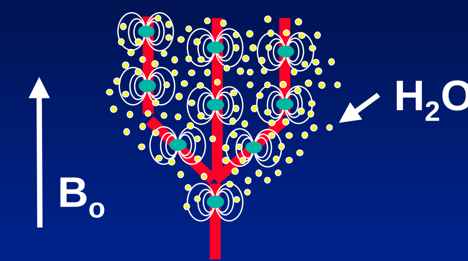
Addition of paramagnetic compound to blood makes signal go down





Signal from water is dephased by local fields,

______________ ↑ ______________ ↓

Conversely,

Reducing amount of a paramagnetic substance in the blood will make the image intensity go up.

______________ ↓ ______________ ↑

What happens during neuronal activation?

Neuronal Activation . . .

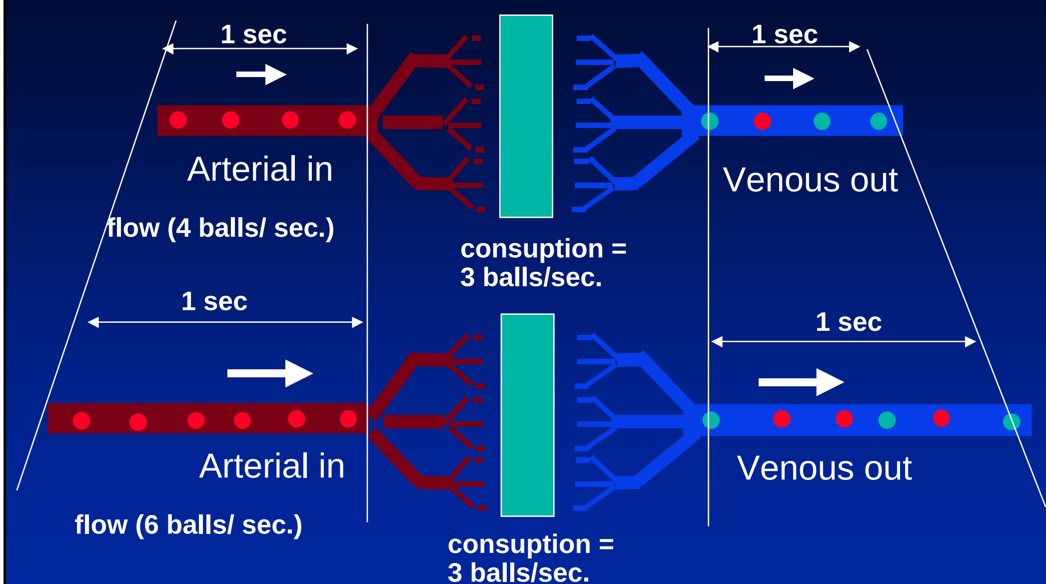
Produces *local* hemodynamic changes
(Roy and Sherrington, 1890)

Increases local blood flow

Increases local blood volume

BUT, relatively little change in oxygen consumption

decrease in deoxygenated red cell concentration



NMR and Activation

Summary:

Flow ↑	increases signal on “T1-weighted” scans
DeoxyHb ↓	increases signal on “T2/T2*-weighted” scans
Blood Vol. ↑	Decreases signal on contrast agent CBV scans.

Why does flow go up so much?

If O2 consumption rises only modestly (15%), why does flow need to go up a lot (50%)?

“Uncoupling” between flow and metabolism?

No real paradox: as flow↑____n oxygen extraction is hampered by decreased capillary transit time.

The simple answer is it takes a lot of flow…

“Balloon model”

Buxton et al. Magn. Reson. Med. 39, p855, 1998

Signal dephasing changes that accompany activation (BOLD effect)

a more detailed look…

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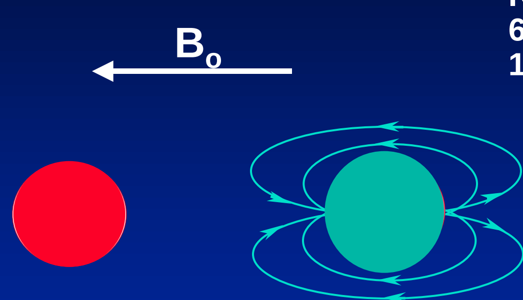
Internal contrast agent: the deoxygenated red blood cell

Red blood cell
6um dia.,
1-2um thick



Oxygenated Red Cell de-Oxygenated Red Cell

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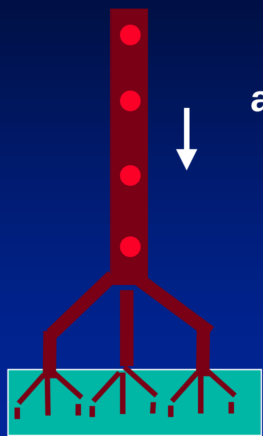
Brain: Arterial side

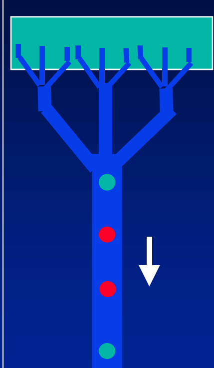


artery

- Capillaries are long and skinny, randomly oriented
- O2 exchange is in capillary

Arterioles,	25um dia., 15% blood Vol.
Capillary,	8um dia., 40% blood Vol.

Brain: venous side



Venules,	25-50um dia., 40% blood Vol.
Collecting veins	40% blood Vol
Veins	

Blood Oxygen saturation ~60% oxygenated for resting individual.

- Venules have the same BV as caps
- Venules have 2x the deOxyHb conc. Of caps.

>> venules are more magnetic.

Venules are ~ randomly oriented

Brain vessel facts

resting state 60% venous oxygen saturation.
80% sat. in capillaries
100% sat. in arteries.

activated state (with 70% increase in flow and 20% increase in CMRO2)
72% venous oxygen saturation
86% sat. in caps.
100% sat. in arteries

What does the water see?

Freely diffusing water is the source of image signal

In 50ms, water diffuses 25um on average
thus moves ~4x diameter of capillary…

Water diffuses readily in and out of red blood cells.
(spends about 5ms in a red blood cell)

In the 50ms timescale of fMRI, only 5% of H20 leaves the cap. bed.

Two water spaces: Extravascular (tissue) and Intravascular (blood)

Water does not exchange between these pools (in <0.1s)

The blood component has 2 sub spaces (capillaries and venules) with different vessel size and oxygenation levels.

Water diffuses freely in the extravascular space.

There is 20x more water in the extravascular space.

T2 or T2* changes?

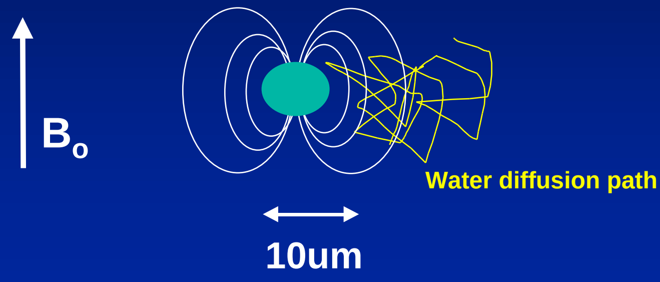
T2 changes require the water dynamically move in a local field distribution.

Water only moves 25um during encoding so the local fields must change significantly on 25um scale to get T2 effect.

Field around red blood cell changes on this scale

Intravascular:
T2 or T2* changes?

Field around red blood cell changes on the scale of mean free path of water.



T2 changes in the blood

Dynamic dephasing from diffusion in vicinity of the magnetic field of the RBC.

Easier to talk about dephasing rate: R2 = 1/T2

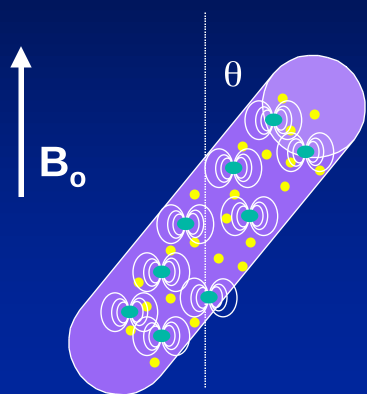
Empirical and Monte Carlo simulations:

$$R_2 = 1/T_2 = 1/T_{2o} + aB_o^2\left[Hematocrit\right]\left(1-O_2Sat\right)^2$$

Blood becomes darker on SE at high field…

Intravasculature: T2* changes

Static dephasing from the different fields inside larger vessel with different orientations.



Field inside vessel:

$$\Delta\nu = \alpha B_o (1 - 3\cos^2\theta)[1 - O_2 Sat]$$

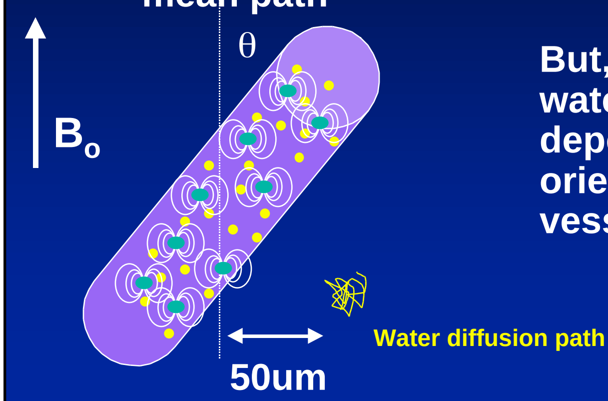
$$\Delta\nu \approx 0 - 10Hz$$

Intravascular summary

Both T2 and T2* changes, must really do a careful simulation to figure out relative contribution.

Extravascular:
T2 or T2* changes?

Field outside large "magnetized" venule is approx. constant on length scale of water mean path



But, field (thus freq.) water experiences will depend on the orientation and size of vessel. Thus T2* effect.

The Boxerman-Weisskoff model

Monte Carlo simulation of dephasing in vascular tree using know size distributions.

Tissue and blood components

Track static and dynamic dephasing.

Include size of RBC ~ size of capillary

Boxerman J et al. Magn. Reson. Med 34 p 4-10
Boxerman J et al. Magn. Reson. Med 34 p 555-566

The B-W model: Intravascular effects

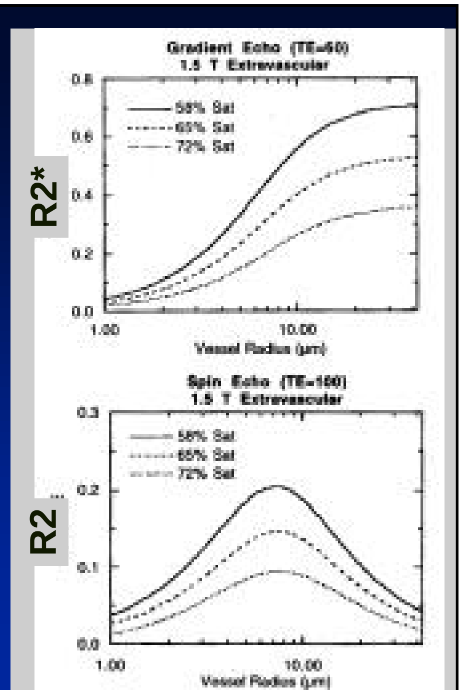
- There are both T2 and T2* effects.
- But don’t forget intravascular space has 20x fewer spins
- Relative importance of blood pool increases at high Bo or for spin echos.

The B-W model at 1.5T: Extravascular effects

T2 vs. T2*

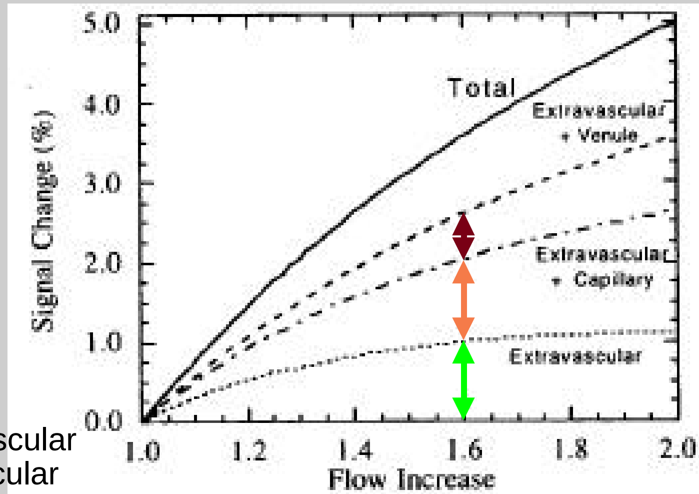
T2* effects (gradient echo) are ~3-4x larger

T2* effects are derived from bigger vessels



The B-W model at 1.5T: Extravascular vs Intra

- Venule
- Capillary
- Extravascular



At 1.5T 2/3 is intravascular
At 3T, 1/2 is intravascular

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Tests of B-W model dephasing flowing spins

Add a bipolar diffusion gradient to grad echo BOLD to remove signal from flowing spins.

Range of flow velocities crushed can be adjusted

spoiling venule flow (>10mm/s) eliminates 30% of BOLD

Spoiling capillary + venule flow (>0.5mm/s) eliminates 60% of signal

The last 30% of the signal must be extravascular…

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Effects of going to higher B_o

Blood T2s become short enough that activation makes the blood go from really dark to very dark.

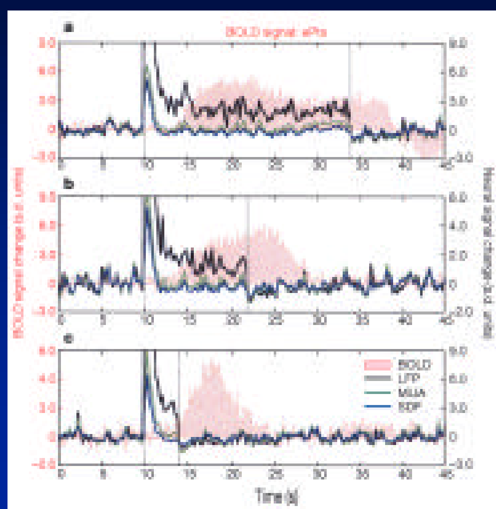
Velocity spoiling that would eliminate 2/3 of the BOLD effect at 1.5Tonly eliminates half at 3T and has no effect at 9.4T.

>> BOLD signal becomes more extravascular at high field.

How does BOLD relate to electrophysiology

Anaesthetized monkeys

BOLD response near electrode tip correlated with LFP measurements



Logothetis et al. Nature 412 p 150, 2001

Practical Acquisition tradeoffs

slice thickness

TE

TR

spatial resolution

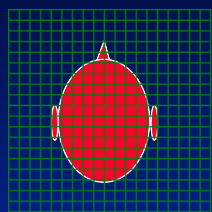
SNR proportional to Voxel Size

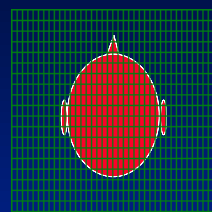
Thinner slice, higher in-plane resolution

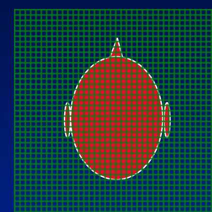
– ***Decreases raw SNR***

? Functional Activation CNR

Matrix Size







64 x 64 Matrix
Isotropic (square)

64 x 128 Matrix
Anisotropic (oblong)

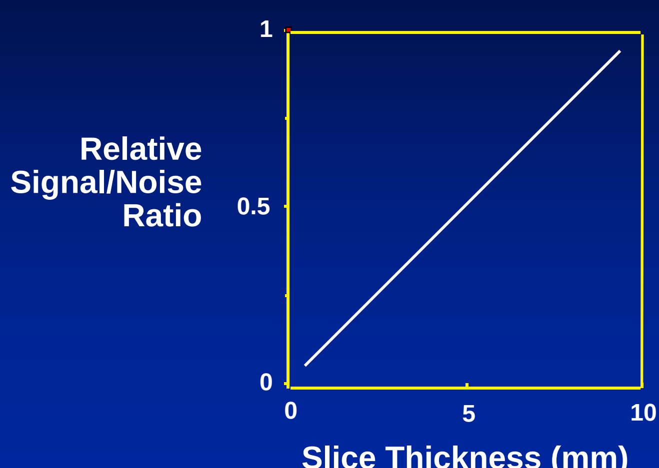
128 x 128 Matrix
Isotropic (square) voxels.

Relative SNR = 1

Relative SNR = 0.5

Relative SNR = 0.25

Slice Thickness and Signal/Noise Ratio



Slice Thickness and fMRI, Less is sometimes more

Thicker Slices → SNR ↑, but:

“Partial Voluming” Actual activation levels may drop

“Susceptibility Artifact” may lower actual SNR

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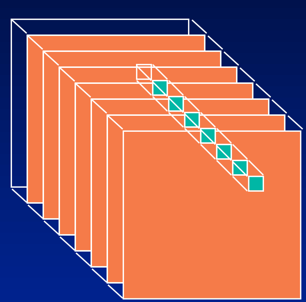
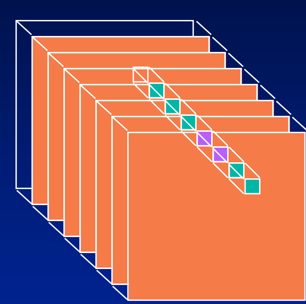
Partial Voluming



vs.



Activation uniformly through thick slice

Activation varies through thick slice

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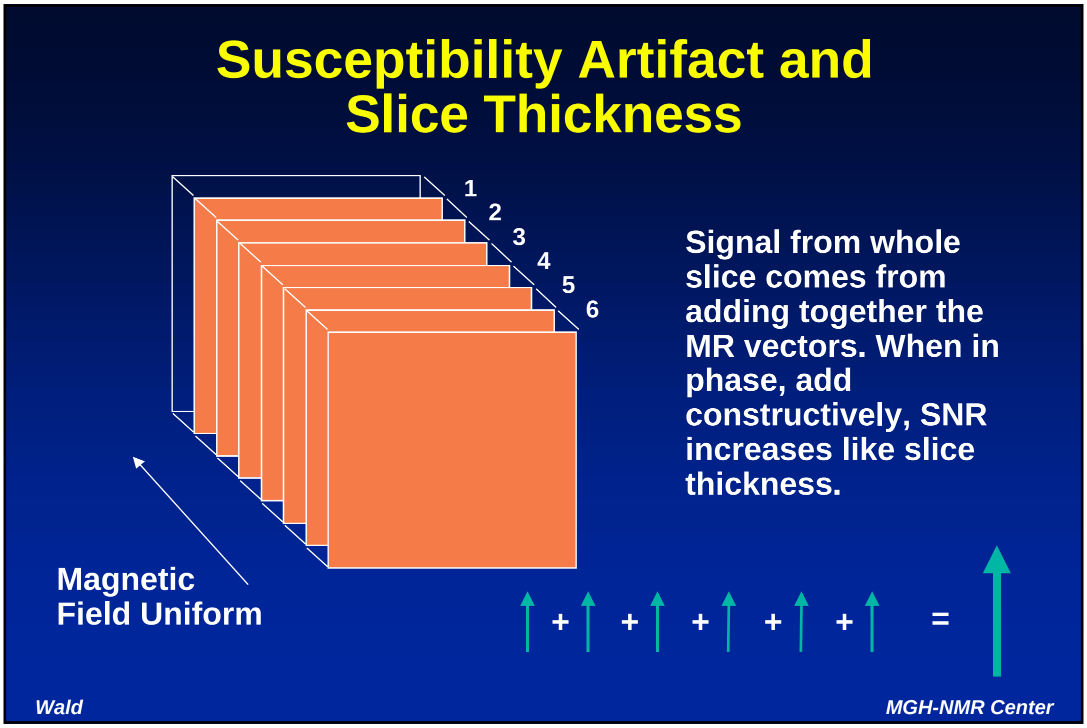
Susceptibility Artifact and
Slice Thickness
1
2
3
4
5
6
Signal from whole slice comes from adding together the MR vectors. When in phase, add constructively, SNR increases like slice thickness.
Magnetic
Field Uniform
+ + + + + =
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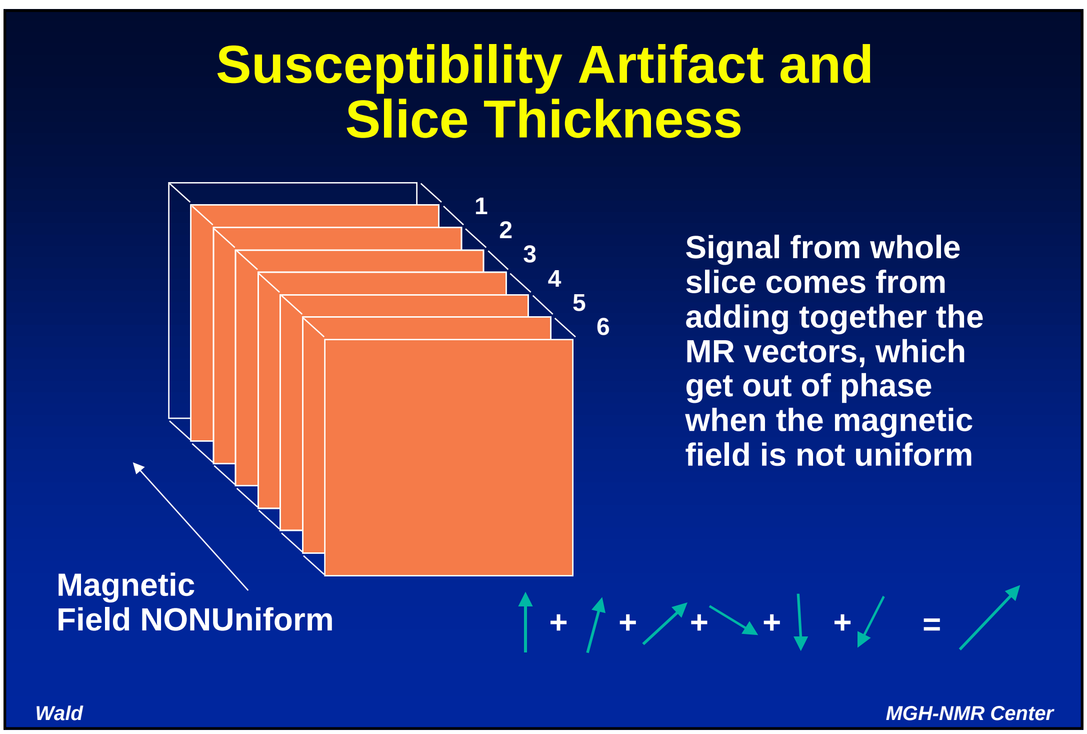
Susceptibility Artifact and
Slice Thickness
1
2
3
4
5
6
Signal from whole slice comes from adding together the MR vectors, which get out of phase when the magnetic field is not uniform
Magnetic
Field NONUniform
+ + + + + =
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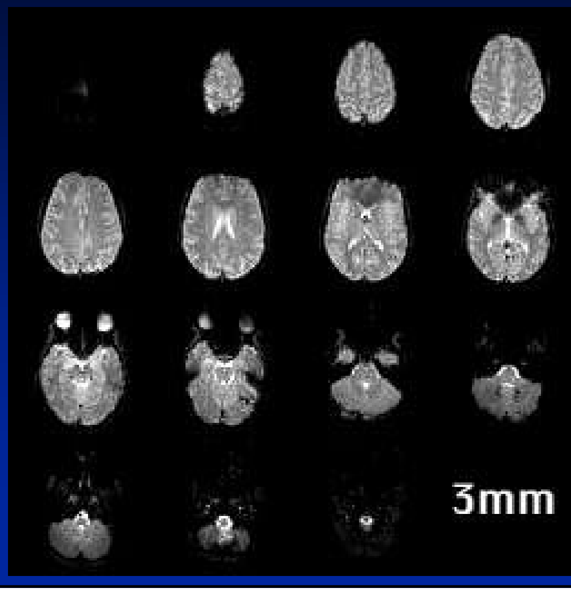
Susceptibility Artifact and Slice Thickness



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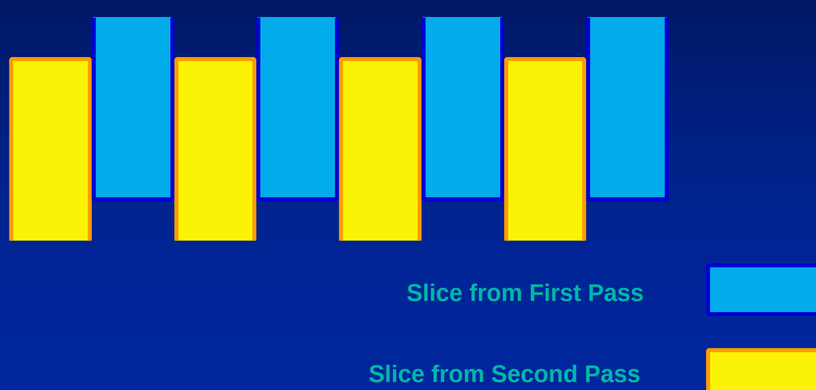
Slice Order

Interleaving: if no gap, then interleave to minimize Crosstalk



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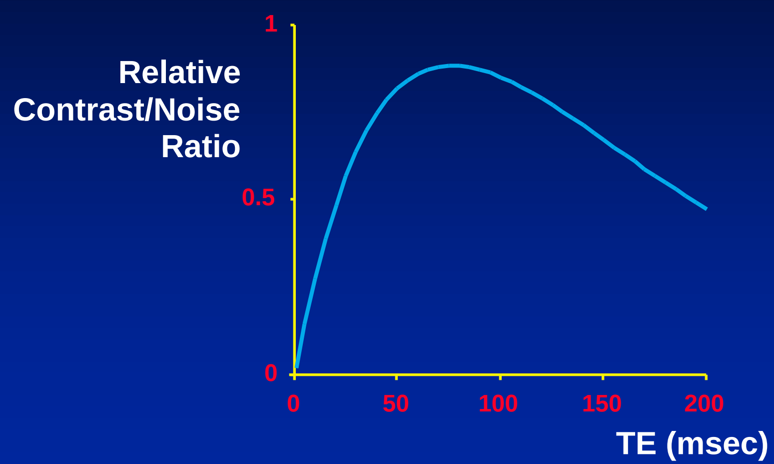
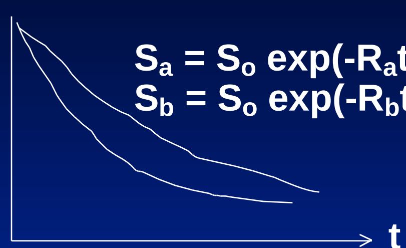
Contrast/Noise Ratio and Echo Time (TE)



Contrast/Noise Ratio and Echo Time (TE)



$S_a = S_o \exp(-R_a t)$
$S_b = S_o \exp(-R_b t)$

$R_a = 1/T_{2a}^*$
$R_b = 1/T_{2b}^*$
$\Delta R = R_a - R_b$

$$\Delta S = S_o e^{-R_a t} - S_o e^{-R_b t}$$

$$\Delta S = S_o e^{-R_a t} - S_o e^{-(Ra-\Delta R)\, t}$$

$$\Delta S = S_o e^{-R_a t}\left(1 - e^{\Delta R t}\right)$$

$$\Delta S = -S_o e^{-R_a t} \Delta R t$$

$$\frac{\partial}{\partial t}(\Delta S) = 0$$

$$t = 1/R_a$$

$$TE = T_{2a}^*$$