HST.583 Functional Magnetic Resonance Imaging: Data Acquisition and Analysis
Fall 2008

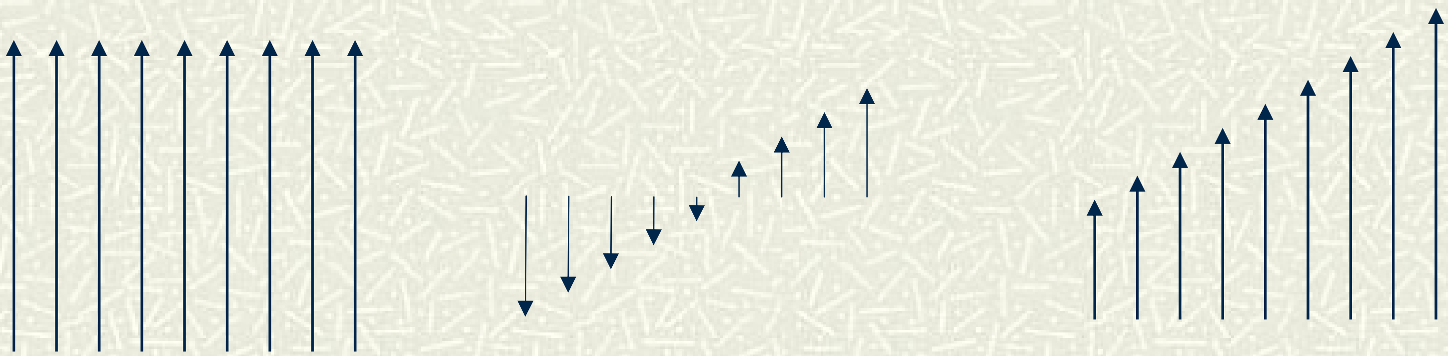
HST.583: Functional Magnetic Resonance Imaging: Data Acquisition and Analysis, Fall 2008
Harvard-MIT Division of Health Sciences and Technology
Course Director: Dr. Randy Gollub.

1) MR image encoding for fMRI

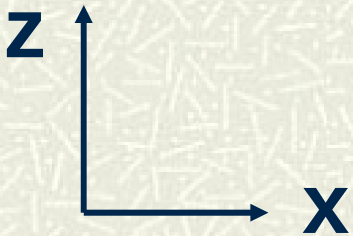
2) BOLD Contrast

Magnetic field gradient: the key to image encoding

B_o | $G_x\,x$ | $B_o + G_x\,x$



Uniform magnet | Field from gradient coils | Total field



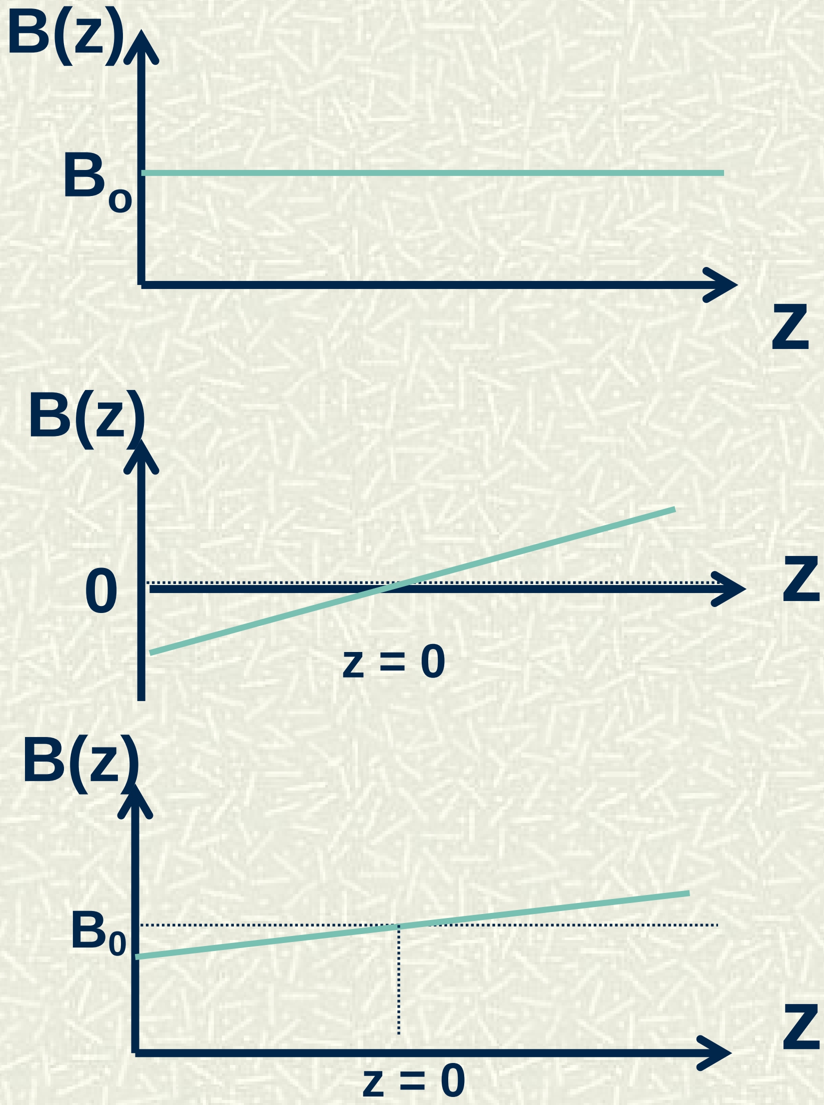
$$G_x = \partial B_z / \partial x$$

Gradient field for MR encoding

The magnet's field is homogeneous.

A gradient coil is a spool of wire designed to provide a linear "trim" field.

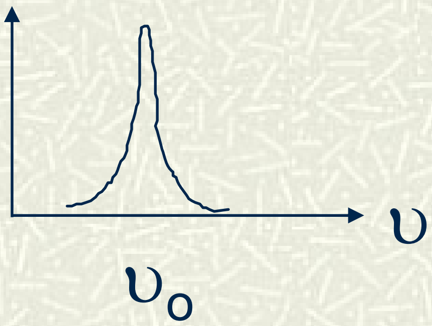
Gradient coil in magnet

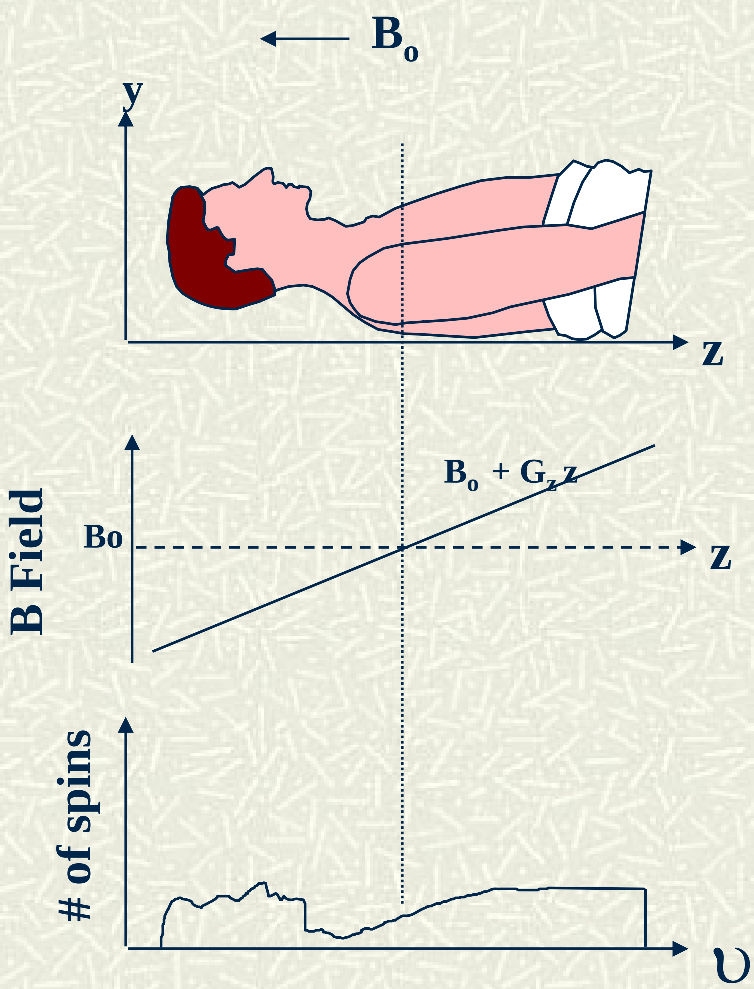


A gradient causes a spread of frequencies

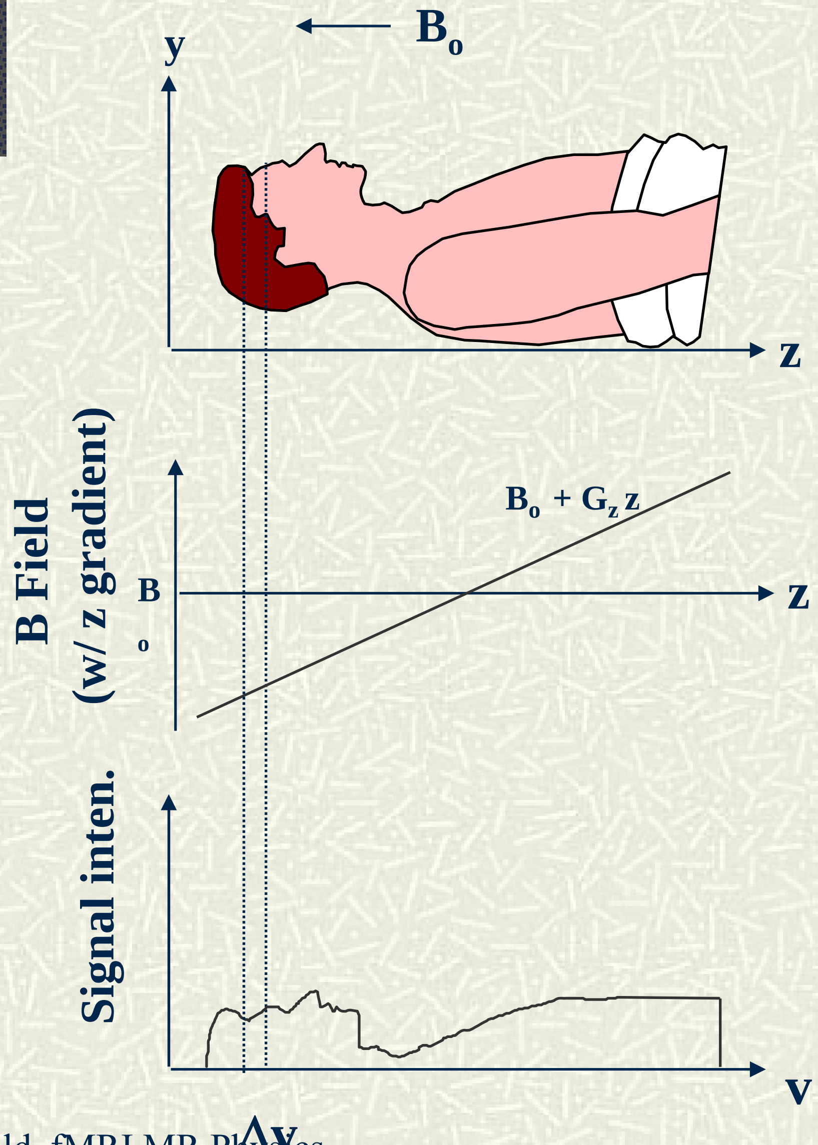
MR frequency of the protons in a given location is proportional to the local applied field.

$$v = \gamma B_{TOT} = \gamma(B_o + G_z\, z)$$

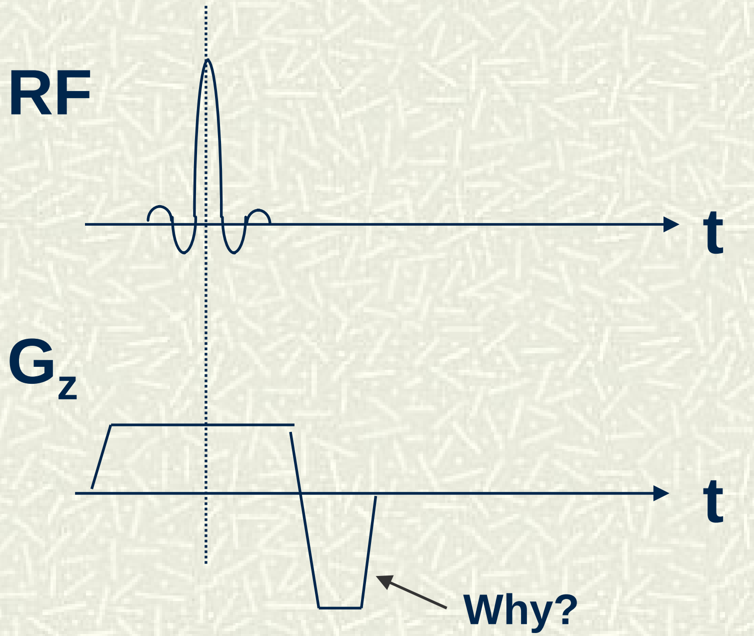




Step one: excite a slice

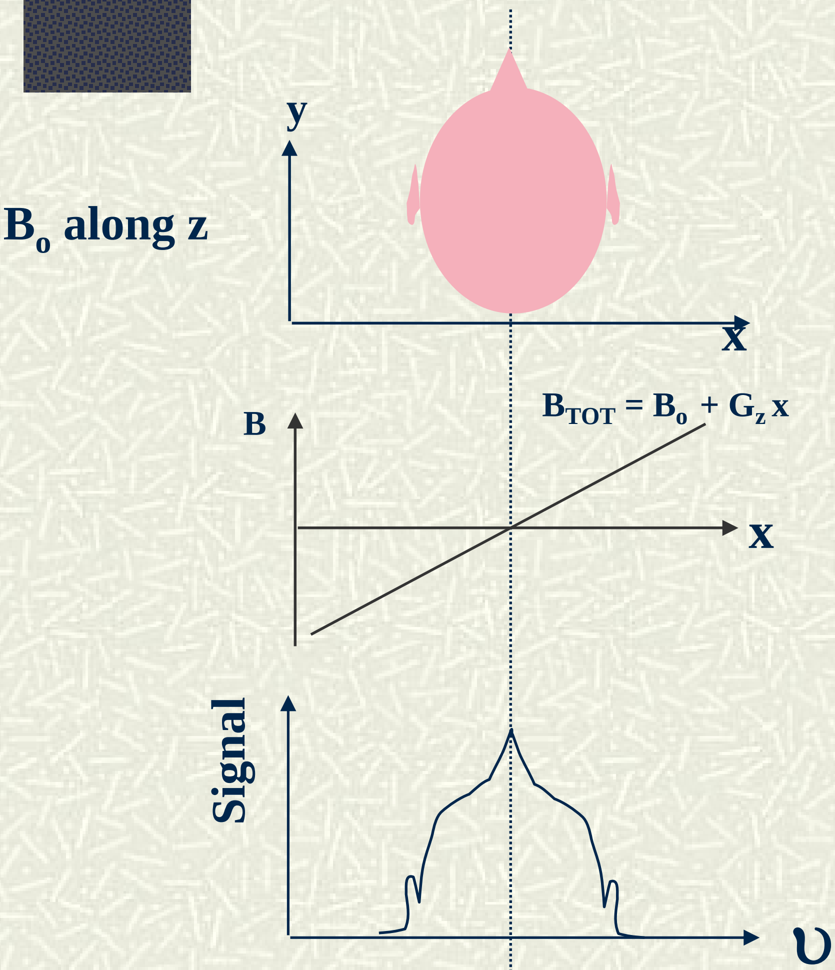


While the gradient is on, excite only band of frequencies.

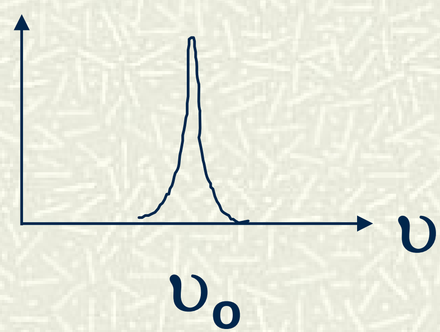


Step two: encode spatial info. in-plane

"Frequency encoding"

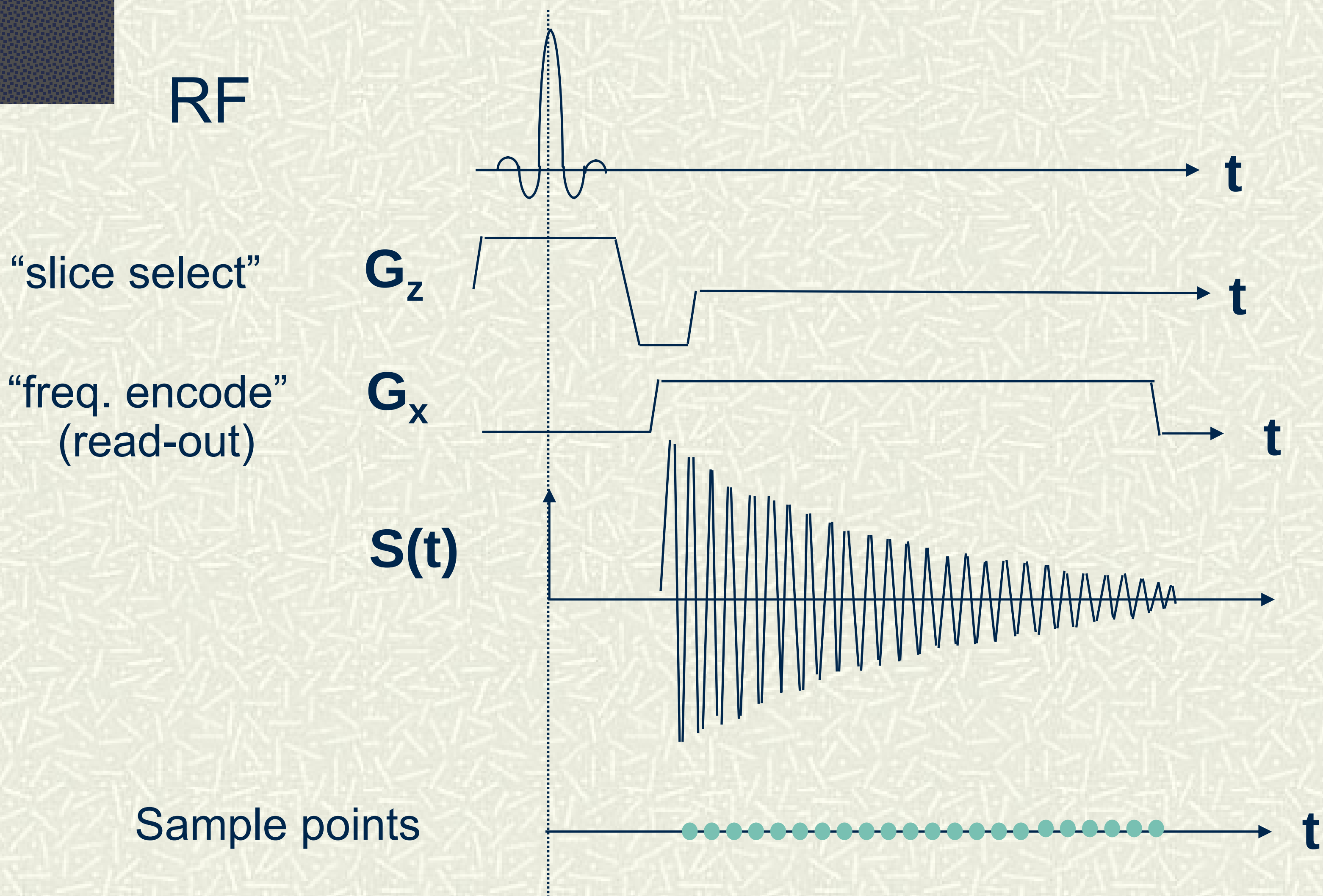


with gradient

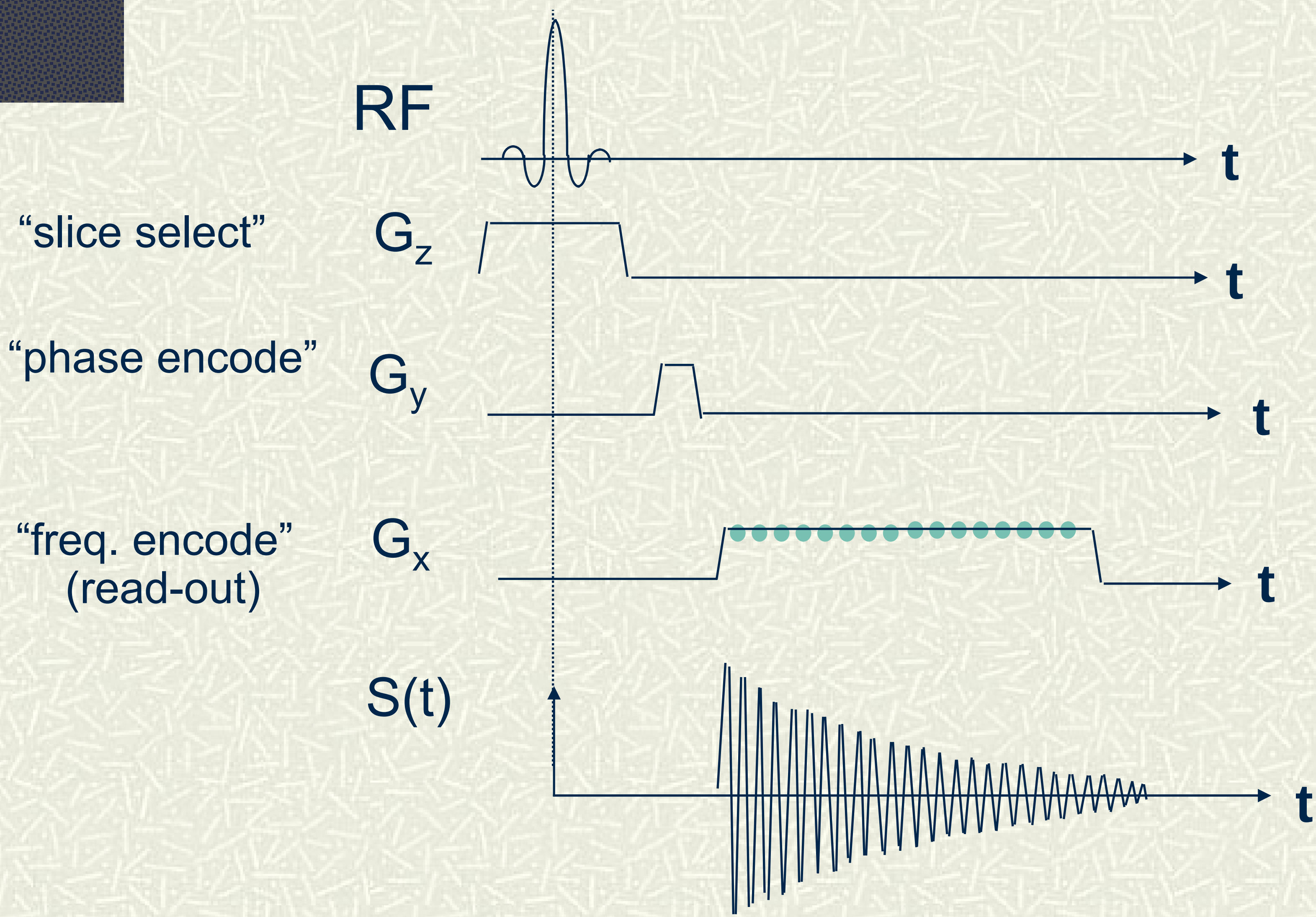


without gradient

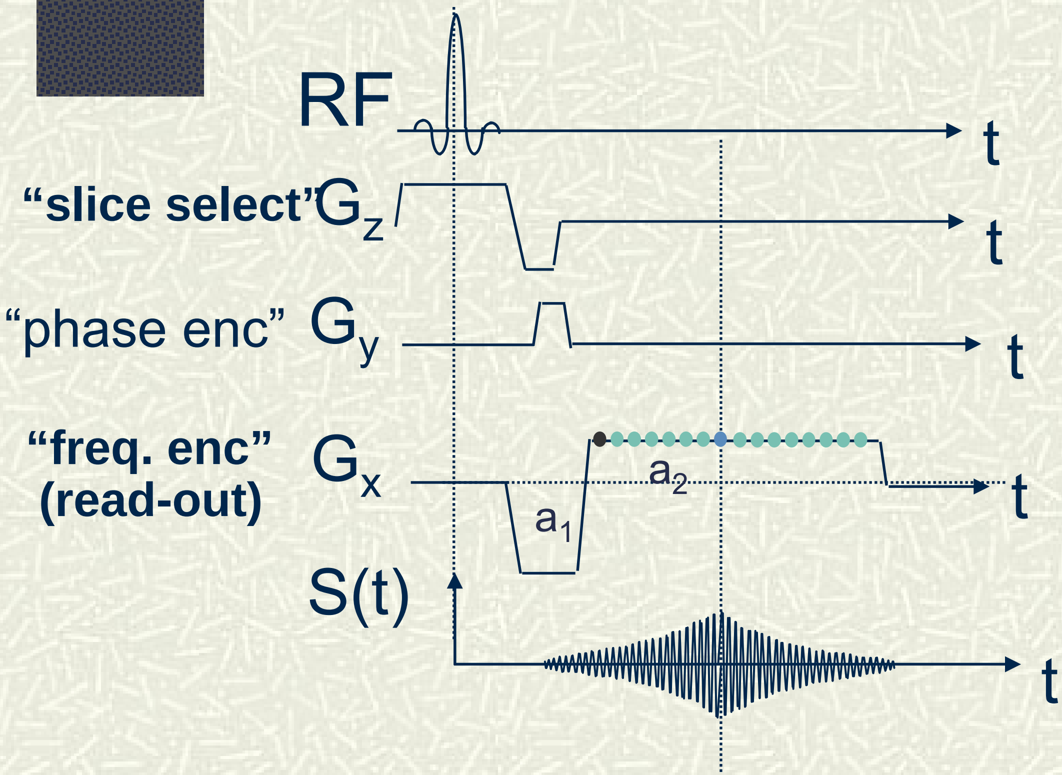
‘Pulse sequence’ so far

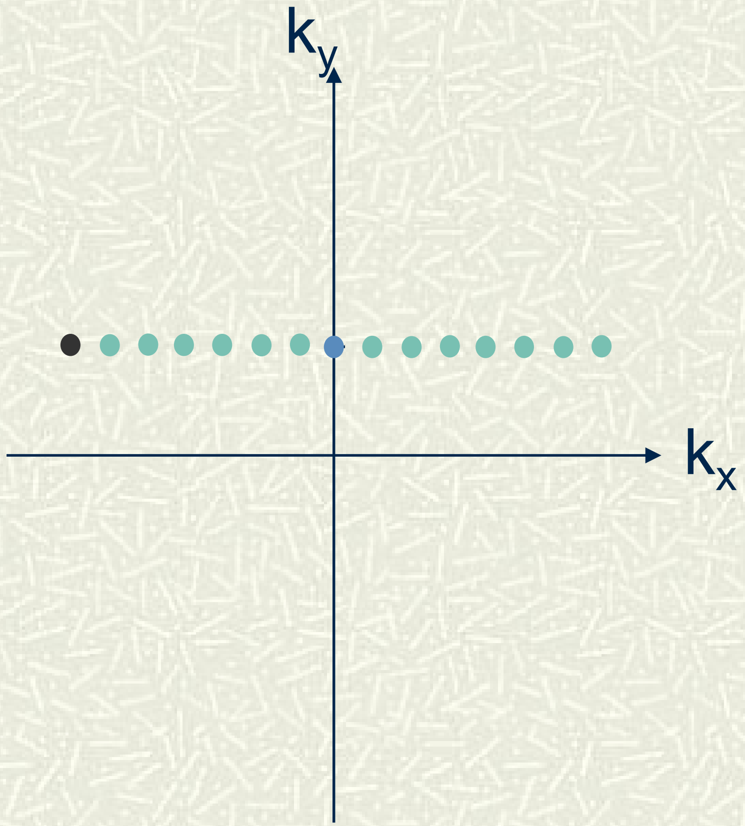


“Phase encoding”



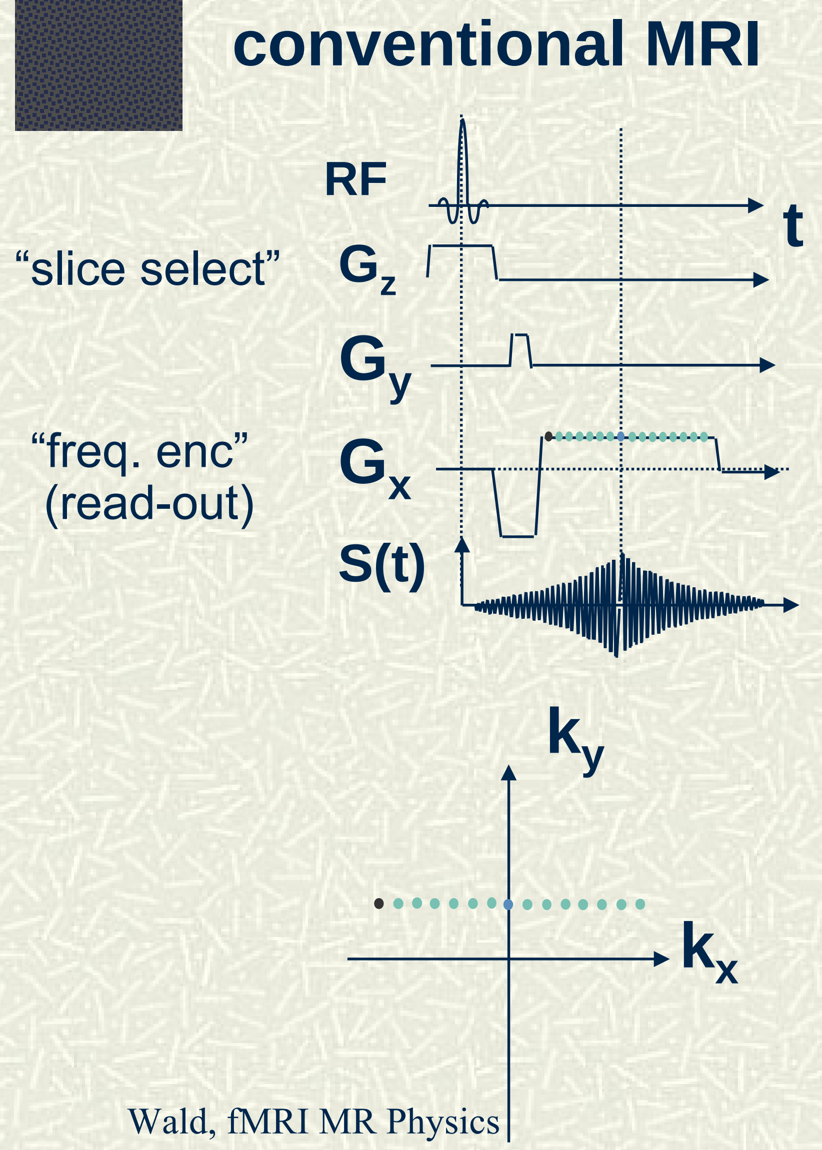
“Spin-warp” encoding

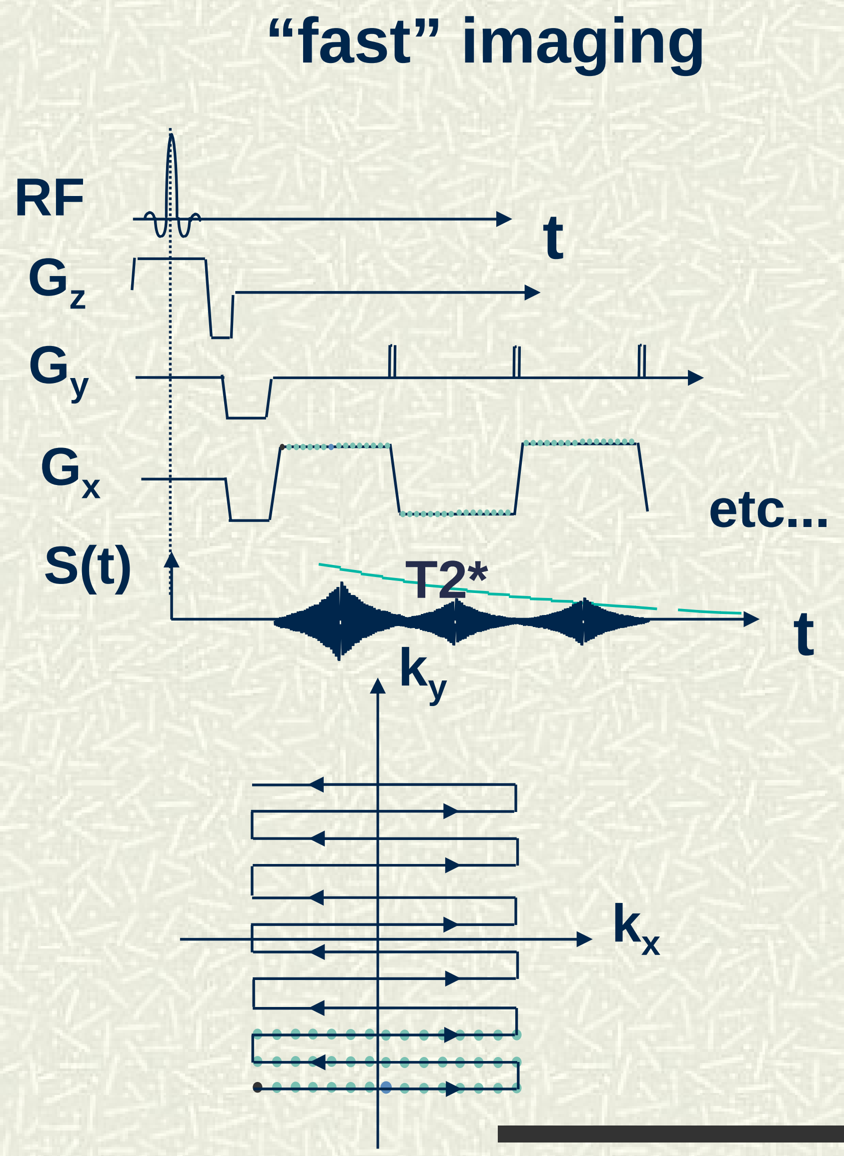




one excitation, one line of kspace...

What's the difference?





"Echo-planar" encoding

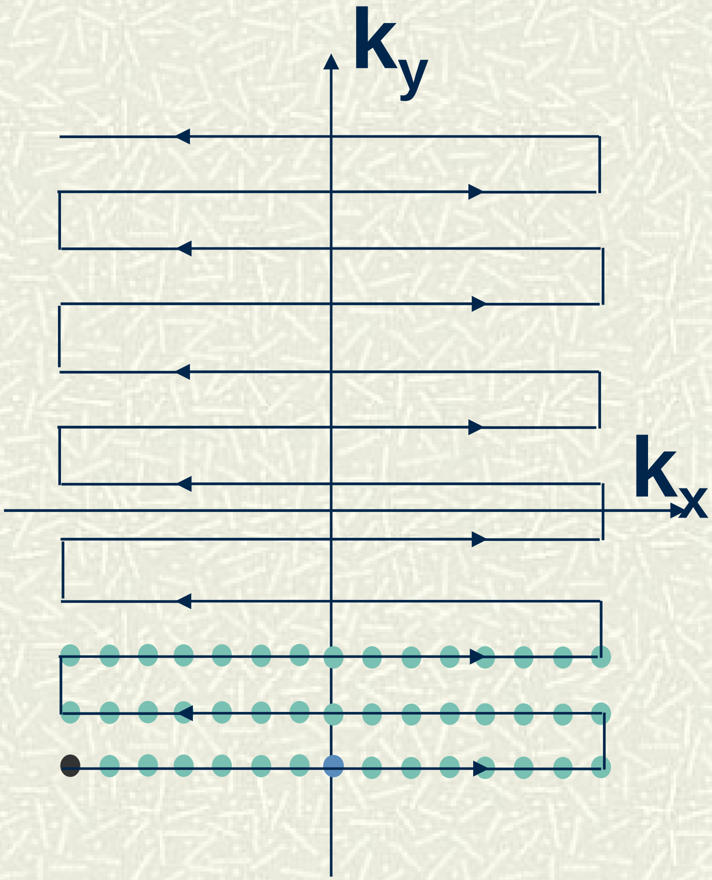
Observations:

• Adjacent points along kx are taken with short Δt (= 5 us). (high bandwidth)

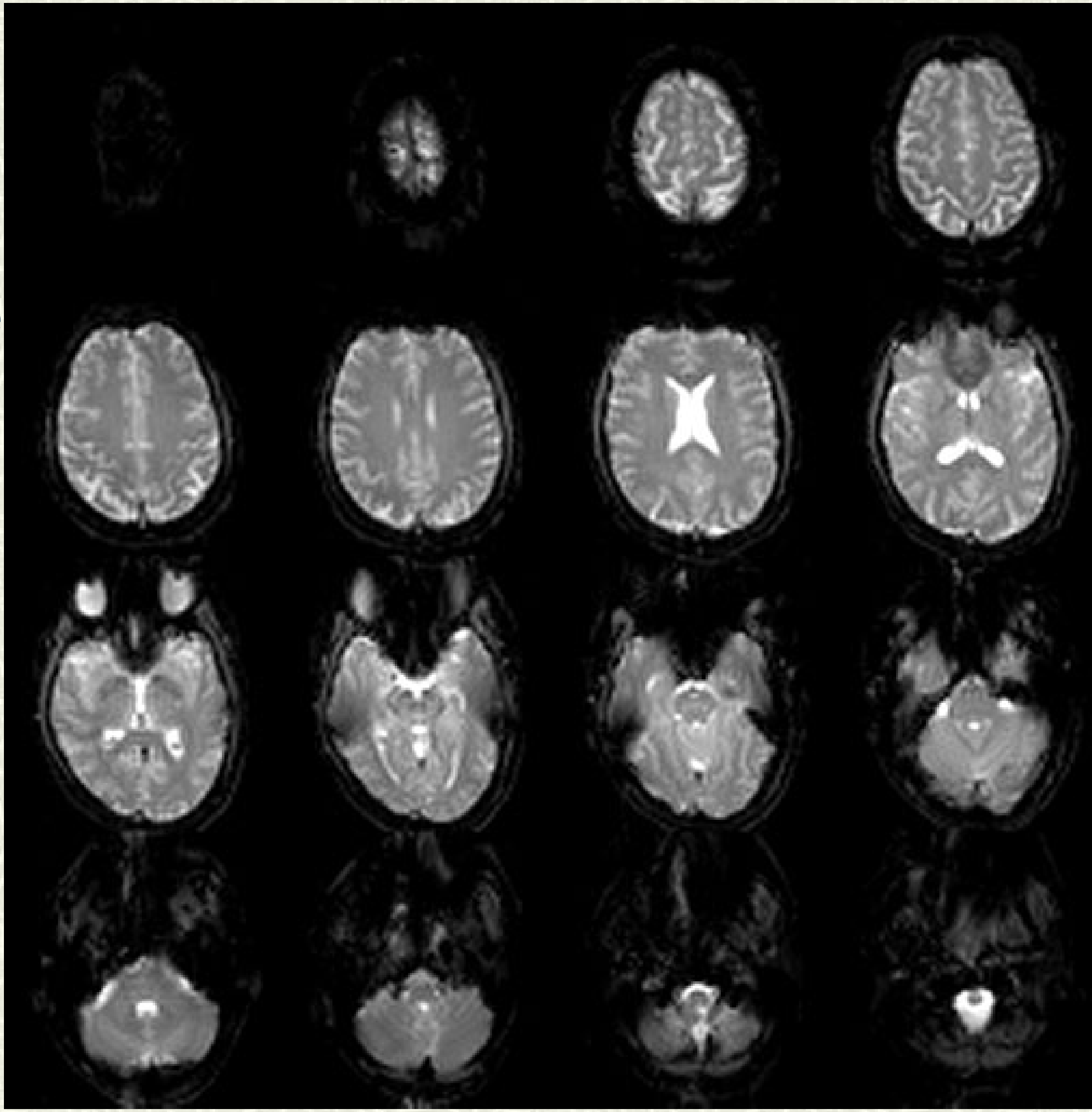
• Adjacent points along ky are taken with long Δt (= 500us). (low bandwidth)

• A given line is read quickly, but the total encode time is longer than conventional Imaging.

• Adjacent lines are traversed in opposite directions.



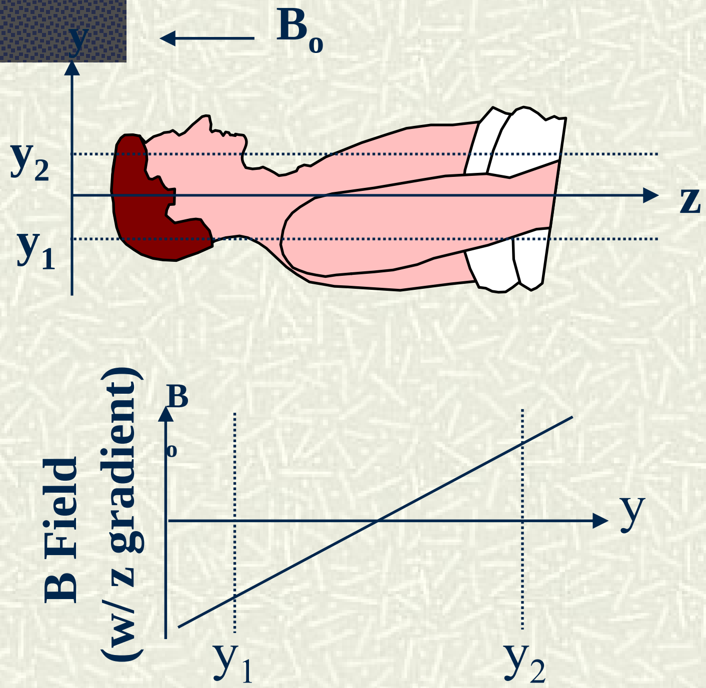
Drawbacks of Single Shot Imaging

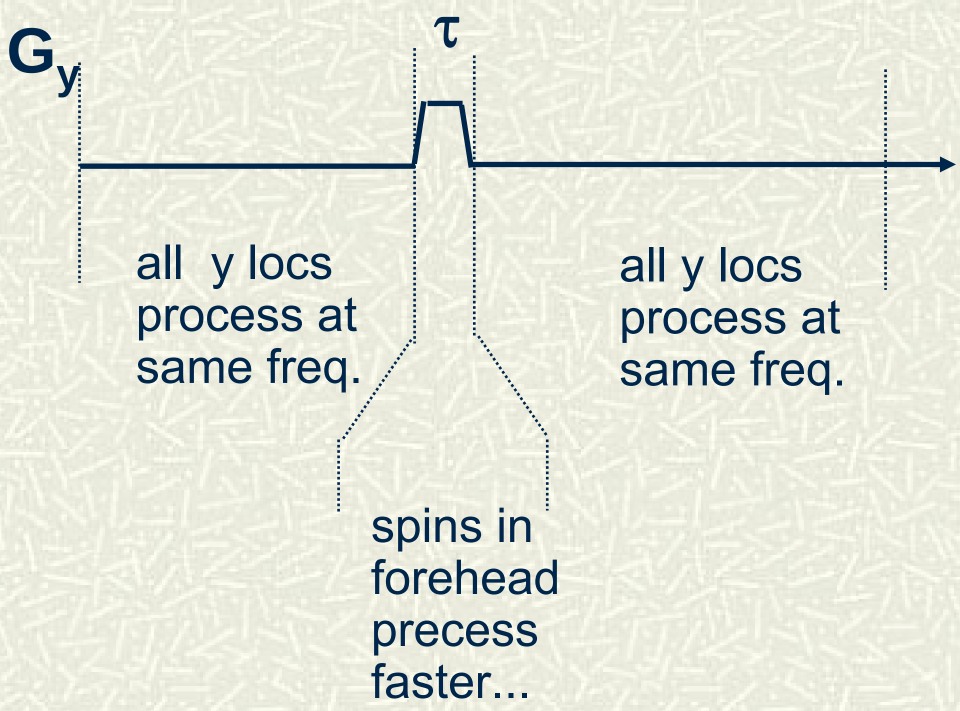


- Require high gradient performance to eliminate susceptibility induced distortions.

- Susceptibility in the head is worse at 3T than 1.5T.

How does blipping on a grad. encode spatial info?

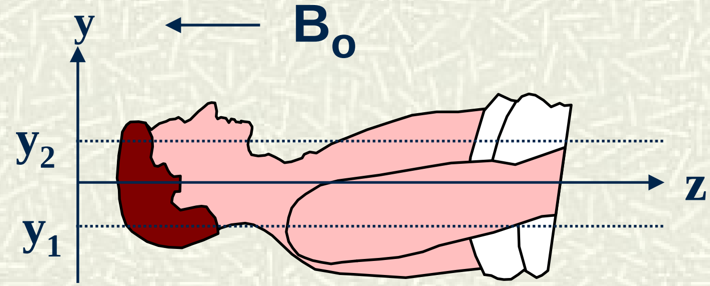




$$\upsilon(y) = \gamma B_{TOT} = \gamma (B_o + \Delta y\, G_y)$$

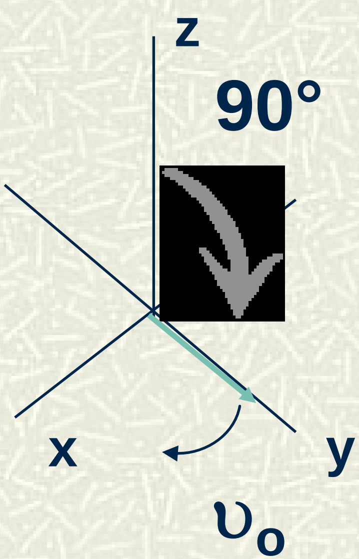
$$\Delta\theta(y) = \Delta\upsilon(y)\, t = \gamma\, \Delta y\, (G_y t)$$

How does blipping on a grad. encode spatial info?

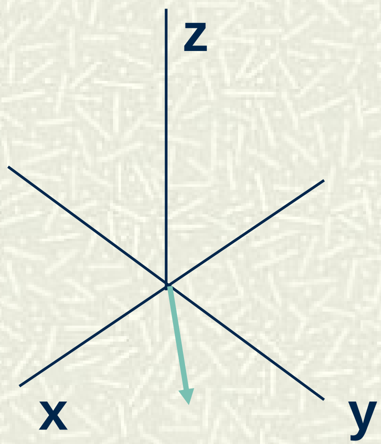


$\theta\ (y) = \upsilon(y)\ \tau \quad = \gamma\ G_y\ \Delta y\ \tau$

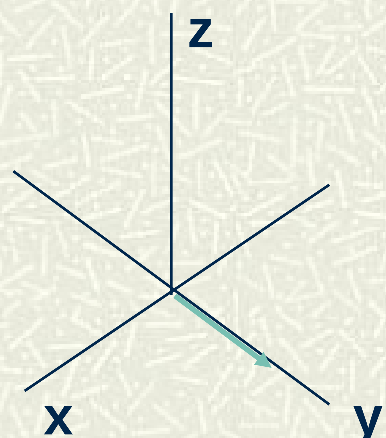
after RF



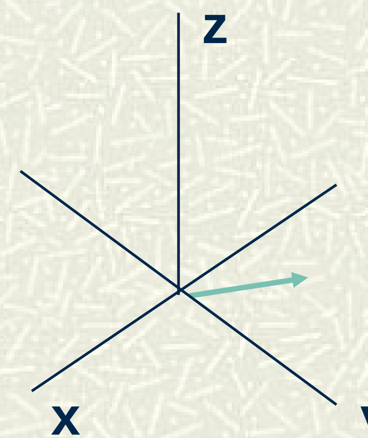
After the blipped y gradient...



position y_2



position 0

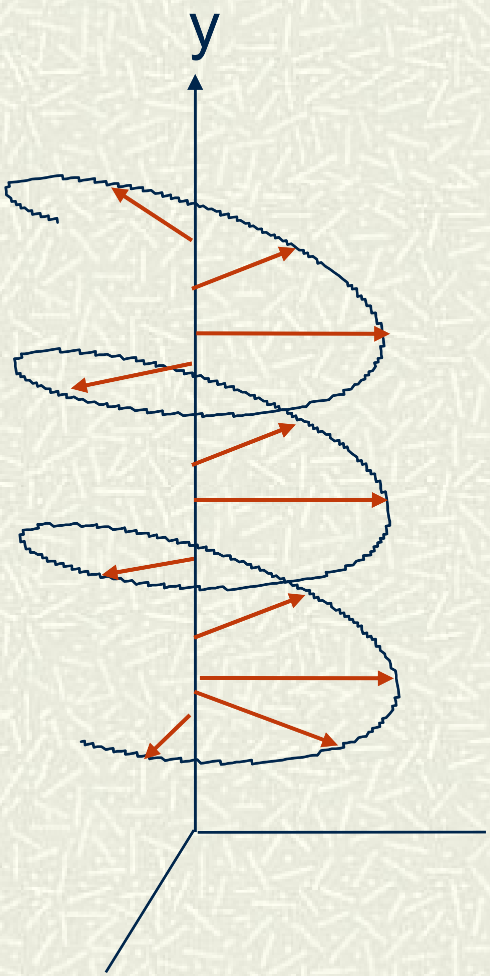


position y_1

How does blipping on a grad. encode spatial info?

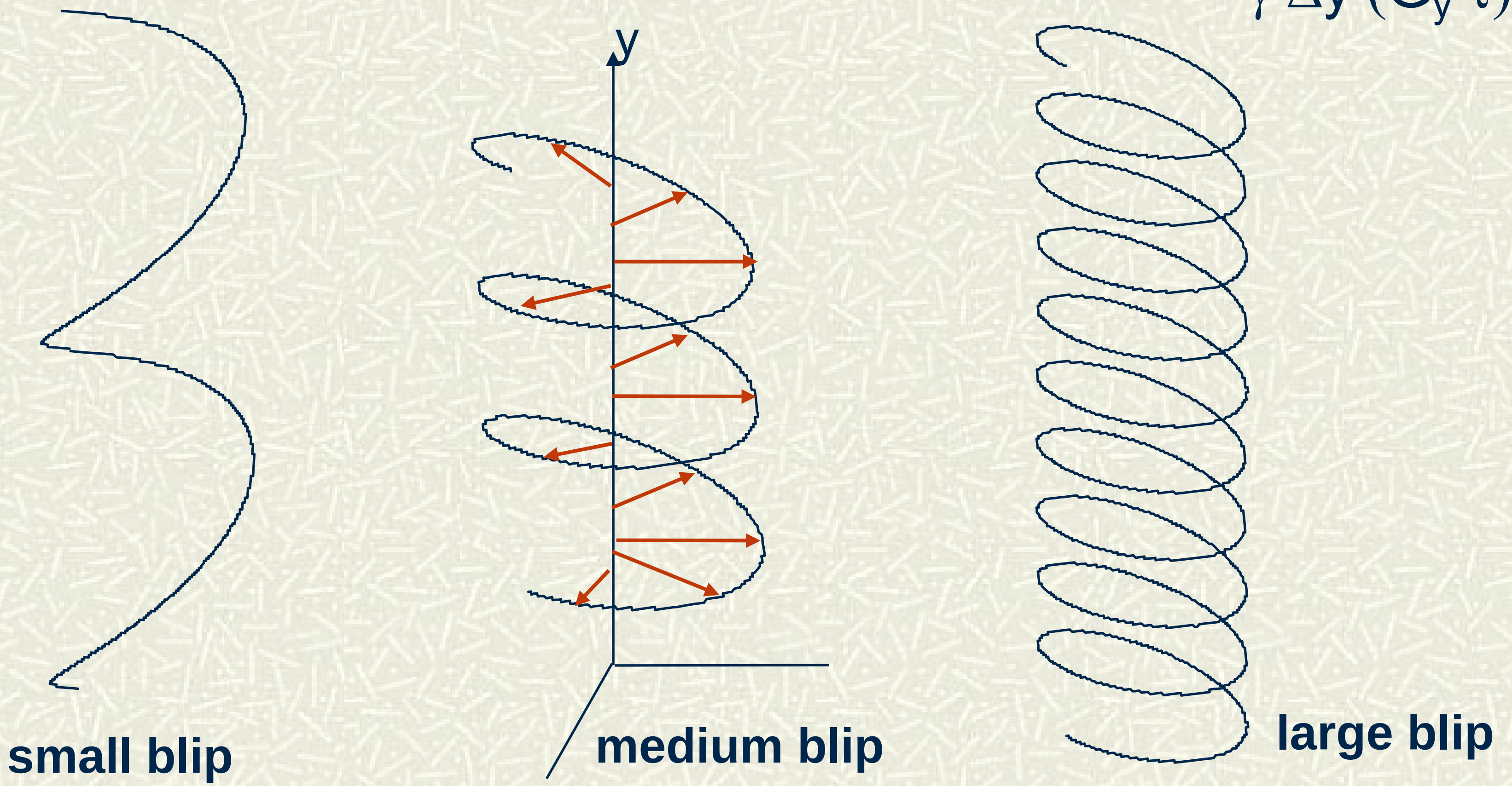
The magnetization
in the xy plane is wound into
a **helix** directed along y axis.

Phases are ‘locked in’ once
the blip is over.

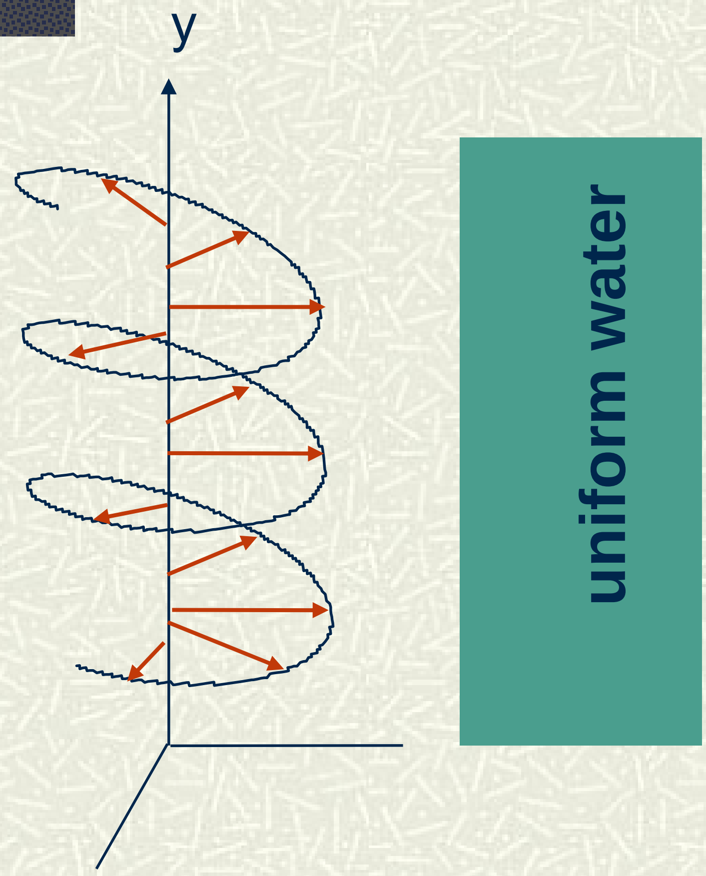


Big gradient blip area means tighter helix

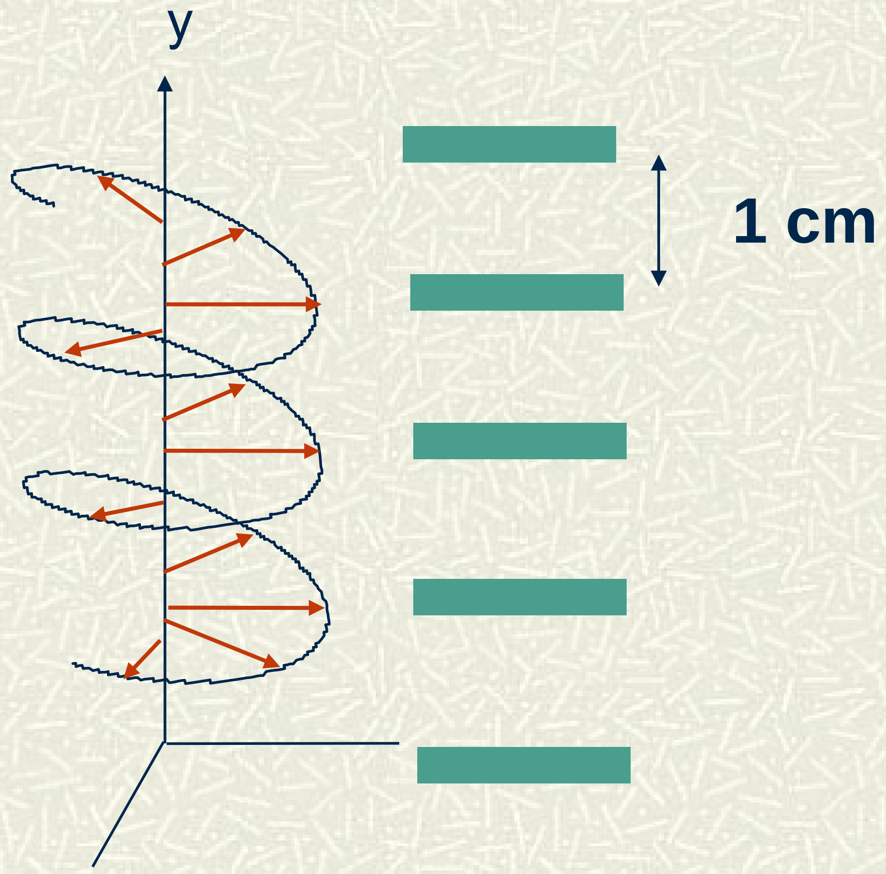
$$\theta(y) = \upsilon(y)\,\tau$$
$$= \gamma\, G_y\, \Delta y\, \tau$$
$$= \gamma\, \Delta y\, (G_y\, \tau)$$



Signal after the blip: Consider 2 samples:

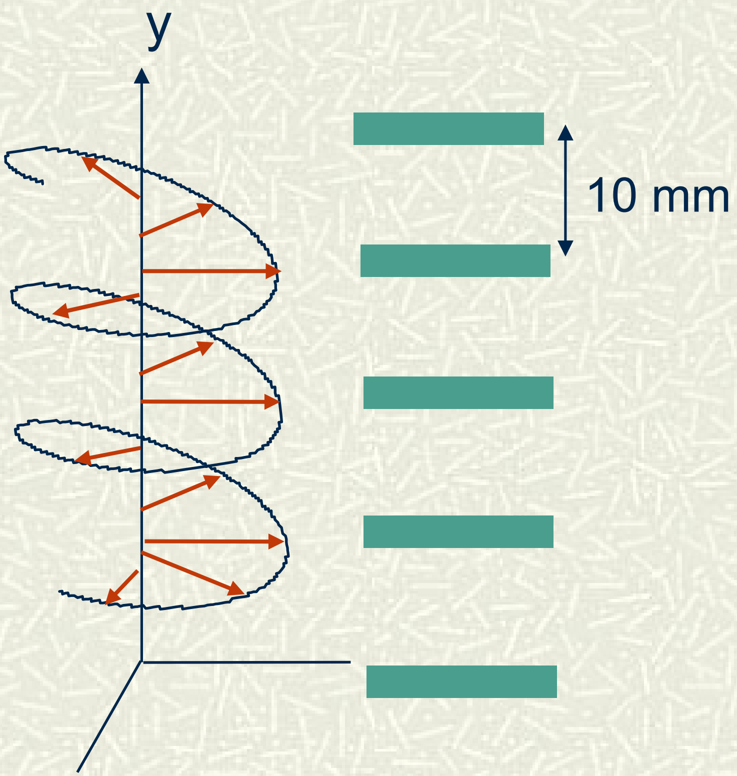


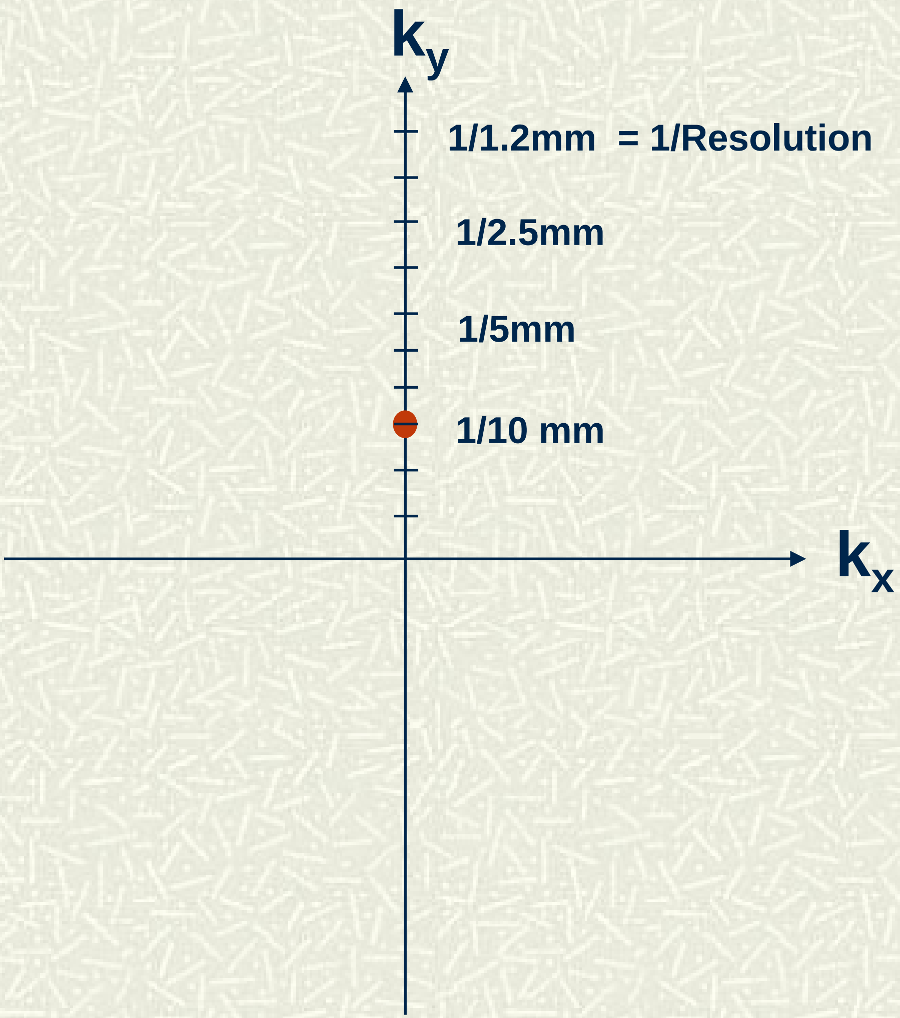
no signal observed



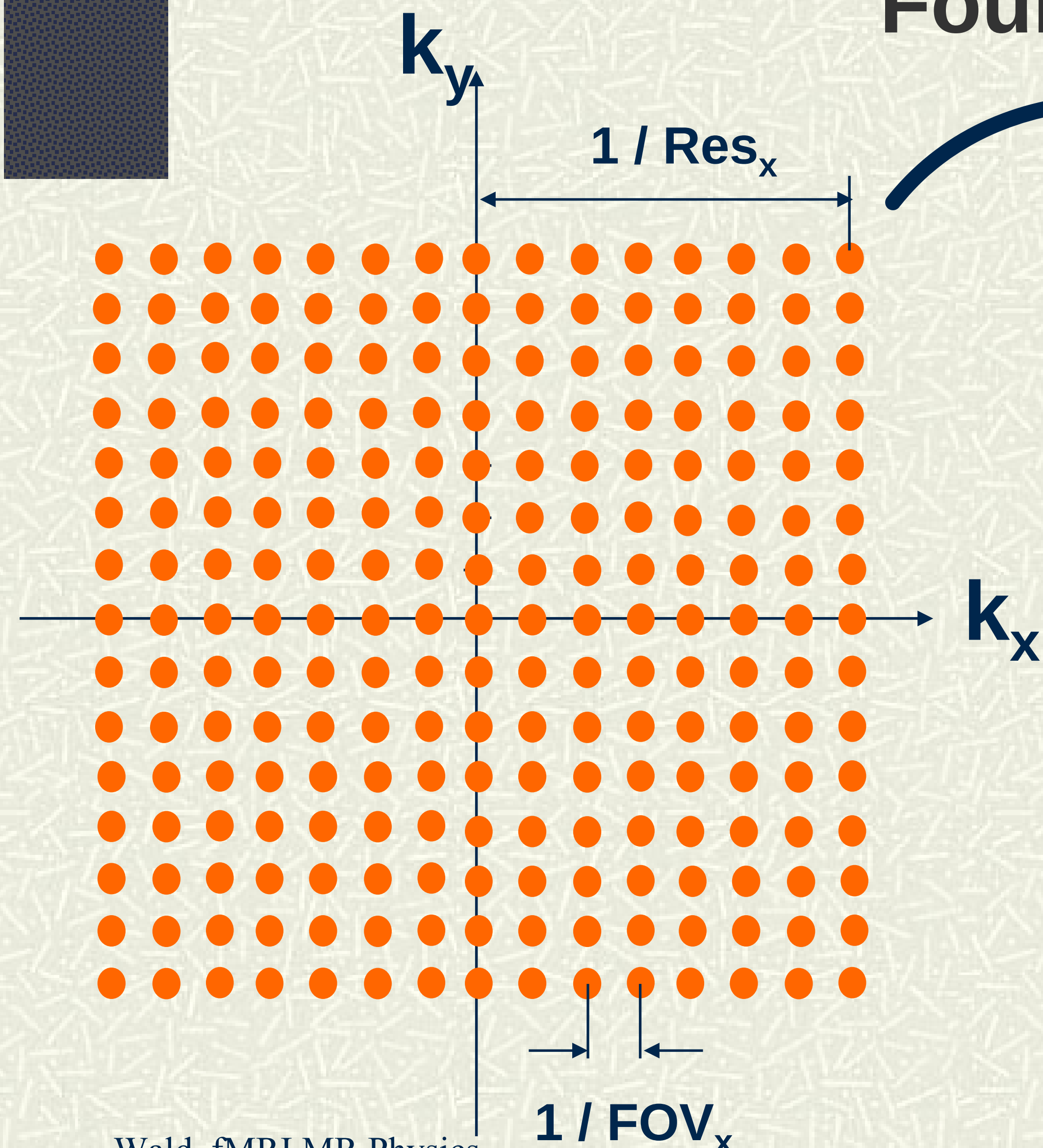
signal is as big as if no gradient

You've measured: intensity at a spatial frequency...



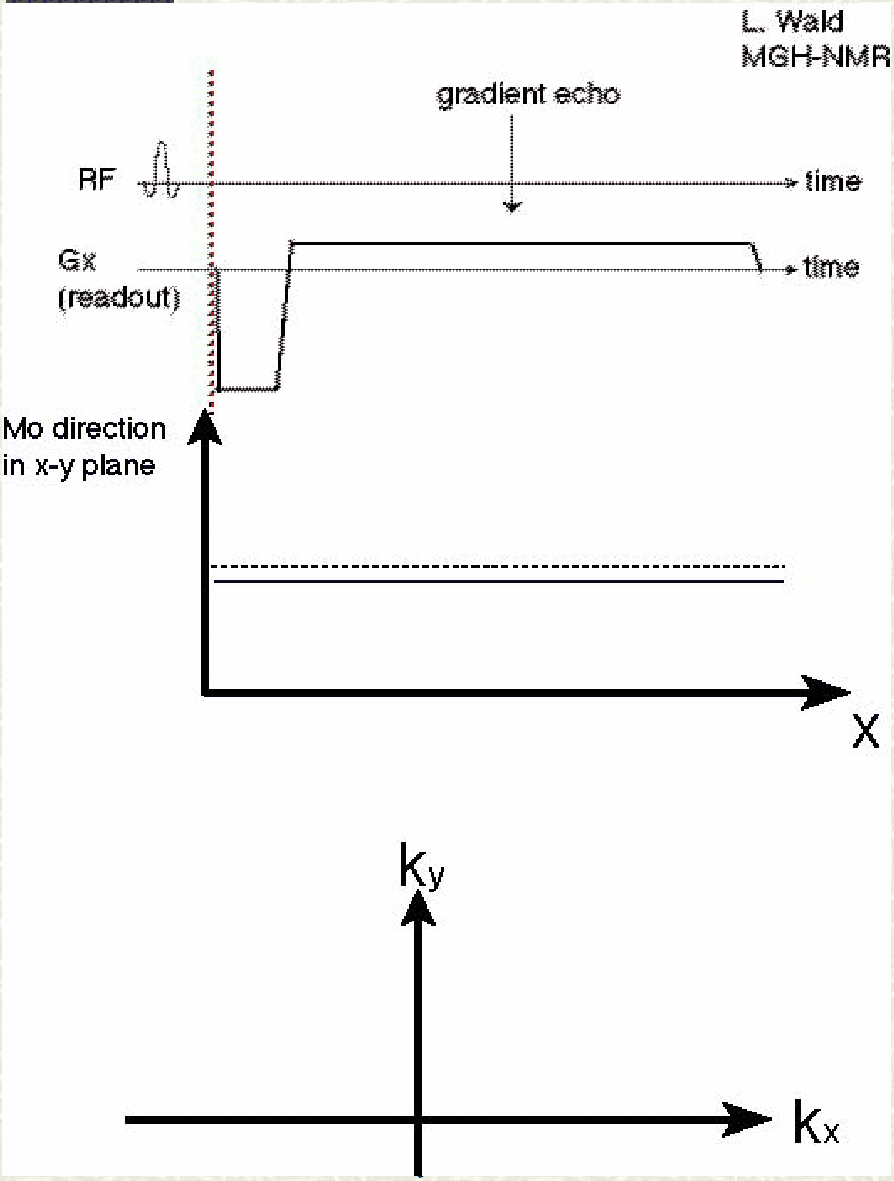


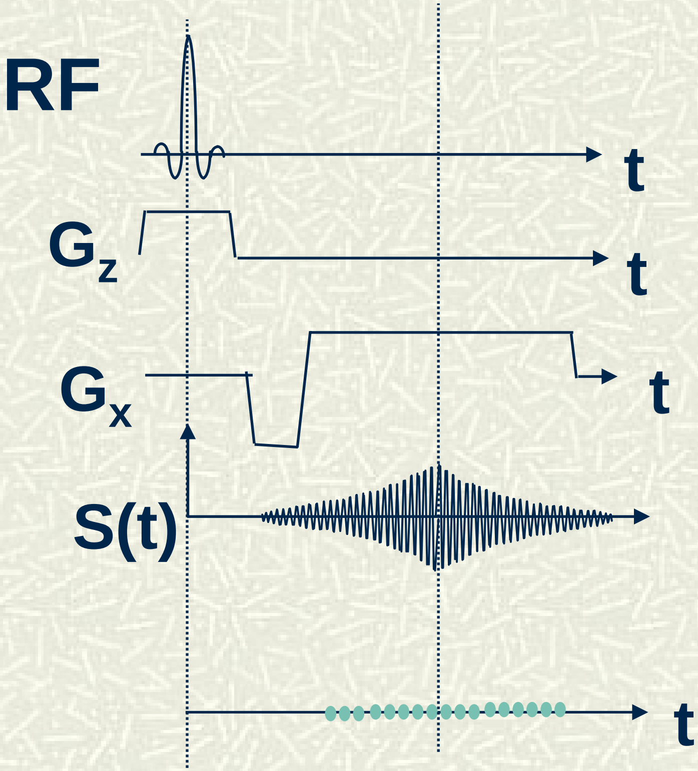
Fourier transform



FOV_x = matrix * Res_x

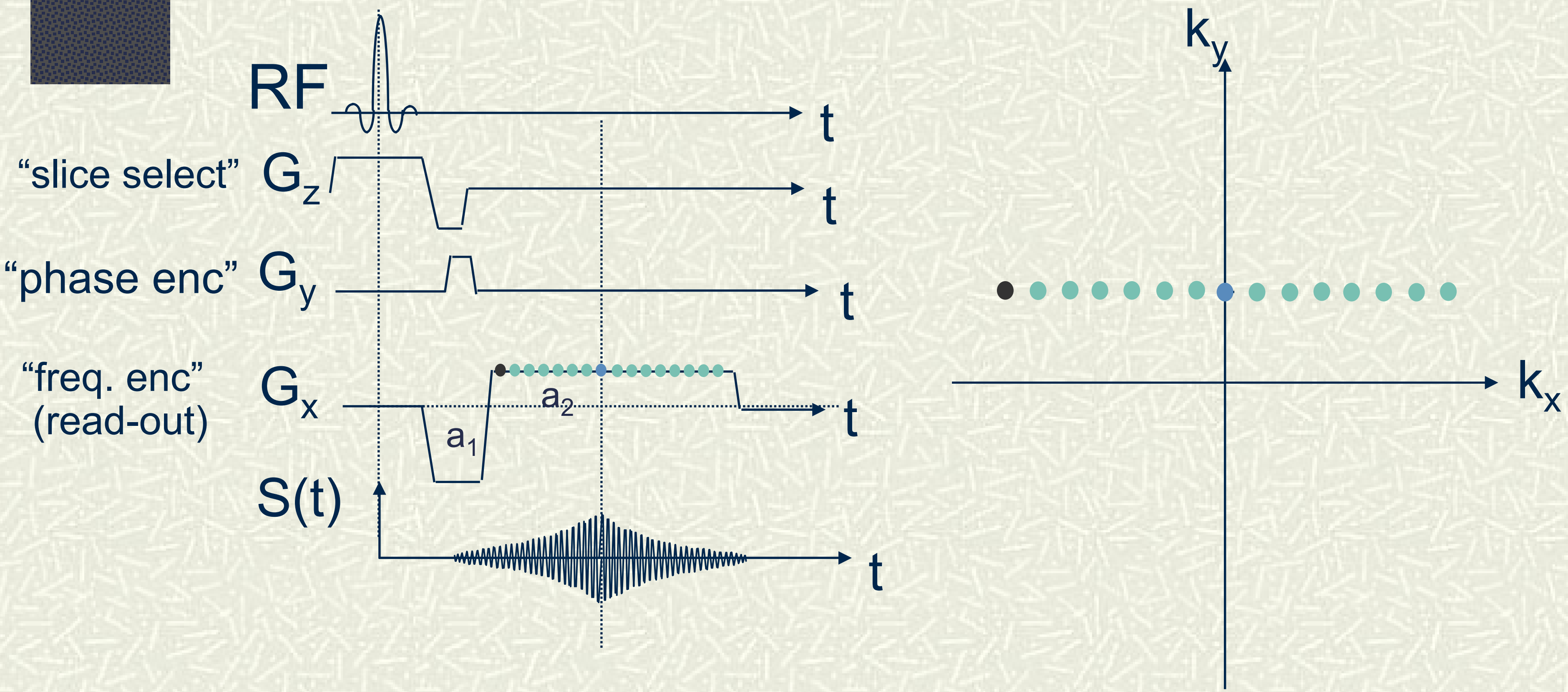
Frequency encoding revisited





Kspace, the movie...

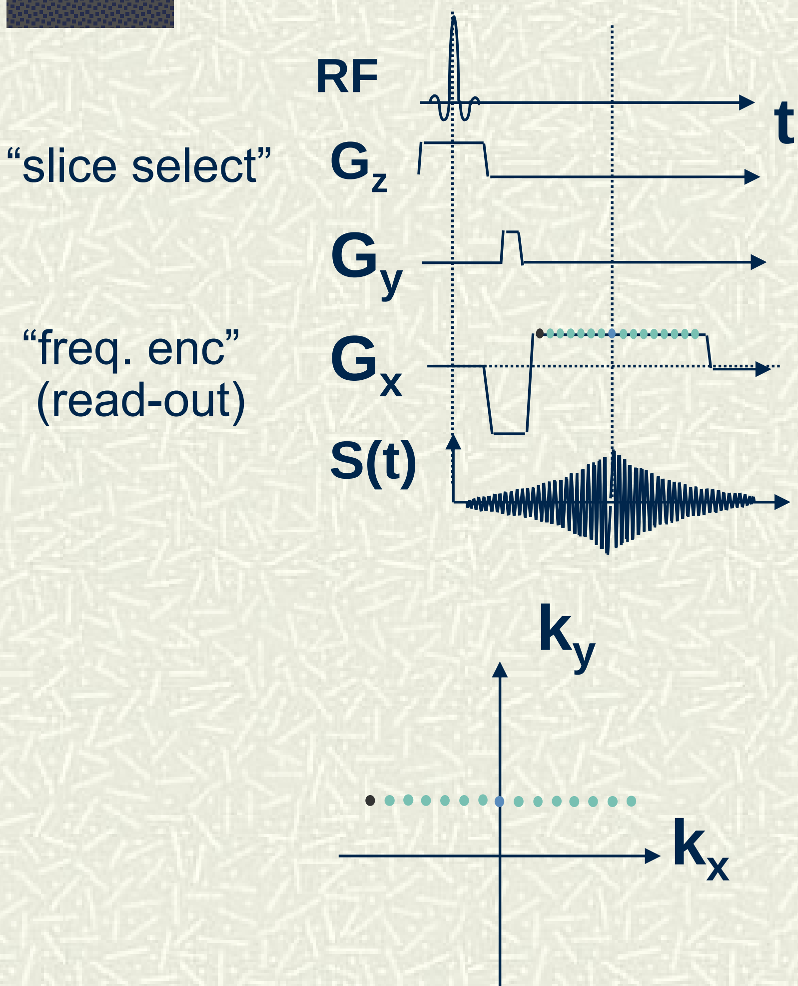
“Spin-warp” encoding



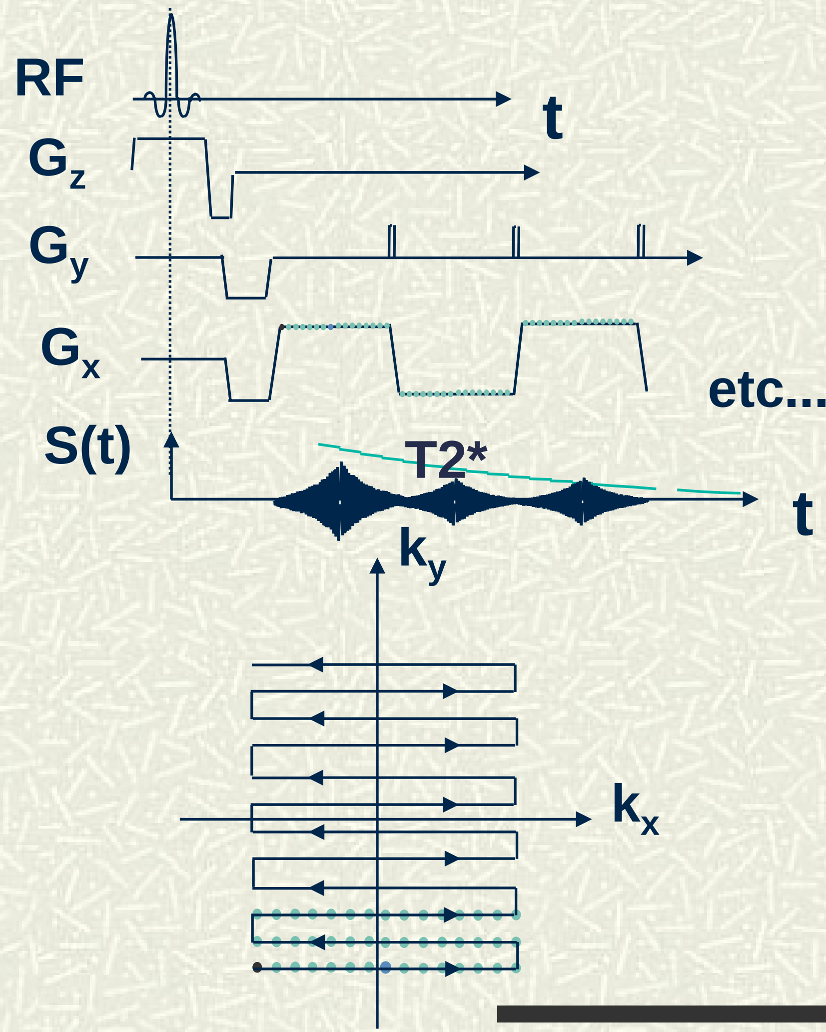
one excitation, one line of kspace...

What's the difference?

conventional MRI



"fast" imaging



"Spin-warp" encoding mathematics

Keep track of the phase...

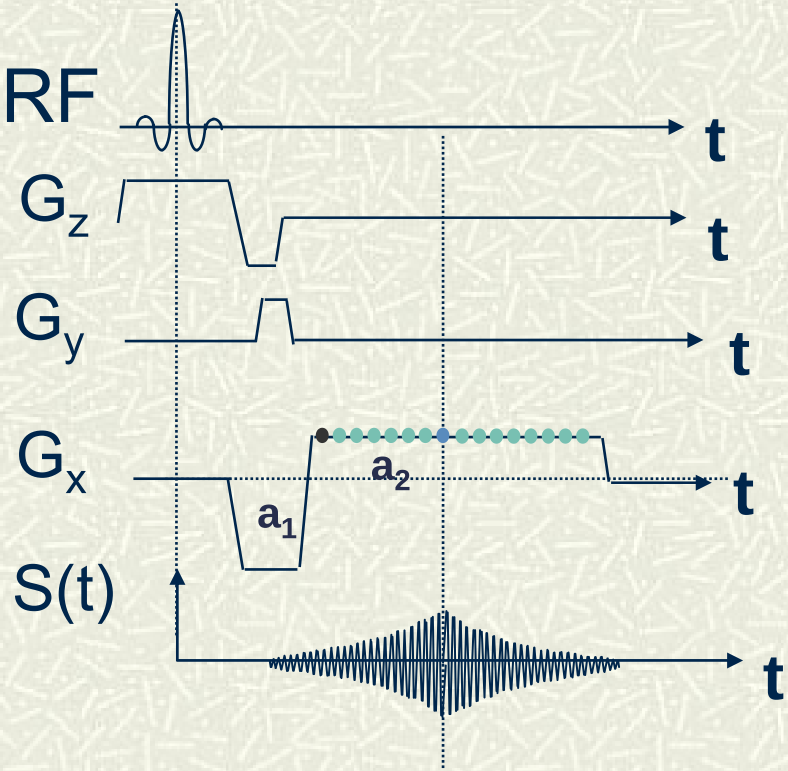
Phase due to readout:

$$\theta(t) = \omega_o t + \gamma\ G_x x t$$

Phase due to P.E.

$$\theta(t) = \omega_o t + \gamma\ G_y y \tau$$

$$\Delta\theta(t) = \omega_o t + \gamma G_x x t + \gamma\ G_y y \tau$$



"Spin-warp" encoding mathematics

Signal at time t from location (x,y)

$$S(t) = \rho(x,y)e^{i\gamma G_x xt + i\gamma G_y y\tau}$$

The coil integrates over object:

$$S(t) = \iint_{object} \rho(x,y)e^{i\gamma G_x xt + i\gamma G_y y\tau}dxdy$$

Substituting $k_x = -\gamma\ G_x\ t$ and $k_y = -\gamma\ G_y\ t$:

$$S(k_x, k_y) = \iint_{object} \rho(x,y)e^{-ik_x x - ik_y y}dxdy$$

"Spin-warp" encoding mathematics

View signal as a matrix in k_x, k_y…

$$S(k_x, k_y) = \iint_{object} \rho(x,y) e^{-ik_x x - ik_y y} dxdy$$

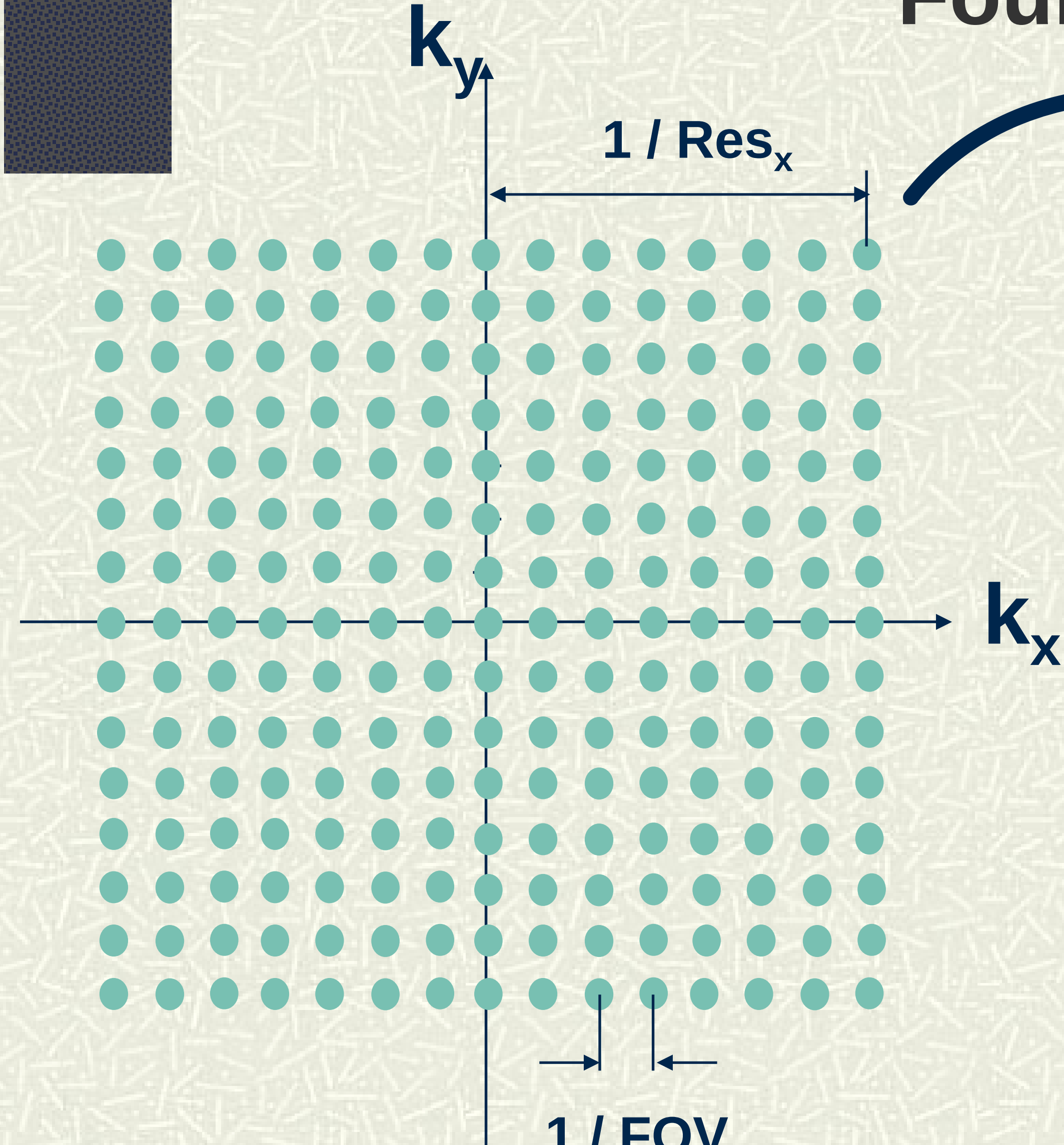
:

Solve for $\rho(x,y,)$

$$\rho(x,y) = FT^{-1}\left[S(k_x,k_y)\right]$$

$$\rho(x,y) = \iint_{kspace} S(k_x,k_y) e^{ik_x x + ik_y y} dk_x dk_y$$

Fourier transform



FOV_x = matrix * Res_x

Blood
Oxygenation
Level
Dependant

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

Ogawa et al.

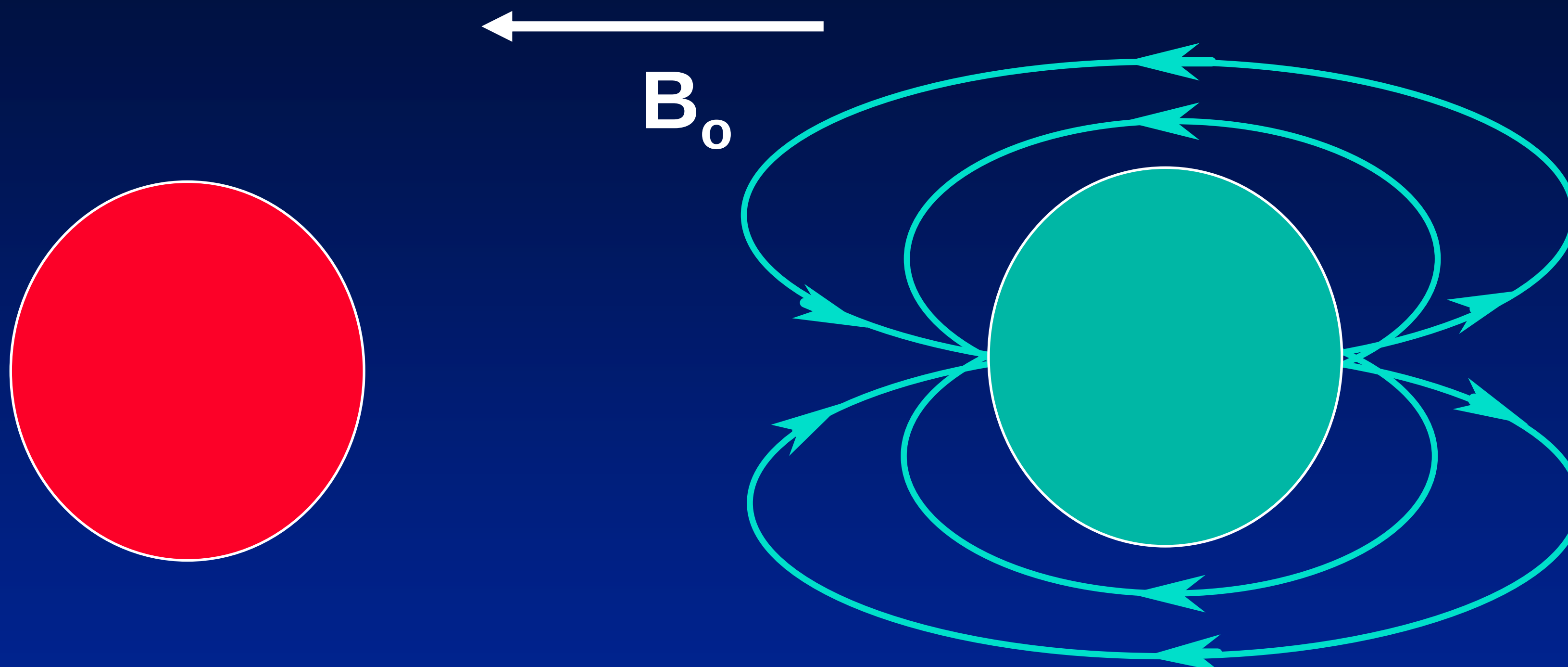
Basis of fMRI

Qualitative Changes during activation

Observation of Hemodynamic Changes

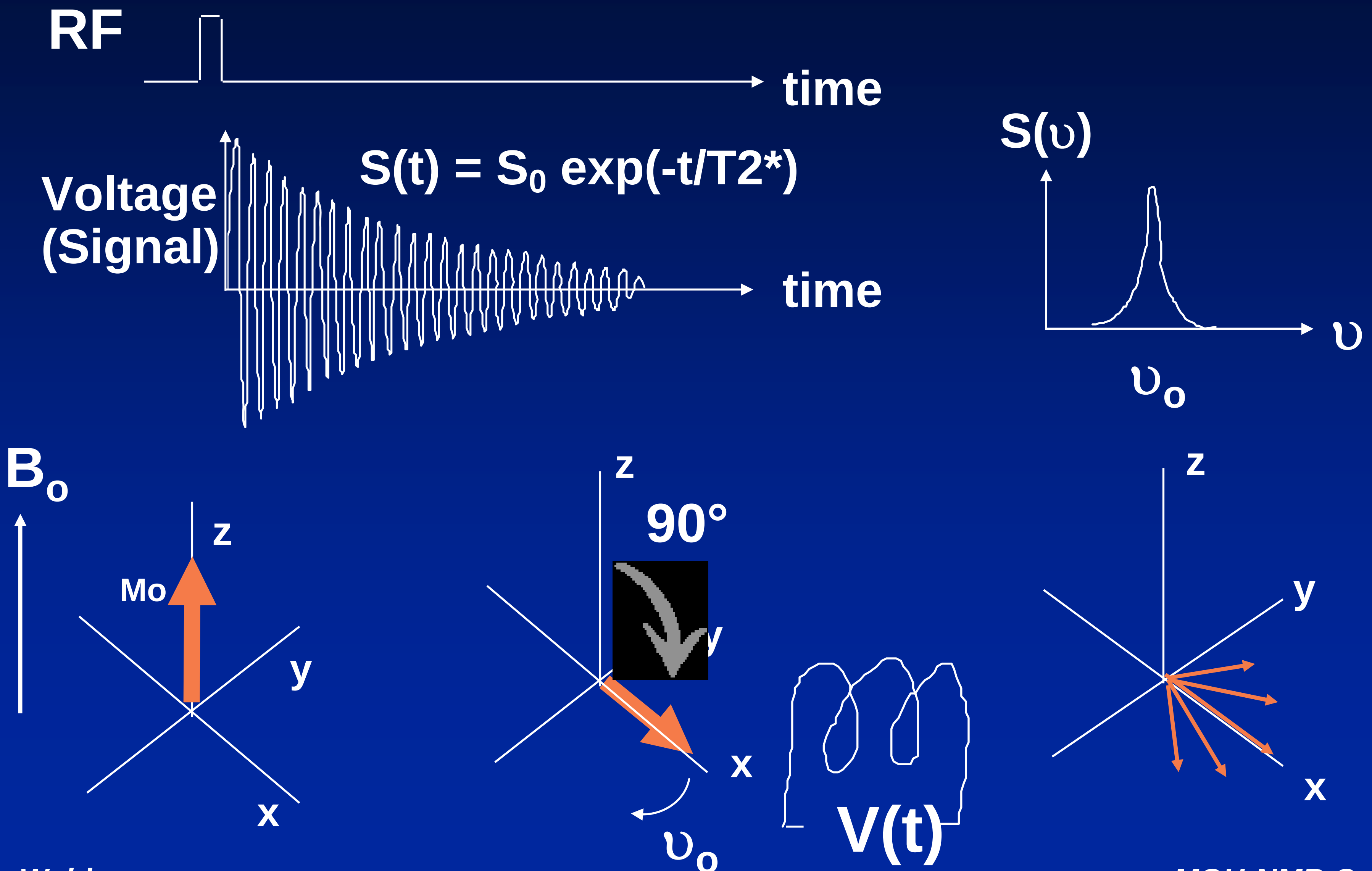
- **Direct Flow effects**
- **Blood Oxygenation effects**

Field Homogeneity and Oxygen State

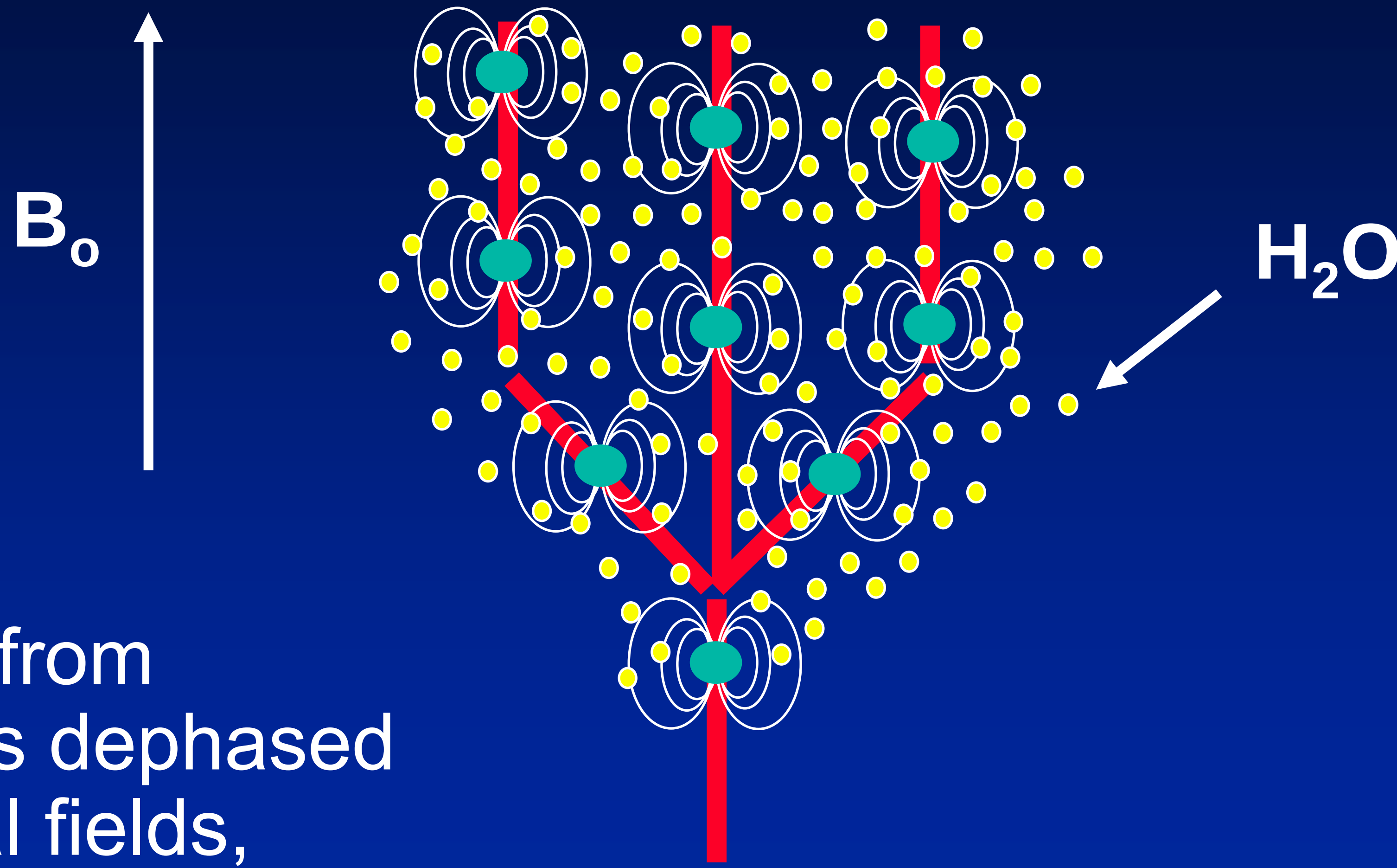


Oxygenated Red Cell **de-Oxygenated Red Cell**

BOLD: blood effects T2*



Addition of paramagnetic compound to blood



Signal from water is dephased by local fields, T_2* shortens, S goes down on EPI

Addition of paramagnetic compound to blood

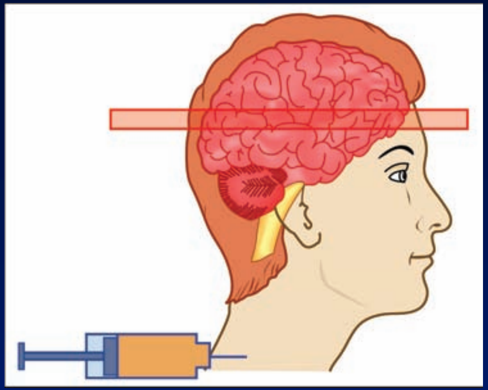
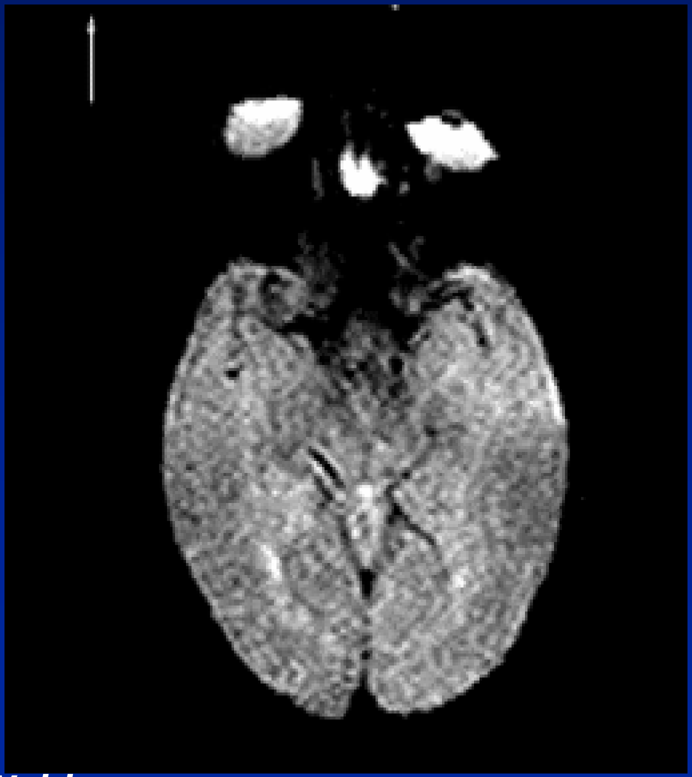
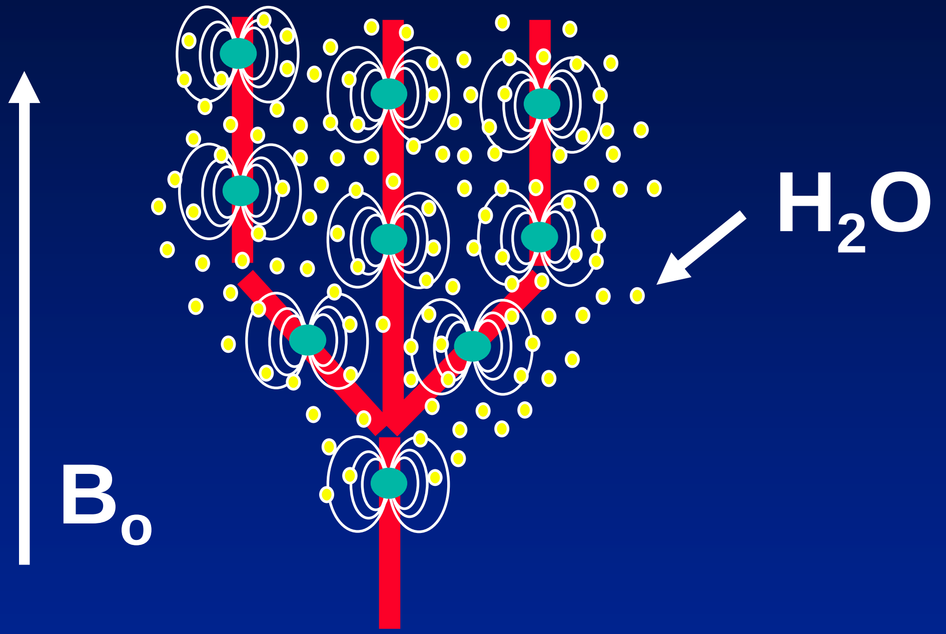


Figure by MIT OpenCourseWare.





Signal from water is dephased by local fields (T2* shortens), S goes down on EPI

Magnetic stuff ↑ MR signal↓

Conversely,

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

Magnetic stuff ↓ MR signal ↑

What happens during neuronal activation?

Neuronal Activation . . .

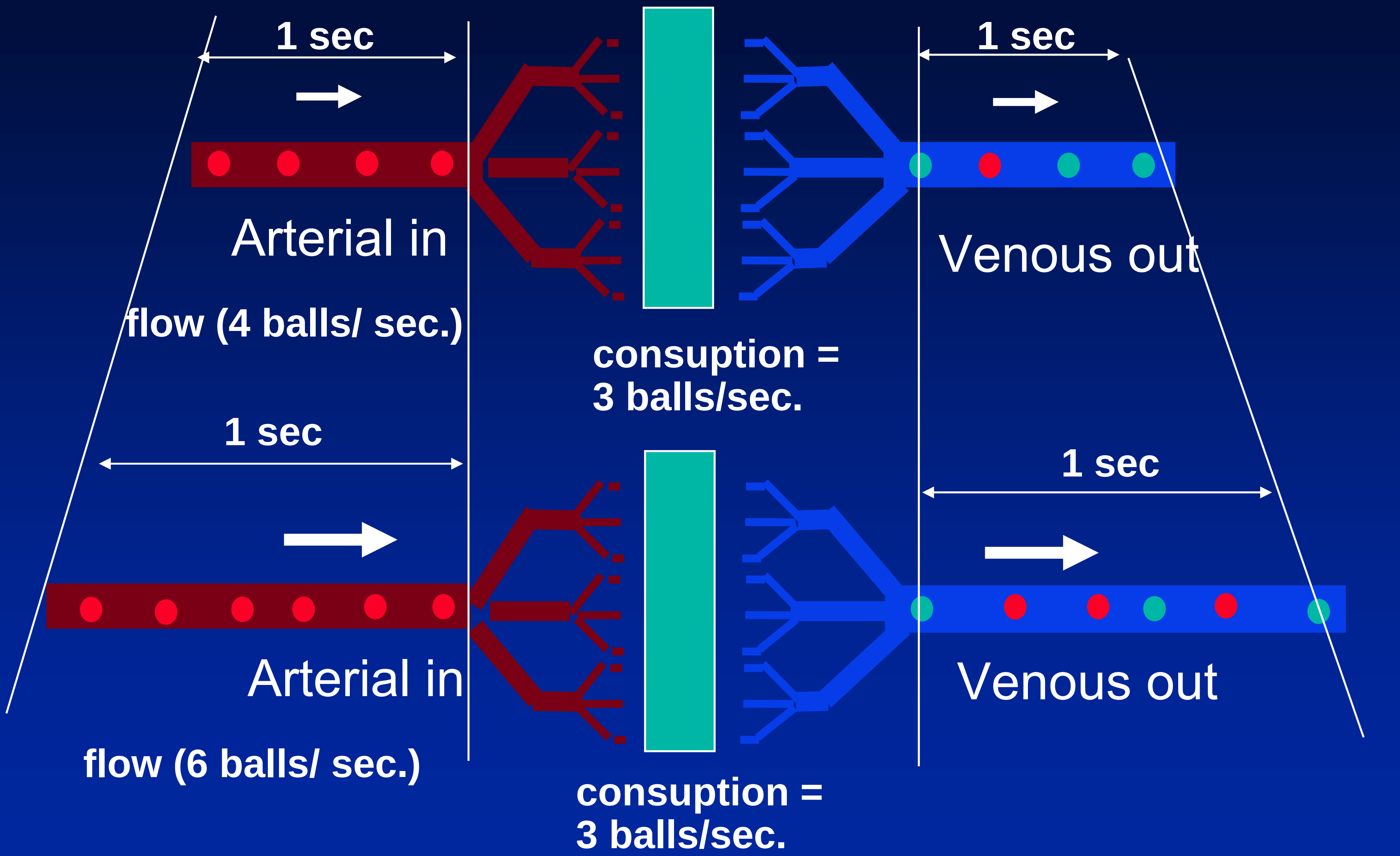
Produces *local* hemodynamic changes
(Roy and Sherrington, 1890)

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" or flow 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?

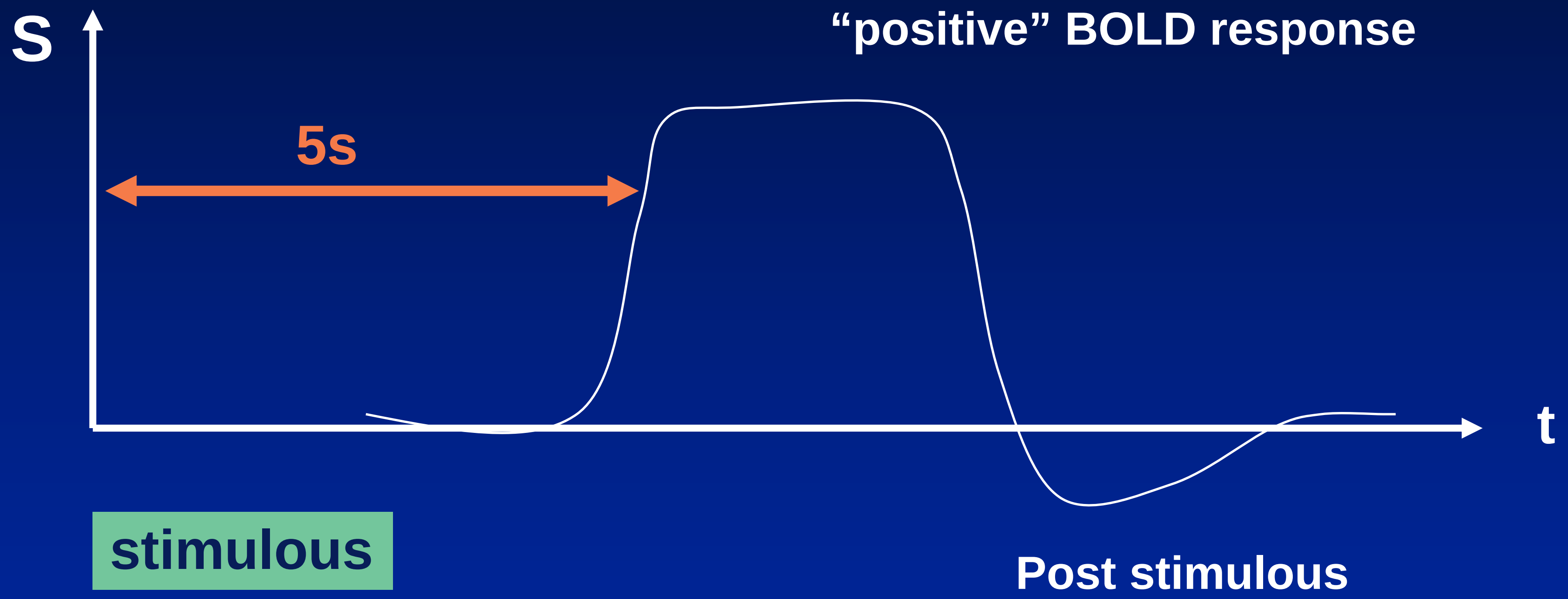
No real paradox: as flow↑ oxygen extraction is hampered by decreased capillary transit time.

The simple answer is it takes a lot of flow increase…

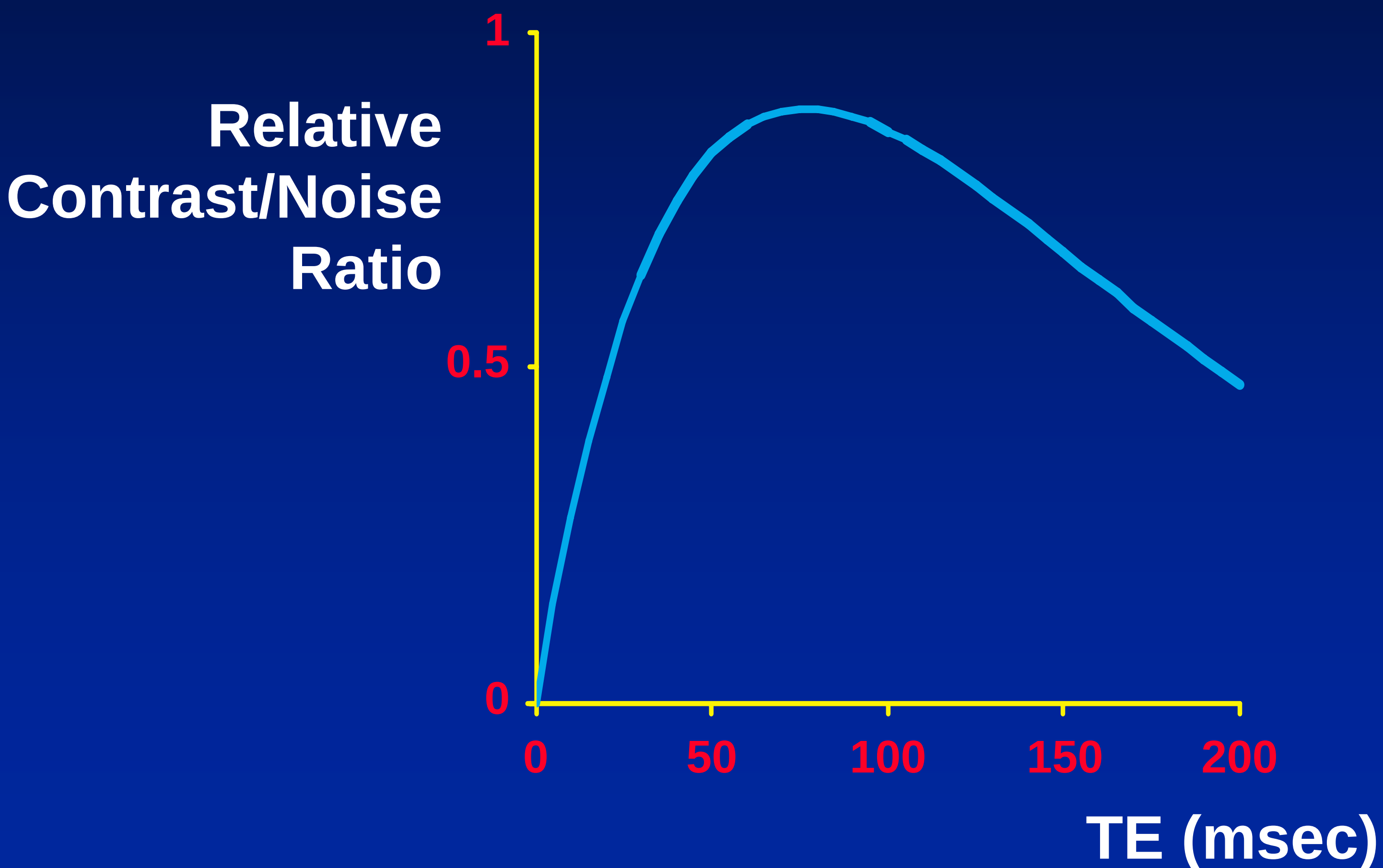
“Balloon model”

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

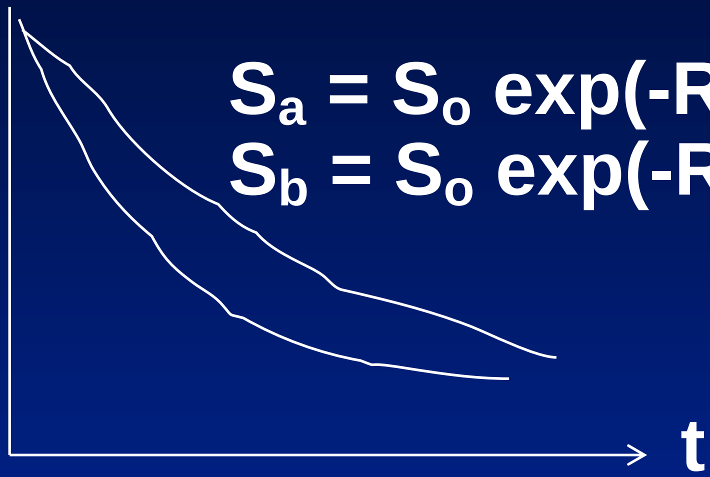
Time response of BOLD



Contrast/Noise Ratio and Echo Time (TE)



Contrast/Noise Ratio and Echo Time (TE)



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

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

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

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

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

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

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

$$t = 1/R_a$$

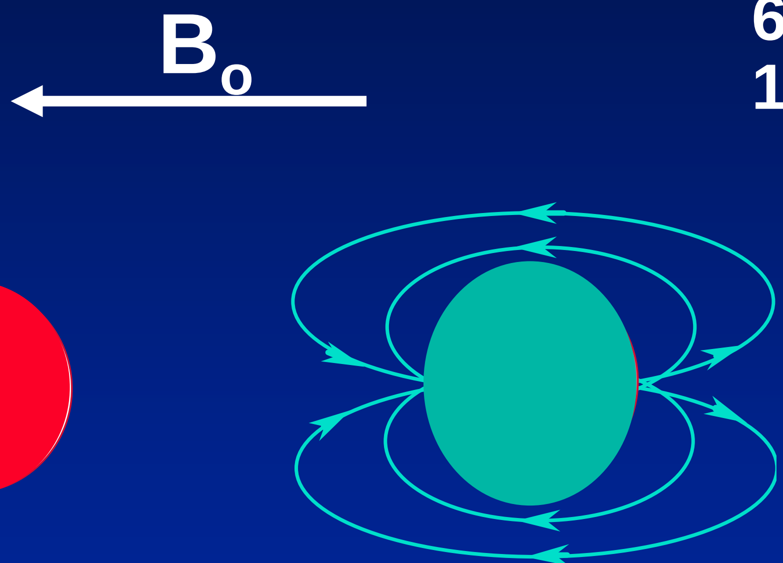
$$TE = T_{2a}^*$$

Signal dephasing changes that accompany activation (BOLD effect)

a more detailed look…

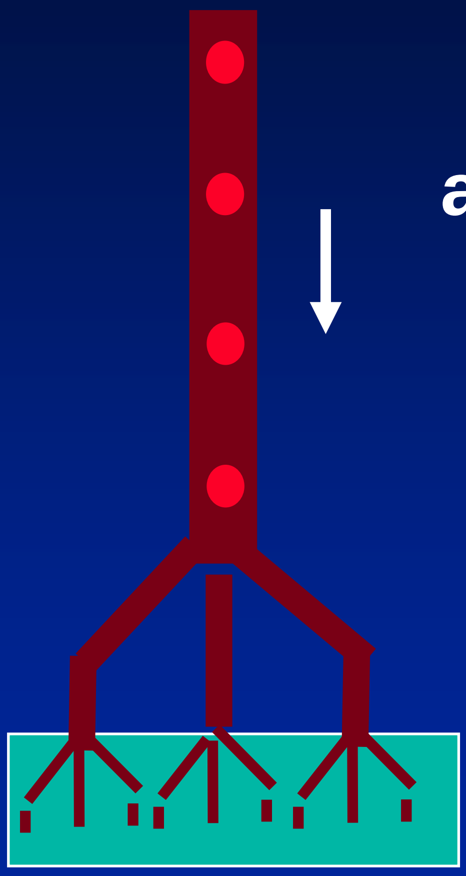
Internal contrast agent: the deoxygenated red blood cell

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



Oxygenated Red Cell **de-Oxygenated Red Cell**

Brain: Arterial side



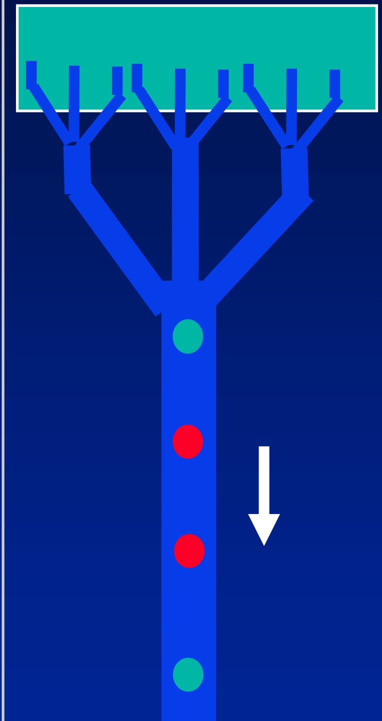
artery

- Capillaries are long and skinny, randomly oriented

- O_2 exchange is in capillary

Arterioles,	**25um dia.,**
Capillary,	**6um dia.,**

Brain: venous side



Venules, 25-50um dia.,

Collecting veins

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, but many veins on surface

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 H_20 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.

Which contributes more to BOLD signal?

T2 or T2* changes?

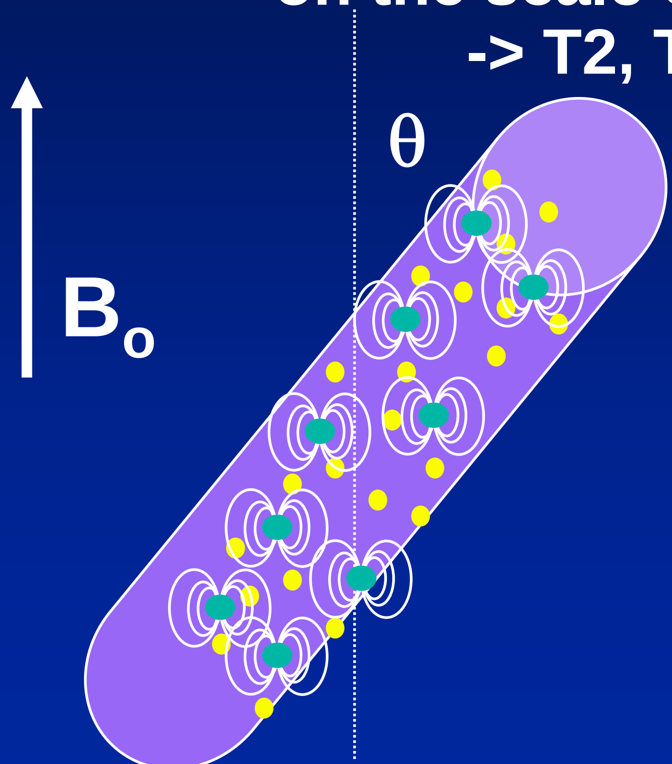
T2 changes require the water dynamically move in a local field distribution.

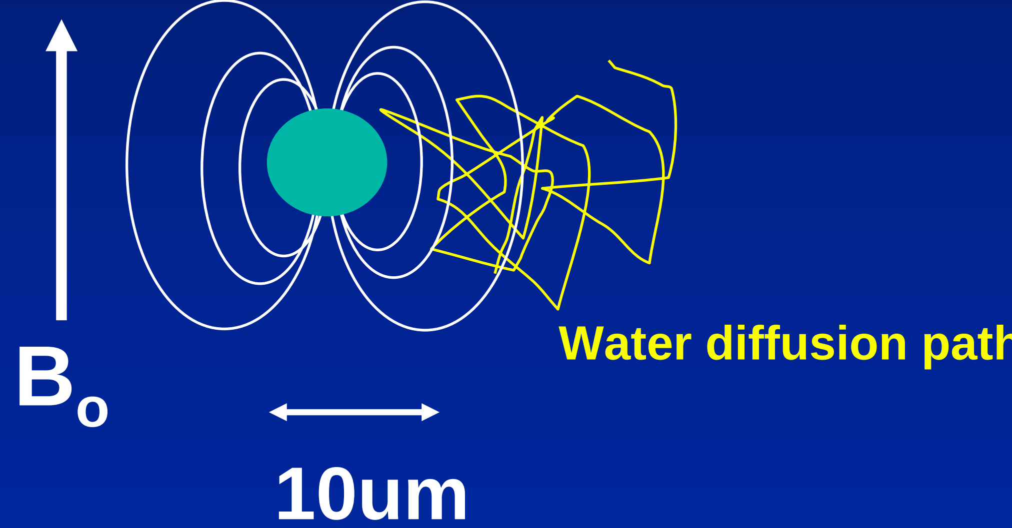
Water diffuses ~25um during encoding.

If field is changing in 25um scale, water will see dynamic dephasing (not refocused by spin echo).

Intravascular:
T2 or T2* changes?

Both: Field around red blood cell changes on the scale of mean free path of water
-> T2, T2* shortens in vessel.





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

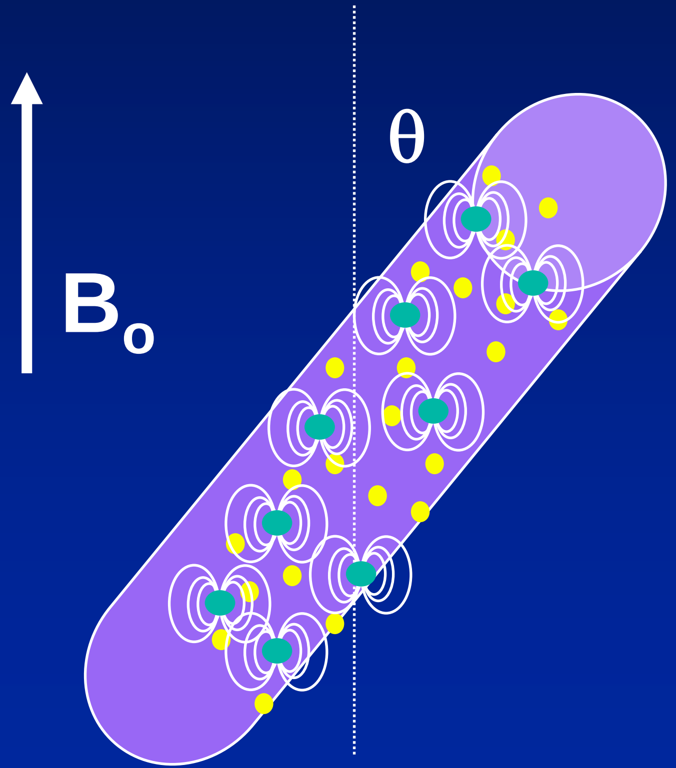
Empirical and Monte Carlo simulations:

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

Blood becomes darker on SE at high field…

Intravasculature: T2* changes

Consider the vessel as uniformly magnetized.
Distribution of angular orientations inside voxel.



Field inside vessel:

$$\Delta\nu = \alpha B_o (1 - 3\cos^2\theta)[1 - O_2Sat]$$

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

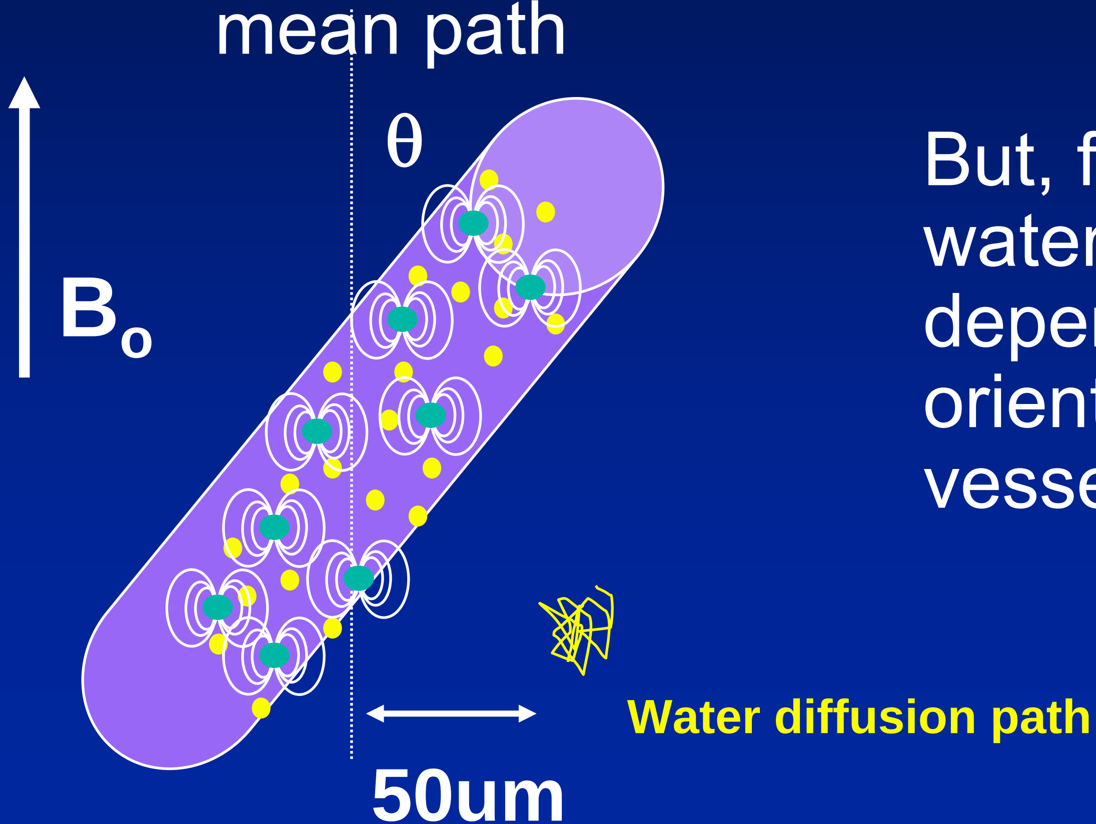
Intravascular summary

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

At high enough field we expect T2 to get very short inside vessels.

Extravascular: T2 or T2* changes?

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

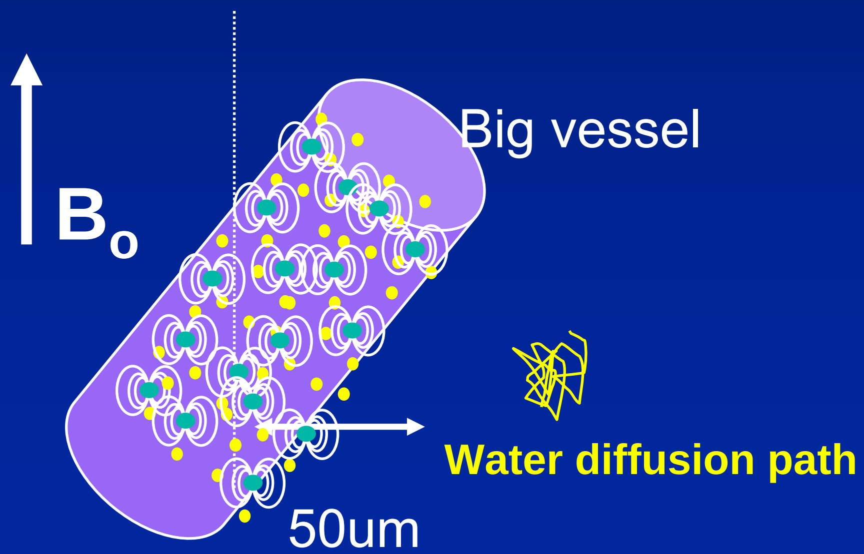


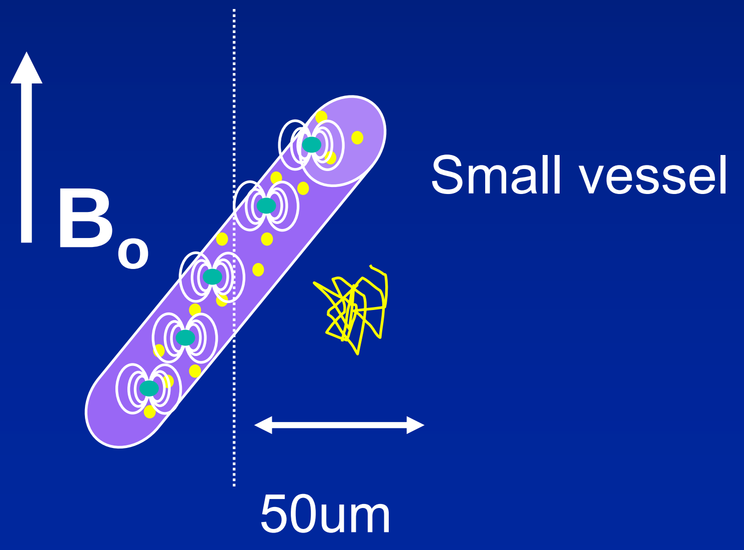
But, field (thus freq.) water experiences will depend on the orientation and size of vessel. Thus T2* effect.

Extravascular summary

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

But, T2 effect mainly comes from the smaller vessels.





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

Good review in fMRI book edited by P. Bandetini

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 B_o 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

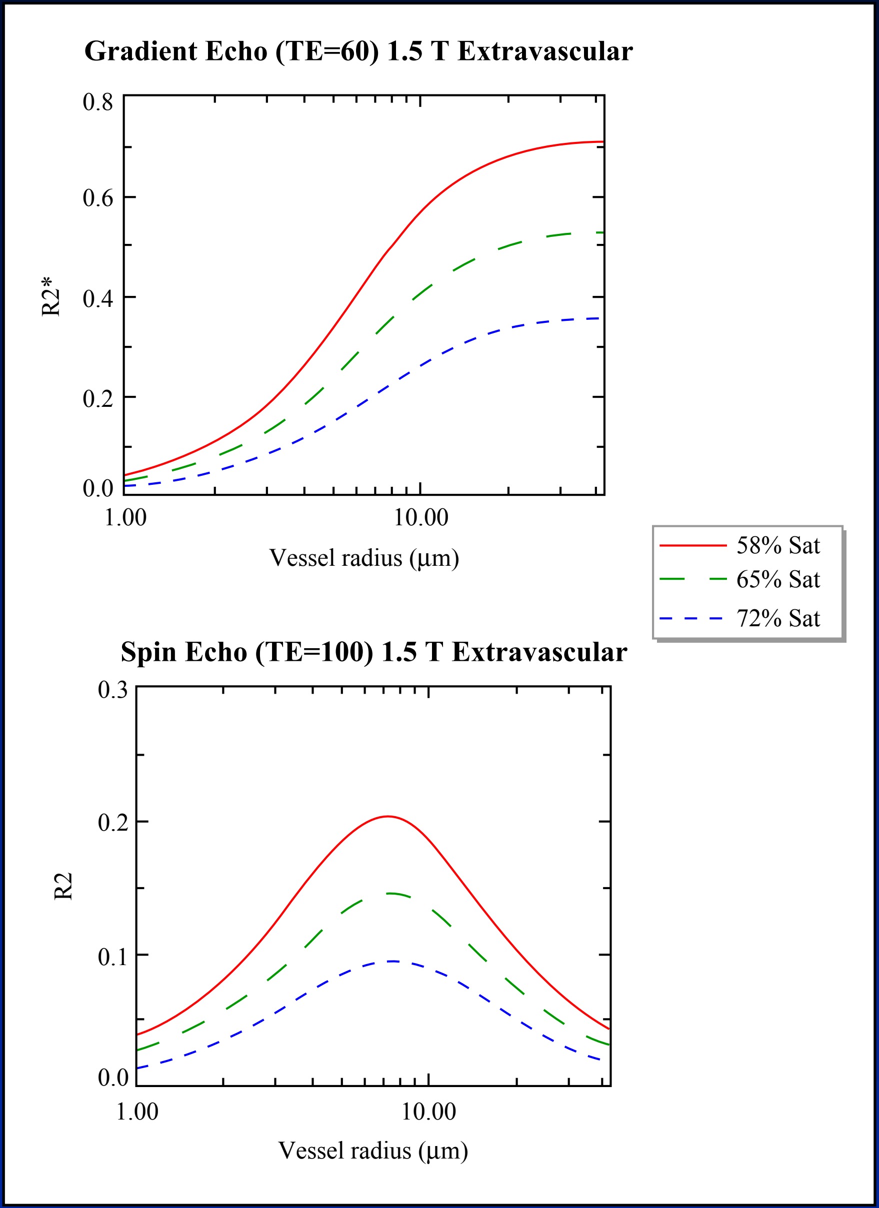


Figure by MIT OpenCourseWare.

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

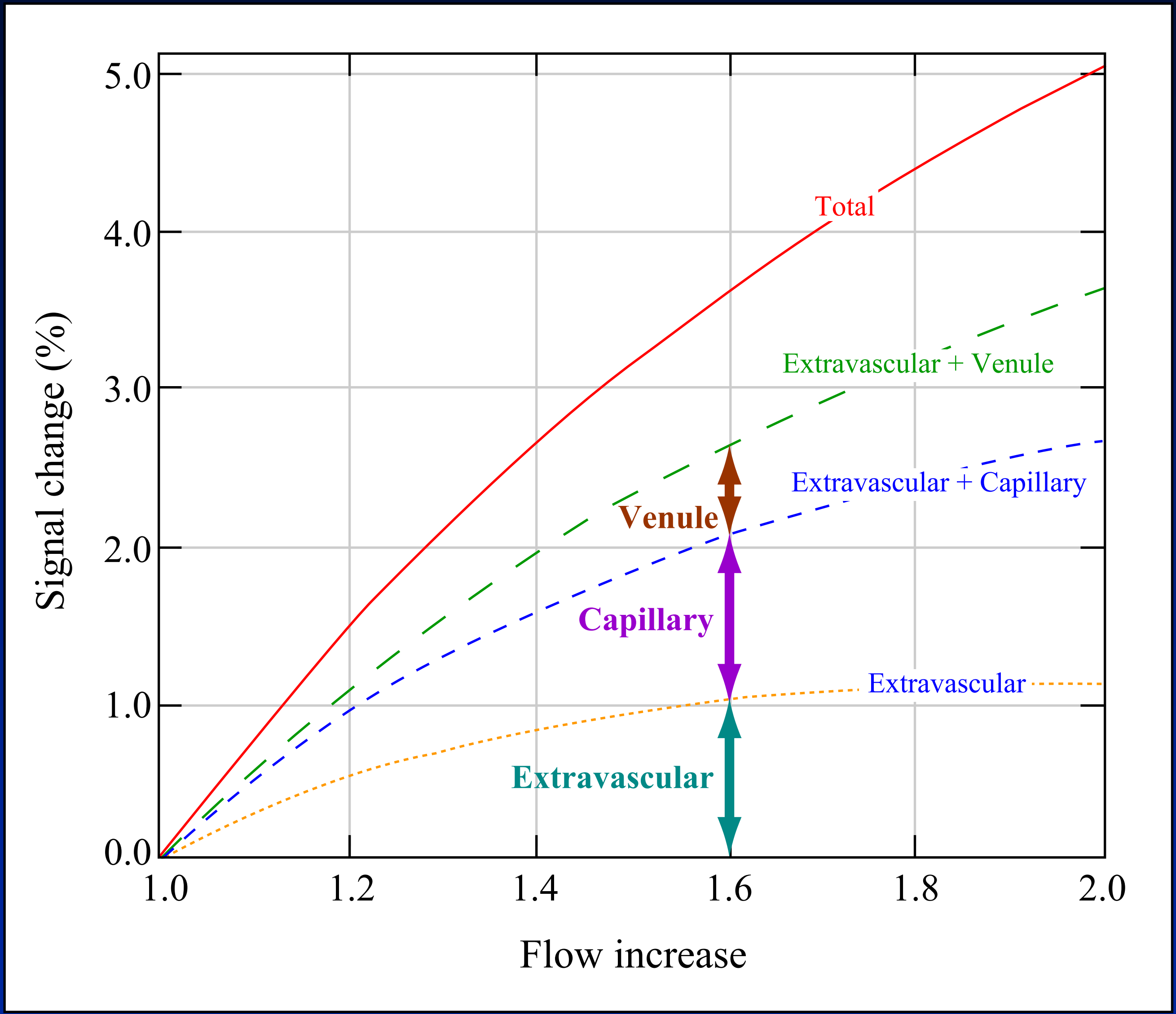


Figure by MIT OpenCourseWare.

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

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…

Effects of going to higher B_o

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

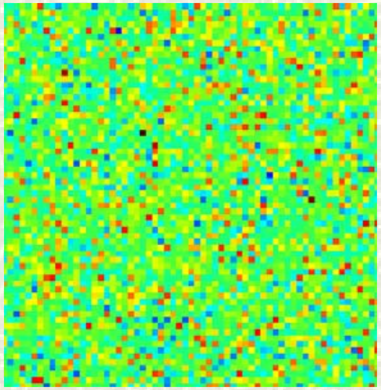
Velocity spoiling that would eliminate 2/3 of the BOLD effect at 1.5Tonly eliminates half at 3T and has no effect at 9.4T.

>> BOLD signal becomes more extravascular at high field.

Measuring Noise Components

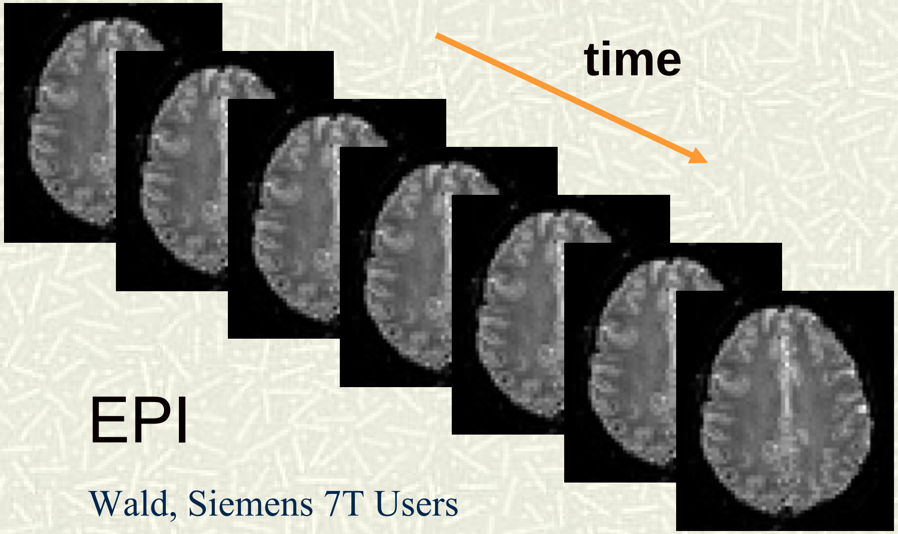
Raw Image Noise, S_0

- EPI, no RF excitation

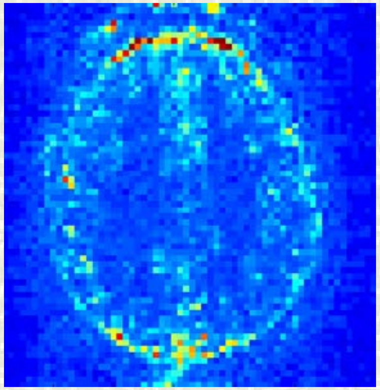


Time Series Noise, $SQRT(s_o + \sigma_P)$

ROI Analysis: frontal, parietal and occipital gray matter



EPI

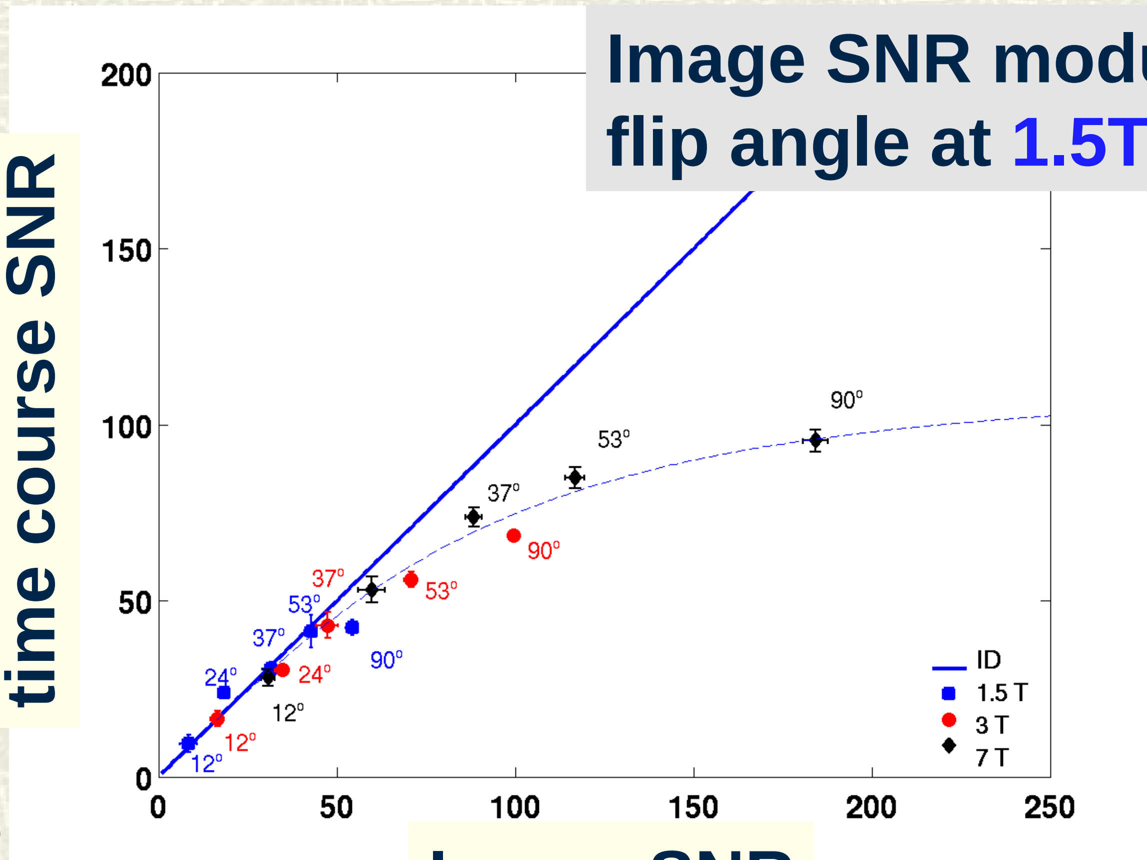


Wald, Siemens 7T Users Meeting 2005

Physiologic noise in fMRI timecourse

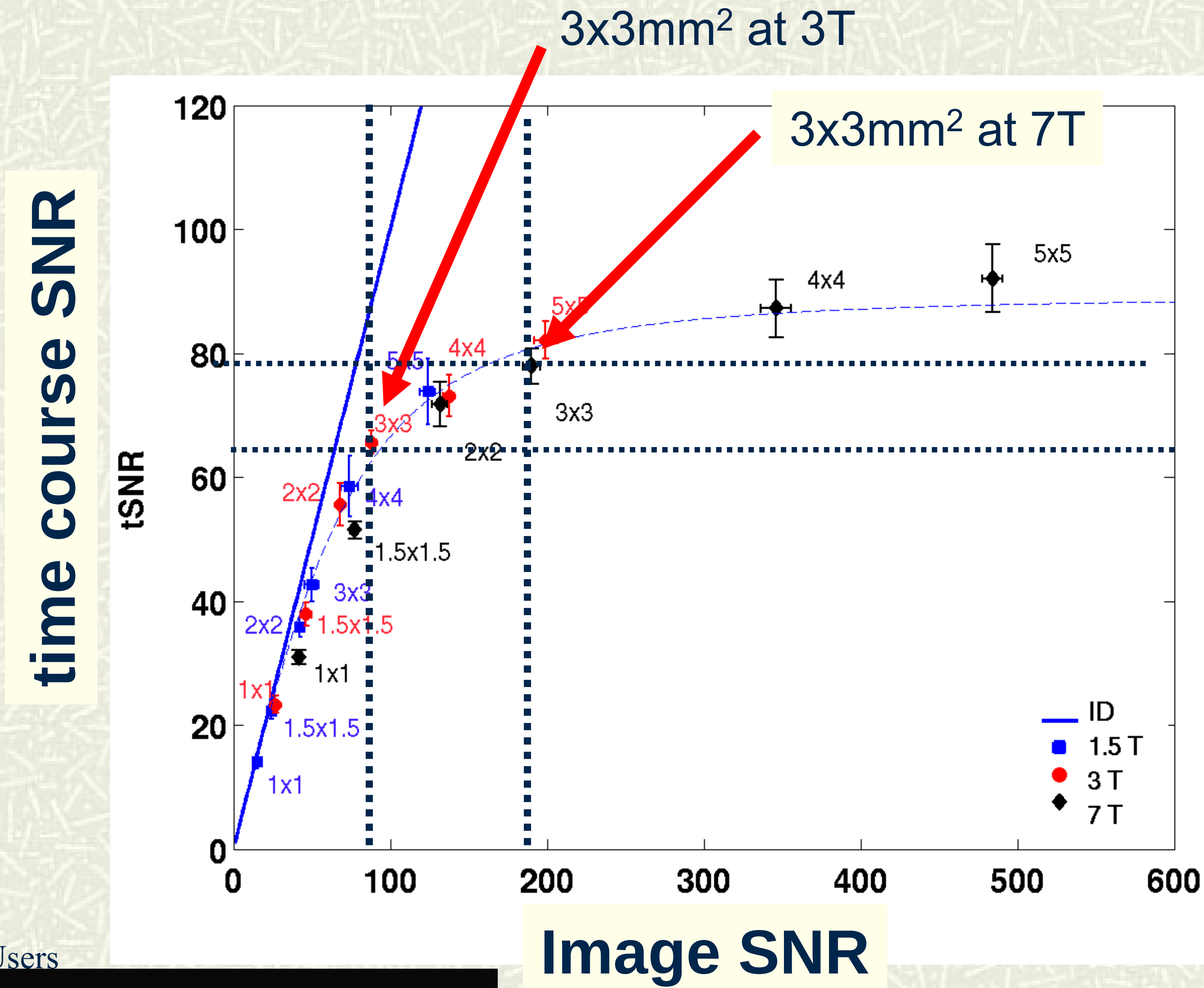
Triantafyllou et al. “Comparison of physiological noise at 1.5 T, 3 T and 7 T and optimization of fMRI acquisition parameters.” Neuroimage. 2005 May 15;26(1):243-50

Image SNR modulated by flip angle at 1.5T, 3T, 7T



Wald, Siemens 7T Meeting 2005

Image SNR modulated by image resolution at 1.5T, 3T, 7T



Wald, Siemens 7T Users

Lesson: keep image SNR below ~100

Physiologic noise in fMRI timecourse

Image SNR modulated by resolution at 1.5T, 3T, 7T

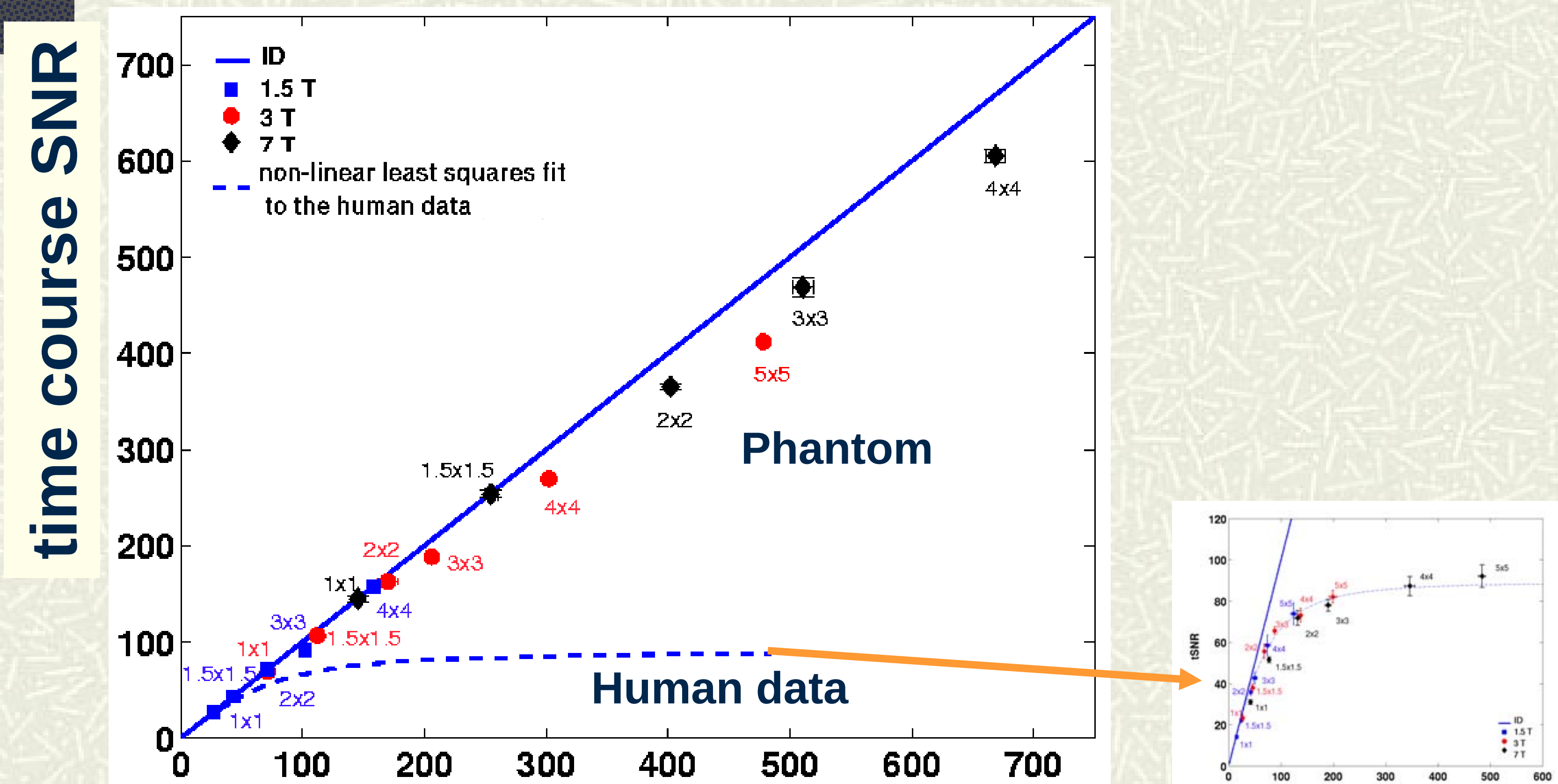
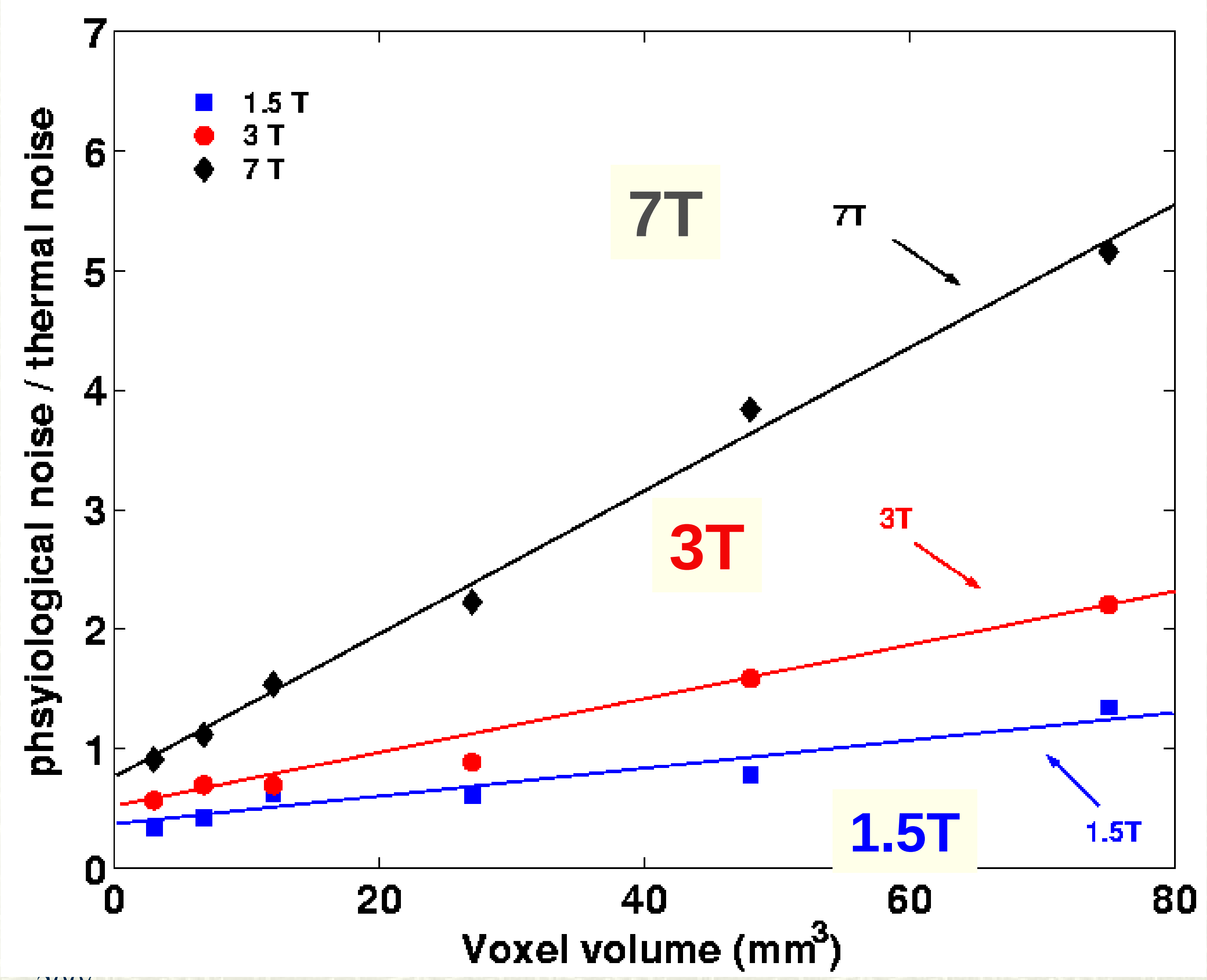


Image SNR

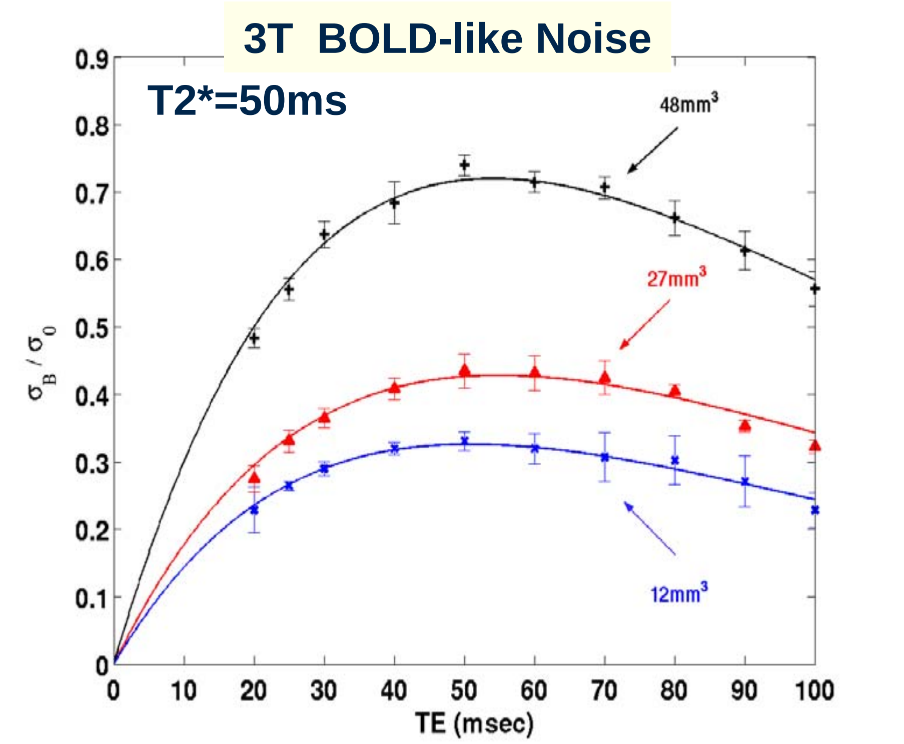
Wald, Siemens 7T Users Meeting 2005

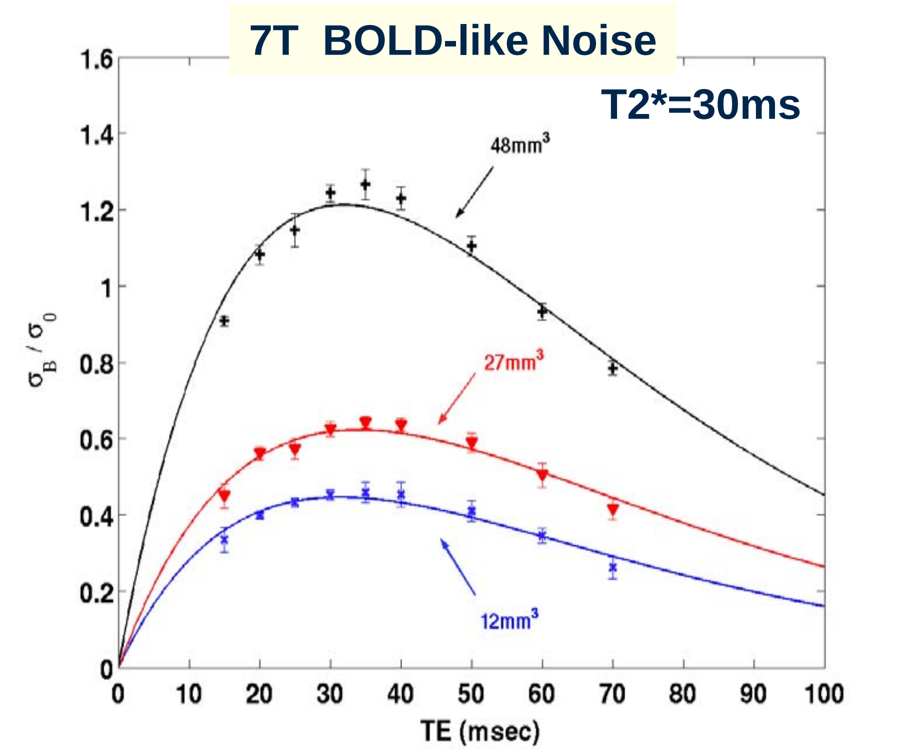
High resolution fMRI is needed at 7T to gain tSNR over 3T…



Wald,
Meeting 2005

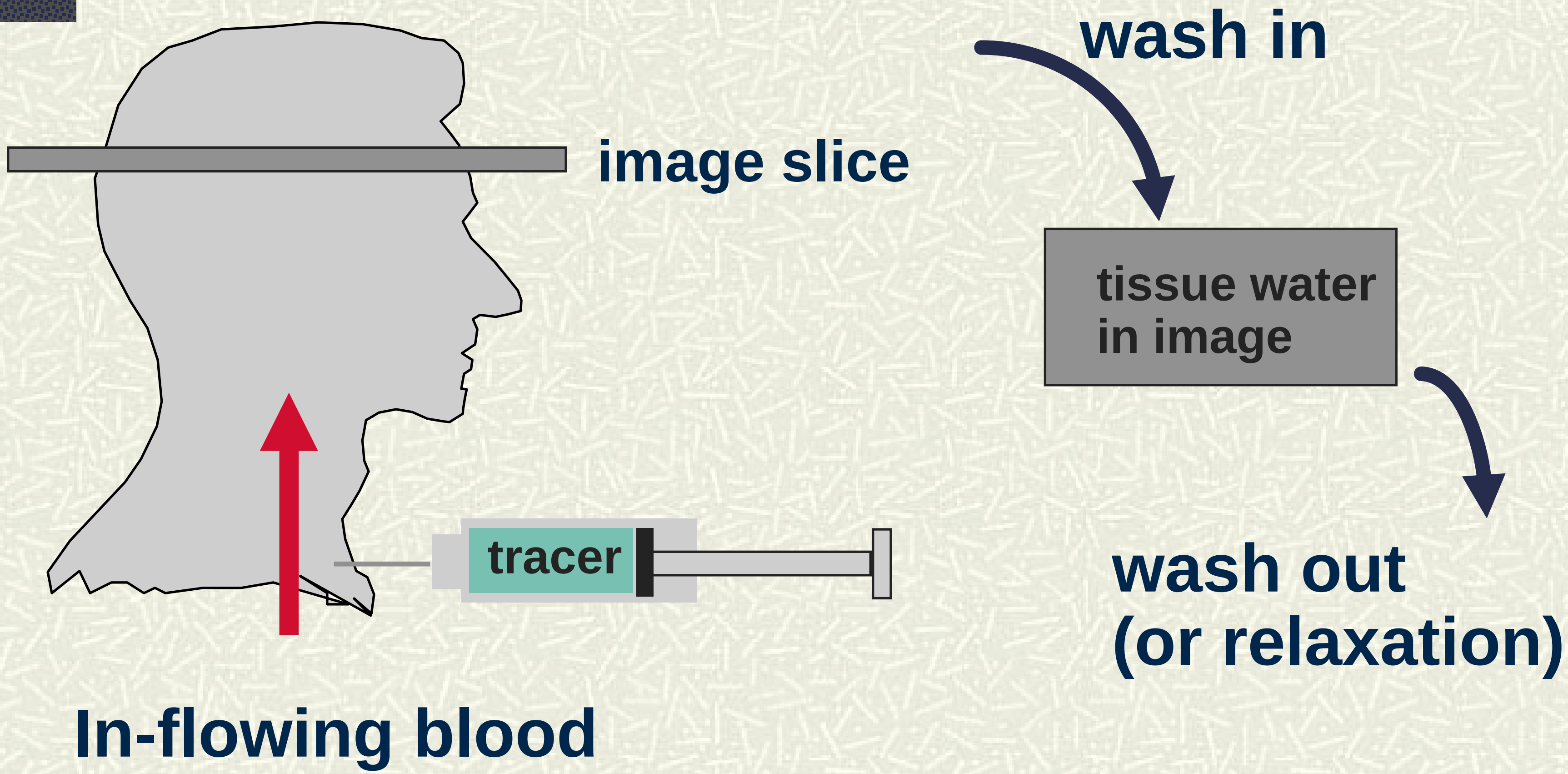
Physiologic noise is "BOLD noise" dominated at 7T





Wald, Siemens 7T Users Meeting 2005

Perfusion Seq. for direct flow measures



Bolus Gd(DTPA) MR CBV
(Intravascular T2* agent)

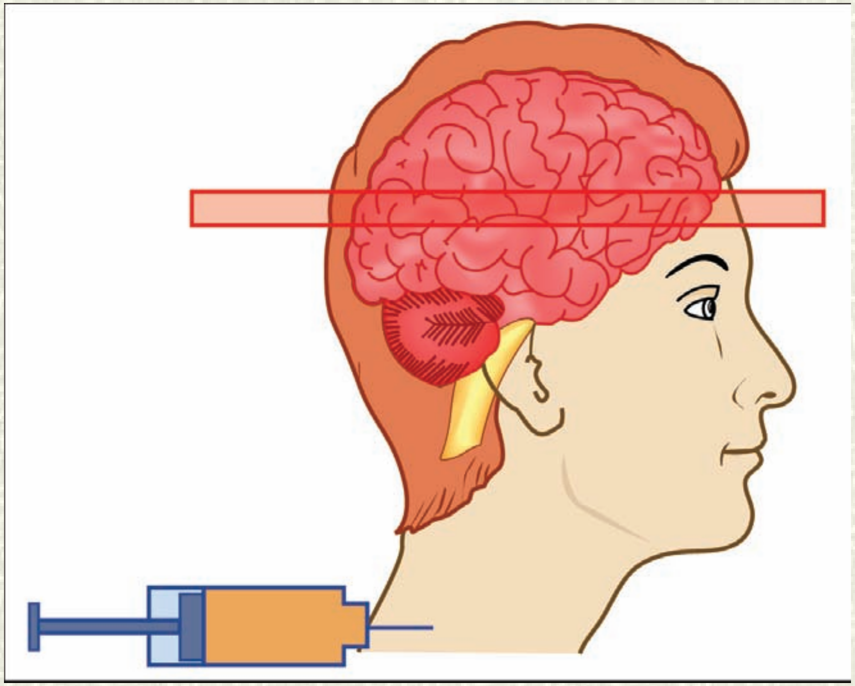
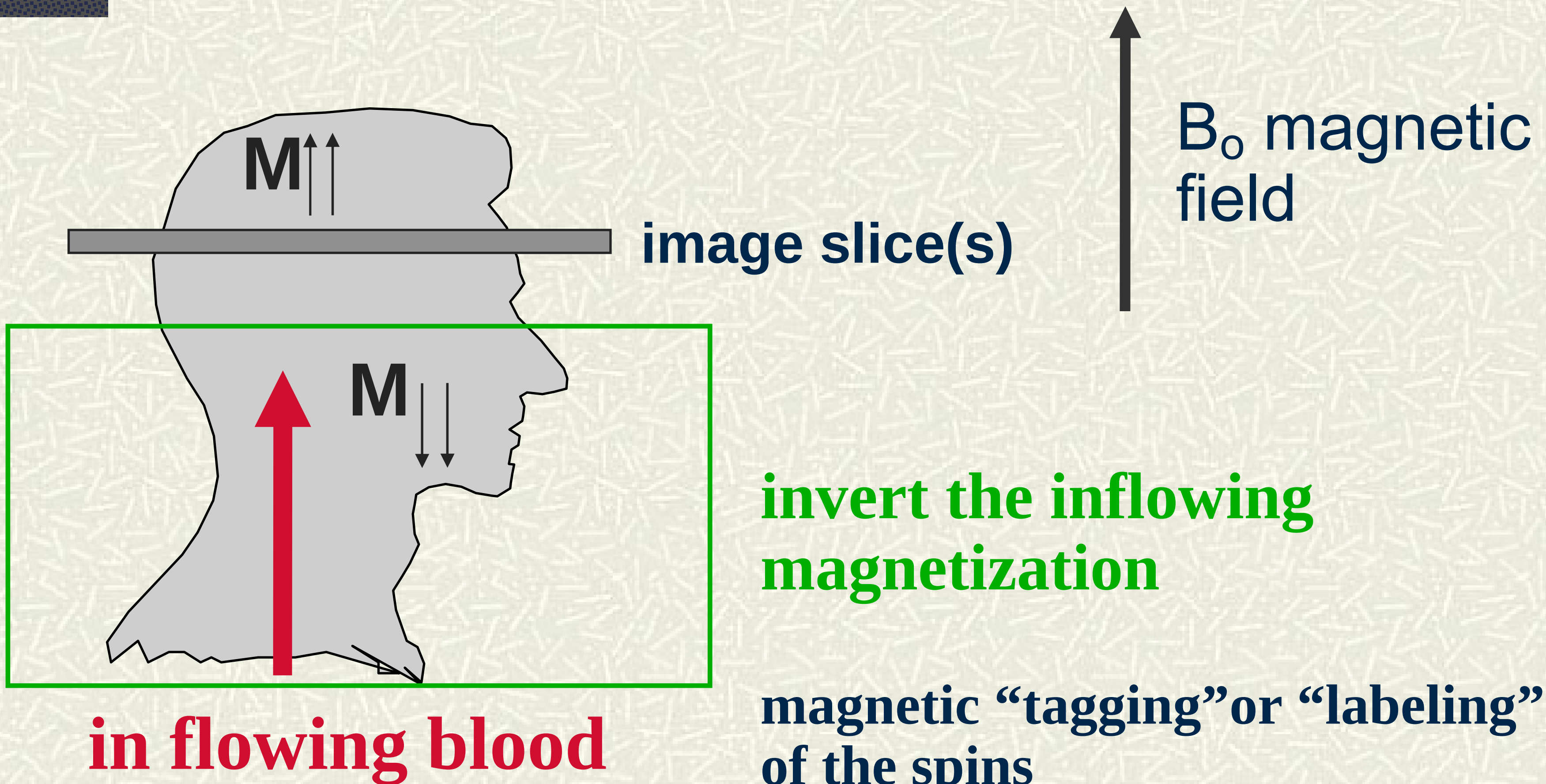


Figure by MIT OpenCourseWare.

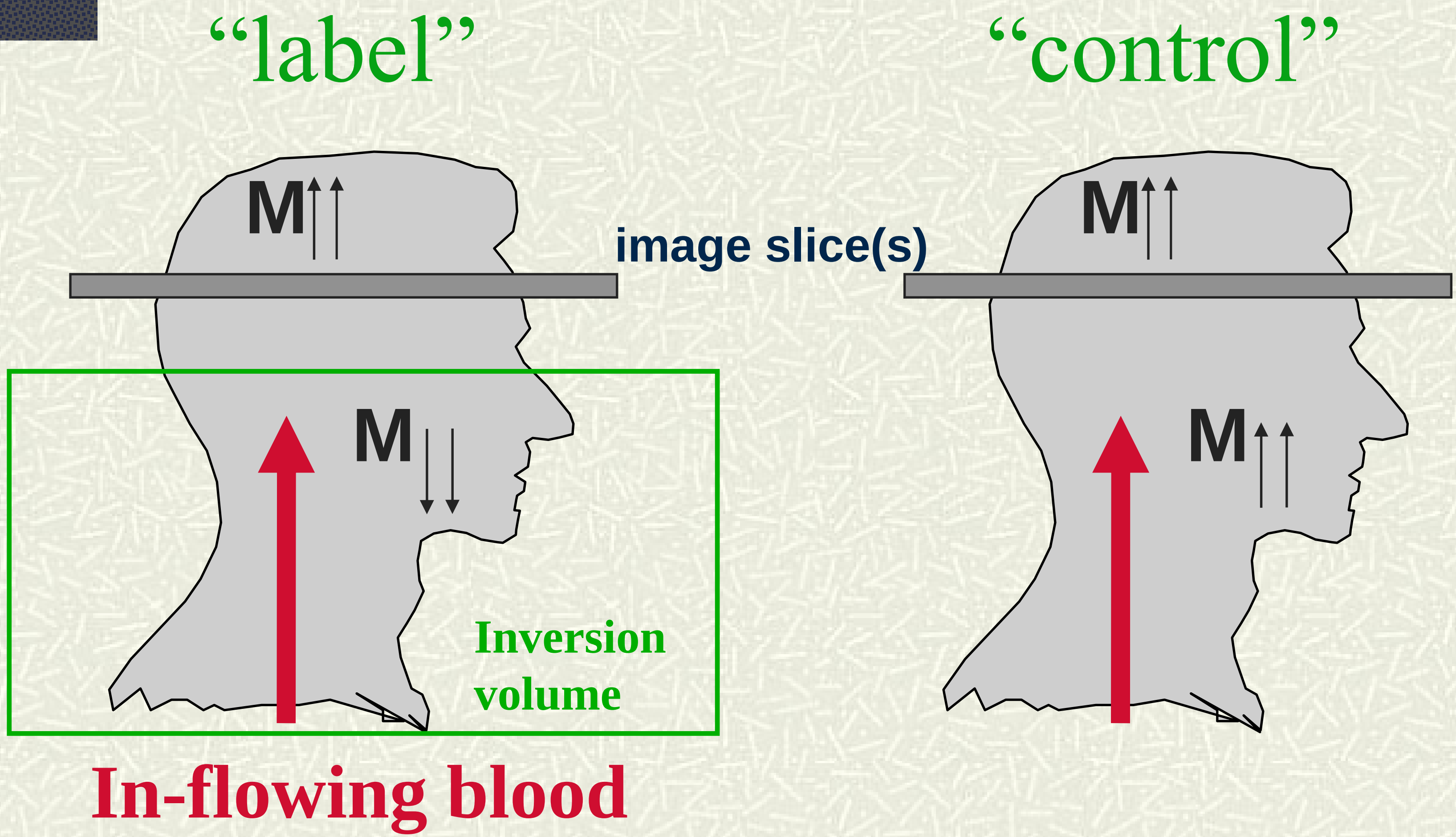
- Agent stays in vessels (in brain)
- Integral of concentration timecourse = **rCBV**
- Flow is needed, but integral is flow independent
- To estimate flow, compare transit time and width to arterial input function.
- T_1 effects occur if BBB broken

Using water as a magnetic tracer: Arterial Spin Labeling



magnetic “tagging”or “labeling” of the spins

How to create a magnetic tracer: Arterial Spin Labeling



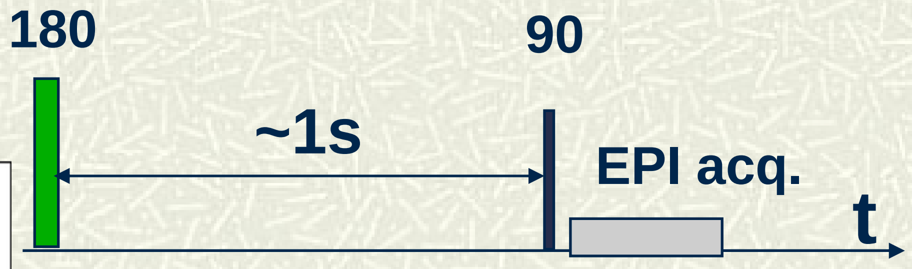
ASL: subtract labeled image from a control image

Effect of the inverted blood water is < 4% reduction of normal signal. (on order of the % blood volume)

=> Requires the labeled image to be subtracted from a control acquisition.

Motion is a big problem...

Pulsed Label ASL (PASL)



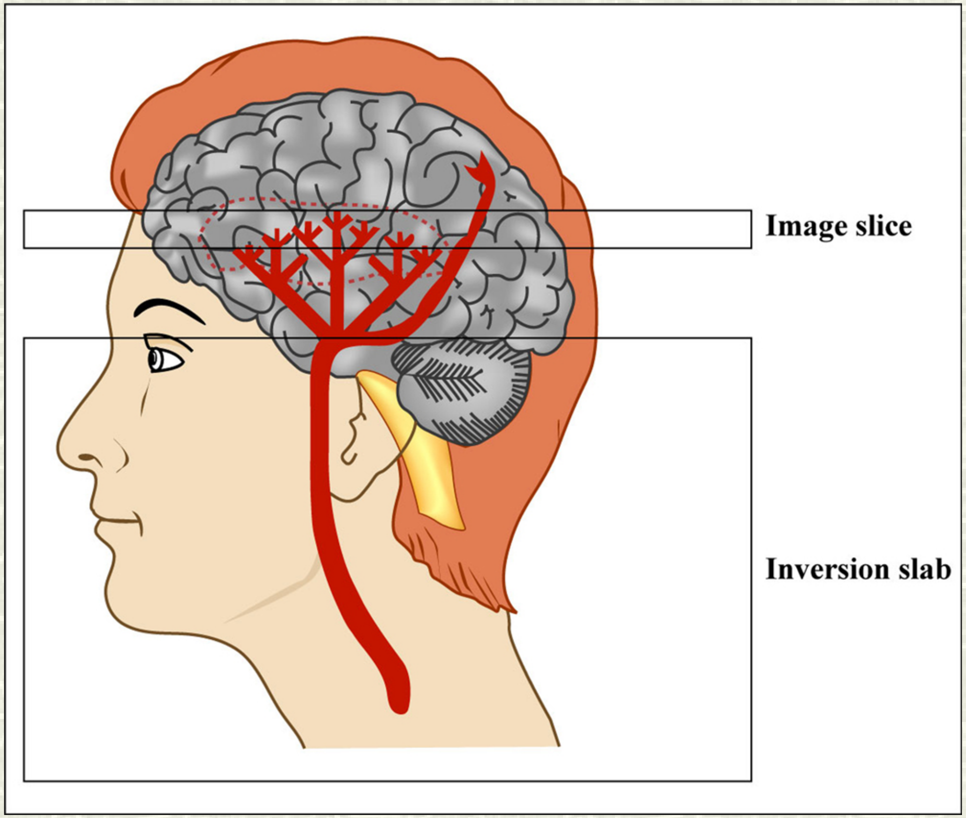


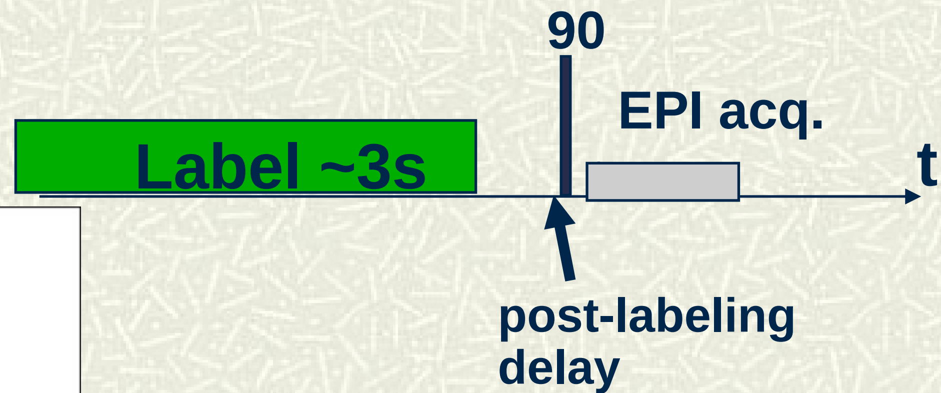
Figure by MIT OpenCourseWare.

T_1 is important

Thru slice arteries relatively dark

Large inversion slab is important

Continuous label ASL (CASL)



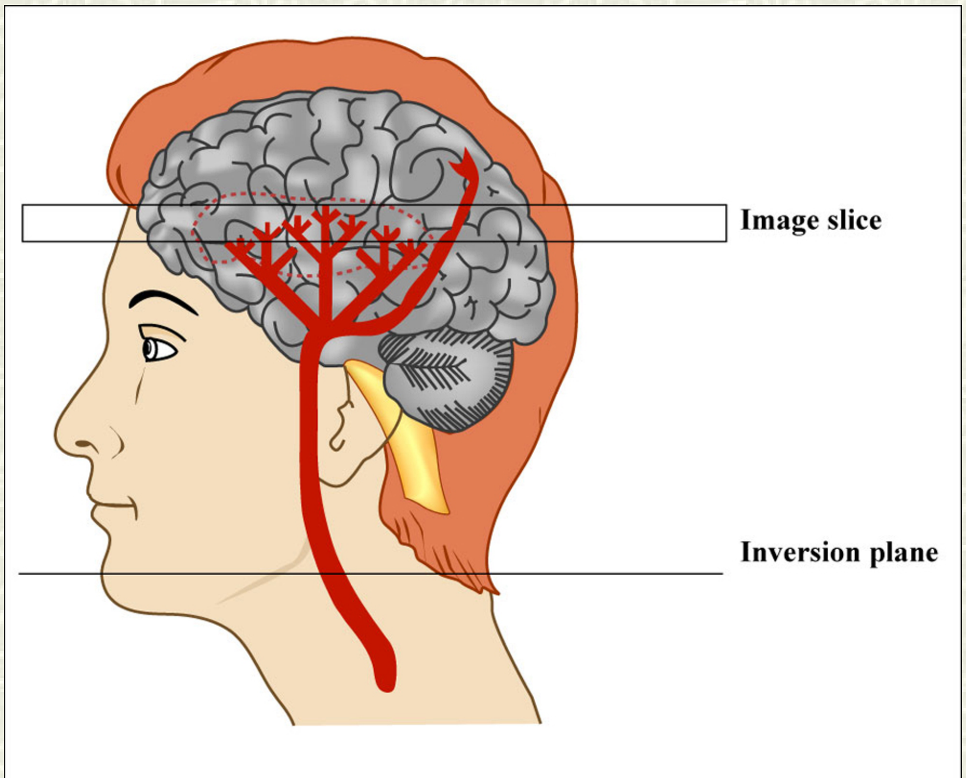


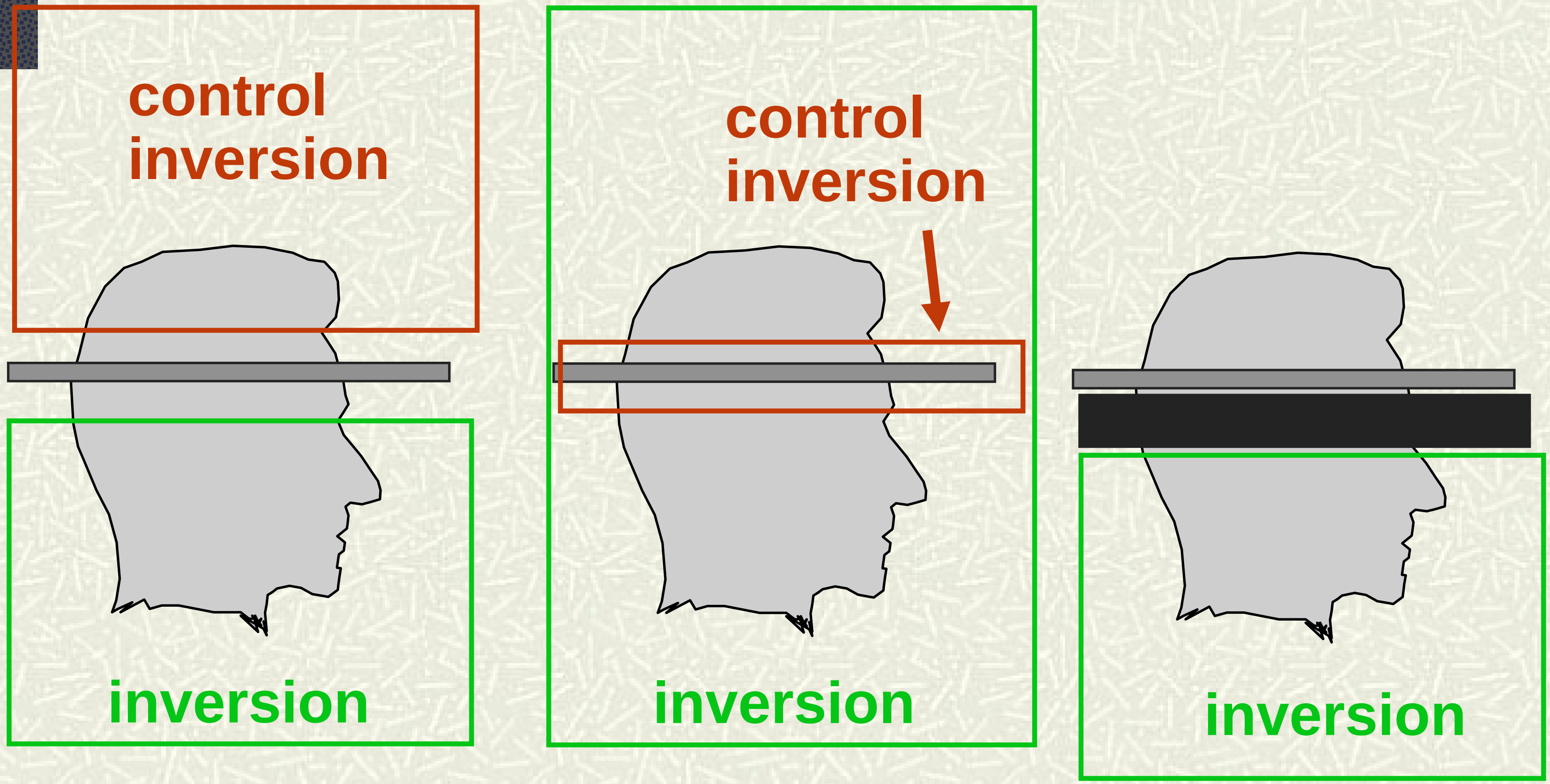
Figure by MIT OpenCourseWare.

T_1 is important

Thru slice arteries relatively dark

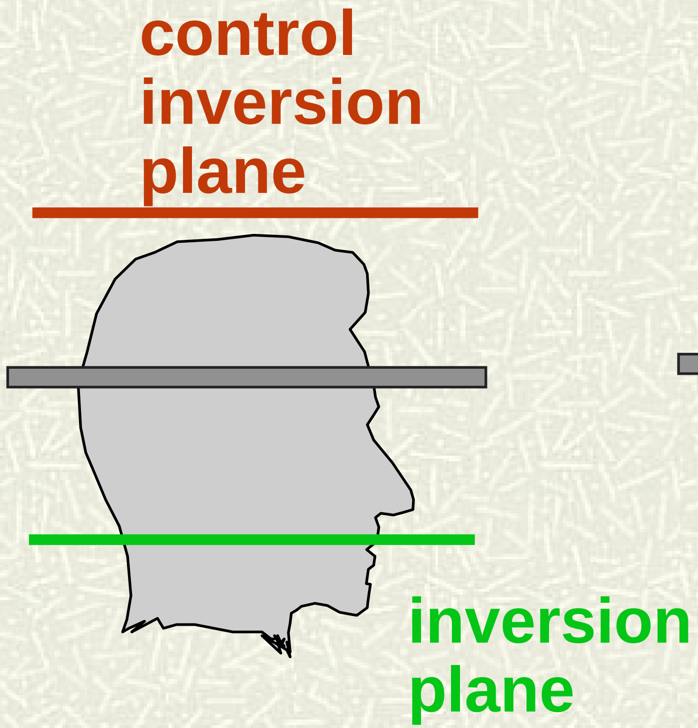
Less transit time sensitive.

Three flavors of pulsed ASL

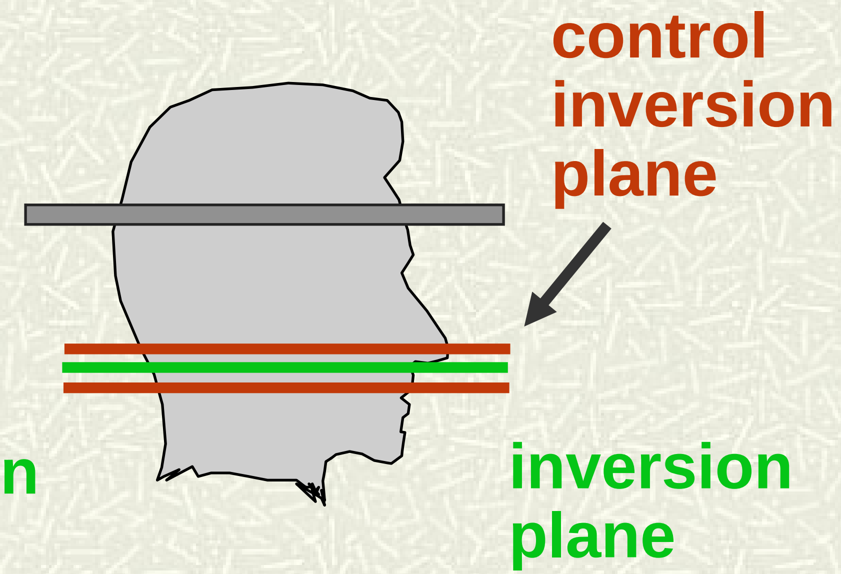


EPISTAR **FAIR** **QUIPPS**

Continuous ASL



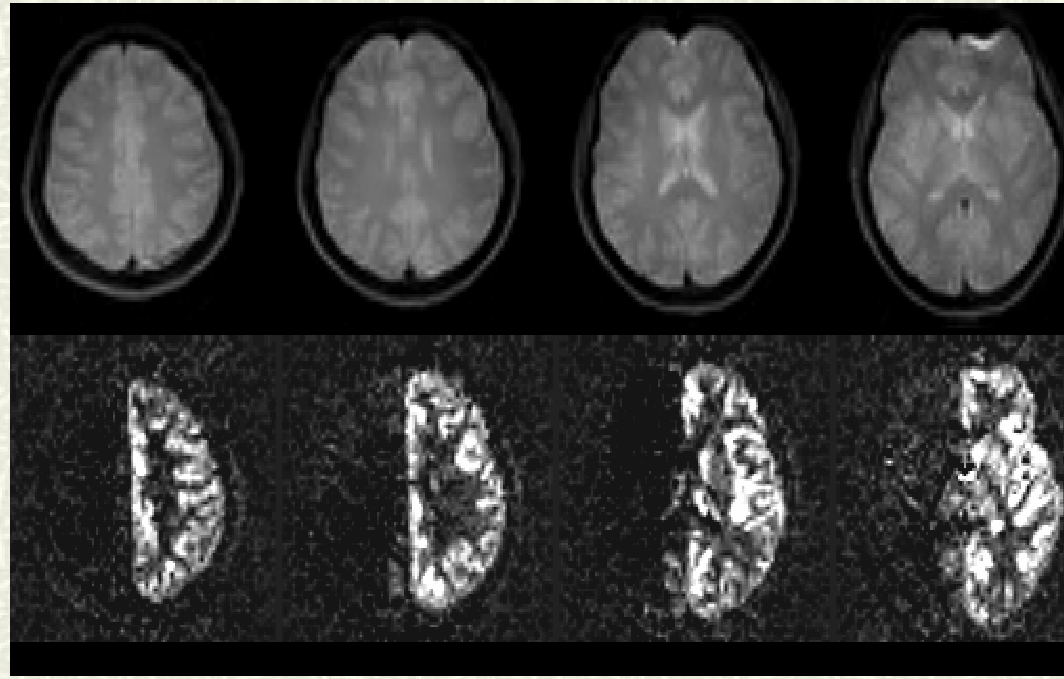
cw adiabatic inversion

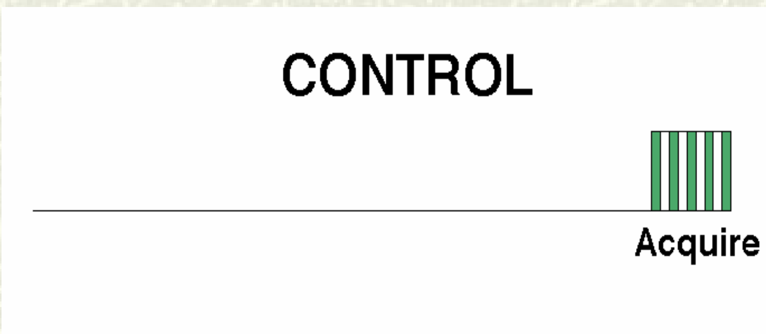


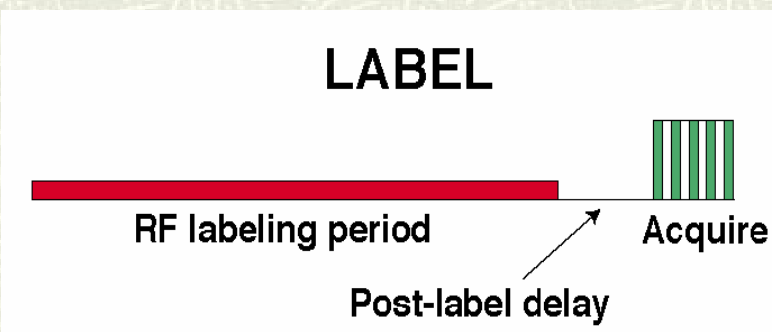
cw adiabatic inversion (Alsop et al.)

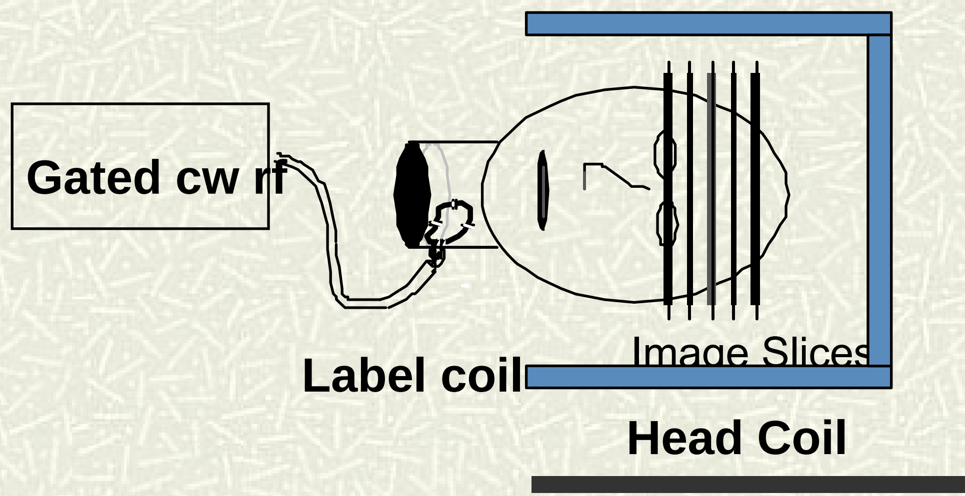
2 coil continuous ASL

Perfusion territory imaging









ASL: confounds

- Labeling and control image should have same effect on static tissue to within 0.1%
- Magnetization Transfer: off resonance saturation
- of image slice during the label but not the control. (esp. continuous ASL)
- Slice profile effects: Label and control have different slice profiles (~1%). (esp. pulsed ASL)

Be sure to...

Pulsed ASL (EPISTAR, FAIR, QUIPPS)	Continous ASL (single coil, two coil)
Use body coil for slab inversion.	Use Alsop's control excitation or 2 coil method to allow multi-slice w/o MT.
Use inversion pulses with high quality spatial profiles	
Use sufficient TI to ensure capillary flow	Use sufficient labeling time to ensure capillary flow.
QUIPPS inferior sat band for transit insensitivity	Post-labeling delay for transit insensitivity

The pros and cons

Pulsed ASL (FAIR, QUIPPS)	**Continous ASL** (single coil, two coil)
Better suited to fMRI	
Limited to axial slices.	Arbitrary slice orientation
veins are labeled in FAIR	Only arteries
Large # of slices cuts into labeling slab volume	# slices doesn't limit label time
Label efficiency not velocity sensitive	Lower efficiency (15-25%) due to Laminar flow.
Label is near imaging slices	~15ms transit delay per cm
Intrinsically less efficient per unit time (~30%)	more SAR intensive

ASL at 7 Tesla

6 minute pASL flow image

1.56mm x 1.56mm x 4mm
(at 3T we do 3mmx 3mm x 5mm)

Four times smaller voxel volumes!