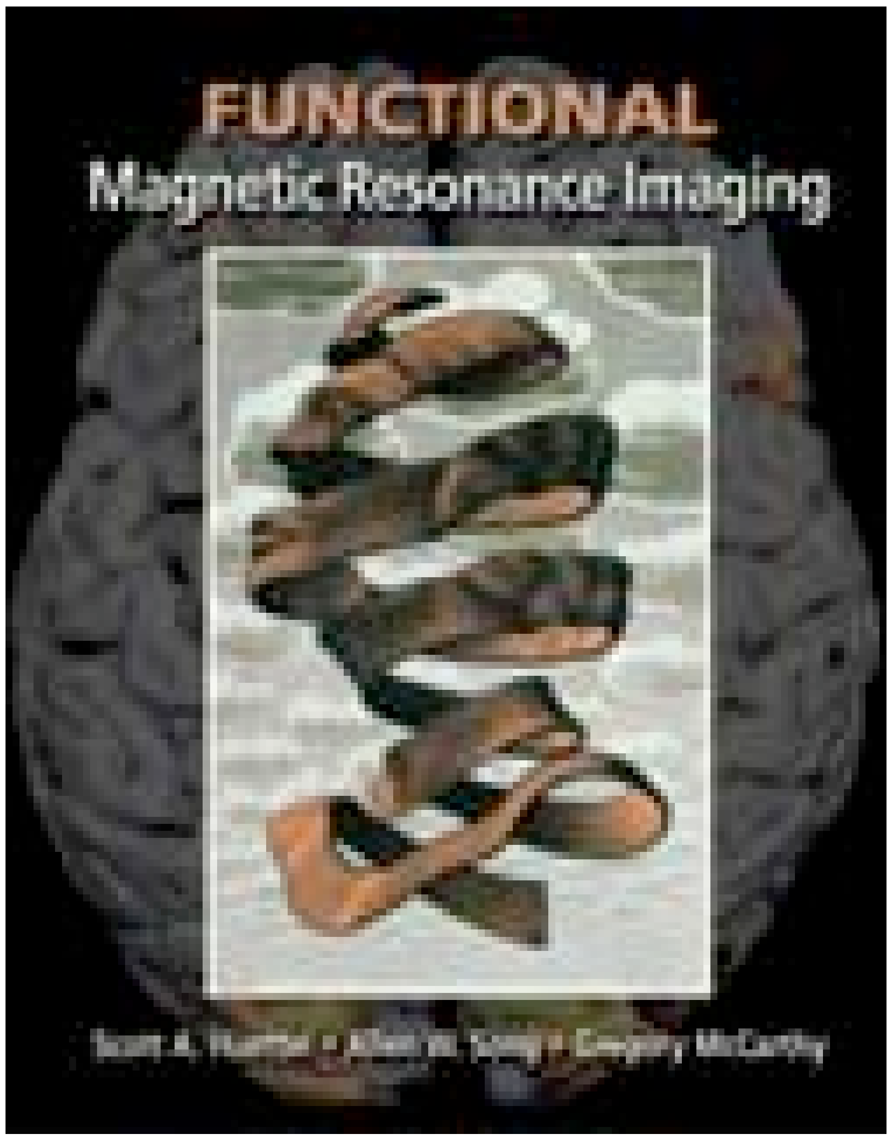
Math Aspects of MRI and FMRI

Souheil Inati

Statistical Analysis and Modeling of Neural Data

Oct. 31, 2007

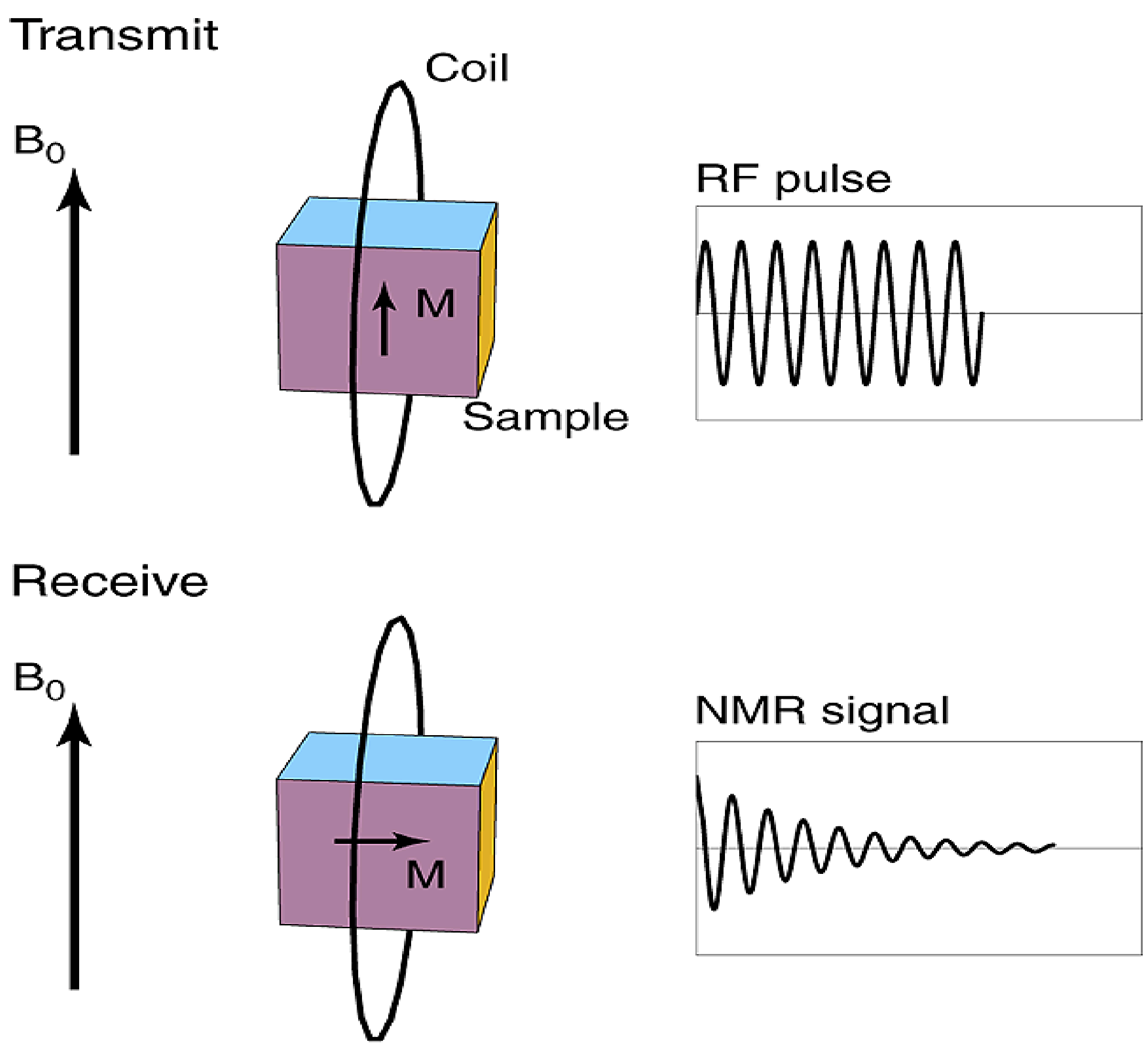
Interrupt early and often.

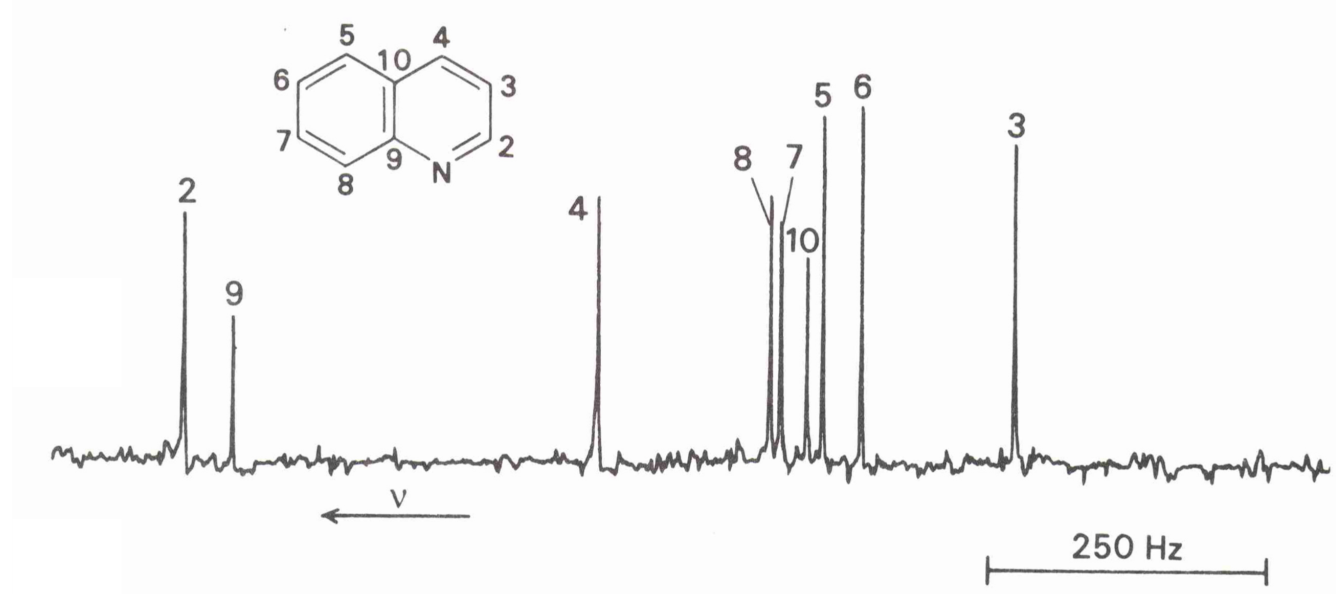


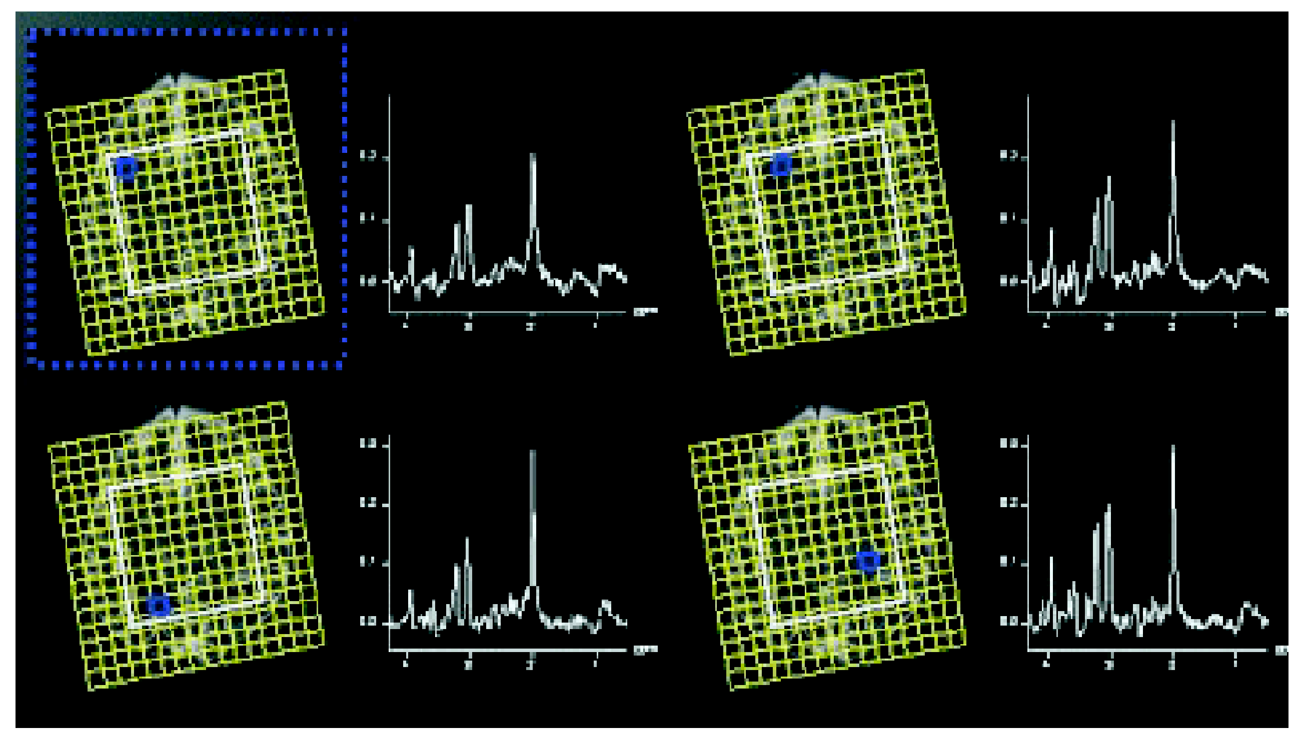
Getting started textbook:
Huettel, Song, and McCarthy

many figures taken from Huettel

NMR Spectroscopy



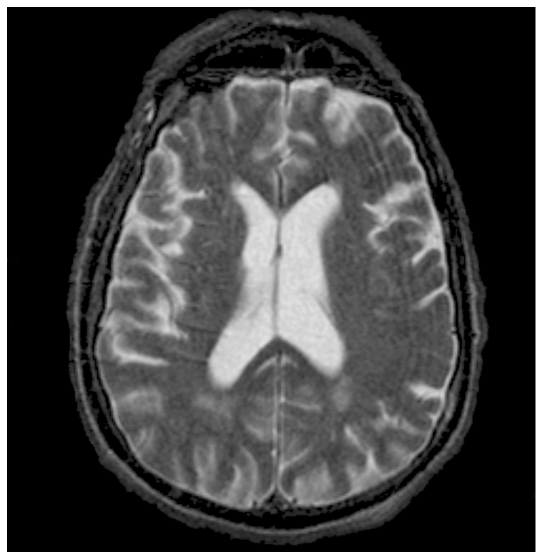


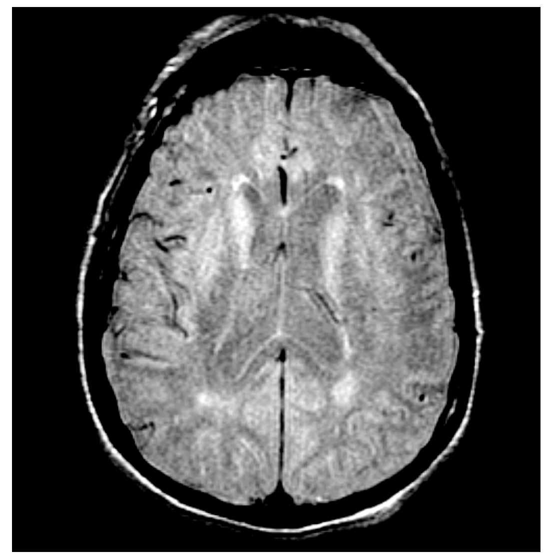


Direct measure of chemical composition

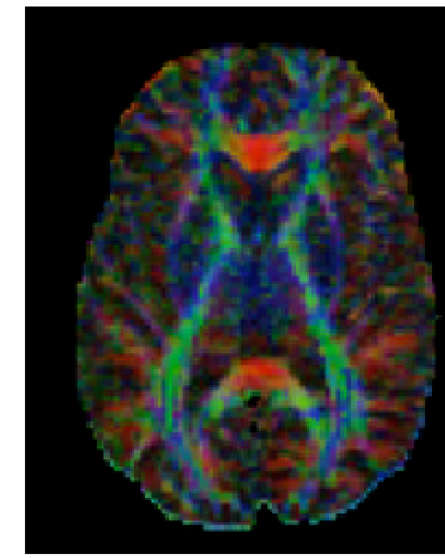
Bread and Butter Clinical MRI


T1


T2

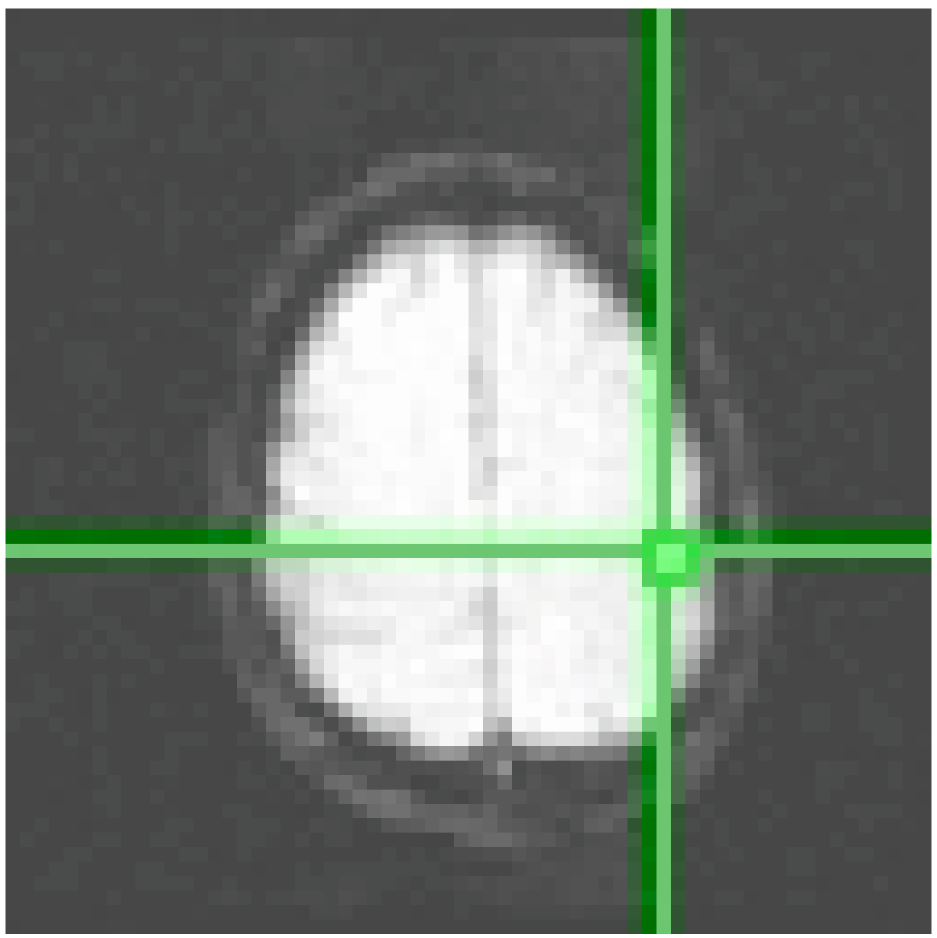

Density

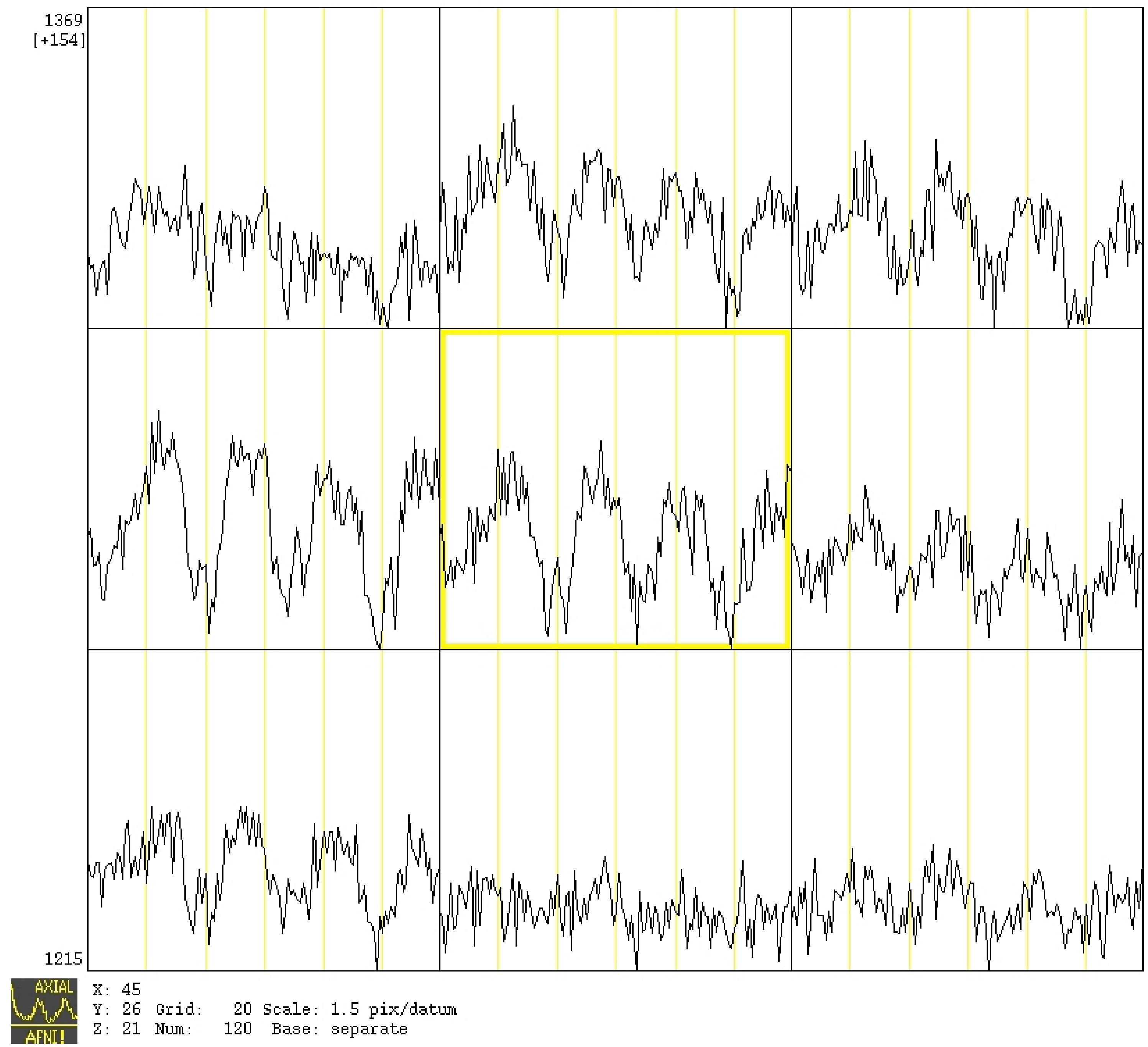

Flow


Diffusion

Images of water density weighted by local microscopic environment

Functional MRI Time Course





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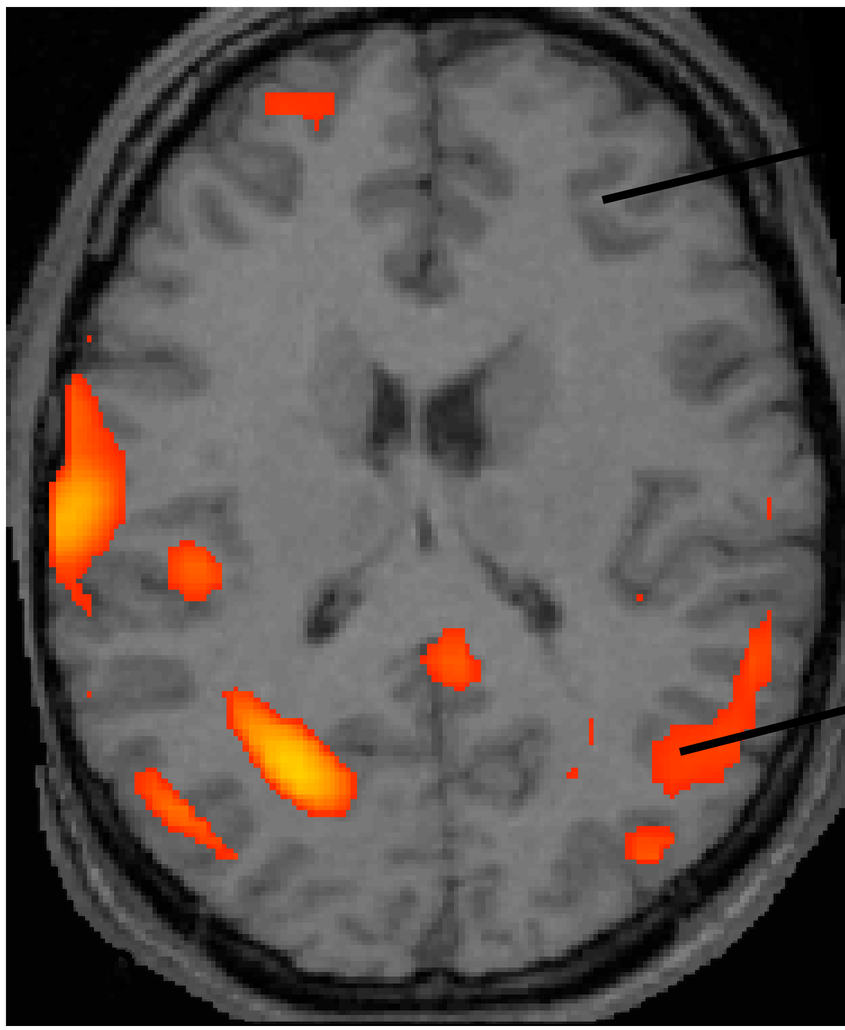
Measure Cognitive Function



Anatomy image (T_1)

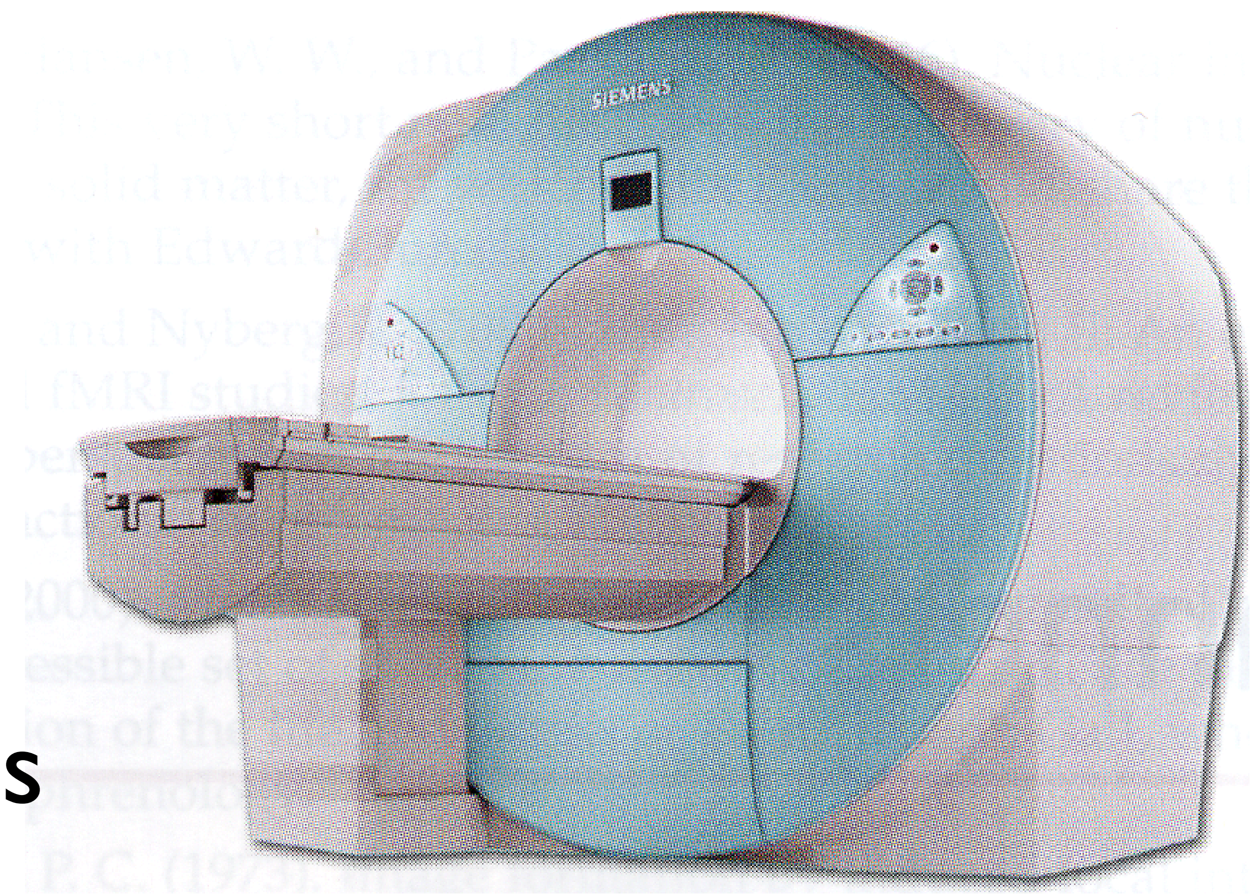
Statistical image overlay:
color ~ P value

BOLD FMRI at 1.5T

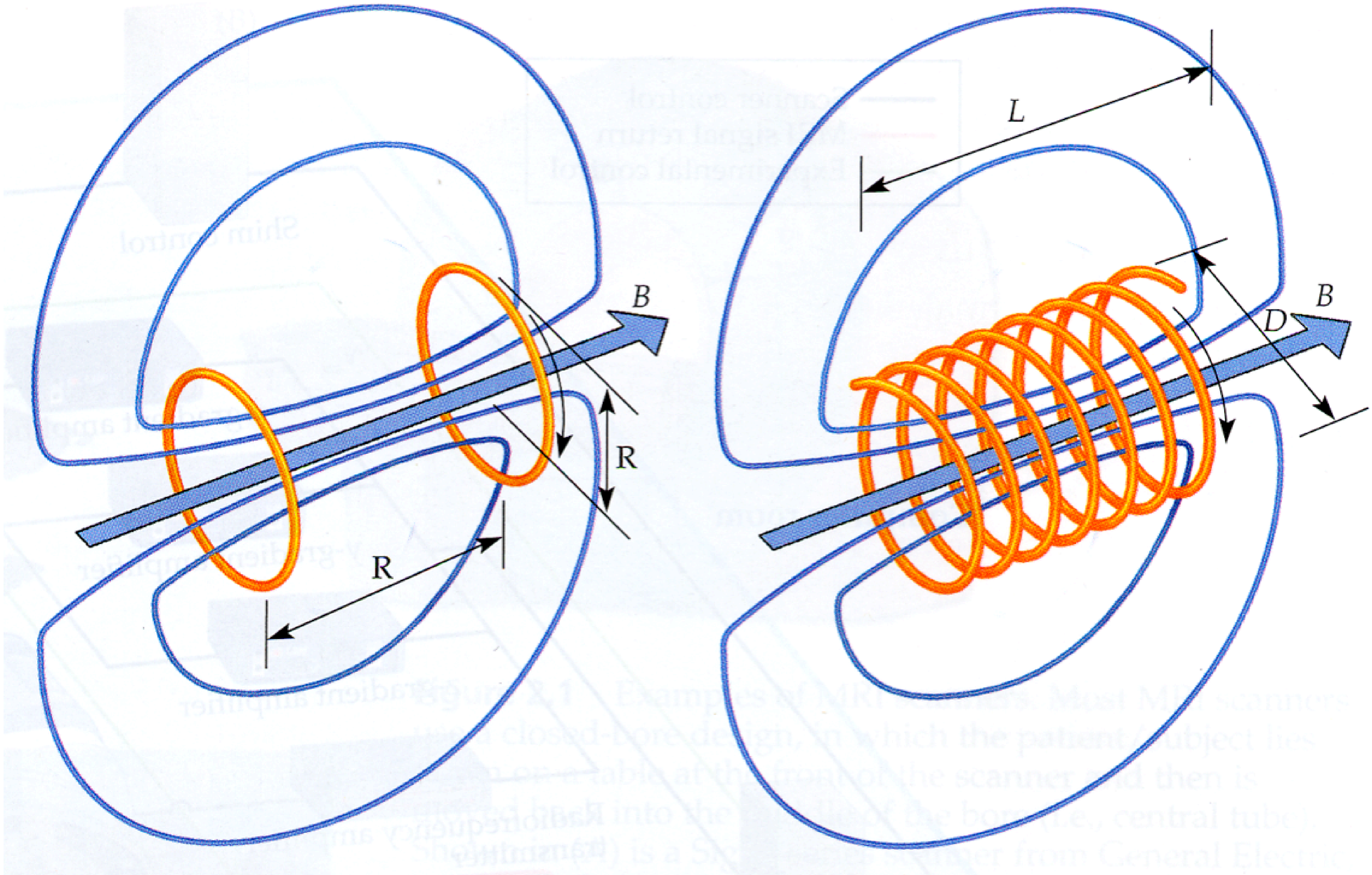
the MRI machine

i.e.

what's inside the ~~donut~~ torus

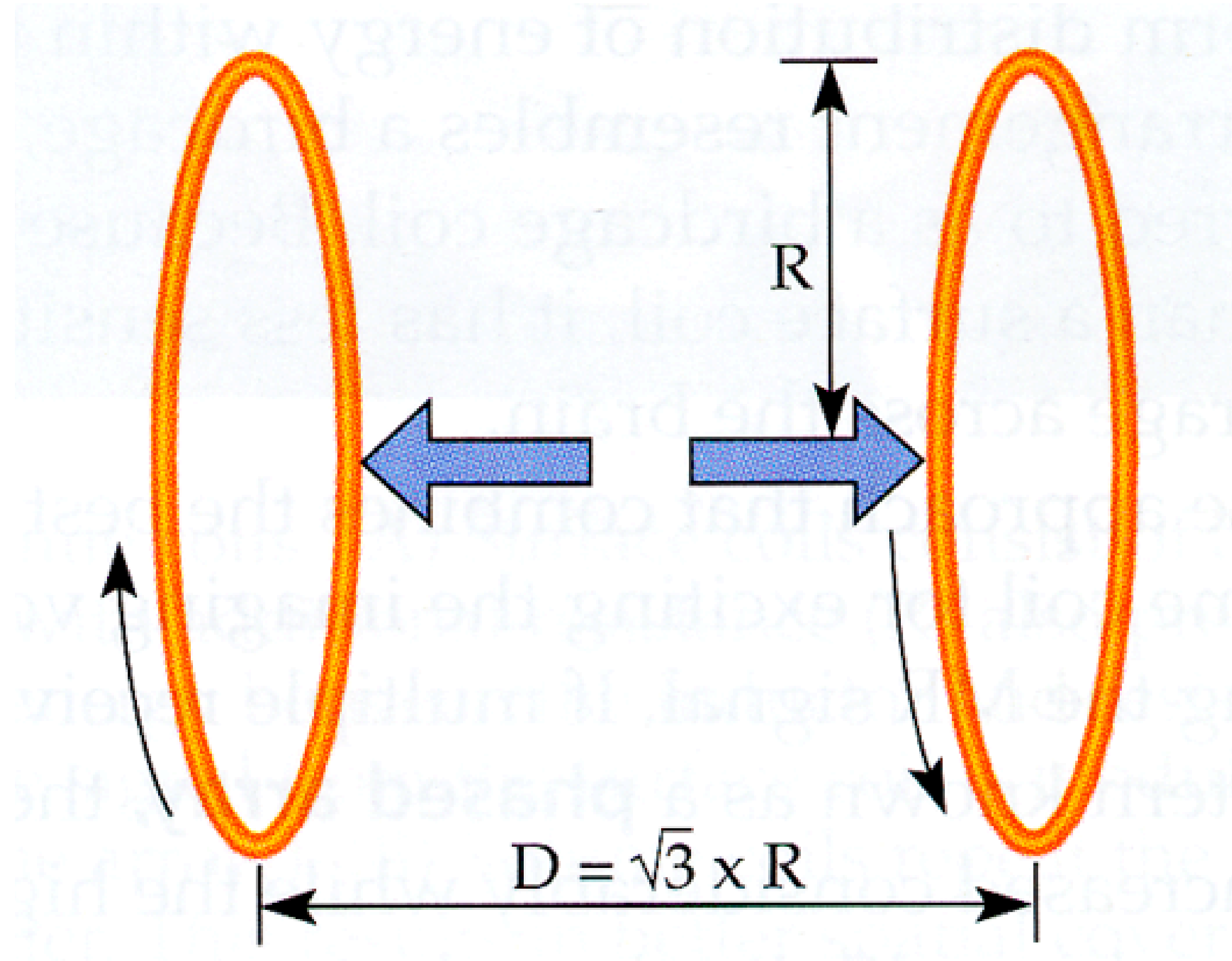


Main Magnetic Field



Helmholtz pair Solenoid

Magnetic Field Gradient

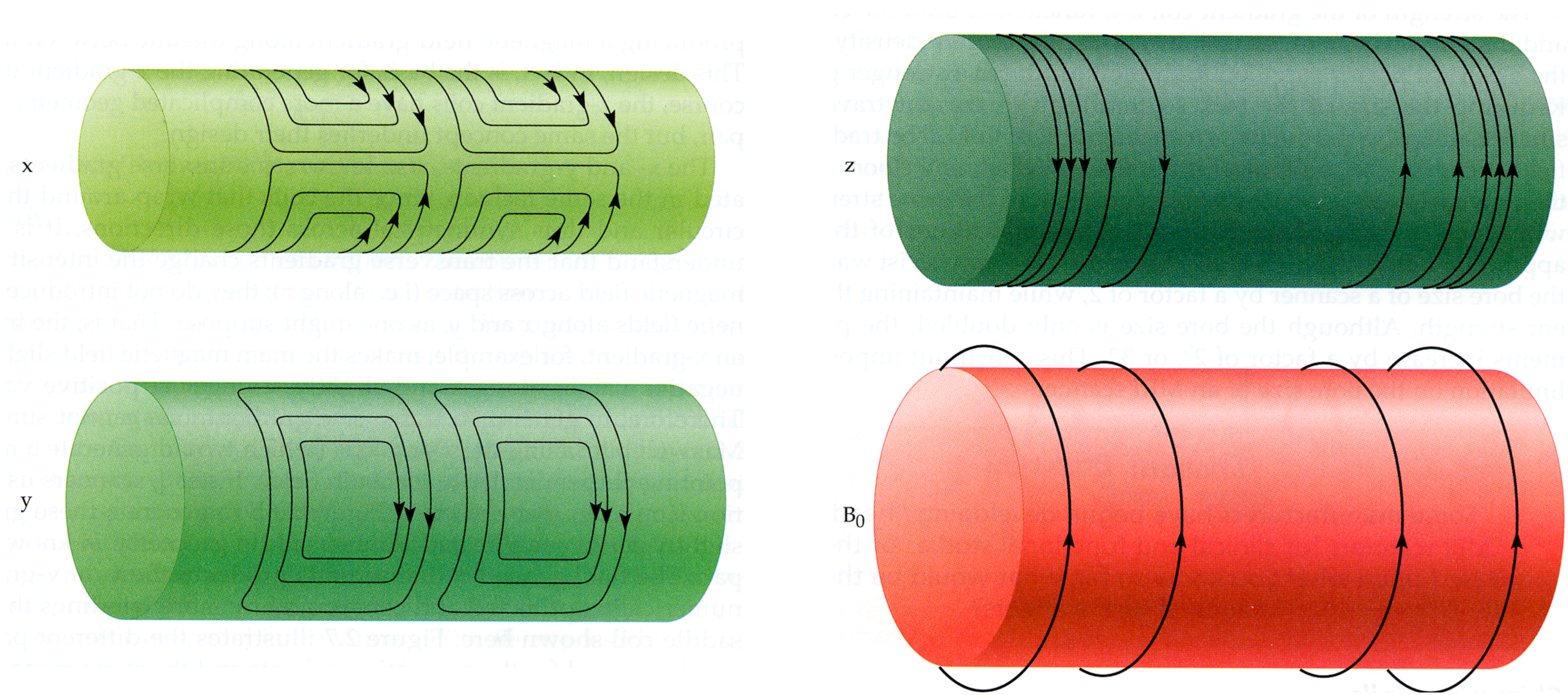


Currents are in opposite directions

1. Field pointing along z
2. Strength linear in z: B=(0,0,Gz)

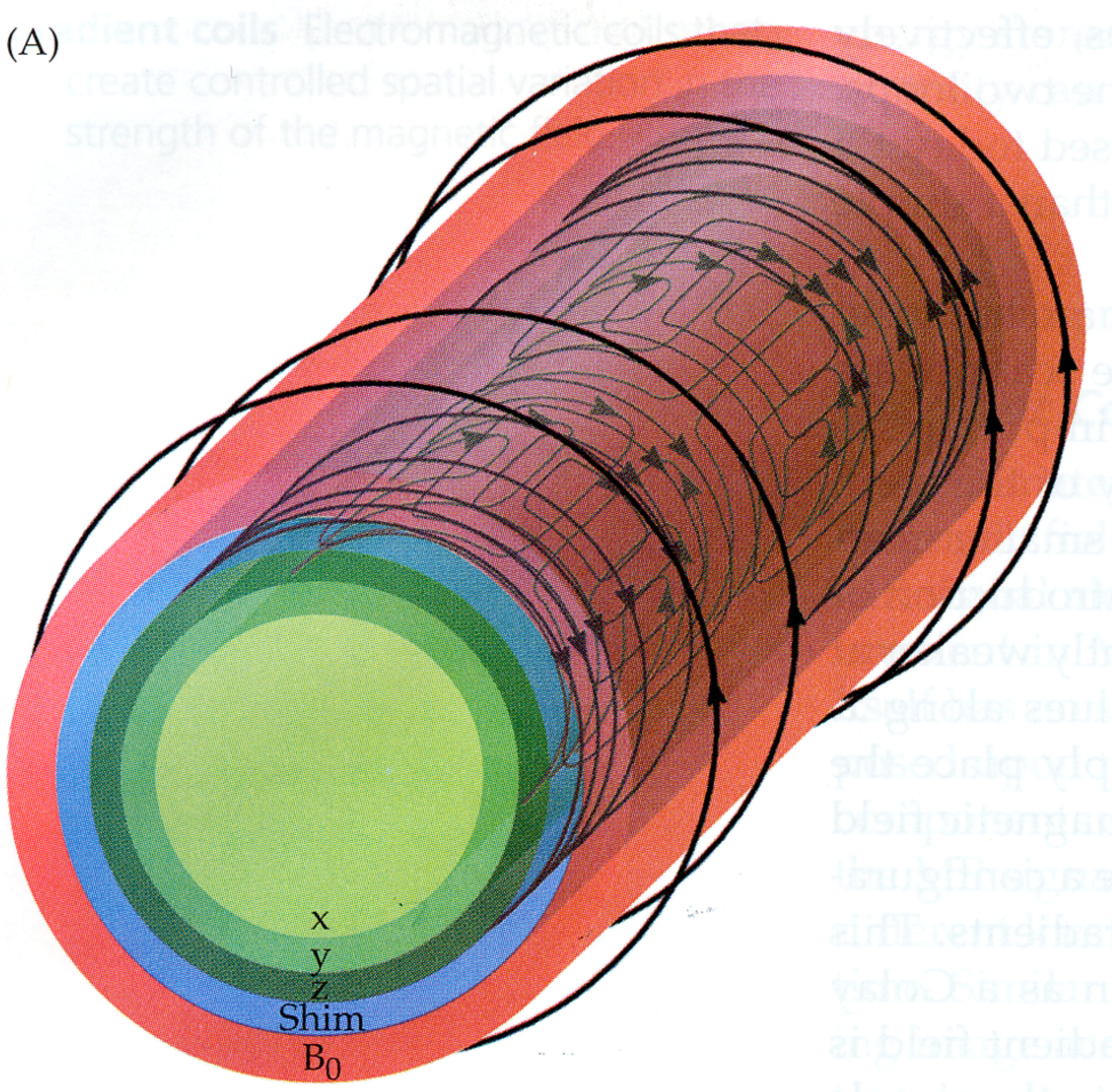
x and y gradients only slightly more complicated

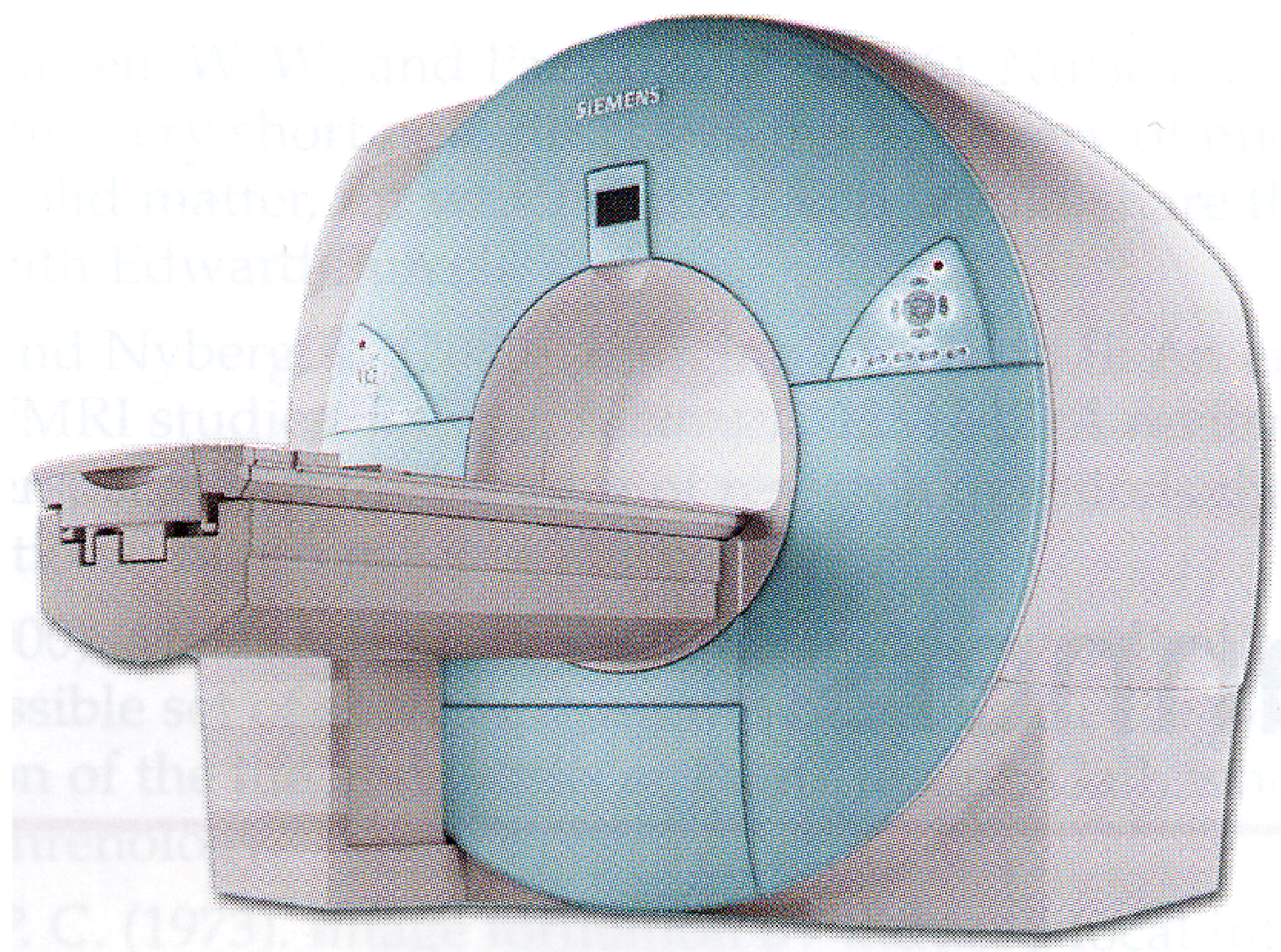
Building an MRI Machine



Main field (B_0) and imaging gradients (G_x, G_y, G_z)

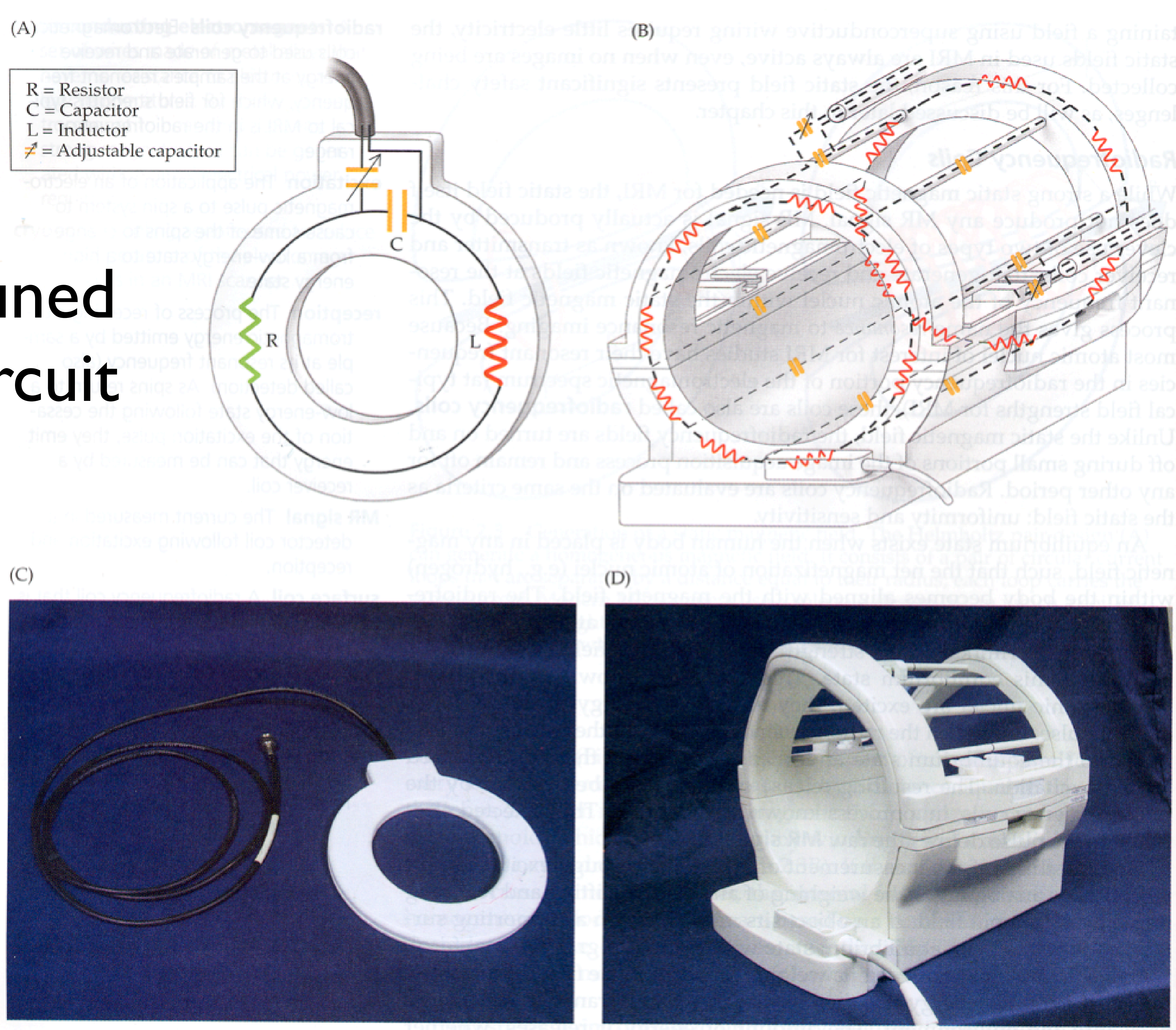
Bulding an MRI Machine



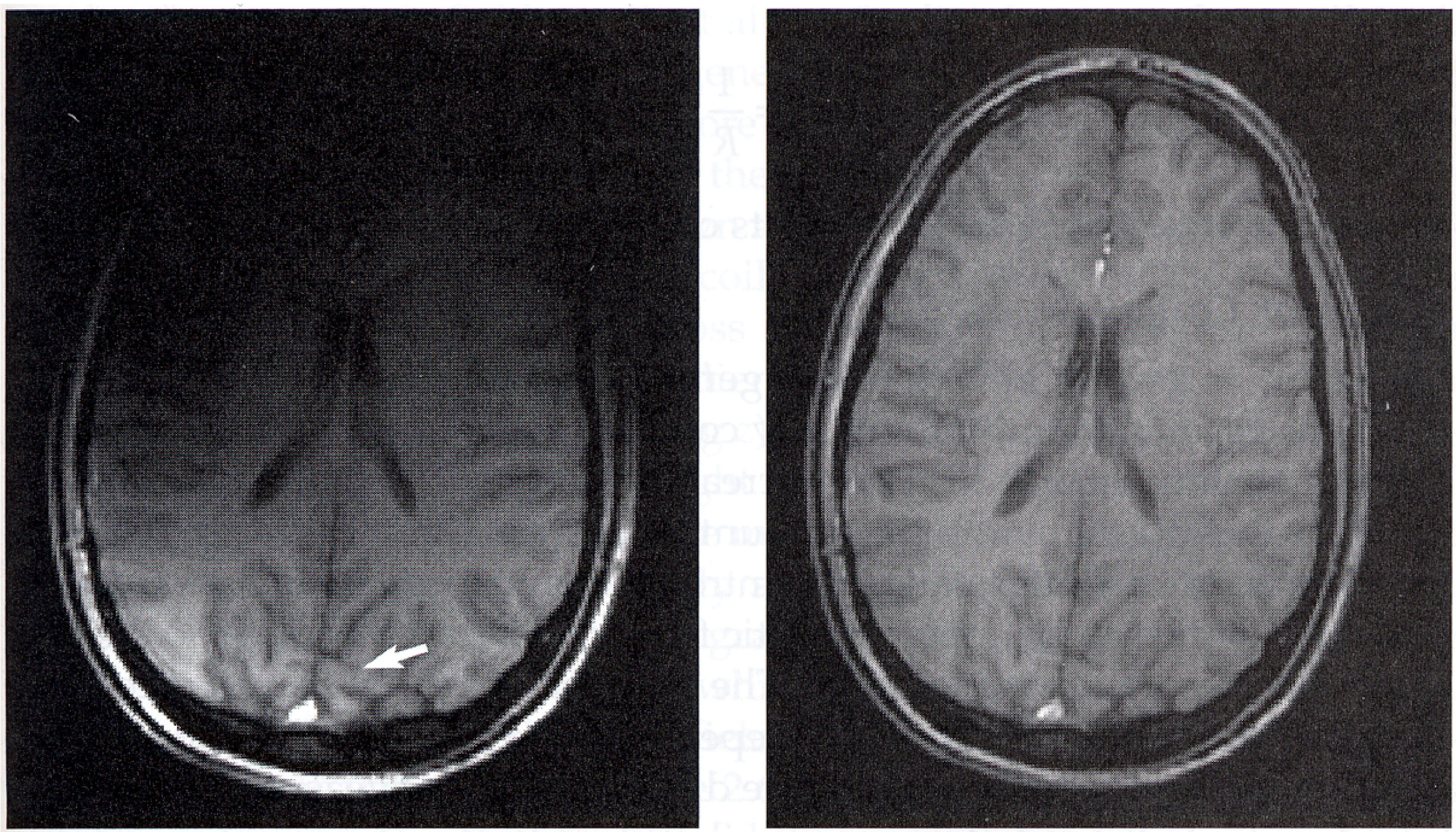


RF Coils

Tuned circuit



Surface Coils vs Volume Coils

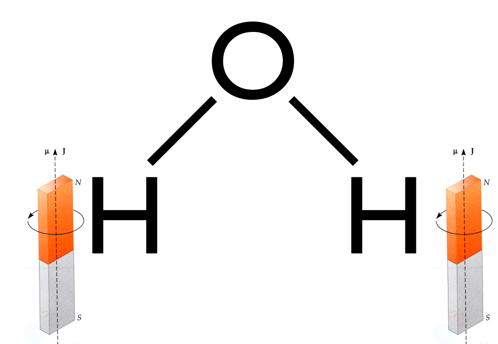


the nuclear spins

i.e.

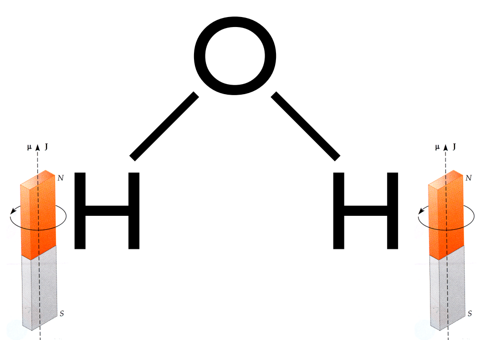
what we're imaging in MRI

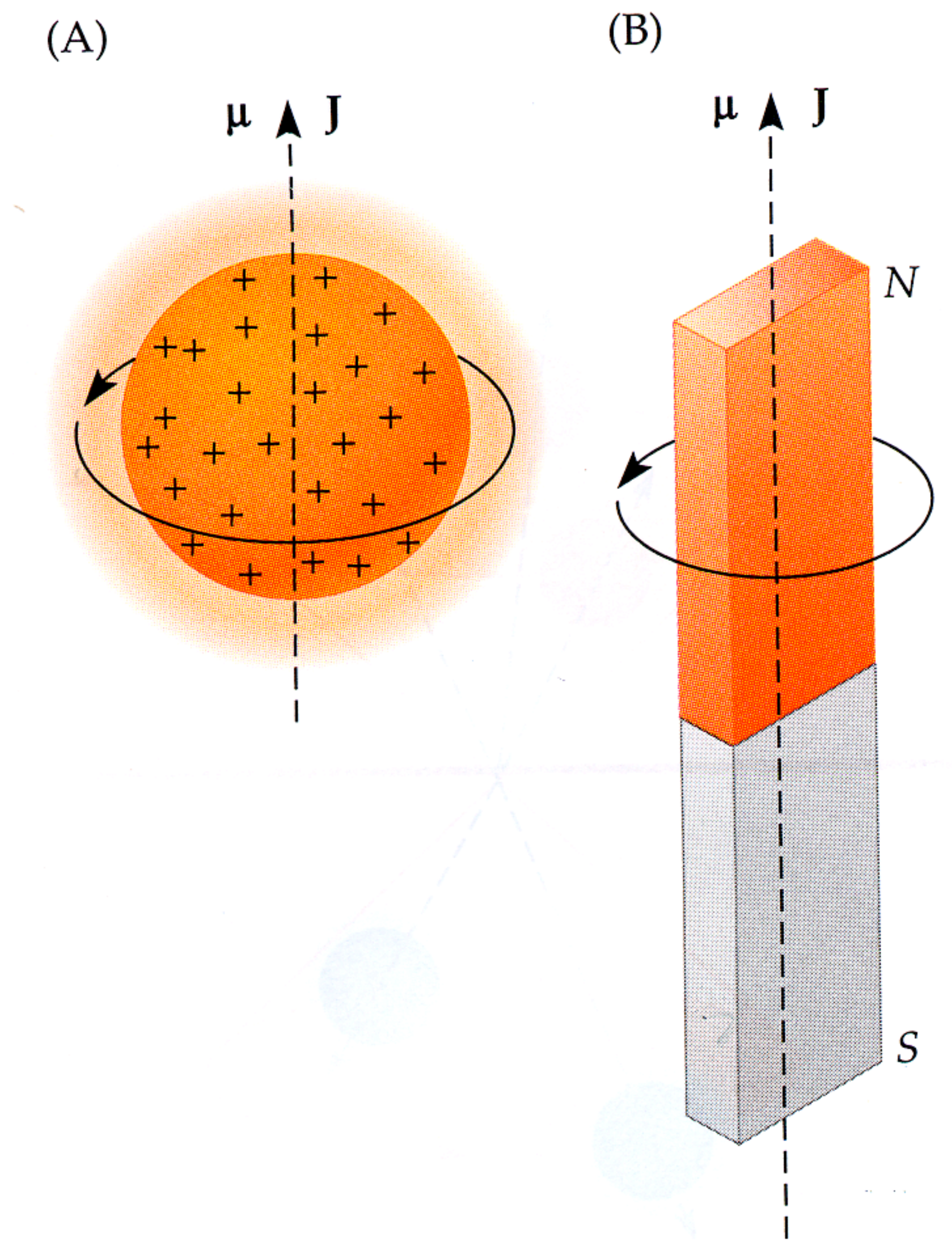
Water: H_2O



Nuclear Spin

Water: H_2O



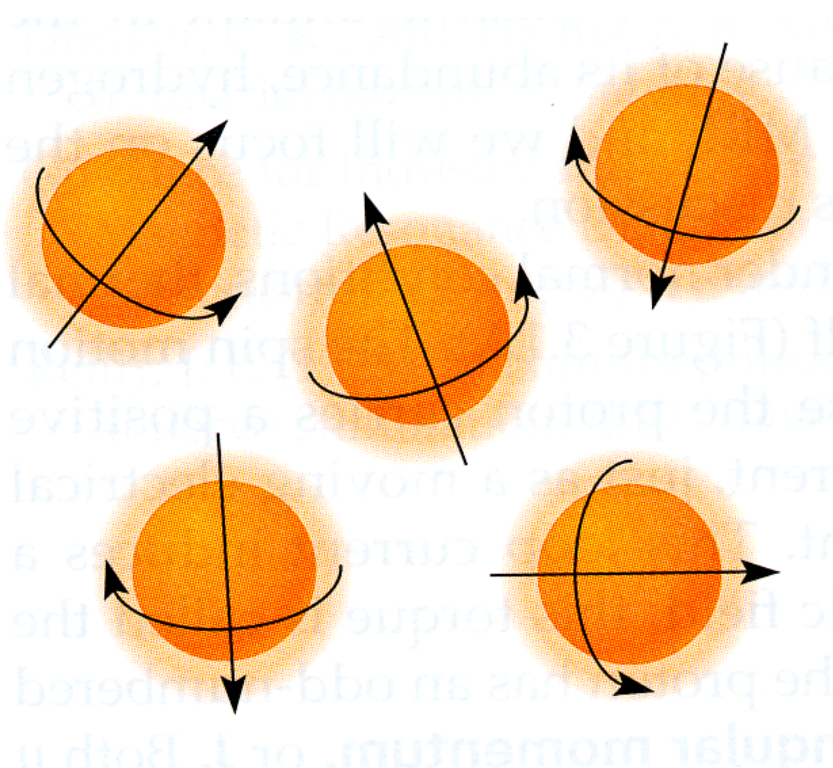


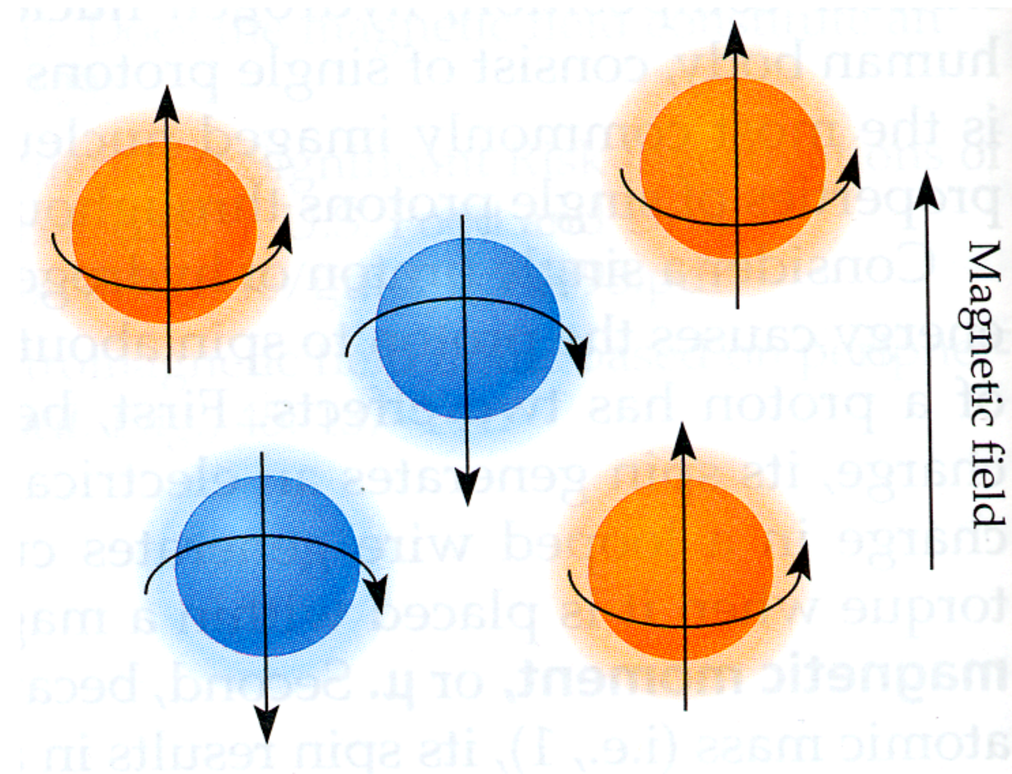
Protons have spin

- angular momentum (J)
- magnetic moment (μ)

Look like small spinning bar magnets

Spins in Magnetic Field

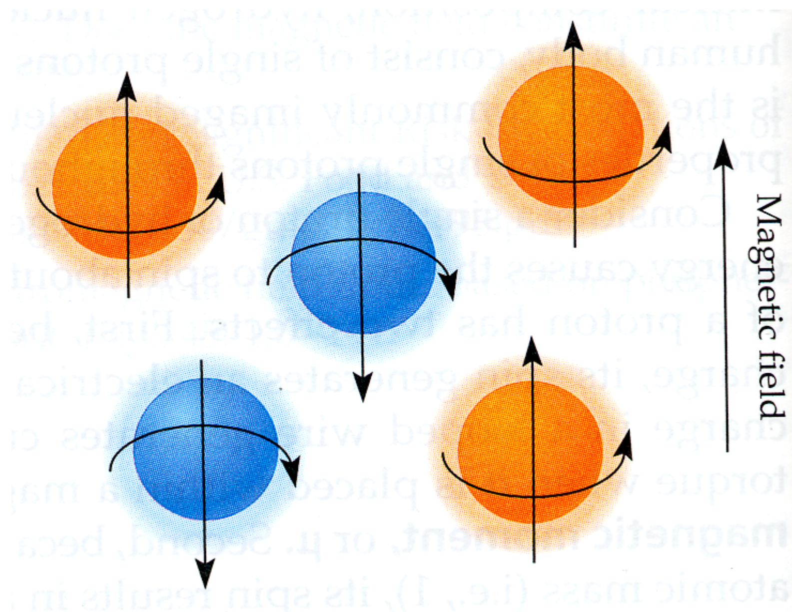


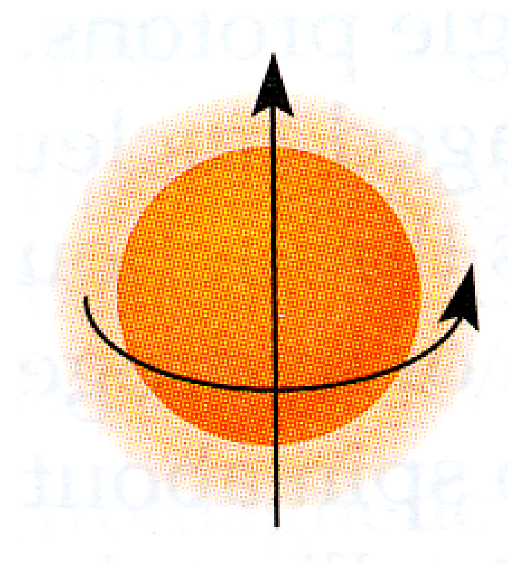


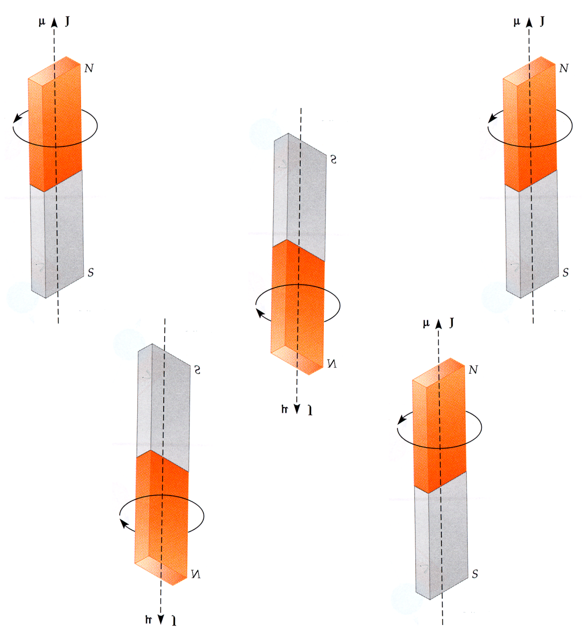
Magnetic Field = 0
Random orientation
One state

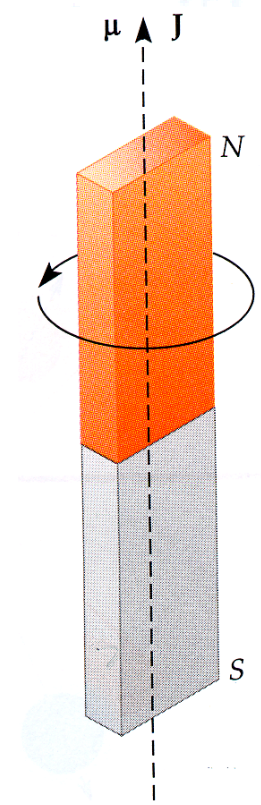
Magnetic Field ≠ 0
Alignment. Two states
orange: parallel, low energy
blue: anti, high energy

Many Spins: Net Magnetization

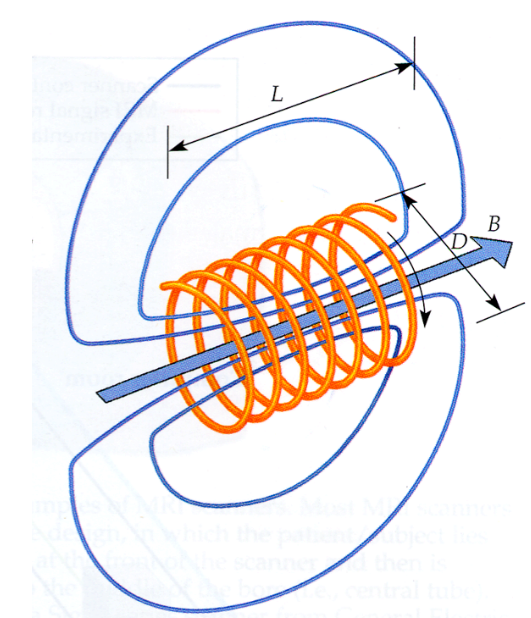




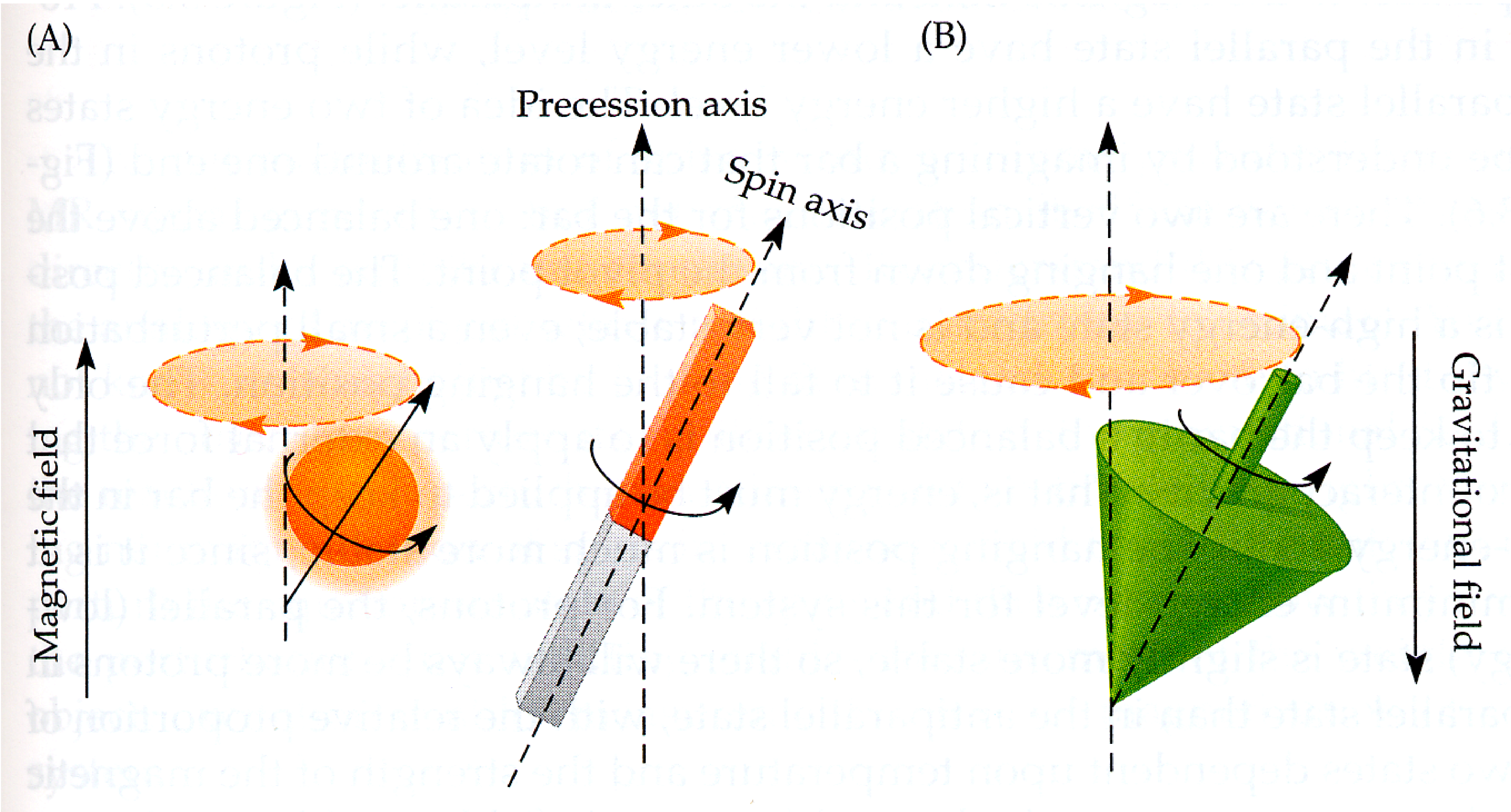




Main Field B0



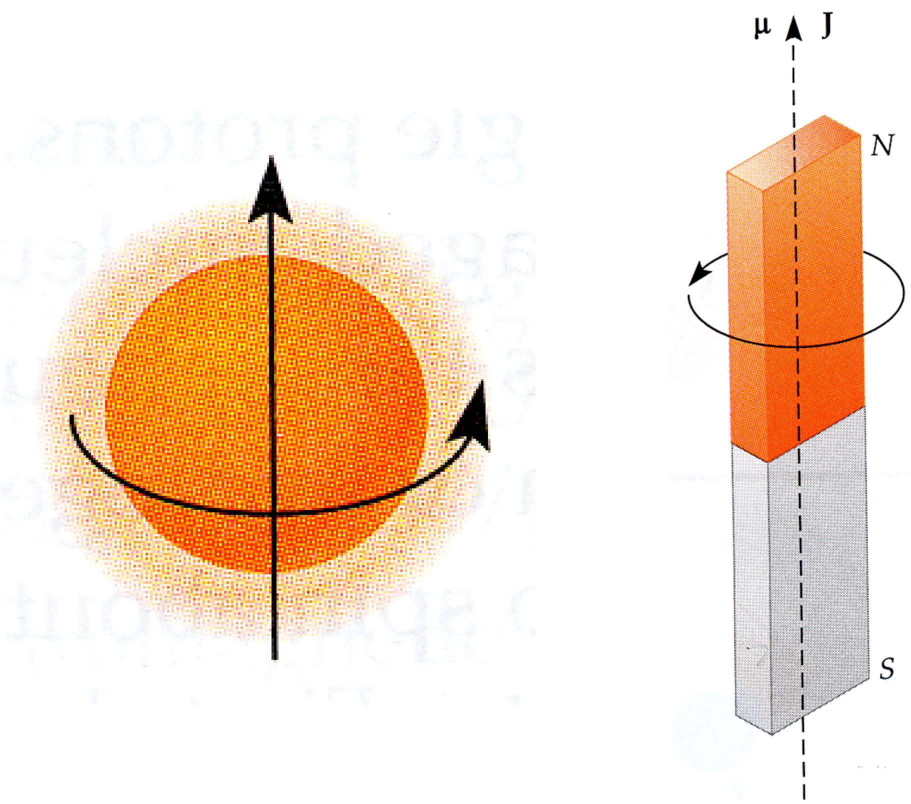
Precession of Spins



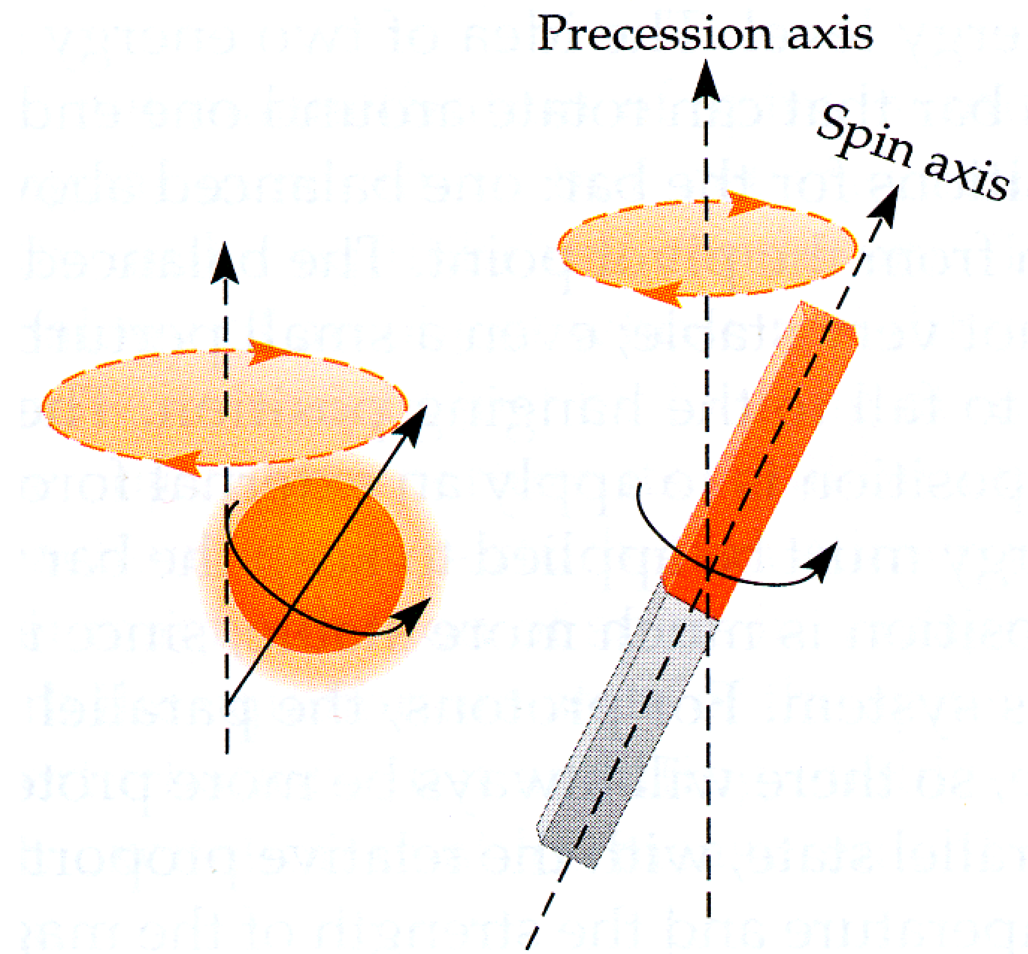
Larmor Equation:
Precession frequency proportional to magnetic field strength

$$\omega = \gamma B$$

The Magnetization Vector



Equilibrium State M_0



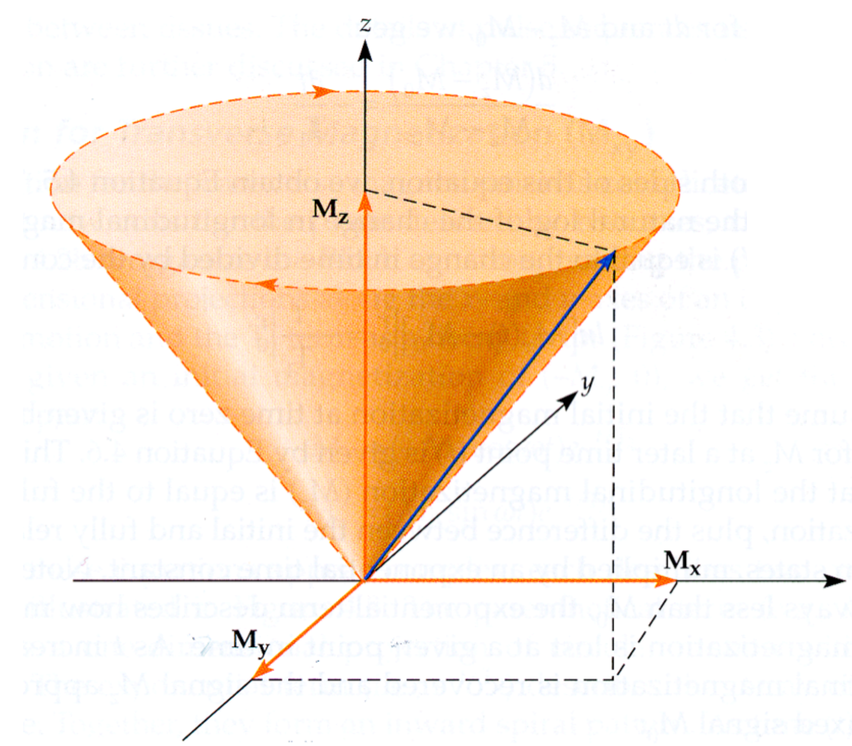
Dynamic State

M_0 proportional to number of spins and strength of magnetic field.

$$M_0 \sim NB_0$$

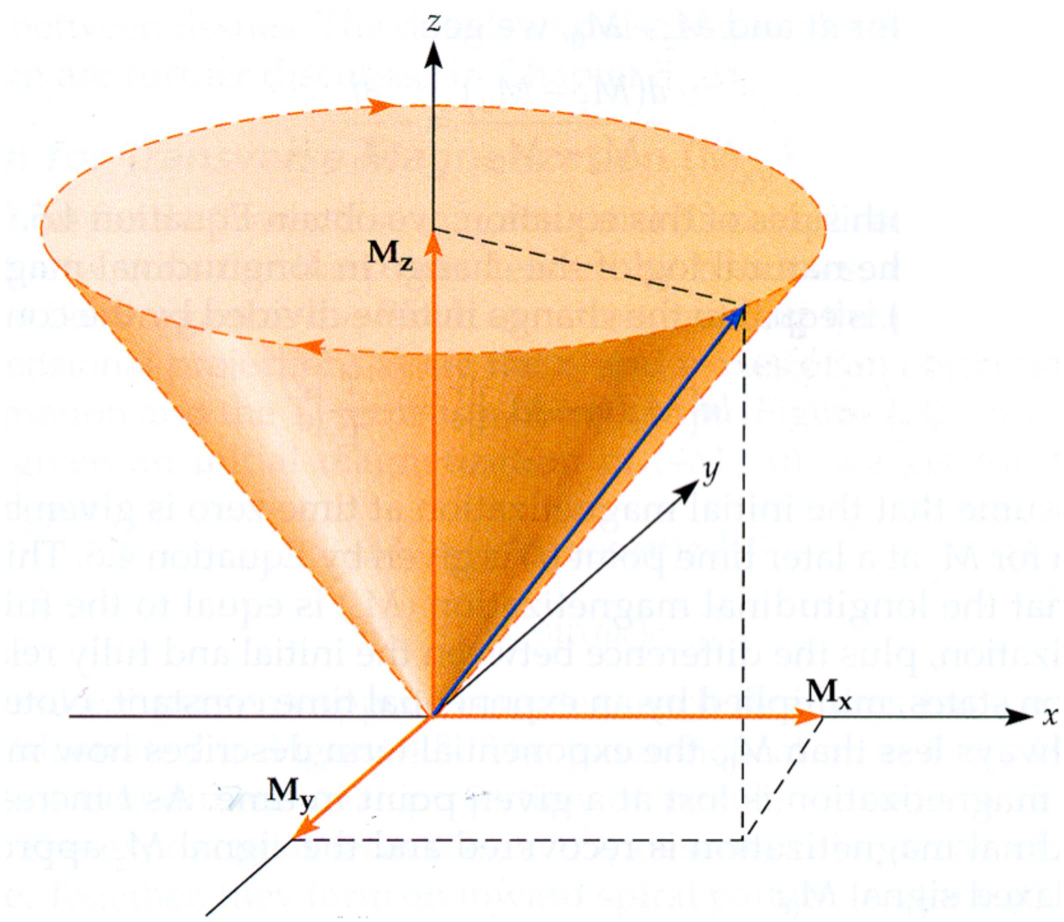
Time Evolution of the Magnetization Vector

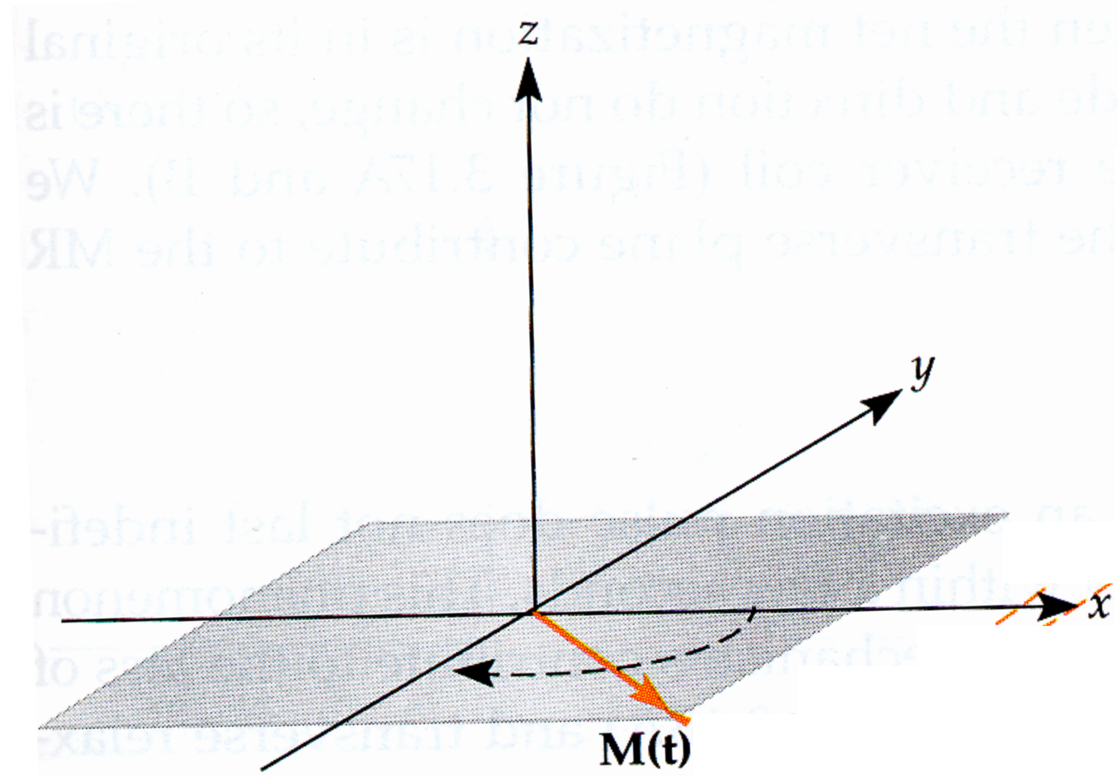
- Equilibrium: M_0 along z.
- Longitudinal Component (M_z):
  - returns to M_0 with time constant T_1
- Transverse Component (M_x,M_y):
  - rotates at larmor frequency
  - decays to 0 with time constant T_2



$$\omega = \gamma B$$

Transverse Magnetization Rotates



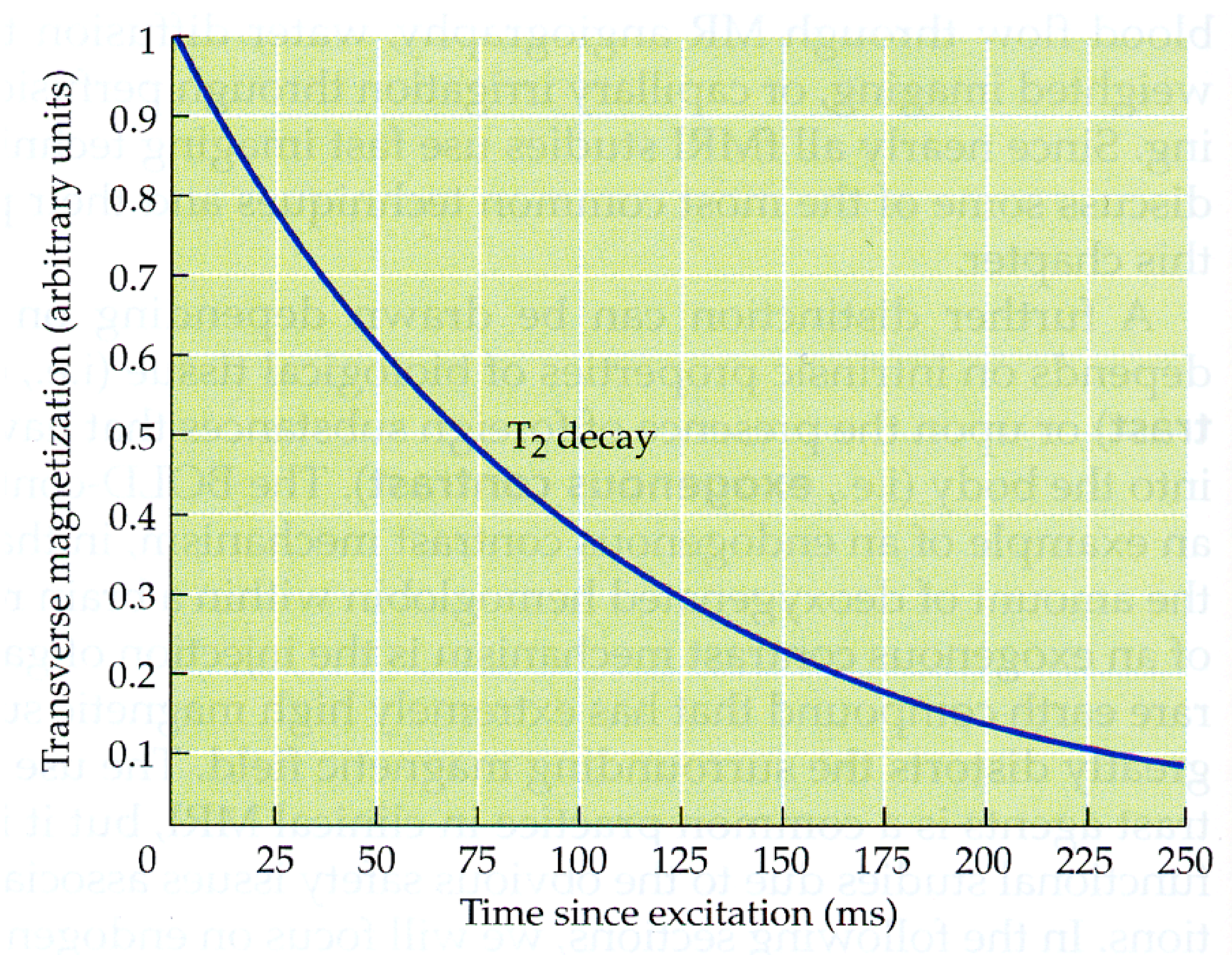


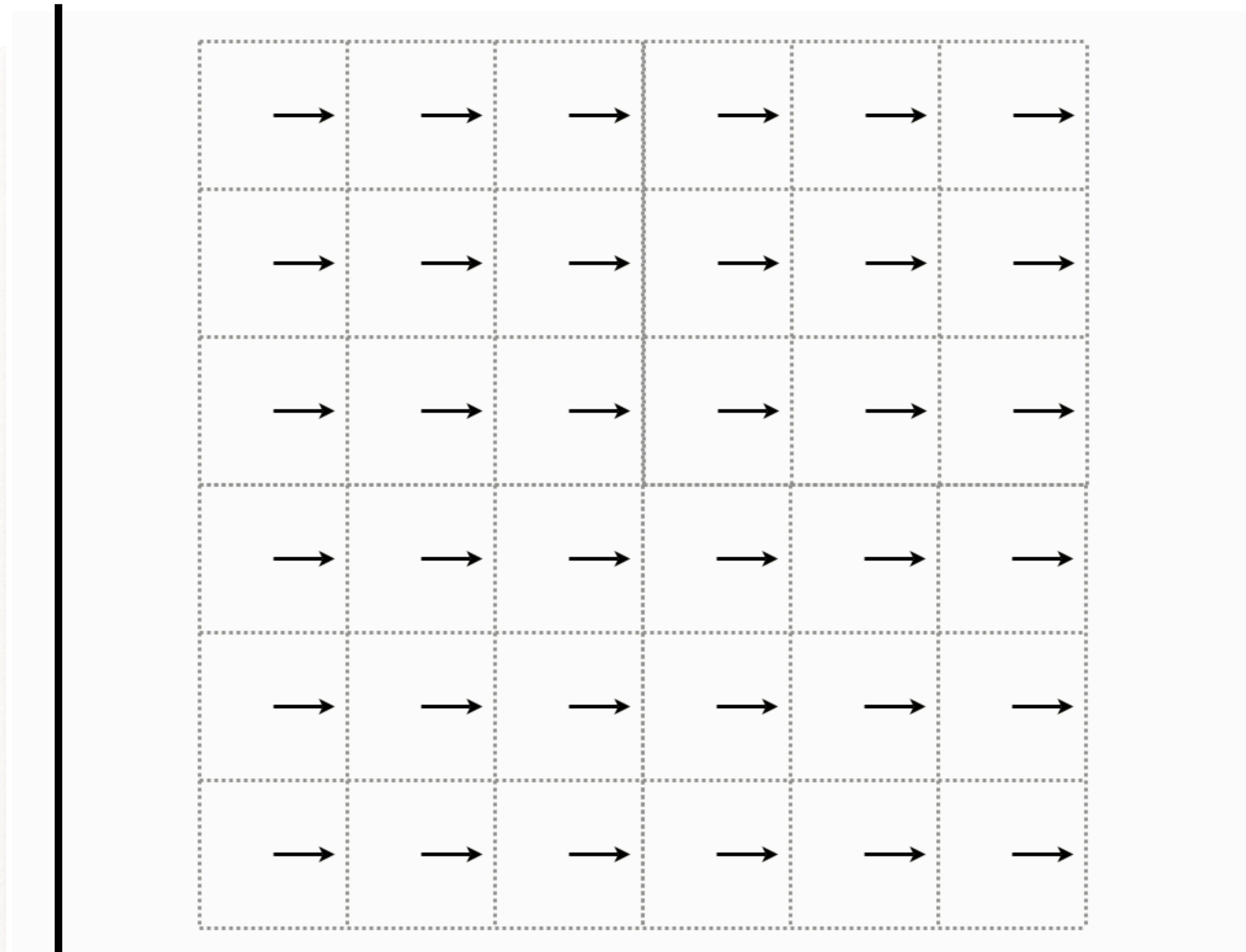
$$\omega = \gamma B$$

	1.5T	3T
1H	64	128
13C	16	32

MHz

Transverse Magnetization Decays





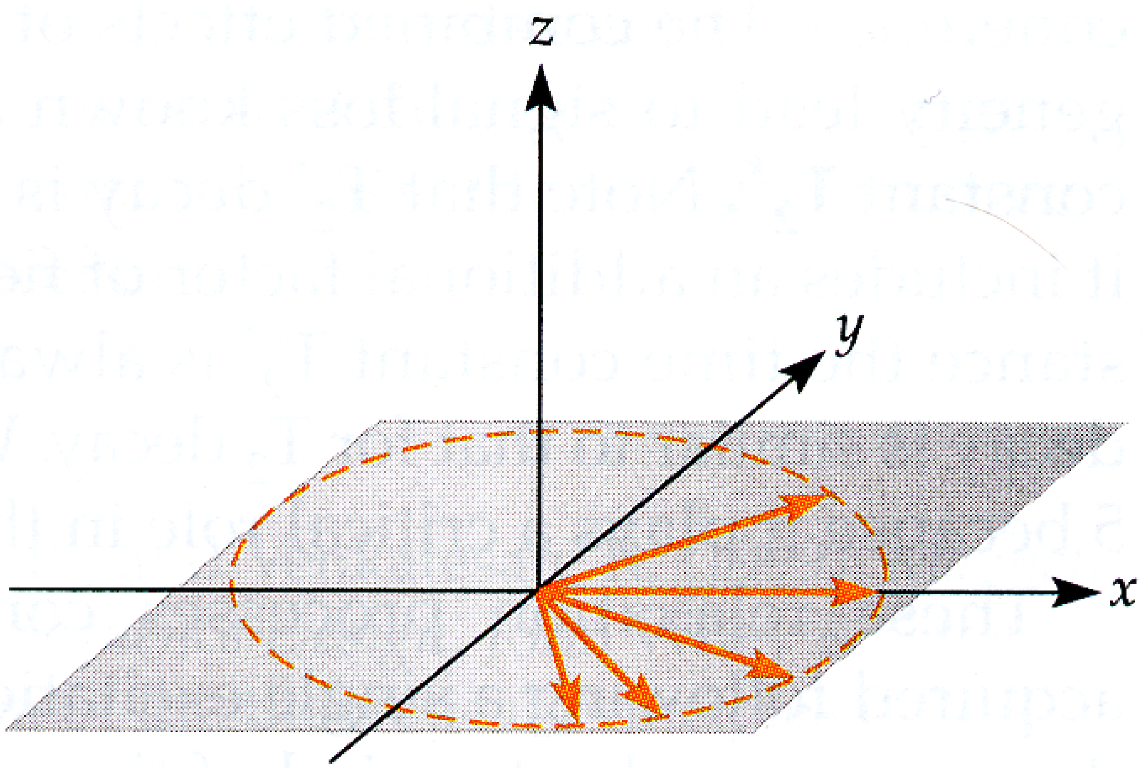
T_2*

T_2: magnetization get's shorter

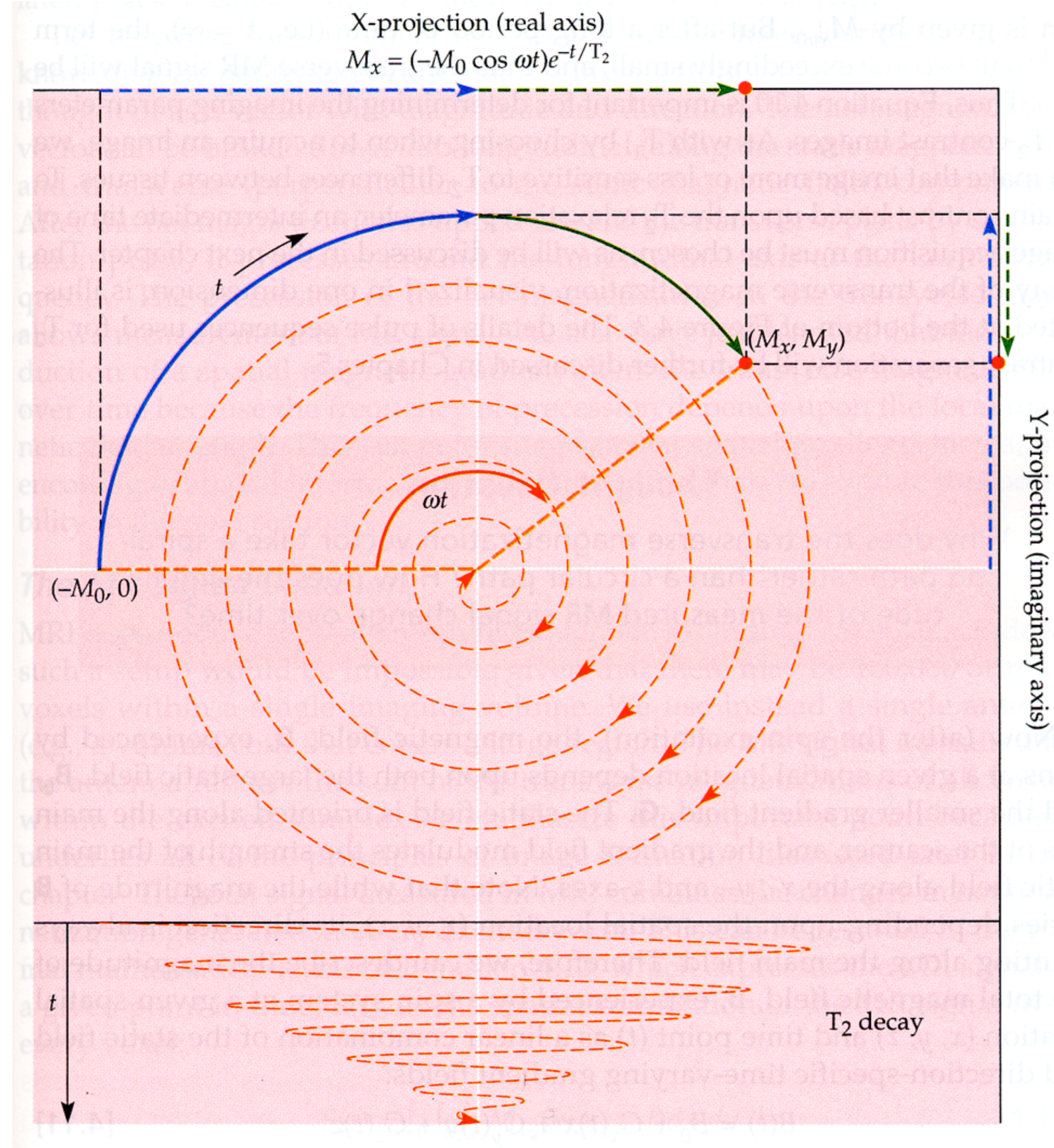
T_2*: magnetization gets out of phase

Non-uniformity in local magnetic field, motion, etc.

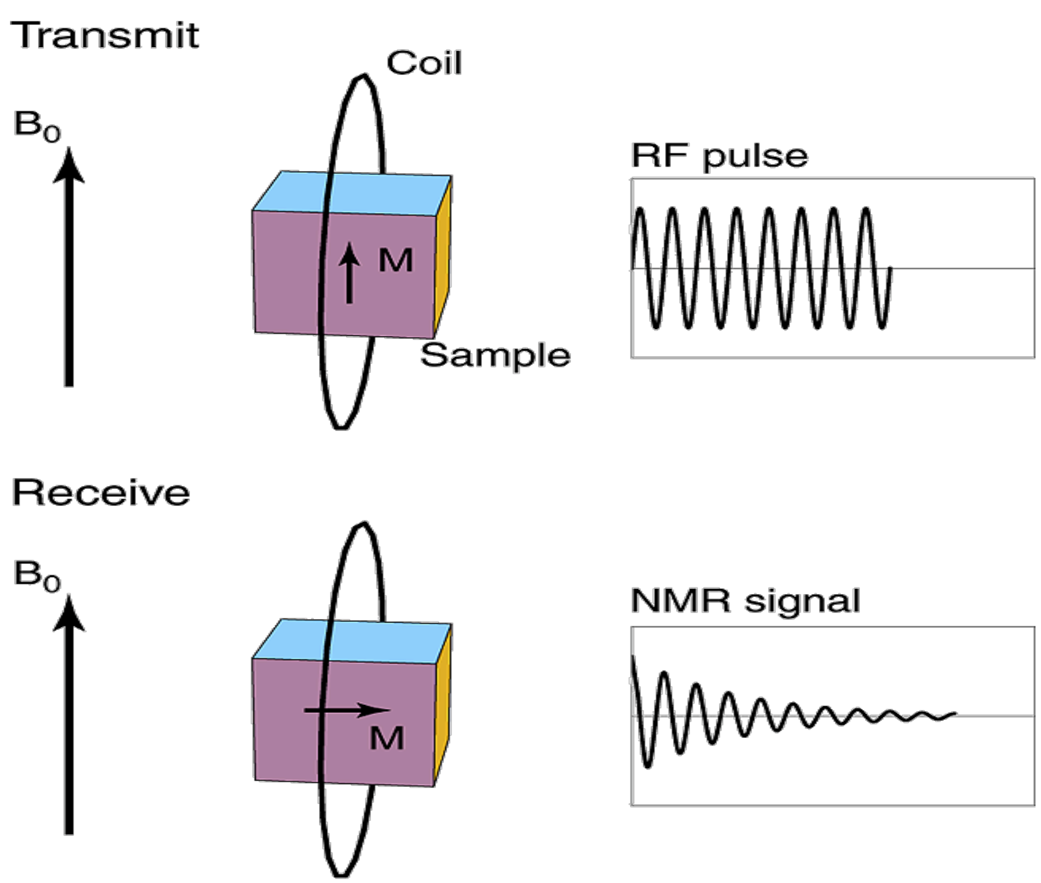
Transverse Magnetization Rotates and Decays

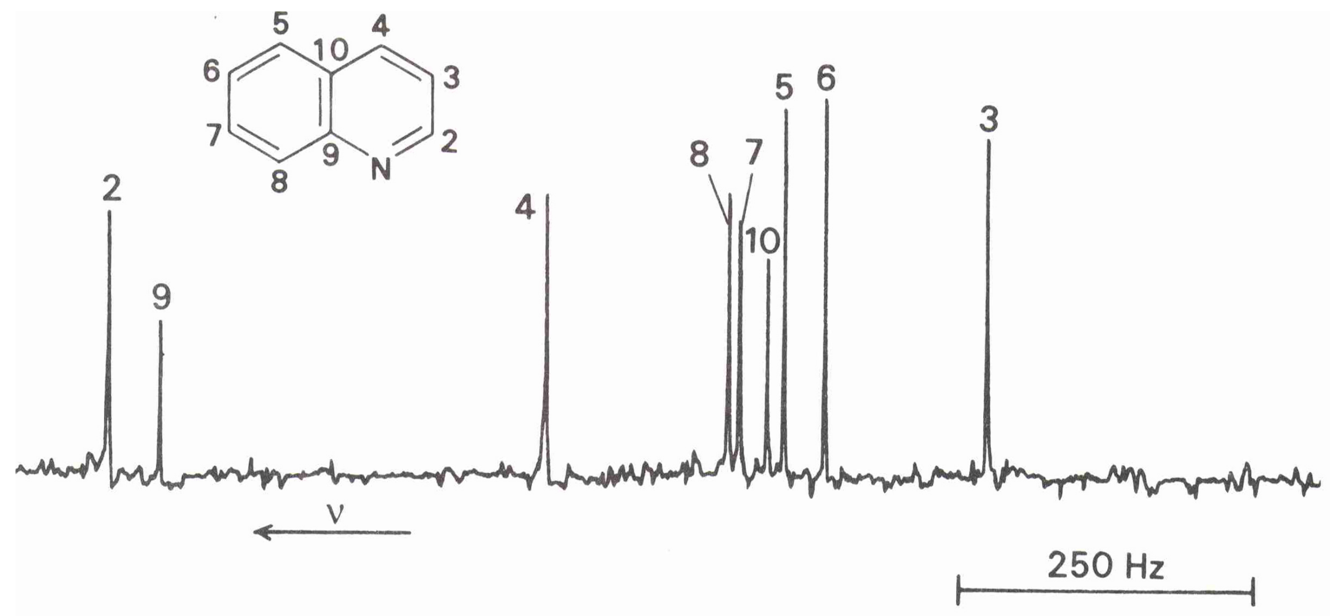


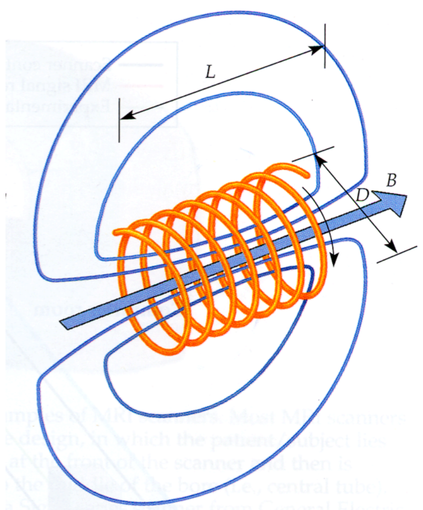
Time constant T_2

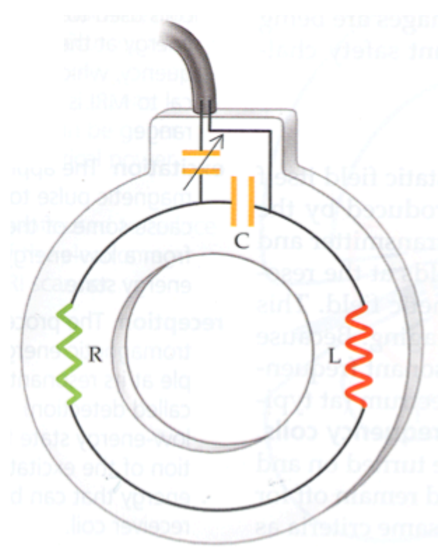


The NMR Experiment





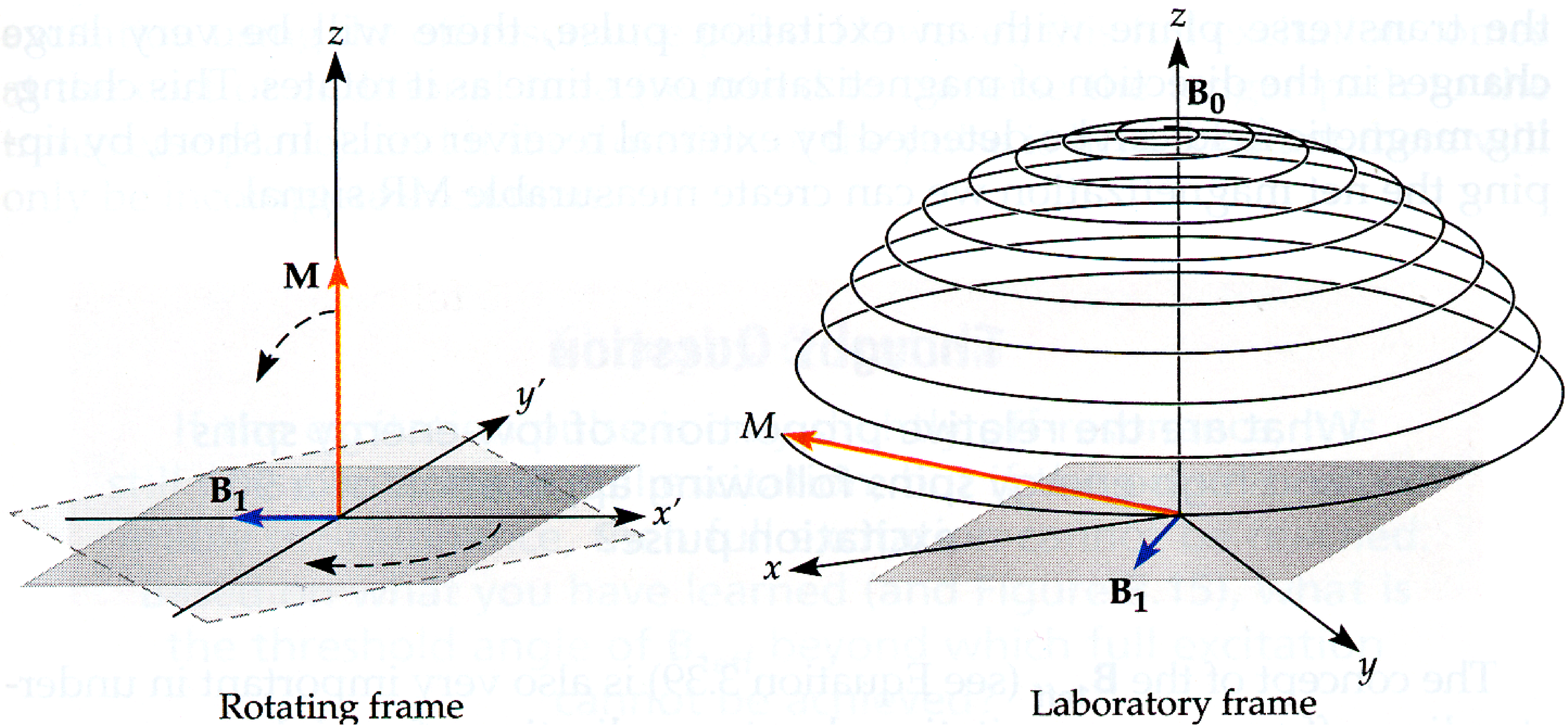




tuned circuit

0) Put sample in magnet
1) Push magnetization into transverse plane
2) Detect NMR signal
3) Produce power spectrum

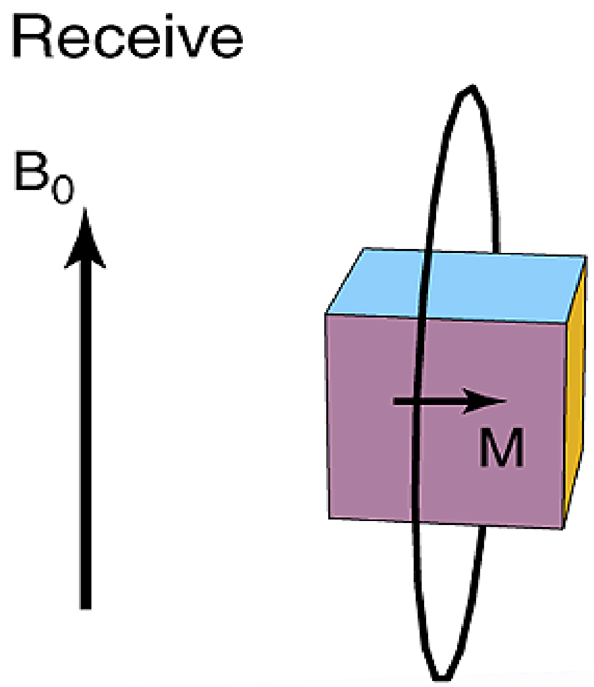
Push the Magnetization

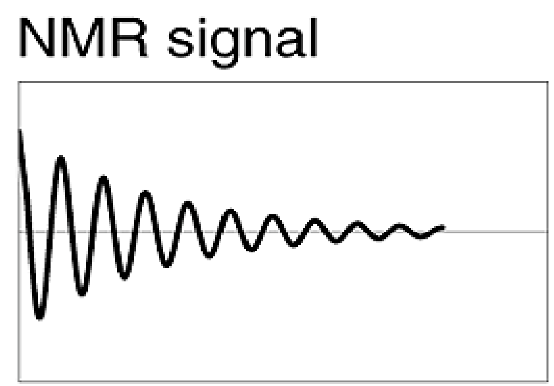


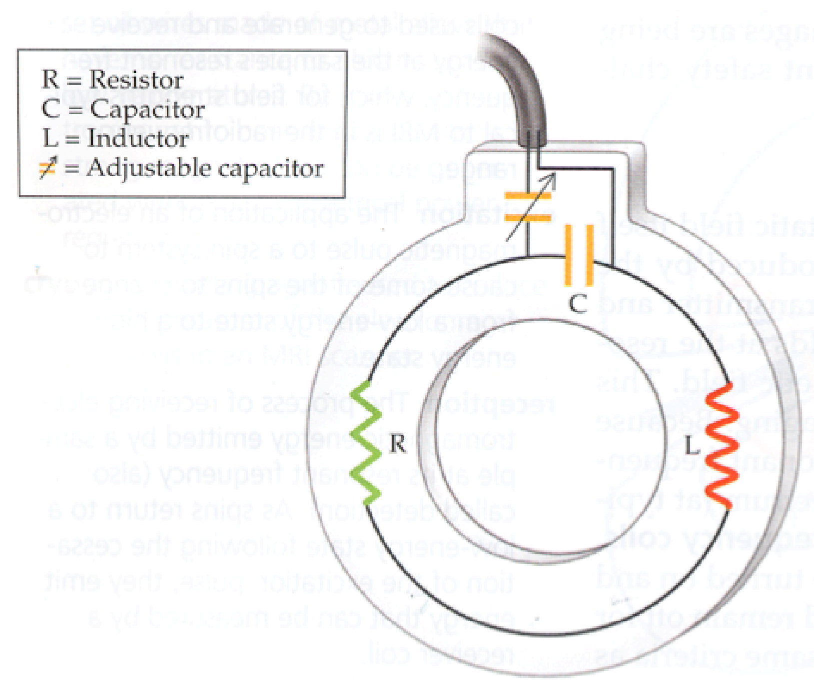
RF pulse frequency must match rotation frequency of M (**resonance**)

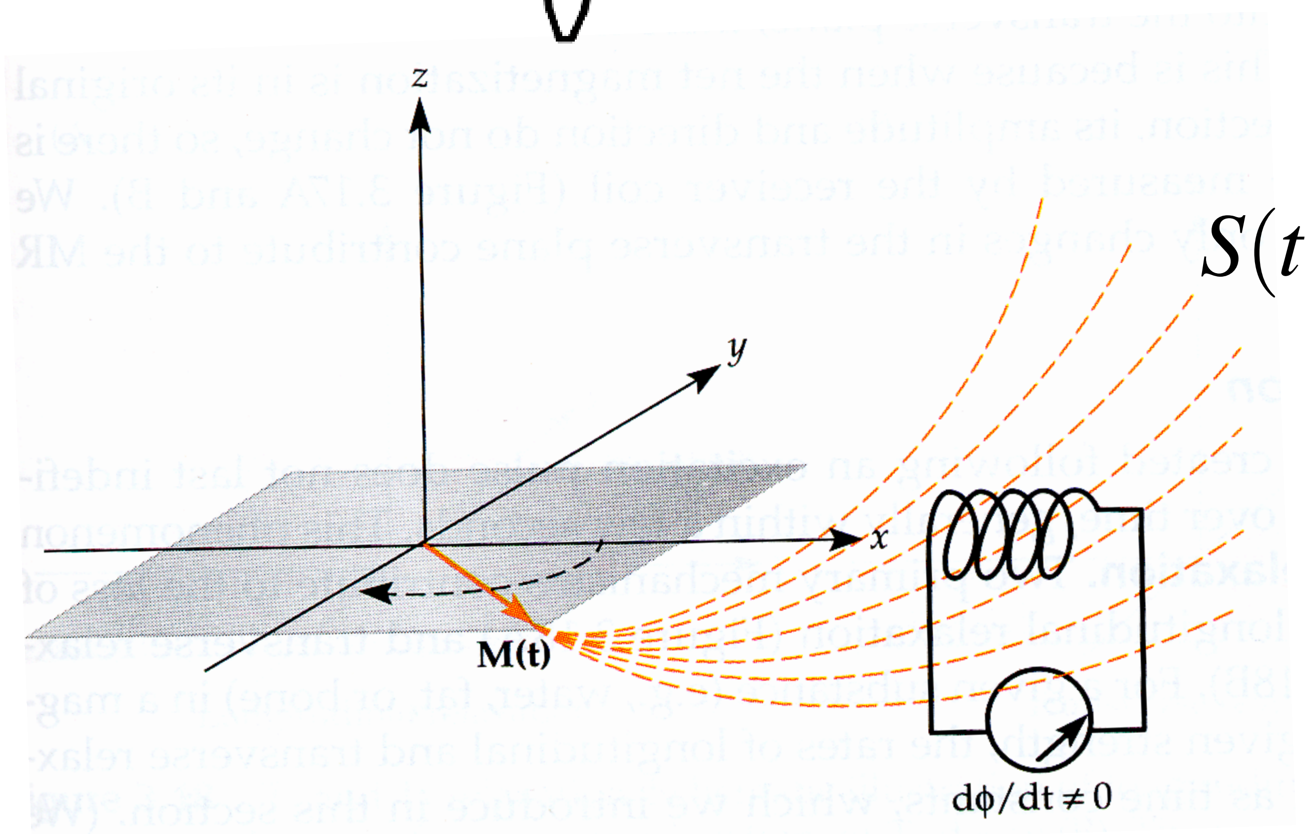
RF pulse amplitude and duration control flip angle

Detect Transverse Magnetization









$$S(t) = \int_x \int_y \int_z M_{xy}(x,y,z,t)\,dxdydz$$

Coil integrates over space

Detect rotating transverse magnetization by induction.

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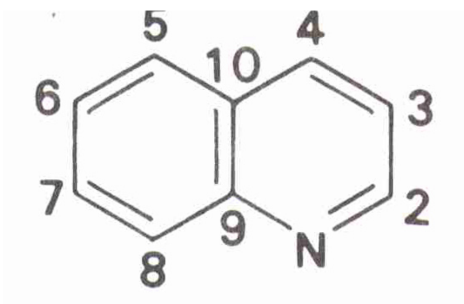
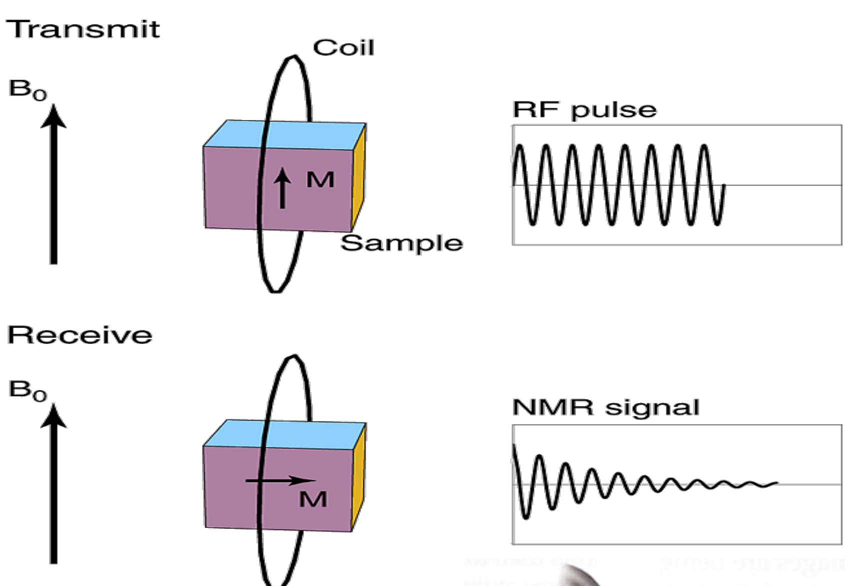
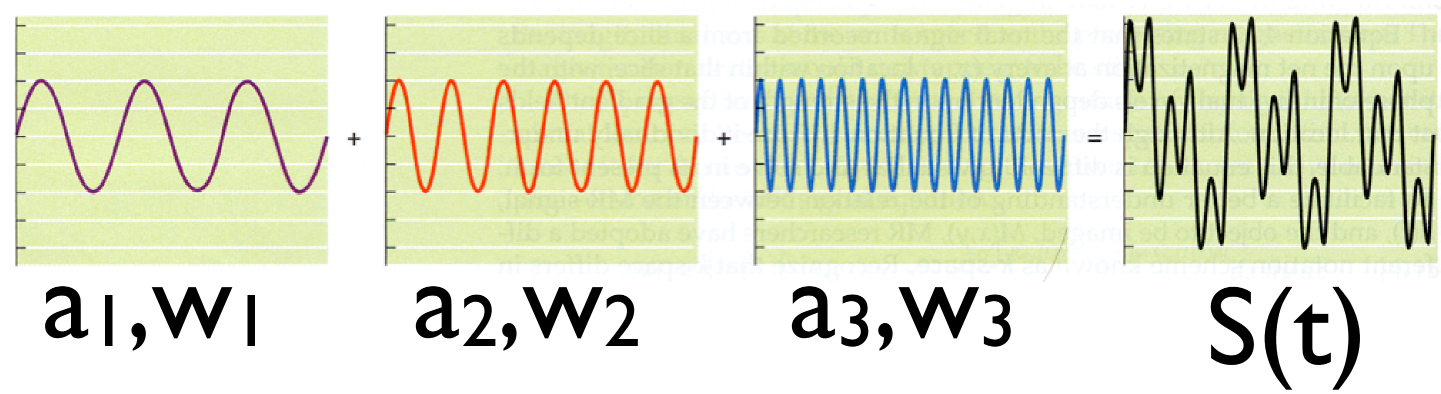
The NMR Experiment



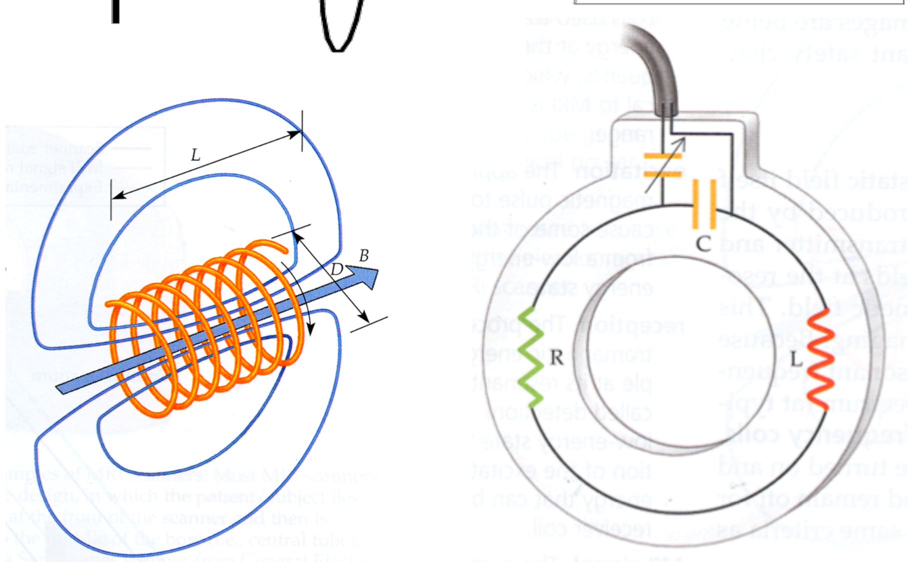
$$\omega_j = \gamma B_j$$

$$M_{xy,j}(t) = a_j e^{-t/T_2} e^{i\omega_j t} \approx a_j e^{i\omega_j t}$$

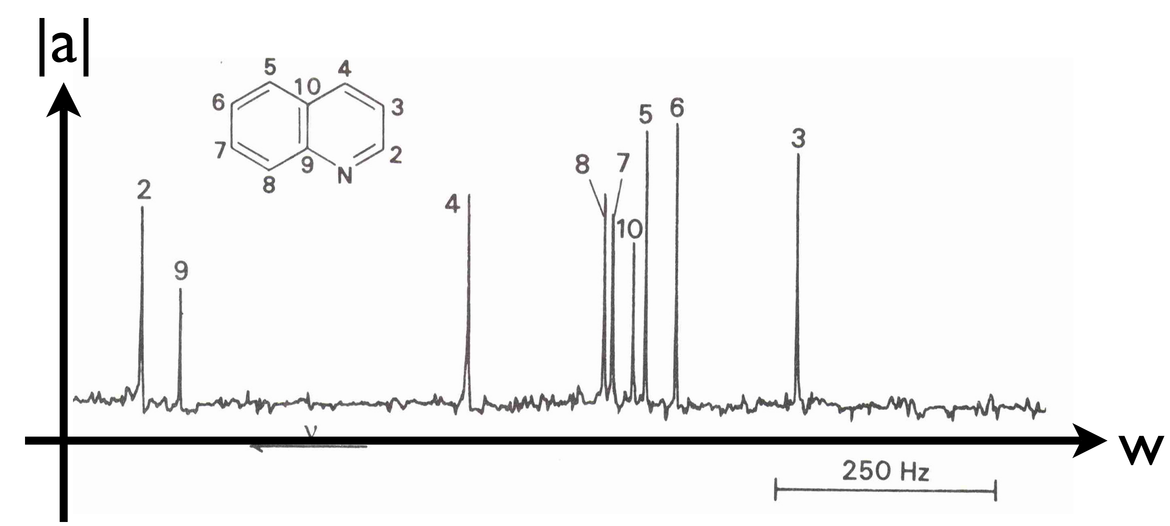




$$S(t) = a_1 e^{i\omega_1 t} + a_2 e^{i\omega_2 t} + a_3 e^{i\omega_3 t} + \ldots$$



Fourier Transform

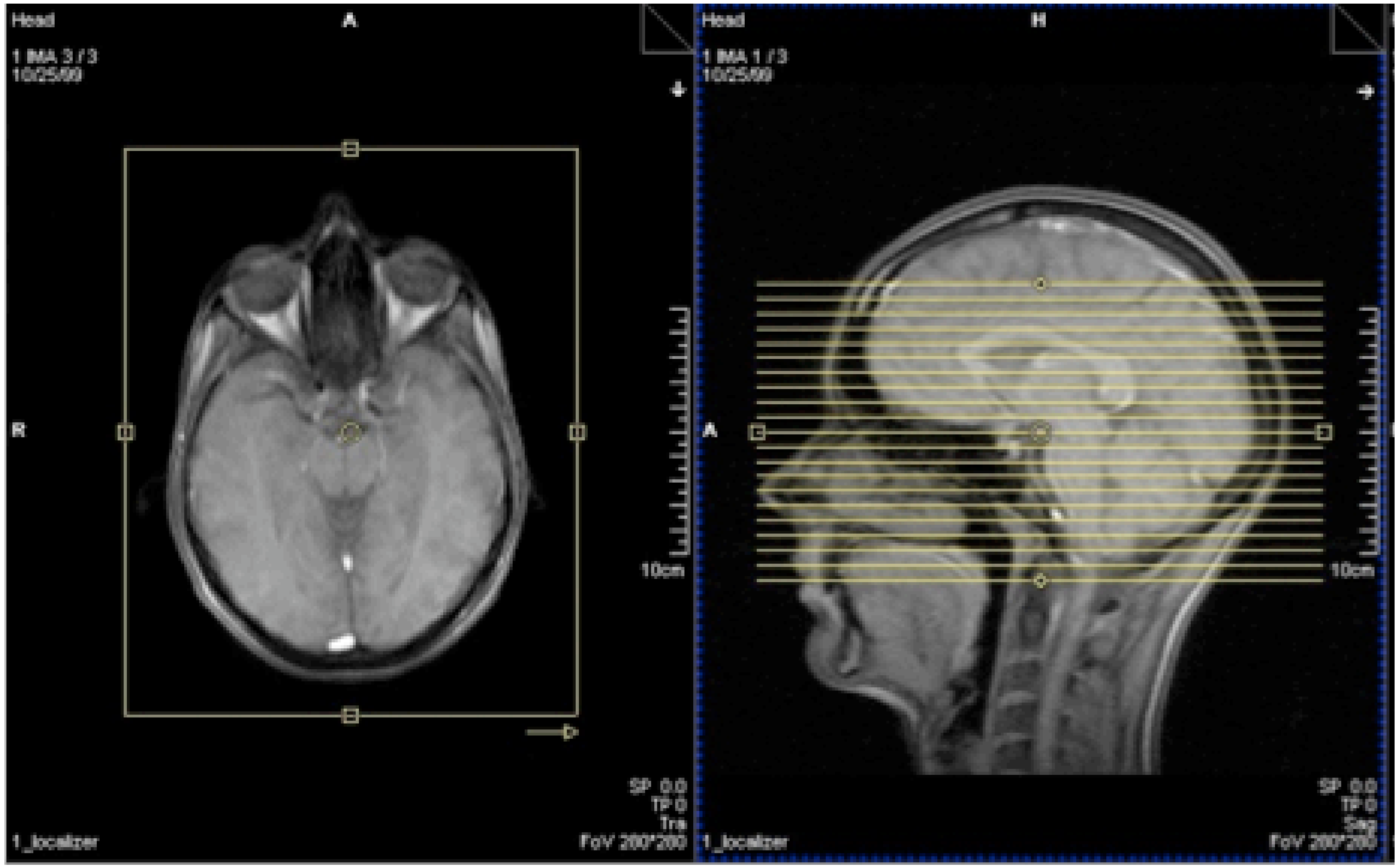


$$S(t) = \int_V C(x,y,z) M_{xy}(x,y,z,t) dV$$

The NMR coil measures the INTEGRAL of the transverse magnetization M_{xy} from all parts of the sample (weighted by the coil sensitivity C).

Problem:
How do we make an image of the magnetization?
i.e. how do we localize the signal?

MRI: Signal Localization



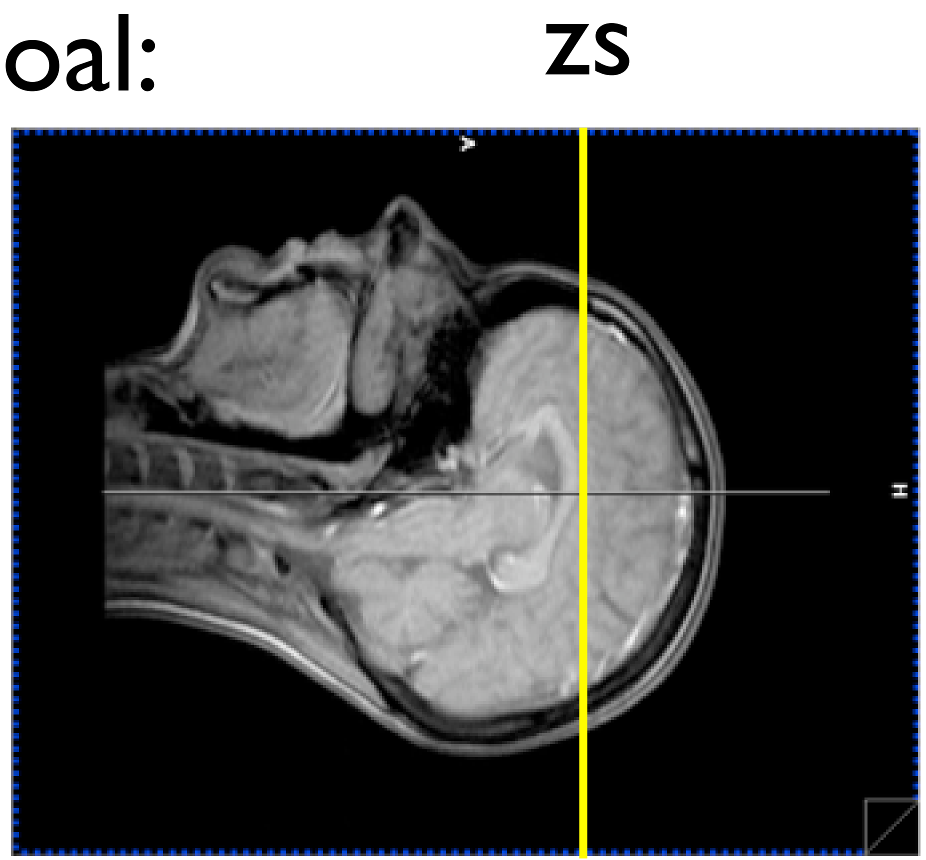
Two ways to localize:
1) Excitation
2) Detection

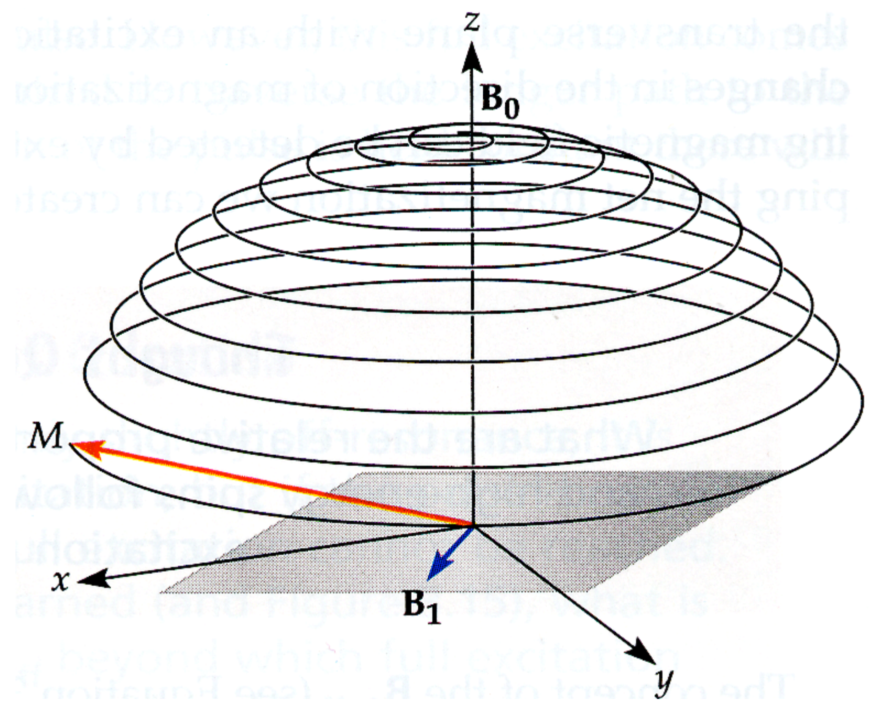
Excite a single "slice"
Encode position in signal
frequency/phase

Slice selection
Spatial localization during excitation

How to Excite a Slice?

Goal:





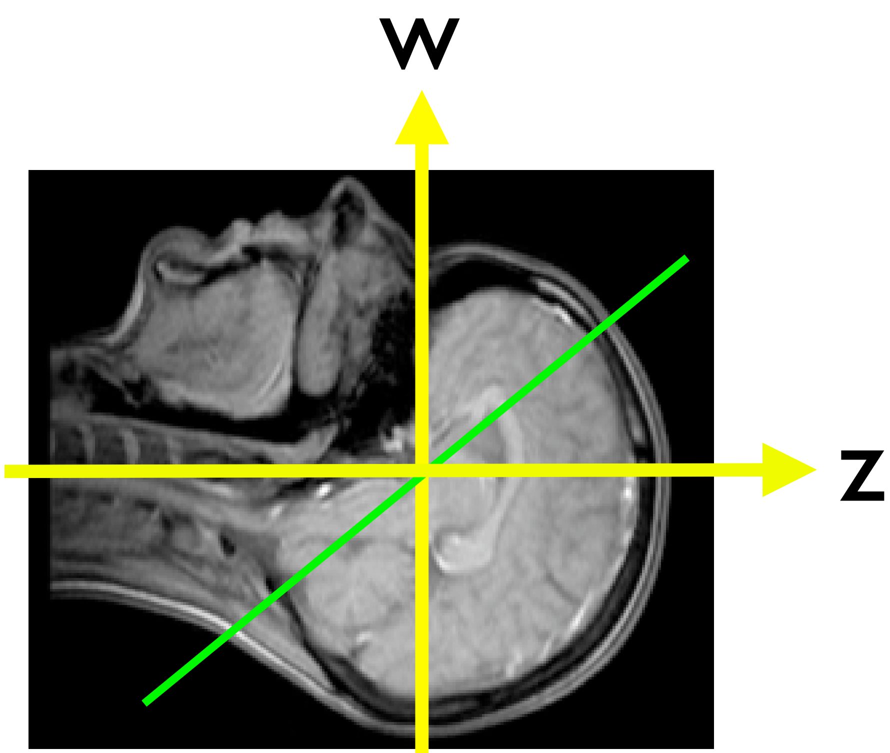
RF pulse only rotates M with matched frequency

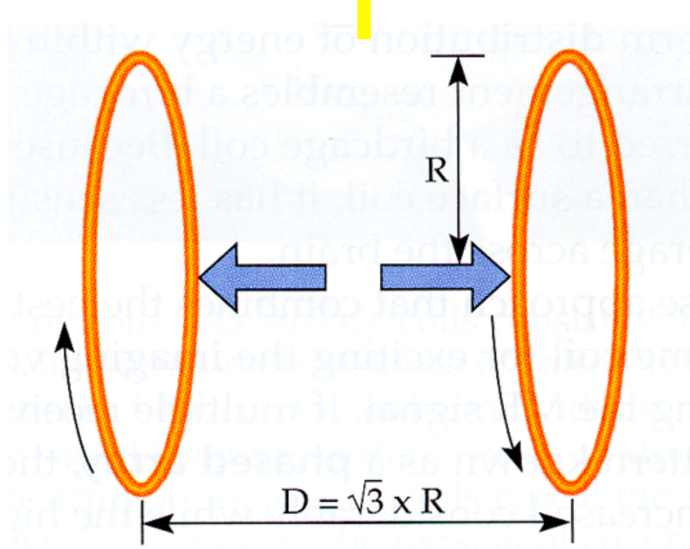
Solution:

1) Make M rotation frequency depend on location
   apply magnetic field using gradient coil
2) Apply RF pulse with appropriate frequency

Excite Slice 1

1) Make M rotation frequency depend on location





Use z gradient coil.

$$B(z) = Gz$$

$$\downarrow$$

$$\omega(z) = \gamma B(z) = \gamma G z$$

Excite Slice 2

2) Apply RF pulse with appropriate frequency

Magnetization rotation frequency

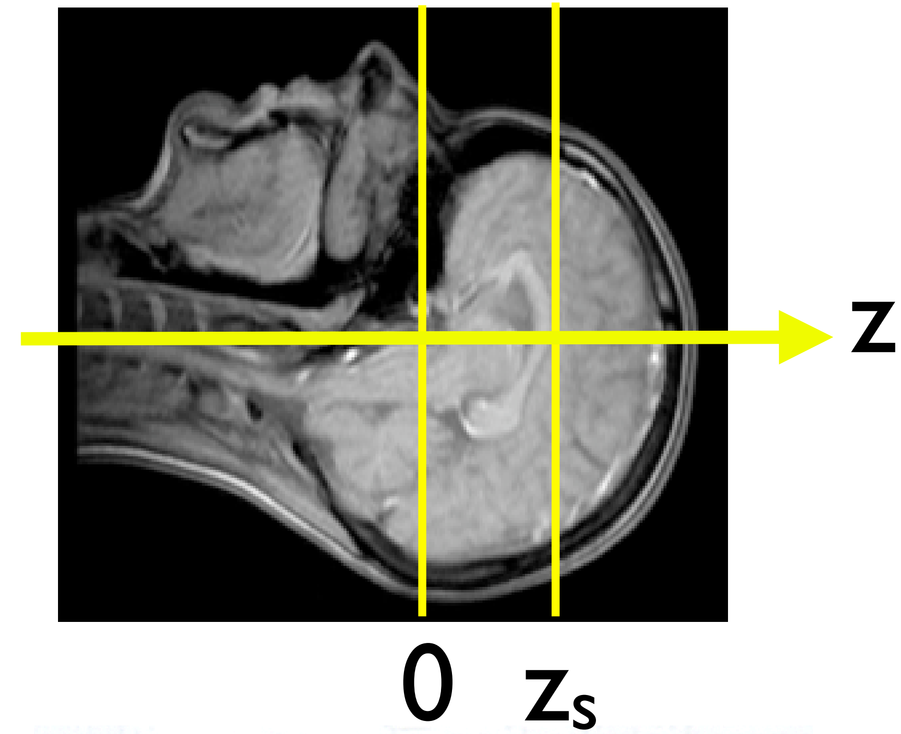
$$\omega(z) = \gamma G z$$

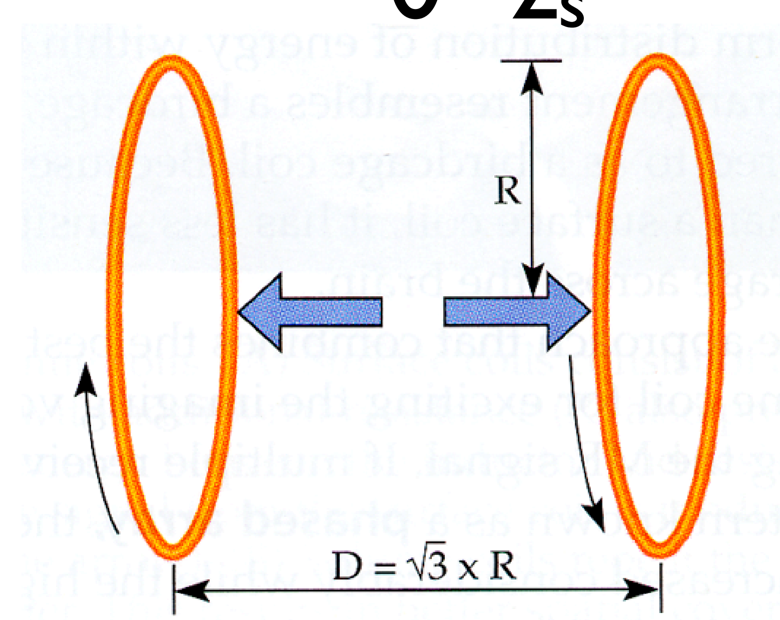
Apply RF pulse with frequency

$$\omega_{RF}$$

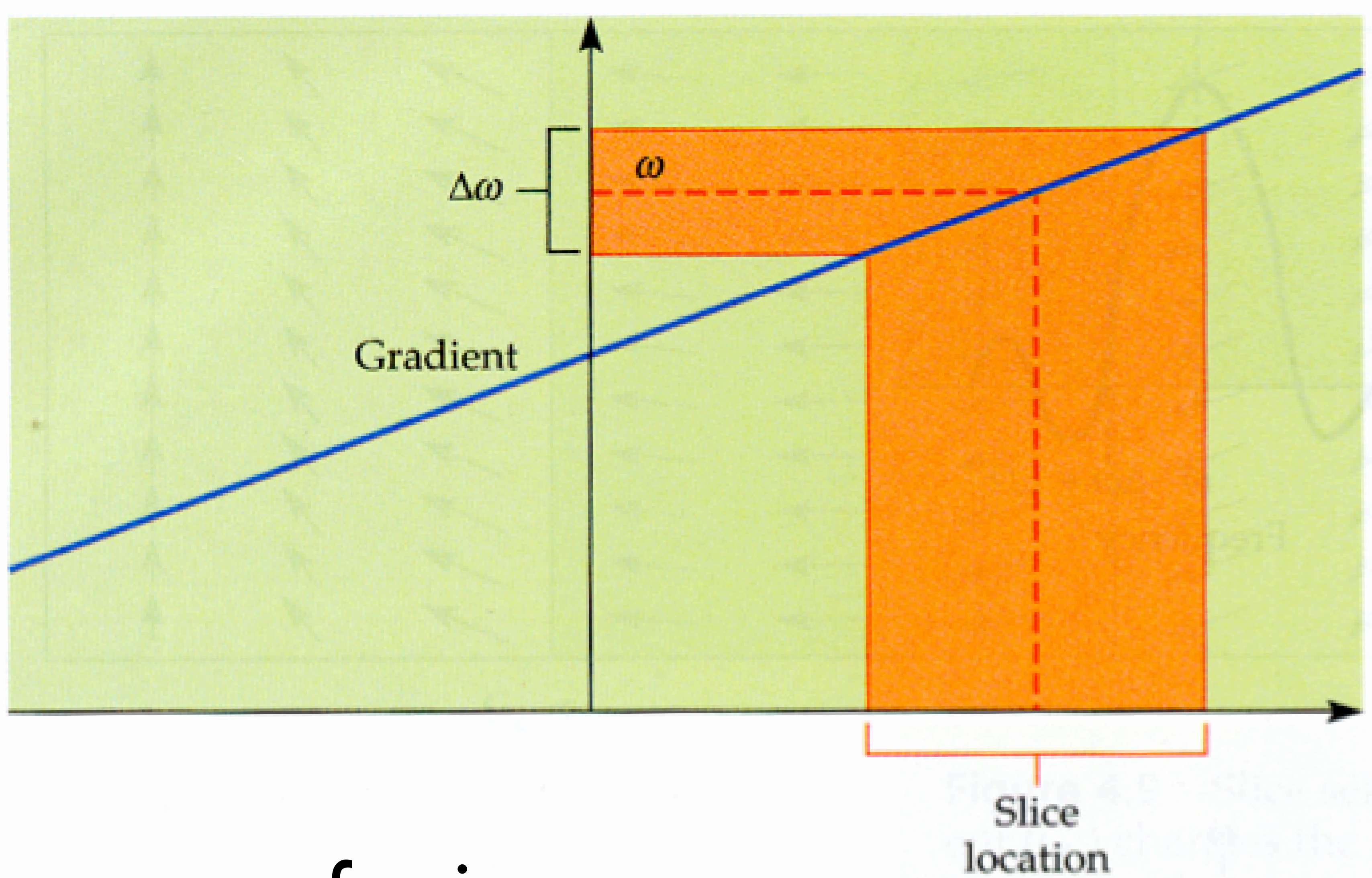
Flip Magnetization in slice at z_s

$$z_s = \frac{\omega_{RF}}{\gamma G}$$





Excite Slice 3



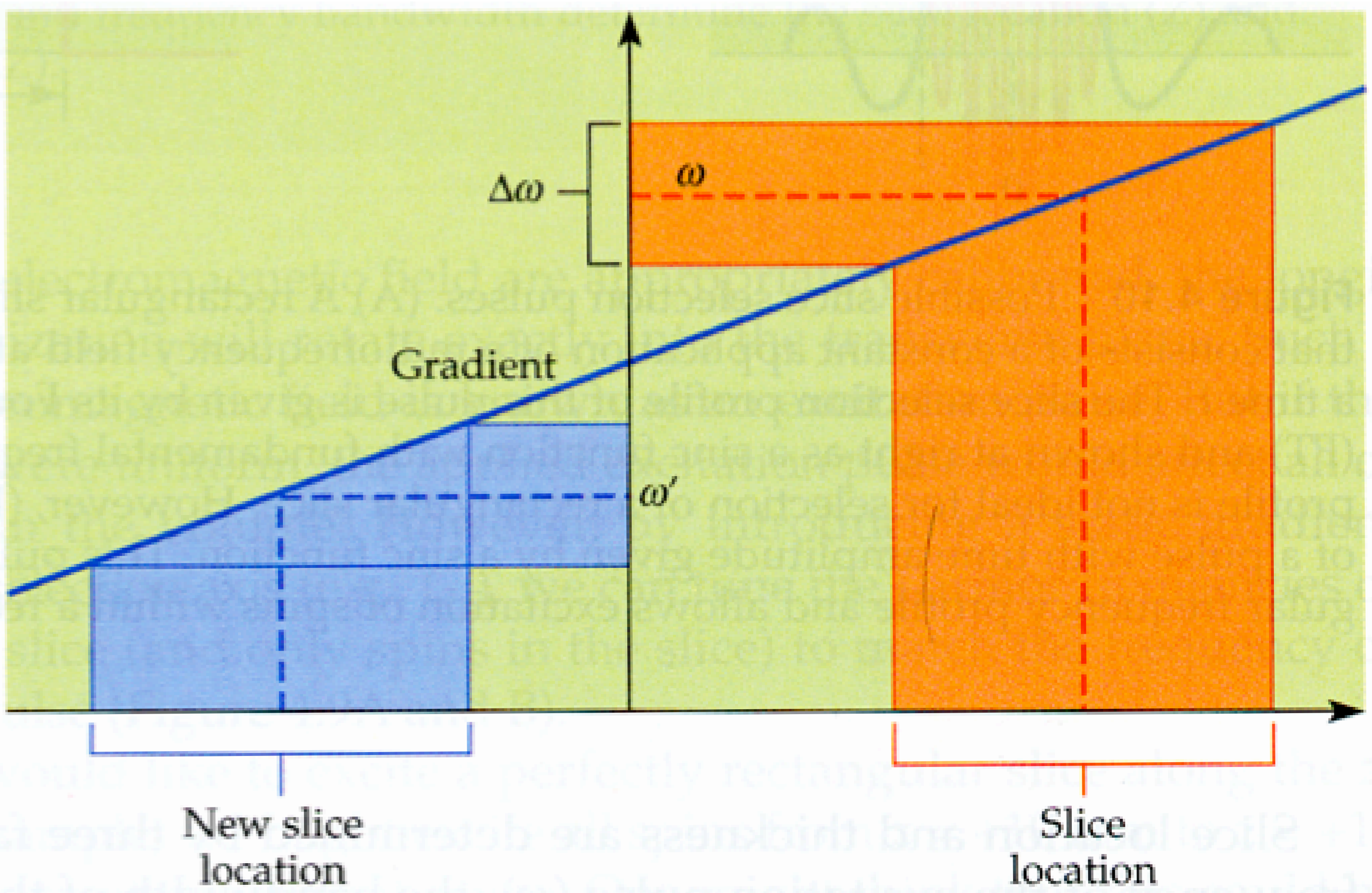
Larmor frequency of spins

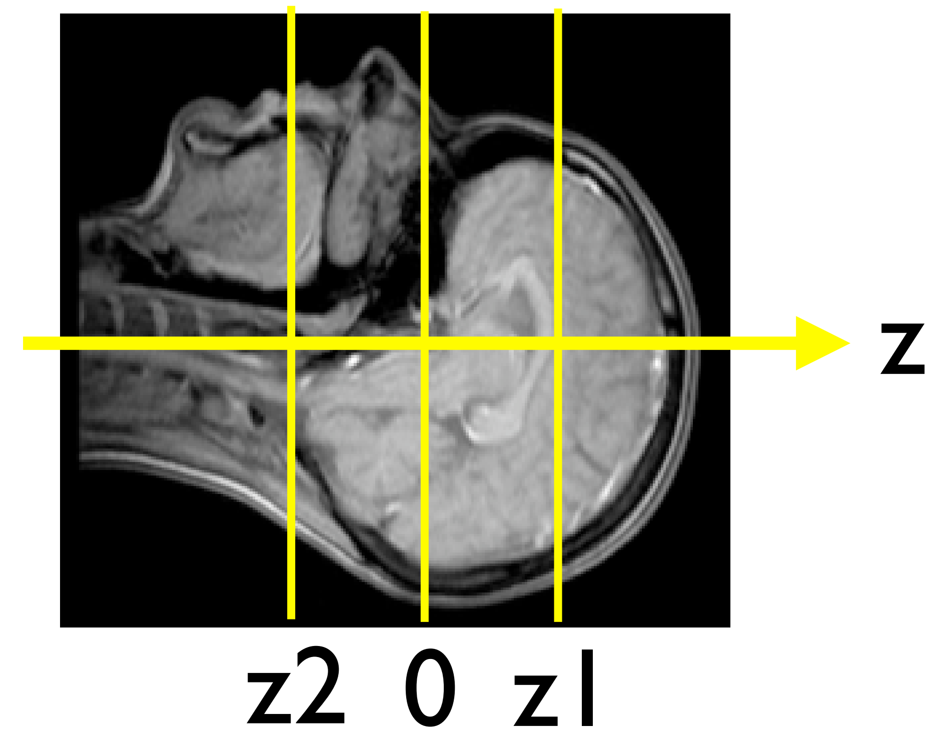
$$\omega(z) = \gamma G z$$

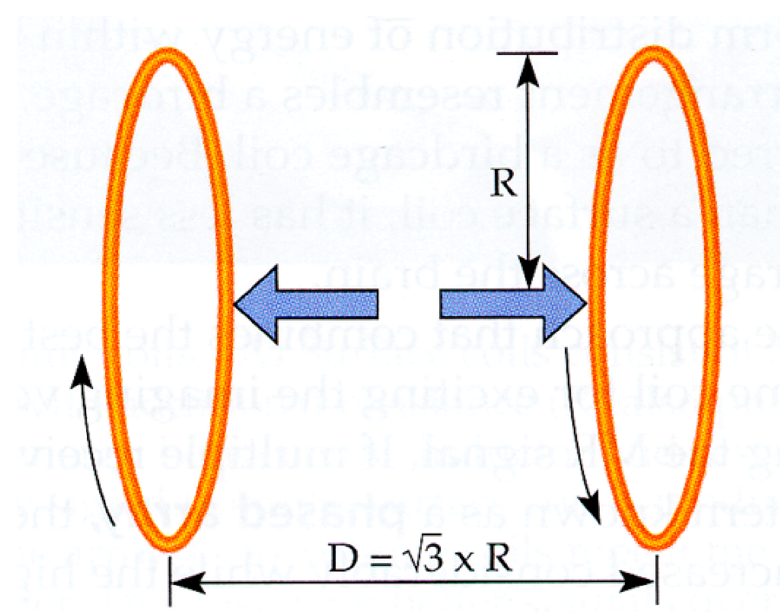
RF excitation has mean, and shape $\omega_{RF}\ ,\ \Delta\omega$

Slice has location and shape

Controlling Slice Location



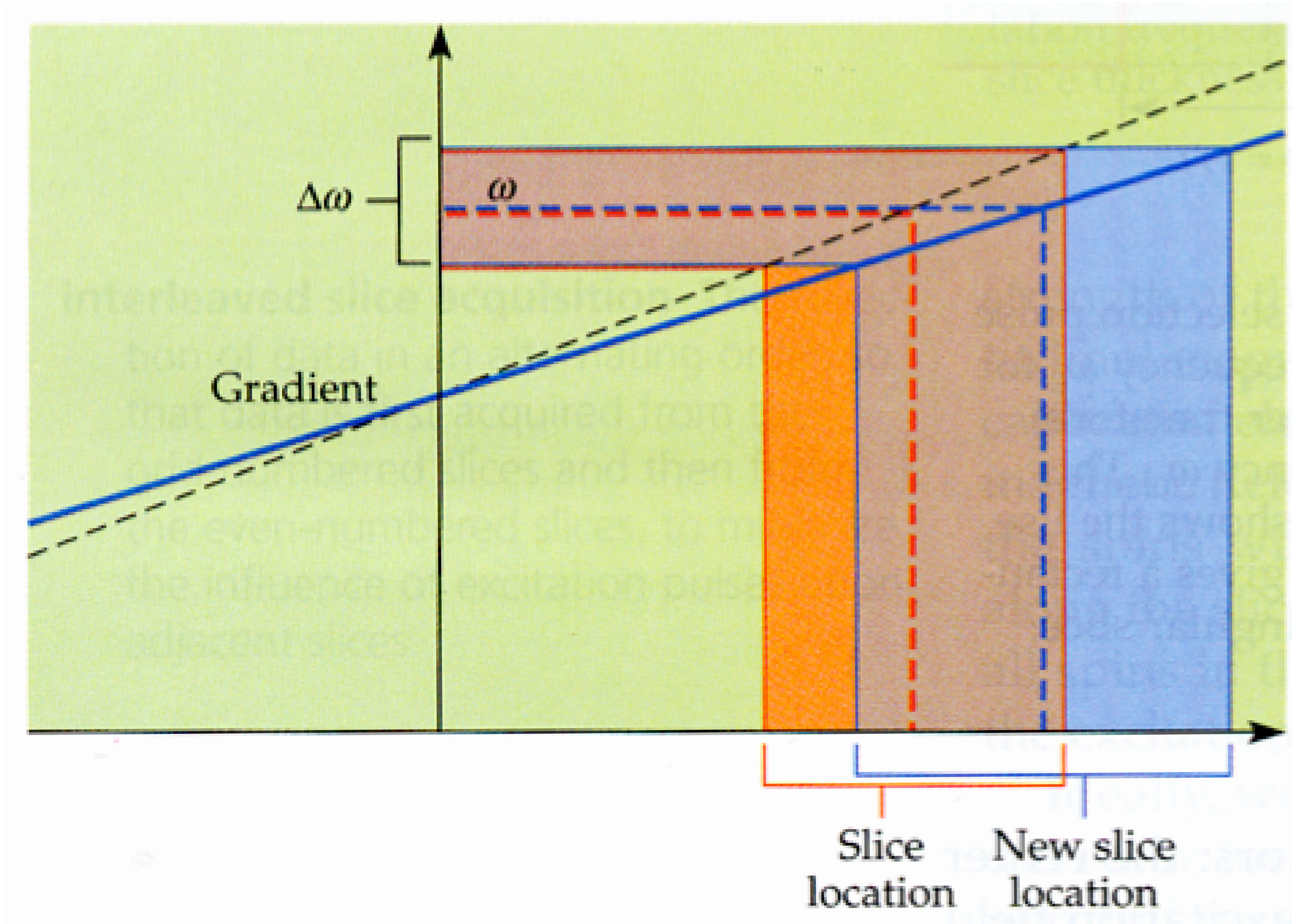




To move slice location, change wRF

$$z_s = \frac{\omega_{RF}}{\gamma G}$$

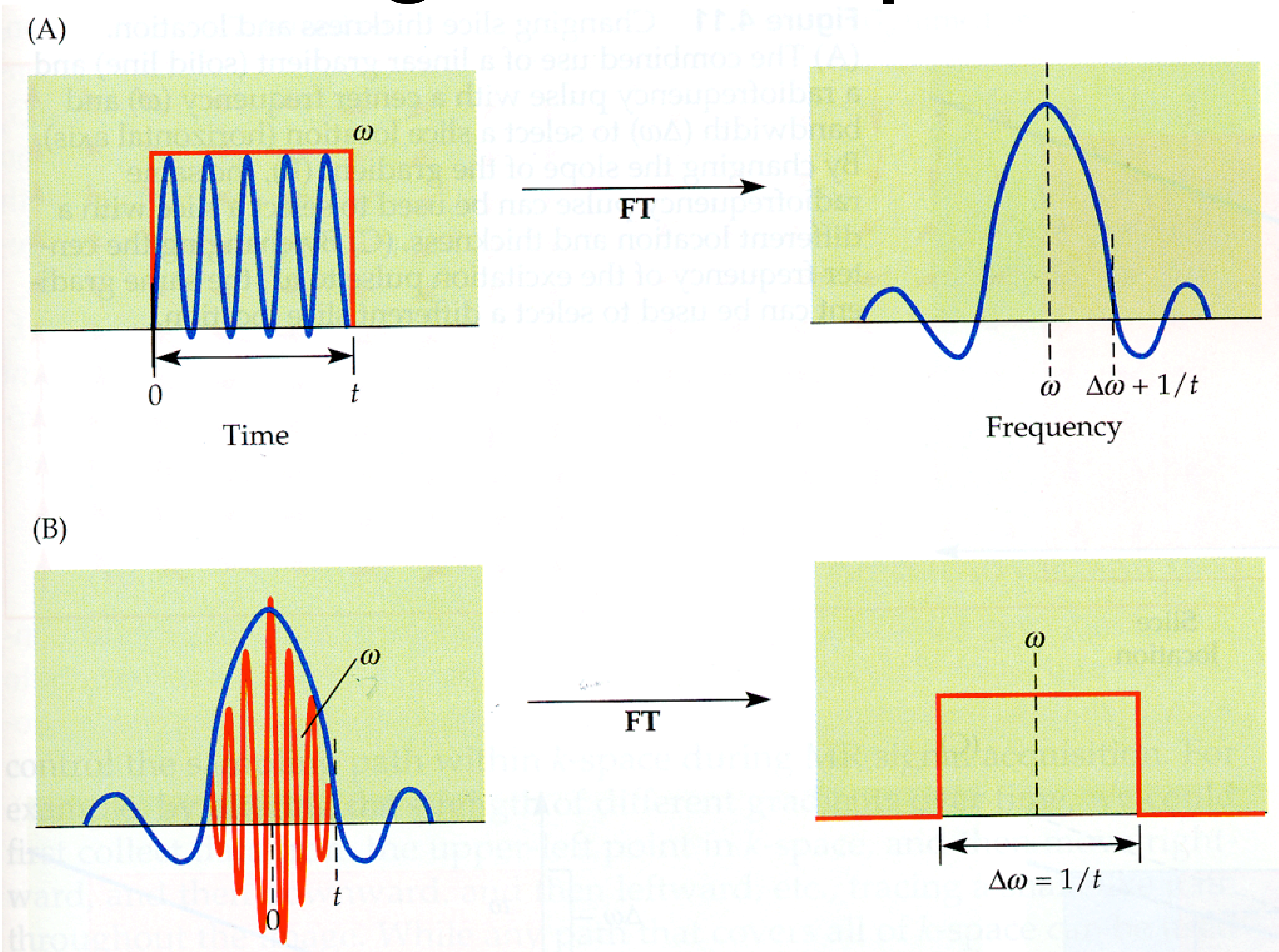
Controlling Slice Width



To change slice width, change gradient amplitude, or RF shape. Bigger G gives thinner slice.

$$z_s = \frac{\omega_{RF}}{\gamma G}$$

Controlling Slice Shape

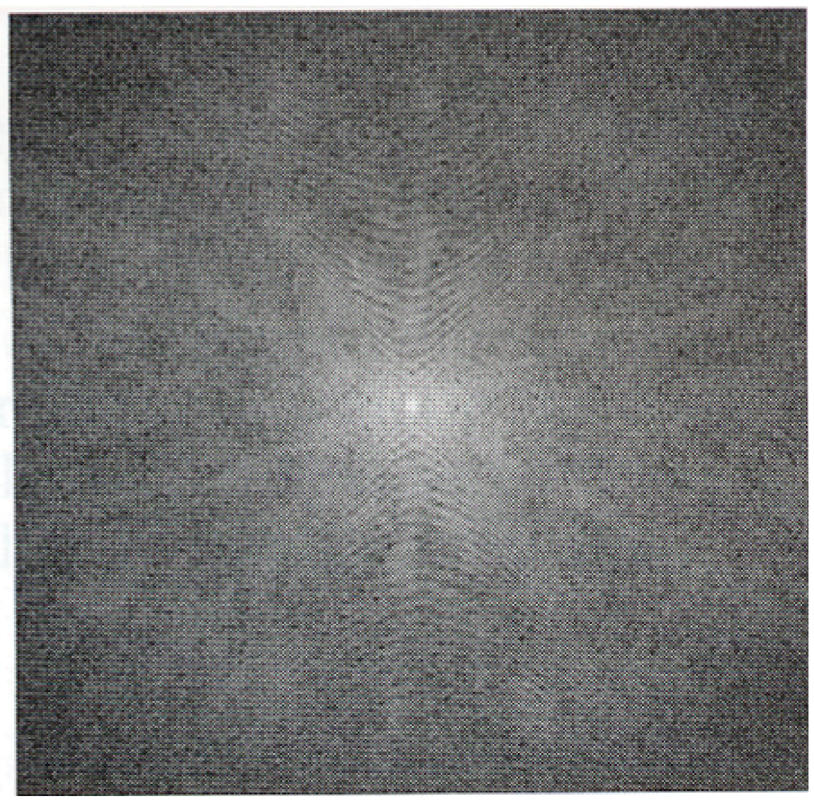


Slice shape depends on RF pulse envelope approximately fourier transform

k-space
Spatial encoding during detection

Spatial Encoding

Nobel prize stuff!
P. Lauterbur



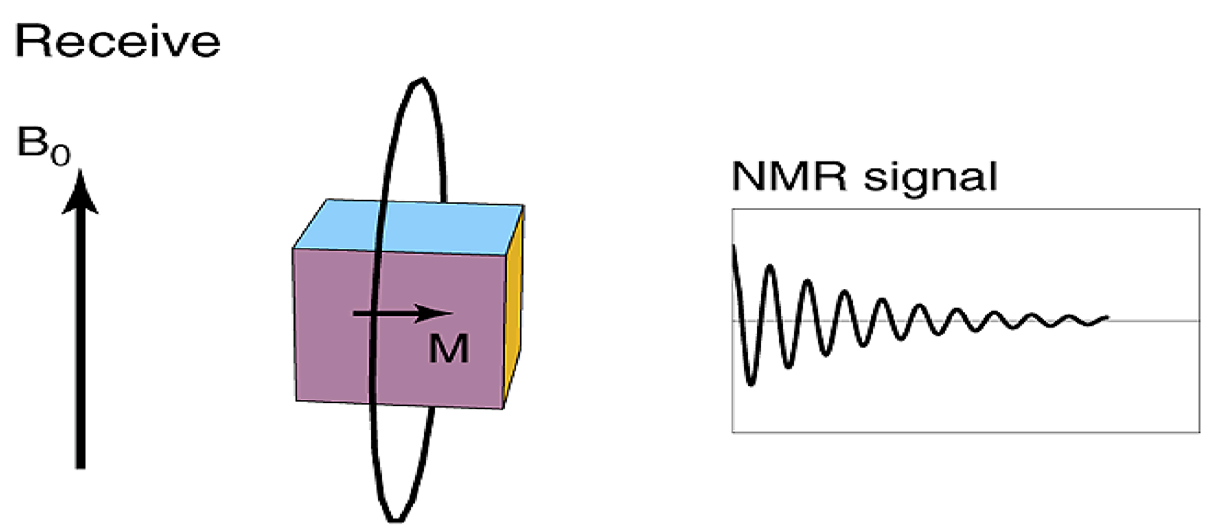
Raw data $S(k_x,k_y)$

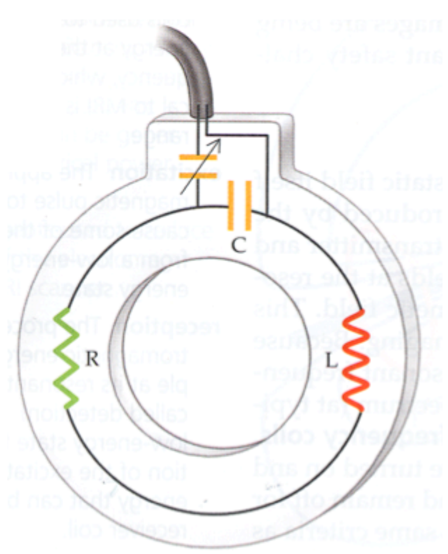
Fourier ⟷ Transform

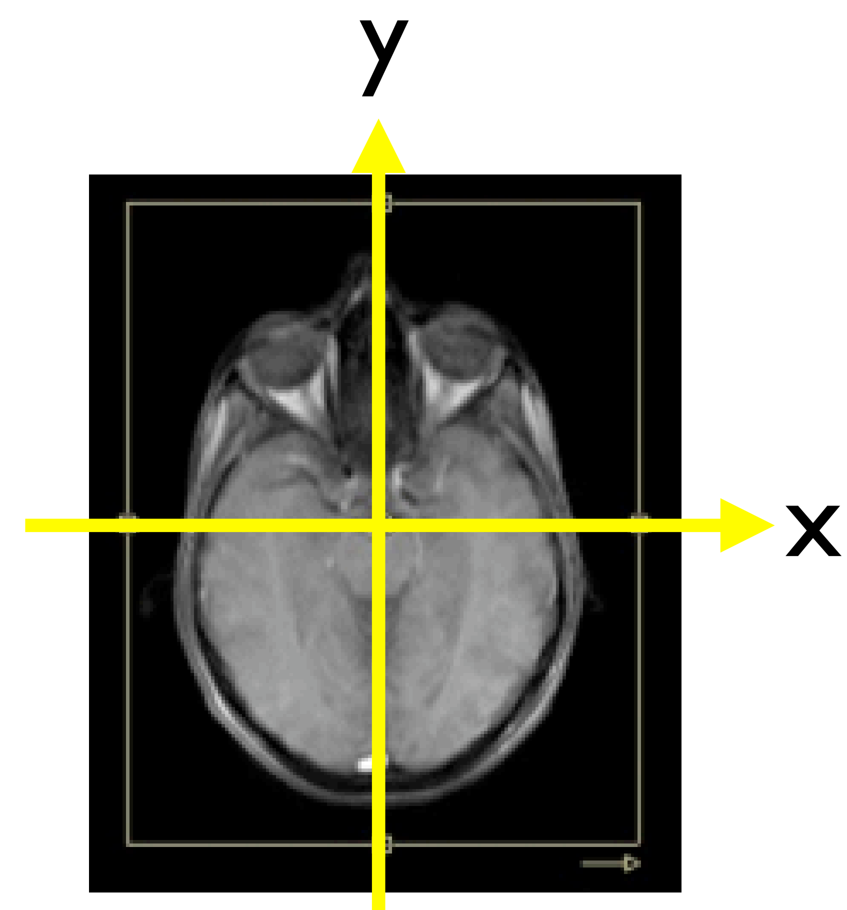
Image $I(x,y)$

$$S(k_x,k_y) = \int_x \int_y I(x,y) e^{i(k_x x + k_y y)} dx dy$$

Encoding 2D Position in Signal





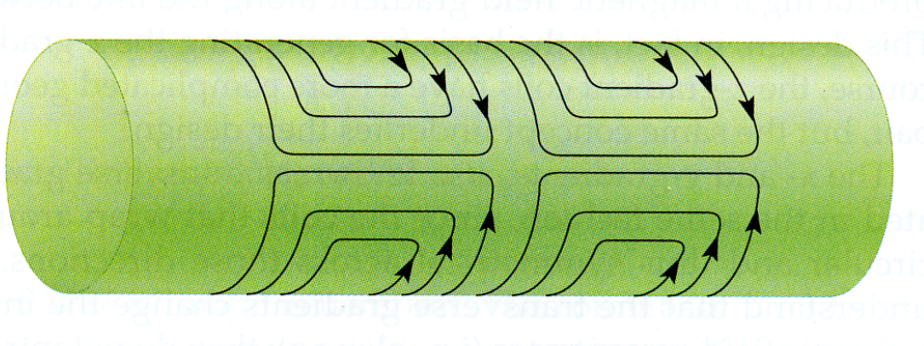


Coil integrates transverse magnetization over space

$$S(t) = \int_V C(x,y,z) M_{xy}(x,y,z,t)\, dV$$

Position Encoded in Phase

Apply gradient in x

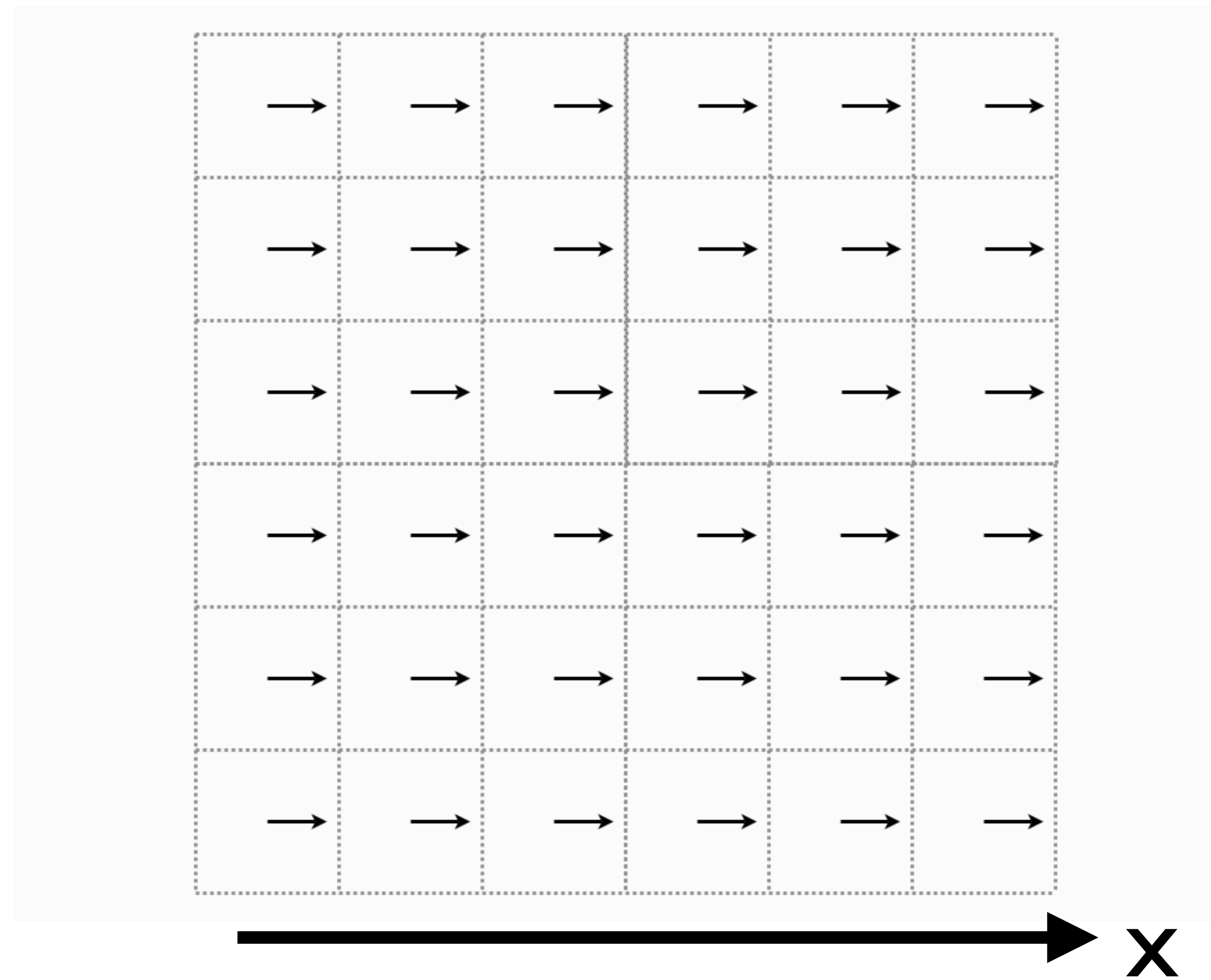


x Gradient

Larmor frequency now depends on x

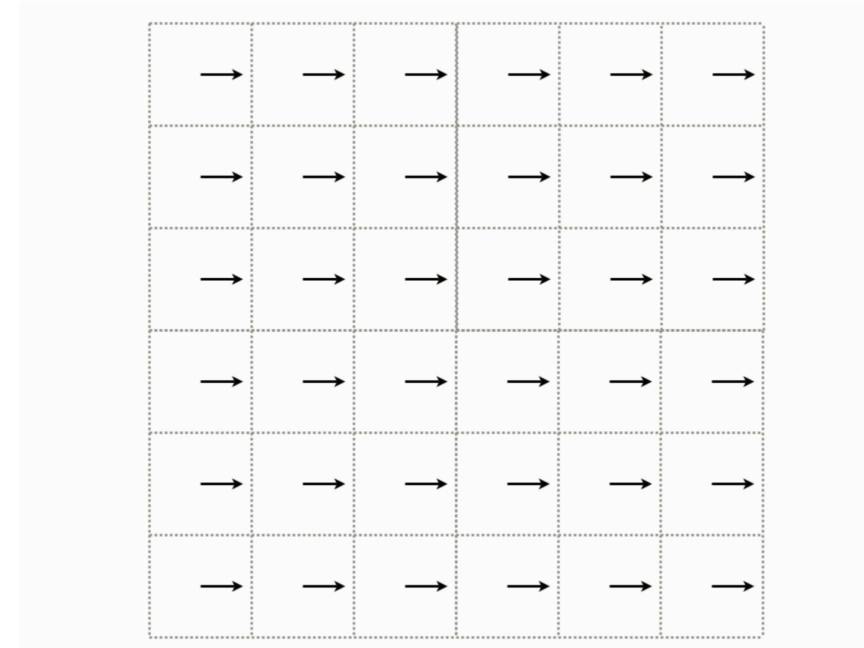
$$\omega(x) = \gamma B(x) = \gamma G x$$

$$S(t) = \int_x \int_y \int_z M_{xy}(x, y, z, t)\, dx\, dy\, dz$$



Phase of magnetization changes with time. Depends on x

The Magical k-Space Formalism



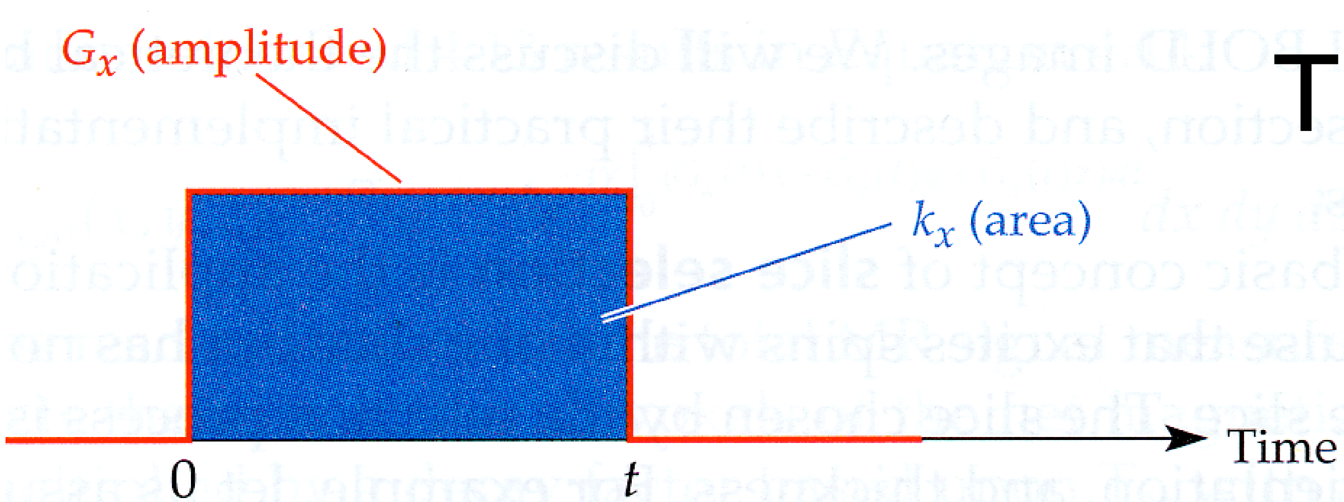
Instantaneous frequency:

$$\omega(x) = \gamma B(x) = \gamma G x$$

Net phase (total rotation angle):

$$\phi(x,y,t) = \int_0^t \omega(x,y,\tau)\,d\tau = \int_0^t \gamma B(x,y,\tau)\,d\tau$$

$$= \int_0^t \gamma\left(G_x(\tau)x + G_y(\tau)y\right)d\tau$$



The k number:

$$k_x \equiv \gamma \int_0^t G_x(\tau)\,d\tau$$

k-Space Formalism 2

NMR signal

$$S(t) = \int_x \int_y \int_z M_{xy}(x,y,z,t)\,dx\,dy\,dz$$

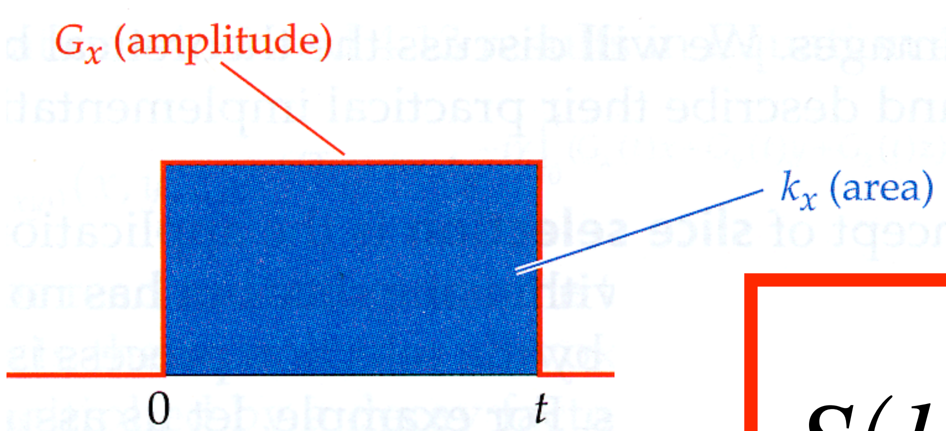
Neglect decay
integrate over z (slice)

$$S(t) = \int_x \int_y M_{xy}(x,y,0)\,e^{i\phi(x,y,t)}\,dx\,dy$$

Write phase(t)
in terms of (k_x, k_y)

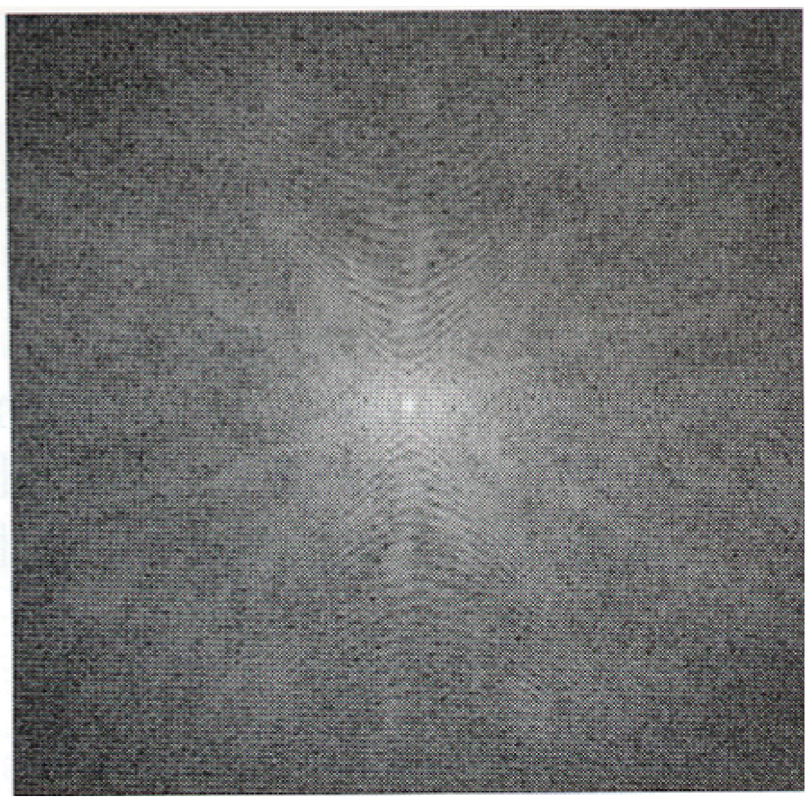
$$\phi(x,y,t) = k_x(t)x + k_y(t)y$$

$$k_x \equiv \gamma \int_0^t G_x(\tau)\,d\tau$$



$$S(k_x,k_y) = \int_x \int_y I(x,y)\,e^{i(k_x x + k_y y)}\,dx\,dy$$

Spatial Encoding and Image Recon



Fourier

Transform

Raw data $S(k_x,k_y)$

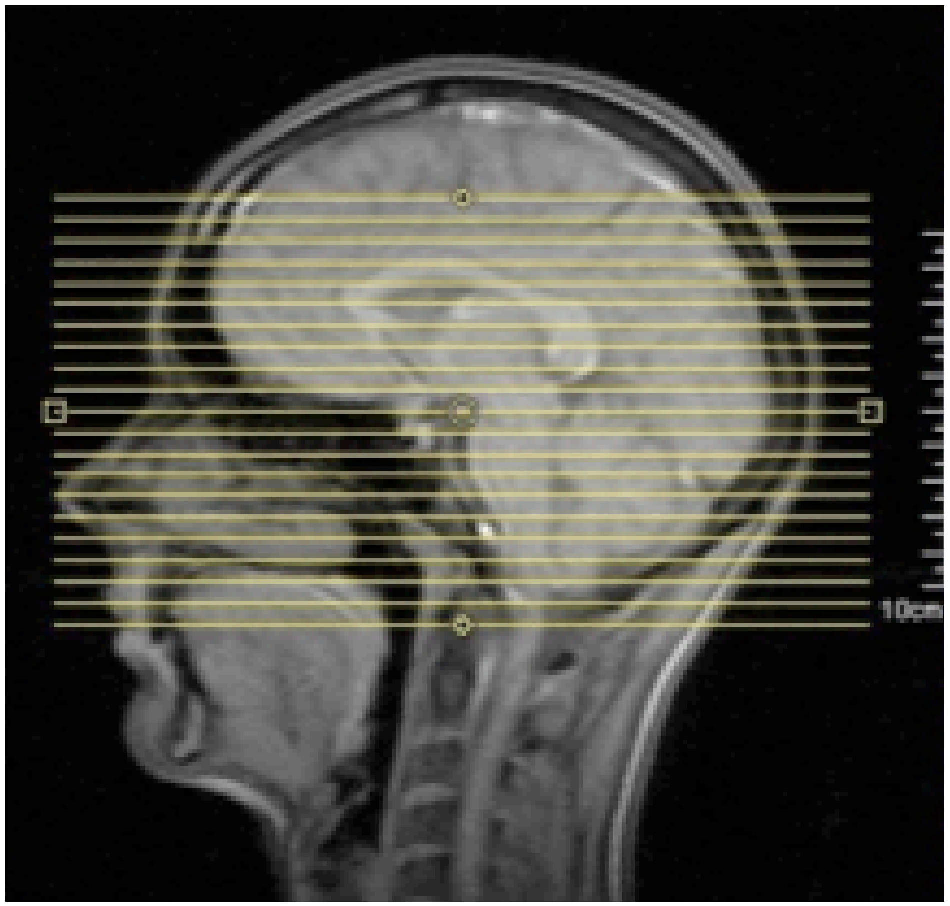
Image $I(x,y)$

$$S(k_x, k_y) = \int_x \int_y I(x,y) e^{i(k_x x + k_y y)} dx dy$$

Make image by inverse FT

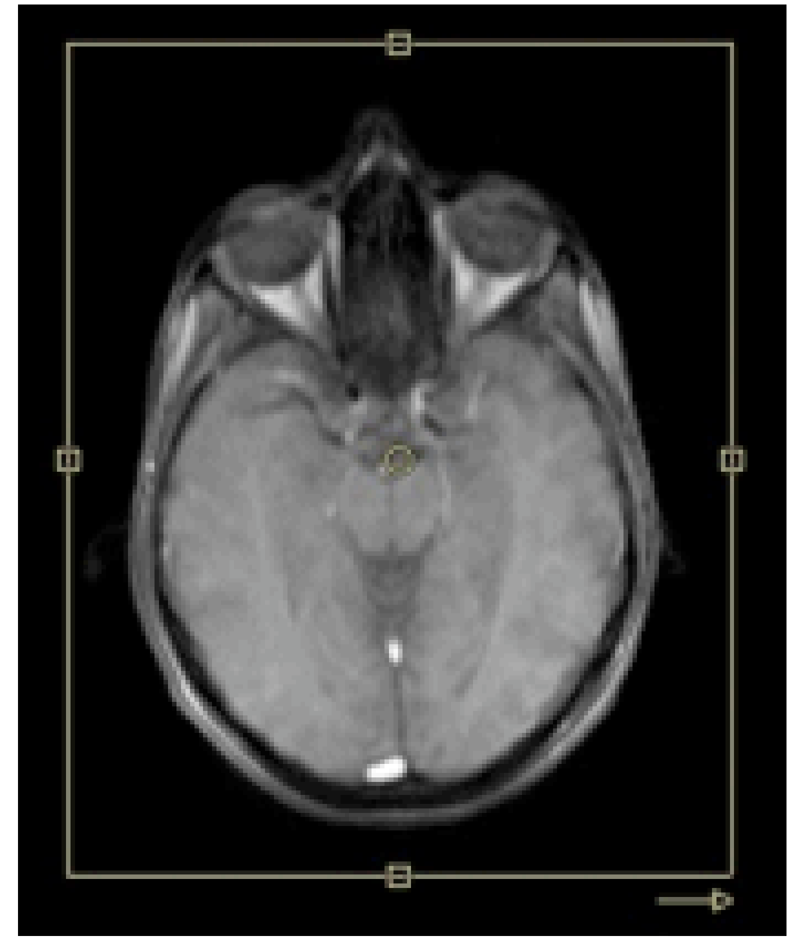
MRI Signal Localization

1)



Excite one slice
at a time

2)

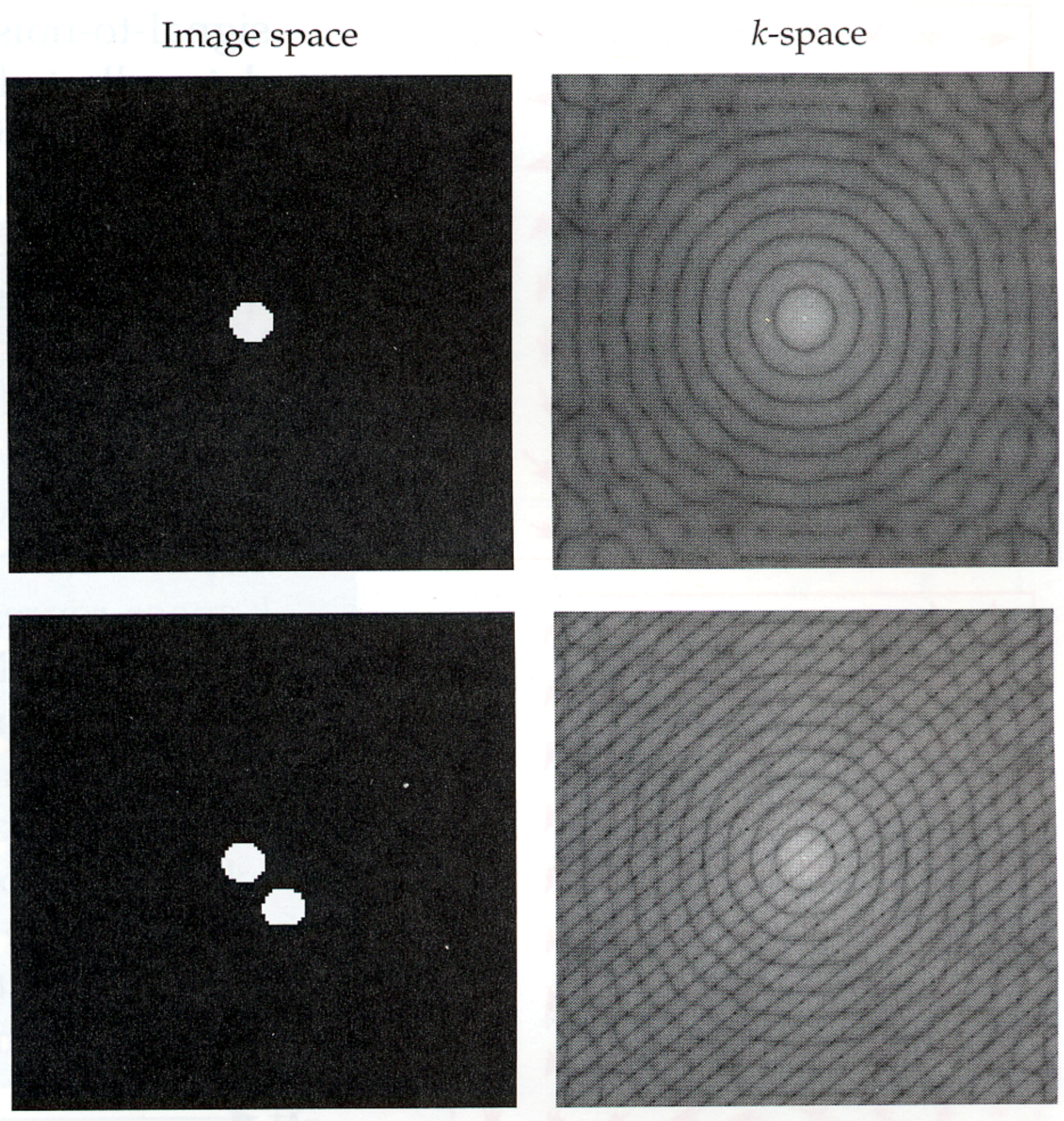


Encode 2D
position in signal

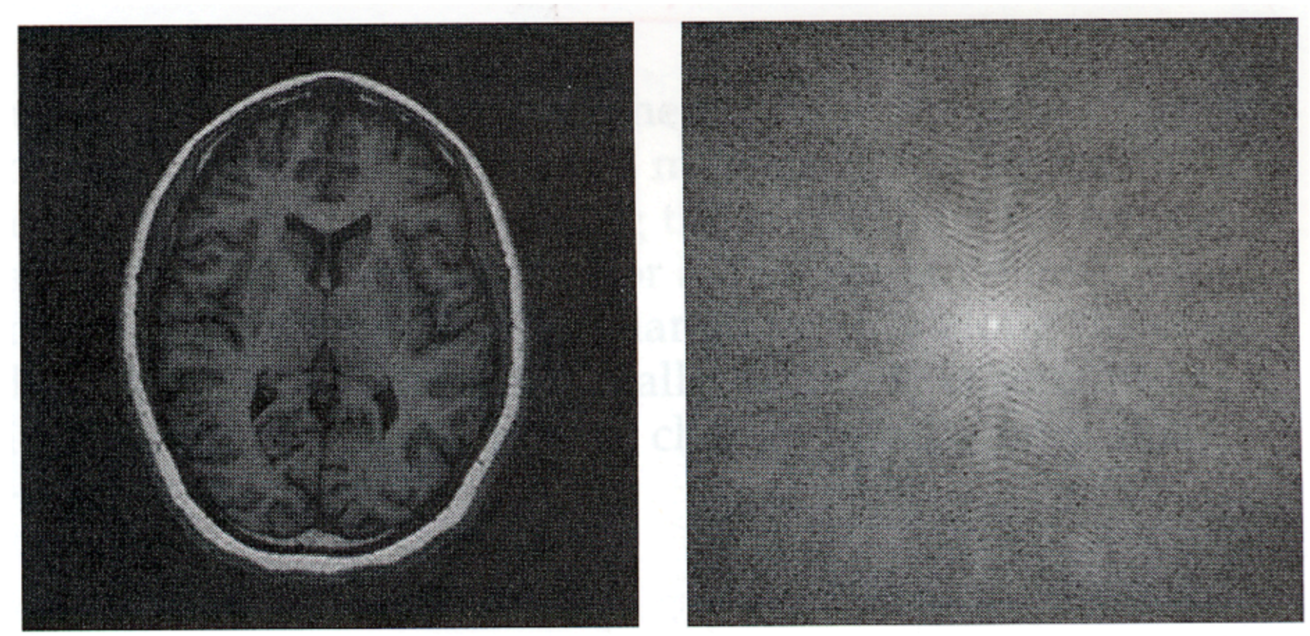
3) reconstruct image from signal:
Inverse Fourier Transform

A little more k-space intuition

Signals Add

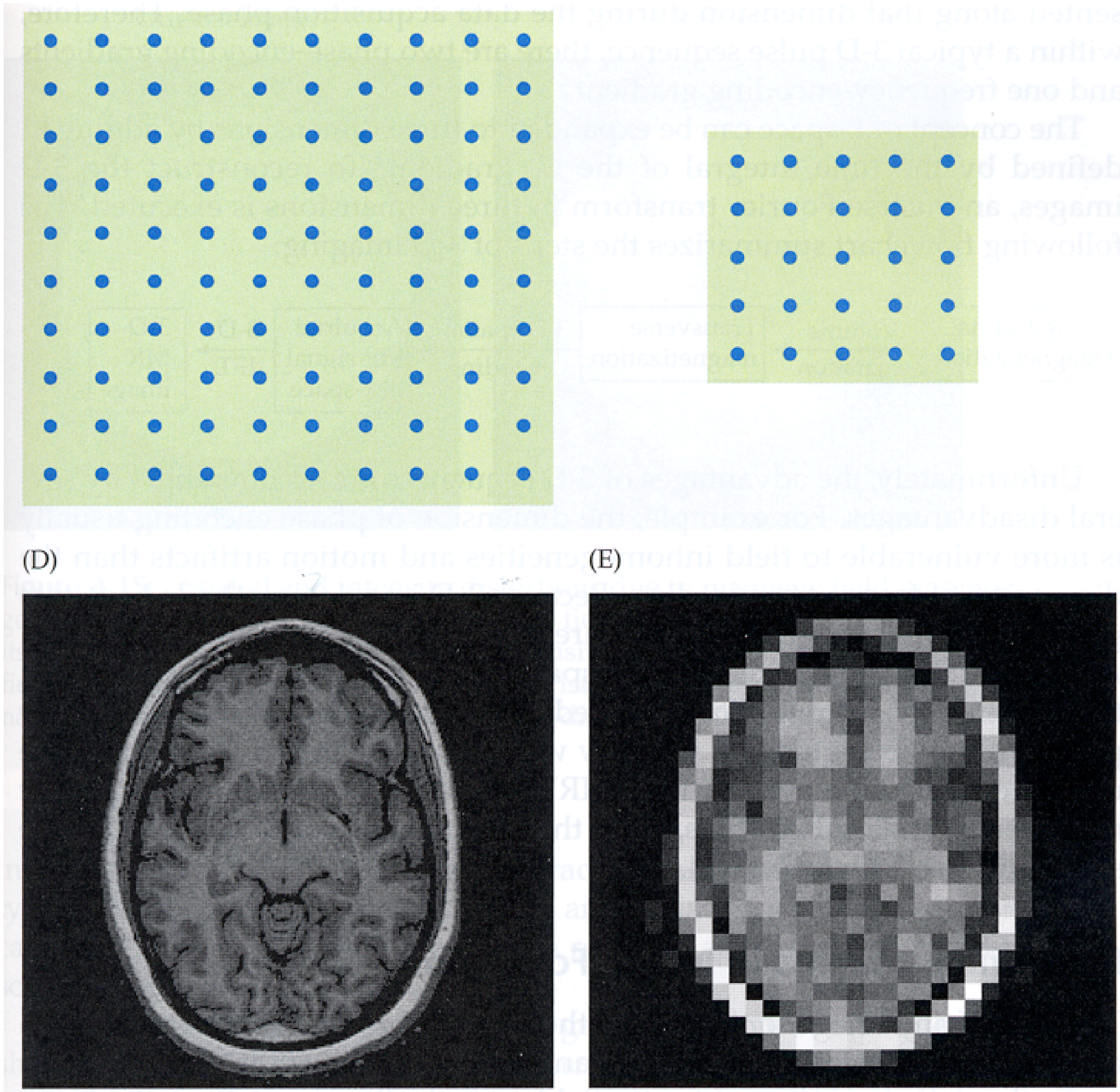


A few point sources

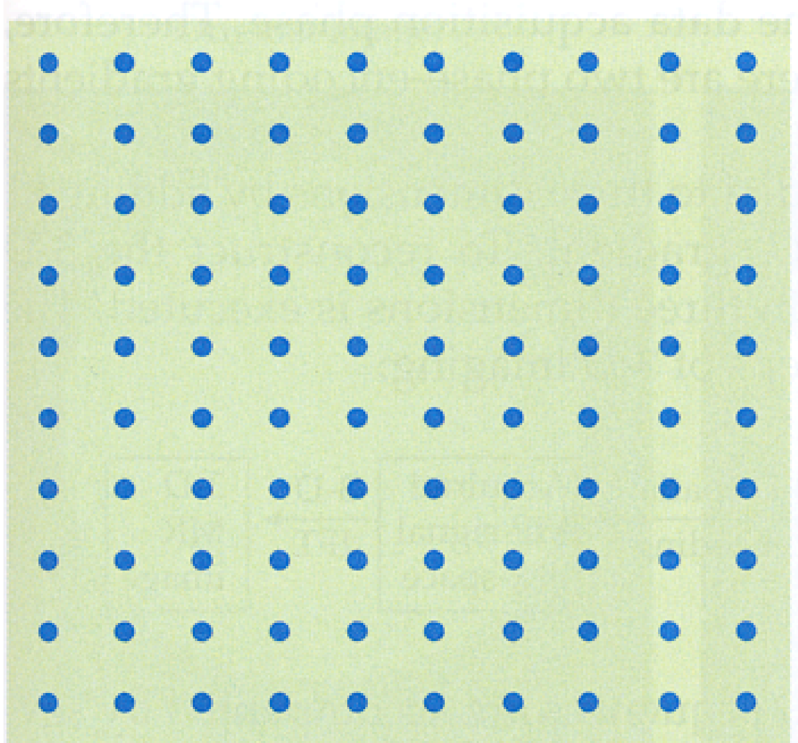


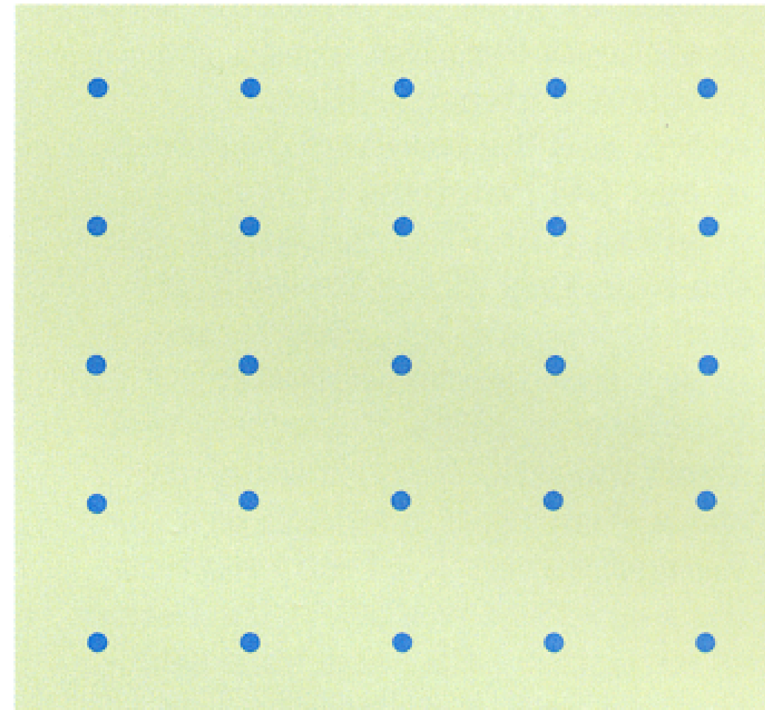
An entire head

Spatial Resolution: extent in k

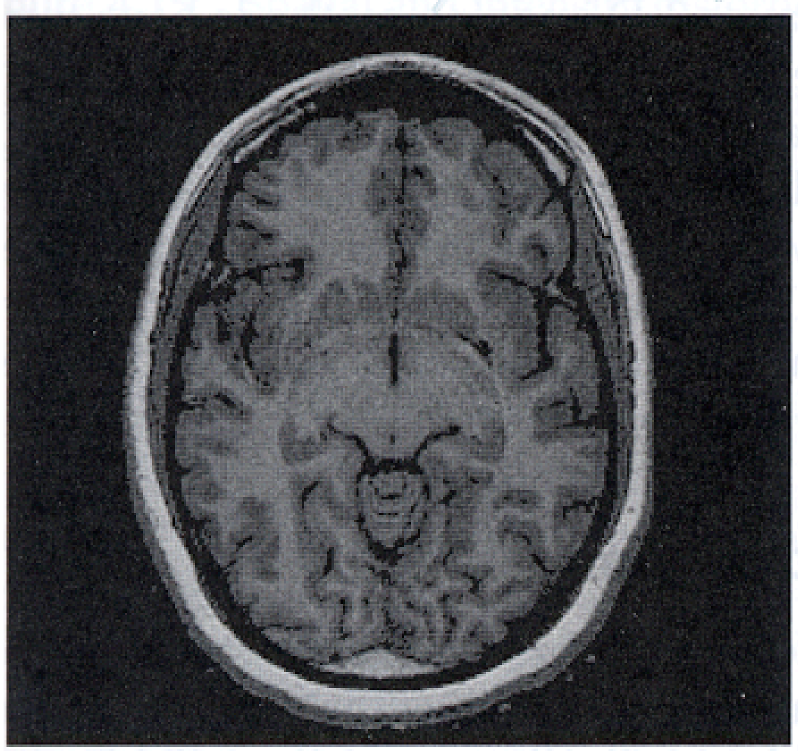


Field of View: spacing in k

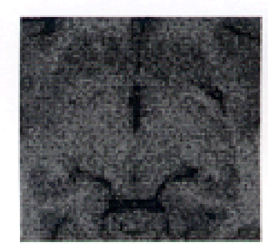




(D)



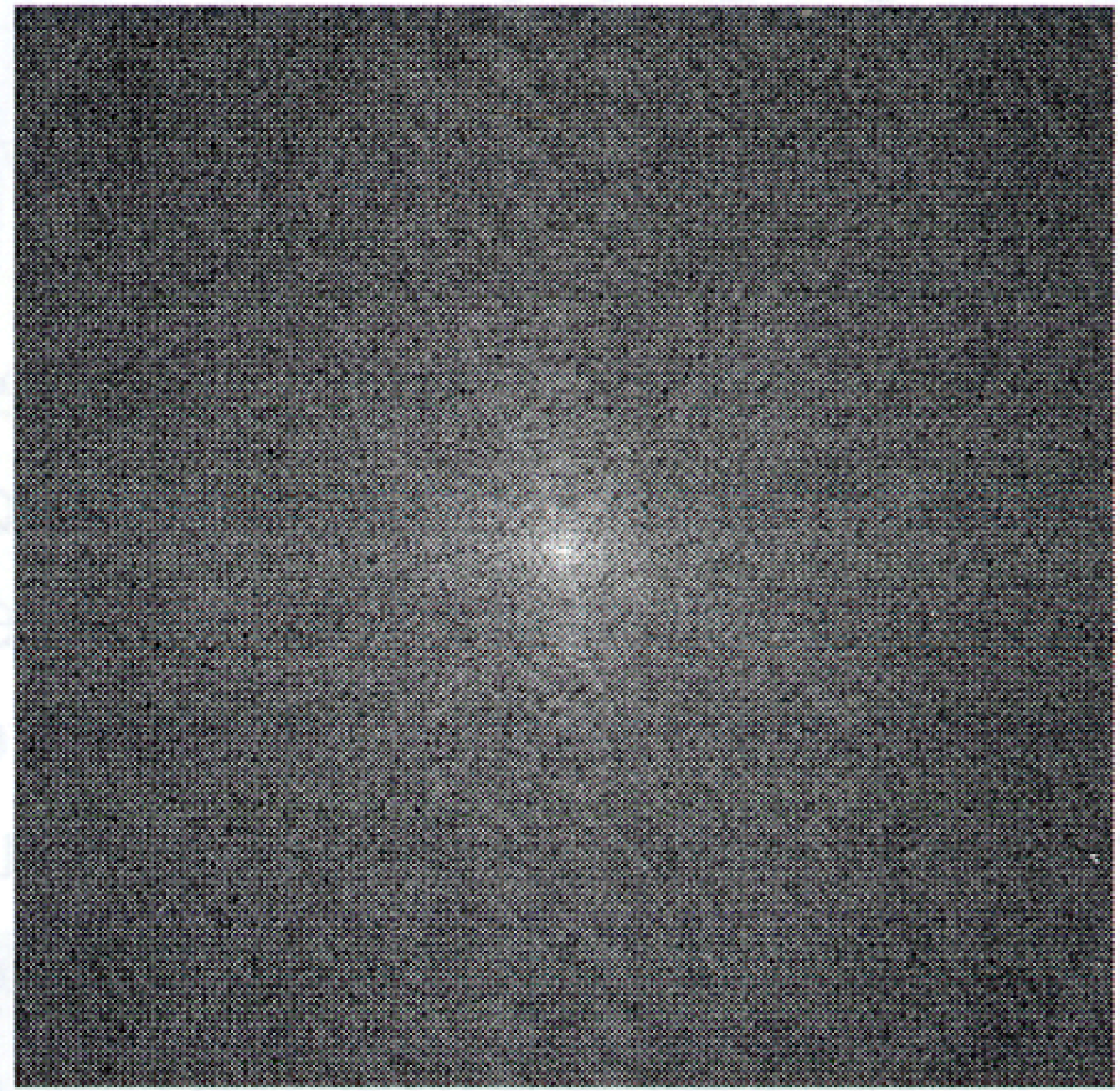
(F)



Watch out for aliasing (wrap)!

Image Space

k-Space

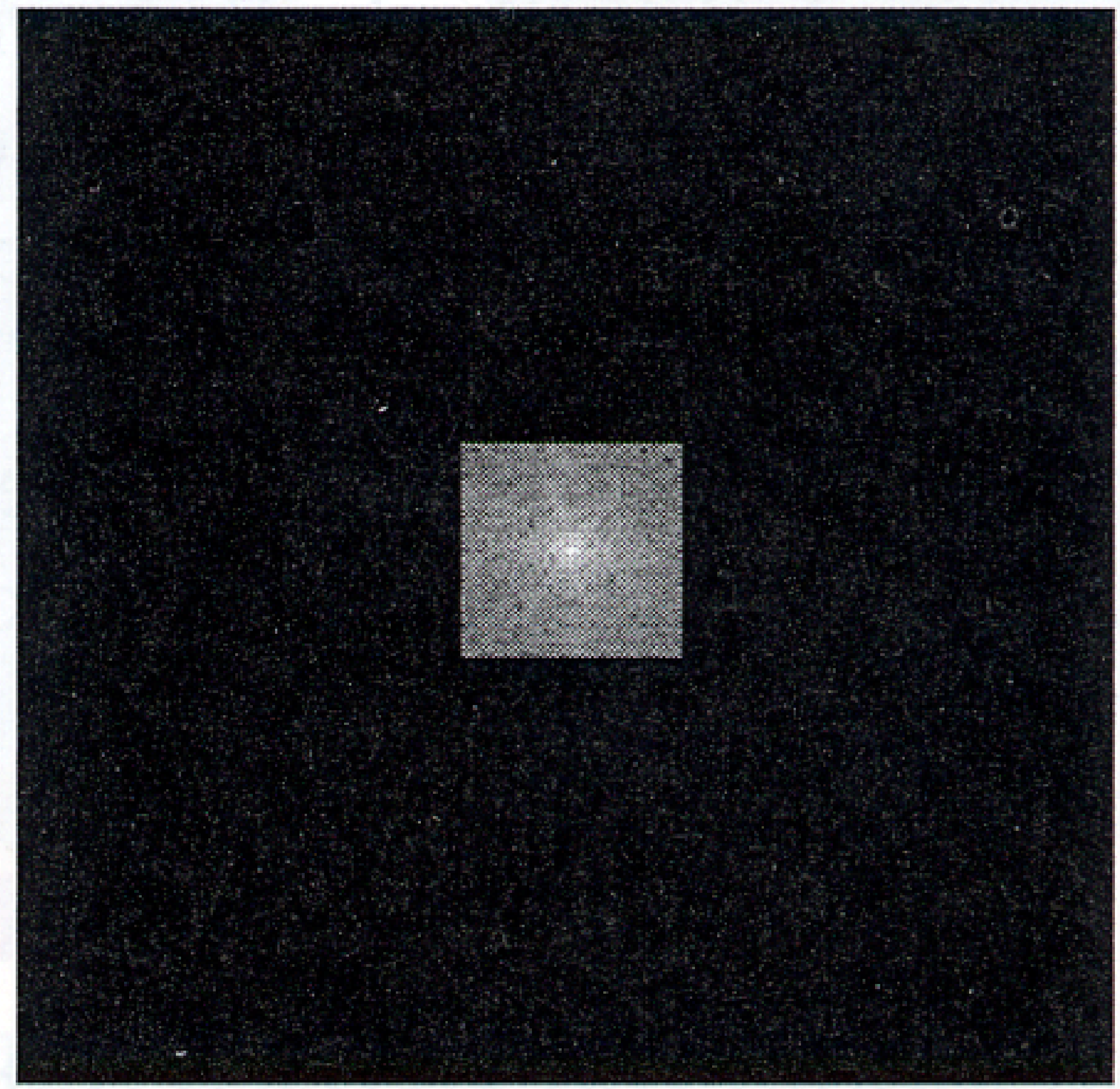


S. Ogawa

Low Spatial Frequency

Image Space

k-Space

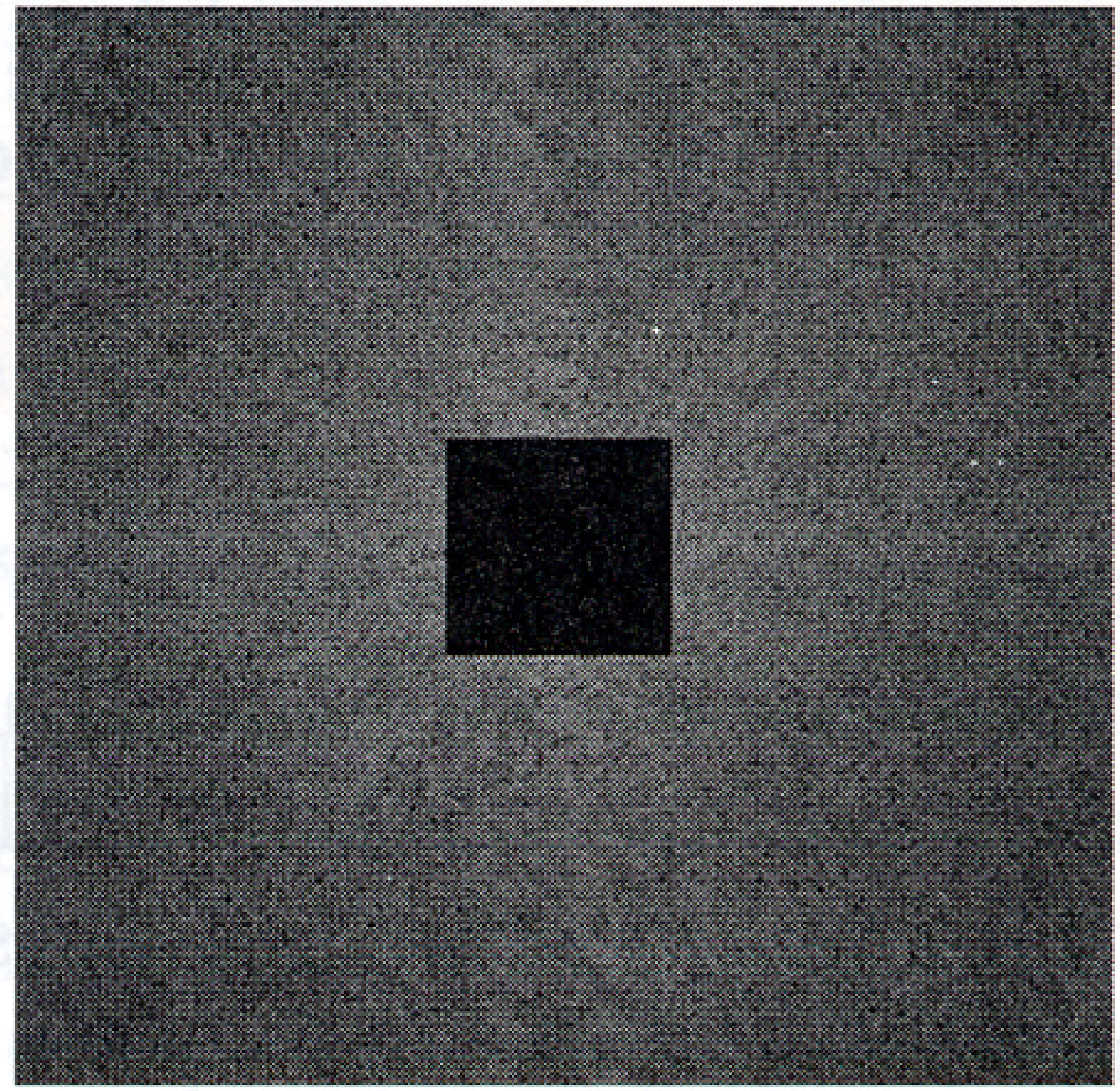


what’s the ringing artifact?

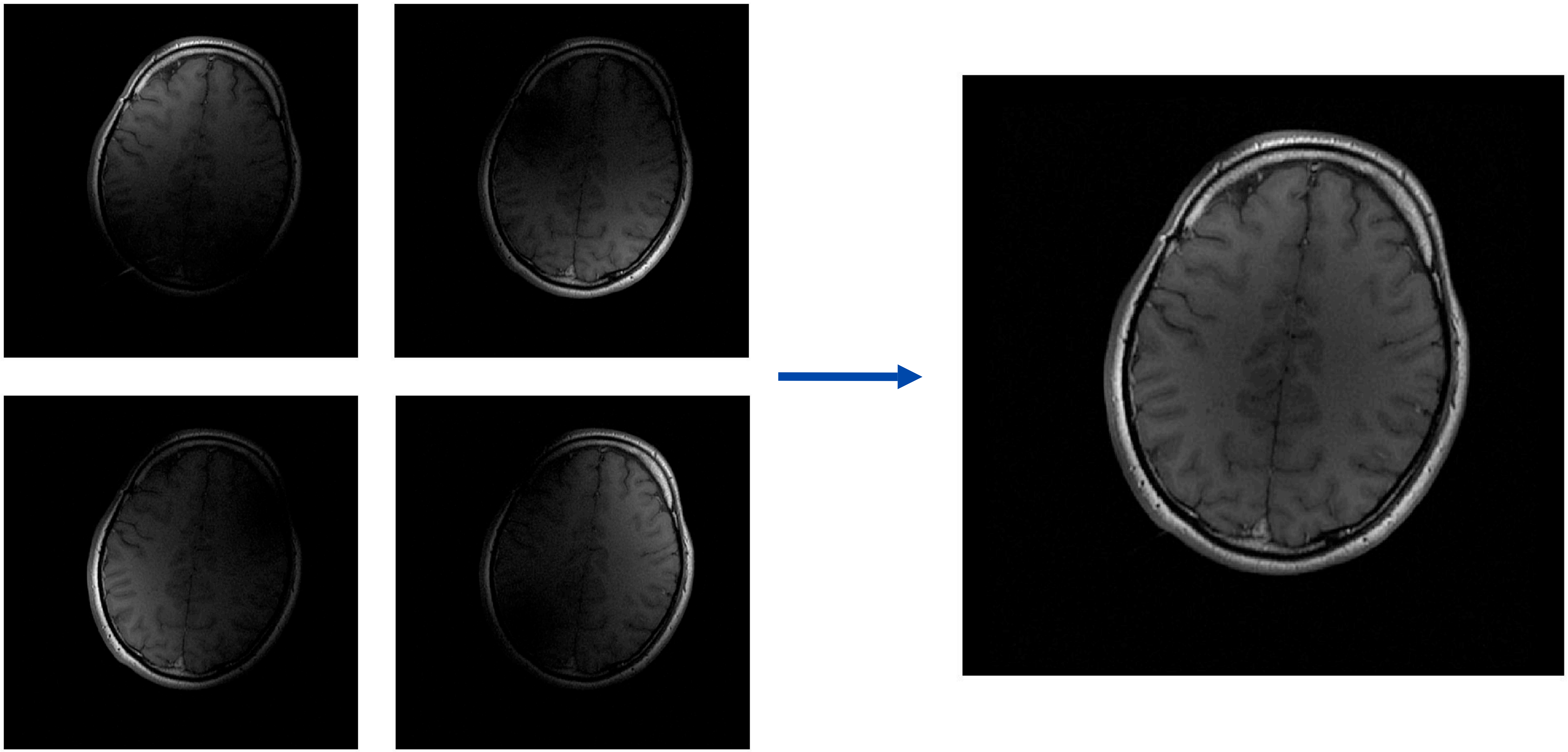
High Spatial Frequency

Image Space

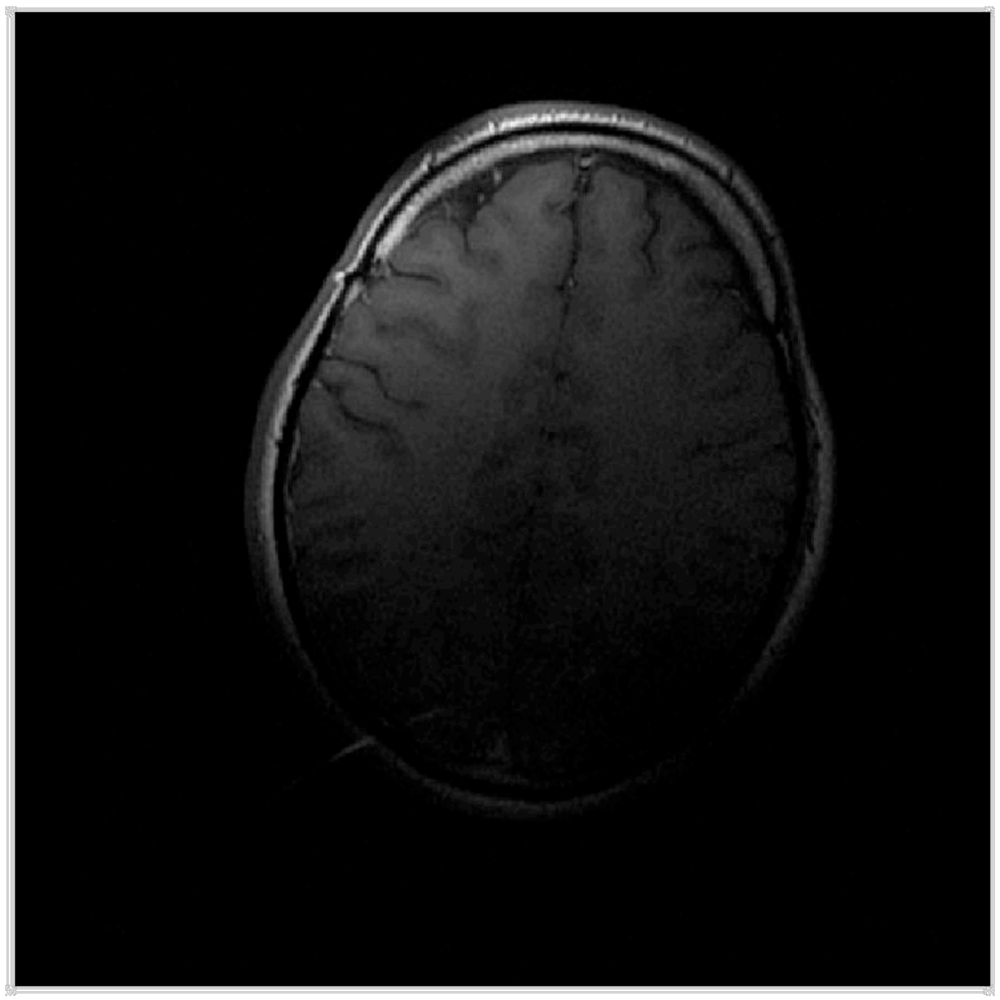
k-Space

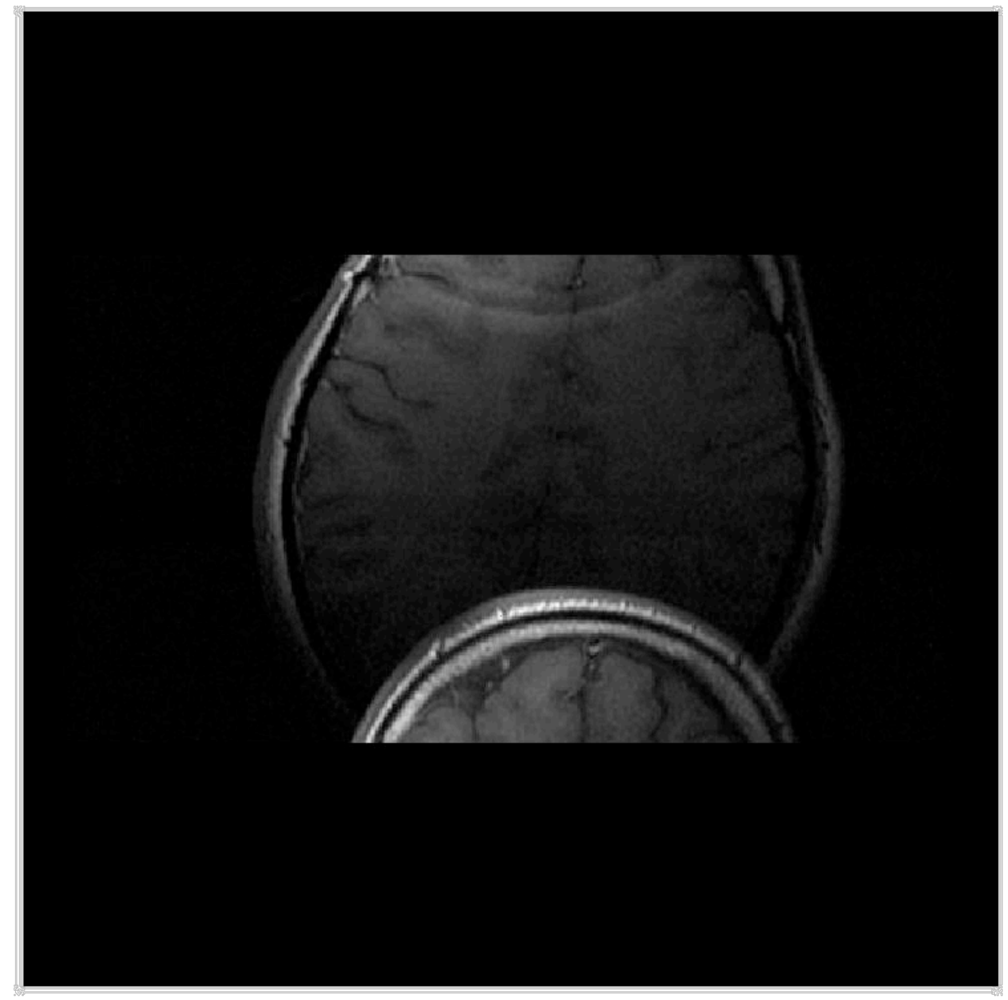


Array Coils



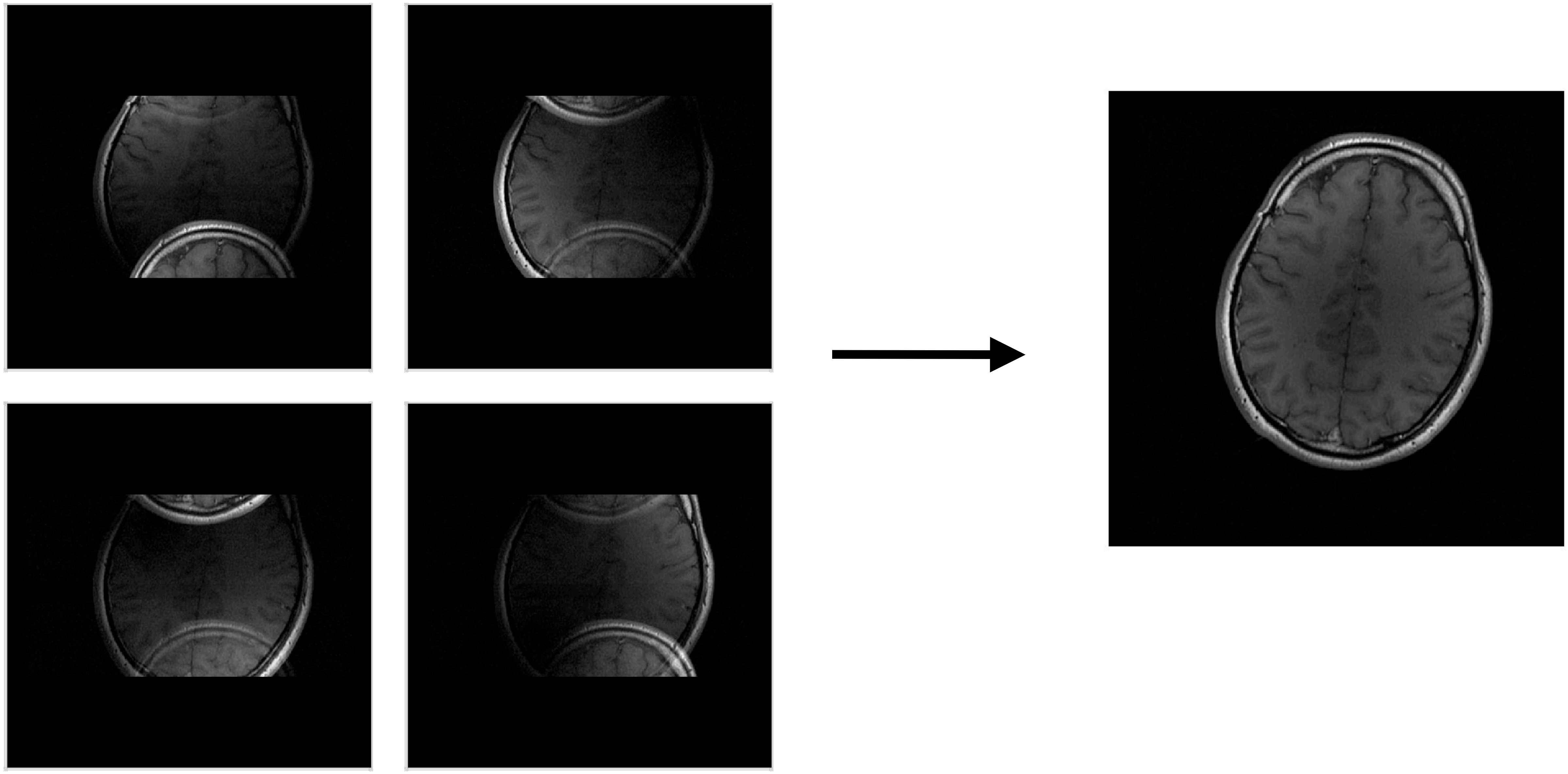
Undersampling and Aliasing





Acquire 1/2 the data (Frequency domain)

Undersampling with a Coil Array



Relative coil sensitivity makes linear system well conditioned i.e. remove aliasing
Noise more spatially correlated

Image reconstruction

Linear System

Discretize the integral and look at the Linear system

How many singular values are not "too small"?

What do the columns of U and V look like?

Construct pseudo-inverse operator

$$s(k) = \int \rho(x) e^{-ikx} dx$$

$$s(k) \approx \sum_n \rho_n e^{-ikx_n} \Delta$$

$$\mathbf{s} = \mathbf{A}\rho$$

$$\mathbf{A} = \mathbf{USV}^{\mathrm{T}}$$

$$[\mathbf{U}, \mathbf{S}, \mathbf{V}] = \mathbf{svd}(\mathbf{A})$$

$$\hat{\rho} = \mathbf{A}^{+}\mathbf{s}$$

Matlab Demo of 1D MRI

Ill-conditioning and resolution

Gibbs ringing

More sampling doesn't always help

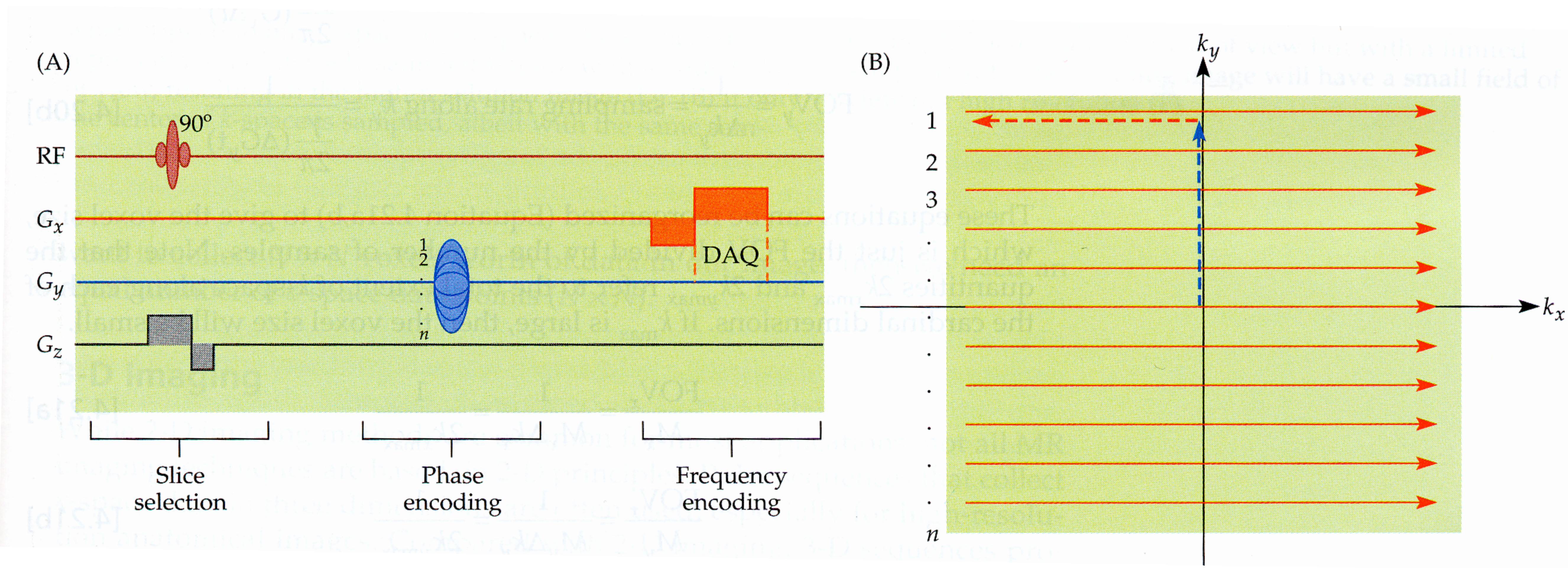
see the m file in the handout

Non-linear methods

Change the model:
Discontinuities + smooth stuff
Solved in 1D
Working on it in 2D

The MRI pulse sequence

Conventional Imaging

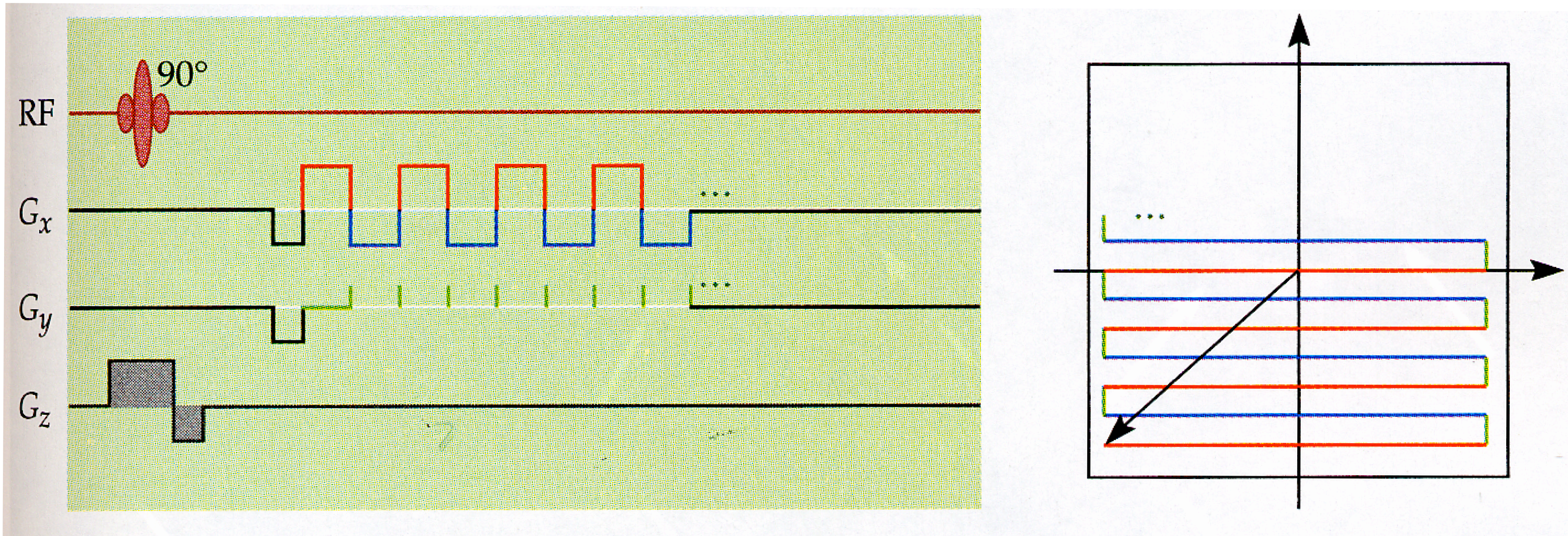


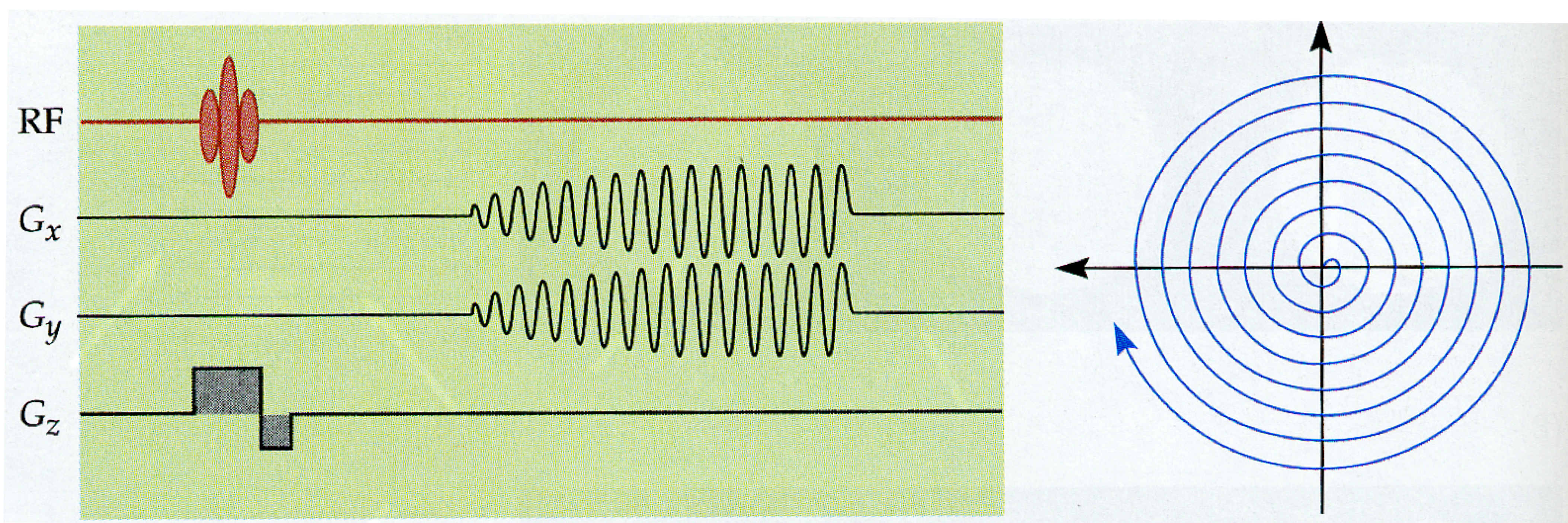
Raster k-space one line at a time.

Echo Planar Imaging

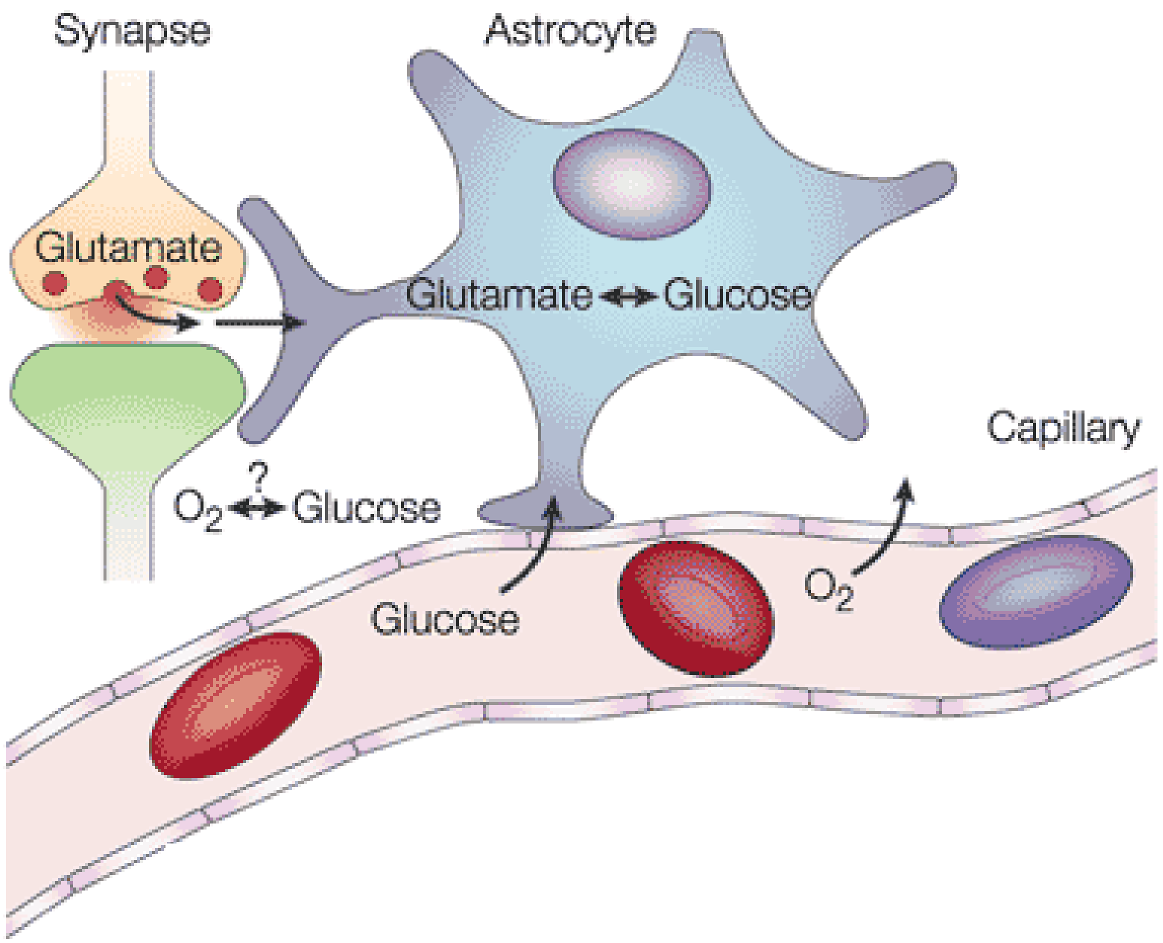
- Different k-space sampling trajectories
  - Conventional EPI
  - Spiral
- Typically 2D, single shot
  - Excite one slice
  - Go through all of k-space in one go
- Artifacts - we'll talk about those later

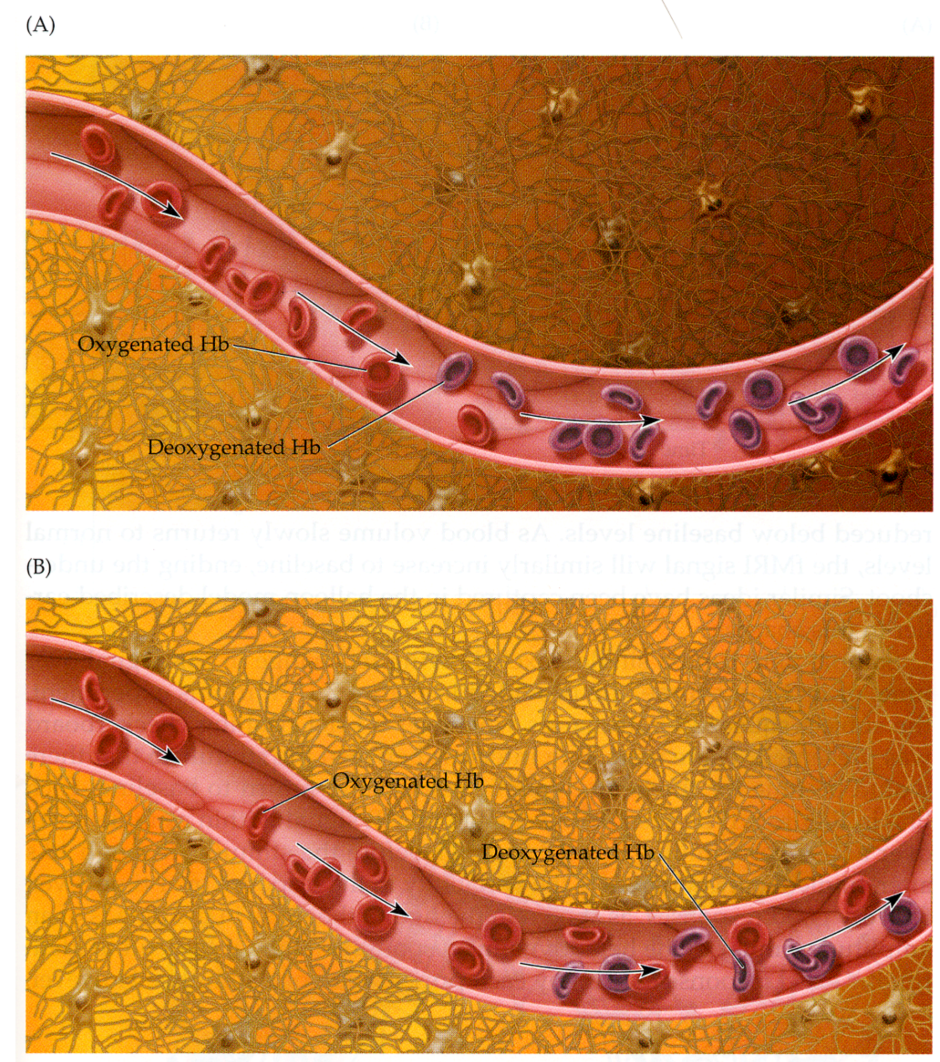
Raster vs. Spiral EPI





A basic description of BOLD FMRI physics



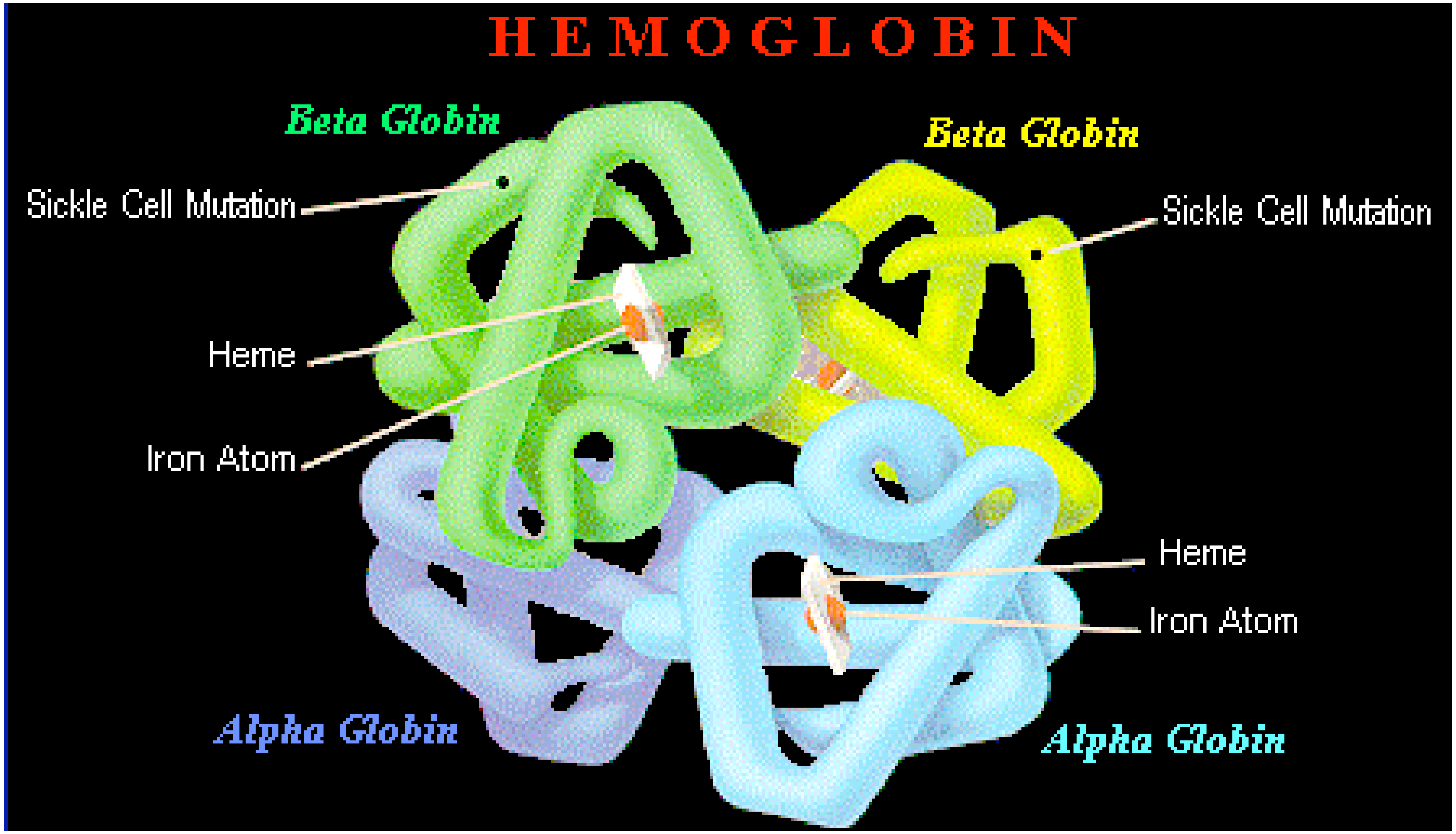


Baseline

Task

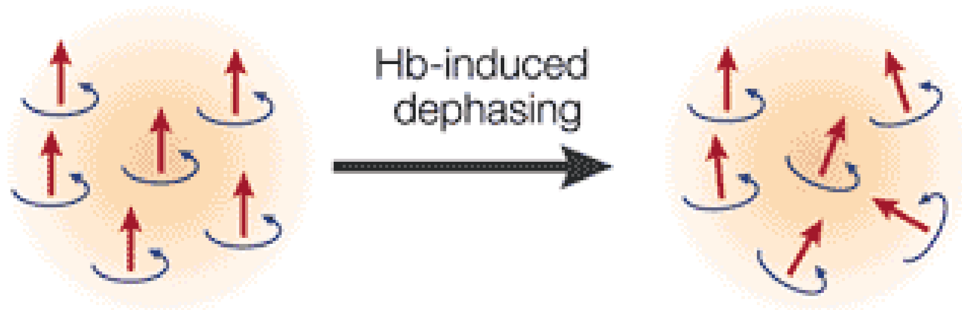
Increased neural activity leads to increased blood flow, blood volume, and oxygen consumption

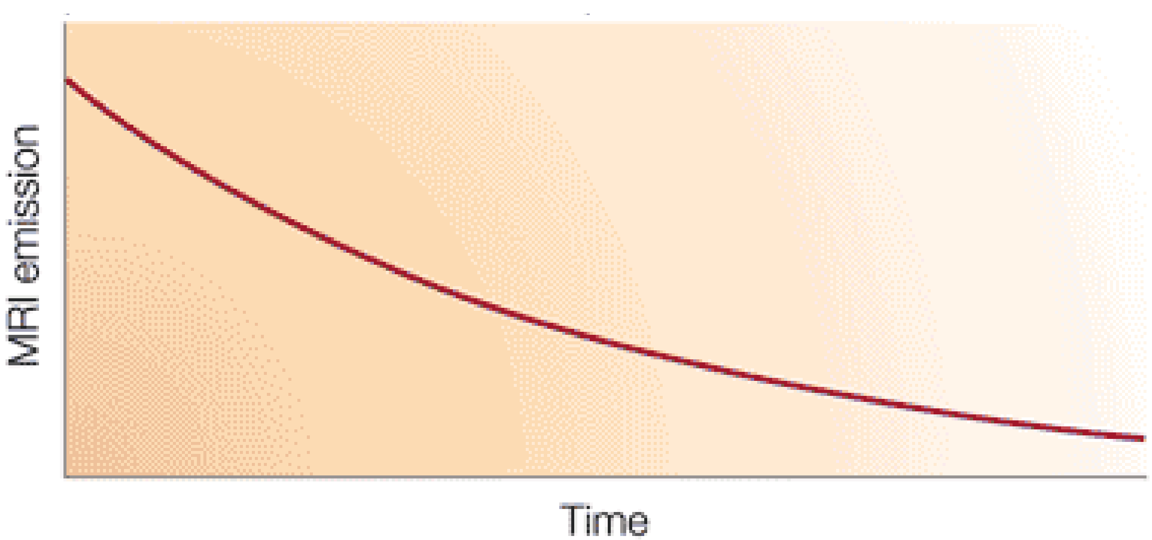
Roy and Sherrington (ought diggedy) without the pretty graphics

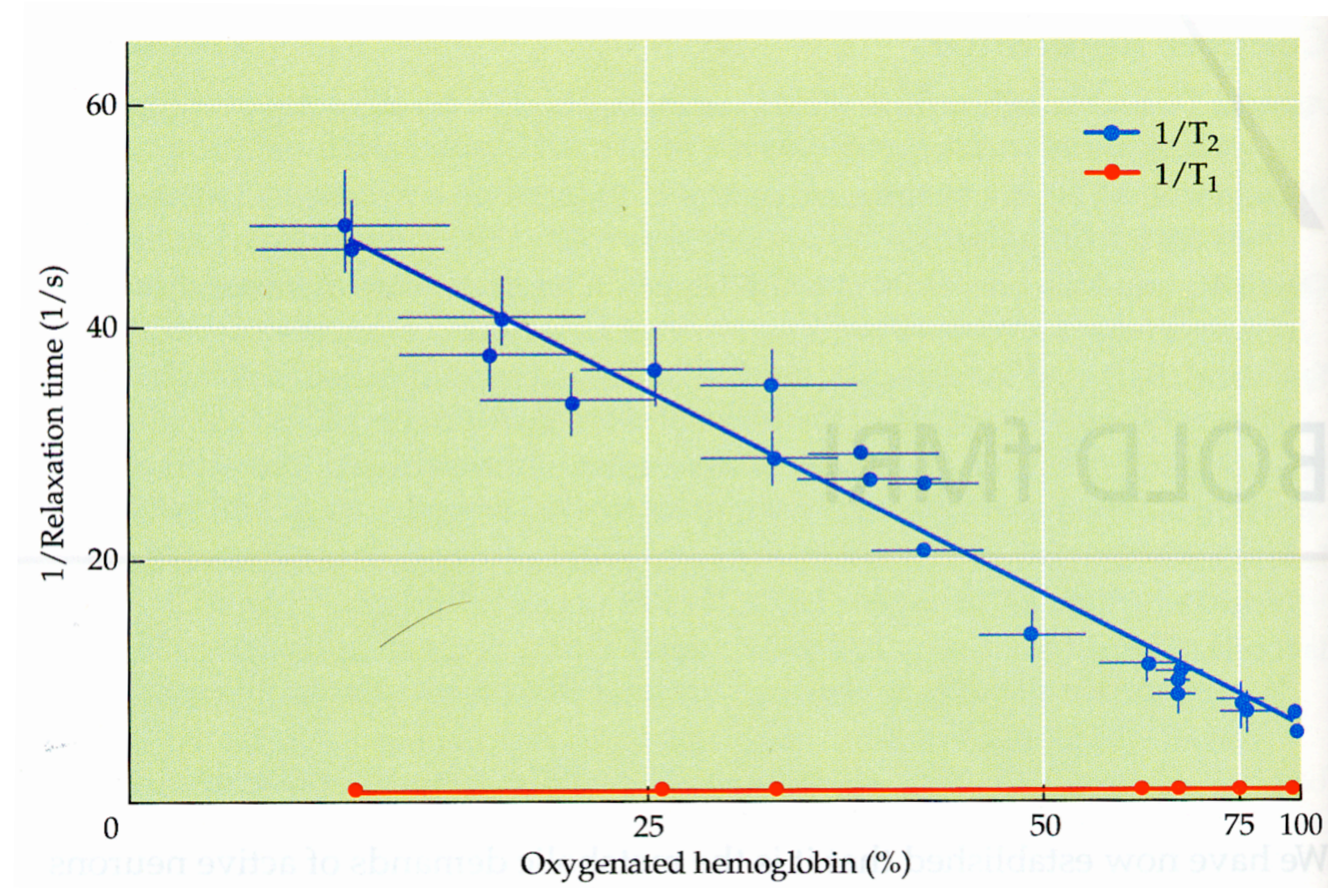


4 Iron atoms
Bind O_2

Oxy-hemoglobin: diamagnetic
Deoxyhemoglobin: paramagnetic ← Pauli 1935
Changes local magnetic field



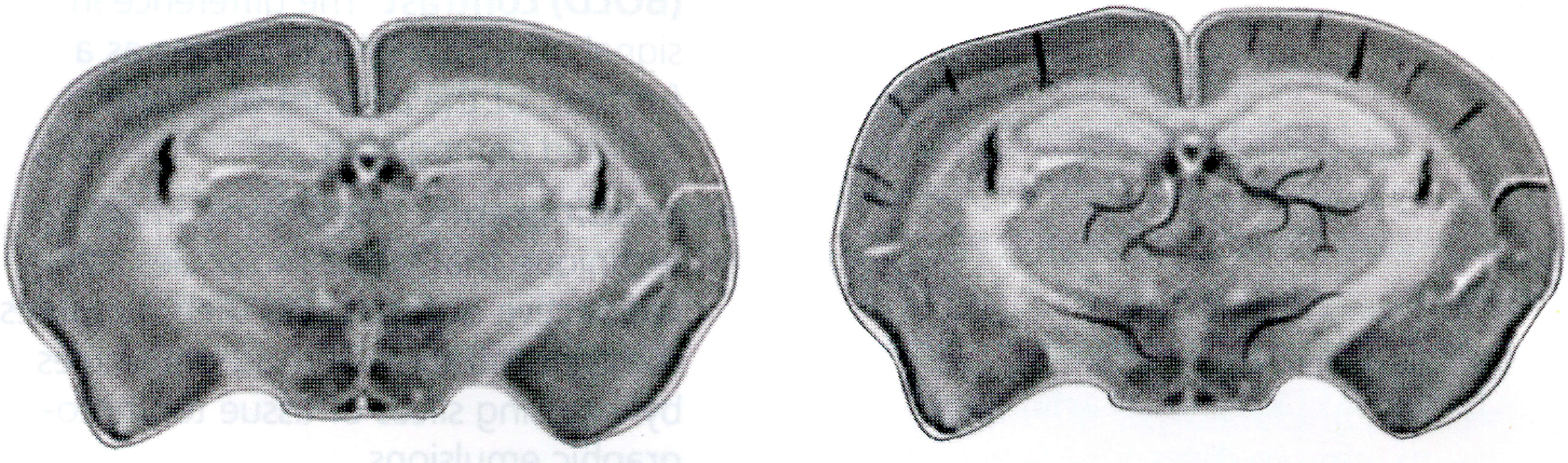




Thulborn 1982

Oxygenation of hemoglobin changes local magnetic field and T_2 of blood

The BOLD Effect

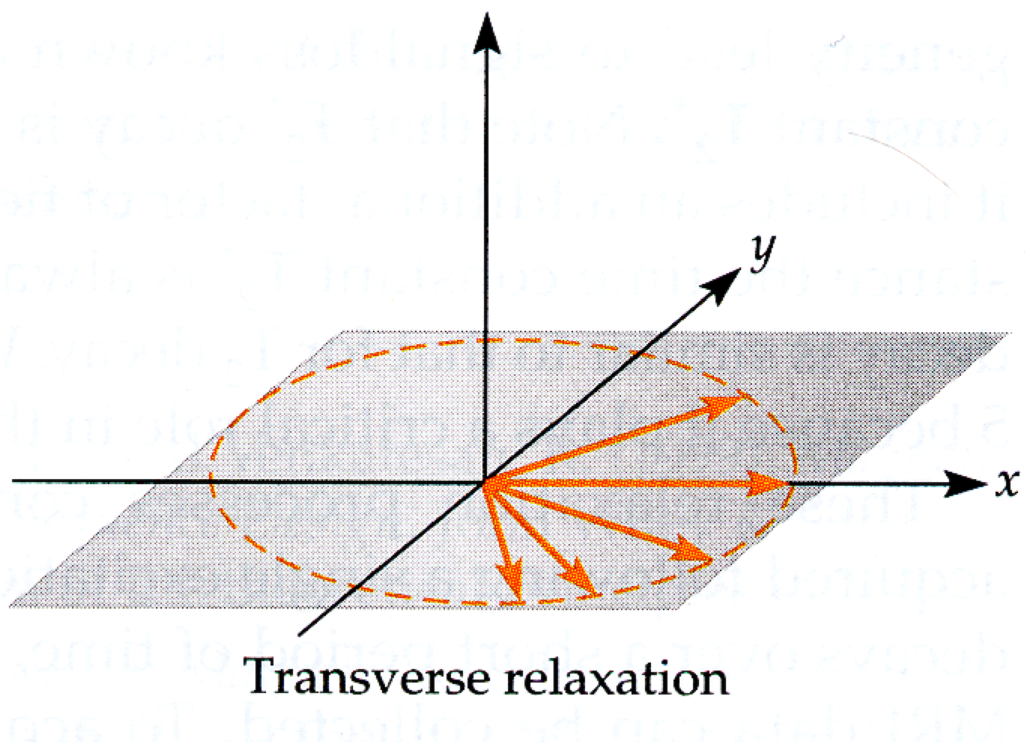


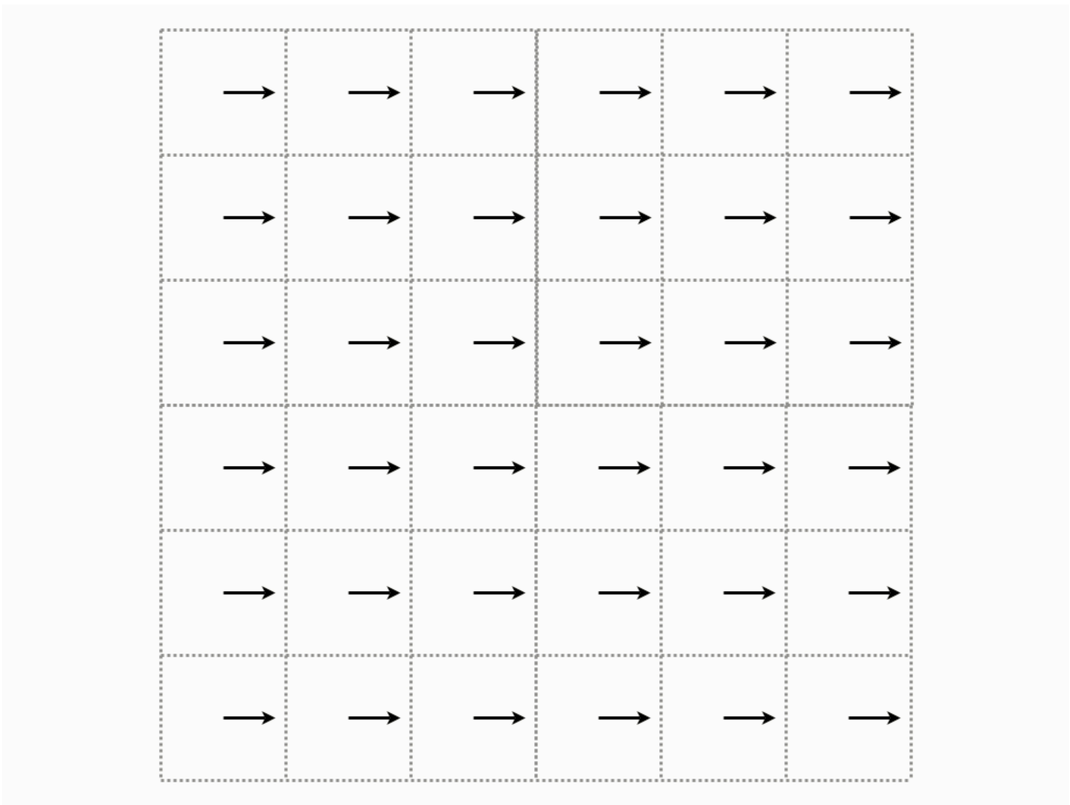
Pure O_2 Normal Air

Oxygenation of blood can be imaged! Ogawa 1990

T_2^* Decay

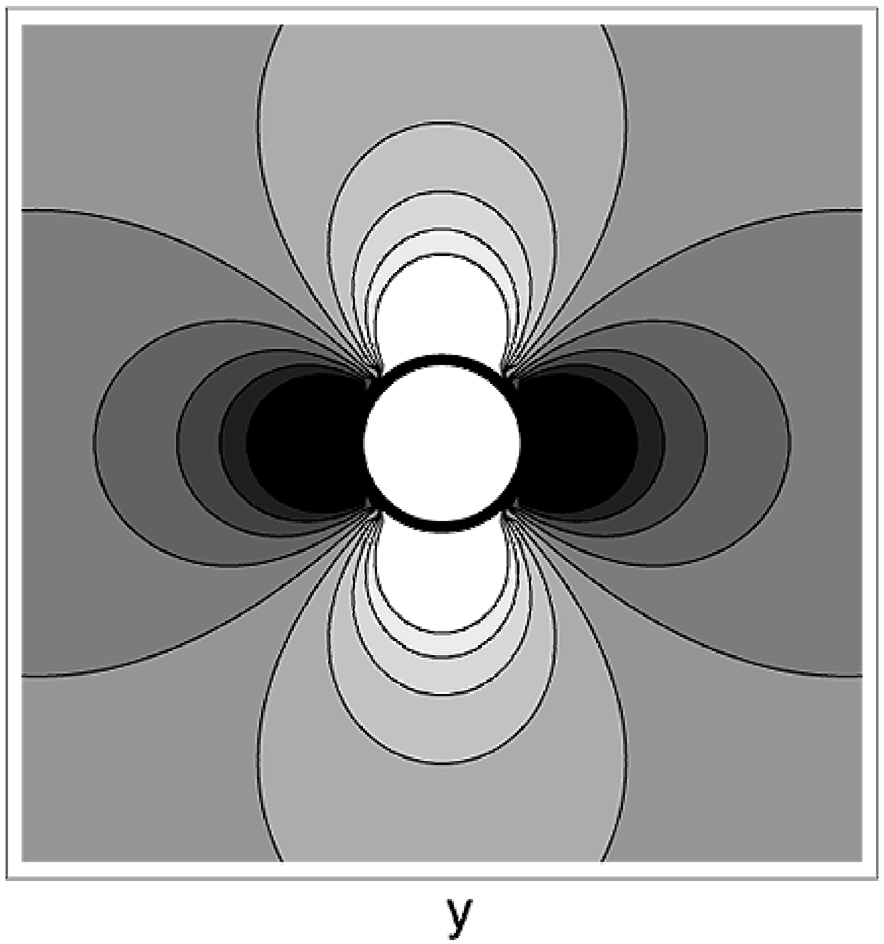
Due to variation of magnetic field INSIDE in a voxel

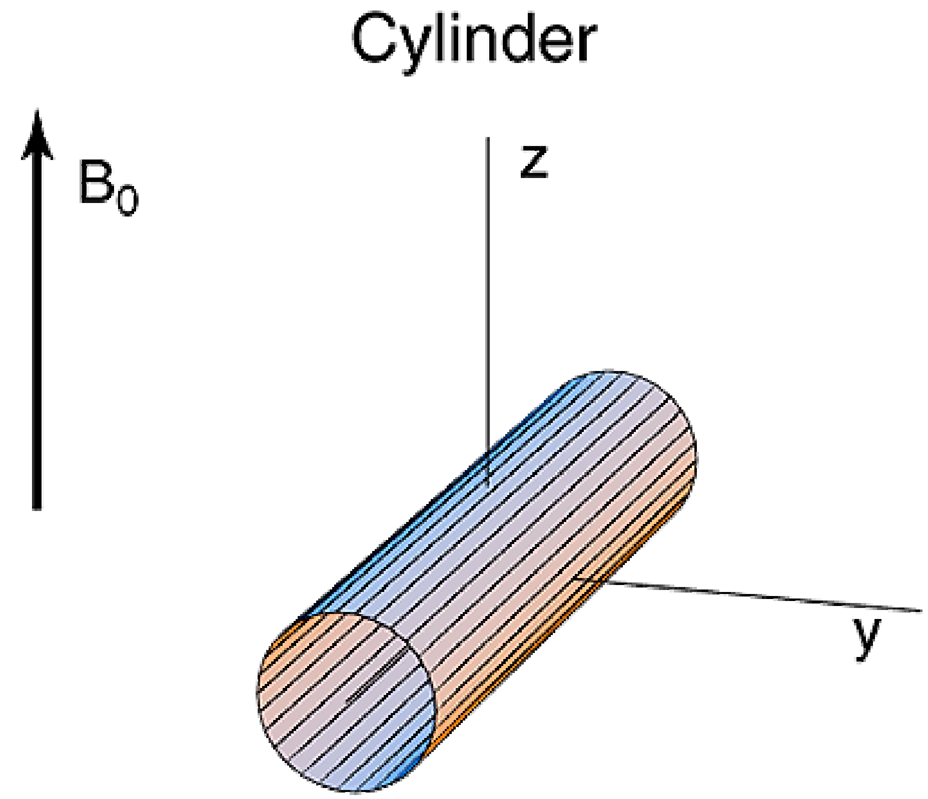




Deoxyhemoglobin in veins changes T_2^*

Magnetic Field Near a Vessel

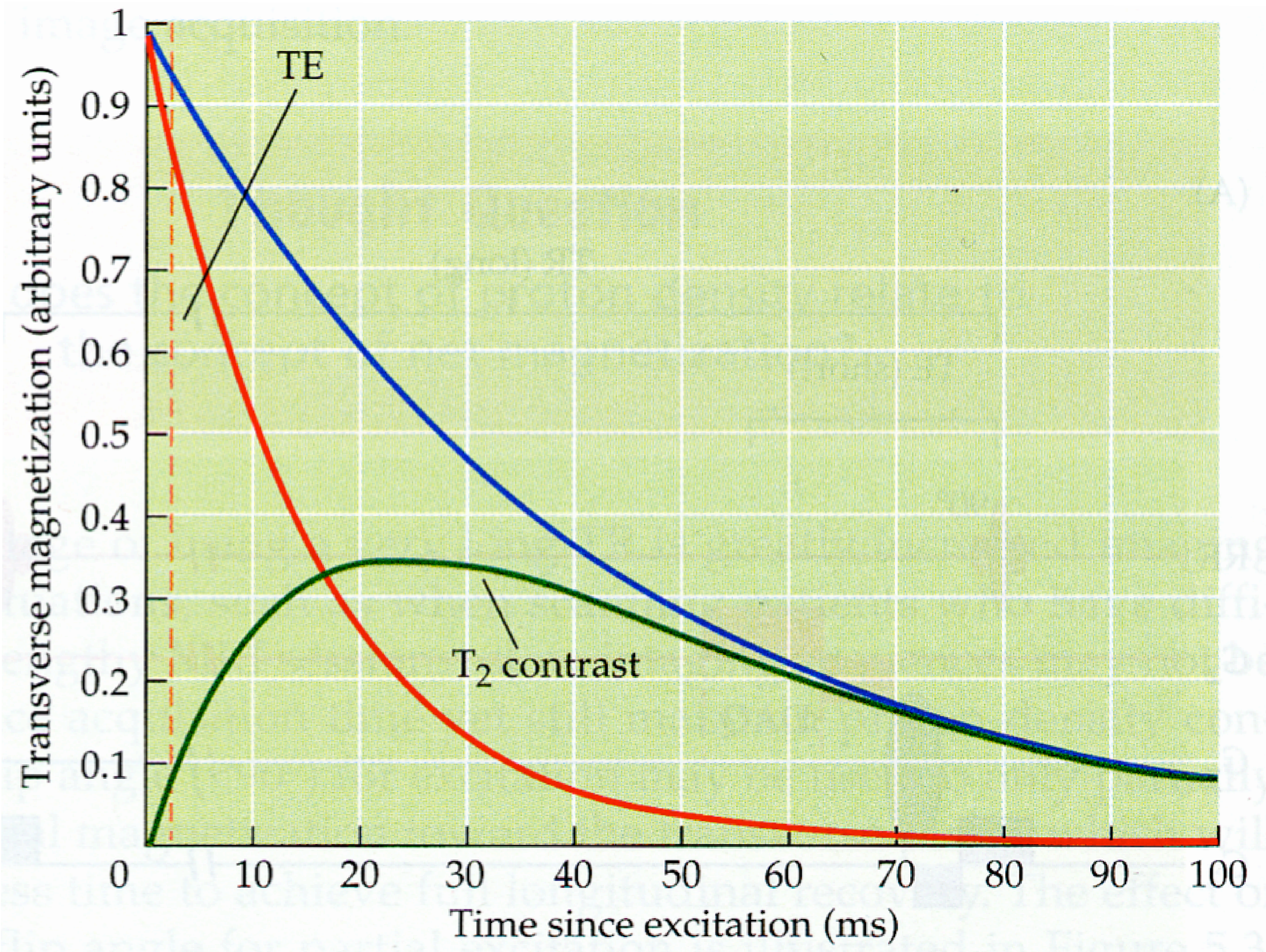




Field depends on several things:

1) Location
2) Vessel orientation relative to B_0
3) Deoxyhemoglobin content

T_2^* Image Contrast



Pick TE to maximize T_2^* sensitivity

Neuronal activation

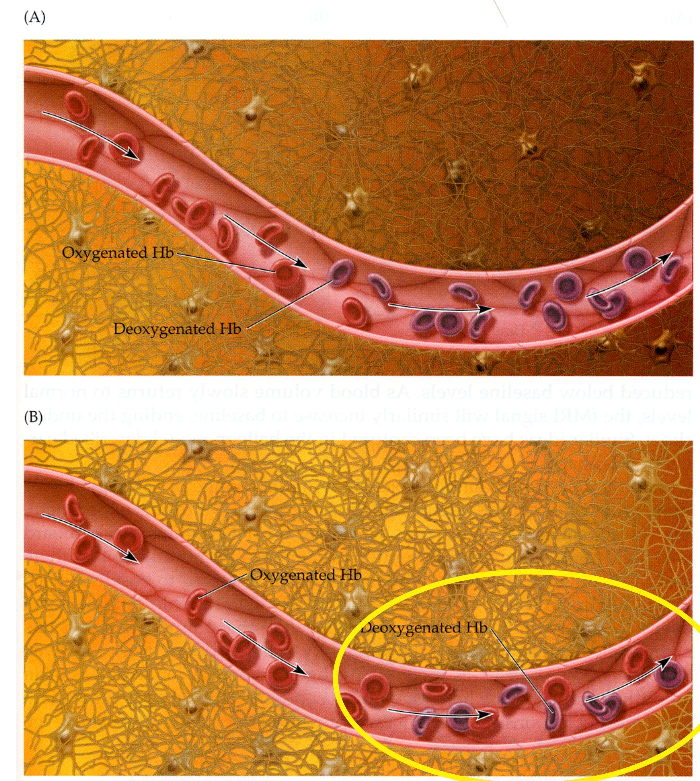
↓

Local hemodynamic changes

- ↑ •Blood flow
- ↑ •Blood volume
- ↑ •oxygen consumption

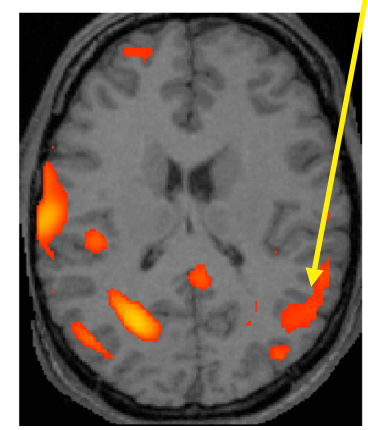
↓

Decrease in venous deoxyHb concentration → Local increase in MR signal



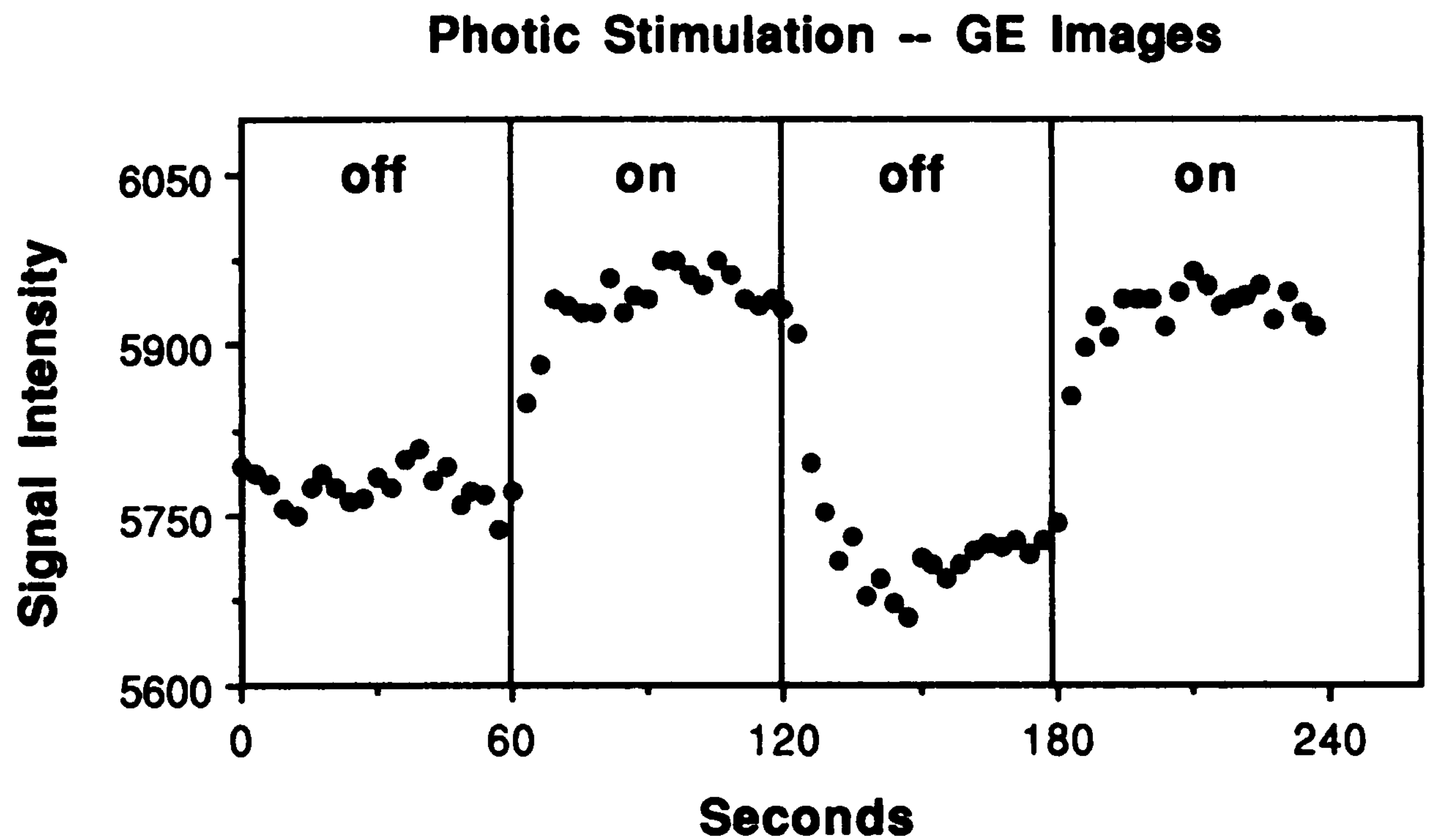
Baseline

Task



Kwong '92
Ogawa '92

Block Design

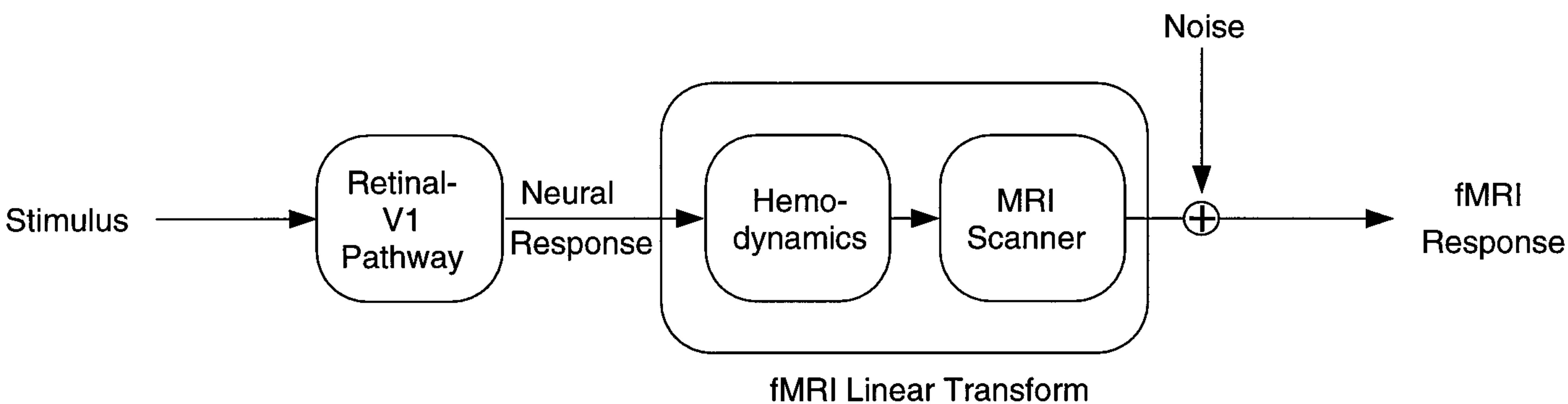


Kwong 92

Inspired by PET studies (90s/image)
Easy to analyze

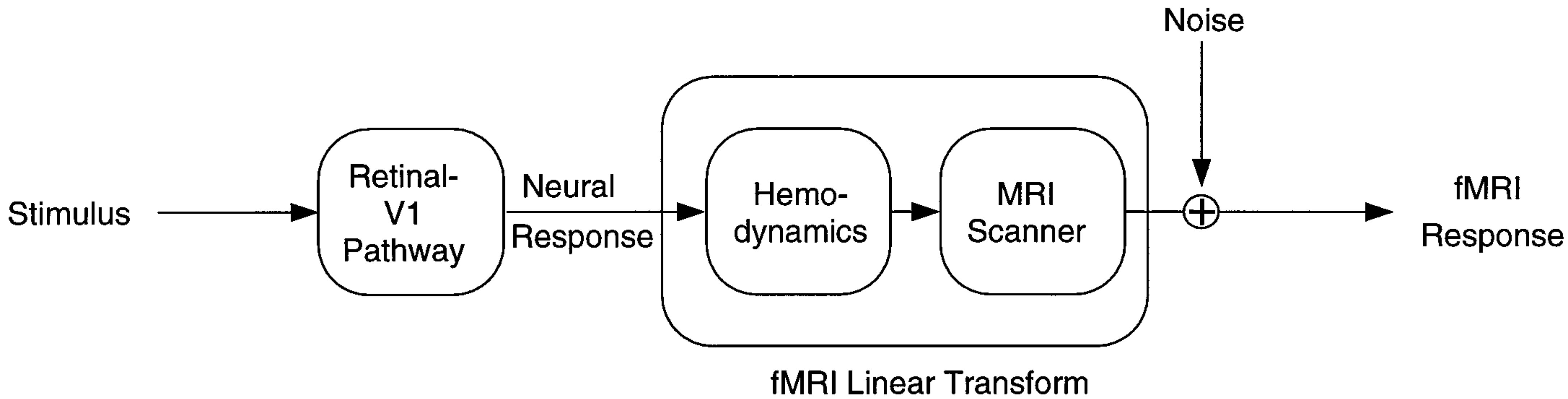
Estimate "average" BOLD response in block

FMRI as a Linear System



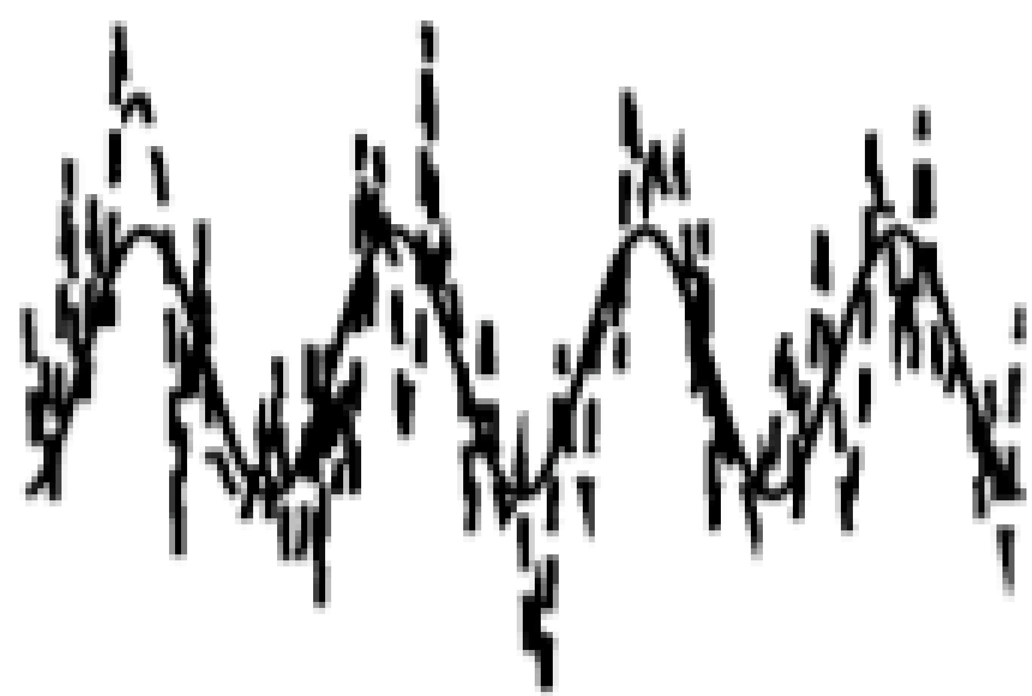
Hypothesis which can be tested.
Boynton and Heeger 96

Periodic Stimulus

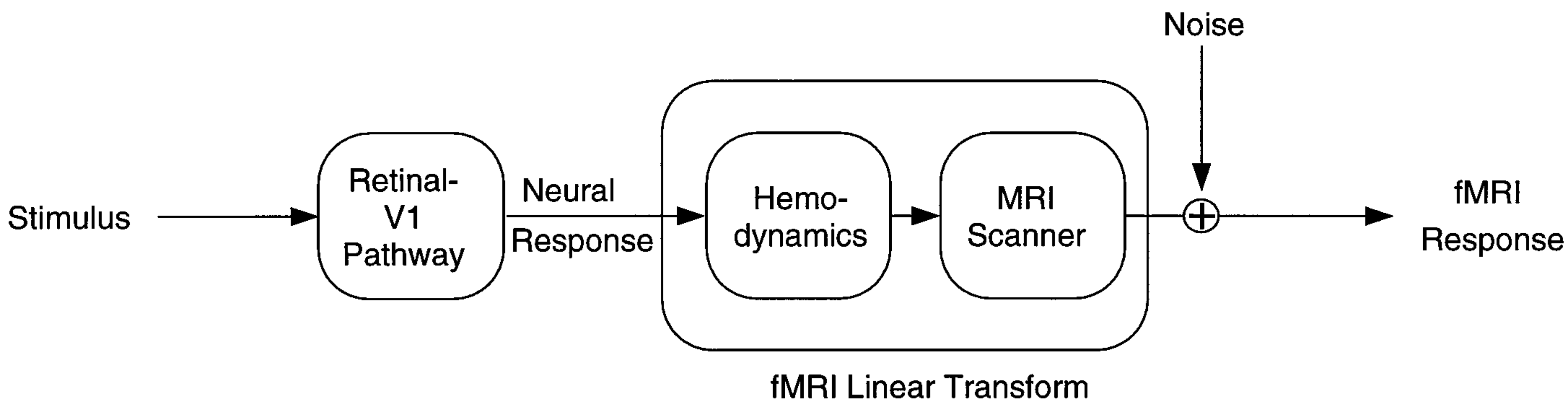


Periodic stimulus produces periodic response

Analysis is easy
Don't need to know HRF



Impulse Stimulus

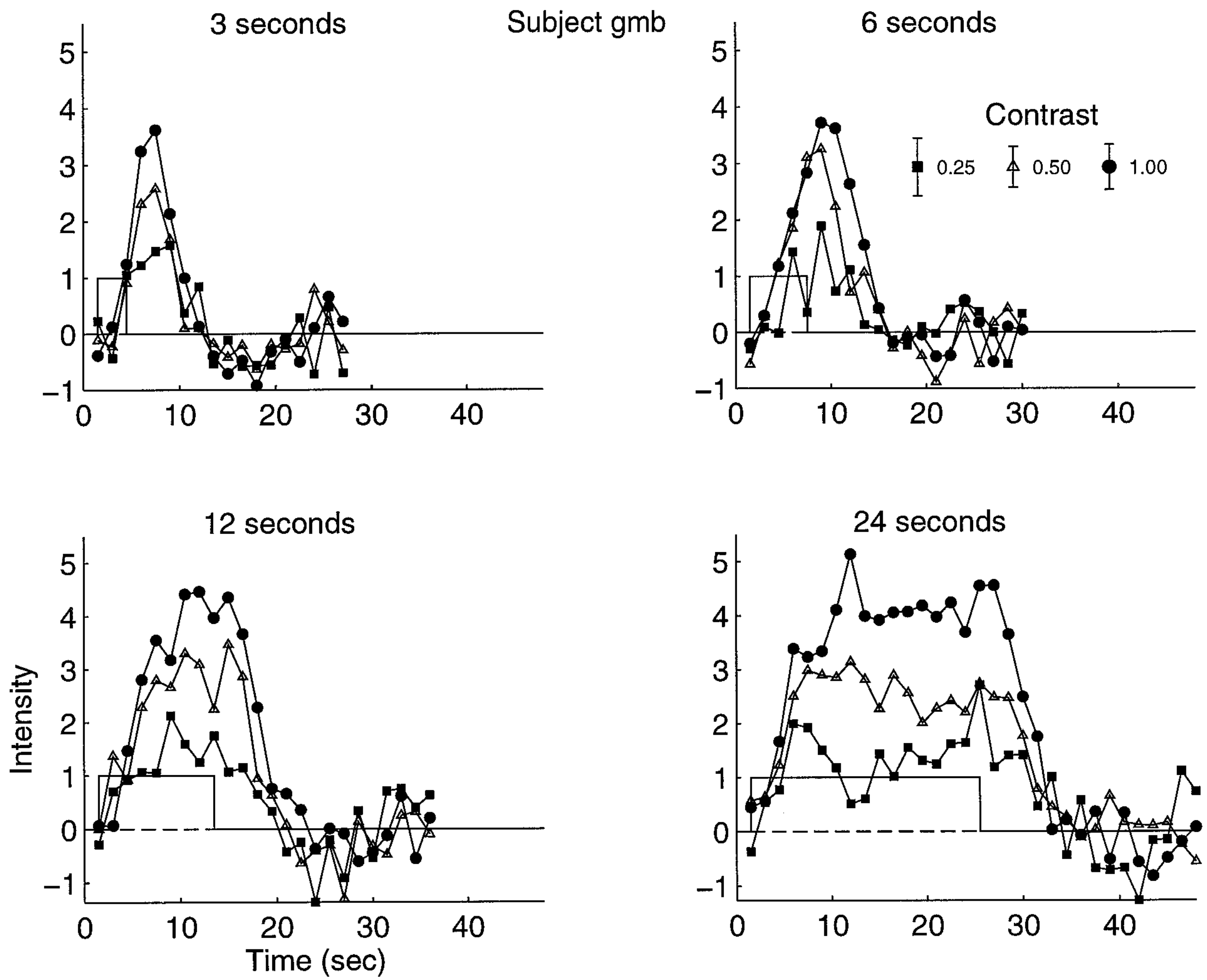


Brief stimulus produces impulse response

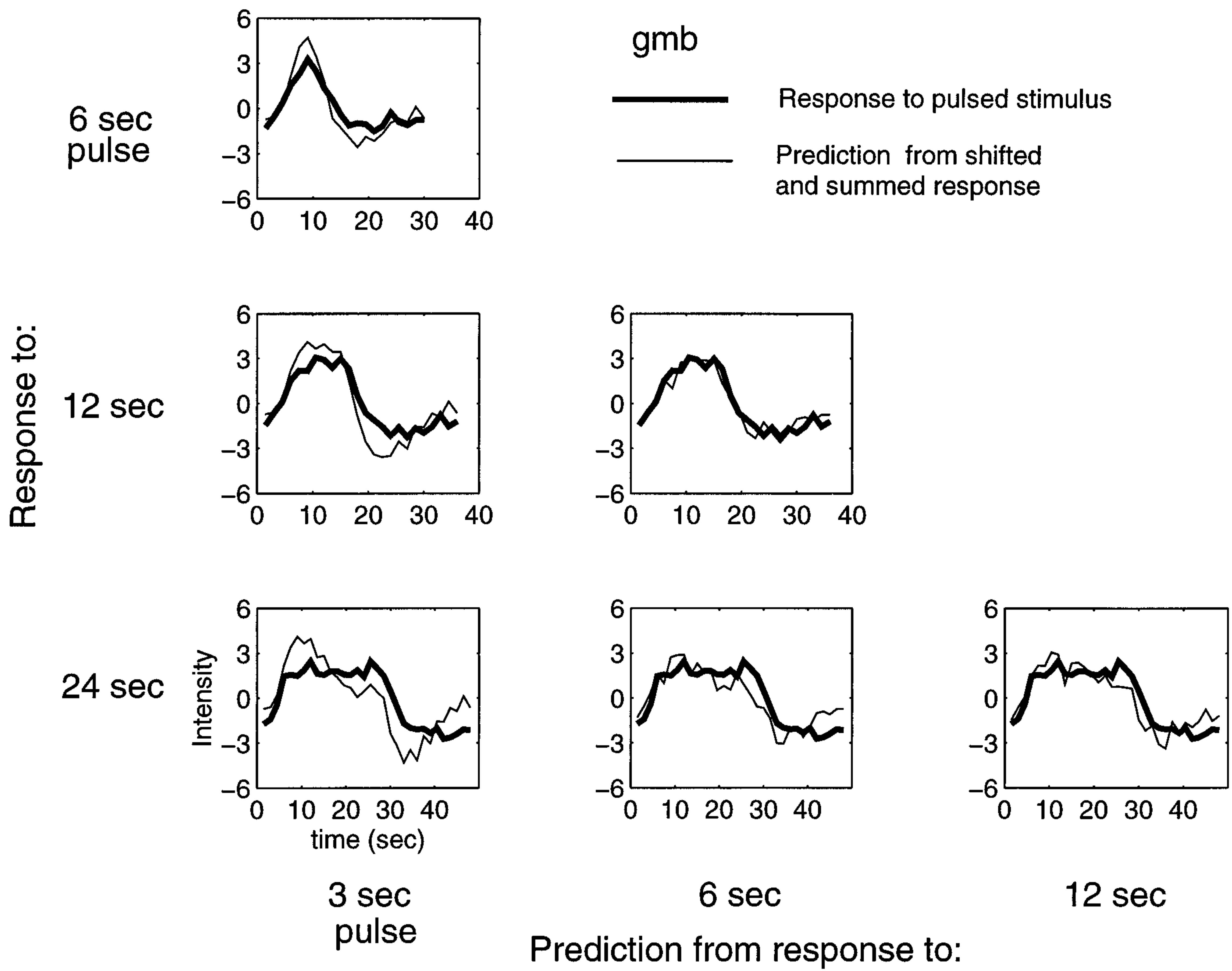
Analysis is easy if events are far apart

Measure Hemodynamic Impulse Response Function (HRF)

Impulse Response and Linearity



Looks like convolution.


gmb
Response to pulsed stimulus
Prediction from shifted and summed response
6 sec pulse
Response to:
12 sec
24 sec
Intensity
time (sec)
3 sec pulse
6 sec
12 sec
Prediction from response to:

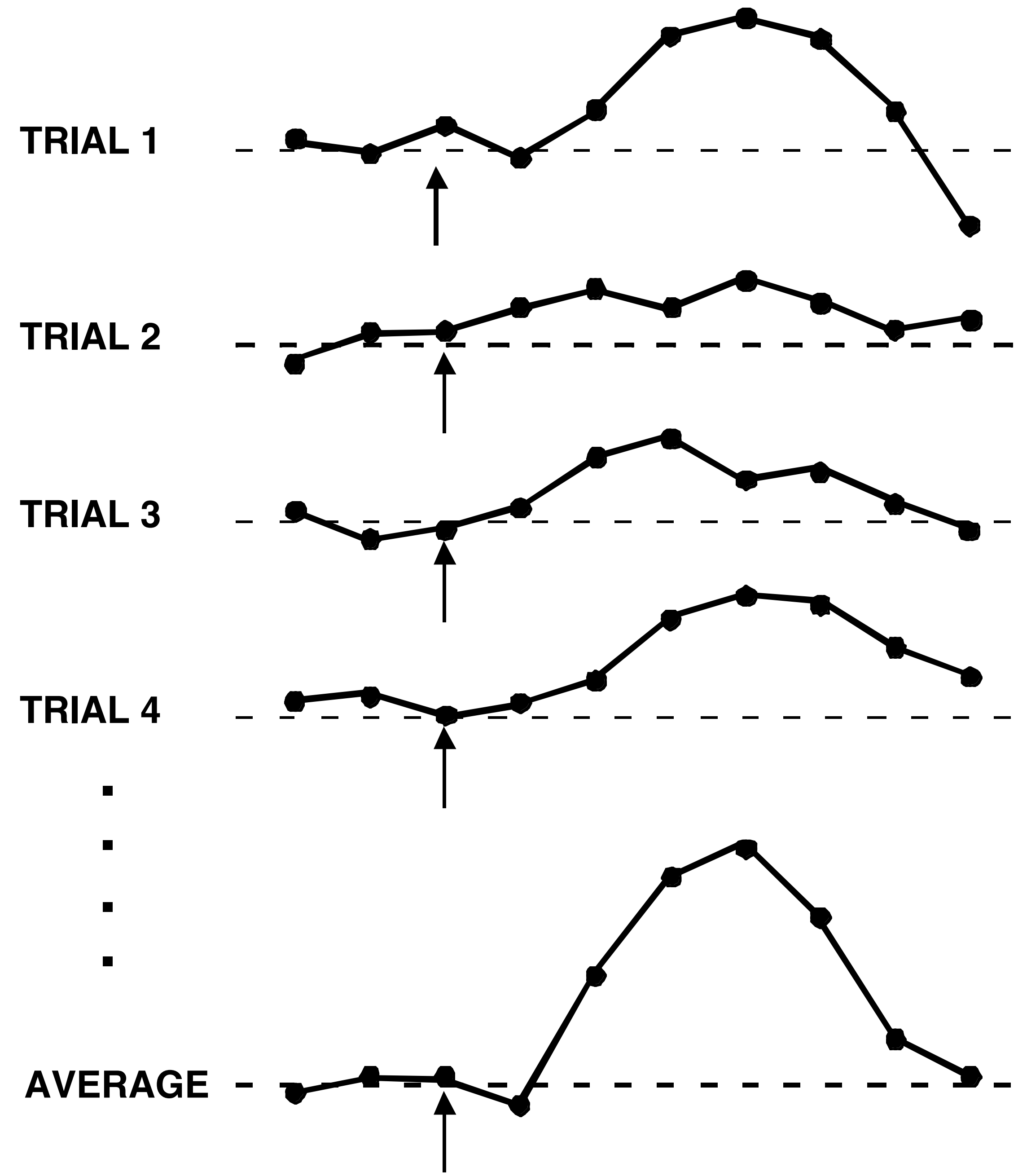
“Trial Triggered” Averaging

Inspired by ERP

If trials widely spaced in time (>20s), can average blocks.

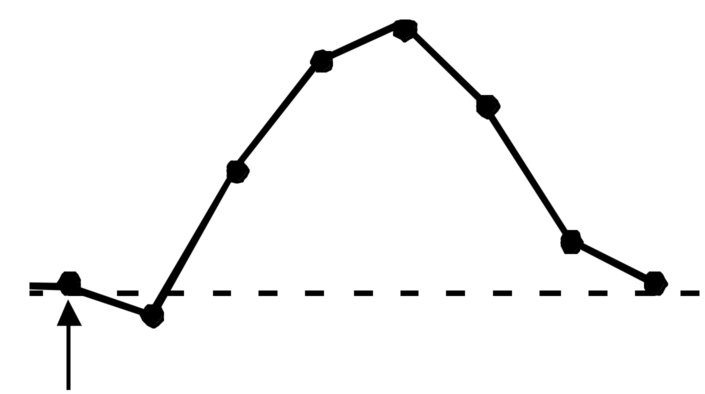
Sync to the beginning of the trial period.

“Slow” event-related



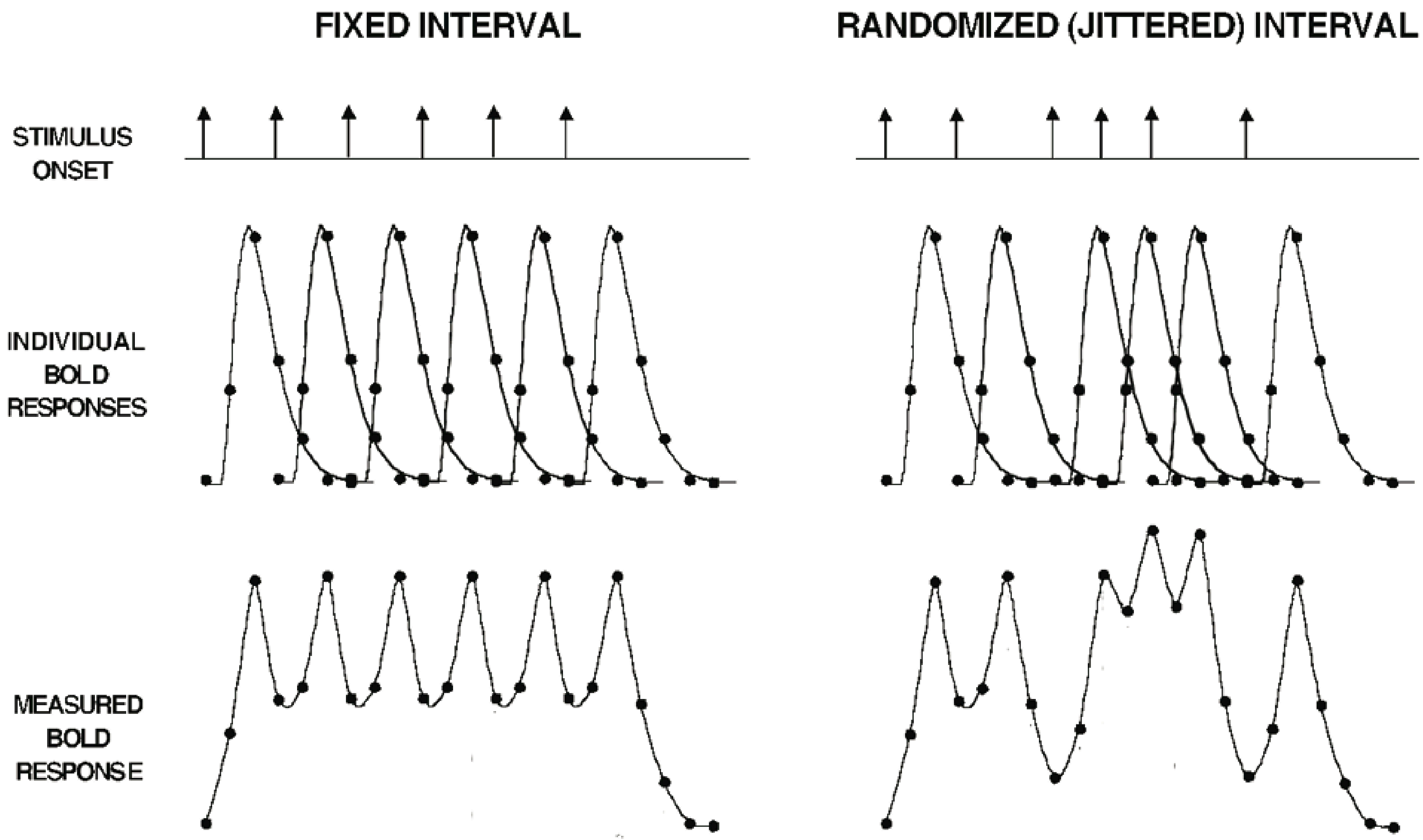
Model for Trial Averaging

$$X = \left[\begin{array}{cccccc}
1 & 0 & 0 & 0 & 0 & 0 \\
0 & 1 & 0 & 0 & 0 & 0 \\
0 & 0 & 1 & 0 & 0 & 0 \\
0 & 0 & 0 & 1 & 0 & 0 \\
0 & 0 & 0 & 0 & 1 & 0 \\
0 & 0 & 0 & 0 & 0 & 1 \\
\hline
1 & 0 & 0 & 0 & 0 & 0 \\
0 & 1 & 0 & 0 & 0 & 0 \\
0 & 0 & 1 & 0 & 0 & 0 \\
0 & 0 & 0 & 1 & 0 & 0 \\
0 & 0 & 0 & 0 & 1 & 0 \\
0 & 0 & 0 & 0 & 0 & 1 \\
\hline
1 & 0 & 0 & 0 & 0 & 0 \\
0 & 1 & 0 & 0 & 0 & 0 \\
0 & 0 & 1 & 0 & 0 & 0 \\
0 & 0 & 0 & 1 & 0 & 0 \\
0 & 0 & 0 & 0 & 1 & 0 \\
0 & 0 & 0 & 0 & 0 & 1
\end{array}\right]
\begin{array}{l}
\text{Trial 1} \\ \\ \text{Trial 2} \\ \\ \text{Trial 3}
\end{array}$$

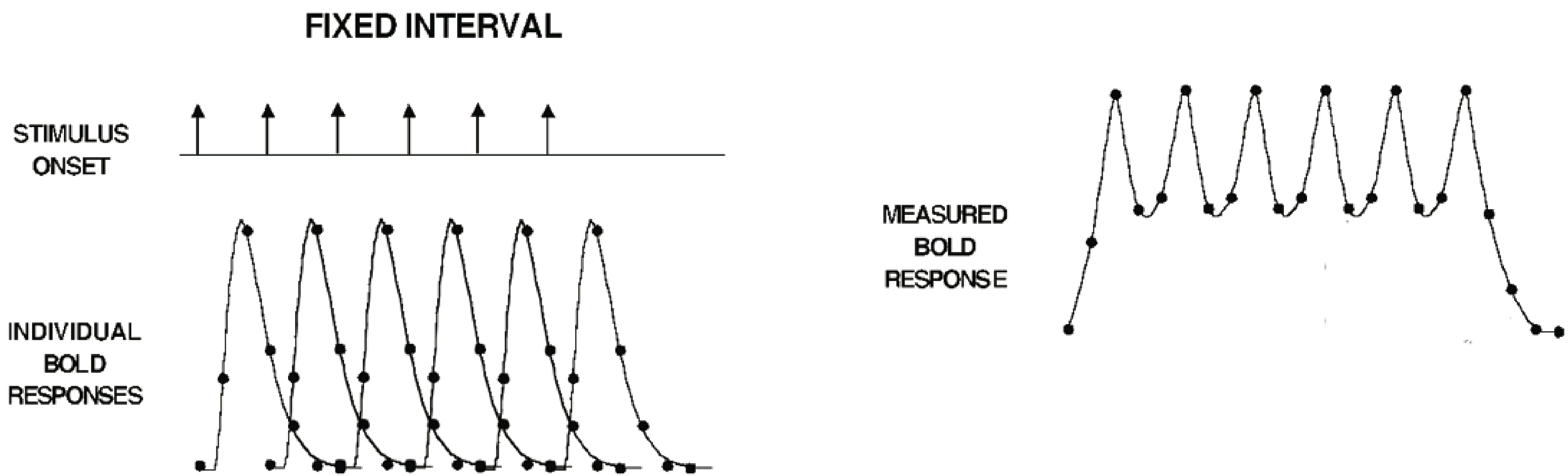


Estimate 6 parameters

Bring Trials Closer Together



Fast ER: Known HRF

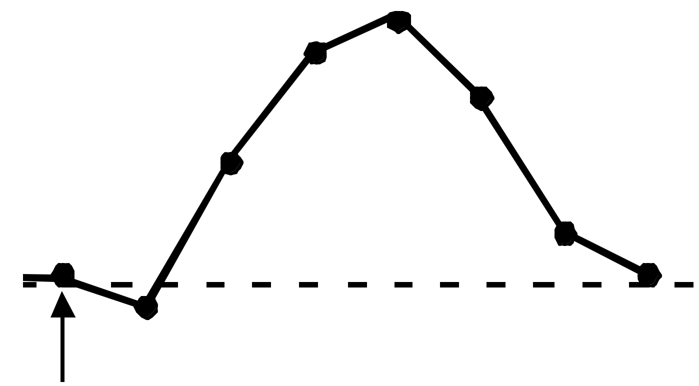


Only a few unknown parameters.
Amplitude of response to each trial type

Model for ER Known HRF

X =

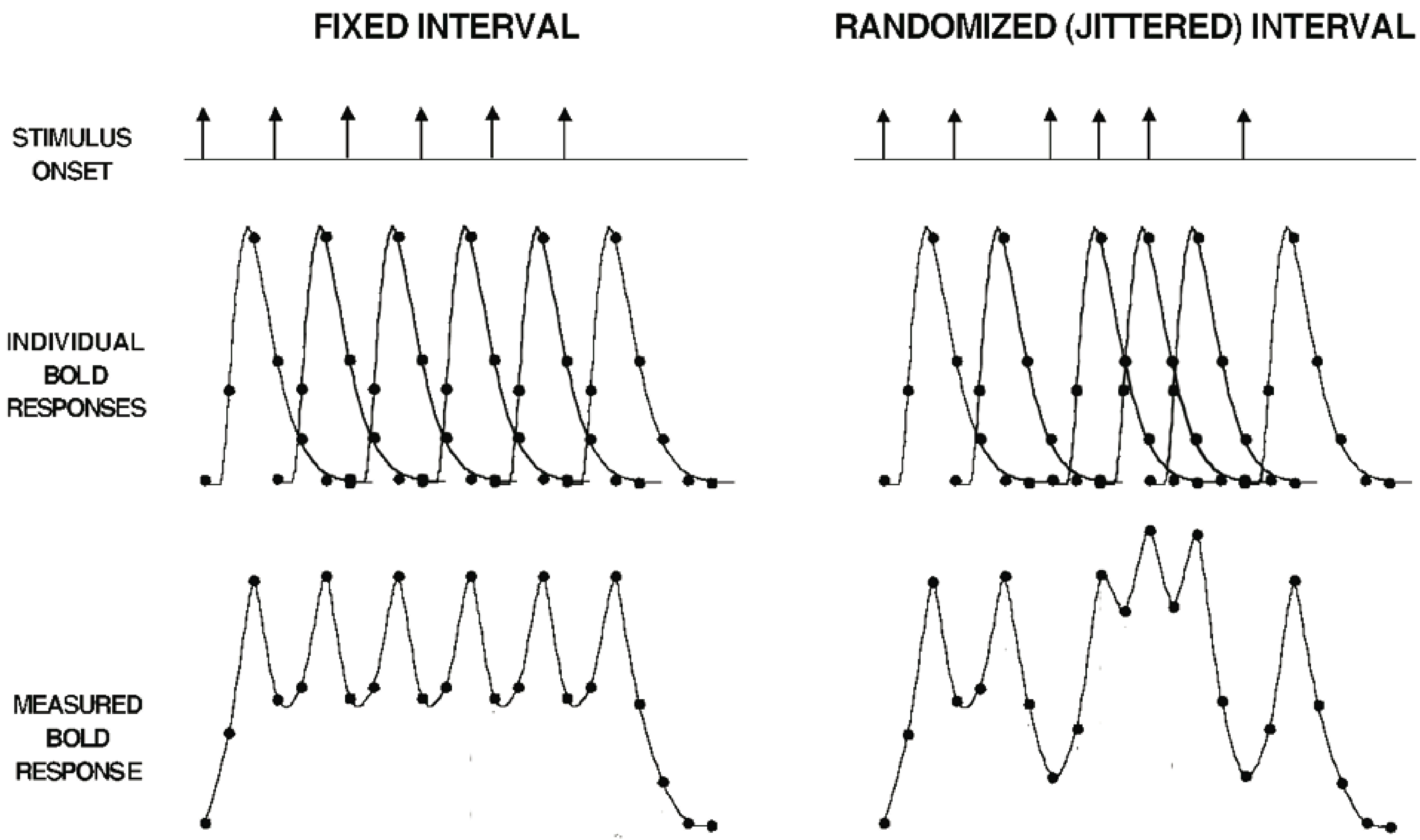
0	0.1000	B
0.1000	1.0000	A
1.0000	3.0000	
3.0000	2.0000	
2.1000	0.1000	A
1.1000	0	B
2.9000	1.1000	B
2.0000	4.0000	
0.1000	5.0000	B
-0.1000	2.2000	A
0.1000	1.0000	A
1.1000	2.9000	.
4.0000	2.0000	
5.0000	0.2000	.
2.1000	0.9000	
0.1000	3.0000	.
0.9000	2.1000	
3.0000	1.1000	
2.0000	2.9000	
0.1000	2.0000	
-0.1000	0.1000	
0	-0.1000	
0	0	



Estimate 1 parameter per trial type

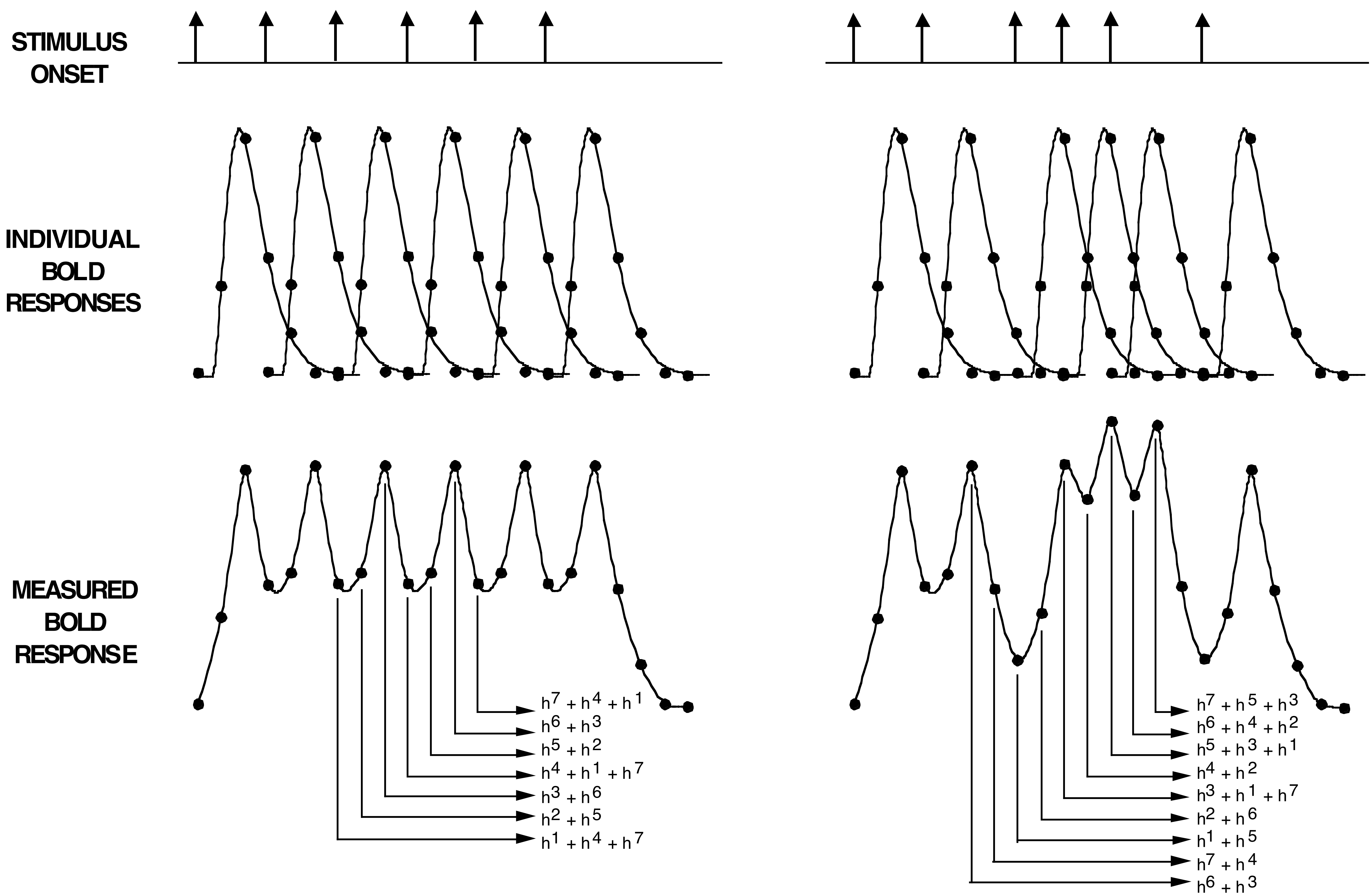
If HRF is wrong, you're in trouble!

Fast ER: Estimate HRF



Many unknown parameters.
Amplitude over time for each trial type

FIXED INTERVAL | RANDOMIZED (JITTERED) INTERVAL



Seven Unknowns, Only Three Independent Equations

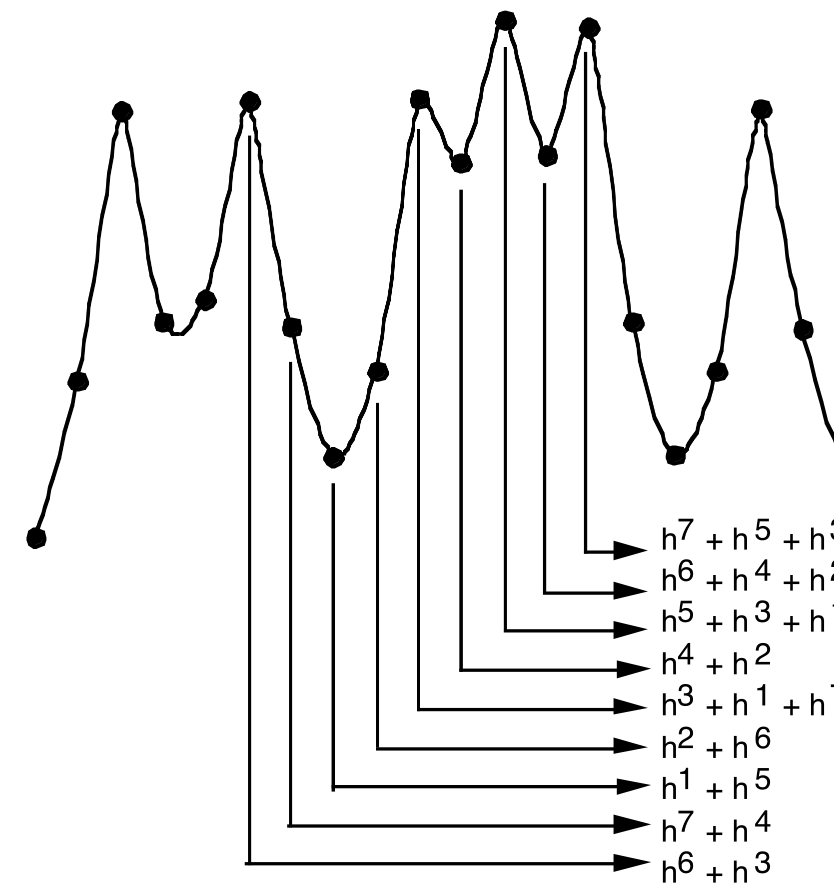
Seven Unknowns, More Than Seven Independent Equations

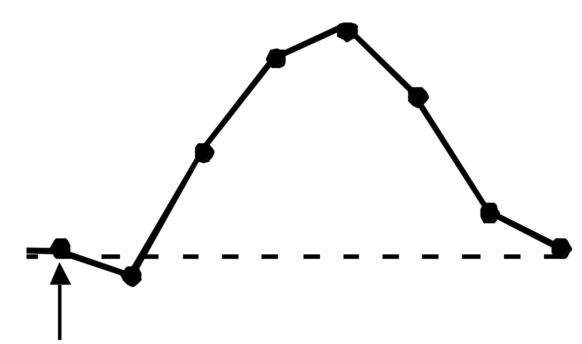
Model for ER Unknown HRF

	XA	XB
A	1 0 0 0 0 0	0 0 0 0 0 0
	0 1 0 0 0 0	0 0 0 0 0 0
B	0 0 1 0 0 0	1 0 0 0 0 0
A	1 0 0 1 0 0	0 1 0 0 0 0
	0 1 0 0 1 0	0 0 1 0 0 0
	0 0 1 0 0 1	0 0 0 1 0 0
B	0 0 0 1 0 0	1 0 0 0 1 0
	0 0 0 0 1 0	0 1 0 0 0 1
	0 0 0 0 0 1	0 0 1 0 0 0
A	1 0 0 0 0 0	0 0 0 1 0 0
	0 1 0 0 0 0	0 0 0 0 1 0
B	0 0 1 0 0 0	1 0 0 0 0 1
	0 0 0 1 0 0	0 1 0 0 0 0
	0 0 0 0 1 0	0 0 1 0 0 0
	0 0 0 0 0 1	0 0 0 1 0 0

X

Betas
h1
h2
h3
h4
h5
h6
g1
g2
g3
g4
g5
g6



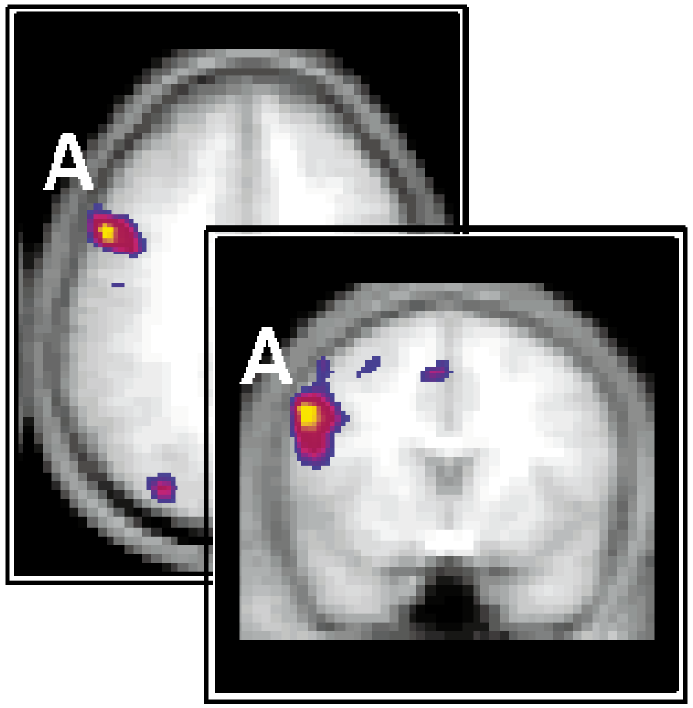


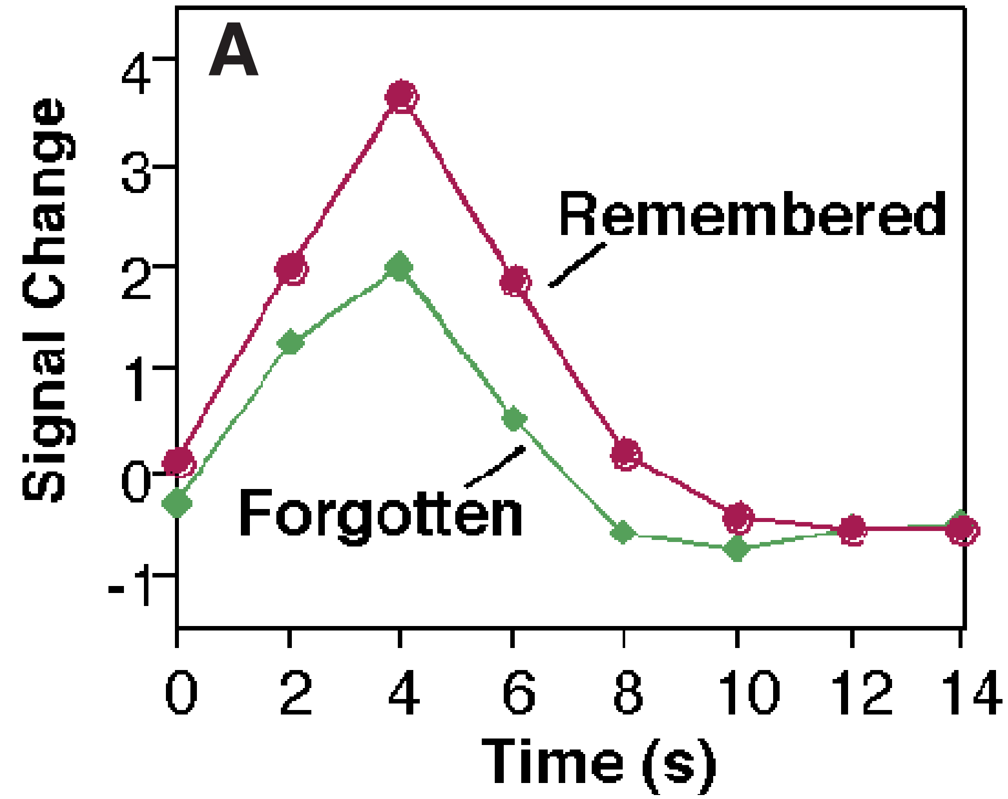
Estimate L parameters per trial type

Sorting After the Fact

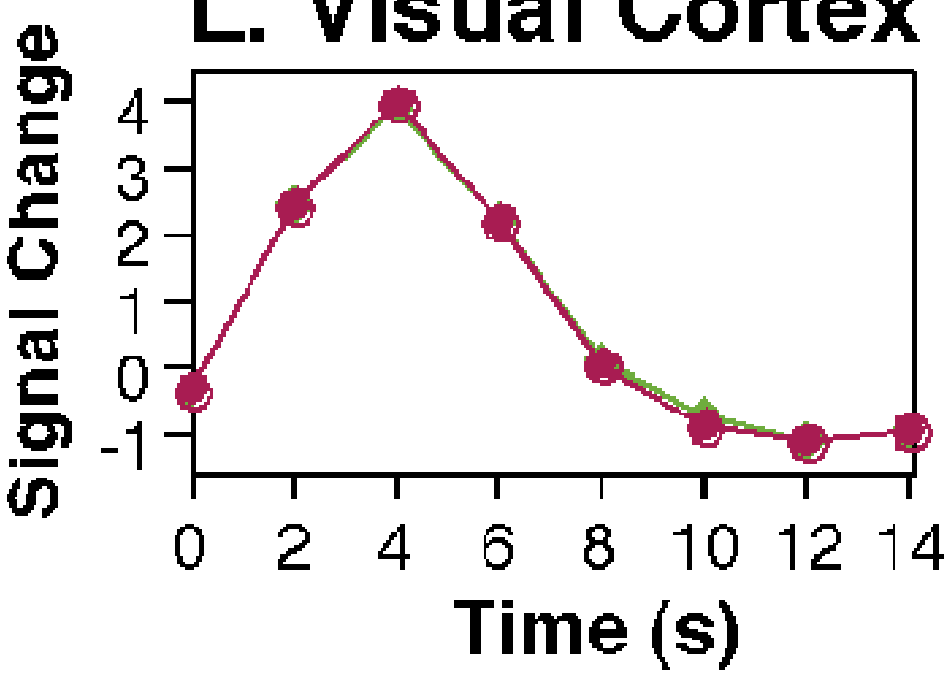
- Wagner, et. al. Science 98
- Behavior may produce sufficient jittering
- Trials were 2s long (750ms word, 1250ms blank)
- Subjects making abstract/concrete decision
- Fixation trials
- Surprise memory test after the session to sort the trials into remembered vs. forgotten

Posterior LIFG

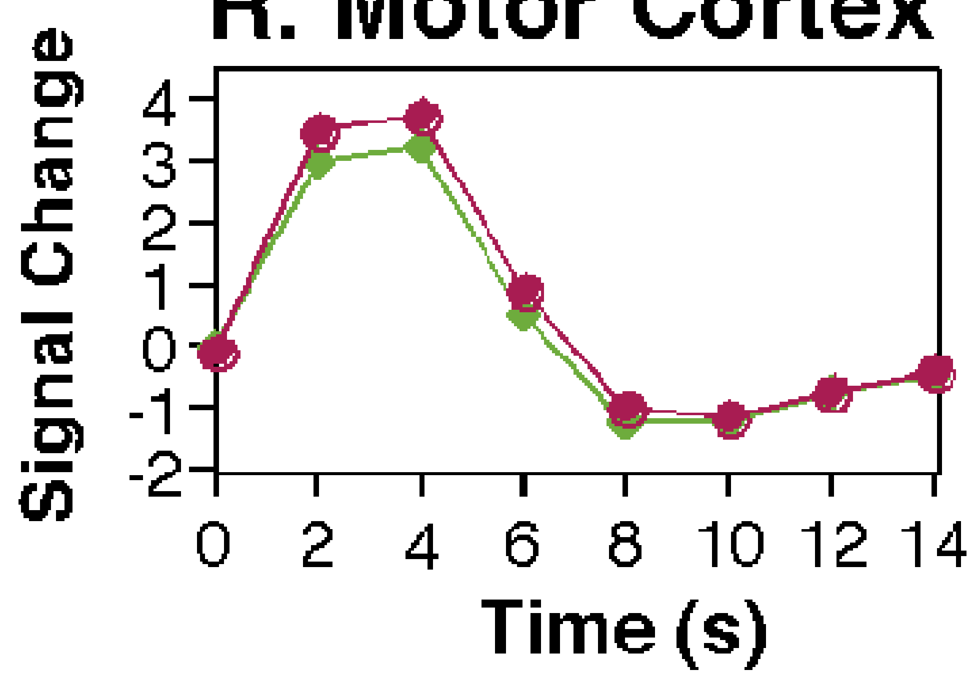




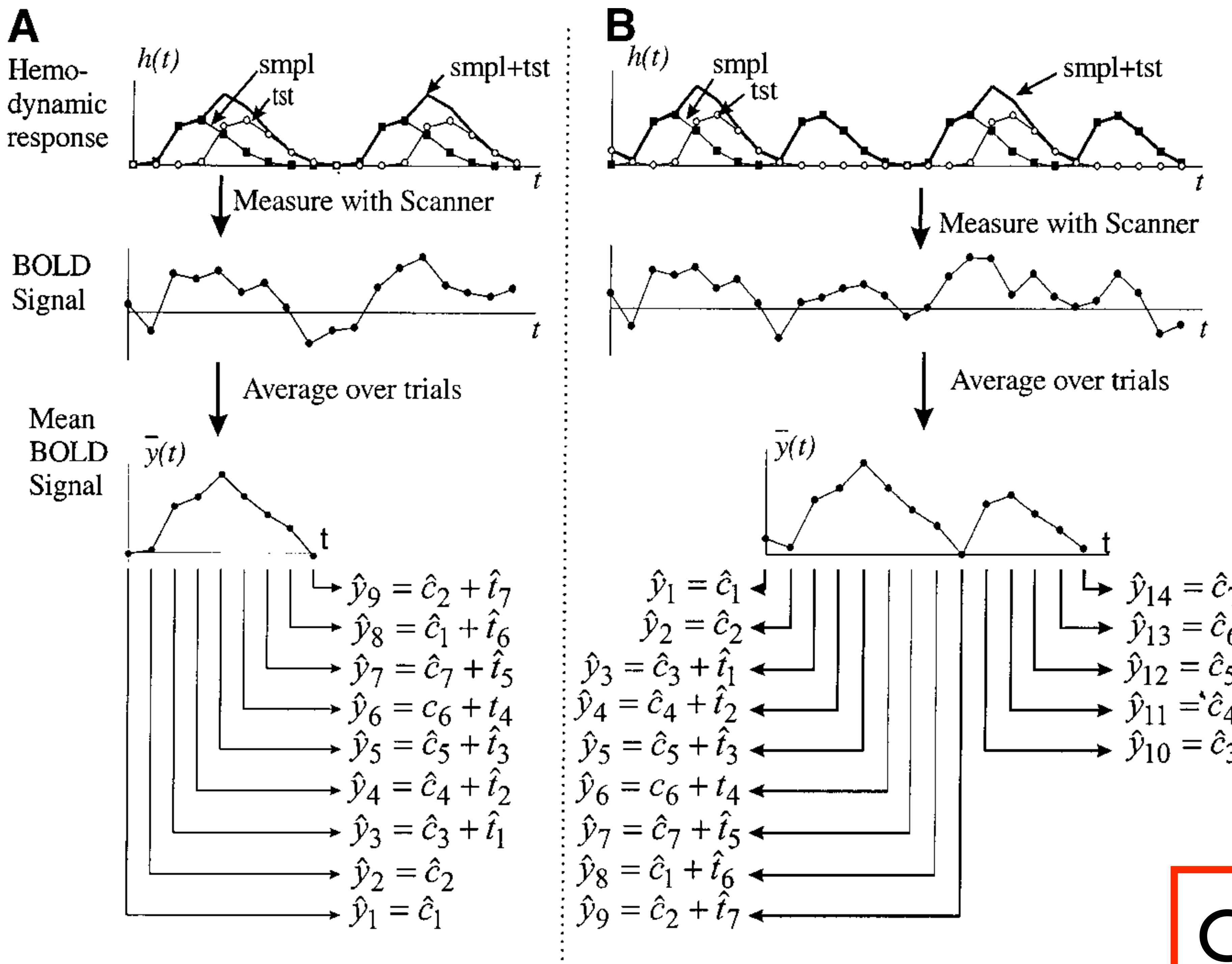
L. Visual Cortex



R. Motor Cortex



Separating Task Components



Caveats?

Ollinger 01, “catch” trials

Bad Designs

When the model matrix is close to "singular"

Bottom line:
  Different sets of parameters fit the data equally well.
  Which one is right?

The pseudoinverse choses the parameter set with the "smallest" amplitude.

Parameter estimates very sensitive to noise

Noise in FMRI

Noise in MRI

Electrical noise in the MRI receiver is white and stationary

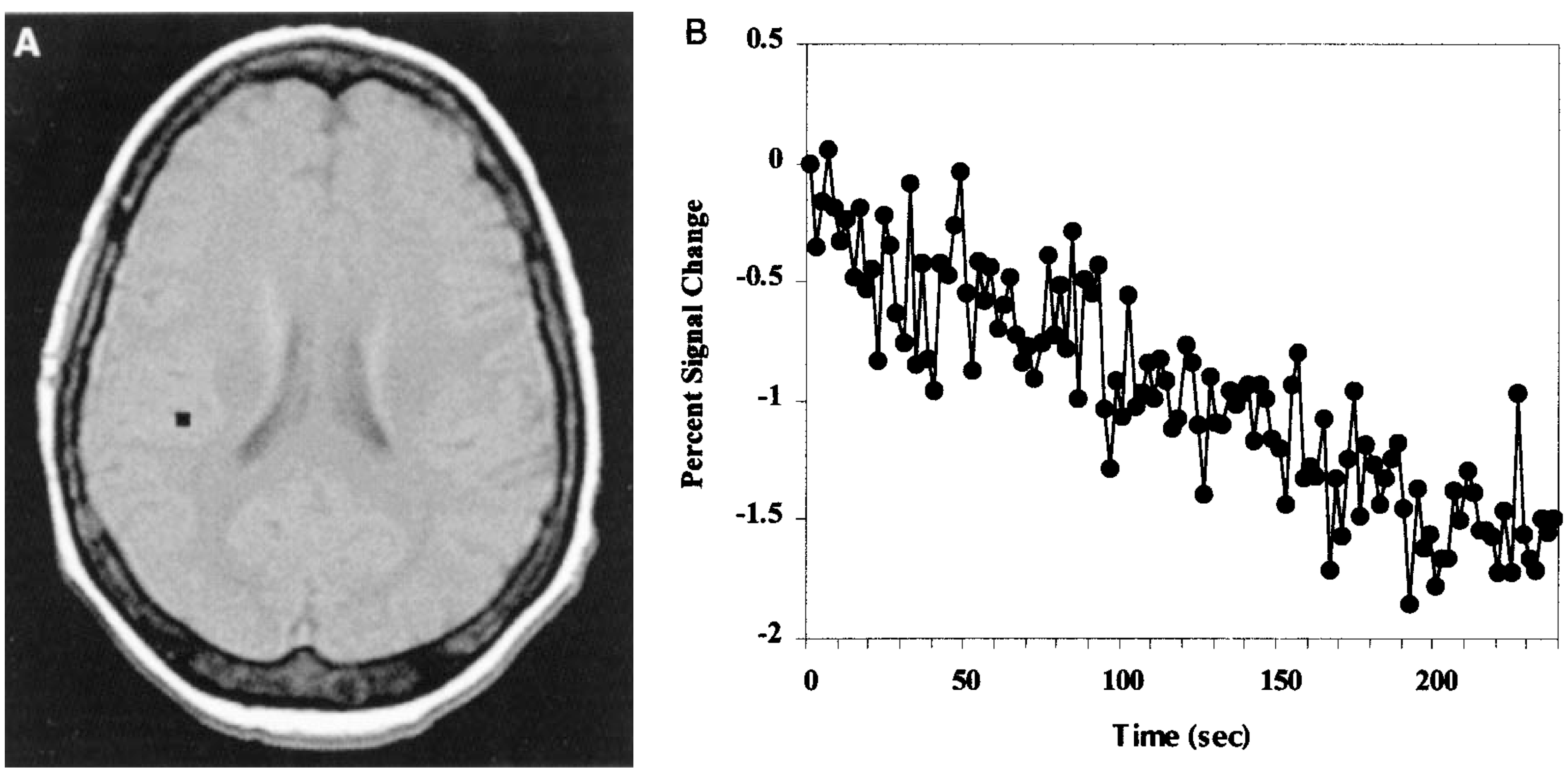
Noise in the reconstructed image has a very small amount of spatial autocorrelation because of the reconstruction process

Also some image artifacts (distortion), stationary if the subject doesn't move too much

Temporal noise in FMRI 1

FMRI noise is not independent in time
autocorrelations and low frequencies:

- instrumental drift
- cognitive junk: attention, thinking about lunch
- even in dead people! see Smith '99



Temporal noise in FMRI 2

For what to do about it
see Heeger notes, MGH stats notes,
Woolrich ‘01 and Liu ’01 (in that order)

Estimation Efficiency and Noise

The noise propagates through the GLM fit:

$$\beta_{est} = \mathrm{X}^{+}(data)$$

$$\beta + \eta_{\beta} = \mathrm{X}^{+}(s + \eta)$$

Truth Noise Truth Noise

pinv(design matrix)

Estimation Efficiency and Noise

$$\beta + \eta_\beta = X^+(s + \eta)$$

If you know the statistics of the noise then you can estimate the error bars on the parameter estimates for the particular choise of desing.

Some designs are more efficient than others. Pick the one that is best, subject to behavioral constraints.