Introduction to Brain Science and fMRI

Jorge Jovicich, Ph.D.
MR Lab Co-Director
Center for Mind Brain Sciences
University of Trento
jorge.jovicich@unitn.it

Tokyo Institute of Technology
February 2011

Lectures Outline

Dates	Topics
Friday Feb 4, 2011 (13:50-16:40)	• Overview of a brain fMRI experiment • Basic MRI concepts ○ Signal source. Image formation. Contrast. Safety. • Anatomical MR images: ○ Acquisition: T1-weighted contrast imaging ○ Analysis: brain segmentation ○ Potential image artifacts
Mon Feb 7, 2011 (13:20-16:30)	• Functional MR images: ○ Acquisition: fast imaging (EPI), BOLD contrast ○ Analysis: pre-processing, designs, statistical analyses ○ Potential image artifacts

Suggested reading materials

- Functional Magnetic Resonance Imaging
  Scott A. Huettel, Allen W. Song and Gregory McCarthy
- What we can do and what we cannot do with fMRI, N. Logothetis, Nature 2008
  (http://www.nature.com/nature/journal/v453/n7197/pdf/nature06976.pdf)
- Seven topics in fMRI, P. Bandettini, J Integrative Neuroscience 2009
  (http://fim.nimh.nih.gov/publications/seven-topics-functional-magnetic-resonance-imaging)
- Stay updated: e.g., pubmed search 'Trends in Neurosciences fMRI' (reviews)

fMRI Educational Links

- http://www.cis.rit.edu/htbooks/mri
- http://www.fmrib.ox.ac.uk/education/graduate-training-course/program/mri-physics/mri-physics-course
- http://psychology.uwo.ca/fmri4newbies/Tutorials.html
- … (stay updated)

The most fundamental goal in neuroscience

Understand relationship between
AND

Operations of the Mind — Brain neurophysiology

Attention

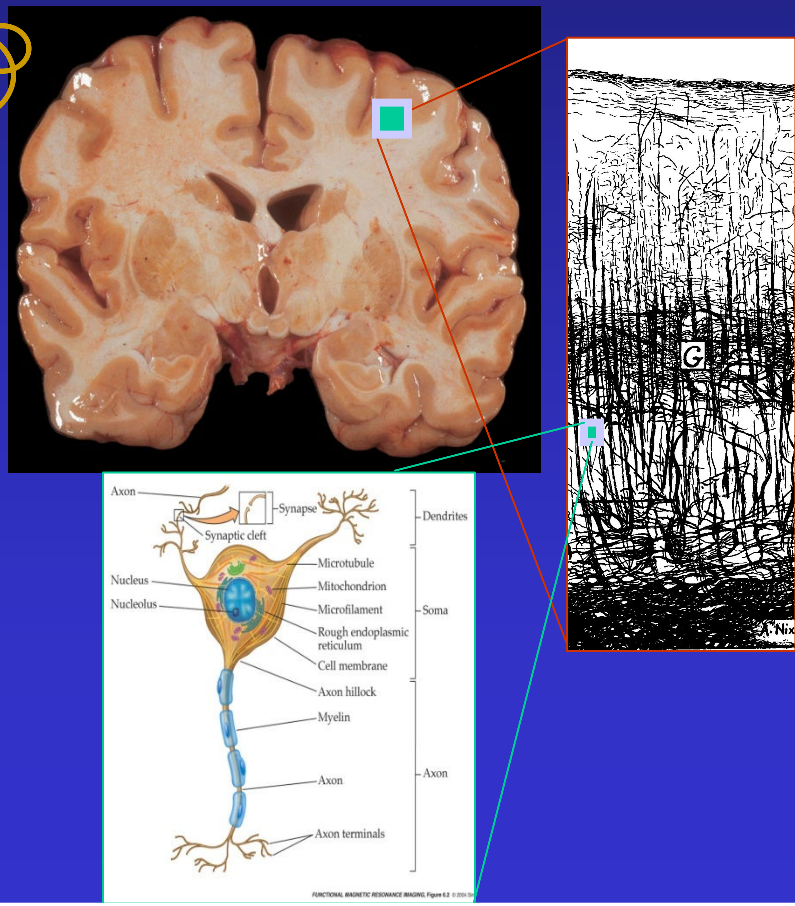
Language

Memory

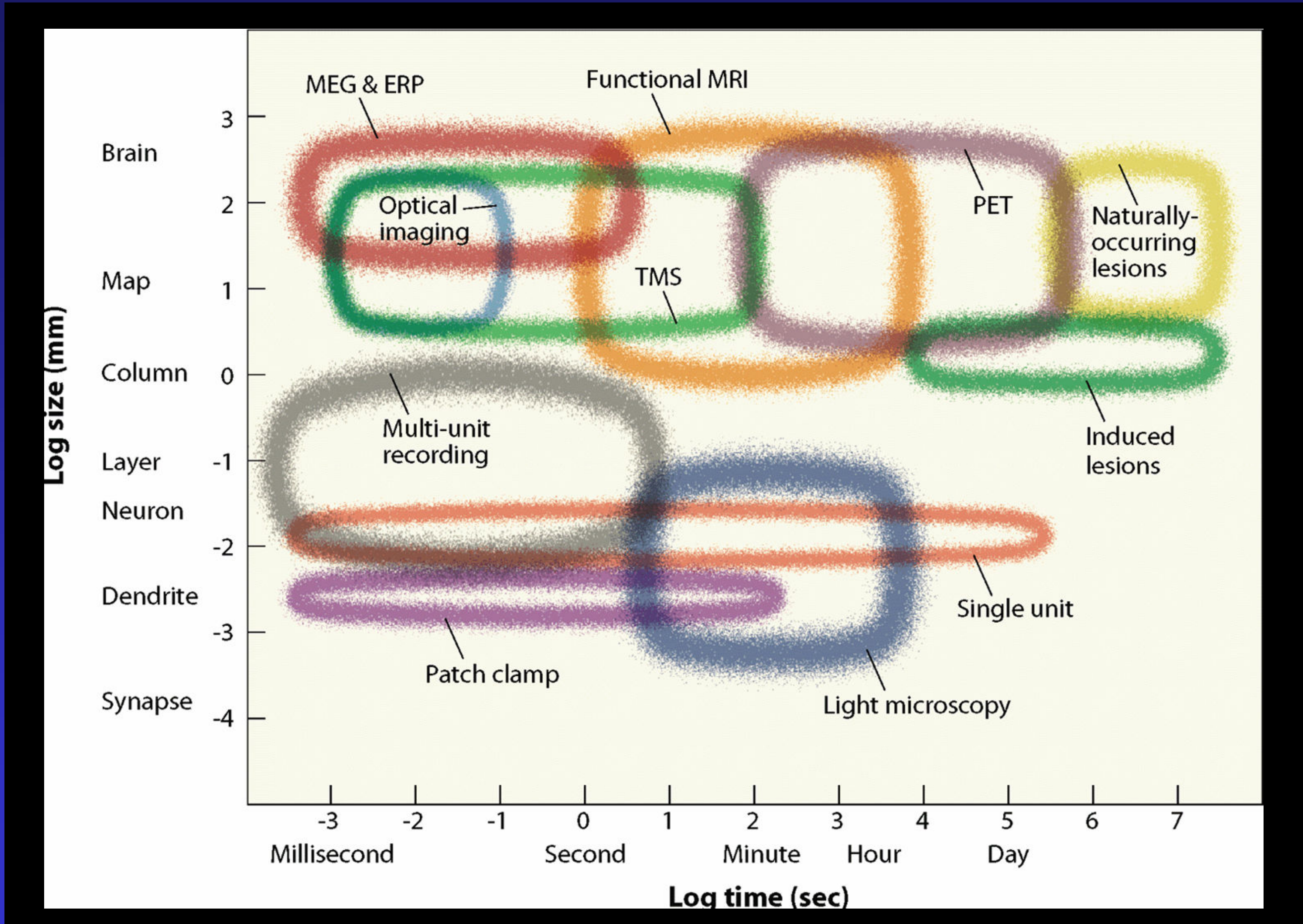
Emotions

Etc.

Senses and their integration



There are many tools to choose from

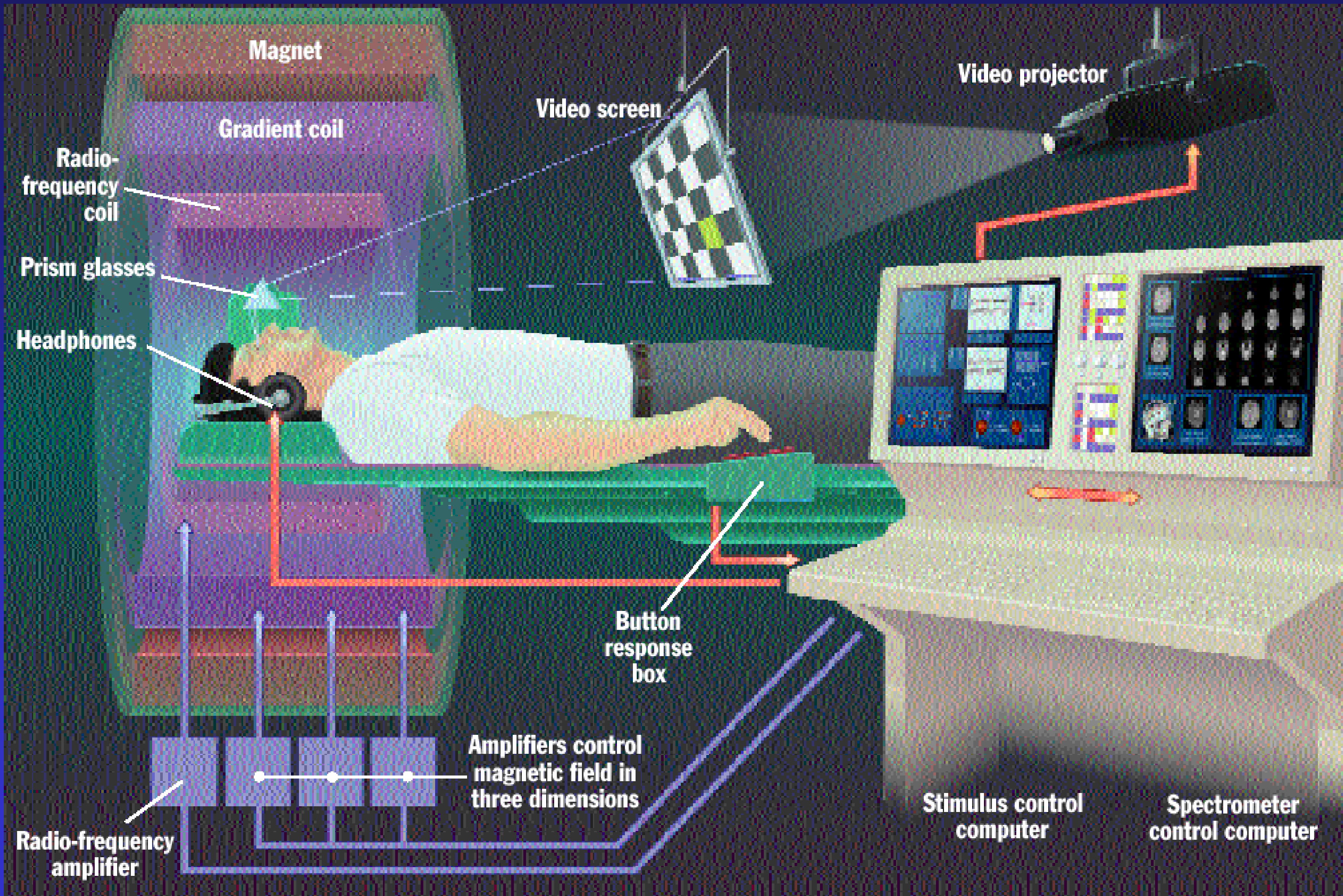


Graph from: Gazzaniga, Ivry & Mangun, *Cognitive Neuroscience*
Slide borrowed from Jody Culham.

First question worth considering

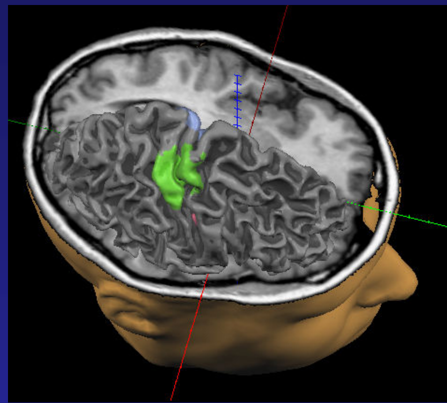
Are my research hypotheses consitent with
the tool used to test them?

Functional MRI setup

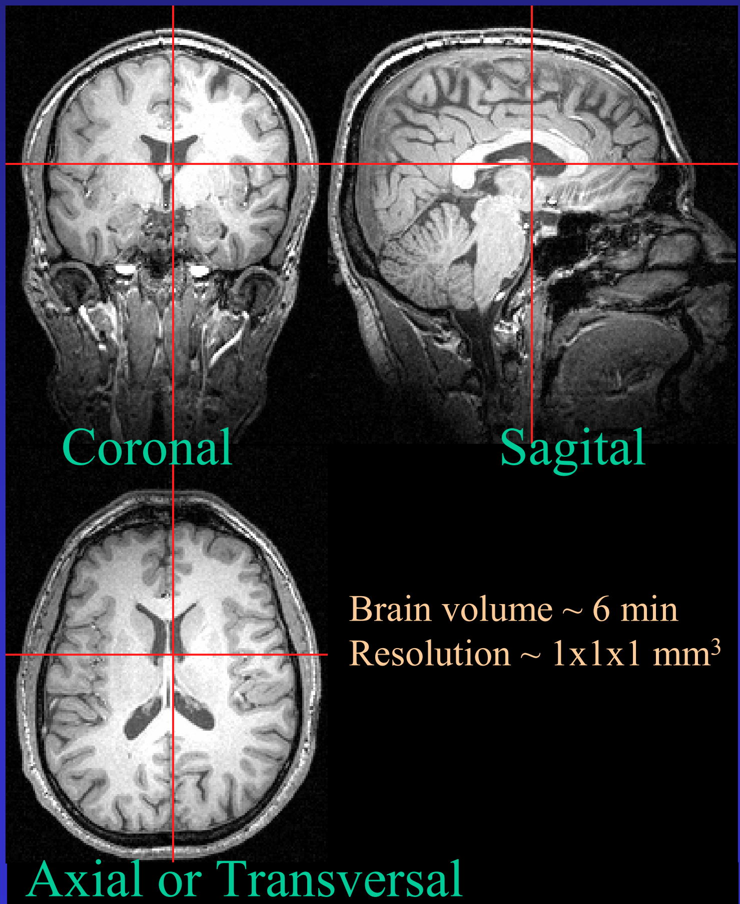


Source: Jody Culham's fMRI for Newbies web site

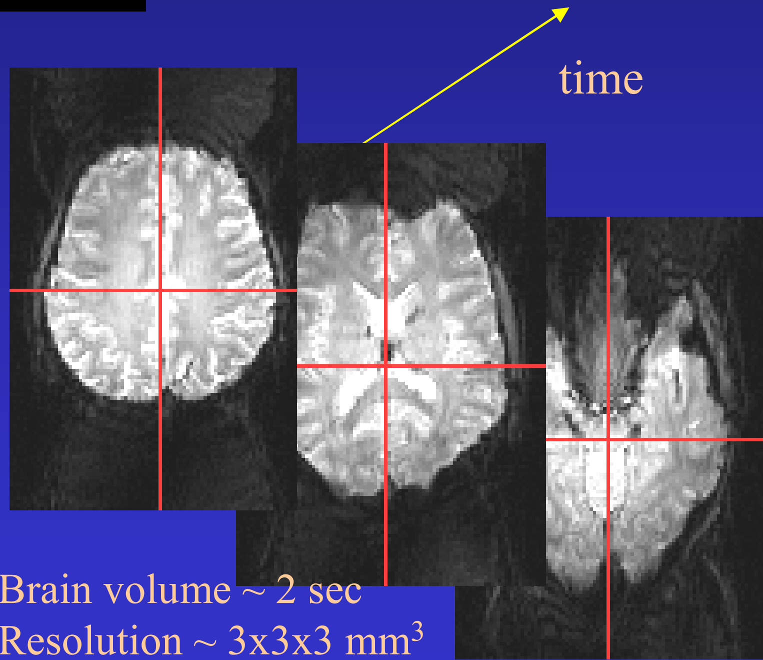
Which MR images are we mostly interested in?



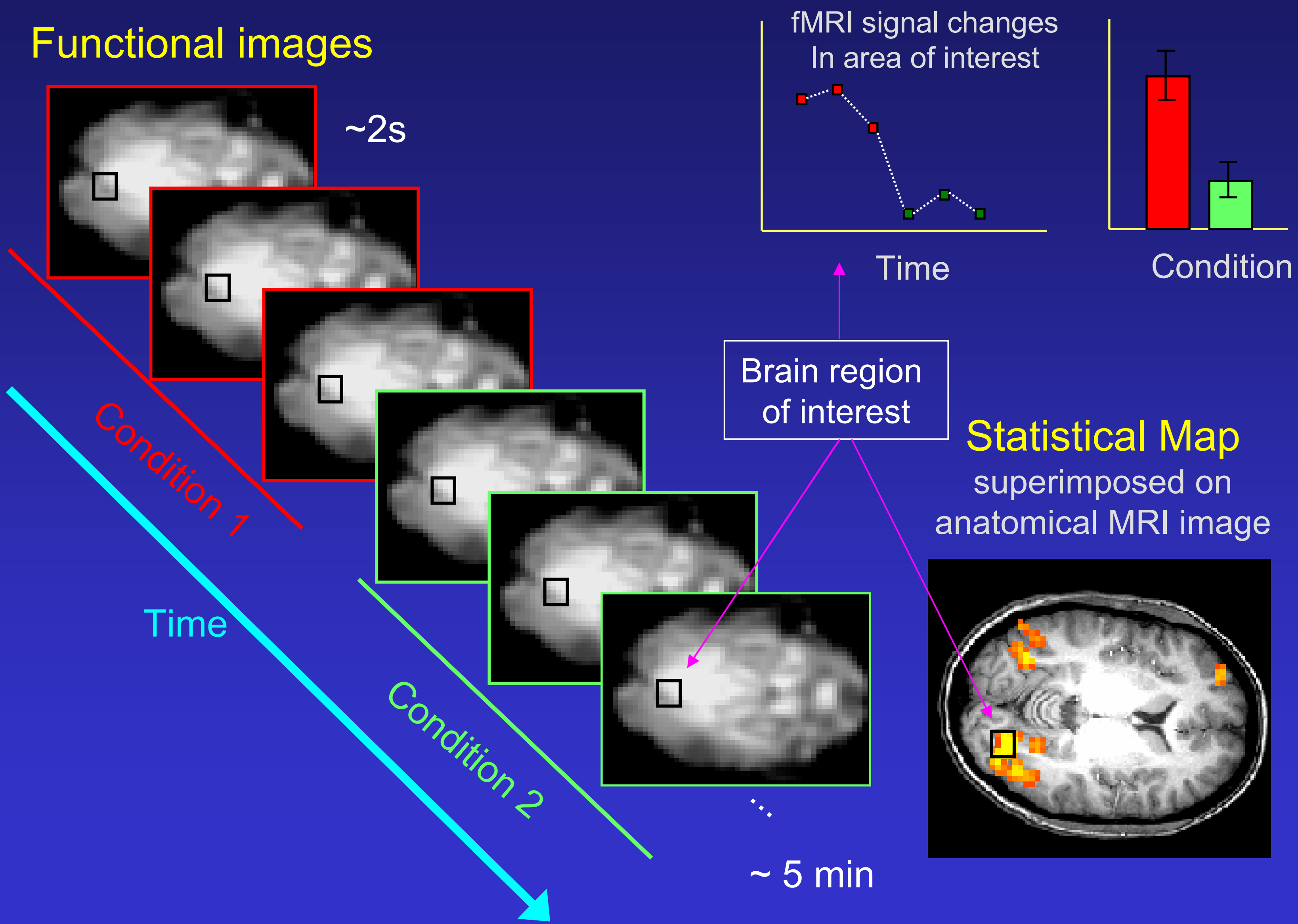
Structural Images



Functional Images



Functional MRI Activation Statistics



Source: Modified from Jody Culham's fMRI Newbies web site

fMRI Experiment Overview

Can some knowledge of physics help me?

- Hypothesis definition & experimental design
- Subject recruitment
- Data Acquisition
- Data Analyses and Interpretation

fMRI Experiment Overview

Can some knowledge of physics help me?

- **Hypothesis definition and experimental design**
  - o Critical literature review: data acquisition and analysis
  - o Definition of your own MR imaging parameters
  - o Plan data acquisition: special needs that might be non-standard?

- **Subject recruitment**
  - o MR Safety issues
  - o Physiological issues (medication that affects blood flow?)

- **Data Acquisition**
  - o Structural scans: basic quality assurance
  - o Functional scans: basic quality assurance

- **Data Analyses and Interpretation**
  - o Structural analyses: should I trust what I get?
  - o Functional analyses: should I trust what I get?

Physics of MR Image Acquisition

- NMR signal & relaxation
- NMR image
- MRI contrast
- MRI safety

So… how do we get the NMR signal?

1) Put subject in a strong static magnetic field (e.g., 4T)

    This creates an equilibrium magnetization

2) Transmit radio waves into subject [2~10 ms, mT]

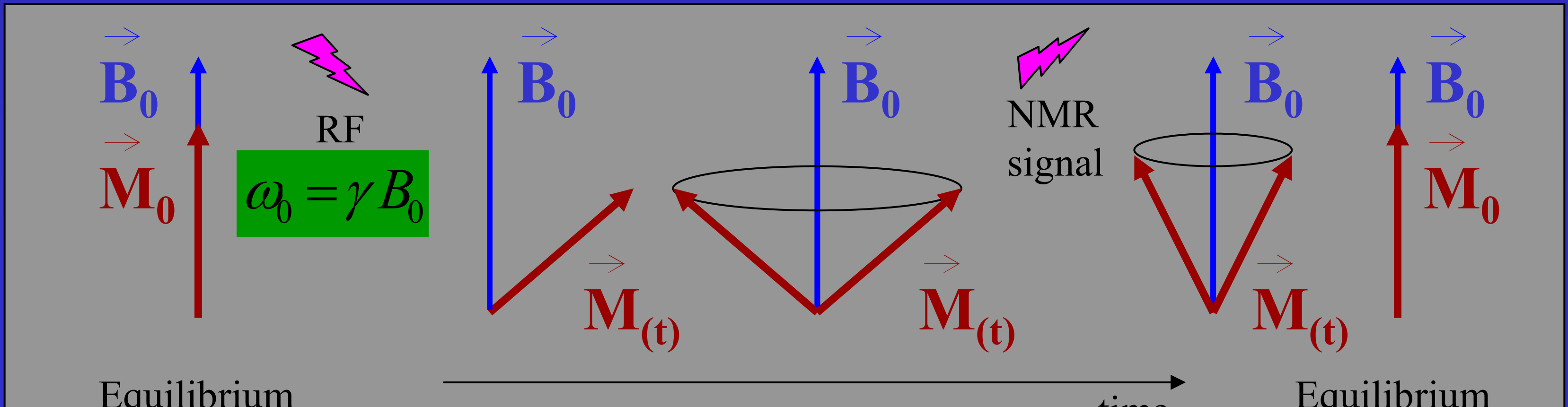
    This excites the magnetization away from equilibrium

3) Turn off radio wave transmitter

4) Receive radio waves re-transmitted by subject

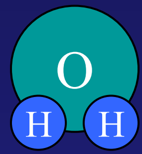
    The magnetization relaxes

5) Convert measured RF data to image (many repetitions)



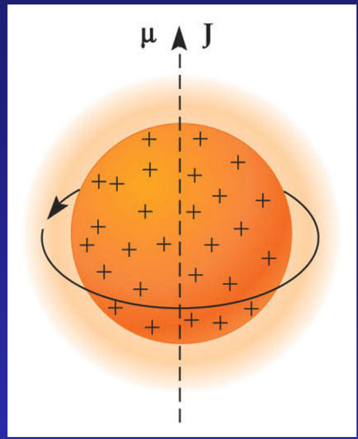
Jorge Jovicich, February 2011

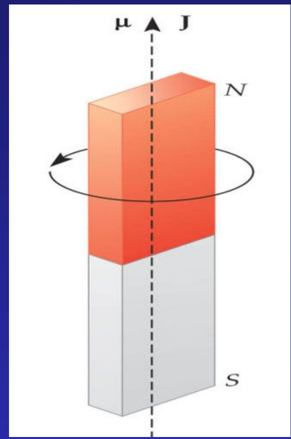
Lets review properties of our sample



Most abundant molecule: water

Sample
(biologic tissue)



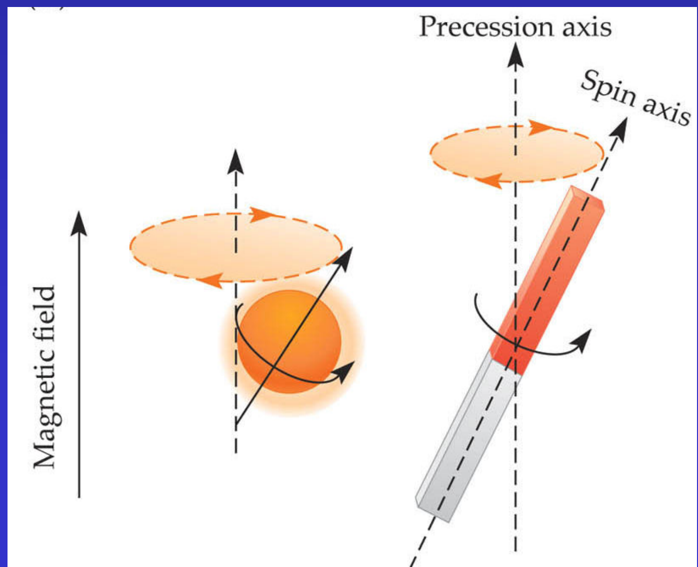


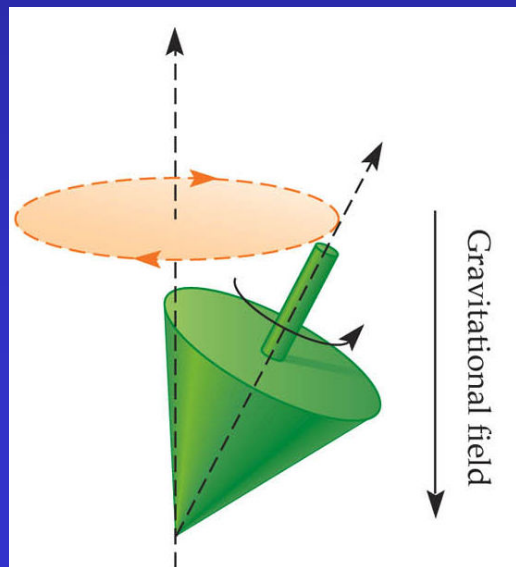
Hydrogen nucleus (proton):

- electric charge
- spin (angular momentum)
- magnetic moment: **μ**
- **μ** precession about local magnetic field

$$\omega = \gamma B$$

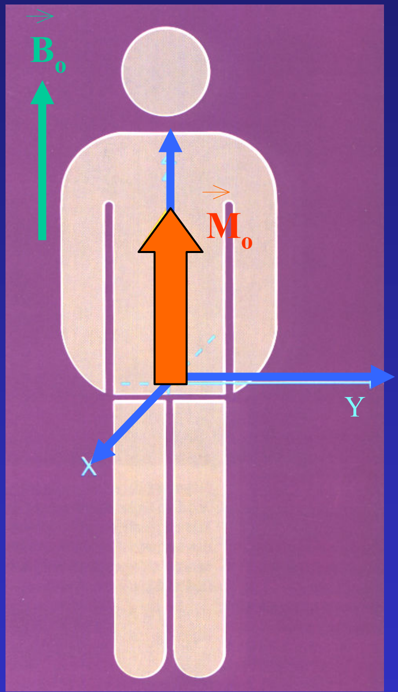
ω: Larmor frequency
γ: giromagnetic ratio (42.58 MHz/T)
B: local magnetic field





The magnetization always wants to precess about the net magnetic field

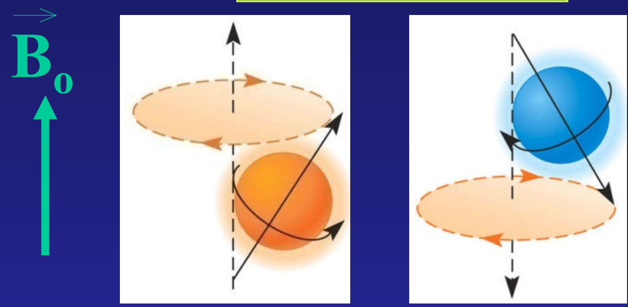
Our sample goes into the magnet...



$\vec{B}_0$: uniform static magnetic field

$\vec{M}_0$: static macroscopic magnetization

One proton



Low energy (E_0, preferred) High energy (E_1)

Two energetic states

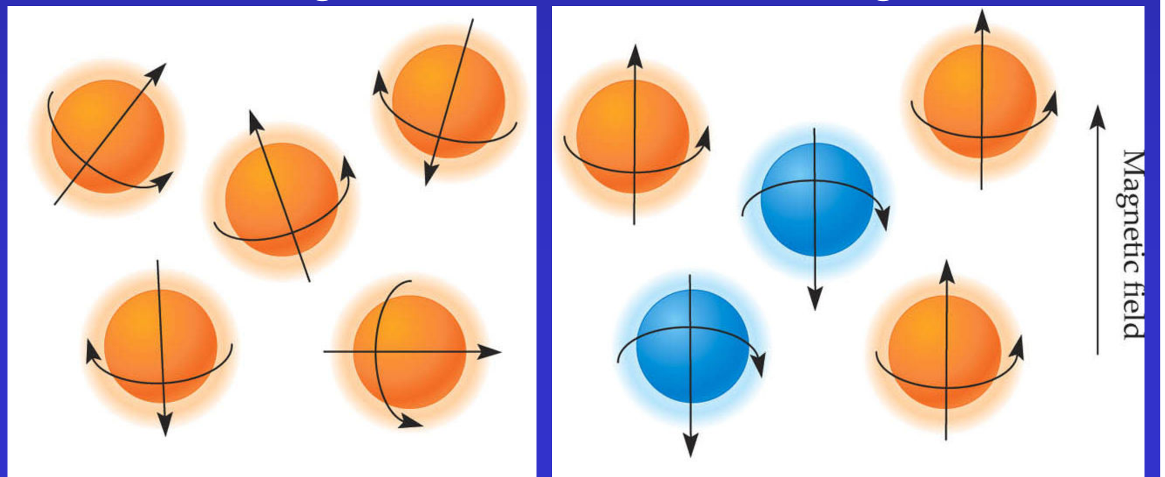
$$\Delta E = E_1 - E_0$$

$$\Delta E = \eta\omega_0 = \eta\gamma \mathbf{B}_0$$

$$\omega_o = \gamma B_o$$

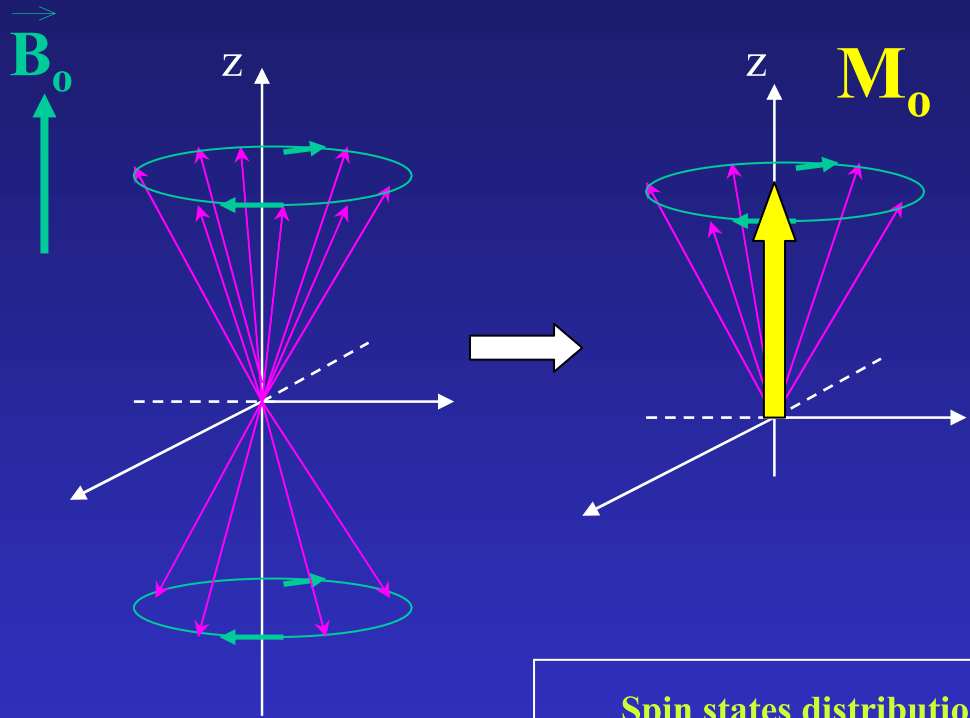
Group of protons

No external magnetic field External magnetic field

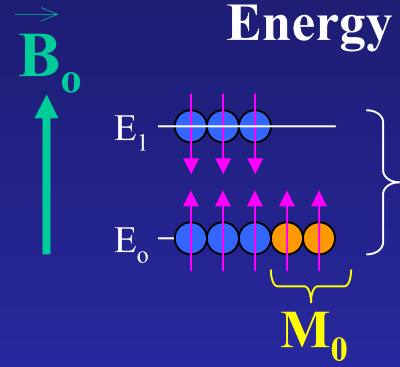


Jorge Jovicich, February 2011

Our sample goes into the magnet... (continued)



Energy states



$$\Delta E = h\,\omega_0$$

$$\omega_o = \gamma\, B_o$$

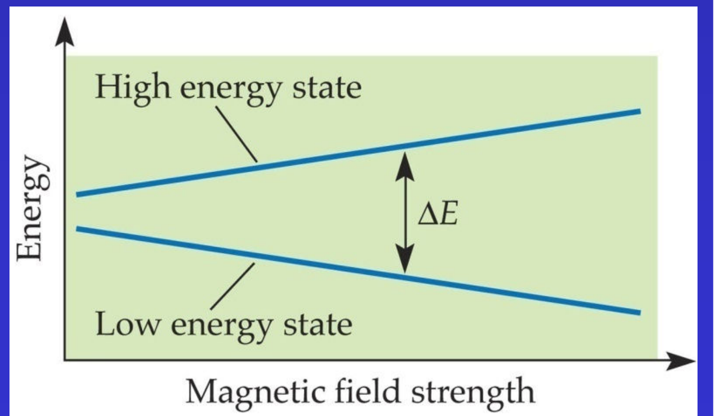
Net Equilibrium magnetization $\mathbf{M_0}$:
- M_z aligned with $\mathbf{B_0}$
- $M_{xy} = 0$

Typical B_0 for MRI:
1.5T = $3\text{x}10^4\ B_{earth}$
4T = $8\text{x}10^4\ B_{earth}$

Spin states distribution

$$\frac{N_1}{N_0} = \exp\left(-\frac{h\,\gamma B_0}{kT}\right)$$

N_1 = # of protons in state E_1
N_0 = # of protons in state E_0
k : Boltzmann's constant
T : temperature



Jorge Jovicich, February 2011

Summary so far:

- *By placing* the sample in the external field we generated a static, longitudinal equilibrium magnetization (M_o)
- We know the precession frequency of each proton ($\omega_o = \gamma B_o$)

- Problem: the magnetization must be moving for detection
- Solution: excitation out of equilibrium so it oscillates

- How? 1) Tilt the magnet or compass suddenly

  2) Drive the magnetization (compass needle) with a periodic magnetic field (ω_o)

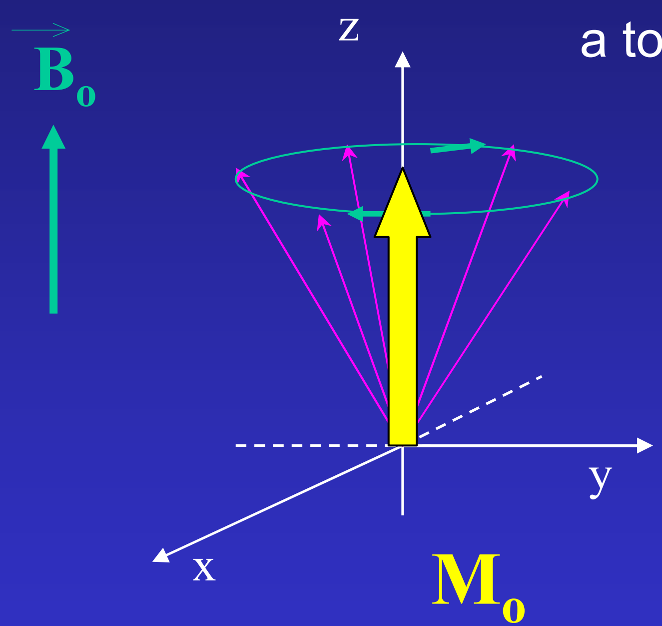
Why magnetic ‘resonance’?

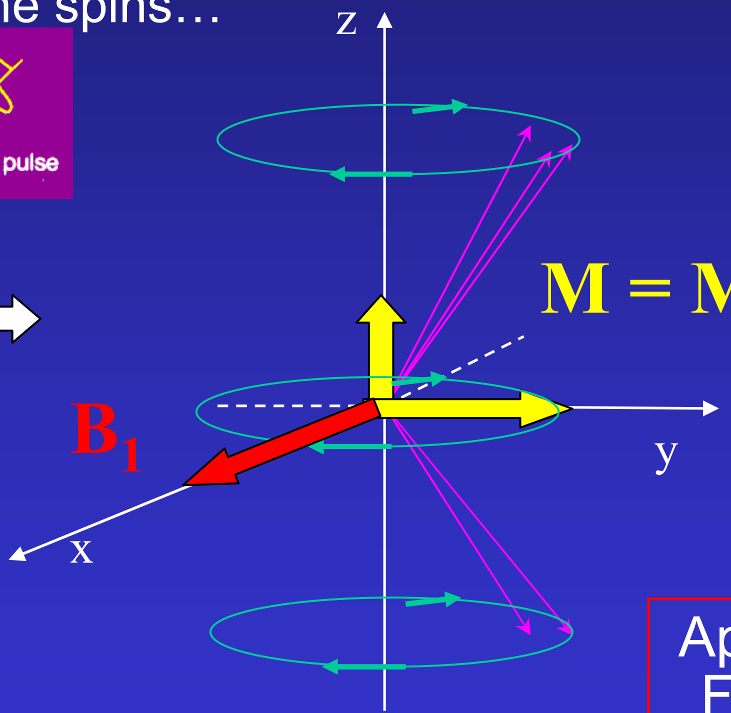
Our sample will absorb energy (i.e., we can play with the magnetization) only if we transmit energy at the Larmor frequency

Excitation of the magnetization: use magnetic resonance

EQUILIBRIUM → **EXCITATION** → **AFTER EXCITATION**

RF Field (B_1) applies a torque to the spins…





$\omega_o = \gamma B_o$

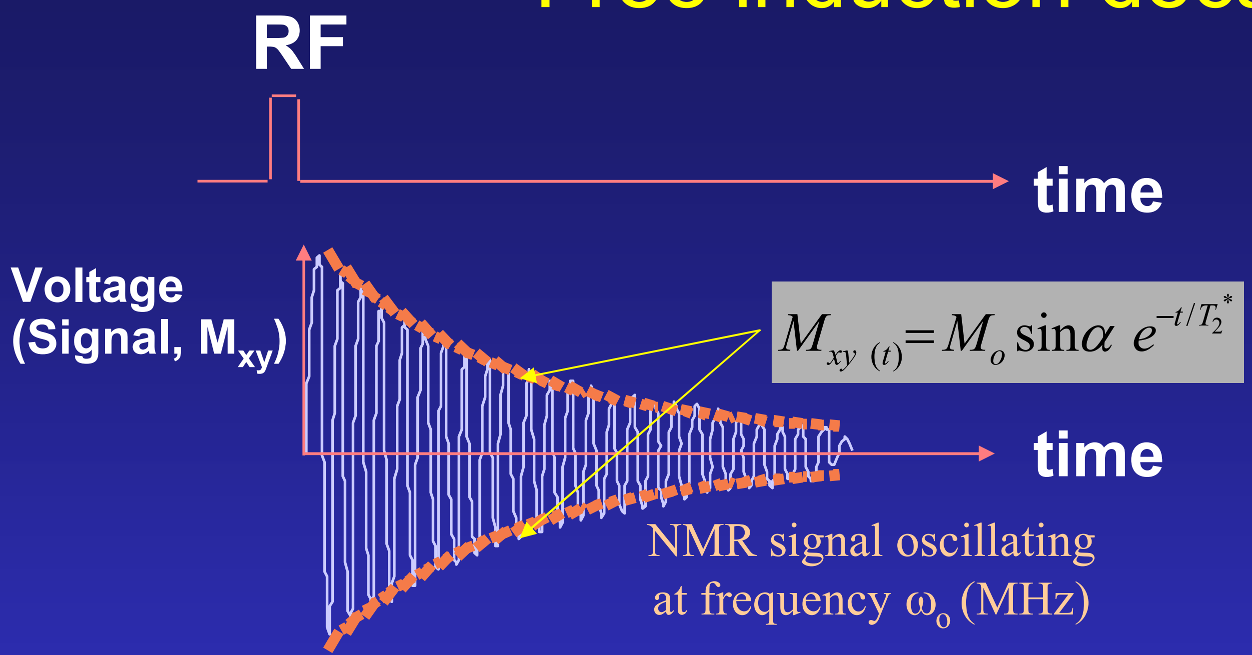
Applied RF Field (B_1)

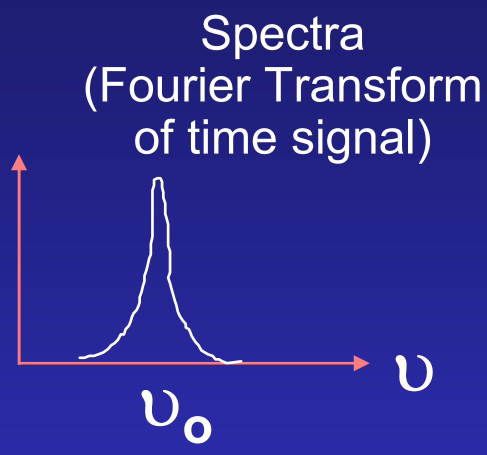
M_z: z is "longitudinal" direction
M_{xy}: x-y is "transverse" plane

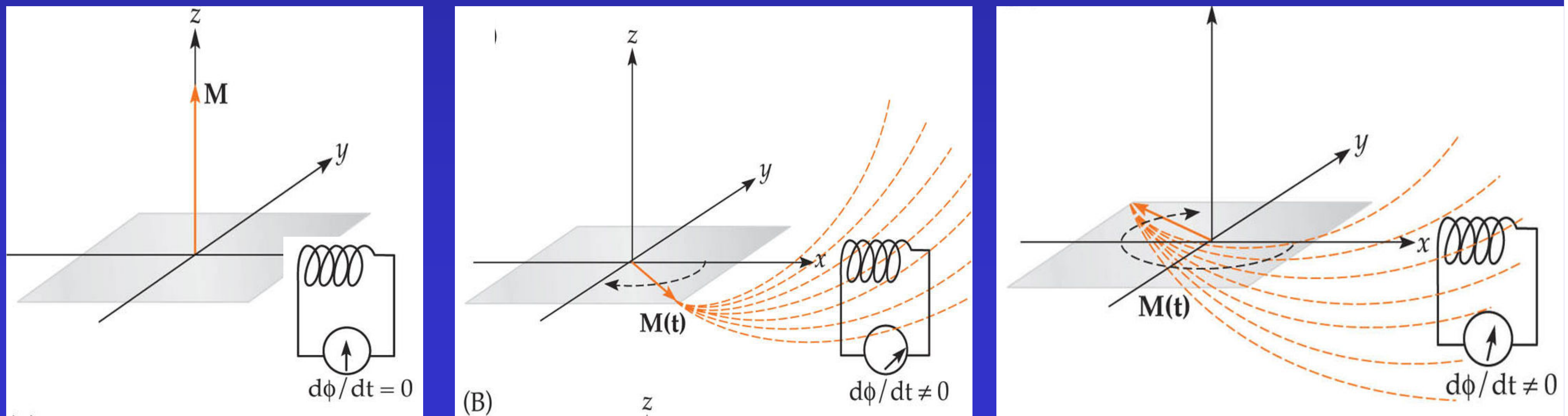
The RF pulse B_1 rotates M_0 about the B_1 field

Jorge Jovicich, February 2011

The NMR Signal:
Free induction decay



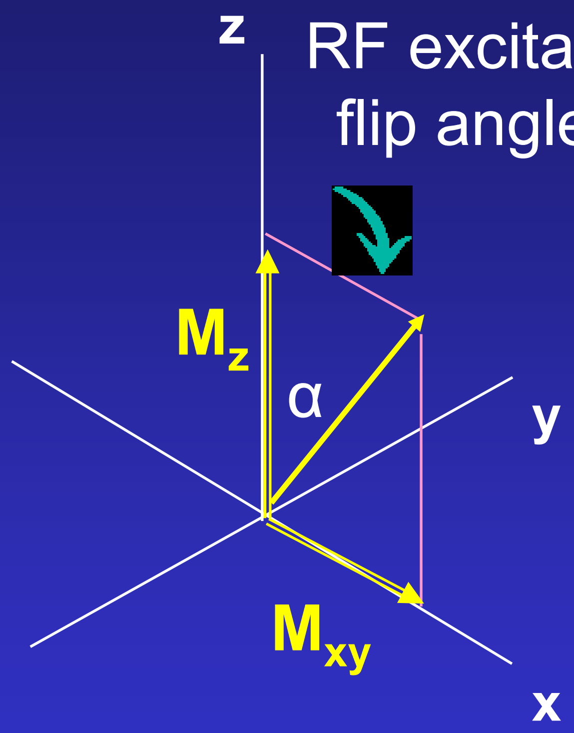


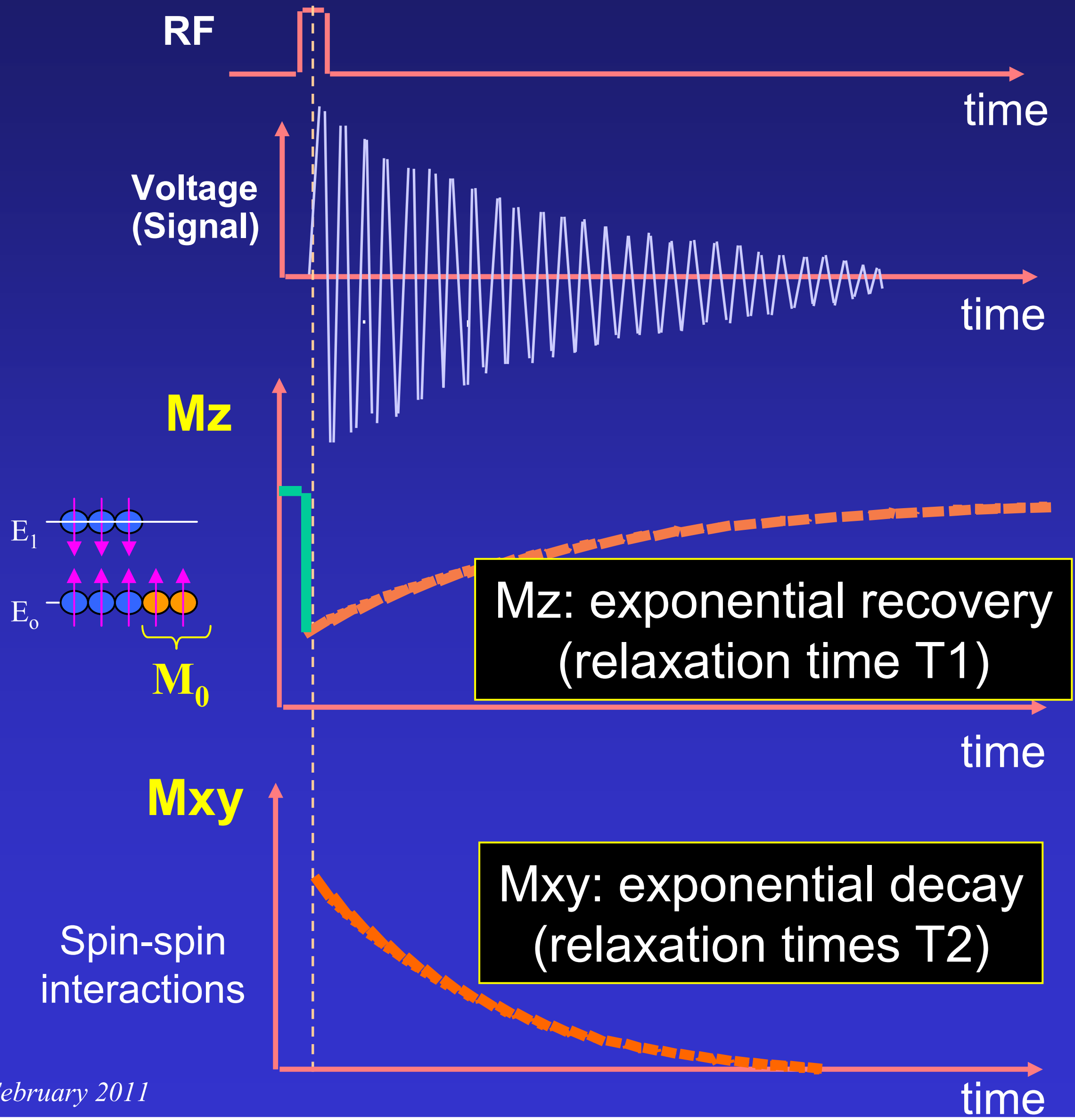


$$\omega_o = \gamma B_o$$

Jorge Jovicich, February 2011

Relaxation of magnetization to equilibrium





$M_z = M \cos(\alpha)$

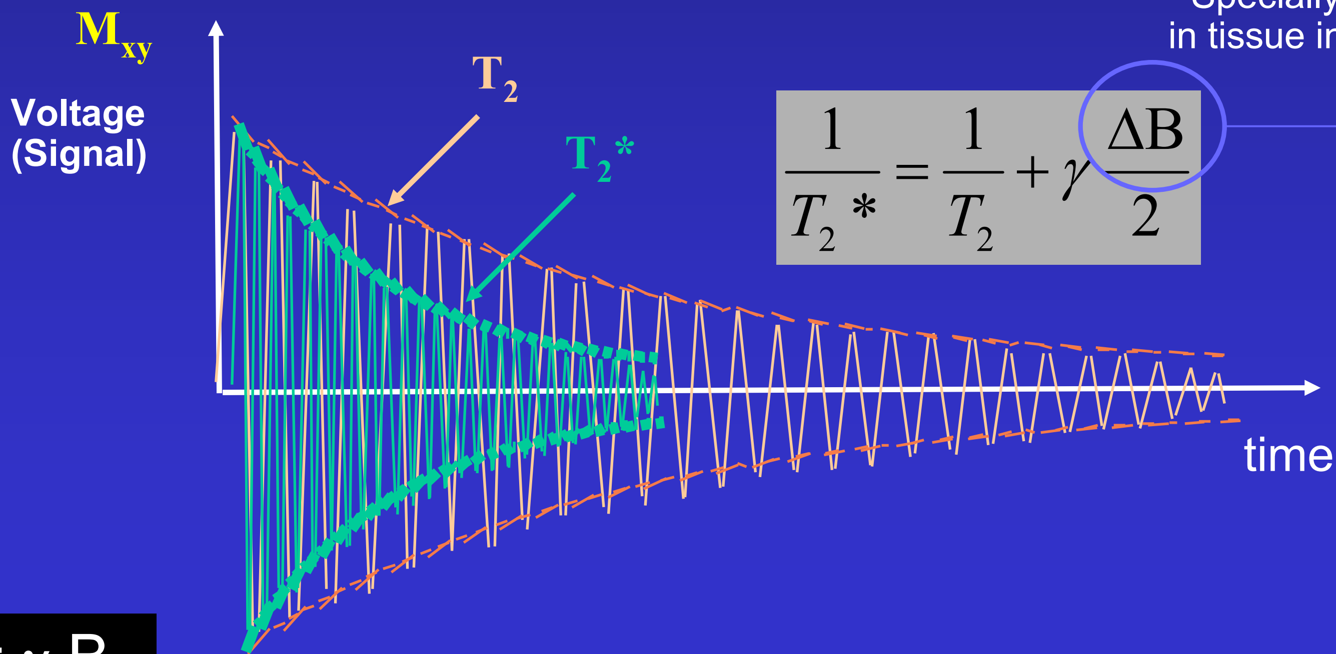
$M_{xy} = M \sin(\alpha)$

$\omega_o = \gamma B_o$

Jorge Jovicich, February 2011

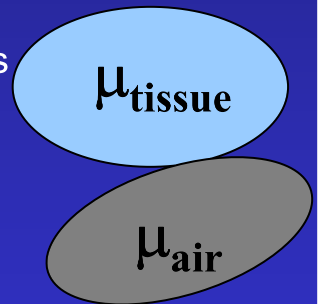
An imperfect world: T_2^* decay

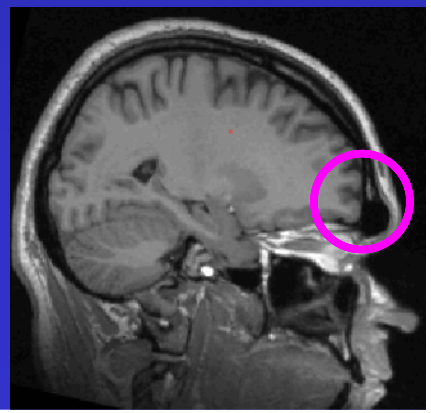
- Real signal decays faster than T_2 predictions
- Pure T_2: random spin-spin interactions with perfect homogeneous external B0
- In reality: Field is inhomogeneous ($B_{real} = B_0 + \Delta B$)
- Signal decay due to random and fixed dephasing effects: T_2^*



$$\frac{1}{T_2^*} = \frac{1}{T_2} + \gamma \frac{\Delta B}{2}$$

Specially strong in tissue interfaces



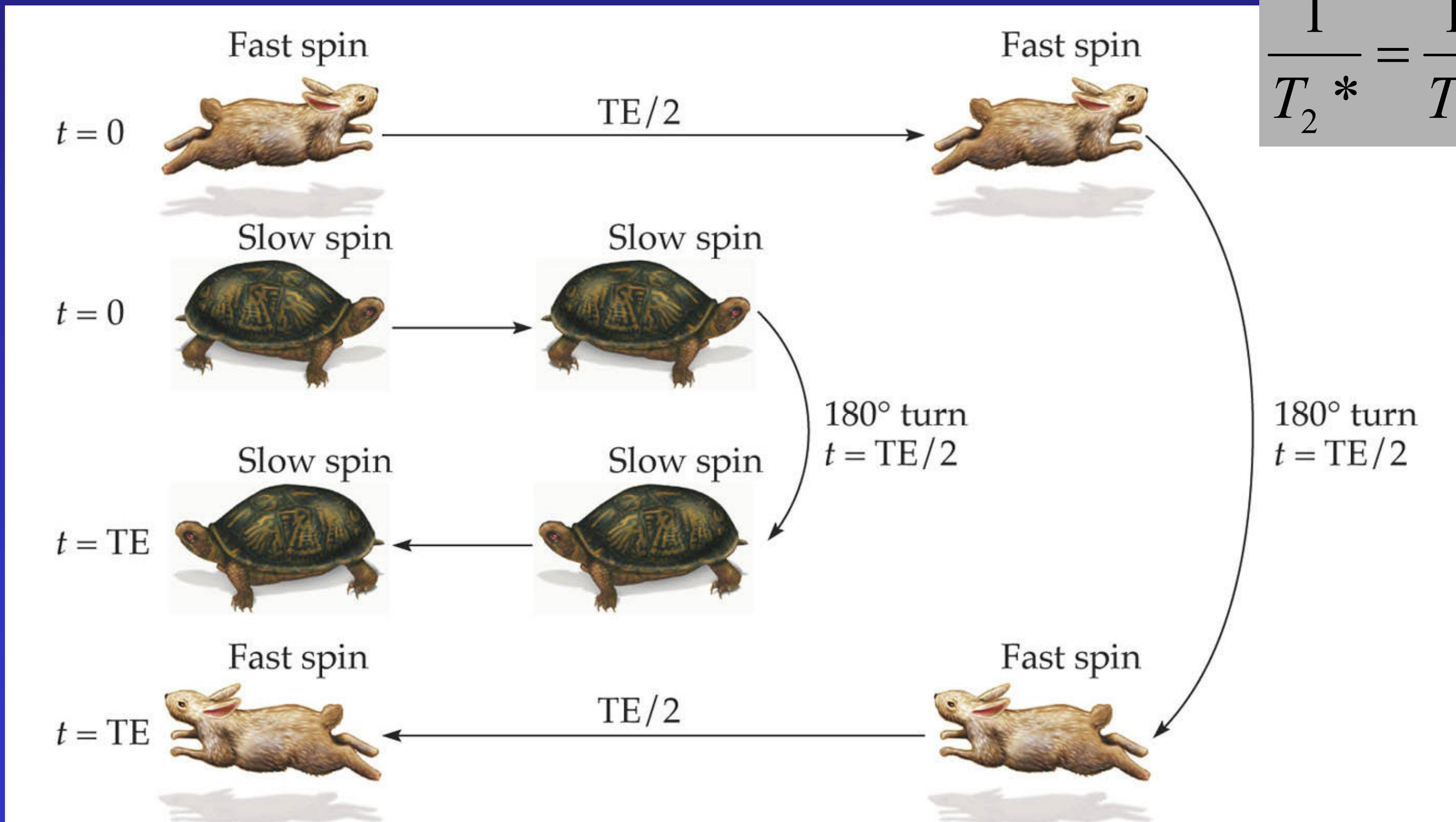


$\omega_o = \gamma B_o$

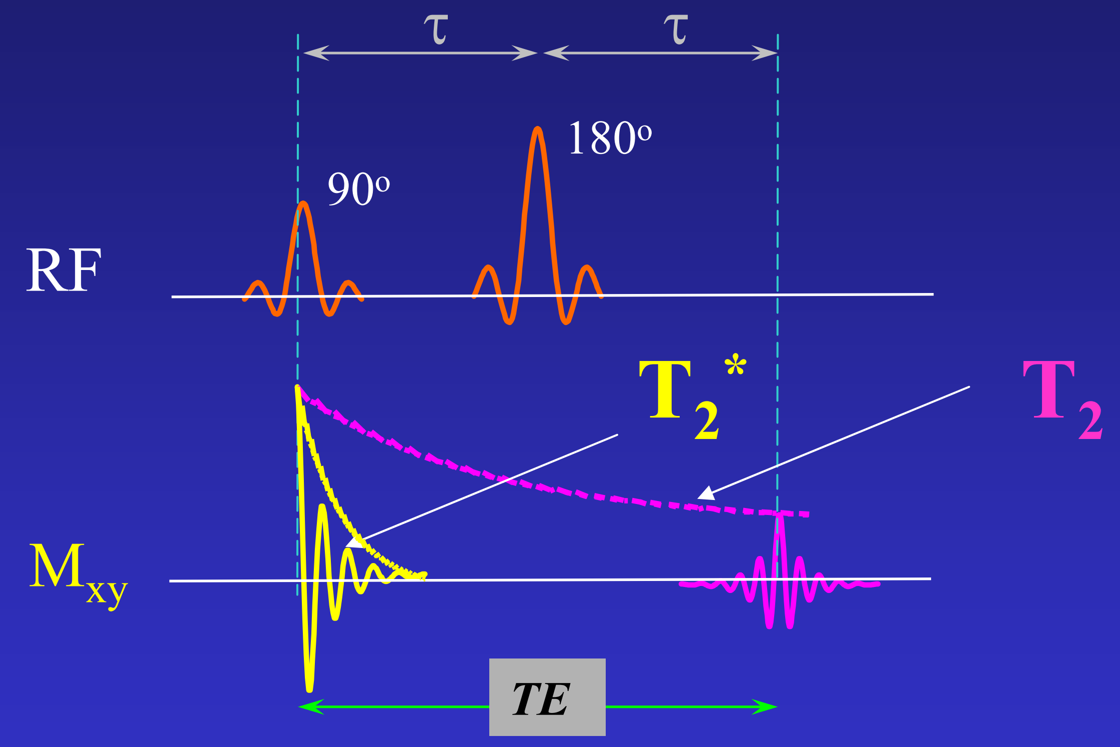
Can we do something about T_2^* signal loss ?

- Dephasing from random motions cannot be recovered
- Dephasing from locally static ΔB can be recovered: spin-echo

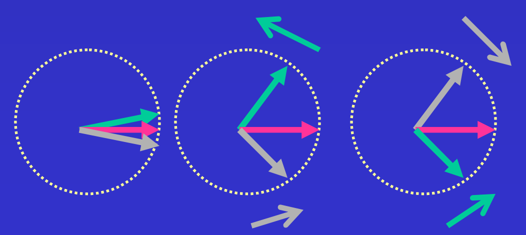
$$\frac{1}{T_2^*} = \frac{1}{T_2} + \gamma \frac{\Delta B}{2}$$



Spin-Echo: recovery of T_2 signal

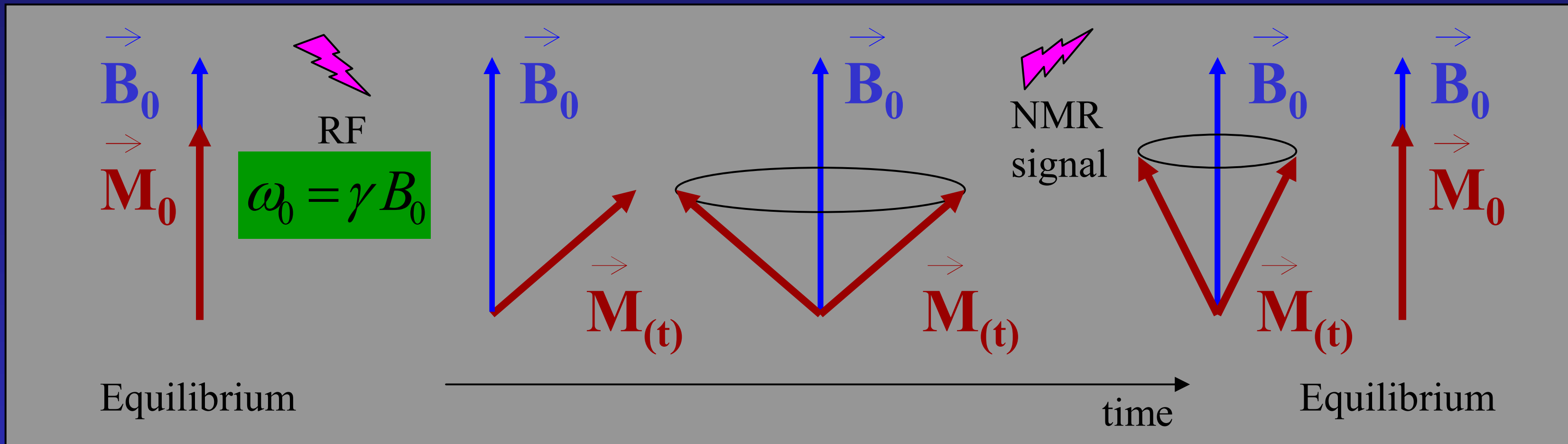


Signal dephasing
in xy plane



Dynamics of the Magnetization

• Geometrical description: damped precession



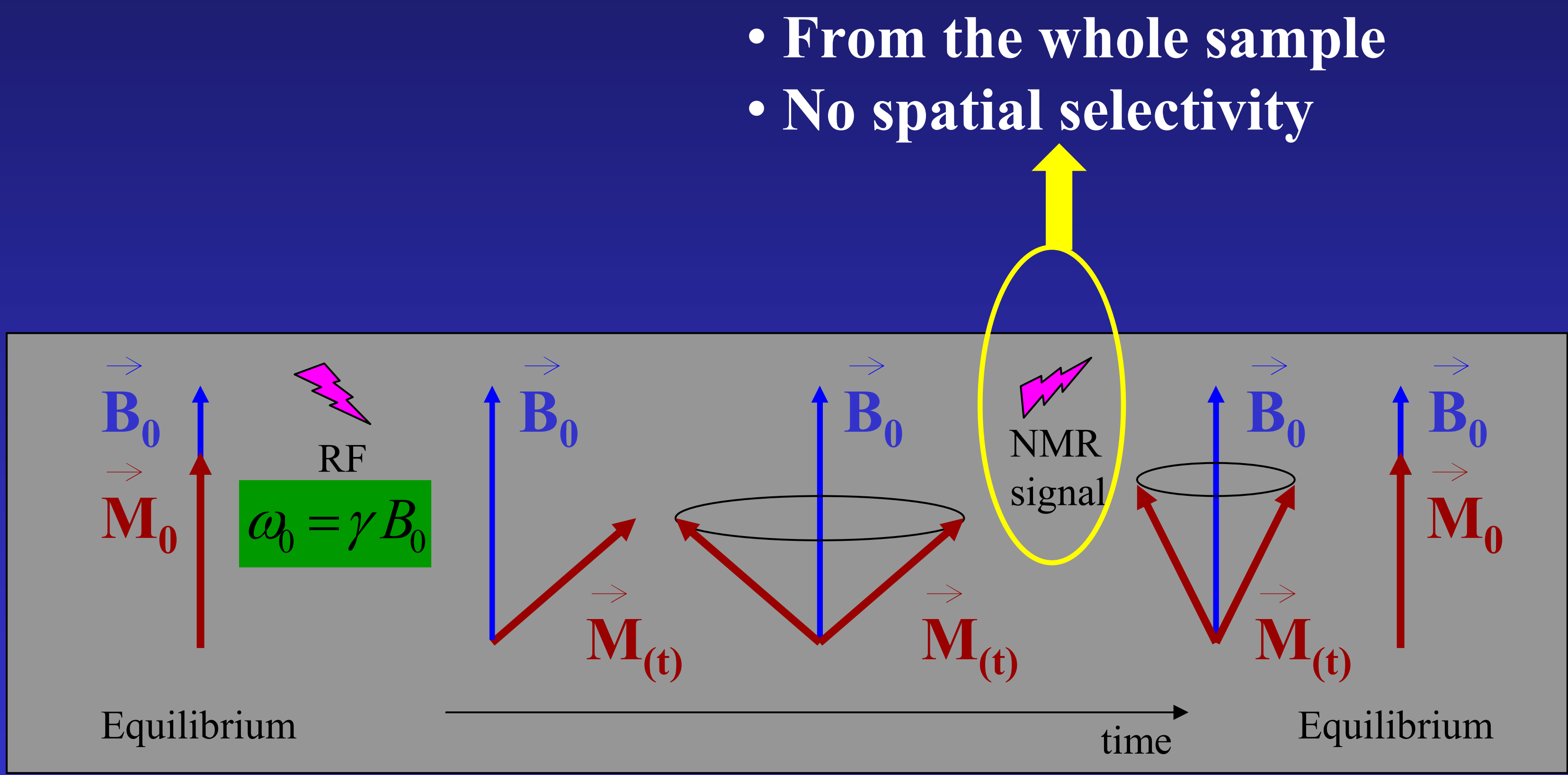
• Mathematical Description: precession + relaxation (Bloch equations)

$$\frac{d\vec{M}_{(t)}}{dt} = \vec{M}_{(t)} \times \gamma \vec{B}_{ext(t)} - \frac{(M_x \hat{i} + M_y \hat{j})}{T_2^*} - \frac{(M_z - M_0)}{T_1} \hat{k}$$

Physics of MR Image Acquisition

- NMR signal & relaxation √
- NMR image
- MRI contrast
- MRI safety

Summary so far:



How can we put spatial information in the signal?

Spatial encoding concepts

$$\omega_{(x)} = \omega_0 + \gamma G_x x$$

<u>linear magnetic field gradient</u>

I know these

Then:

If I can <u>measure</u> this → I can <u>calculate</u> this

Spatial encoding concepts

- **Key points so far**:
  - Magnetic field gradients encode spatial information in the frequency of the NMR signal: $\omega_{(x)} = \omega_0 + \gamma\, G_x\, x$
  - So: the **spatial information** is in the **signal frequency**
  - But: the NMR signal measured is a signal that changes in time.
  - So: To get spatial information we need to transform temporal information into frequency information

We need a Fourier Transform 'massage'

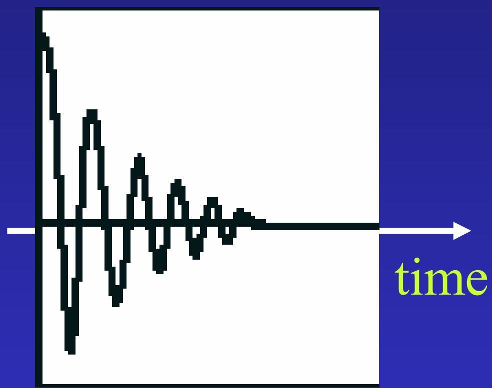
to transform the measured signal (time)

into an image (signal of frequency)

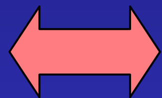
Spatial encoding concept

What is the Fourier Transform of a signal?

Signal Intensity as function of time

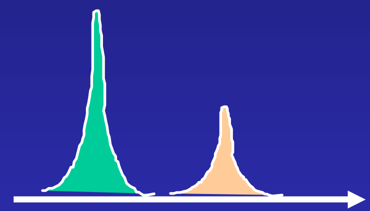


Fourier Transform



Equivalent descriptions!

Signal Intensity as function of frequency



Joseph Fourier (1768-1830)

Signal as function of time

$$s_{(t)} = \frac{1}{2\pi} \int_{-\infty}^{+\infty} S_{(w)} e^{i\omega t} \mathrm{d}\omega$$

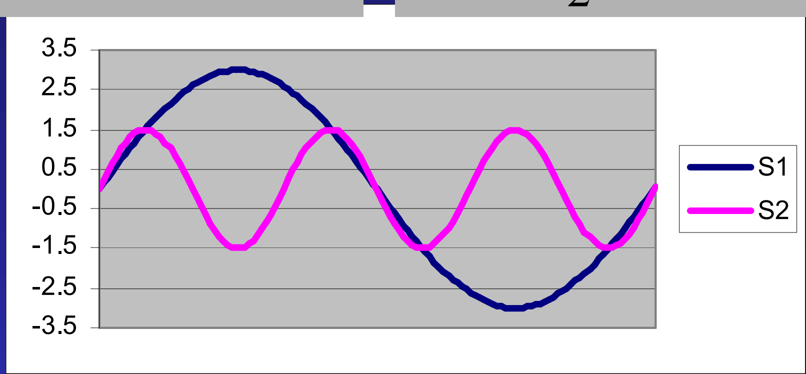
Signal as function of frequency

$$S_{(\omega)} = \int_{-\infty}^{+\infty} s_{(t)} e^{-i\omega t} \mathrm{d}t$$

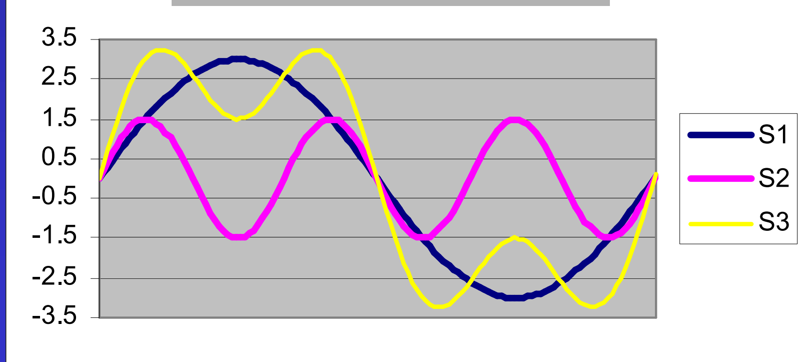
Fourier Transform concepts
(frequency and time signals)

$$s_{1(t)} = A\sin(w_0 t)$$

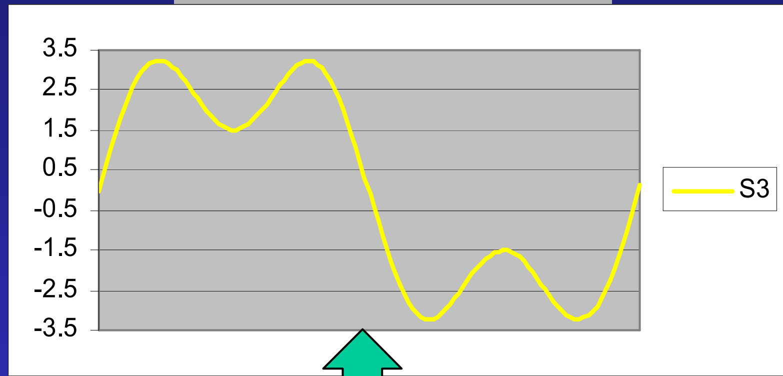
$$s_{2(t)} = \frac{A}{2}\sin(3w_0 t)$$

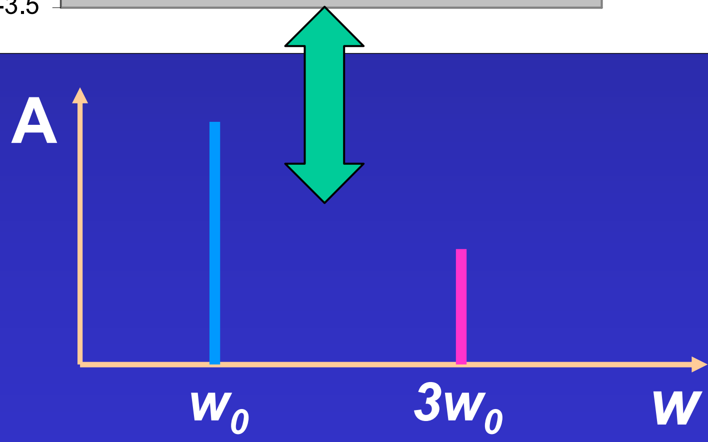


$$s_{3(t)} = s_{1(t)} + s_{2(t)}$$



$$s_{3(t)} = s_{1(t)} + s_{2(t)}$$



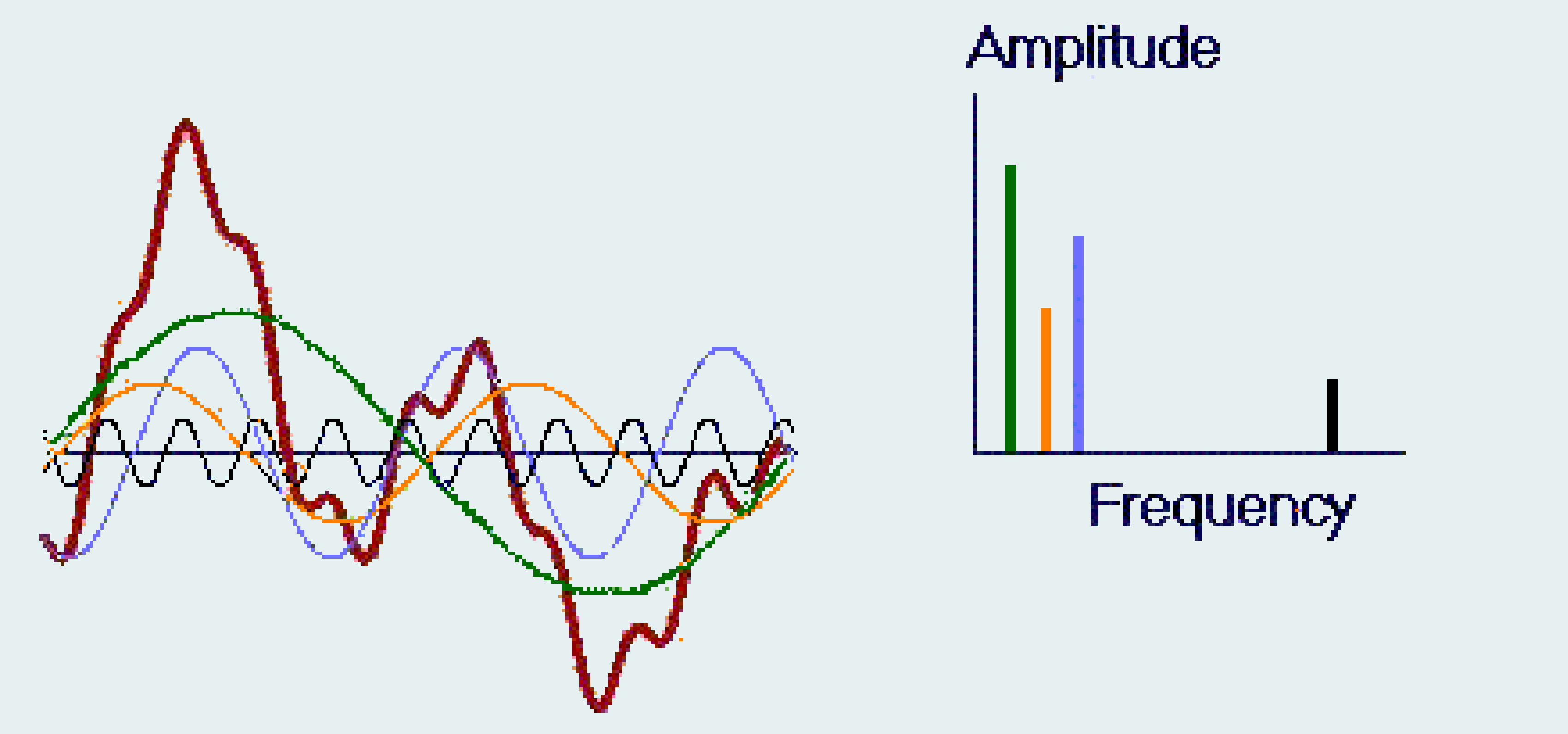


Frequency space of signal S_3

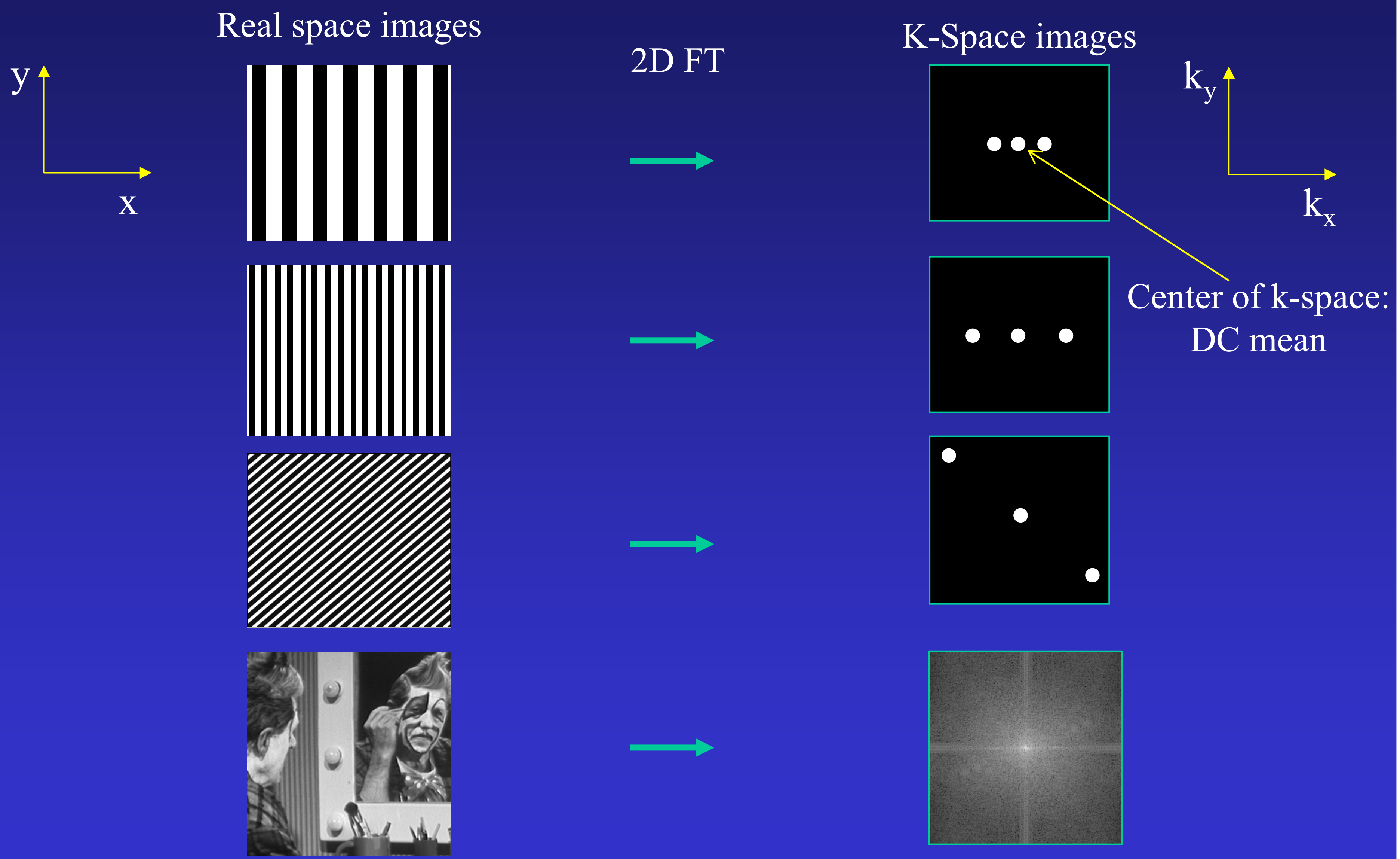
FT: strength of signal at each frequency

Jorge Jovicich, February 2011

Fourier Transform concepts
(frequency and time signals)



Fourier Transform concepts: Spatial frequency



Jorge Jovicich, February 2011

Modified from: http://homepages.inf.ed.ac.uk/rbf/HIPR2/fourier.htm

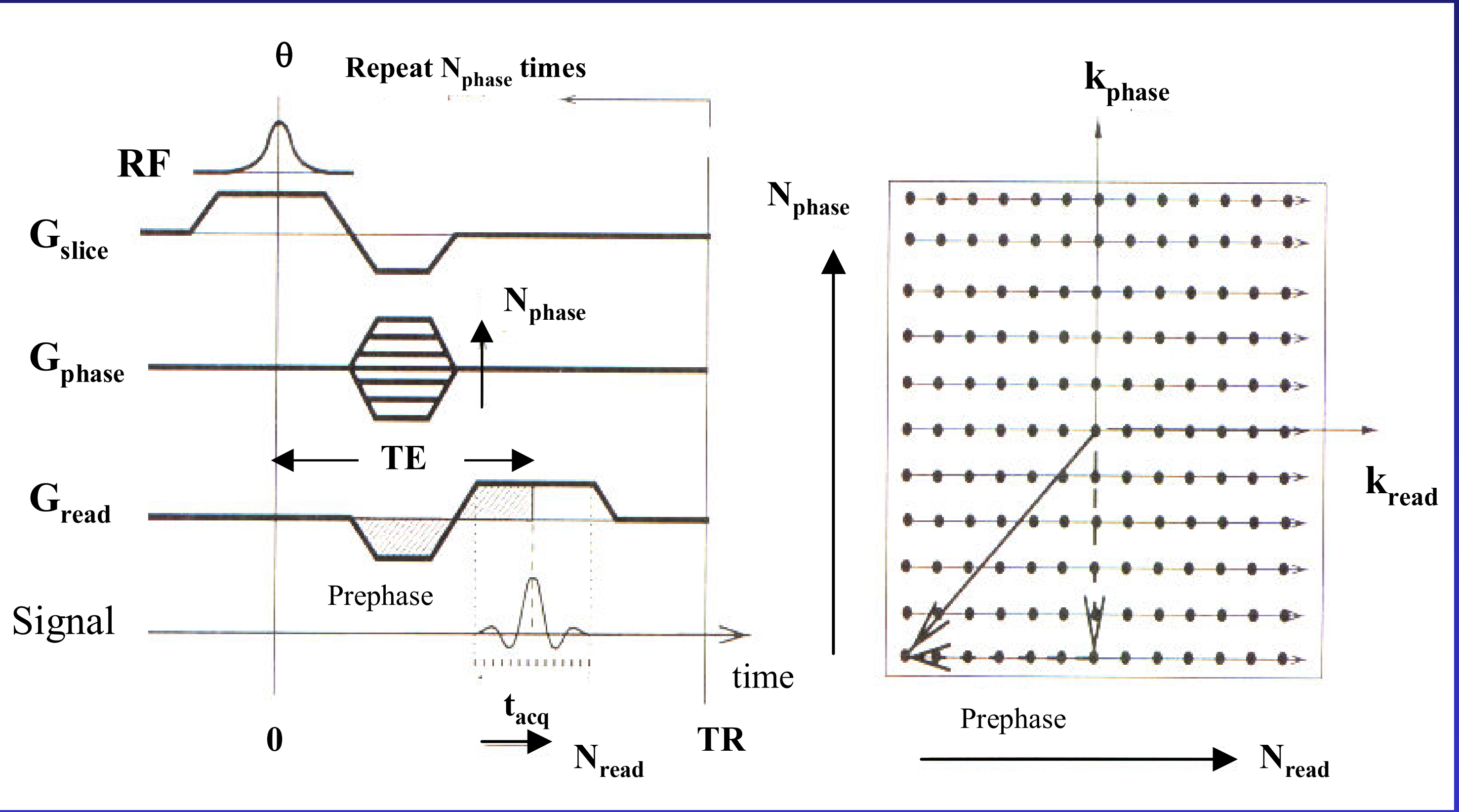
Spatial Encoding in MRI

Key concept: $\omega_{(\vec{r})} = \gamma \left(B_0 + \vec{G} . \vec{r} \right)$

Three orthogonal gradients are used

- **Slice Selection**
  - Location
  - Thickness
  - Rephasing/Refocussing
- **Frequency Encoding**
  - Fourier Transform
  - FOV
  - Gradient Echo Formation
- **Phase Encoding**
  - Phase / Frequency Equivalency
  - FOV

Conventional spin-warp 2D MRI sequence

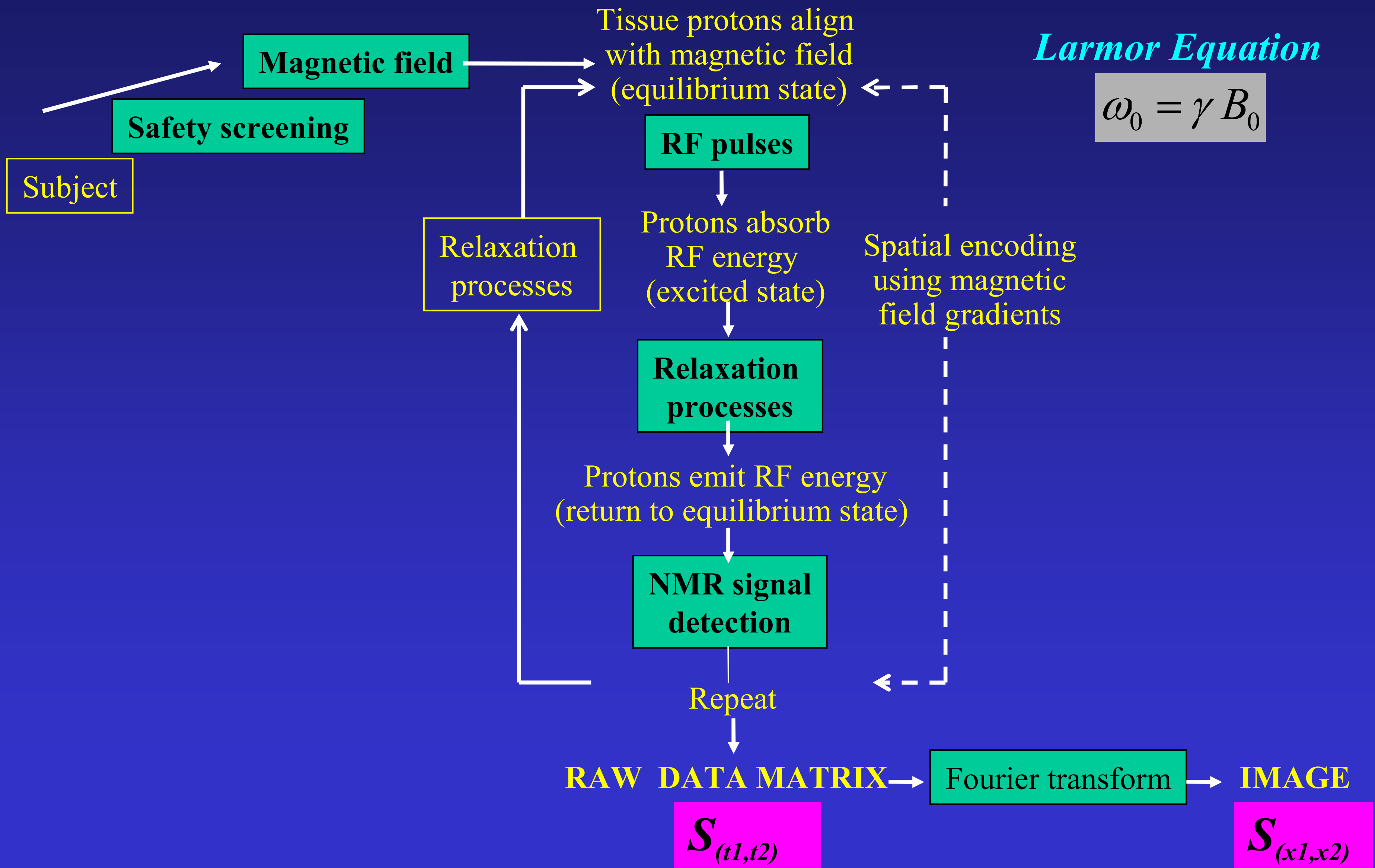


The signal we measure is in spatial frequency space (*k*-space)

$$k_{(t)} = \frac{\gamma}{2\pi}\int_0^t G_{(t')}\,dt'$$

Jorge Jovicich, February 2011

Overview of an MRI procedure



Larmor Equation

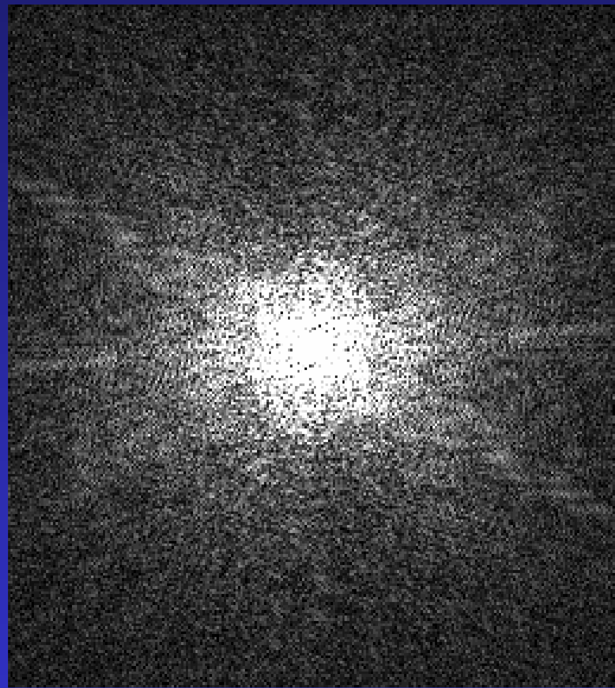
$$\omega_0 = \gamma B_0$$

Jorge Jovicich, February 2011

K-space

Reconstructed

Measured



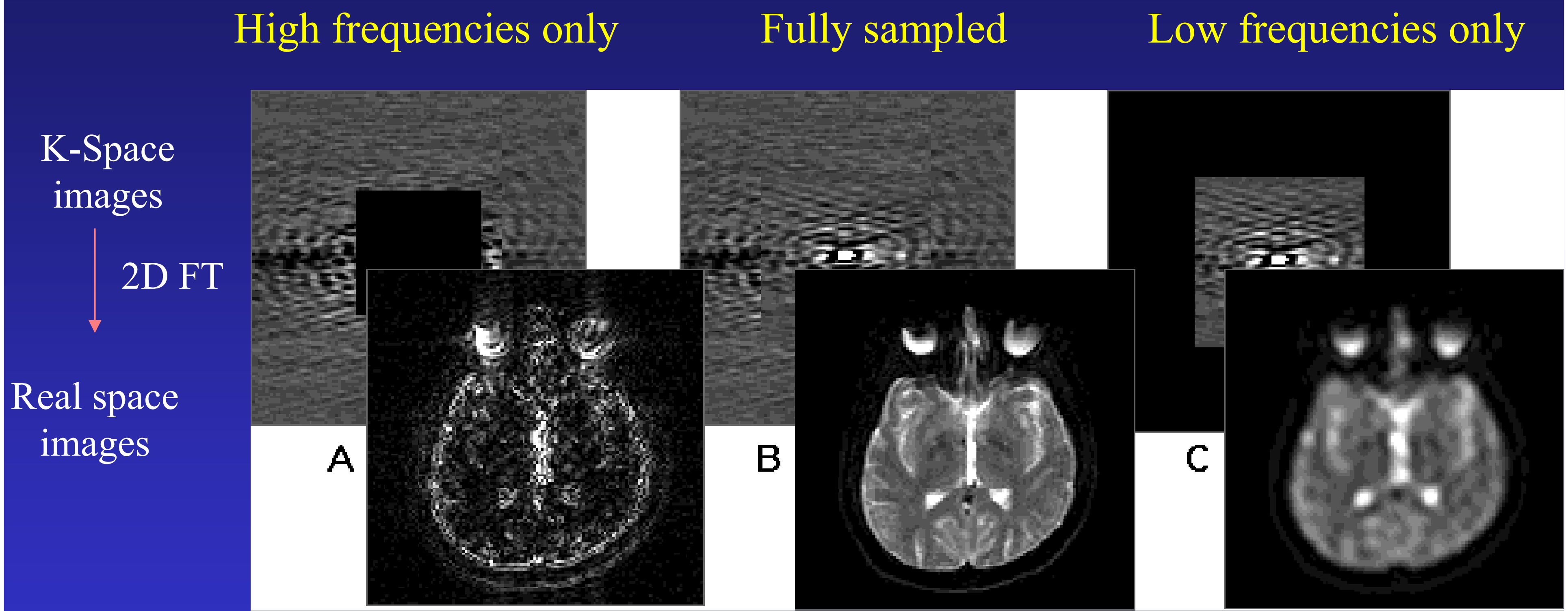
Fourier Transform

Image space (magnitude)

k-space (magnitude)

From L. Wald

Understanding *k* - space



K-Space: spatial frequency information of the image

- Center: low frequencies ⇒ global features, image intensity (C)
- Periphery: high frequencies ⇒ sharp features, edges (A)

Images from: http://thelonius.loni.ucla.edu/AMR/EPITheory.html

Physics of MR Image Acquisition

- NMR signal & relaxation √
- NMR image √
- MRI contrast
- MRI Safety & compatibility

Do we normally want such a contrast?

Image Contrast Definition

- **Goal**: maximize the contrast of interest **(USEFUL IMAGES!)**
- **Contrast**: difference in MR signals between different tissues

Tissue 1 → T_1, T_2, T_2^*, ρ, Diffusion, Flow → S_1

Tissue 2 → T_1, T_2, T_2^*, ρ, Diffusion, Flow → S_2

Water protons' mobility/environment: T_1, T_2, T_2^*, ρ, Diffusion, Flow

MR signal: S_1, S_2

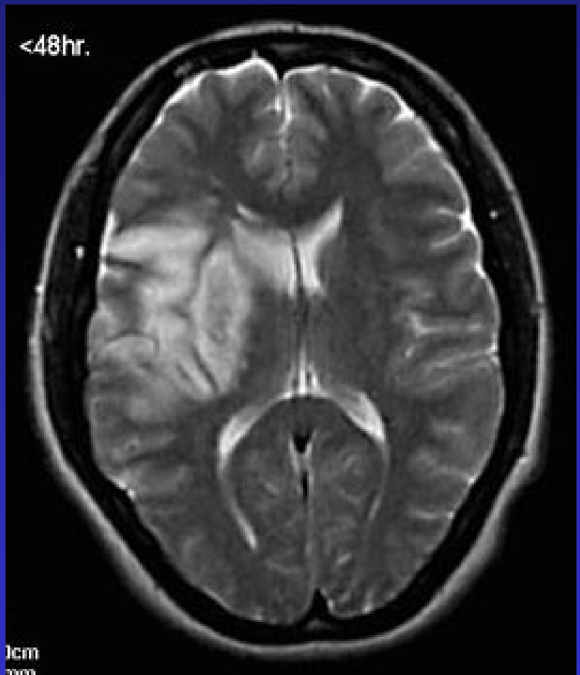
Contrast to Noise ratio:

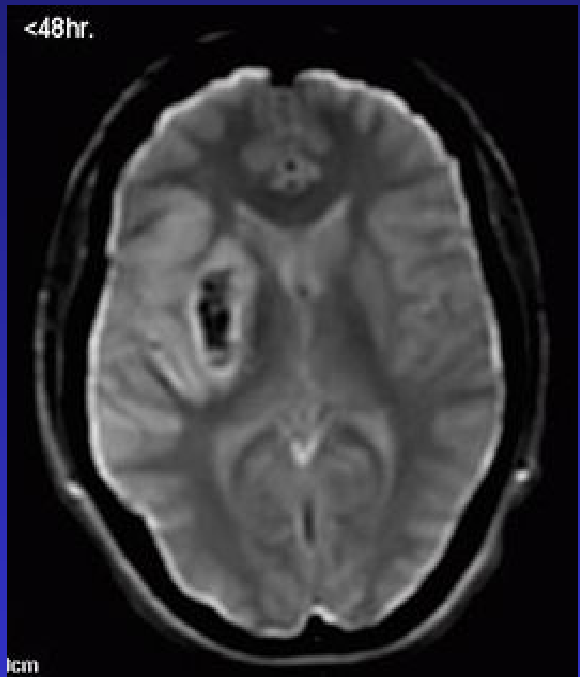
$$CNR = \frac{S_1 - S_2}{\sqrt{\sigma_1^2 + \sigma_2^2}}$$

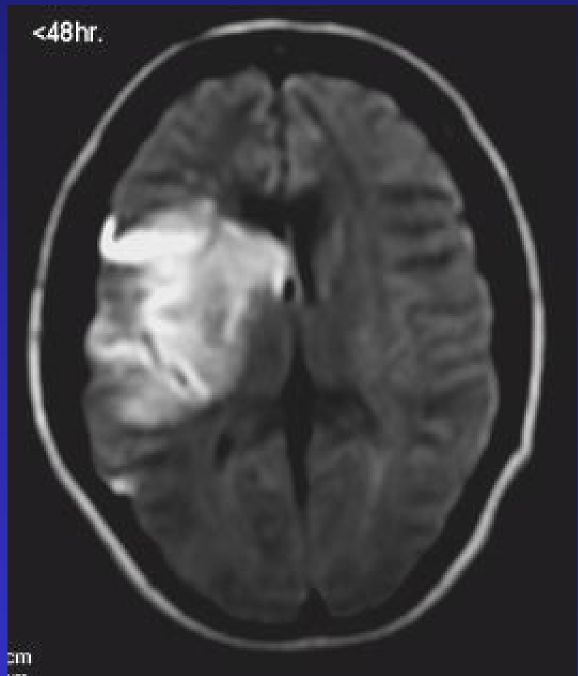
Some examples?

MRI Contrast: Some Examples

< 48 hours post ictual acute infarct in right hemisphere







T_2-weighted
(infarct detection)

T_2*-weighted
(presence of blood)

Diffusion-weighted
(full infarct extent)

How do we do this?

Images from Toshiba Image gallery

Jorge Jovicich, February 2011

Image Contrast: What can we manipulate?

Tissue Properties: fixed

Tissue	T_1^+	T_2 (ms)	ρ*
Fat	260	84	0.90
White Matter	780	90	0.72
Gray Matter	920	100	0.84
CSF	3000	300	1.00

T1 values for $B_0 = 1.5T$

ρ*: % H_2O relative to CSF

Experimental Variables

- Pulse sequence
- Pulse sequence parameters
  - Repetition time: TR
  - Echo time: TE
  - Inversion time: TI
  - RF flip angle: α
- Contrast agent

What's the effect of these variables?

Image Contrast: Weighting the MR Signal

- **General MRI pulse sequence: combination of contrasts**

Signal Intensity:

$$S(x,y) = k \times \rho \times T_1 \times T_2 \times \ldots$$

- **Contrast Weighting: maximize one term, minimize the others**

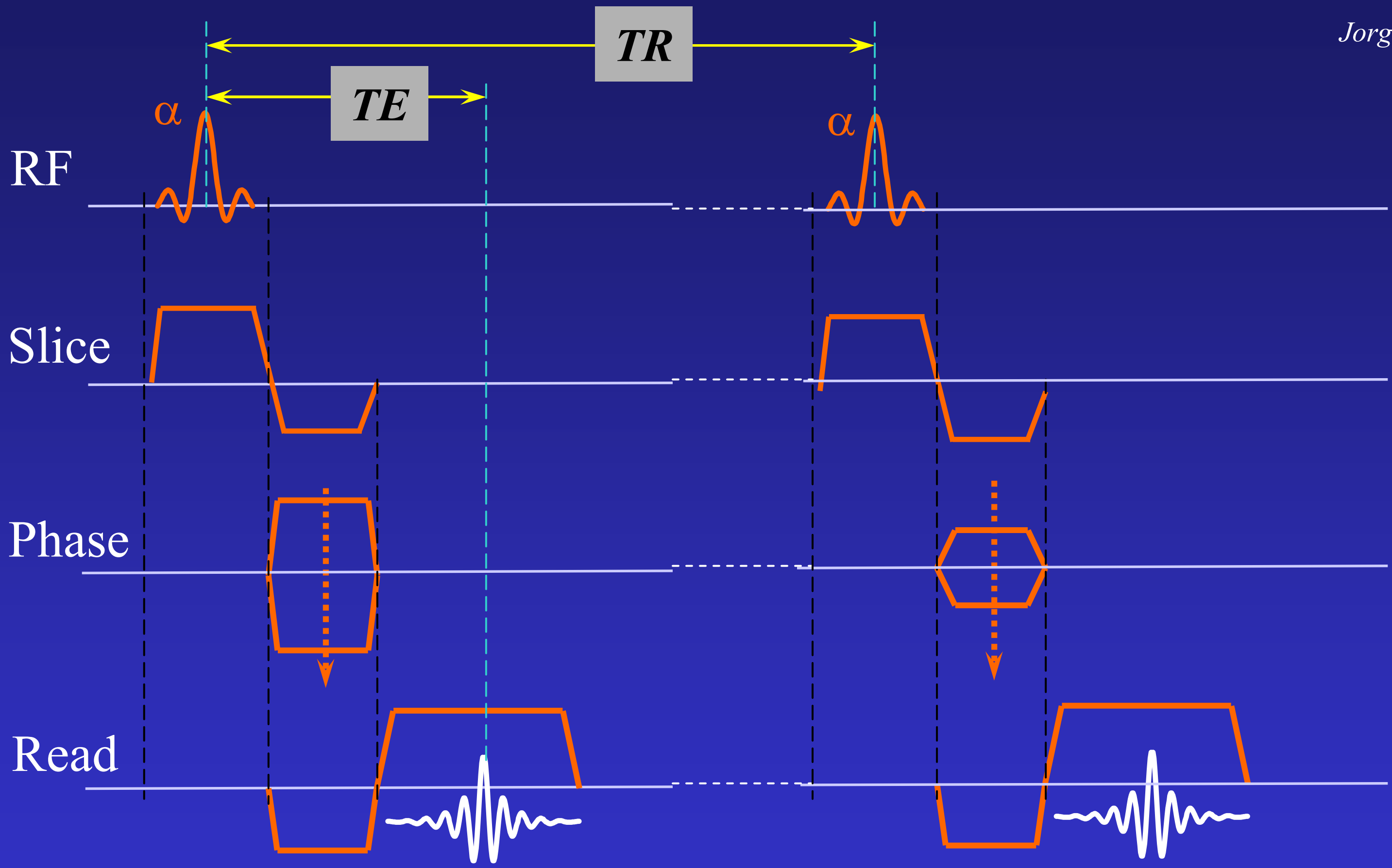
Example: T_1-weighting

$$S(x,y) = k \times \rho \times T_1 \times T_2 \times \ldots$$

by choosing adequate sequence & sequence parameters

Basic Gradient Echo Sequence

Jorge Jovicich, February 2011

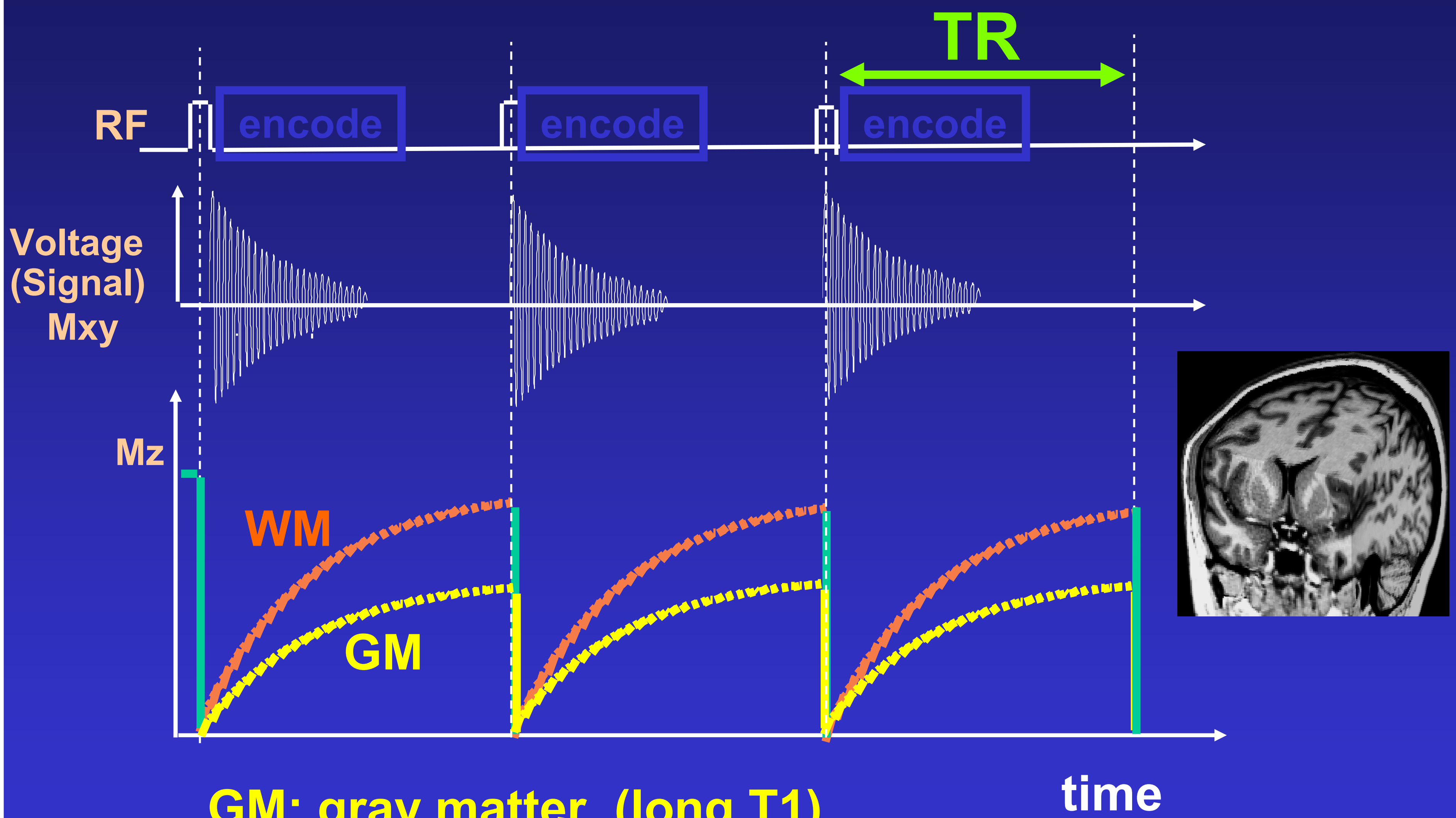


MR Signal:

$$S_{GRE} = M_0 \sin\alpha \left[1 - \exp\left(-\frac{TR}{T_1}\right)\right] \exp\left(-\frac{TE}{T_2^*}\right)$$

To first approximation, the MRI signal intensity can be approximated to the signal peak measured at the center of k-space

Repetition Time (TR): T1 contrast

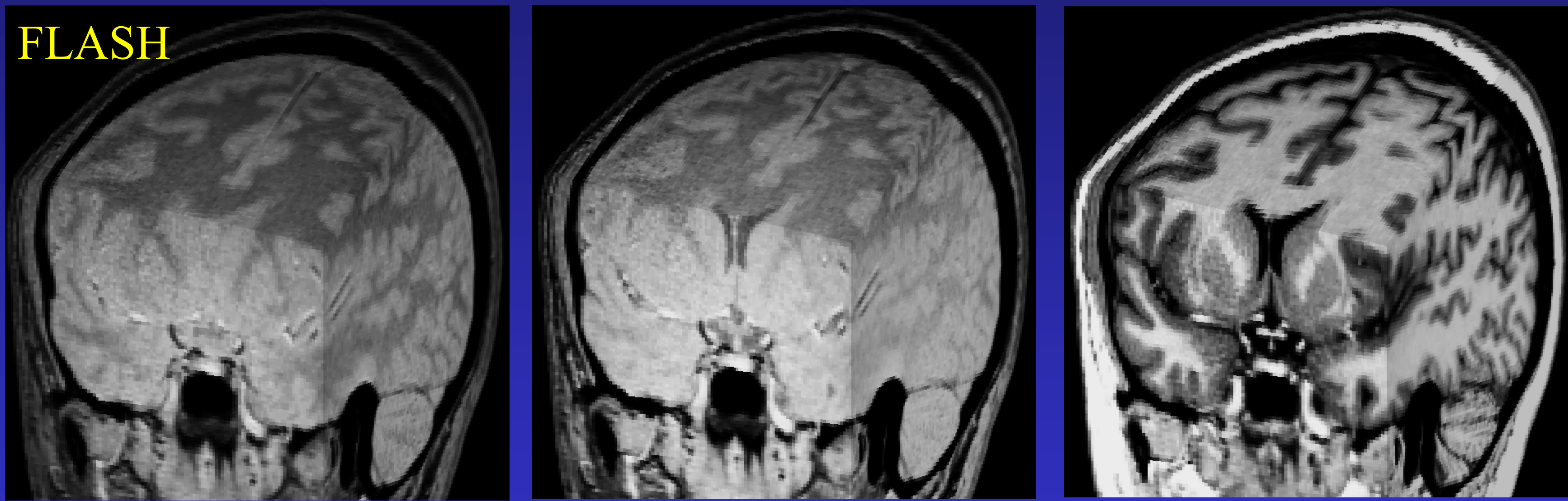


GM: gray matter (long T1)
WM: white matter (short T1)

Courtesy of L. Wald

Gradient Echo Sequence

Proton Density Weighting → T_1 Weighting



FA = 3° **FA = 5°** **FA = 30°**

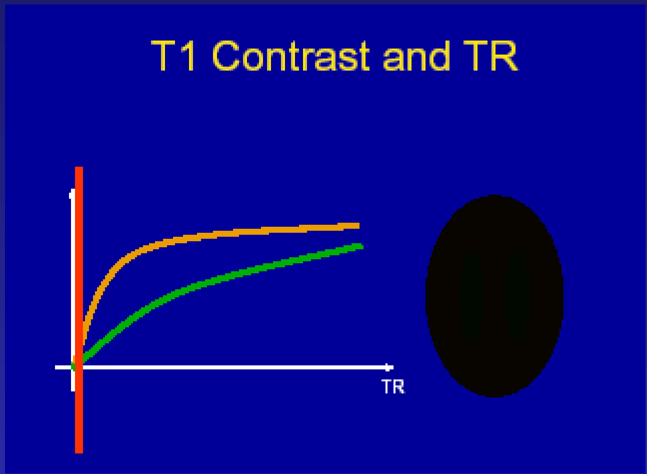
Manipulating contrast with flip angle

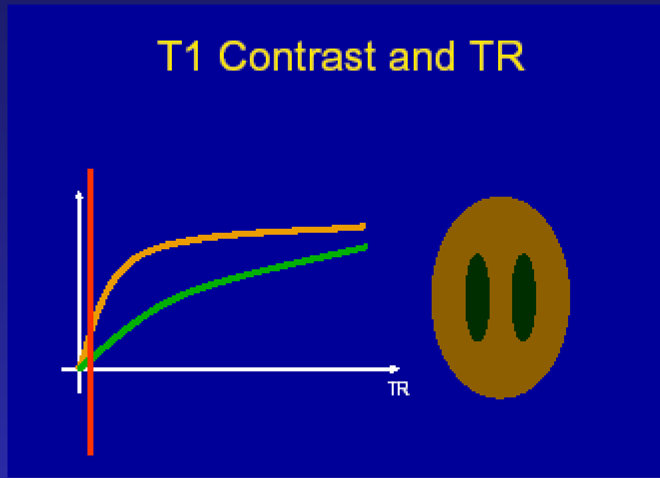
MR Signal:

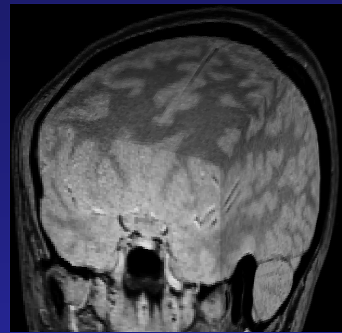
$$S_{GRE} = M_0 \sin\alpha \left[1 - \exp\left(-\frac{TR}{T_1}\right)\right] \exp\left(-\frac{TE}{T_2^*}\right)$$

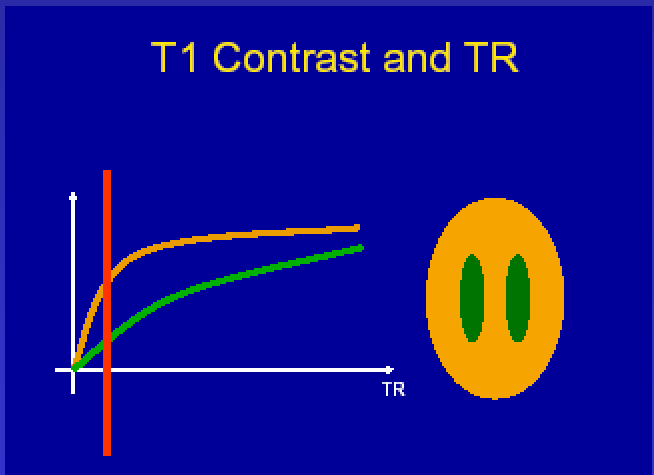
Courtesy of A. Dale and B. Fischl

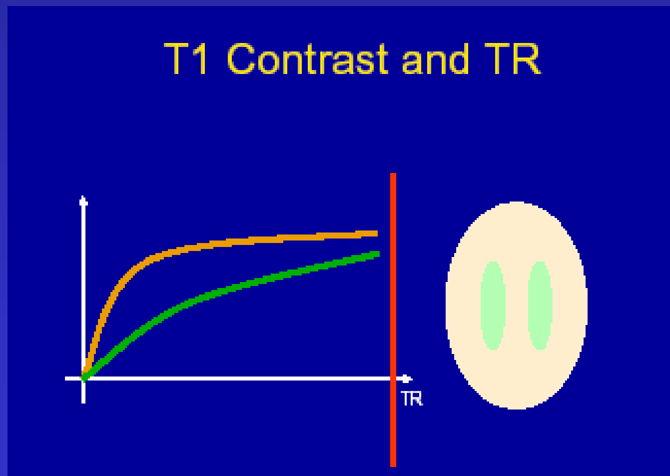
T1 relaxation: how can it be used?











To optimize the contrast to noise ratio between tissues we need to know T1 of the tissues of interest

Physics of MR Image Acquisition

- NMR signal & relaxation √
- NMR image √
- MRI contrast √
- MRI Safety & Compatibility

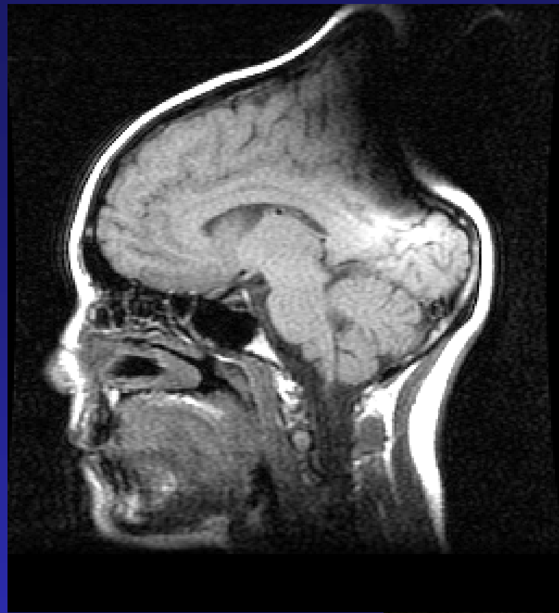
Lets reflect a moment about safety

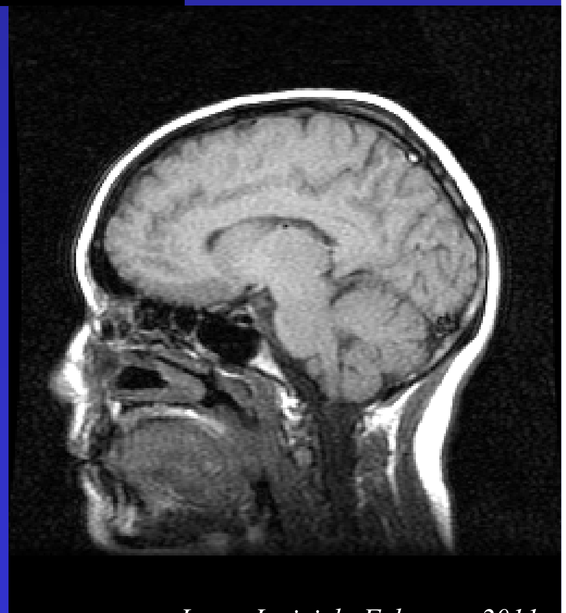
- *Risks and risk reductions in the MR environment*
  - Static magnetic field (B0) PROJECTILE!!
  - Radiofrequency power deposition (B1) HEATING!!
  - Gradient magnetic fields (Gx, Gy, Gz) PERIPHERAL NERVE STIMULATION
  - Other concerns (the subject) Acoustic noise, Cryogenics, Claustrophobia, etc.

- *Practicing Safe Imaging- minimize risks*
- *Ethical Conduct of fMRI Research involving Human Subjects*

Lets reflect a moment about safety

From: www.symplyphysics.com/flying_objects.html





Boy, 6, killed in MRI Accident (July 31, 2001)

A 6-year-old boy died two days after he was smashed in the head by a metal oxygen canister that was pulled by magnetic force into the MRI machine where he was being examined, Westchester Medical Center officials said yesterday.

Subjective Distress in the MRI Environment

- Incidence of distress among clinical MRI is high
- Distress factors:
  - confined space, noise, restriction of movement
- Distress ranges:
  - from mild anxiety to full blown panic attack
- Distress consequences:
  - Study interruption, subject motion, disrupt image quality

Minimizing Subjective Distress

- Careful screening
- Complete explanations
- Make them comfortable in the scanner
- Maintain verbal contact
- Give them the panic button

Safety is Your Responsibility

- Become familiar and READ materials posted on your institution's Human Subjects web site
  - Emergency information (scan stop, phones, reporting)
  - MR operation and periodic safety training
  - MR safety rules
  - Screening subject for MR compatibility
    - Things that rule out a subject
    - Things that might rule out a subject
    - What not to bring or wear in the scanner
  - Scan protocol in the event of possible abnormality

MR Compatibility

- Peripheral equipment working in the magnet room needs testing:
  - Safety for MR staff and volunteers/patients
    - Start with simple magnet test outside magnet room
    - Ideally use nothing that could move in the field
  - Proper work of equipment in the MR environment
    - Test specifications from vendor under YOUR working conditions
  - Minimal effects on the quality of the MRI
    - Phantom and human tests
    - Check for spikes and RF interference artifacts
    - Check for SNR inhomogeneities and losses
    - Evaluate all acquisition protocols you expect to use

Physics of MR Image Acquisition

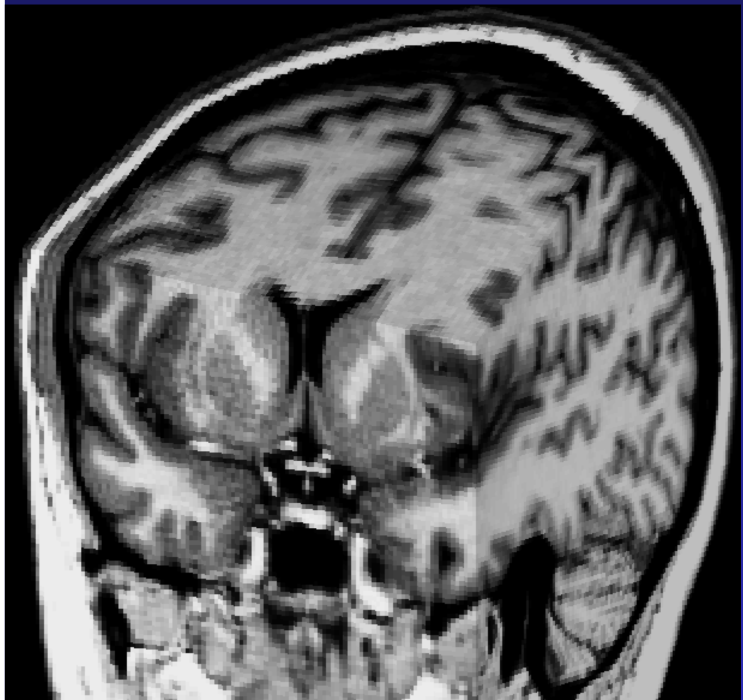
- NMR signal & relaxation √
- NMR image √
- MRI contrast √
- MRI Safety & Compatibility √

Dates	Topics
Friday Feb 4, 2011 (13:50-16:40)	• Overview of a brain fMRI experiment • Basic MRI concepts ○ Signal source. Image formation. Contrast. Safety. • Anatomical MR images: ○ Acquisition: T1-weighted contrast imaging ○ Analysis: brain segmentation ○ Potential image artifacts
Mon Feb 7, 2011 (13:20-16:30)	• Functional MR images: ○ Acquisition: fast imaging (EPI), BOLD contrast ○ Analysis: pre-processing, designs, statistical analyses ○ Potential image artifacts

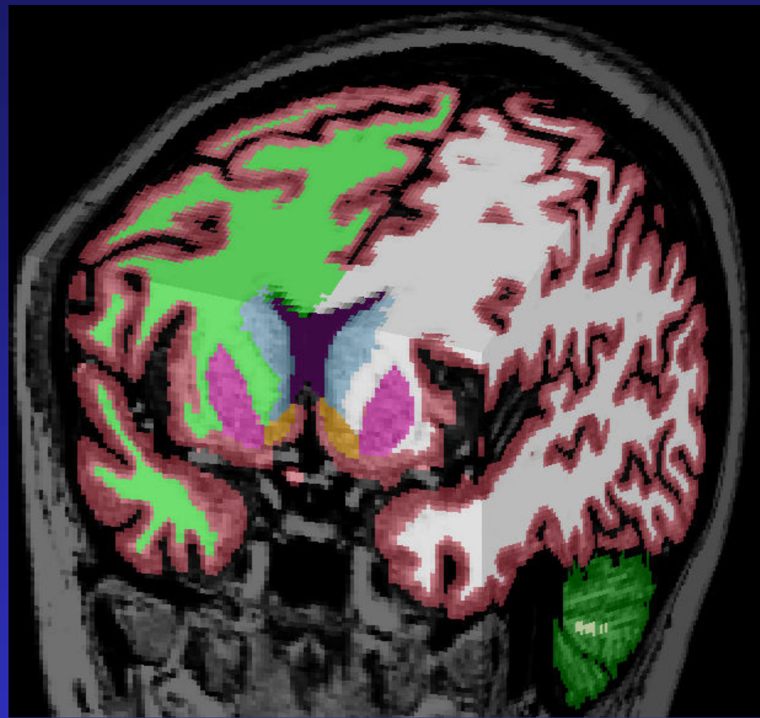
Structural MRI: why?

- Cortical segmentation
  - Across session image co-registration (within subject)
  - Across subjects image co-registration (group studies)
  - Multimodal integration (MEG, EEG, diffusion MRI, etc.)
  - Cortical thickness measures and correlates to function
- Subcortical segmentation
  - Automatic regions of interest (ROI) definition
  - Multimodal integration
  - Subcortical volumes estimation and correlates to function

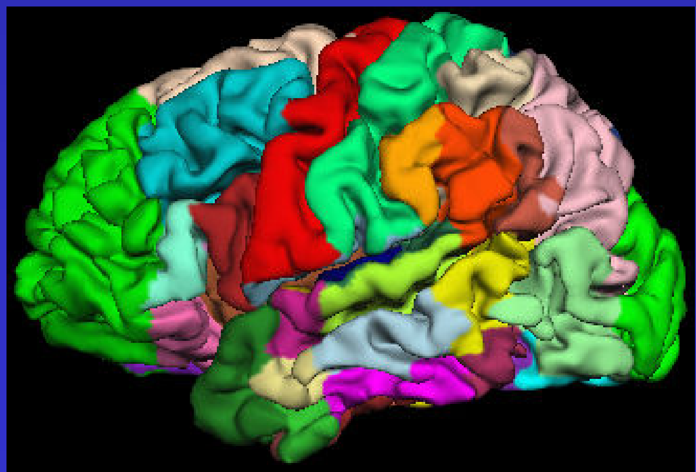
Structural MRI: why?

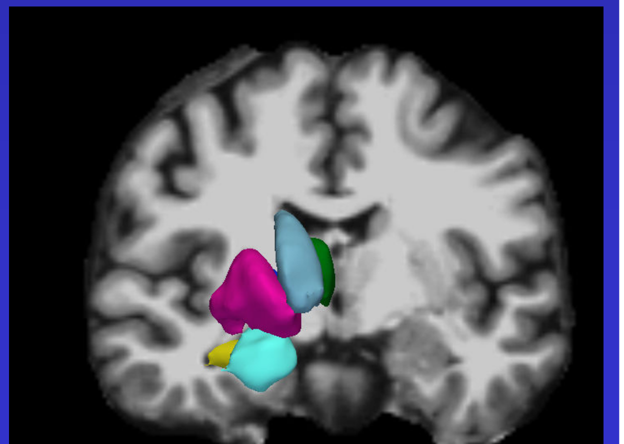


Automatic full brain segmentation



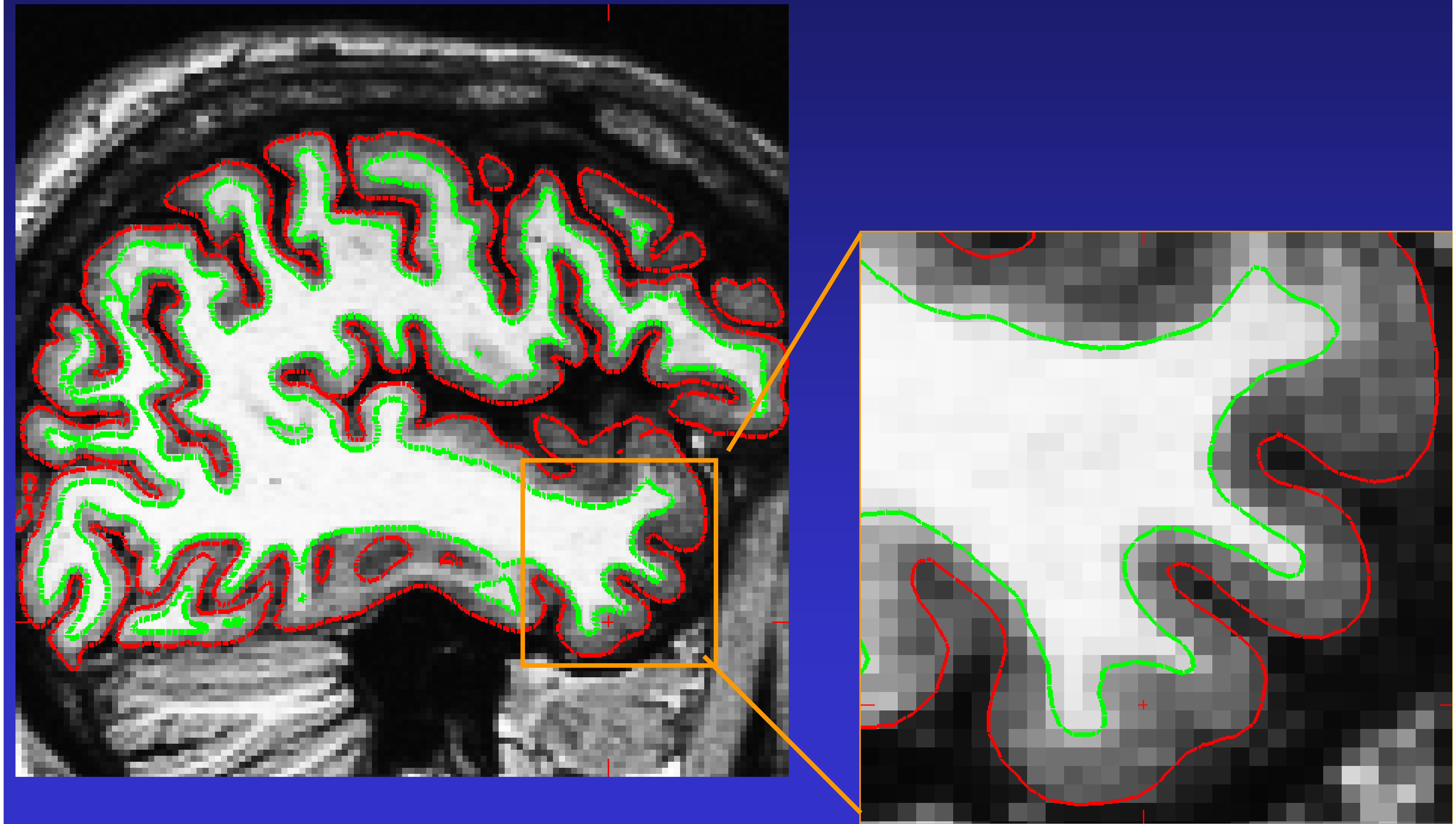
Cortical & Subcortical Surface models



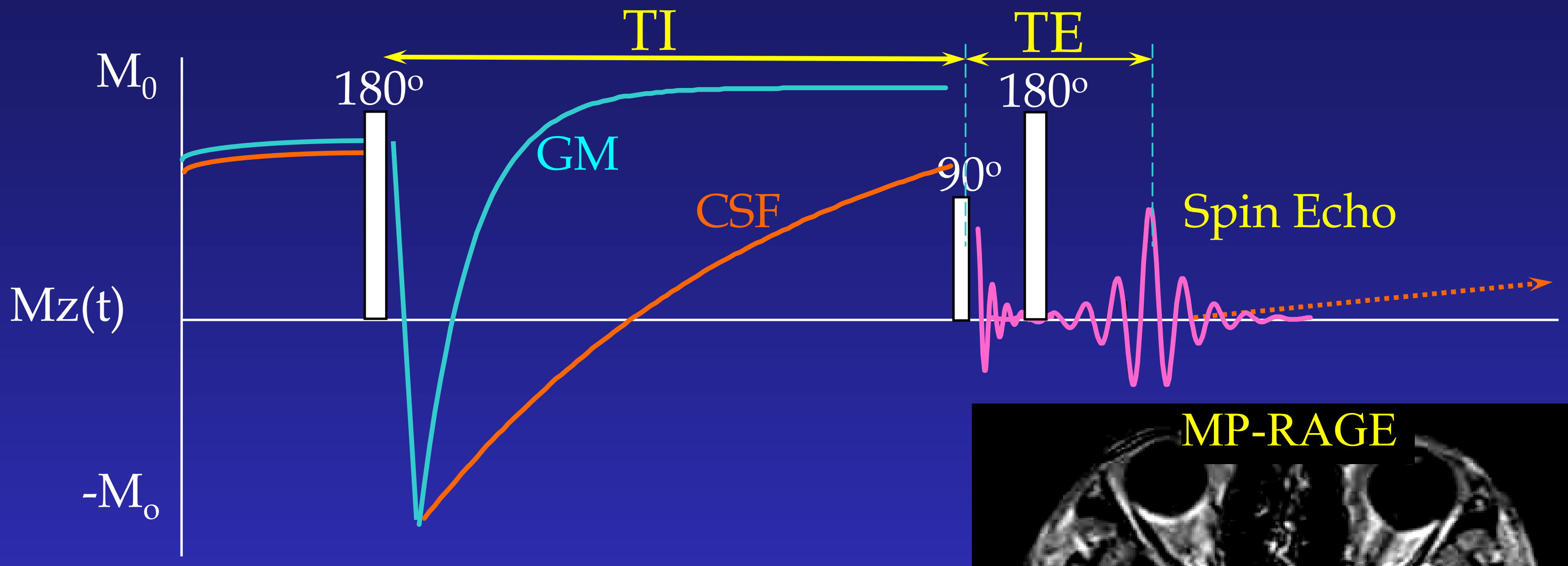


Jorge Jovicich, February 2011

Structural images matter for fMRI

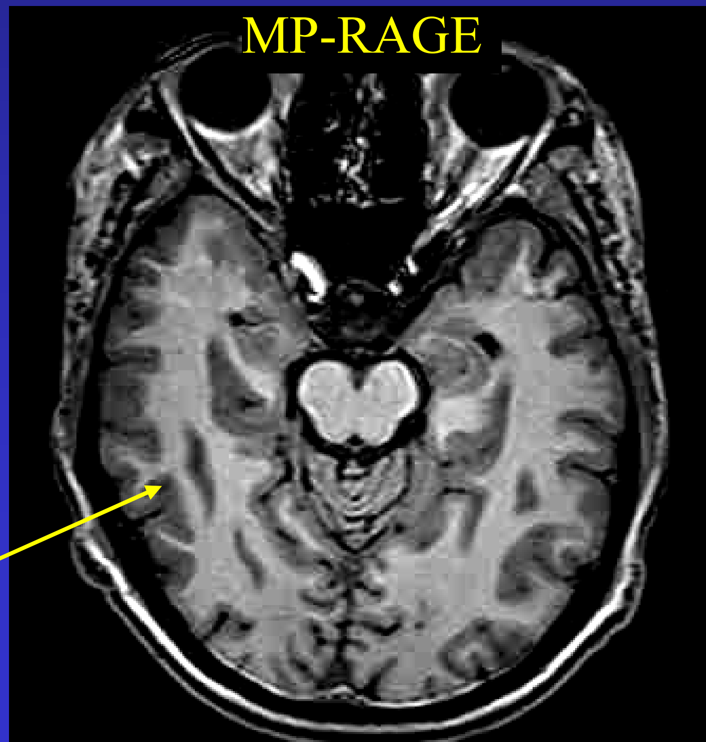


Enhanced T_1-weighting: Inversion Recovery



180° Inversion: prepare magnetization prior to Spin Echo detection

$$\text{Signal} \propto \rho(1-2e^{-TI/T1}+e^{-TR/T1})\,e^{-TE/T2}$$

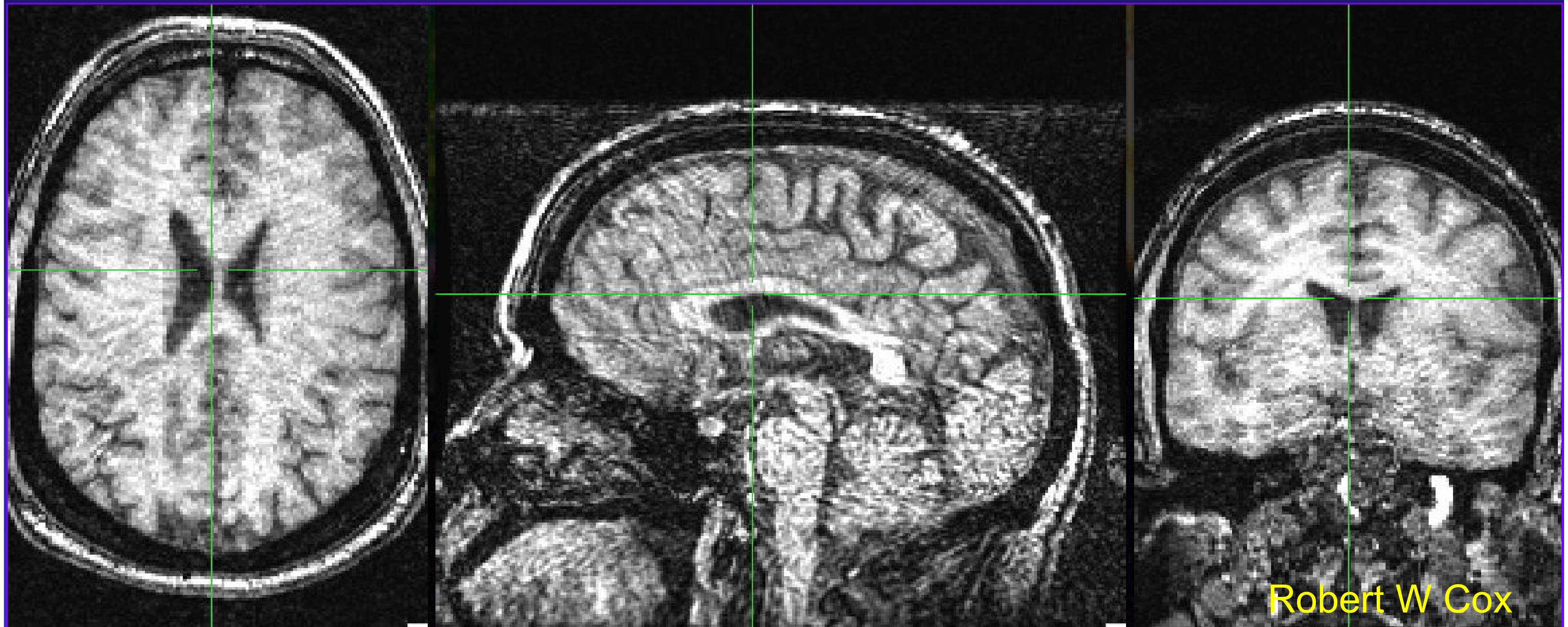


Excellent gray/white matter contrast

MR Image Artifacts

- Image quality assurance during acquisition
- Artifacts can reflect
  - General problems with the MR system
  - Problems with peripheral equipment
  - Problems with the particular acquisition protocol
  - Inappropriate volunteer
- Examples of artifacts in brain structural MRI

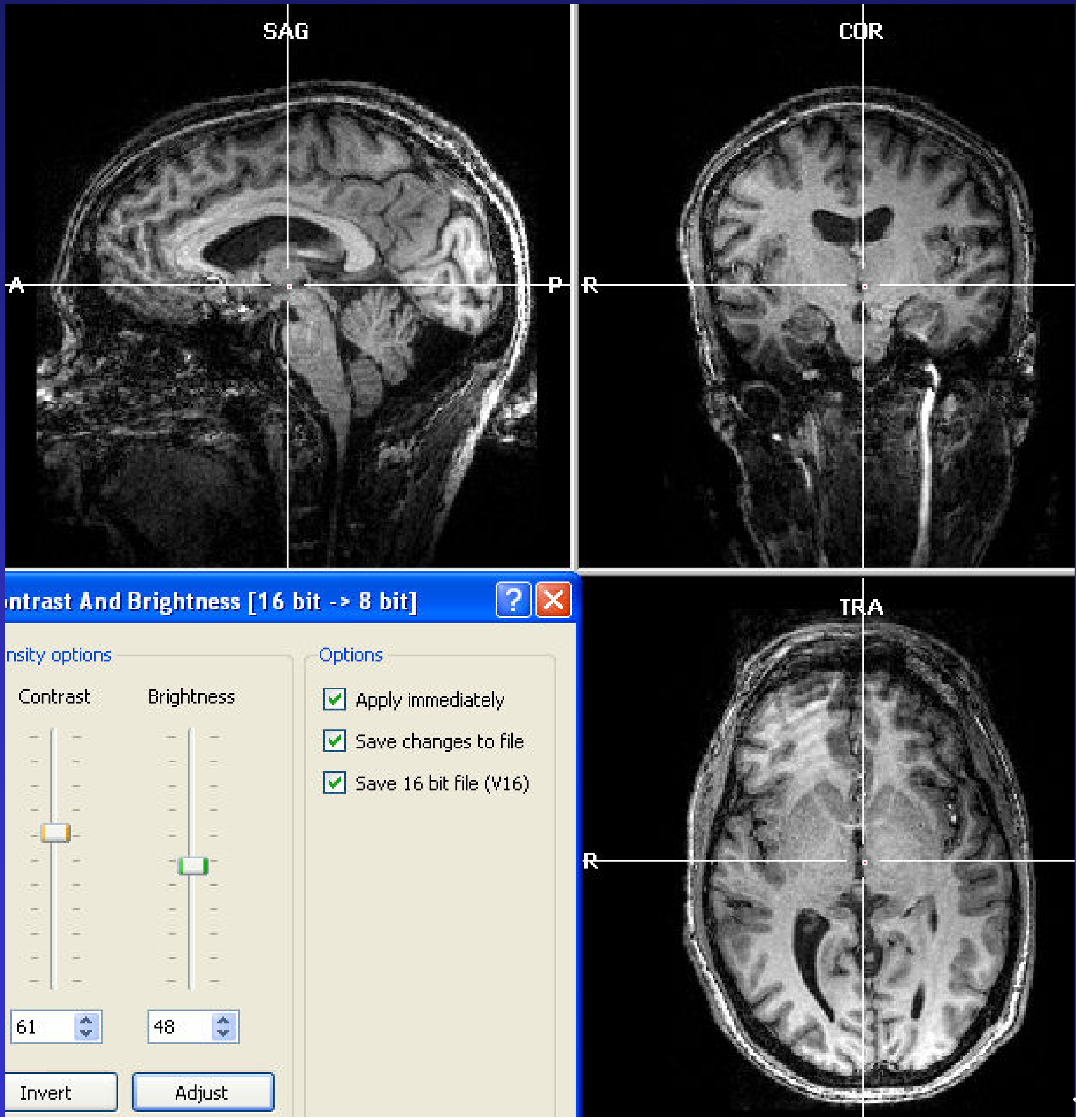
MR Image Artifacts: Structural



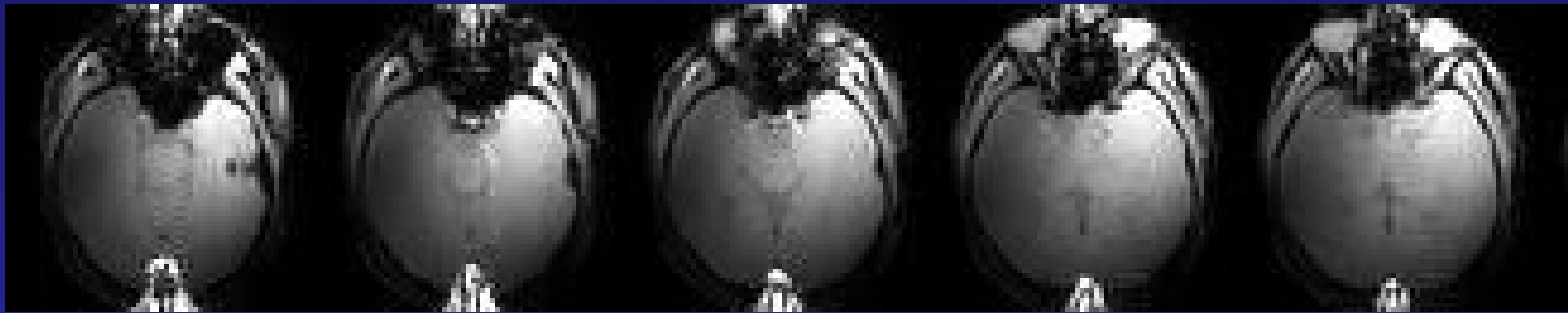
- <u>Subject moved head during acquisition</u>
  - Ghosting and ringing artifacts
  - Might be OK for some clinical purposes, but not much use for most quantitative brain research

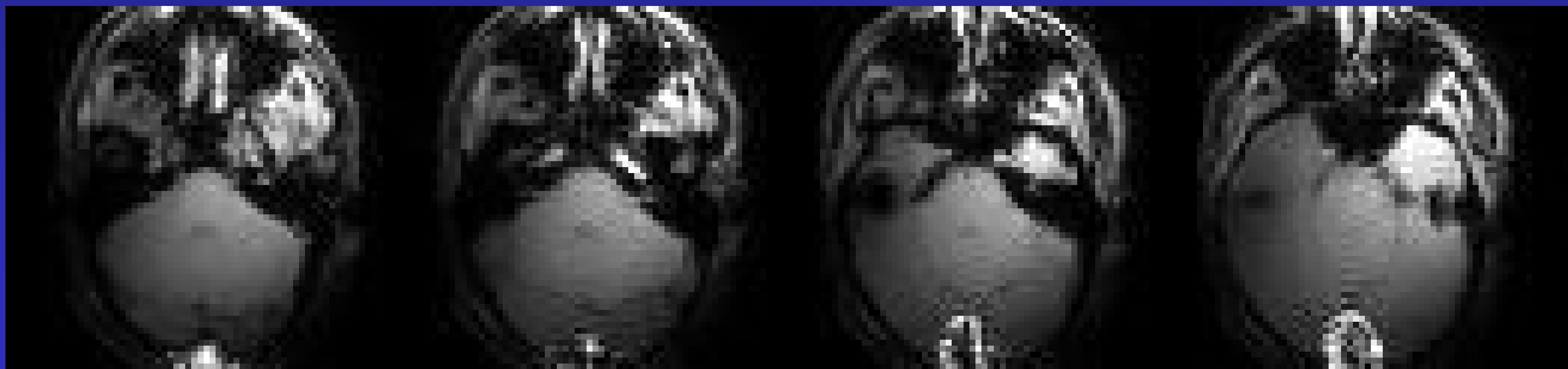
Jorge Jovicich

MR Image Artifacts: Structural



MR Image Artifacts: Structural

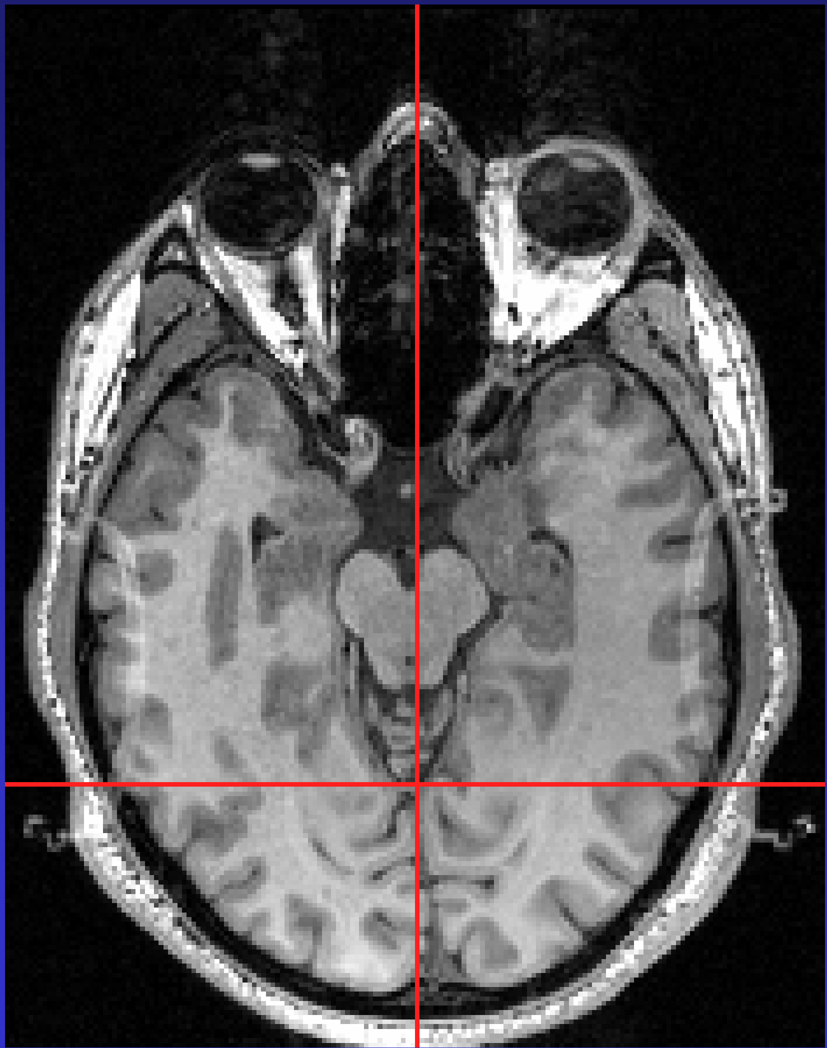




- <u>Wrap around artifact</u>
  - Frequency aliasing: the nose that is outside the field of view gets folded to the back of the brain
  - The structural image cannot be used for quantitative information in the area of the artifact

Jorge Jovicich

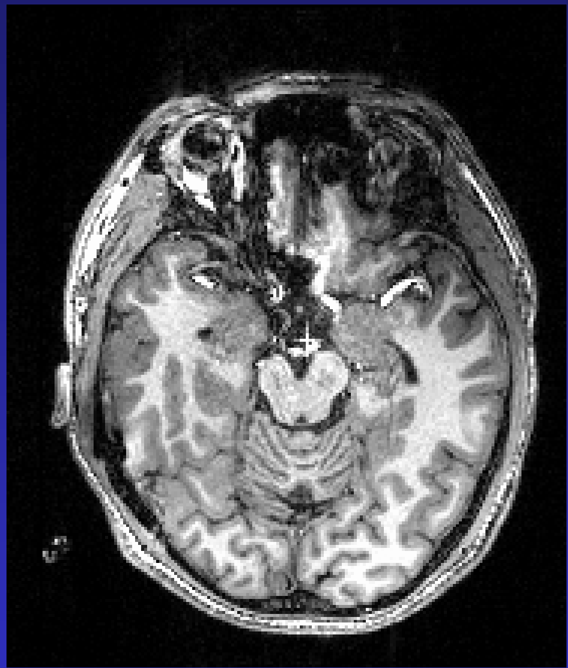
MR Image Artifacts: Structural

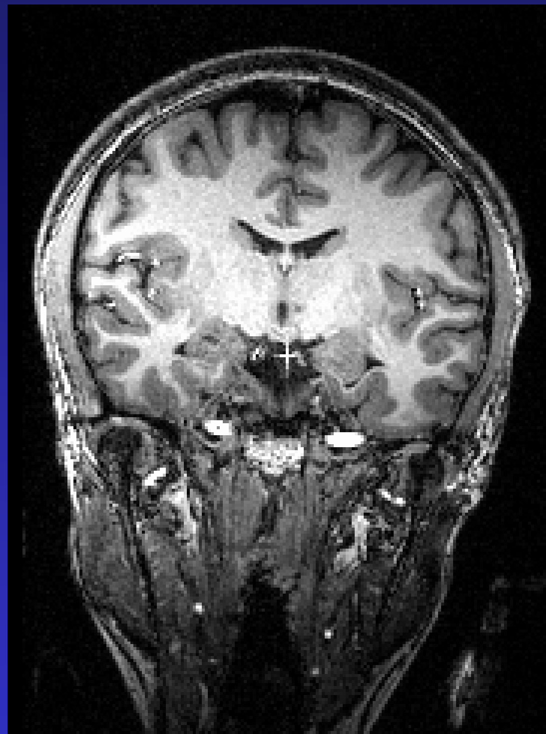


- Wrap around artifact
  - Frequency aliasing: the headphones outside the field of view get folded into the brain
- Eye motion artifact
  - Does not affect brain signal here

Jorge Jovicich

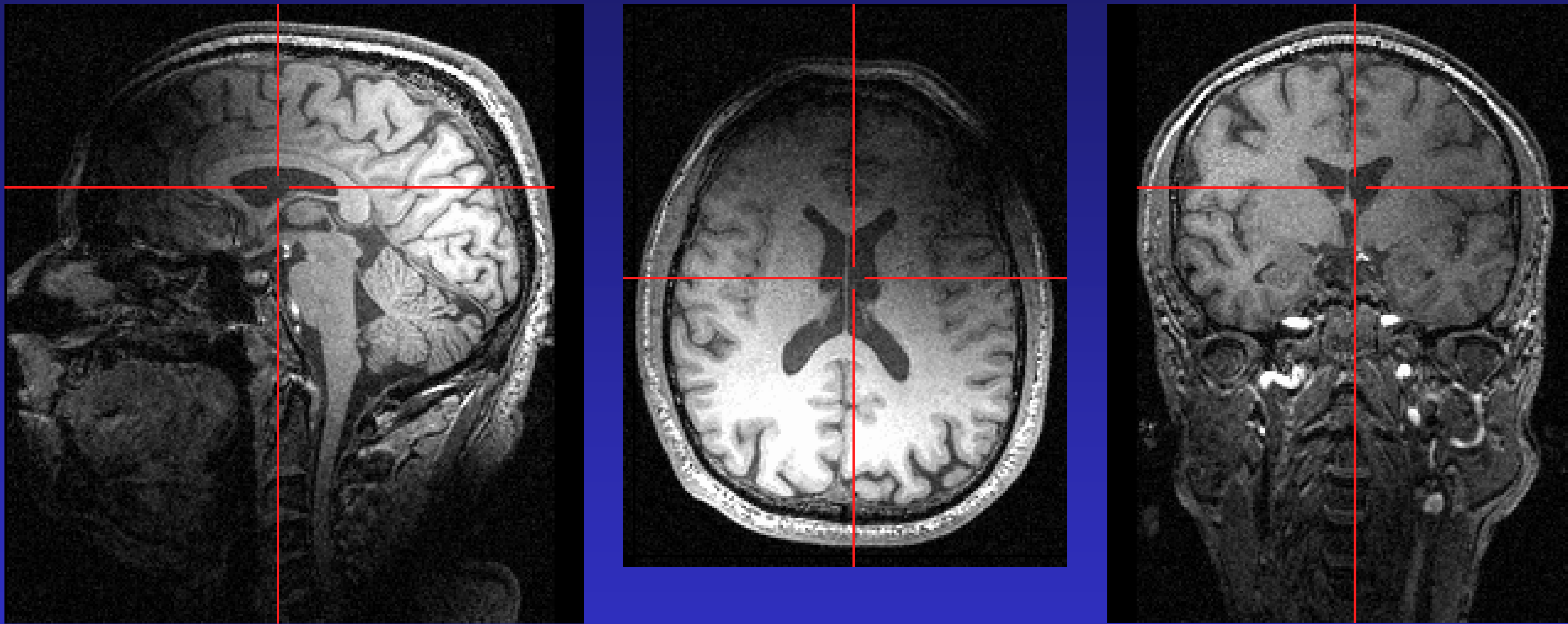
MR Image Artifacts: Structural





- <u>Central point artifact</u>
  - DC offset in receiver chain, after Fourier Transform gives the sinc function profile at he center of the field of view

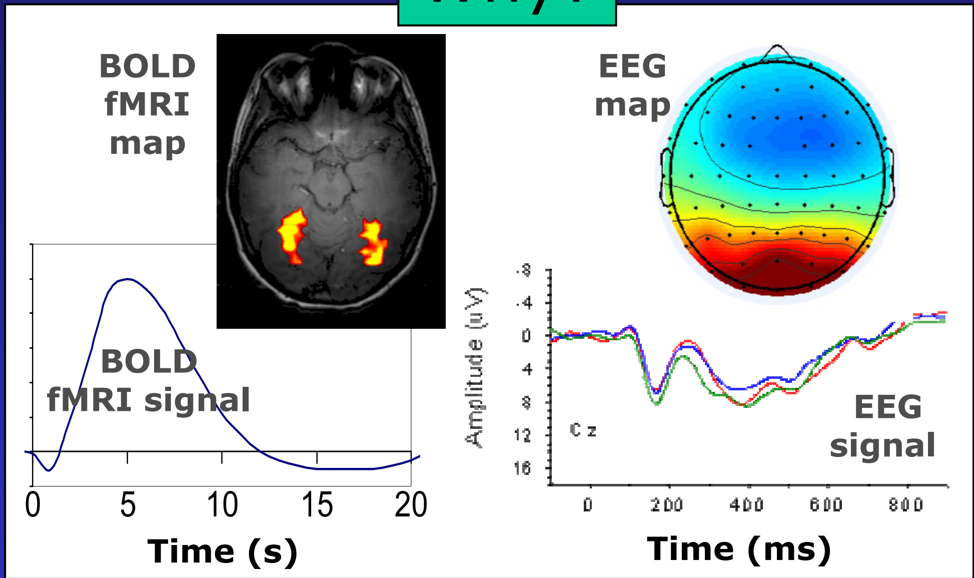
MR Image Artifacts: Structural



- <u>Image intensity and contrast inhomogeneities</u>
  - Bad head positioning inside RF coil and/or problems with RF transmission/reception chain

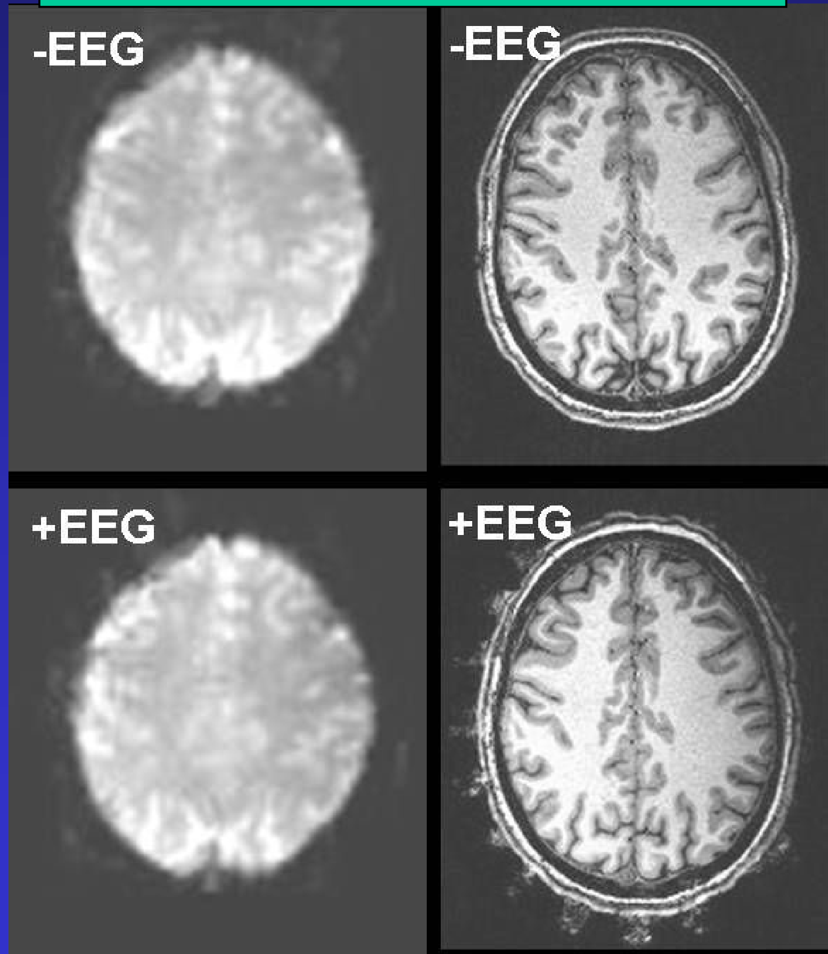
Simultaneous EEG-fMRI at 4T

Why?



How?

Effects on MRI quality

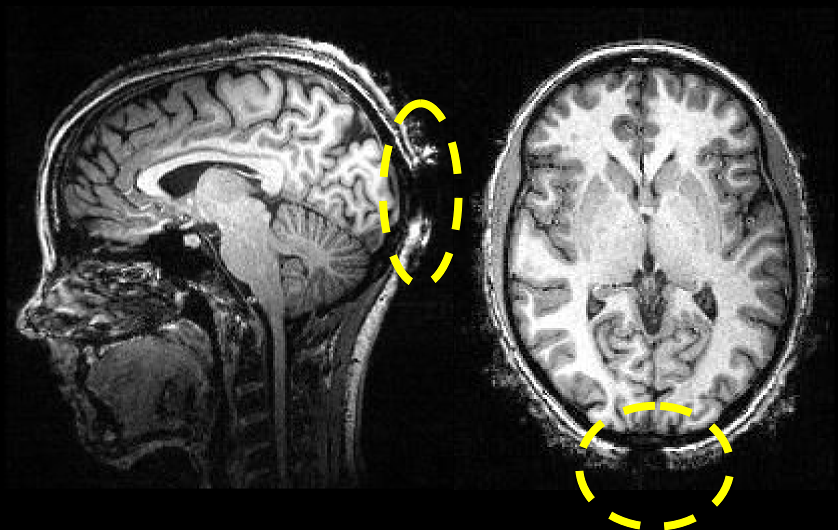


Jorge Jovicich

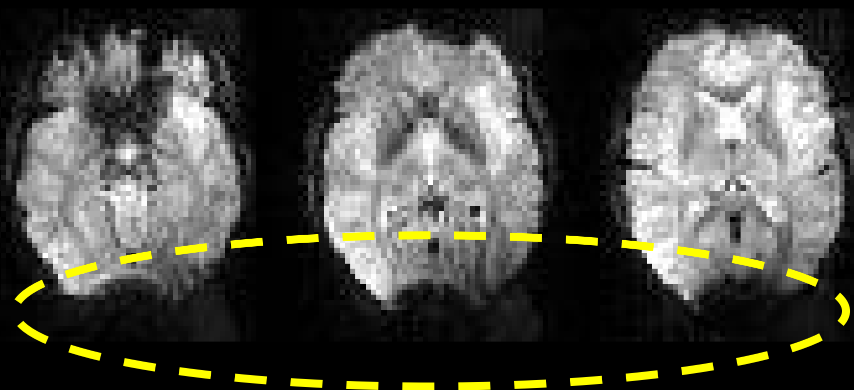
Simultaneous EEG-fMRI at 4T: faulty electrode

With EEG cap

3D MPRAGE

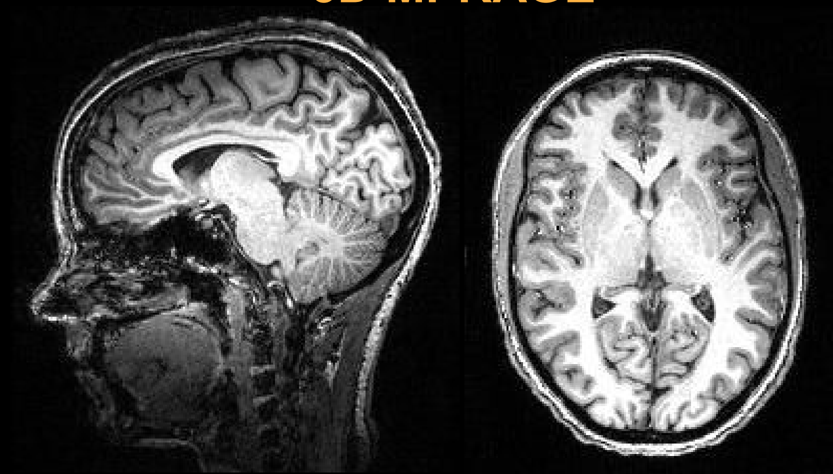


2D EPI

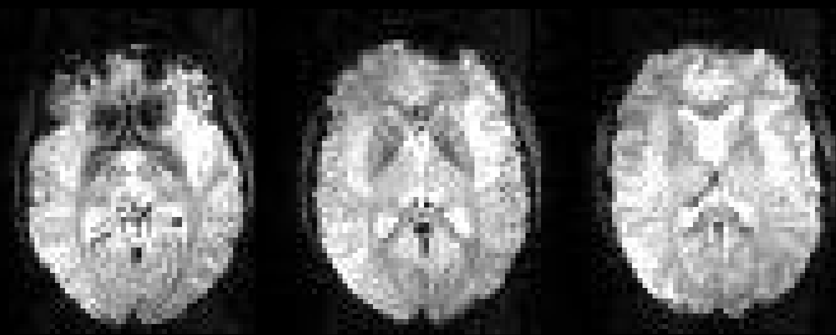


Without EEG cap

3D MPRAGE

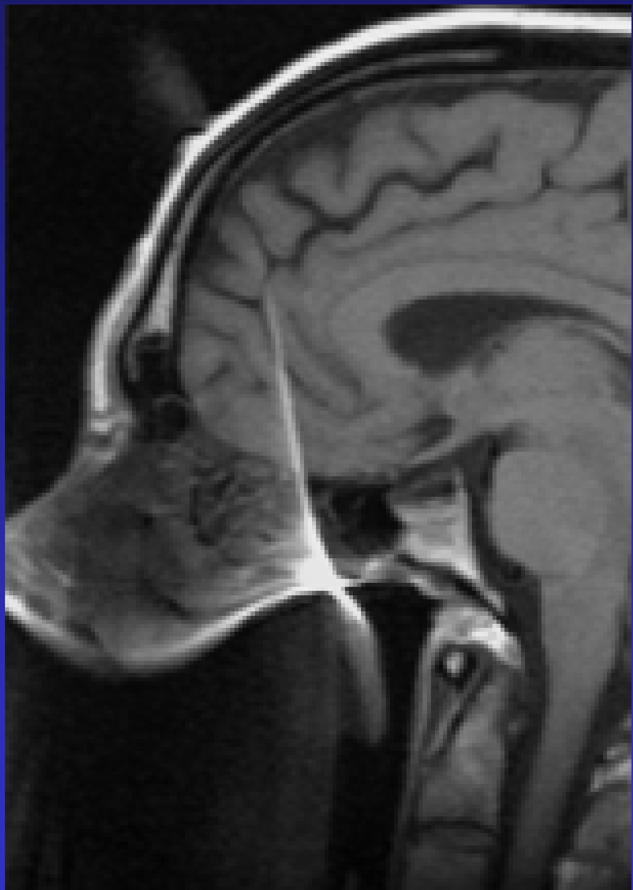


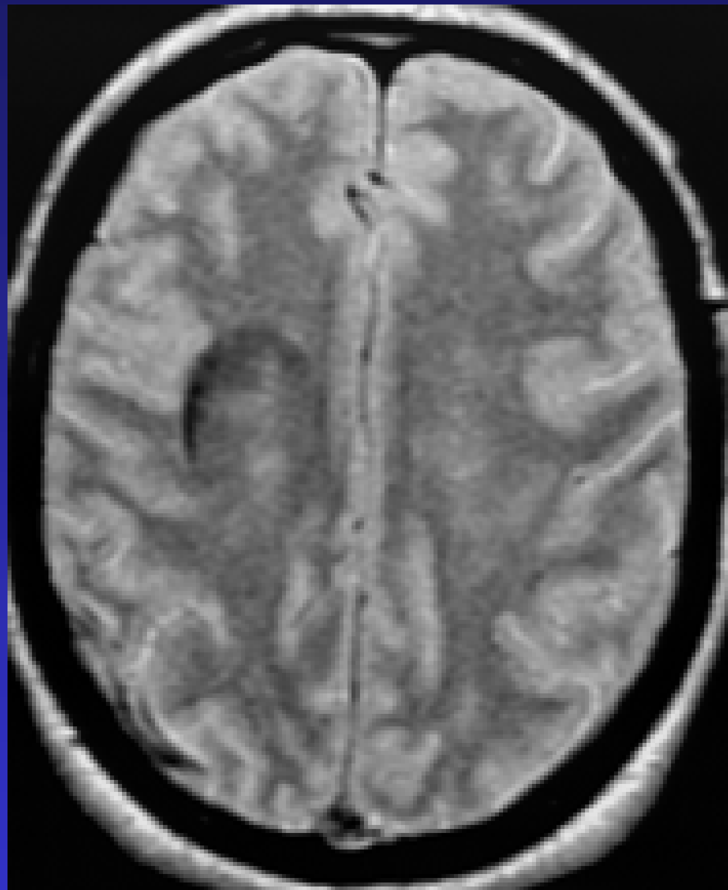
2D EPI



Jorge Jovicich

MR Image Artifacts: Structural



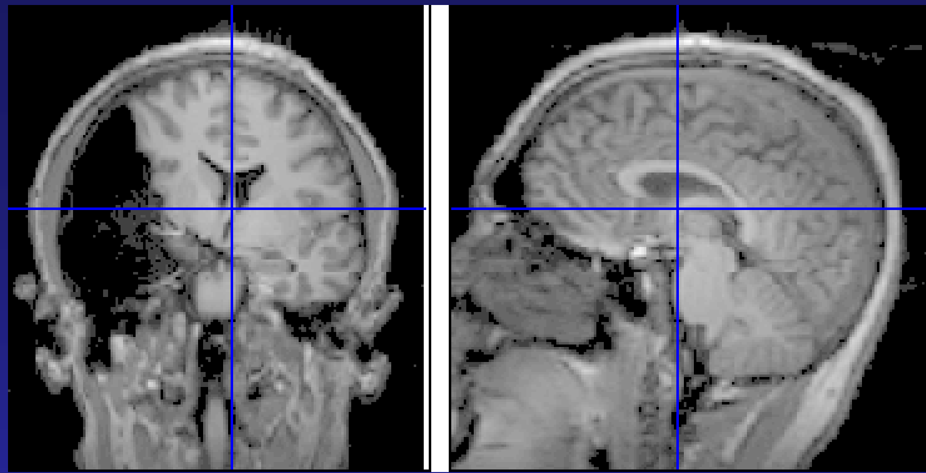


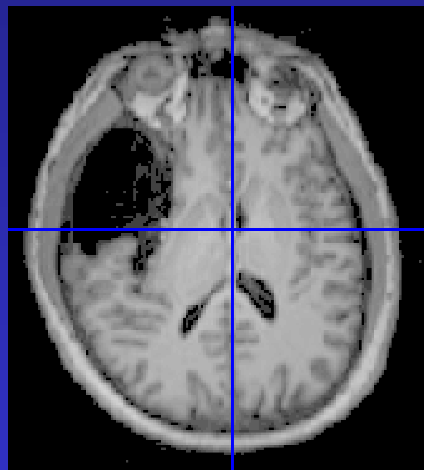
- Dental work
  - Artifacts can extend well beyond the mouth area

Jorge Jovicich

A special ‘normal’ volunteer

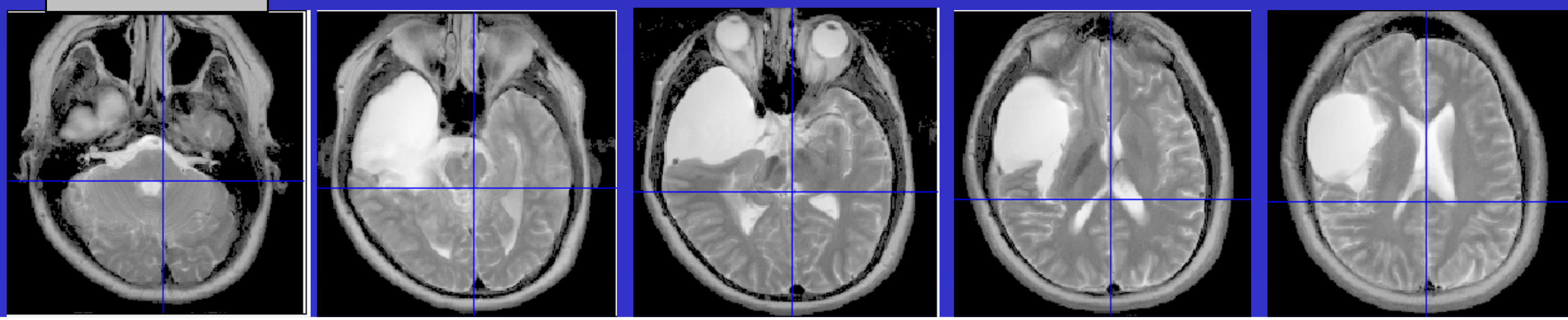
- Always check anatomical MRI
- If suspicious:
  - check with MD
  - run CLINICAL-BRAIN protocol (T1,T2,FLAIR,Diffusion)
  - just use the default parameters
  - but set slices to cover all head!
  - run your fMRI?
  - what to tell the subject?





3DSagittalT1

T2 Axials



Jorge Jovicich, February 2011

MR Image Artifacts

- EXAMPLES IN STRUCTURAL MRI
  - Motion
  - Wrap around
  - SNR and CNR inhomogeneities
  - Interference with other equipment (e.g., EEG)
  - Central point artifact
  - Interference from tooth implants
  - Unexpected anatomy
  - …

Dates	Topics
Friday Feb 4, 2011 (13:50-16:40)	• Overview of a brain fMRI experiment • Basic MRI concepts ○ Signal source. Image formation. Contrast. Safety. • Anatomical MR images: ○ Acquisition: T1-weighted contrast imaging ○ Analysis: brain segmentation ○ Potential image artifacts
Mon Feb 7, 2011 (13:20-16:30)	• Functional MR images: ○ Acquisition: fast imaging (EPI), BOLD contrast ○ Analysis: pre-processing, designs, statistical analyses ○ Potential image artifacts