Radio spectroscopies, NMR, ESR, MRI

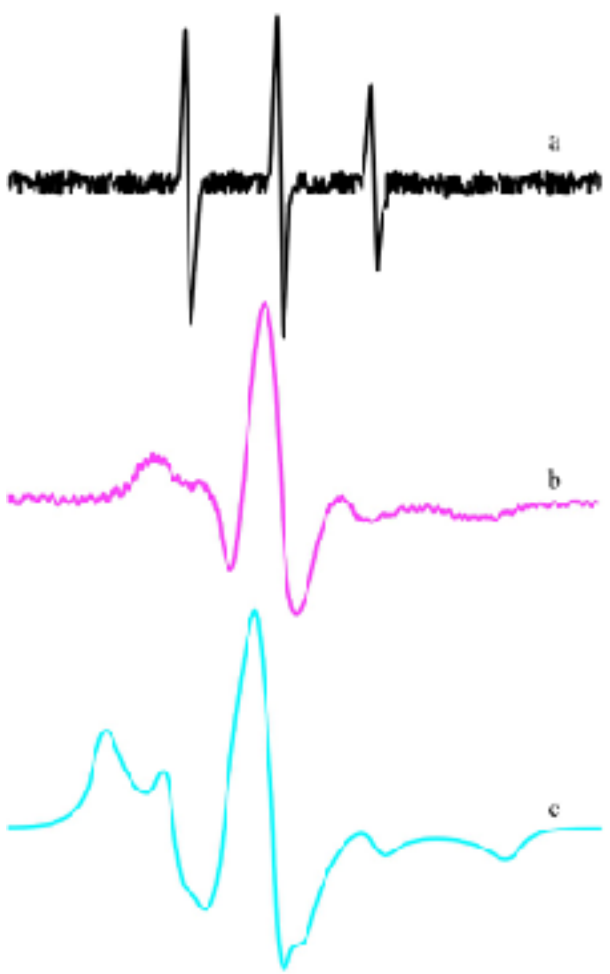
Miklós Kellermayer

Radiospectroscopies

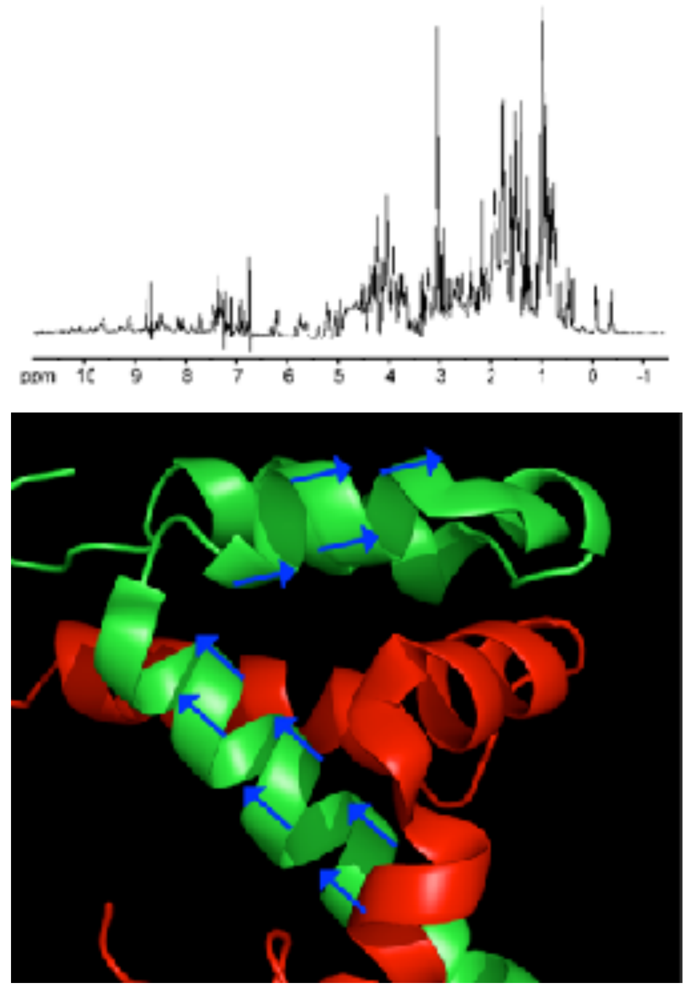
Revolutionized physics, chemistry, biology and medicine

- Electronspin resonance (ESR, electron paramagnetic resonance - EPR)
- Nuclear Magnetic Resonance (NMR, MRI)

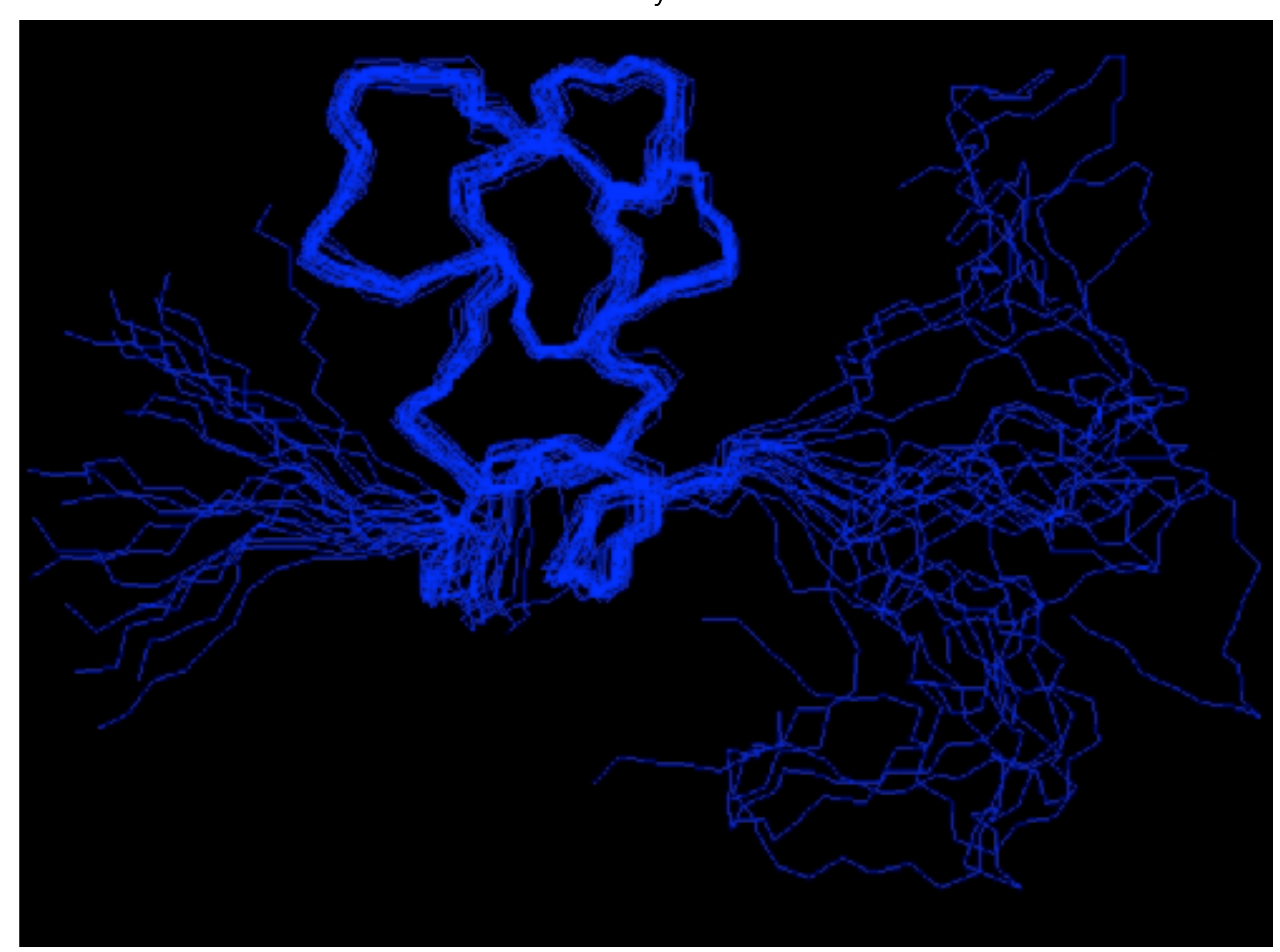
EPR spectroscopy



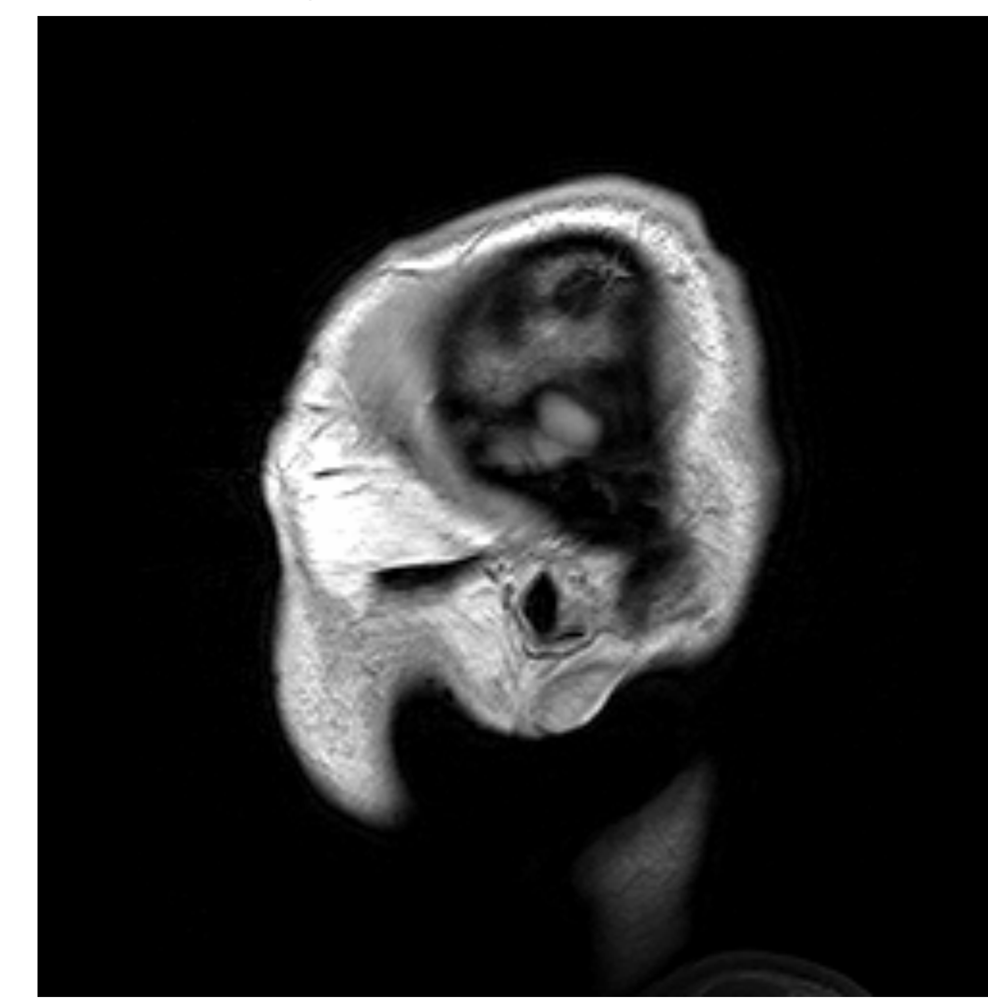
NMR spectroscopy



Protein molecular dynamics with NMR



High-resolution, anatomical MRI

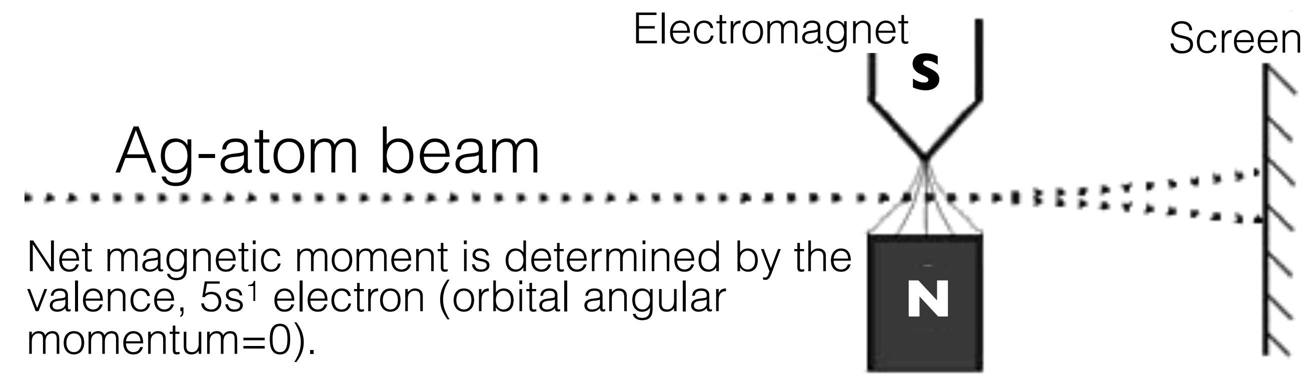


Atomic, molecular systems may behave as elementary magnets

Stern-Gerlach experiment (1922)

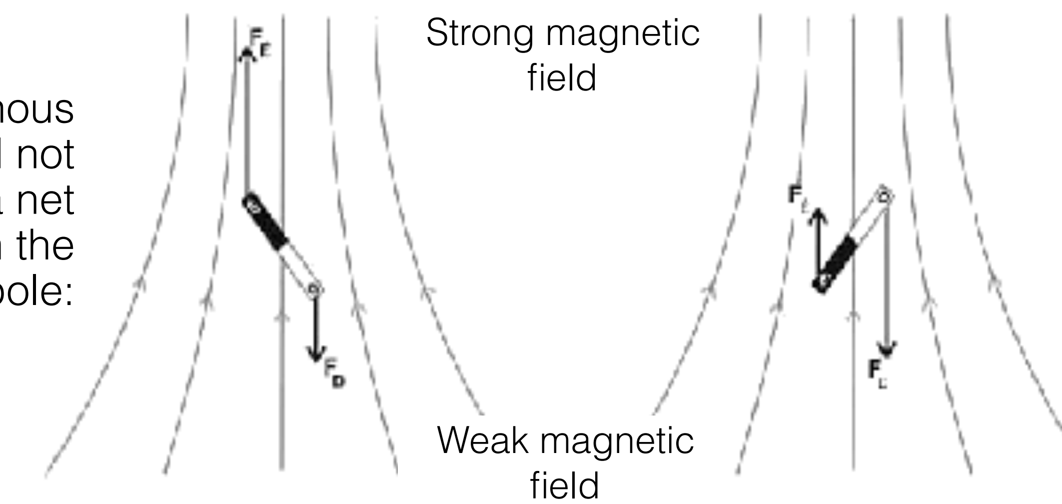

Otto Stern
(1888-1969)


Walther Gerlach
(1889-1979)



The beam splits in two.

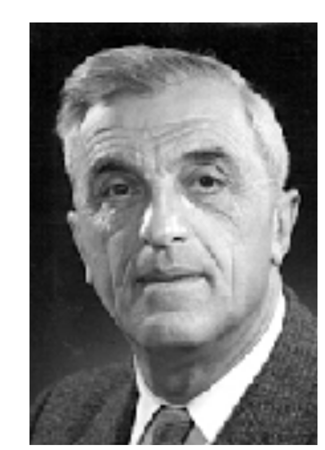
In an inhomogenous magnetic field not only torque, but a net force also acts on the magnetic dipole:



The spin magnetic moment may attain two discrete values.

Nuclear magnetic resonance, (NMR)
Nobel-prize, 1952


Isidor Rabi
(1898-1988)

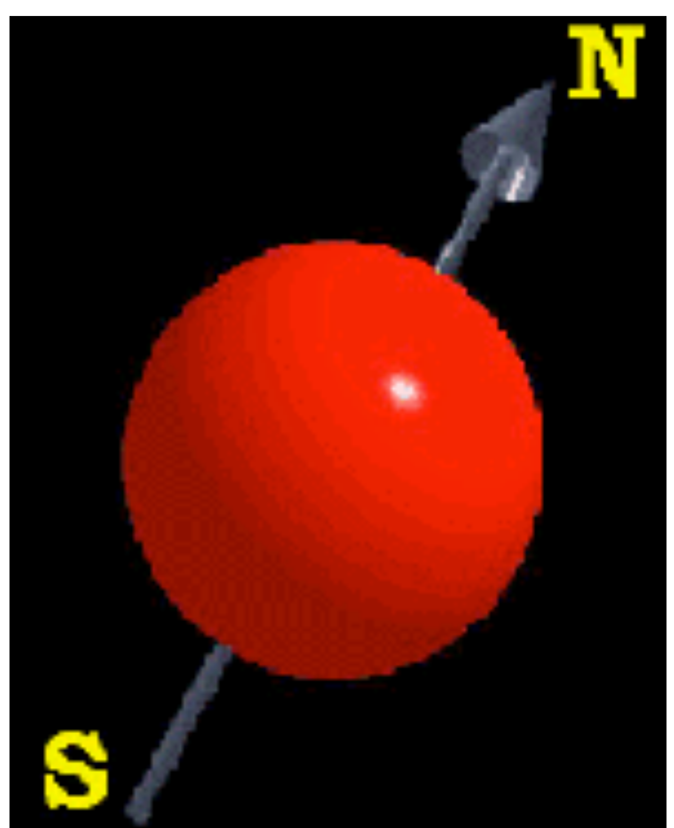

Felix Bloch
(1905-1983)


Edward Mills Purcell
(1912-1997)

Magnetic resonance: resonance-absorption of electromagnetic energy by a material placed in magnetic field.

Systems with net spin: elementary magnets

- Elementary particles (p, n, e) have their own *spin*.
- Depending on the number of elementary particles and organizational principles (e.g., Pauli principle), ***net spin*** emerges within the system.
- Atomic nucleus: odd mass number - half nuclear spin (^{1}H, ^{13}C, ^{15}N, ^{19}F, ^{31}P); even mass number, odd atomic number - whole nuclear spin; even mass and atomic number - zero nuclear spin.
- Electron: net electron spin within a molecular system containing a stable unpaired electron (e.g., free radicals).
- Because of ***charge*** and ***net spin, magnetic moment*** emerges.



Nuclear magnetic moment:

$$M_N = \gamma_N L$$

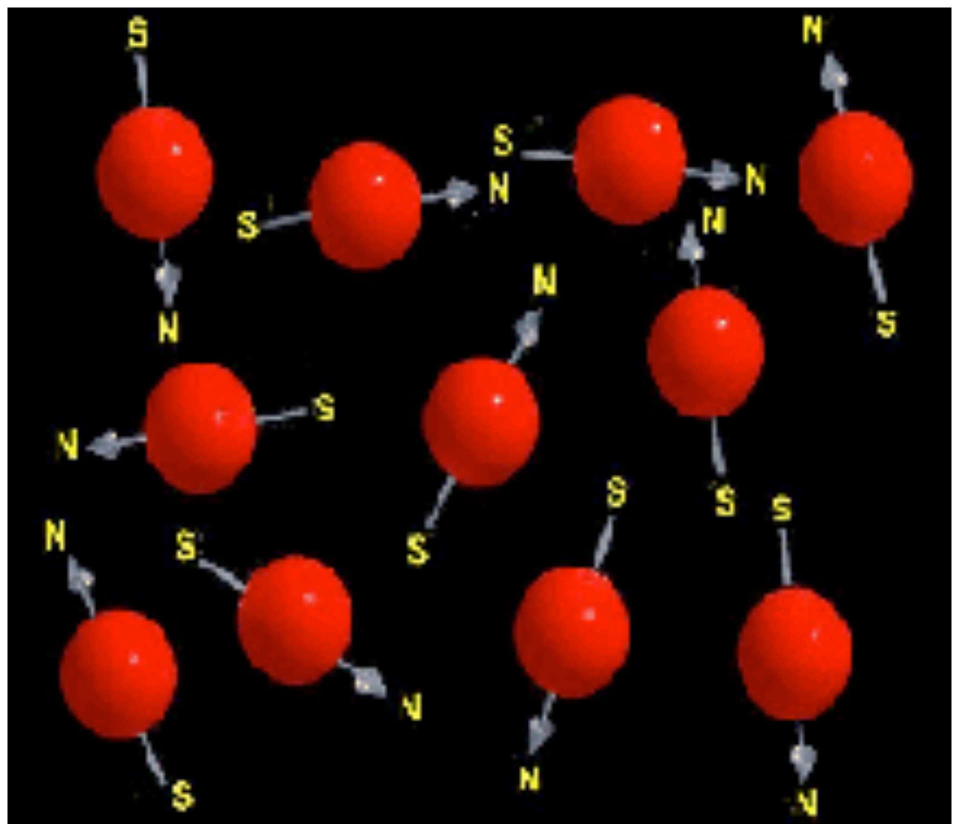
γ_N = gyromagnetic ratio (ratio of magnetic moment and angular momentum.)
L = nuclear spin ($L = \sqrt{l(l+1)}\hbar$), l= spin quantum number.

Magnetic moment of the electron:

$$M_e = -g\mu_\beta\sqrt{S(S+1)}$$

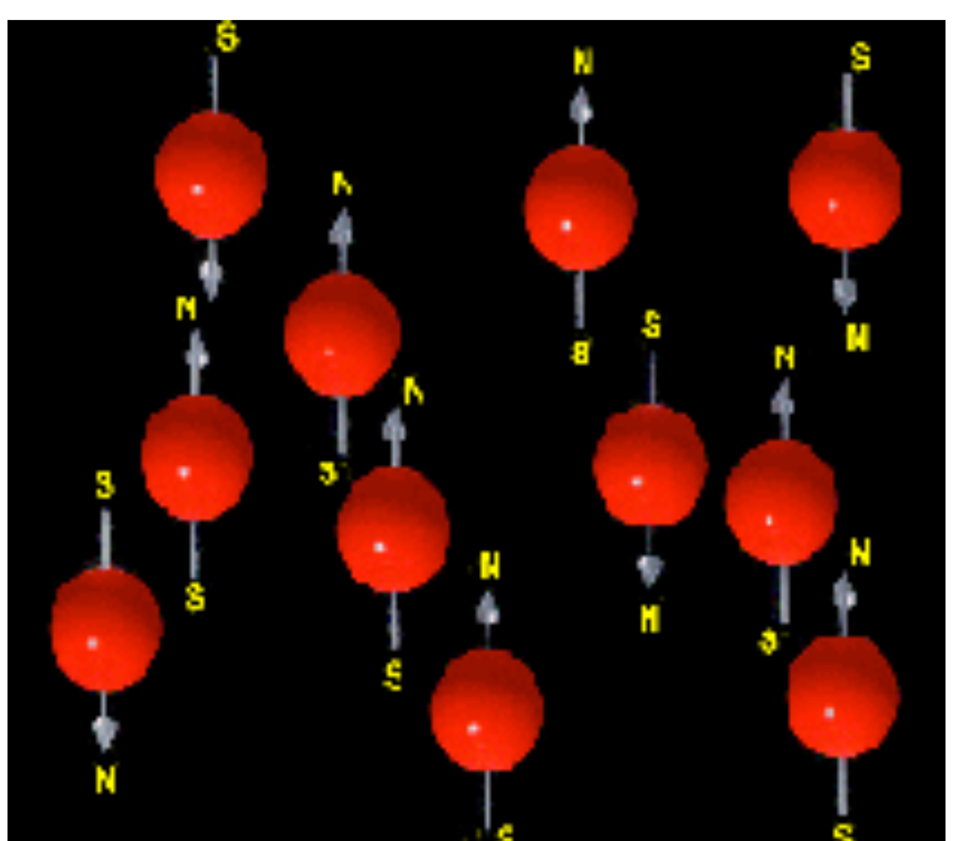
g = electron's g-factor (dimensionless number that describes the relationship between magnetic moment and gyromagnetic ratio)
μ_β = Bohr's magneton (unit of the electron's magnetic moment)
S = spin quantum number

In external magnetic field the elementary magnets orient



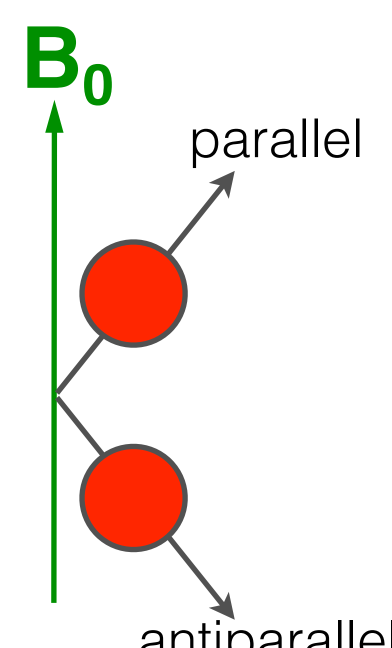
In absence of magnetic field:
random orientation of elementary magnets

Paramagnetism: magnetism emerging in external magnetic field (caused by the orientation of magnetic dipoles).

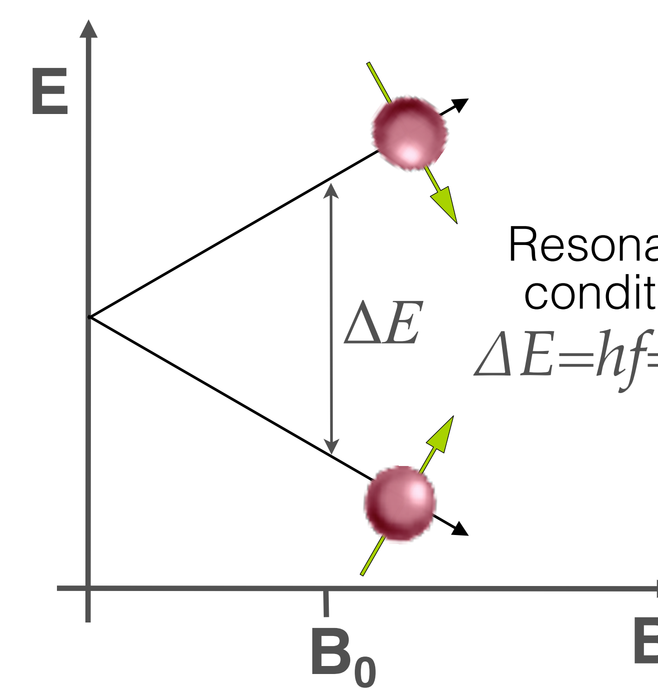


In magnetic field:

elementary magnets orient



energy levels split

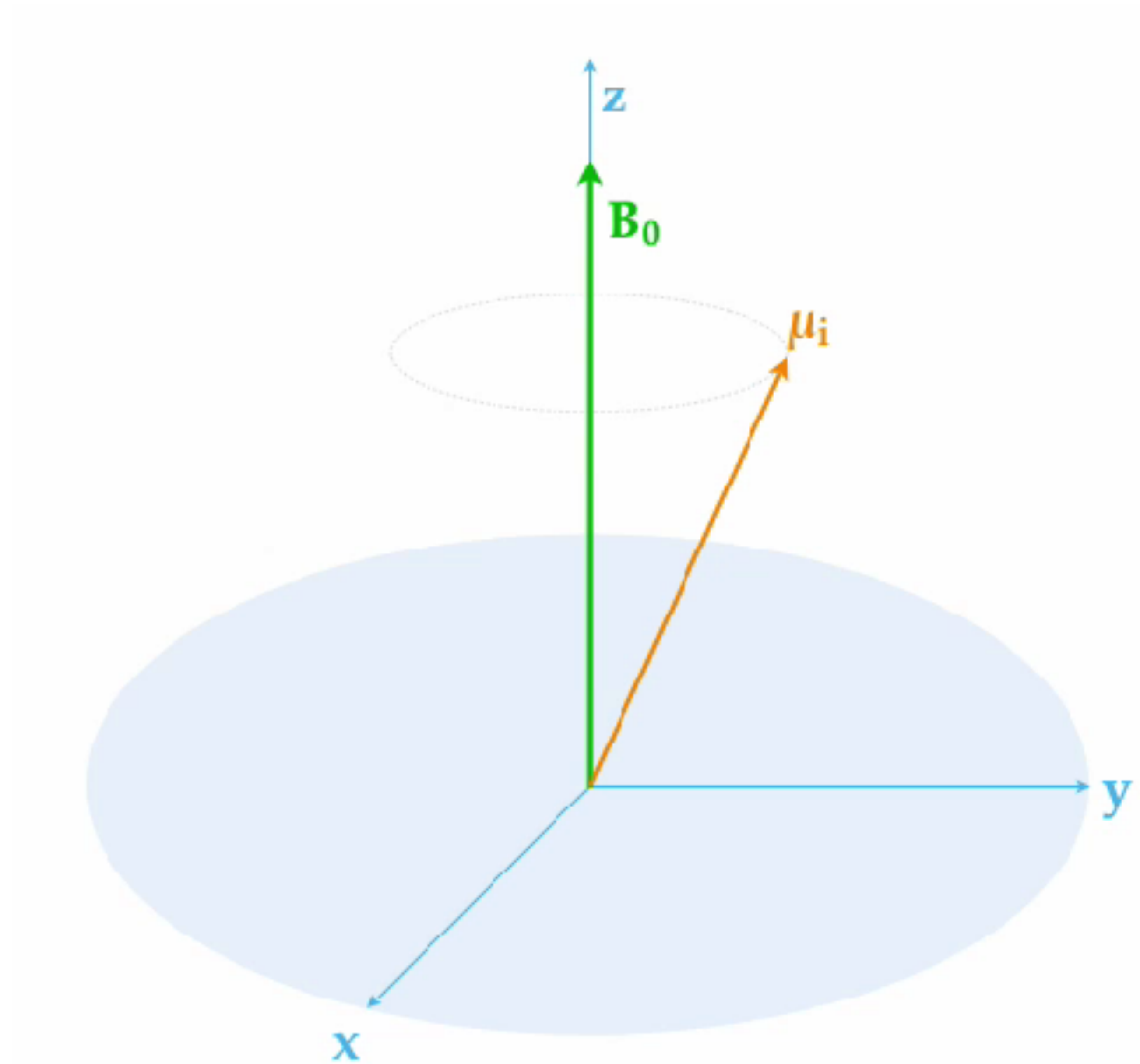


Resonance condition:
$\Delta E = hf = \mu B_0$

Edward Purcell, 1946

Oriented elementary magnets do precessional motion

Precession of a top



Precession of an elementary magnetic moment (μ_i) in magnetic field (B_0) within a reference *xyz* space

Precession or Larmor frequency:

$$\omega_0 = \gamma B_0$$

$$f_{Larmor} = \frac{\gamma}{2\pi} B_0$$

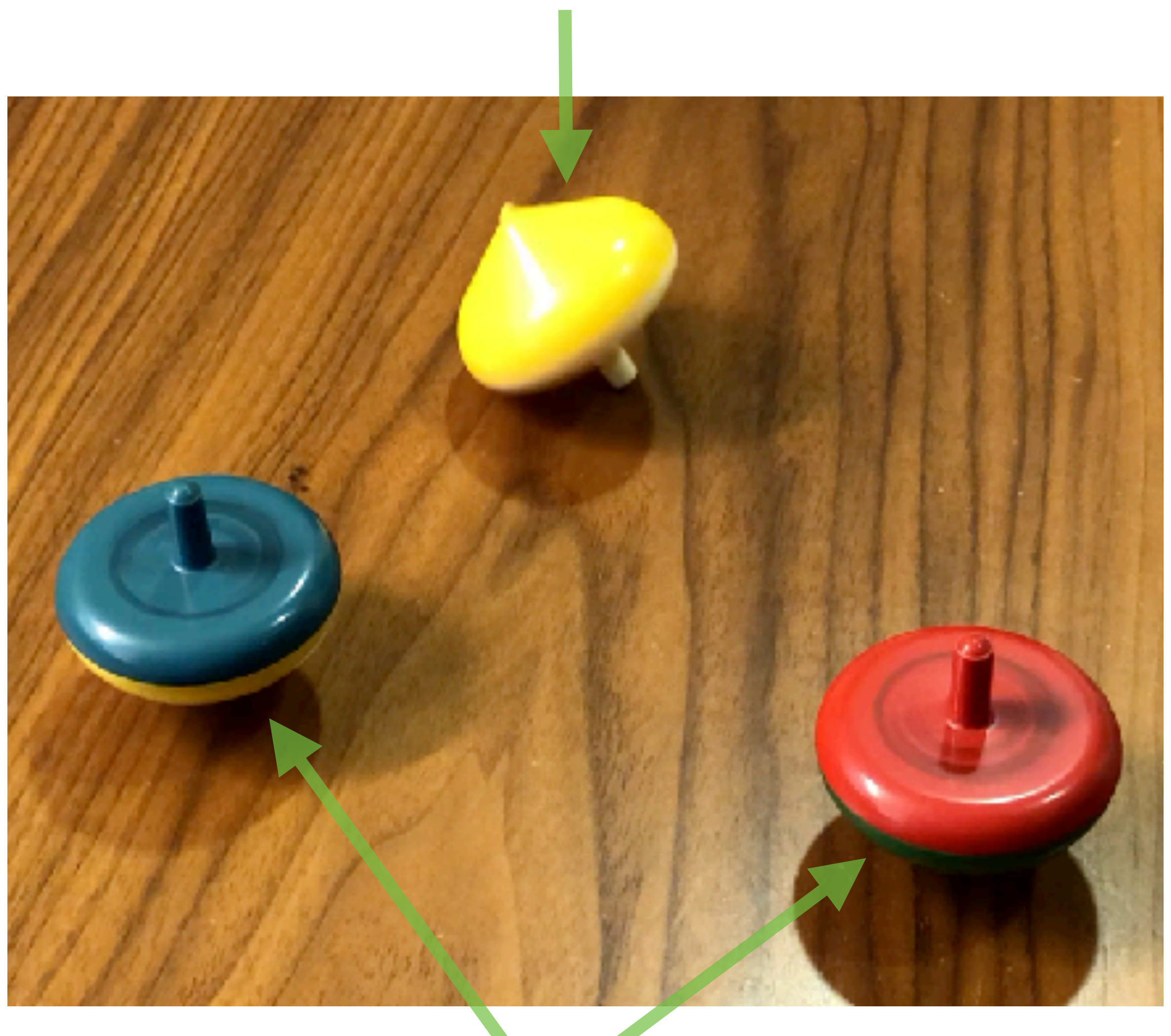
Resonance condition:

$$\Delta E = \frac{h\omega_0}{2\pi}$$

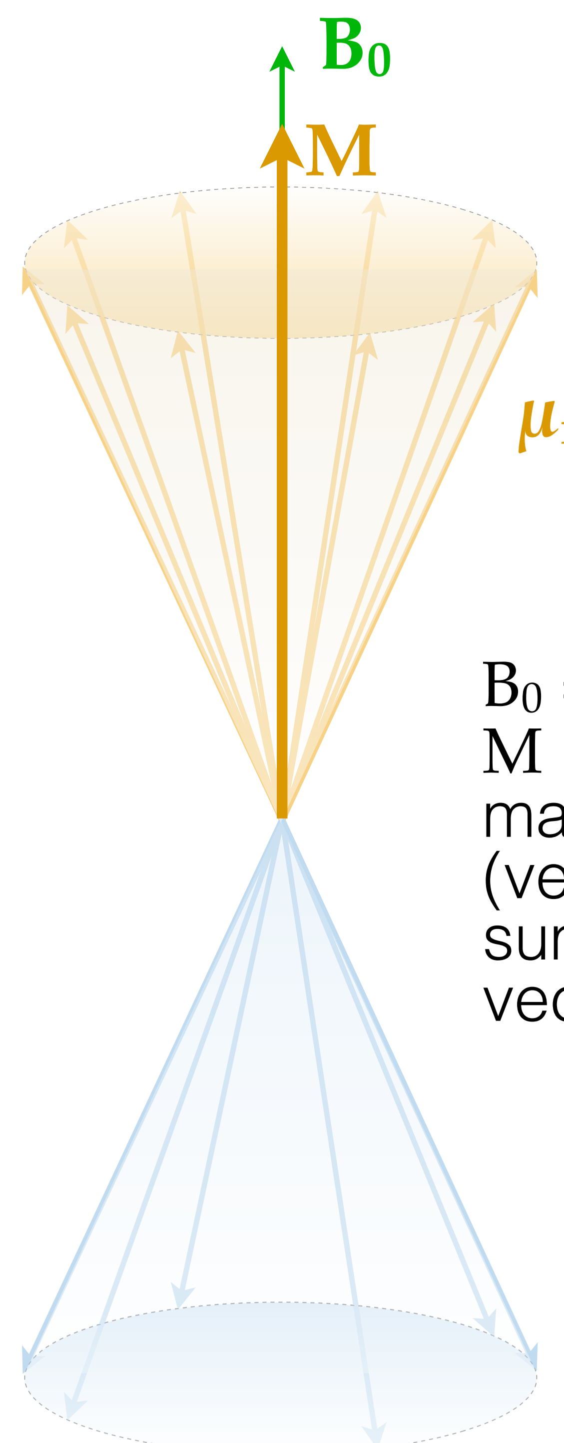
Felix Bloch, 1946

Net (macrosopic) magnetization

Due to spin access in different energy states



Low-energy state
parallel in case of proton (^1H)



High-energy state
antiparallel in case of ^1H

B_0 = magnetic field
M = net magnetization (vectorial quantity, sum of elementary vectors μ_i)

Ratio of low- and high-energy spin polulations is determined by the Boltzmann distribution:

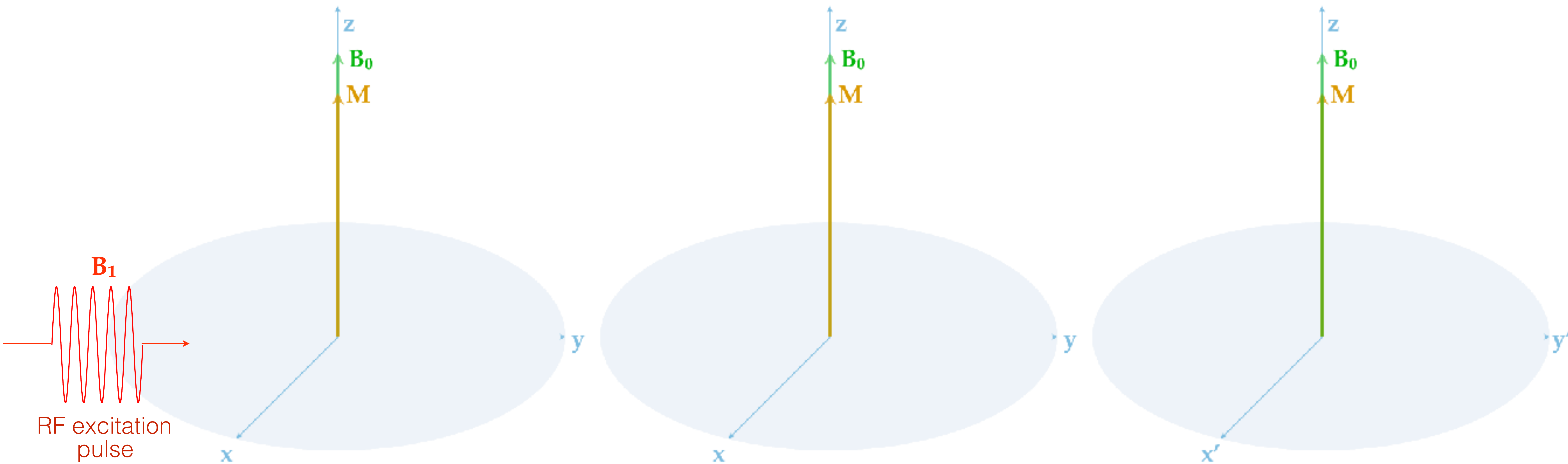
$$\frac{N_{antiparallel}}{N_{parallel}} = e^{-\frac{\Delta E}{k_B T}}$$

N.B.: magnetic field in MRI is 20-50-thousand times as strong as the earth's magnetic field.

Excitation

Resonance condition, Larmor frequency

Employed electromagnetic radiation: radiowaves (NMR, MRI), microwaves (ESR)



Excitation in the real coordinate system (x, y, z)

Concept of the rotating frame of reference: x’, y’, z coordinate system rotating around the z-axis, together with M

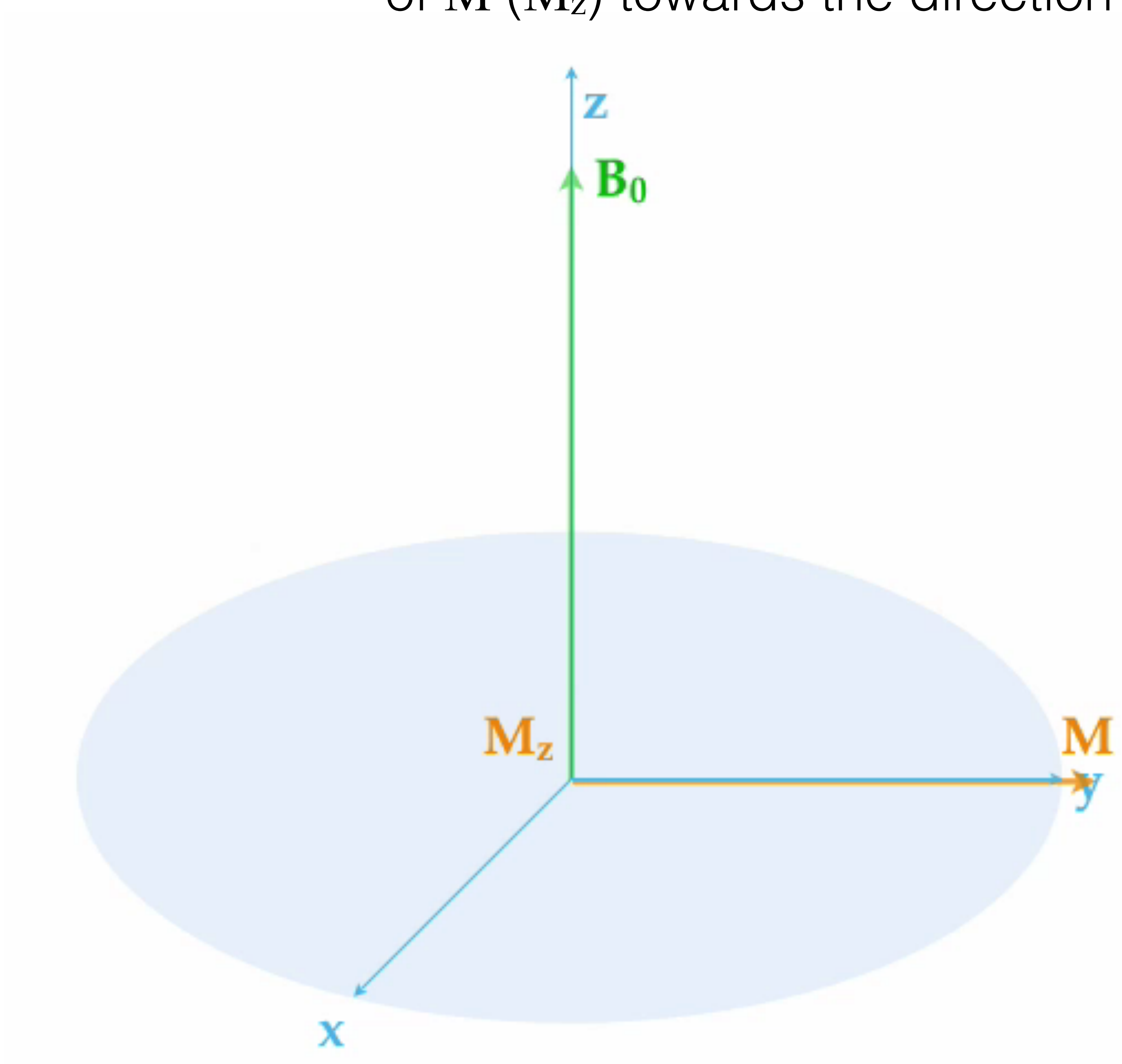
Excitation within the rotating frame of reference: the net magnetization vector (M) is tilted from its oriented state into the *xy*-plane (transverse plane)

B_0 = magnetic field
M = net magnetization
B_1 = irradiated radio frequency wave

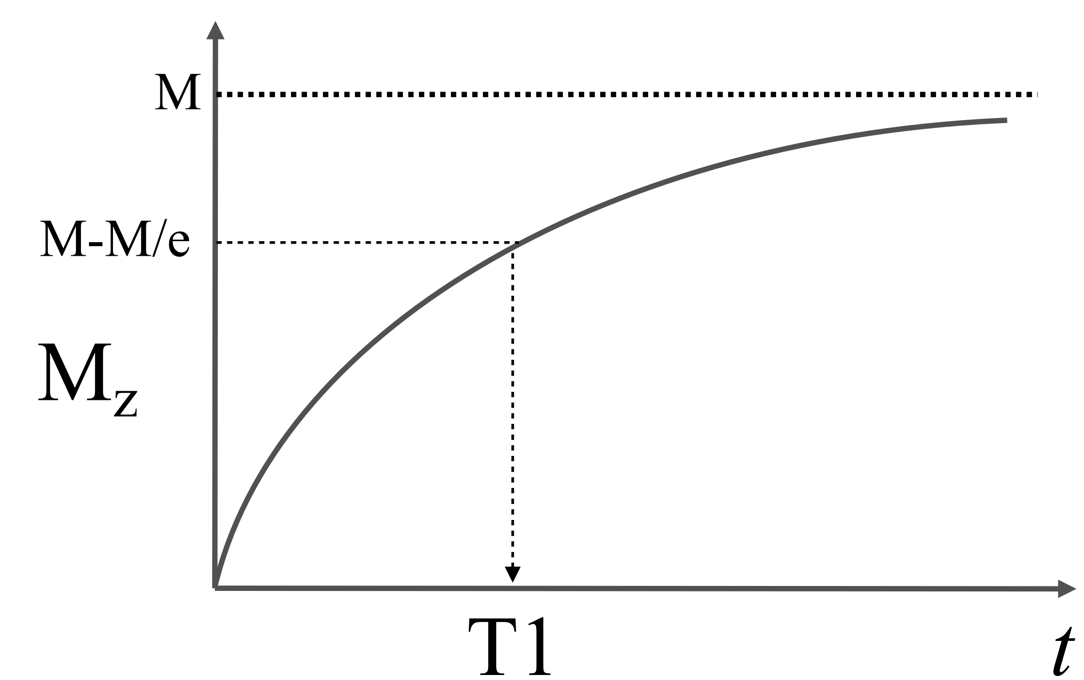
Spin-lattice relaxation

T1 or longitudinal relaxation

T1 relaxation process: return (relaxation) of the z-axis vectorial component of M (M_z) towards the direction of the external magnetic field



M_z: z-axis vectorial component of M



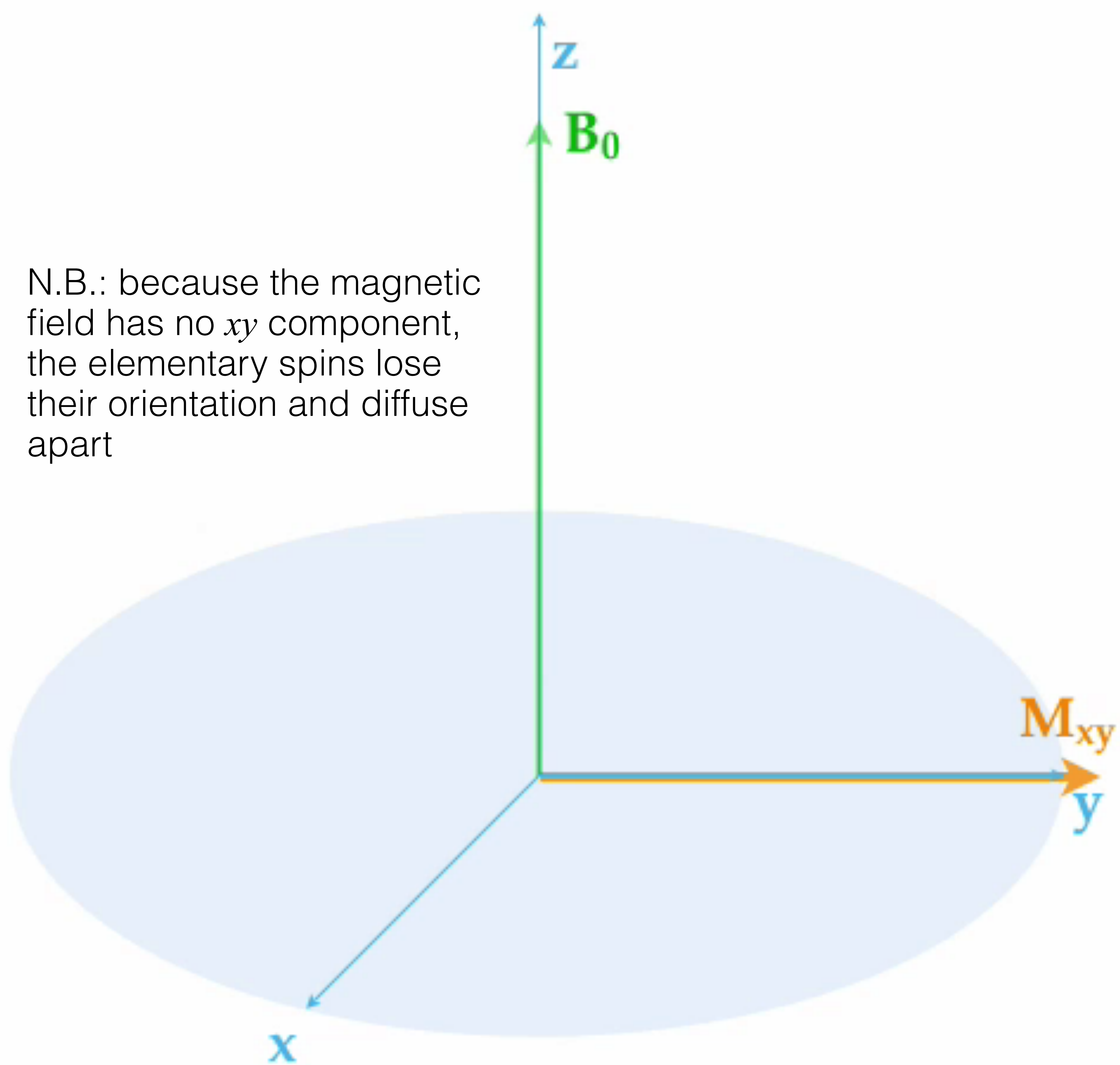
T1 relaxation time:
depends on interaction
between elementary magnet (proton)
and its environment (lattice)

Spin-spin relaxation

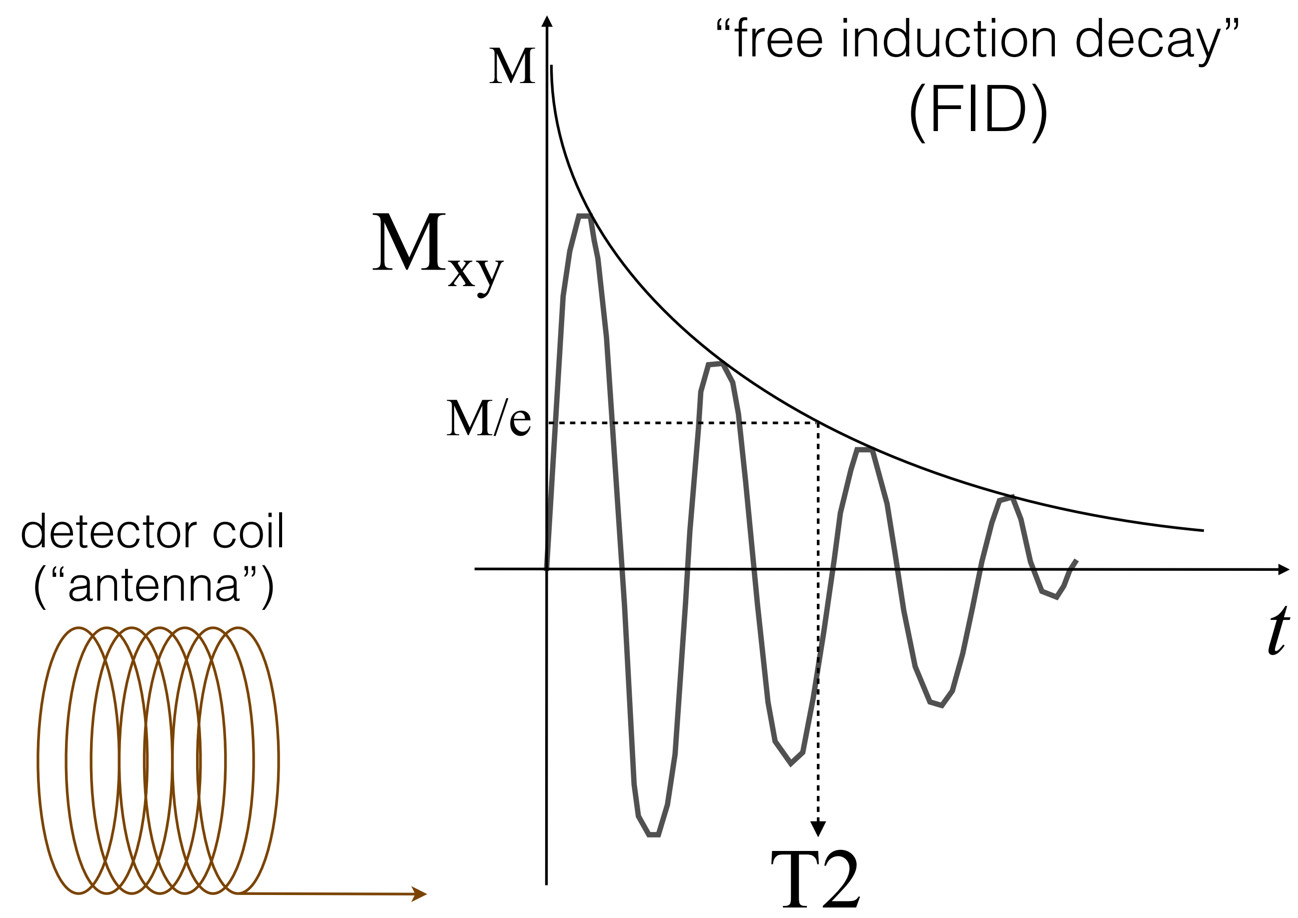
T2 or transverse relaxation

T2 relaxation process: diffusion (spreading) of the elementary magnetic moments (μ_i) resulting in the decay of the transverse(xy)-plane vectorial component of $\mathbf{M}$ ($\mathbf{M}_{xy}$)

N.B.: because the magnetic field has no xy component, the elementary spins lose their orientation and diffuse apart



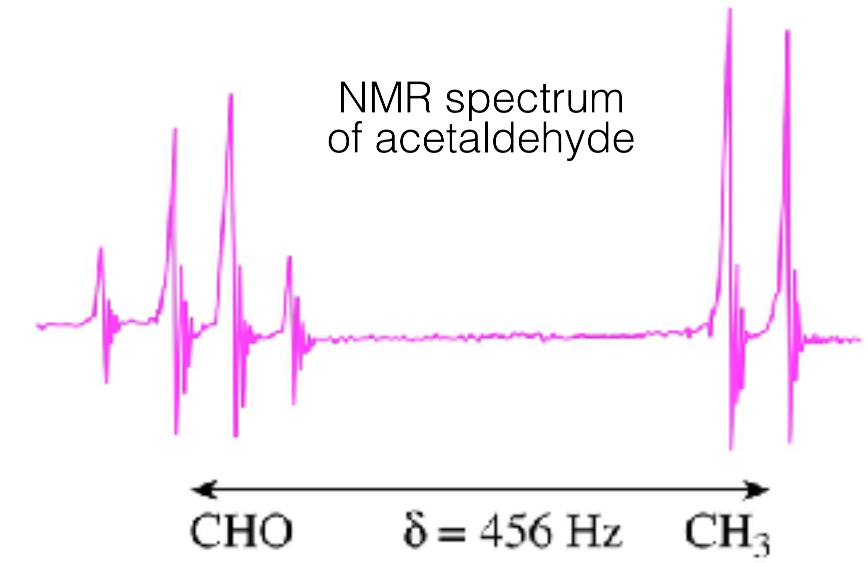
M_{xy}: xy-plane vectorial component of M



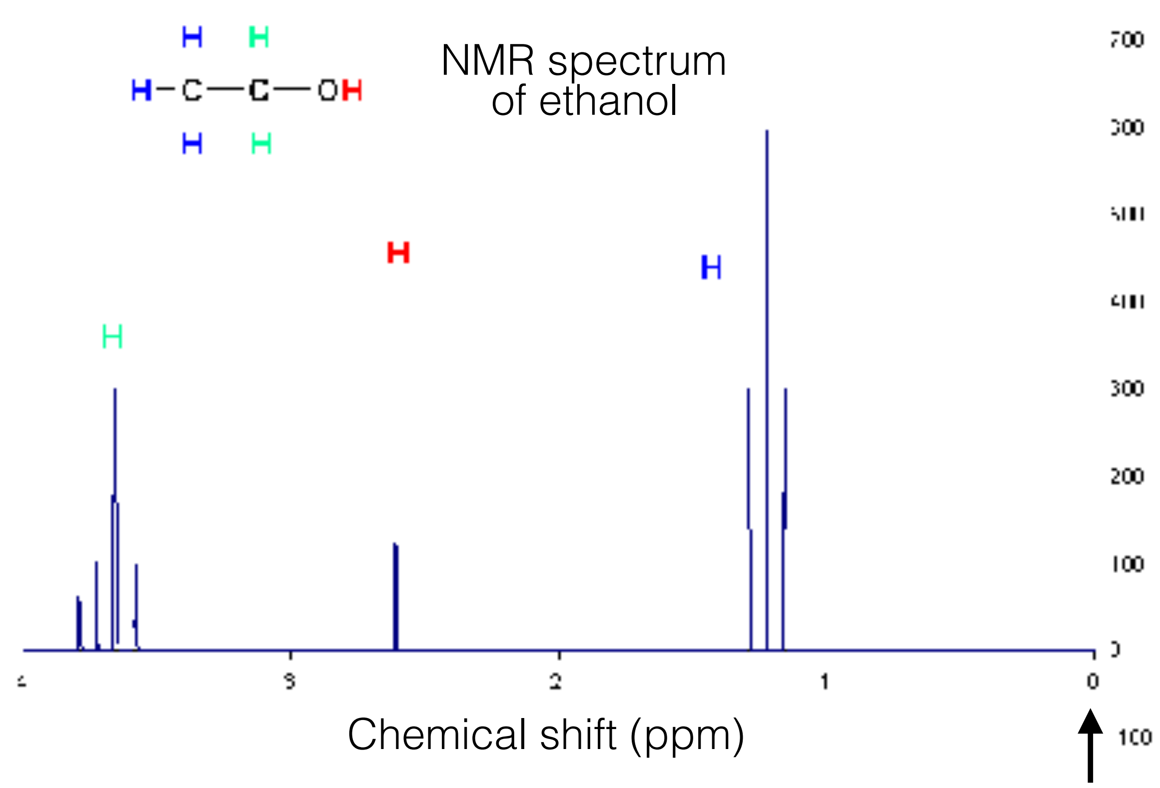
T2 relaxation time:
depends on interaction between elementary magnets (spins, protons);
process occurs in the transverse (xy) plane

NMR spectroscopy

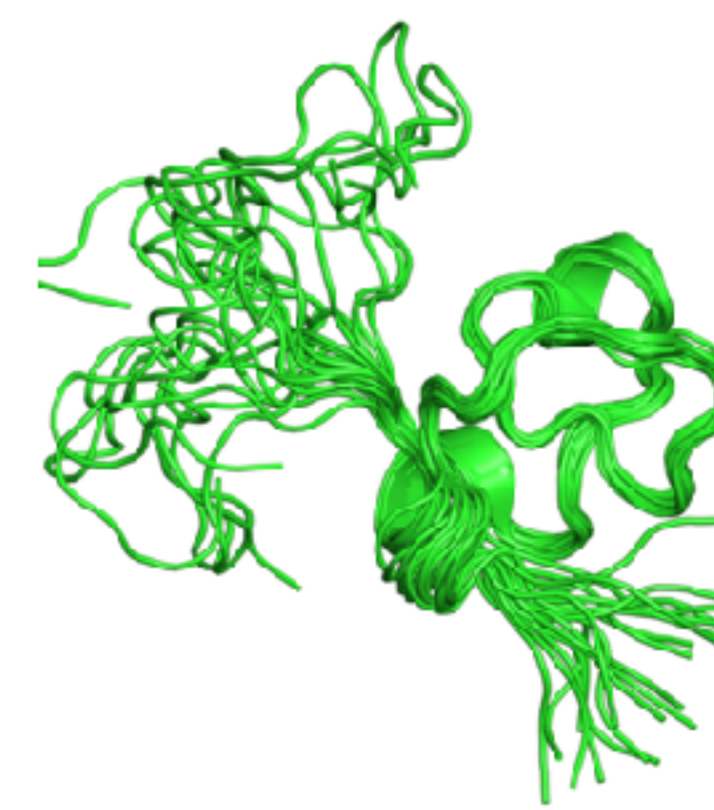
- NMR spectroscopy or Magnetic Resonance Spectroscopy (MRS)
- Spectroscopic method for measuring the local magnetic field around atomic nuclei. We measure the resonance frequencies of the nuclei positioned in the magnetic field.
- NMR spectrometer: superconducting magnet (cooled with liquid He), large magnetic field (spectral resolution is proportional to field strength).
- NMR spectrum: intensity of absorbed electromagnetic radiation as a function of frequency.
- The area under the "NMR-line" is proportional to the number of absorbing atomic nuclei.
- The electron cloud distorts the local magnetic field, therefore the frequency condition is shifted: "chemical shift". Chemical structure determination is possible.
- Protein NMR: possibility of measuring dynamics and the detection of disordered protein elements



900 MHz NMR, 21.1 T magnet



Reference (TMS, tetramethylsilane)

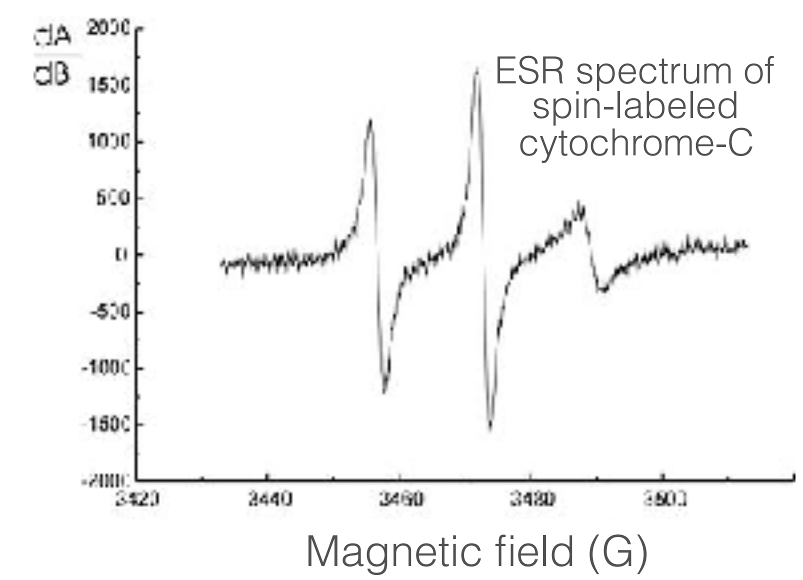


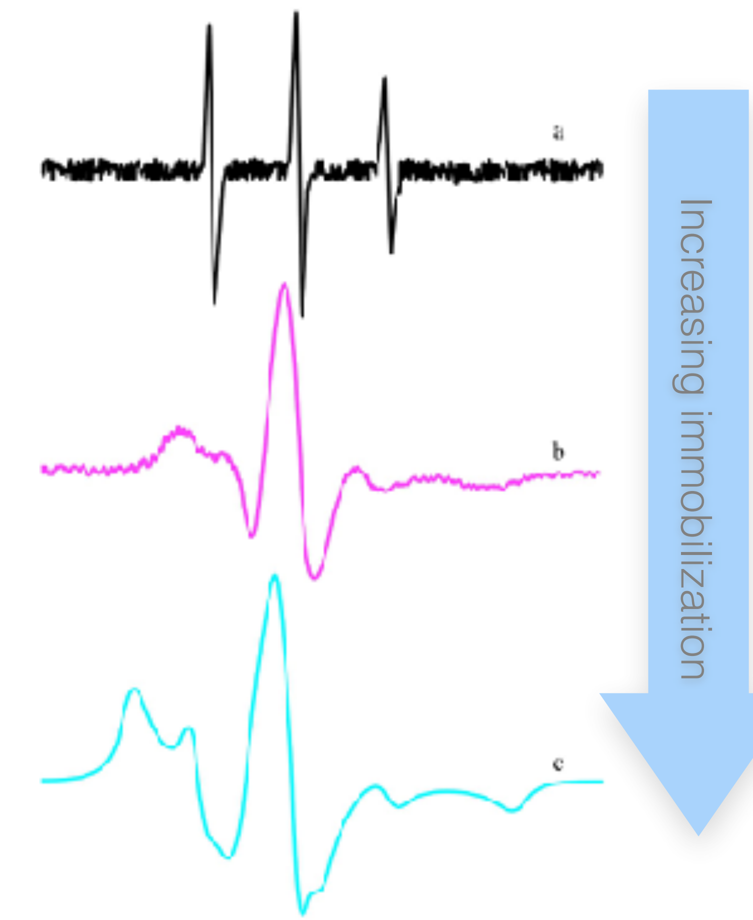
Somatomedin B domain (superimposed structures)

ESR spectroscopy

- Electron spin resonance (ESR) or electron paramagnetic resonance (EPR) spectroscopy.
- Specteroscopic method for investigating materials containing unpaired electron.
- EPR spectrum: intensity of electromagnetic radiation as a function of magnetic field.
- Magnetic field is lower, but radiation frequencies are greater (microwave) than in NMR.
- Spin-labeling: attachment of a chemical containing a stable unpaired electron. Site-directed spin labeling: spin labeling of reactive (mostly -SH) residues introduced into the targeted protein by molecular biological tools (point mutation).
- Dynamics of rotational motion can be measured ub the 10^{-4} - 10^{-2} s time range.

Jevgenyij Zavoisky, 1944

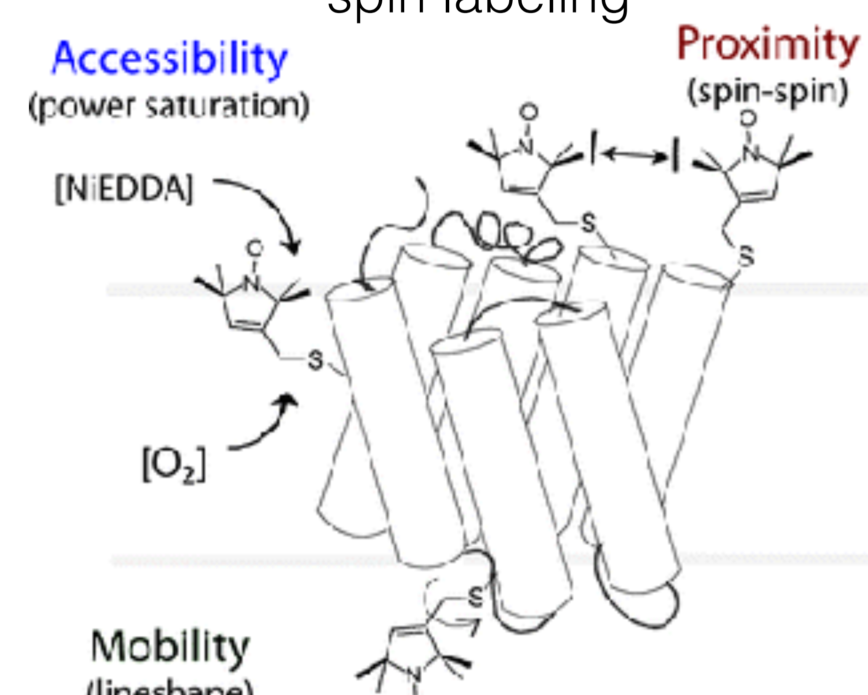




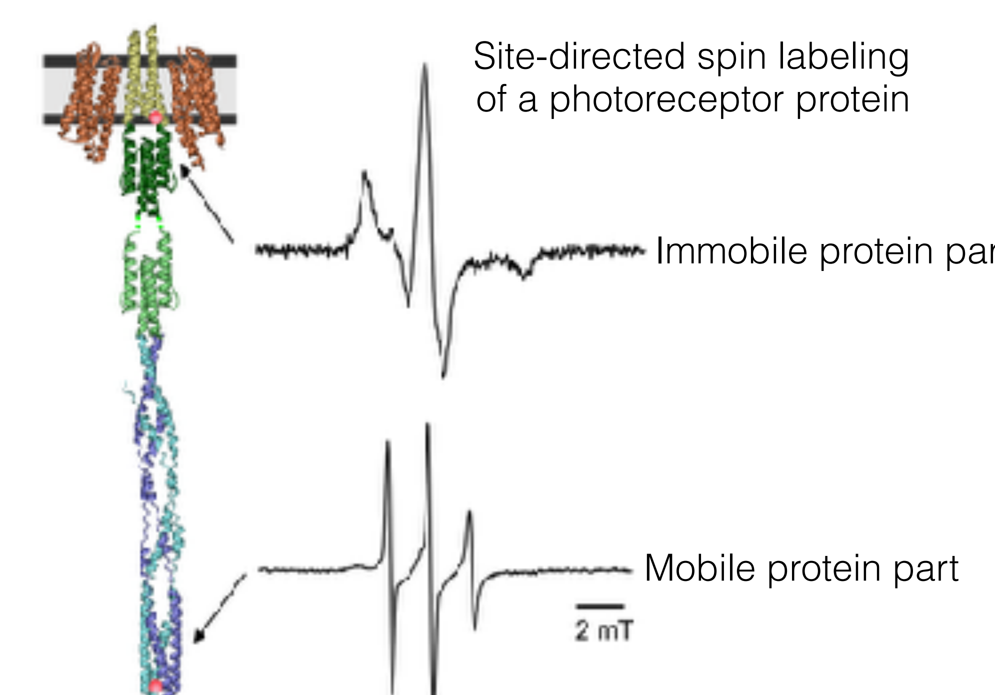
Effect of immobilization on the ESR spektrum

ESR spectroscopy workstation

Site-directed spin labeling



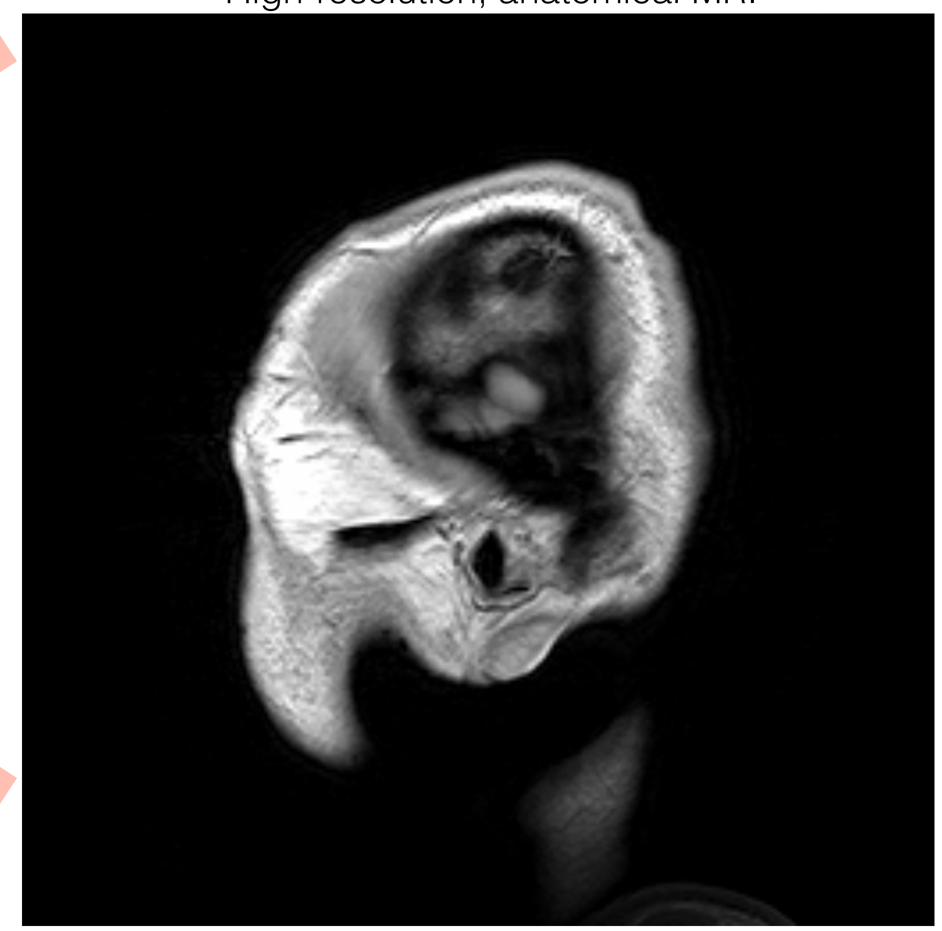
Site-directed spin labeling of a photoreceptor protein



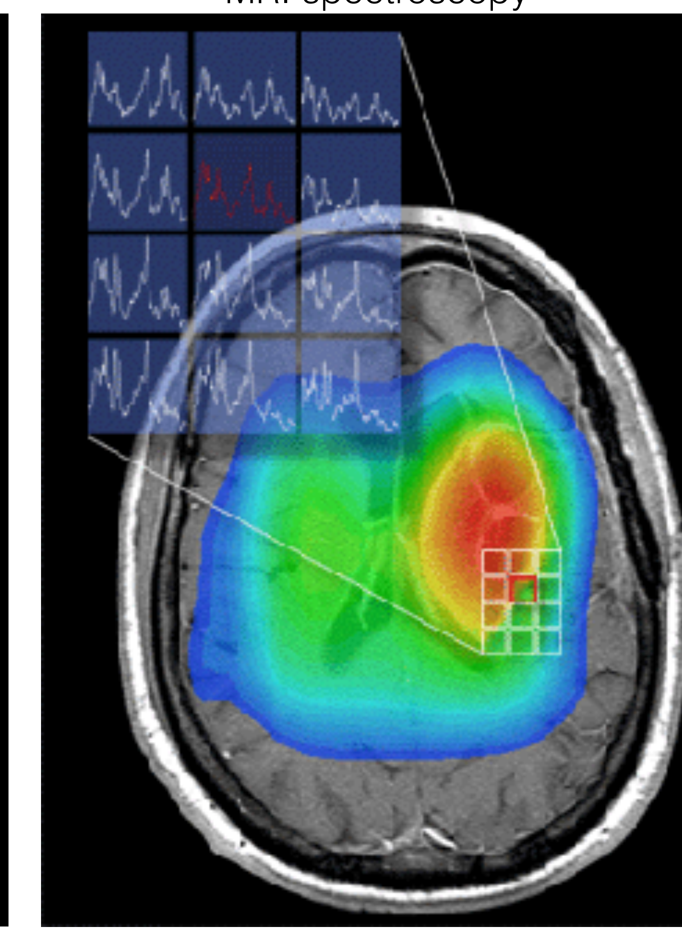
MRI is a revolutionary device

Non-invasive

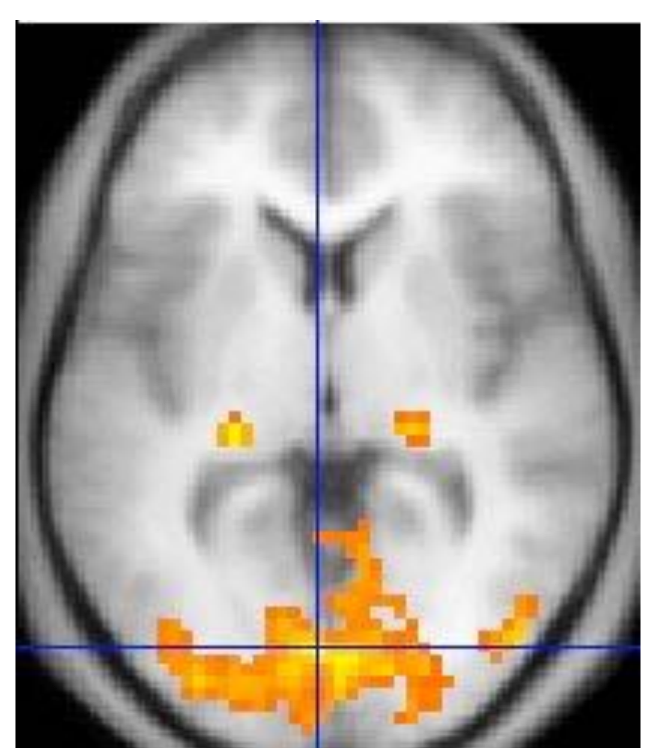
High-resolution, anatomical MRI



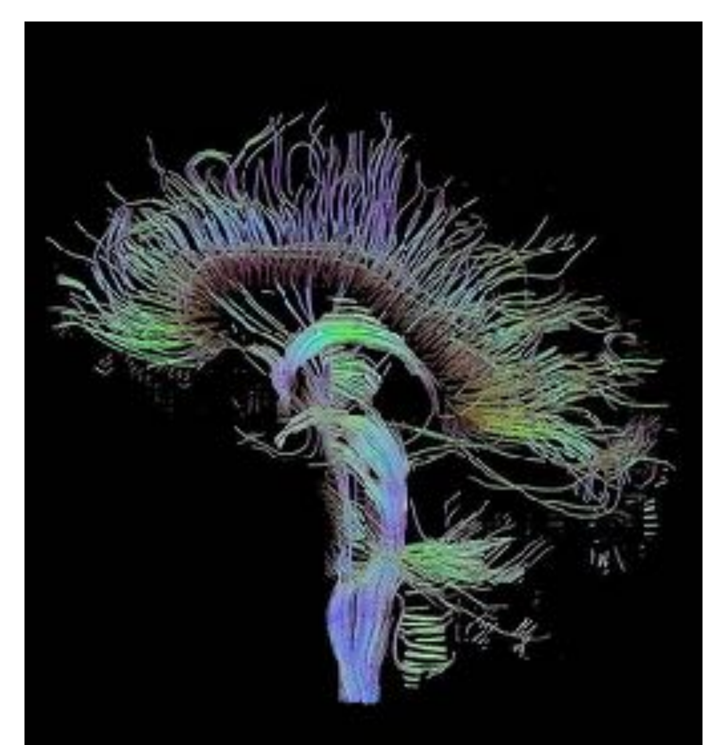
MRI spectroscopy



MRI angiography



Functional MRI (fMRI)



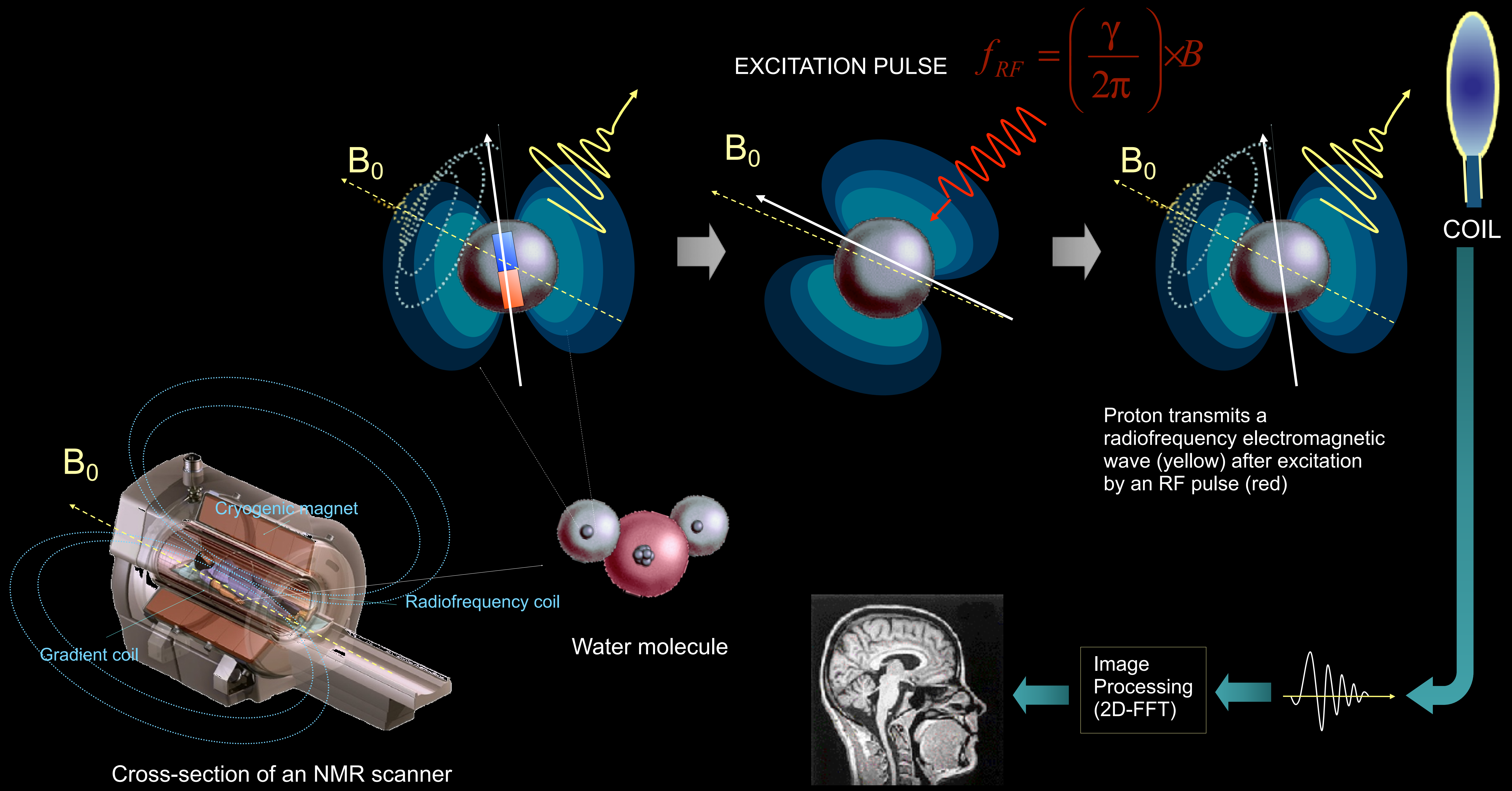
Diffusion MRI (tractography)

Musculoskeletal MRI

MRI History

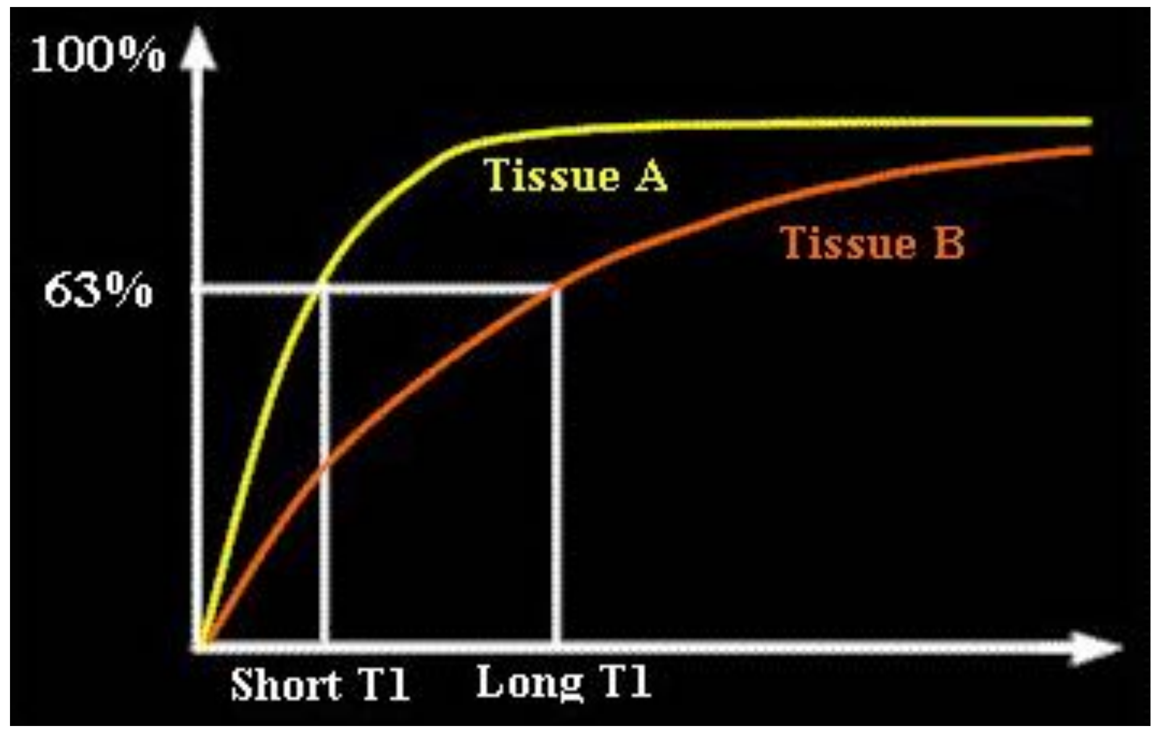
- 1970 - Raymond Damadian: T1 and T2 relaxations of neoplastic and normal tissues are different.
- 1972 - Raymond Damadian: US patent
- 1973 - Paul Lauterbur: 2D MR imaging method
- 1974 - Peter Mansfield: 3D MR imaging method
- 1977 - Raymond Damadian: first MR scanner ("focused field" method)
- 2003 - Nobel-prize: Paul Lauterbur, Peter Mansfield
- NMR/MRI: method which has received the most Nobel-prizes (7)
  Otto Stern (1942), Isidor Rabi (1944), Felix Bloch, Edward Purcell (1952), Norman Ramsey (1989), Richard Ernst (1991), Kurt Wüthrich (2002), Paul Lauterbur, Peter Mansfield (2003)

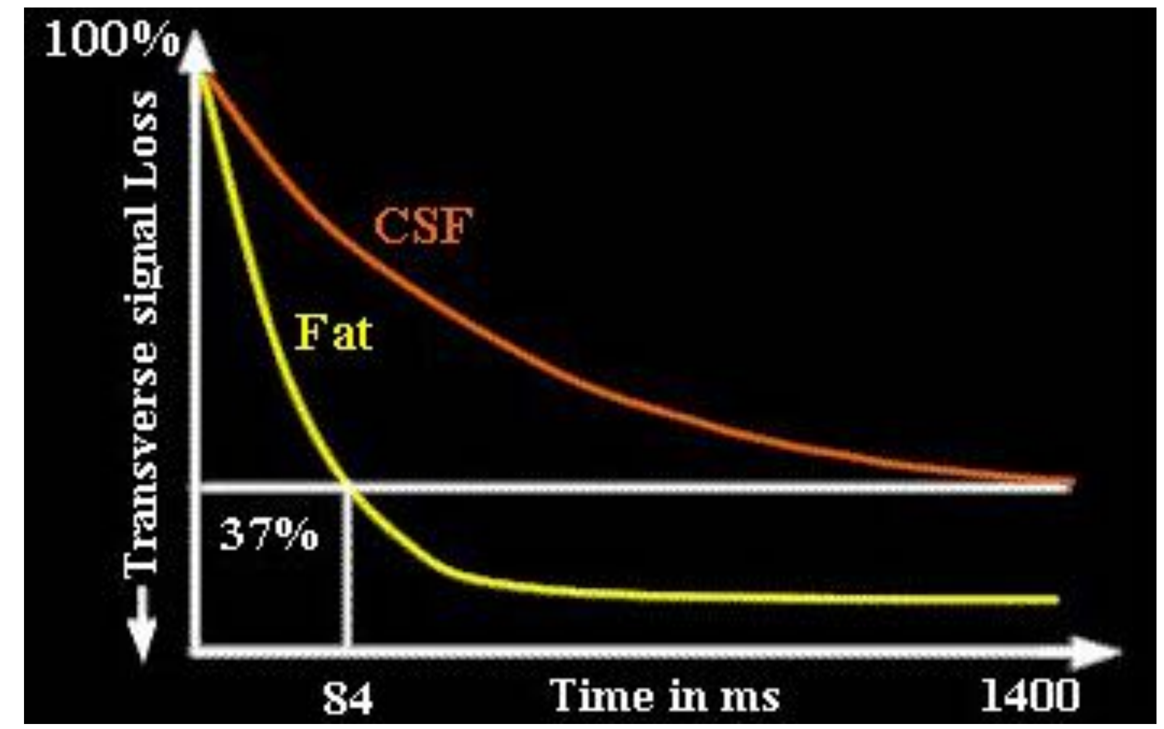
MRI: the human body is macroscopically magnetized

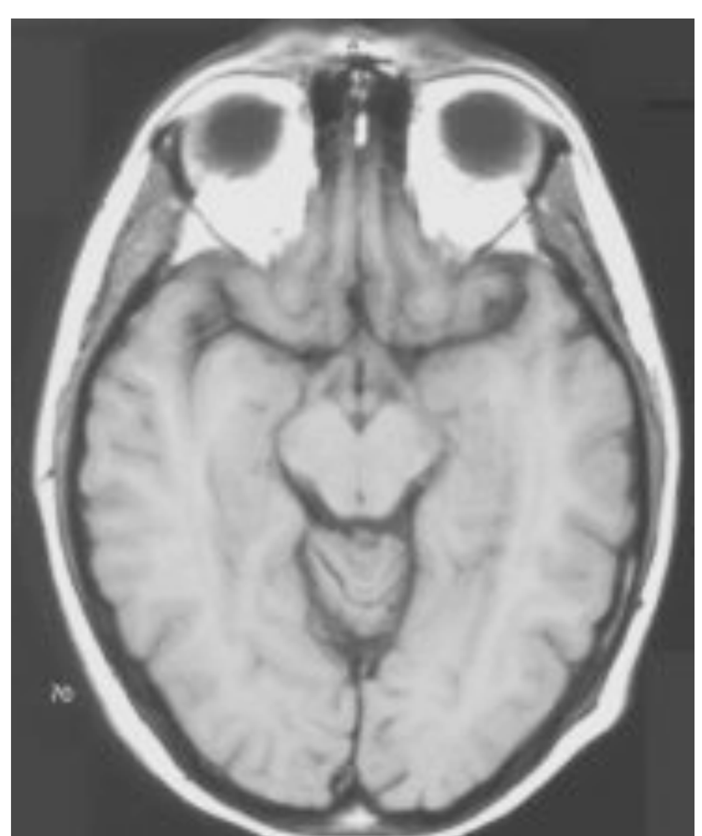


MRI 1: contrast

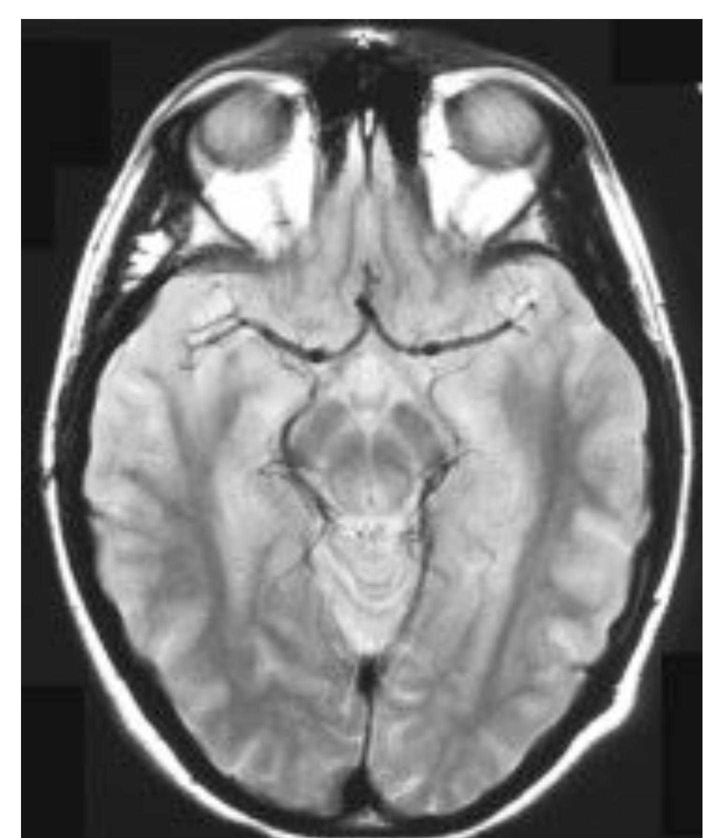
Color contrast based on spin density (proton density, PD) and relaxation times (T1, T2)



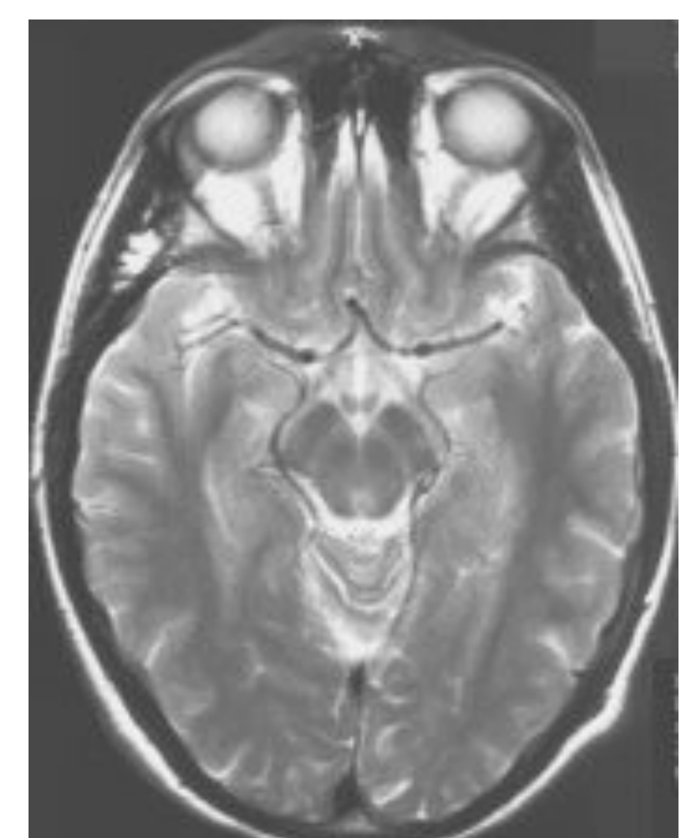




T1-weighting



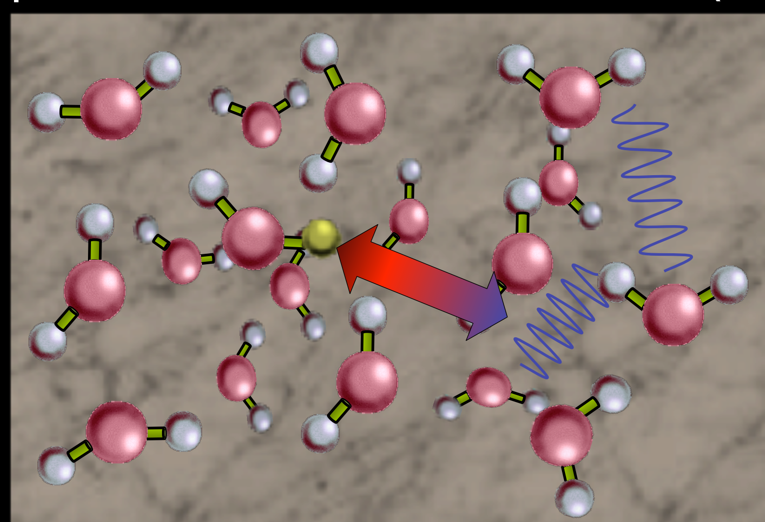
proton density-weighting



T2-weighting

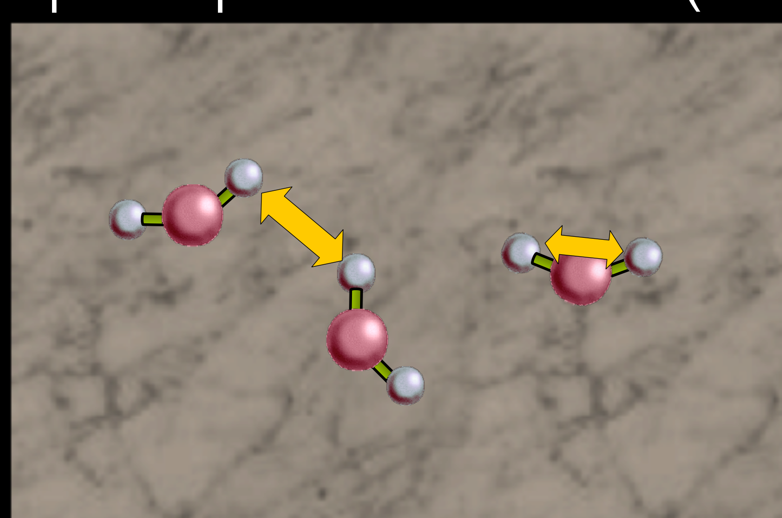
Relaxation-time based contrast mechanisms

Spin-lattice relaxation (T1)

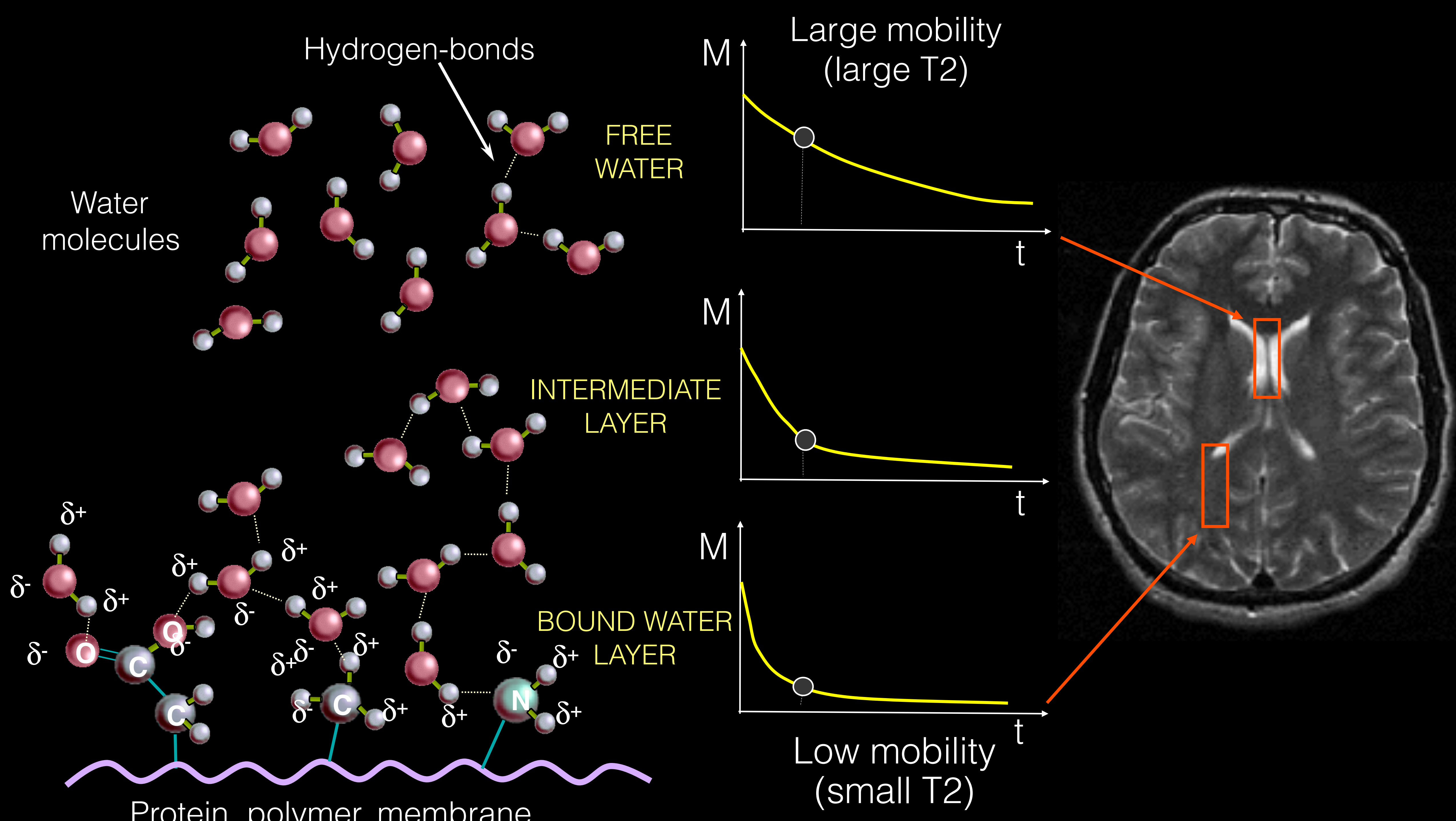


- Restoration of longitudinal magnetization
- Energy transfered to lattice

Spin-spin relaxation (T2)

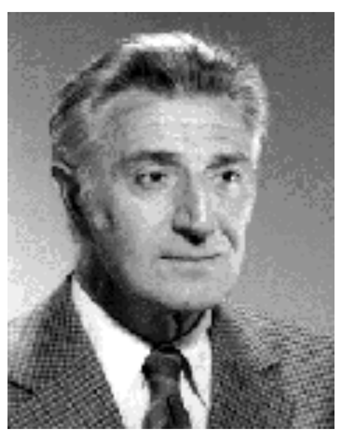


- Dephasing of transverse magnetization
- Energy transferred between spins

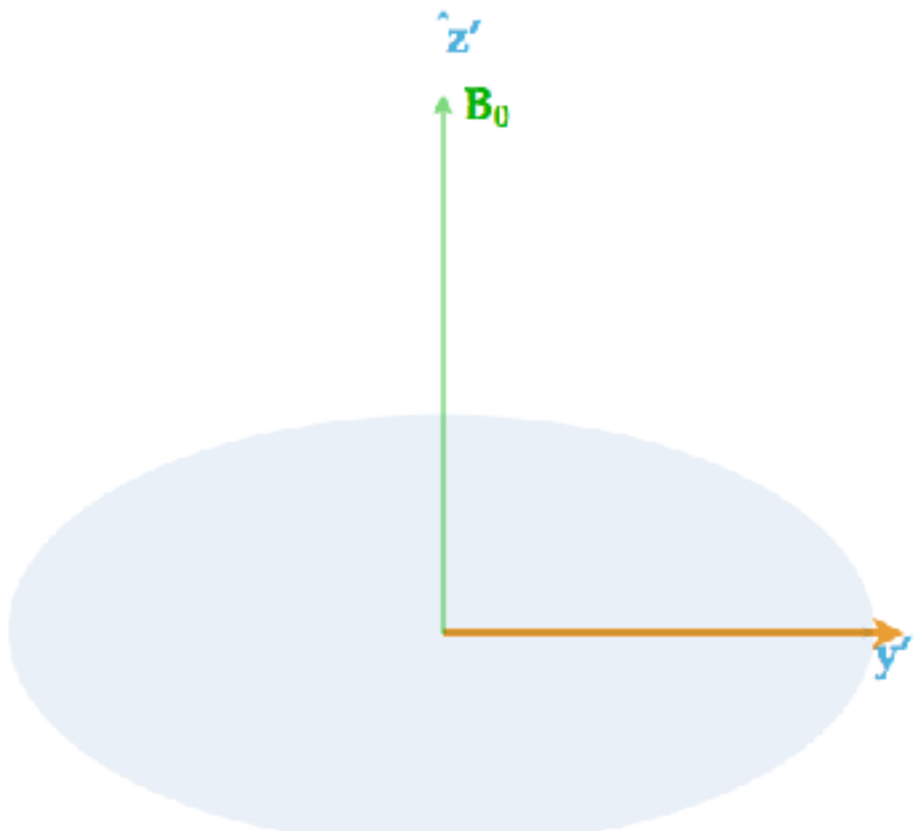


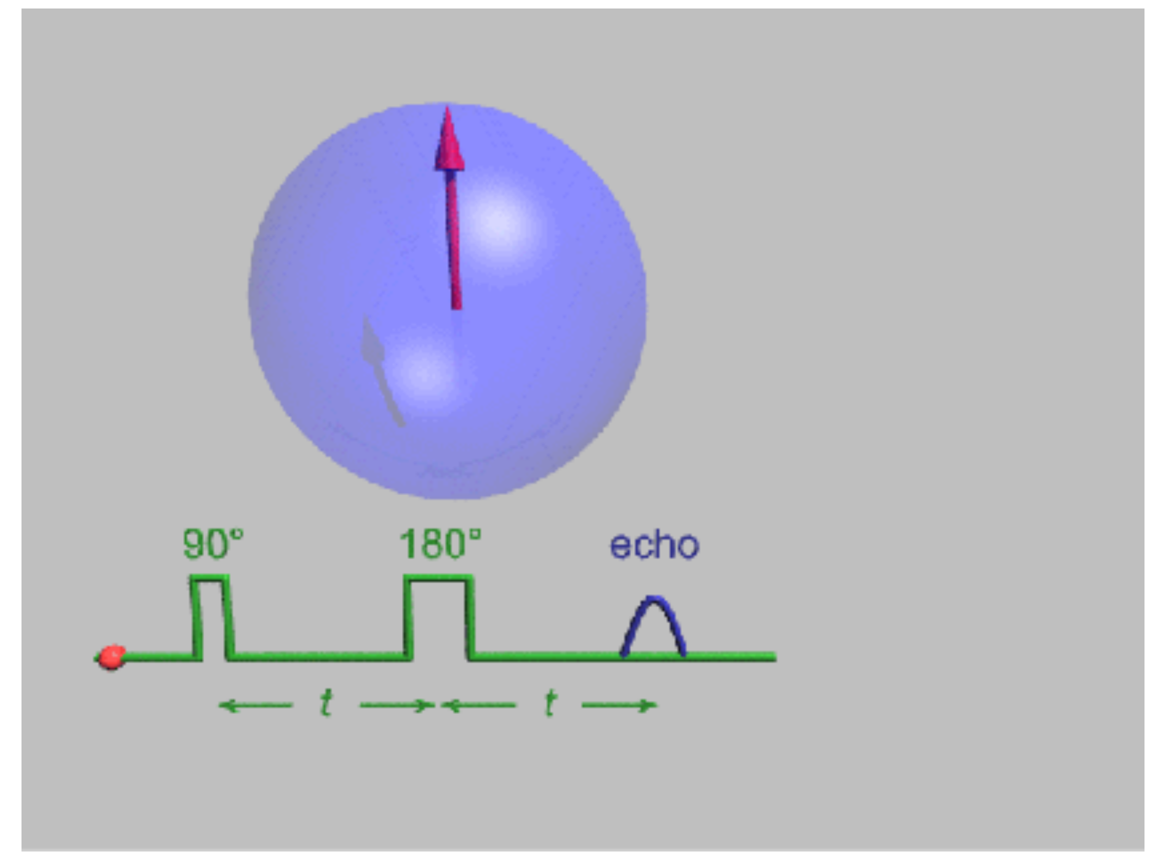
Measuring relaxation time: the spin-echo experiment

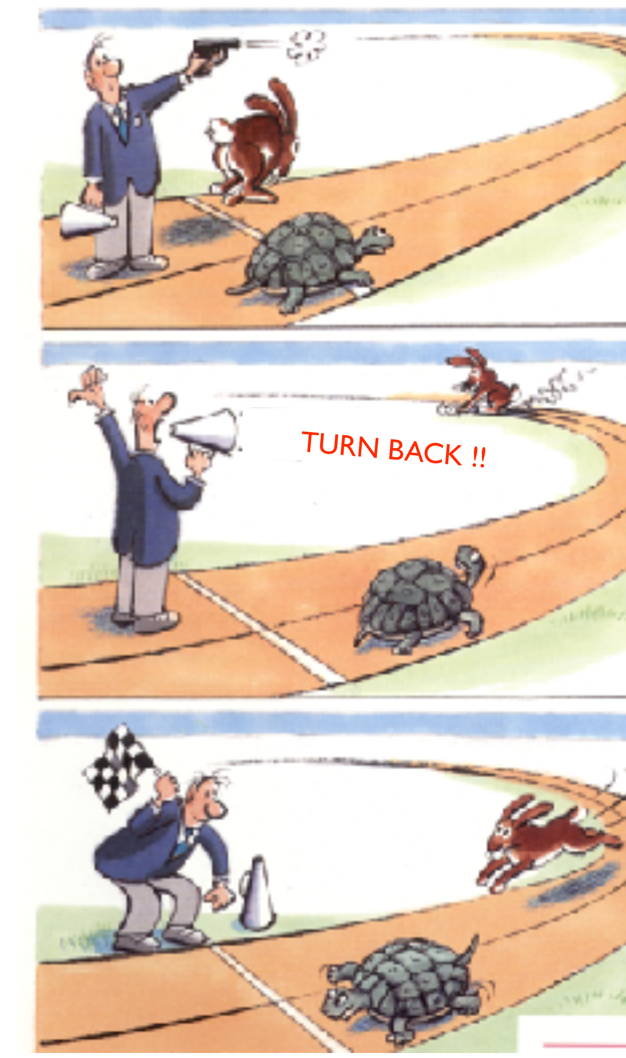
Repeating excitation, refocusing and “echo” pulses: spin-echo sequence

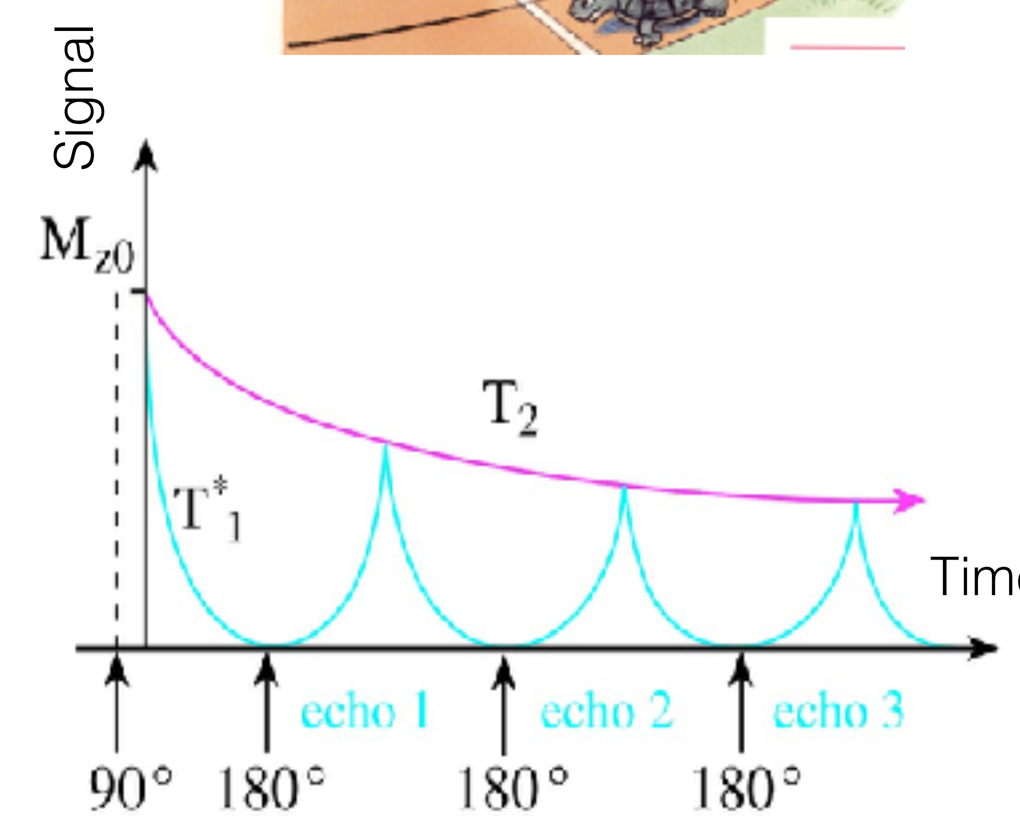


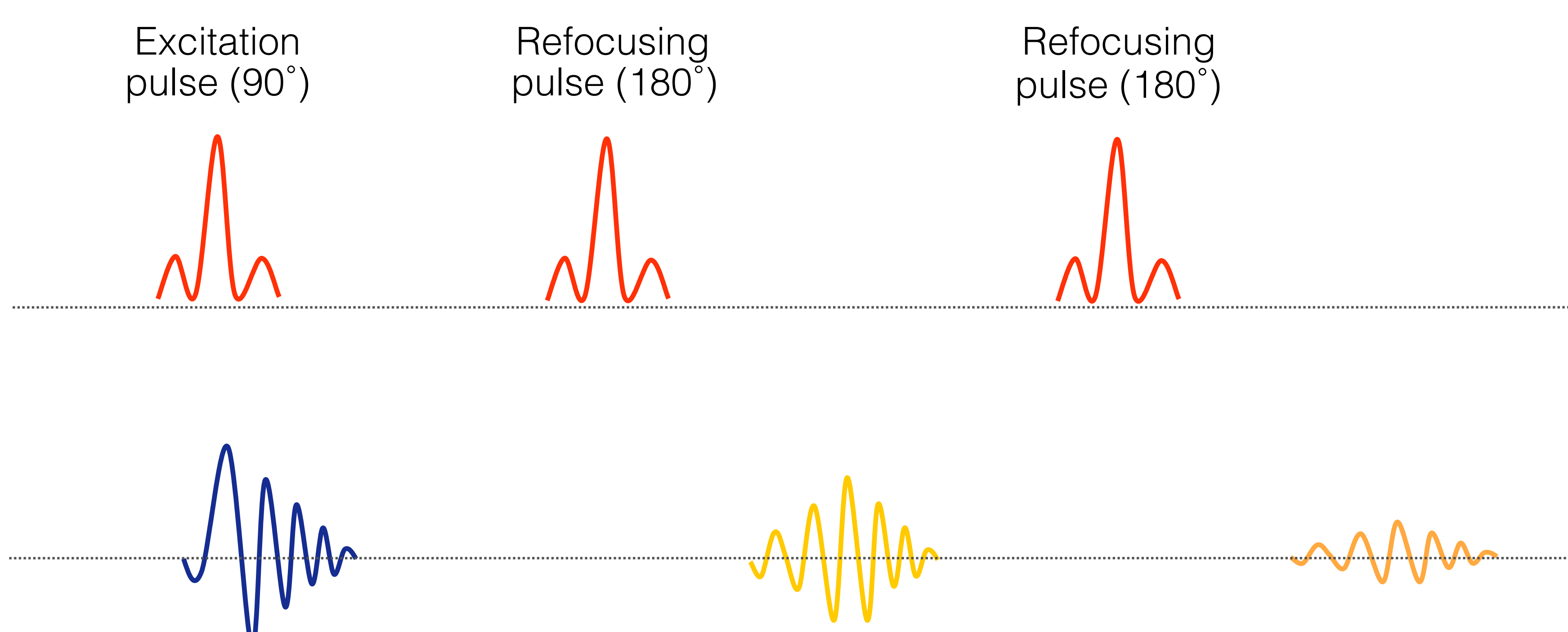
Erwin Hahn, 1949





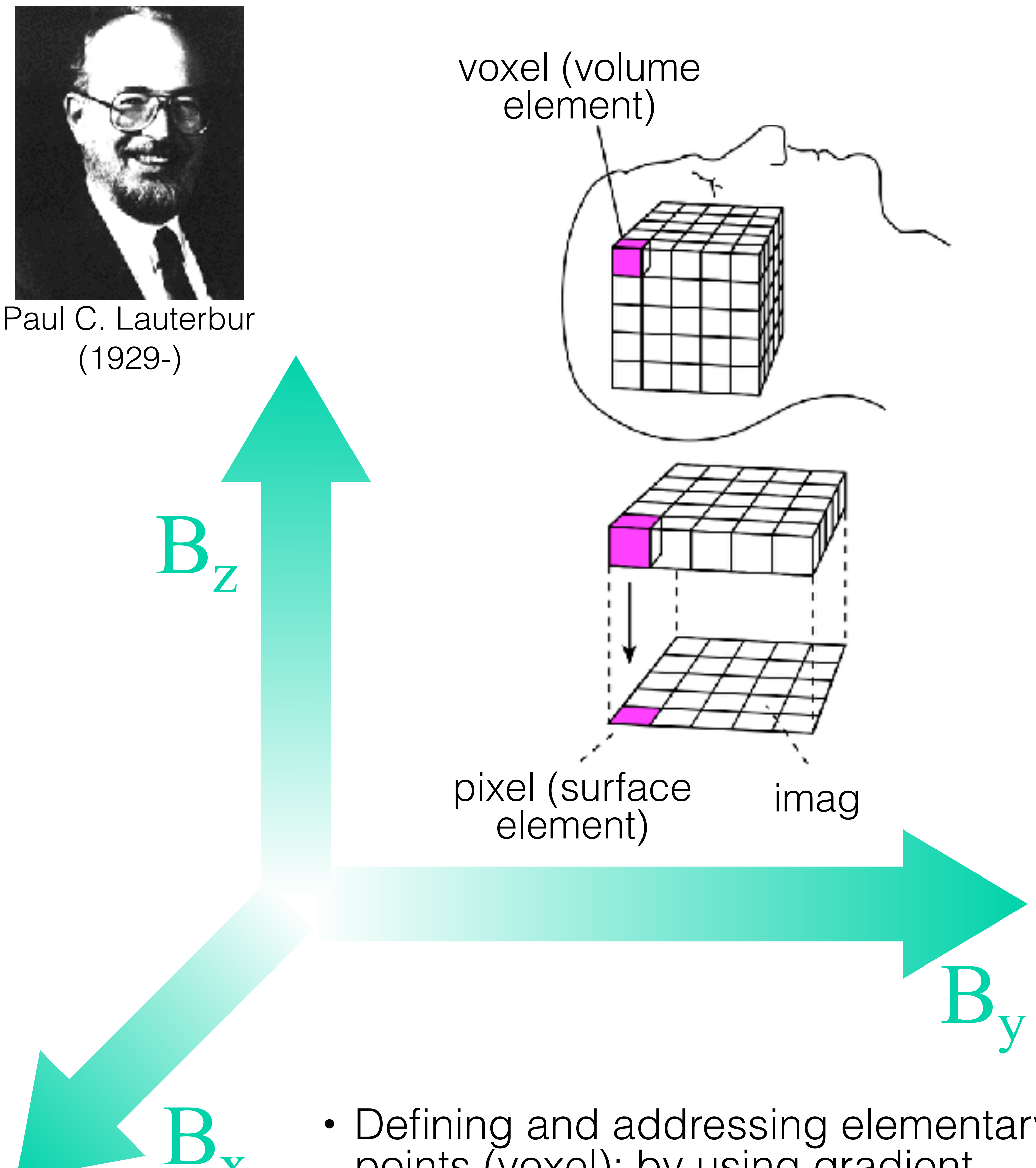


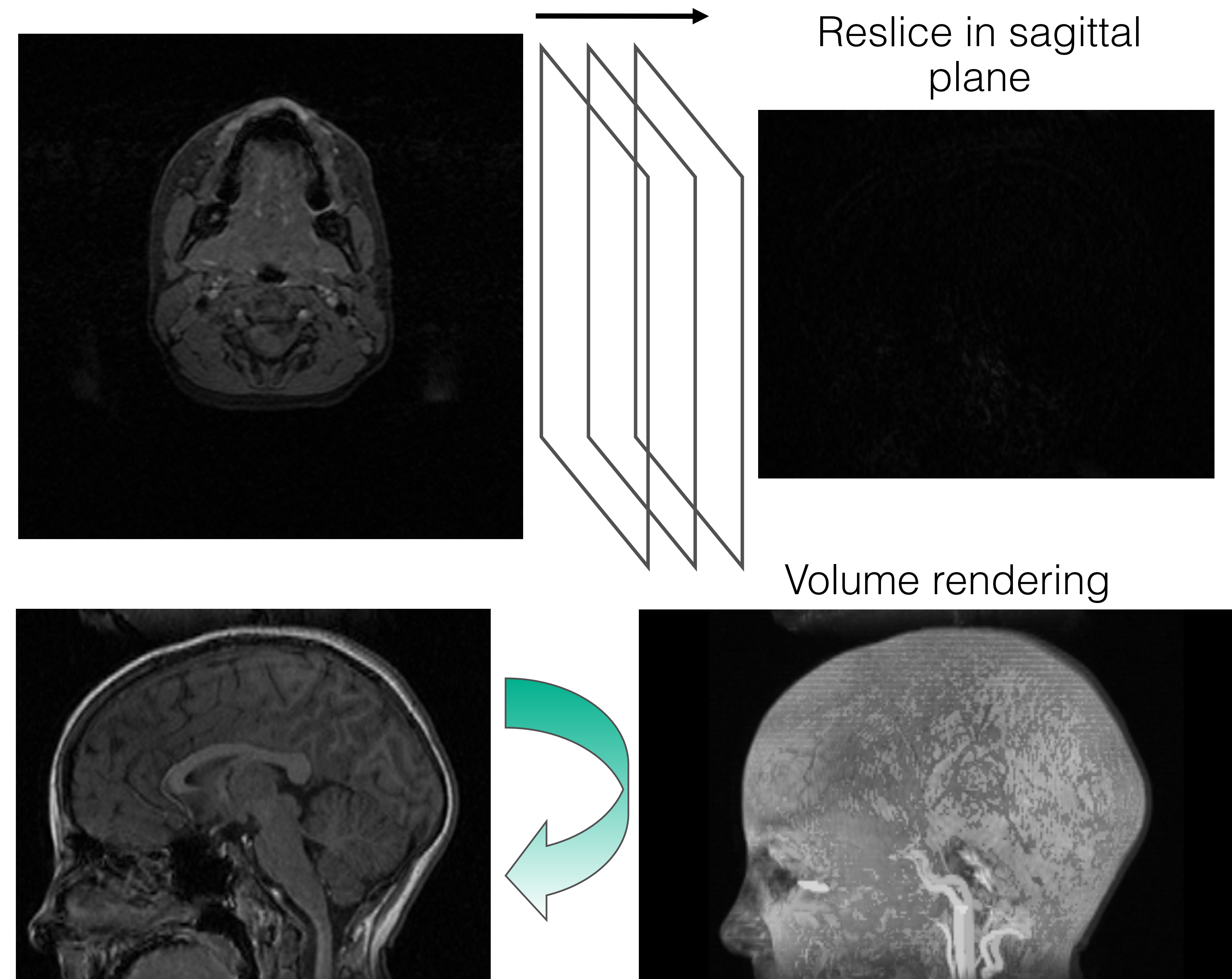




Knocking sounds in MRI: pulse generation

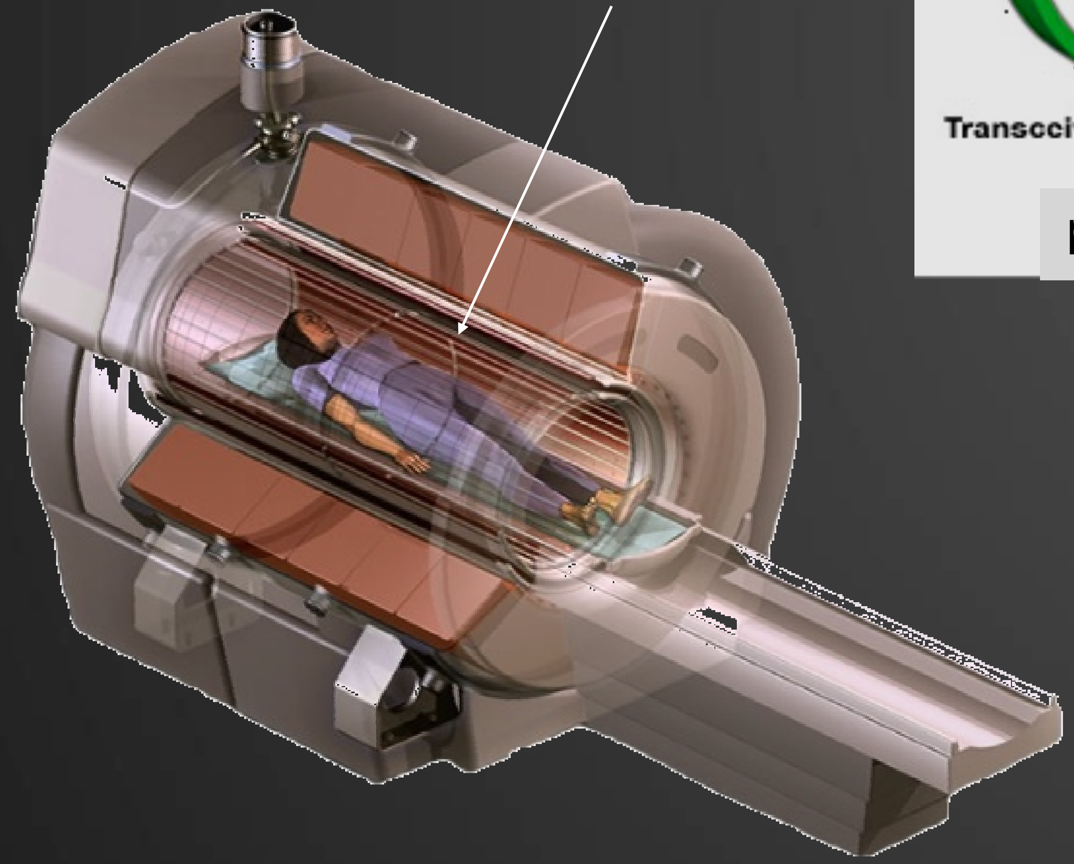
MRI 2: spatial encoding

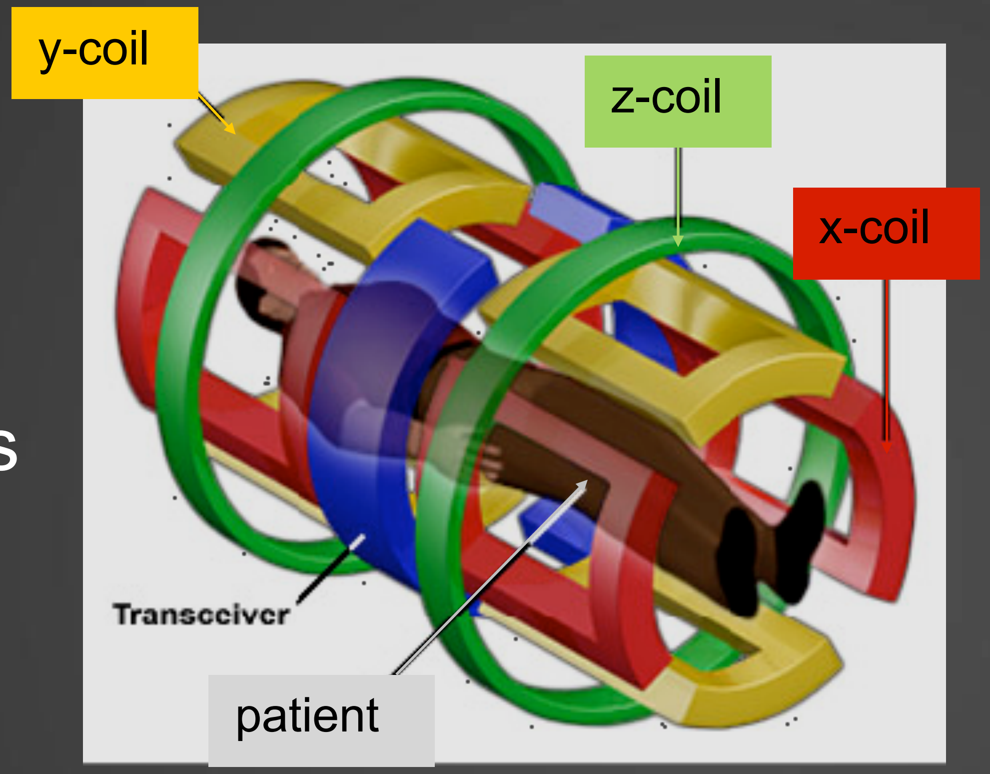




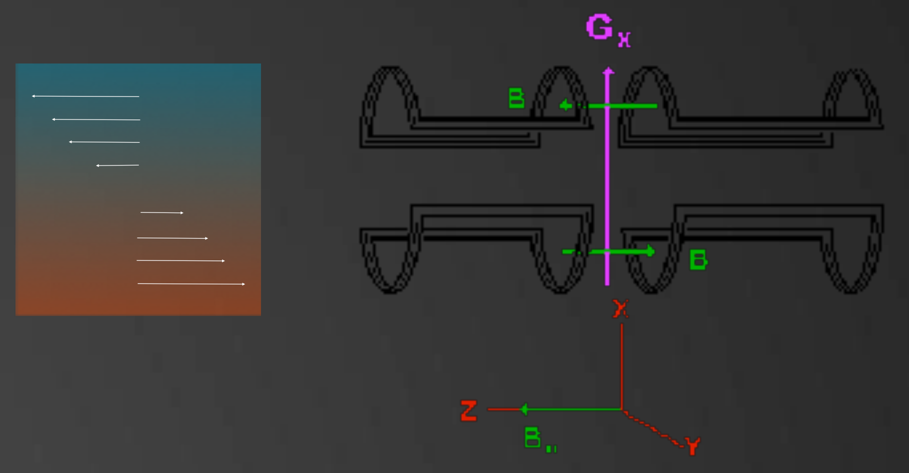
- Defining and addressing elementary 3D points (voxel): by using gradient magnetic field
- Foundations: resonance condition

Generation of gradient fields: with gradient coils

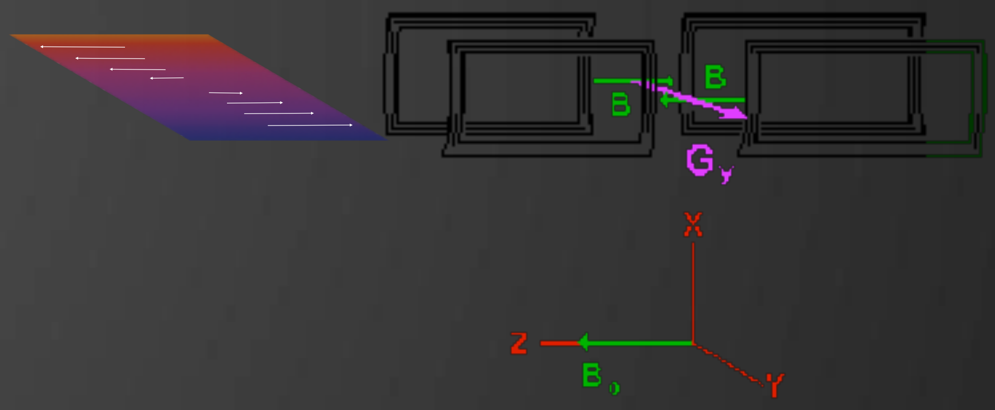




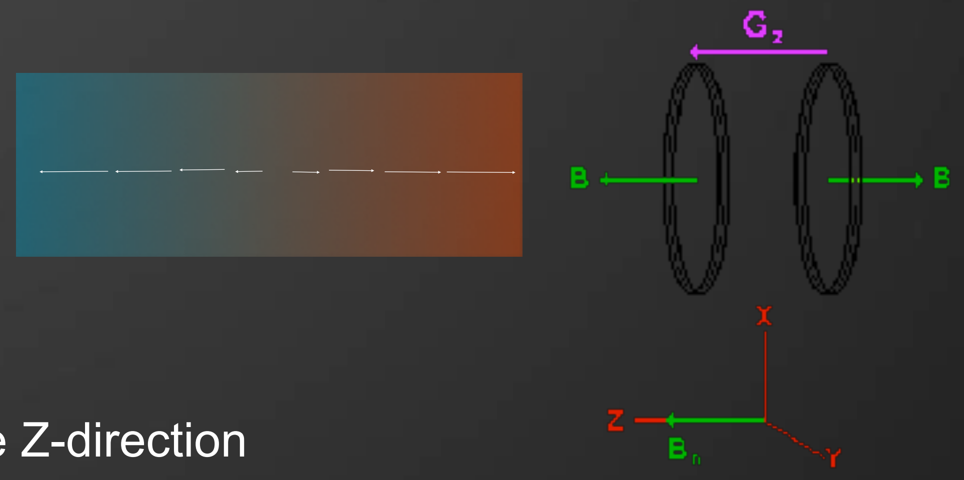
X-gradient coil



Y-gradient coil



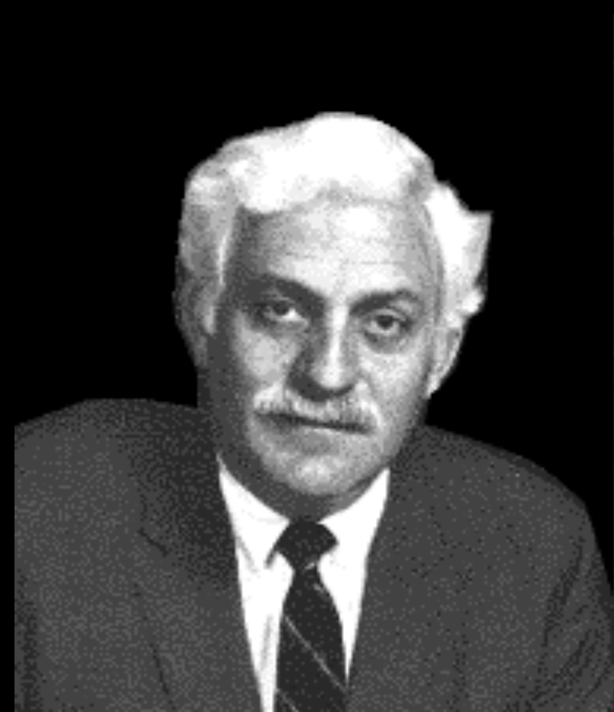
Z-gradient coil



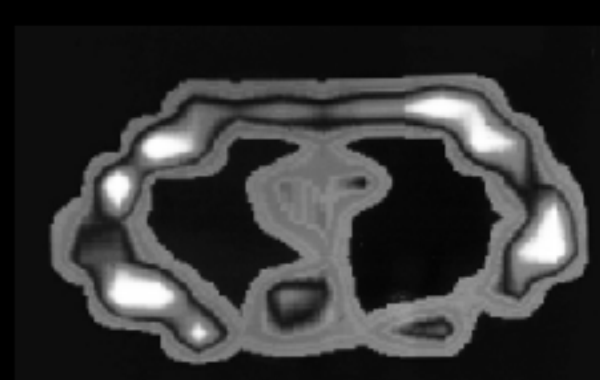
IMPORTANT NOTE:
The magnetic field is always in the Z-direction

Spatial encoding with focused field (FONAR)

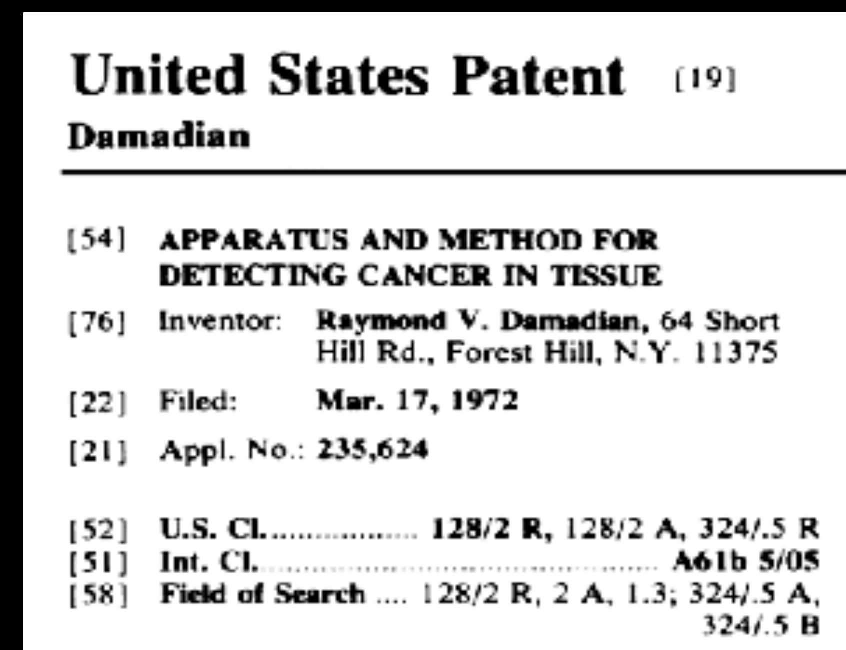
Downstate Medical Center - Brooklyn, 1972



Raymond V. Damadian

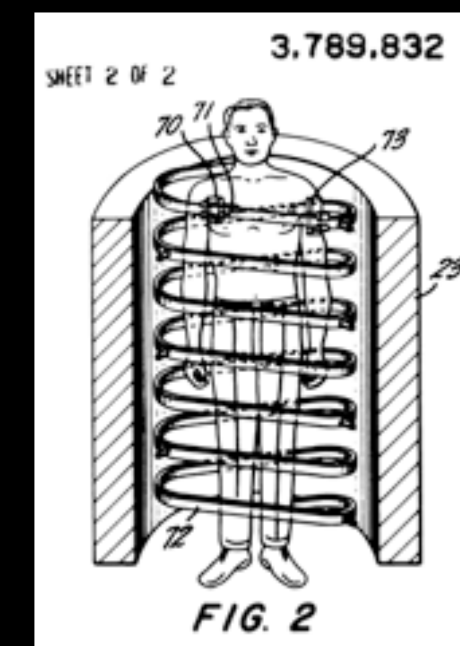


First MRI scan

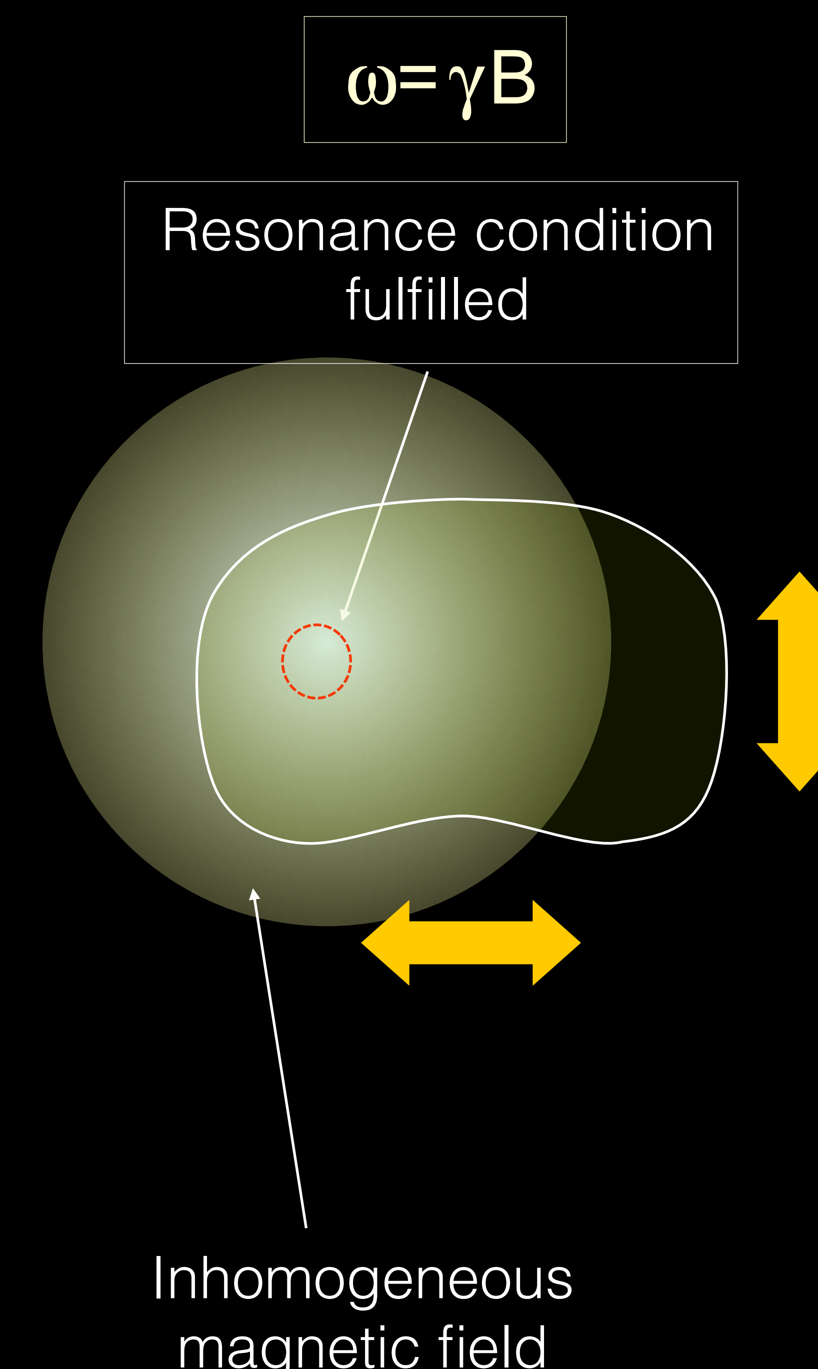


United States Patent [19]
Damadian

[54] APPARATUS AND METHOD FOR DETECTING CANCER IN TISSUE
[76] Inventor: Raymond V. Damadian, 64 Short Hill Rd., Forest Hill, N.Y. 11375
[22] Filed: Mar. 17, 1972
[21] Appl. No.: 235,624
[52] U.S. Cl. .... 128/2 R, 128/2 A, 324/.5 R
[51] Int. Cl. A61b 5/05
[58] Field of Search .... 128/2 R, 2 A, 1.3; 324/.5 A, 324/.5 B



1970: detection of lengthened relaxation times in cancerous tissues
1972: theoretical development of human in vivo 3D NMR
1977: first human MRI image (very slow scan)

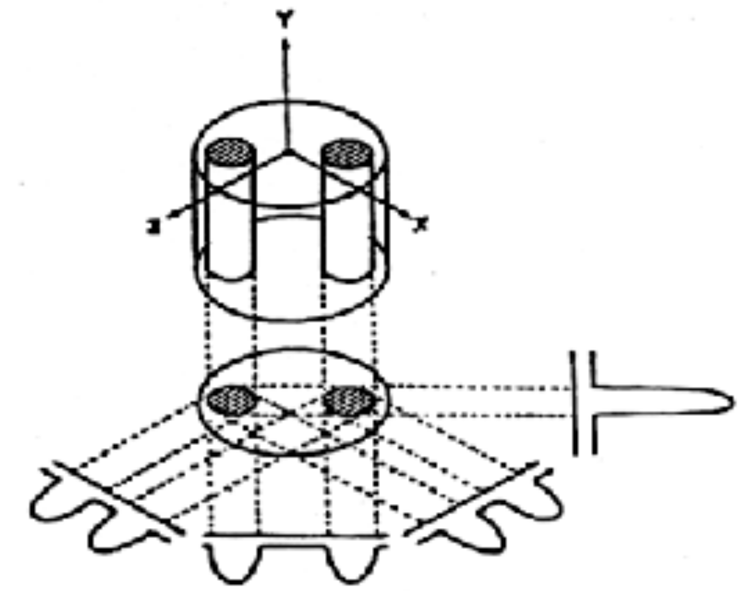


MRI 3: image reconstruction

1. Back projection
- as in CT scanning


Paul Lauterbur, 1973, Illinois


Peter Mansfield, 1973, Nottingham

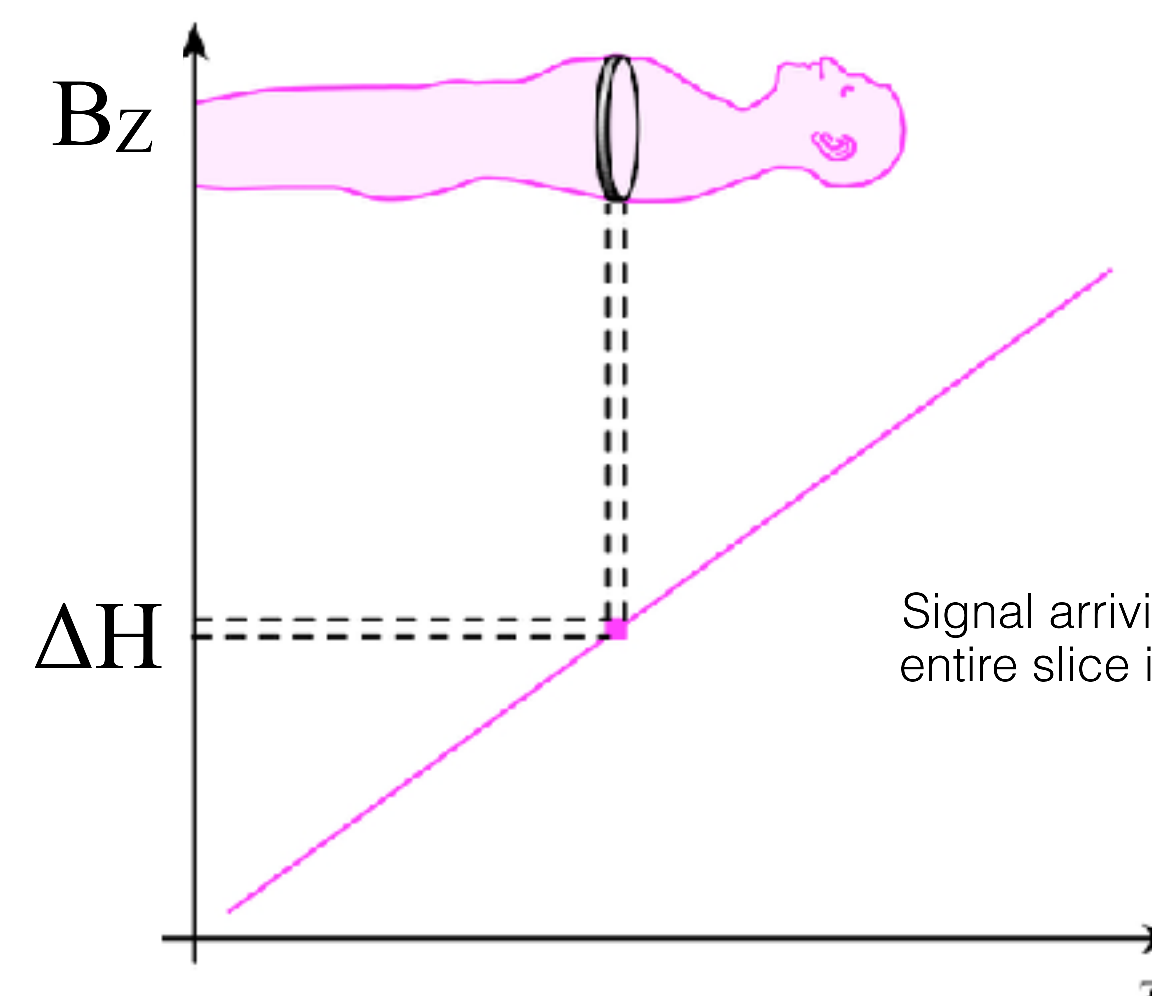

Principle of back projection


Reconstructed image (cross section of two test tubes)

2. 2D Fourier transformation
- currently used method
- „NMR Fourier Zeugmatography"


Richard Ernst, 1974, Zürich

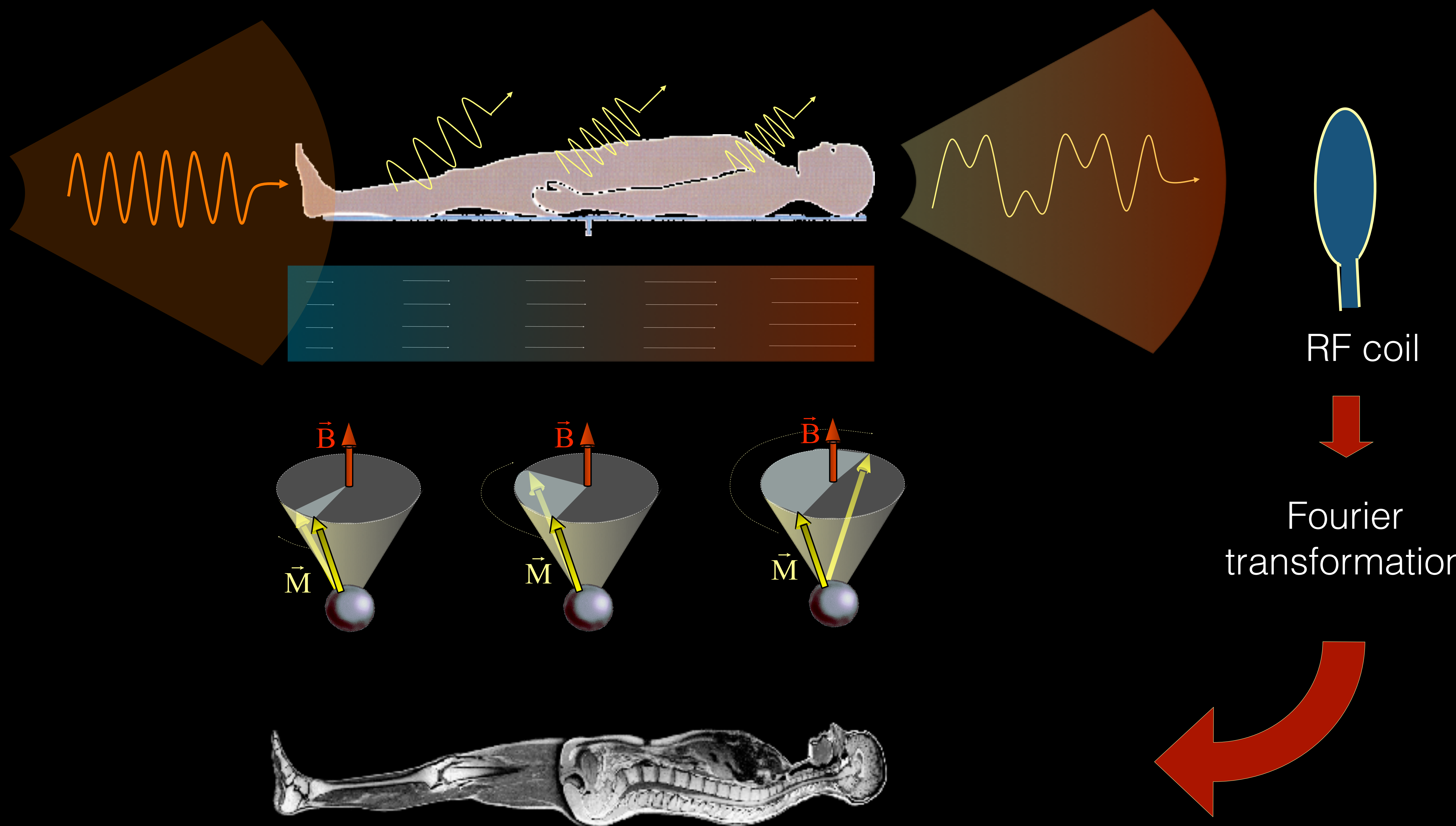

"MRI Scanner Mark One", Aberdeen, Scotland



Signal arriving from an entire slice is analyzed

MRI: spatial coding and image reconstruction

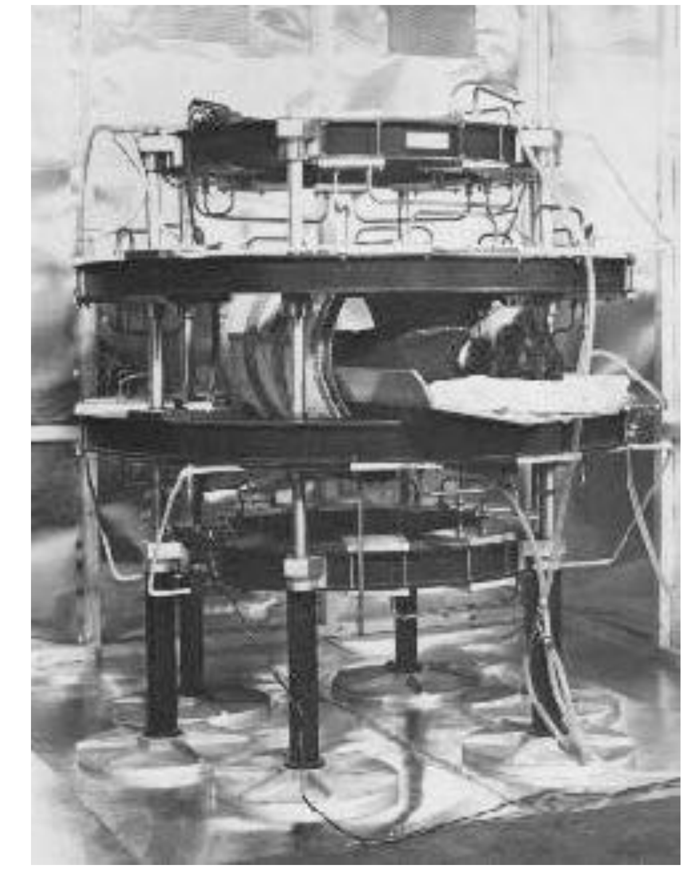
based on the resonance condition (B_0-dependent ω)



MRI 4: scanners

Early times


Indomitable (Damadian)

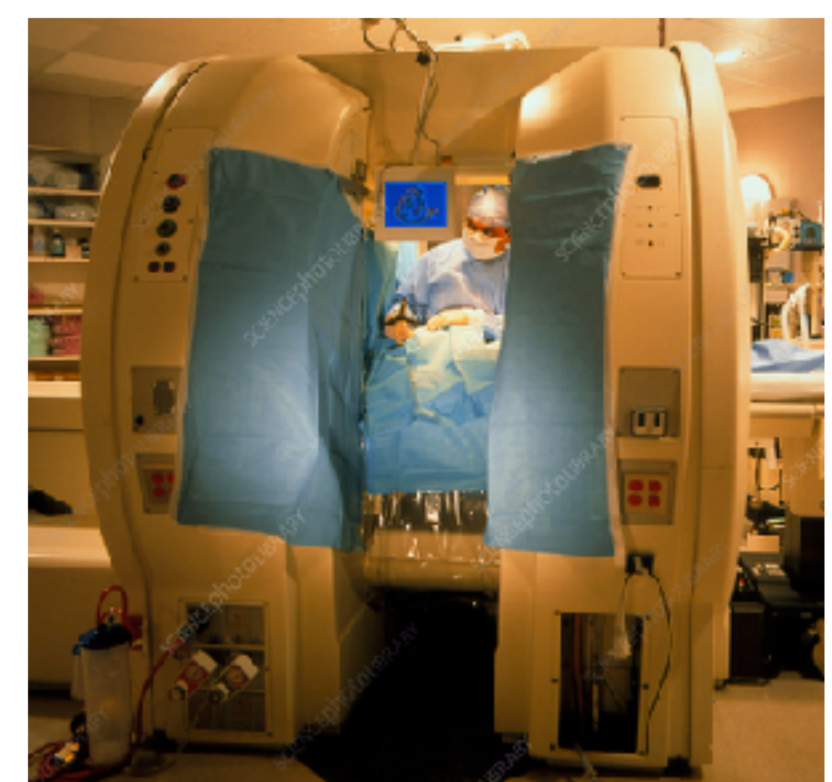


MRI Scanner Mark One (Ernst)

Present

3T MRI

Open MRI unit



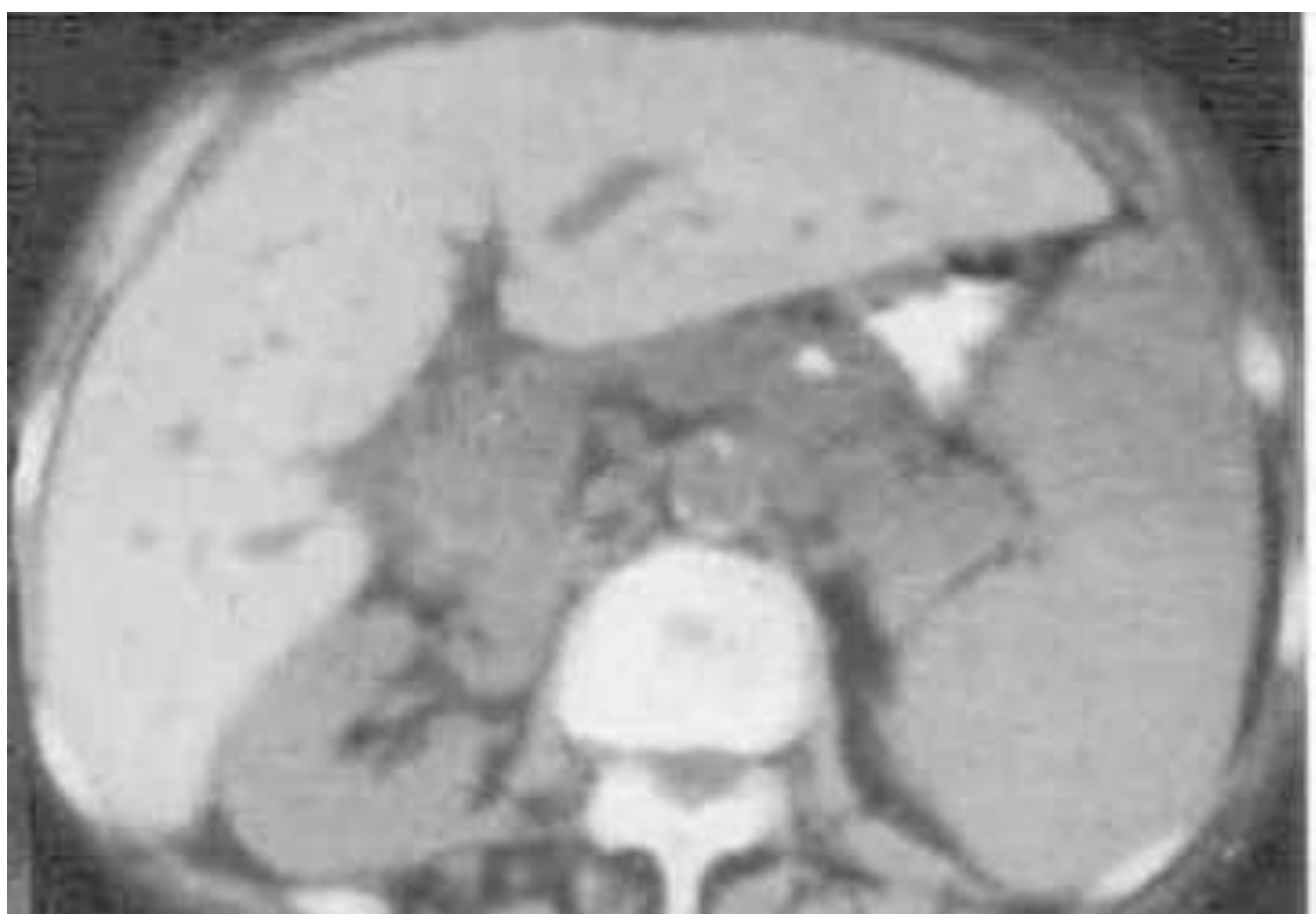
Interventional MRI unit


Mobile MRI

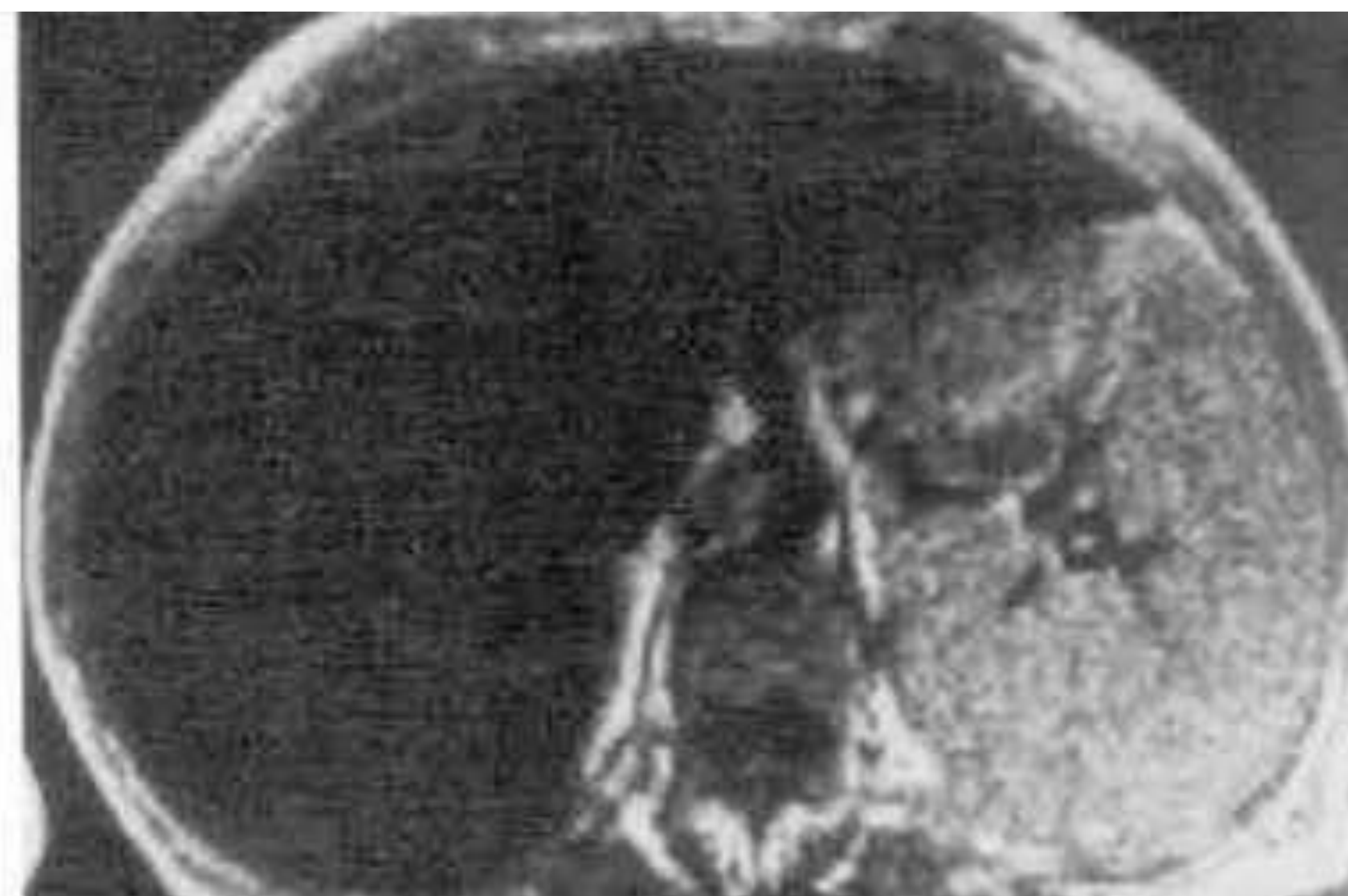
MRI 5: contrast agents

Positive: paramagnetic elements (T1 contrast): Gd, Mn

Negative: superparamagnetic, ferromagnetic (T2 contrast): FeIII, MnII



CT

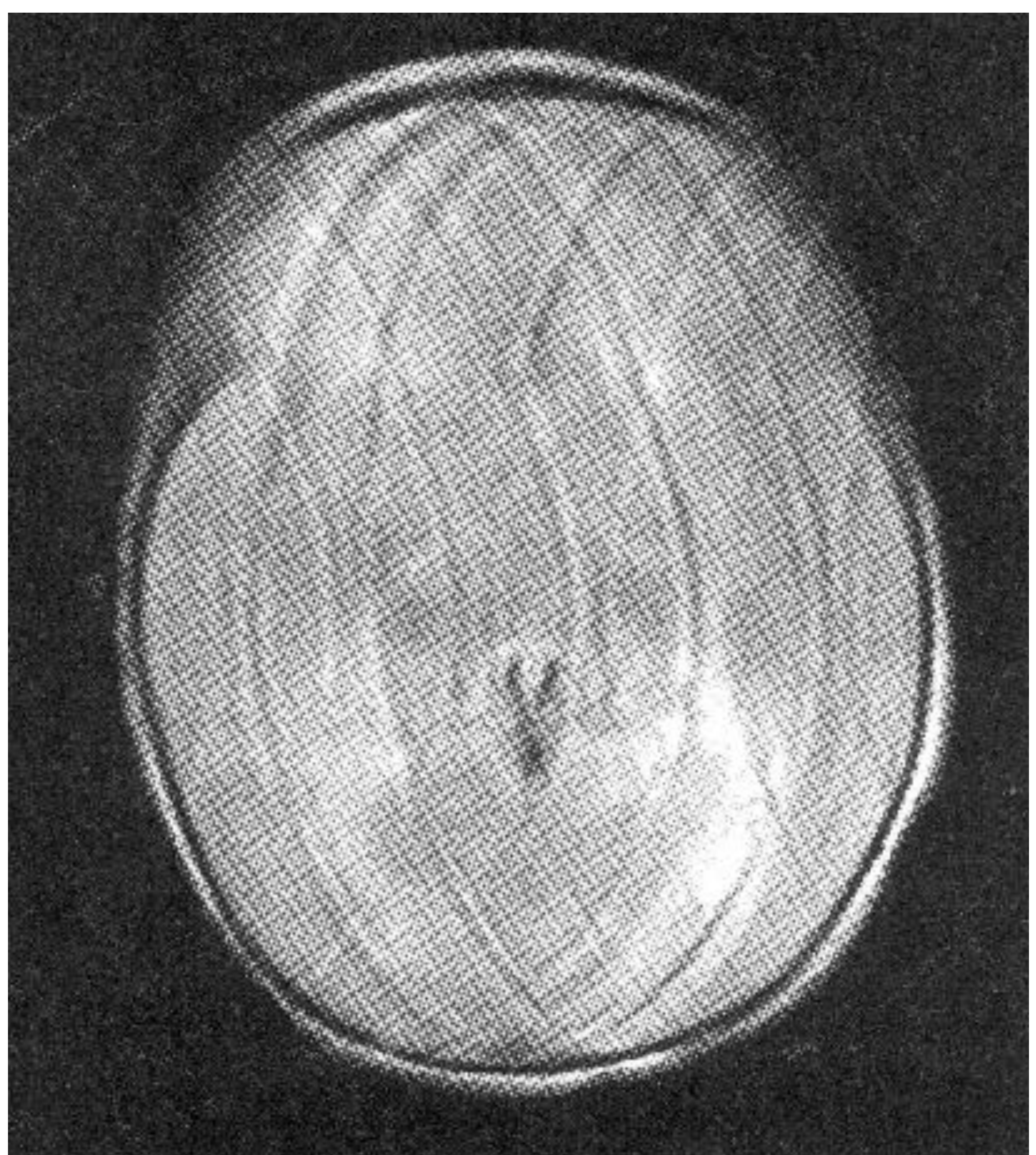


MR T2

Haemochromatosis hepatis (iron accumulation in liver)

MRI 6:artefacts

- Motion
- Metals (implants, injury)



Motion artefact

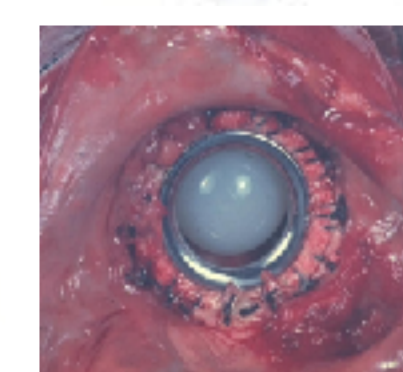
Metal in the orbit of the eye

MRI 7: dangers, contraindications

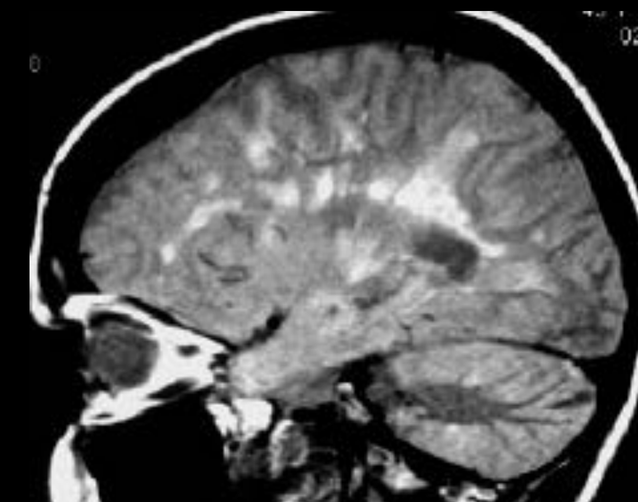
- Static magnetic field - metal objects
  Contraindications: implanted devices (pacemaker, defibrillator, hearing aids, drug delivery devices), neurostimulators, brain aneurysm clamps, early cardiac valve implants
- Gradient field - induced current
- Radio frequency field - thermal effects (lens, testis)



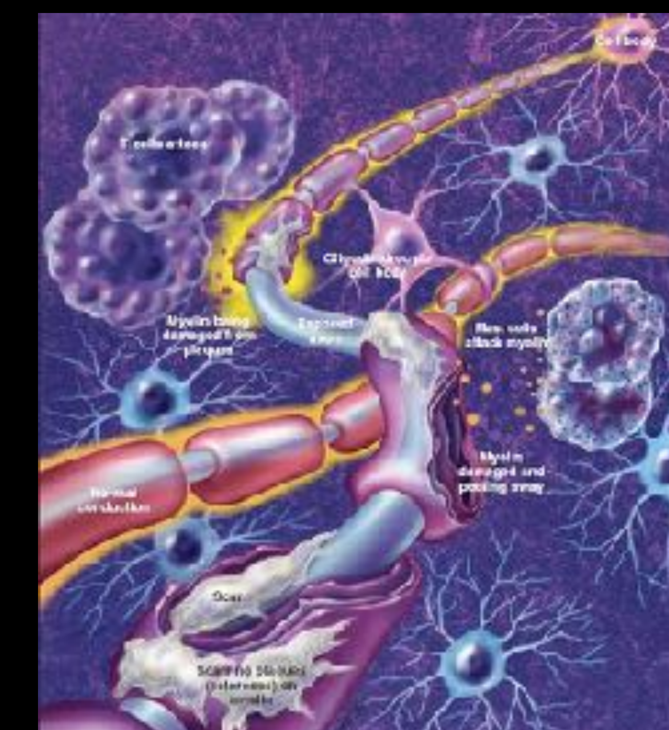




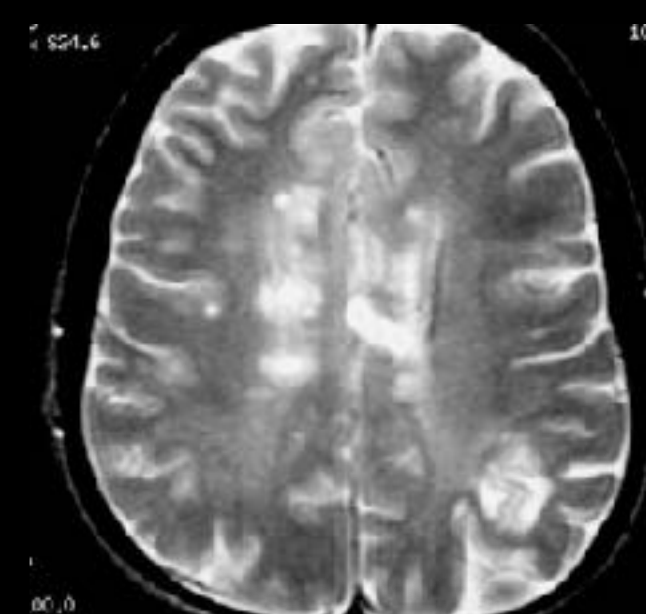
Applications: Anatomical imaging - Multiple sclerosis



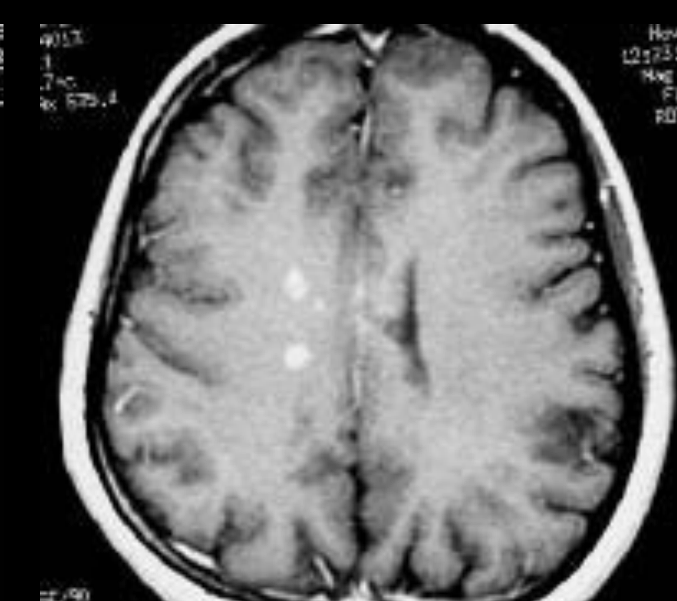
Proton density
(sagital)



Proton density
(transverse)



T2 weighted
(transverse)

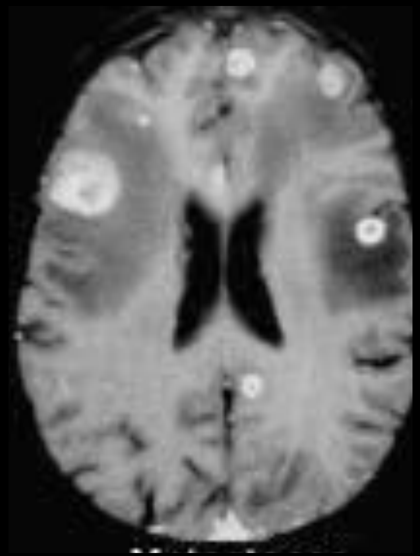


T1 weighted
With contrast agent

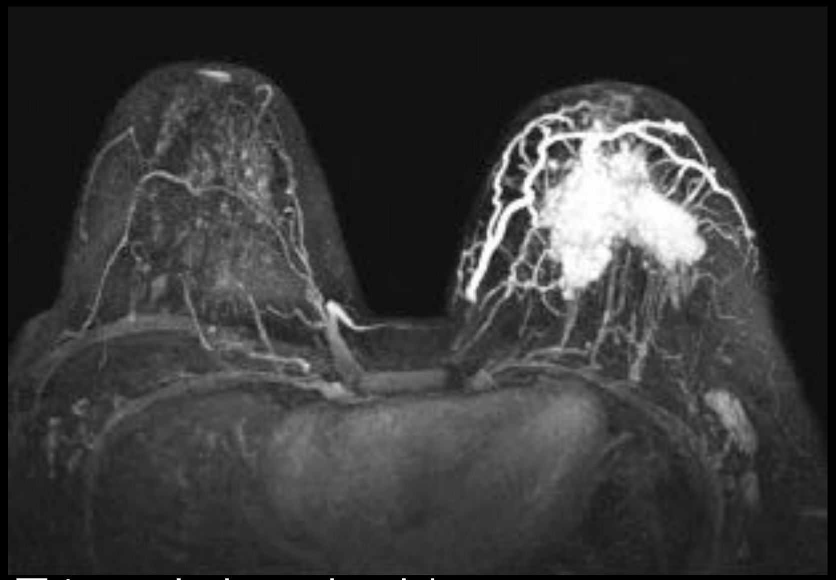
Anatomical imaging: Oncology

T2 weighted
(chondrosarcoma)

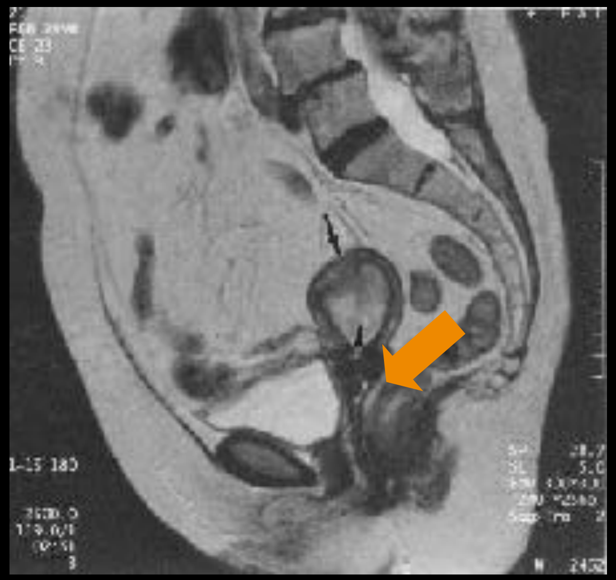
T2 weighted
(cyst)



Protondensity
(Brain metastasis)



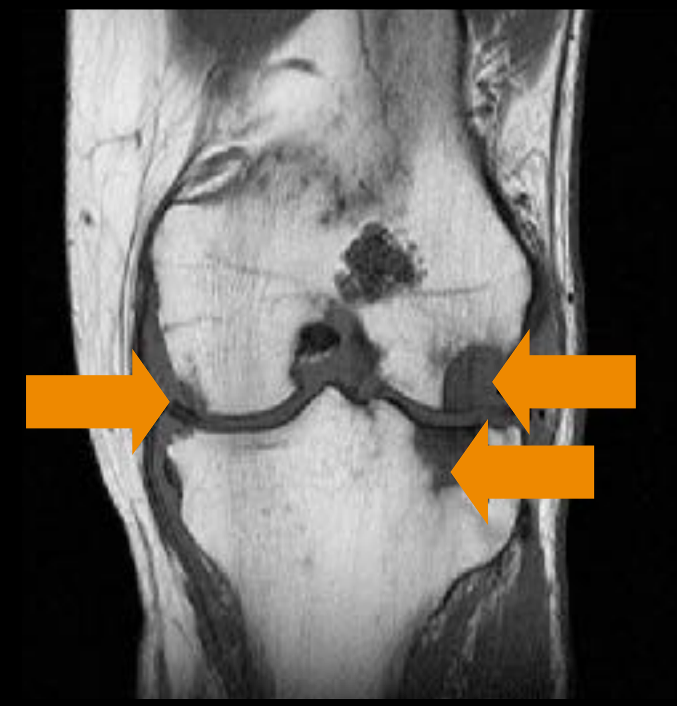
T1 weighted with contrastagent
(Breast carcinoma)



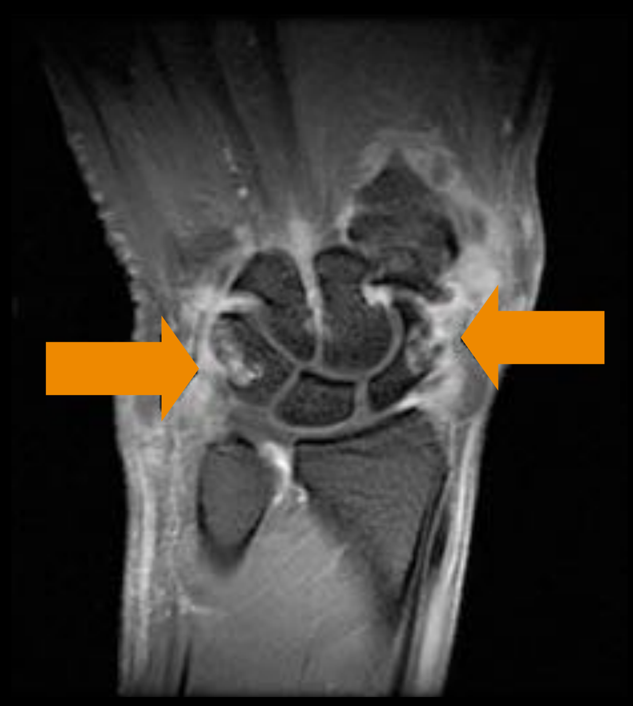
T2 weighted
(cervix carcinoma)

T2 weighted
(prostate tumor)

Anatomical imaging
Bone and soft tissue



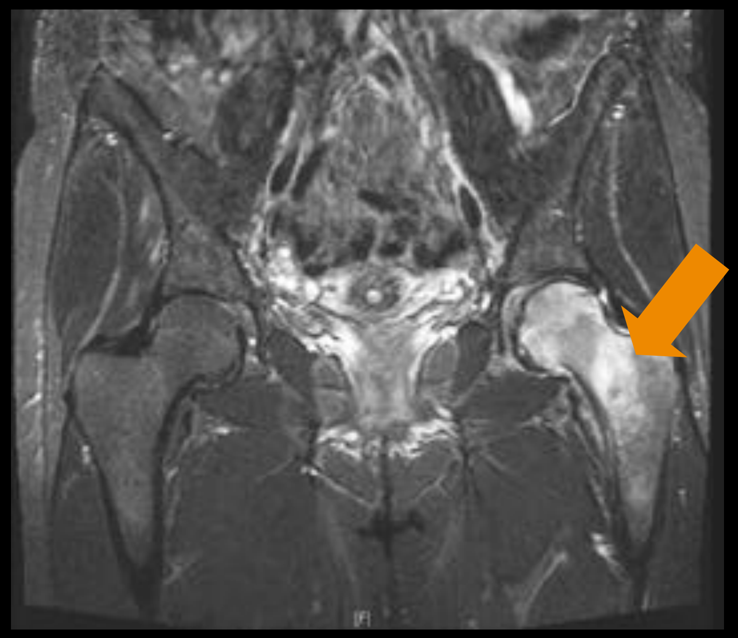
Rheumatoid arthritis
knee



Rheumatoid arthritis
whrist

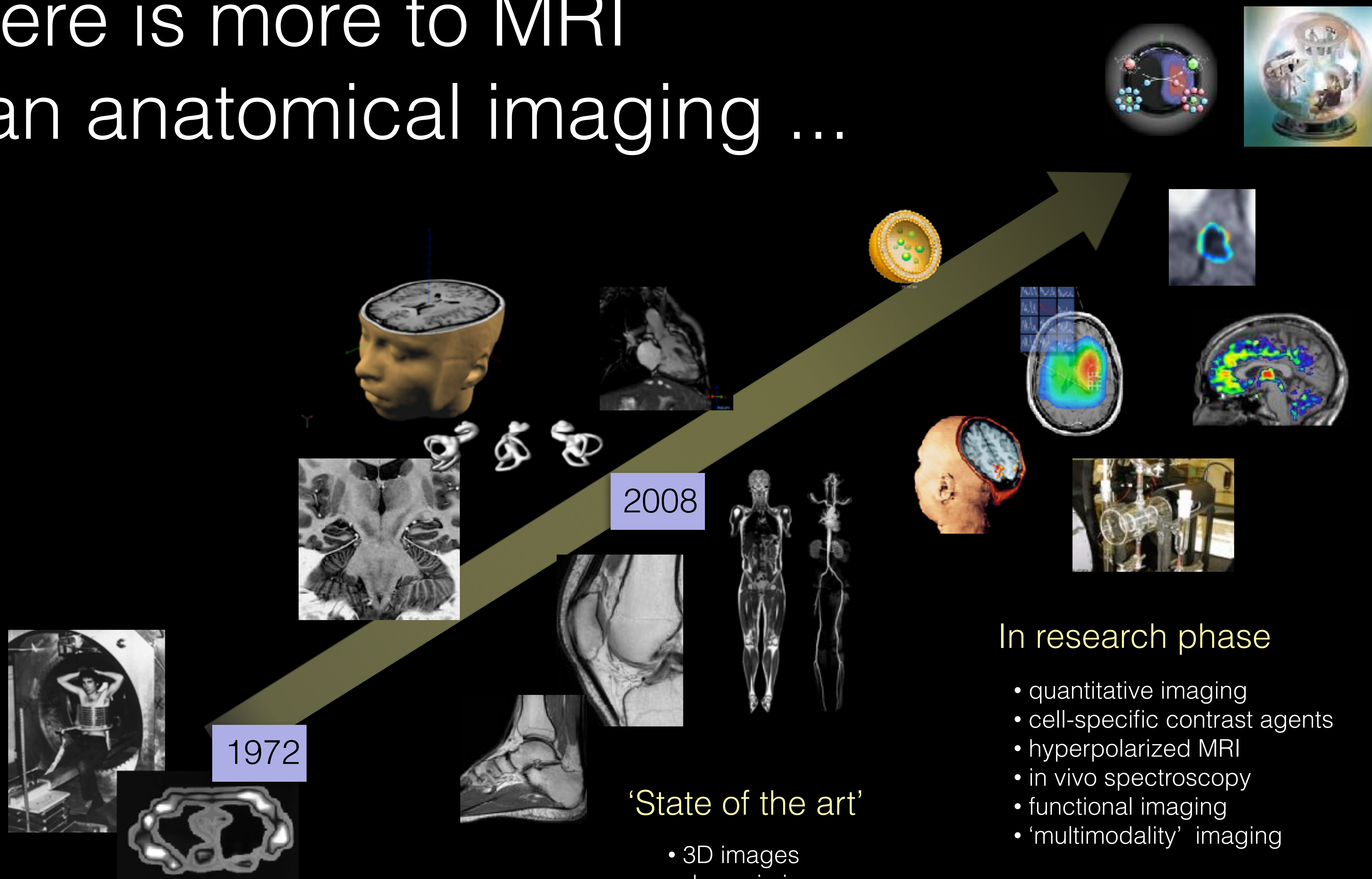
T2 weighted
(torn ligaments)

T2 weighted
(hernia)



Osteoporosis (femur)

There is more to MRI than anatomical imaging ...



First NMR images

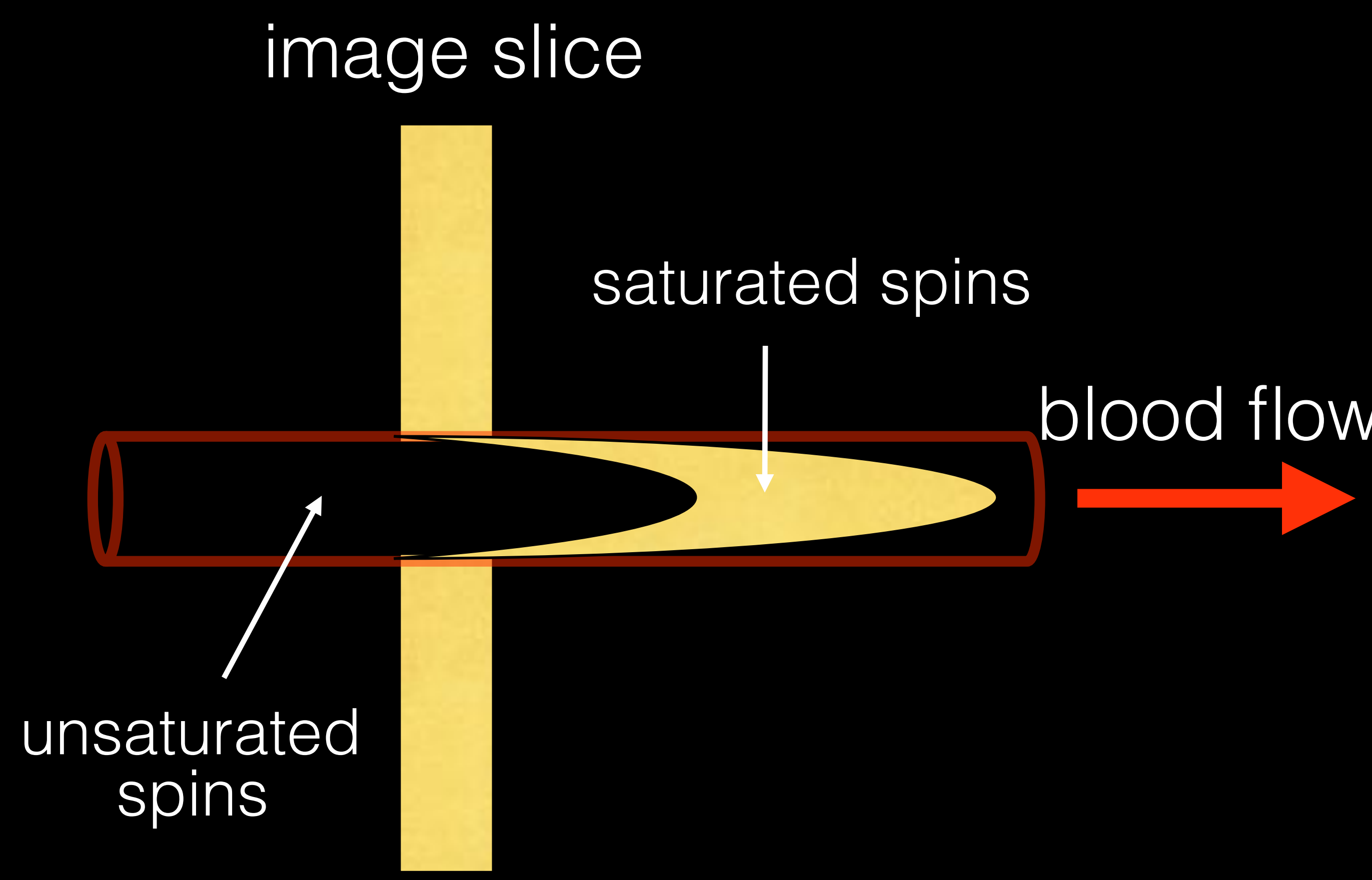
‘State of the art’

- 3D images
- dynamic images
- sharp image resolution

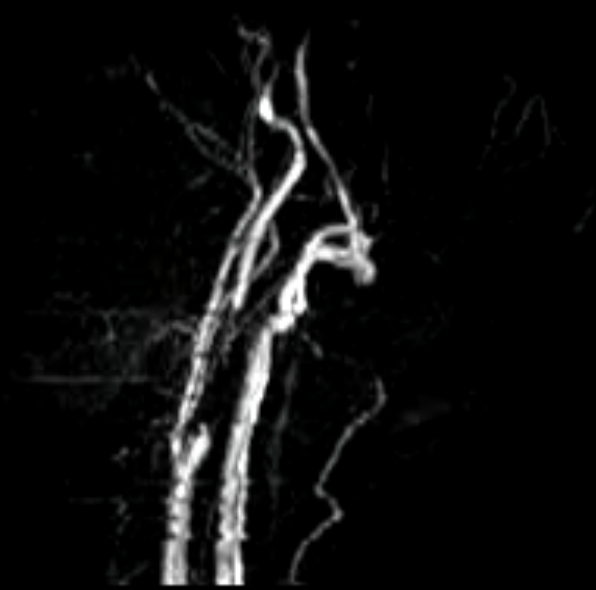
In research phase

- quantitative imaging
- cell-specific contrast agents
- hyperpolarized MRI
- in vivo spectroscopy
- functional imaging
- ‘multimodality’ imaging

MRI:
Non-invasive angiography

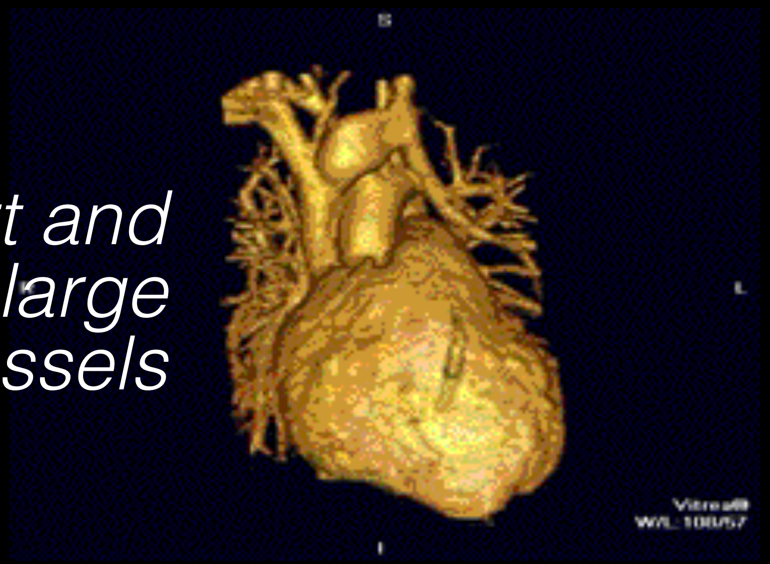


Arteria carotis



Circulus arteriosus Willisii

Heart and large vessels



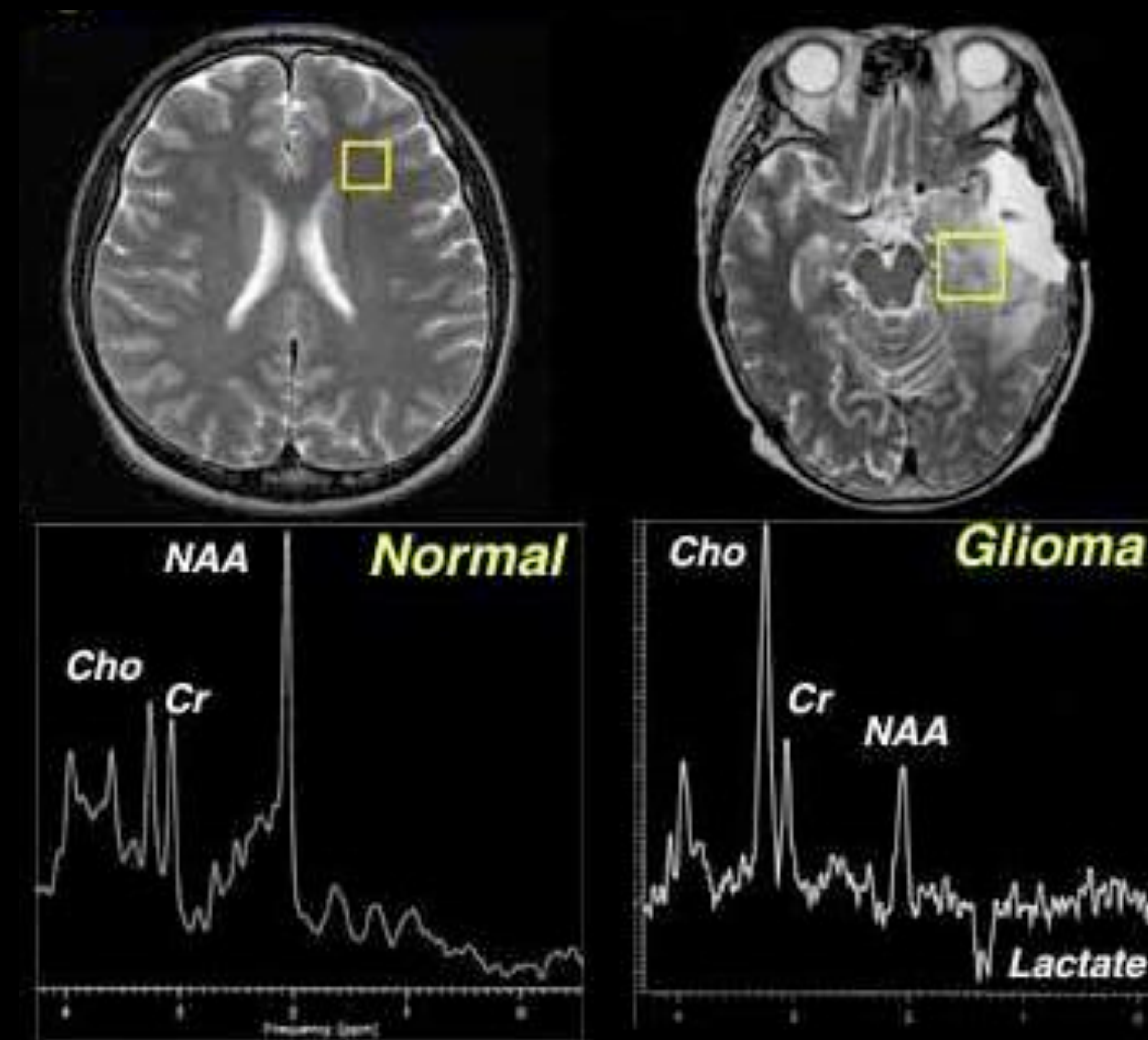
Time-resolved MRI
(ECG-gating required)

Blood flow across the cardiac chambers

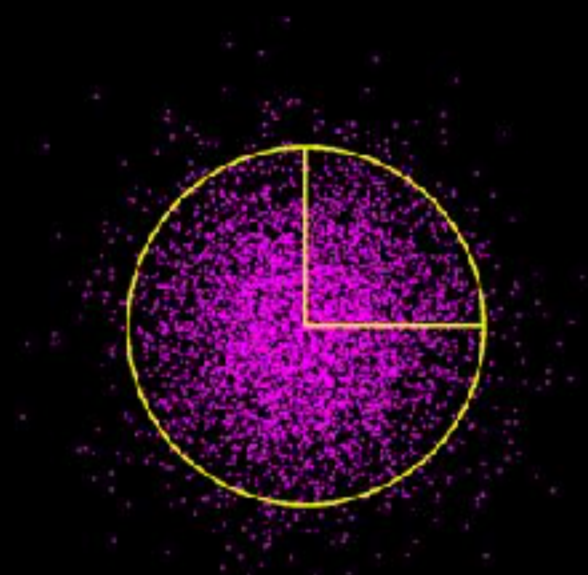
Opening and closing of aorta valve

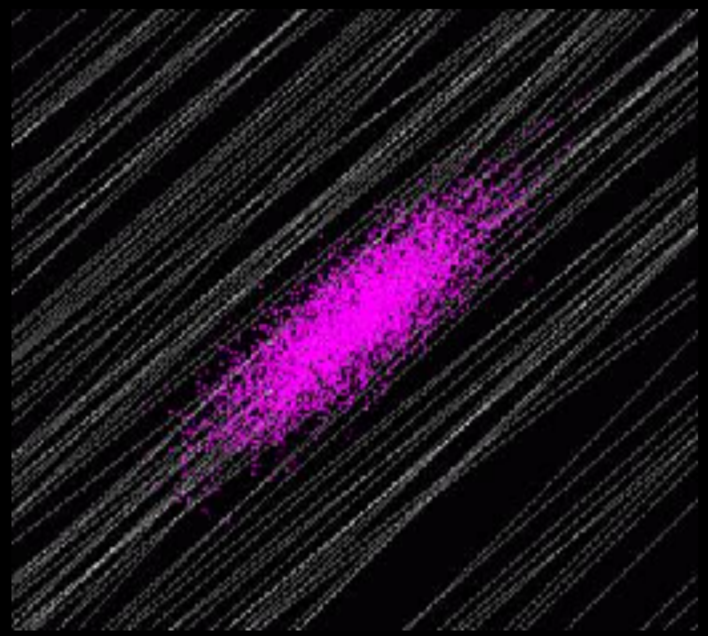
MR Spectroscopy

- Chemical shift
- Identification of metabolites
- Tumor diagnostics

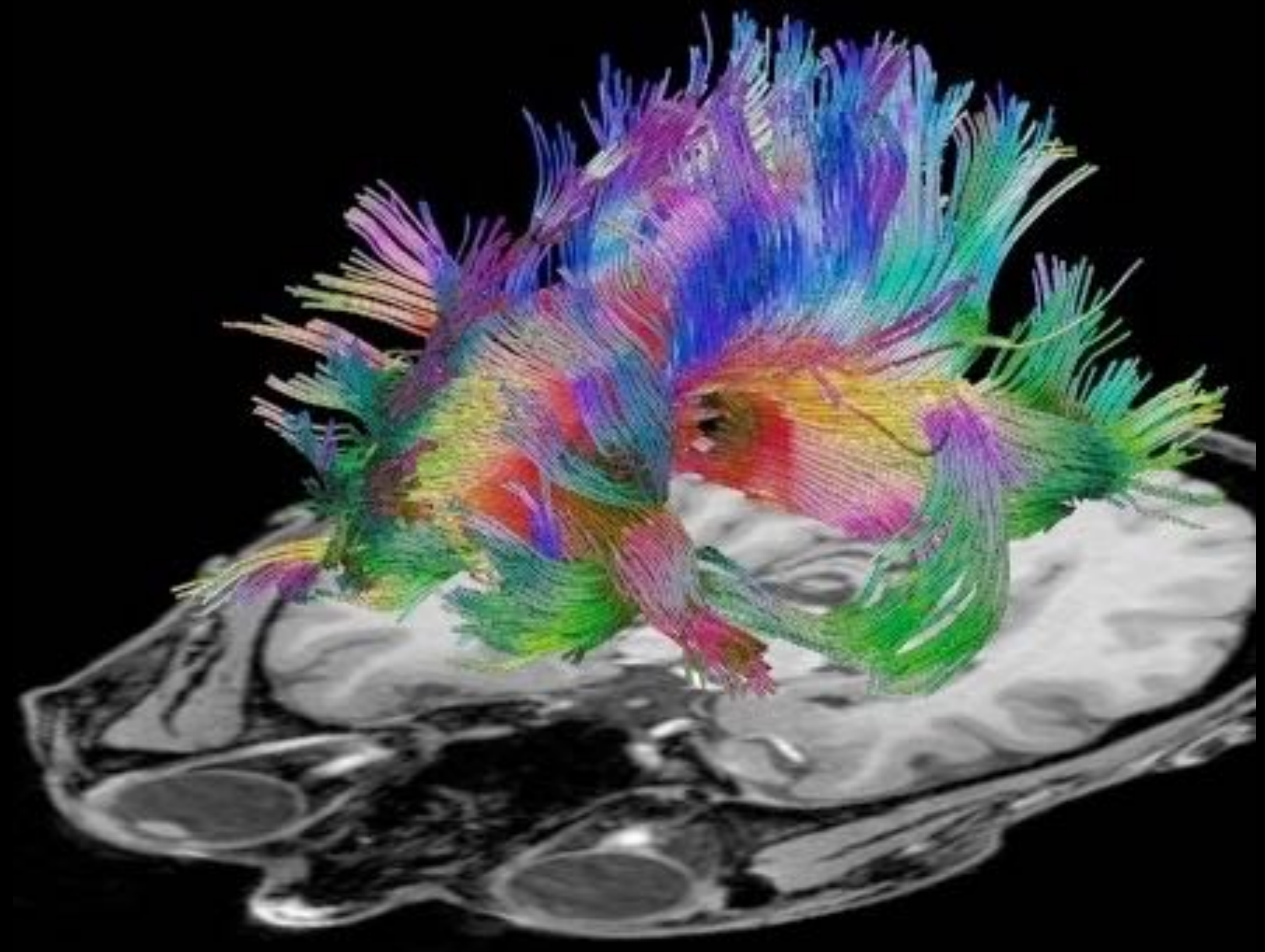


Diffusion imaging





Anisotropic water diffusion:
contrast generation

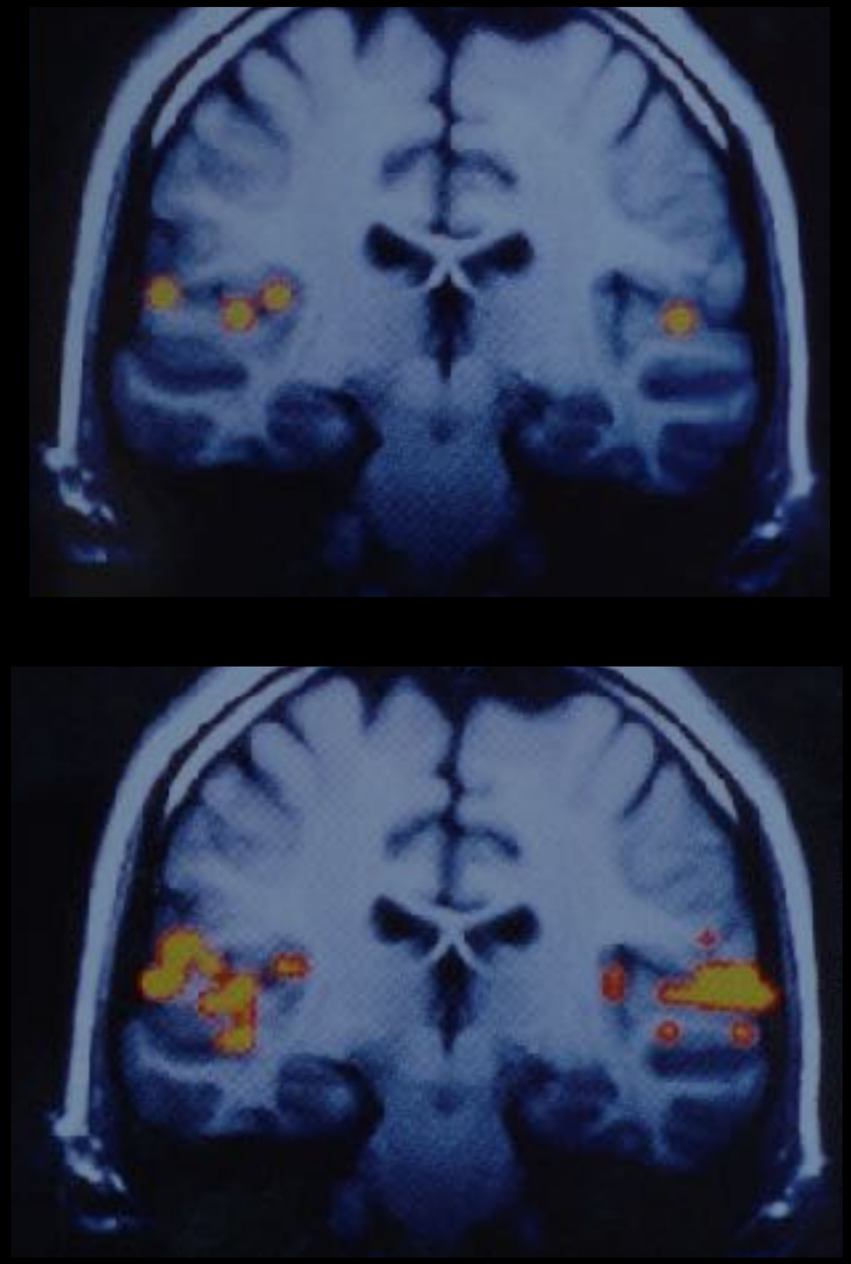


Imaging neural tracts:
tractography

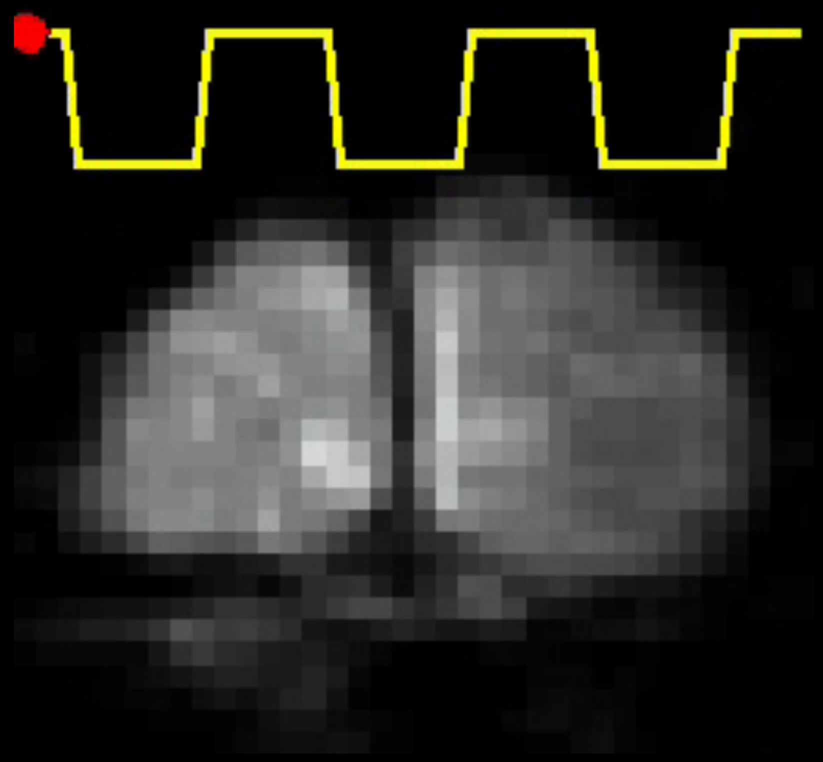
Corpus callosum

Functional MRI (fMRI)

High time resolution images recorded synchronously with physiological processes



Activation in the acoustic cortex



Effect of light pulses on the visual cortex

Superposition of MRI and PET

Intracranial tumor

PET signal: cortical areas activated during eye movement
Volume rendering