Radio spectroscopies, NMR, ESR, MRI

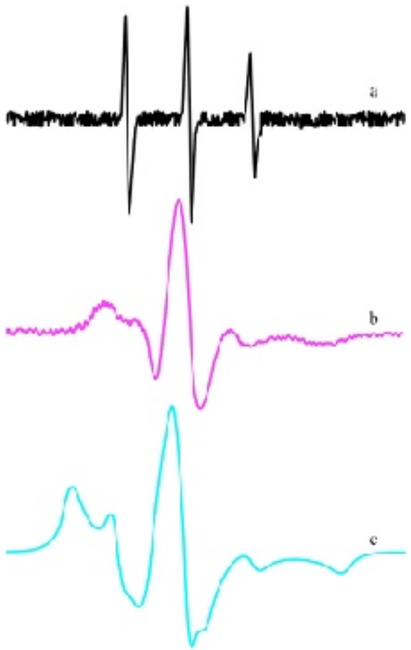
Miklós Kellermayer

Radiospectroscopies

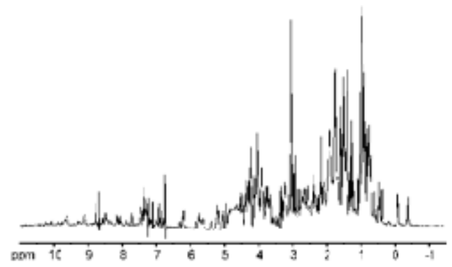
Revolutionized physics, chemistry, biology and medicine

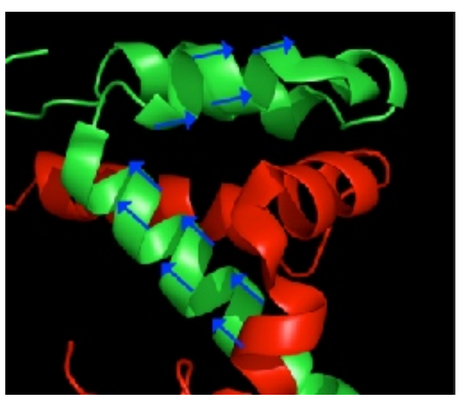
- Electronspin resonance (ESR, electron paramagnetic resonance - EPR)
- Nuclear Magnetic Resonance (NMR, MRI)

EPR spectroscopy

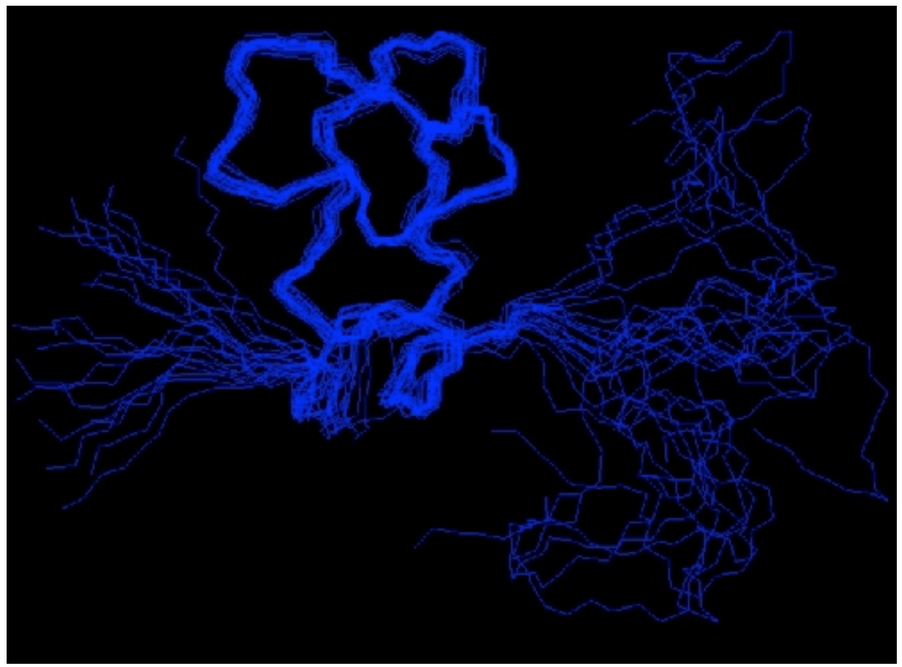


NMR spectroscopy

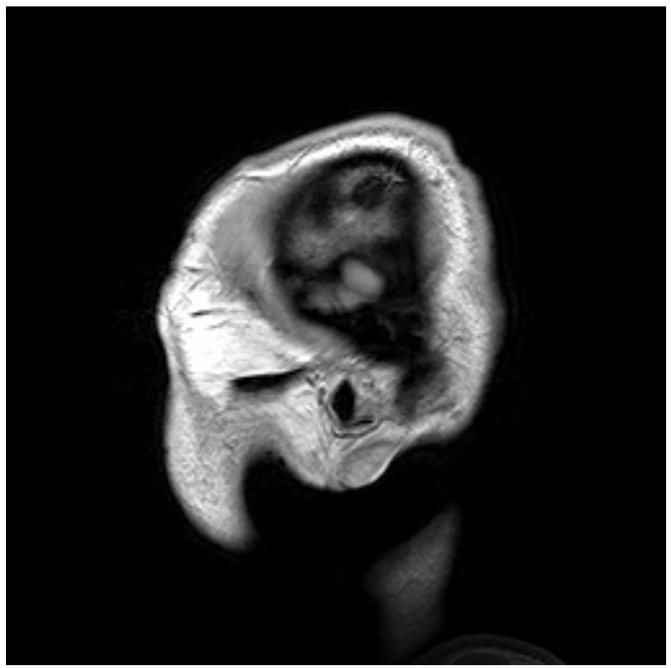




Protein molecular dynamics with NMR



High-resolution, anatomical MRI

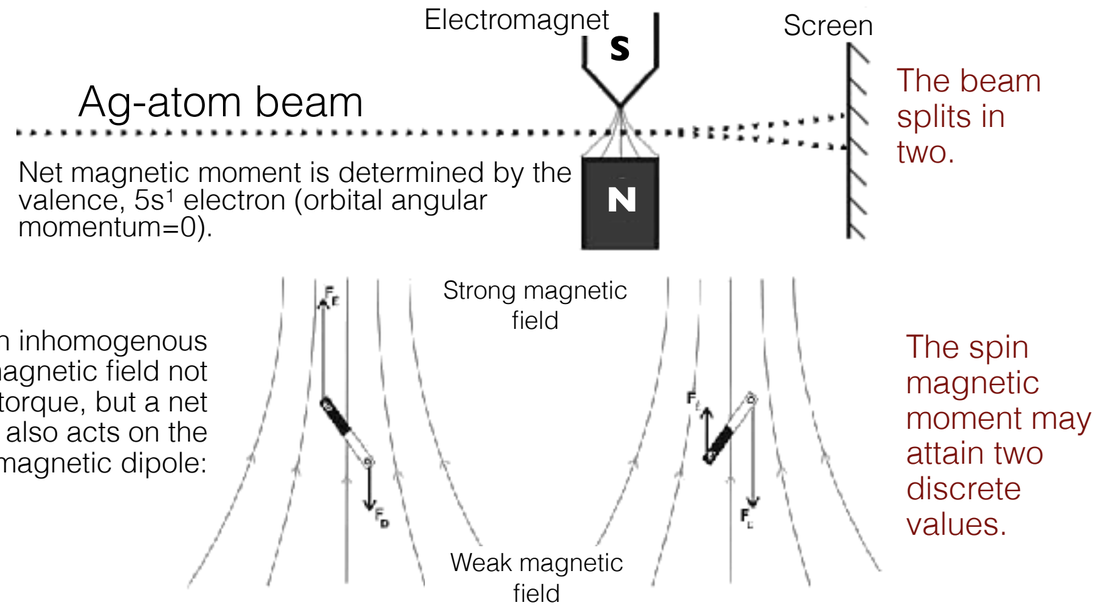


Atomic, molecular systems may behave as elementary magnets

Stern-Gerlach experiment (1922)

Otto Stern
(1888-1969)

Walther Gerlach
(1889-1979)



Net magnetic moment is determined by the valence, $5s^1$ electron (orbital angular momentum=0).

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)

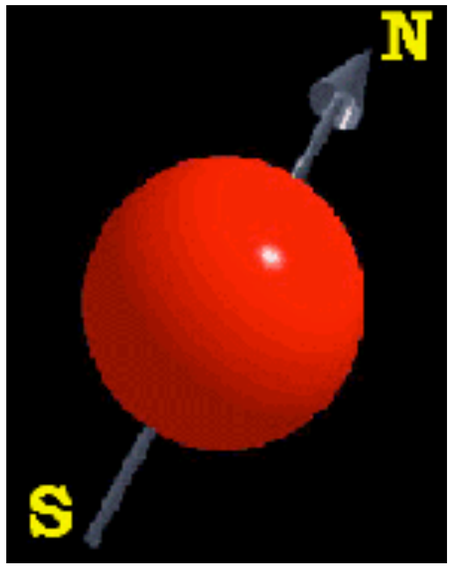
Felix Bloch
(1905-1983)

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:

$$M_N = \gamma_N L$$

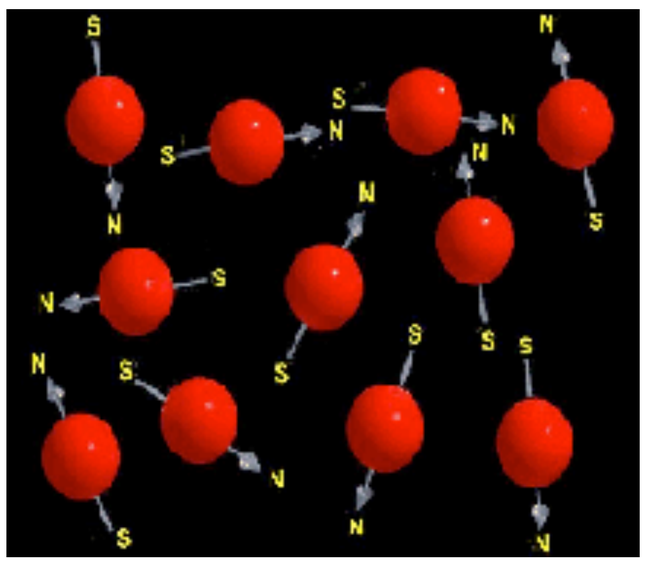
γ_N = gyromagnetic ratio (ratio of magnetic moment and angular momentum.)
L = nuclear spin ($L = \sqrt{l(l+1)}\hbar$), l= spin quantum number.

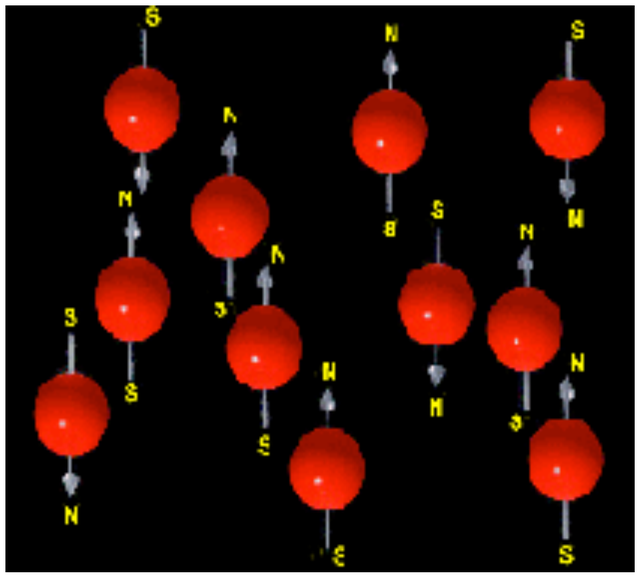
Magnetic moment of the electron:

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

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



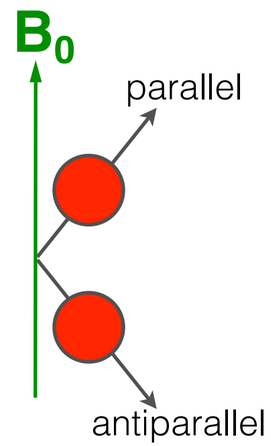


In absence of magnetic field:
random orientation of elementary magnets

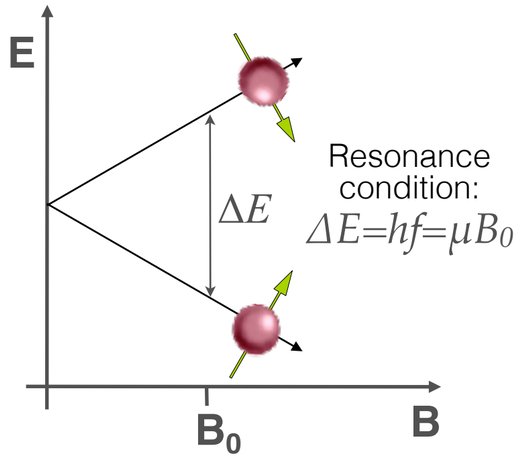
Paramagnetism: magnetism emerging in external magnetic field (caused by the orientation of magnetic dipoles).

In magnetic field:

elementary magnets orient



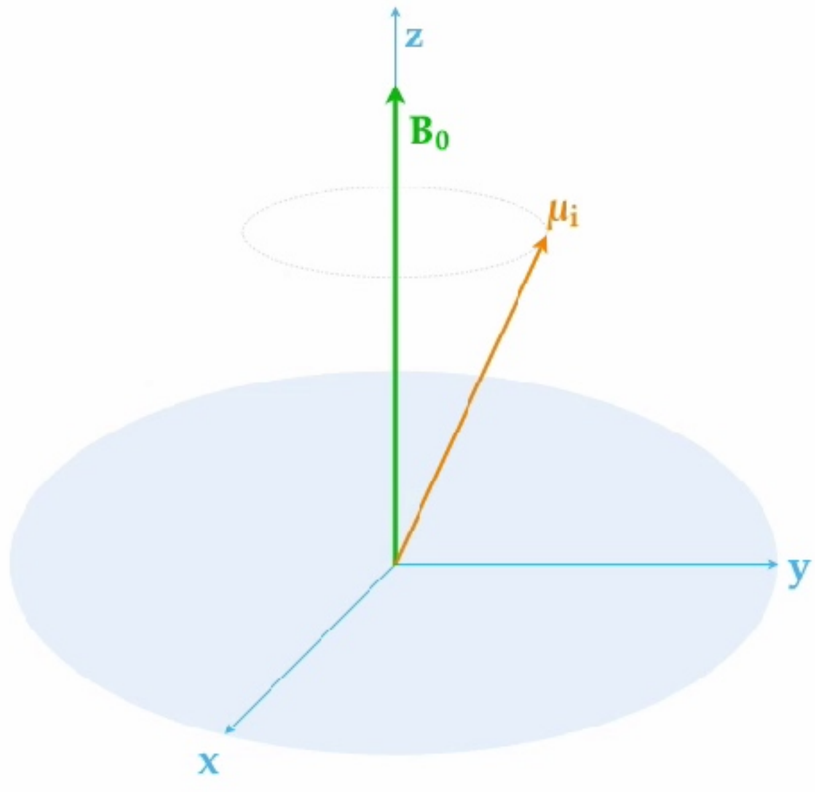
energy levels split



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:

$$\omega_0 = \gamma B_0$$

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

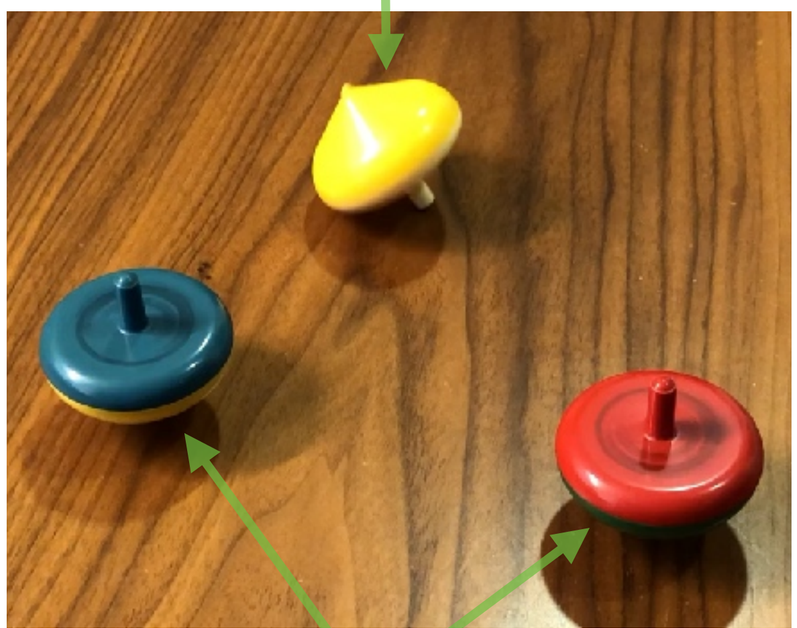
Resonance condition:

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

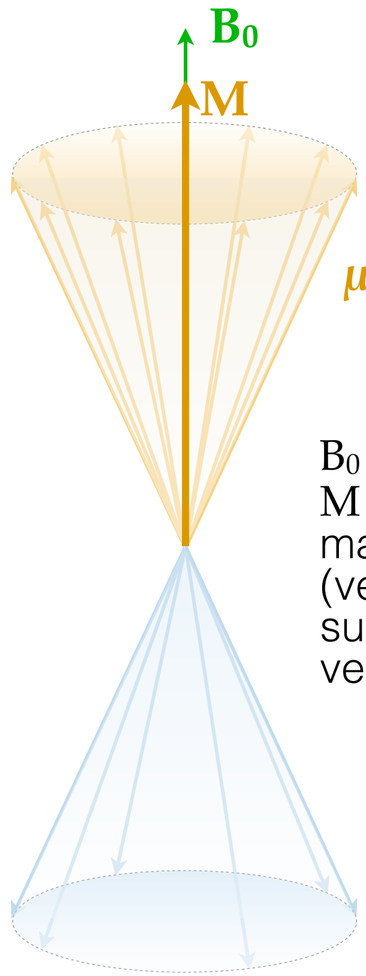
Felix Bloch, 1946

Net (macrosopic) magnetization

Due to spin access in different energy states



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



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

High-energy state
antiparallel in case of ^{1}H

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

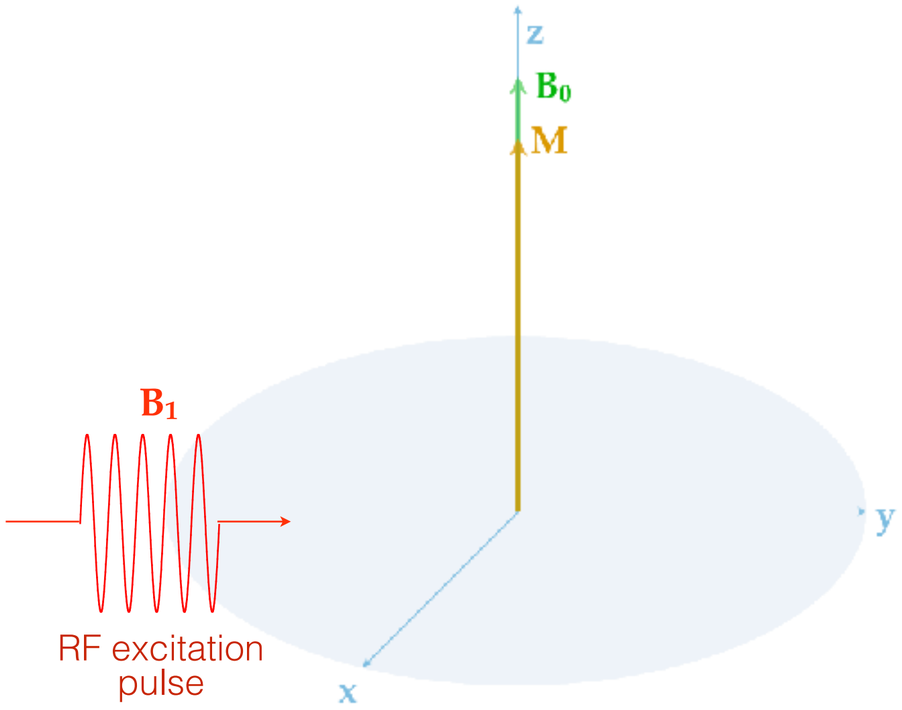
$$\frac{N_{antiparallel}}{N_{parallel}} = e^{-\frac{\Delta E}{k_B T}}$$

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

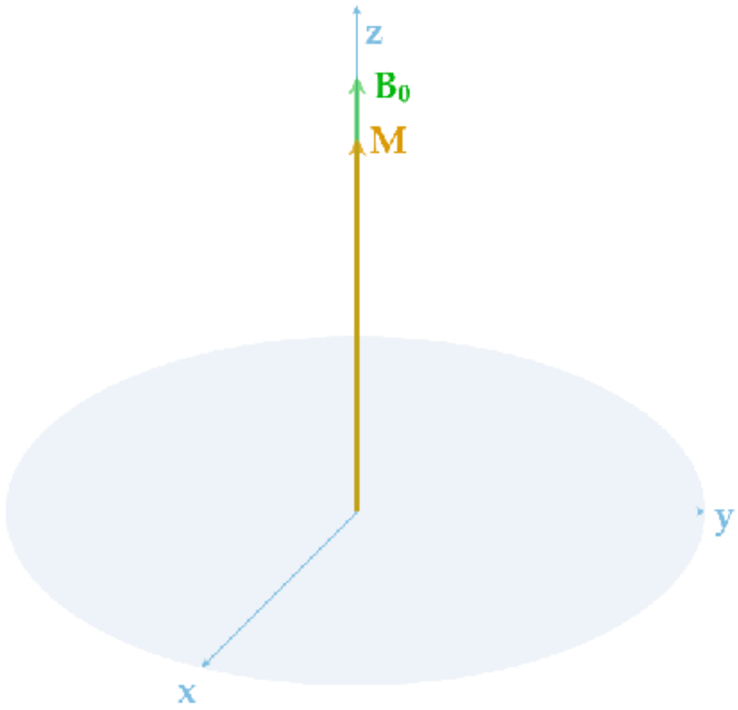
Excitation

Resonance condition, Larmor frequency

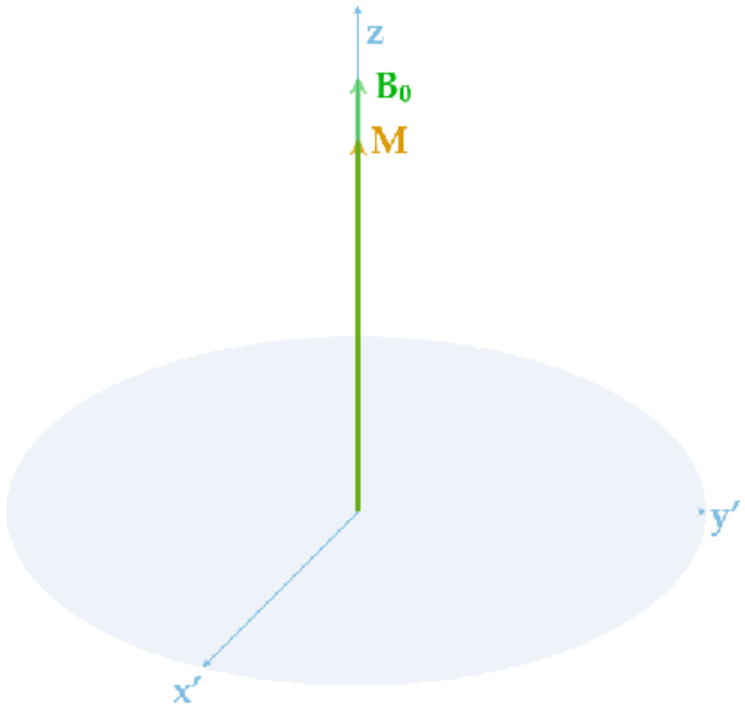
Employed electromagnetic radiation: radiowaves (NMR, MRI), microwaves (ESR)



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



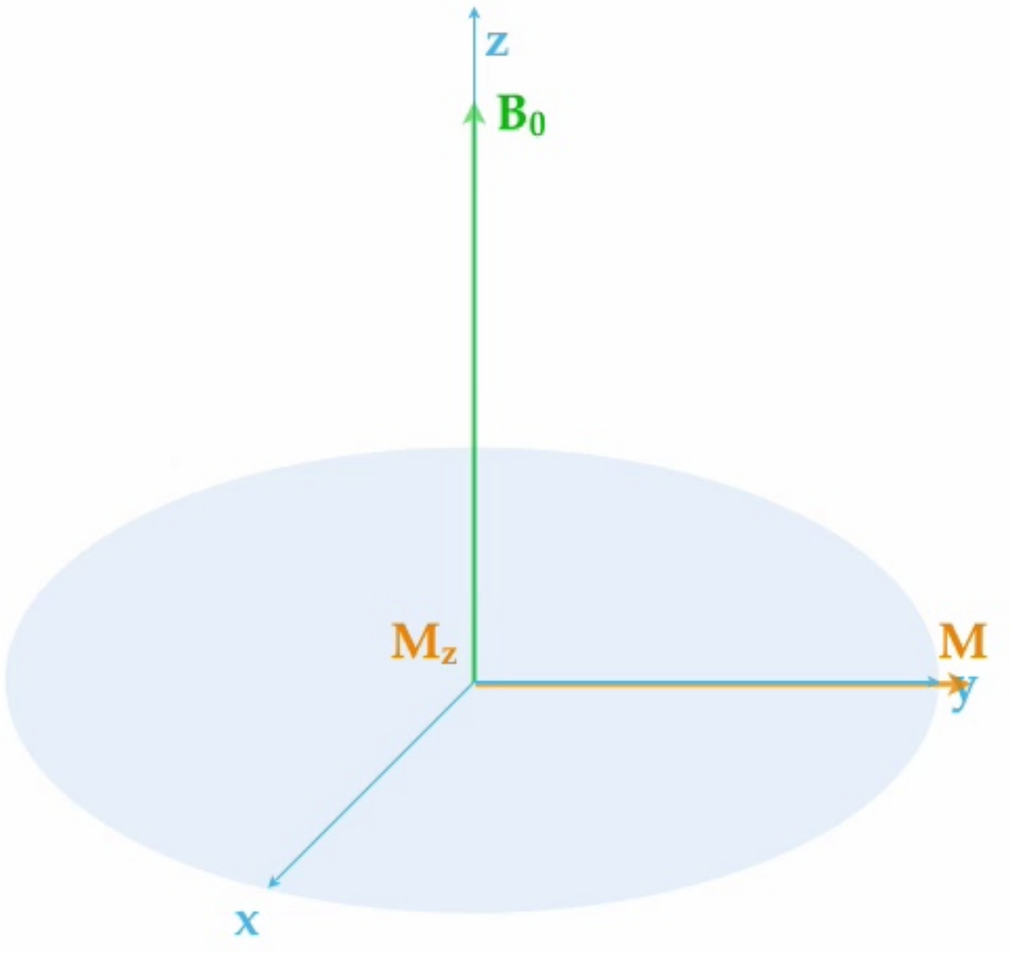
Excitation within the rotating frame of reference: the net magnetization vector (M) is tilted from its oriented state into the *xy*-plane (transverse plane)

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

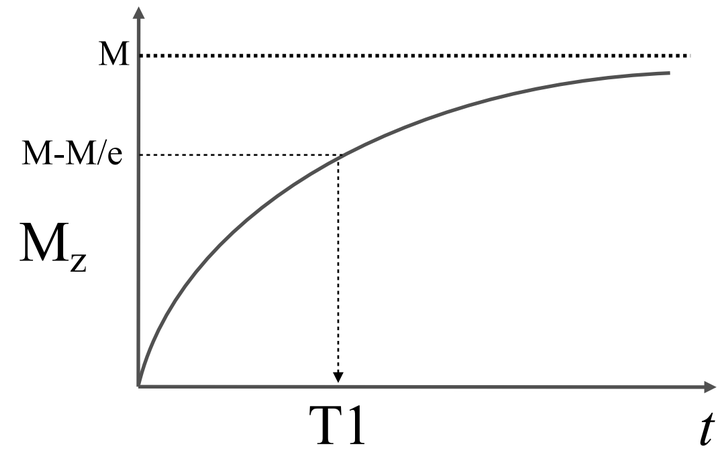
Spin-lattice relaxation

T1 or longitudinal relaxation

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



$\mathbf{M_z}$: z-axis vectorial component of $\mathbf{M}$



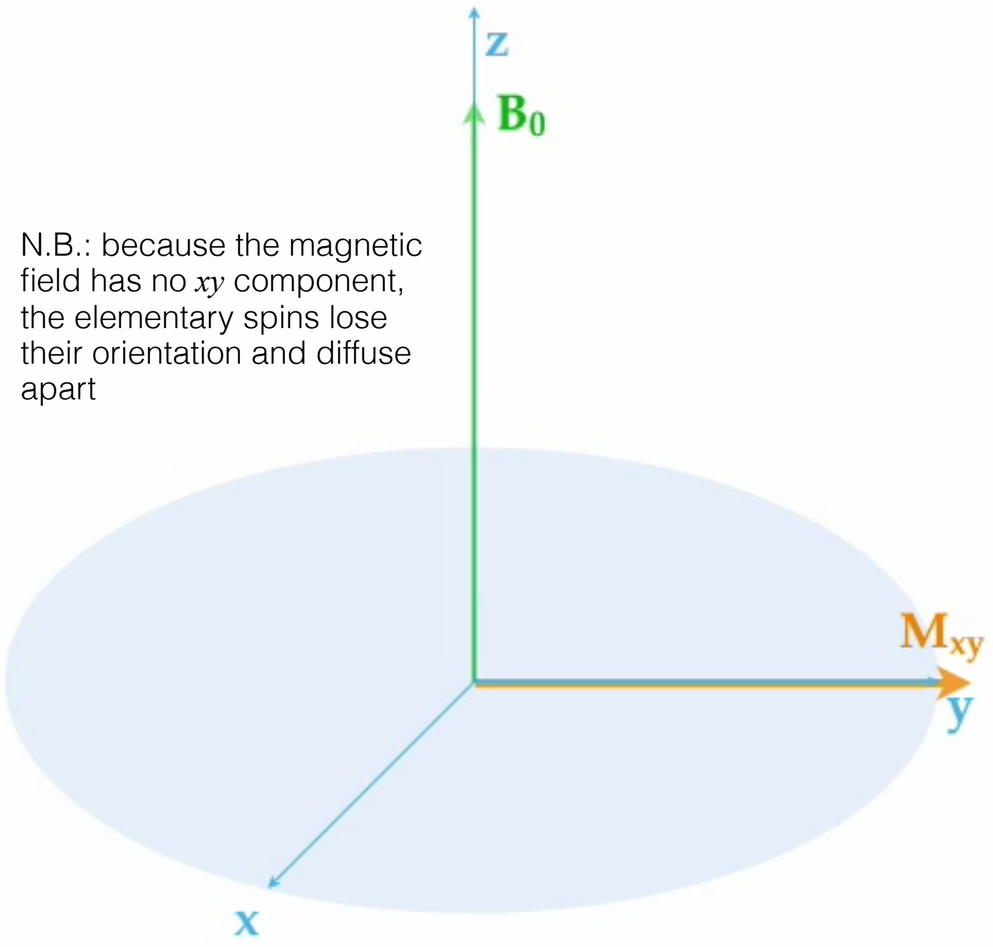
T1 relaxation time:
depends on interaction
between elementary magnet (proton)
and its environment (lattice)

Spin-spin relaxation

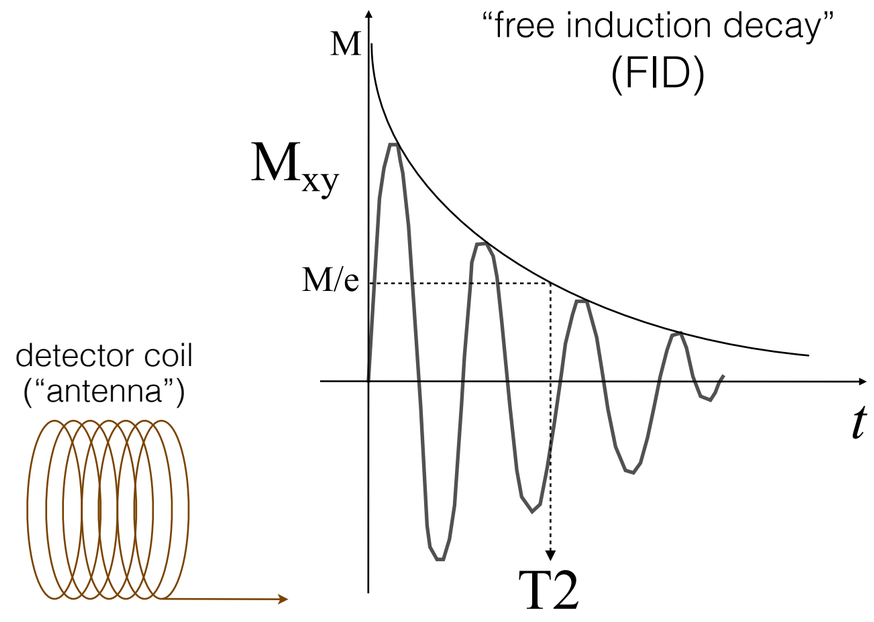
T2 or transverse relaxation

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



$\mathbf{M}_{xy}$: xy-plane vectorial component of $\mathbf{M}$

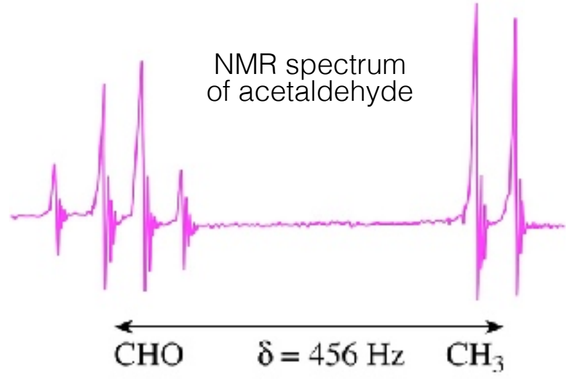


"free induction decay"
(FID)

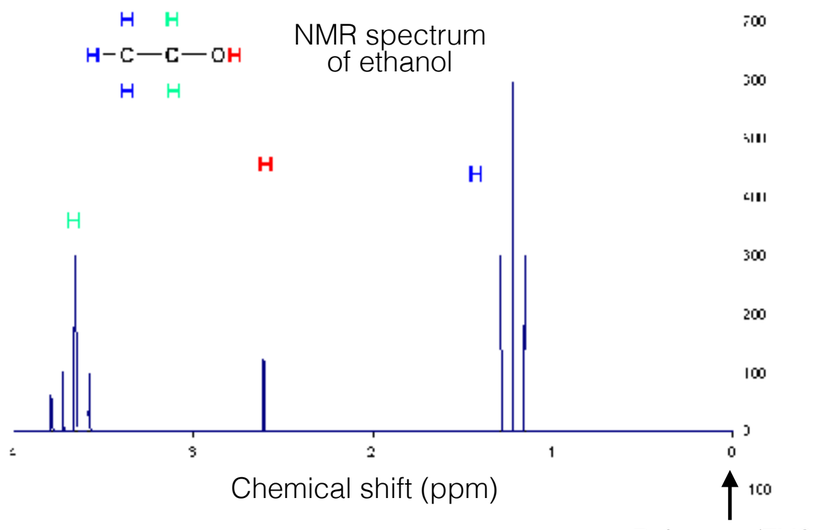
T2 relaxation time:
depends on interaction between elementary magnets (spins, protons);
process occurs in the transverse (xy) plane

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

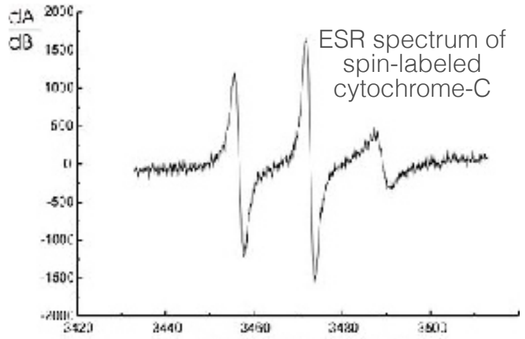


Somatomedin B domain
(superimposed structures)

ESR spectroscopy

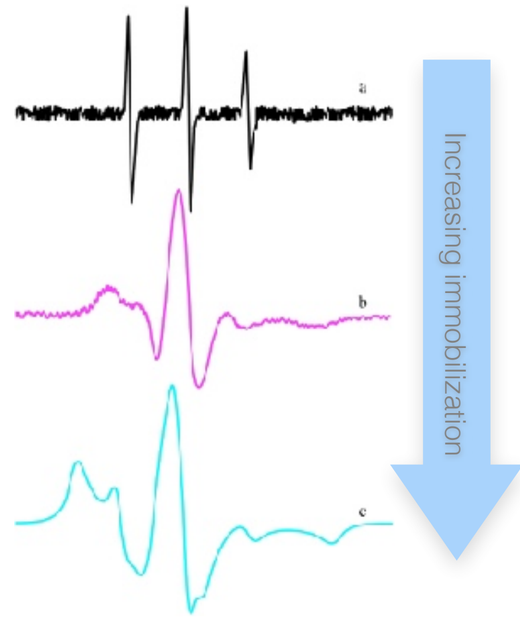
- Electron spin resonance (ESR) or electron paramagnetic resonance (EPR) spectroscopy.
- Spectroscopic method for investigating materials containing unpaired electron.
- EPR spectrum: intensity of electromagnetic radiation as a function of magnetic field.
- Magnetic field is lower, but radiation frequencies 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



ESR spectrum of spin-labeled cytochrome-C

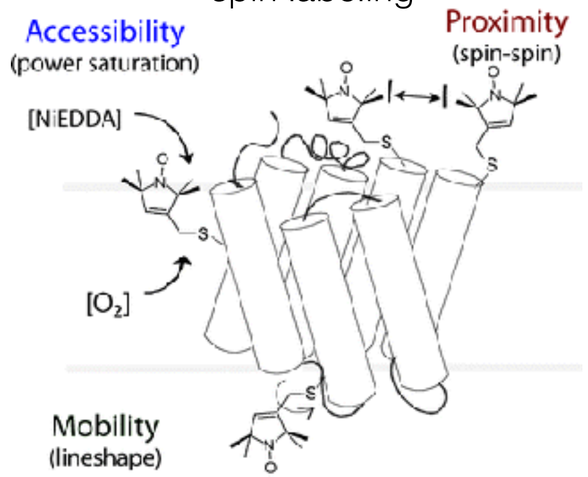
Magnetic field (G)

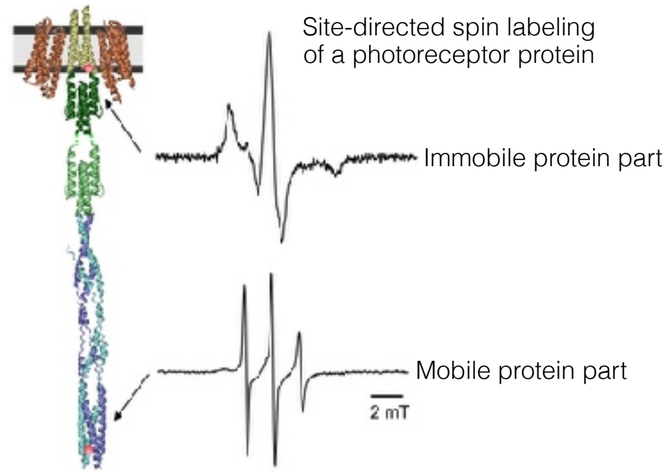


Effect of immobilization on the ESR spektrum

ESR spectroscopy workstation

Site-directed spin labeling

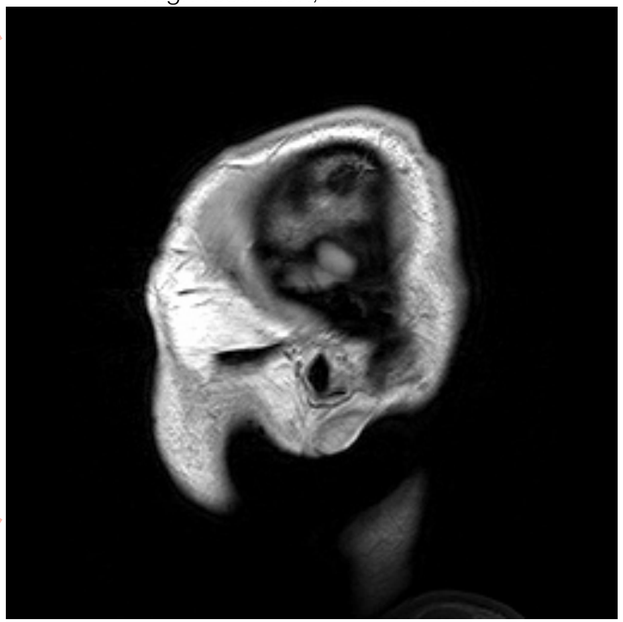




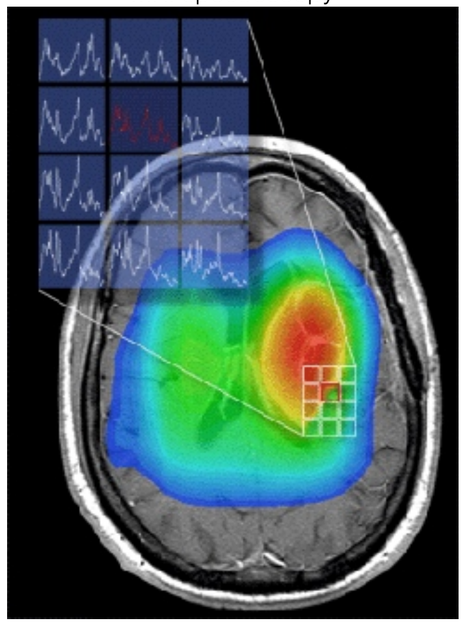
MRI is a revolutionary device

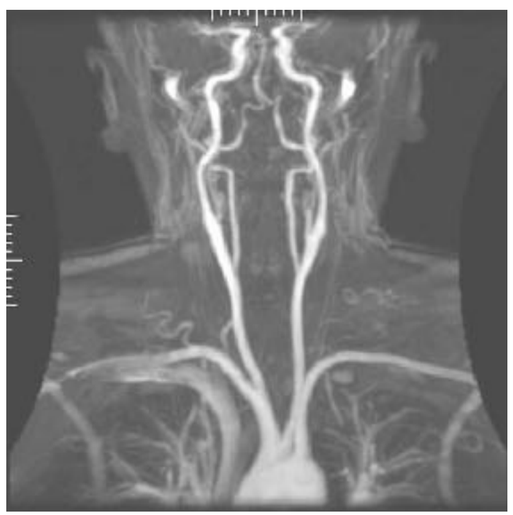
Non-invasive

High-resolution, anatomical MRI

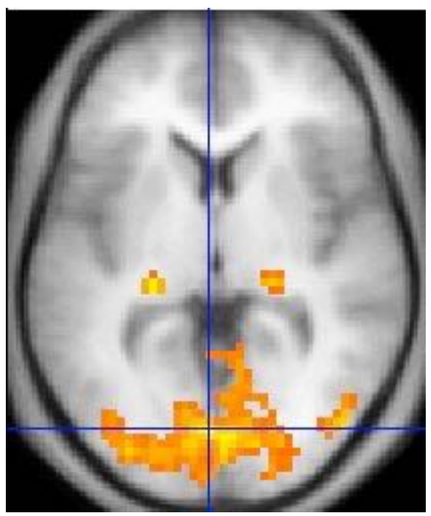


MRI spectroscopy

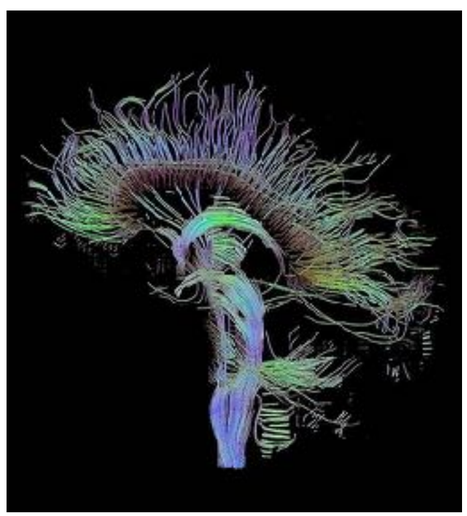




MRI angiography



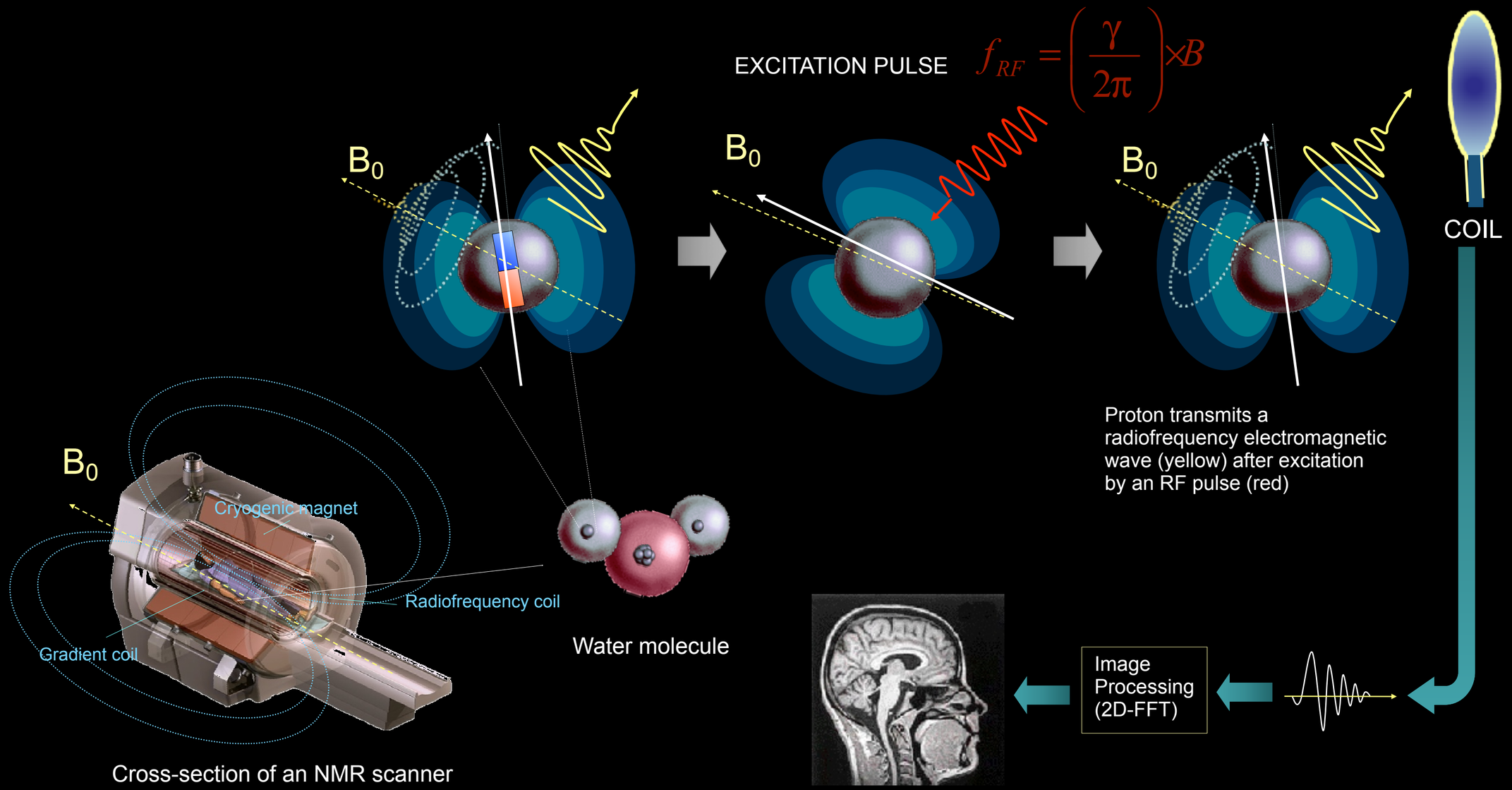
Functional MRI (fMRI)



Diffusion MRI (tractography)

Musculoskeletal MRI

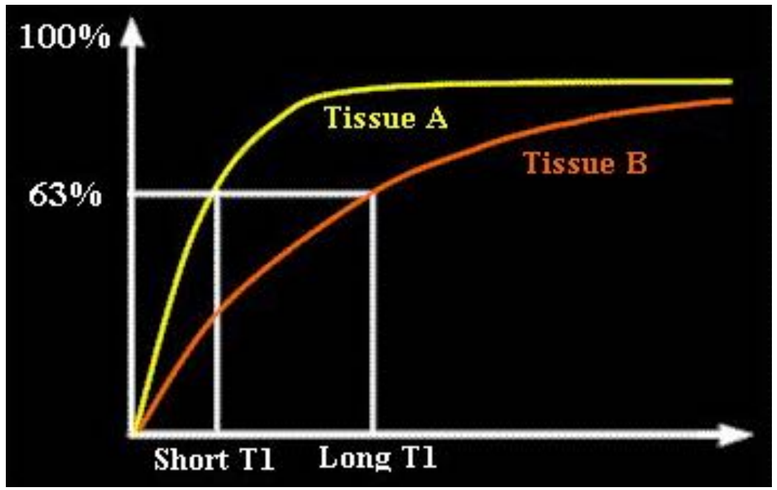
MRI: the human body is macroscopically magnetized

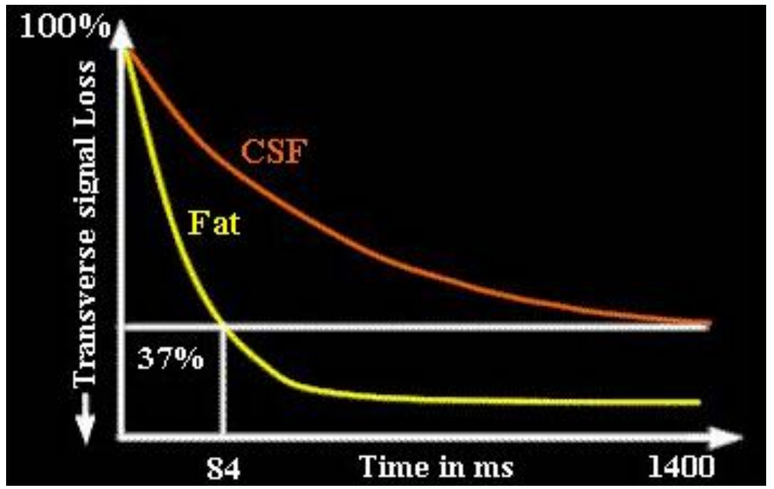


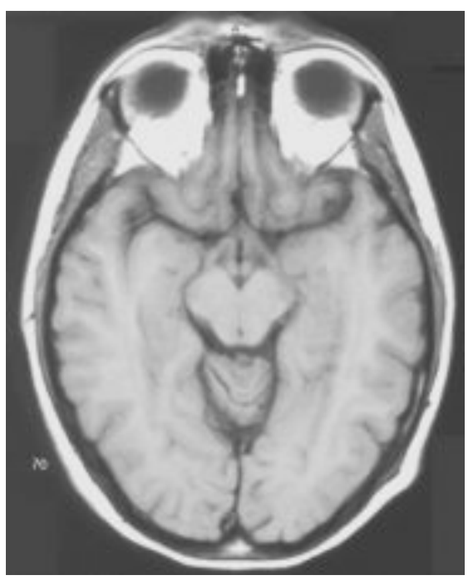
Cross-section of an NMR scanner

MRI 1: contrast

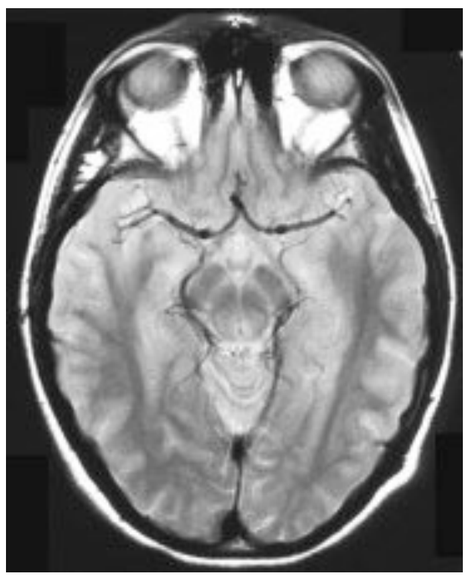
Color contrast based on spin density (proton density, PD) and relaxation times (T1, T2)



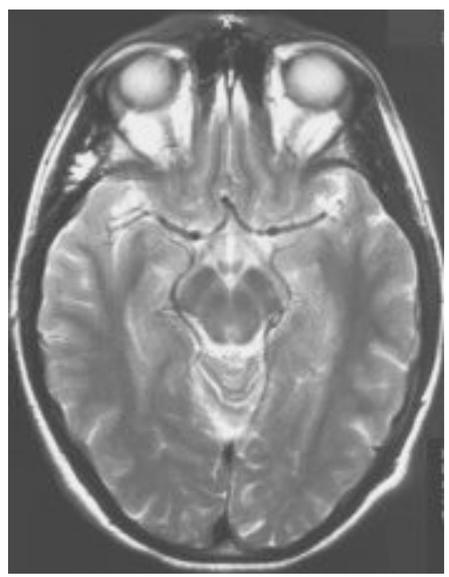




T1-weighting



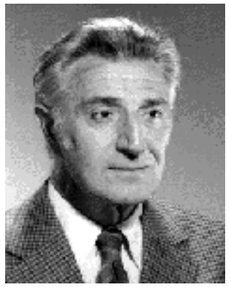
proton density-weighting



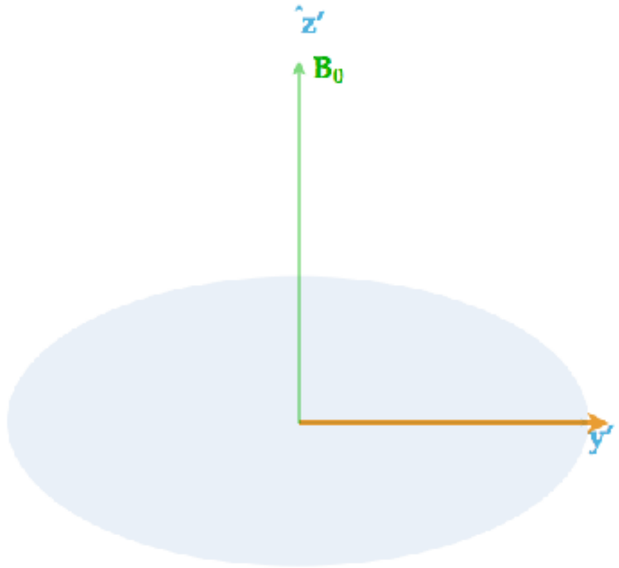
T2-weighting

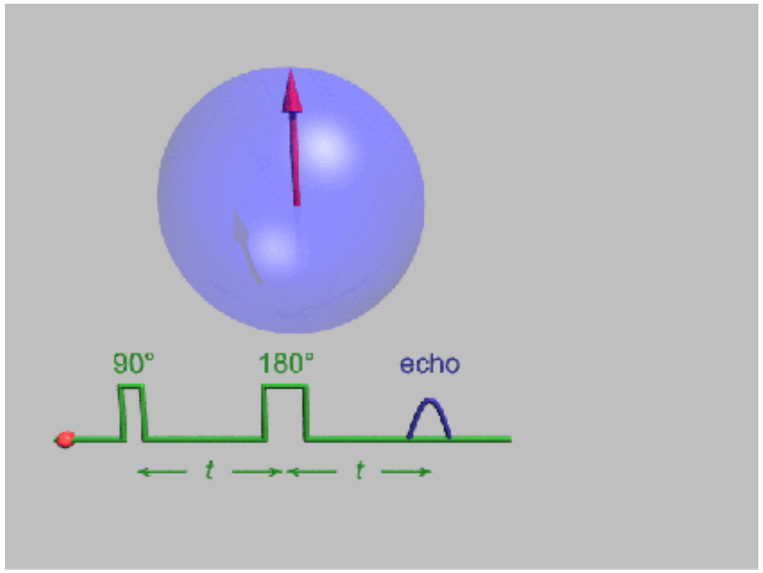
Measuring relaxation time: the spin-echo experiment

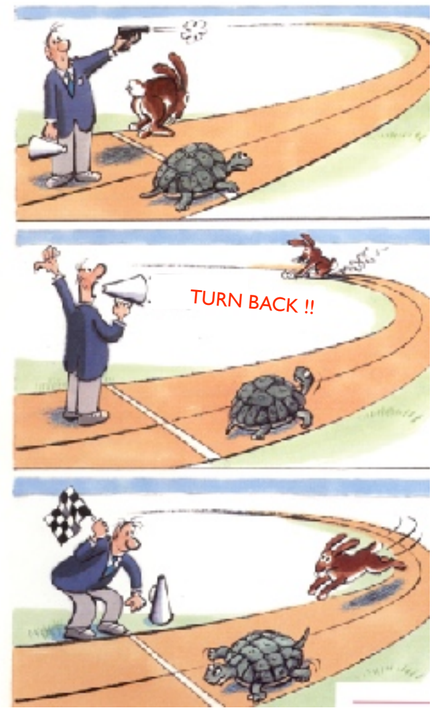
Repeating excitation, refocusing and “echo” pulses: spin-echo sequence



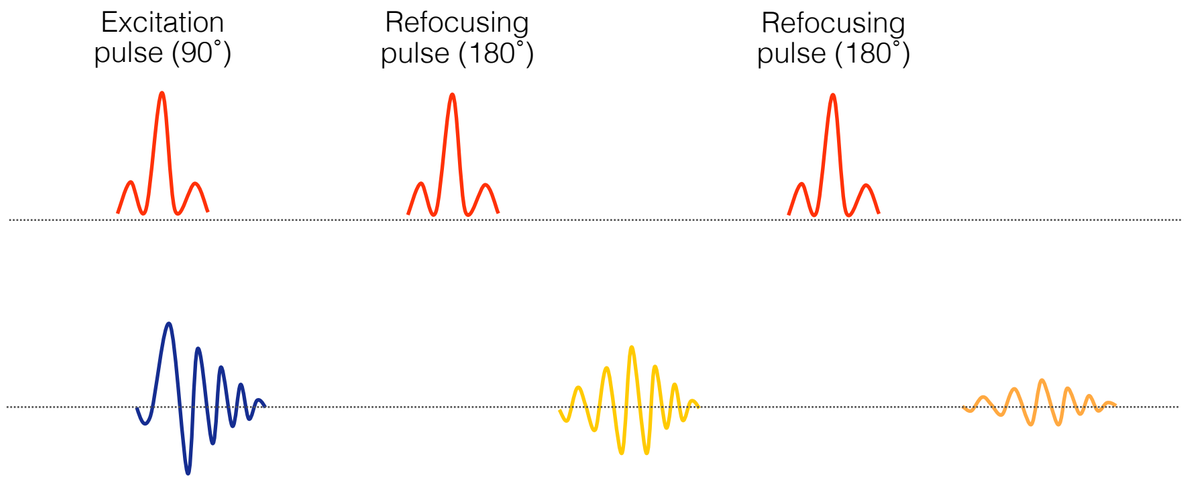
Erwin Hahn, 1949

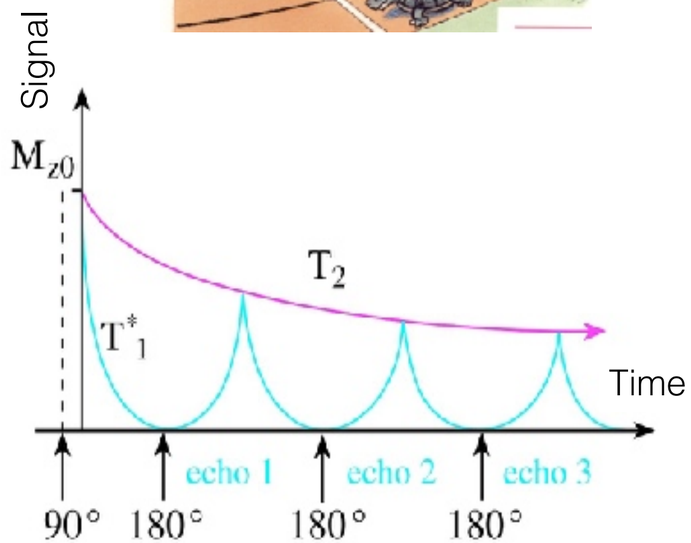






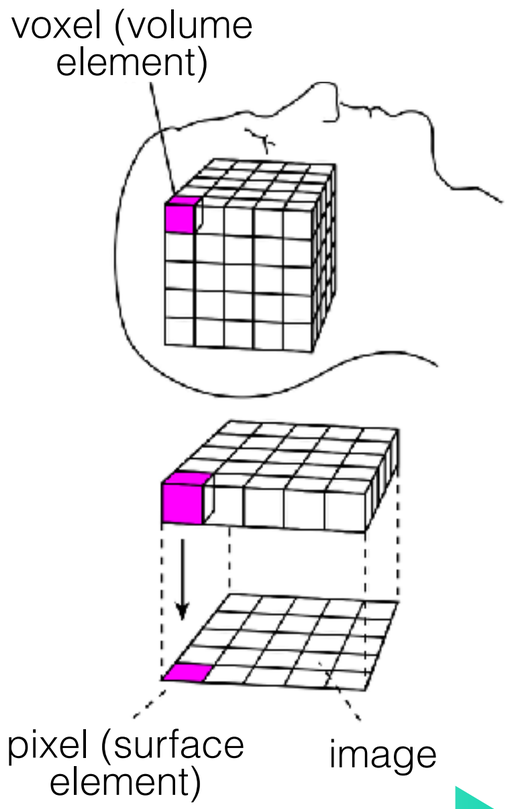
Knocking sounds in MRI: pulse generation

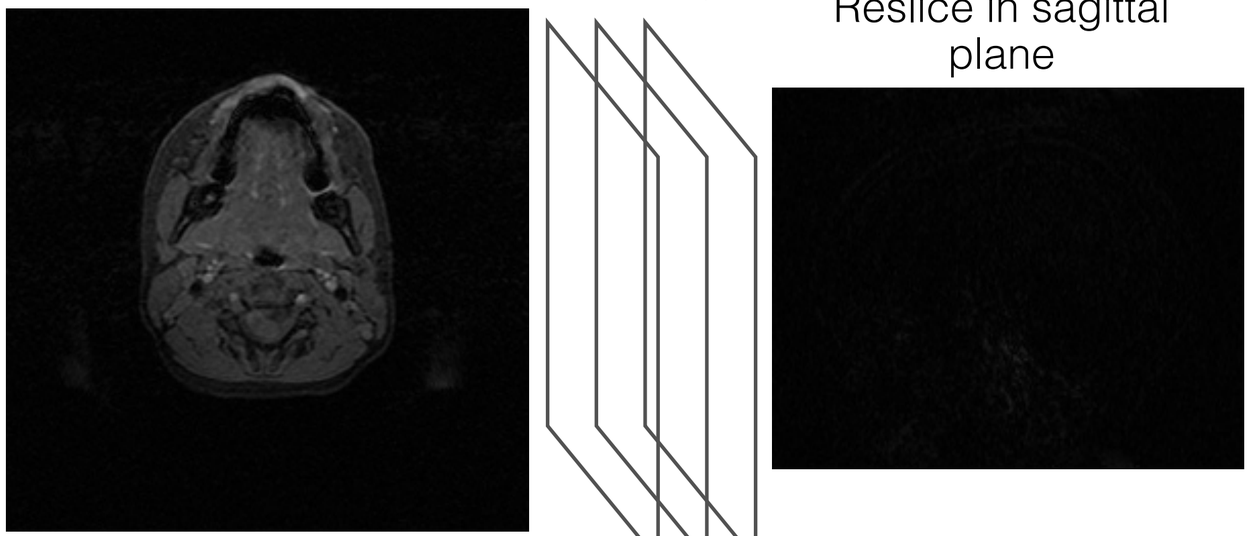


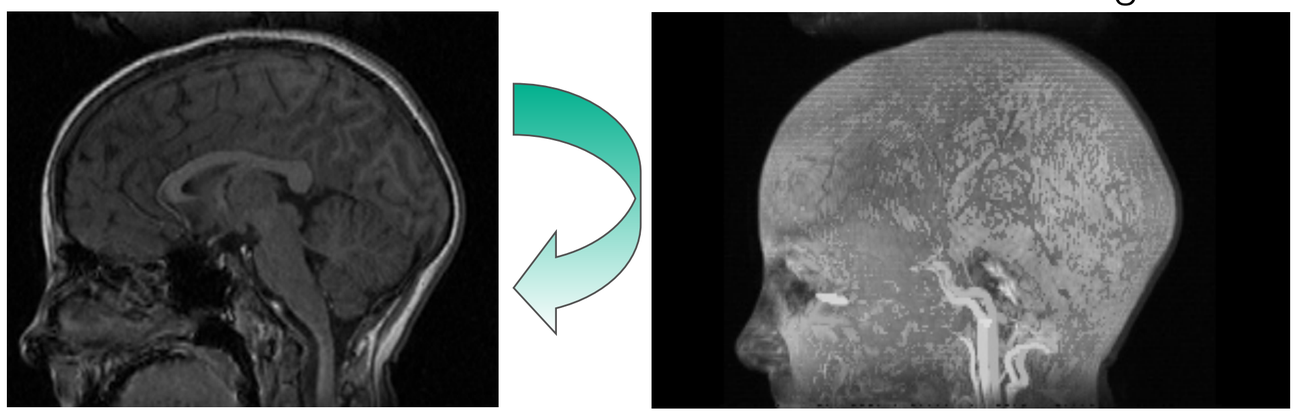


MRI 2: spatial encoding

Paul C. Lauterbur
(1929-)



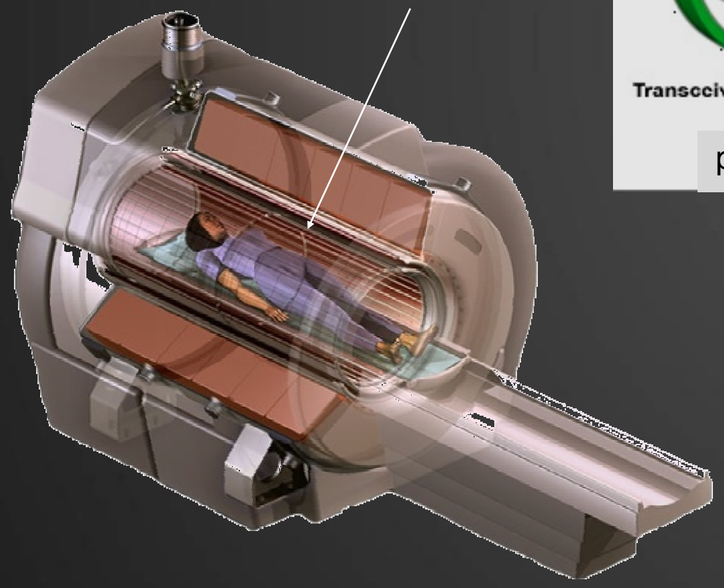


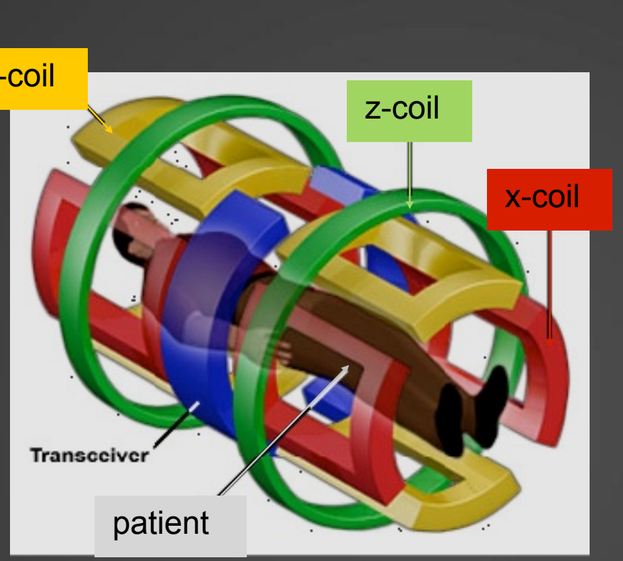


- Defining and addressing elementary 3D points (voxel): by using gradient magnetic field
- Foundations: resonance condition

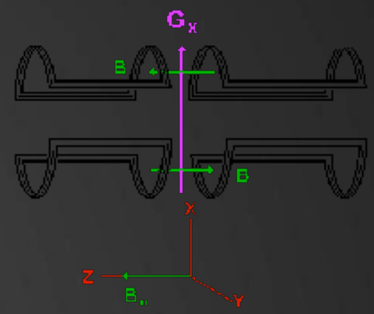
Generation of gradient fields: with gradient coils

Gradient coils

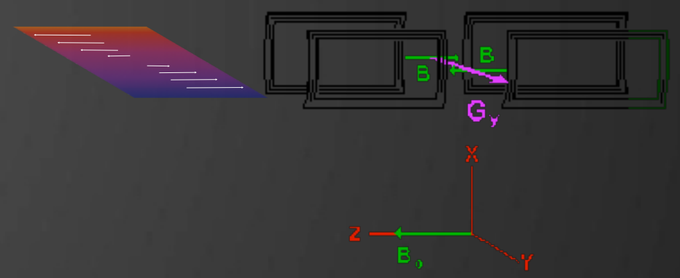




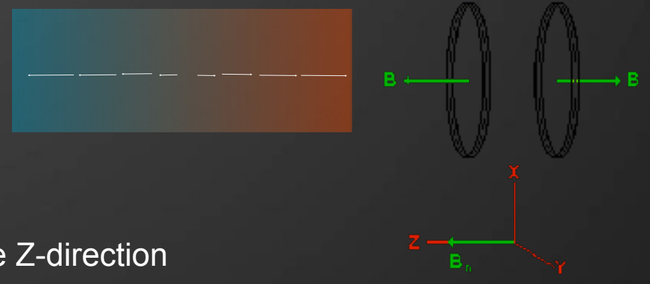
X-gradient coil



Y-gradient coil



Z-gradient coil



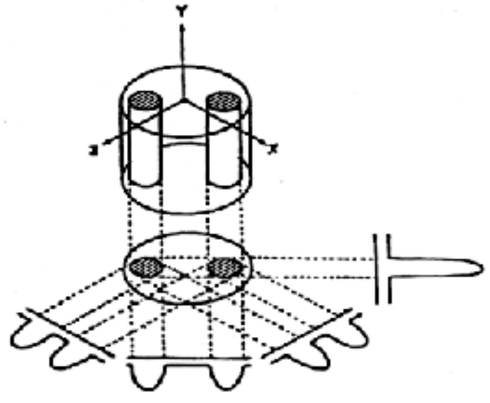
IMPORTANT NOTE:
The magnetic field is always in the Z-direction

MRI 3: image reconstruction

1.Back projection
- as in CT scanning

Paul Lauterbur, 1973, Illinois

Peter Mansfield, 1973, Nottingham

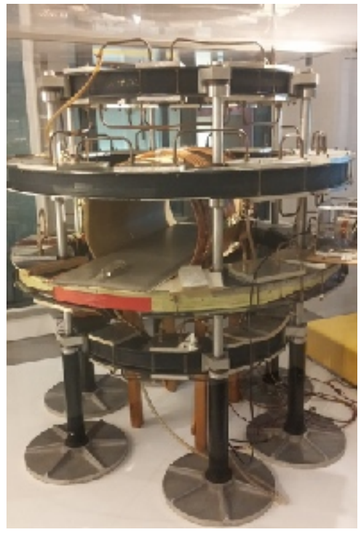


Principle of back projection

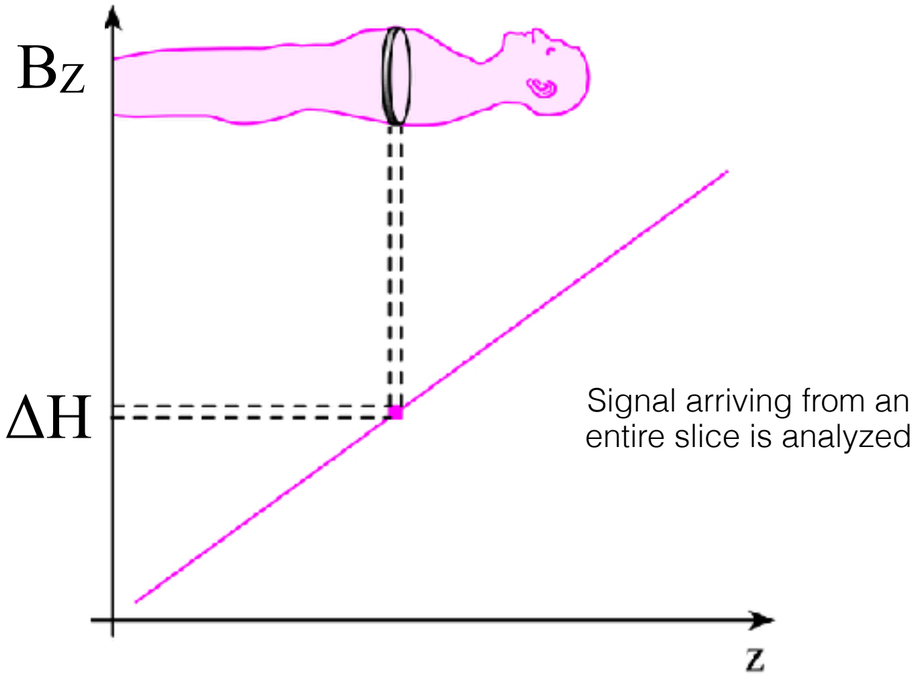
Reconstructed image (cross section of two test tubes)

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

Richard Ernst, 1974, Zürich



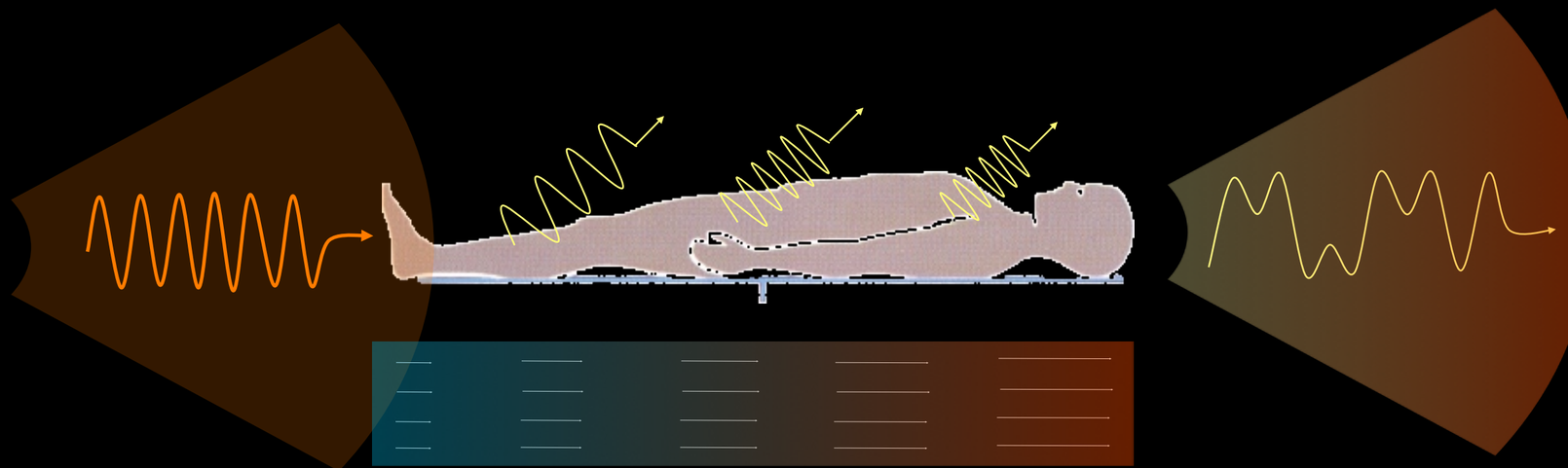
“MRI Scanner Mark One”, Aberdeen, Scotland

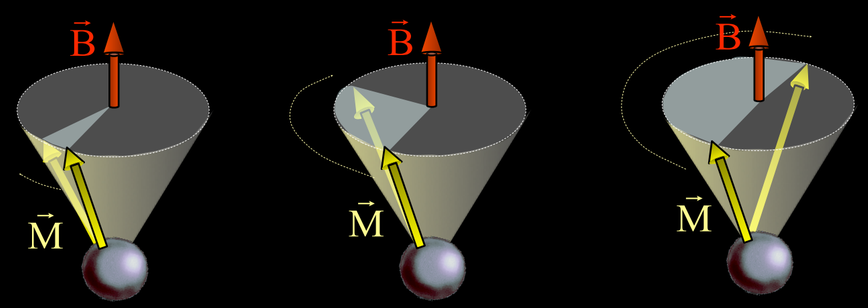


Signal arriving from an entire slice is analyzed

MRI: spatial coding and image reconstruction

based on the resonance condition ($\mathbf{B_0}$-dependent ω)





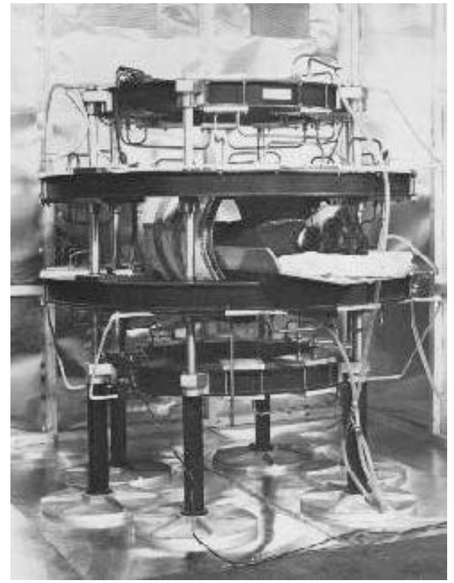
RF coil

Fourier transformation

MRI 4: scanners

Early times

Indomitable (Damadian)



MRI Scanner Mark One (Ernst)

Present

3T MRI

Open MRI unit

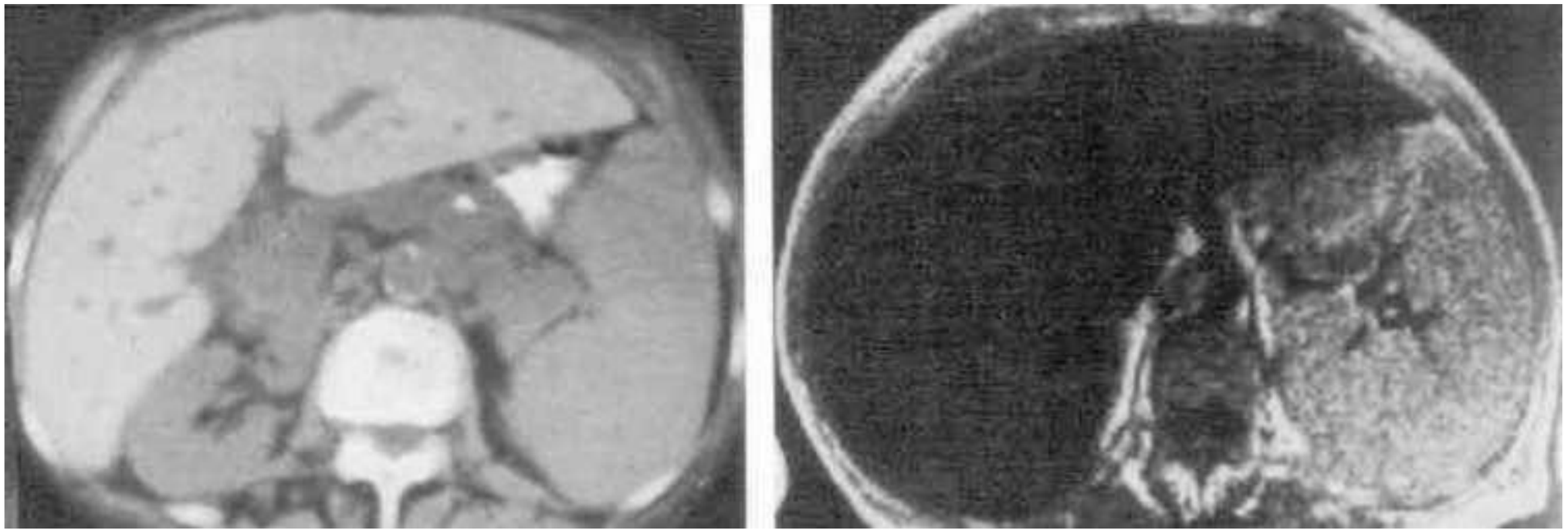
Interventional MRI unit

Mobile MRI

MRI 5: contrast agents

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

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

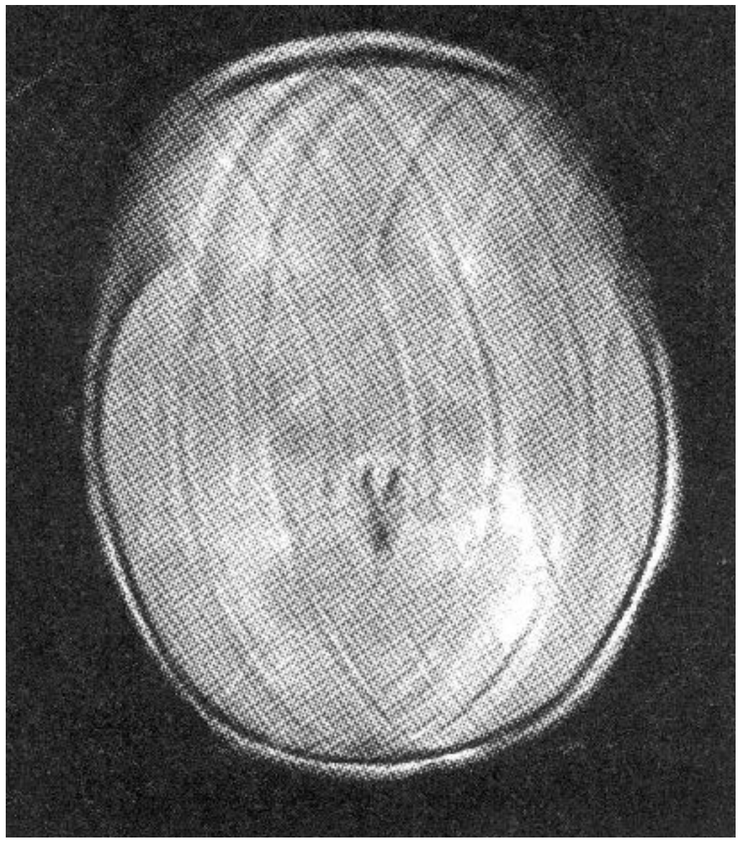


CT MR T2

Haemochromatosis hepatis (iron accumulation in liver)

MRI 6:artefacts

- Motion
- Metals (implants, injury)



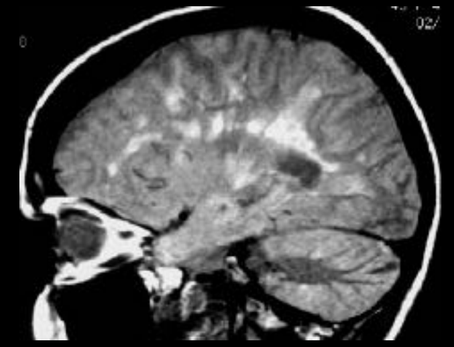
Motion artefact

Metal in the orbit of the eye

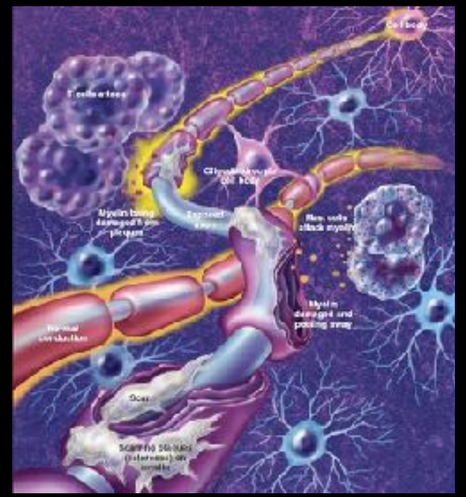
MRI 7: dangers, contraindications

- 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)

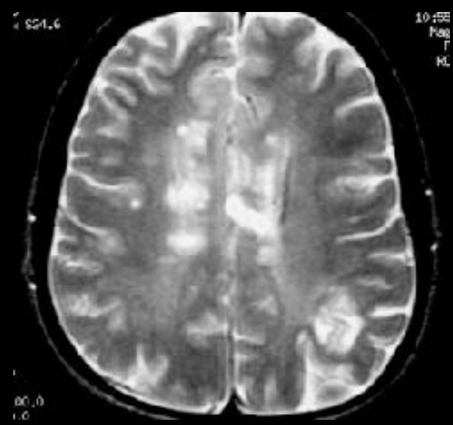
Applications: Anatomical imaging - Multiple sclerosis



Proton density
(sagital)



Proton density
(transverse)



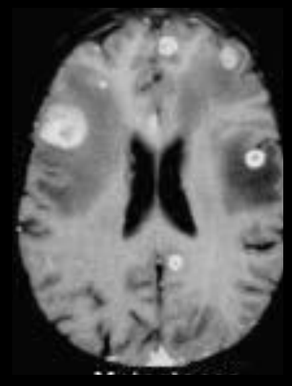
T2 weighted
(transverse)

T1 weighted
With contrast agent

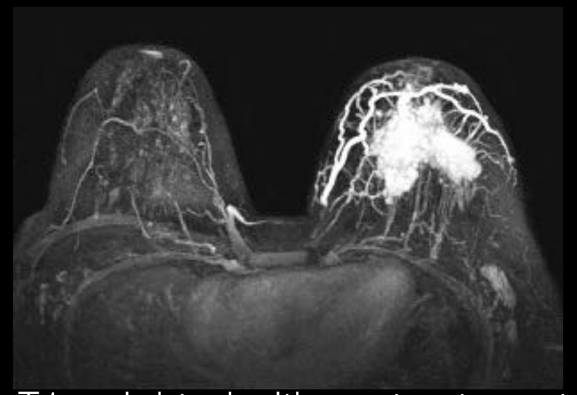
Anatomical imaging: Oncology

T2 weighted
(chondrosarcoma)

T2 weighted
(cyst)

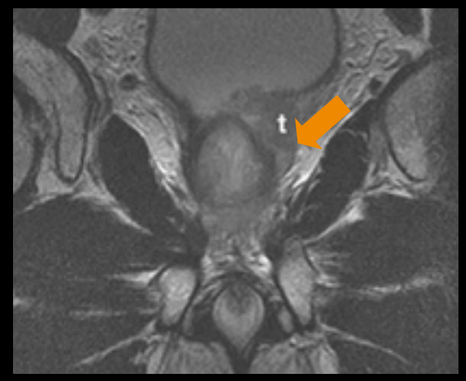


Proton density
(Brain metastasis)



T1 weighted with contrastagent
(Breast carcinoma)

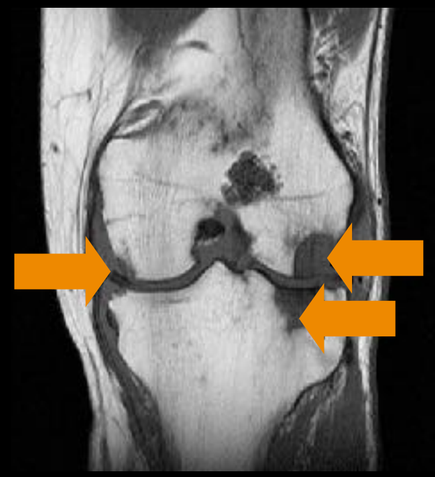
T2 weighted
(cervix carcinoma)



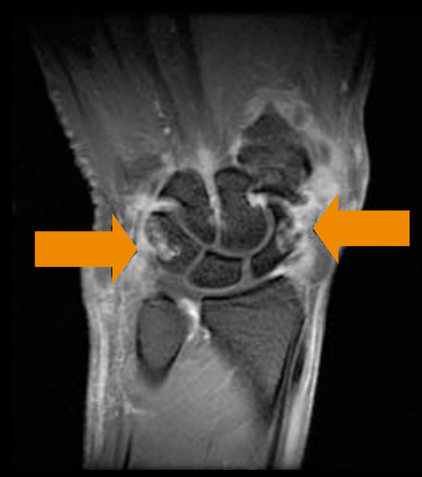
T2 weighted
(prostate tumor)

Anatomical imaging
Bone and soft tissue

T2 weighted
(torn ligaments)

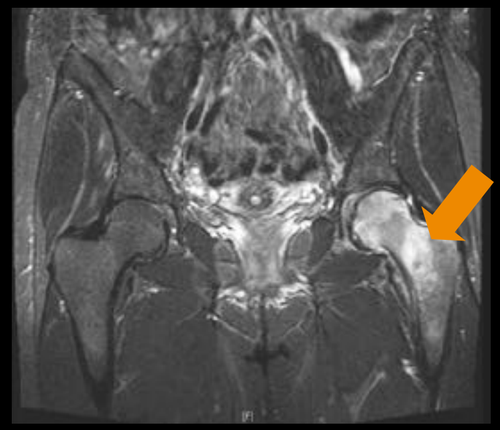


Rheumatoid arthritis
knee



Rheumatoid arthritis
whrist

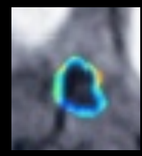
T2 weighted
(hernia)

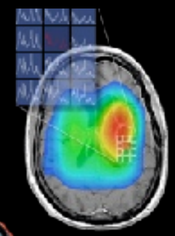
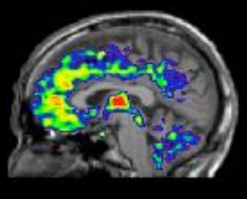
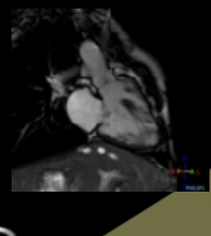
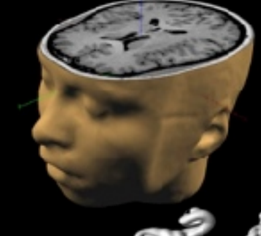


Osteoporosis (femur)

There is more to MRI than anatomical imaging ...









2008

‘State of the art’

- 3D images
- dynamic images
- sharp image resolution

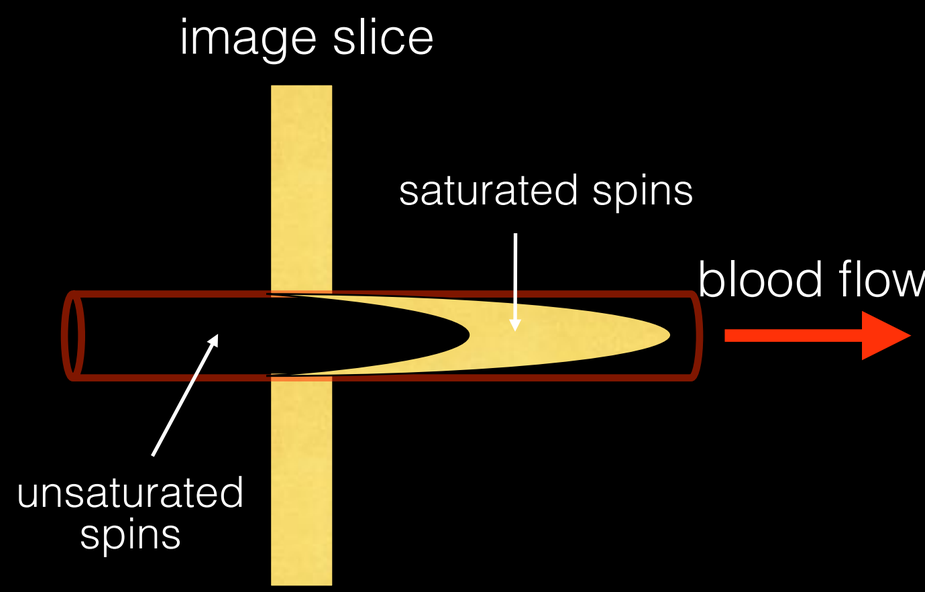
1972

First NMR images

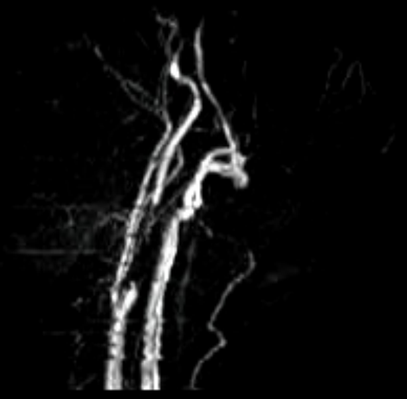
In research phase

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

MRI:
Non-invasive angiography

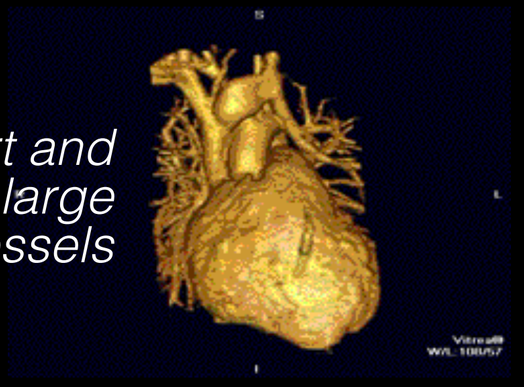


Arteria carotis

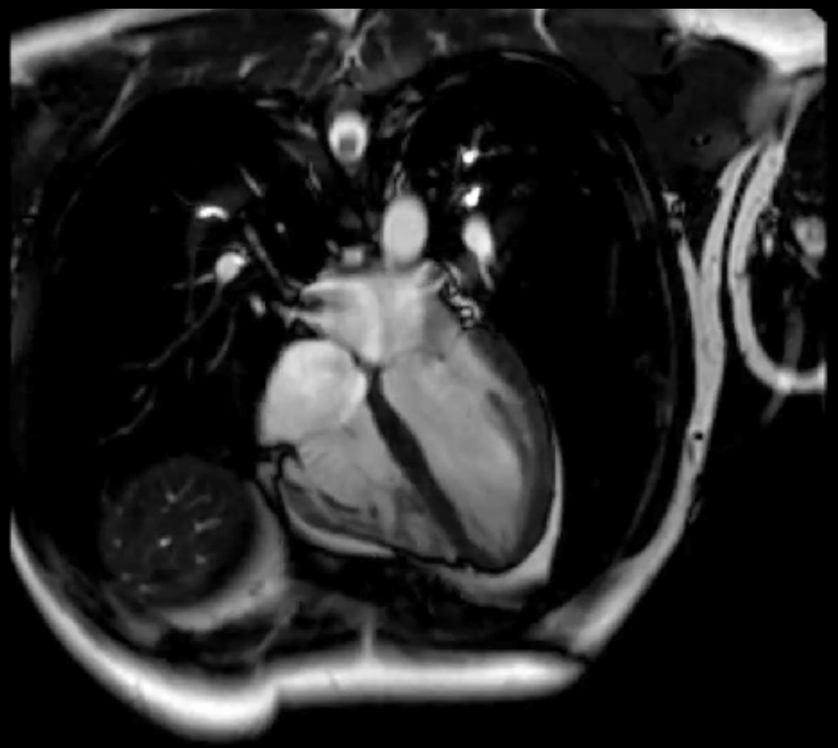


Circulus arteriosus Willisii

Heart and large vessels



Time-resolved MRI
(ECG-gating required)

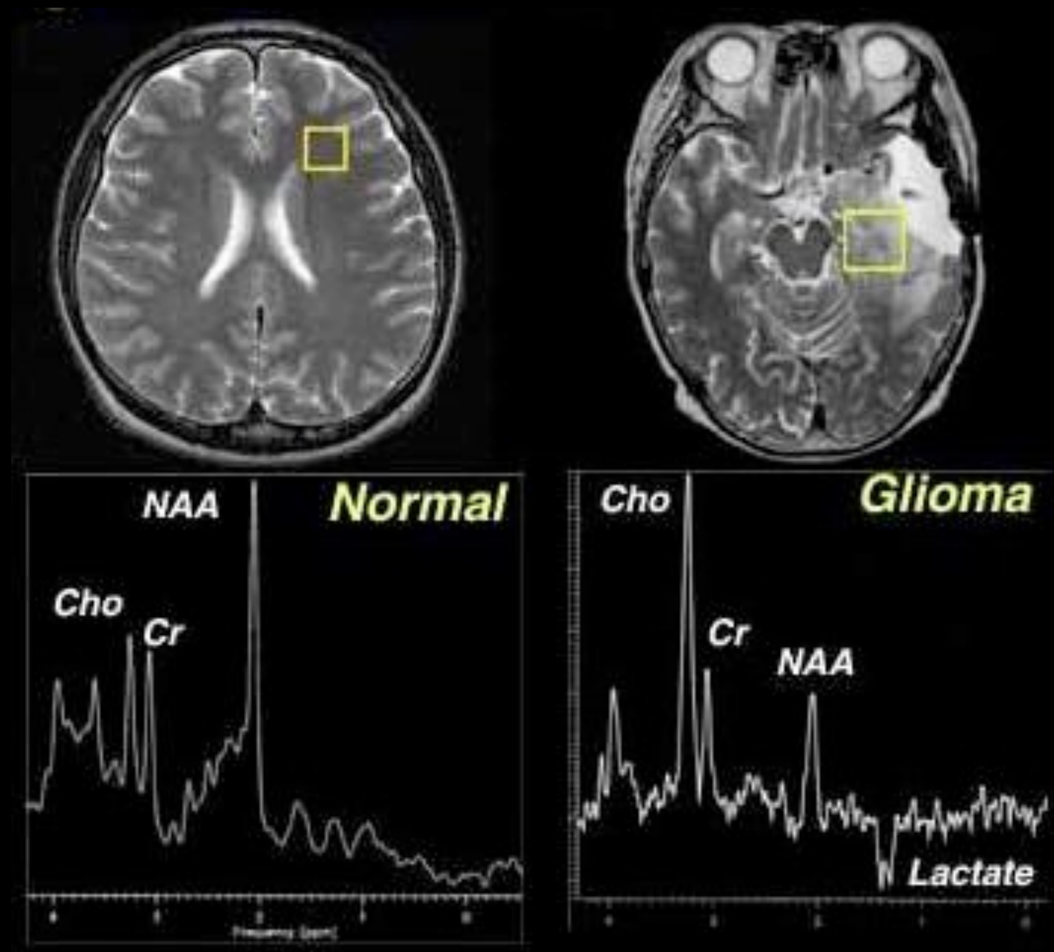


Blood flow across the cardiac chambers

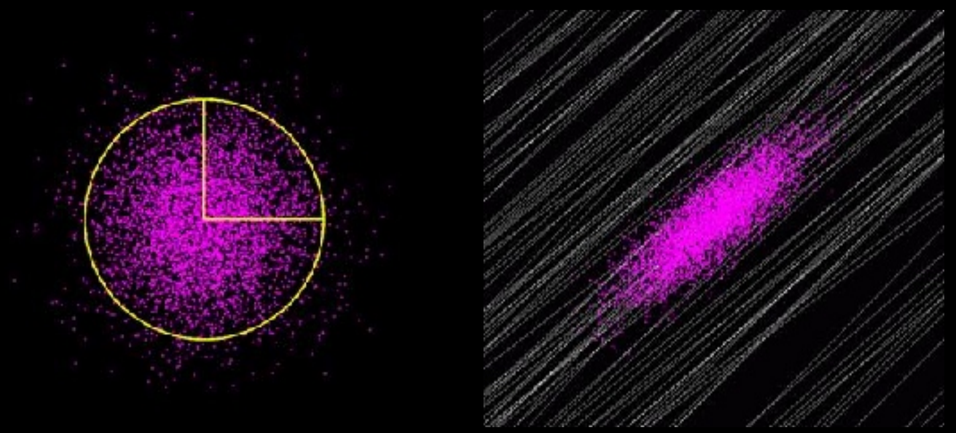
Opening and closing of aorta valve

MR Spectroscopy

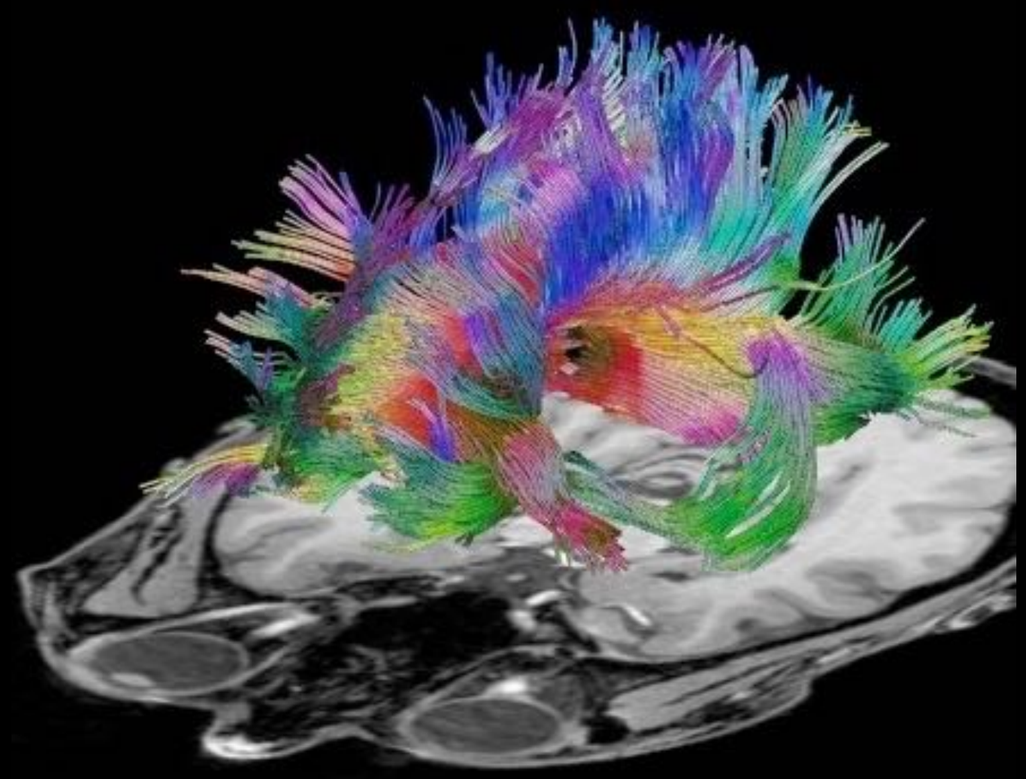
- Chemical shift
- Identification of metabolites
- Tumor diagnostics



Diffusion imaging



Anisotropic water diffusion:
contrast generation

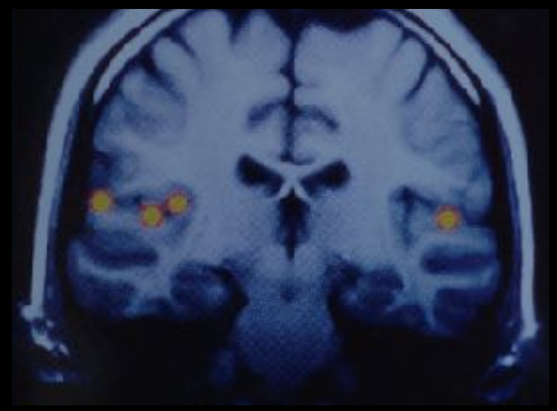


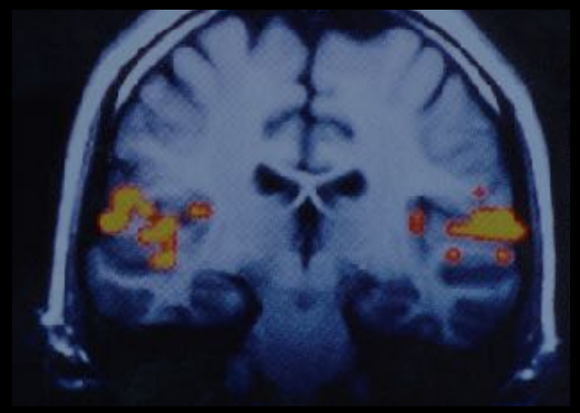
Imaging neural tracts:
tractography

Corpus callosum

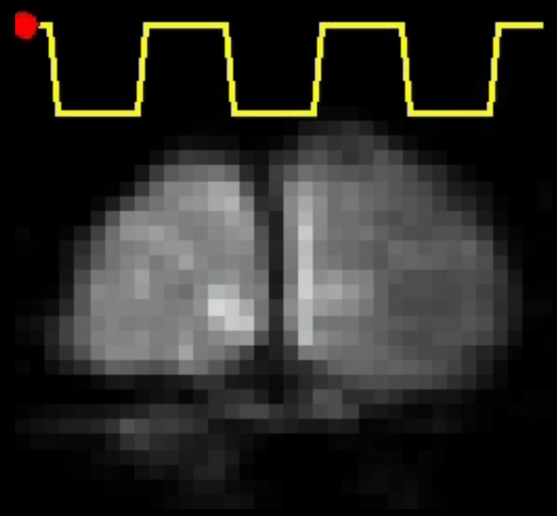
Functional MRI (fMRI)

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