Functional Brain MRI

Part 1

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fMRI: Methods and Applications

- **Christian Windischberger**
- **March 16th - 20th**
- **14:00 – 17:30**
- **MRCE, seminar room**
- **Further questions:**
  - Tel.: 6463, 81-6090
  - Email: christian.windischberger@meduniwien.ac.at

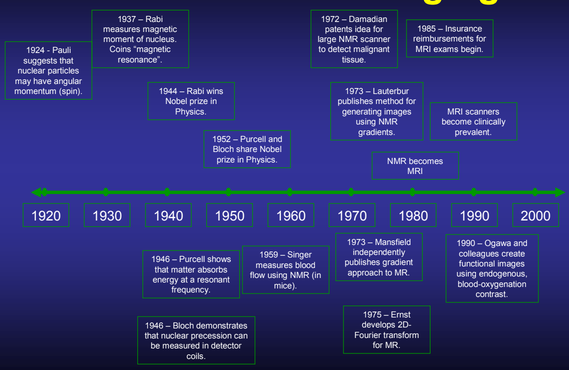
Who are we?

- **Centre of Excellence “High Field MR”**
  - Joint Unit of Center for Biomedical Engineering and Physics and Dept. Radiology
  - Uses, maintains, and supports a research-dedicated MRI scanner (3.0T)
  - New 3T research scanner at the end of 2006
  - New 7T research scanner at the end of 2007
  - Scientific Research

Outline for Today

- **History of MRI**
- **MRI basics**
  - Spin
  - RF Excitation
  - Relaxation
  - Echoes
  - Bloch equations

Timeline of MR Imaging



Discovery of Nuclear Magnetic Resonance Absorption (1946)


Felix Bloch

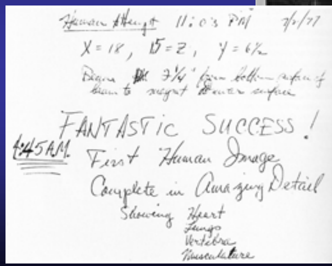

Edward Purcell

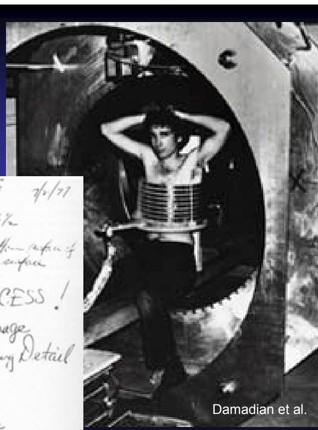
- **Bloch and Purcell independently discovered how to measure nuclear moment of bulk matter (1946)**
- **They showed that energy applied at a resonant frequency was absorbed by matter, and the re-emission could be measured in detector coils**
- **They shared the 1952 Nobel Prize in Physics**

Early Uses of NMR

- **Most early NMR was used for chemical analysis**
  - No medical applications
- **1971 – Damadian publishes and patents idea for using NMR to distinguish healthy and malignant tissues**
  - “Tumor detection by nuclear magnetic resonance”, *Science*
  - Proposes using differences in relaxation times
  - No image formation method proposed
- **1973 – Lauterbur describes projection method for creating NMR images**
  - Mansfield (1973) independently describes similar approach

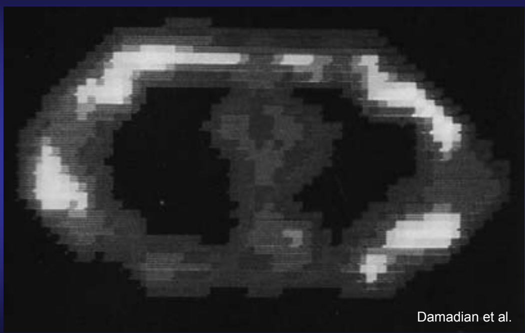
in the beginnings





Damadian et al.

Thoracic imaging …



Damadian et al.

The first images

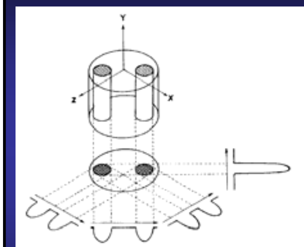


Fig. 1 Relationship between a three-dimensional object, its two-dimensional projection along the Y-axis, and four one-dimensional projections at 45° intervals in the XZ-plane. The arrows indicate the gradient directions.

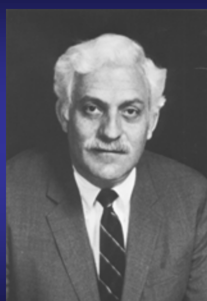
Fig. 2 Proton nuclear magnetic resonance zeugmatogram of the object described in the text, using four relative orientations of object and gradients as diagrammed in Fig. 1.

Lauterbur, P.C. (1973). Image formation by induced local interaction: Examples employing nuclear magnetic resonance. *Nature*, 242, 190-191.

2003 Nobel Prize Winners

Paul Lauterbur **Peter Mansfield**

2003 Nobel Prize



Raymond Damadian


This Year's Nobel Prize in Medicine

The Shameful Wrong That Must Be Righted

This year the committee that awards The Nobel Prize for Physiology or Medicine did the one thing it has no right to do: it ignored the truth. Eminent scientists, leading medical textbooks and the historical facts are in disagreement with the decision of the committee. So is the U. S. Patent Office. Even Alfred Nobel's will is in disagreement. The committee is attempting to rewrite history.

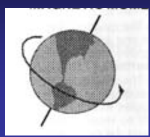
The Nobel Prize Committee to Physiology or Medicine chose to award the prize, not to the medical doctor/research scientist who made the breakthrough discovery on which all MRI technology is based, but to two scientists who later made technological improvements based on his discovery.

New York Times
October 9, 2003

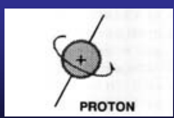
NMR Basics

Spin

- Spin (angular momentum) is a fundamental property of nature



- Protons, electrons, and neutrons possess spin

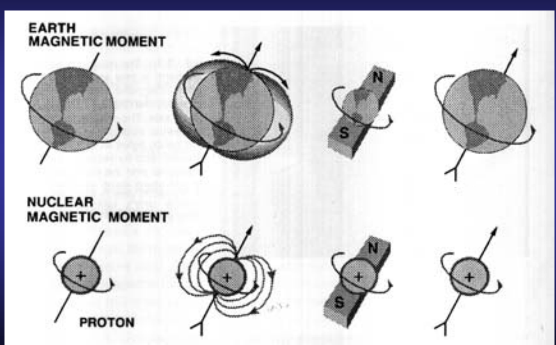


Nuclear Spin

- Atomic nuclei can have spin *I* of integer, half-integer or zero value

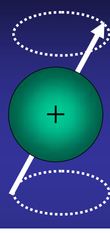
Z	A	I	${}^{A}_{Z}E$
even	even	0	${}^{12}_{6}C$, ${}^{16}_{8}O$
odd	odd	$\frac{1}{2}, \frac{3}{2}, \frac{5}{2}, \ldots$	${}^{1}_{1}H$, ${}^{15}_{7}N$, ${}^{19}_{9}F$, ${}^{31}_{15}P$
even	odd	$\frac{1}{2}, \frac{3}{2}, \frac{5}{2}, \ldots$	${}^{13}_{6}C$, ${}^{17}_{8}O$
odd	even	1,2,3,. . .	${}^{2}_{1}H$, ${}^{14}_{7}N$

Spin and magnetic moment



Spin and magnetic moment

- **Due to inner structure of the nucleons (charged quarks) this angular momentum (spin) is related to a magnetic moment**
- **This can be thought of an electric current which produces a magnetic field**



$$\vec{\mu} = \gamma \vec{I}$$

γ ... gyromagnetic ratio

Nuclear spin

- **Particles with opposite spins can pair up and cancel out the effect**
- **NMR can only be performed with certain nuclei**
- **The most commonly used are:**

nucleus	$\nu_0 = \frac{\omega_0}{2\pi}$ [MHz] (for 1 T)	*rel. natural abundance [%]*	*relative abundance in biol. systems [.]*	*sensitivity relative to ^1H [.]*
^{1}H	42.58	99.98	1	1
^{2}H	6.56	0.016	$6.2 \cdot 10^{-5}$	$9.7 \cdot 10^{-3}$
^{13}C	10.71	1.11	$2.5 \cdot 10^{-4}$	$1.6 \cdot 10^{-2}$
^{19}F	40.05	100	$6.3 \cdot 10^{-5}$	$8.3 \cdot 10^{-1}$
^{23}Na	11.26	100	10^{-3}	$9.3 \cdot 10^{-2}$
^{31}P	17.24	100	$1.4 \cdot 10^{-3}$	$6.6 \cdot 10^{-2}$

Magnetic Moments

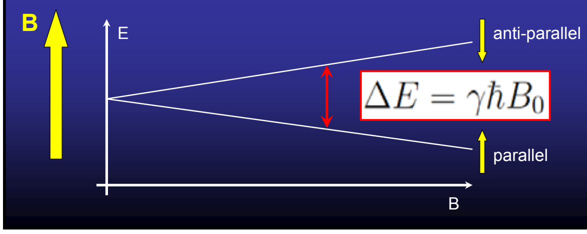
- Proton: μ_P=1,41 10^{-26} J/T
- Neutron μ_N=9,65 10^{-27} J/T
- For a given spin quantum number s there are 2s+1 possible orientations along the magnetic field axis
- s=1/2 → 2 possible orientations
  - parallel
  - anti-parallel

Spins within an external magnetic field

- When particles with spin are placed in a magnetic field of strength B_0, spins orient themselves parallel to (low energy state) or anti-parallel the field (high energy state)

Magnetic Moments

- **Spins in external magnetic field**
  → splitting of energy levels
- **Example: Hydrogennucleus (s=1/2)**



Energy difference

$$\Delta E = \gamma\hbar B_0$$

The difference between these energy states is proportional to the applied magnetic field B_0

$$h\nu_0 = \Delta E = \hbar\omega_0$$

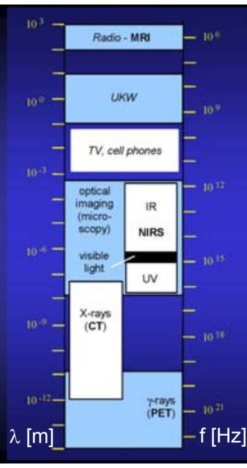
- ν **... frequency [MHz]**
- ω_0 **... angular frequency [MHz]**
- B_0 **... Magnetic field [T]**
- γ **... gyromagnetic ratio**

Energy difference

Energy is proportional to frequency

$$h\nu_0 = \Delta E$$

MRI is able to make high resolution images despite the low energy involved due to the resonance of many spins



Larmor equation

$$\omega_0 = \gamma \cdot B_0$$

$\omega_0 = 2\pi\, \nu_0$ ... Larmor frequency [MHz]

B_0 … magnetic field [T]

γ ... gyromagnetic ratio

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Population densities

- Population densities of a spin ensemble in thermal equilibrium follow the Boltzmann distribution

$$n_i = N \cdot p_i = N \cdot \frac{e^{-\frac{E_i}{kT}}}{\sum_i e^{-\frac{E_i}{kT}}}$$

Energy levels

$$E_{+\frac{1}{2}} = \frac{e^{-\frac{\hbar\gamma B_0}{2kT}}}{e^{-\frac{\hbar\gamma B_0}{2kT}} + e^{+\frac{\hbar\gamma B_0}{2kT}}}$$

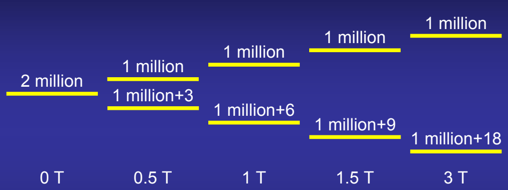
$$E_{-\frac{1}{2}} = \frac{e^{+\frac{\hbar\gamma B_0}{2kT}}}{e^{-\frac{\hbar\gamma B_0}{2kT}} + e^{+\frac{\hbar\gamma B_0}{2kT}}}$$

Population densities

$$\frac{n_{-\frac{1}{2}}}{n_{+\frac{1}{2}}} = \frac{e^{+\frac{\hbar\gamma B_0}{2kT}}}{e^{-\frac{\hbar\gamma B_0}{2kT}}} = e^{\frac{\hbar\gamma B_0}{kT}} = e^{\frac{\Delta E}{kT}}$$

at 3 T and 300 K: ΔN ca. 10^7/mol

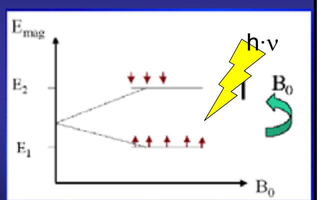
More signal at higher field



At 3 Tesla, for every **2 million** protons, there are **18** more protons aligned with the field than there are aligned against the field

Magnetization of a spin population

- Spins can undergo transitions between the two energy states by the absorption of a photon
- Energy difference ΔE is related to frequency of photon by Planck's constant *h*



Nuclear magnetic resonance

- The detection of radiant transitions by means of high frequency methods is called nuclear resonance
- A solitary transition between a nucleus' Zeeman niveaus can never be observed directly
- A measurable effect will only result if a large number of nuclei simultaneously contributes to resonance

(N)MR in a nutshell I

- **RF pulses are used to excite spins of nuclei with odd mass numbers**
- **Signal emitted during return to baseline is detected**
- **Nuclei: H (^{1}H)**
  C (^{13}C)
  P (^{31}P)
  Na (^{23}Na) a.s.o.

(N)MR in a nutshell II

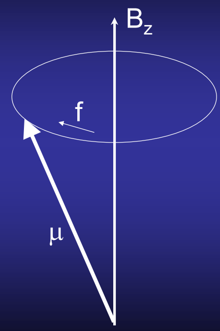
- **Using RF pulse population densities of both levels are changed**
  → overall magnetization changes
- **Resonance: *Larmor frequency***

$$\hbar\omega=\Delta E=\hbar\gamma B$$
$$f=\gamma B/2\pi$$

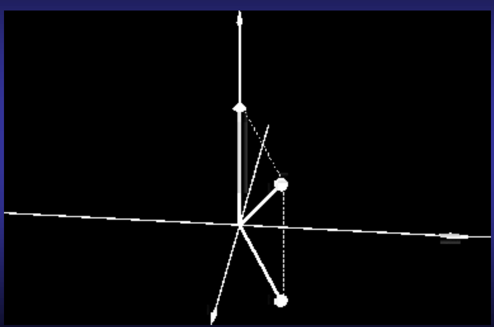
Classic Model

A magnetic moment μ precesses around B at the Larmor frequency $f=\gamma.B/2\pi$

For hydrogen: 42 MHz/T



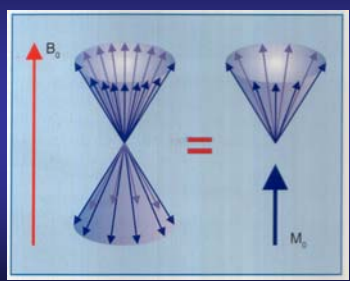
Classic Model



Courtesy: RW Cox

Macroscopic magnetisation

All magnetization vectors within the body add up to a net magnetization parallel to B_0



Magnetic Moments

- Spins in external magnetic field
  → splitting of energy levels
- Animation:
  file:///C:/Dokumente%20und%20Einstellungen/chris/Eigene%20Dateien/Daten/Vortr%E4ge/fmri_VO/anims/precess.htm

Macroscopic magnetisation

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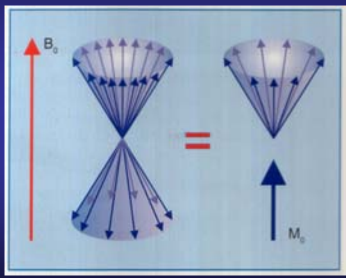
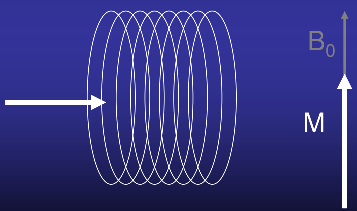


How to get a Signal

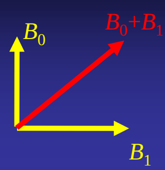
- Need varying magnetic field to induce voltage

$$U \propto \frac{dB}{dt}$$



How to rotate *M*

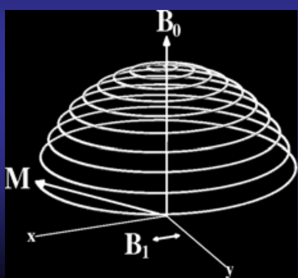
- **A way that does *not* work:**
  - Turn on a second big magnetic field B_1 perpendicular to main B_0 (for a few seconds)
  - Then turn B_1 off; *M* is now not parallel to magnetic field B_0



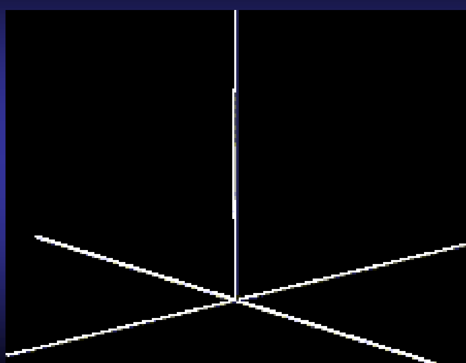
- **This fails because cannot turn huge (Tesla) magnetic fields on and off quickly**
  - But it contains the kernel of the necessary idea:
    A magnetic field B_1 perpendicular to B_0

RF-Fields

- **Apply a magnetic field perpendicular to B0 that rotates at precession frequency**
- B_1 will cause M to spiral away from B_0
- B_1 frequency must be close to Larmor frequency ("resonance")

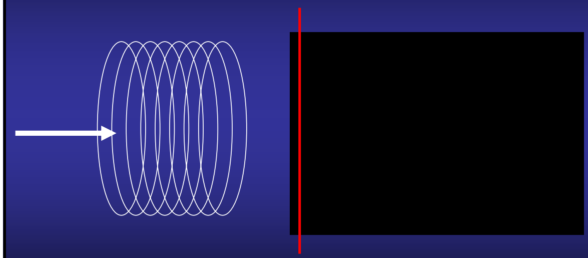


RF-Excitation

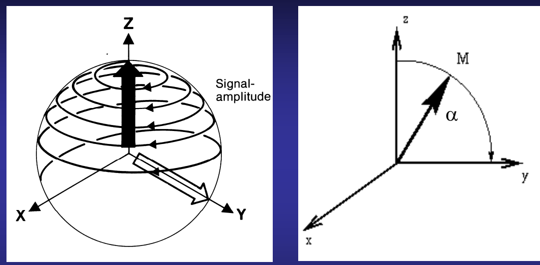


Courtesy: RW Cox

Induced Signal

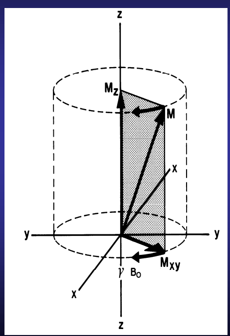


A view from the roundabout



- An observer in the surrounding laboratory will see M_0 spiral down to the XY plane (or even to the Z-axis)
- An observer riding on the M_0 vector sees the external world rotating about him. M_0 then seems to tip α ° towards XY

Longitudinal and Transversal Components of Magnetization M



Magnetization **M** is composed of

Mz - Longitudinal component parallel to the external magnetic field B_0

and

Mxy - Transversal component perpendicular to the external magnetic field B_0

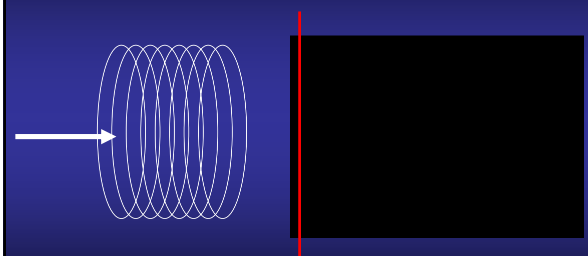
▪ Only transverse magnetization can be measured with receive coil

▪ Both components show different relaxation behavior

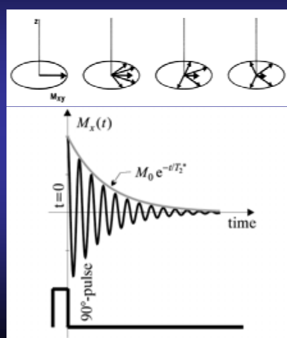
Relaxation: Nothing Lasts Forever

- In absence of external B_1, *M* will go back to being aligned with static field B_0 — this is called relaxation
- Part of *M* perpendicular to B_0 shrinks [M_{xy}]
  - This part of *M* is called *transverse magnetization*
  - It provides the detectable RF signal
- Part of *M* parallel to B_0 grows back [M_z]
  - This part of *M* is called *longitudinal magnetization*
  - Not directly detectable, but is converted into transverse magnetization by externally applied B_1

Induced Signal with Relaxation



Transverse Relaxation



The transversal magnetization M_{xy} is dephasing due to different Larmor frequencies experienced by the magnetization at different locations with a characteristic time constant T_2^*

$$M_{xy} = M_0 \exp(-t/T_2^*)$$

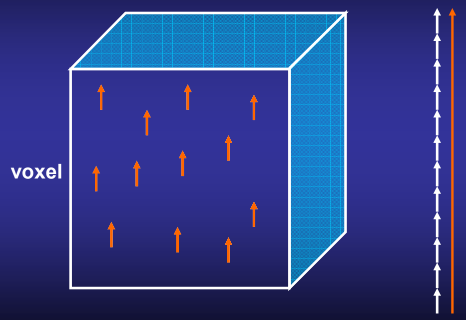
T_2^* is due to inhomogeneities of the main (static) magnetic field

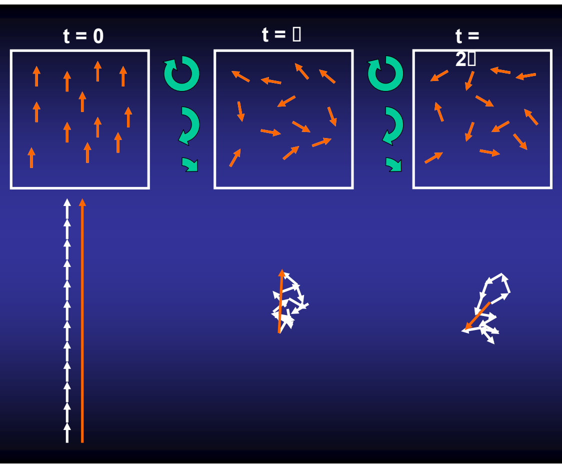
to get the relaxation time T_2 a special pulse has to be used

Loss if Phase Coherence

I need coffee for survival
I need coffee for survival
I need coffee for survival
I need coffee for survival
I need coffee for survival
I need coffee for survival
I need coffee for survival
I need coffee for survival

Spin Summation





Transverse Relaxation and Signal

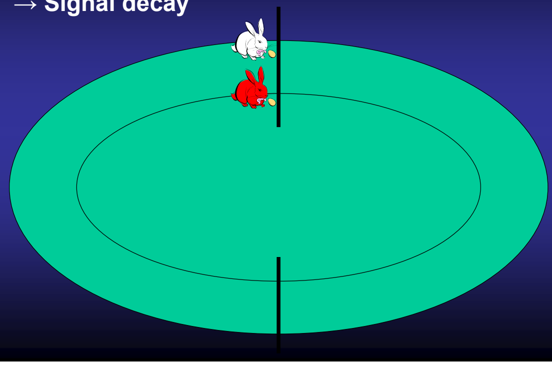
- Random frequency differences inside intricate tissue environment cause RF signals (from M_{xy}) to *dephase*
- Measurement = sum of RF signals from many places
- Measured signal decays away over time [brain $T_2^* \approx 40$ ms at 3 T]
- At a microscopic level (microns), M_{xy} signals still exist; they just add up to zero when observed from outside (at the RF coil)

Transverse Relaxation and Signal

- Contents of tissue can affect local magnetic field
- Signal decay rate depends on tissue structure and material
- Measured signal strength will depend on tissue details
- If tissue contents change, NMR signal will change
  - e.g., oxygen level in blood affects signal strength

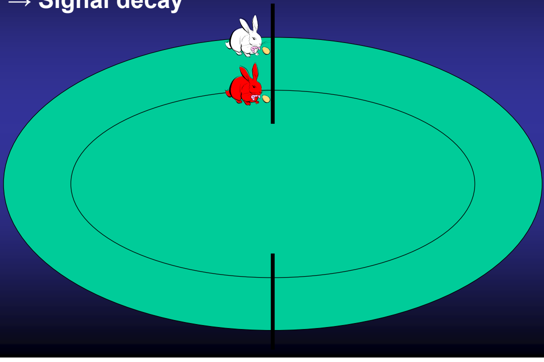
Hahn Spin Echo I

- Different spins rotate at different rates → Signal decay

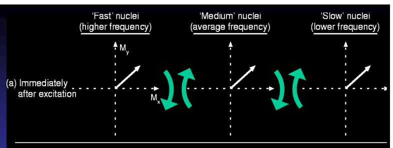


Hahn Spin Echo II

- Different spins rotate at different rates
  → Signal decay



- The “magic” trick: *inversion* of the magnetization *M*
- Apply a second *B*1 pulse to produce a flip angle of 180° about the *y*-axis

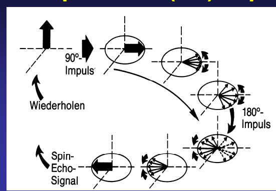


Courtesy: RW Cox

Spin Echo Animation

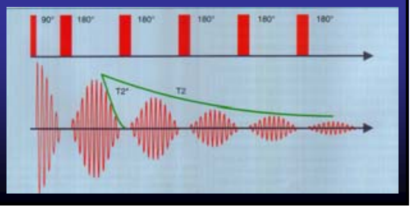
- [..\anims\spinecho.avi]

Spin-echo (SE) experiment to determine T_2

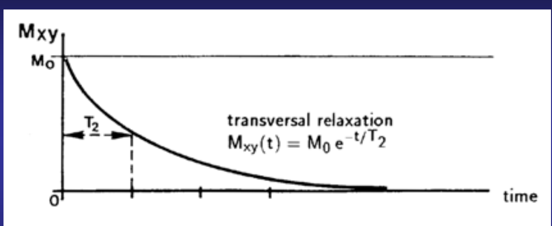


A 180° degree RF-pulse flips the dephasing magnetization back and an echo forms at echo time TE

Multiple 180° degree RF-pulses can reveal the real T_2 decay

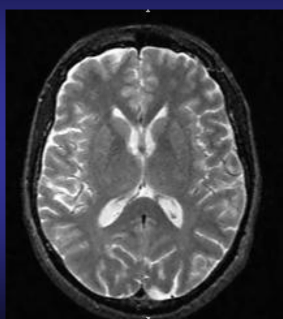


Spin-echo (SE) experiment to determine T_2



$M_{xy} = M_0 \exp(-t/T_2^*)$

T_2 Relaxation

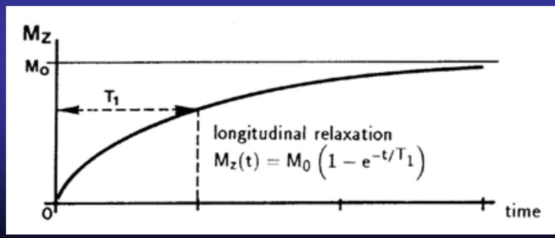


T_2-Relaxation

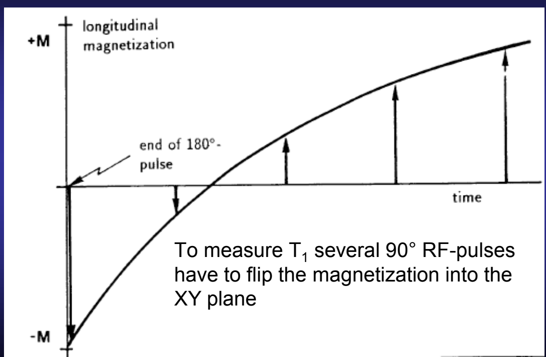
- **Spin echo doesn't work forever (TI can't be too big)**
- **Main reason: water molecules diffuse around randomly**
  - About 5-10 microns during 10-100 ms readout window
  - ➔ They "see" different magnetic fields and so their precession frequency changes from fast to slow to fast to ....
  - This process cannot be reversed by the inversion RF pulse
  - Time scale for irreversible decay of M_{xy} is called T2

T_1-Relaxation

After excitation with an 90° RF pulse Mz relaxes back to the equilibrium state with the characteristic time constant T1



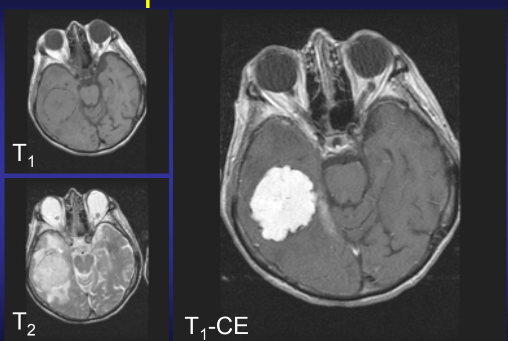
T_1-Relaxation



T_1-Relaxation

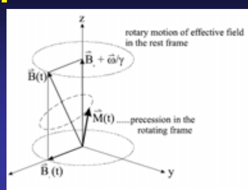
- **Longitudinal relaxation of M_z back to "normal" (T1)**
- **Caused by internal RF magnetic fields in matter**
  - Thermal agitation of H_2O molecules
- **Can be enhanced by magnetic impurities in tissue**
  - ➔ Drugs containing such impurities can alter T1, T2, and T2* — contrast agents (e.g., Gd-DTPA, MION)

T_1-Relaxation



Bloch equations

The complex interaction between RF excitation and relaxation processes is described by the Bloch equations



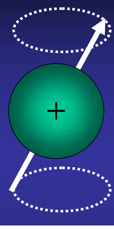
$$\frac{dM_x}{dt} = -\frac{M_x}{T_2}$$

$$\frac{dM_y}{dt} = -\frac{M_y}{T_2}$$

$$\frac{dM_z}{dt} = -\frac{M_z - M_0}{T_1}$$

Spin and magnetic moment

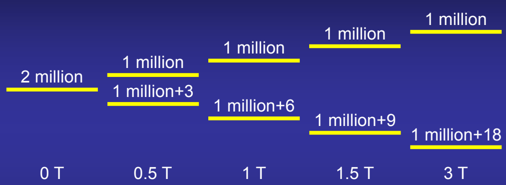
- Due to inner structure of the nucleons (charged quarks) this angular momentum (spin) is related to a magnetic moment
- This can be thought of an electric current which produces a magnetic field



$$\vec{\mu} = \gamma \vec{I}$$

γ ... gyromagnetic ratio

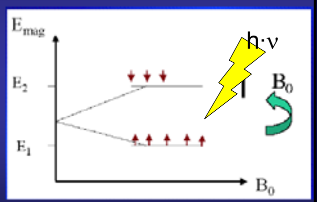
More signal at higher field



At 3 Tesla, for every **2 million** protons, there are **18** more protons aligned with the field than there are aligned against the field

Magnetization of a spin population

- Spins can undergo transitions between the two energy states by the absorption of a photon
- Energy difference ΔE is related to frequency of photon by Planck's constant *h*



Larmor equation

$$\omega_0 = \gamma \cdot B_0$$

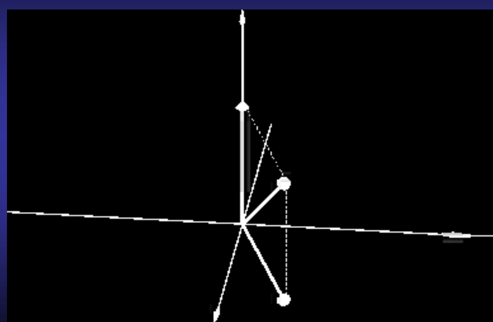
$\omega_0 = 2\pi \nu_0$ ... **Larmor frequency [MHz]**

B_0 **... magnetic field [T]**

γ ... **gyromagnetic ratio**

nucleus	$\nu_0 = \frac{\omega_0}{2\pi}$ [MHz] (for 1 T)	*rel. natural abundance [%]*	*relative abundance in biol. systems [.]*	*sensitivity relative to ^1H [.]*
^{1}H	42.58	99.98	1	1
^{2}H	6.56	0.016	$6.2 \cdot 10^{-5}$	$9.7 \cdot 10^{-3}$
^{13}C	10.71	1.11	$2.5 \cdot 10^{-4}$	$1.6 \cdot 10^{-2}$
^{19}F	40.05	100	$6.3 \cdot 10^{-5}$	$8.3 \cdot 10^{-1}$
^{23}Na	11.26	100	10^{-3}	$9.3 \cdot 10^{-2}$
^{31}P	17.24	100	$1.4 \cdot 10^{-3}$	$6.6 \cdot 10^{-2}$

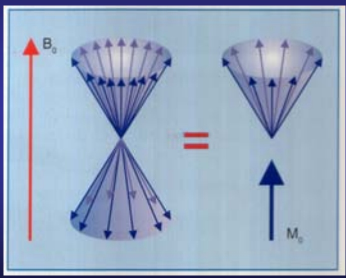
Classic Model



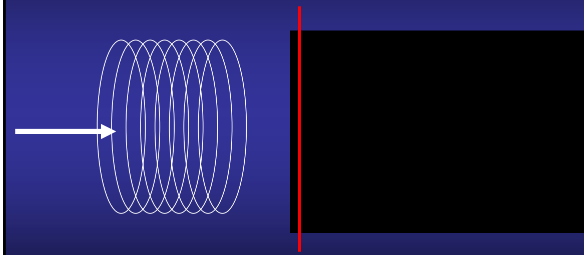
Courtesy: RW Cox

Macroscopic magnetisation

All magnetization vectors within the body add up to a net magnetization parallel to B_0



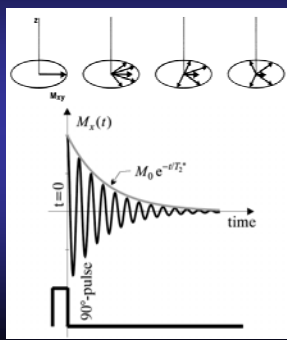
Induced Signal



Loss if Phase Coherence

I need coffee for survival
I need coffee for survival
I need coffee for survival
I need coffee for survival
I need coffee for survival
I need coffee for survival
I need coffee for survival
I need coffee for survival

Transverse Relaxation



The transversal magnetization M_{xy} is dephasing due to different Larmor frequencies experienced by the magnetization at different locations with a characteristic time constant T_2^*

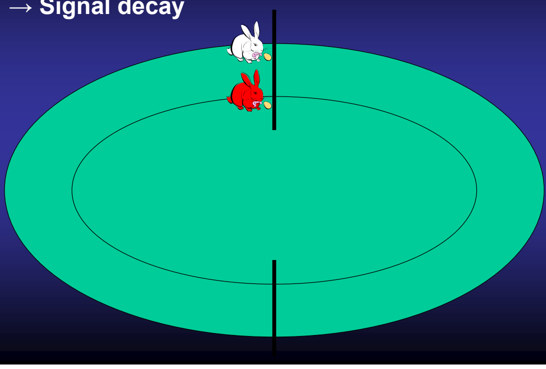
$$M_{xy} = M_0 \exp(-t/T_2^*)$$

T_2^* is due to inhomogeneities of the main (static) magnetic field

to get the relaxation time T_2 a special pulse has to be used

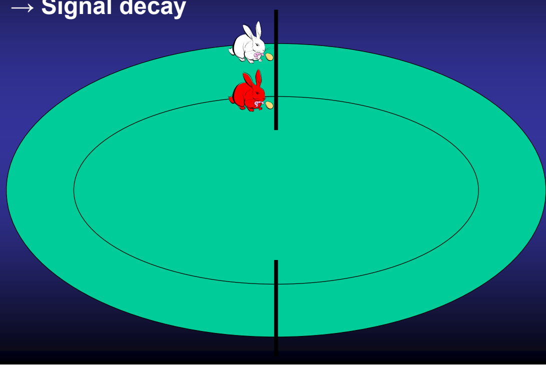
Hahn Spin Echo I

- Different spins rotate at different rates → Signal decay

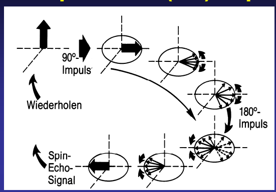


Hahn Spin Echo II

- Different spins rotate at different rates → Signal decay

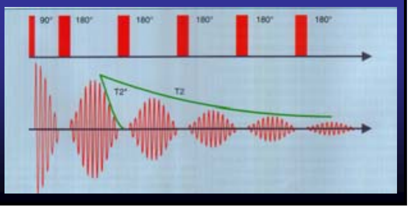


Spin-echo (SE) experiment to determine T_2



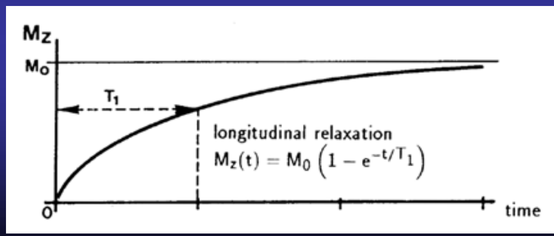
A 180° degree RF-pulse flips the dephasing magnetization back and an echo forms at echo time TE

Multiple 180° degree RF-pulses can reveal the real T_2 decay

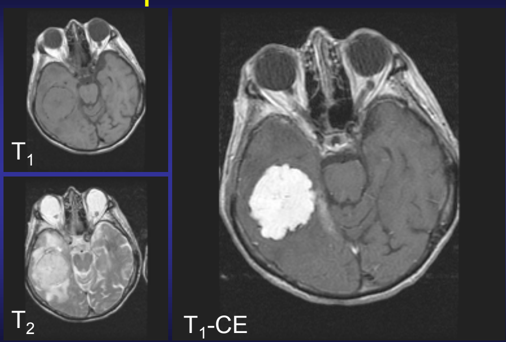


T_1-Relaxation

After excitation with an 90° RF pulse Mz relaxes back to the equilibrium state with the characteristic time constant T1

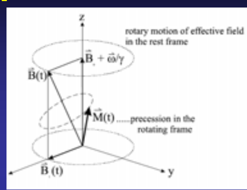


T_1-Relaxation



Bloch equations

The complex interaction between RF excitation and relaxation processes is described by the Bloch equations



$$
\begin{aligned}
\frac{\mathrm{d}M_x}{\mathrm{d}t} &= -\frac{M_x}{T_2} \\
\frac{\mathrm{d}M_y}{\mathrm{d}t} &= -\frac{M_y}{T_2} \\
\frac{\mathrm{d}M_z}{\mathrm{d}t} &= -\frac{M_z - M_0}{T_1}
\end{aligned}
$$