

# Introduction to NMR

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# Brief History of NMR

- First detection of NMR
- MSNMR
- FT NMR
- 2D NMR
- 2D-NMR and protein structure
- Development of MRI

# Outline

- Concept of SPIN
  - Spin angular momentum
  - Spin quantum # of various spins
  - Boltzman factor and sensitivity
  - Interaction of magnetic moment and  $B_0$
  - Status of the magnetization in laboratory
  - Larmor precession
    - Rotating frame
    - Application of RF field

# History of NMR

- 1926 Pauli's prediction of nuclear spin
- 1932 Detection of nuclear magnetic moment by Stern using molecular beam
  - 1936 First theoretical prediction of NMR by Gorter; his attempt to detect the first NMR did not work (LiF &  $\text{K}[\text{Al}(\text{SO}_4)_2]12\text{H}_2\text{O}$ ) at low temp.

# History of NMR

- 1945 First NMR of solution (Bloch et al for H<sub>2</sub>O) and solids (Purcell et al for parafin)
- 1949 Discovery of chemical shifts
- 1952 Nobel prize in Physics to Bloch and Purcell

# First NMR spectrum observed by Bloch

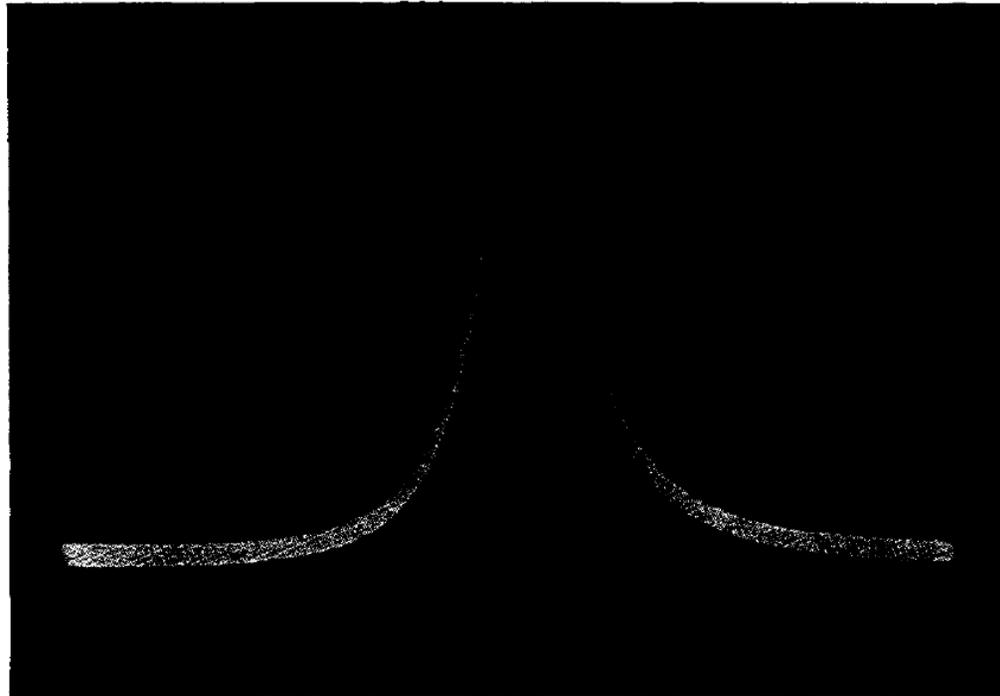


Fig. 3. A resonance line of protons in water, containing  $\text{MnSO}_4$  as a paramagnetic catalyst and obtained from the phase component of the nuclear induction signal which corresponds to absorption. The photograph is that of the trace on a cathode-ray oscillograph with the *vertical deflection* arising from the rectified and amplified signal, and the *horizontal deflection* corresponding to different values of the constant field.

# First NMR spectrum

- $^1\text{H}$  NMR of paraffin obtained by Purcell and that of EtOH obtained by Bloch,

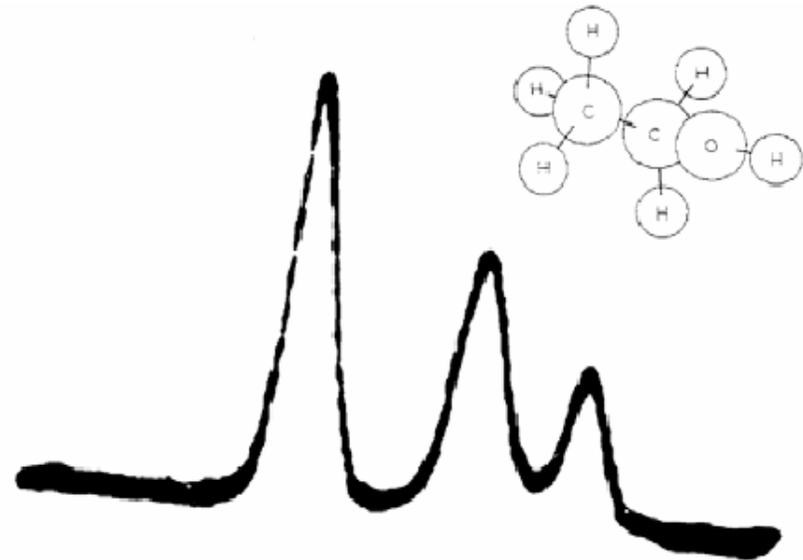
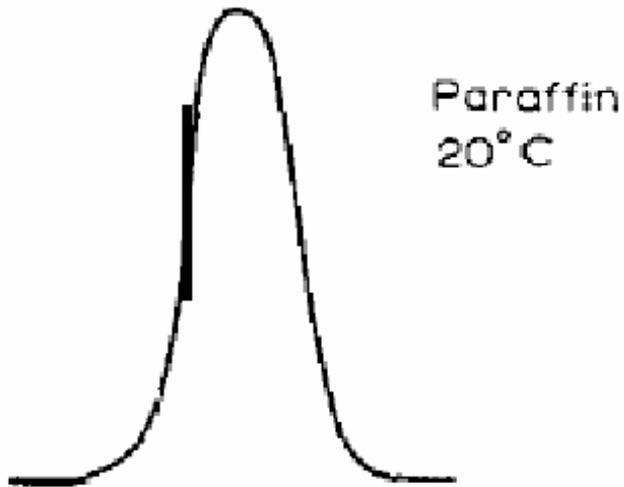


Fig. 6. The proton resonance in ethyl alcohol, observed with high resolution. The three lines arise from the  $\text{CH}_3$  hydrogens, from the  $\text{CH}_2$  hydrogens, and from the  $\text{OH}$  hydrogen, respectively.

The Nobel Prize in Physics 1952

"for their development of new methods for nuclear magnetic precision measurements and discoveries in connection therewith"

- Felix Bloch
  - Stanford University
  - 1905-1983
- Edward M. Purcell
  - Harvard University
  - 1912-1997



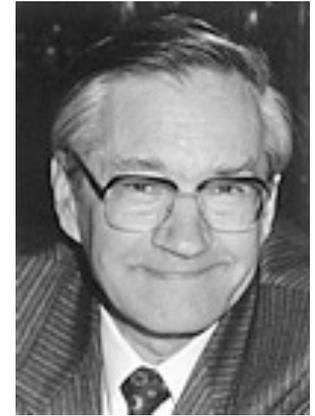
"Dr Bloch and Dr Purcell! You have opened the road to new insight into the micro-world of nuclear physics. Each atom is like a subtle and refined instrument, playing its own faint, magnetic melody, inaudible to human ears. By your methods, this music has been made perceptible, and the characteristic melody of an atom can be used as an identification signal. This is not only an achievement of high intellectual beauty - it also places an analytic method of the highest value in the hands of scientists."

From *Les Prix Nobel en 1952*, Editor Göran Liljestränd,  
[Nobel Foundation], Stockholm, 1953

# History of NMR

- 1958 High resolution Solid-state NMR by Magic-angle spinning
- 1964 First pulse FT NMR by Ernst and Anderson at Varian
- 1971 Jeener's proposal of 2 PULSE 2D EXPERIMENT
- 1972 Lauterbur's MRI EXPERIMENT
- 1974 First demonstration of 2D NMR by Ernst (COSY)
- 1979 2D  $^1\text{H}/^1\text{H}$  NOESY; correlation with through-space transfer useful for structural determination

# History of NMR



- 1980 NMR protein structure by Wuthrich
- 1990 3D and  $^1\text{H}/^{15}\text{N}/^{13}\text{C}$  Triple resonance
- NMR of protein (MW 30K)
- 1992 Nobel Prize in Chemistry to Ernst
- 1997 Ultra high field ( $\sim 800$  MHz) & TROSY(MW 100K)

- Richard R. Ernst
- "for his contributions to the development of the methodology of high resolution nuclear magnetic resonance (NMR) spectroscopy"
- Full Nobel prize in Chemistry 1991

# History of NMR

- 2002 Nobel Prize in Chemistry to Wuthrich
- 2002 Structural determination of protein in solids



- Kurt Wuthrich
- for his development of nuclear magnetic resonance spectroscopy for determining the three-dimensional structure of biological macromolecules in solution”
- 1/2 Nobel prize in Chemistry 2002

# The Nobel Prize in Physiology or Medicine 2003

for their discoveries concerning Magnetic Resonance Imaging

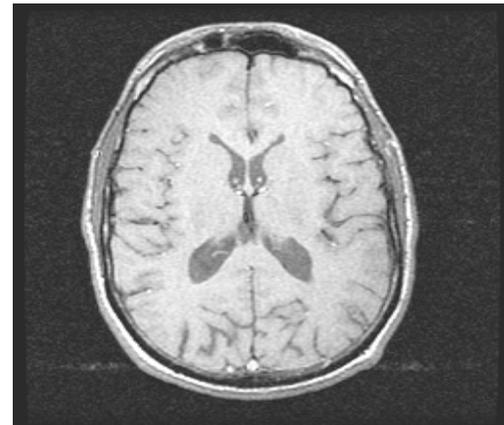
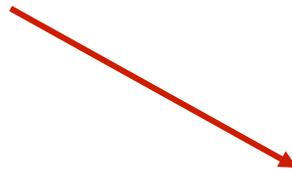
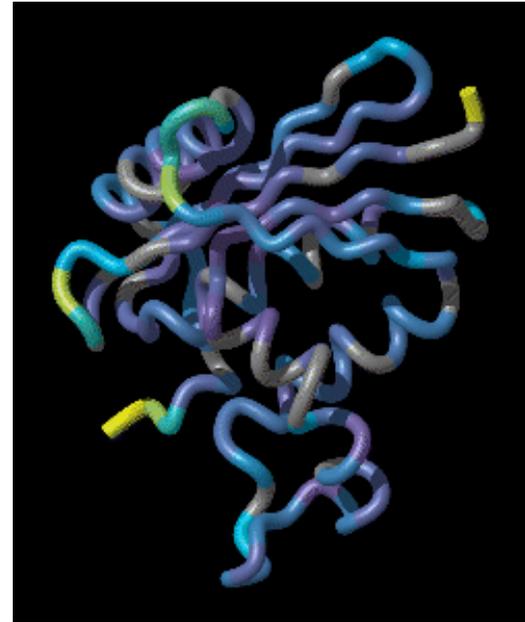


Paul C Lauterbur



**Peter Mansfield**

- NMR/MRI



# Course

- Details on the spin-choreography in different settings
  - Theory and Practicals
  - Organic molecules, Biomolecules
  - Structure and function of human organs
  - applications in biomedicine/clinical setting
- **Challenges:** visualizing/imaging single cell, and single molecule/protein misfolding/enhanced polarization/etc

# Spin

- Spin of a particle is its intrinsic angular momentum
- The total angular momentum spin  $I$

$$\sqrt{I(I+1)}\hbar$$

- It is purely quantum mechanical phenomena
- It comes in multiples of  $1/2$
- Unpaired electrons, neutrons, and protons each possess a spin of  $1/2$
- Example
  - ${}^2\text{H}$ , one electron, 1 proton and 1 neutron
  - Total nuclear spin=1, total electronic spin= $1/2$

# Properties of particles

Particle	Rest mass (kg)	Charge	Spin
Electron	$9.109 \cdot 10^{-30}$	$-e$	$1/2$
Neutron	$1.675 \cdot 10^{-26}$	0	$1/2$
Proton	$1.673 \cdot 10^{-26}$	$+e$	$1/2$
Photon	0	0	1

# Spin properties

- Nuclear spin and composition of a nucleus:
  - Fermions : Odd mass nuclei (i.e. those having an odd number of nucleons) have fractional spins.
  - Examples  $I = 1/2$  (  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{19}\text{F}$  ),  $I = 3/2$  (  $^{11}\text{B}$  ) &  $I = 5/2$  (  $^{17}\text{O}$  ).
- Bosons : Even mass nuclei composed of odd numbers of protons and neutrons have integral spins.
- Examples  $I = 1$  (  $^2\text{H}$ ,  $^{14}\text{N}$  ).
- Even mass nuclei composed of even numbers of protons and neutrons have zero spin (  $I = 0$  ). Examples are  $^{12}\text{C}$ , and  $^{16}\text{O}$ .

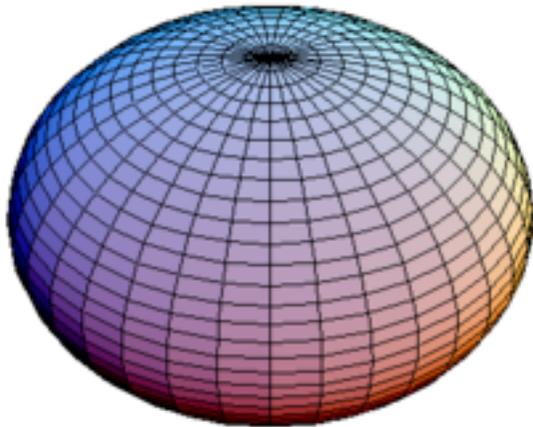
# Nuclear spins

Nuclei (mass #)	Unpaired protons	Unpaired Neutrons	Net Spin	g(MHz/ T)
$^1\text{H}$	1	0	1/2	42.58
$^2\text{H}$	1	1	1	6.54
$^{31}\text{P}$	1	0	1/2	17.25
$^{23}\text{Na}$	1	2	3/2	11.27
$^{14}\text{N}$	1	1	1	3.08
$^{13}\text{C}$ (6p+7n)	0	1	1/2	10.7
$^{19}\text{F}$	1	0	1/2	40.08

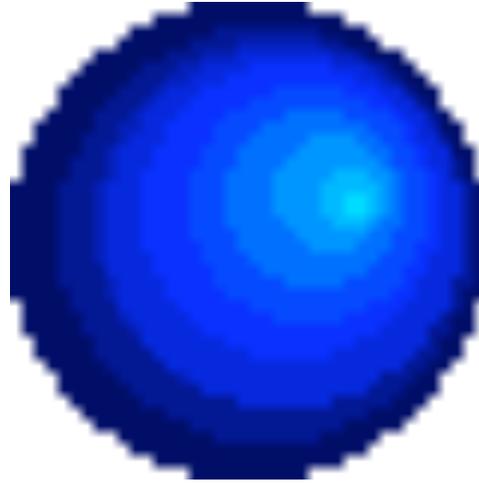
# Nuclear Spin

- Spin  $1/2$  nuclei have a spherical charge distribution, and their nmr behavior is the easiest to understand.
- Nuclei with nonspherical charge distributions may be analyzed as prolate or oblate spinning bodies.
- All nuclei with non-zero spins have magnetic moments ( $\mu$ ), but the nonspherical nuclei also have an electric quadrupole moment ( $eQ$ ).

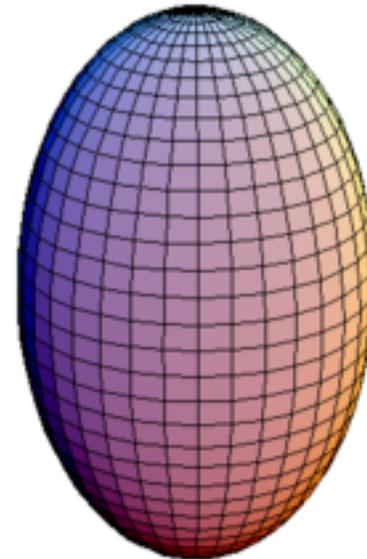
# Prolate and oblate



Oblate



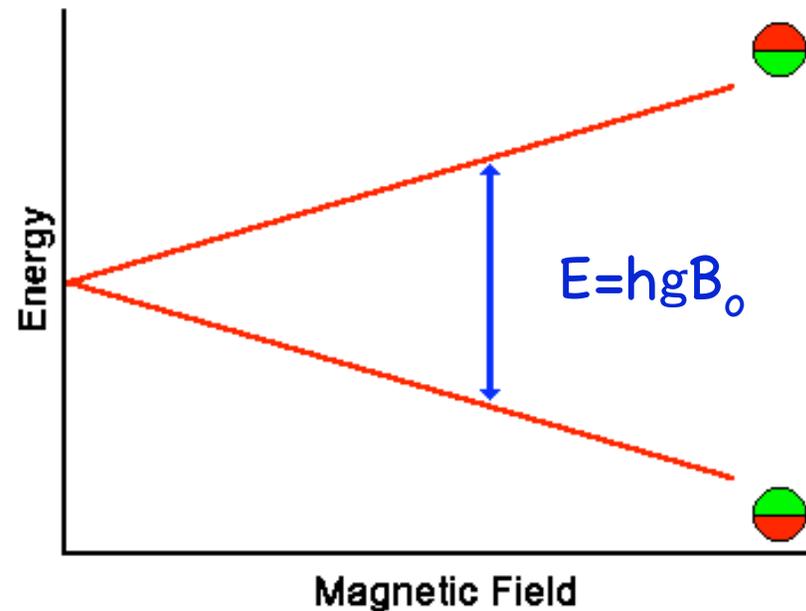
Sphere



Prolate

# Resonance

- Two spin states in the magnetic field
- Energy needed to cause a transition  $E=hgB_0$
- When the energy of the photon matches the energy difference between the two spin states an absorption of energy occurs (Resonance!)

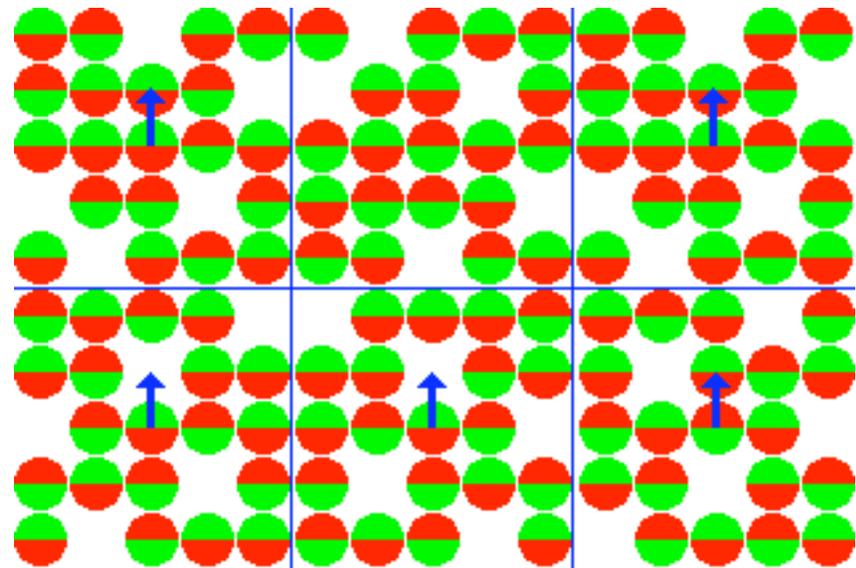


What is the size of nuclear magnetic resonance signal?

- What is the net magnetization from a collection of nuclear spins or from a sample?

# Boltzman Distribution

- Magnetic field due to each spin in each spin pocket is represented by a magnetization vector
- At room temperature, the number of spins in the lower energy level,  $N_+$ , slightly more than that in upper level  $N_-$ .
- $N_-/N_+ = \exp(-DE/kT)$   
DE is the energy difference between the spin states; k is the Boltzman Constant.

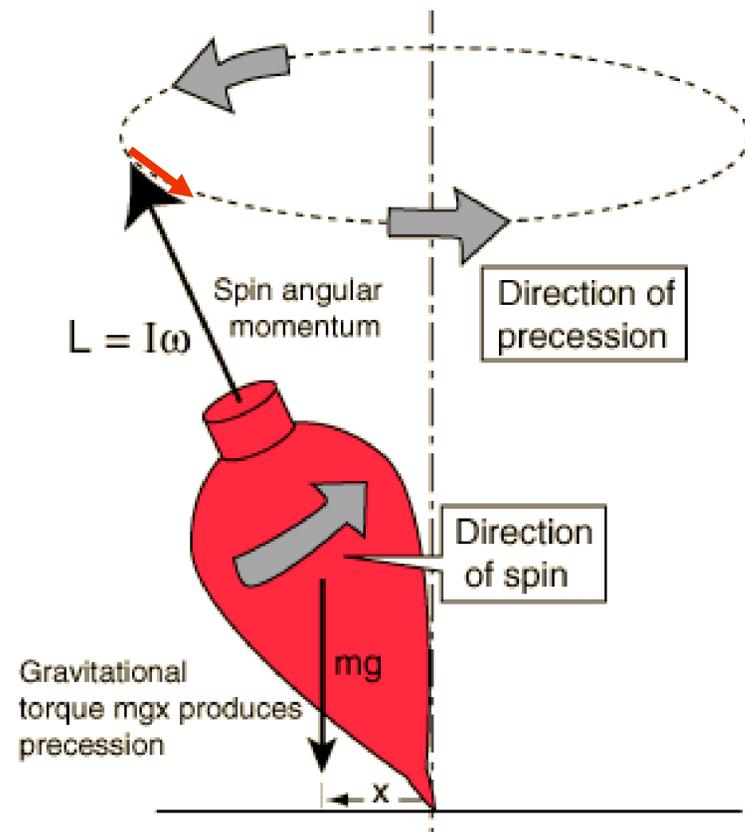


# Boltzman factor

- Boltzman factor
- $N$ =total number of spins
- $(N_+/N)=\exp((1/2)E/kT)=\sim 1+(E/kT)$
- $(N_-/N)=\exp((-1/2)E/kT)=\sim 1-(E/kT)$
- Boltzman factor= $b=(N_+-N_-)/N=E/kT$
- $K=1.3805 \times 10^{-23}$  J/Kelvin
- $T=300$  k
- $E= h\nu=6.626 \times 10^{-34}$  Js  $\times 100$  MHz
- $b= 1.599 \times 10^{-5}$
- How is the Boltzman factor changes with  $B_0$  and or  $T$ ?

# Spinning top

- Rapidly spinning top will precess in a direction determined by the torque exerted by its weight
- The torque. →



# Nuclear magnetic dipole moment

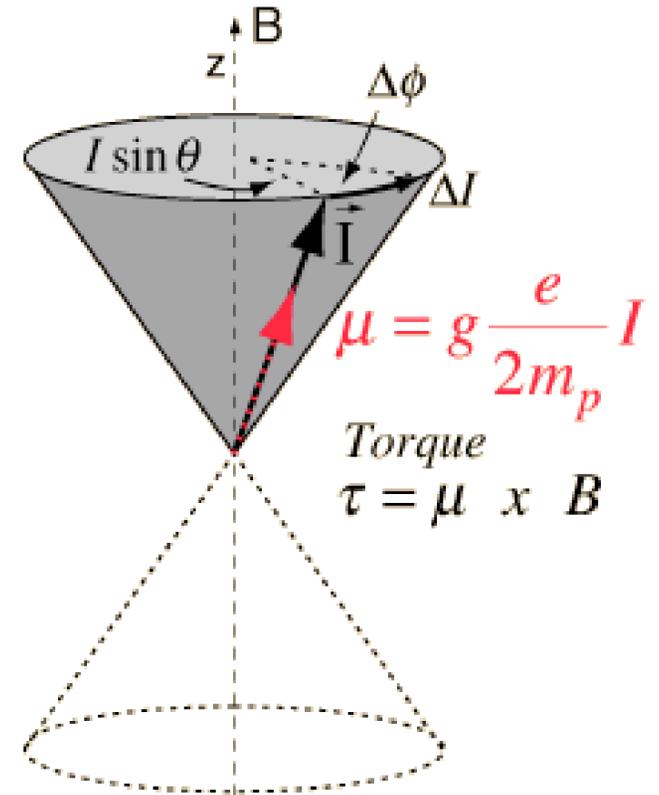
- Associated with each rotating object there will be an angular momentum
- Each nuclear spin possesses a **magnetic moment** arising from the angular momentum of the nucleus
- The magnetic moment is a vector perpendicular to the current loop
- In a magnetic field ( $B$ ) the magnetic moment will behave like magnetic dipole



$$\mu = IA$$

# Larmor frequency

- When a magnetic moment directed at some angle w.r.t.  $B_0$  direction, the field will exert a torque on the magnetic moment. This causes it to precess about the magnetic field direction.
- Torque is the rate of change of the nuclear spin angular momentum  $I$

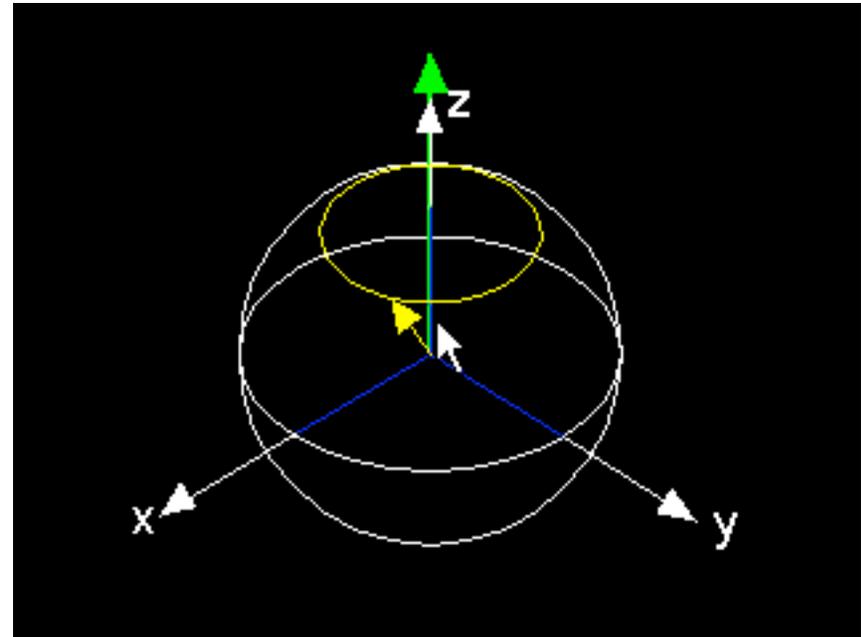


# Larmor precession

<http://www.quantum-physics.polytechnique.fr/en/larmor.html>

# Larmor Precession

- Precession of the magnetization vector around the z-axis of the magnetic field



# Bloch's NMR probe

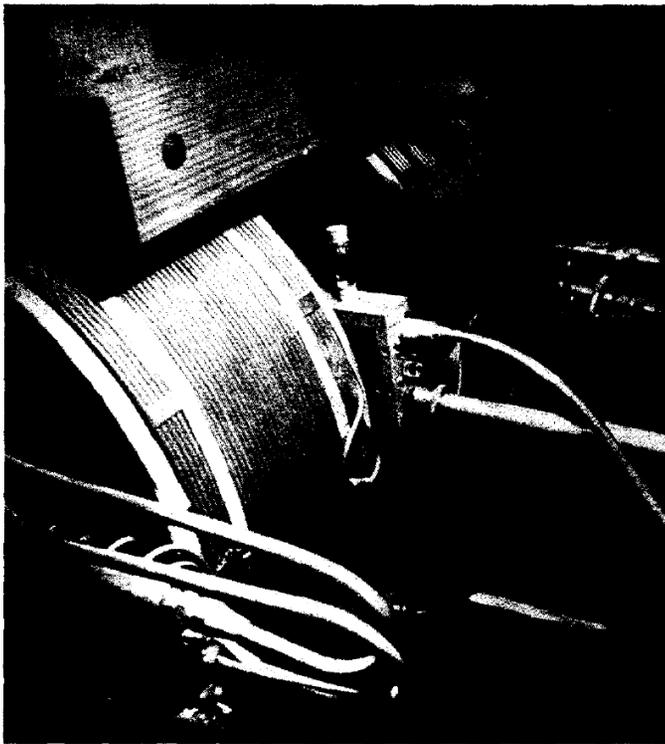


Fig. 2. The same head as in Fig. 1, about to be inserted in the gap of an electromagnet and containing a sample test tube. The two protruding lucite rods between the leads reach into the interior of the head and carry small copper disks; a fine adjustment of the coupling is achieved by rotation of these «paddles».

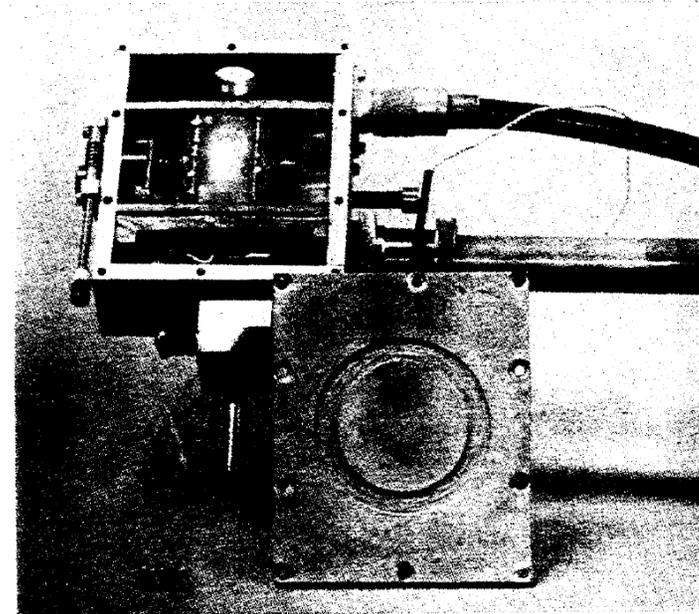


Fig. 1. The «head» of the crossed-coil arrangement with the cover plate removed. The bottom tube to the right contains the leads to the transmitter coil, which is wound in two sections visible in black in the head. The black cable leads from the receiver coil to the amplifier; the receiver coil is wound with a vertical axis inside the hollow lucite piece between the two sections of the transmitter coil. The sample test tubes are placed in its interior through the circular hole at the top of the supporting frame.

# MRI: Magnet and Coils

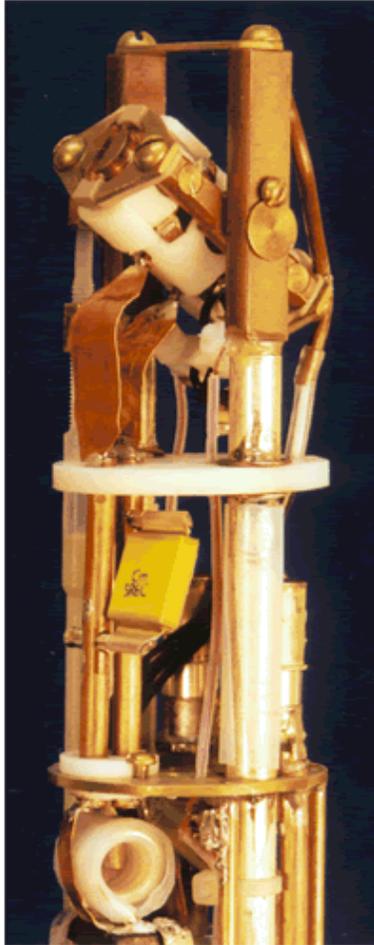


300-900 MHz



8.5-170 MHz

# MRI: Magnet and Coils

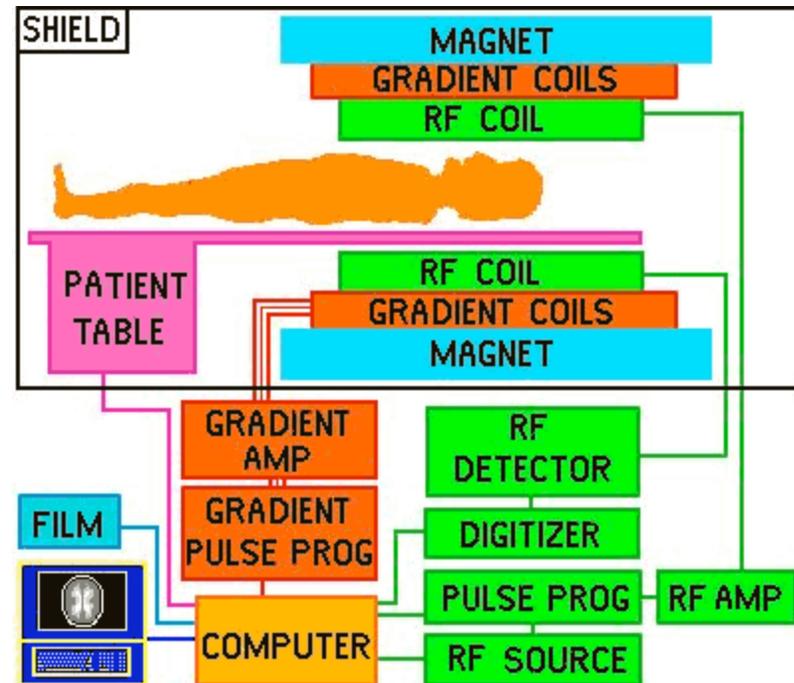


5-10 ml



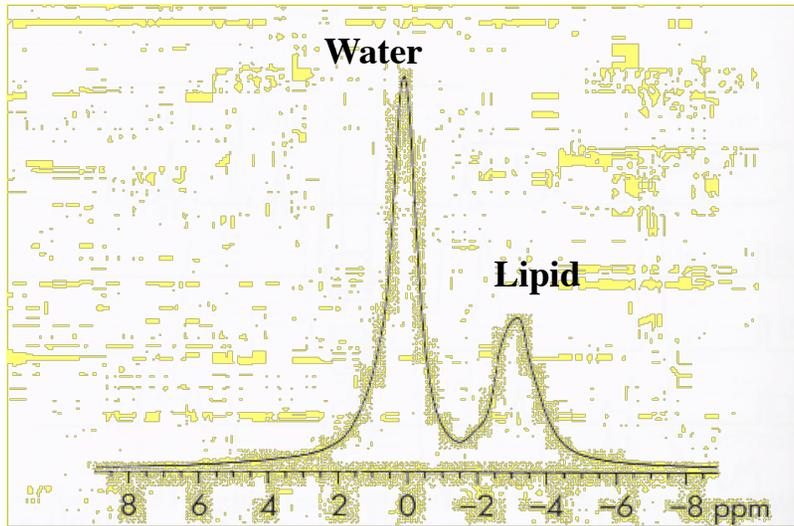
50-4000 ml

# MRI scanner



MRI

Bulk

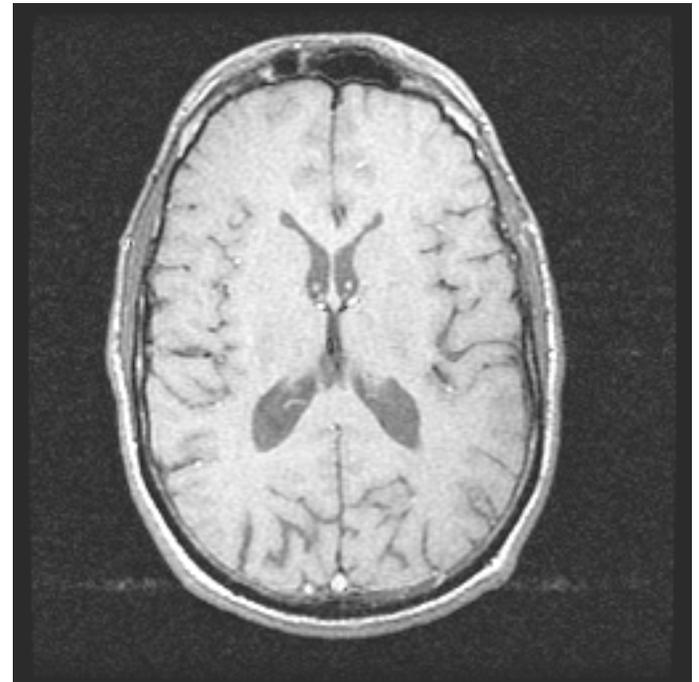


Water

Fat



Spatial





# fMRI?

