核磁共振與磁振造影

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核磁共振 Nuclear Magnetic Resonance (NMR)

This technique observes signals from nuclear spins to obtain the structural & dynamical information of the sample.
Nuclear spin

The Bohr model of H atom

Nuclear spin (自旋) \( I \) \( \rightarrow \) An intrinsic property of the nucleus

Nuclear magnetic moment (磁矩) \( \mu_I = \gamma_n \hbar I \)

Can be though of as a strange tiny magnet 小磁矩(鐵)

Why & how to observe nuclear spins?
Timeline I

1946: Discovery of nuclear magnetic resonance phenomenon
   Purcell et al. (Harvard) & Bloch et al. (Stanford)

1949: Chemical shift

1952: Nobel Prize in physics - Bloch and Purcell
   for their development of new methods for nuclear magnetic precision
   measurements and discoveries in connection therewith
1960s: Solid state NMR – Waugh
NMR imaging was demonstrated

1966: Ernst and Anderson
Fourier Transform technique for NMR

1970: 2D NMR

1980s: Macromolecular structure determination in solution by NMR.

1973: Back projection MRI (P. Lauterbur)

1975: Fourier Imaging – R. Ernst

1977: the first study performed on a human took place

1991: Nobel prize in Chemistry - Ernst

for his contributions to the development of the methodology of high resolution NMR spectroscopy
1990s: Heteronuclear multi-dimensional NMR permit the determination of protein structure up to 50 KDA. MRI become a major radiological tool in medical diagnostic.

2002: Nobel prize in Chemistry - Wüthrich (1/2)
   for his development of NMR spectroscopy for determining the 3D structure of biological macromolecules in solution.

2003: Nobel Prize in Physiology or Medicine – Lauterbur and Mansfield discoveries concerning magnetic resonance imaging

Kurt Wüthrich  
Paul C. Lauterbur  
Sir Peter Mansfield
Solid-state NMR spectrometer (固態核磁共振儀)
$H_0$: Static Magnetic Field

$H_1(t)$: Alternating Field with frequency $\omega$

Set-up
A bare nuclear spin in a magnetic field $H_0$

Quantum mechanics tells us:  μ_I precession with the Larmor frequency $\omega_L$

2 states for $^1$H nuclear spin (I =1/2)

$m = -1/2$

$1/2$

Energy difference between the states (levels)
$\Delta E = \gamma_n \hbar H_0 = \hbar \omega_L$

What happened?

Low-energy state
up

high-energy state
down
Nuclear magnetization $M_z$ is what we are going to measure.

A powerful magnetic field $H_0$ is used to produce the nuclear magnetization.
Principle of magnetic resonance

Apply radio frequency field $H_1(t)$ with frequency $\omega_0$,
when $\hbar \omega_0 = \Delta E \Rightarrow$ resonance occurs

$m = -\frac{1}{2}$

$\Delta E = \gamma_n \hbar H_0$

Therefore, $\omega_0 = \gamma_n H_0$

$M_z$ is destroyed
Detect the NMR signal

Radio frequency (RF) fields with frequency $\omega_0$ are used to systematically alter the alignment of this magnetization, causing the hydrogen nuclei to produce a rotating magnetic field detectable by the scanner.

- **$H_1(t)$ on**
  - $M_0 = M_z$
  - Knock down $M_0$

- **$H_1(t)$ off**
  - $M_0$ rotates in x-y plane, the coil pick up the signal.
  - $V \propto \frac{dM_0(t)}{dt}$ 感應電動勢

- NMR spectrum
  - a signal at $\omega_0$ (frequency)
Each species of atom has its own $\gamma_n$ value

- Signal appears at different frequency (position) → Site assignment

For the same spin:

- Increase $H_0$ → $\omega_0$ increases → Signal shifts to higher frequency

Basics of MRI
In addition to $H_1$ and $H_0(t)$, the nuclear spin in materials also senses the fields produced by:

- Other nuclear spins
- Electron spins (Knight shift)
- Electron orbital motion (chemical shift)
- Electric quadrupole effect
- ……

The above fields will affect the energy difference $\Delta E$ affect the position and shape of the signal in frequency

$\text{Cu: } 3d^{10}4s^1$

$\text{O: } 2s^2p^4$

Insulator (絕緣體) eg. $\text{Cu}_2\text{O}$

Conductor (導體) eg. $\text{Cu}$

Ferromagnet (鐵磁性物質)
The applications of NMR in physics

Probing the electronic properties
- Electron spins (Knight shift)
- Electric quadrupole effect

- superconductors:
  For a conventional superconductor, electrons form pairs (cooper pairs) in the superconducting state.

  spin singlet $S=0$

  First observed by NMR

- the magnetic materials
The applications of NMR in chemistry

NMR is chemists’s eyes - a technique of analytical chemistry

- Identify functional group by probing electron orbital motion (chemical shift)

  Protons ($^1$H) spectrum from CH$_3$CH$_2$OH

  Peak assignments (which peak is what) can be done using NMR Database

  Frequency

- determine the structure of many compounds
The applications of NMR in bio- & medical-related fields

- living tissue (chemical shift)
- Biomolecules: Lipids, Proteins, nucleic acids, including RNA and DNA

Macromolecules

Sequence 3D structure

nsp1 protein
MDSNTVSSFQ VDCFLWHVRK
RFADQELGDA PFLDRLRDRQ
KSLRGRGSTL GLDIRTATRE
GKHIVERILE EESDEALKMT
IASVPAPRYL TEMTLEEMSR
DWLMLPKQK VTGSLCIRMD
QAIMDKDIIL KANFSVIFNR
LEALILLRAF TDEGAIVGEI
SPLPSLPGHT EEDVKNAIGV
LIGGLEWNDN TVRVSETLQR
FTWRSSDENG RSPLPPKQKR
KMERTIEPEV (230 amino acids)

Each amino acid contains C, N, H, O

Non-destructive technique
Earth Field NMR (EFNMR)

Make use of earth magnetic field (30~60 μT, protons resonate ~ 2kHz)

→ A special case of low field NMR

- investigating the structure of ice crystals in polar ice-fields, to rocks and hydrocarbons in the field.
- Detect ferrous objects (鐵磁性物質) on land and at sea

- Earth's field MRI scanners

Advantage: Portability - to analyze substances on site lower cost

Antarctic (南極)
Superconducting magnet

An electromagnet that is built using superconducting coils

- operate at liquid helium temperature (4K) to achieve SC state
- produce stronger magnetic fields than ordinary iron-core electromagnets
- no power is lost to ohmic resistance in the windings
- cheaper to operate

SC coil: niobium-titanium (NbTi)
or niobium-tin (Nb3Sn)
Higher field $\rightarrow$ larger signal (signal/noise)

800 MHz, 18.8 T NMR spectrometer

900 MHz, 21.2 T NMR Magnet
NMR

- narrow line
  - Solution NMR
  - High resolution SS NMR (magic angle spinning)

- wide line
  - Solid-state NMR

- image
  - MRI
Magnetic resonance imaging (MRI) 磁振造影
Was called Nuclear magnetic resonance imaging (NMRI)
Now called Magnetic resonance imaging (MRI) to avoid using “Nuclear”.

- An imaging technique (used to map the inside of human body)
- Relatively new technique compared with X-ray radiography (over 110 years)
- Based on the principles of nuclear magnetic resonance (NMR)
Recall ~~~

Signal appears at $\omega_0 = \gamma_n H_0$

For the same spin:

Increase $H_0$ $\rightarrow$ $\omega_0$ increases $\rightarrow$ Signal shifts to higher frequency

Signal (peak) position is proportional to the field strength
Principle of imaging

Idea - using magnetic field gradients to introduce spatial localization

A third field $\delta H(x)$ is needed to provide a gradient field

$$\omega_0 = \gamma_n H_0$$

$$\omega_0 = \gamma_n H_0 + \delta H(x)$$

Frequency coding

(frequency tells you which location the signal is from)
Data processing

$\delta H(x)$

$\delta H(y)$

Typical field: 1 ~ 3 T

Typical field gradient:

20 - 100 mT/m
MRI scanner

takes about 45 minutes to complete each body part.

no ionizing radiation

Non-destructive technique

1.5 T scanners: 1 ~1.5 million USD.
3.0T scanners: 2 ~2.3 million USD.
Animal MRI

Cod in MRI swimtunnel (In vivo MR studies) horses
Field safety

- Earth’s magnetic field 30~60 µT (0.03~0.06 mT) depending on location
- Direct current (DC) transmission lines: 0.02 mT
- Small magnets (audio speakers components, battery-operated motors, microwave ovens, refrigerator magnets) : 1-10 mT
- MRI: 1~3T
- NMR: up to ~21T (shielding to 0.5mT at 2m from field center)

Exposure limit:

The general public: 40 mT
Occupational whole-body exposure: 2T
The end