Nuclear Magnetic Resonance (NMR)

**Nuclear**
- In the Nucleus

**Magnetic**
- Involves Magnets

**Resonance**
- In the Nucleus
Introduction

• NMR is the most powerful tool available for organic structure determination.
• It is used to study a wide variety of nuclei:
  – $^1$H
  – $^{13}$C
  – $^{15}$N
  – $^{19}$F
  – $^{31}$P
Nuclear Spin

• A nucleus with an odd atomic number or an odd mass number has a nuclear spin.
• The spinning charged nucleus generates a magnetic field.
When placed in an external field, spinning protons act like bar magnets.
Two Energy States

The magnetic fields of the spinning nuclei will align either with the external field, or against the field. A photon with the right amount of energy can be absorbed and cause the spinning proton to flip.
The basis of NMR spectroscopy

Electromagnetic radiation of frequency

Increasing energy

α-spin

β-spin

Copyright © mottfolio.com
• The nucleus of a hydrogen atom has a very weak magnetic spin, it behaves like a weak compass needle.

• If a molecule containing hydrogen is placed in a strong magnetic field, the magnetic hydrogen nucleus can line up with the field or line up against it!

  - Nucleus spin aligned with the field - Low energy!
  - Nucleus spin aligned against the field - High energy!

• Which is the high energy orientation?
Excited state = High energy

Add Energy

Aligned = Low Energy

Energy Released

Back to low energy ground state

• When the spin falls back into line with the magnetic field it releases energy. We detect this energy and it provides information on:

• The environment of the hydrogen in the molecule

• How many hydrogen atoms are in that environment.
NMR is a very detailed method of chemical analysis for organic compounds. It can tell us the number of hydrogen atoms in a molecule and their related positions in the carbon chain.

The nucleus of each hydrogen atom behaves like a tiny magnet, which usually lines up with an applied magnetic field. However, if we add energy, the tiny magnet can flip over so that it aligns against the magnetic field.

When the external energy is removed, the magnetic nucleus must, once again, fall back in line with the magnetic field and release its extra energy. We detect this released energy and use it to gather information about the hydrogen which was excited.
The NMR Spectrometer
OBTAINING SPECTRA

• a liquid sample is placed in a tube which spins in a magnetic field

• solids are dissolved in deuterated solvents (CDCl$_3$) or solvents without H’s (CCl$_4$) [solvents with hydrogen atoms in them will produce peaks in the spectrum]

• TMS, tetramethylsilane, (CH$_3$)$_4$Si, is added to provide a reference signal.

• In practice, the radio wave interacts with the nuclei to cause a rotation of the nuclear magnets.

• The rotating magnet produces an electrical current in a wire placed around the sample, and this is what is detected.

• In principle, a detector could record the difference in the signal that it receives compared to the original signal and cause an absorption peak to appear on the chart recorder.
TETRAMETHYLSILANE - TMS

PROVIDES THE REFERENCE SIGNAL

The molecule contains four methyl groups attached to a silicon atom in a tetrahedral arrangement. All the hydrogen atoms are chemically equivalent.

- **non-toxic liquid** - SAFE TO USE
- **inert** - DOESN’T REACT WITH COMPOUND BEING ANALYSED
- has a **low boiling point** - CAN BE DISTILLED OFF AND USED AGAIN
- all the **hydrogen atoms are chemically equivalent** - PRODUCES A SINGLE PEAK

- given the chemical shift of $\delta = 0$
- the position of all other signals is measured relative to TMS
chemical environments of Hydrogen

• If all the hydrogen atoms in a compound are bonded to a common carbon atom, then only one absorption would be observed in the 1H NMR spectrum of the molecule.

• For example, the methane molecule, CH₄, has four chemically equivalent hydrogen atoms and has only one peak in its NMR spectrum.

• Hydrogen in different structural arrangements (or chemical environments) give rise to peaks at different positions in the NMR spectrum.

For example, the butane molecule, CH₃-CH₂-CH₂-CH₃, gives rise to two peaks in the NMR spectrum.

One peak is due to resonance involving the terminal hydrogens in the methyl groups, −CH₃, at the end of the molecule; the other is due to the hydrogens in the methylene groups, −CH₂−, in the centre of the molecule.

This occurs because the nuclei of the hydrogen atoms are shielded by other electrons in the molecule to different extents.

The hydrogen nuclei are said to be in different chemical environments.
CHEMICAL SHIFT

- each proton type is said to be chemically shifted relative to a standard (usually TMS)

- the chemical shift is the difference between the field strength at which it absorbs and the field strength at which TMS protons absorb

- the delta ($\delta$) scale is widely used as a means of reporting chemical shifts

- the TMS peak is assigned a value of ZERO ($\delta = 0.00$)

- all peaks of a sample under study are related to it and reported in parts per million

$$\delta = \frac{(\text{frequency of signal} - \text{frequency of TMS}) \times 10^6}{\text{frequency of TMS}}$$
Information from $^1$H-nmr spectra:

1. **Number of signals**: How many different types of hydrogen's in the molecule.

2. **Position of signals (chemical shift)**: What types of hydrogen's.

3. **Relative areas under signals (integration)**: How many hydrogen's of each type.

4. **Splitting pattern**: How many neighboring hydrogen's.
LOW RESOLUTION SPECTRA

- low resolution nmr gives 1 peak for each environmentally different group of protons

LOW RESOLUTION SPECTRUM OF 1-BROMOPROPAANE
HIGH RESOLUTION SPECTRA

- high resolution gives more complex signals - doublets, triplets, quartets, multiplets
- the signal produced indicates the number of protons on adjacent carbon atoms

The splitting pattern depends on the number of hydrogen atoms on adjacent atoms.
1. Number of signals: How many different types of hydrogens in the molecule.

\[ \text{CH}_3\text{CHCH}_2\text{CH}_3 \quad \text{Br} \]

Four

\[ \text{Cl-CH}_2\text{CH}_2\text{CH}_2\text{-Cl} \]

Two
One

CH₃C–C–CH₃

Br

Two

CH₃CH₂-Br

One

CH₃C=C–CH₃

CH₃C=C–CH₃

One

CH₃CHCHCH₃

CH₃

Cl

Two

<table>
<thead>
<tr>
<th>Type of Proton</th>
<th>Approximate $\delta$</th>
<th>Type of Proton</th>
<th>Approximate $\delta$</th>
</tr>
</thead>
<tbody>
<tr>
<td>alkane ($\text{--CH}_3$)</td>
<td>0.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>alkane ($\text{--CH}_2$)</td>
<td>1.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>alkane ($\text{--CH}$)</td>
<td>1.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\text{O}$ $\text{--C--CH}_3$</td>
<td>2.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\text{O}$ $\text{--C}≡\text{C--H}$</td>
<td>2.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\text{R}--\text{CH}_2--\text{X}$</td>
<td>3–4</td>
<td>$\text{R}--\text{COOH}$</td>
<td>10–12</td>
</tr>
<tr>
<td>($\text{X = halogen, O}$)</td>
<td></td>
<td>$\text{R}--\text{OH}$</td>
<td>variable, about 2–5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$\text{Ar}--\text{OH}$</td>
<td>variable, about 4–7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$\text{R}--\text{NH}_2$</td>
<td>variable, about 1.5–4</td>
</tr>
</tbody>
</table>

Note: These values are approximate, as all chemical shifts are affected by neighboring substituents. The numbers given here assume that alkyl groups are the only other substituents present. A more complete table of chemical shifts appears in Appendix 1.
3. Integration (relative areas under each signal): how many hydrogens of each type.

\[
\text{a} \quad \text{CH}_3 \\
\text{a} \quad \text{H}_3\text{C} - \text{C} - \text{CH}_3 \\
\text{a} \quad \text{Br} \\
\text{a} \quad 9 \text{ H}
\]

\[
\text{a} \quad \text{CH}_3\text{CH}_2\text{-Br} \\
\text{a} \quad 3 \text{ H} \\
\text{b} \quad 2 \text{ H}
\]

\[
\text{a} \quad \text{b} \quad \text{c} \\
\text{CH}_3\text{CH}_2\text{CH}_2\text{-Br} \\
\text{a} \quad 3 \text{ H} \\
\text{b} \quad 2 \text{ H} \\
\text{c} \quad 2 \text{ H}
\]

\[
\text{a} \quad \text{b} \quad \text{a} \\
\text{CH}_3\text{CHCH}_3 \\
\text{Cl} \\
\text{a} \quad 6 \text{ H} \\
\text{b} \quad 1 \text{ H}
\]
MULTIPLICITY (Spin-spin splitting)

- low resolution nmr gives 1 peak for each environmentally different group of protons
- high resolution gives more complex signals - doublets, triplets, quartets, multiplets
- the signal produced indicates the number of protons on adjacent carbon atoms

Number of peaks = number of chemically different H’s on adjacent atoms + 1

- 1 neighbouring H: 2 peaks “doublet” 1:1
- 2 neighbouring H’s: 3 peaks “triplet” 1:2:1
- 3 neighbouring H’s: 4 peaks “quartet” 1:3:3:1
- 4 neighbouring H’s: 5 peaks “quintet” 1:4:6:4:1

Signals for the H in an O-H bond are unaffected by hydrogens on adjacent atoms - get a singlet
Spin-spin splitting is illustrated in the high-resolution $^1$H NMR spectrum of ethanol.
4. Splitting pattern: How many neighboring hydrogens

\[
\begin{align*}
\text{CH}_3 & \quad \text{a} \\
\text{H}_3\text{C}-\text{C}-\text{CH}_3 & \quad \text{a} \quad \text{Br} \quad \text{a} \\
& \quad \text{a} \quad 9 \text{ H singlet} \\
\text{CH}_3\text{CH}_2\text{CH}_2\text{-Br} & \quad \text{a} \quad \text{b} \quad \text{c} \\
& \quad \text{a} \quad 3 \text{ H triplet} \\
& \quad \text{b} \quad 2 \text{ H complex} \\
& \quad \text{c} \quad 2 \text{ H triplet} \\
\text{CH}_3\text{CH}_2\text{-Br} & \quad \text{a} \quad \text{b} \\
& \quad \text{a} \quad 3 \text{ H triplet} \\
& \quad \text{b} \quad 2 \text{ H quartet} \\
\text{CH}_3\text{CHCH}_3 & \quad \text{a} \quad \text{b} \quad \text{a} \\
& \quad \text{a} \quad 6 \text{ H doublet} \\
& \quad \text{b} \quad 1 \text{ H septet}
\end{align*}
\]
\[
\text{CH}_3\text{CHCH}_2\text{CH}_3 \quad \text{Br}
\]
\[
\text{a} \quad 3 \text{ H triplet}
\]
\[
\text{b} \quad 3 \text{ H doublet}
\]
\[
\text{c} \quad 2 \text{ H complex}
\]
\[
\text{d} \quad 1 \text{ H complex}
\]

\[
\text{Cl-CH}_2\text{CH}_2\text{CH}_2\text{-Cl}
\]
\[
\text{a} \quad 2 \text{ H quintet}
\]
\[
\text{b} \quad 4 \text{ H triplet}
\]

\[
\text{CH}_3\text{CH}_2\text{-OH}
\]
\[
\text{a} \quad 6 \text{ H singlet}
\]
\[
\text{b} \quad 3 \text{ H triplet}
\]
\[
\text{c} \quad 2 \text{ H quartet}
\]
\[
\text{d} \quad 1 \text{ H singlet}
\]
cyclohexane

\[
\begin{array}{c}
\text{a singlet } 12\text{H}
\end{array}
\]
2,3-dimethyl-2-butene

\[
\begin{align*}
\text{H}_3\text{C} & \quad \text{C} \quad \text{CH}_3 \\
\text{H}_3\text{C} & \quad \text{C} \quad \text{CH}_3
\end{align*}
\]

a singlet 12H
benzene

\[
\{ \text{a singlet 6H} \}
\]
ethyl bromide

$\text{CH}_3\text{CH}_2\text{-Br}$

a    triplet   $3\text{H}$
b    quartet   $2\text{H}$
1-bromopropane

CH₃CH₂CH₂-Br

a  triplet  3H
b  hextate  2H
c  triplet  3H
Chloropropane

\[ \text{CH}_3\text{CHCH}_3\text{Cl} \]

- a: doublet, 6H
- b: septet, 1H
ethanol

CH$_3$CH$_2$-OH

a   triplet   3H
b   singlet   1H
c   quartet   2H
Propanol

\[ CH_3CH_2CH_2-OH \]

- a: triplet, 3H
- b: complex, 2H
- c: singlet, 1H
- d: triplet, 2H
In addition to the NMR spectrum, the NMR spectrometer has drawn what is termed ‘an integrated spectrum trace’.

The height of each step is a measure of the area under the peak.

It is proportional to the number of hydrogen atoms (protons) resonating at this point in the NMR spectrum.

In this case there are three steps, which are in the ratio of 1 : 2 : 3 (from left to right).
MRI

- Magnetic resonance imaging, noninvasive
- “Nuclear” is omitted because of public’s fear that it would be radioactive.
- Only protons in one plane can be in resonance at one time.
- Computer puts together “slices” to get 3D.
- Tumors readily detected.
Magnetic resonance imaging (MRI) uses NMR for medical diagnosis.

The patient is placed inside a cylinder that contains a very strong magnetic field (usually generated by a superconducting magnet).

Radio waves then cause the hydrogen atoms in the water molecules of the body to resonate.

Each type of body tissue emits a different signal, reflecting the different hydrogen density of the tissue.

Computer software then translates these signals into a three-dimensional picture.
MRI does not ‘see’ bone and can only produce images of soft tissues such as blood vessels, cerebrospinal fluid, bone marrow and muscles.

This occurs because the amount of water in bone is very small compared to the amount in soft tissue.

MRI is used to detect brain tumors, damage caused by multiple sclerosis (MS) or strokes, joint injuries, heart disease (caused by the narrowing of arteries) and herniated discs.

It is regarded as a harmless procedure except to those patients who have metal implants, such as a pacemaker, joint pins, shrapnel or artificial heart valves.