NMR Spectroscopy
NMR Phenomenon

- **Nuclear Magnetic Resonance**

  A spinning charged particle generates a magnetic field.

  A nucleus with a spin angular momentum will generate a magnetic moment ($\mu$).

  If these tiny magnets are placed in an applied magnetic field ($B_0$), they will adopt two different states - one aligned with the field and one aligned against the field. The energy difference between these two states is what we are observing with NMR.
Nuclear Spin States

When EM waves at this energy are directed at the nuclei - it will absorb. Spins will flip from lower energy to higher energy. At that energy, nuclei are “In Resonance”.
Many nuclei are “NMR Active”

- Spin Quantum Number $I \neq 0$
  - $^1H$ -- $I = \frac{1}{2}$; $^{13}C$ -- $I = \frac{1}{2}$
  - $^{12}C$, $^{16}O$ -- $I = 0$ -- Can’t be observed

Other nuclei that are NMR active

- $^2H$ (D), $^{14}N$, $^{19}F$, $^{31}P$
NMR Instrumentation

Sample in tube

Radiofrequency generator

Detector and amplifier

Display

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NMR is the basis for MRI
To summarize

A spinning charged particle generates a magnetic field. A nucleus with a spin angular momentum will generate a magnetic moment (m).

When placed in a magnetic field \( B_0 \), they will adopt two different states - one aligned with the field and one aligned against the field.

Energy difference between the states at a particular magnet strength. In the \( R_f \) range of the EM Spectrum.
Methyl Acetate - Carbon NMR

\[
\text{H}_3\text{C} - \text{C} = \text{O} - \text{O} - \text{CH}_3
\]

solvent

171.143
77.425
77.000
76.575
51.427
20.564

ppm
Electronic Shielding - Local Environments

\[ B_{\text{effective}} = B_0 - B_{\text{local}} \]

Actual magnetic field felt by the nucleus
Methyl Acetate - Proton NMR

\[
\text{H}_3\text{C} - \text{C} - \text{O} - \text{CH}_3
\]
Methyl Acetate - Carbon NMR

H₃C\[\text{C} \text{O}\text{O}\text{CH}_3\]

solvent

171.143

\[\text{O} \text{O} \text{C} \text{C}\]

77.425 77.000 76.575

51.427

20.564

ppm
The difference in resonance frequency of a nuclei relative to a standard:

- Most Shielded
- Relatively Inert
- Volatile

Resonance of standard is set to 0

\[
\text{H}_3\text{C} - \text{Si} - \text{CH}_3
\]

TMS (TetraMethylSilane)
X-Axis - frequency axis

NMR Spectrum

<table>
<thead>
<tr>
<th>Low Field</th>
<th>High Field</th>
</tr>
</thead>
<tbody>
<tr>
<td>Little electron shielding</td>
<td>More electron shielding</td>
</tr>
<tr>
<td>(more electron withdrawing groups)</td>
<td>(less electron withdrawing groups)</td>
</tr>
</tbody>
</table>

peaks measured as a shift (in Hz) away from TMS

Reference TMS

10 Hz

0
Different Spectrometer Frequencies

- Each specific instrument has its own magnetic field strength - resonance occurs at different frequencies.

100 MHz NMR
300 MHz NMR

Reference TMS
\[ \delta = \text{ppm} = \frac{\text{Chemical Shift from TMS (Hz)}}{\text{Spectrometer Frequency (MHz)}} \]

100 MHz NMR
300 MHz NMR

\[ \frac{100 \text{ Hz}}{100 \text{ MHz}} = 1.0 \text{ ppm} \]

\[ \frac{300 \text{ Hz}}{300 \text{ MHz}} = 1.0 \text{ ppm} \]
C\textsubscript{13} NMR

- Difficult - Carbon 13 only 1.1\% of all carbon.
- Number of different carbons
- Functional Group Regions

\[ \delta \] ppm

\[ \begin{array}{c}
\text{C-O} \\
\text{C-N} \\
\text{C-X}
\end{array} \]
C13 NMR

(a) Intensity

Chemical shift (δ)

200 180 160 140 120 100 80 60 40 20 0 ppm

(b) Intensity

Chemical shift (δ)

200 180 160 140 120 100 80 60 40 20 0 ppm

OH
Symmetry in molecules can make carbons “Chemically Equivalent”
Some molecules have more than one mirror plane.
The intensity of the peaks roughly correlates with the number of hydrogens on the carbon.
$^{13}$C NMR Regions
Bromooctanal
Alanine Me-Ester HCl

\[
\begin{align*}
\text{H}_3\text{C} & \quad \text{NH}_3\text{Cl} \\
\text{O} & \quad \text{OCH}_3 \\
\end{align*}
\]
Alaninol

\[
\text{H}_3\text{C}-\text{CH}_2-\text{NH}_2-\text{OH}
\]
Alaninol - phthalimide

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

\[
\begin{align*}
\text{OH} & \quad \text{O} \\
\end{align*}
\]
A - normal C13

B - CH carbons only

C - Odd # up (CH3 and CH) Even # down (CH2)
Example from 13.7

\[
\begin{align*}
\text{Cl} & \quad \text{KOH ethanol} \\
\text{C} & \quad \text{KOH ethanol} \\
\text{Cl} & \quad \text{KOH ethanol}
\end{align*}
\]

or

\[
\begin{align*}
\text{C} & \quad \text{KOH ethanol} \\
\text{Cl} & \quad \text{KOH ethanol} \\
\text{Cl} & \quad \text{KOH ethanol}
\end{align*}
\]

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A Real Example

In the alkane region there would only be 4 peaks due to symmetry.

In the alkane region there would be 6 different peaks.
The Answer Is . . .

The Answer Is . . .
Proton NMR

- Number of chemically different hydrogens
- Relative Ratios of protons (peak size)
- How many neighboring hydrogens
- Chemical shifts and functional groups
Proton Equivalency

**Homotopic**

\[
\begin{align*}
\text{replace H's - same} \\
\end{align*}
\]

**Enantiotopic**

\[
\begin{align*}
\text{replace H's - enantiomers} \\
\end{align*}
\]

**Diastereotopic**

\[
\begin{align*}
\text{replace H's - diastereomers} \\
\end{align*}
\]
Range 0-10 ppm
### Typical NMR Chemical Shifts

<table>
<thead>
<tr>
<th>Functional Group</th>
<th>Type</th>
<th>$^1$H Chemical Shift (ppm)</th>
<th>$^{13}$C Chemical Shift (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\equiv$C−H</td>
<td>Alkane</td>
<td>0.7 - 1.8</td>
<td>10 - 60</td>
</tr>
<tr>
<td>$\equiv$C−C−H</td>
<td>Allylic or next to carbonyl</td>
<td>1.6 - 2.4</td>
<td>30 - 60</td>
</tr>
<tr>
<td>$\equiv$X−C−H</td>
<td>next to halogen or alcohol</td>
<td>2.5 - 4.0</td>
<td>20 - 85</td>
</tr>
<tr>
<td>C−O=C−H</td>
<td>next to oxygen of an ester</td>
<td>4.0 - 5.0</td>
<td>50 - 85</td>
</tr>
<tr>
<td>$\equiv$C−H</td>
<td>vinylic</td>
<td>4.5 - 6.5</td>
<td>110 - 150</td>
</tr>
<tr>
<td></td>
<td>aromatic</td>
<td>6.5 - 8.0</td>
<td>110 - 140</td>
</tr>
<tr>
<td></td>
<td>aldehyde</td>
<td>9.7 - 10.0</td>
<td>190 - 220</td>
</tr>
<tr>
<td>O−H</td>
<td>alcohol</td>
<td>varies widely</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>will exchange with D$_2$O</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>carbonyl of ester, amide, or</td>
<td>N/A</td>
<td>165 - 185</td>
</tr>
<tr>
<td></td>
<td>carboxylic acid (X = O, N)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>O−C−X</td>
<td>carbonyl of ketone or aldehyde</td>
<td>N/A</td>
<td>190 - 220</td>
</tr>
</tbody>
</table>
Methyl Acetate

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

Area under peak corresponds to the number of H’s for that resonance
Triphenyl Methanol
Ethyl Acetate

\[
\text{H}_3\text{C} - \overset{\text{O}}{\text{C}} - \overset{\text{O}}{\text{C}} - \overset{\text{H}_2}{\text{C}} - \overset{\text{CH}_3}{\text{C}}
\]
- Protons on adjacent carbons also have an effect
- Resonances will split into \( n+1 \) number of peaks

\[
\begin{align*}
\text{C} & \quad \text{C} \\
H_a & \quad H_b \\
H_b & \quad \downarrow \\
\end{align*}
\]

\[J\]  

\[
\begin{align*}
1^H \text{NMR (without coupling)} \\
1^H \text{NMR (with coupling)}
\end{align*}
\]
Two hydrogens split neighbors into a triplet

1H NMR (without coupling)

1H NMR (with coupling)
Every splitting can be broken down into a series of doublets.

$^{1}\text{H NMR}$ (without coupling)

$^{1}\text{H NMR}$ (with coupling)

1 : 2 : 1
Spin Spin Splitting

- Three neighbors - Quartet

\[ \text{C} - \text{C} - \text{H}_b \]

\[ H_a \quad H_b \]

\[ H_b \]

\[ \text{1H NMR (without coupling)} \]

\[ \text{1H NMR (with coupling)} \]

\[ \text{1 : 3 : 3 : 1} \]
Higher Spin Spin Splitting

Pascal’s Triangle

<table>
<thead>
<tr>
<th></th>
<th>singlet</th>
<th>1</th>
</tr>
</thead>
<tbody>
<tr>
<td>doublet</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>triplet</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>quartet</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>quintet</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>sextet</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>septet</td>
<td>1</td>
<td>6</td>
</tr>
</tbody>
</table>

H_a will split into 7 peaks

C=C=C=H

H_b

64 different combinations of 6 spins
Summary of Spin Spin Splitting

- Proton resonance split into n+1 number of peaks.
- Relative ratio of peaks depends on number of spin states of the neighbors.
- Adjacent protons will couple with the same coupling constant.
- Protons farther away usually do not couple.
- Chemically equivalent protons cannot couple (e.g. ClCH₂CH₂Cl).
Doublet Splitting

Methyl sees 1 neighbor, Methine sees 3
Note that the OH (and NH) usually don’t couple.
1,1,2-Trichloroethane
2-Bromopropane
Butanone
Sometimes peaks overlap
Multiple Coupling
Every splitting can be broken down into a series of doublets.

\[ \begin{align*}
H_a & \quad H_b \\
\text{C} & \text{C} \quad H_b
\end{align*} \]

\[ ^1H \text{ NMR (without coupling)} \]

\[ \begin{align*}
1 & : 2 : 1
\end{align*} \]
Coupling with the same $J$

$J_{a-b} = 5$ Hz

$J_{a-c} = 5$ Hz

Coupling with $H_b$

Coupling with $H_c$
Coupling with different $J$ values

$J_{a-b} = 5 \text{ Hz}$

$J_{a-c} = 10 \text{ Hz}$

Coupling with $H_b$

Coupling with $H_c$

Coupling with $H_c$

Coupling with $H_b$
- Multiple Coupling

- $J_{H1-H2} = 6 \text{ Hz}, J_{H2-H3} = 12 \text{ Hz}$
Cinnemaldehyde

Proton on C2

$J_{2-3} = 12 \text{ Hz}$

$J_{1-2} = 6 \text{ Hz}$

6.73 δ
Multiple Coupling - Identical $J$

$J_{a-b} = 5 \text{ Hz}$

$J_{a-c} = 5 \text{ Hz}$

Coupling with $H_b$

Coupling with $H_c$

Coupling with $H_c$
$J_{a-b} = 10 \text{ Hz}$  
$J_{a-c} = 5 \text{ Hz}$

**Diagram:**

- Coupling with $H_b$
- Coupling with $H_a$
- Coupling with $H_c$
Nitropropane

\[ \text{CH}_3\text{CH}_2\text{CH}_2\text{NO}_2 \]
Strategies for Determining Unknows

- Given the Molecular Formula - calculate degrees of unsaturation.
- Identify functional groups
- Identify pieces of the structure
- Put the pieces together in a reasonable way
- Double check that your structure matches all the data given.