NMR Theory

NMR = Nuclear Magnetic Resonance Spectroscopy

Spectroscopy is the interaction of matter with energy.

NMR uses low energy radiation from the radio frequency (RF) region of the electromagnetic spectrum.
NMR Theory

Only certain nuclei are NMR active.

Only nuclei containing odd mass numbers or odd atomic numbers will give NMR signals. These nuclei possess a property known as **nuclear spin**.

The proton ($^1\text{H}$) for example:
- 1 proton, 1 electron, 0 neutrons
- Nuclear Spin = $+\frac{1}{2}$ and $-\frac{1}{2}$

In the absence of any external stimuli, there is an equal probability of a proton being in either the $\alpha$ or the $\beta$ state.
NMR Theory

Every distinct proton in a molecule exists in a distinct chemical environment and thus requires a different RF frequency to cause excitation from the $\alpha$ to the $\beta$ state.

This results in each distinct proton providing a distinct signal in the NMR spectrum.

NMR Instrument
Chemically Equivalent/Distinct Hydrogen

Protons that exist in different chemical environments give rise to different NMR signals.

Equivalent protons correspond to the same NMR signal.
Chemically Equivalent/Distinct Hydrogen

\[
\begin{align*}
H_3C & \quad O \quad C \quad CH_3 \\
H_3C & \quad C \quad CH_3
\end{align*}
\]

Chemically Equivalent/Distinct Hydrogen

\[
\begin{align*}
H_3C & \quad O \quad C \quad CH_3 \\
H_3C & \quad C \quad NH_2
\end{align*}
\]
Chemically Equivalent/Distinct Hydrogen

\[ \text{H}_3\text{C} = \text{H} \]

Chemically Equivalent/Distinct Hydrogen

\[ \text{Cl} \]

\[ \text{Cl} \]

\[ \text{Cl} \]

\[ \text{Cl} \]
Chemically Equivalent/Distinct Hydrogen

Enantiotopic and Diastereotopic Protons

The Chemical Equivalence Test (X Test):
When the equivalency of two protons is in question, draw the compound twice. In one, replace one H with X. In the second, replace the other H with X.

• If the two are identical – the protons are identical.
• If the two are enantiomers – the protons are enantiotopic, but are still equivalent and thus result in the same NMR signal.
• If the two are diastereomers – the protons are diastereotopic and are not equivalent. These protons result in two different NMR signals.

Identical Protons:
Chemically Equivalent/Distinct Hydrogen

Enantiotopic and Diastereotopic Protons

Enantiotopic Protons:

Diastereotopic Protons:
Chemically Equivalent/Distinct Hydrogen

Enantiotopic and Diastereotopic Protons

One Last Example:

OH

Chemical Shift

Increasing Chemical Shift
Chemical Shift

A decrease in electron density around a nucleus deshields that nucleus and moves the signal downfield.

Increasing $\delta$

\[ \text{F} \rightarrow \text{CH}_3 \quad \text{Cl} \rightarrow \text{CH}_3 \quad \text{Br} \rightarrow \text{CH}_3 \quad \text{I} \rightarrow \text{CH}_3 \quad \text{H} \rightarrow \text{CH}_3 \]

Chemical Shift

A decrease in electron density around a nucleus deshields that nucleus and moves the signal downfield.

Increasing $\delta$

\[ \text{Cl} \rightarrow \text{CH} \quad \text{Cl} \rightarrow \text{CH}_2 \quad \text{Cl} \rightarrow \text{CH}_3 \quad \text{H} \rightarrow \text{CH}_3 \]
Chemical Shift

Deshielding effects are diminished with distance.

Attached electron withdrawing groups deshield a proton.
Increasing the # of alkyl groups deshields a proton.

The chemical shift of protons attached to sp² hybridized carbon atoms are unusually high.

This is due to a phenomenon known as magnetic anisotropy where the loosely held π electrons move in a circular path in the presence of a magnetic field.

This induced magnetic field reinforces the magnetic field applied by the instrument resulting in a larger deshielding effect.
Chemical Shift

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Chemical Shift

General Regions in a $^1$H NMR Spectrum

Integration (Peak Height)

The area under the signal is proportional to the number of protons that signal corresponds to.
Integration (Peak Height)

The area under an NMR signal is proportional to the number of protons that signal corresponds to.
Integration (Peak Height)

**Case 1:** Integration values accurately reflect the number of H.

![Compound structure with integration values](image1)

**Case 2:** Whole number integrations values that do not integrate for enough total H.

![Compound structure with integration values](image2)
Integration (Peak Height)

Case 3: One or more integration values are less than 1.

\[
\begin{array}{c|c|c}
C_4H_8O & 0.153 & 0.230 \\
2 & 1 & 0
\end{array}
\]

Case 4: Integration values appear as very large numbers

\[
\begin{array}{c|c|c}
C_6H_{12}O & 2950 & 1475 & 8840 \\
1 & 3 & 4
\end{array}
\]

\[\text{Structure: } \text{CH}_3\text{C(O)}\text{CH}_3\]
Case 5: The height of integral symbols printed on the spectrum reflect the area under the curve.

C₃H₇Cl

Peak Ratio – 1 : 1 : 1.5
2 : 2 : 3
x 2
Integration (Peak Height)

In some cases the integrals may all be connected together.
Coupling (Splitting)

The signal corresponding to a particular proton will split due to the protons on adjacent atoms.

The most common coupling that is observed is between protons on adjacent carbon atoms.

Simple coupling follows the n+1 rule.

\[ n = \# \text{ of protons on the adjacent carbon.} \]
Many names describing the same phenomenon....

- **Splitting or Spin-Spin-Splitting** – refers to a proton signal being split due to neighboring protons.

- **Coupling** – refers to one type of proton being “coupled” to neighboring proton(s). This results in splitting of the signal.

- **Multiplicity** – this refers to the type of splitting observed. If the signal is split into two peaks, the multiplicity is said to be a doublet.
**Coupling (Splitting)**

**What gives rise to signal splitting?**

![Chemical structures](image)

**Predicting connectivity using signal splitting**

![NMR spectra](image)
Coupling (Splitting)

**Common Features:**
1. The most common coupling occurs from non-equivalent proton that are separated by 3-bonds.

2. Coupling will be observed between protons separated by two bonds if the two protons are chemically distinct.
Coupling (Splitting)

Common Features:
3. Coupling between protons separated by 4 or more bonds is not generally observed.

![Chemical structure]

Common Features:
4. Coupling is usually not observed through oxygen and nitrogen.

![Chemical structure]

Alcohol and amine proton NMR signals usually show up as a singlet.
Coupling (Splitting)

Common Features:
5. Chemically equivalent protons do not couple!

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

Example:

\[
\begin{align*}
\text{HO} & \quad \text{O} \\
\text{O} & \quad \text{C} \quad \text{HO} \\
\text{H} & \quad \text{H} \quad \text{H} \\
\text{H} & \quad \text{H} \quad \text{H} \\
\text{H} & \quad \text{H} \quad \text{H} \\
\end{align*}
\]
The Coupling Constant

For every split signal in an NMR spectrum, a coupling constant can be calculated.

Essentially, a coupling constant is a measure of the interaction between coupled protons.

Coupling constants are also known as J-values and reported in Hz.
Calculating the Coupling Constant

Subtract the chemical shift values of two adjacent peaks in a split signal and multiple that value by the operating frequency of the NMR spectrometer.

![Spectrum recorded on 300 MHz spectrometer]

\[ J = 8.1 \text{ Hz} \]

Typical Coupling Constants

<table>
<thead>
<tr>
<th>Structure</th>
<th>( J ) (Hz)</th>
<th>Structure</th>
<th>( J ) (Hz)</th>
<th>Structure</th>
<th>( J ) (Hz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \text{H}_2\text{C} - \text{H} - \text{R} )</td>
<td>6 – 8</td>
<td>( \text{H} - \text{H} )</td>
<td>12 – 15**</td>
<td>( \text{H} - \text{H} )</td>
<td>12 – 18</td>
</tr>
<tr>
<td>( \text{H}_3\text{C} - \text{H} - \text{H} )</td>
<td>5 – 7</td>
<td>( \text{H} - \text{H} )</td>
<td>6 – 9</td>
<td>( \text{H} - \text{H} )</td>
<td>7 – 12</td>
</tr>
<tr>
<td>( \text{H} - \text{R}_1 - \text{H} - \text{R}_2 )</td>
<td>2 – 12*</td>
<td>( \text{H} - \text{H} )</td>
<td>1 – 3</td>
<td>( \text{H} - \text{H} )</td>
<td>0.5 – 3</td>
</tr>
<tr>
<td>( \text{HO} - \text{H} - \text{H} )</td>
<td>0.5 – 3</td>
<td>( \text{H} - \text{H} )</td>
<td>0 – 1</td>
<td>( \text{H} - \text{H} )</td>
<td>3 – 11*</td>
</tr>
</tbody>
</table>

*Depends on the H-C-H dihedral angle.

**Must be diastereotopic
NMR Spectroscopy

Dr. Joshua Osbourn – Dept. of Chemistry, West Virginia University

1. Theory of NMR Spectroscopy
2. Spectrum Basics
3. Chemically Equivalent and Distinct Hydrogen
4. Chemical Shift
5. Integration (Peak Height)
6. Coupling (Splitting)
7. Complex Splitting
8. Special Features to Lookout For
9. Examples – $^1$H NMR
10. Carbon-13 NMR

Complex Splitting

Sometimes coupling is more complex than n+1. This occurs when a proton is coupled to two or more non-equivalent protons.

\[
\begin{align*}
\text{H} & \quad \text{O} \\
\text{O} & \quad \text{H} \\
\text{H} & \quad \text{H}
\end{align*}
\]
Complex Splitting

Sometimes coupling is more complex than n+1. This occurs when a proton is coupled to two or more non-equivalent protons.
Complex Splitting

Sometimes coupling is more complex than n+1.

\[
\begin{array}{c}
\text{Cl} \\
\text{H} \\
\text{H} \\
\text{O} \\
\text{H} \\
\text{H} \\
\end{array}
\]
Overlapping Signals

Protons that are chemically distinct, yet have similar chemical environments can potentially overlap creating a multiplet.

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NMR Solvents

Deuterated solvents are typically used in NMR spectroscopy.

- Deuterated solvents are ones in which all of the hydrogen in the molecule have been replaced by deuterium.
- Deuterium absorptions are not detected in the range that is observed for $^1$H NMR.

![Diagram of NMR solvents]

TMS – Internal Standard

Oftentimes the NMR solvent is spiked with 0.1% trimethylsilane (TMS) which serves as an internal standard.

![Diagram of TMS]
**D₂O Shake**

Shaking an alcohol with D₂O results in rapid exchange of the OH proton with deuterium, which eliminates the –OH resonance.

When a sample containing an –OH group is very pure and completely dry, coupling through the alcohol will be observed.

Typically alcohols are contaminated with a small amount of water, acid, or base which collapses the OH signal into a singlet.
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Example 1 – C\(_7\)H\(_8\)O
Example 2 – $\text{C}_8\text{H}_9\text{BrO}$

Example 3 – $\text{C}_5\text{H}_{10}\text{O}_2$
Example 4 – C$_3$H$_9$N

Example 5 – C$_{10}$H$_{12}$O$_2$

IR Data: 1720, 1610, 1505, 1210, 1010 cm$^{-1}$
Example 6 – C$_3$H$_7$BrO

Example 7 – C$_9$H$_{20}$
Example 8 – $\text{C}_7\text{H}_{14}\text{O}_2$

Example 9 – $\text{C}_6\text{H}_{12}\text{O}$
Example 10 – $\text{C}_6\text{H}_{10}\text{O}_2$

IR Data: 3100 (broad, strong); 1730, 1650 cm$^{-1}$

A Terminal Alkene
An Internal Alkene