Advanced NMR Topics
Second Order Effects in NMR

- Splitting does not follow N+1; cannot be solved graphically
  - Different intensities
  - Additional peaks
  - Cannot directly measure coupling constants
Causes of Second Order Spectra

- Strong Coupling
- Virtual Coupling
- Magnetic non-equivalence
Strong Coupling

- Compare coupling constant (J) to difference in shift (Δν)
- If Δν < 5J, then second order
- Simplified by higher field instrument
- 60MHz: Δν=0.3ppm(60Hz/ppm) = 18Hz; J= 18 Hz
- 360MHz: Δν=0.3ppm(360Hz/ppm) = 108Hz; J= 18 Hz
Pople Coupling Nomenclature

• Spin system named by how close protons are in shift: A, M, X
• AX2 system: one proton coupled to two protons with distant chemical shift (first order)
• AB2 system: one proton coupled to two protons with similar shift (second order)
• AMX3: one proton coupled to one proton coupled to three protons, all distant chemical shift (first order)
First and Second order systems

- http://www.chem.wisc.edu/areas/reich/nmr/05-hmr-07-pople.htm
Some molecules with $A_2B_2/A_2X_2$ patterns:

- Change from $A_2X_2$ to $A_2B_2$

\[ v_{AB} = 200 \text{ Hz} \]
\[ J_{AB} = 10 \text{ Hz} \]

\[ v_{AB} = 70 \text{ Hz} \]

\[ v_{AB} = 25 \text{ Hz} \]

http://www.chem.wisc.edu/areas/reich/chem605/index.htm
Virtual Coupling

CH₃CH₂CH₂CH₂OH

(a)

(b)
Magnetic Equivalence

- Chemical equivalence
- Magnetic equivalence
- AA’BB’ system: disubstituted benzene
- Deceptively simple spectra
Modern C-13 NMR Spectroscopy
C-13 Sensitivity

- Only 1% natural abundance
- Split by protons
- $^{13}\text{C}/^1\text{H} J = 125 \text{ Hz}$ for sp$^3$ carbon
- Solution to problem: Broadband Decoupling
  - No splitting observed
  - Increases signal
DEPT NMR

- Distorsionless Enhancement by Polarization Transfer
- Transfer signal from protons to carbon

<table>
<thead>
<tr>
<th>Type of $^{13}$C spectrum</th>
<th>$\text{CH}_3$</th>
<th>$\text{CH}_2$</th>
<th>$\text{CH}$</th>
<th>$C$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Broadband-decoupled $^{13}$C</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>DEPT(45)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>0</td>
</tr>
<tr>
<td>DEPT(90)</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
</tr>
<tr>
<td>DEPT(135)</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>0</td>
</tr>
</tbody>
</table>
2D NMR

• 2 basic experiments – COSY and HETCOR
• COSY
  – H-H Correlation spectroscopy
  – $^1$H spectra on x and y axes
• HETCOR
  – Heteronuclear correlation spectroscopy
  – $^{13}$C on one axis, $^1$H on the other (same sample)

• There are many more 2D experiments – these are two of the most common
Reading a COSY spectrum

- X-axis = $^1$H spectrum
- Y-axis = $^1$H spectrum
- Diagonal = reference points (mirror plane: C=D)
- Off-diagonal peaks = *coupled protons*
Isopentyl acetate

A = 1-2 coupling
B =
C =
How to read a HETCOR spectrum

• X-axis = $^{13}\text{C}$ spectrum
• Y-axis = $^1\text{H}$ spectrum
• No diagonal (no mirror plane)
• Peaks indicate a $^{13}\text{C}$ and the $^1\text{H}$’s directly attached to it.
Isopentyl acetate

In the C-13 spectrum, which carbon signal is furthest upfield? From induction, we might think that it is carbon 1, but...
• Very useful for
  – Finding overlapping proton signals
  – Identifying diasteriotopic carbon and protons atoms
Interpret all NMR spectra for 6-chlorohexanol (don’t need to calculate coupling constants):

Note: These NMR spectra were obtained in a solvent in which acidic protons are visible, and coupling to these protons is observed.
$^1$H NMR 600 MHz

$^{13}$C NMR 150.9 MHz
COSY 600 MHz

![COSY spectrum diagram](image)
HETCOR 600 MHz
Ribavirin

- Anti-viral
- Used to treat hepatitis C
- Guanosine analog—inhibitor or viral RNA synthesis
Riboflavin DEPT
Ribavirin COSY
Ribavirin HETCOR