Second Order Spectra

BCMB/CHEM 8190
First Order and Second Order NMR Spectra

• The "weak coupling" or "first order" approximation assumes that, for simple coupled systems, the difference between the Larmor frequencies of the coupled nuclei is large compared to the coupling constant between them:

\[ \Delta \nu \gg J \]

• When the frequency difference approaches the coupling constant, the spectra are said to be "second order"

\[ \Delta \nu \sim J \]

• The simple rules presented for first order spectra (multiplicity, number of peaks, peak intensities, chemical shifts of multiplets, values and measurement of coupling constants) do not necessarily apply to second order spectra

• **Importantly**, as \( B_0 \) increases, Larmor frequencies decrease and \( \Delta \nu \) decreases, but \( J \) is \( B_0 \) independent, so \( \Delta \nu \rightarrow J \) and spectra become second order

• Spin systems for second order spectra will use letters close in the alphabet (AB, ABC), to indicate similarity in frequencies
Second Order Spectrum Example: Acrylonitrile

- Shown is an "ideal" first order spectrum (AMX) for acrylonitrile
- Are 12 peaks, equal intensities (predicted for first order)

For δ_A=6.3 ppm, δ_B=6.1 ppm, δ_C=5.6 ppm:

<table>
<thead>
<tr>
<th></th>
<th>800 MHz</th>
<th></th>
<th>60 MHz</th>
</tr>
</thead>
<tbody>
<tr>
<td>J_AB</td>
<td>-2 Hz</td>
<td>Δν_AB</td>
<td>160 Hz</td>
</tr>
<tr>
<td>J_AC</td>
<td>11 Hz</td>
<td>Δν_AC</td>
<td>560 Hz</td>
</tr>
<tr>
<td>J_BC</td>
<td>16 Hz</td>
<td>Δν_BC</td>
<td>400 Hz</td>
</tr>
</tbody>
</table>

- At lower B_0 (as Δν → J ) the spectrum becomes second order
- In first order spectra, can't discern the sign of the coupling (by looking at the spectra). Not always the case for second order
Field dependence of second order spectra

- As $\Delta \nu \rightarrow J$, a number of noticeable effects
  - peak intensities deviate from what is expected for first order
  - number of peaks changes (can get peaks for "forbidden" transitions)
  - signals become unrecognizable with respect to first order expectations
Field dependence of second order spectra

simulated spectra

60 MHz

90 MHz

200 MHz

400 MHz
Peak Intensities and Transition Probabilities

- Recall for pairs of spin $\frac{1}{2}$ nuclei, the product wavefunctions ($\alpha\alpha$, $\beta\alpha$, $\alpha\beta$, and $\beta\beta$), in the limit of first order spectra (AX), are good solutions to Schrödinger's equation
  - they form a complete orthonormal set
- Can write wavefunctions for more complex Hamiltonians by making linear combinations of all members of the set (this is how second order spectra are treated)
  \[ \psi = c_1\alpha\alpha + c_2\alpha\beta + c_3\beta\alpha + c_4\beta\beta = \sum_j c_j\psi_j \]
- Recall, the probability of being in some state, $\psi$, is
  \[ \psi^*\psi \]
- Thus, the probability ($\rho$) of (mostly) being in one ($j$) of our well-defined basis states is
  \[ \rho_{jj} \propto c_j^* c_j \]
- The transition probability, the probability of starting in one state ($k$) and ending in another ($l$), is
  \[ \rho_{k\rightarrow l} \propto (c_k^* c_k) (c_l^* c_l) \]
Peak Intensities and Transition Probabilities

- The *transition probability*, the probability of starting in one state \((k)\) and ending in another \((l)\), is
  \[
  \rho_{k\rightarrow l} \propto \begin{pmatrix} c_k^* & c_k \end{pmatrix} \begin{pmatrix} c_l^* & c_l \end{pmatrix}
  \]

- If we know we start in state \(k\) \((c_k^* c_k = 1)\), then we only need to solve for the probability that we are going to end up in state \(l\) (peak intensities)

- This requires consideration of the time dependence (for transitions to occur), hence Schrödinger's time dependent equation (time derivative of the wavefunction)
  \[
  \hat{H} \psi(t) = -i \hbar \frac{d(\psi(t))}{dt} \quad \psi = \sum_j c_j \varphi_j
  \]

- So, to see how \(c_l\) changes with time (in unit time, what is the probability of going from state \(k\) to \(l\))
  \[
  \frac{d(c_l)}{dt} = \langle \phi_l | \hat{H}' | \phi_k \rangle \quad \text{integrated from } t = 0 \text{ to } 1
  \]

- Last thing: have to square the result to get intensities
  \[
  \rho_{k\rightarrow l} \propto \left| \langle \phi_l | \hat{H}' | \phi_k \rangle \right|^2
  \]
Understanding second order spectra

- Pure first order (AX) spectrum: HF
  - even at low field strength, Larmor frequencies of $^1\text{H}$ and $^{19}\text{F}$ are MHz apart (at 2.35 T, 100 MHz $^1\text{H}$ and 94 MHz $^{19}\text{F}$, $\Delta \nu \sim 6,000,000$ Hz), and the one-bond HF coupling constant is $\sim 500$ Hz, so, $\Delta \nu \gg J$

- Transition energies when $J = 0$ (i.e. no coupling)
  - for spin 1, $\alpha\alpha \rightarrow \beta\alpha$ and $\alpha\beta \rightarrow \beta\beta$ energies are equal
  - for spin 2, $\alpha\alpha \leftrightarrow \alpha\beta$ and $\beta\alpha \leftrightarrow \beta\beta$ energies are equal

- Transition energies when $J > 0$ (i.e. positive coupling)
  - when $J > 0$, $\Delta E$ for transitions to/from the highest energy state ($\beta\beta$) increases compared to $J = 0$, $\Delta E$ for transitions to/from the lowest energy state ($\alpha\alpha$) decrease compared to $J = 0$
Understanding second order spectra

- Peak intensities for "pure" first order (AX) spectrum: HF
  - the intensities of the signals in each multiplet should be identical
  - we can calculate the probabilities for single quantum ($\Delta m = 1$) interconversions, which should, therefore, all be the same

- For the first order system, we'll write the Hamiltonian as
  \[ \hat{H}' = \gamma B_1 (\hat{I}_{x1} + \hat{I}_{x2}) \]
  - we can leave out the time dependence (rotating frame)
  - use $B_1$ (rf field) which interacts with the magnetic moment ($\gamma I_x$, assuming $B_1$ acts along x-axis)

- Example: evaluate for $\beta\beta \rightarrow \alpha\beta$ transition
  \[ \rho_{\beta\beta \rightarrow \alpha\beta} \propto \left| \langle \beta\beta | \gamma B_1 (I_{x1} + I_{x2}) | \alpha\beta \rangle \right|^2 \]
  (recall $\hat{I}_x | \alpha \rangle = 1/2 \beta$ \hspace{1cm} $\hat{I}_x | \beta \rangle = 1/2 \alpha$)

  \[ = \gamma B_1 \left[ \left| \langle \beta\beta | (I_{x1}) | \alpha\beta \rangle + \langle \beta\beta | (I_{x2}) | \alpha\beta \rangle \right|^2 \right] \]

  \[ = \gamma B_1 \left[ \left| 1/2 \langle \beta\beta | \beta\beta \rangle + 1/2 \langle \beta\beta | \alpha\alpha \rangle \right|^2 \right] \]

  \[ = \gamma B_1 \left[ 1/2 + 0 \right|^2 \]

- Evaluate all four transitions:
  \[ \rho_{\alpha\alpha \rightarrow \alpha\beta} = \rho_{\alpha\alpha \rightarrow \beta\alpha} = \rho_{\alpha\beta \rightarrow \beta\beta} = \rho_{\beta\alpha \rightarrow \beta\beta} \]

- What about $\alpha\alpha \rightarrow \beta\beta$ ???
Understanding second order spectra

- Consider a "pure" second order ($A_2$) spectrum ($H_2$, $H_2O$, etc.)
  - expect single peak (equivalent nuclei have identical chemical shifts)
  - coupling does not result in peak splitting........why?

- Problem: $\alpha\alpha$, $\alpha\beta$, $\beta\alpha$, $\beta\beta$ are not individually good solutions to Schrödinger's equation for equivalent nuclei
  - recall, when not first order, must include $I_xI_x$ and $I_yI_y$ in the scalar coupling term of the Hamiltonian (first order approximation no longer valid)
  - also, $\alpha\beta$ and $\beta\alpha$ imply they are distinguishable (can't be for identical nuclei)
  - $\alpha\alpha$ and $\beta\beta$ are OK

- Solution: use linear combinations of $\alpha\beta$ and $\beta\alpha$
  \[
  \frac{(\alpha\beta + \beta\alpha)}{\sqrt{2}} \quad \frac{(\alpha\beta - \beta\alpha)}{\sqrt{2}}
  \]

- So, we can then solve for the 4 possible transition probabilities
  \[
  \rho_{k\rightarrow l} \propto \left| \langle \phi_l \mid \hat{H}' \mid \phi_k \rangle \right|^2
  \]
Understanding second order spectra

- Solve for one of the transitions

\[ \rho_{\beta\beta \to (\alpha\beta + \beta\alpha)} \propto |\beta\beta|, (\gamma B_1(I_{x1} + I_{x2}) \mid (\alpha\beta + \beta\alpha) / \sqrt{2})|^2 \]

\[ = |\gamma B_1 \langle \beta\beta \mid I_{x1} \mid (\alpha\beta + \beta\alpha) / \sqrt{2} \rangle + \gamma B_1 \langle \beta\beta \mid I_{x2} \mid (\alpha\beta + \beta\alpha) / \sqrt{2} \rangle|^2 \]

\[ = |\gamma B_1 [(\langle \beta\beta \mid I_{x1} \mid (\alpha\beta) / \sqrt{2} \rangle + \langle \beta\beta \mid I_{x1} \mid (\beta\alpha) / \sqrt{2} \rangle + \langle \beta\beta \mid I_{x2} \mid (\alpha\beta) / \sqrt{2} \rangle + \langle \beta\beta \mid I_{x2} \mid (\beta\alpha) / \sqrt{2} \rangle]^2 \]

\[ = |\gamma B_1 [(1/2)/\sqrt{2} \langle \beta\beta \mid \beta\beta \rangle + (1/2)/\sqrt{2} \langle \beta\beta \mid \alpha\alpha \rangle + (1/2)/\sqrt{2} \langle \beta\beta \mid \alpha\alpha \rangle + (1/2)/\sqrt{2} \langle \beta\beta \mid \beta\beta \rangle]^2 \]

\[ = |\gamma B_1 [1/\sqrt{2}]^2 \]

\[ = 1/2 (\gamma B_1)^2 \]

- Result

- two transitions of equal energy and equal probability (i.e. one peak)
- two transitions of with different energies, but zero probability (not allowed)

- All solutions

\[ \rho_{\beta\beta \to (\alpha\beta + \beta\alpha)} \propto 1/2 (\gamma B_1)^2 \]

\[ \rho_{\beta\beta \to (\alpha\beta - \beta\alpha)} = 0 \]

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\[ \alpha\alpha \quad (\alpha\beta + \beta\alpha)/\sqrt{2} \quad (\alpha\beta - \beta\alpha)/\sqrt{2} \]
"Intermediate" behavior of 2\textsuperscript{nd} order spectra

- AB systems are "intermediate" between AX and A\textsubscript{2}
  - as $\Delta \nu \rightarrow J$ an AX system becomes AB
  - inner peaks of doublets more intense than outer peaks ("roof effect")
  - $J$ can still be measured as distance between peak centers
  - chemical shifts are not center of doublets, but weighted averages of peak intensities ("center of gravity"), and can be determined knowing

$$\delta_A - \delta_B = \sqrt{(\delta_1 - \delta_4)(\delta_2 - \delta_3)}$$

outer lines are not observed, but couplings still exist
ABX systems

- ABX systems raise additional complications
  - for 'X', can't necessarily deduce coupling constant from peak separation
  - example: coupling of H5 (A), H5' (B) and H4 (X) in ribose rings
  - may consider using Karplus relationship to deduce torsion angle from $J_{45}$ and $J_{45}'$
  - splitting in ABX spectrum in X signal is equal to $(J_{45}+J_{45}')/2$
  - can't conclude $J_{45} = J_{45}'$

- Helpful to simulate spectra