

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:

$$\Delta\nu \gg J$$

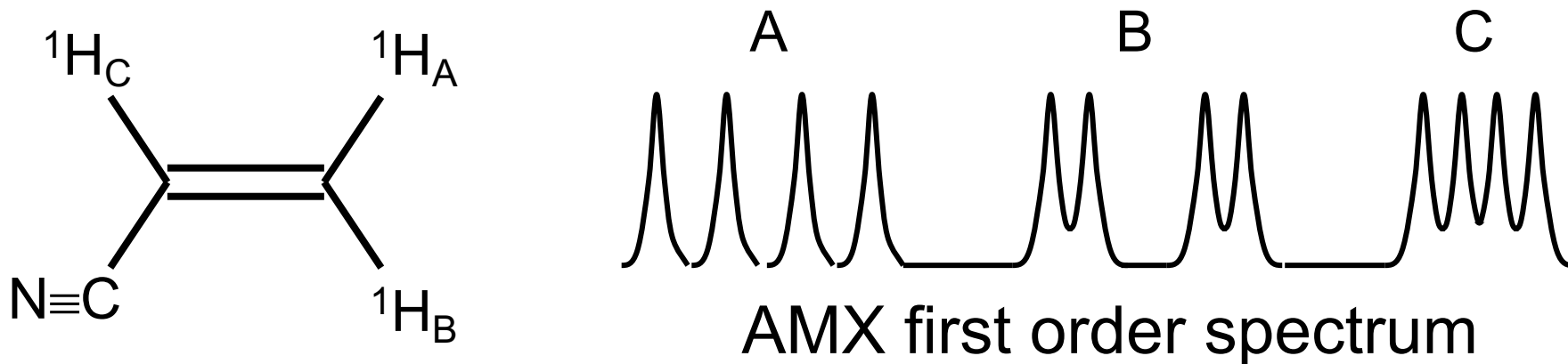
- When the frequency difference approaches the coupling constant, the spectra are said to be "second order"

$$\Delta\nu \sim J$$

- 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 decreases, 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)



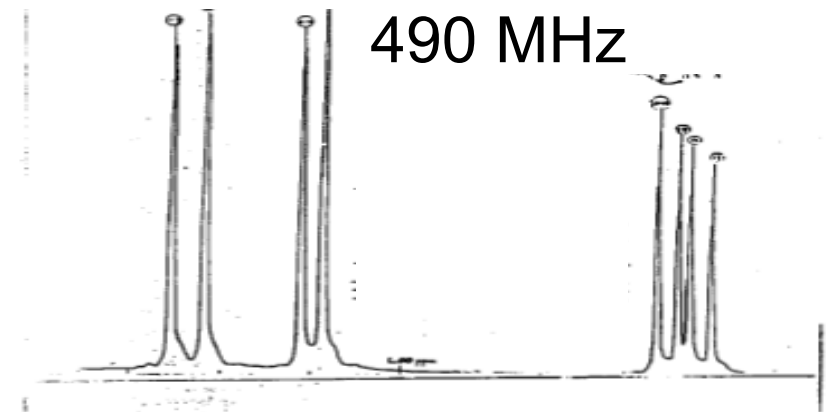
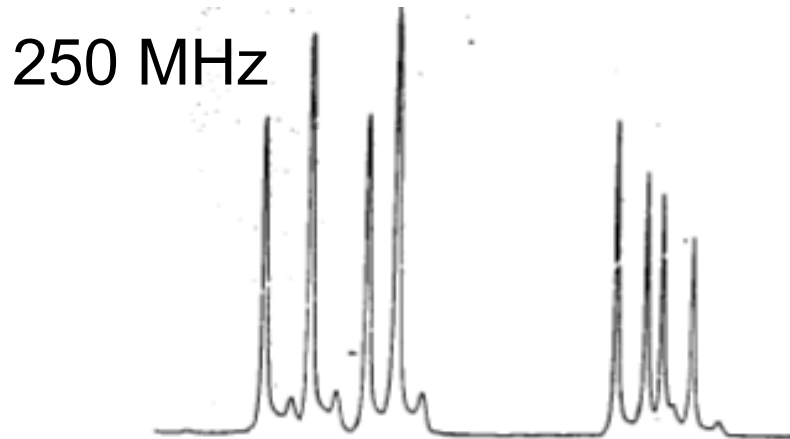
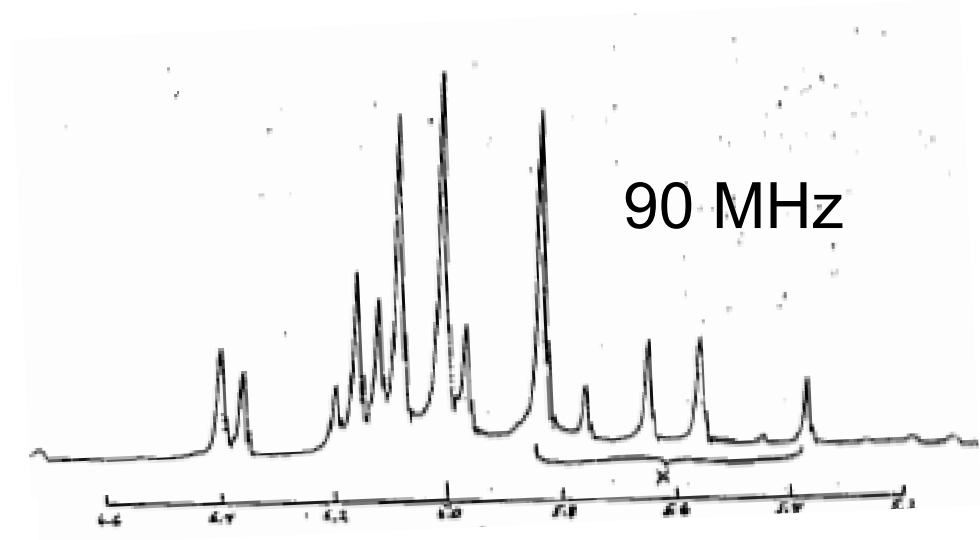
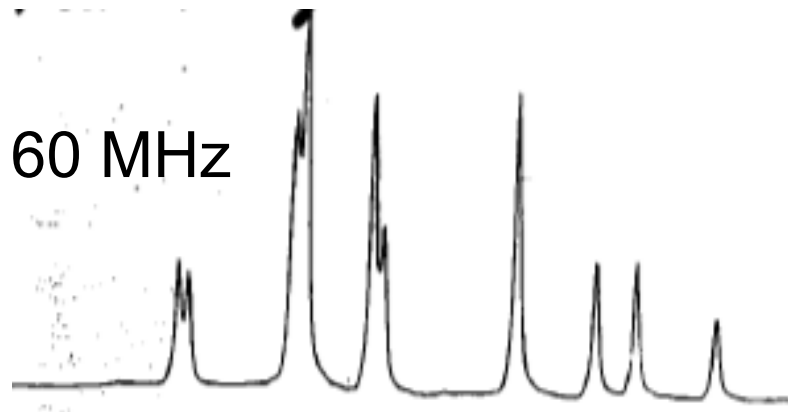
For $\delta_\text{A}=6.3$ ppm, $\delta_\text{B}=6.1$ ppm, $\delta_\text{C}=5.6$ ppm:

	<u>800 MHz</u>	<u>60 MHz</u>
$J_\text{AB} = -2$ Hz,	$\Delta\nu_\text{AB} = 160$ Hz	$\Delta\nu_\text{AB} = 12$ Hz
$J_\text{AC} = 11$ Hz,	$\Delta\nu_\text{AC} = 560$ Hz	$\Delta\nu_\text{AC} = 42$ Hz
$J_\text{BC} = 16$ Hz,	$\Delta\nu_\text{BC} = 400$ Hz	$\Delta\nu_\text{BC} = 30$ Hz

- At lower B_0 (as $\Delta\nu \rightarrow J$) 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

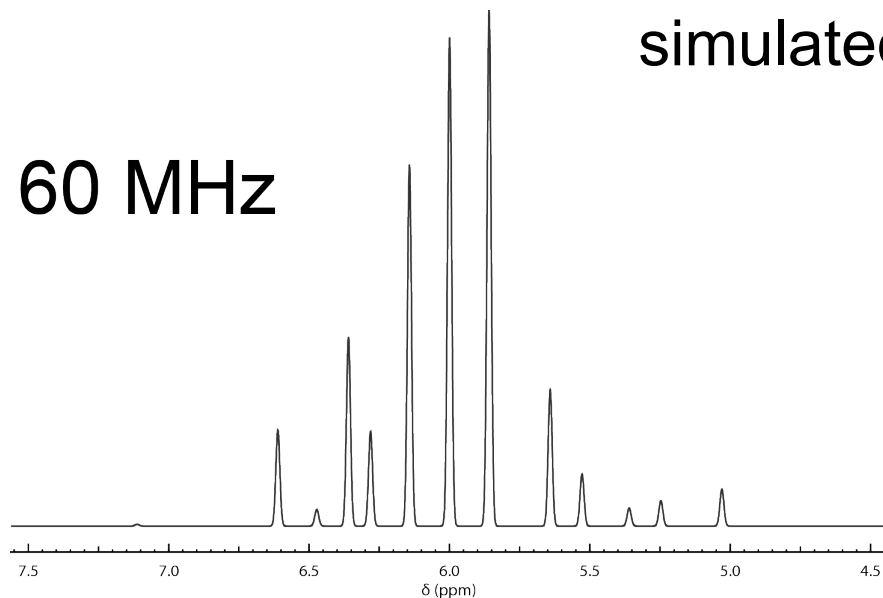
- As $\Delta\nu \rightarrow J$, a number of noticeable effects
 - peak intensities deviate from what is expected for first order
 - number of peaks changes (can get peaks for "forbidden" transitions)
 - signals become unrecognizable with respect to first order expectations



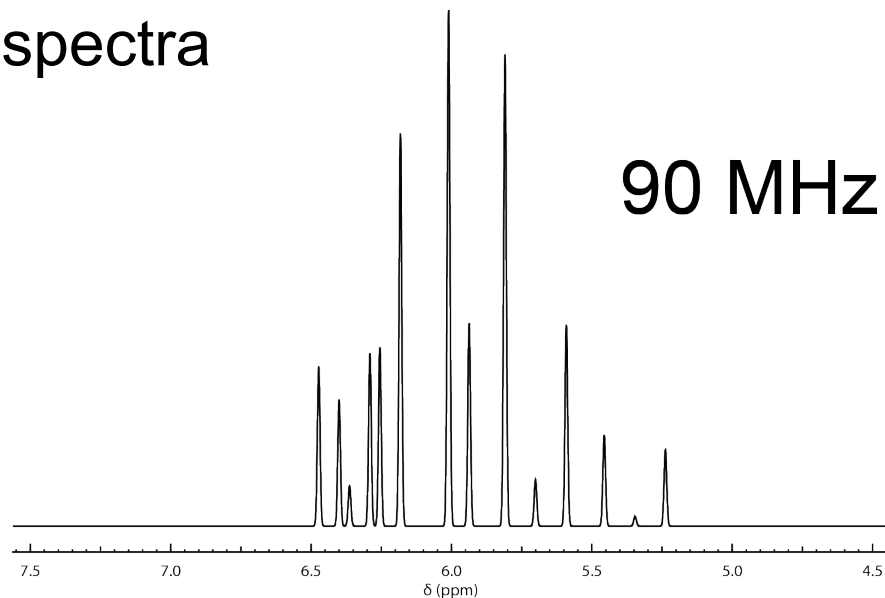
Field dependence of second order spectra

simulated spectra

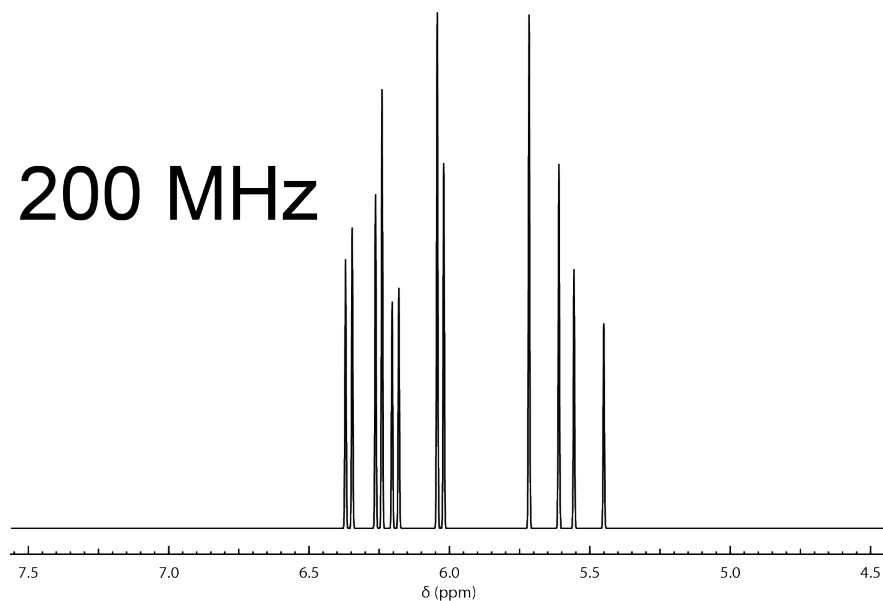
60 MHz



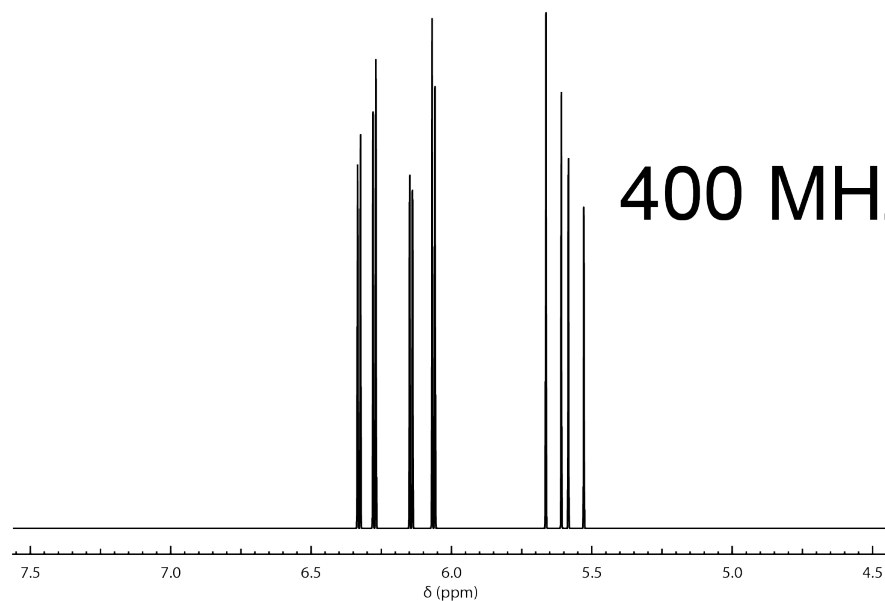
90 MHz



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)

$$\psi = c_1\alpha\alpha + c_2\alpha\beta + c_3\beta\alpha + c_4\beta\beta = \sum_j c_j \varphi_j$$

- Recall, the probability of being in some state, ψ , is

$$\psi^* \psi$$

- Thus, the probability (ρ) 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

$$\rho_{k \rightarrow l} \propto \begin{pmatrix} c_k^* & c_k \end{pmatrix} \begin{pmatrix} c_l^* \\ c_l \end{pmatrix}$$

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)

$$\hat{H}\psi(t) = -i\hbar \, d(\psi(t))/dt \qquad \psi = \sum_j c_j \varphi_j$$

- So, to see how c_l changes with time (in unit time, what is the probability of going from state k to l)

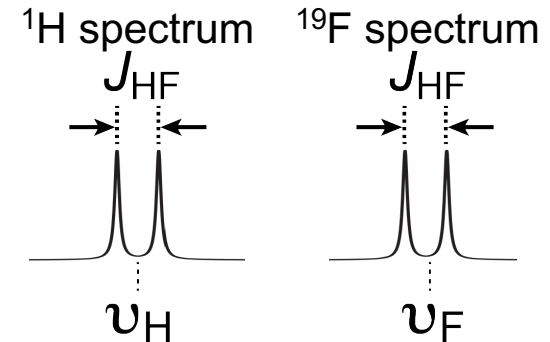
$$d(c_l)/dt = \langle \phi_l | \hat{H}' | \phi_k \rangle \quad \text{integrated from } t = 0 \text{ to } 1$$

- Last thing: have to square the result to get intensities

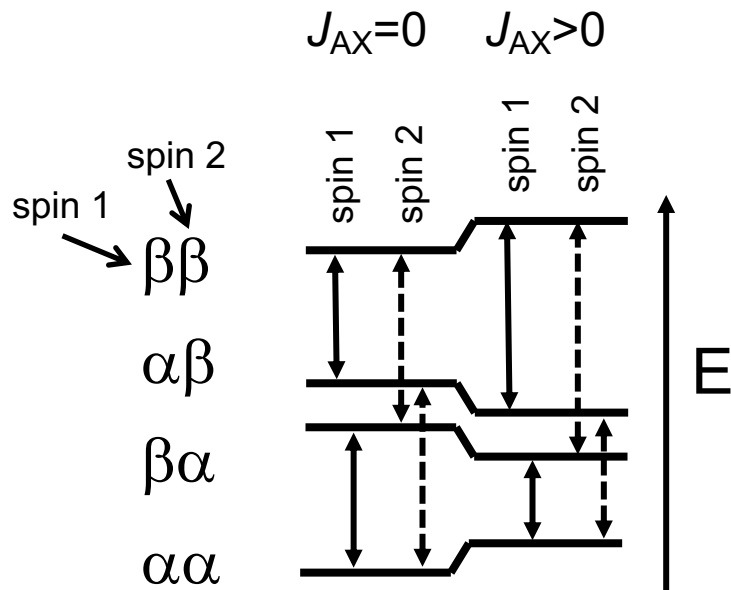
$$\rho_{k \rightarrow l} \propto \left| \langle \phi_l | \hat{H}' | \phi_k \rangle \right|^2$$

Understanding second order spectra

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

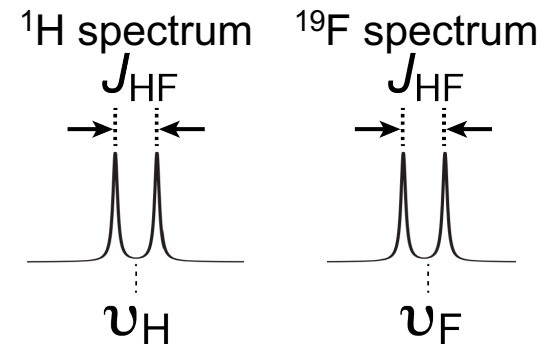


- Transition energies when $J = 0$ (i.e. no coupling)
 - for spin 1, $\alpha\alpha \rightarrow \beta\alpha$ and $\alpha\beta \rightarrow \beta\beta$ energies are equal
 - for spin 2, $\alpha\alpha \rightarrow \alpha\beta$ and $\beta\alpha \rightarrow \beta\beta$ energies are equal
- Transition energies when $J > 0$ (i.e. positive coupling)
 - when $J > 0$, ΔE for transitions to/from the highest energy state ($\beta\beta$) increases compared to $J = 0$, ΔE 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 (γI_x , assuming B_1 acts along x-axis)
- Example: evaluate for $\beta\beta \rightarrow \alpha\beta$ transition ($\rho_{k \rightarrow l} \propto |\langle \phi_l | \hat{H}' | \phi_k \rangle|^2$)

$$\rho_{\beta\beta \rightarrow \alpha\beta} \propto |\langle \beta\beta | \gamma B_1 (I_{x1} + I_{x2}) | \alpha\beta \rangle|^2 \quad (\text{recall } \hat{I}_x |\alpha\rangle = 1/2 \beta \quad \hat{I}_x |\beta\rangle = 1/2 \alpha)$$

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

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

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

- 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 $I_x I_x$ and $I_y I_y$ 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 $\beta\alpha$

$$(\alpha\beta + \beta\alpha)/\sqrt{2} \quad (\alpha\beta - \beta\alpha)/\sqrt{2}$$
- So, we can then solve for the 4 possible transition probabilities

$$\rho_{k \rightarrow l} \propto \left| \langle \phi_l | \hat{H}' | \phi_k \rangle \right|^2$$

$$\rho_{\beta\beta \rightarrow (\alpha\beta + \beta\alpha)} \propto \left| \langle \beta\beta | \gamma B_1 (I_{x1} + I_{x2}) | (\alpha\beta + \beta\alpha) / \sqrt{2} \rangle \right|^2 \quad \rho_{\beta\beta \rightarrow (\alpha\alpha + \beta\alpha)} \propto \left| \langle \alpha\alpha | \gamma B_1 (I_{x1} + I_{x2}) | (\alpha\beta + \beta\alpha) / \sqrt{2} \rangle \right|^2$$

$$\rho_{\beta\beta \rightarrow (\alpha\beta - \beta\alpha)} \propto \left| \langle \beta\beta | \gamma B_1 (I_{x1} + I_{x2}) | (\alpha\beta - \beta\alpha) / \sqrt{2} \rangle \right|^2 \quad \rho_{\beta\beta \rightarrow (\alpha\alpha - \beta\alpha)} \propto \left| \langle \alpha\alpha | \gamma B_1 (I_{x1} + I_{x2}) | (\alpha\beta - \beta\alpha) / \sqrt{2} \rangle \right|^2$$

Understanding second order spectra

- Solve for one of the transitions

$$\begin{aligned}
 \rho_{\beta\beta \rightarrow (\alpha\beta + \beta\alpha)} &\propto \left| \langle \beta\beta | \gamma B_1 (I_{x1} + I_{x2}) | (\alpha\beta + \beta\alpha) / \sqrt{2} \rangle \right|^2 \\
 &= \left| \gamma B_1 \langle \beta\beta | I_{x1} | (\alpha\beta + \beta\alpha) / \sqrt{2} \rangle + \gamma B_1 \langle \beta\beta | I_{x2} | (\alpha\beta + \beta\alpha) / \sqrt{2} \rangle \right|^2 \\
 &= \left| \gamma B_1 \left[\langle \beta\beta | I_{x1} | (\alpha\beta) / \sqrt{2} \rangle + \langle \beta\beta | I_{x1} | (\beta\alpha) / \sqrt{2} \rangle + \langle \beta\beta | I_{x2} | (\alpha\beta) / \sqrt{2} \rangle + \langle \beta\beta | I_{x2} | (\beta\alpha) / \sqrt{2} \rangle \right] \right|^2 \\
 &= \left| \gamma B_1 \left[(1/2)/\sqrt{2} \langle \beta\beta | \beta\beta \rangle + (1/2)/\sqrt{2} \langle \beta\beta | \alpha\alpha \rangle + (1/2)/\sqrt{2} \langle \beta\beta | \alpha\alpha \rangle + (1/2)/\sqrt{2} \langle \beta\beta | \beta\beta \rangle \right] \right|^2 \\
 &= \left| \gamma B_1 \left[(1/2)/\sqrt{2} + 0 + 0 + (1/2)/\sqrt{2} \right] \right|^2 \\
 &= \left| \gamma B_1 \left[1/\sqrt{2} \right] \right|^2 \\
 &= 1/2 (\gamma B_1)^2
 \end{aligned}$$

- All solutions

$$\rho_{\beta\beta \rightarrow (\alpha\beta + \beta\alpha)} \propto 1/2 (\gamma B_1)^2$$

$$\rho_{\beta\beta \rightarrow (\alpha\beta - \beta\alpha)} = 0$$

$$\rho_{\alpha\alpha \rightarrow (\alpha\beta + \beta\alpha)} \propto 1/2 (\gamma B_1)^2$$

$$\rho_{\alpha\alpha \rightarrow (\alpha\beta - \beta\alpha)} = 0$$

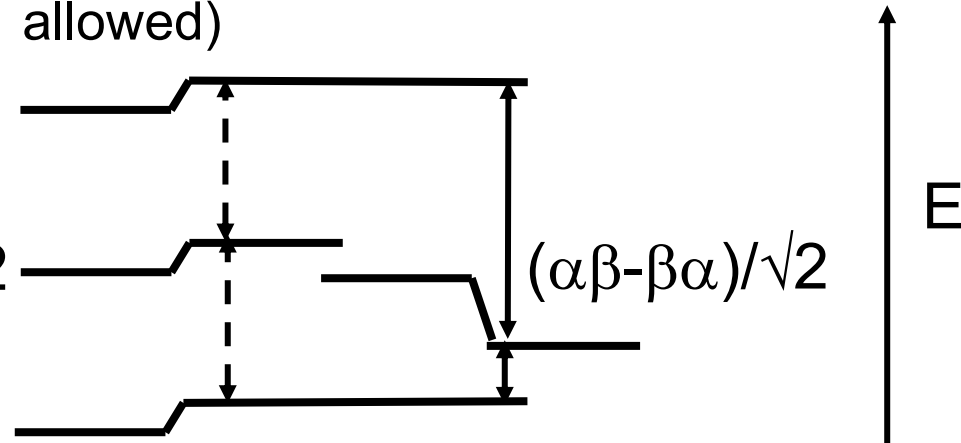
$\beta\beta$

$(\alpha\beta + \beta\alpha)/\sqrt{2}$

$\alpha\alpha$

Result

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



"Intermediate" behavior of 2nd order spectra

- AB systems are "intermediate" between AX and A₂
 - 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

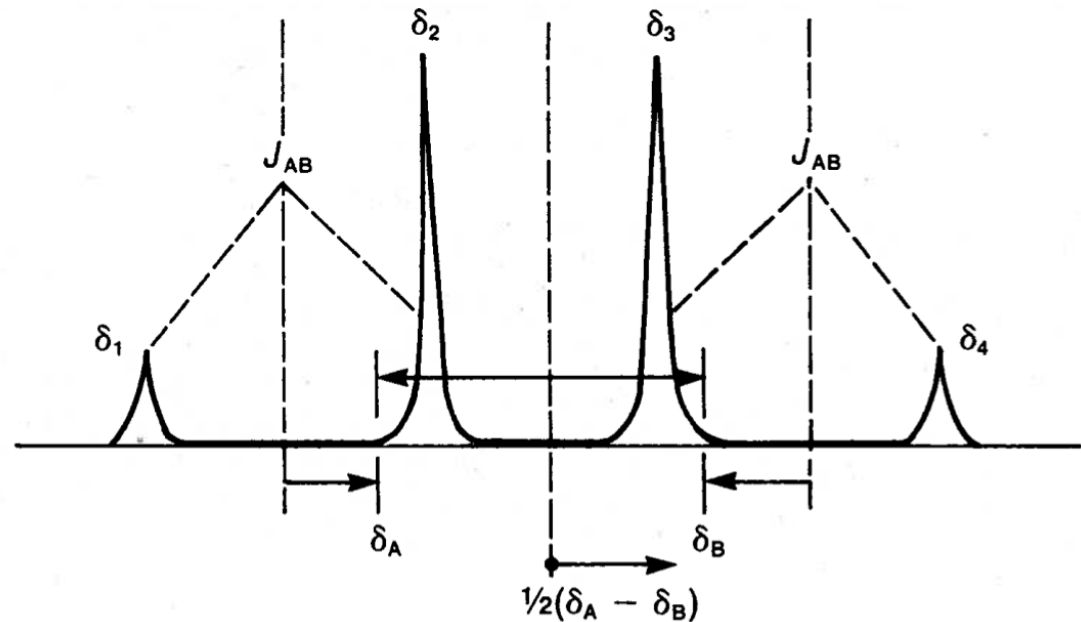
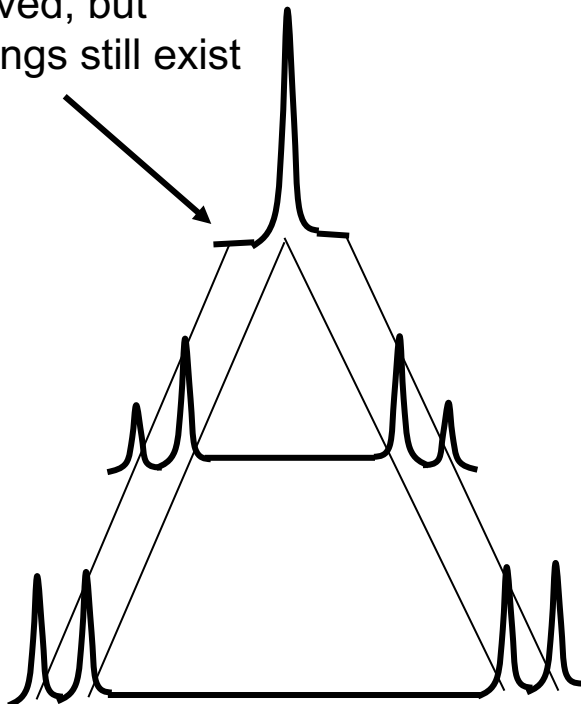
$$\delta_A - \delta_B = \sqrt{(\delta_1 - \delta_4)(\delta_2 - \delta_3)}$$

outer lines are not observed, but couplings still exist

H₂
O

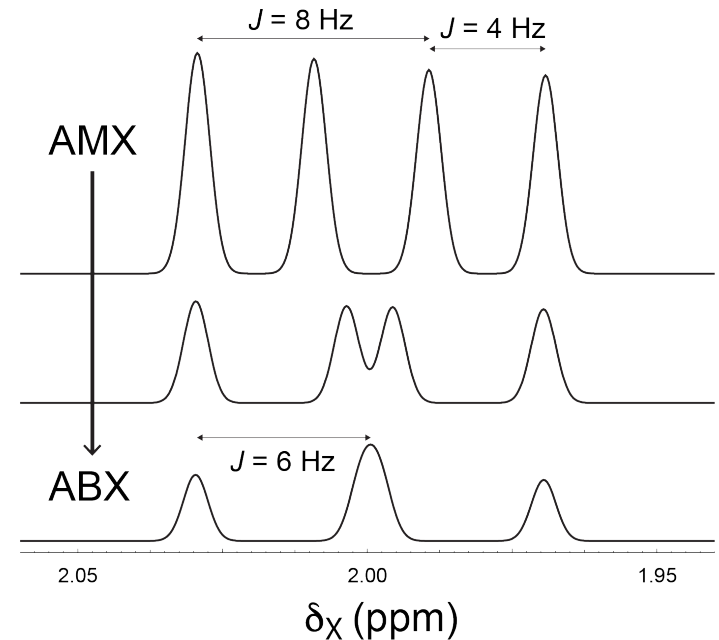
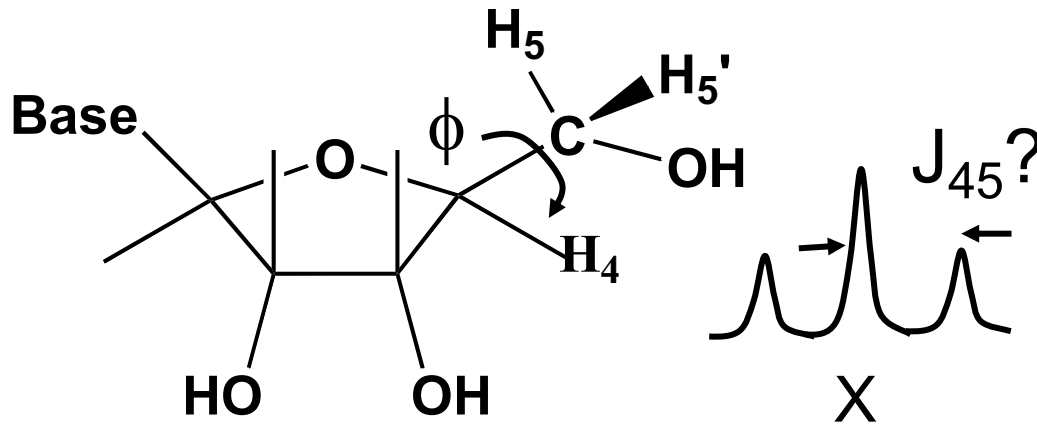
AB

HF



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
 - software: S.A. Smith, *J. Magn. Res.*, **166**, 75 (1994)
M.Veshtort, R.G.Griffin, *J Magn. Res.*, **178**, 248-282 (2006)