

BCMB/CHEM 8190

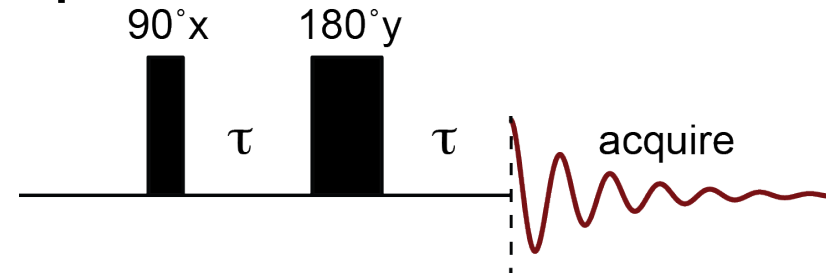
Spin Operators and QM Applications

Quantum Description of NMR Experiments

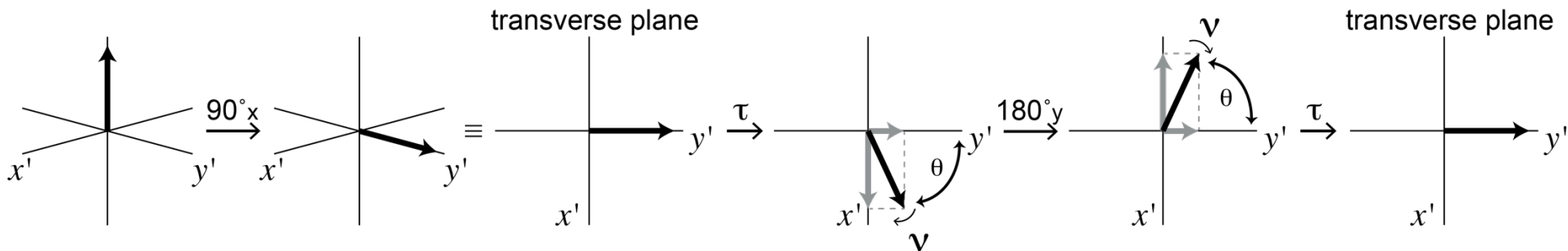
- Not all experiments can be described by the Bloch equations
- A quantum description is necessary for understanding many NMR experiments and designing new ones
- Many important building blocks of experiments (COSY- and INEPT-based magnetization transfers, multiple quantum states, etc.) require a quantum treatment
- Hamiltonians and Schrödinger's equation
- Density matrix (quantum mechanical methods for treating collections of spins)
- Liouville-VonNeuman equation (density operator time evolution)
- Product operators, transformation rules
- Examples

Some Pulse Sequences/Elements Have Classical (Bloch) Explanations

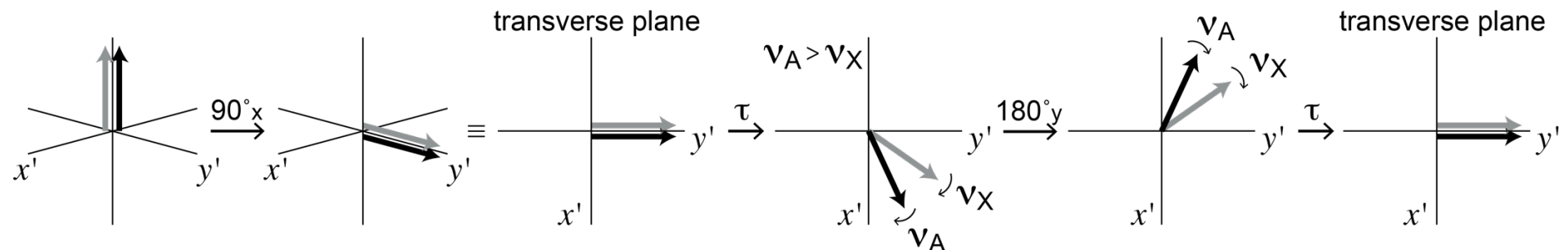
- We'll first examine an important pulse sequence element, the spin-echo element



- This element can be used to eliminate (refocus) the effects of magnetic field homogeneity or chemical shift evolution
- Here's a single spin example (chemical shift refocusing):



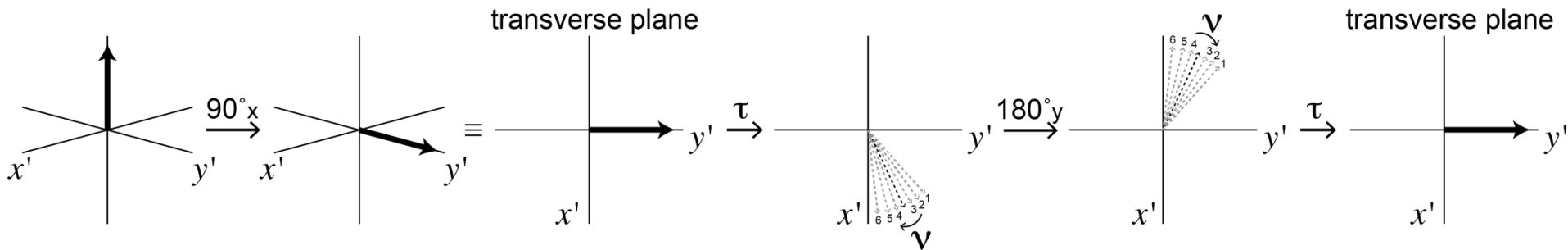
- Example with two independent spins (i.e. NOT coupled)



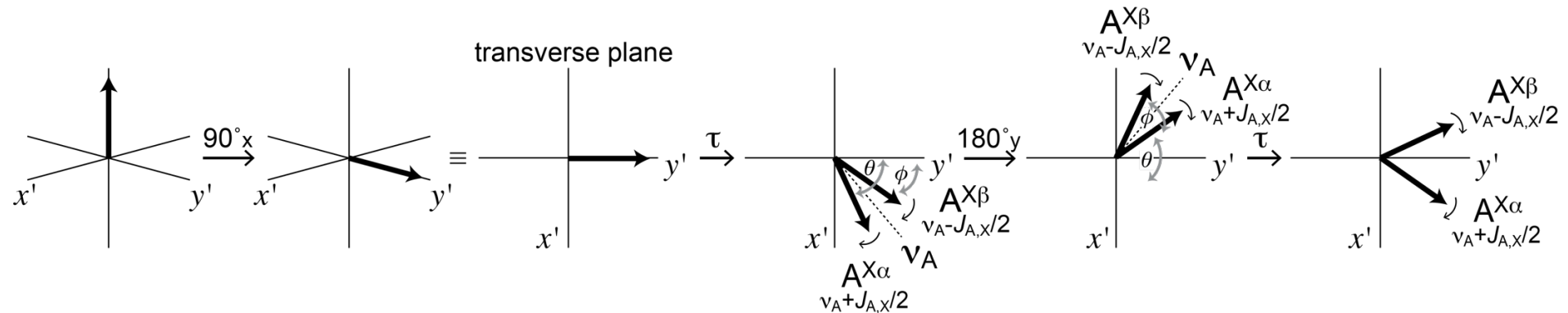
- Chemical shifts refocused (no net evolution)

Some Pulse Sequences/Elements Have Classical (Bloch) Explanations

- Magnetic field inhomogeneity refocusing example
 - can reduce linebroadening due to magnetic field inhomogeneity using this element
 - can use it also to measure T_2 (i.e. remove magnetic field inhomogeneity part)

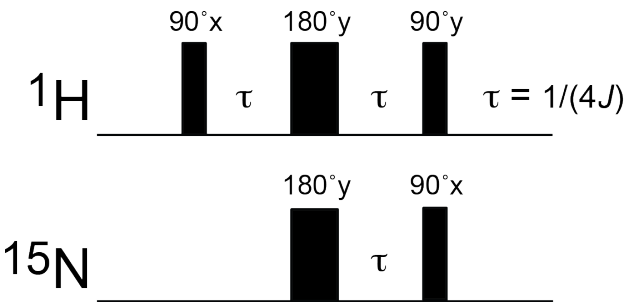


- Homonuclear coupling is not refocused by spin-echo
 - the 180° pulse reflects the vectors as expected
 - the 180° pulse ALSO acts on the other (coupled) spin, changing all α states to β , and β to α , so the vectors "change places" ("rule" based on quantum mechanics)



Some Sequences Need More Quantum Explanations

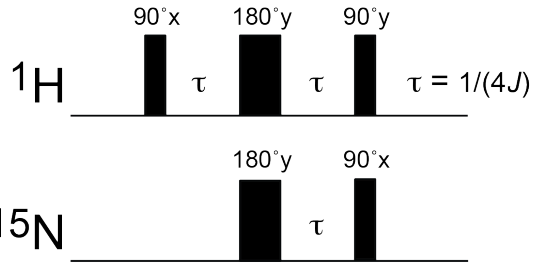
Mixing by Scalar Coupling of Directly Bonded Nuclei: the INEPT and HSQC Experiments



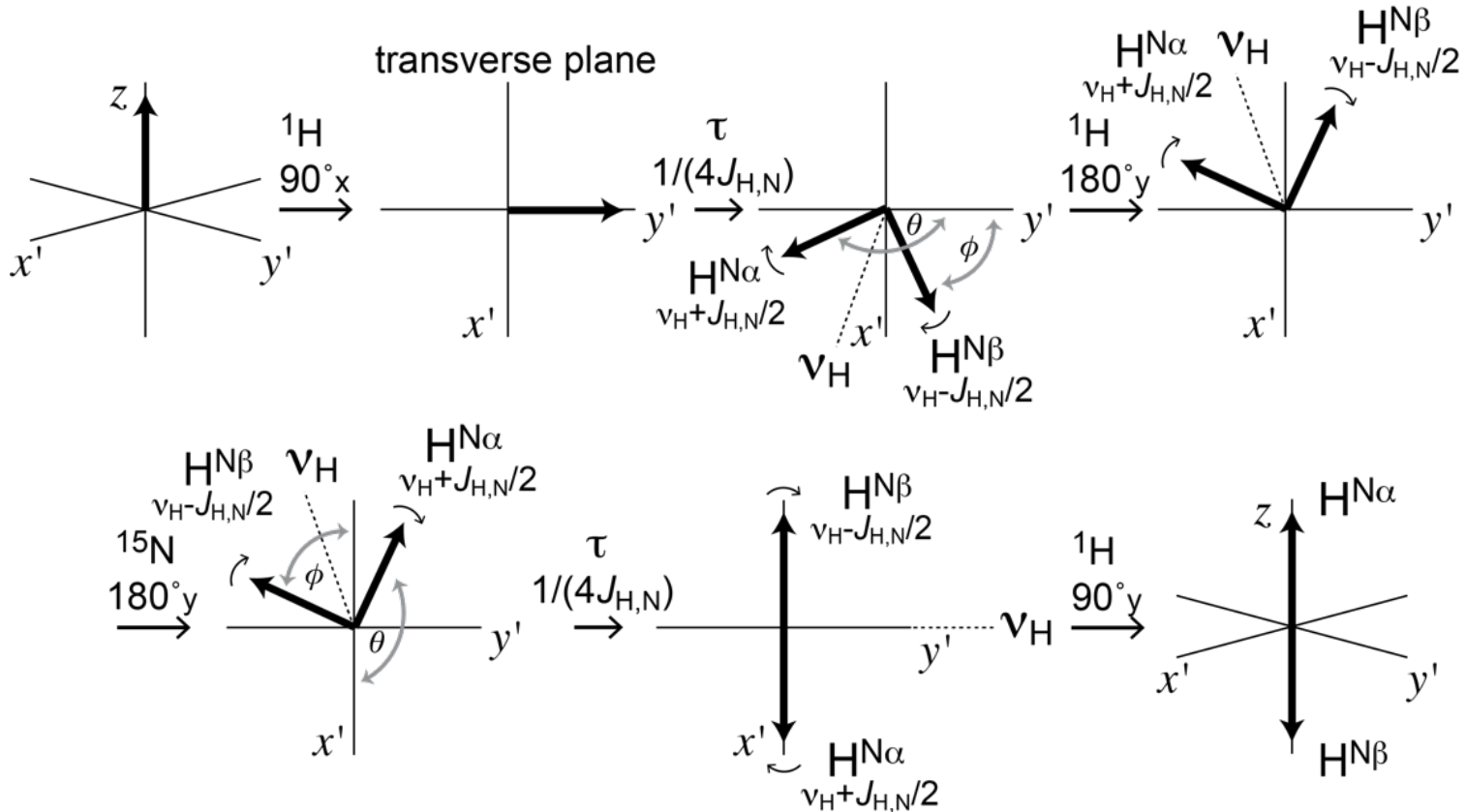
- INEPT: Insensitive Nuclei Enhanced by Polarization Transfer
- One of the most important pulse sequence elements for biomolecular NMR

- Purpose (of INEPT) is to improve the polarization (population difference between α and β states) of lower γ nuclei (^{13}C , ^{15}N) by transferring the polarization from a high γ nucleus (^1H)
- Result is improved sensitivity for low γ nuclei
- Sensitivity improved by $\sim \gamma^1\text{H}/\gamma^{15}\text{N}$

INEPT

 ^1H pulses don't excite ^{15}N frequencies ^{15}N pulses don't excite ^1H frequencies

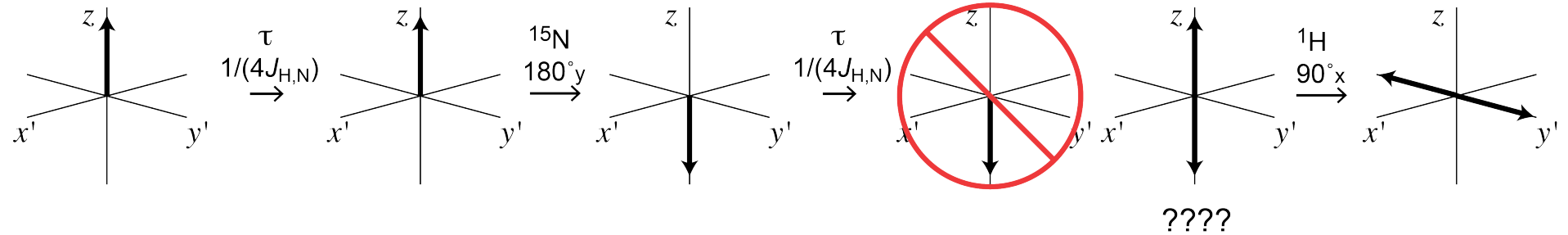
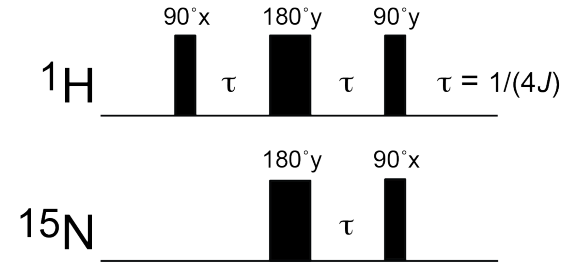
- ^1H magnetization readily understood
 - vectors move apart by $2\pi J_{\text{H,N}}\tau$ during τ ($\pi/2$ radians or 90° for $\tau = 1/(4J_{\text{H,N}})$)
 - the ^1H 180° pulse reflects the vectors as expected
 - the ^{15}N 180° pulse exchanges the vectors (converts all ^{15}N α states to β , and β to α)
 - vectors antiphase after second τ



INEPT

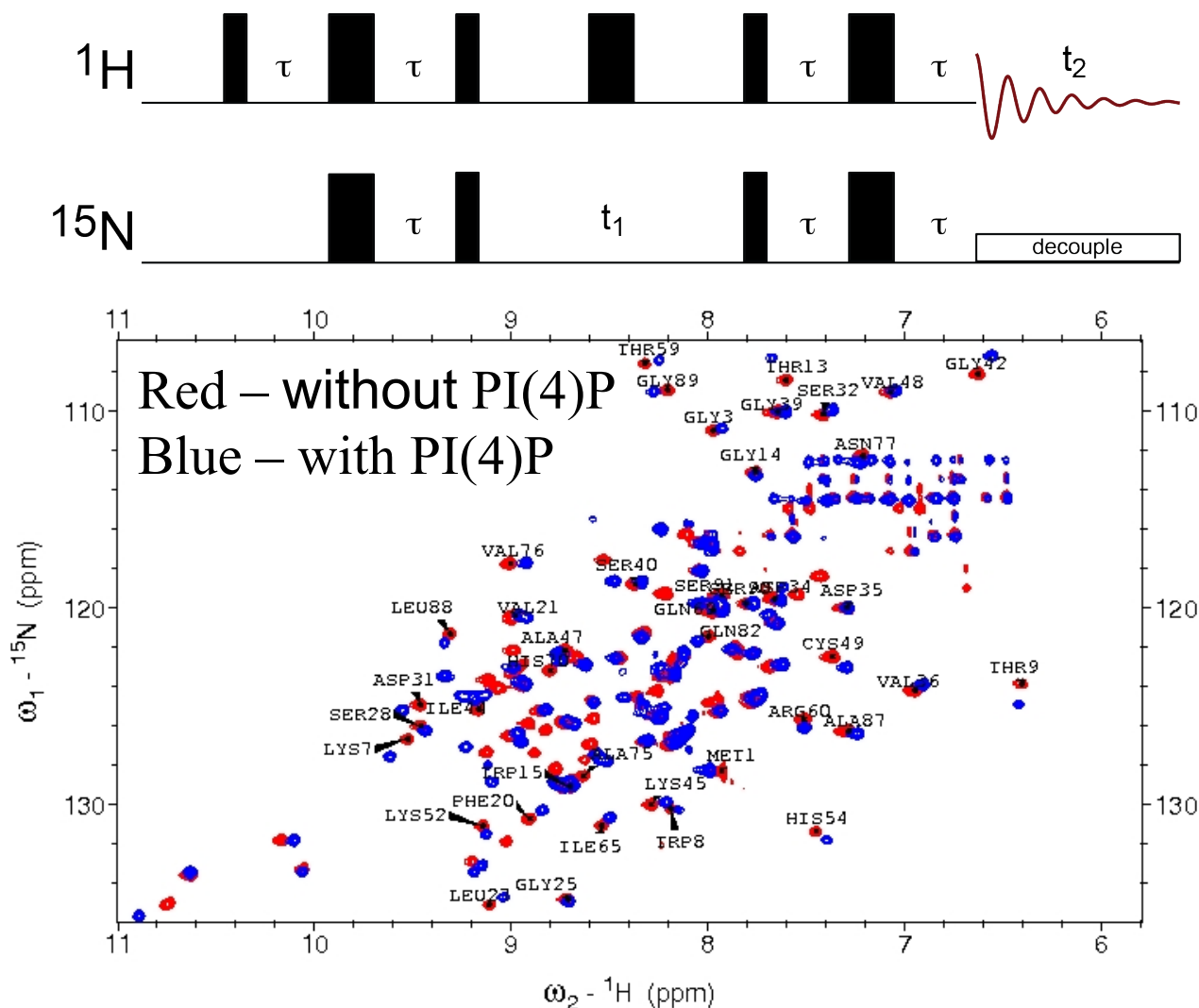
- ^{15}N magnetization not easily understood without quantum approach

- τ -180- τ : 180 moves $N^{H\alpha}$ and $N^{H\beta}$ to $\pm z$
- not clear how this is accomplished
- clearly vector diagrams alone can't give correct answer without more input



HSQC Spectrum of ^1H - ^{15}N Amides in a Protein

- Heteronuclear Single Quantum Coherence (based on INEPT)
- Workhorse experiment for biomolecular NMR



Phosphoinositide interactions with PH domain of FAPP1 at a bicelle surface

Quantum Mechanics Fundamentals (Spin Operations)

- To find the value of some observable (μ), quantum mechanically we calculate the expectation value
- Here, the expectation of the magnetic moment (μ) is the result of the operator ($\hat{\mu}$) operating on spin wavefunction (ψ) multiplied (on the left) by the complex conjugate of the wavefunction (ψ^*), integrated over all spin space

$$\langle \mu \rangle = \langle \psi | \hat{\mu} | \psi \rangle = \int \psi^* \hat{\mu} \psi d\tau \quad \hat{\mu} - \text{magnetic moment operator} \quad \psi - \text{spin wavefunction}$$

- For calculating spin systems we'll need *spin wavefunctions*

$$\psi = \alpha, \beta \text{ (single spins } 1/2), \alpha\alpha, \alpha\beta, \beta\alpha, \beta\beta \text{ (two spins } 1/2)$$

- for α and β , $m=+1/2$ and $m=-1/2$

- for two spins (weakly coupled, $\Delta v \gg J$), just take products ($\alpha\alpha$, $\alpha\beta$, etc.)

- All of these wavefunctions must be solutions to Schrödinger's equation

$$\hat{H}\psi = E\psi$$

- \hat{H} (*Hamiltonian* operator) operates on ψ to give back the energy (E) and ψ

- a discrete set of energies and a discrete set of associated wavefunctions

- The expectation value of the *Hamiltonian* operator is energy

$$\langle \psi | \hat{H} | \psi \rangle = E$$

Quantum Mechanics Fundamentals (Spin Operations)

- These wavefunctions must be *normalized*

$$\int \psi^* \psi \, dt = \langle \psi | \psi \rangle = 1$$

- $\psi^* \psi$, probability of finding our particle at some point in space
- so, sum of all probabilities (all space) should = 1

- The Hamiltonian is the magnetic moment operator interacting with the magnetic field

$$\hat{H}_z = -\hat{\mu} \cdot B_0$$

- dot product is projection on z axis

- Magnetic moments in terms of spin operators

$$\hat{\mu}_z = \gamma \hat{I}_z \quad \mu_z = \gamma I_z = m \gamma \hbar \quad \alpha, m = +1/2 \quad \beta, m = -1/2$$

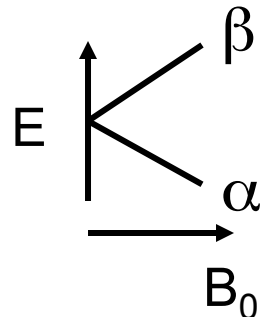
- Operations (remember normalization, $\langle \alpha | \alpha \rangle = 1$, $\langle \beta | \beta \rangle = 1$)

$$\hat{I}_z |\psi_m\rangle = m \hbar \psi_m \quad \hat{I}_z |\alpha\rangle = +1/2 \hbar \alpha \quad \hat{I}_z |\beta\rangle = -1/2 \hbar \beta$$

$$E_{zm} = \langle \psi_m | -\hat{\mu}_z \cdot B_0 | \psi_m \rangle = \langle \psi_m | -m \gamma \hbar B_0 | \psi_m \rangle = -m \gamma \hbar B_0 \langle \psi_m | \psi_m \rangle = -m \gamma \hbar B_0$$

$$E_{z\alpha} = \langle \alpha | -\hat{\mu}_z \cdot B_0 | \alpha \rangle = \langle \alpha | -1/2 \gamma \hbar B_0 | \alpha \rangle = -1/2 \gamma \hbar B_0 \langle \alpha | \alpha \rangle = -1/2 \gamma \hbar B_0$$

$$E_{z\beta} = \langle \beta | -\hat{\mu}_z \cdot B_0 | \beta \rangle = \langle \beta | -(-1/2) \gamma \hbar B_0 | \beta \rangle = 1/2 \gamma \hbar B_0 \langle \beta | \beta \rangle = 1/2 \gamma \hbar B_0$$



Hamiltonian Operator Containing Primary Observables for High Resolution NMR

- Hamiltonian for ensemble of spins

$$\hat{H}_z = \underbrace{-\gamma B_0 \sum_i (1 - \sigma_i) \hat{I}_{zi}}_{\text{chemical shift}} + \underbrace{\sum_{j>i} 2\pi J \hat{I}_i \cdot \hat{I}_j}_{\text{scalar coupling}} + \underbrace{\sum_{j>i} 2\pi \hat{I}_i \cdot D \cdot \hat{I}_j}_{\text{dipolar coupling}}$$

- written as frequency (rad/s), not energy, for convenience (i.e. \hbar missing)

- Zeeman (chemical shift) term (\hat{I}_z) includes shielding ($1-\sigma$)
- Scalar coupling term: expected product of moments ($\hat{I}_i \cdot \hat{I}_j$)
 - is complicated by the fact that $\mathbf{I}_i = \mathbf{I}_{ix} + \mathbf{I}_{iy} + \mathbf{I}_{iz}$, so $\mathbf{I}_i \cdot \mathbf{I}_j = \mathbf{I}_{ix} \cdot \mathbf{I}_{jx} + \mathbf{I}_{iy} \cdot \mathbf{I}_{jy} + \mathbf{I}_{iz} \cdot \mathbf{I}_{jz}$
 - for "first order" spectra ($\Delta\nu \gg J$), only z terms significant, so can simplify:

$$\sum_{j>i} 2\pi J \hat{I}_i \cdot \hat{I}_j \approx \sum_{j>i} 2\pi J \hat{I}_{iz} \cdot \hat{I}_{jz}$$

- this is an important simplification, because our spin functions (α , β , $\alpha\beta$, $\alpha\beta$, etc.) are only solutions to Schrodinger's equation when only I_z operators are present (not I_x , I_y)

- Dipolar coupling (through space interactions) term
 - important for solids NMR, relaxation, but not simple solution experiments (we'll return to this later)

Some other spin operators:

- Can't totally ignore I_x and I_y operators
 - necessary for describing "second order" spectra (strong coupling, $\Delta\nu \sim J$)
 - important for considering RF pulses (applied in x-y plane)
- The operations (rules) are:

$$\hat{I}_x|\alpha\rangle = 1/2\beta \quad \hat{I}_x|\beta\rangle = 1/2\alpha \quad \hat{I}_y|\alpha\rangle = 1/2i\beta \quad \hat{I}_y|\beta\rangle = -1/2i\alpha \quad \hat{I}_z|\alpha\rangle = 1/2\alpha \quad \hat{I}_z|\beta\rangle = -1/2\beta$$

$$\hat{I}_{y1}|\alpha\beta\rangle = 1/2i\beta\beta \quad \hat{I}_{y2}|\alpha\beta\rangle = -1/2i\alpha\alpha \quad \hat{I}_{y1}\hat{I}_{y2}|\alpha\beta\rangle = 1/4\beta\alpha \quad \hat{I}_{z1}\hat{I}_{z2}|\alpha\beta\rangle = -1/4i\alpha\alpha$$
- Keep in mind: the α and β spin functions are *not* eigenfunctions of Hamiltonians that include I_x and I_y operators (I_x and I_y change the wavefunctions)
- If any I_x and I_y operators are included in the Hamiltonian, these product functions ($\alpha\alpha$, $\beta\alpha$, $\alpha\beta$, $\beta\beta$) are no longer eigenfunctions of the Hamiltonian (not solutions to Schrödinger's equation)
- However these spin functions form a complete orthonormal set

$$\langle\psi_i\psi_j|\psi_m\psi_n\rangle = 1 \text{ when } i = m \text{ AND } j = n, \text{ otherwise } \langle\psi_i\psi_j|\psi_m\psi_n\rangle = 0$$
- Because of this, we can use linear combinations of the set to describe more complex functions and get good solutions

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

More Operators

- I^2 operator

$$\hat{I}^2 |\psi\rangle \equiv \hat{\mathbf{I}} \cdot \hat{\mathbf{I}} |\psi\rangle = I(I+1)\psi \quad \text{for spin } 1/2, \hat{I}^2 |\psi\rangle = 3/4 \psi$$

- I^2 can be written in terms of I_x , I_y and I_z

$$\hat{I}^2 = \hat{I}_x \hat{I}_x + \hat{I}_y \hat{I}_y + \hat{I}_z \hat{I}_z$$

- exercise: given this relationship, show that $\hat{I}^2 |\alpha\rangle = 3/4 \alpha$

$$\begin{aligned} \hat{I}^2 |\alpha\rangle &= \hat{I}_x \hat{I}_x |\alpha\rangle + \hat{I}_y \hat{I}_y |\alpha\rangle + \hat{I}_z \hat{I}_z |\alpha\rangle = \hat{I}_x 1/2 \beta + \hat{I}_y 1/2 i \beta + \hat{I}_z 1/2 \alpha = \hat{I}_x \hat{I}_x + \hat{I}_y \hat{I}_y + \hat{I}_z \hat{I}_z \\ &= 1/4 \alpha + 1/4 \alpha + 1/4 \alpha = 3/4 \alpha \end{aligned}$$

- Raising and lowering ("shift") operators

- for electronic wavefunctions, we found it convenient to write p orbitals (p_x , p_y , p_z) in terms of their angular momentum projections (p_1 , p_0 , p_{-1})
- similarly, here we write I_x and I_y in terms of the raising and lowering ("shift") operators I_+ and I_- (these change m by ± 1)

$$\hat{I}_x = (\hat{I}_+ + \hat{I}_-)/2 \quad \hat{I}_y = (\hat{I}_+ - \hat{I}_-)/2i$$

$$\hat{I}_+ = \hat{I}_x + i\hat{I}_y \quad \hat{I}_- = \hat{I}_x - i\hat{I}_y$$

- example:

$$\hat{I}_+ |\beta\rangle = \hat{I}_x |\beta\rangle + i\hat{I}_y |\beta\rangle = 1/2 \alpha + i (-i 1/2 \alpha) = 1/2 \alpha + 1/2 \alpha = \alpha$$

$$\hat{I}_+ |\alpha\rangle = 0 \quad \hat{I}_- |\alpha\rangle = \beta \quad \hat{I}_+ |\beta\rangle = \alpha \quad \hat{I}_- |\beta\rangle = 0$$

Using Operators: Energy Levels for an AX Spin System in Solution

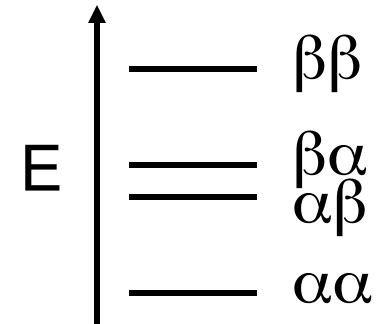
- Spin systems are designated by letters of the alphabet according to the frequency difference between the nuclei
 - for 2 spins, AX designates a "first order" spin system
 - for first order systems, the frequency difference between the nuclei is large (hence letters that are far apart in the alphabet) compared to J ($\Delta\nu \gg J$)

- Hamiltonian

$$\hat{H}_z = -\gamma B_0 \sum_i (1 - \sigma_i) \hat{I}_{zi} + \sum_{j>i} 2\pi J \hat{I}_i \cdot \hat{I}_j$$

- recall $\nu_i = \gamma B_0 (1 - \sigma_i) / (2\pi)$, rewrite in terms of frequencies

$$\hat{H} = -h\nu_A \hat{I}_{Az} - h\nu_X \hat{I}_{Xz} + hJ_{AX} \hat{I}_{Az} \hat{I}_{Xz}$$



- Find the expectation value (recall $\hat{I}_z |\alpha\rangle = 1/2 \alpha$ and $\hat{I}_z |\beta\rangle = -1/2 \beta$)

- example: $\alpha\alpha$

$$\begin{aligned} \langle \alpha\alpha | \hat{H} | \alpha\alpha \rangle &= \langle \alpha\alpha | -h\nu_A \hat{I}_{Az} | \alpha\alpha \rangle - \langle \alpha\alpha | h\nu_X \hat{I}_{Xz} | \alpha\alpha \rangle + \langle \alpha\alpha | hJ_{AX} \hat{I}_{Az} \hat{I}_{Xz} | \alpha\alpha \rangle \\ &= \langle \alpha\alpha | -h\nu_A 1/2 | \alpha\alpha \rangle - \langle \alpha\alpha | h\nu_X 1/2 | \alpha\alpha \rangle + \langle \alpha\alpha | hJ_{AX} 1/4 | \alpha\alpha \rangle \\ &= -h\nu_A 1/2 \langle \alpha\alpha | \alpha\alpha \rangle - h\nu_X 1/2 \langle \alpha\alpha | \alpha\alpha \rangle + hJ_{AX} 1/4 \langle \alpha\alpha | \alpha\alpha \rangle \\ &= -h\nu_A 1/2 - h\nu_X 1/2 + hJ_{AX} 1/4 \end{aligned}$$

One Quantum Transitions:

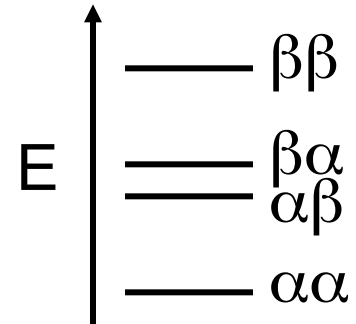
- Here are the energies for the four energy levels

$$\langle \alpha\alpha | \hat{H} | \alpha\alpha \rangle = -h\nu_A/2 - h\nu_X/2 + hJ_{AX}/4 = -h(\nu_A + \nu_X)/2 + 1/4 hJ_{AX}$$

$$\langle \alpha\beta | \hat{H} | \alpha\beta \rangle = -h\nu_A/2 + h\nu_X/2 - hJ_{AX}/4 = -h(\nu_A - \nu_X)/2 - 1/4 hJ_{AX}$$

$$\langle \beta\alpha | \hat{H} | \beta\alpha \rangle = +h\nu_A/2 - h\nu_X/2 - hJ_{AX}/4 = h(\nu_A - \nu_X)/2 - 1/4 hJ_{AX}$$

$$\langle \beta\beta | \hat{H} | \beta\beta \rangle = +h\nu_A/2 + h\nu_X/2 + hJ_{AX}/4 = h(\nu_A + \nu_X)/2 + 1/4 hJ_{AX}$$



- Now calculate the energies of the transitions

$$\begin{aligned} \Delta E_{\alpha\alpha \rightarrow \beta\alpha} &= E_{\beta\alpha} - E_{\alpha\alpha} = h(\nu_A - \nu_X)/2 - 1/4 hJ_{AX} - [-h(\nu_A + \nu_X)/2 + 1/4 hJ_{AX}] \\ &= h\nu_A/2 - h\nu_X/2 + h\nu_A/2 + h\nu_X/2 - 1/4 hJ_{AX} - 1/4 hJ_{AX} \\ &= h\nu_A - hJ_{AX}/2 \end{aligned}$$

$$1. \Delta E_{\alpha\alpha \rightarrow \beta\alpha} = h(\nu_A - J_{AX}/2) \quad 3. \Delta E_{\alpha\alpha \rightarrow \alpha\beta} = h(\nu_X - J_{AX}/2)$$

$$2. \Delta E_{\alpha\beta \rightarrow \beta\beta} = h(\nu_A + J_{AX}/2) \quad 4. \Delta E_{\beta\alpha \rightarrow \beta\beta} = h(\nu_X + J_{AX}/2)$$

