

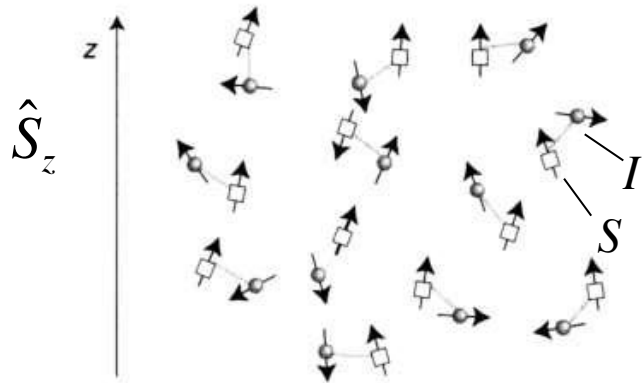
# Lecture #3

## Nuclear Spin Hamiltonian

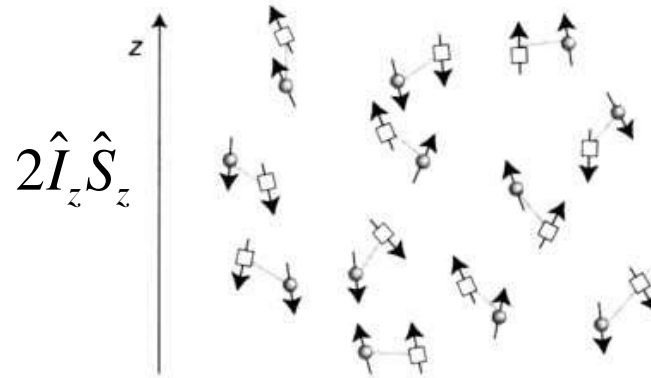
- Topics
  - Liouville-von Neuman equation
  - Time-averaged versus instantaneous spin Hamiltonian
  - Chemical shift and J, dipolar, and quadrupolar coupling
- Reading assignments
  - van de Ven: Chapters 2.1-2.2
  - Levitt, Chapters 7 (optional)

# Coherences

- Nuclear spins can be thought of as weak magnetic dipoles, each with a well defined direction of polarization.
- Summing the polarization across many spins can result in net phase coherences.



Net tendency for S spins to be  $+z$   
 No net tendency for I spins in any direction



No net tendency for I or S spins to be  $\pm z$   
 If I or S is  $\pm z$ , increased probability paired spin is  $\pm z$

# The Spin Density Operator

- Spin density operator,  $\hat{\sigma}(t)$ , is the mathematical quantity that describes a statistical mixture of spins and the associated phase coherences that can occur, as encountered in a typical NMR or MRI experiment.
- $\hat{\sigma}(t)$  is usually expressed as a linear combination of basis operators, e.g.  $\{\frac{1}{2}\hat{E}, \hat{I}_x, \hat{S}_x, \hat{I}_y, \hat{S}_y, \dots, 2\hat{I}_z\hat{S}_z\}$  (the 16 two-spin product operators)

- Coherences (signals) observable with an Rf coil:

$$M_x = \gamma\hbar \text{Tr}\{\hat{\sigma}\hat{I}_x\} = \gamma\hbar \overline{\langle \hat{I}_x \rangle} \quad M_y = \gamma\hbar \text{Tr}\{\hat{\sigma}\hat{I}_y\} = \gamma\hbar \overline{\langle \hat{I}_y \rangle}$$

- Some coherences not directly observable with an Rf coil:

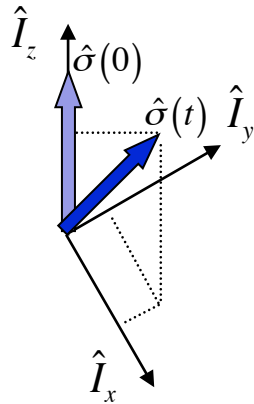
$$M_z = \gamma\hbar \overline{\langle \hat{I}_z \rangle} \quad C_{xz} = \gamma\hbar \overline{\langle 2\hat{I}_x\hat{S}_z \rangle} \quad C_{zz} = \gamma\hbar \overline{\langle 2\hat{I}_z\hat{S}_z \rangle}$$

“antiphase x”  “longitudinal two-spin order”

- The goal is to describe how these quantities evolve in time.

# Liouville-von Neumann Equation

- Time evolution of  $\hat{\sigma}(t)$ :



$$\frac{\partial}{\partial t} \hat{\sigma} = -i\hat{H}\hat{\sigma}$$

$\hat{H}$  is the Hamiltonian operator and corresponds to the energy of the system ( $\mathcal{E}/\hbar$ ).

- $\hat{H}$  can often be expressed as sum of a large static component plus a small time-varying perturbation:  $\hat{H} = \hat{H}_0 + \hat{H}_1(t)$ , leading to...

$$\frac{\partial}{\partial t} \hat{\sigma} = \underbrace{-i\hat{H}_0 \hat{\sigma}}_{\text{Rotations}} - \underbrace{\hat{\Gamma}(\hat{\sigma} - \hat{\sigma}_B)}_{\text{Relaxation}} \quad \text{(Compare with Bloch's equations)}$$

Relaxation superoperator (a function of  $\hat{H}_1$ )

- The key, yet again, is finding the Hamiltonian!

# Spin-Lattice Disconnect

- Complete QM description of a molecule involves lots of terms in the Hamiltonian (nuclear spin, molecular motion, electron-nucleus interactions, etc).

$$\hat{H} = \underset{\text{lattice}}{\hat{H}_l} + \underset{\text{spin}}{\hat{H}_s} + \underset{\text{interaction term}}{\hat{H}_i}$$

- Previously, we assumed a negligible interaction between the nuclear spins and the lattice:

$$\hat{H} \approx \hat{H}_l + \hat{H}_s \quad \text{and just solved} \quad \frac{\partial}{\partial t} \hat{\sigma} = -i\hat{H}_s \hat{\sigma}$$

- Now we need to take a closer look at the interaction term, which includes effects such as spin operator coefficients that depend on molecular orientation, etc.

# The Nuclear Spin Hamiltonian

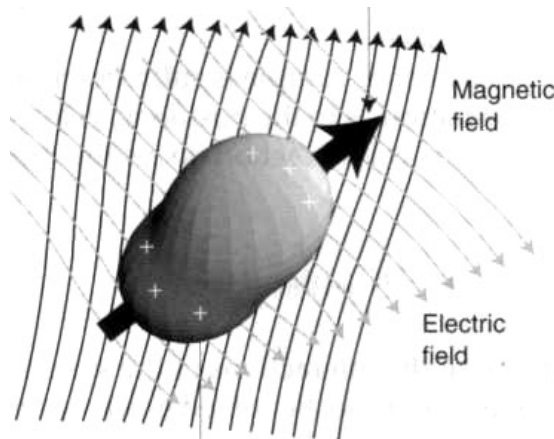
- $\hat{H}$  is the sum of different terms representing different physical interactions.  
$$\hat{H} = \hat{H}_1 + \hat{H}_2 + \hat{H}_3 + \dots$$

Examples:

- 1) interaction of spin with  $B_0$
- 2) interactions with dipole fields of other nuclei
- 3) nuclear-electron couplings

- In general, we can think of an atomic nucleus as a lumpy magnet with a (possibly non-uniform) positive electric charge
- The spin Hamiltonian contains terms which describe the orientation dependence of the nuclear energy

$$\hat{H} = \hat{H}^{elec} + \hat{H}^{mag}$$



The nuclear magnetic moment interacts with magnetic fields

The nuclear electric charge interacts with electric fields

# Electromagnetic Interactions

- Magnetic interactions

$$\hat{H}^{mag} = -\vec{\mu} \cdot \vec{B} = -\gamma \hbar \vec{I} \cdot \vec{B}$$

↙ magnetic moment
↖ local magnetic field

- Electric interactions

Nuclear electric charge distributions can be expressed as a sum of multipole components.

monopole
dipole
quadrupole

$$C(\vec{r}) = C^{(0)}(\vec{r}) + C^{(1)}(\vec{r}) + C^{(2)}(\vec{r}) + \dots$$

Symmetry properties:  $C^{(n)}=0$  for  $n>2I$  and odd interaction terms disappear

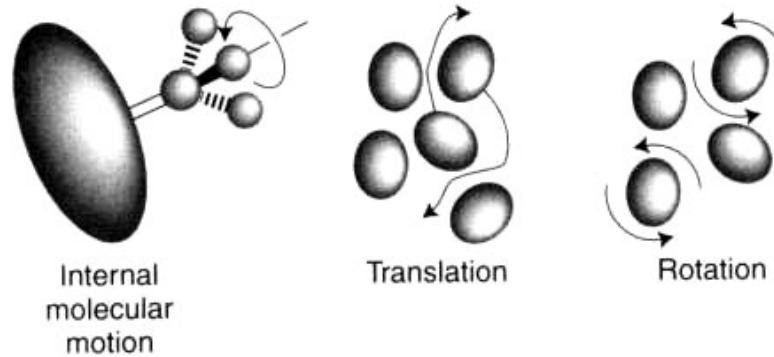
→  $\hat{H}^{elec} = 0$  (for spin  $I = 1/2$ )

→  $\hat{H}^{elec} \neq 0$  (for spin  $I > 1/2$ )

Hence, for spin- $1/2$  nuclei there are no electrical energy terms that depend on orientation or internal nuclear structure, and they behave exactly like point charges! Nuclei with spin  $> 1/2$  have electrical quadrupolar moments.

# Motional Averaging

- Molecular motion



- Previously, we used averaging to simplify the Hamiltonian

Molecular orientation depends on time and Hamiltonian terms can be written as  $\hat{H}_{\text{int}}^0(\Theta(t))$ . These terms were replaced by their time averages:

$$\underbrace{\overline{\hat{H}}_{\text{int}}^0}_{\text{Secular Hamiltonian}} = \frac{1}{\tau} \int_0^{\tau} \hat{H}_{\text{int}}^0(\Theta(t)) dt \xrightarrow{\text{ergodicity}} \overline{\hat{H}}_{\text{int}}^0 = \int \hat{H}_{\text{int}}^0 p(\Theta) d\Theta$$

Isotropic materials:  $\overline{\hat{H}}_{\text{int}}^{\text{isotropic}} = \frac{1}{N} \int \hat{H}_{\text{int}}^0(\Theta) d\Theta$

$p(\Theta)$  = probability density for molecule having orientation  $\Theta$

normalization

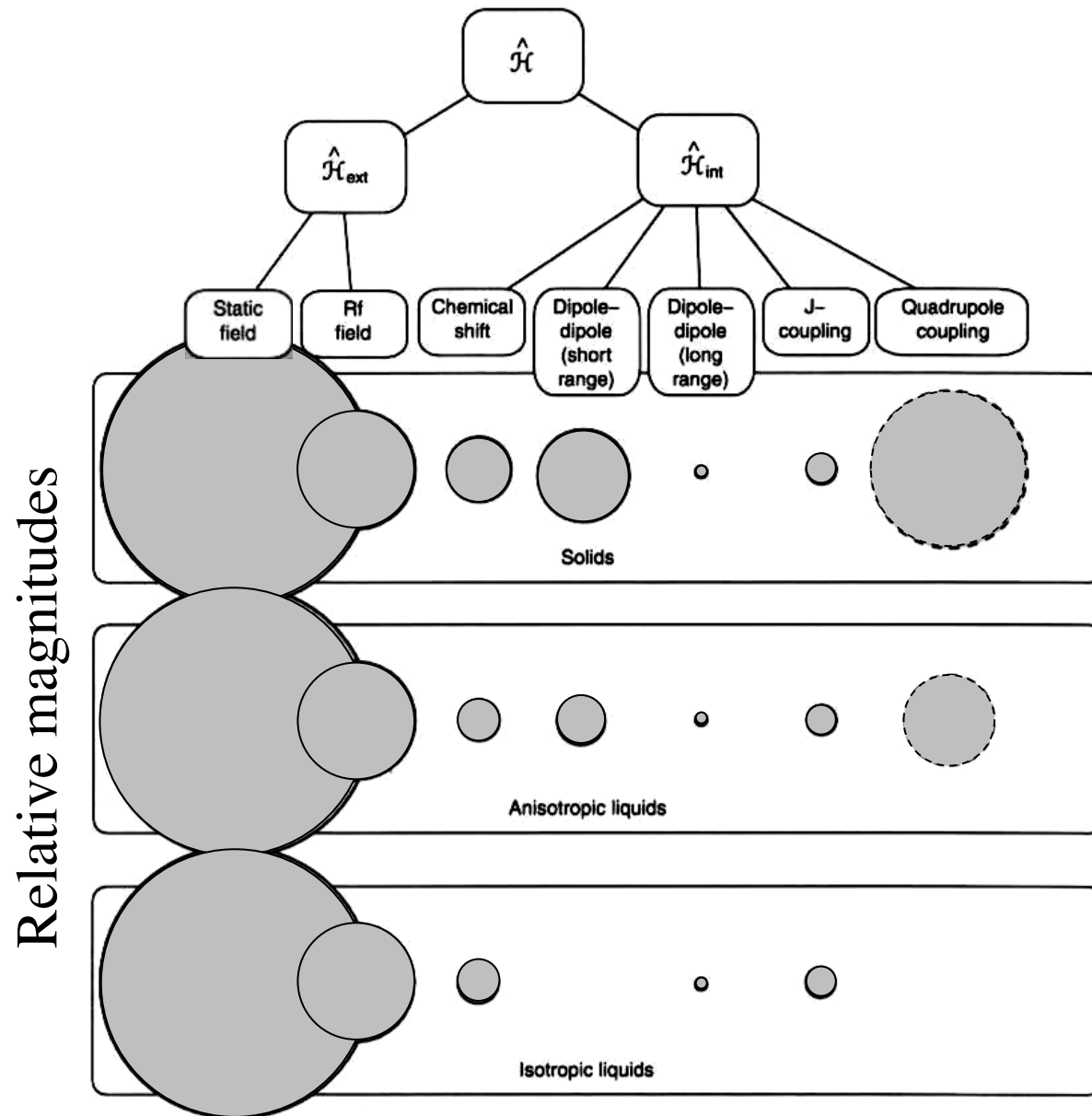
- We no longer want to make this approximation. Instead, the time variations will be analyzed as perturbations.

What does "secular" mean?

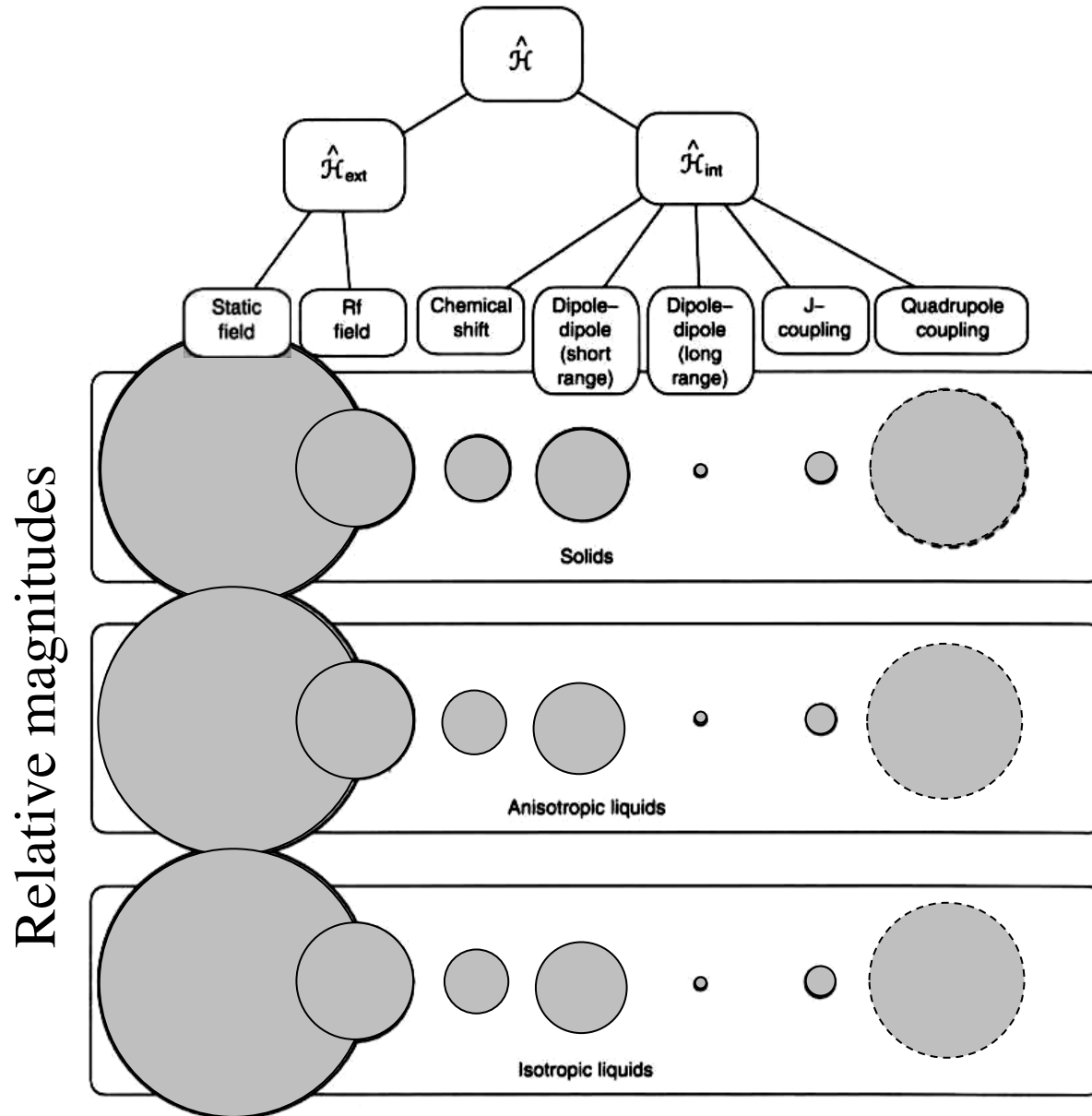




# Time-averaged Spin Hamiltonian



# Instantaneous Spin Hamiltonian



# Simplifications

- In general, the nuclear spin Hamiltonian is quite complicated.
- We'll regularly make use of two simplifications.
  1. For terms in the Hamiltonian that are periodic, we use a change of basis.

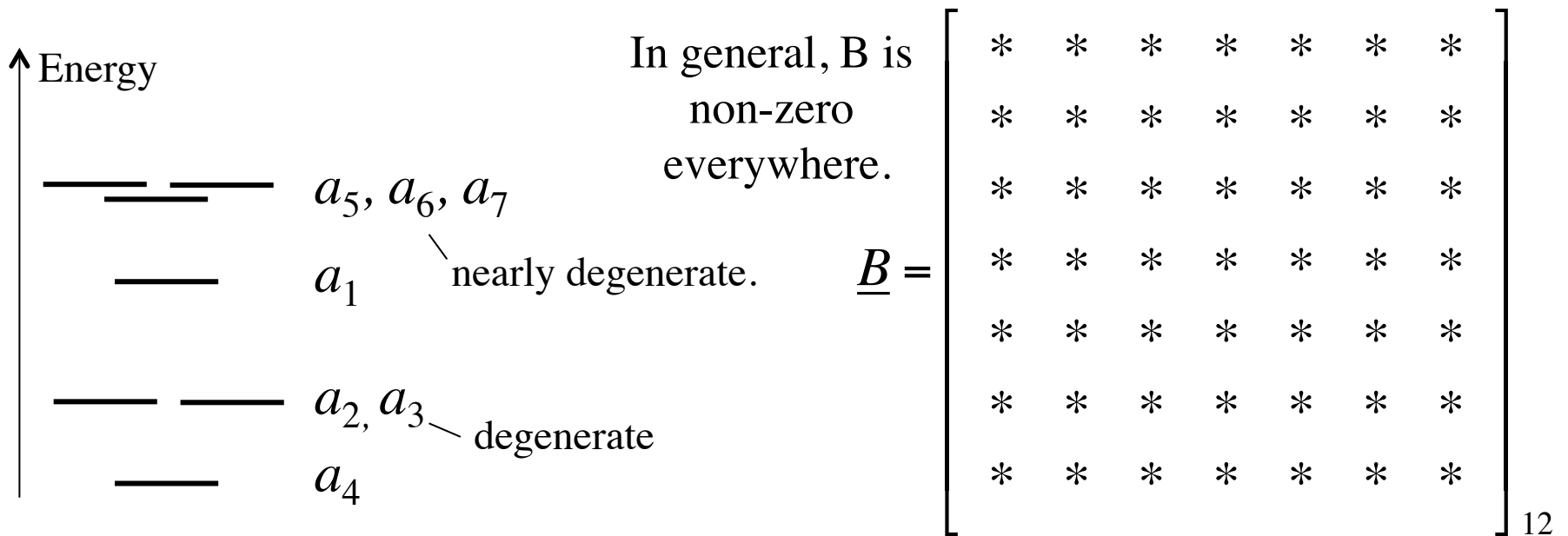
$$\underbrace{\hat{H}'}_{\text{rotating frame}} = e^{-i\omega t \hat{I}_z} \underbrace{\hat{H}}_{\text{laboratory frame}} = e^{-i\omega t \hat{I}_z} \hat{H} e^{i\omega t \hat{I}_z}$$

$$\hat{H}(t) = -\omega_0 \hat{I}_z - \omega_1 (\hat{I}_x \cos \omega t - \hat{I}_y \sin \omega t) \quad \longrightarrow \quad \hat{H}_{eff} = -(\omega_0 - \omega) \hat{I}_z - \omega_1 \hat{I}_x$$

2. The secular approximation

# The Secular Approximation

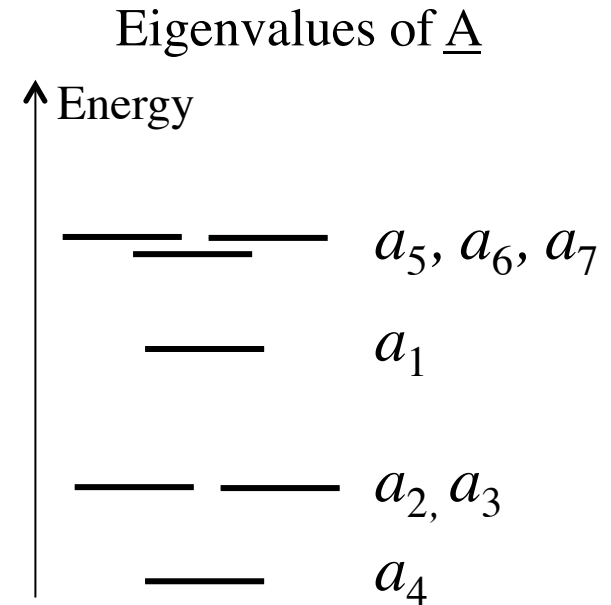
- The large  $B_0$  field dominates some of the internal spin interactions.
- Consider the general case of  $\hat{H} = \hat{A} + \hat{B}$   
 “large”      “small”
- Choosing the eigenkets,  $\hat{A}|i\rangle = a_i|i\rangle$ , as an orthonormal basis set, then  $\underline{A} = \text{diag}(a_1, a_2, \dots, a_n)$ .
- Example: let the eigenvalues of  $\underline{A}$  have the following pattern:



# The Secular Approximation

- The secular approximation of  $\underline{B}$  is:

$$\underline{B}^0 = \begin{bmatrix} * & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & * & * & 0 & 0 & 0 & 0 \\ 0 & * & * & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & * & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & * & * & * \\ 0 & 0 & 0 & 0 & * & * & * \\ 0 & 0 & 0 & 0 & * & * & * \end{bmatrix}$$



- Mathematically  $\underline{B}^0 = \sum_n b_{nn} |n\rangle\langle n| + \sum'_{m \neq n} b_{mn} |m\rangle\langle n|$

where the ' indicates summation only over terms which connect degenerate or nearly degenerate states of  $\underline{A}$ .

- This is equivalent to omitting terms for which  $|b_{mn}| \ll |a_m - a_n|$ .
- The secular approximation for the Hamiltonian is:  $\hat{H} \approx \hat{A} + \hat{B}^0$ .

# Secular Approximation Example

- Consider a spin in a large field  $B_0$  to which we add an  $x$  gradient  $G_x$ .
- We actually can't create the field  $G_x x \vec{z}$  alone (see Laplace's Eqn)
- We really have:  $\vec{B} = B_0 \vec{z} + G_x x \vec{z} + \Delta B_x(x, y, z) \vec{x} + \Delta B_y(x, y, z) \vec{y}$

In MRI, these are often called "Maxwell" or "concomitant gradient" terms.

$$\text{Hence: } \hat{H} = -\gamma \vec{B} \cdot \vec{I} = -\gamma B_0 \hat{I}_z - \gamma G_x x \hat{I}_z - \gamma \Delta B_x \hat{I}_x - \gamma \Delta B_y \hat{I}_y = \hat{A} + \hat{B}$$

$$\text{where } \hat{A} \Rightarrow \underline{A} = \frac{1}{2} \begin{bmatrix} \gamma B_0 & 0 \\ 0 & -\gamma B_0 \end{bmatrix} \text{ and } \hat{B} \Rightarrow \underline{B} = \frac{1}{2} \begin{bmatrix} \gamma G_x x & \gamma(\Delta B_x + i\Delta B_y) \\ \gamma(\Delta B_x - i\Delta B_y) & -\gamma G_x x \end{bmatrix}$$

- However,  $B_0 \gg G_x x, \Delta B_x, \Delta B_y \Rightarrow |a_1 - a_2| = \gamma B_0 \gg \gamma |\Delta B_x \pm i\Delta B_y|$

$$\text{hence } \underline{B}^0 = \frac{1}{2} \begin{bmatrix} \gamma G_x x & 0 \\ 0 & -\gamma G_x x \end{bmatrix}$$

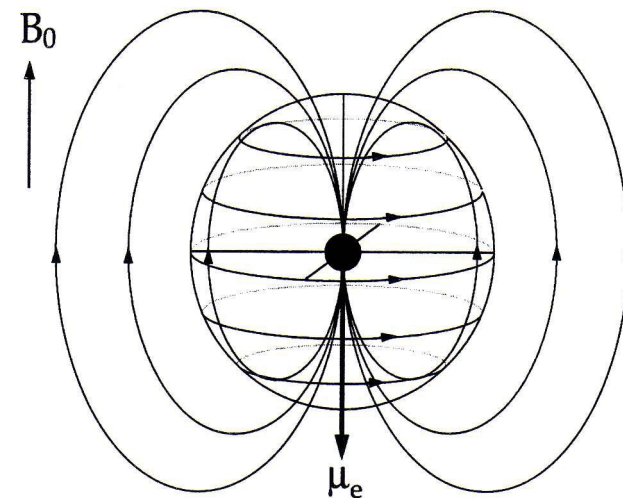
- The secular approximation is:  $\hat{H} = -\gamma \vec{B} \cdot \vec{I} \approx \hat{A} + \hat{B}^0 = -\gamma (B_0 + \gamma G_x x) \hat{I}_z$

i.e. we can safely ignore the "Maxwell" terms as is routinely done in MRI (with just a few exceptions, particularly at low field)

# $B_0$ -Electron Interactions

When a material is placed in a magnetic field it is magnetized to some degree and this modifies the field...

**Shielding:** Electrons in an atom circulate about  $B_0$ , generating a magnetic moment opposing the applied magnetic field. →



- Global effects: magnetic susceptibility

$$B_0^s = (1 - \chi)B_0$$

field inside sample
bulk magnetic susceptibility
applied field

Hereafter we'll use " $B_0$ " to refer to the internal field.

- Local effect: Chemical Shift

Different atoms experience different electron cloud densities.



$$B = B_0(1 - \sigma)$$

shielding constant  
 (Don't confuse with the spin density operator!)

# The Zeeman Hamiltonian

- The interaction energy between the magnetic field,  $\vec{B}$ , and the magnetic moment,  $\vec{\mu} = \gamma\vec{I}$ , is given by the Zeeman Hamiltonian.

Classical:  $E = -\gamma\vec{B} \cdot \vec{I}$   $\rightarrow$  QM:  $\hat{H}_{zeeman} = -\gamma\vec{B} \cdot \hat{I}$

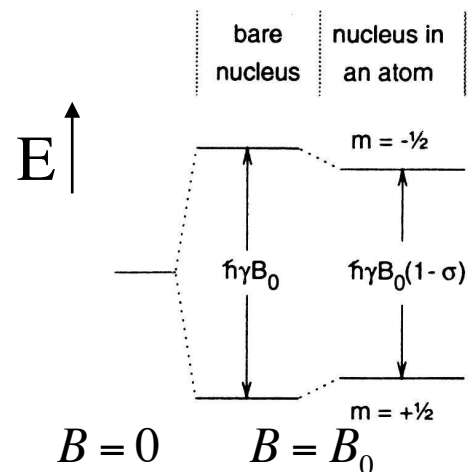
- The formal correction for chemical shielding is:

$$\hat{H}_{zeeman} = -\gamma\hat{I}(1 - \underline{\sigma})\vec{B} \quad \text{where} \quad \underline{\sigma} = 3 \times 3 \text{ shielding tensor}$$

- In vivo*, rapid molecular tumbling averages out the non-isotropic components.  $\sigma = \sigma_{iso} = \text{Tr}(\underline{\sigma}/3)$

- Hence for  $\vec{B} = [0, 0, B_0]$ :

$$\hat{H}_{Zeeman} = -\gamma(1 - \sigma)B_0\hat{I}_z$$





A little foreshadowing...

# Chemical Shielding Tensor

- Electron shielding is in general anisotropic, i.e. the degree of shielding depends on the molecular orientation.
- The shielding tensor can be written as the sum of three terms:

$$\underline{\sigma} = \begin{bmatrix} \sigma_{xx} & \sigma_{xy} & \sigma_{xz} \\ \sigma_{yx} & \sigma_{yy} & \sigma_{yz} \\ \sigma_{zx} & \sigma_{zy} & \sigma_{zz} \end{bmatrix} = \sigma_{iso} \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix} + \underline{\sigma}^{(1)} + \underline{\sigma}^{(2)}$$

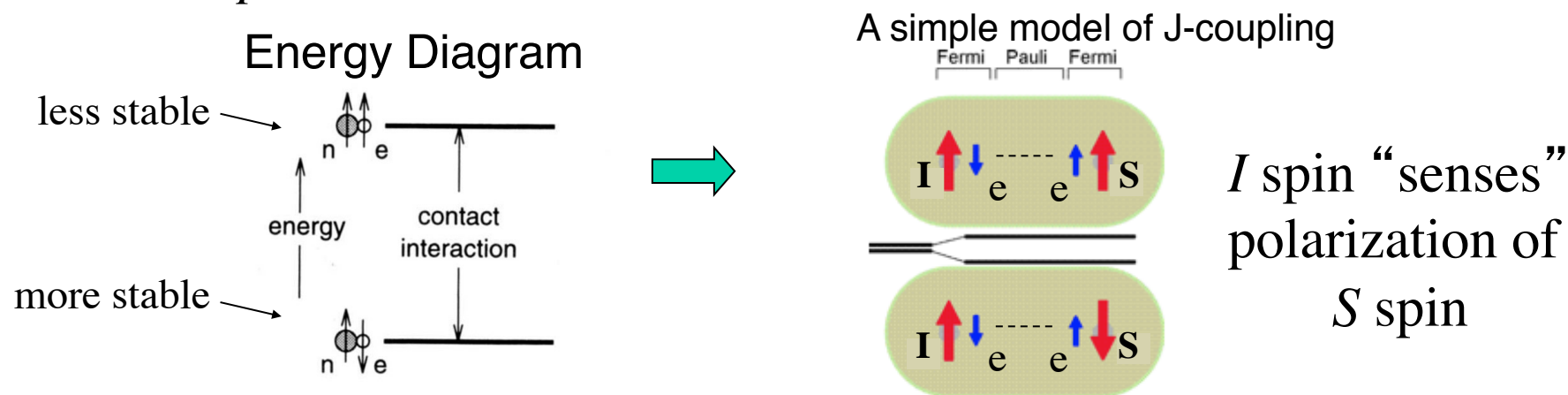
$= \frac{1}{3}(\sigma_{xx} + \sigma_{yy} + \sigma_{zz})$

See Kowalewski, pp 105-6 for details.  
 antisymmetric      symmetric and traceless

- Both  $\underline{\sigma}^{(1)}$  and  $\underline{\sigma}^{(2)}$  are time-varying due to molecular tumbling.
- $\underline{\sigma}^{(2)}$  gives rise to a relaxation mechanism called chemical shift anisotropy (CSA). (to be discussed later in the course)
- $\underline{\sigma}^{(1)}$  causes only 2<sup>nd</sup> order effects and is typically ignored.

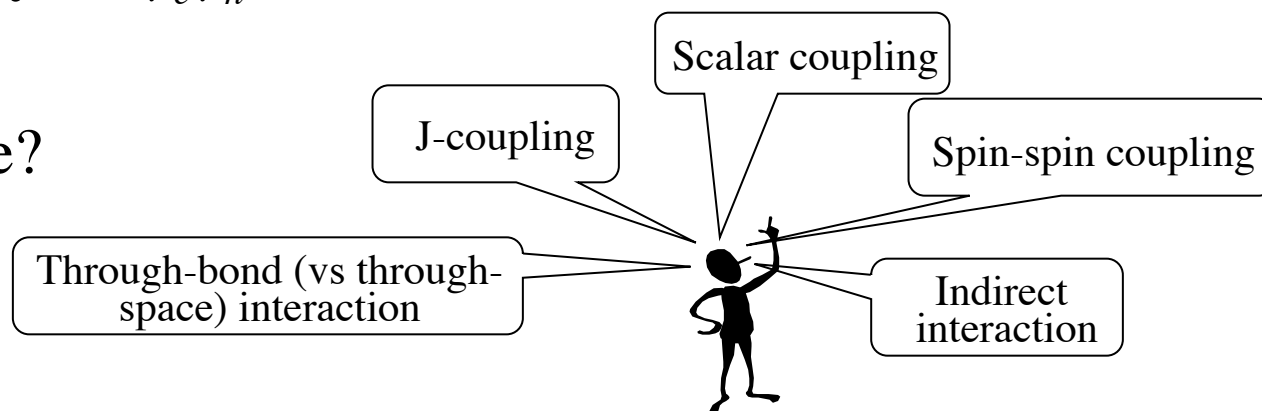
# J-Coupling: Mechanism

- At *very* small distances (comparable to the nuclear radius), the dipolar interaction between an electron and proton is replaced by an *isotropic* interaction called “Fermi contact interaction”.

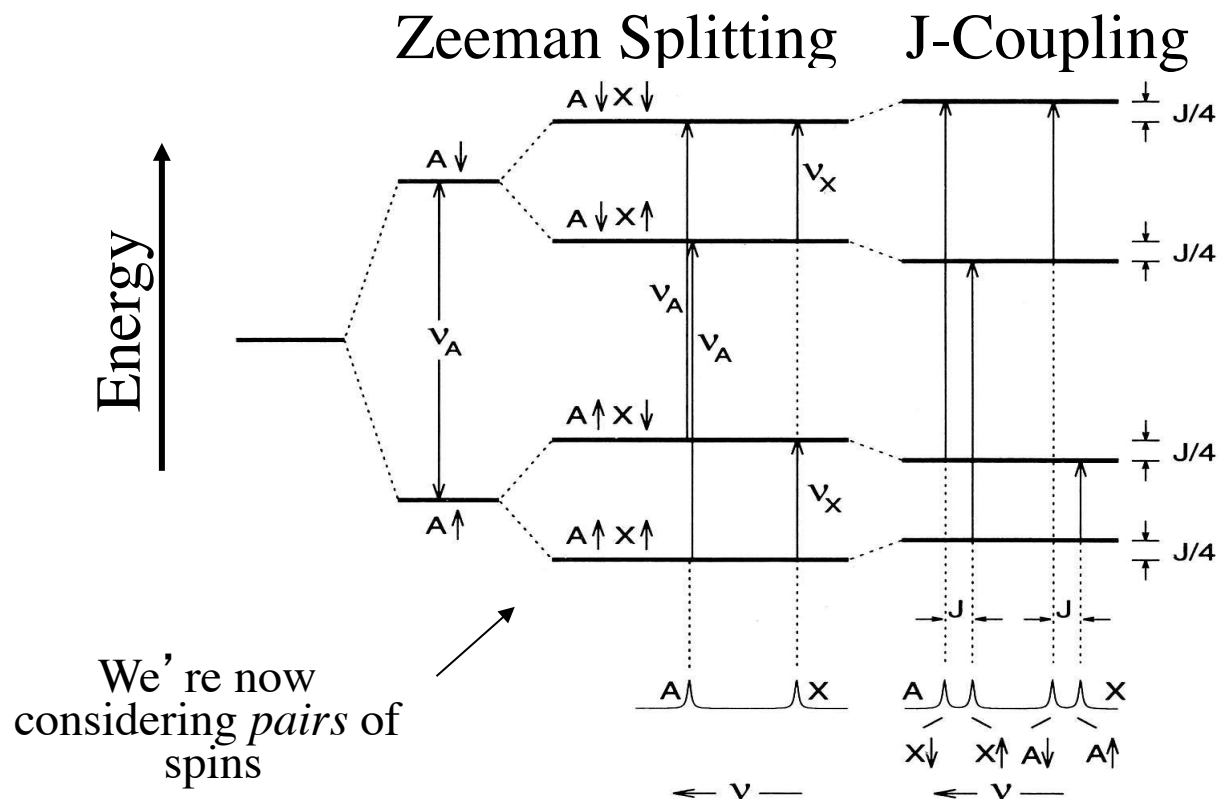


- Interaction energy  $\propto -\gamma_e \gamma_n \hat{I} \cdot \hat{S}$  ← independent of molecular orientation

- What’s in a name?



# J-Coupling: Energy Diagram



- The J-Coupling Hamiltonian

$$\hat{H}_J = \hat{I} \underline{J} \hat{S} = 2\pi \hat{I} \cdot \hat{S} = 2\pi J (\hat{I}_x \hat{S}_x + \hat{I}_y \hat{S}_y + \hat{I}_z \hat{S}_z)$$

J-coupling constant (Hz)

“product operators” 19

A little foreshadowing...

# J-Coupling and Relaxation

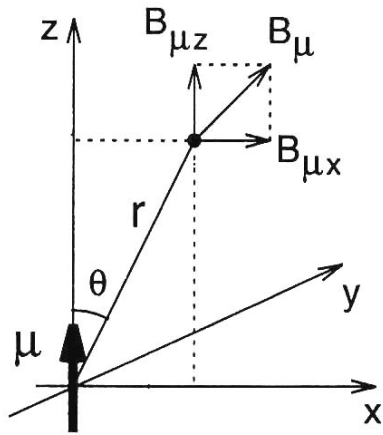
- Because  $J$  is unchanged with molecular tumbling, J-coupling typically does not contribute to relaxation.

$$\hat{H}_J = 2\pi J \hat{I} \cdot \hat{S} \quad \text{where} \quad J(\Theta(t)) = J$$

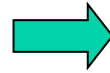
- However, there are a few cases where  $J$  can become “effectively” time-varying.
  - Case 1: the S spin is engaged in chemical exchange
  - Case 2: the  $T_1$  of the S spin itself is  $\ll 1/J$ .
- These cases are called scalar relaxation of the first and second kind respectively, and both are important for the study of MRI contrast agents.

# Magnetic Dipoles

- Nuclei with spin  $\neq 0$  act like tiny magnetic dipoles.



Dipole at origin



$$B_{\mu x} = \left( \frac{\mu_0}{4\pi} \right) \left( \frac{\mu}{r^3} \right) (3 \sin \theta \cos \theta)$$

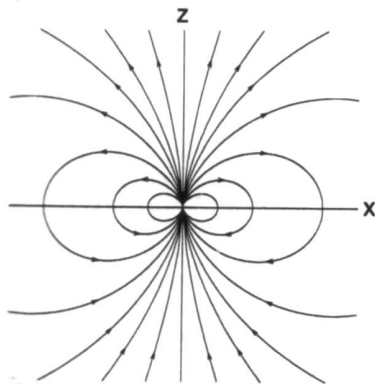
$$B_{\mu y} = 0$$

permeability of free space

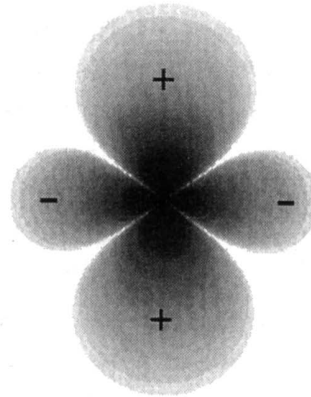
$$B_{\mu z} = \left( \frac{\mu_0}{4\pi} \right) \left( \frac{\mu}{r^3} \right) (3 \cos^2 \theta - 1)$$

falls off as  $r^3$

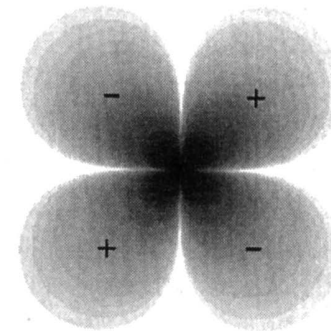
Magnetic Field in  $y=0$  plane



Lines of Force



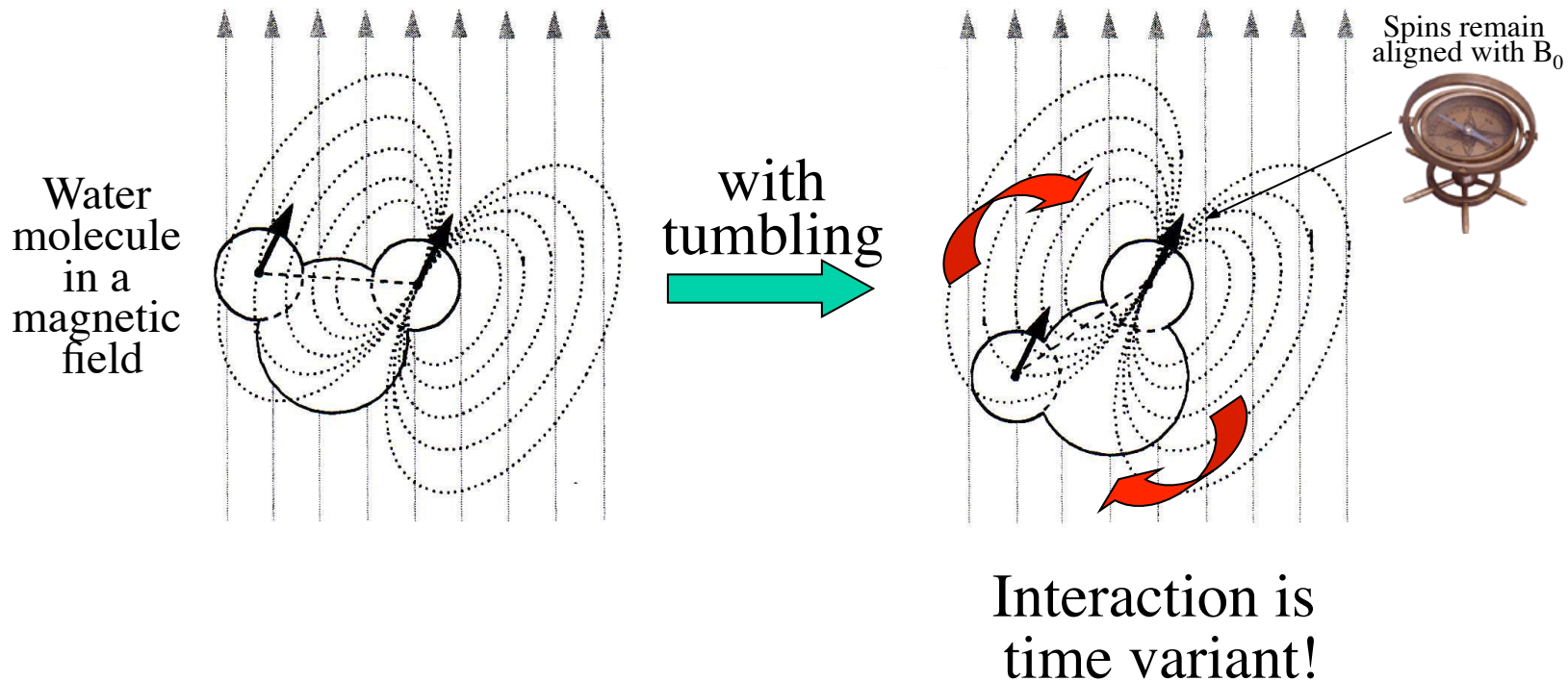
$B_{\mu z}$



$B_{\mu x}$

# Dipolar Coupling

- Dipole fields from nearby spins interact (i.e. are coupled).
- Rapid fall off with distance causes this to be primarily a intramolecular effect.



# The Nuclear Dipolar Coupling Hamiltonian

- Mathematically speaking, the general expression is:

$$\hat{H}_{dipole} = -\frac{\mu_0 \gamma_I \gamma_S}{4\pi r^3} \hbar \left( \hat{I} \cdot \hat{S} - \frac{3}{r^2} (\hat{I} \cdot \vec{r})(\hat{S} \cdot \vec{r}) \right) \quad \text{where } \vec{r} \text{ vector from spin } I \text{ to spin } S$$

- Secular approximation:

$$\hat{H}_{dipole} = d \left( 3\hat{I}_z \hat{S}_z - \hat{I} \cdot \hat{S} \right) \quad \text{where } d = -\frac{\mu_0 \gamma_I \gamma_S}{4\pi r^3} \hbar (3 \cos^2 \Theta_{IS} - 1)$$

dipole coupling constant
angle between  $B_0$  and vector from spins I and S

- With isotropic tumbling, the time average of  $\hat{H}_{dipole} = 0$
- However, the temporal variations of  $\hat{H}_{dipole}(t)$  are typically the dominant source of  $T_1$  and  $T_2$  relaxation in vivo.

# Quadrupolar Interactions

- Nuclei with spin  $I > \frac{1}{2}$  have a electrical quadrupolar moment due to their non-uniform charge distribution.
- This electrical quadrupole moment interacts with local electric field gradients
  - Static E-field gradients results in shifts of the resonance frequencies of the observed peaks.
  - Dynamic (time-varying) E-field gradients result in relaxation.
- Quadrupolar coupling Hamiltonian (secular approximation):

$$\hat{H}_Q = \frac{3eQ}{4I(2I-1)\hbar} V_0 \left( 3\hat{I}_z^2 - \hat{I} \cdot \hat{I} \right)$$

Looks like an interaction of a spin with itself.

Electric field gradient – dependent on molecular orientation



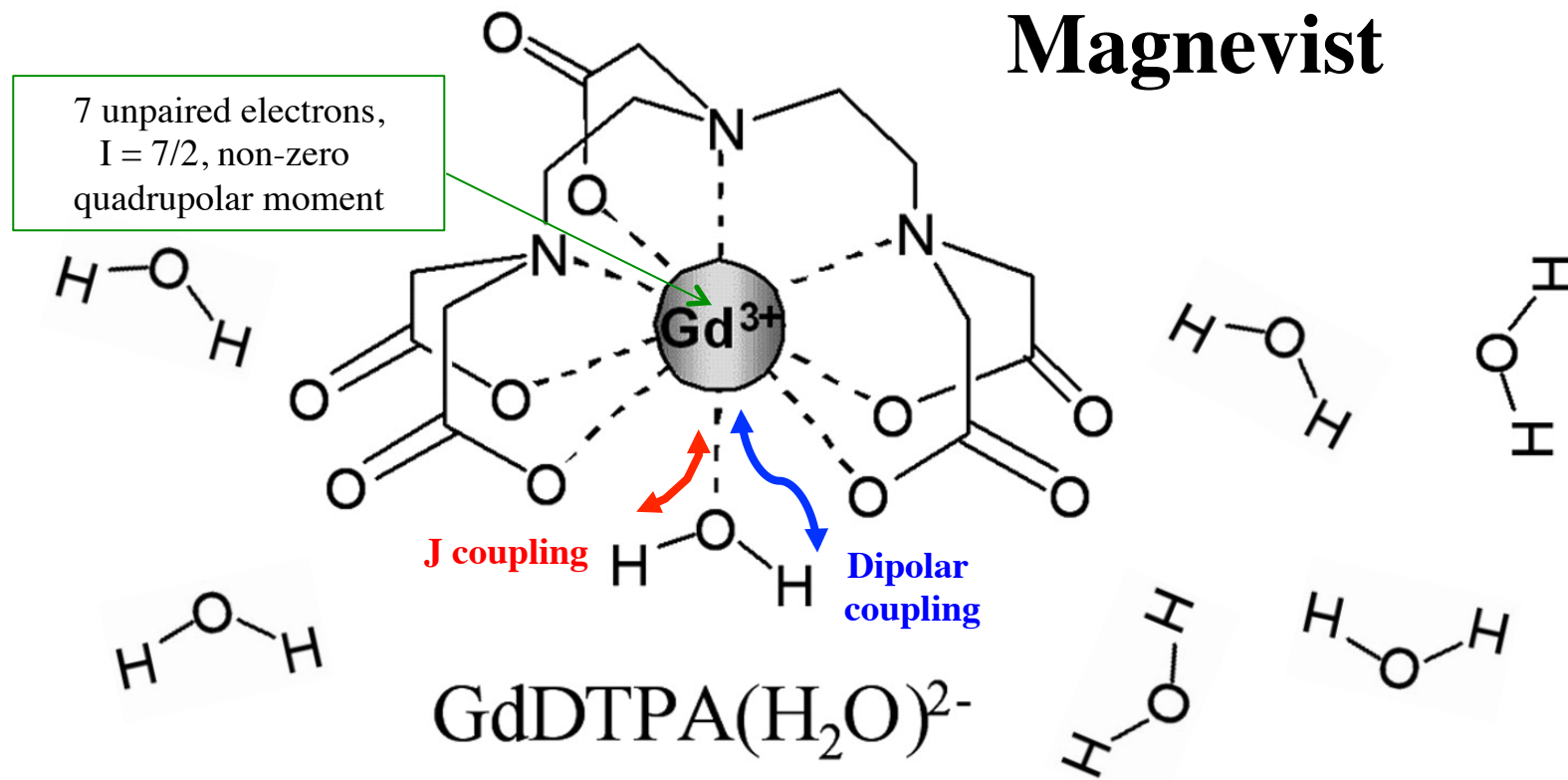
What's the spin of  $\text{Gd}^{3+}$  with its 7 unpaired electrons?



A little foreshadowing...

# Nucleus-unpaired electron couplings

- Both nuclear-electron J and dipolar coupling occur.
- Important for understanding MR contrast agents.



# Summary: Nuclear Spin Hamiltonian

$$\hat{H} = \underbrace{-\gamma_I \hat{I}(1 - \underline{\sigma}_I) \vec{B}}_{\text{Zeeman terms}} - \underbrace{\gamma_S \hat{S}(1 - \underline{\sigma}_S) \vec{B}}_{\text{Zeeman terms}} + \underbrace{2\pi J (\hat{I} \cdot \hat{S})}_{\text{J-coupling}} + \underbrace{d \left( 3\hat{I}_z \hat{S}_z - \hat{I} \cdot \hat{S} \right)}_{\text{Dipolar coupling}} + \underbrace{\eta Q \left( 3\hat{I}_z^2 - \hat{I} \cdot \hat{I} \right)}_{\text{Quadrupolar coupling (+S spin term)}}$$

- Major relaxation mechanisms important for MRI (+ contrast agents)
  - $d(t)$  gives rise to dipolar relaxation
  - $\underline{\sigma}(t)$  gives rise to chemical shift anisotropy (CSA)
  - $\eta(t)$  gives rise to quadrupolar relaxation
  - “ $J(t)$ ” gives rise to scalar relaxation of the 1<sup>st</sup> and 2<sup>nd</sup> kind
  - Plus, we also need to figure out how include chemical exchange effects
  - At the end, we’ll add Rf excitation when computing  $T_{1\rho}$ :  $\hat{H}_{Rf} = -\omega_1^I \hat{I}_x - \omega_1^S \hat{S}_x$

Next lecture:  
Basics of Relaxation