6– NMR Interactions: 
Zeeman and CSA

6.1 Zeeman Interaction

Up to this point, we have mentioned a number of NMR interactions - Zeeman, quadrupolar, dipolar - but we have not looked at the nature of these interactions and others. In order to do NMR spectroscopy, we need to look at each NMR interaction in detail.

Recall that written in terms of a Hamiltonian, the Zeeman interaction is given as:

$$\hat{H}_Z = -\gamma \hbar B_0 \hat{I}_z = \omega_0 \hbar \hat{I}_z.$$  \hspace{1cm} (6.1)

As already mentioned, the Zeeman interaction is not really of interest to NMR spectroscopists. The interactions that are of interest are the chemical shift (or chemical shift anisotropy - CSA), the scalar interaction (also known as J-coupling), the dipolar interaction, and, for spins with $I > 1/2$, the quadrupolar interaction. All of these interactions
result in small perturbations of the resonance away from the Larmor frequency (i.e. a small change in the separation of the energy levels we have dealt with up to this point). The table below lists the magnitude of these interactions or perturbations.

<table>
<thead>
<tr>
<th>Interaction</th>
<th>Order of Magnitude</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zeeman</td>
<td>$10^8$ Hz</td>
</tr>
<tr>
<td>Chemical Shift</td>
<td>$10^3$ Hz</td>
</tr>
<tr>
<td>Scalar</td>
<td>$1 - 100$ Hz</td>
</tr>
<tr>
<td>Dipolar</td>
<td>$10^3$ Hz</td>
</tr>
<tr>
<td>Quadrupolar</td>
<td>$10^6$ Hz</td>
</tr>
</tbody>
</table>

Together these interactions form the “internal” Hamiltonian

$$\hat{H}_{int} = \hat{H}_{cs} + \hat{H}_J + \hat{H}_d + \hat{H}_Q.$$ (6.2)

### 6.2 Chemical Shift/Crossed Spin-Addressability (CSA)

The chemical shielding interaction arises because of the interaction of the nuclear spin with surrounding electrons, i.e. the chemical shift depends on how the
nuclear spin is affected by its electronic environment (e.g. electronegativity, hybridization, hydrogen bonding). As a result of this, the local magnetic field felt by each nucleus is given by

$$\vec{B}_k = (1 - \sigma_k)\vec{B}_0. \quad (6.3)$$

and the frequency of precession of the spin changes to:

$$\omega_{0k} = -\gamma_k(1 - \sigma_k)B_0, \quad (6.4)$$

where $\sigma_k$ is the chemical shielding anisotropy (CSA) for the spins $k$ in the system.
The CSA is a tensor: a $n^{th}$-rank tensor in $m$-dimensional space is a mathematical object that has $n$ indices and $m^n$ components and obeys certain transformation rules. Each index of a tensor ranges over the number of dimensions of space. Tensors are generalizations of scalars (that have no indices), vectors (that have exactly one index), and matrices (that have exactly two indices) to an arbitrary number of indices (http://mathworld.wolfram.com/Tensor.html). The chemical shielding tensor is a $3 \times 3$ matrix.

A typical example used to illustrate the effects of electrons on the nuclear spin is that of benzene:

(http://www.chembio.uoguelph.ca/driguana/NMR/RINGCUR1.HTM)
The $^1H$’s feel an effective field which is larger than $\vec{B}_0$ and are said to be deshielded. To understand the concept of “shielding” and “deshielding”, think of the $^1H$’s in an OH and a CH group:
Since using units of frequency (Hz) will depend on $\vec{B}_0$, chemical shifts are typically reported in ppm:

$$\delta = \text{ppm} = \text{Chemical Shift from TMS (Hz)}$$

Spectrometer Frequency (MHz)

<table>
<thead>
<tr>
<th>$100 \text{ Hz}$</th>
<th>$300 \text{ Hz}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$100 \text{ MHz}$</td>
<td>$300 \text{ MHz}$</td>
</tr>
</tbody>
</table>

Overall, typical $^1H$ chemical shifts are:

In terms of a Hamiltonian, the chemical shift is thus given by
\[ \hat{H}_{cs} = \gamma \hat{I} \sigma B_0, \quad (6.5) \]

or written out explicitly,

\[ \hat{H}_{cs} = \gamma (\hat{I}_x \sigma_{xx} + \hat{I}_y \sigma_{yy} + \hat{I}_z \sigma_{zz}) B_0 \quad (6.6) \]

in the principal axis frame of reference (PAS), a frame of reference defined relative to the chemical shift tensor components.

### 6.3 Definition of the CSA Components

The chemical shift is an anisotropic parameter (i.e. it has a directional dependence) which is characterised by a tensor, the ”shape” of which is illustrated below:
The shape of these three-dimensional ellipsoids is defined by the principal tensor components $\sigma_{xx}$, $\sigma_{yy}$, $\sigma_{zz}$, (or alternately, $\sigma_{11}$, $\sigma_{22}$, $\sigma_{33}$ - which will be defined below). Other important definitions stemming from these are that of the isotropic chemical shift, $\sigma_{iso}$, given by,

$$\sigma_{iso} = \frac{\sigma_{11} + \sigma_{22} + \sigma_{33}}{3}$$

(6.7)
and the anisotropy parameter, \( \eta \), given by,

\[
\eta = \frac{\sigma_{yy} - \sigma_{xx}}{\sigma_{zz} - \sigma_{iso}}. \tag{6.8}
\]

Note that these two equations are defined once in terms of \( \sigma_{xx}, \sigma_{yy}, \) and \( \sigma_{zz} \), and once with \( \sigma_{11}, \sigma_{22}, \) and \( \sigma_{33} \). These two notations are not interchangeable (though in the literature, they are often interchanged)!

If we were sitting in the reference frame of tensor, then the overall chemical shift would be given by:

\[
\delta = \sigma_{xx}^{PAS} + \sigma_{yy}^{PAS} + \sigma_{zz}^{PAS}. \tag{6.9}
\]

It is, however, often more convenient to define the chemical shift anisotropy with respect to the laboratory frame of reference (LF), i.e. the frame of reference where the static magnetic field \( \vec{B}_0 \) is along the z-direction (the observable).
In this case, the overall chemical shift is given by

\[
\delta = \sigma_{xx}^{PAS} (\cos \alpha \sin \beta)^2 + \sigma_{yy}^{PAS} (\sin \alpha \sin \beta)^2 + \sigma_{zz}^{PAS} (\cos \beta)^2.
\] (6.10)

For example, the \(^{15}N\) chemical shift tensor in a peptide plane
where an additional dependence on $\theta$ is introduced to relate the CSA to the NH bond.

As a result:

$$\delta = \sigma_{11} \sin^2(\alpha - \theta) \sin^2(\beta) + \sigma_{22} \cos^2(\beta) + \sigma_{33} \cos^2(\alpha - \theta) \sin^2(\beta).$$  \hspace{1cm} (6.11)

### 6.4 Notation for CSA components

As mentioned above there are two sets of notations for the principal components of the chemical shift tensors:

$\sigma_{xx}, \sigma_{yy}, \sigma_{zz}$, or $\sigma_{11}, \sigma_{22}, \sigma_{33}$. 

For the $\sigma_{xx}$, $\sigma_{yy}$, $\sigma_{zz}$ version, the following definition applies:

$$|\sigma_{zz} - \sigma_{iso}| \geq |\sigma_{xx} - \sigma_{iso}| \geq |\sigma_{yy} - \sigma_{iso}| \quad (6.12)$$

i.e. for $\sigma_{zz} - \sigma_{iso} > 0$,

\[ \sigma_{zz} \quad \sigma_{iso} \quad \sigma_{yy} \quad \sigma_{xx} \]

whereas for $\sigma_{zz} - \sigma_{iso} < 0$,

\[ \sigma_{xx} \quad \sigma_{yy} \quad \sigma_{iso} \quad \sigma_{zz} \]

For the $\sigma_{11}$, $\sigma_{22}$, $\sigma_{33}$ version, the following definition applies:

$$\sigma_{11} \geq \sigma_{22} \geq \sigma_{33} \quad (6.13)$$

i.e.

\[ \sigma_{11} \quad \sigma_{22} \quad \sigma_{iso} \quad \sigma_{33} \]
The relationship between both notations is:

\[
\begin{align*}
\sigma_{xx} &= \sigma_{iso} - \sigma_{11}, \\
\sigma_{yy} &= \sigma_{iso} - \sigma_{22}, \\
\sigma_{zz} &= \sigma_{iso} - \sigma_{33}. 
\end{align*}
\] (6.14)

and thus,

\[
\sigma_{xx} + \sigma_{yy} + \sigma_{zz} = 0.
\] (6.15)

6.5 CSA Spherical Tensor Representation

As previously mentioned, it is possible to write the density matrix in terms of spherical tensors. Along the same lines, it is also possible to write the Hamiltonian in terms of spherical tensor components. This representation is useful to
represent the Hamiltonian in terms of spatial functions and operators which have well defined transformation properties. The most suitable choice are irreducible spatial tensors and irreducible spin operators, such that

\[ \hat{\mathcal{H}} = \sum_{l} \sum_{m=-l}^{l} (-1)^m A_{l,m}^{(\mu)} T_{l,-m}^{(\mu)} \]  

(6.16)

where \( \mu \) represents the type of interaction involved (e.g. dipolar, quadrupolar,...), \( l \) is the angular momentum quantum number or rank of the tensor, \( m \) is the magnetic quantum number, \( A_{l,m}^{(\mu)} \) are spatial tensor components, and \( T_{l,-m}^{(\mu)} \) are the irreducible spin tensor operators.

For the CSA interaction, the tensor components are defined as follows - Spin part:

\[
T_{20} = \frac{1}{\sqrt{6}} 2I_z B_0 \\
T_{2\pm1} = \pm \frac{1}{2} I^\pm B_0 \\
T_{2\pm2} = 0
\]

(6.17)
Spatial part in PAS:

\[ A_{20}^{PAS} = \sqrt{\frac{3}{2}} \gamma (\sigma_{zz} - \sigma_{iso}) \]
\[ A_{2\pm1}^{PAS} = 0 \]
\[ A_{2\pm2}^{PAS} = -\frac{1}{2} \gamma (\sigma_{zz} - \sigma_{iso}) \eta \]

(6.18)

To obtain the spatial part in any arbitrary frame, we need to transform or rotate to a different coordinate system. The rotations in three-dimensional space are represented by the Euler angles \((\alpha, \beta, \gamma)\), and are denoted \(R(\alpha, \beta, \gamma)\):
In other words,

$$R(\alpha, \beta, \gamma) = R_z(\alpha)R_Y(\beta)R_Z(\gamma).$$  \hspace{1cm} (6.19)

The convention of rotation varies from text to text - so beware of the definition used!

So to go from the PAS to the LAB frame, we use $R(\alpha, \beta, \gamma)$ and to do the reverse rotation, i.e. from LAB $\rightarrow$ PAS, we use the notation $R(\phi, \Theta, \chi)$.

Transforming the spatial tensors from PAS $\rightarrow$ LAB, we get

$$A_{20}^{LAB} = \sqrt{\frac{3}{8}} \gamma(\sigma_{zz} - \sigma_{iso}) \left[ (3\cos^2 \beta - 1) - \eta \sin^2 \beta \cos 2\alpha \right]$$
\[ A_{2 \pm 1}^{LAB} = \pm \frac{1}{2} \gamma (\sigma_{zz} - \sigma_{iso}) [(3 + \eta \cos 2\alpha) \cos \beta \mp i \eta \sin 2\alpha] \]
\[ \times \sin \beta e^{\mp i \gamma} \]
\[ A_{2 \pm 2}^{LAB} = \frac{1}{2} \gamma (\sigma_{zz} - \sigma_{iso}) e^{\mp 2i \gamma} \]
\[ \times \left[ \frac{3}{2} \sin^2 \beta - \frac{\eta}{2} (1 + \cos^2 \beta) \cos 2\alpha \pm i \eta \cos \beta \sin 2\alpha \right] \]

(6.20)

6.6 Determining the CSA

The methods used to measure the chemical shift anisotropy of a particular nucleus depend primarily on the state of the sample, i.e. whether the solid is a powder or microcrystalline sample, or whether it is a single crystal. In the case of powdered samples, the molecules have a statistical distribution of possible orientations with respect to the magnetic field \( \vec{B}_0 \). For single crystals, on the other hand, all the molecules are aligned in the same direction in a crystalline lattice. Thus for a given crystal orientation, the molecules will have a particular alignment in the magnetic field \( \vec{B}_0 \).

In the figure below are illustrated the spectra one would obtain for:

- a) a powder sample with \( \sigma_{11} \neq \sigma_{22} \neq \sigma_{33} \)
b) a powder sample with $\sigma_{11}$ and $\sigma_{22} = \sigma_{33}$ and

- c) a single crystal.

The spectrum in a), with its broad "powder pattern", is typical of functional groups that have very asymmetric electronic environments, such as, for example, the carbonyl group (C=O). The spectrum in b) illustrates the case of an axially symmetric tensor, with two of the three tensor components being equal. This occurs for moieties where there is a threefold symmetry axis through the nucleus, such as for N in NH$_3$ groups. Note that in the case of nuclei with symmetric electronic environments, such as C in methane, all the tensors components are equal and the spectrum collapses to a single peak at the isotropic position $\sigma_{iso}$. The spectrum in c) can also represent the chemical shift for a particular crystallite in the magnetic field. If there are a number of inequivalent sites in the crystal, these would be reflected in the spectra in that there would be one line for every crystallographic inequivalency. The particular chemical shift measured depends on the orientation and thus by changing the orientation of the crystal, one gets a new measurement for the chemical shift.
Measuring the CSA from powders

The simplest way to measure the CSA from a powder sample is to record a "powder pattern" such as those shown in a) and b) in the figure above, and then to fit the spectra to extract the tensor parameters. The biggest
limitation in using this method is when there are a number of similar nuclei to detected at once. This results in overlapped powder patterns, making a straightforward determination of the principal components difficult, if not impossible.

To alleviate this problem, there are a number of other one-dimensional methods and two dimensional methods that can be used to separate the isotropic chemical shifts of the different nuclei. Two examples are given in the figures below.

1) Slow spinning/ fitting of sidebands using the Herzfeld-Berger method:
Figure 4  (a) MAS spectrum of 1,2,3-trimethoxybenzene (shown in inset) at a spinning rate of 6.0 kHz. (b) Spinning sideband pattern obtained for 1,2,3-trimethoxybenzene at a spinning rate of 1106 ± 5 Hz

2) Magic Angle Turning experiments:

Figure 1. Pulse sequence of the chemical shift and CSA correlation experiment using slow magic angle spinning. The last segment of the evolution period is incorporated into the acquisition period, and all of the narrow pulses are 90° pulses.

<table>
<thead>
<tr>
<th>step</th>
<th>$\phi_1$</th>
<th>$\phi_2$</th>
<th>$\phi_3$</th>
<th>receiver</th>
<th>blocks</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$+x$</td>
<td>$-y$</td>
<td>$-y$</td>
<td>$+x$</td>
<td>real</td>
</tr>
<tr>
<td>2</td>
<td>$+x$</td>
<td>$+x$</td>
<td>$-x$</td>
<td>$+x$</td>
<td>real</td>
</tr>
<tr>
<td>3</td>
<td>$+x$</td>
<td>$-y$</td>
<td>$+x$</td>
<td>$+x$</td>
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</tr>
<tr>
<td>4</td>
<td>$+x$</td>
<td>$+x$</td>
<td>$-y$</td>
<td>$+x$</td>
<td>imaginary</td>
</tr>
</tbody>
</table>

$^a$The simultaneous phase alternation ($+x$ and $-x$) of the spin-lock phase $\phi_1$ and the receiver phase can be added to the listed phase cycle.
ref: A. Orendt, "Chemical Shift Tensor Measurement in Solids", Encyclopedia of NMR, Grant and Harris (eds.).
Measuring the CSA from single crystals

In this case, the simplest way to measure the CSA tensor components is to measure the chemical shift for a number of crystal orientations. To do this, the crystal is mounted in the probe on a goniometer, a device that allows the user to keep track of how much the crystal has been rotated by. Spectra are then recorded for rotation step sizes of 5-10 degrees, until the crystal has been rotated by a full 180 degrees in one direction. The process is then repeated with the crystal rotated by 90 degrees in an orthogonal direction and then again 90 degrees to that, i.e.

The resulting chemical shift positions are then plotted as a function of rotation angle to yield:
This curve is then fitted to the function in equation 6.10 to extract $\sigma_{11}$, $\sigma_{22}$, $\sigma_{33}$.

Again as with powders, this method is limited to crystals that do not have too many magnetically inequivalent molecules, otherwise the lines would be overlapped. As for the powder samples, two-dimensional methods can be used to circumvent this problem. For more details, see A. Orendt, "Chemical Shift Tensor Measurement in Solids".

Methods to calculate CSAs

In recent years, reliable density functional methods
(DFT) to calculate the CSAs for given nuclei, in specific molecules, have been developed. These methods currently reproduce the experimental results for $\sigma_{11}$, $\sigma_{22}$ and $\sigma_{33}$ to within ca. 2-3 ppm. For more details, see:


Example: Chemical shift calculation of methyl groups in antamanide, as a function of dihedral angle.
6.7 Importance of Chemical Shift/CSA

1. Identification of compounds (e.g. in combination with IR and MS data)

2. Identification of secondary structure in proteins: e.g. the $^1H^\alpha$ chemical shift depends on backbone dihedrals
This also applies to other resonances such as HA, CA, CB, CO, and N.

TALOS, a program which uses the chemical shift info of these five nuclei can be used to predict backbone
dihedral angles - and therefore secondary structure (http://spin.niddk.nih.gov/bax/software/TALOS/).

3. Relaxation (modulation of CSA through rotation of the molecule).

4. In solids, orientation of a molecule with respect to the external magnetic field (e.g. a membrane protein aligned on a glass slide)