A) Introduction
   i) Challenges of solid state
   ii) What can we study?
   iii) Review of NMR interactions

B) Averaging – Magic angle sample spinning

C) Polarization transfer - CP
Linewidth comparison

Solution State: 1H 12-25 Hz
13C 5-15 Hz
15N 4-7 Hz

Solid State: 1H ca. 10 000 Hz
13C ca. 5000 Hz
15N ca. 7000 Hz
\[ H = H_z + H_{cs} + H_J + H_D (\pm H_Q) \]

**Zeeman**

\[ H_z = -\gamma B_0 I_z \]

**Chemical Shift**

\[ H_{cs} = -\gamma \sigma B_0 I \]

- environment
- orientation

**Scalar**

\[ H_J = \sum \sum 2\pi J_{kj} I_k \cdot I_j \]

- connectivities
- dihedral angles

**Dipolar**

\[ H_D = b_{12} [(I_1 \cdot I_2) r^3 - 3(\langle I_1 \cdot r \rangle)(\langle I_2 \cdot r \rangle) r^5] \]

\[ b_{12} = \frac{\mu_0 \gamma_1 \gamma_2 h^2}{16\pi^3} \]
Solution State

Averaging due to isotropic tumbling

\[ H = H_z + H_{cs} + H_J + H_\theta ( + H_Q ) \]

Only the isotropic part of \( H_{cs} \) and \( H_J \) remain

These interactions are on the order of \( H_z \), therefore high resolution can be achieved.
Solid State

No averaging

Single crystal

Powder

\[ H = H_z + H_{cs} + H_J + H_D (+ H_Q) \]

The interactions of interest are on the order of 10-1000 Hz (\(10^6\) Hz in the case of \(H_Q\)) and conserve their anisotropic character.
Intermediate Regime: Residual Dipolar Couplings

\[ H = H_z + H_{cs} + H_J + H_D \]

The dipolar coupling is not fully averaged and is on the order of Hz.
Resolution in the Solid State

\[ H = H_z + H_{cs} + H_J + H_D \ (H_Q) \]

\[ P_2(\cos \theta) = (3 \cos^2 \theta - 1) \]

Use the angular dependence of some of the Interactions to:

1) Average

Magic Angle Sample Spinning (MAS)

For \( \theta = 54.7^\circ \),

\[ \langle P_2(\cos \theta) \rangle = 0 \]

2) Make use of the angular dependence

Oriented Methods

- mechanically

For \( \theta = \theta_i \),

\[ P_2 = (3 \cos^2 \theta_i - 1) \]
MAS

Solution State:  
$^1\text{H}$ 12-25 Hz  
$^{13}\text{C}$ 5-15 Hz  
$^{15}\text{N}$ 4-7 Hz

Solid State:  
$^1\text{H}$ ca. 100 Hz  
$^{13}\text{C}$ ca. 100 Hz  
$^{15}\text{N}$ ca. 40 Hz
Oriented Methods

Solution State:  
\(^1\text{H}\) 12-25 Hz  
\(^{13}\text{C}\) 5-15 Hz  
\(^{15}\text{N}\) 4-7 Hz

Solid State:  
\(^1\text{H}\) ca. 1000 Hz  
\(^{13}\text{C}\) ca. 300 Hz  
\(^{15}\text{N}\) ca. 300 Hz
So why bother with solid state NMR? if resolution is poor and (as we will see) the theory is complex!
1) Membrane proteins constitute 20-40% of the proteins encoded by known genomes and are important drug targets (e.g. dopamine receptors, ABC transporters)

YET

Only 368 out of a total of 20057 (1.8%) structures determined and deposited in the Protein Databank are of membrane protein structures

STRUCTURAL INFORMATION IS NEEDED TO GAIN INSIGHT INTO FUNCTION

Recent developments in solid state NMR have made it possible to undertake structural studies of peptides and proteins.
Hagfish slime is 99.996% seawater, 0.002% mucin (glycoprotein) and 0.002% protein fibre. The fibres were hypothesized to contain both rigid and mobile regions. $^{13}$C spectra collected with and without cross-polarization show very different carbonyl carbon lineshapes, supporting the two-phase model for the fibres.

Bloch decay spectra clearly show a sharp feature in the carbonyl region, while CP spectra clearly show a broad component.
Solution or solid?
Ubiquitin

1998


2004

What has made this possible?

Sample preparation:
- labelling strategies
- recrystallization/precipitation

Assignment strategies:
- $^{13}\text{C}-^{13}\text{C}$ correlation experiments
- $^{13}\text{C}-^{15}\text{N}$ correlation experiments
- $^{13}\text{C}-^{1}\text{H}$ or $^{15}\text{N}-^{1}\text{H}$ correlation experiments

Structural parameters from:
- chemical shifts
- torsion angle measurements
- distance measurements

Straus, S.K. Phil. Trans. B. 2004
Interactions in solid state

<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

$$\hat{H}_{int} = \hat{H}_{cs} + \hat{H}_{J} + \hat{H}_{d} + \hat{H}_{Q}.$$
Chemical shift:

$$\hat{\mathcal{H}}_{cs} = \gamma (\hat{I}_x \sigma_{xx} + \hat{I}_y \sigma_{yy} + \hat{I}_z \sigma_{zz}) B_0$$

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

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

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:

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

Spatial part in PAS:

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

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

$$\eta = \frac{\sigma_{yy} - \sigma_{xx}}{\sigma_{zz} - \sigma_{iso}}.$$
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 \(R(\alpha, \beta, \gamma)\):
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 $\text{LAB} \rightarrow \text{PAS}$, we use the notation $R(\phi, \Theta, \chi)$. 

\[ R(\alpha, \beta, \gamma) = R_z(\alpha)R_y(\beta)R_z(\gamma). \]
Transforming the spatial tensors from PAS $\rightarrow$ LAB, we get

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

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

$\ast \quad \sin \beta e^{\mp i \gamma}$

$$A_{2\pm 2}^{LAB} = \frac{1}{2} \gamma (\sigma_{zz} - \sigma_{iso}) e^{\mp 2i \gamma}$$

$\ast \quad \left[ \frac{3}{2} \sin^2 \beta - \frac{\eta}{2} (1 + \cos^2 \beta) \cos 2\alpha \pm i \eta \cos \beta \sin 2\alpha \right]$
Scalar coupling:

\[ \hat{\mathcal{H}}_J = \sum_k \sum_j 2\pi J_{k,j} \vec{I}_k \cdot \vec{I}_j \]

Spherical tensor notation:

\[
\begin{align*}
T_{10} & = -\frac{1}{2\sqrt{2}}(I_+S_- - I_-S_+) \\
T_{1\pm1} & = \frac{1}{2}(I_zS_\pm - I_\pm S_z) \\
T_{20} & = \frac{1}{\sqrt{6}}(3I_zS_z - \mathbf{I} \cdot \mathbf{S}) \\
T_{2\pm1} & = \pm\frac{1}{2}(I_zS_\pm + I_\pm S_z) \\
T_{2\pm2} & = \frac{1}{2}I_\pm S_\pm
\end{align*}
\]
Dipolar interaction:

\[ \hat{\mathcal{H}}_D = \frac{\mu_0 \gamma_1 \gamma_2 \hbar^2}{16\pi^3} \left[ (\vec{I}_1 \cdot \vec{I}_2) r^{-3} - 3(\vec{r} \cdot \vec{I}_1)(\vec{r} \cdot \vec{I}_2) r^{-5} \right]. \]
\[
\hat{\mathcal{H}}_D = \frac{\mu_0 \gamma_1 \gamma_2 \hbar^2}{16 \pi^3 r^3} \left[ A + B + C + D + E + F \right]
\]

where

\[
A = \hat{I}_{1z} \hat{I}_{2z} (1 - 3\cos^2 \theta)
\]

\[
B = -\frac{1}{4} \left[ \hat{I}_1^+ \hat{I}_2^- + \hat{I}_1^- \hat{I}_2^+ \right] (1 - 3\cos^2 \theta)
\]

\[
C = -\frac{3}{2} \left[ \hat{I}_1^+ \hat{I}_{2z} + \hat{I}_{1z} \hat{I}_2^+ \right] \sin \theta \cos \theta e^{-i\phi}
\]

\[
D = -\frac{3}{2} \left[ \hat{I}_1^- \hat{I}_{2z} + \hat{I}_{1z} \hat{I}_2^- \right] \sin \theta \cos \theta e^{i\phi}
\]

\[
E = -\frac{3}{4} \hat{I}_1^+ \hat{I}_2^+ \sin^2 \theta e^{-2i\phi}
\]

\[
F = -\frac{3}{4} \hat{I}_1^- \hat{I}_2^- \sin^2 \theta e^{2i\phi}
\]
Thus the Hamiltonian in the case of homonuclear coupling (between like spins) is

\[
\hat{\mathcal{H}}_D = -\frac{\mu_0 \gamma_1 \gamma_2 h^2}{16\pi^3 r^3} \frac{1}{2} (3 \cos^2 \theta - 1) [3 \hat{I}_{1z} \hat{I}_{2z} - \vec{\hat{I}}_1 \cdot \vec{\hat{I}}_2] 
\]  

(8.13)

whereas in the case of heteronuclear coupling, it is given by

\[
\hat{\mathcal{H}}_D = -\frac{\mu_0 \gamma_1 \gamma_2 h^2}{16\pi^3 r^3} (3 \cos^2 \theta - 1) \hat{I}_{1z} \hat{I}_{2z}.
\]  

(8.14)
Spherical tensor notation:

\[ T_{10} = 0 \]
\[ T_{1\pm 1} = 0 \]
\[ T_{20} = \frac{1}{\sqrt{6}} (3I_z S_z - \mathbf{I} \cdot \mathbf{S}) \]
\[ T_{2\pm 1} = \mp \frac{1}{2} (I_z S_{\pm} + I_{\pm} S_z) \]
\[ T_{2\pm 2} = \frac{1}{2} I_{\pm} S_{\pm} \]

\[ A_{20} = \sqrt{\frac{3}{2}} d_{IS} (3 \cos^2 \beta - 1) \]
\[ A_{2\pm 1} = \pm \frac{3}{2} d_{IS} \sin(2\beta) e^{\pm i\gamma} \]
\[ A_{2\pm 2} = \frac{3}{2} d_{IS} (\sin^2 \beta) e^{\pm i\gamma}. \]
Quadrupolar interaction:

\[
\hat{H}_Q = \frac{3eQ}{4I(2I - 1)\hbar} [V_{zz}(3\hat{I}_z^2 - \hat{I} \cdot \hat{I}) ] \\
+ (V_{xx} - V_{yy})(\hat{I}_x^2 - \hat{I}_y^2) \\
+ 2V_{xy}(\hat{I}_x\hat{I}_y + \hat{I}_y\hat{I}_x) \\
+ 2V_{xz}(\hat{I}_x\hat{I}_z + \hat{I}_z\hat{I}_x) \\
+ 2V_{yz}(\hat{I}_y\hat{I}_z + \hat{I}_z\hat{I}_y)].
\]
\[ Q = \frac{eQV}{2I(2I - 1)h} \]

\[ V = \begin{pmatrix} V_{xx} & 0 & 0 \\ 0 & V_{yy} & 0 \\ 0 & 0 & V_{zz} \end{pmatrix} \]
Spherical tensor notation:

\[ T_{20} = \frac{1}{\sqrt{6}} \left[ 3I_z^2 - I(I + 1) \right] \]

\[ T_{2\pm 1} = \pm \frac{1}{2} \left[ I^\pm I_z + I_z I^\pm \right] \]

\[ T_{2\pm 2} = \frac{1}{2} (I^\pm)^2 \]

\[ A_{20}^{PAS} = \frac{e^2 qQ \sqrt{6}}{4I(2I - 1)\hbar} \]

\[ A_{2\pm 1}^{PAS} = 0 \]

\[ A_{2\pm 2}^{PAS} = -\frac{e^2 qQ \eta^Q}{4I(2I - 1)\hbar} \]
Spatial parts in arbitrary frame:

\[ A_{20} = \frac{e^2 q Q}{4I(2I - 1)\hbar} \sqrt{\frac{3}{2}} \left[ (3\cos^2 \beta - 1) - \eta^Q \sin^2 \beta \cos 2\alpha \right] \]

\[ A_{2 \pm 1} = \pm \frac{e^2 q Q}{4I(2I - 1)\hbar} \sin(\beta) e^{\pm i\gamma} \left[ (3 + \eta^Q \cos(2\alpha)) \cos \beta \mp i\eta^Q \sin(2\alpha) \right] \]

\[ A_{2 \pm 2} = \frac{e^2 q Q}{4I(2I - 1)\hbar} e^{\pm 2i\gamma} \]

\[ \left[ \frac{3}{2} \sin^2 \beta - \frac{\eta^Q}{2} (1 + \cos \beta) \cos(2\alpha) \pm i\eta^Q \cos \beta \sin(2\alpha) \right] \]