Biomolecular NMR 2005

• Biomolecular NMR - short history ~ 1985 first protein structure
• Compared to X-ray ~ 1953 first protein structure
• Today ~ 15 % of structures in the PDB come via NMR – higher for nucleic acids
• New challenges need new methods – NMR is still an evolving science
NMR References 2005


NMR and Biology: Recognition

- 1952 - Bloch and Purcell – Nobel Prize in Physics
- 1991 – Richard Ernst – Nobel Prize in Chemistry
- 2002 – Kurt Wuthrich – Nobel Prize in Chemistry
- 2003 – Lauterbur and Mansfield – Nobel Prize in Physiology and Medicine
Computers Were Primitive in 1966
Varian HR 220

Early Superconducting Magnets Required a Lot of Care And Feeding
High Field (220 MHz), but Still 1D CW NMR
80’s Approach: 2D $^1$H-$^1$H NMR
assign resonances, collect NOE’s, calculate structure
NMR Moved from 1D to 2D to 3D with the Help of Rf Pulse Sequences, Gradients, and Fourier Transform

\[
\begin{align*}
\text{(HB)CBCA(CO)NH} & \\
\text{HNCACB} & \\
\end{align*}
\]
Structural Challenges – for 2005

• ~35,000 genes identified in the Human Genome
• Sequencing in progress on Over 1500 organisms >1000 viruses, >100 bacteria, yeast, C elegans, arabidopsis
• Only about half can be classified as to function (based on sequence homology)
• Massive amounts of parallel information will help (structural information is one source)
Growth in sequence information greatly exceeds structure determination capacity
Can NMR Make a Unique Contribution?
Membrane Proteins, Protein-Protein Interactions, Ligand Binding

Unstructured Regions in Proteins
% with rmsd > 4 Å

NMR
Xray
Spin Properties

\[ \vec{\mu} = \gamma \vec{I} \quad I_z = \hbar m \quad E = -\vec{\mu} \cdot \vec{B}_0 \]

for \( I = 1/2 \)

\[ m = -1/2 \quad \nu = \mu B_0 / \hbar \]

\[ m = 1/2 \]

\[ p = \exp(-E_i / kT) / Z \]

\[ M_z = \gamma \hbar \sum_i \rho_i m_i N_0 \]

\[ = N_0 \gamma \hbar B_0 I(I+1) \]

\[ \frac{2}{3kT} \]
**NMR Active Isotopes Exist for Nearly Every Element**

http://bouman.chem.georgetown.edu/NMRpt/NMRPerTab.html

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## Select an element by clicking on it:

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*La | Ce | Pr | Nd | Pm | Sm | Eu | Gd | Tb | Dy | Ho | Er | Tm | Yb | Lu |

**Ac | Th | Pa | U | Np | Pu | Am | Cm | Bk | Cf | Es | Fm | Md | No | Lr |
Spin ½ Nuclei are Most Useful in Biomolecular NMR

Carbon

Note: Resonance frequencies are quoted relative to a resonance frequency of exactly 100 MHz for 1H.

Isotope: 13C

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<th>Property</th>
<th>Value</th>
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<td>Spin</td>
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<tr>
<td>Natural abundance</td>
<td>1.108%</td>
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<tr>
<td>Magnetogyric ratio (rad/T s)</td>
<td>$6.7283 \times 10^7$</td>
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<td>Relative receptivity</td>
<td>$1.76 \times 10^{-4}$</td>
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<tr>
<td>Magnetic moment</td>
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<td>Quadrupole moment $Q/m(2)$</td>
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<tr>
<td>Resonance frequency</td>
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Nuclear Properties

• Reference: Cottingham & Greenwood (1986)
• Not all nuclei have magnetic moments, Why?
• Not all nuclei are equally abundant, Why?
• Spins vary, Why?
• Magnetogyric ratios vary, Why?
Fundamental Particle Properties

Stern Gerlach experiment: Na atom - 1 unpaired electron
Two spots implies quantized moments: +/- 1/2
protons and neutrons are also spin 1/2 particles
Current Loop Model for Magnetic Moments

\[ \vec{M} = i \vec{S} \]

- \( i \) in Coulomb s\(^{-1}\)
- \( S \) in m\(^2\)
- \( M \) in JT\(^{-1}\) (Tesla)

Estimates: 
- \( i = -ev/(2\pi r) \)
- \( S = \pi r^2 \)
- \( M \) (or \( \mu \)) = -erv/2

\[ \vec{\mu} = -e(\vec{r} \times \vec{v})/2, \quad \vec{L} = m_e \vec{r} \times \vec{v}, \quad \vec{\mu} = -e/(2m_e) \vec{L} = \gamma \vec{L} = \gamma \hbar/(2\pi l) \]

\( \gamma = -g \left( e/(2m_e) \right), \quad g = \text{Lande g factor} \)
Values of Particle Magnetogyric Ratios

Electron: \( g \approx 2, \quad \gamma_e = -17.7 \times 10^{10} \text{T}^{-1}\text{s}^{-1} \)

Proton: expect \( 1/m_p \) dependence, \( 1/2000 \) and positive
\( 2.7 \times 10^8 \text{T}^{-1}\text{s}^{-1} \)

Neutron: similar mass to proton
\( -1.8 \times 10^8 \text{T}^{-1}\text{s}^{-1} \)
Shell Model of the Nucleus

Simple Rules:

a) spherical particle in a box potential
\[ \psi = R_{nl}(r) \ Y_{l}^{m}(\theta,\phi), \ E(n,l) \]
ladder of energy levels like H atom, but all ls allowed

b) strong coupling of spin and orbit angular momentum
quantized total: \( j = l \pm 1/2 \) for spin 1/2 particle
larger \( j \), lower energy (usually)
Shell Model Rules Continued

c) Treat protons and neutrons separately and fill from bottom up assuming \(2j + 1\) degeneracy.

d) Assume particle pair strongly within levels: only unpaired spins count - total spin angular momentum given by \(j\) of level for unpaired spin.

e) Sign of moment depends on sign of moment for fundamental particle but changes sign when moment subtracts instead of adds to \(l\) in giving \(j\).
## Energy Level Diagram

<table>
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<th>j</th>
<th>degeneracy</th>
<th>total</th>
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<tr>
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Examples of Nuclear Properties

• $^{16}_8$O - most abundant in Earth’s crust. 8 protons, 8 neutrons - 2 magic #s. All particles paired - no moment.

• $^{13}_6$C - 6 protons, 7 neutrons. All protons paired. One neutron unpaired in $1p_{1/2}$. $j = l - 1/2$. Therefore, negative moment subtracts from $l$. Positive $\gamma$ spin $1/2$ particle