Introduction to Nuclear Magnetic Resonance Spectroscopy

Dr. Dean L. Olson, NMR Lab Director
School of Chemical Sciences
University of Illinois

Called figures, equations, and tables are from “Principles of Instrumental Analysis, 6th Ed.” Skoog, Holler, and Crouch, 2007; Thompson Corp.

http://www.cis.rit.edu/htbooks/nmr/
NMR basic layout & components

- Superconducting Magnet
- Console (Transceiver)
- Workstation
- NMR Probe (the transceiver antenna placed inside magnet bore; only seen from below)
NMR basic layout & components
A variety of configurations; UIUC has all Agilent/Varian equipment

NMR Workstation Computer and Superconductive Magnet

NMR console:
Latest Agilent/Varian Style
NMR components

- **Workstation computer**
- **NMR Console**
  - Creates and receives pulses
- **Magnet** (inside a Dewar)
  - Overhead perspective; solenoid inside
- **NMR Probe**: really a transceiver antenna (inside magnet)

Photos from www.jeol.com
Nuclear Magnetic Resonance

- NMR is based on the behavior of a sample placed in an electromagnet and irradiated with radiofrequency waves: 60 – 900 MHz ($\lambda \approx 0.5$ m)
  - The magnet is typically large, strong, $$, and delivers a stable, uniform field – required for the best NMR data; New 500 MHz Bruker: $910K$
  - A transceiver antenna, called the NMR probe, is inserted into the center bore of the magnet, and the sample is placed inside the probe
    - Sample can be in a narrow tube, or
    - Sample can flow in via an autosampler
- Qualitative or Quantitative; liquid or solid
- Universal proton (others) detector; non-destructive
NMR, continued

- **NMR** is a chemical analysis technique
- **MRI** = magnetic resonance imaging; usually an imaging technique, but has also become a chemical method called functional MRI (fMRI)
  - MRI is also non-destructive
  - Prof. Paul Lauterbur, UIUC, Nobel Laureate for Medicine or Physiology, 2003, with Sir Peter Mansfield, U. Nottingham
  - MRI is really **NMRI**; the MRI industry cleverly omitted the “nuclear” from their product for easier marketing to the public
A plaque just outside Chemical Life Sciences Laboratory A commemorating Paul Lauterbur, Professor of Chemistry, U of Illinois. Nobel Prize, 2003 for MRI

Another plaque, outside Noyes Lab (SE corner), honors Herb Gutowsky Professor of Chemistry, U of Illinois. He was the first to “apply the nuclear magnetic resonance method to chemical research. His experimental and theoretical work on the chemical shift effect and its relation to molecular structure.”

NMR components

Magnet (inside a Dewar)

Overhead perspective; solenoid inside

NMR Probe (inside magnet)

Pneumatic Legs (to stabilize vibrations)
U. Bristol, United Kingdom
14.1 Tesla magnet

Termed a
“600 MHz” magnet

600 MHz is the frequency (energy) at which the proton (1H) nucleus spin resonates – in a magnet of this strength (14.1 Tesla)

1000 MHz is equivalent to 23.5 Tesla

Varian became Agilent in late 2010; Agilent left the NMR business in November 2014; a shocker
The magnet is superconducting, always charged, but not powered, and surrounded by liquid helium (4.2 K) and the LHe is surrounded by liquid nitrogen (77 K). The current is “coasting”, that is, persistent, uniform, & stable.

The big white tanks outside Noyes and RAL hold liquid N$_2$ for NMR and other cold stuff. No high pressures are involved; vented. T = -196°C.

U. Bristol, United Kingdom
14.1 Tesla magnet

Termed a “600 MHz” magnet

600 MHz is the frequency at which the proton (¹H) nucleus spin resonates – in a magnet of this strength.
NMR magnet cut-away

In the Atrium of Chemical Life Sciences Lab A
A typical NMR sample tube: 7-8 inches long; 5 mm outer diameter. Inserted into the NMR probe from above either manually or using automation.

NMR sample handling options

- Spinning tube NMR
- Sample syringe
- Sample vial
- Automated Flow NMR – Chem 237
- Pumps and solvents
- Autosampler
How does NMR work?

**B₀** = Static Magnetic Field
from the big supercon magnet:
Persistent Field

Probe Coils create the **Transverse (B₁)** Field
from a current pulse of **time t**
2 Helmholtz Coils: One inside the other for tube NMR. One coil for protons, the other for carbon. The inner coil is the most sensitive.

Solenoidal Microcoil for flow NMR; one coil does it all
NMR depends on the spin of the nucleus under study – the most common is $^1H$

- **Nuclear spin in an applied magnetic field**
  - A magnetic dipole, $\mu$, is produced
  - The spin **precesses**
  - The spin is quantized
  - $^1H$ has a **spin quantum number** of either $+\frac{1}{2}$ (low E) or $-\frac{1}{2}$ (high E)
  - Many nuclei have suitable spin quantum numbers for NMR:
    - $^{13}C$ (only 1.1% abundance)
    - $^{19}F$
    - $^{31}P$
    - $^{14}N$
  - Many nuclei are **not** NMR active:
    - $^{12}C$ (sadly) & $^{16}O$ (also sadly)

Fig. 19-2
Think about the **precession** of the nuclear spin:
It’s how the nucleus absorbs and releases energy

The pulse ends here. Energy release begins.

The Free Induction Decay or FID

https://www.youtube.com/watch?v=A0dl4_wxr1c
NMR depends on the spin of the nucleus under study: the magnetogyric ratio

\[ \gamma = \frac{\mu}{p} \]

\( \gamma \) = magnetogyric ratio
\( \mu \) = dipole moment
\( p \) = angular momentum

Magnetogyric ratio = gyromagnetic ratio: It’s different for each type of nucleus. The bigger the better.

Eqn. 19-1, slightly modified to be a ratio

---

**TABLE 19-1 Magnetic Properties of Important Nuclei with Spin Quantum Numbers of 1/2**

<table>
<thead>
<tr>
<th>Nucleus</th>
<th>Magnetogyric Ratio, radian T(^{-1}) s(^{-1})</th>
<th>Isotopic Abundance, %</th>
<th>Relative Sensitivity(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(^1)H</td>
<td>(2.6752 \times 10^8)</td>
<td>99.98</td>
<td>1.00</td>
</tr>
<tr>
<td>(^{13})C</td>
<td>(6.7283 \times 10^7)</td>
<td>1.11</td>
<td>0.016</td>
</tr>
<tr>
<td>(^{19})F</td>
<td>(2.5181 \times 10^8)</td>
<td>100.00</td>
<td>0.83</td>
</tr>
<tr>
<td>(^{31})P</td>
<td>(1.0841 \times 10^8)</td>
<td>100.00</td>
<td>0.066</td>
</tr>
</tbody>
</table>

\(^a\)At constant field for equal number of nuclei.
In a magnetic field, the spin has two quantized energy states called high and low.

\[ E = -\frac{\gamma m \hbar}{2\pi} B_o \]

\[ E_{-1/2} = \frac{\gamma \hbar}{4\pi} B_o \]

\[ E_{+1/2} = -\frac{\gamma \hbar}{4\pi} B_o \]

\[ \Delta E = \frac{\gamma \hbar}{2\pi} B_o \]

\( m = \) spin quantum number
\( m = -\frac{1}{2} \) for high energy; opposed
\( m = +\frac{1}{2} \) for low energy; aligned

\( \Delta E = \) high - low

\( B_o \) in Tesla (T)
\( \) and \( E \) in Joules (J);
\( B_o \) is the static field.
In a magnetic field, the spin has two quantized energy states called high and low.

\[ E_{+1/2} = -\frac{\gamma}{4\pi} \frac{h}{B_0} \]

Low E; aligned

\( m = \) spin quantum number
\( m = -\frac{1}{2} \) for high energy; opposed
\( m = +\frac{1}{2} \) for low energy; aligned

Fig. 19-2
In a magnetic field, the spin has **two** quantized energy **states** called **high** and **low**.

![Diagram](image)

- **High E; opposed**
  - $m = -\frac{1}{2}$
  - Magnetic moments
  - $B_0$
  - $\mu_z$

- **Low E; aligned**
  - $m = +\frac{1}{2}$
  - Magnetic moments
  - $B_0$
  - $\mu_z$

**Energies**

- **Applied field $B_0$**
  - $E = \frac{\gamma h}{4\pi} B_0$
  - $m = -\frac{1}{2}$

- **No field**
  - $\Delta E = \frac{\gamma h}{2\pi} B_0$
  - $E = -\frac{\gamma h}{4\pi} B_0$
  - $m = +\frac{1}{2}$

**Fig. 19-1**
$\Delta E$ depends on the applied $B_o$

$$E_{-1/2} = \frac{\gamma h}{4\pi} B_o$$

$$E_{+1/2} = -\frac{\gamma h}{4\pi} B_o$$

Slope $= \frac{\gamma h}{4\pi}$

The stronger the magnet, the larger the $\Delta E$

http://www2.chemistry.msu.edu/faculty/reusch/VirtTxtJml/Spectrpy/nmr/nmr1.htm
So, where does the NMR signal come from?

The NMR probe coil both transmits and receives: it’s a transceiver.

The spin is **pulsed** by the NMR probe, then the **spin relaxation** produces the signal.
At equilibrium, the low spin state is slightly favored – otherwise, no NMR signal.

\[
\frac{N_{\text{Hi}}}{N_{\text{Lo}}} = e^{\left(-\frac{\gamma h B_o}{2\pi k T}\right)}
\]

Boltzmann Distribution Equation for quantum spin states in a magnetic field

In Example 19-2 (p. 501), for 1,000,000 atoms of hydrogen, \(^1\text{H}\), in the high energy state:

- \(B_o = 4.69\) Tesla (termed a 200 MHz spectrometer; named after H frequency)
- \(T = 20^\circ\text{C}\)
- \(\gamma = 2.6752 \times 10^8\ T^{-1}\ \text{sec}^{-1}\)
- \(N_{\text{Hi}} / N_{\text{Lo}} = 0.999967\)
- For \(N_{\text{Hi}} = 1,000,000\) then \(N_{\text{Lo}} = 1,000,033\)
- \(\Delta N = 33\) or just 33 ppm of all the spins present are available for NMR because all the rest of the spins are in a dynamic equilibrium
- *This is why NMR is a relatively insensitive technique → unfortunate.*

Thus, big $$$ magnets.
What does NMR data look like?

This is the acquired signal from the spin relaxation. The precession rotates and each one gives a wave.

https://www.youtube.com/watch?v=A0dl4_wxr1c

Time (a few sec of relaxation after 1 pulse)

A signal is seen for each type of proton and each has its own frequency (energy) depending on its own electronic environment.

This is what you look at and analyze: An NMR spectrum

Same normalized scale for all magnet strengths

\[
\frac{\Delta \nu}{\nu_{\text{reference}}} \times (1 \times 10^6) = \text{shift in ppm, } \delta
\]
Understanding NMR Spectra

Deshielded protons absorb more energy*

Increasing Frequency at Fixed Magnetic Field
Increased Shielding by Extranuclear electrons

Si is not electron withdrawing

Cl₃C\(=\text{O}\)

Cl\(=\text{C}\)=Cl

H₃C-NO₂

H₃C-S=O

H₃C-Si-CH₃

H₂C-O-CH₂

H₂C-C≡O

H₃C-C-CH₃

*The e- are pulled away from the H and do a poor job of protecting the nucleus from the magnetic field

Oxygen is electron withdrawing

http://www2.chemistry.msu.edu/faculty/reusch/VirtTxtJml/Spectrpy/nmr/nmr1.htm
Understanding NMR Spectra

Increasing Frequency at Fixed Magnetic Field

The Separation of Resonance Signals (in Hz) Increases with Increasing Field Strength

http://www2.chemistry.msu.edu/faculty/reusch/VirtTxtJml/Spectrpy/nmr/nmr1.htm
Understanding NMR Spectra

Chemical Shift

\[ \delta = \left( \frac{\nu_{\text{samp}} - \nu_{\text{ref}}}{\nu_{\text{ref}}} \right) \times 10^6 \]

Small magnet \( B_0 = 2.34 \, T \) \{
- 7.34 ppm at 734 Hz
- 5.30 ppm at 530 Hz
\}

Large magnet \( B_0 = 11.75 \, T \) \{
- 3670 Hz
- 2650 Hz
- 1075 Hz
\}

http://www2.chemistry.msu.edu/faculty/reusch/VirtTxtJml/Spectrpy/nmr/nmr1.htm
Understanding NMR Spectra

Increasing Frequency at Fixed Magnetic Field
Increased Shielding by Extranuclear electrons

These ppm are for ALL magnets

http://www2.chemistry.msu.edu/faculty/reusch/VirtTxtJml/Spectrpy/nmr/nmr1.htm
NMR Spectral Nomenclature

- Deshielded
- High frequency
- Downfield
- Low field

Left side of spectrum

- Shielded
- Low frequency
- Upfield
- High field

Right side of spectrum

*The e- are pulled away from the H and do a poor job of protecting the nucleus from the magnetic field

http://www2.chemistry.msu.edu/faculty/reusch/VirtTxtJml/Spectrpy/nmr/nmr1.htm
But, the spins couple - they interact

For 2 proton neighbors:
• Each proton has its own spin
• The spin can be $+\frac{1}{2}$ or $-\frac{1}{2}$
• We can draw all the combinations:

Skoog, Page 515

Relative spin population

$B_0 \rightarrow$

Field direction

High E; opposed

Possible spin orientations of methylene protons

Low E; aligned

Degenerate: both cases have the same energy

$\begin{align*}
\text{Relative spin population:} & \quad 1 \quad 2 \quad 1 \\
\text{Field direction:} & \quad B_0 \rightarrow \\
\text{Possible spin orientations:} & \quad \text{High E; opposed} \quad \text{Low E; aligned}
\end{align*}$
But, the spins couple - they interact

For 3 proton neighbors:
- Each proton has its own spin
- The spin can be $+\frac{1}{2}$ or $-\frac{1}{2}$
- We can draw all the combinations:

Relative spin population

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>3</th>
<th>3</th>
<th>1</th>
</tr>
</thead>
</table>

High E; opposed

Low E; aligned

Degenerate: all 3 cases have the same energy
The principle of multiplicity: the $n + 1$ rule and peak splitting

$n$ is the number of adjacent (neighboring) protons that are in a different chemical environment

**Multiplicty, $m = n + 1$**

<table>
<thead>
<tr>
<th>Number of Equivalent Protons, $n$</th>
<th>Multiplicity, $(n + 1)$</th>
<th>Relative Peak Areas</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>1 1</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>1 2 1</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>1 3 3 1</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>1 4 6 4 1</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
<td>1 5 10 10 5 1</td>
</tr>
<tr>
<td>6</td>
<td>7</td>
<td>1 6 15 20 15 6 1</td>
</tr>
<tr>
<td>7</td>
<td>8</td>
<td>1 7 21 35 35 21 7 1</td>
</tr>
</tbody>
</table>
The principle of multiplicity: a signal gets split based on what it’s next to

\[ m = n + 1 \]

<table>
<thead>
<tr>
<th>No Coupled Hydrogens</th>
<th>( n = 0 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>[ \text{H} ] C C C H</td>
<td>1</td>
</tr>
<tr>
<td>[ \text{H} ] C C C [ \text{H} ]</td>
<td>2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>One Coupled Hydrogen</th>
<th>( n = 1 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>[ \text{H} ] C C C H</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Two Coupled Hydrogens</th>
<th>( n = 2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>[ \text{H} ] C C C [ \text{H} ]</td>
<td>4</td>
</tr>
</tbody>
</table>

The splitting is called J coupling.

Proximity is important.

Pascal's Triangle:

- Singlet
- Doublet
- Triplet
- Quartet
Do they split – or not?

Determining Equivalent Hydrogens in $^1$H NMR Spectroscopy

The hydrogens in the structure of a molecule can be grouped together based on their individual molecular environments (i.e., where each hydrogen is located in the molecule’s structure). Hydrogens that are in identical molecular environments in a molecule are chemically equivalent. Chemically equivalent hydrogens have the same chemical shift in a $^1$H NMR spectrum, so they show up as a single signal.

For example, all six hydrogens in ethane are chemically equivalent; they are all in the same molecular environment, so only one signal is seen in ethane’s $^1$H NMR spectrum.

![Ethane structure]

This will yield a spectrum with one NMR singlet.
Protons are not split by identical neighbors.

Chemically equivalent hydrogens are called homotopic hydrogens. Two hydrogens must be in identical molecular environments for them to be homotopic.

http://cobalt.rocky.edu/~barbaroj/equivalent_hydrogens.pdf
Do they split – or not?

Hydrogens in a molecule that are in different molecular environments are **chemically nonequivalent**. Chemically nonequivalent hydrogens have different chemical shifts in the $^1\text{H}$ NMR spectrum of the compound and show separate signals. For example, the eight hydrogens in propane are not chemically equivalent. The six methyl hydrogens are chemically equivalent, as are the two methylene hydrogens, but the two methylene hydrogens are in a different molecular environment than the six methyl hydrogens.

![Propane molecule diagram](http://cobalt.rocky.edu/~barbaroj/equivalent_hydrogens.pdf)

The methyl hydrogens and the methylene hydrogens in propane are chemically nonequivalent. These two groups of nonequivalent hydrogens have different chemical shifts and will show up as two separate signals in a $^1\text{H}$ NMR spectrum. Chemically nonequivalent hydrogens are called **heterotopic hydrogens**. In order for two hydrogens to be heterotopic, they must be in different molecular environments. In theory, every group of nonequivalent hydrogens gives rise to a separate signal in the $^1\text{H}$ NMR spectrum.
$^1$H-NMR Spectrum of Propane

$\text{CH}_3 - \text{CH}_2 - \text{CH}_3$

a b a

a (triplet)

b (septet)

Area ratios??
$^1$H-NMR Spectrum of Propane

CH$_3$ – CH$_2$ – CH$_3$

a         b       a

b (septet)

Area ratios??

a (triplet)
Relative total areas: B:C:A
3:2:3

Splitting relative areas 1:3:3:1

Most deshielded protons

90-MHz Magnet

Splitting relative areas 1:2:1

Least deshielded protons

J_{AC} = 7.2 \text{ Hz}
NMR Data Interpretation – Example 2

See if you can work out the spectral details yourself! (areas in green)

Most shielded protons?

90-MHz Magnet
NMR Chemical Shifts – helps interpret data

Proton Chemical Shift Ranges*

* For samples in CDCl₃ solution. The δ scale is relative to TMS at δ = 0.
To get a predicted NMR spectrum, all you need is a ChemDraw Structure, and the Mnova software we provide free to everyone on campus:

http://www.scs.illinois.edu/nmr/handouts/mnova.php
Other Things NMR Can Mean
	no membership required