Introduction to Nuclear Magnetic Resonance Spectroscopy

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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

- Workstation
- Console (Transceiver)
- Superconducting Magnet
- 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
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
  - 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 is also becoming 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**

- 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
NMR components

Magnet (inside a Dewar)

Overhead perspective; solenoid inside

NMR Probe (inside magnet)

Pneumatic Legs (to stabilize vibrations)

NMR Probe
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 (14.1 Tesla)

1000 MHz is equivalent to 23.5 Tesla

Varian is now Agilent as of late 2010

B₀ = Static Magnetic Field
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.

The magnet is superconducting, always charged, but not powered, and surrounded by liquid helium (4.2 K) and the He 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 N₂ for NMR and other cold stuff. No high pressures are involved; vented.
NMR magnet cut-away

In the Atrium of Chemical Life Sciences Lab A
A typical NMR sample tube: 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
- Automated flow NMR

Pumps and solvents

Sample syringe

Sample vial

Autosampler
How does NMR work?

\[ B_0 = \text{Static Magnetic Field} \]

from the big supercon magnet: persistent

Probe Coils create the Transverse \( B_1 \) Field from a current pulse of time \( t \)
2 Helmholtz Coils: 1 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.

http://www.bioc.aecom.yu.edu/labs/girvlab/nmr/course/COURSE_2010/Lab_1.pdf
NMR depends on the **spin of the nucleus** under study – the most common is $^1\text{H}$

- **Nuclear spin in an applied magnetic field**
  - A magnetic dipole, $\mu$, is produced
  - The spin precesses
  - The spin is quantized
  - $^1\text{H}$ 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:
    - $^{13}\text{C}$ (only 1.1% abundance)
    - $^{19}\text{F}$
    - $^{31}\text{P}$
    - $^{14}\text{N}$
  - Many nuclei are **not** NMR active:
    - $^{12}\text{C}$ (sadly) & $^{16}\text{O}$ (also sadly)
NMR depends on the spin of the nucleus under study: the magnetogygycric ratio

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

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

Magnetogygycric 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>
<thead>
<tr>
<th>Nucleus</th>
<th>Magnetogygycric 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.

- **m** = spin quantum number
- **m = - ½** for high energy; opposed
- **m = + ½** for low energy; aligned

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

Low E; aligned
In a magnetic field, the spin has **two** quantized energy **states** called high and low.

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

$\Delta E = \frac{\mu B_x}{I}$

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

Proton Spin Energy Differences

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.

The Boltzmann Distribution Equation for quantum spin states in a magnetic field is given by:

$$\frac{N_{Hi}}{N_{Lo}} = e^{\left(\frac{-\gamma h B_0}{2 \pi k T}\right)}$$

In Example 19-2 (p. 501), for 1,000,000 atoms of hydrogen, $^1$H, in the high energy state:
- $B_0 = 4.69$ Tesla
- $T = 20 ^\circ C$
- $\gamma = 2.6752 \times 10^8 \text{ T}^{-1} \text{ sec}^{-1}$
- $N_{Hi} / N_{Lo} = 0.999967$
- For $N_{Hi} = 1,000,000$ then $N_{Lo} = 1,000,033$
- $\Delta N = 33$ 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.

Time (a few sec of relaxation for 1 pulse)

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

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

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

Same normalized scale for all magnet strengths.
Understanding NMR Spectra

Deshielded protons absorb more energy*

Increasing Frequency at Fixed Magnetic Field

Increased Shielding by Extranuclear electrons

Si is not electron withdrawing

*The e- are pulled away from H and do a poor job of blocking 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
Understanding NMR Spectra

Chemical Shift

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

Increasing Frequency at Fixed Magnetic Field

Small magnet  \( B_o = 2.34 \text{ T} \) \{ 734 Hz \}

Large magnet  \( B_o = 11.75 \text{ T} \) \{ 3670 Hz \}

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

These ppm are for ALL magnets

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

- Deshielded
- High frequency
- Downfield
- Low field

- Shielded
- Low frequency
- Upfield
- High field

*The e- are pulled away and do a poor job of blocking the magnetic field

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

For 2 protons:
• 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

Skoog, Page 515

- High E; opposed
- Low E; aligned

Possible spin orientations of methylene protons

Degenerate: both cases have the same energy
But, the spins couple - they interact

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

<table>
<thead>
<tr>
<th>Relative spin population</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

\[ \text{Multiplicity, } m = n + 1 \]

### TABLE 19-3 Relative Intensities of First-Order Multiplets (\( I = 1/2 \))

<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</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>6</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>7</td>
<td>8</td>
<td>1</td>
</tr>
</tbody>
</table>

Pattern follows Pascal’s triangle

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The principle of multiplicity: a signal gets split based on what it’s next to.

- No Coupled Hydrogens, $n = 0$
- One Coupled Hydrogen, $n = 1$
- Two Coupled Hydrogens, $n = 2$
- Three Coupled Hydrogens, $n = 3$

The splitting is called J coupling.

Proximity is important.
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.

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.
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 \(^1\)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.

\[
\text{Propane:} \quad \begin{array}{c}
\text{H} & \text{H} & \text{H} \\
\text{H} & \text{C} & \text{C} & \text{C} & \text{H} \\
\text{H} & \text{H} & \text{H}
\end{array}
\]

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 \(^1\)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 \(^1\)H NMR spectrum.)

http://cobalt.rocky.edu/~barbaroj/equivalent_hydrogens.pdf
$^1$H-NMR Spectrum of Propane

CH$_3$ – CH$_2$ – CH$_3$

a  b  a

a (triplet)

b (septet)

Area ratios??
NMR Data Interpretation – Example 1

Relative total areas:
C:B:A
2:3:3

Most deshielded protons?

Splitting relative areas
1:3:3:1

Splitting relative areas
1:2:1

90-MHz Magnet

90 MHz Magnet
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 CDCl$_3$ solution. The δ scale is relative to TMS at δ = 0.
NMR data interpretation – watch the video!

http://mestrelab.com/software/mnova-nmrpredict-desktop/
Other Things NMR Can Mean

no membership required

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Nightingale Moon Records

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