NMR
NMR is a nondestructive technique that gives exact positions of atoms in the molecule. Before NMR organic chemical structure was always ambiguous or inferred. NMR changes all that.

Order of topics
1. Practical NMR. How to use NMR to assign chemical structure.
2. Modern NMR – 2D and DEPT.

$^1$H NMR
$^1$H is 99.99% abundant. What are the other forms of H?

A little bit of how NMR works:
When you put a molecule in an external magnetic field, the electrons around the $^1$H affect the way that the $^1$H aligns in the magnetic field, this alignment relates to energy in that there is an easy alignment and a hard alignment with the external magnetic field. Easy alignment is low energy and harder alignment is high energy. The NMR spectrum is split into regions corresponding to the energies created by the interactions of the orbitals surrounding the H.

http://www.shu.ac.uk/schools/sci/chem/tutorials/molspec/nmr1.htm

Nuclear spin and the splitting of energy levels in a magnetic field

Subatomic particles (electrons, protons and neutrons) can be imagined as spinning on their axes. In many atoms (such as $^{12}$C) these spins are paired against each other, such that the nucleus of the atom has no overall spin. However, in some atoms (such as $^1$H and $^{13}$C) the nucleus does possess an overall spin. The rules for determining the net spin of a nucleus are as follows;

1. If the number of neutrons and the number of protons are both even, then the nucleus has NO spin.
2. If the number of neutrons plus the number of protons is odd, then the nucleus has a half-integer spin (i.e. 1/2, 3/2, 5/2)
3. If the number of neutrons and the number of protons are both odd, then the nucleus has an integer spin (i.e. 1, 2, 3)

The overall spin, $I$, is important. Quantum mechanics tells us that a nucleus of spin $I$ will have $2I + 1$ possible orientations. A nucleus with spin 1/2 will have 2 possible orientations. In the absence of an external magnetic field, these orientations are of equal energy. If a magnetic field is applied, then the energy levels split. Each level is given a magnetic quantum number, $m$.

**Energy levels for a nucleus with spin quantum number 1/2**

When the nucleus is in a magnetic field, the initial populations of the energy levels are determined by thermodynamics, as described by the Boltzmann distribution. This is very important, and it means that the lower energy level will contain slightly more nuclei than the higher level. It is possible to excite these nuclei into the higher level with electromagnetic radiation. The frequency of radiation needed is determined by the difference in energy between the energy levels. The difference is about 1 in a million or ppm.
Imagine a nucleus (of spin 1/2) in a magnetic field. This nucleus is in the lower energy level (i.e. its magnetic moment does not oppose the applied field). The nucleus is spinning on its axis. In the presence of a magnetic field, this axis of rotation will precess around the magnetic field;

If energy is absorbed by the nucleus, then the angle of precession, \( q \), will change. For a nucleus of spin 1/2, absorption of radiation “flips” the magnetic moment so that it opposes the applied field (the higher energy state).

http://www.shu.ac.uk/schools/sci/chem/tutorials/molspec/nmr1.htm
The frequency of precession is termed the *Larmor frequency*, which is identical to the transition frequency.

The magnetic field at the nucleus is not equal to the applied magnetic field; electrons around the nucleus shield it from the applied field. The difference between the applied magnetic field and the field at the nucleus is termed the *nuclear shielding*. Consider the s-electrons in a molecule. They have spherical symmetry and circulate in the applied field, producing a magnetic field which opposes the applied field. This means that the applied field strength must be increased for the nucleus to absorb at its transition frequency. This *upfield shift* is also termed *diamagnetic shift*.

The energies are plotted on a scale of about 0-10
0 relates to low energy and 12 relates to high energy transitions.
0 is called shielded and >10 is called deshielded meaning that the proton is less or more susceptible to the external magnetic field.
0 is called upfield and 10 is called downfield – this is historical when NMR was done on chart recorders.
**Chemical shift**  The energy of the NMR absorption is related to functional group.

- 0-2 \( \text{H-C saturated} \) \( \text{sp}^3\text{C-H} \)
- 2-3 \( \text{H-C allyl} \) \( \text{sp}^2\text{C-sp}^3\text{C-H} \)
- 3-4 \( \text{H-C-EN} \ (\text{EN}=\text{N,O,F,Cl,Br,I}) \) usually \( \text{sp}^3\text{C-H} \)
- 5-6 \( \text{H-C vinyl} \) \( \text{sp}^2\text{C-H} \)
- 6-8 \( \text{H-C aromatic} \) \( \text{sp}^2\text{C-H} \)

You can have multiple effects. \( \text{CH}_2\text{Cl} \) \( \text{CH}_2\text{Cl}_2 \) \( \text{CHCl}_3 \)

Every Cl exerts about a 2 ppm shift. Assumes that a normal proton in a completely saturated environment is about 1 ppm. (0-2 ppm).

NMR scale is based on minute differences from the magnetic field. The absolute energy scale is in Hz. Hz is an energy unit because \( E = h \nu \) and \( \nu \) is frequency \( c/\lambda \). We use relative energy differences based on the strength of the magnetic field. If the field is 200 MHz, a ppm is how many Hz? ________________

How many Hz/ppm for a 400 MHz magnetic field? ________________

Real NMR spectra

![NMR spectra CH4 and H3C-Cl](image)

Note. Is the \(^1\text{H}\) NMR scale based on 0 being methane?

![NMR spectra H2C-Cl and HC-Cl](image)

What would the \(^1\text{H}\) spectrum of \( \text{CCl}_4 \) look like?
Organic Compounds with many $^1$H's.

Integration = relative number of protons. Area under peaks. A ratio of number of protons. Integration is not intensity, but might be for some resonances. Which spectrum for which molecule?

Predict the ratios of the proton areas in these compounds:

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

Below are peaks based on equivalence.
Equivalence. Many times H’s have degenerate energy transitions in the NMR. The analytical method is to identify symmetry elements. Or alternatively, replace an H with an X. If replacing various H’s leads to the same isomer, then the H is called equivalent. This is a unique kind of $^1$H.

http://www.cem.msu.edu/~reusch/VirtualText/Spectrpy/nmr/nmr1.htm#nmr2
**Spin-Spin Splitting** – The interaction of local magnetic fields on H’s on neighboring C’s

Splitting = \( n + 1 \) nearest neighbors in a Pascal’s triangle intensity pattern:

<table>
<thead>
<tr>
<th># neighbors</th>
<th>lines</th>
<th>label</th>
<th>intensity ratios</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 neighbors</td>
<td>1 line</td>
<td>singlet</td>
<td>1</td>
</tr>
<tr>
<td>1 neighbors</td>
<td>2 lines</td>
<td>doublet</td>
<td>1 1</td>
</tr>
<tr>
<td>2 neighbors</td>
<td>3 lines</td>
<td>triplet</td>
<td>1 2 1</td>
</tr>
<tr>
<td>3 neighbors</td>
<td>4 lines</td>
<td>quartet</td>
<td>1 3 3 1</td>
</tr>
<tr>
<td>4 neighbors</td>
<td>5 lines</td>
<td>pentet</td>
<td>1 4 6 4 1</td>
</tr>
<tr>
<td>5 neighbors</td>
<td>6 lines</td>
<td>sextet</td>
<td>1 5 10 10 5 1</td>
</tr>
<tr>
<td>6 neighbors</td>
<td>7 lines</td>
<td>septet</td>
<td>1 6 15 20 15 6 1</td>
</tr>
</tbody>
</table>

Patterns look like this when equivalent or near-equivalent sets of protons are nearest neighbors.

**Neighbor H – H Interactions**

[Image of H-H interactions]

**Geminal Hydrogens**

[Image of geminal hydrogens]

**Vicinal Hydrogens**

[Image of vicinal hydrogens]

**Important Note** Equivalent \(^1\)Hs do not split each other. Splitting must be for non-equivalent \(^1\)Hs. Why?

Analyze ethanol:

[Image of ethanol spectrum]

**Applied field**

[Image of applied field for methylene protons]

**Spin orientations of methylene protons**

[Image of spin orientations for methylene protons]

**Methyl triplet**

**Methylene quartet**

[Image of methyl and methylene quartet]

[Image of applied field for methyl protons]

**Spin orientations of methyl protons**

[Image of spin orientations for methyl protons]
Examples: How many nearest neighbors?

http://www.cem.msu.edu/~reusch/VirtualText/Spectrpy/nmr/nmr1.htm#nmr2

The coupling constant is called $J$. Note sets of coupled H's will always have the same $J$.

$J$ values depend on hybridization, geometry and other electronic factors.

$J$ is always measured in Hz.

How many bonds is a normal $J$ coupling?

Range of $J$ couplings

Vicinal Coupling

\[ \text{H}_3\text{C}-\text{CH}_2-\text{CH}_3 \]

0 Hz

\[ \text{H}_3\text{C}-\text{CH}_2-R \]

6 - 8 Hz

Geminal Coupling

\[ \text{X} \text{H} \text{Y} \]

1 – 3 Hz

Coupling through Pi bonds:

\[ \text{H} \text{H} \]

12 - 18 Hz
Long Range coupling through Pi bonds.

$R_2C\equiv\text{H}$

3 – 8 Hz

$\text{H}^+_\text{O} \quad \text{H}^+_\text{R}_2\equiv\text{H}$

1 – 3 Hz

Coupling Patterns for nonequivalent Hydrogens

No Coupled Hydrogens

One Coupled Hydrogen

Two Coupled Hydrogens

Three Coupled Hydrogens

http://www.cem.msu.edu/~reusch/VirtualText/Spectrpy/nmr/nmr1.htm#nmr2
Common $^1$H NMR Patterns: Match the groups and assign peaks. Ethyl, Propyl and Isopropyl: $\text{C}_2\text{H}_5\text{Br}$

- $\text{C}_2\text{H}_5\text{Br}$
- $\text{C}_3\text{H}_7\text{Br}$
- $\text{C}_3\text{H}_7\text{Br}$
The 4-carbon molecules:
\[ \text{C}_4\text{H}_9\text{Br}: \text{Butyl, Isobutyl, sec-Butyl, ter-Butyl} \]

Which butyl is missing? What would the \(^1\)H NMR of the missing group look like?
$^{13}$C NMR  Like proton NMR but different. $^{13}$C NMR is based on 0 – 200 ppm. Since this is 20 times $^1$H, just multiply by 20.

1. Chemical shifts are not as predictable as proton, but this is a guide.
   - 0-40  H-C saturated
   - 40-60  H-C allyl
   - 60-80  H-C-EN (EN=N,O,F,Cl,Br,I)
   - 100-120  H-C vinyl
   - 120-160  H-C aromatic with the bonus of C=O, around 200 ppm.

2. Integration = not used too much. It is difficult to integrate $^{13}$C.

3. Splitting = we usually ignore splitting. We usually blast the splitting away with microwave energy. Most $^{13}$C NMR spectra that you will see are a forest of lines. $^{13}$C is about 1.1% of the C in any molecule. Therefore, what are the chances of two $^{13}$C being next to each other? What are the chances of two $^1$H – $^1$H being near each other?

4. Equivalence. This is the main point of $^{13}$C NMR. You can tell at a glance the number of unique carbons that are present in a molecule. This is very useful indeed.

Here are some examples of what $^{13}$C NMR look like.

C$_3$H$_7$Br  The two propyl spectra are clearly indicative of the actual structure.
Notice how the top two spectra are ambiguous, but the bottom two are clearly indicative of the correct structure. What would you need to distinguish the top two?
Problem Solving H-NMR spectra
1. Take formula and derive the degrees of unsaturation.
2. Determine the number of H’s by integration and match the formula.
3. Determine the chemical shift regions of each H.
4. Create fragments ready to assemble.
5. Assemble fragments based on splittings.

C₉H₁₂O
Degrees of unsaturation
More C_2H_4O IR shows broad peak between 3300-3600

![NMR spectrum of C_2H_4O with labels for peaks at 2H, 1H, and 9H at different ppm values.]

![NMR spectrum of another compound with labels for peaks at 5H, 2H, 2H, 1H, and 2H at different ppm values.]

NMR-02-926
NMR-06-238
More C₉H₁₂O. IR shows broad peak between 3300-3600.
A strong IR peak at 1700 cm\(^{-1}\) and at 1250 cm\(^{-1}\)

\[ C_6H_{10}O_2 \]

\[ {^{13}}C \text{ NMR} \]
Enhancements on $^{13}$C NMR

Consider $C_8H_{10}$

DEPT spectrum of ethyl benzene

http://www.chem.ucla.edu/cgi-bin/webspectra.cgi?Problem=bp21&Type=D
In the DEPT spectra, the C with an odd number of attached H have a positive phase (up) and those with an even number of H have a negative phase (down).

2-D NMR


http://www.cis.rit.edu/htbooks/nmr/chap-10/j4-1.htm
More H-H COSY

http://www.chem.ualgary.ca/courses/351/Carey5th/Ch13/ch13-2dnmr-1.html#hetcor
$^1H^{13}C$ COSY

http://www.chem.ucalgary.ca/courses/351/Carey5th/Ch13/ch13-2dnmr-1.html#hetcor