Short Summary of 1H-NMR Interpretation

I. Number of Signal Sets
II. Integration   These **must be simple whole-number ratios** (2:1, 3:1, 3:2, etc..)

III. "Chemical Shifts" of the Signal Sets

9's (9.0-10.0)   **Aldehyde** sp^2 hybridized C-H's

7's (6.5-8.4)   **Aromatic** sp^2 hybridized C-H's

5's (4.8-6.8)   **Alkene** sp^2 hybridized C-H's

3's (2.8-4.5)   **Oxygenated** or **Halogenated** sp^3 hybridized C-H's.
Oxygenated sp^3–carbons are routinely present for the following functional groups that contain oxygen single bonds:
- **alcohols**, (usually signal in 3's)
- **ethers**, (usually signal in 3's)
- **esters** (usually signal in low 4's)

2's (1.8-2.8)   **Allylic** sp^3 hybridized C-H's (sp^3 hybridized C-H's that has a double bond attached to the sp^3 hybridized C). Allylic signals routinely appear when one of the following double-bonded functional groups is present:
- **carbonyls**, (ketones, esters, aldehydes, acids, amides)
- **alkenes**, or
- **aromatics**

1's (0.7-2.0) sp^3 hybridized C-H's, with **no attached Functional Groups**
- **Note:** Many molecules with non-functional alkyl portions will give a lot of signal in this area.

0-12   **Alcohol/Acid** O-H hydrogens (N-H hydrogens likewise)
(anywhere!)
- **Alcohols** (usually 1-4 area)
- **carboxylic acids** (usually 10-12 area)

1. Recognize OH's..
2. Check zones. Each one gives you a yes/no regarding the featured group.
3. End-Check: Do your actual chemical shifts match your proposed structure?
4. The regions are somewhat approximate, and have some spillover.
5. The impact of functional groups is roughly additive for multi-functional molecules. An sp^3-hybridized C-H with two attached oxygens can come in the 5's, or an sp^3-hybridized C-H that is doubly allylic can come in the 3's.

IV. Splitting
- ❑ **N-1 Rule:**   N lines ➔ **N-1 neighbor H's** (H's directly attached to carbons attached to the C-H group causing the signal)
  - The N-1 Rule is useful when working from spectrum to actual structure
- ❑ **N+1 Rule:**   N neighbor H's ➔ **N+1 lines**
  - The N+1 Rule is useful when working from structure to actual spectrum

Note: OH hydrogens don't participate in splitting (normally)

Short Summary of C13-NMR Interpretation

1. **Count how many lines** you have. **This will tell you how many types of carbons** you have. (Symmetry equivalent carbons will give a single line.)
    a. Each "unique" carbon gives a separate line.
    b. Symmetry duplicates give the same line.
    c. If there are more carbons in your formula than there are lines in your spectrum, it means you have symmetry.

2. **Check diagnostic frequency windows** ("chemical shift windows") of the lines **to provide yes-or-no answers regarding the presence or absence of key functional groups** in your molecule.

    220-160   C=O carbonyl carbons, sp^2 hybridized
    160-100   C alkene or aromatic carbons, sp^2 hybridized
    100-50   C-O oxygen-bearing carbons, single bonds only, sp^3 hybridized
    50-0   C alkyl carbons, no oxygens attached, sp^3 hybridized

3. **Check Splitting**. C13 NMR's are often acquired as "decoupled" spectra, in which each carbon signal appears as a singlet. However, at the cost of extra time and/or complexity it is also possible to get "coupled" C13 NMR's with splitting. These splitting values are very useful, and follow the N+1/N-1 rules (the number of lines is one greater than the number of attached H's). (Other experimentally preferable but conceptually complex "HSQC" two-dimensional NMR experiments can provide the same information more quickly.)
    Quartert (q)   CH$_3$
    Triplet (t)   CH$_2$
    Doublet (d)   CH
    Singlet (s) C (no attached hydrogens).
    • Note: The use of DEPT NMR or other techniques can also be used to establish whether carbons are CH$_3$, CH$_2$, CH, or carbons without any attached hydrogens.

4. **Signal Height/Size**
    a. Carbons without any attached H's are short.   This is common for carbonyls (aldehydes are the only carbonyl carbons that have hydrogens attached) and for substituted carbons in a benzene ring.
    b. Symmetry duplication multiplies signal height (if you have two copies of a carbon, the line will probably be taller than normal!)

5. **Aromatics, Symmetry, and C-13 Signals**. Most aromatics have symmetry, and both the number of aromatic lines and the splitting of the aromatic lines can be indicative of the substitution pattern on a benzene. Mono- and para-disubstituted benzenes have symmetry.

    4 lines s, d, d, d   Monosubstituted benzene.   (Has symmetry).
    4 lines s, s, d, d   Para-disubstituted benzene.   (Has symmetry).
    6 lines s, s, d, d, d, d   Ortho- or meta-disubstituted benzene. (Has no symmetry).

Summary of IR (Infrared) Interpretation

1. **Check for Diagnostic Signals**
    3500-3200   OH or NH
    1800-1640   C=O
    3500-2500 + 1800-1640   CO$_2$H
2. **Further Information in the "Carbonyl Zone"**
    <1700   Unsaturated C=O
    >1700   Saturated C=O
    1720-1700   Saturated ketones, aldehydes, acids
    1750-1735   Saturated ester

Hundreds of Practice Problems, and Thousands of Spectra.
- Looking at spectra and practicing NMR problems helps. There are many opportunities.

Here are several:
1. **Jasperse practice problems**:
    - Problems: http://www.mnstate.edu/jasperse/Chem360/NMR-Problems-Jasperse.pdf
    - Answers: http://www.mnstate.edu/jasperse/Chem360/NMR%20Problem%20Answers.pdf
    - The above site is linked from both the Jasperse Chem 342 and Chem 360 websites.
    - Some of these we will work in class together for practice, but there will be lots more you can practice on.
    - Even if I do work them in class, doing it fresh a day or more later may be much like working it fresh.

2. **Jasperse practice-test problems**:
    - http://www.mnstate.edu/jasperse/Chem360/Practice%20Tests/Chem360PracticeTests.html
    - These will the four versions of "test 2" practice tests linked.
    - Included will be links to the practice test movie sessions that I recorded in which I discuss some of the logic.

3. **Web Spectra site** (UCLA):   Has about 75 problems of varying level of difficulty. Formulas are provided.
    - **www.chem.ucla.edu/~webspectra**

4. **Organic Structure Elucidation site** (Notre Dame): (64 problems)
    - http://www.nd.edu/~smithgrp/structure/workbook.html
    - Click the "Do the Problems" link on the left to access the problems page.

5. **NMR's for over 14,000 chemicals**. (These aren't problems, but if you enter the name or formula or CAS number for something,
- **http://riodb01.ibase.aist.go.jp/sdbs/cgi-bin/cre_index.cgi?lang=eng**

The four facets of 1H NMR spectroscopy: (13.3-13)

1. The <u>number of signal sets</u>
    - The number of signal sets tells how many types of symmetry-unique hydrogen are present
    - Symmetry-duplicate hydrogens give the same signal sets

2. The <u>chemical shifts</u> (where the signals appear)   (Most complex facet)
    - The chemical shifts reflect the chemical environment of each type of hydrogen
        a. Whether attached to an sp^3 or and sp^2 carbon
        b. What kind of functional groups might be attached to the carbon on which the hydrogen is attached.
        c. Whether attached to carbon versus to oxygen or nitrogen

3. The <u>integration</u> (size/area) of each signal set   (Simplest facet, once you know how)
    - The integrated area for each signal set reflects how many hydrogens are responsible.
        a. 3H $\rightarrow$ CH_3 group (or 2H and 1H groups superimposed)
        b. 2H $\rightarrow$ CH_2 group (or two nonequivalent 1H groups superimposed)
        c. 1H $\rightarrow$ CH or OH group

4. The <u>splitting</u> (number of lines) in each signal set
    - The splitting provides information about what is connected to a given carbon
        a. N lines $\rightarrow$ N-1 "neighbor" H's (when working from spectrum to structure)
        b. N neighbors $\rightarrow$ N+1 lines (when predicting spectrum from structure)

Summary of Steps in Beginner 1H NMR Interpretation:

1. If provided with a chemical formula, calculate elements of unsaturation
    - This helps to put you on the alert for the presence of double bonds, rings, or aromatics
2. **Count how many signal sets** you have.
- **This will tell you how many types of hydrogen-bearing carbons** you have.
- Hydrogens attached to symmetry-equivalent carbons will give equivalent signals)
- Asymmetric signals indicate two or more overlapping signal sets
3. Check the **<u>integration</u>** of each signal set.
    - 3H $\rightarrow$ CH_3 group   2H $\rightarrow$ CH_2 group   1H $\rightarrow$ CH or OH group
    - The above are true if there isn't any accidental overlapping
    - Clean CH_3 or CH_2 signal sets will normally have reasonable shape symmetry
        a. Ex, if you have a nice symmetric 3H signal, conclude you have a CH_3
        b. But if you have a complex, unsymmetric 3H, do not assume it's really a CH_3.
    - Effective recognition and integration of signal sets can help you know how many CH_3's and CH_2's you have in your molecule
4. **Check diagnostic "chemical shift" windows** of the lines
    - Use yes-or-no checklist regarding the presence of key functional groups
    - Things can get more complicated if two or more functional groups are both affecting a common signal set.
    - Chemical shift information can quickly tell you whether hydrogens are attached to arenas or alkenes, and tell whether a CH_2 or CH_3 or CH signal set is attached to a single-bond oxygens or a carbonyl or an aromatic.

5. Check the **splitting** of each signal set.
    *   A signal set with N lines means that there are N-1 hydrogens attached to carbons directly connected to the carbon that holds the signal set hydrogens
    *   The splitting tells you nothing about the signal set itself (for example, whether it is a CH_3 or a CH_2 group). But it can tell you for example whether a CH_3 group (for example) is connected to a CH_2 group or a CH group, or perhaps to an oxygen or a carbonyl carbon that doesn't have any directly attached hydrogens.
    *   Etc.
6. Try to find any sure things that you can as soon as you can.
7. Try to use integration to find any clean 3H signals that indicate CH_3 groups. Then use splitting and/or chemical shifts to track down what the CH_3 group is connected to, etc..

Other Practical Tips
1. Try to recognize any easy and obvious sure-thing components, for example:
    a. Aryl groups (chemical shift in the 7's, a 4H or 5H integral depending on whether di- or mono-substituted)
    b. CH_3 methyl groups (based on clean 3H integration)
    c. Isopropyl groups (6H doublet)
    d. Alcohol OH: integrates for only 1H, and normally doesn't have the splitting that a CH hydrogen does
2. Try to work from end(s) toward the middle
    *   If you know you have a CH_3 group, you can write it down for sure, and then try to figure out via splitting and/or chemical shifts what it's connected to, etc.
3. Recognizing "end groups" can give you an idea whether you have a straight chain or have branching
    * CH_3
    *   Cl, Br
   *   OH
    * C_6H_5

The Number of Signal Sets
1. Nonequivalent H's have different chemical environments and give different signals

2. Symmetry-equivalent H's have the same chemical environment and give the same signal
    *   Thus the number of signal sets tells you how many different types of hydrogens are present

3. On an **achiral** molecule (alkenes and rings excepted), hydrogens on a common carbon will be equivalent.
    *   all three H's on a CH_3 group will be equivalent
    *   both H's on a CH_2 group will be equivalent.

Example: How many H-NMR Signal Sets Would each of the following produce?
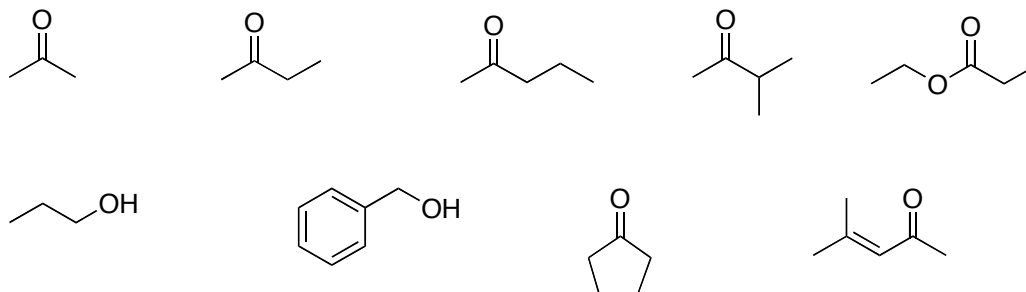
4. For chiral molecules, substituted rings, and alkenes, cis-trans relationships can often make the two hydrogens in a CH_2 group non-equivalent
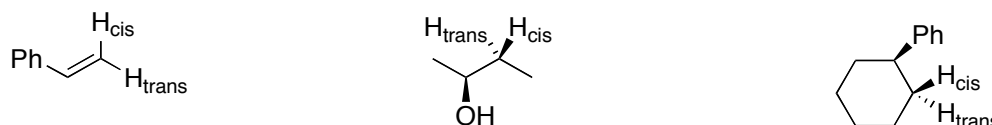

5. **Beware of overlaps!**
    *   Often two signal sets will show at about the same place. If you think you have a CH_3 group when in fact it's overlapping CH_2 and CH signals, you can get very confused…
    *   Overlaps normally don't have the clean symmetry that a clean signal set has
6. **Beware of Symmetry Duplication**
    *   Isopropyl groups are most common, and t-butyl groups on occasion
        o   Integrations of 6H or 9H can help recognize these
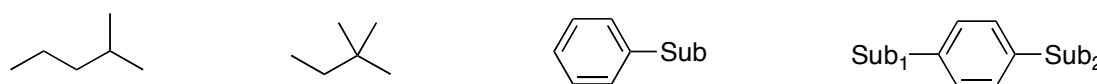
Integration   (Section 13-7)
1. All hydrogens give an equal amount of signal
    *   The area produced is measured or "integrated" by the spectrometer
    *   The measured area is normally referred to as the "integral"
2. When there is symmetry duplication of a hydrogen, the resulting signal will be multiplied accordingly!
    *   Since all three H's on a CH_3 group are equivalent, they will sum to provide a signal set that integrates for 3H
3. Technical notes:
    a.   The key is not the signal height, but rather the signal **area**.
    b.   The signal **area** is measured by "integration lines". Make sure to differentiate integration marks, and what they mean, from signal lines themselves.
4. **The relative areas of the signal-set integrals directly correlates the ratios of H's**
    *   The integrals **must be simple whole-number ratios** (2:1, 3:1, 3:2, etc..)
    *   You can't have half a hydrogen or one-third of a hydrogen atom!

5. <u>Clean sets involving equivalent H's give clean, symmetric signal sets:</u>
   a. 1H → CH or OH
   b. 2H → CH_2
   c. 3H → CH_3
   d. 6H → 2 equivalent CH_3 groups
   e. 5H in aryl region → monosubstituted benzene (even if not clean set)
   f. 4H in aryl region → disubstituted benzene (even if not clean set)
6. <u>Unsymmetrical messy sets involving overlapping signal sets:</u>   (these will routinely not look nice and symmetric…)
   a. 3H → CH_2 overlapping an OH or CH
   b. 4H → two overlapping but not exactly equivalent CH_2 groups; or a CH_3 overlapping an OH or CH
   c. 5H → common in the 7's, for 5 overlapping arene H's; also common in the 1's, when a CH_3 and CH_2 overlap
7. Recognizing 3H → methyl groups, or 6H → isopropyl groups is really helpful

<u>Ways to Determine the Integration (Focus on the types of spectra that you'll see for test)</u>
   • Identify the integration line as opposed to the actual spectrum itself
1. Measure the raw areas for each signal set
   a. For class/test problems, use the grid lines
   b. For lab, the spectrometer will often measure an integral number for you
   c. For class or lab, if you prefer to use a ruler to measure, that's common to
2. Convert the raw areas into relative area ratios (Example, Handout problem 1)

Raw areas:

<u>Three Ways to do this:</u>
   1. Divide any raw area by the smallest raw area

Ratio	Means	Ratio	Means	Ratio	Means	Ratio	Means
1		1.5		2		3	

   2. Since some of our class/test NMR's will have 10 gridlines, you can take 10 gridlines/actual number of hydrogens (if formula is provided) to figure out the gridlines-per-hydrogen ratio
   • You can then use this to convert your raw integrals into actual Hydrogen counts

   Ex: 10 grids/7 H's = 1.4 grids/1 H
        or

   Ex: $\dfrac{2.9 \text{ grids}}{10 \text{ grids}} = \dfrac{x \text{ H's}}{7 \text{ H's}}$

Splitting   (Section 13.7-11)

*   The number of lines in a signal set tell us nothing about the C-H's themselves that cause the signal (whether it's a CH_3 or CH_2 group, whether it's an sp^3 or sp^2 carbon, whether it's allylic or oxygenated…).
*   But the splitting tells us something else that is really useful: what kind of CH groups are attached to the group of interest! Splitting tells us nothing about the group itself, but it does provide great information about neighbor groups.

Rules of "Splitting"
❑   **N-1 Rule: N lines ➔ N-1 neighbor H's** (H's directly attached to carbons attached to the C-H group causing the signal)
*   The N-1 Rule is useful when working from spectrum to actual structure
❑   **N+1 Rule: N neighbor H's ➔ N+1 lines**
*   The N+1 Rule is useful when predicting a spectrum for a structure

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N+1 Rule (Given structure, how many lines a spectrum should give)

	a	b	c	d			a	b	c	d	e
Neighbors	2	3+2	2	0	Neighbors	0	-	2	2+3	2
Lines	3	6	3	1	Lines	1	-	3	6	3

(Notice: OH doesn't split...)

N-1 Rule (Given spectrum, how many neighbors a structure should have)

Lines	1 (s)inglet		Lines	2 (d)oublet	
Neighbors	0		Neighbors	1	
Lines	3 (t)riplet		Lines	4 (q)uartet	
Neighbors	2		Neighbors	3	etc.

1. Physics Origin: hydrogens are quantized little magnets. Having neighbor hydrogens is equivalent to having local magnets that can either reinforce the external field (spin up) or counteract the external magnetic field (spin down).
    -   The number of lines and the relative intensity of the lines reflects simple statistical possibilities in terms of neighbor hydrogen magnets being spin up or spin down.
        -   With one neighbor magnet, the probability of spin up vs spin down is comparable → 1:1 doublet
        -   With two neighbor magnets, they can be spin up/down in three different arrangements of 1:2:1 probability → 1:2:1 triplet
        -   Etc.

Lines Neighbors	2 (d)oublet 1 neighbor	3 (t)riplet 2 neighbors	4 (q)uartet 3 neighbors

Neighbor
Hydrogen
Spin States

2. Neighbor C-H hydrogens participate in splitting (always)
3. Neighbor OH hydrogens usually don't participate in splitting (~75% of the time). But sometimes they do (about 25% of the time).
    -   They can have widely varying and rapidly changing hydrogen-bonding arrangements
4. Splitting from H's further distant than neighbor carbons sometimes occurs, but usually the amount of splitting is too small to worry about
5. Splitting nicknames:
    -   1 line = singlet (s)   2 lines = doublet (d)   3 lines = triplet (t)
    -   4 lines = quartet (q)   5 lines = pentet (p)   >5 lines = multiplet (m)
6. Limitation to the N-1/N+1 rules: it is only reliable if all of the neighbor hydrogens are equivalent. However, the rules actually are accurate only if the neighbor H's are equivalent.
    -   The rule can break down when some of the neighbor H's differ significantly from each other
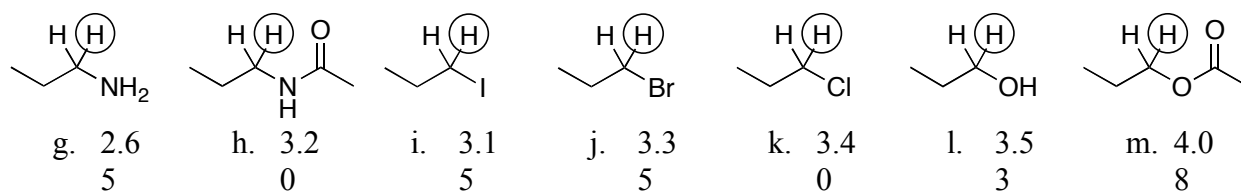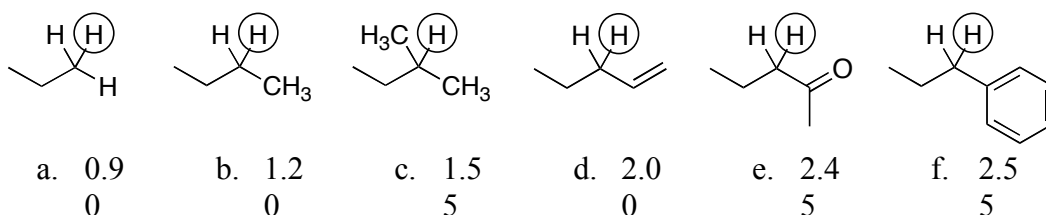   -   The more nonequivalent the neighbor hydrogens, the less the N-1/N+1 rules apply
        -   Neighbor hydrogens on acyclic and sp^3 carbons tend to be pretty similar
        -   Alkenes or aldehyde hydrogens (on sp^2 carbons) tend to split rather differently than hydrogens on sp^3 carbons
        -   Splitting involving cis versus trans hydrogens on rings or alkenes tend to split rather differently from each other and from hydrogens on acyclic sp^3 systems.
        -   Chiral centers can mess up the splitting even on acyclic systems

 **"Chemical Shifts" of the Signal Sets (Section 13.5)**
- The following apply when only one functional group is impacting
- If two or more are impacting, then signal sets can appear outside of these windows

1's (0.7-2.0) sp^3 hybridized C-H's, with **no attached Functional Groups**
- **Note:** Many molecules with non-functional alkyl portions will give a lot of signal in this area.
- **This is the default place for** sp^3 **C-H's, when no functional group is shifting them to higher number**

2's (1.8-3.1)   **Allylic** sp^3 hybridized C-H's (sp^3 hybridized C-H's that has a double bond attached to the sp^3 hybridized C). Allylic signals routinely appear when one of the following double-bonded functional groups is present:
- +1 Adjustment factor
- **carbonyls**, (ketones, esters, aldehydes, acids, amides)
- **alkenes**, or
- **aromatics**

3's (2.8-4.5)   **Oxygenated** sp^3 hybridized C-H's (halogenated and nitrogenated alkyl C-H's will also come in this window, although no candidates for today's lab). Oxygenated sp^3–carbons are routinely present for the following functional groups that contain oxygen single bonds:
- +2 Adjustment factor
- **alcohols**, (usually signal in 3's)
- **ethers**, (usually signal in 3's) or
- **esters** (usually signal in low 4's)
- **More general: heteroatom substituents (O, Cl, Br, I) usually have a +2 adjustment factor, N a +1.5-2.0 adjustment factor.**

5's (4.8-6.8)   **Alkene** sp^2 hybridized C-H's

7's (6.5-8.4)   **Aromatic** sp^2 hybridized C-H's

9's (9.0-10.0)   **Aldehyde** sp^2 hybridized C-H's

0-12 (anywhere!)   **Alcohol/Acid** O-H hydrogens (N-H hydrogens likewise)
- **alcohols**, (normally 1.5-3.0)
- **carboxylic acids** (usually 10-12)

1. Replacement of H by more electronegative atom/group "deshields" a proton and moves it "downfield", to a higher number
    a. "methine" (CH) → "methylene" (CH₂) → "methyl" (CH₃) (case "a" vs "b" vs "c")
        • sequential replacement of hydrogens by more electronegative carbons moves the signal "downfield"
    b. See the electronegativity pattern as you go from: H (0.9) – C (1.2) – N (2.6) – I (3.2) – Br (3.3) – Cl (3.4) to O (3.5) (case "a" vs "b" vs "g" vs "i-l")
        • sequential replacement of hydrogens (or carbons) by any more electronegative substituents moves a signal "downfield"
    c. See the electronegativity pattern between amine (2.7) versus amide (3.2) (case "g" vs "h"), and alcohol/ether oxygen (3.5) versus ester oxygen (4.1) (case "l" vs "m")
        • the electron-withdrawing carbonyl attachment on the nitrogen or oxygen makes it effectively more electronegative and moves the signal "downfield"

| a. 0.9 0 | b. 1.2 0 | c. 1.5 5 | d. 2.0 0 | e. 2.4 5 | f. 2.5 5 |

| g. 2.6 5 | h. 3.2 0 | i. 3.1 5 | j. 3.3 5 | k. 3.4 0 | l. 3.5 3 | m. 4.0 8 |

2. The allylic factor has the same basis: sp² carbons are more electronegative than sp³ carbons, so replacing an sp³ with an sp² "deshields"

1.20   2.00   2.45
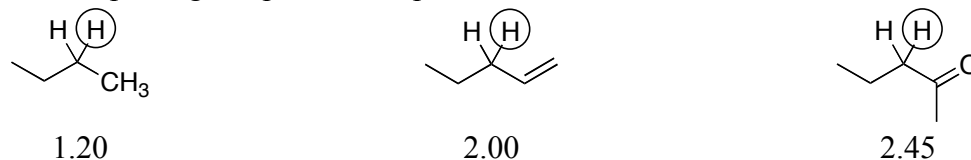
3. An electron-withdrawing carbonyl on a heteroatom makes the heteroatom effectively more electronegative.   So ester versus ether and amide versus amine has the same electronegativity basis.


2.65   3.20   3.53   4.08
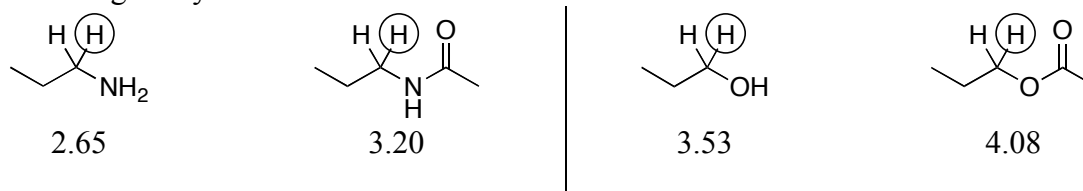
4. **Additivity values can be used to predict chemical shifts when two or more functional groups are acting**

Vinyl	Carbonyl ("Acyl")	Aryl	Amino	Amido	Halo	Hydroxy/ Alkoxy	Carbonyloxy
0.8	1.2	1.3	1.5	2	2.2	2.3	2.8

- Default reference points: CH_3 0.90 CH_2 1.20   CH 1.50
- Memorize the following qualitative additivity values:
  a. Double-bonded carbons (vinyl, acyl, aryl) → +1
  b. Oxygen or Halogen → +2

Predict the chemical shifts for the circled hydrogens, using the specific chart additivity values and using the qualitative memorized ones:
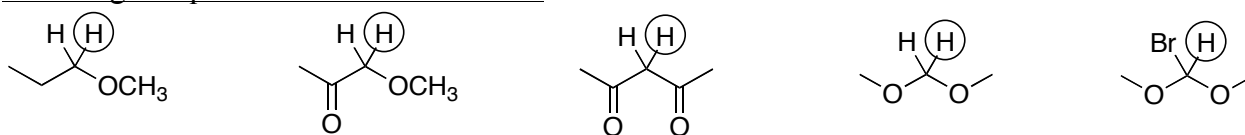
5. Strong hybridization effect: hydrogens on sp^2 carbons routinely above 5, those on sp^3 carbons normally come below 5.

| 1.20 | 5.4 | 7.1 | 9.7 |
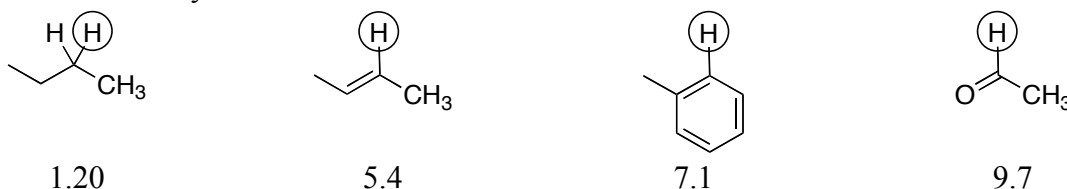
6. Functional Groups further away have reduced but sometimes significant impact.
   - Direct "α" attached functional groups have a large impact
   - When the functional group is "β" it makes a difference, but not large
   - When the functional group is "γ" or further, it makes no difference
   - Sometimes a couple of "β" substituents can add up and push a signal set out of it's normal window

α-CH_2 3.5
β-CH_2 1.3
γ-CH_2 1.2
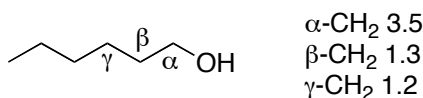
Key: The impact of two or more functional groups can sometimes deceptively push a signal into a window that you assume means something else
   - A signal in the 3's normally implies an oxygenated (or halogenated) carbon. But it could also result from a double allylic carbon with two carbonyls attached.
   - A signal in the 5's is normally implies an alkene, but it might also result from an sp^3-hybridized carbon that has two oxygen attachments.
   - Etc.

7. **Recognize OH's.**.
   a. An OH can come anywhere, and can easily cause you to make a mistaken conclusion about a feature group. For example, if you have an OH and it comes in the 2's, and you conclude that you have an allylic C-H, that might send you down a bad blind alley. Thus it is really helpful to recognize OH's when they appear so that they don't confuse you.

   b. Recognition factors for OH signals:
      1. They always **integrate for 1H**, never for 2H or 3H
      2. They **lack sharp splitting**, and often **appear as singlets, often somewhat broad**. C-H signals tend to be sharper, and any C-H signal set that integrates for 1H will have significant splitting. The only way to have a 1H that doesn't split is for it to be an OH.
      3. They come anywhere, but often in the 1.5-3.0 range
      4. If you have an alcohol OH signal, of course you will also have some C-H signals in the 3.0-4.5 area.

8. **Check each of the zones. Each one gives you a tentative yes or no answer about the presence of absence of the featured group**.
   - Do I have something in the 9's? If yes → aldehyde
   - Do I have something in the 7's? (Other than a solvent singlet…)? If yes → aromatic
   - Do I have something in the 5's? If yes → alkene
   - Do I have something in the 3's? If yes → alcohol, ether, or ester (or OH)
   - Do I have something in the 2's? If yes → ketone, aromatic, or alkene (or OH)
   - Do I have something in the 1's? If yes → some nonfunctional alkyl carbons (or OH)

Caution: Mistaken conclusions can sometimes be drawn from two sources:
   a. An OH in the 2's or 3's, from which you falsely conclude that you have allylic or oxygenated C-H's
   b. A signal that appears where it does because of the effect of two (or more) functional groups, rather than just one.

Standard Summary Format and Predicting H-NMR's   There is a standard summary report format for H-NMR's which **addresses 1. chemical shift, 2. integration, and 3. splitting**. Normally an **interpretation/correlation** with the actual structure is also included.

Ex: $CH_3OCH_2CH_2CH_2C(O)CH_3$ (I'll number the carbons from left to right…)

> Standard report format (approximate chemical shift range, integration, splitting, and interpretation of which signal correlates to which group in the structure…)
> > 3's, 3H, s (CH_3-1)
> > 3's, 2H, t (CH_2-2)
> > 1's, 2H, p (CH_2-3)
> > 2's, 2H, t (CH_2-4)
> > 2's, 3H, s (CH_3-6)

Predict the NMR for the Following Structure, Using the Standard Summary Format
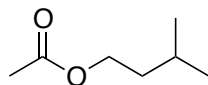
Review + Summary
1. Use your formula to count elements of unsaturation
2. Count **how many signal sets** you have.
3. Check the **integration** of each signal set.
   - 3H → CH_3 group   2H → CH_2 group   1H → CH or OH group
4. Check the **splitting** of each signal set.
   - N lines → N-1 neighbor hydrogens
5. Check **"chemical shift" windows** of the lines to provide information regarding the **presence or absence of key functional groups** in your molecule.
   - ❑ Beware of misinterpreting overlapping signals
   - ❑ Beware of being confused by signal sets caused by OH's or caused by two or more functional groups impacting chemical shift
   - ❑ Steps 4 and 5 are definitely interchangeable
6. **Use "tracking" to work from known components (normally CH₃ end groups, or C₆H₅ end group, or OH end groups) down the chain**
   - **Integration** can tell whether it's a CH_3, CH_2, or CH causing a particular signal set
   - **Chemical shift** and/or **splitting** can then tell you what else may be **attached**
     - a. **Chemical shift** tells if a **functional group** is attached
     - b. **Splitting** tells what **CH, CH2, or CH3** groups are attached
7. **End-Check: Check that the structure you believe you actually have would give the number of signal sets you have, the chemical shifts you have, the integrations you have, and the splittings that you have. If not, your structure needs to be corrected!**

^{13}C NMR (Sections 13.14-19)
- ^{13}C is NMR active, ^{12}C is not
- Signals are much weaker, C-13 spectra are harder to get
    - o C-13 gives about $1/10,000^{th}$ as strong a signal as H-NMR
    - o Because the natural abundance is only 1%, and the inherent sensitivity is only 1%
- A result is that for C-13 NMR, one or more of the following is usually true:
    1. Take longer
    2. Not as clean a baseline
    3. Higher sample/solvent concentration used
    4. Data processing tricks used in order to shorten the process. These often result in:
        - o Loss of splitting information ("decoupled" C-13 NMR's in lab…)
        - o Loss of integration information (our C-13 NMR's in lab…)

Summary of C-13 NMR Interpretation:
1. **Count how many lines** you have in a decoupled carbon spectrum. **This will tell you how many types of carbons** you have. (Symmetry equivalent carbons can at times cause the number of lines to be less than the number of carbons in your structure.)
2. **Check diagnostic frequency windows** ("chemical shift windows") of the lines **to provide yes-or-no answers regarding the presence or absence of key functional groups** in your molecule.
3. If **splitting** information is provided via a coupled carbon spectrum, or a DEPT NMR spectrum is provided, or a phase-sensitive 2-dimensional NMR is provided, use tools like these to decide which carbons are CH_3, CH_2, CH, and no-H C's.

1. **Count how many lines** you have. **This will tell you how many types of carbons** you have.
    1. Each "unique" carbon gives a separate line.
    2. Symmetry duplicates give the same line.
    3. If there are more carbons in your formula than there are lines in your spectrum, it means you have some symmetry.

Q: How many lines would show in the C-13's for the following?
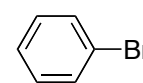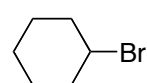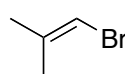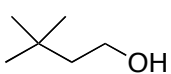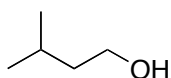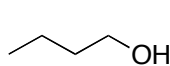
2. **Chemical Shifts: Where do the Lines Come?**

220-160   C=O carbonyl carbons, sp^2 hybridized

> 160-180 → typically ester
> • for formulas that have two oxygens, being able to recognize ester group helps a ton
> 180-220 → other carbonyls (ketone, aldehyde, carboxylic acid, amide)

160-100   C alkene or aromatic carbons, sp^2 hybridized

> • If a molecule has alkene or aromatic, it's usually easy to tell which it is based on chemical formula or on the number of lines in the 100-160 zone (2 for alkene, usually more for aromatics

100-50   C-O oxygen-bearing carbons, single bonds only, sp^3 hybridized
80-30   C-N nitrogen bearing carbons, single bonds only, sp^3 hybridized
80-30   C-X halogen bearing carbons, single bonds only, sp^3 hybridized

50-0   C alkyl carbons, no oxygens attached, sp^3 hybridized

> • This is the default zone for sp^3 carbons with no attached heteroatoms
> • Allylic carbons still fall into the 50-0 zone, unlike in H-NMR where allylic hydrogens are distinct

• Halogens or nitrogens complicate things a bit, because they can appear on either side of the 50-divider.
• But for formulas involving only C, H, and O, the 50-divider is very, very useful.

Using the "Oxygen Zones" for Oxygenated Systems

			220-160 Zone	100-50 Zone
One-Oxygen Formulas	Ketone, Aldehyde		180-220	
	Alcohol			One
	Ether			Two
Two-Oxygen Formulas	Acid		180-220	
	Ester		160-180	One
	Aldehyde/Ketone And Alcohol		180-220	One
	Aldehyde/Ketone And Ether		180-220	Two

3. **Splitting** in a coupled carbon NMR spectrum.
   - C13 NMR's are normally acquired as "decoupled" spectra, in which each carbon signal appears as a singlet, for reasons of speed and simplicity.
   - However, at the cost of extra time and at the expense of some simplicity, it is also possible to get "coupled" C13 NMR's with splitting. The C-13 atoms are split by directly attached hydrogens.
   - These splitting values are very useful, and follow the N+1/N-1 rules (the number of lines is one greater than the number of attached H's).

| Quartert (q)	CH_3
Triplet (t)	CH_2
Doublet (d)	CH
Singlet (s)	C (no attached hydrogens)

   - Coupled C-13 has at last two drawbacks:
     1. The signal to noise ratio and thus the sensitivity is a lot worse.
     2. Overlap: With coupled C-13 NMR, there are a lot more lines, and overlapping of lines becomes normal and confusing for non- simple molecules.

4. **DEPT NMR.**
   - "Distortionless Enhanced Polarization Transfer" is another technique that can unambiguously assign carbons as methyl (CH_3), methylene (CH_2), methyne (CH), or quaternary (no attached hydrogens).
   - One or two DEPT experiments are done in conjunction with a decoupled C-13 NMR.
   - DEPT 90: only methine (CH) carbons show, and they point up
   - DEPT 135: both methine (CH) and methyl (CH_3) carbons point up, and methylene (CH_2) carbons point down.
   - Quaternary carbons won't appear in DEPT 90 or DEPT 135.
   - By combining information from a decoupled, DEPT90, and DEPT135 NMR, you can unambiguously identify which carbons are of which type.

5. **Aromatics, Symmetry, Splitting.** Most aromatics have symmetry, and both the number of aromatic lines and the splitting of the aromatic lines can be indicative of the substitution pattern on a benzene. Mono- and para-disubstituted benzenes have symmetry.

4 lines	s, d, d, d	Monosubstituted benzene. (Has symmetry)
4 lines	s, s, d, d	Para-disubstituted benzene. (Has symmetry)
6 lines	s, s, d, d, d, d	Ortho- or meta-disubstituted benzene. (Has no symmetry)
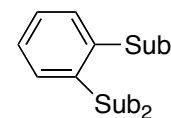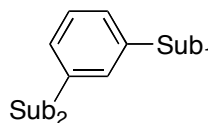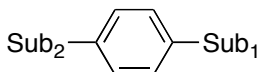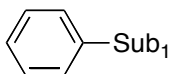
6. **Signal Height/Size**   Unlike 1H-NMR, where integration is really important, signal size is not very important in C-13 NMR.
   a. Signal amplification tricks (to save time) compromise accurate integration
   b. Even when lines have equal area, a narrower one looks much taller than a fatter one
   c. Two patterns that can be somewhat helpful.
      1. Carbons without any attached H's are short. Common in:
         a. carbonyls (aldehydes are the only carbonyl carbons that have hydrogens attached)
         b. substituted carbons in aromatic rings.
         c. T-butyl carbons
      2. Symmetry duplication multiplies signal height (if you have two copies of a carbon, the line will probably be taller than normal!)

Problem Solving and C-13

Alone	In Support with H-NMR
1. Calculate EU	Look for obvious things
2. Symmetry? Check lines versus formula	1. Carbonyls? (any, and if so ester or aldehyde?)
3. Look for Obvious Things	
• Oxygen zones, aryl zone…	2. Oxygen zones?
4. Use Splitting	3. Aromatic or alkene, and if so with what kind of substitution pattern?
5. Look for ends groups	
• Methyl, phenyl, OH, halogen	4. Symmetry?
	5. CH_3, CH_2, CH count

2-Dimensional NMR (Carey section 13.18,19)
   1. In a 2-D NMR experiment, one spectrum gets plotted on the x-axis, another on the y-axis, and atoms that are coupled to each other give "cross peaks".
      • This enables you to tell which atoms are connected or coupled to each other
      • This is sometimes a faster or easier way to establish chain connectivity than simply relying on splitting to figure out which groups are neighbors.

   2. Hydrogen-Hydrogen 2D ("COSY"): the hydrogen NMR of the sample is printed on both axes, but you can use the cross-peaks to identify which hydrogens are split by which other hydrogens

   3. Carbon-Hydrogen 2D ("HSQC" or "HMQC"): the hydrogen NMR is plotted on one axid, the carbon NMR on the other. A hydrogen signal will give a cross peak with the carbon to which it is attached.
      • A phase-sensitive version can differentiate methylene (CH_2) carbons from methyl (CH_3) or methine. Experiments like these are often faster and more informative than DEPT or coupled carbon NMR's.

Infrared Spectroscopy (13.20-22)
- Examples, Contrast to NMR
- Much more complex than NMR
  - In NMR, we expect to explain everything, and we can solve full structures
- In IR, two typical uses:
  a. Functional Group Identification: focus on a few key zones (our use)
  b. "Fingerprint" matchups of unknowns to knowns (we won't do)

Major overall zones:
1600-3600 useful (stretching, useful for functional group ID)
1600-600 vibrations "fingerprint", always busy, not very useful for function group ID

Major Bands that are of some Functional Group Interest
3500-2700   N-H, O-H, C-H single bonds
2300-2100   CN, CC triple bonds
1800-1580   C=O, C=N, C=C double bonds

Practical Feature Groups
1. O-H/N-H Zone (except when O-H is a carboxylic acid O-H): 3500-3200
   - **Alcohol Recognition**
   - Amines or amides
   - Signals are sometimes rather broad due to hydrogen-bonding
   - Note: when looking at an actual spectrum, focus in specifically on the 3500-3200 range, don't just look generally around 3000
     o Because every organic molecule will have a big C-H signal around 2900-3000
     o That is *not* interesting or informative, and should *not* be mistaken for proof of alcohol
   - In contrast to alcohol O-H, <u>carboxylic acid O-H signals are extremely broad, ranging somewhere within 3500-2200</u>

2. Carbonyl Zone: Around 1710 ± 80
   - Very strong signal
   - First thing to check
   1700 rule
   - carbonyls >1700 are "saturated": no attached double-bonded carbons
   - carbonyls <1700 are "unsaturated": an sp^2 attached carbon (i.e. alkene or aromatic)
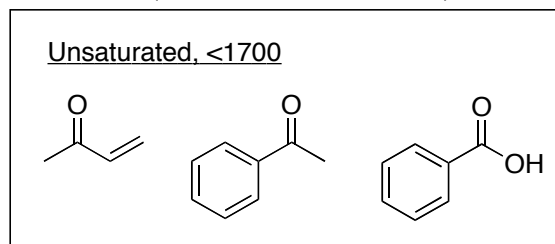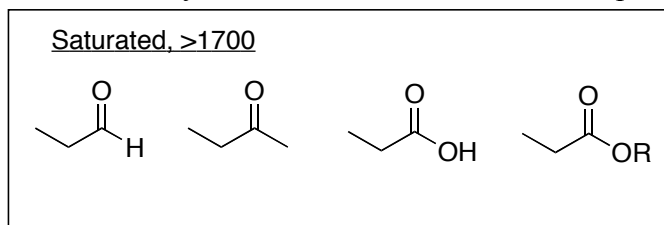
Esters versus Ketones/Aldehydes/Acids
   - Saturated esters 1735-1750
   - Saturated ketones/aldehydes/acids: 1700-1720
   - Very useful for recognizing when a two-oxygen formula contains an ester

Carboxylic Acids (versus hydroxy ketones)
- Acid has both a carbonyl in the ~1700 zone and a broad hydroxyl spread somewhere in the 3500-2200 zone
- A formula with two oxygens that has one as ketone and one as alcohol would give a carbonyl in the ~1700 zone but a tighter alcohol O-H in the 3500-3200 zone
- Very useful for quick recognition of carboxylic acids

Using the "Oxygen Zones" for Oxygenated Systems

			Carbonyl Zone	Hydroxyl Zone
One-Oxygen Formulas	Ketone, Aldehyde		1700-1720 (if saturated, <1700 if not)	
	Alcohol			3500-3200
	Ether			
Two-Oxygen Formulas	Acid		1700-1720 (if saturated, <1700 if not)	3500-3200 (**broad**)
	Ester		1735-1750 (if saturated)	
	Aldehyde/Ketone And Alcohol		1700-1720 (if saturated, <1700 if not)	3500-3200 (**broad**)
	Aldehyde/Ketone And Ether		1700-1720 (if saturated, <1700 if not)	

Practical Use for IR: Fast recognition of key functional group information
-helpful support for an NMR solution, if you know what functionality is present.

Summary of IR (Infrared) Interpretation
Check for Diagnostic Signals

3500-3200	OH or NH
1800-1641	C=O
3500-2500 + 1800-1640	CO_2H

Further Information in the "Carbonyl Zone"

<1700	Unsaturated C=O
>1700	Saturated C=O
1720-1701	Saturated ketones, aldehydes, acids
1750-1735	Saturated ester