

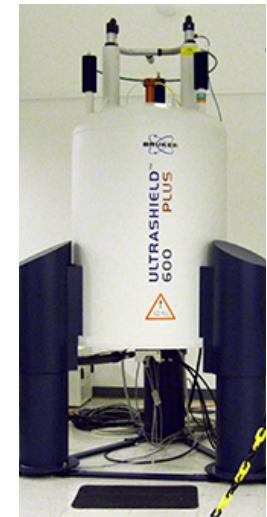
Ch 1b Lecture 9

January 28th, 2013

Next few lectures – *Light/matter interactions*,
or, An Introduction to Spectroscopy.

Today: NMR spectroscopy, or
“Magnets are a chemist’s best friend.”

Reading: Review OGC sections 4.5-4.7 as needed, OGC section 20.4; RC Section 9-10

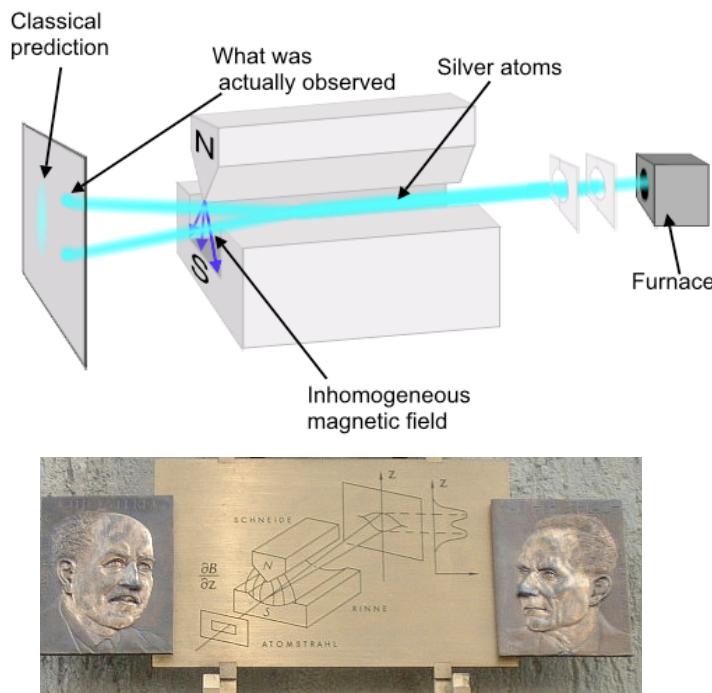


Quick review of last lecture(s):

- The Born-Oppenheimer approximation suggests we can decouple electronic and nuclear degrees of freedom.
- The rovibrational degrees of freedom are sensitive to molecular structure, forces.
- Electronic spectroscopy accesses excited molecular orbital(s), can be pushed to the single molecule limit. All require time dependent E&M fields with $\Delta E = h\nu_{\text{photon}}$.

Nuclear Magnetic Resonance (NMR) Spectroscopy:

Unlike the techniques previously covered, NMR *requires* the application of a constant external field. Why?



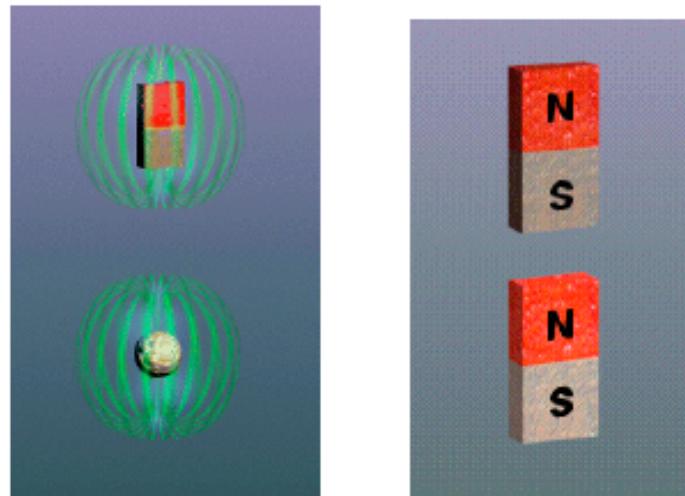
1922, Frankfurt Institute for
Theoretical Physics

Recall (or learn about) the Stern-Gerlach experiment, which ultimately came to be interpreted as a demonstration of the two m_s values of spin-1/2 ($S=1/2$) particles (p. 184, OGC). For molecules with unpaired electrons, EPR can be used to measure electron spin density:



Nuclear Magnetic Resonance (NMR) Spectroscopy:

- many nuclei have non-zero spin
- a spinning charge has a magnetic dipole moment, μ
- magnetic moments can interact with an external magnetic field B_0 and with nearby nuclei with non-zero spin. They behave in some ways like small bar magnets.



No nuclear spin, no external magnetic field, no NMR.

Nuclear Magnetic Resonance (NMR) Spectroscopy:

Before we get to the detailed results, some highlights:

- Only nuclei of certain elements/isotopes have non-zero spins and can thus be used in NMR.
- NMR spectra result from changes in spin orientation upon interaction with a time dependent EM field.
- The nature of the NMR spectrum is exquisitely sensitive to the nuclear environment.
- Especially when combined with IR spectra and mass spectrometry, NMR can be used to characterize the structure and dynamics of molecular systems.
- The related technique of Magnetic Resonance Imaging (MRI) provides a non-invasive means of imaging living organisms with non-ionizing radiation.

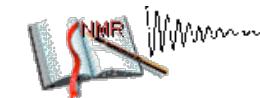
Nuclear Magnetic Resonance (NMR) Spectroscopy:

There are many web-based tutorials on NMR and MRI,
some with excellent animations of the key ideas. A few:

[http://www2.chemistry.msu.edu/faculty/reusch/VirtTxtJml/
Spectrpy/nmr/nmr1.htm](http://www2.chemistry.msu.edu/faculty/reusch/VirtTxtJml/Spectrpy/nmr/nmr1.htm)



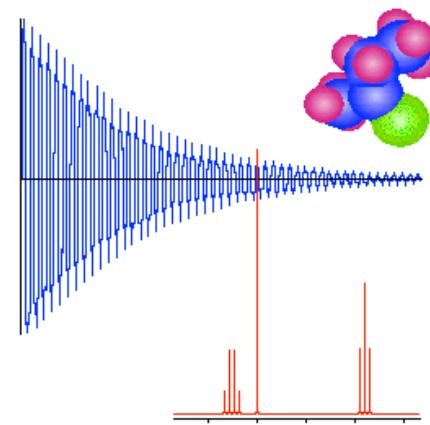
<http://www.chem.queensu.ca/facilities/nmr/nmr/webcourse/>



<http://www.cis.rit.edu/htbooks/nmr/>

The Basics of NMR

Joseph P. Hornak, Ph.D.



Nuclear Magnetic Resonance (NMR) Spectroscopy:

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$I = 1/2$: ^1H , ^{13}C , ^{19}F , ^{29}Si , ^{31}P , ...

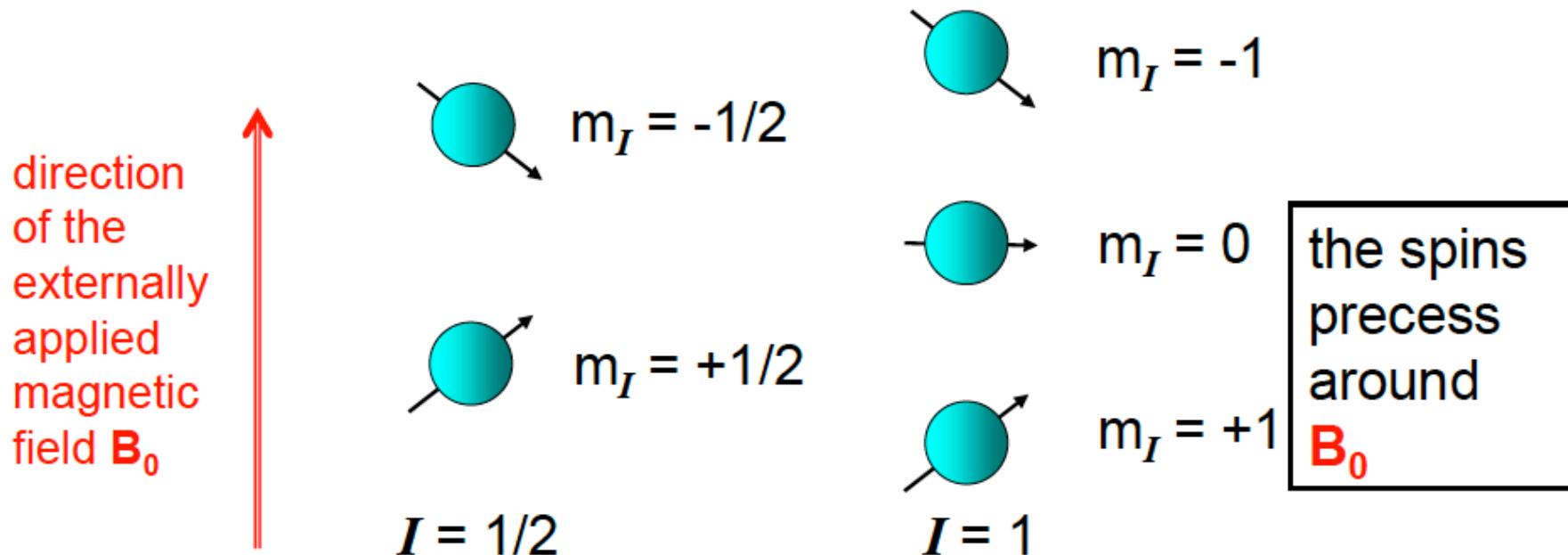
$I > 1/2$: ^2H ($I=1$), ^{14}N ($I=1$), ^{23}Na ($I=3/2$), ^{17}O ($I=5/2$), ...

$I = 0$: ^{12}C , ^{16}O , ^{32}S , ... No NMR!

A nucleus with the spin quantum # I has $2I + 1$ possible spin states:

$$m_I = -I, -I+1 \dots I-1, I,$$

that give possible orientations of the nuclear spin angular momentum



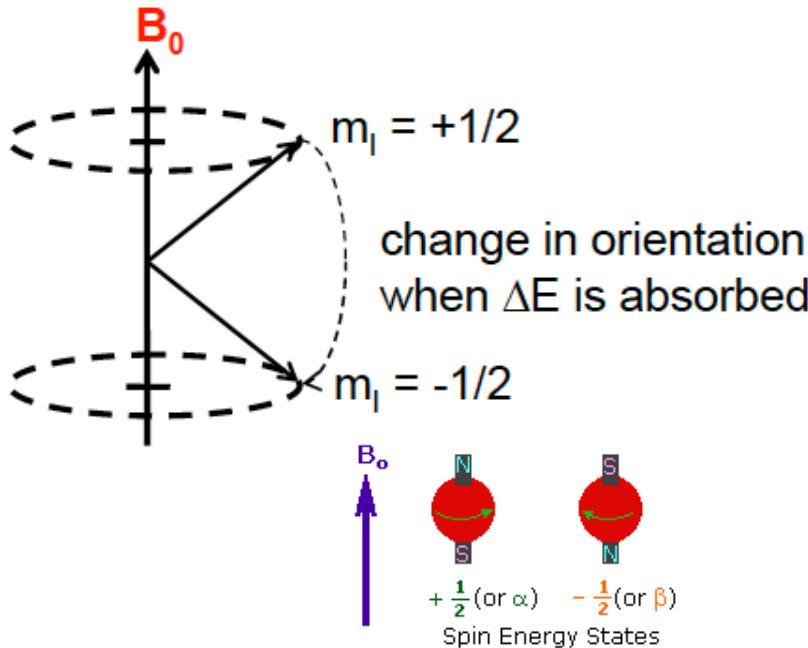
Nuclear Magnetic Resonance (NMR) Spectroscopy:

Relative abundances (%) of common isotopes

Carbon	^{12}C	100	^{13}C	1.11		
Hydrogen	^1H	100	^2H	0.016		
Nitrogen	^{14}N	100	^{15}N	0.38		
Oxygen	^{16}O	100	^{17}O	0.04	^{18}O	0.20
Sulfur	^{32}S	100	^{33}S	0.78	^{34}S	4.40
Chlorine	^{35}Cl	100			^{37}Cl	32.5
Bromine	^{79}Br	100			^{81}Br	98.0

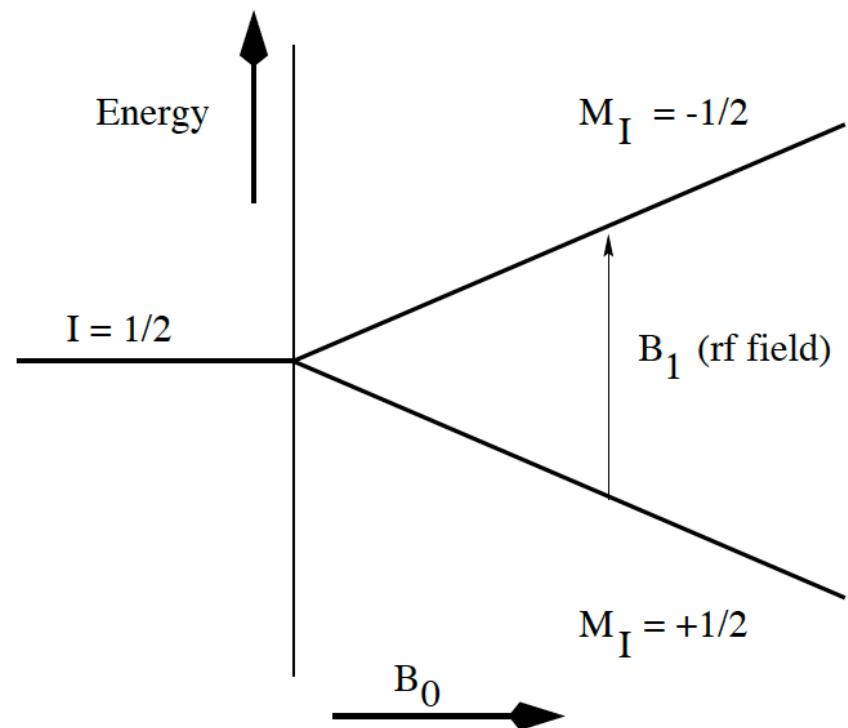
Thus, proton NMR widely used!

Nuclear Magnetic Resonance (NMR) Spectroscopy:



- The magnetic moment μ depends on both m_I and the **magnetogyric ratio γ** such that $\mu = \gamma \cdot m_I (h/2\pi)$
- With an applied RF field B_1 , the selection rule is $\Delta m_I = \pm 1$, and so $v_{\text{NMR}} = \gamma \cdot B_0 / 2\pi$.

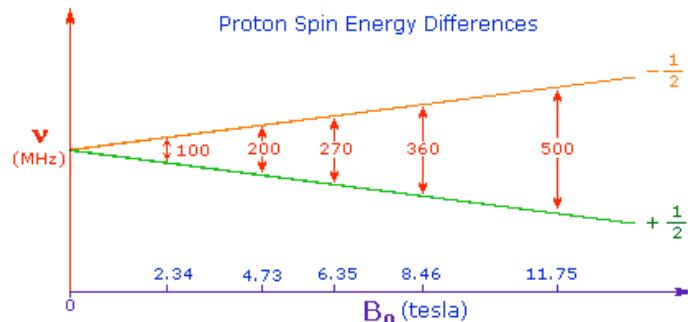
- For a magnetic moment μ , the energy of interaction with an applied DC field B_0 is $E = -\mu \cdot B_0$.



Nuclear Magnetic Resonance (NMR) Spectroscopy: ¹⁰

Each isotope has a specific γ :

nuclei	spin	γ (10^7 rad sec $^{-1}$ T $^{-1}$)
^1H	1/2	26.7522
^2H	1	4.1066
^{13}C	1/2	6.7283



hence the NMR frequencies are isotope-specific.

At $B_0 = 11.7$ T, $\nu(^1\text{H}) = 500$ MHz and $\nu(^{13}\text{C}) = 125$ MHz

OGC uses a different notation:

$$\Delta E = h\nu = g_N \beta_N H$$

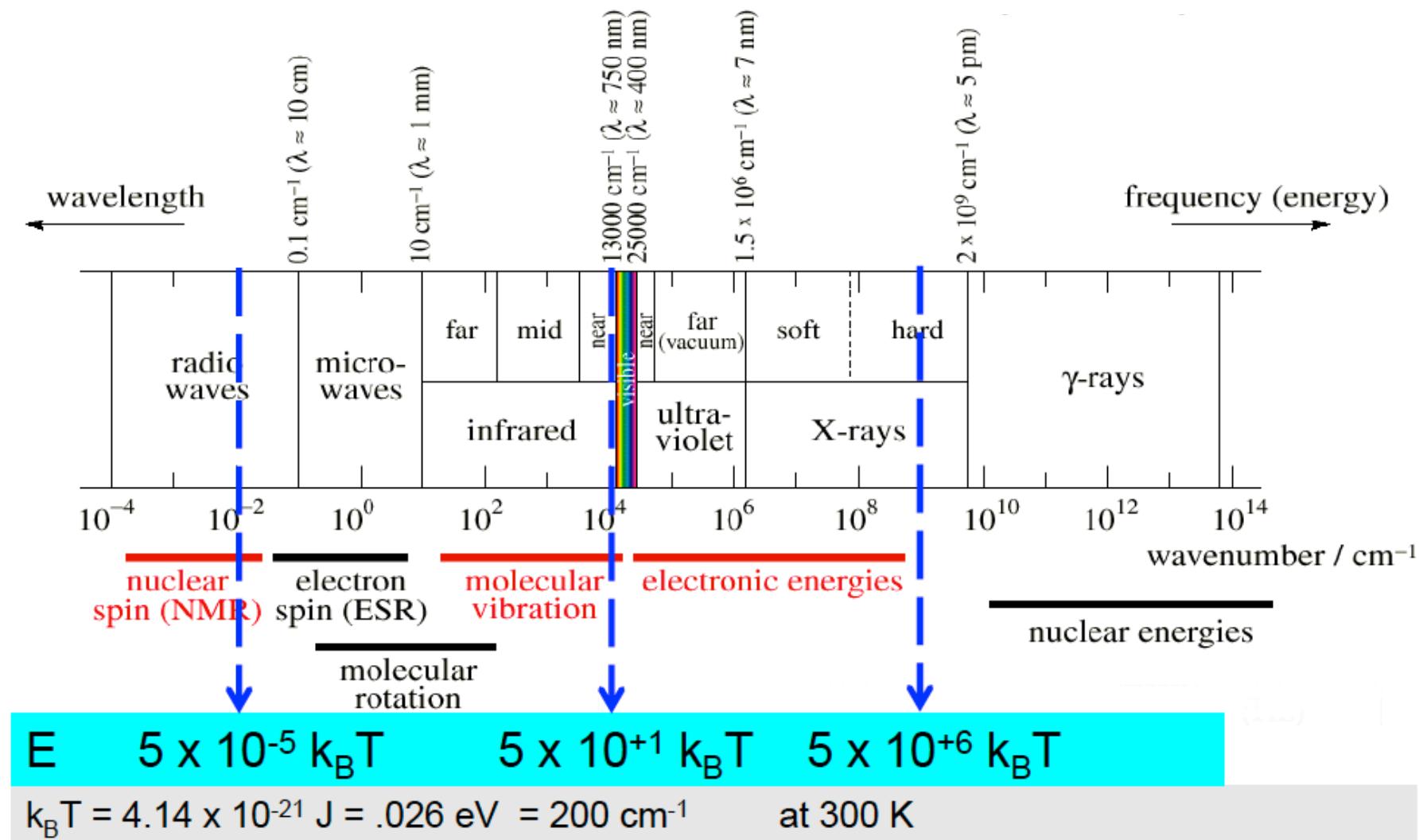
g_N nuclear g factor = 5.585 (^1H); 0.857 (^2H); 1.405 (^{13}C)

β_N nuclear magneton = $eh/(4\pi m_p)$ in SI units

m_p = mass of proton

Thus, NMR is a radiofrequency technique at achievable field strengths.

Nuclear Magnetic Resonance (NMR) Spectroscopy:



Magnetic, not electric, dipole interaction, and very small ΔE . Implications?

Nuclear Magnetic Resonance (NMR) Spectroscopy:

Leads to weak transitions, and so significant samples are needed...

		fraction in ground state	
ν	$h\nu$	300 K	3 K
50 MHz	$3.32 \times 10^{-26} \text{ J}$	0.500002	0.50020
500 MHz	$3.32 \times 10^{-25} \text{ J}$	0.500020	0.50201

$$\begin{aligned} \text{fraction ground state} &= \frac{\text{state}\left(+\frac{1}{2}\right)}{\text{state}\left(+\frac{1}{2}\right) + \text{state}\left(-\frac{1}{2}\right)} = \frac{1}{1 + \text{state}\left(-\frac{1}{2}\right) / \text{state}\left(+\frac{1}{2}\right)} \\ &= \frac{1}{1 + \exp[-\Delta E / k_B T]} \end{aligned}$$

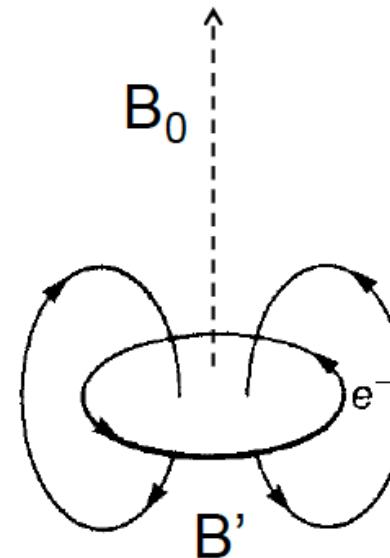
$$h = 6.63 \times 10^{-34} \text{ J sec}; k_B = 1.38 \times 10^{-23} \text{ J K}^{-1}$$

$$k_B T = 4.14 \times 10^{-21} \text{ J at 300 K}; 4.14 \times 10^{-23} \text{ J at 3 K}$$

Nuclear Magnetic Resonance (NMR) Spectroscopy:

If this were it... all compounds would show a single proton NMR peak. Fortunately, there is more!

Protons in different **chemical environments** absorb at slightly different energies. Electrons in motion create their own local magnetic field. In organic molecules this field is opposed to the applied field. The electrons therefore shield the protons because the protons experience a field smaller than the applied field.



induced magnetic field

$$B_{\text{eff}} = B_0 + B' < B_0 \text{ at nucleus: shielding}$$

$$B = B_0(1 - \sigma) \quad \text{or} \quad v_{\text{NMR}} = \gamma B_0 (1 - \sigma) / 2\pi$$

Nuclear Magnetic Resonance (NMR) Spectroscopy:

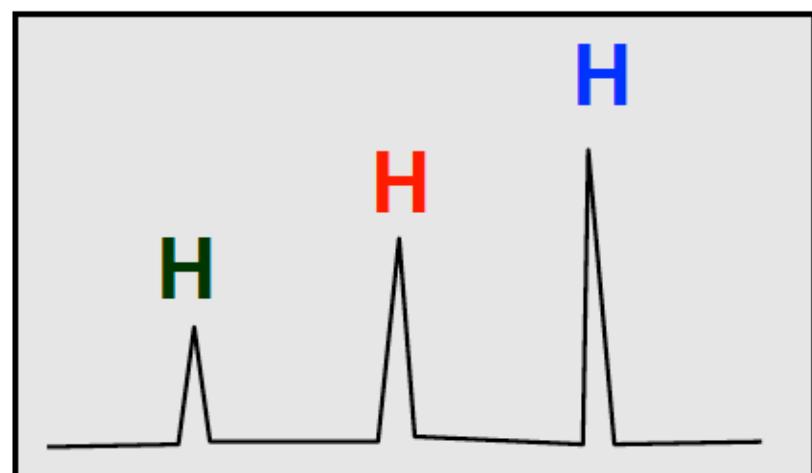
Because of these so-called *chemical shifts*...



Each type of H-atom is in a different chemical environment
They should all exhibit different NMR absorption resonance frequencies

To first approximation:

Intensity is proportional to #
of equivalent H-atoms

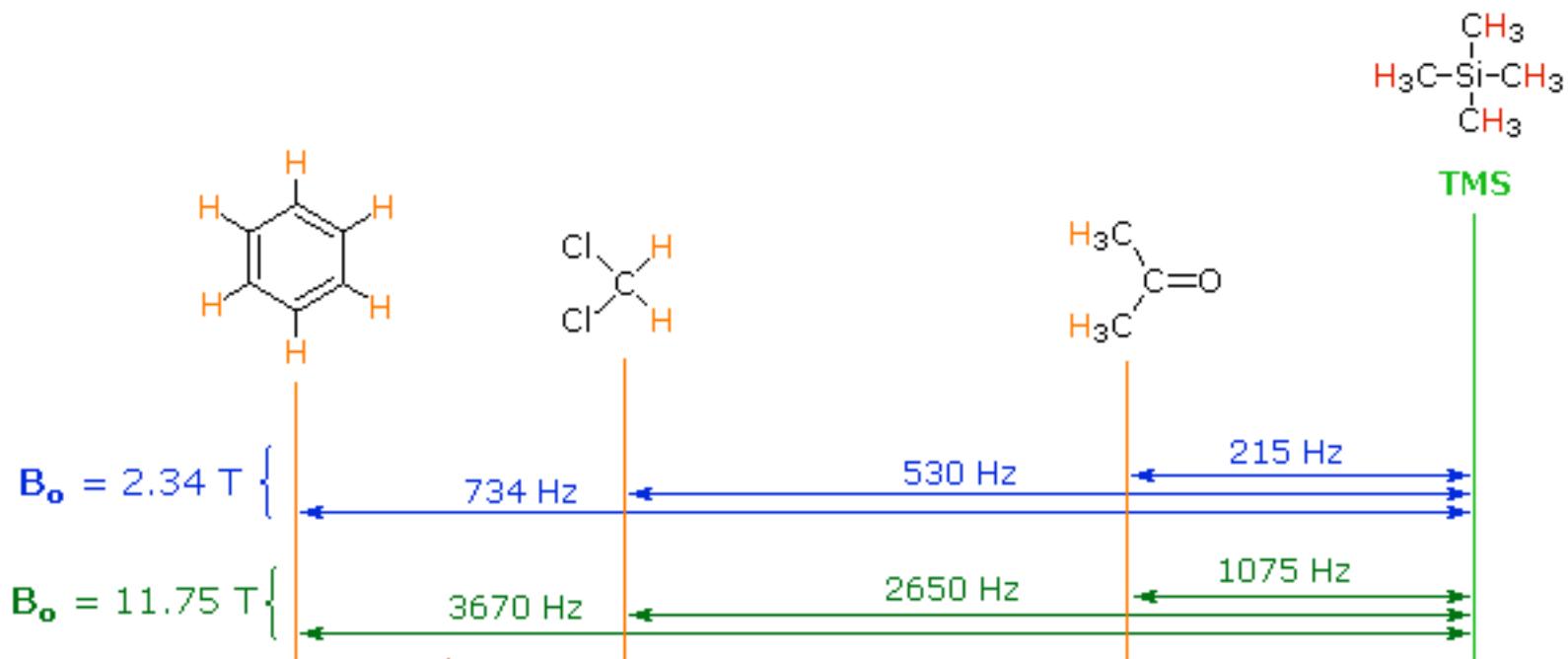


$$\int \text{Intensity} =$$

Nuclear Magnetic Resonance (NMR) Spectroscopy:

Protons in different chemical environments
therefore absorb at different frequencies:

— Increasing Magnetic Field at Fixed Frequency →
← Increasing Frequency at Fixed Magnetic Field —



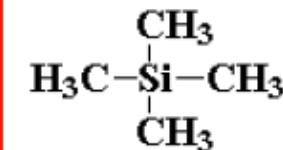
The Separation of Resonance Signals (in Hz) Increases with Increasing Field Strength

Would like a system that is B_0 independent!

Nuclear Magnetic Resonance (NMR) Spectroscopy:

These frequency shifts are measured relative to a standard
e.g. for ^1H and ^{13}C NMR, tetramethylsilane (TMS): $(\text{CH}_3)_4\text{Si}$

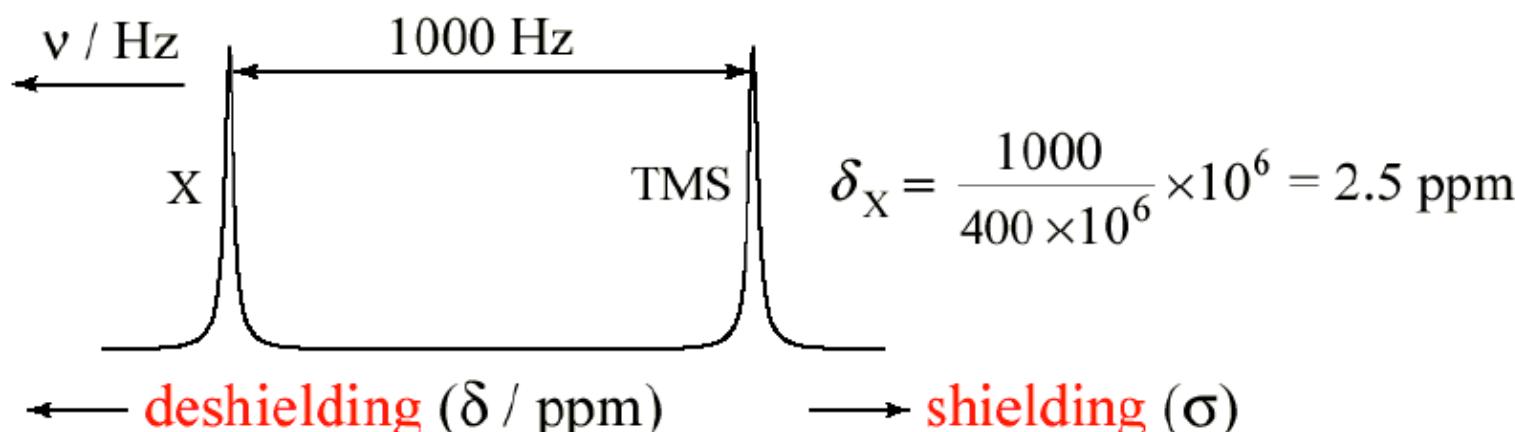
$\nu_X - \nu_{\text{TMS}}$ would depend on B_0 , therefore the
chemical shift (or ppm) scale is defined:



tetramethylsilane

$$\delta_X = \frac{\nu_X - \nu_{\text{TMS}}}{\nu_{\text{TMS}}} \times 10^6 \approx \frac{\nu_X - \nu_{\text{TMS}}}{\nu_0} \times 10^6 \text{ ppm}$$

operating frequency
(e.g. 400 MHz for ^1H)

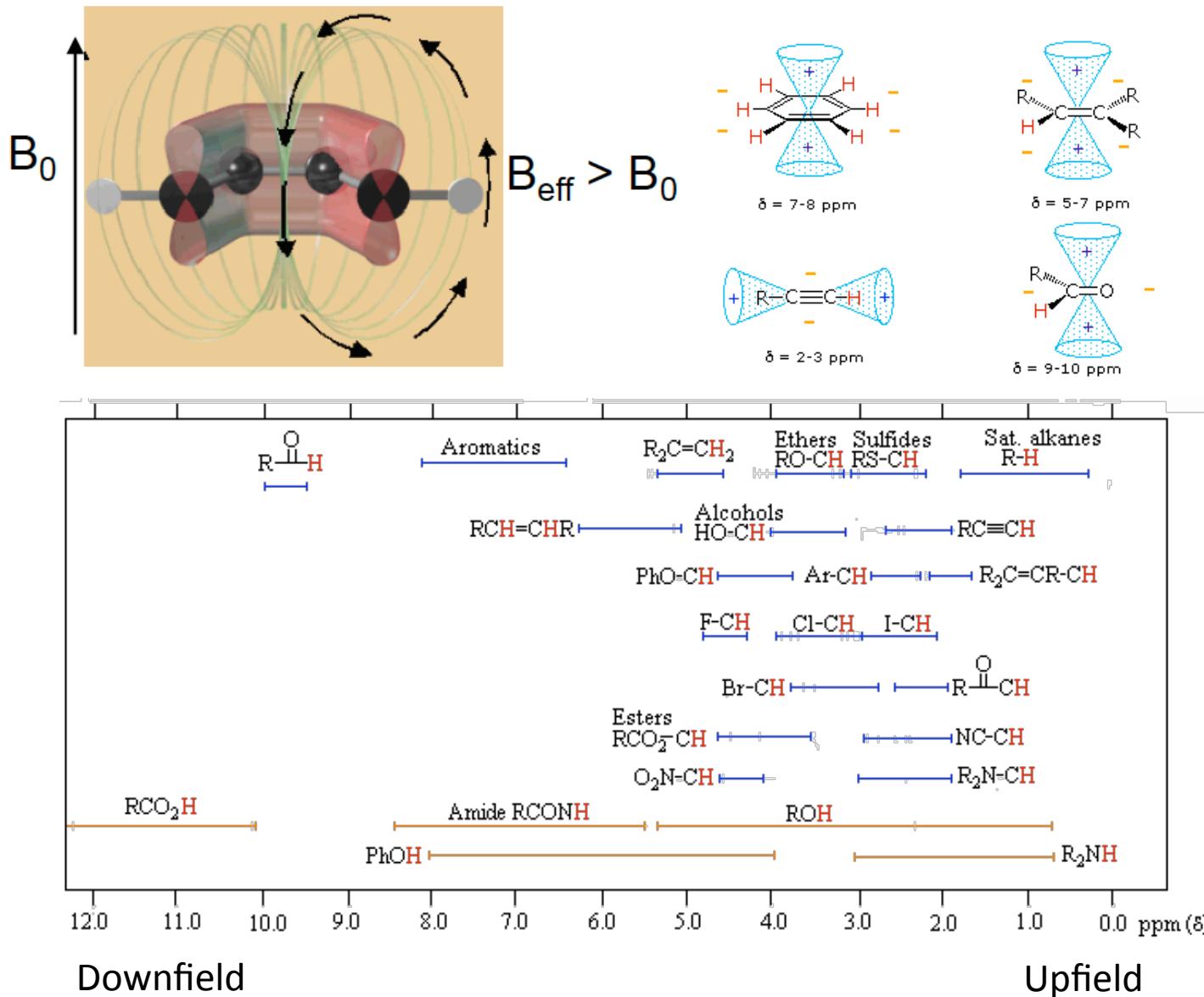


Tetramethylsilane with 12 chemically identical protons, and 4 chemically identical carbons, is used as the standard for both ^{13}C and ^1H NMR.

Nuclear Magnetic Resonance (NMR) Spectroscopy:

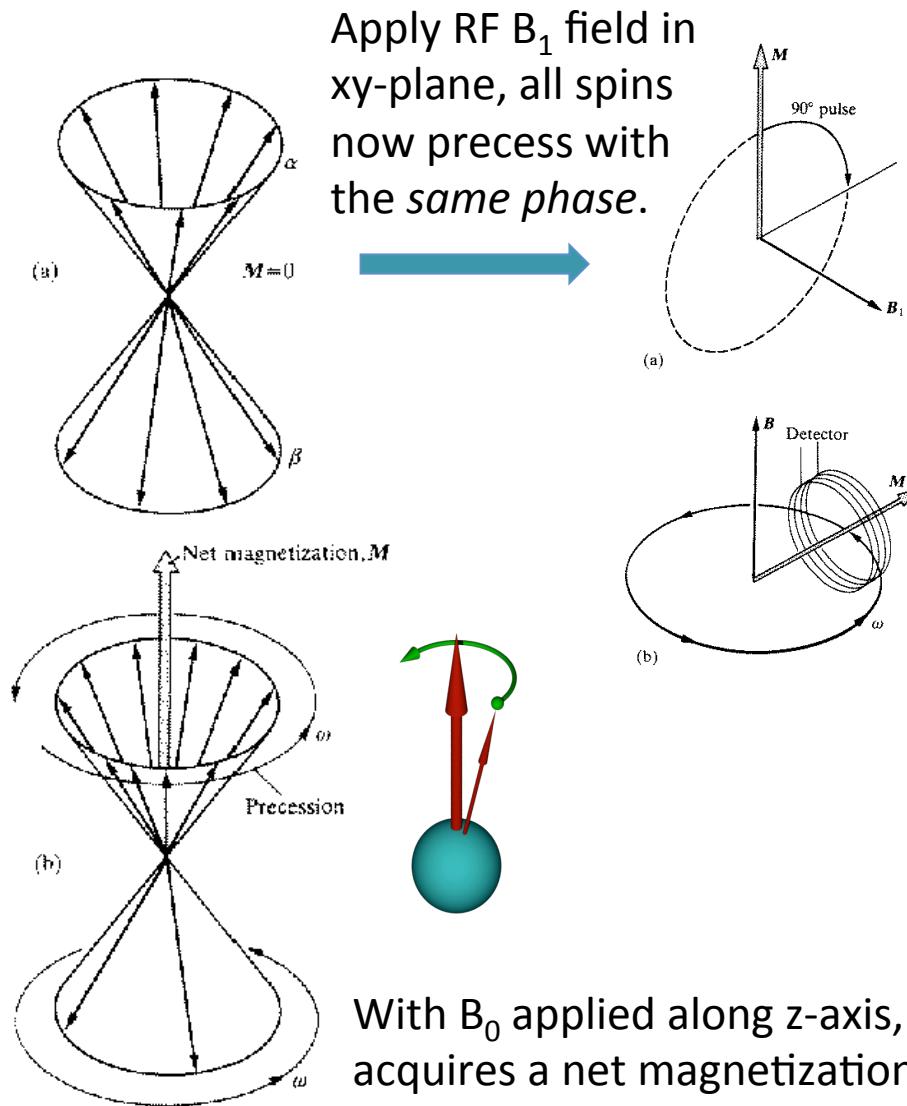
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Chemical Shift Overview



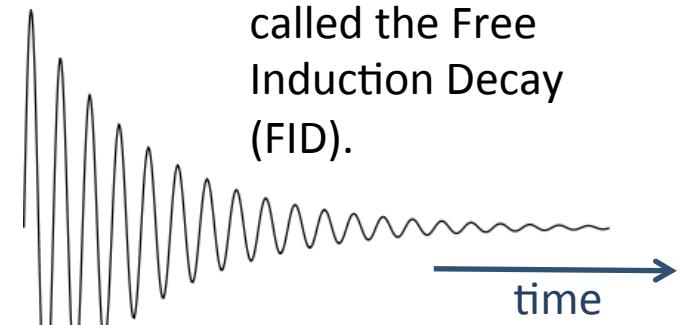
- Electronegative groups tend to de-shield protons.
- The π -system of alkenes, carbonyls and aromatics tend to de-shield protons.
- Protons attached to O or N atoms are often involved in hydrogen bonds and tend to have highly variable chemical shifts.

Fourier Transform (FT-)NMR Spectroscopy:

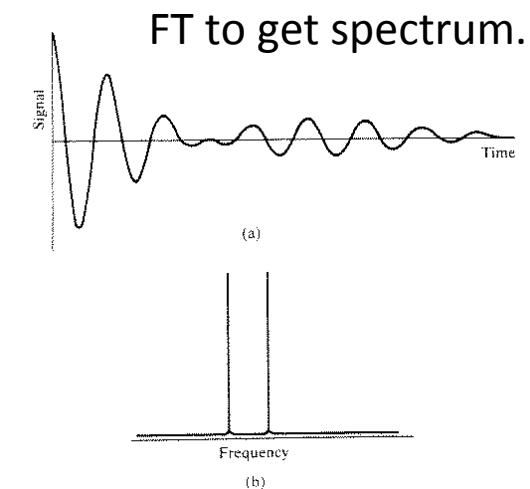


With B_0 applied along z-axis, the sample acquires a net magnetization (more spins along the field than anti-parallel).

Detect xy-plane emission, this is called the Free Induction Decay (FID).



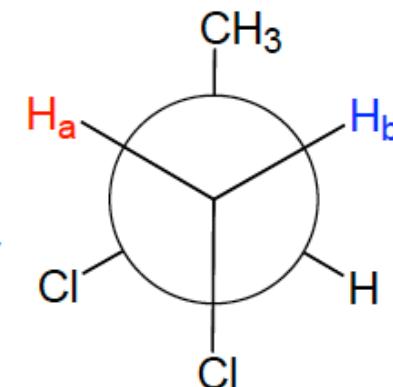
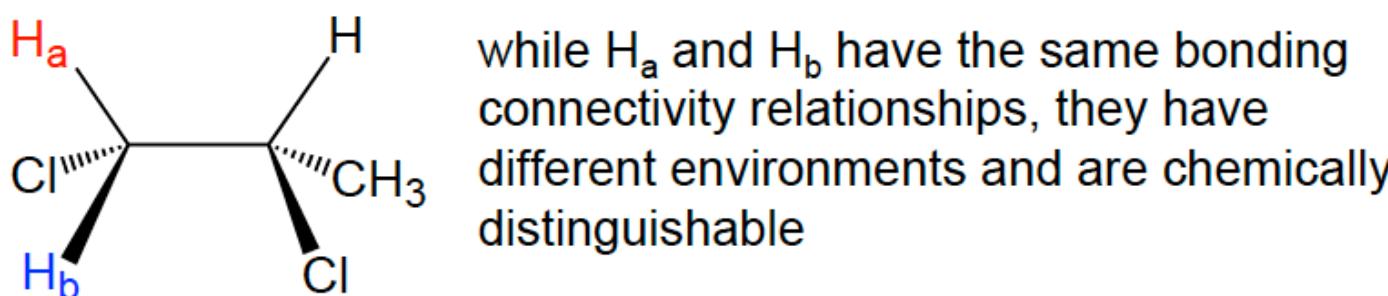
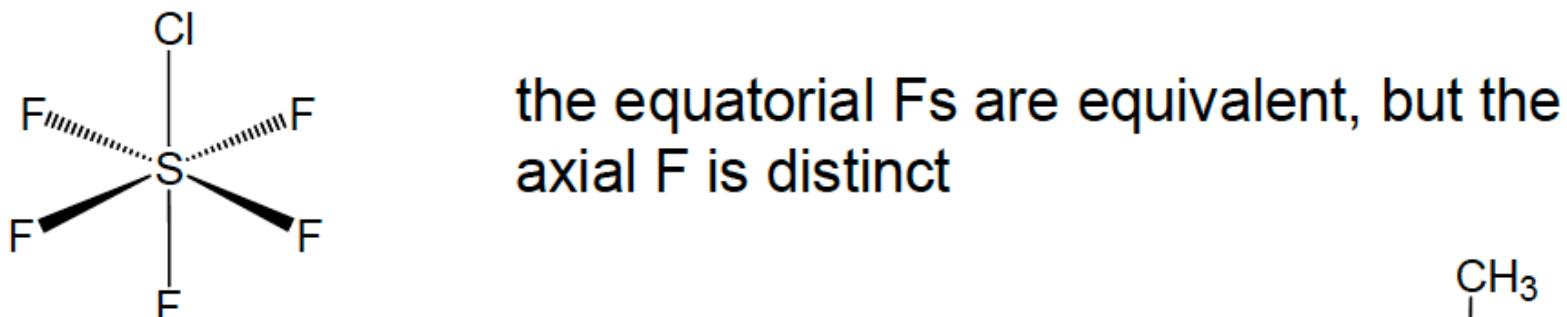
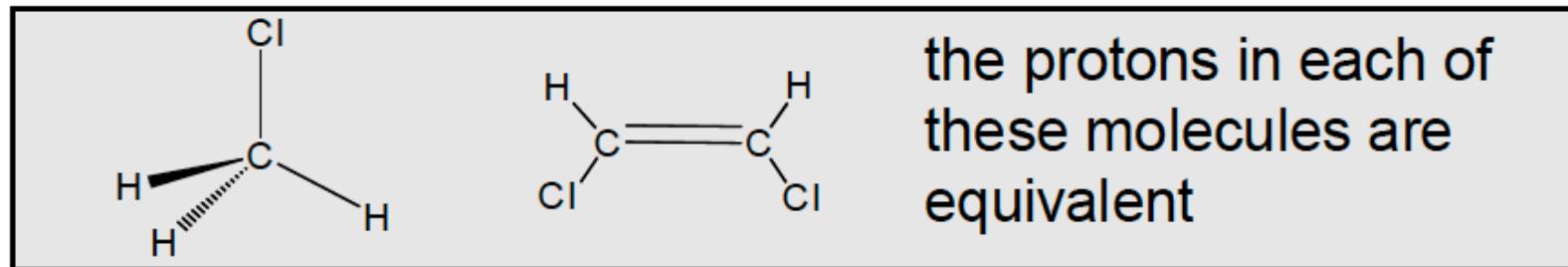
Spins dephase in ~1 sec (liquids).



Nuclear Magnetic Resonance (NMR) Spectroscopy:

Chemical Shifts & Equivalent Nuclei

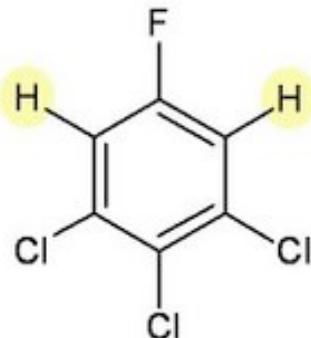
In general, we expect separate peaks for chemically distinct nuclei (protons in this lecture). Nuclei that are identical due to symmetry are called **equivalent**.



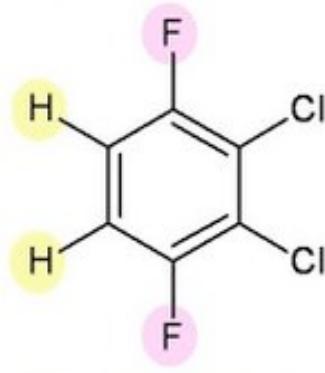
Nuclear Magnetic Resonance (NMR) Spectroscopy:

Chemical Shifts: Chemical & Magnetic Equivalence

Magnetic and Chemical Equivalence



Magnetically
Equivalent Protons



Chemically Equivalent
Protons
Chemically Equivalent
Fluorines

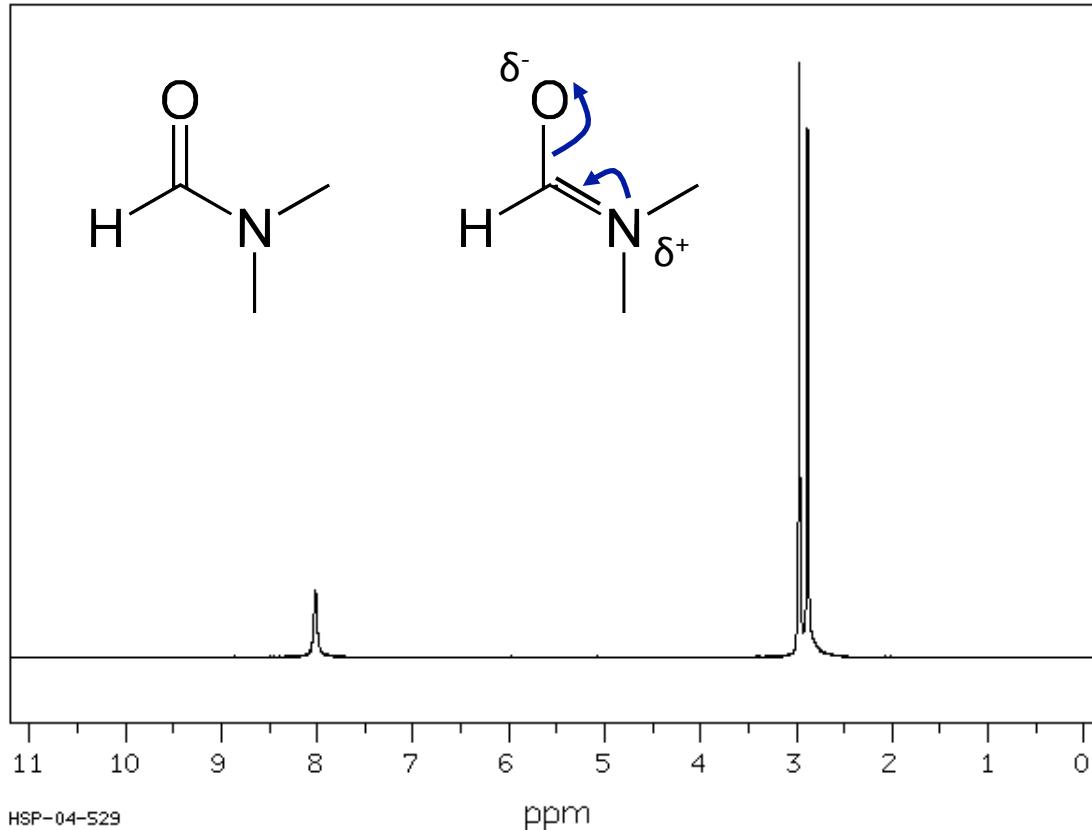
If nuclei do not have the same chemical shift (are isochronous) then they are neither chemically nor magnetically equivalent. All chemically or magnetically equivalent nuclei have the same chemical shift, but there are cases of non-equivalent nuclei having a fortuitously identical chemical shift.

If the two nuclei being considered are isochronous, one should consider how they couple to a third magnetic nucleus in the molecule which is not equivalent to them. If the coupling to the third magnetic nucleus is different for each of the nuclei being considered, then the nuclei are chemically but not magnetically equivalent to one another. If the coupling to the third magnetic nucleus is identical (and this is true for every magnetic nucleus other than those being considered) then the two nuclei are both magnetically and chemically equivalent.

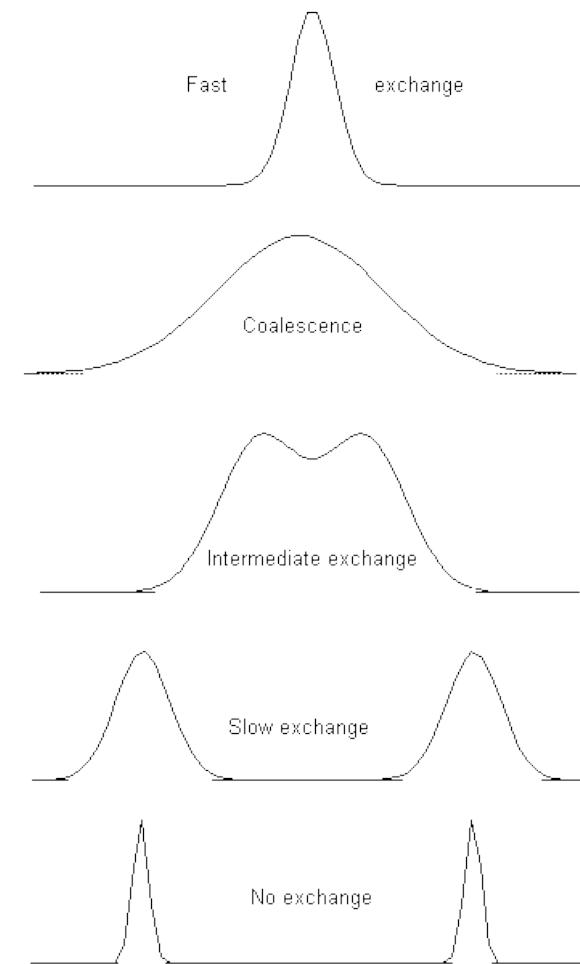
Why do we care?

Nuclear Magnetic Resonance (NMR) Spectroscopy:

Chemical Shifts: Chemical & Magnetic Equivalence



Room temperature proton NMR spectrum of N,N-dimethylformamide.



What do you think will happen near $\delta=3$ ppm if the temperature is increased?

Nuclear Magnetic Resonance (NMR) Spectroscopy:

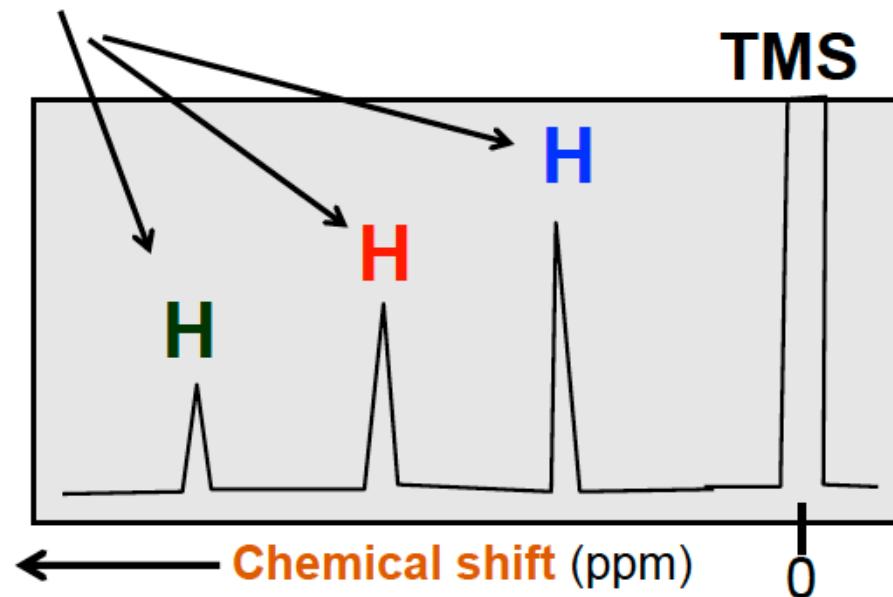
Equivalent H-atoms are degenerate

However, the energy levels may be split by adjacent H-atoms
(this is where much of the chemical information comes from)

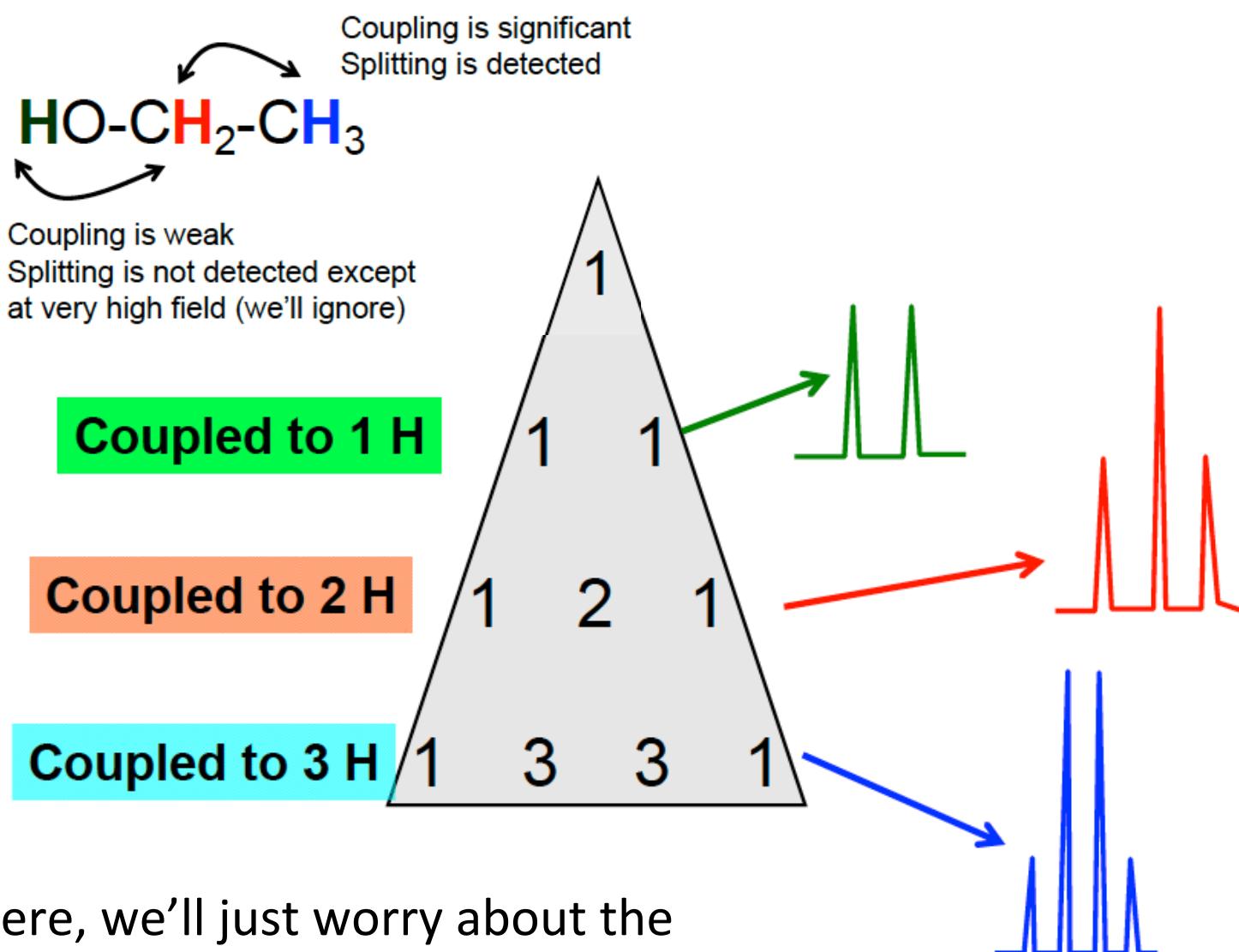


H is influenced by H
H is influenced by H and H
H is influenced by H

These peaks will split

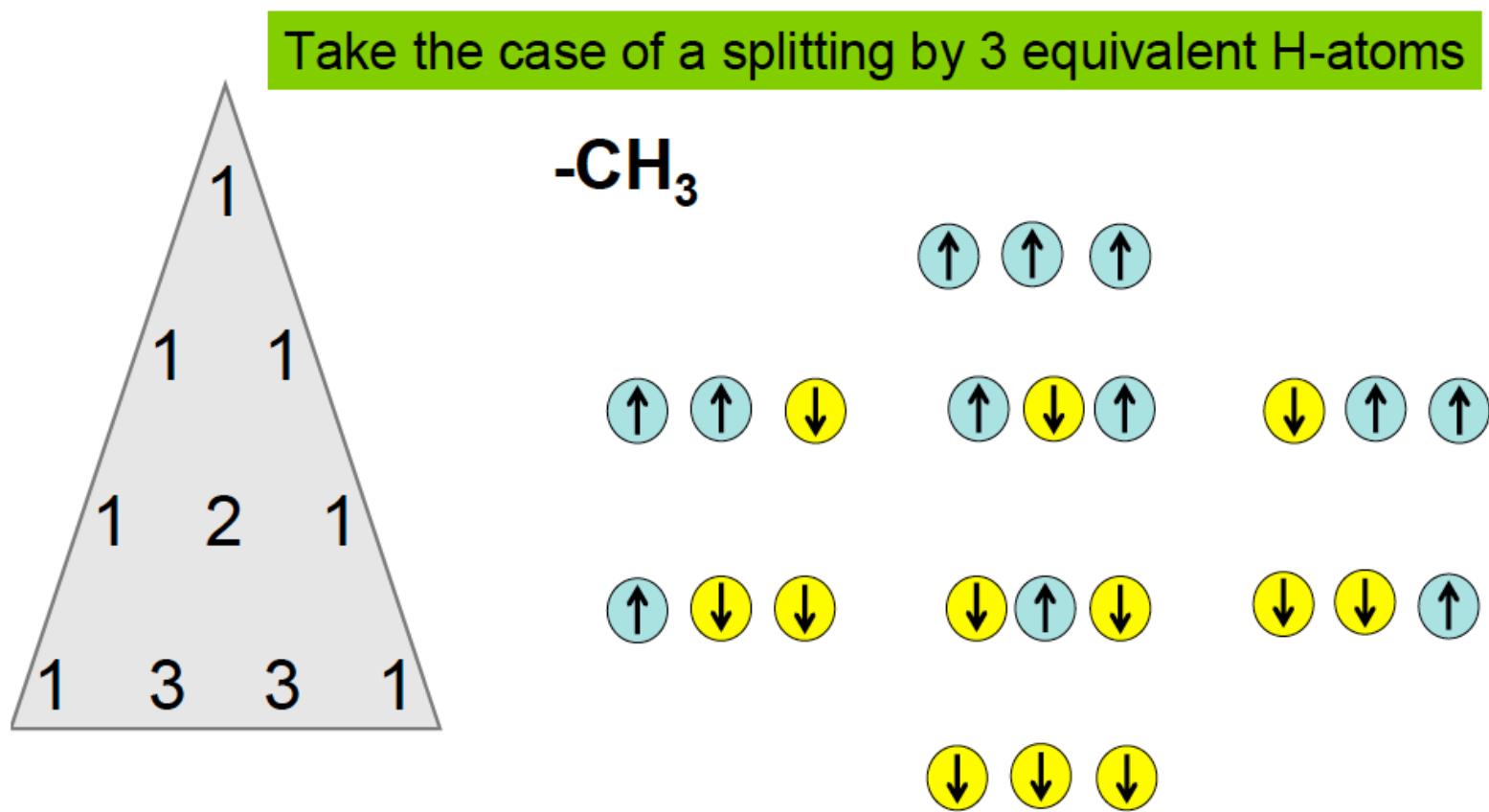


Nuclear Magnetic Resonance (NMR) Spectroscopy:



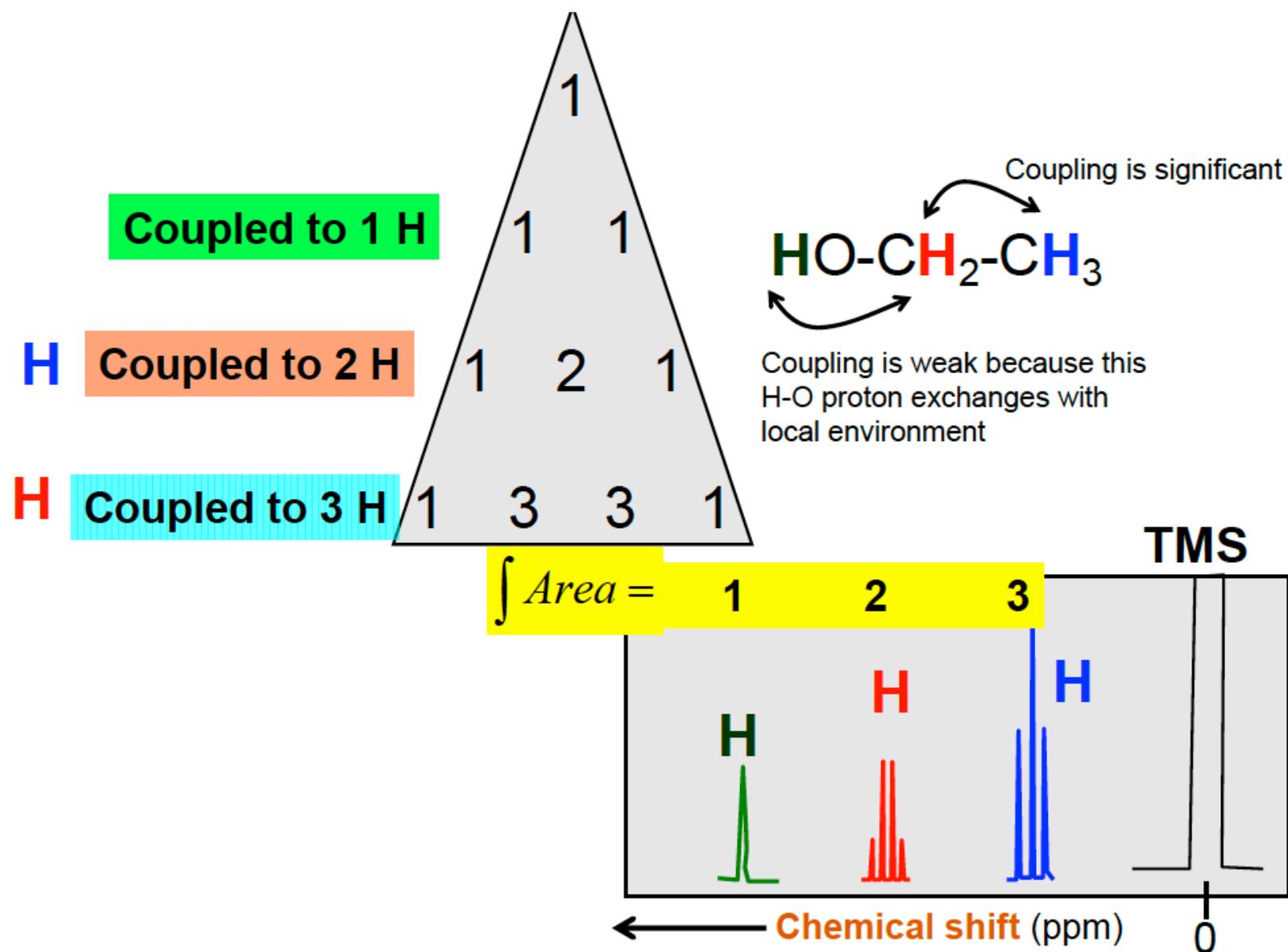
Nuclear Magnetic Resonance (NMR) Spectroscopy:

Pascal's Triangle & Spin-Spin Splittings:



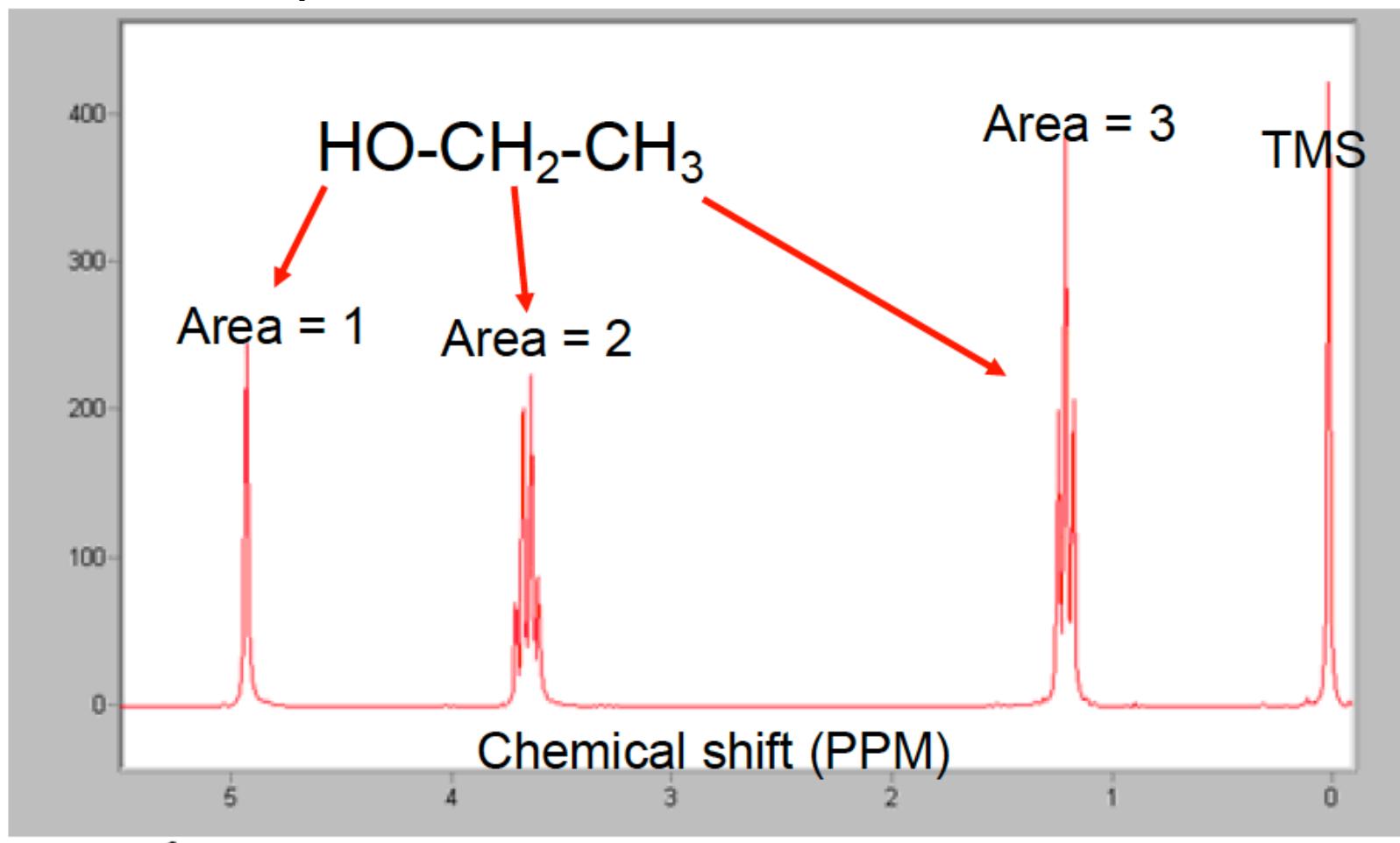
Here, we'll just worry about the coupling of protons on *adjacent* nuclei.

Nuclear Magnetic Resonance (NMR) Spectroscopy:



Nuclear Magnetic Resonance (NMR) Spectroscopy:

^1H NMR Spectrum of Ethanol:

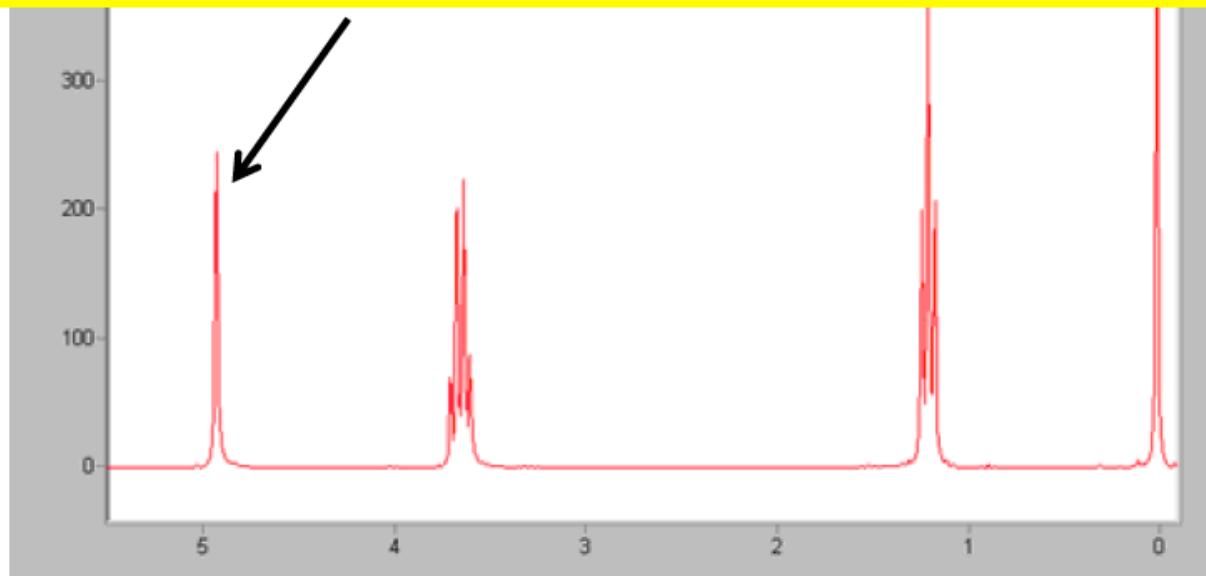


increasing B experienced by nucleus;
increasing ν at fixed B.

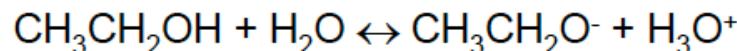
Nuclear Magnetic Resonance (NMR) Spectroscopy:

^1H NMR Spectrum of Ethanol:

why isn't the OH proton also a triplet?



when traces of water are present, the OH proton exchanges with water



This proton exchange disrupts the spin-spin coupling between the OH and CH_2 protons, so only a single OH proton is observed.

At low temperatures and with pure ethanol, the OH signal is a triplet and the CH_2 signal is a(n) ???

Nuclear Magnetic Resonance (NMR) Spectroscopy: ^{28}Si



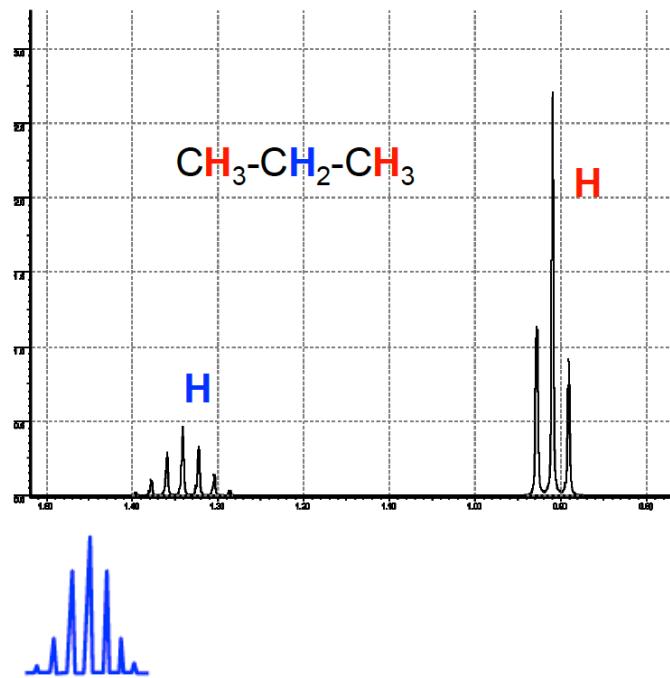
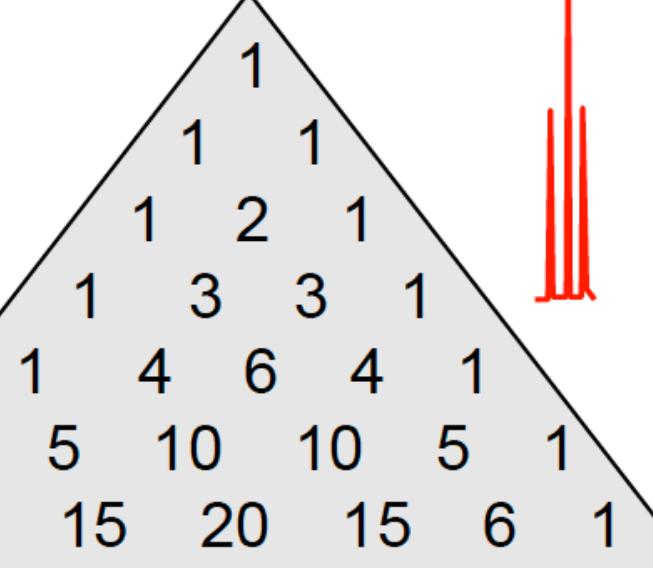
What do we expect to see?

Two types of protons 6:2 intensity ratio

Coupled to 2 H

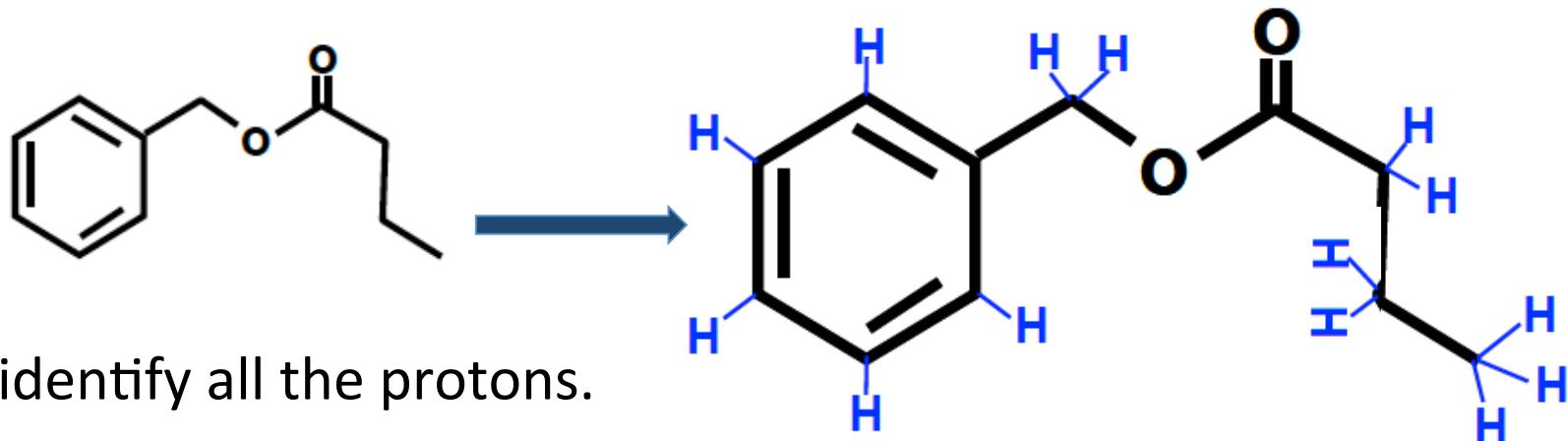
H

Coupled to 6 H

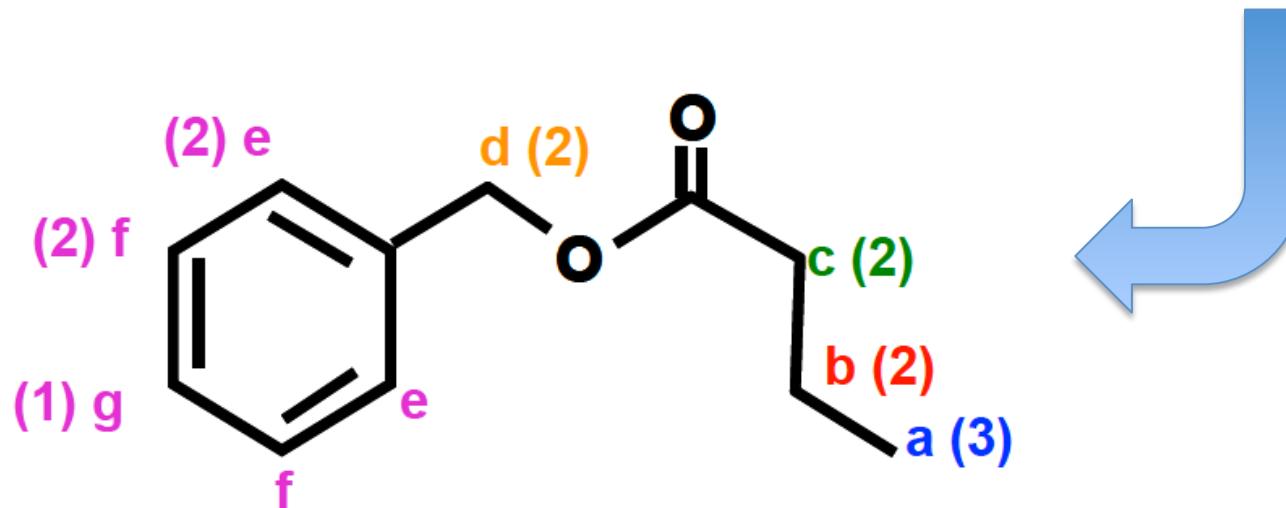


Nuclear Magnetic Resonance (NMR) Spectroscopy:

How about this molecule?



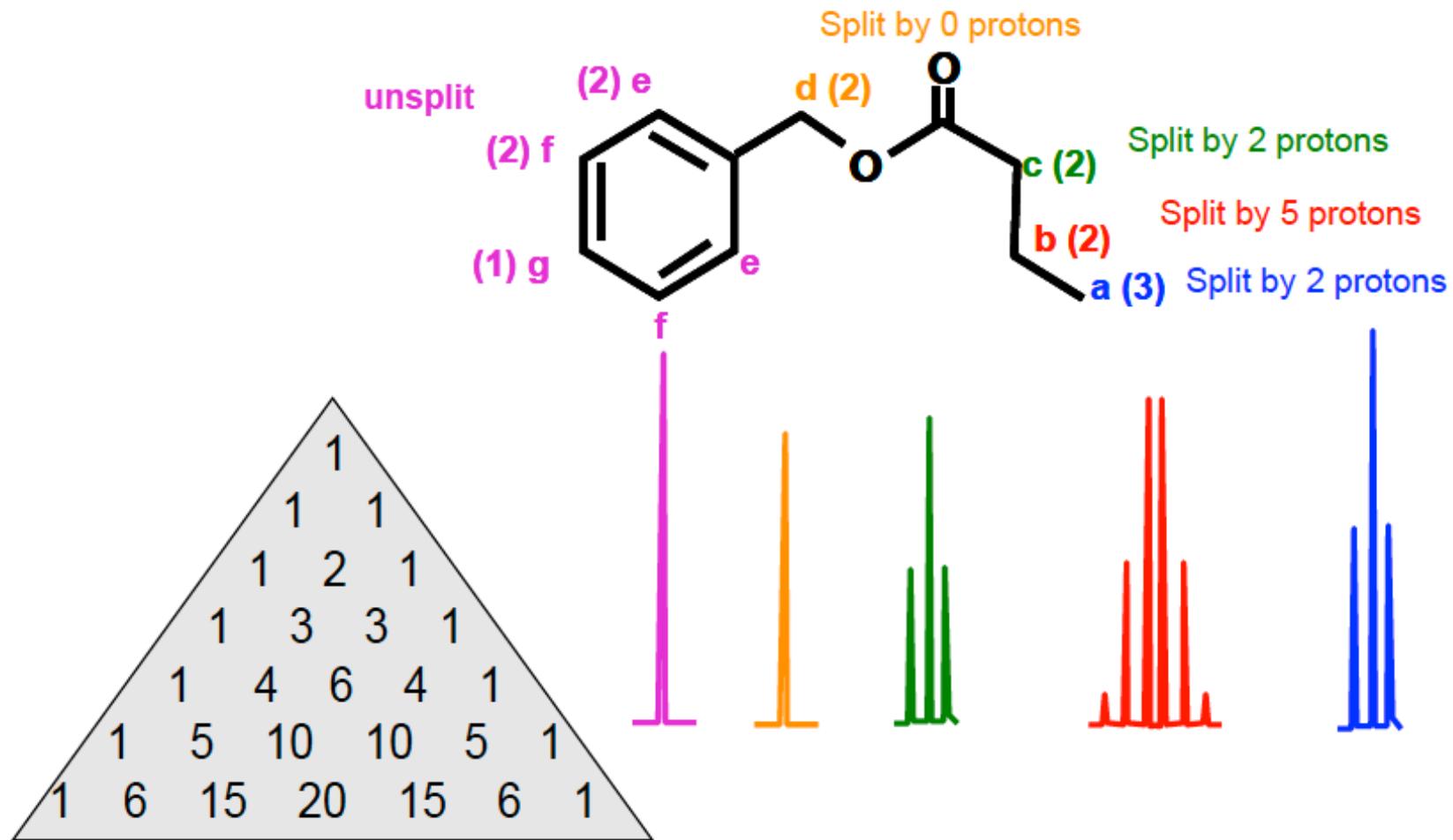
First, identify all the protons.



Next, identify which protons are unique.

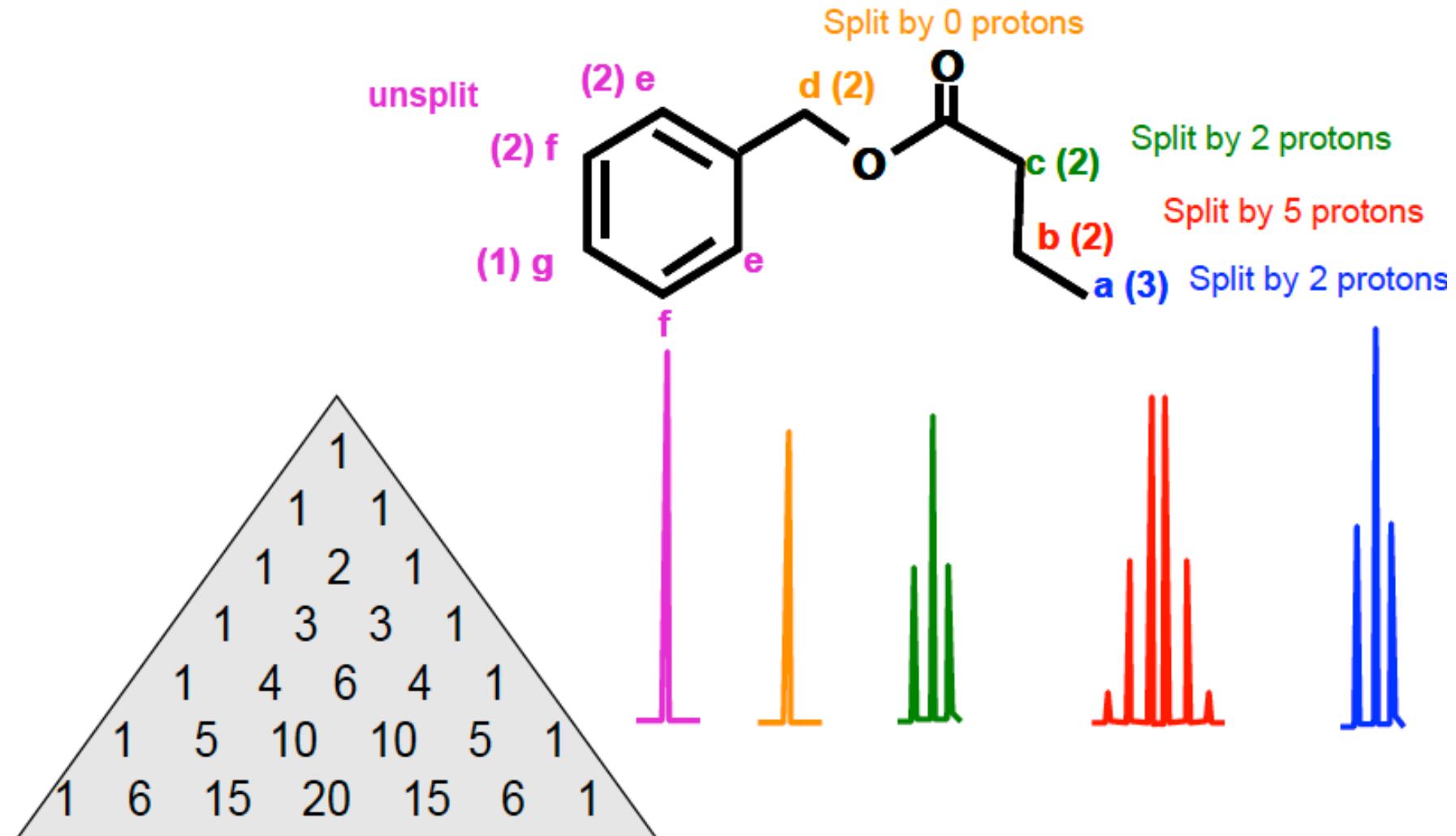
Nuclear Magnetic Resonance (NMR) Spectroscopy:

Then, identify the spin-spin splittings using Pascal's triangle:



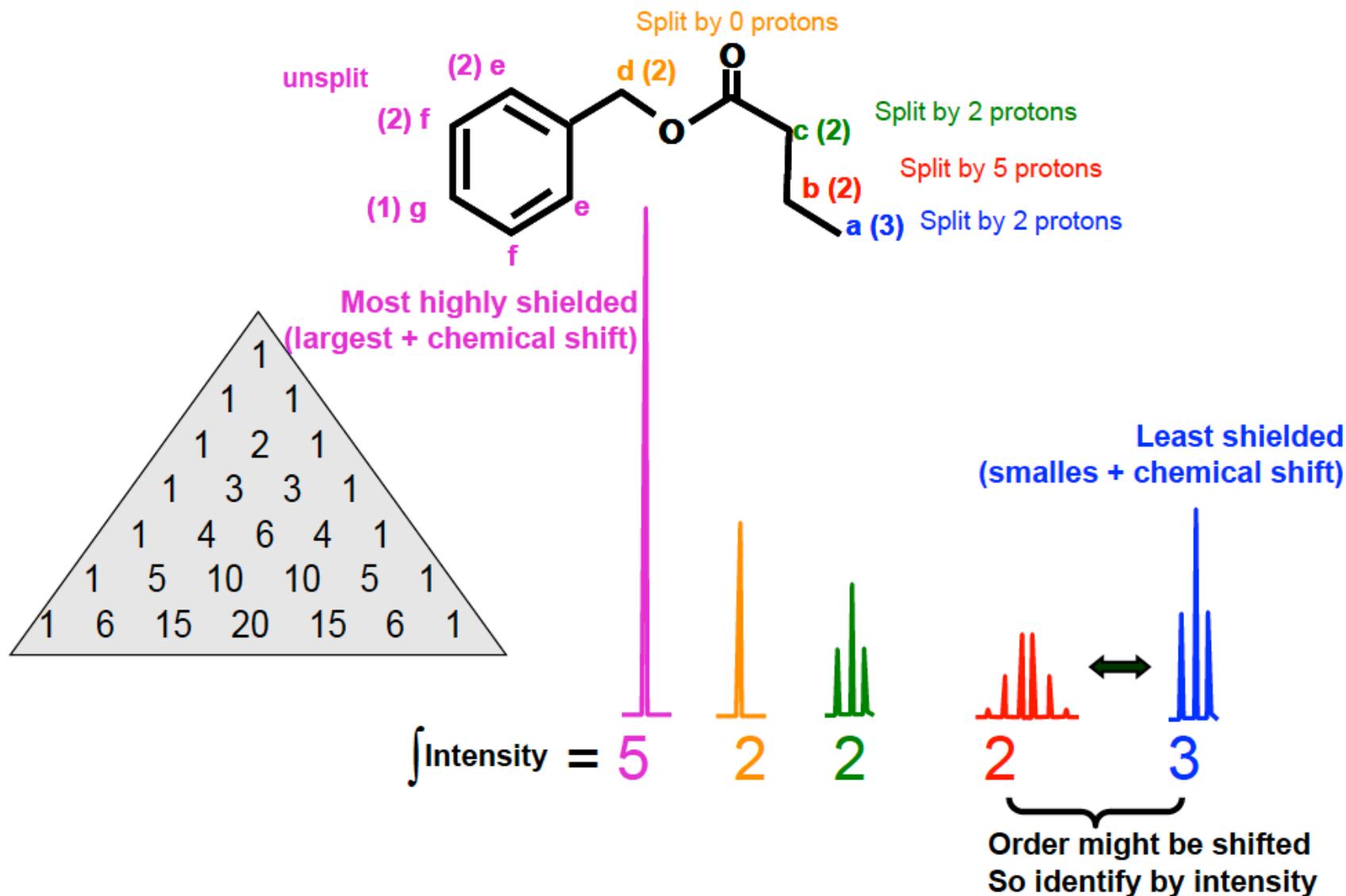
Nuclear Magnetic Resonance (NMR) Spectroscopy:

Don't forget we can estimate the relative intensites as well:

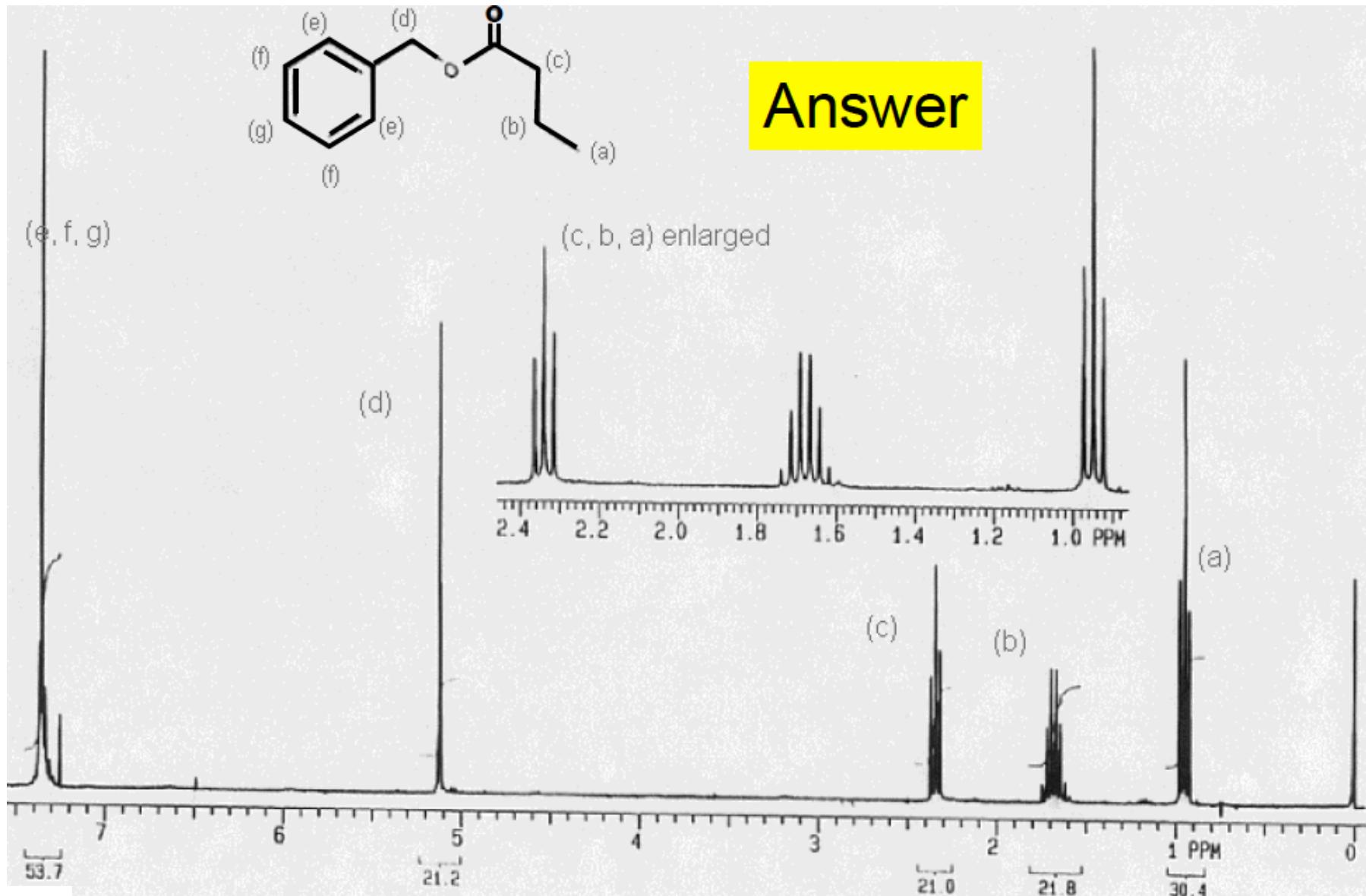


Nuclear Magnetic Resonance (NMR) Spectroscopy:

Finally, estimate the chemical shifts:



Nuclear Magnetic Resonance (NMR) Spectroscopy:

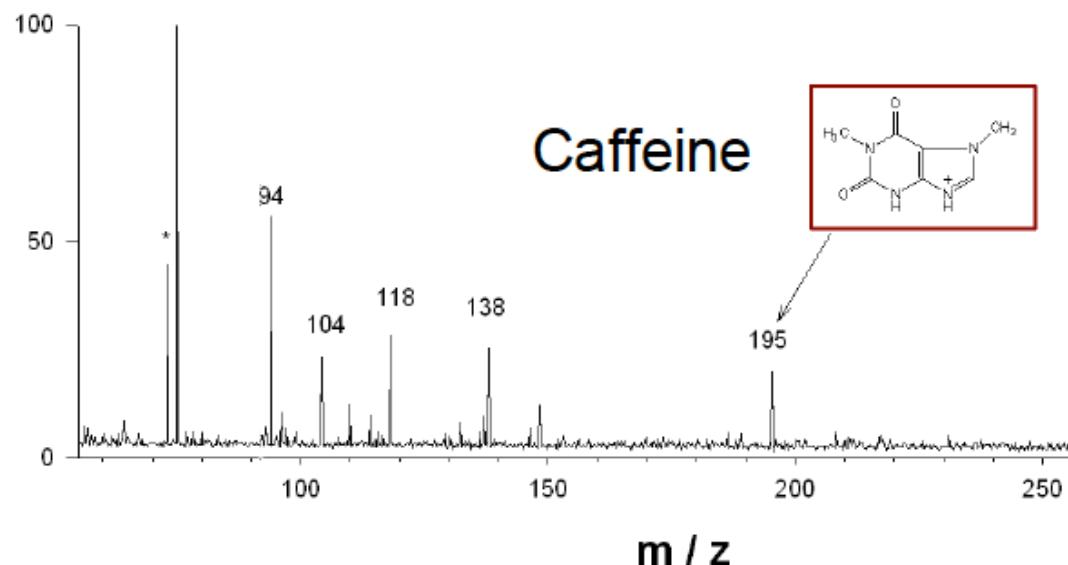


Nuclear Magnetic Resonance (NMR) Spectroscopy:

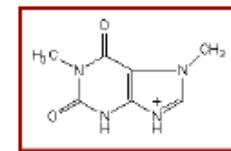
Let's work a couple of combined IR/NMR problems. Often in such problems you are given the molecular weight/formula. How?

Mass Spectrometry:

A Powerful Tool for Chemical Analysis and
Molecular Structure Determination



Caffeine



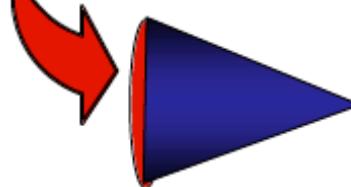
Organic
Compounds in
Peet's Coffee

OGC pp. 19-21

[www.cem.msu.edu/~reusch/VirtualText/Spectrpy/
MassSpec/masspec1.htm](http://www.cem.msu.edu/~reusch/VirtualText/Spectrpy/MassSpec/masspec1.htm)

Mass spectrometer components

Sample



Ionization

Electron ionization (EI)

Chemical ionization (CI)

Photoionization

Fast atom bombardment

Field ionization

Atmospheric pressure CI

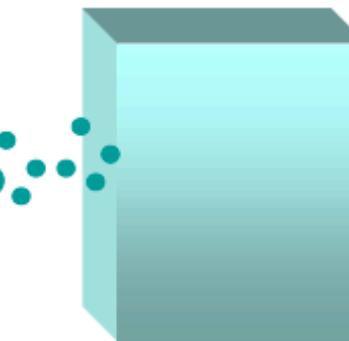
Particle impact

Electrospray

MALDI

DART (most recent)

....



Mass Analysis

Magnetic sector

Quadrupole filter

Ion trap (linear)

Time-of-flight

FTMS

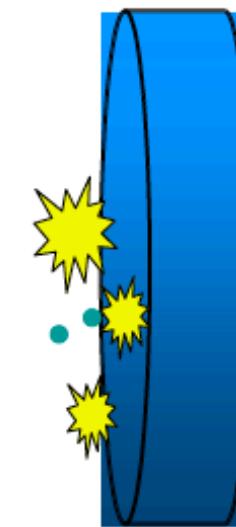
Orbitrap

Tandem and hybrids

Triple quad, TOF-TOF

Q-trap and q-TOF

....



Detection

Electron multiplier

Channeltron

Microchannel plate

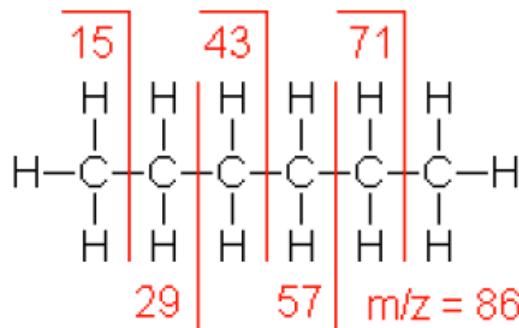
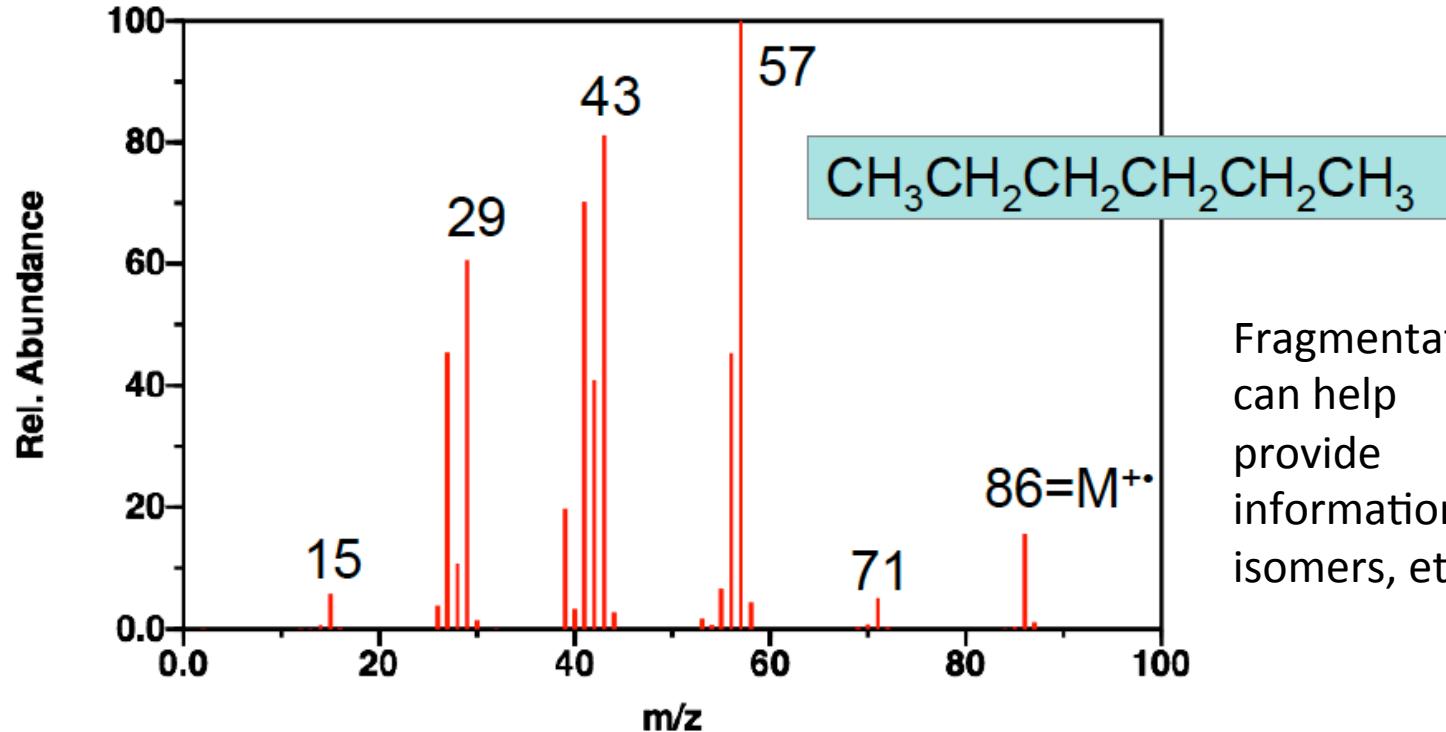
Faraday cup

Photomultiplier

....

Mass Spectrometry: High resolution gives MW

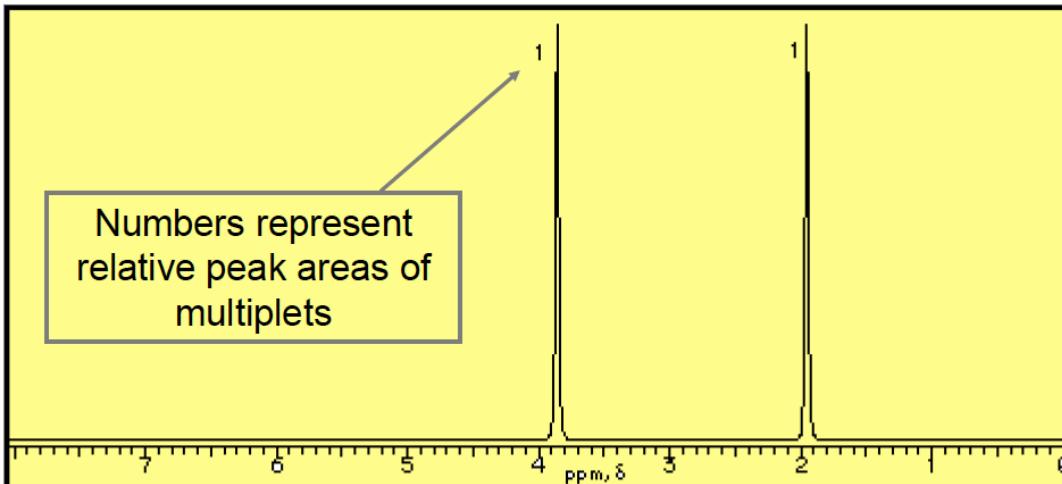
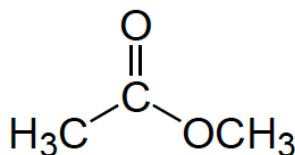
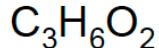
Hexane C_6H_{14} MW = 86.18



Alkanes fragment extensively due to the delocalized charge in the molecular ion

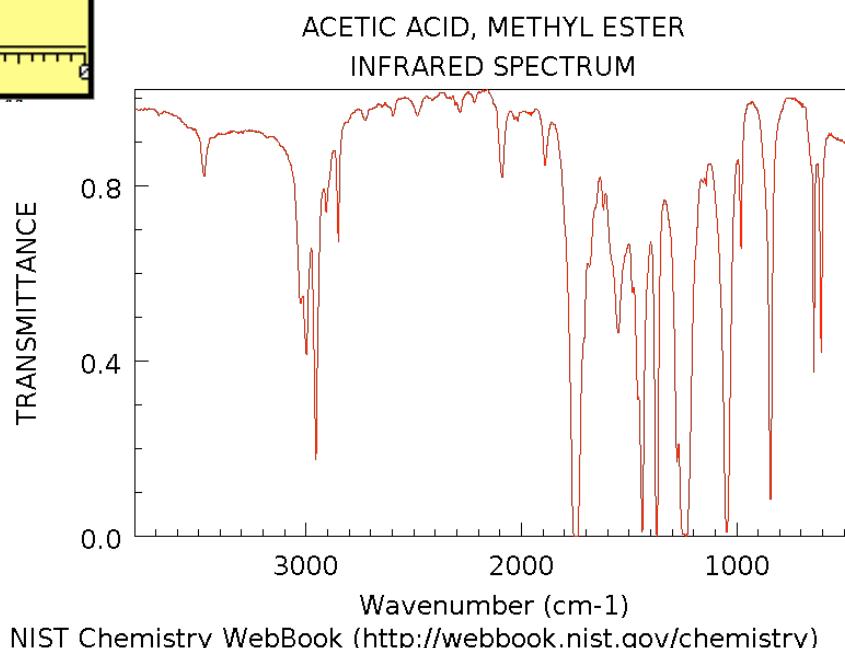
Nuclear Magnetic Resonance (NMR) Spectroscopy:

^1H NMR spectra of methyl acetate



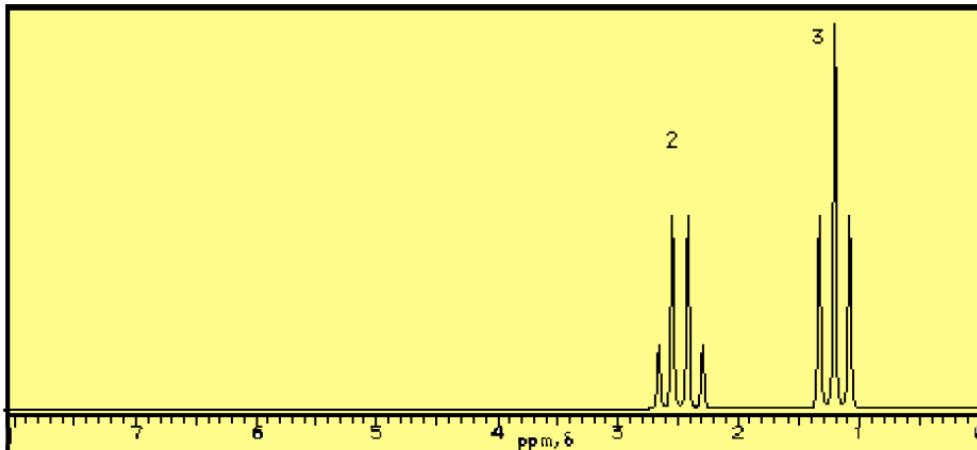
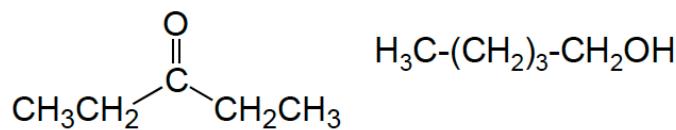
The IR spectrum shows no hydrogen bonding but a carbonyl peak and a C-O stretch, so it's got to be an ester. Only answer, given the formula, is methyl acetate.

Proton NMR shows only two distinct protons, not on adjacent carbon nuclei (no splittings).



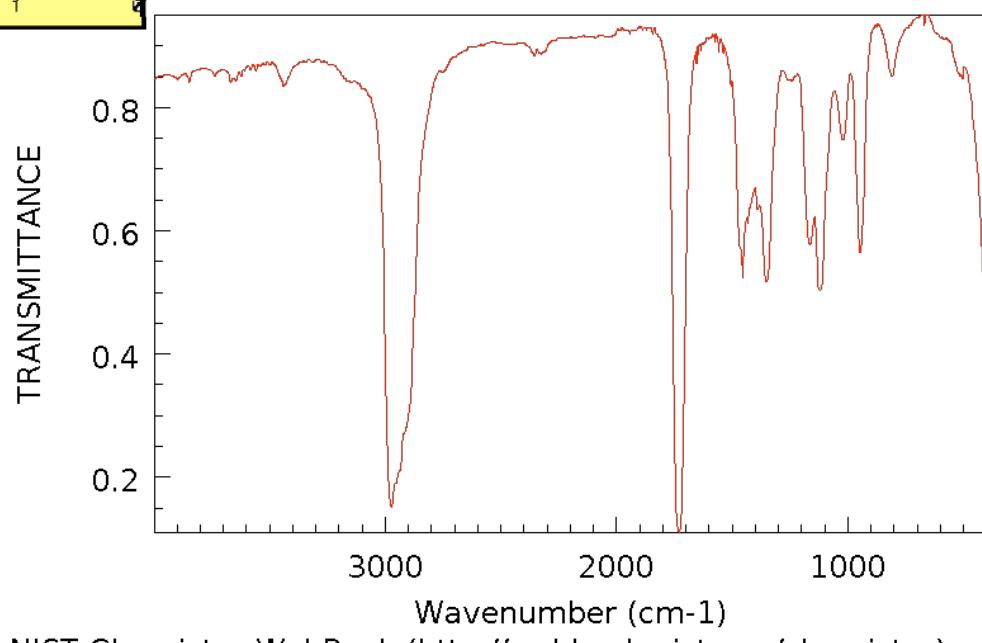
Nuclear Magnetic Resonance (NMR) Spectroscopy:

formula
 $C_5H_{10}O$



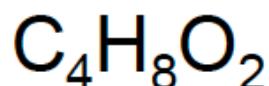
Classic ethyl group pattern in proton NMR (2/3 intensity ratio in quartet/triplet), intensity ratios demand diethyl, not n-pentyl...

Again, IR spectrum shows no hydrogen bonding and a strong carbonyl signature, so in this case it's ketone given the formula, not an alcohol.

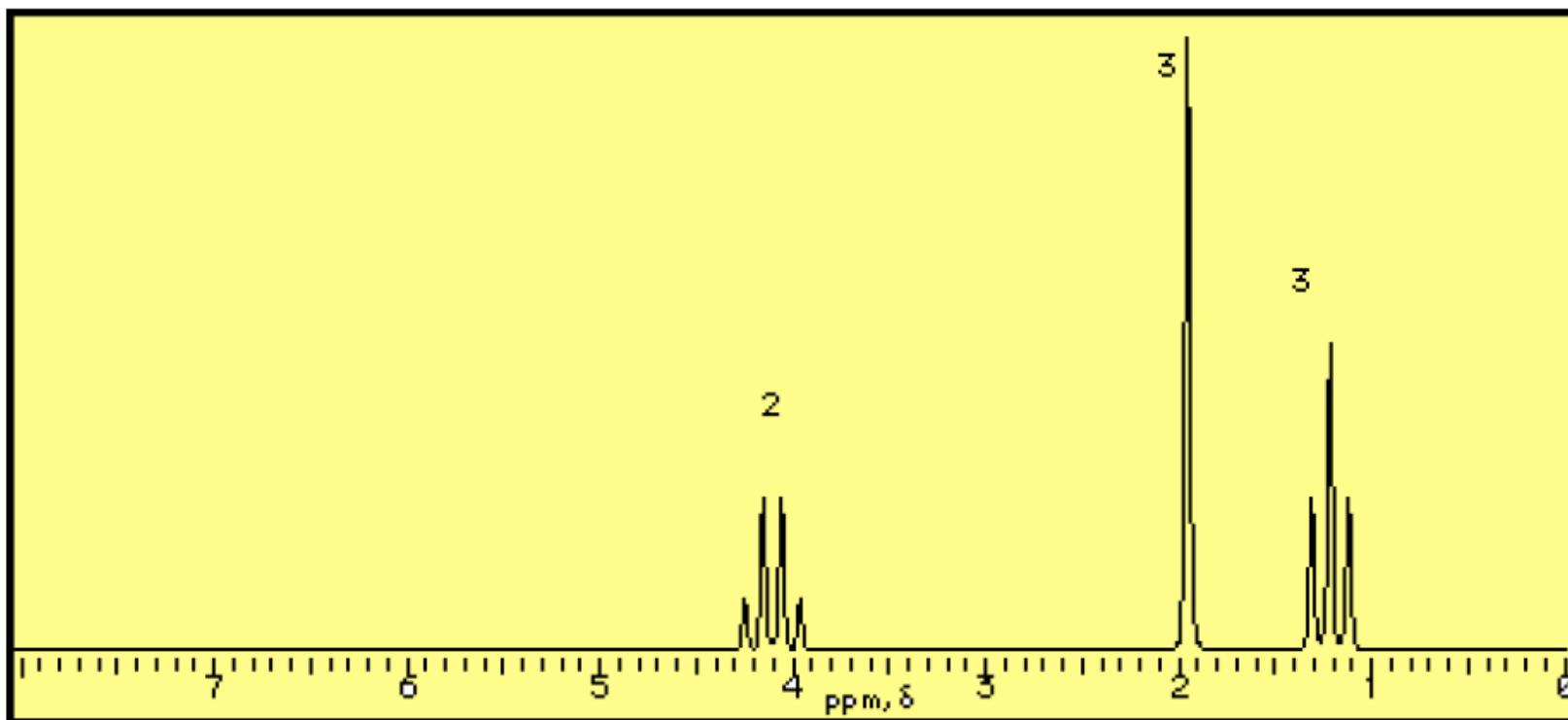


Nuclear Magnetic Resonance (NMR) Spectroscopy:

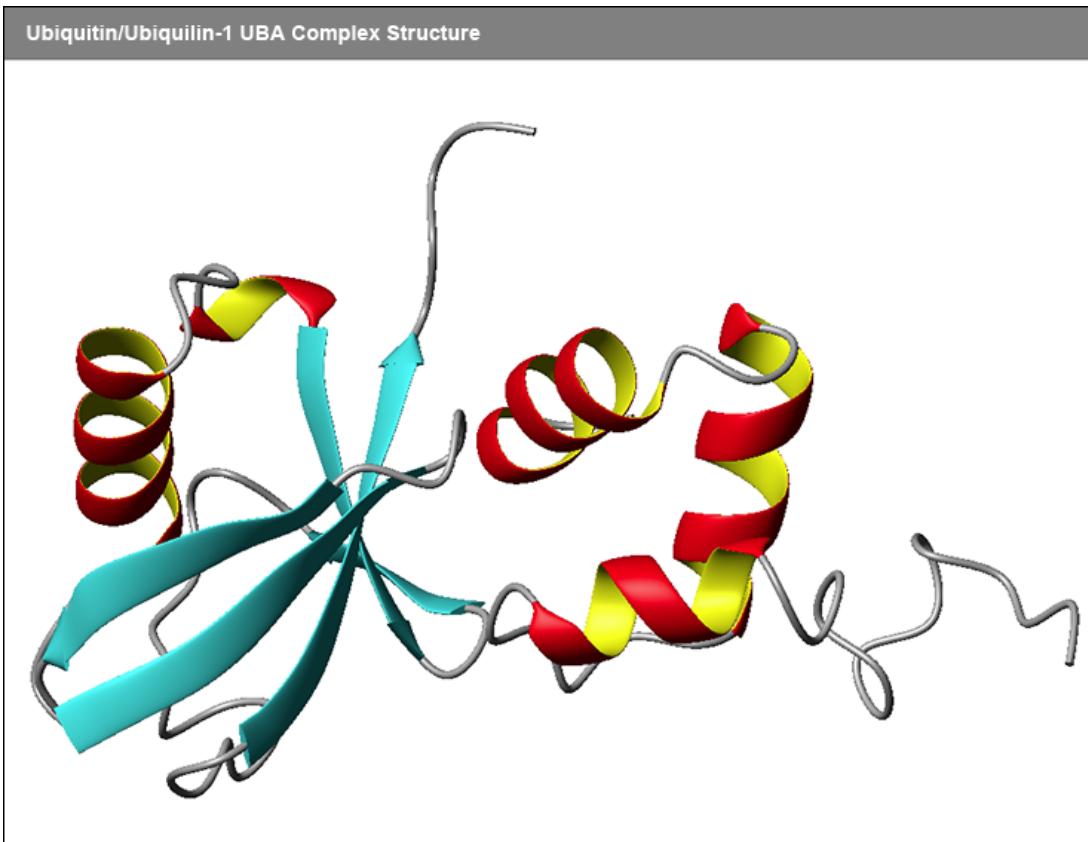
Should be easy:



What is the correct structure?

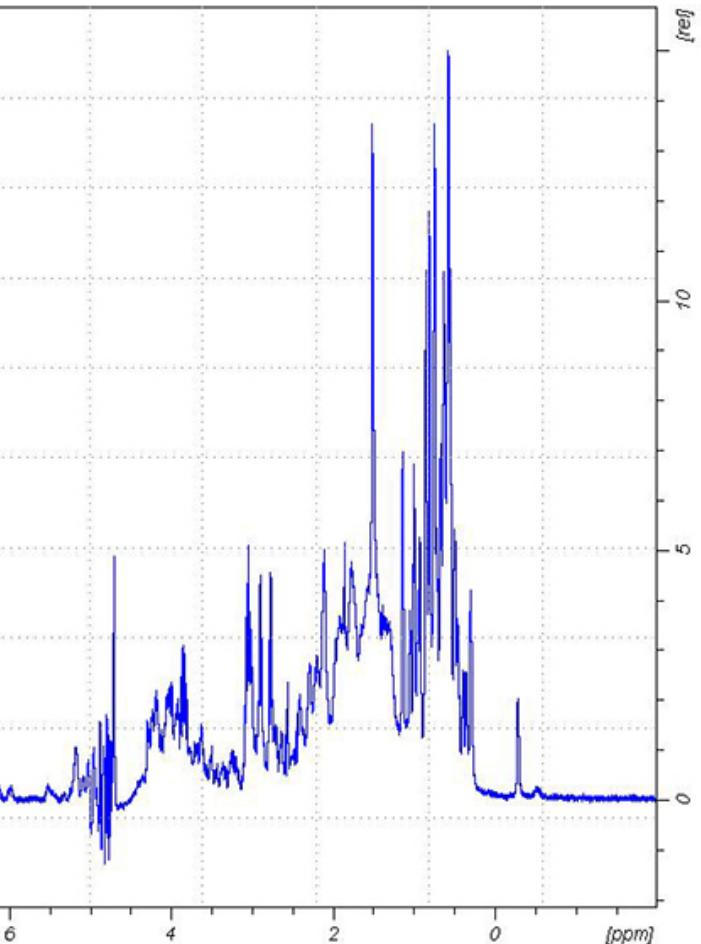


Can NMR probe “the greasy stuff”?



Ubiquitin: “Only” 8.5 kD in size...

Yet the proton NMR spectrum is *very* complex!



Earlier we showed that IR & UV (CD) spectra probed the *secondary* structure. NMR can determine the *tertiary* (3D) structure of a protein.
How is this possible?

Can NMR probe “the greasy stuff”?

The key is to couple and uncouple spins from each other using pulse sequences. High B field of enormous help here!

