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Instrumentation Facility

Massachusetts
Institute of
Technology

Introduction to NMR

Part 1

Revised 2/19/07
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What is an NMR?

- Niobium-tin-copper clad coil wound like a spool of thread. The current runs through this coil, creating the magnetic field.
- This coil is submerged in liquid helium (boiling point -452.1°F, -268.9°C, 4^{o}K – Brrr!!!!) .
- Liquid He chamber surrounded by liquid nitrogen (boiling point -320.5°F, -195.8°C, 77^{o}K).
- Sample and spinner lowered using air from the top, down through the bore, until it nests in the top of the probe.

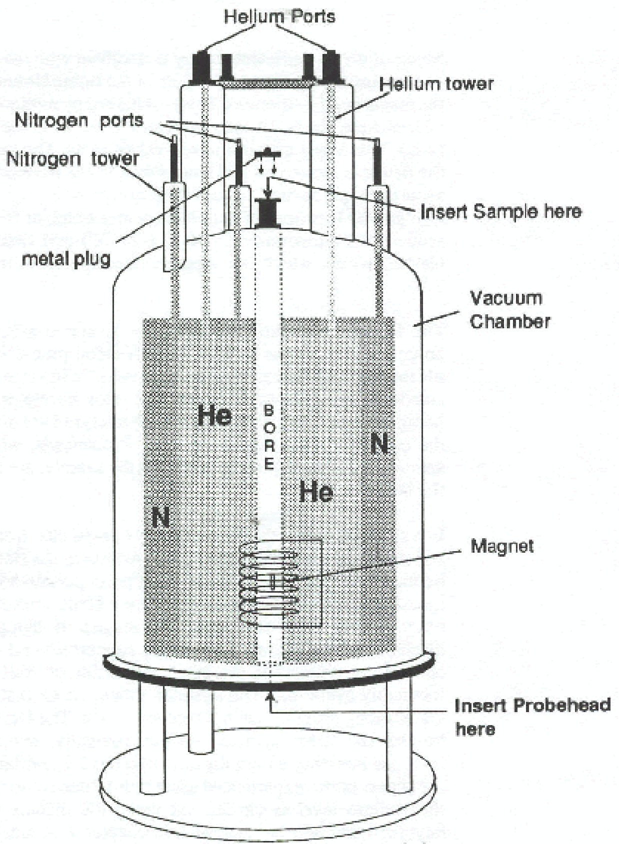


Figure 3.B Magnet and dewar

NMR Safety

- NMR magnets are ***ALWAYS*** live!!! You cannot turn off an NMR like you would a light switch.
- Nothing ferromagnetic allowed in the magnet's field! This includes most tools (hammers, wrenches, screwdrivers) and many metal items like paper clips, staples, bobby pins, barrettes, costume jewelry, wallet chains, metal buckets, floor buffers, and metal chairs.
- No watches, cellphones, iPods, or other digital media. These items can be damaged by the magnetic field.
- No credit and ATM cards.
- No pacemakers or metallic implants within 15 feet of the NMR.
- If you have a question about an item, please ask a DCIF staff member.

Be smart and be safe!

Where does the NMR signal come from?

Quantum Spin Number

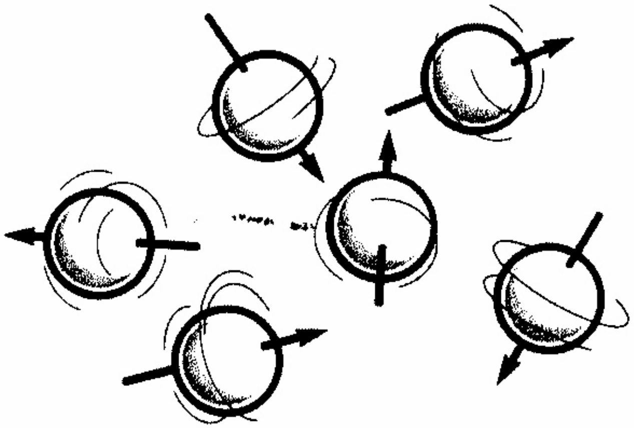
- Only nuclei that posses a property called **spin** can be “seen” by a NMR.
  - If a nucleus can have more than one energy state in a magnetic field, the **quantum spin number** (**I**) is not 0, and energy transitions for this nucleus are possible.
  - **I** depends on the number of protons (Z) and neutrons (n) in a nucleus.

I=0	**#Z is even**	**#n is even**	**mass # even**	**NO NMR SIGNAL!!!** **^{12}C and ^{16}O are not NMR active!**
I=1	**#Z is odd**	**#n is odd**	**mass # is even**	**SIGNAL!!** **^{2}H and ^{14}N**
I=1/2, 3/2, 5/2…..			**mass # is odd**	**SIGNAL!!** **^{1}H, ^{13}C, ^{15}N**

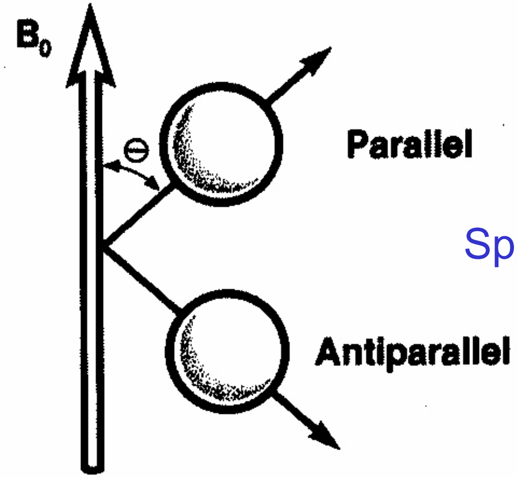
Where does the NMR signal come from?

The Zeeman Effect

- When inserted in a magnetic field (B_0) nuclei that possess *spin* align themselves according to their energy states.
  - This effect on their alignment is called the *Zeeman Effect*.



No B_0



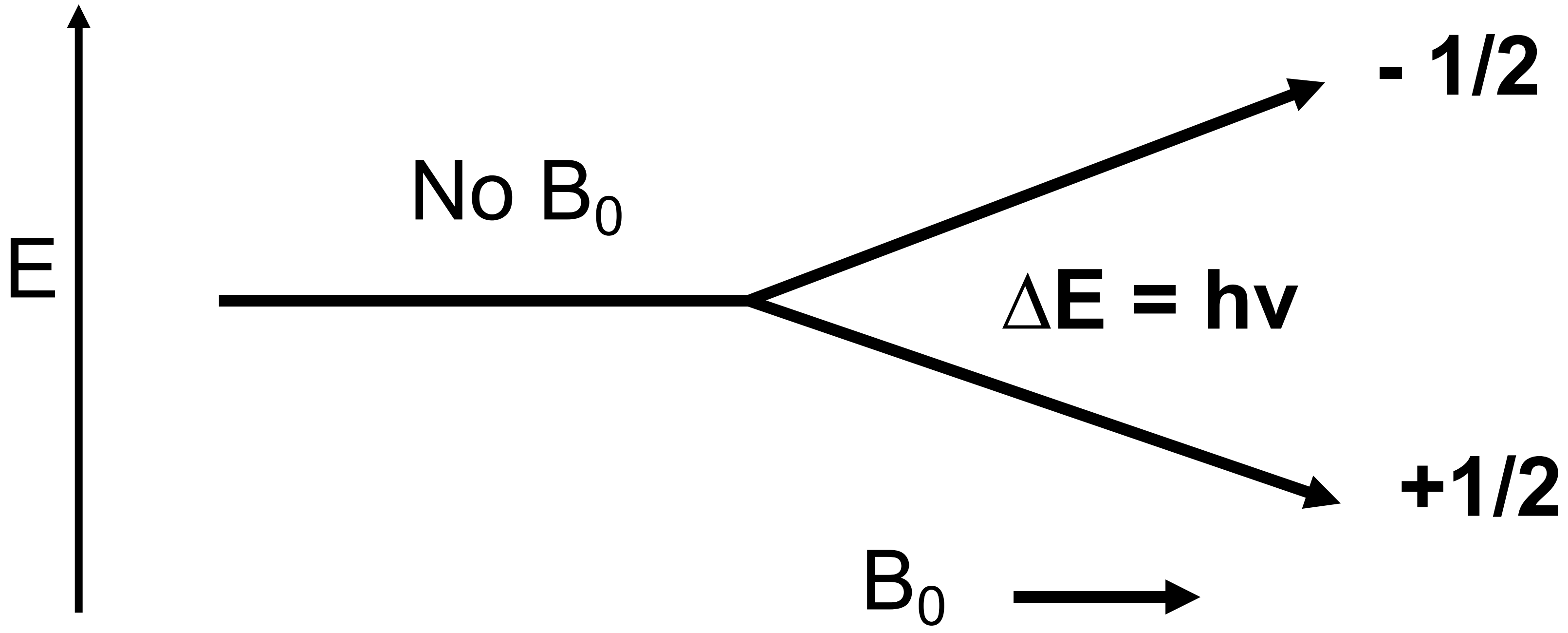
Spin=1/2

B_0

The Zeeman Effect

Energy levels if I=1/2

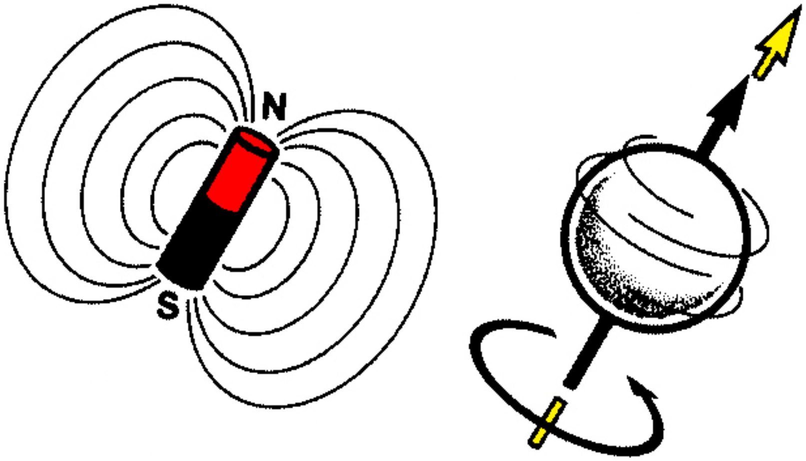
- The spins are said to be split into two populations, -1/2 (anti-parallel) and +1/2 (parallel), by B_0.
  - +1/2 is the lower energy state.



Where does the NMR signal come from?

Magnetic Moments

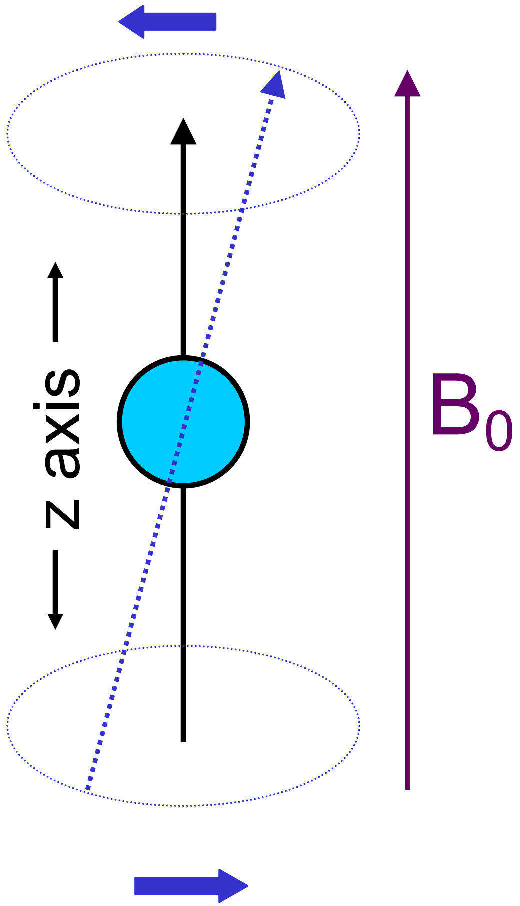
- Spinning, charged nuclei generate a magnetic field and possess a *magnetic moment* (μ).
  - This magnetic moment is a vector, and is partially aligned along the magnetic field (B_0) axis (the z axis).



Where does the NMR signal come from?

Larmor Precession

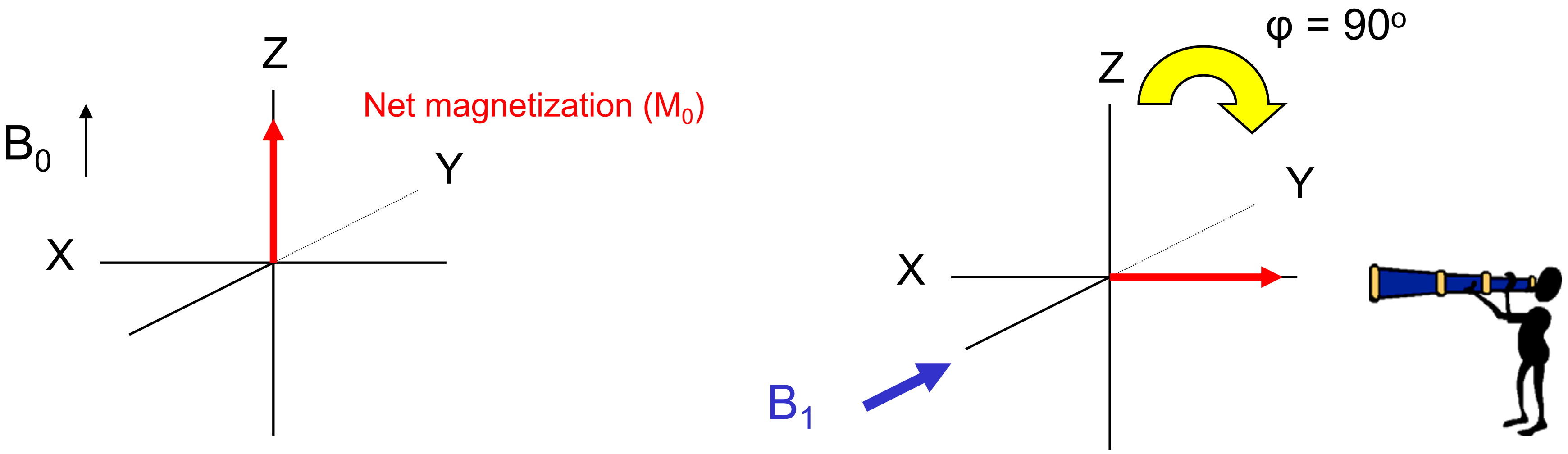
- These vectors are not exactly parallel to the z axis, they *precess*, much like a spinning top does.
- Within B_0, there is tendency for more spins to precess with a component aligned with the +z (+1/2 or parallel) direction.
  - Boltzmann! There are more spins in the lower energy state (+z direction or N+).
  - This population difference results in a net magnetization (M_0) vector in the +z direction.
  - There is a small component in the x and y direction, but this cancels out.



Where does the NMR signal come from?

Tip me over!

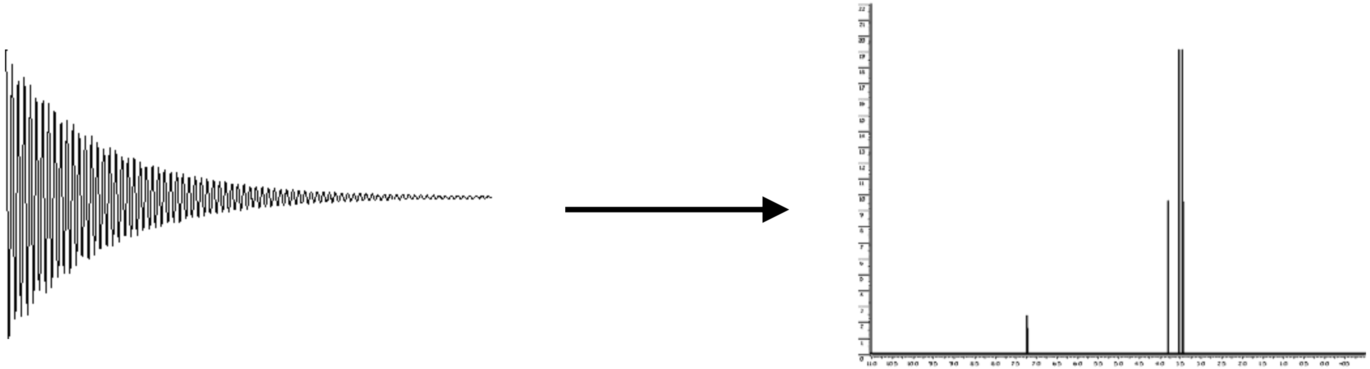
- Nuclei in B_0.
  - Zeeman effect → Boltzmann distribution.
- A second magnetic field is applied (B_1) at radio frequencies (a *pulse*).
  - The length and amplitude of the pulse determine how much the net magnetization vector is tipped from the z direction into the xy plane.
    - A 90^0 pulse tips M_0 fully into the xy plane.
- We “see” only what is tipped into the xy plane.
  - This is collected as a FID.
  - Relaxes back to ground state (along z-axis) and awaits next pulse.



Fourier Transform

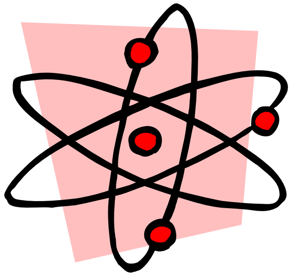
Time → Frequency

- FID (free induction decay) – sinusoidal, exponential function modulated by a decay function.
  - Net magnetization (M_0) was tipped into xy plane, and allowed to relax back to the z direction. FID collected during this time.
  - Must translate the time domain into the frequency domain
    - Amplitude vs. time → amplitude vs. frequency
    - A computer *Fourier transforms* (lots of math!) the FID into what we know as a NMR spectrum.



What kind of Information does a 1D spectrum give us?

- **Chemical shift** (δ) – chemical environment.
- **Scalar coupling** (J) – through bond coupling, provides conformational info. Good shimming allows measurement of small J-couplings.
- **Integration** – area under a curve, provides ratio of number of atoms in a particular chemical environment. Flat baseline + well phased spectrum = good integration (assuming sufficient relaxation delay).
- **NOE** (nuclear Overhauser effect) – through space coupling – who is next to who? Spatial orientation of groups. NOE experiments are experiments in which 'cross relaxation' occurs due to dipole-dipole interaction.
  - In decoupled carbon spectra, the NOE 'enhances' the carbon signal through the irradiation of protons near to carbons, and 'collapsing' multiplets into singlets. The enhancement varies from carbon to carbon, and thus decoupled carbon spectra are NOT quantitative.

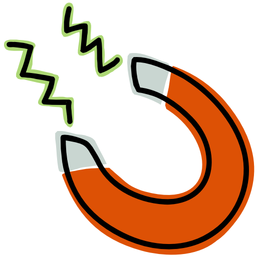


Important Relationships

Remember this!!!

$E=hv$	E=energy h=Planck's Constant v=frequency (Nv)
$\Delta E=hB_0\gamma$	γ=gamma (gyromagnetic ratio)
$v/B_0 = \gamma$	Field and frequency are **directly proportional**!

As you increase the field of your magnet, you get a greater resonance frequency. This is why larger magnets are often more desirable.



Changes in the Resonance Frequency

Why everyone resonates at a different frequency

- Which nucleus
- Field of magnet
- Electron Density
- Scalar coupling

Varian 900 MHz NMR

Which Nucleus

Sensitivity and the Gyromagnetic Ratio

I = n (1)	mass # is even	I		abundance	γ (10^7 rad $T^{-1}s^{-1}$)
H – 2	*2*	*1*	*Q*	*0 .015 %*	*4.11*
N – 14	*14*	*1*	*Q*	*99.63*	*1.93*
I = n (1/2)	mass # is odd	I			
H – 1	*1*	*½*		*99.98*	*26.76*
C – 13	*13*	*½*		*1.11*	*6.73*
N – 15	*15*	*½*		*0.37*	*-2.71*
F – 19	*19*	*½*		*100*	*25.18*
P – 31	*31*	*½*		*100*	*10.84*
Si – 29	*29*	*½*		*4.7*	*-5.32*
V – 51	*51*	*7/2*		*99.76*	*7*
Sn – 117	*117*	*½*		*7.61*	*-9.5*

Q – Quadrupole moment. Happens when the charge not evenly distributed across nucleus.
γ (gamma) is a set value.

** You can see why ^{1}H easy to “see” in NMR – high abundance, and large γ **

Which Nucleus

Sensitivity of ^{1}H vs ^{13}C

$$\frac{^{1}H}{^{13}C} = \frac{\gamma^{3}H}{\gamma^{3}C} = \frac{(26.7519)^{3}}{(6.7283)^{3}} = 63$$

Factor in abundance….

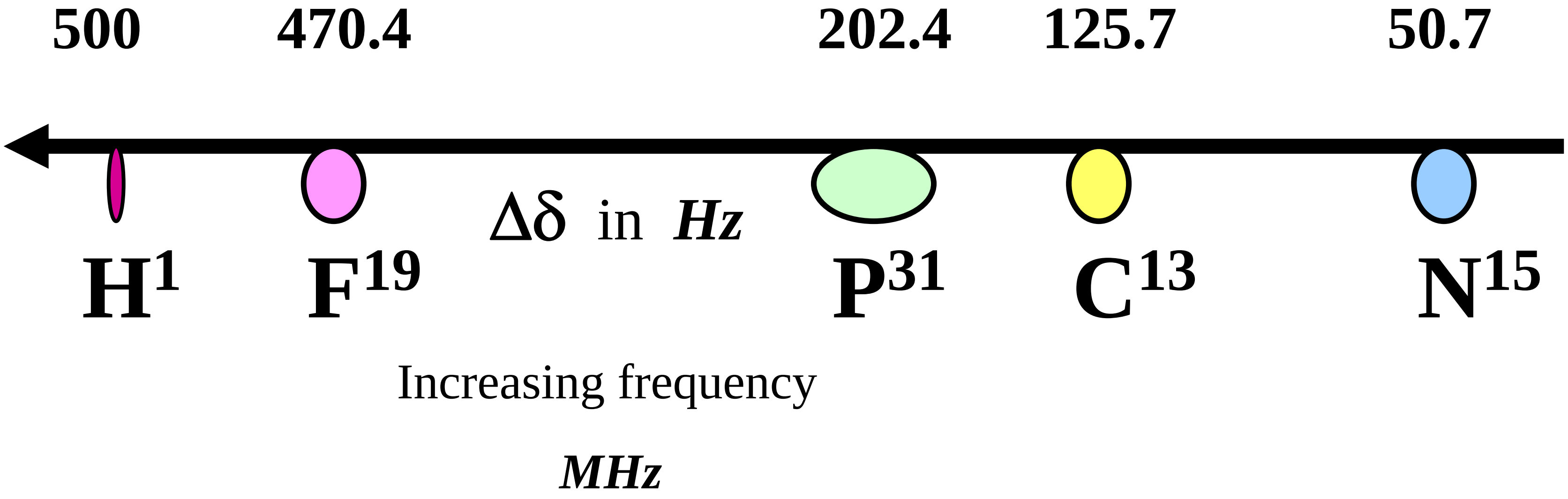
$$\frac{^{1}H}{^{13}C} = \frac{(99.98)}{(1.108)} \quad x \quad 63 \quad = 5672$$

^{1}H is 5672 times more sensitive than ^{13}C. That's why you need many more ^{13}C scans to get a decent spectrum.

Which Nucleus

Different nucleus means different frequency

- Different nuclei resonate at different frequencies in MHz.
  - When talking about 500 MHz NMR, we are referring to the resonance frequency of proton in that particular strength magnetic field.
  - This is why probes need to be tuned in MHz when switching between certain nuclei. ^{1}H and ^{19}F are typically tuned on one channel, while ^{31}P, ^{13}C, and ^{15}N on another.



500 **470.4** **202.4** **125.7** **50.7**

$\Delta\delta$ in ***Hz***

H^1 **F^{19}** **P^{31}** **C^{13}** **N^{15}**

Increasing frequency

MHz

Field of Magnet

Boltzmann revisited

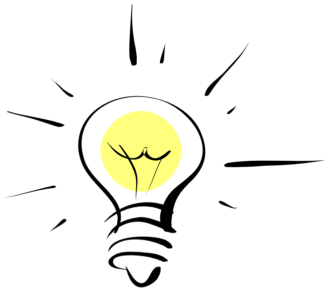
- If spin = ½, then each spin will align itself in one of 2 possible orientations (Remember Zeeman???).
- At room temp, the number of spins in the lower energy level (N+) is slightly greater than the number in the upper level (N-).

$N-/N+ = e^{-\Delta E/kT}$ k is Boltzmann's Constant

- The NMR signal depends on this difference in population.

The greater the field B_0, the greater the population difference.

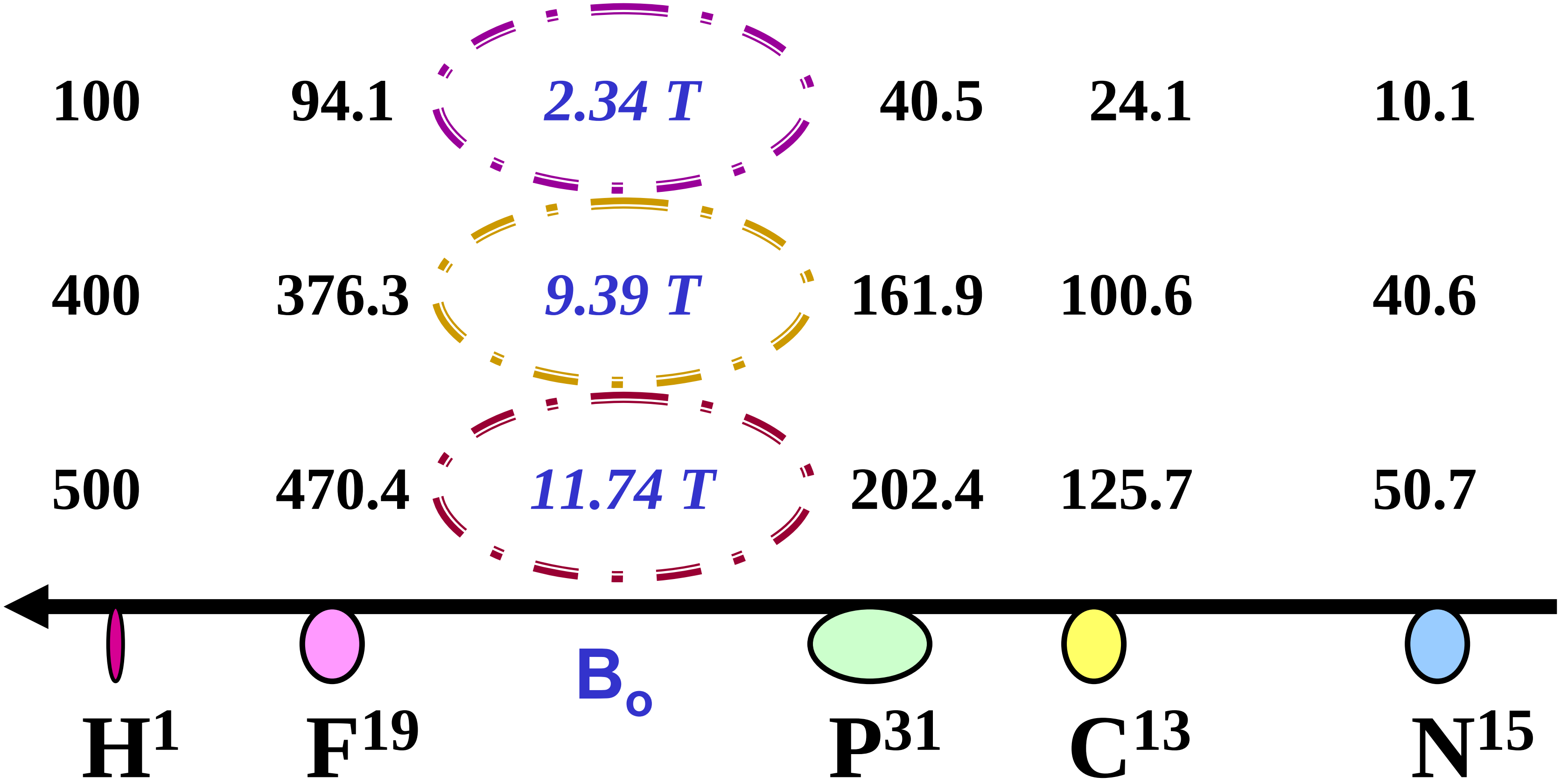
Greater difference = more signal



Field of Magnet

Changing the field of the magnet

Different strength fields (in *Telsa*) mean different resonance frequencies.



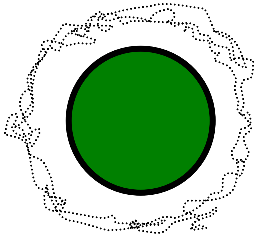
H^1	F^{19}	B_o	P^{31}	C^{13}	N^{15}
100	**94.1**	***2.34 T***	**40.5**	**24.1**	**10.1**
400	**376.3**	***9.39 T***	**161.9**	**100.6**	**40.6**
500	**470.4**	***11.74 T***	**202.4**	**125.7**	**50.7**

Increasing frequency

MHz

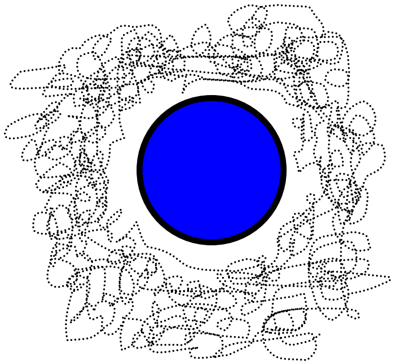
Electron Density

How chemical shift works



Carbonyl

- Less e^- density
- Nucleus ‘deshielded’ from B_0
- Feels the field (B_{eff}) more

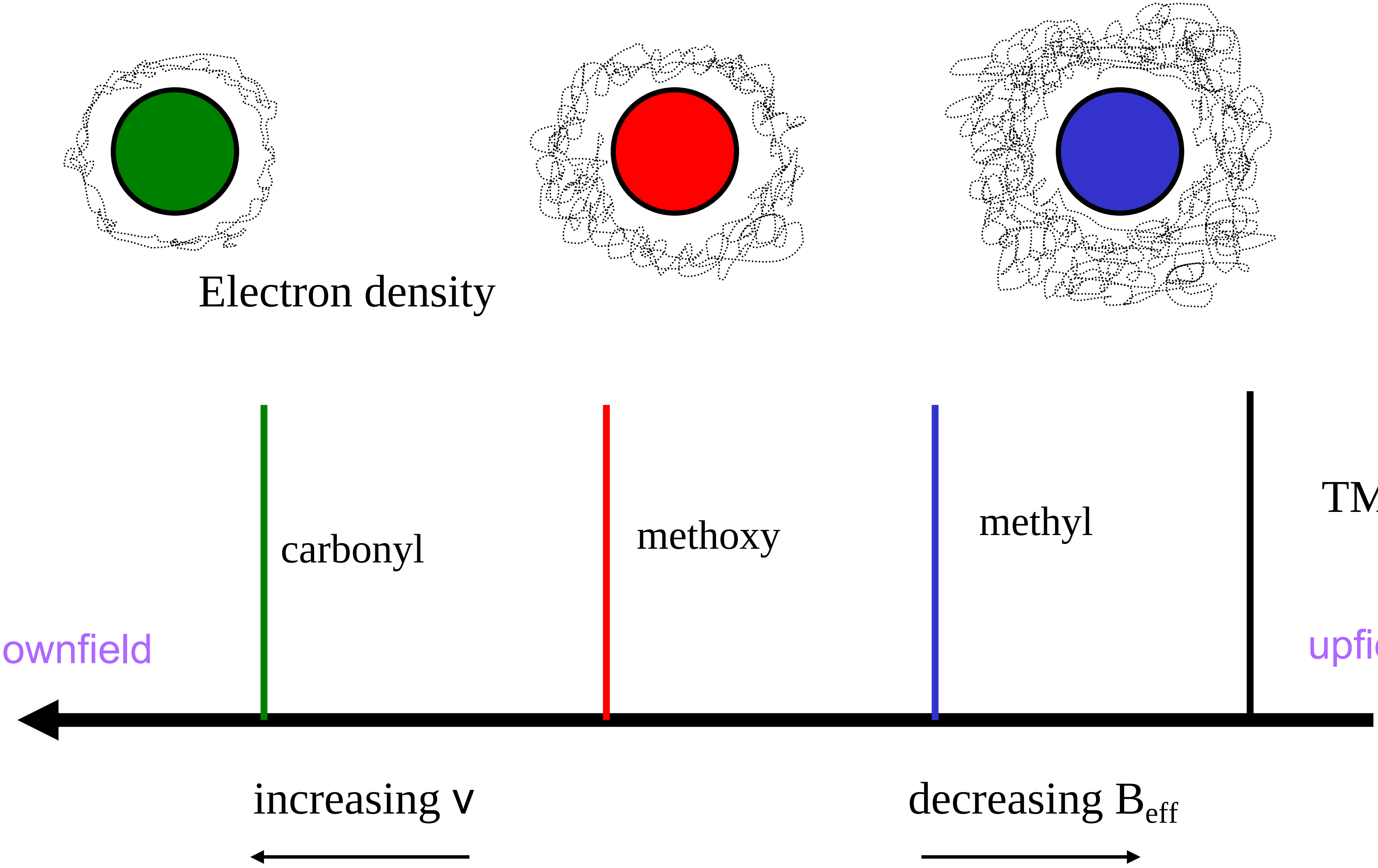


Methyl

- More e^- density
- Nucleus ‘shielded’ from B_0 by e^-
- Feels the field (B_{eff}) less

Electron Density

How chemical shift works



Electron density

carbonyl

methoxy

methyl

TMS

downfield

upfield

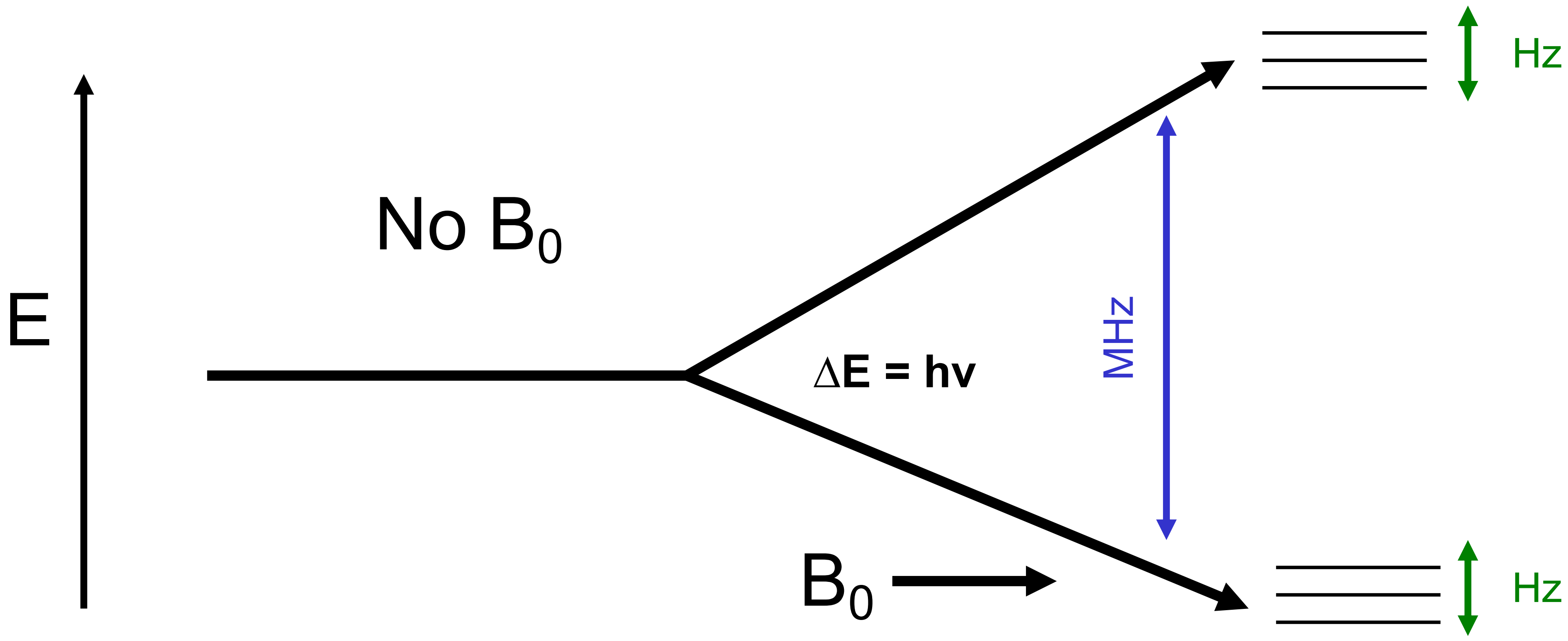
increasing ν

decreasing B_{eff}

Electron Density

How chemical shift works

- Electron density gives us small (0-20,000 Hz) changes in energy levels.
  - Gives us chemical shift (δ) in Hz.



No B_0

E

$\Delta E = hv$

MHz

Hz

Hz

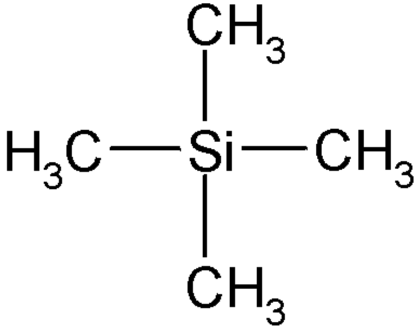
B_0

Electron Density

ppm and Hz

- Chemical shift in Hz is field dependent.
  - Coupling is always in Hz and is NOT field dependent. Therefore, the larger the field, the clearer the coupling, as δ >> J.
- Chemical shift in ppm is NOT field dependent.
  - ppm is parts per million. It is a ratio, so no units.
  - δ Hz / v MHz = ppm. Field of magnet does not matter.

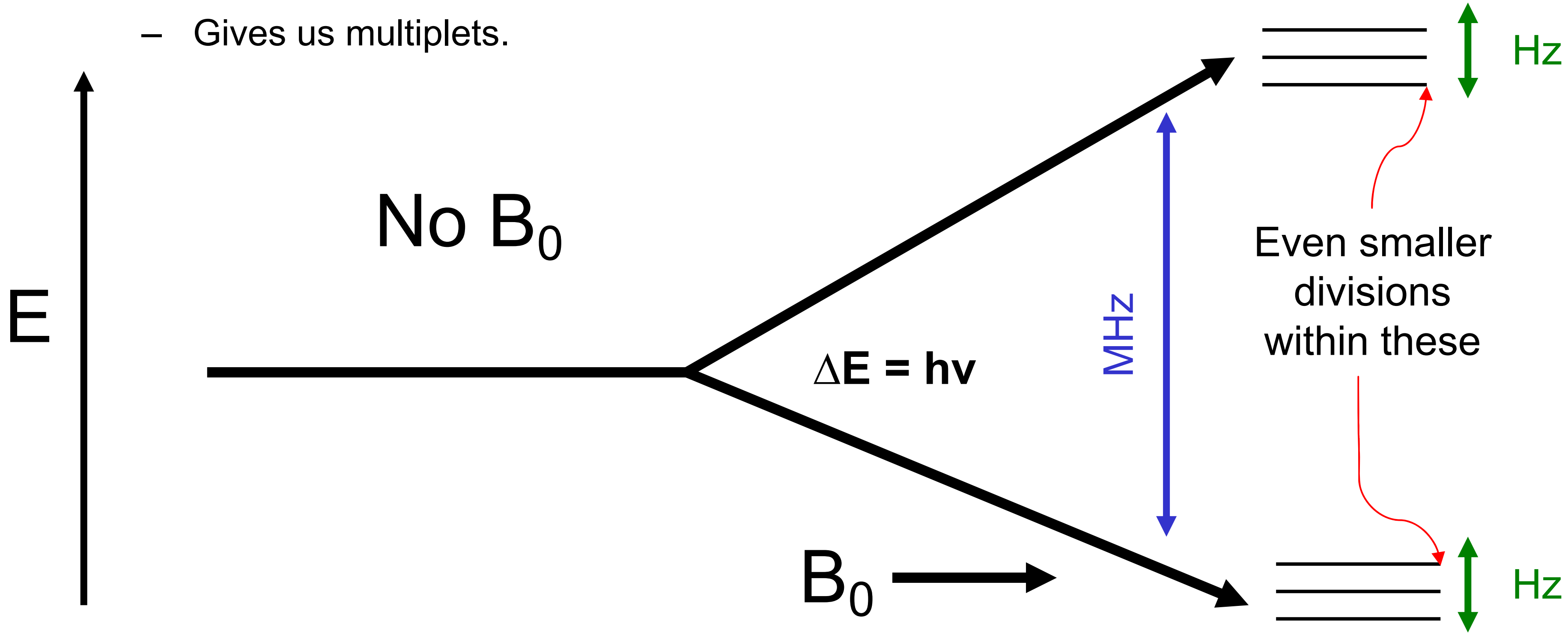
- ^1H and ^{13}C referenced to TMS (tetramethylsilane) = 0
  - In D_2O, TMSP used instead of TMS.
- ^{31}P generally references to phosphoric acid (85%) = 0
- ^{15}N generally referenced to nitric acid = 0
- ^{19}F generally referenced to CCl_3F = 0



Coupling

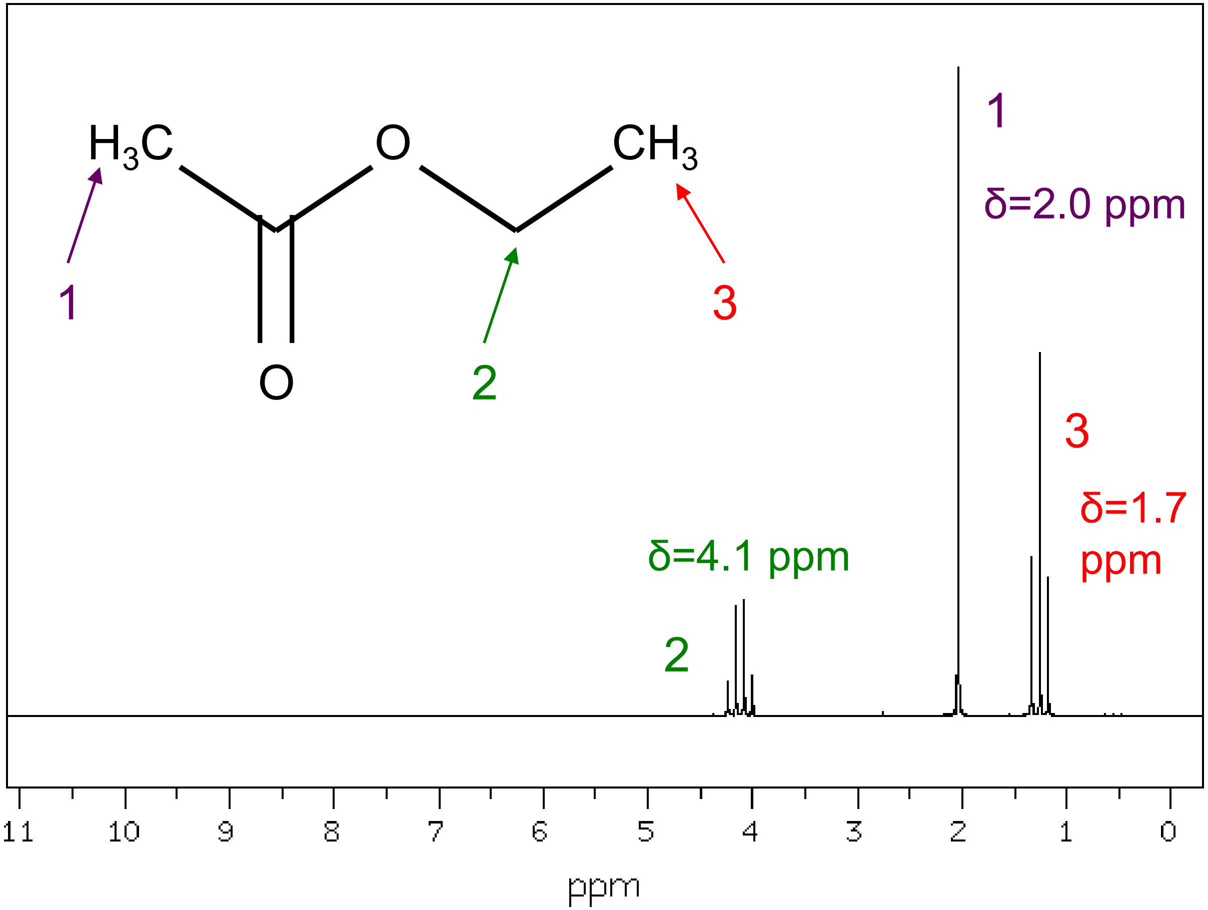
Scalar (J) Couplings

- J couplings – through bond coupling, gives us small changes (0-500 Hz) in energy levels.
  - The spin state of one nucleus can create a slightly different B_{eff} in a neighboring nucleus.
  - Gives us multiplets.



Coupling

Ethyl acetate



Spin-Spin Splitting patterns

1. Singlet. 3 equivalent protons. Not coupled to any neighboring protons.
2. Quartet. 2 equivalent protons. Split (1:3:3:1) because coupled to the 3 ^{1}Hs at the 2 position.
3. Triplet. 3 equivalent protons. Split (1:2:1) because coupled to the 2 ^{1}Hs at the 3 position.

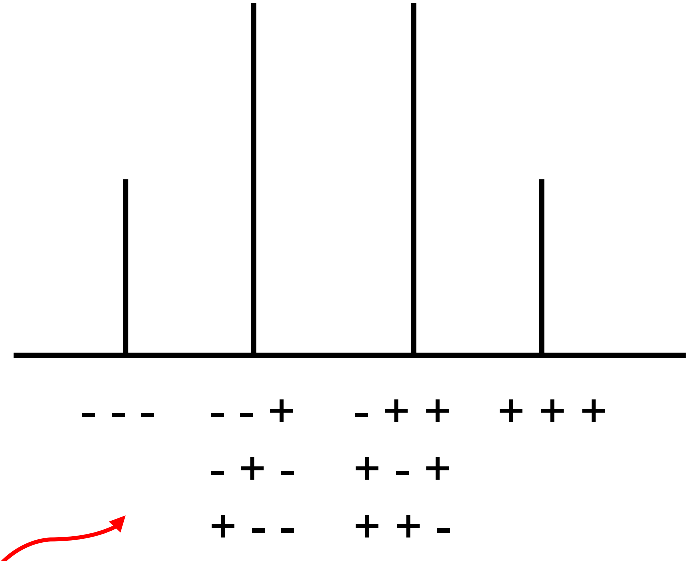
Multiplicity = N (# of neighbors) + 1

Coupling

Spin-Spin Splitting

$—CH_2—CH_3$

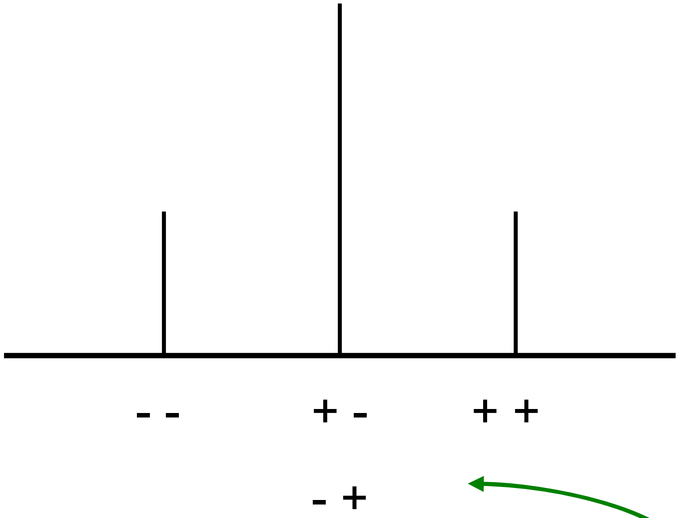
CH_2 Resonance
Quartet (1:3:3:1)



Spin states of neighboring

CH_3 protons

CH_3 Resonance
Triplet (1:2:1)



Spin states of neighboring

CH_2 protons

Credits

Special thanks to…..

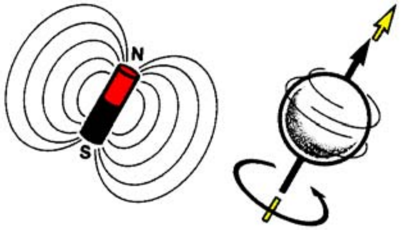
Kathleen Gallagher, University of New Hamsphire.

Jeremy N. S. Evans - BIOMOLECULAR NMR SPECTROSCOPY, Oxford Press, 1995

Varian Associates, Inc.

Joseph P. Hornak – Rensallear Institute of Technology

http://www.cis.rit.edu/htbooks/nmr/bnmr.htm



End of Part 1