Introduction to Nuclear Magnetic Resonance Spectroscopy

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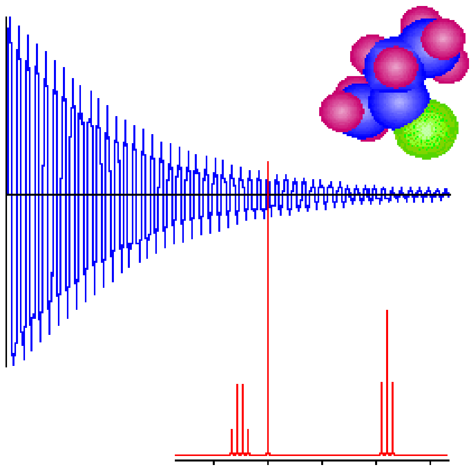
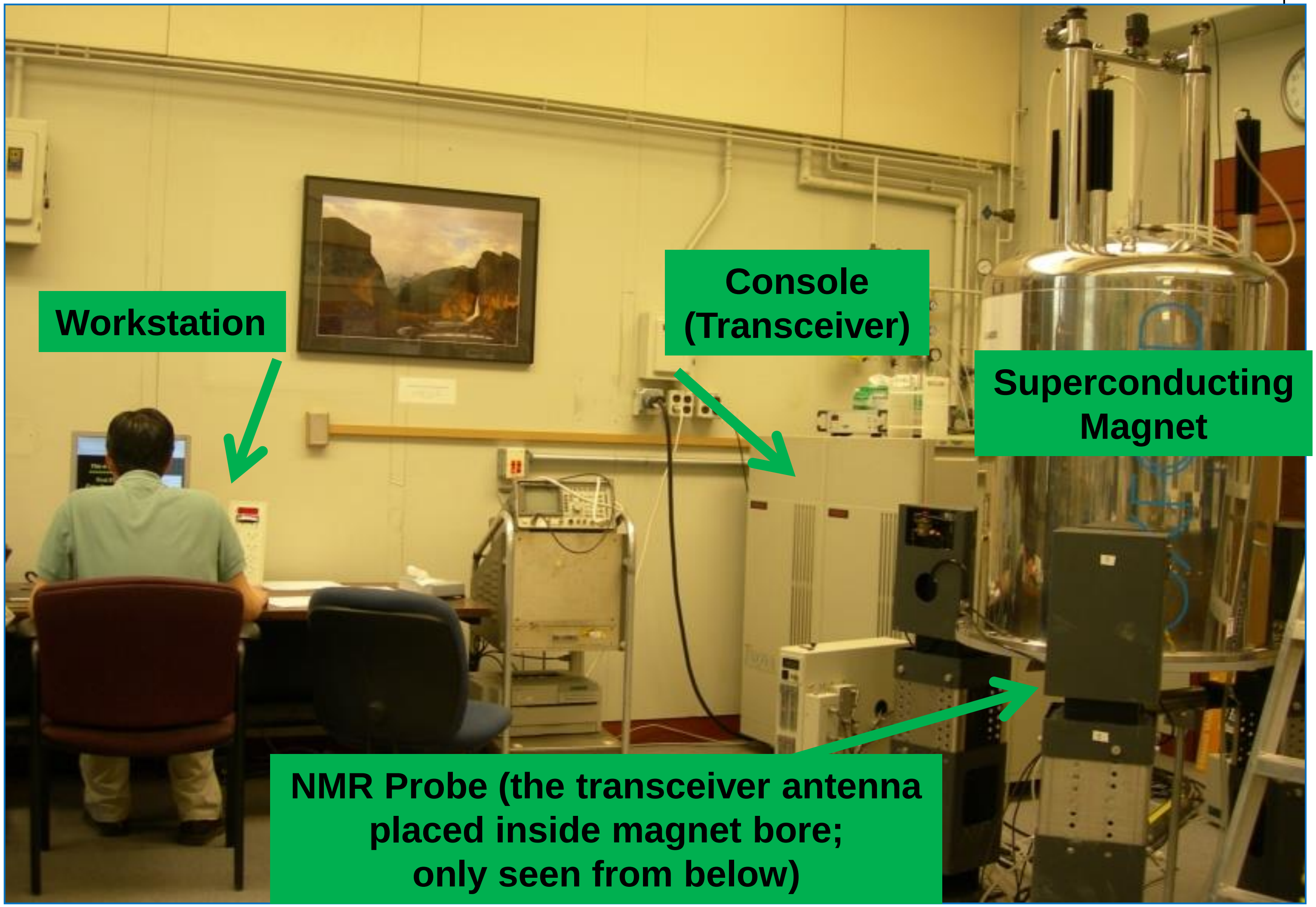
University of Illinois



Called figures, equations, and tables are from "Principles of Instrumental Analysis, 6th Ed." Skoog, Holler, and Crouch, 2007; Thompson Corp.

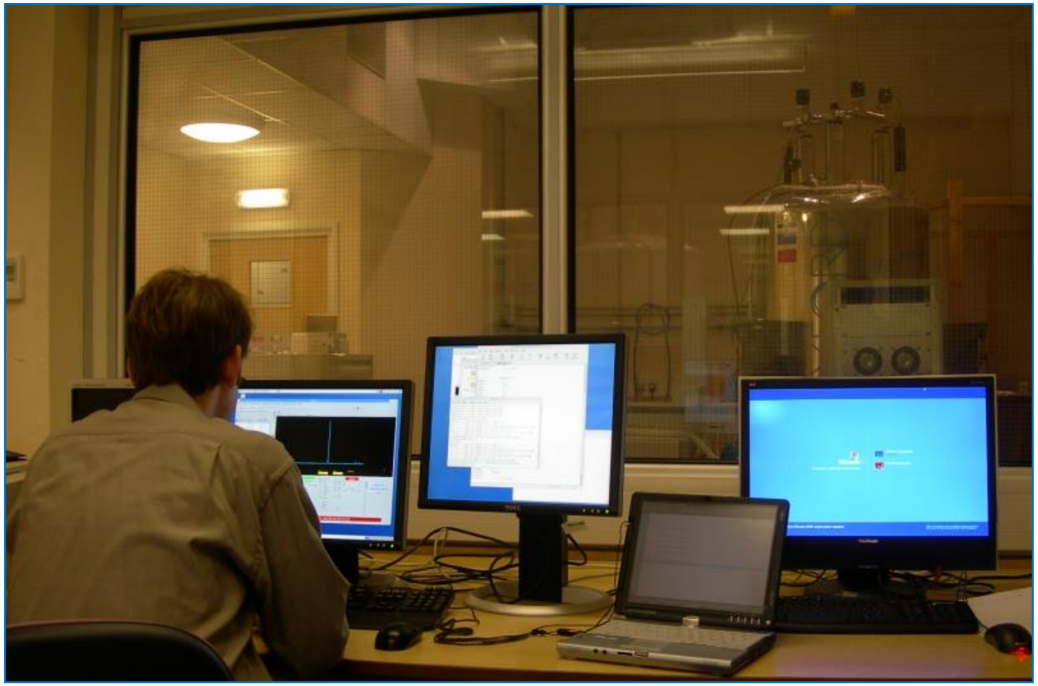
http://www.cis.rit.edu/htbooks/nmr/

NMR basic layout & components



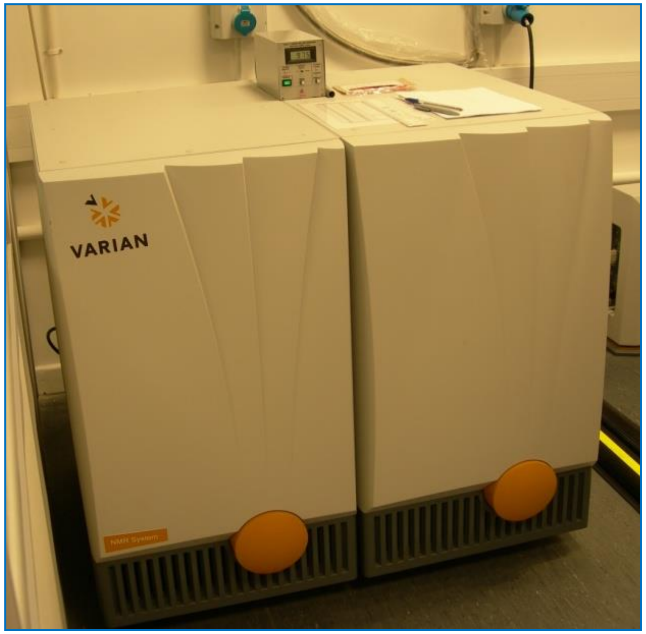
NMR basic layout & components

A variety of configurations; UIUC has all Agilent/Varian equipment



NMR Workstation Computer and Superconductive Magnet

NMR console: Latest Agilent/Varian Style

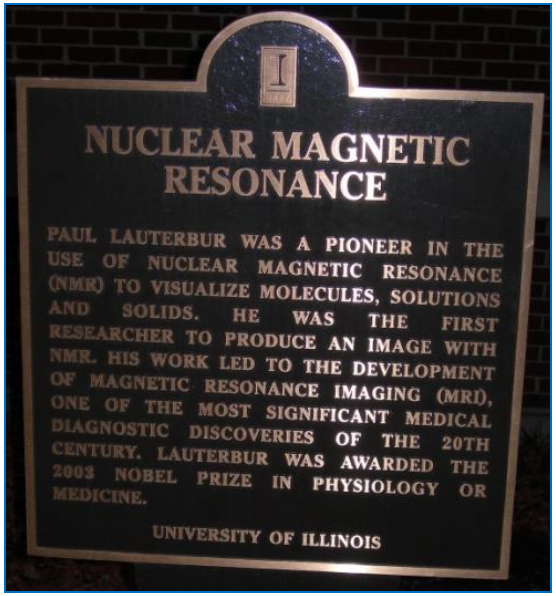


Nuclear Magnetic Resonance

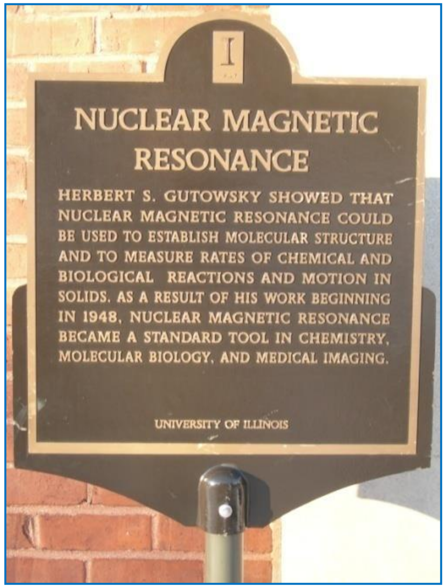
- **NMR is based on the behavior of a sample placed in an electromagnet and irradiated with radiofrequency waves: 60 – 900 MHz (λ ≈ 0.5 m)**
  - **The magnet is typically large, strong, $$$, and delivers a *stable*, *uniform* field – required for the best NMR data**
  - **A transceiver antenna, called the NMR probe, is inserted into the center bore of the magnet, and the sample is placed inside the probe**
    - **Sample can be in a narrow tube, or**
    - **Sample can flow in via an autosampler**
- **Qualitative or Quantitative; liquid or solid**
- **Universal proton (others) detector; non-destructive**

NMR, continued

- **NMR is a chemical analysis technique**
- **MRI = magnetic resonance imaging; usually an imaging technique, but is also becoming a chemical method called functional MRI (fMRI)**
  - **MRI is also non-destructive**
  - **Prof. Paul Lauterbur, UIUC, Nobel Laureate for Medicine or Physiology, 2003, with Sir Peter Mansfield, U. Nottingham**
  - **MRI is really NMRI; the MRI industry cleverly omitted the "nuclear" from their product for easier marketing to the public**



A plaque just outside Chemical Life Sciences Laboratory A commemorating **Paul Lauterbur,** Professor of Chemistry, U of Illinois. Nobel Prize, 2003 for MRI



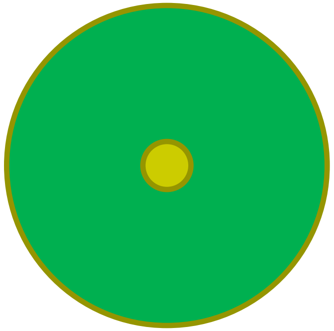
Another plaque, outside Noyes Lab (SE corner), honors **Herb Gutowsky** Professor of Chemistry, U of Illinois.

He was the first to "apply the nuclear magnetic resonance method to chemical research. His experimental and theoretical work on the **chemical shift effect and its relation to molecular structure.**"

http://en.wikipedia.org/wiki/Herbert_S._Gutowsky

NMR components

Magnet (inside a Dewar)



Overhead perspective; solenoid inside

Workstation computer

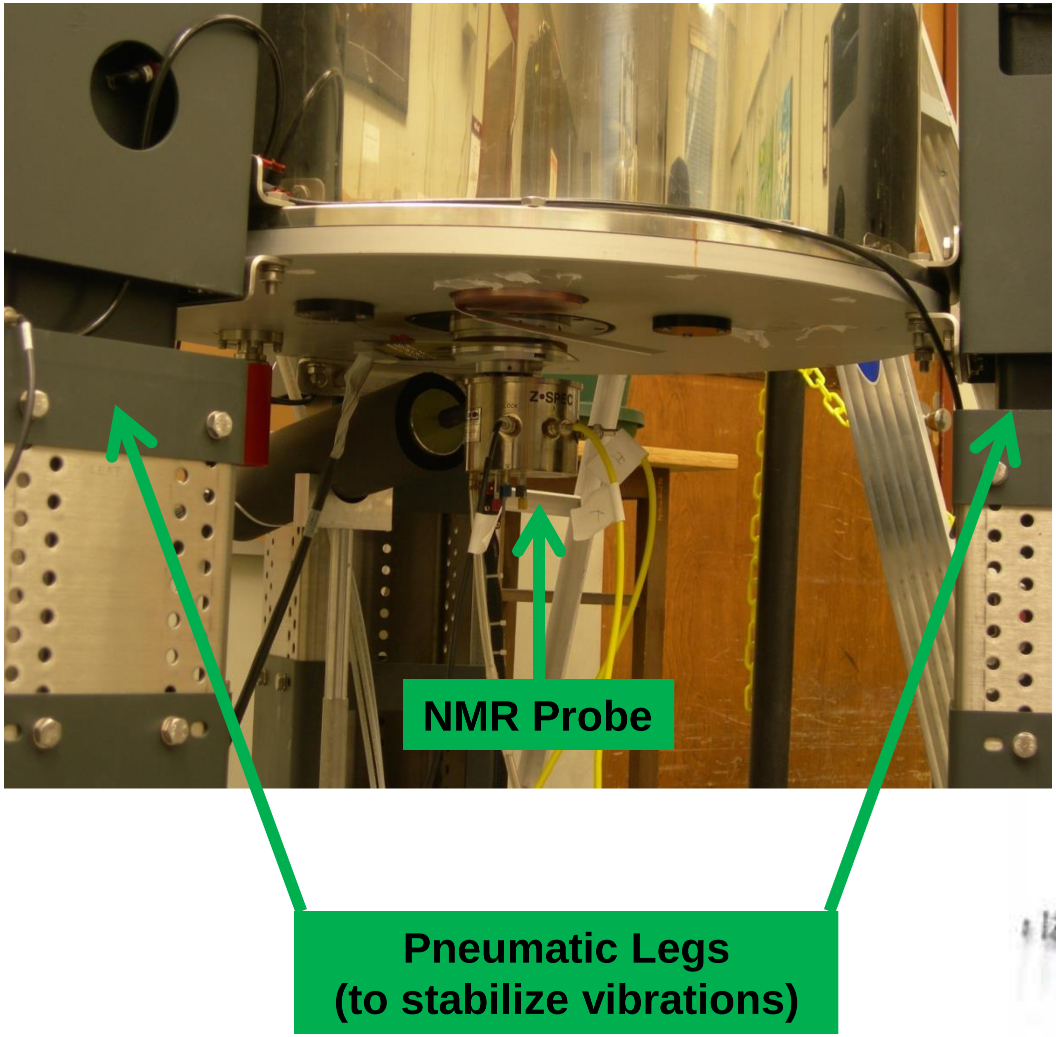
NMR Console

(creates and receives pulses)

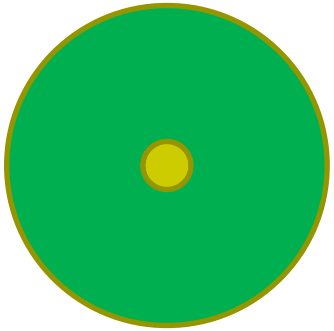
NMR Probe: really a transceiver antenna) (inside magnet)

Photos from www.jeol.com

NMR components

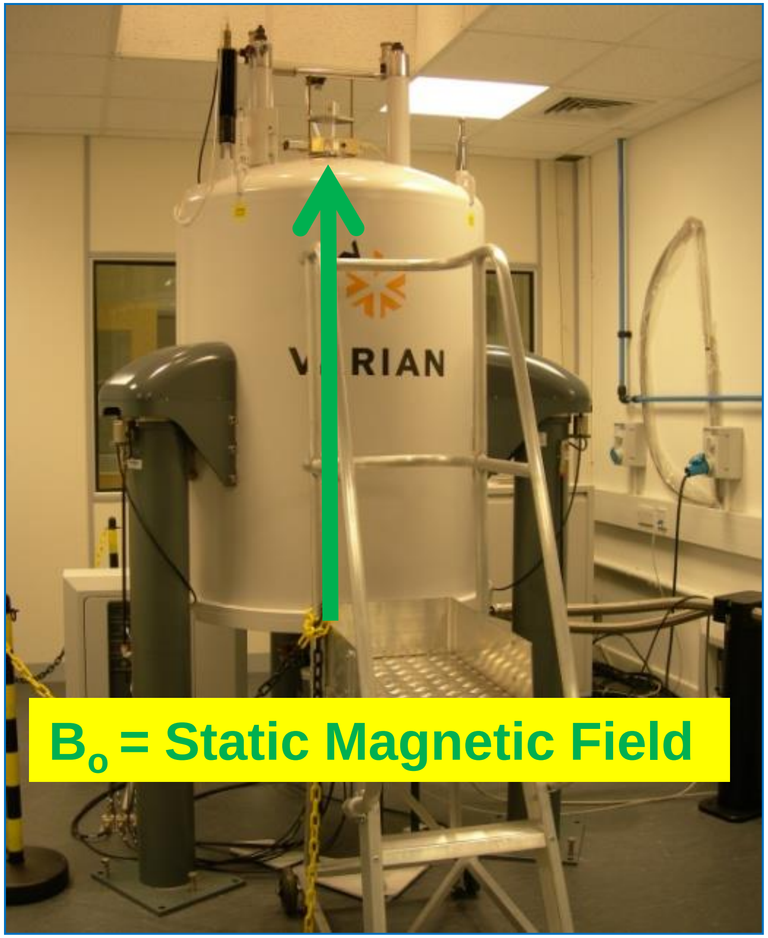


Magnet
(inside a Dewar)



Overhead perspective; solenoid inside

NMR Probe
(inside magnet)



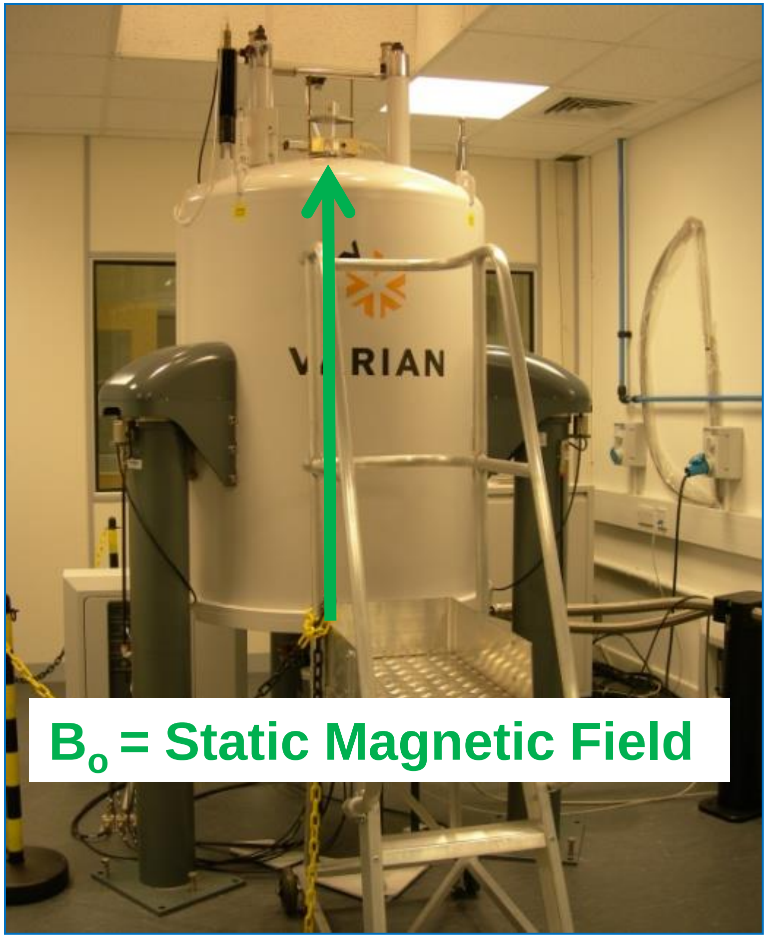
Varian is now Agilent
as of late 2010

U. Bristol, United Kingdom
14.1 Tesla magnet

Termed a
"600 MHz" magnet

600 MHz is the frequency
at which the proton (^1H) nucleus
spin resonates –
in a magnet of *this strength*
(14.1 Tesla)

1000 MHz is equivalent to 23.5 Tesla



U. Bristol, United Kingdom
14.1 Tesla magnet

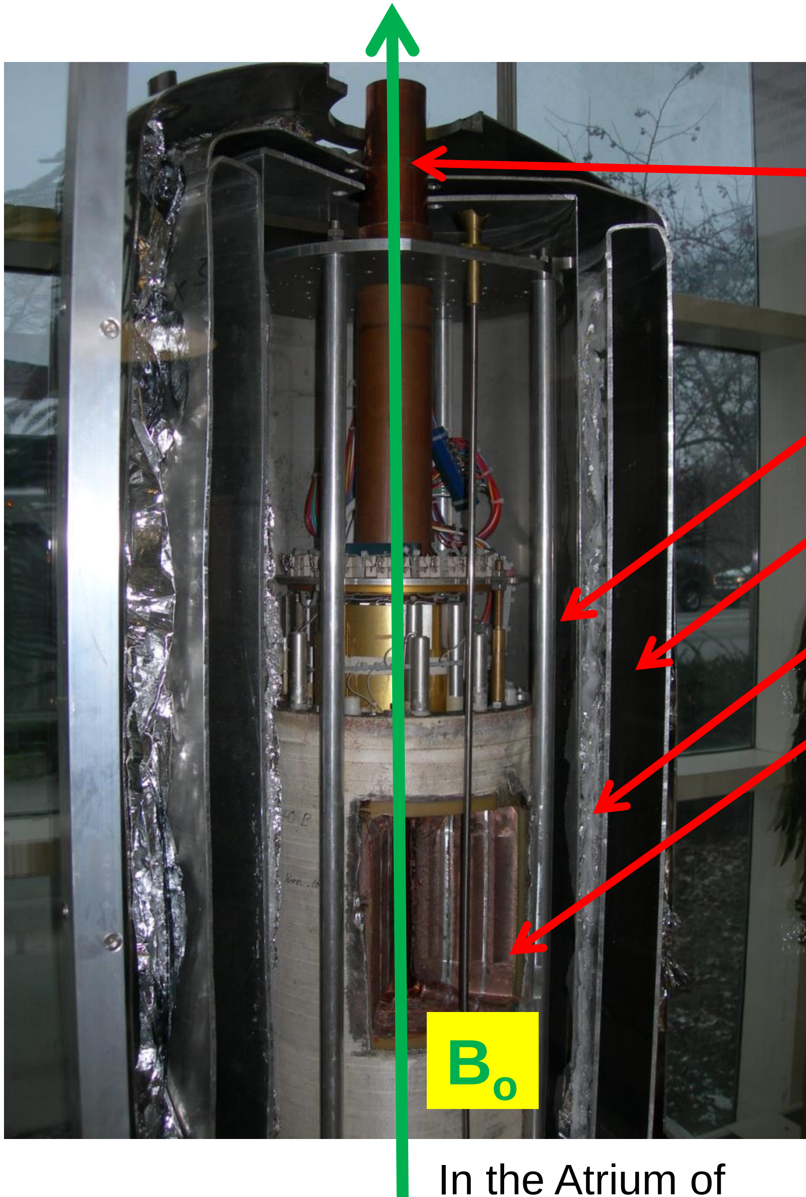
Termed a
"600 MHz" magnet

600 MHz is the frequency at which the proton (^1H) nucleus spin resonates – in a magnet of *this strength*.

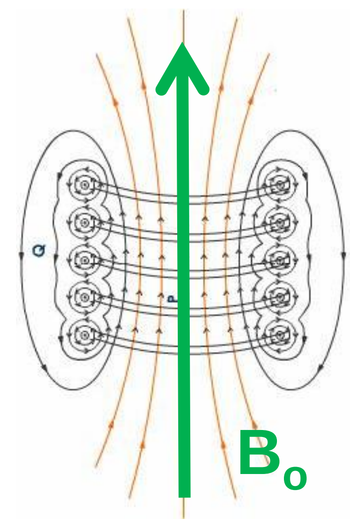
The magnet is *superconducting*, always charged, but *not powered*, and surrounded by liquid helium (4.2 K) and the He is surrounded by liquid nitrogen (77 K).
The current is "coasting", that is, persistent, uniform & stable.

The big white tanks outside Noyes and RAL hold liquid N_2 for NMR and other cold stuff.
No high pressures are involved; vented.

NMR magnet cut-away



In the Atrium of
Chemical Life Sciences Lab A



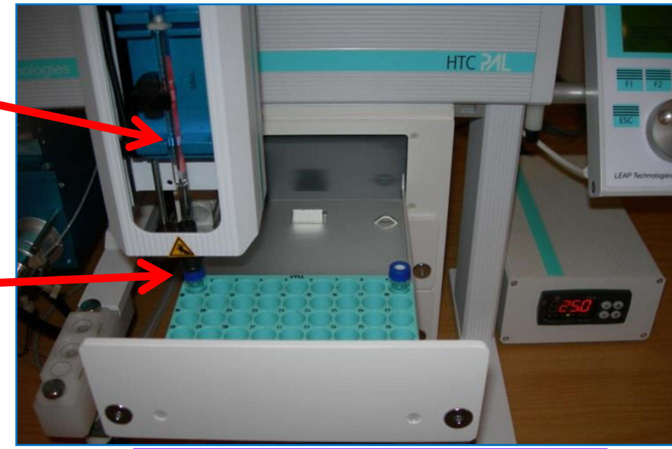
NMR sample handling options

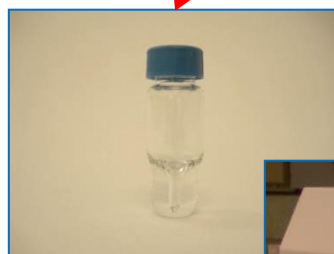
Spinning tube NMR

A typical NMR sample tube: 8 inches long; 5 mm outer diameter. Inserted into the NMR probe from above either manually or using automation.

Sample syringe

Sample vial





Automated flow NMR

Pumps and solvents

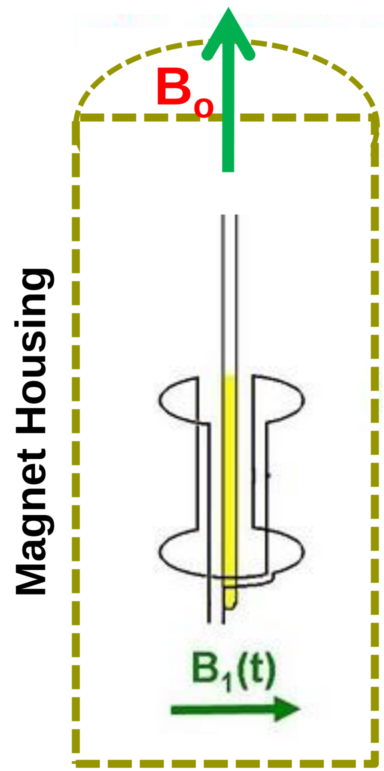
Autosampler

How does NMR work?

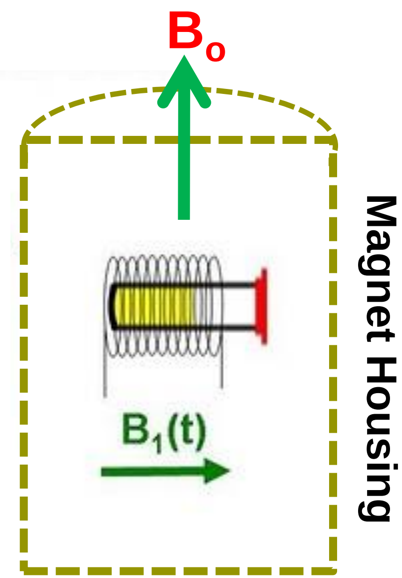
B_o = Static Magnetic Field

from the big supercon magnet: persistent

Probe Coils create the Transverse (B_1) Field from a current pulse of time t

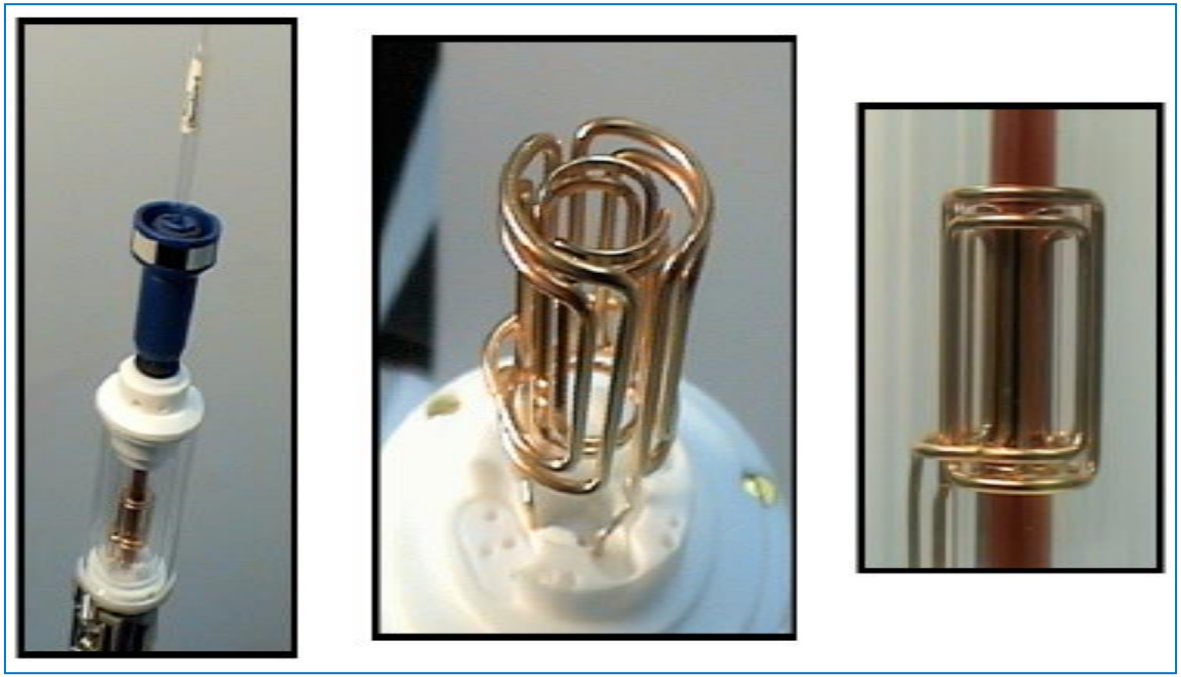


Helmholtz Coil

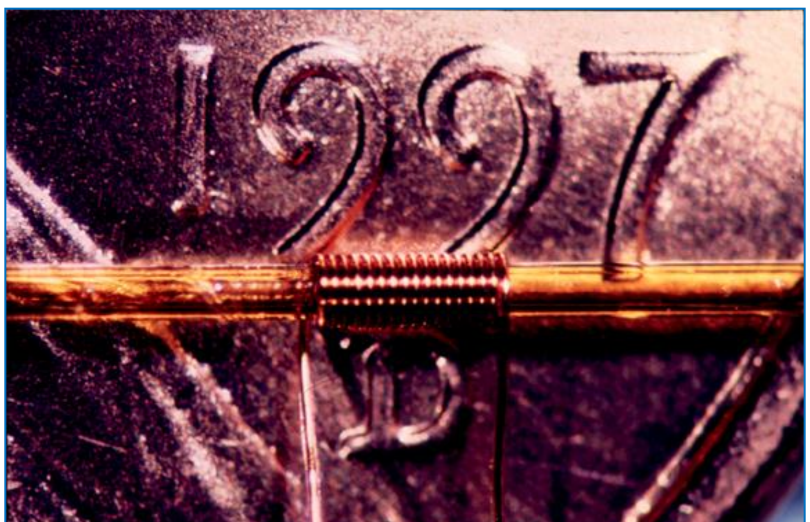


Solenoid Coil

http://u-of-o-nmr-facility.blogspot.com/2008/03/probe-coil-geometry.html



2 Helmholtz Coils:
1 inside the other
for tube NMR. One
coil for protons, the
other for carbon. The
inner coil is the
most sensitive.



Solenoidal
Microcoil
for flow NMR;
one coil
does it all

http://www.bioc.aecom.yu.edu/labs/girvlab/nmr/course/COURSE_2010/Lab_1.pdf

NMR depends on the spin of the nucleus under study – the most common is ^{1}H

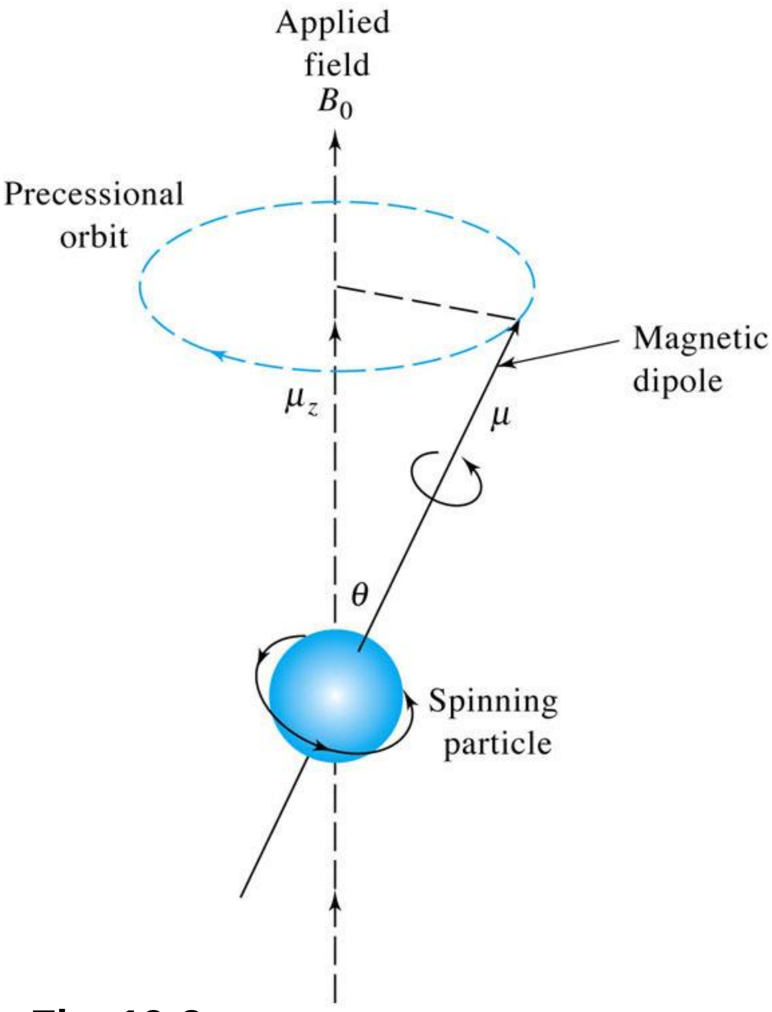


Fig. 19-2

- **Nuclear spin in an applied magnetic field**
  - **A magnetic dipole, μ, is produced**
  - **The spin precesses**
  - **The spin is quantized**
  - **^{1}H has a spin quantum number of either +½ (low E) or – ½ (high E)**
  - **Many nuclei have suitable spin quantum numbers for NMR:**
    - **^{13}C (only 1.1% abundance)**
    - **^{19}F**
    - **^{31}P**
    - **^{14}N**
  - **Many nuclei are not NMR active:**
    - **^{12}C (sadly) & ^{16}O (also sadly)**

NMR depends on the spin of the nucleus under study: the magnetogyric ratio

$$\gamma = \frac{\mu}{p}$$

γ = magnetogyric ratio

μ = dipole moment

p = angular momentum

Magnetogyric ratio = gyromagnetic ratio: It's different for each type of nucleus. The bigger the better.

Eqn. 19-1, slightly modified to be a ratio

TABLE 19-1 Magnetic Properties of Important Nuclei with Spin Quantum Numbers of 1/2

Nucleus	Magnetogyric Ratio, radian T^{-1} s^{-1}	Isotopic Abundance, %	Relative Sensitivity[a]
^{1}H	2.6752×10^{8}	99.98	1.00
^{13}C	6.7283×10^{7}	1.11	0.016
^{19}F	2.5181×10^{8}	100.00	0.83
^{31}P	1.0841×10^{8}	100.00	0.066

[a] At constant field for equal number of nuclei.

In a magnetic field, the spin has two quantized energy states called high and low

$$E = -\frac{\gamma m h}{2\pi} B_o$$

$$E_{-1/2} = \frac{\gamma h}{4\pi} B_o$$

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

B_o in Tesla (T)
and E in Joules (J)
B_o is the static field.

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

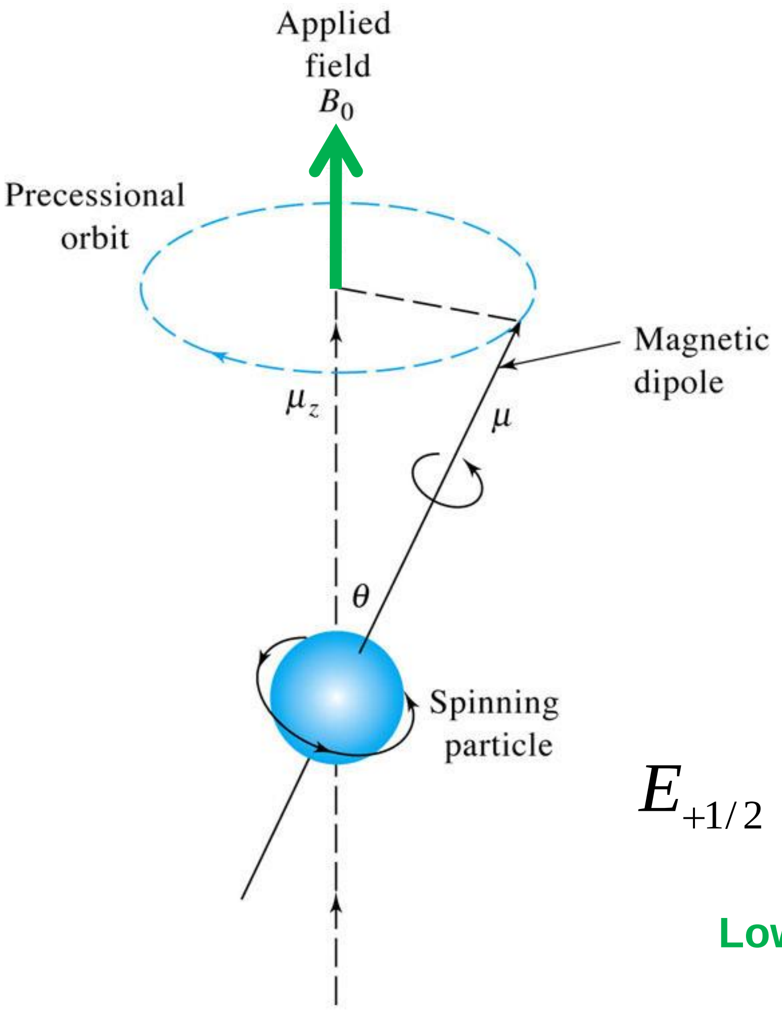
High E; opposed

Low E; aligned

$$\Delta E = \frac{\gamma h}{2\pi} B_o$$

ΔE = high - low

In a magnetic field, the spin has two quantized energy states called high and low



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

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

Low E; aligned

Fig. 19-2

In a magnetic field, the spin has two quantized energy states called high and low

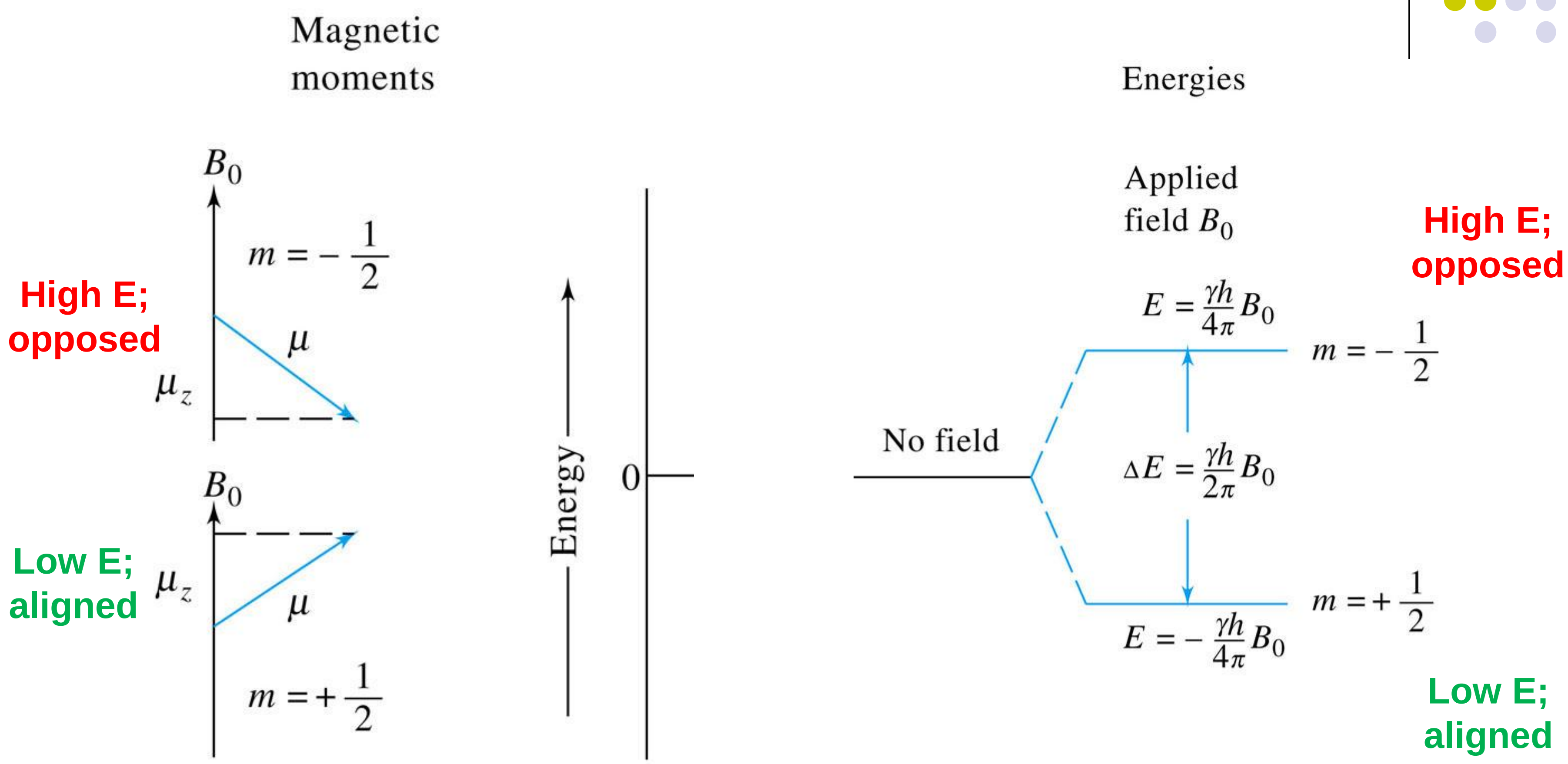
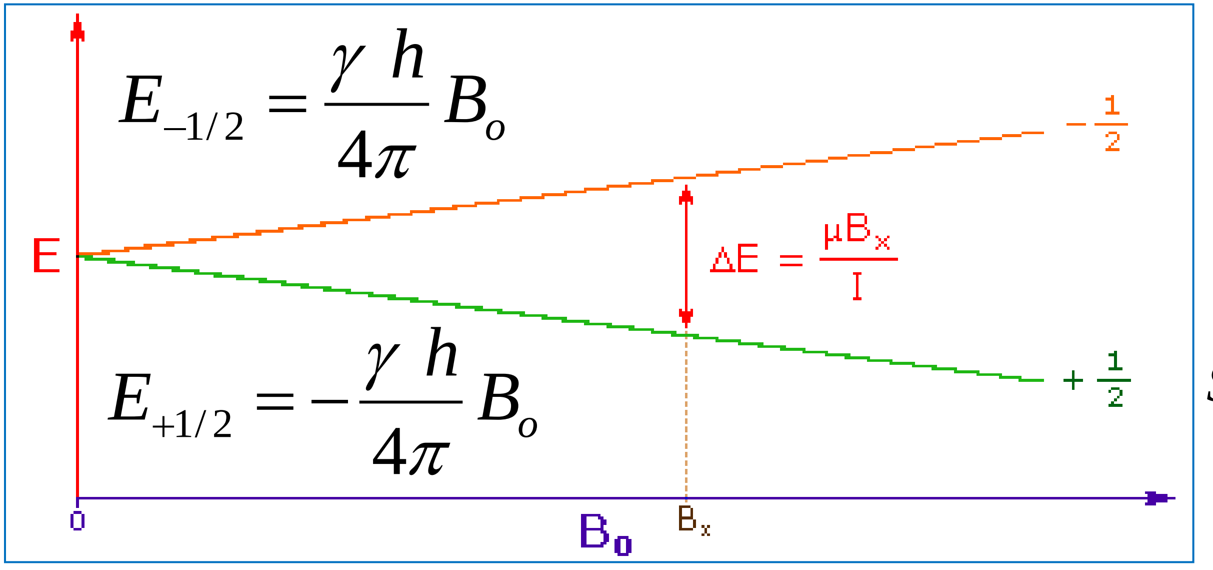


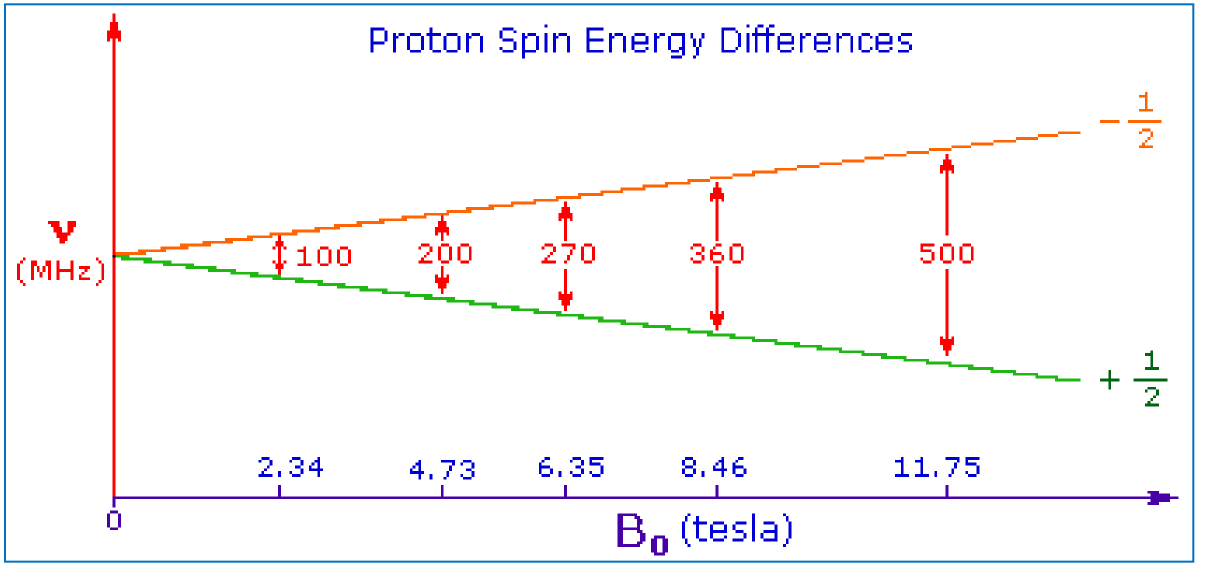
Fig. 19-1

ΔE depends on the applied B_o



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

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



The stronger the magnet, the larger the ΔE

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

So, where does the NMR signal come from?

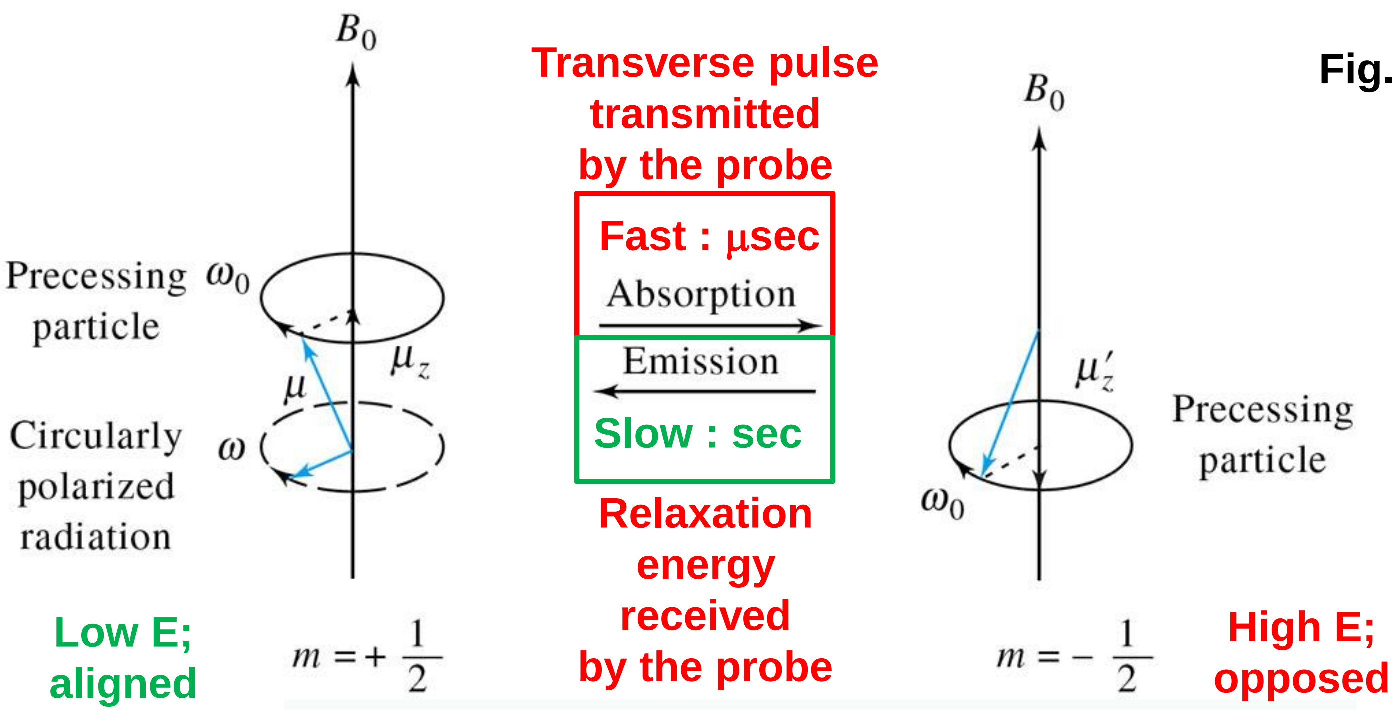


Fig. 19-3

The NMR probe coil both transmits and receives: it's a transceiver.

The spin is pulsed by the NMR probe, then the spin relaxation produces the signal.

At equilibrium, the low spin state is slightly favored – otherwise, no NMR signal

Everything else cancels.

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

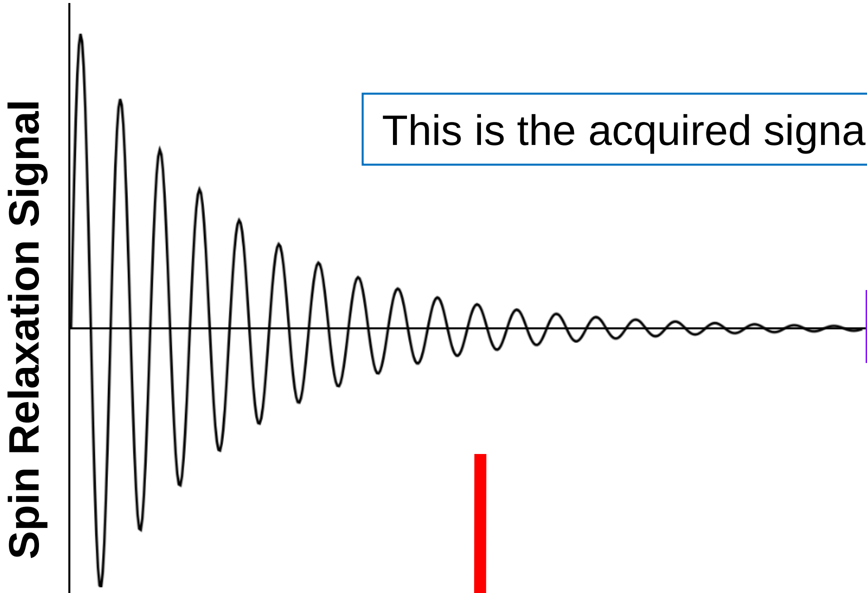
Boltzmann Distribution Equation for quantum spin states in a magnetic field

In Example 19-2 (p. 501), for 1,000,000 atoms of hydrogen, ^1H, in the high energy state:

- **B_o = 4.69 Tesla**
- **T = 20°C**
- **$\gamma = 2.6752 \times 10^8\ T^{-1}\ sec^{-1}$**
- **N_{Hi} / N_{Lo} = 0.999967**
- **For N_{Hi} = 1,000,000 then N_{Lo} = 1,000,033**
- **ΔN = 33 or just 33 ppm of all the spins present are available for NMR because all the rest of the spins are in a dynamic equilibrium**
- ***This* is why NMR is a relatively *insensitive* technique → unfortunate.**

Thus, big $$$ magnets.

What does NMR data look like?



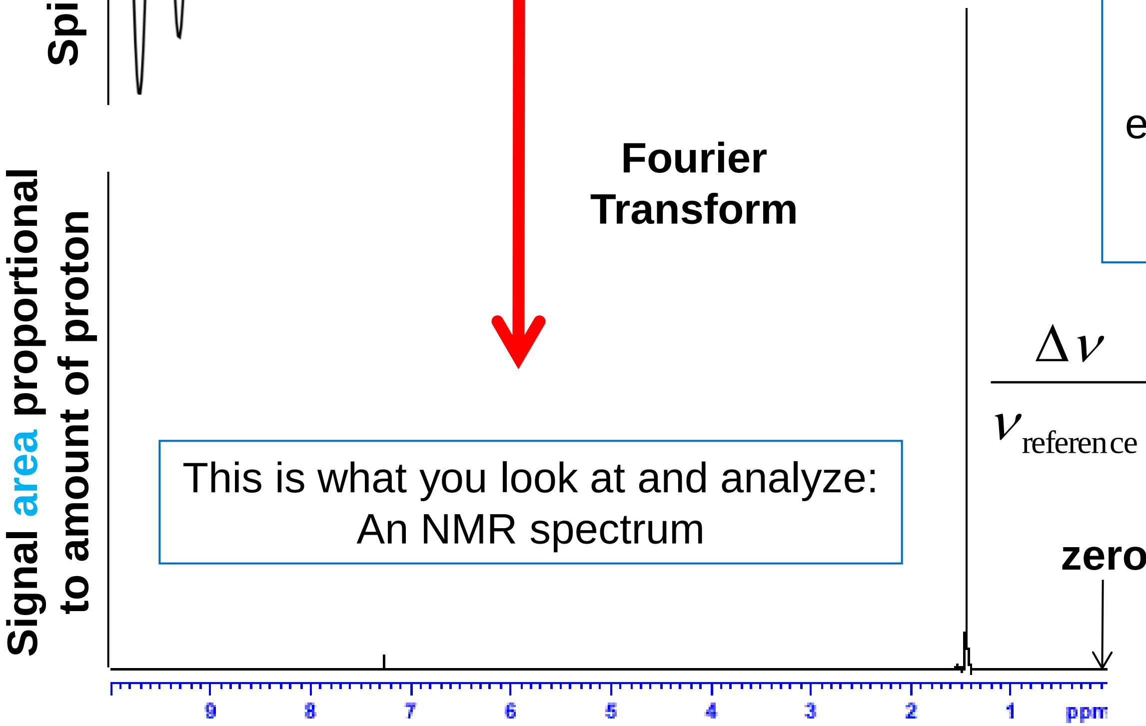
This is the acquired signal from the spin relaxation.

Time (a few sec of relaxation for 1 pulse)

Fourier Transform

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

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



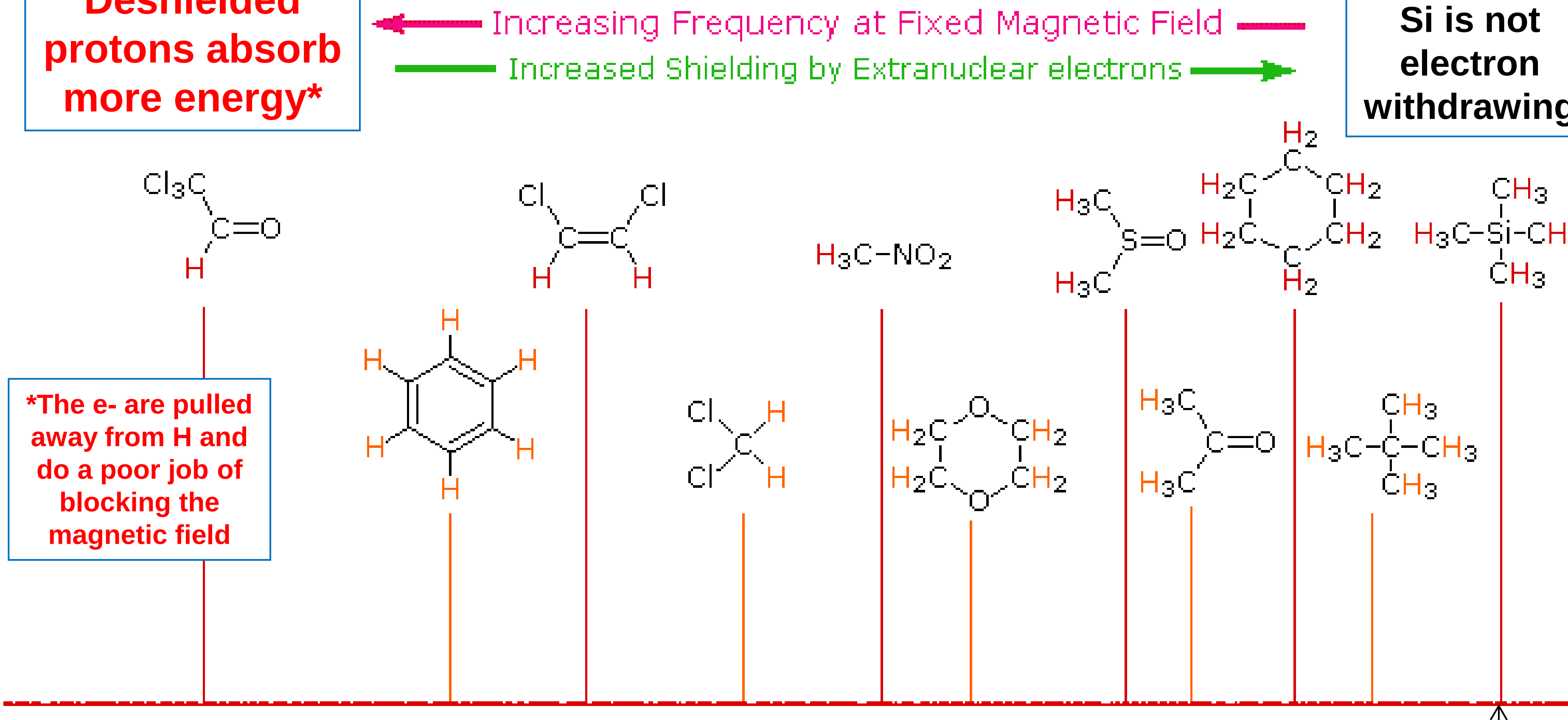
This is what you look at and analyze: An NMR spectrum

Same normalized scale for all magnet strengths

Understanding NMR Spectra

Deshielded protons absorb more energy*

Si is not electron withdrawing



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

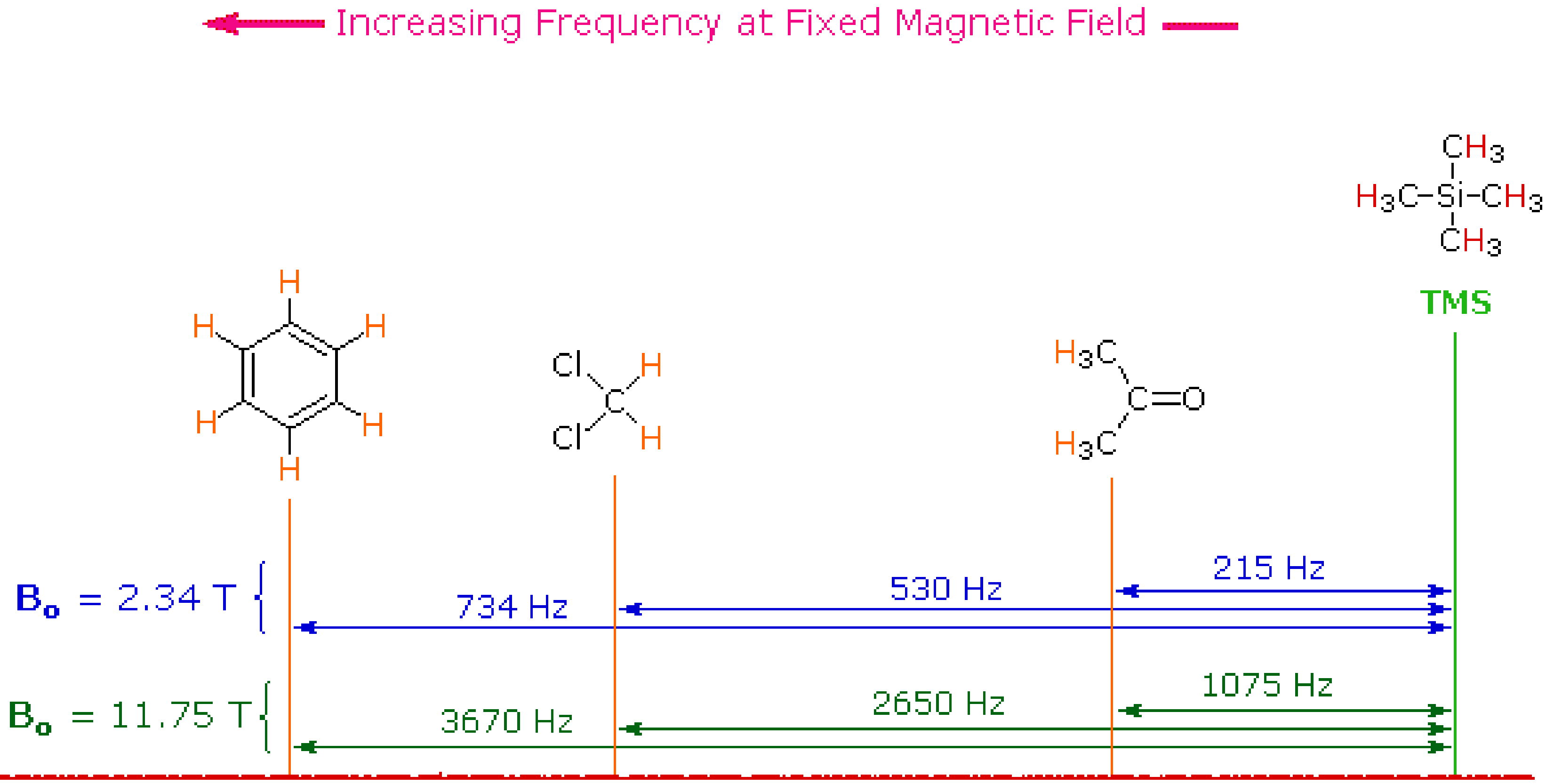
[1]H NMR Resonance Signals for some Different Compounds

zero set by TMS (tetramethyl silane)

Oxygen is electron withdrawing

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

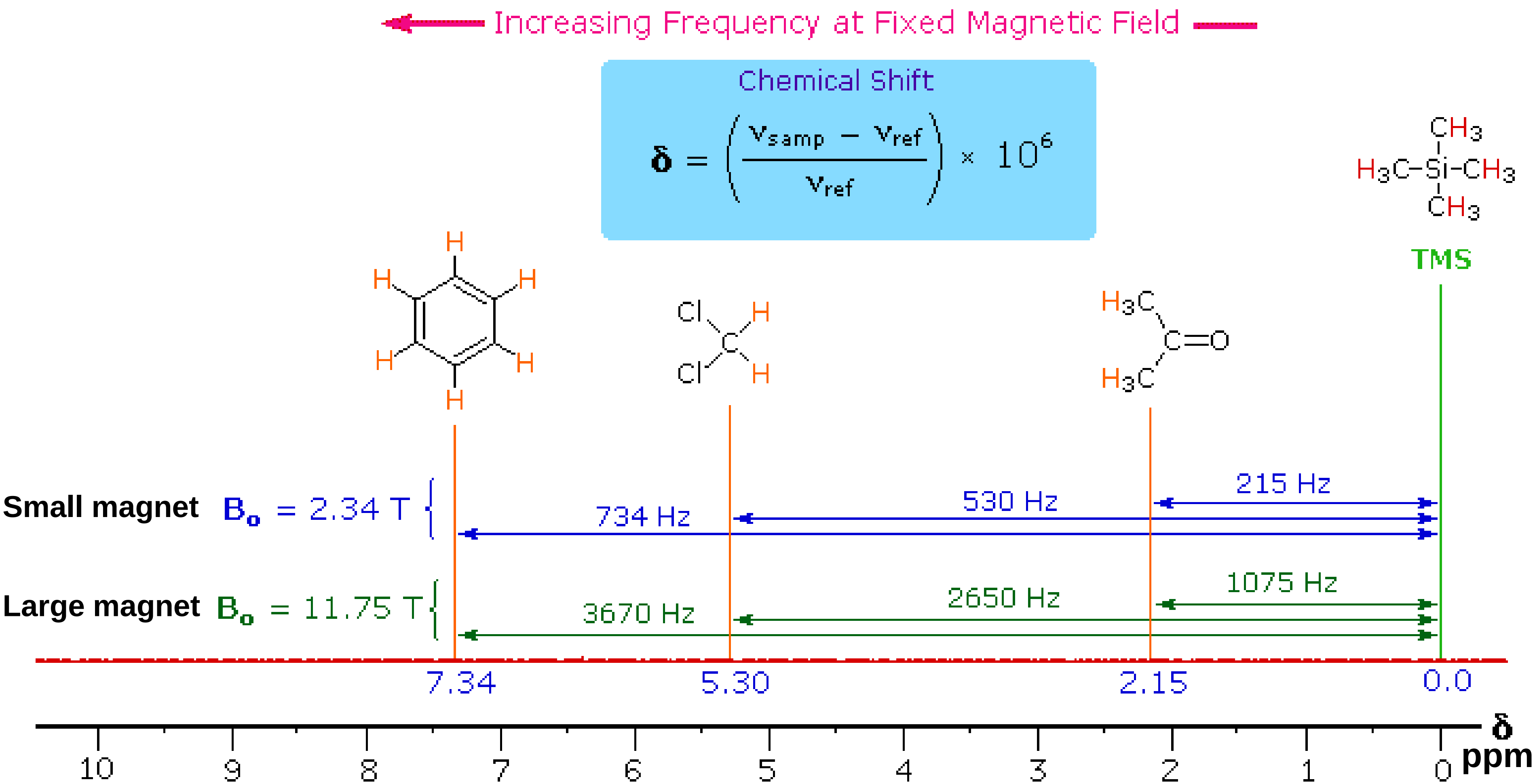
Understanding NMR Spectra



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

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

Understanding NMR Spectra



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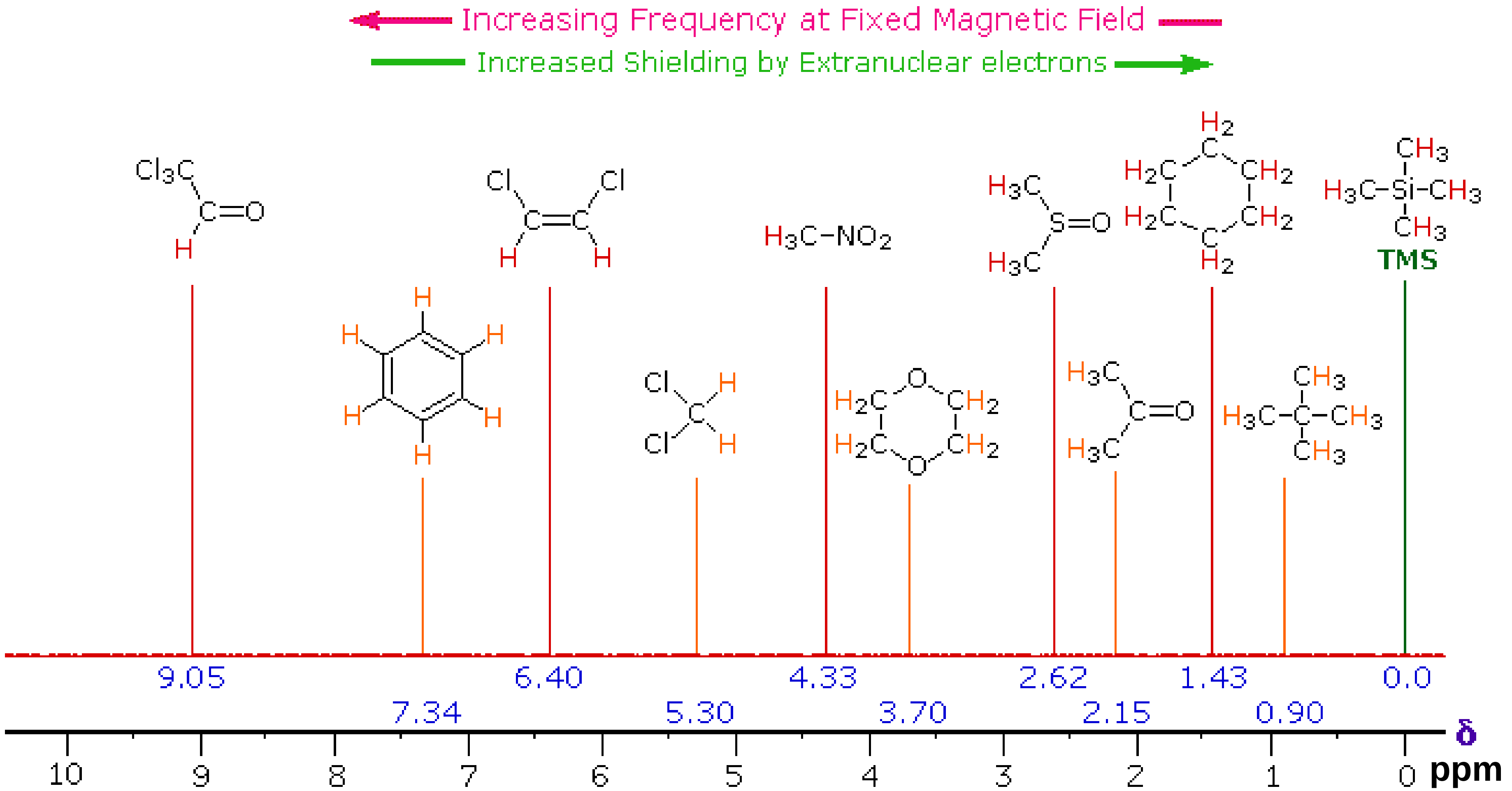
Understanding NMR Spectra



These **ppm** are for **ALL** magnets

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

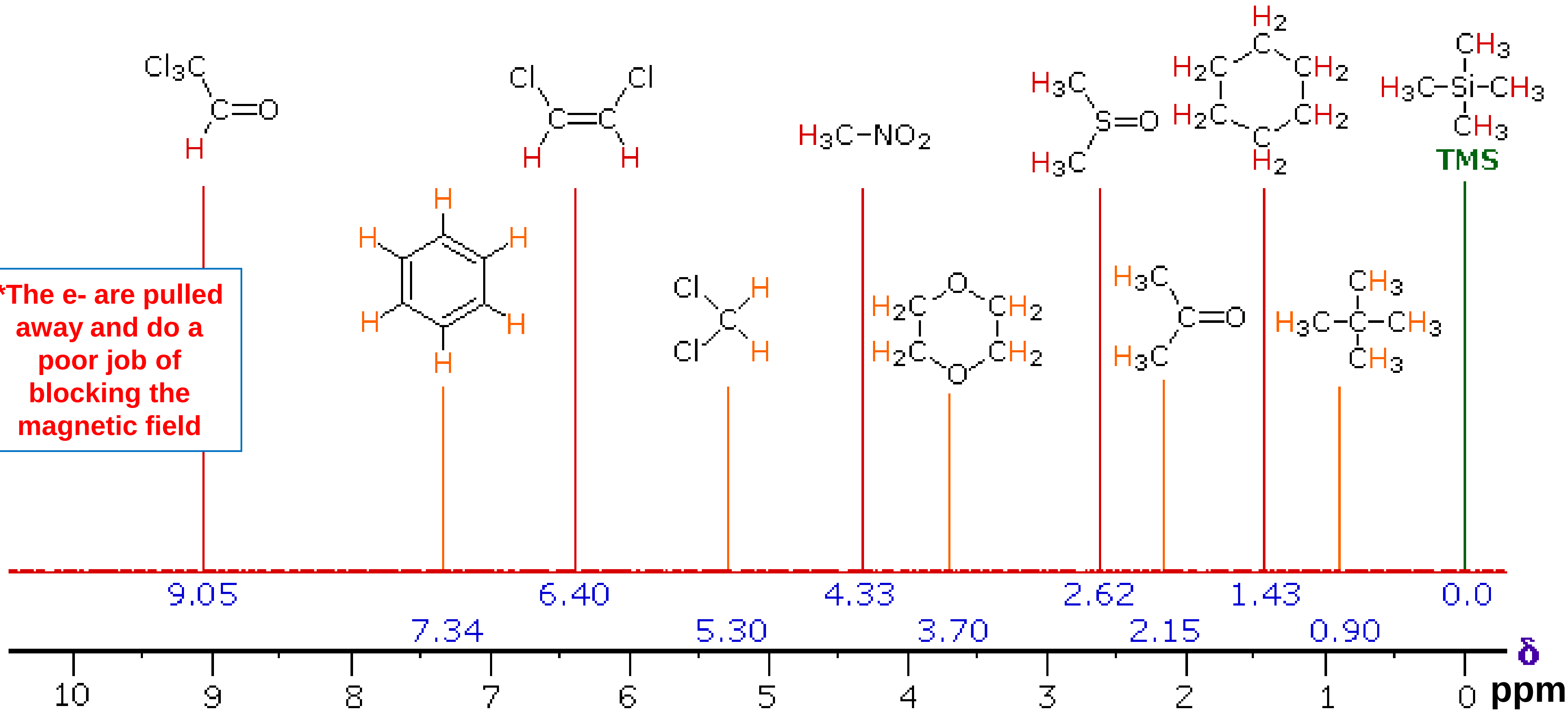
NMR Spectral Nomenclature

Left side of spectrum

- Deshielded
- High frequency
- Downfield
- Low field

Right side of spectrum

- Shielded
- Low frequency
- Upfield
- High field



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

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

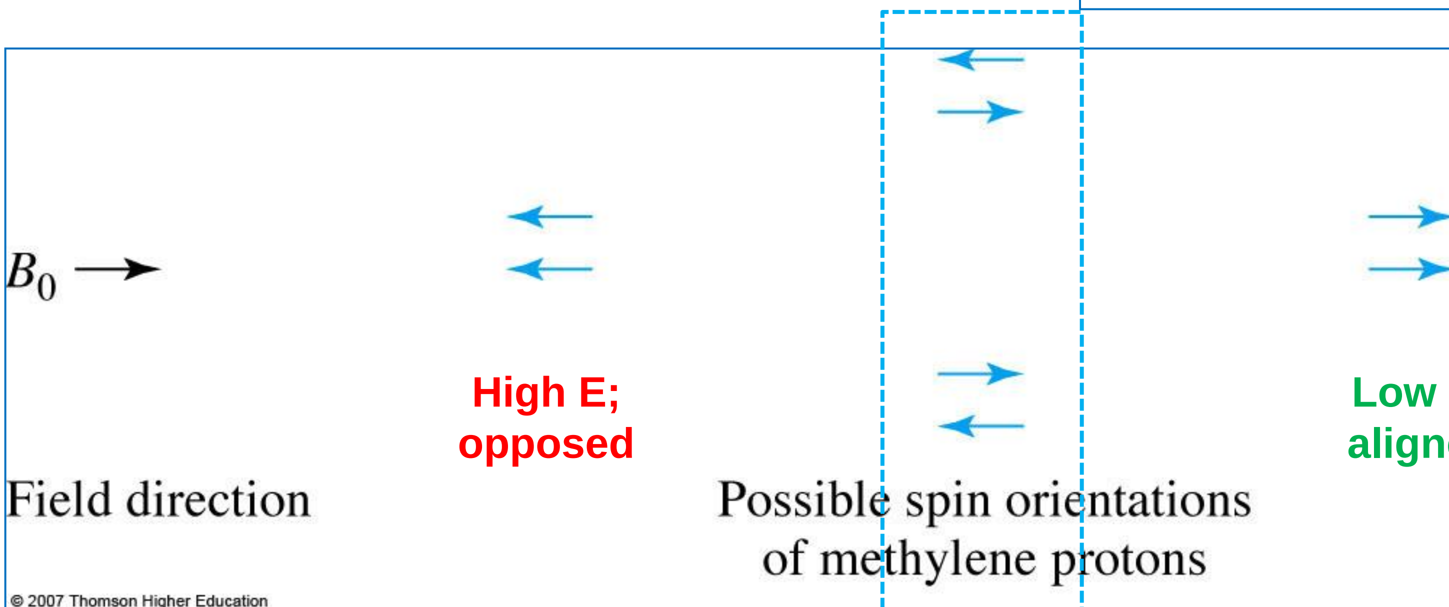
But, the spins couple - they interact

For 2 protons:

- **Each proton has its own spin**
- **The spin can be +½ or –½**
- **We can draw all the combinations:**

Degenerate: both cases have the same energy

Skoog, Page 515



Relative spin population	1	2	1

But, the spins couple - they interact

For 3 protons:
- **Each proton has its own spin**
- **The spin can be +½ or –½**
- **We can draw all the combinations:**

Degenerate: all 3 cases have the same energy

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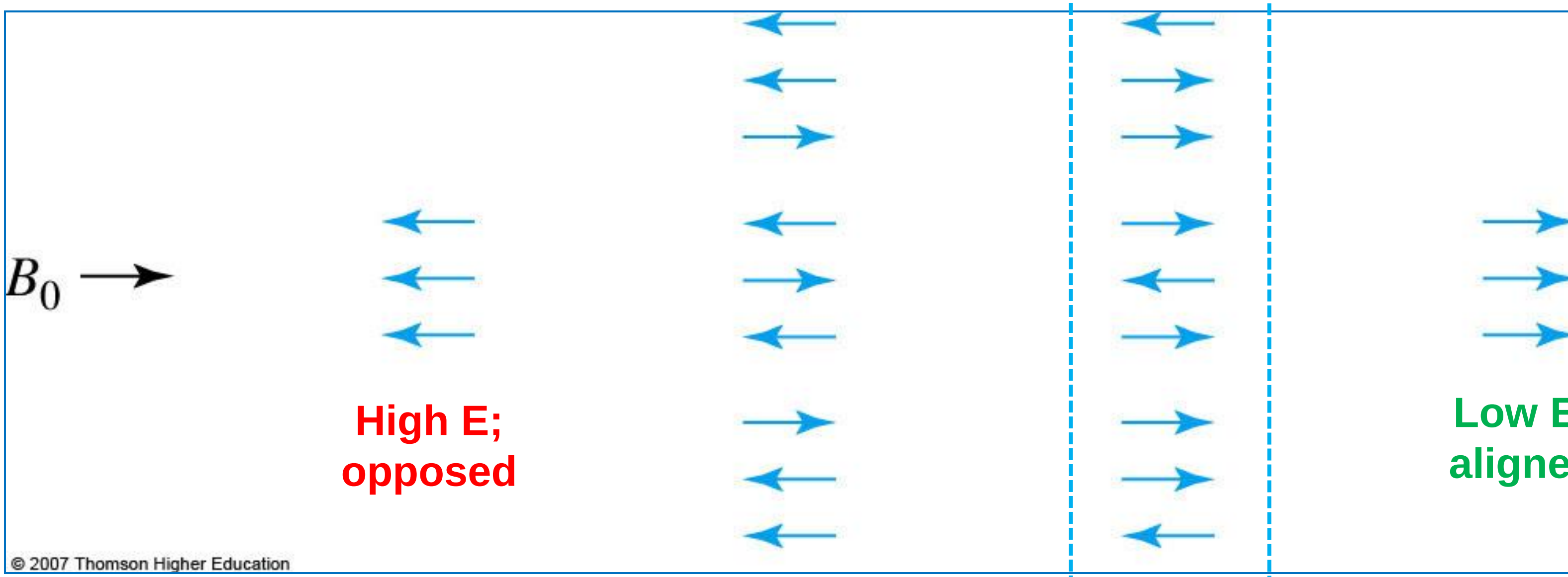


Relative spin population	**1**	**3**	**3**	**1**

The principle of multiplicity: the n + 1 rule and peak splitting

n **is the number of adjacent (neighboring) protons that are in a different chemical environment**

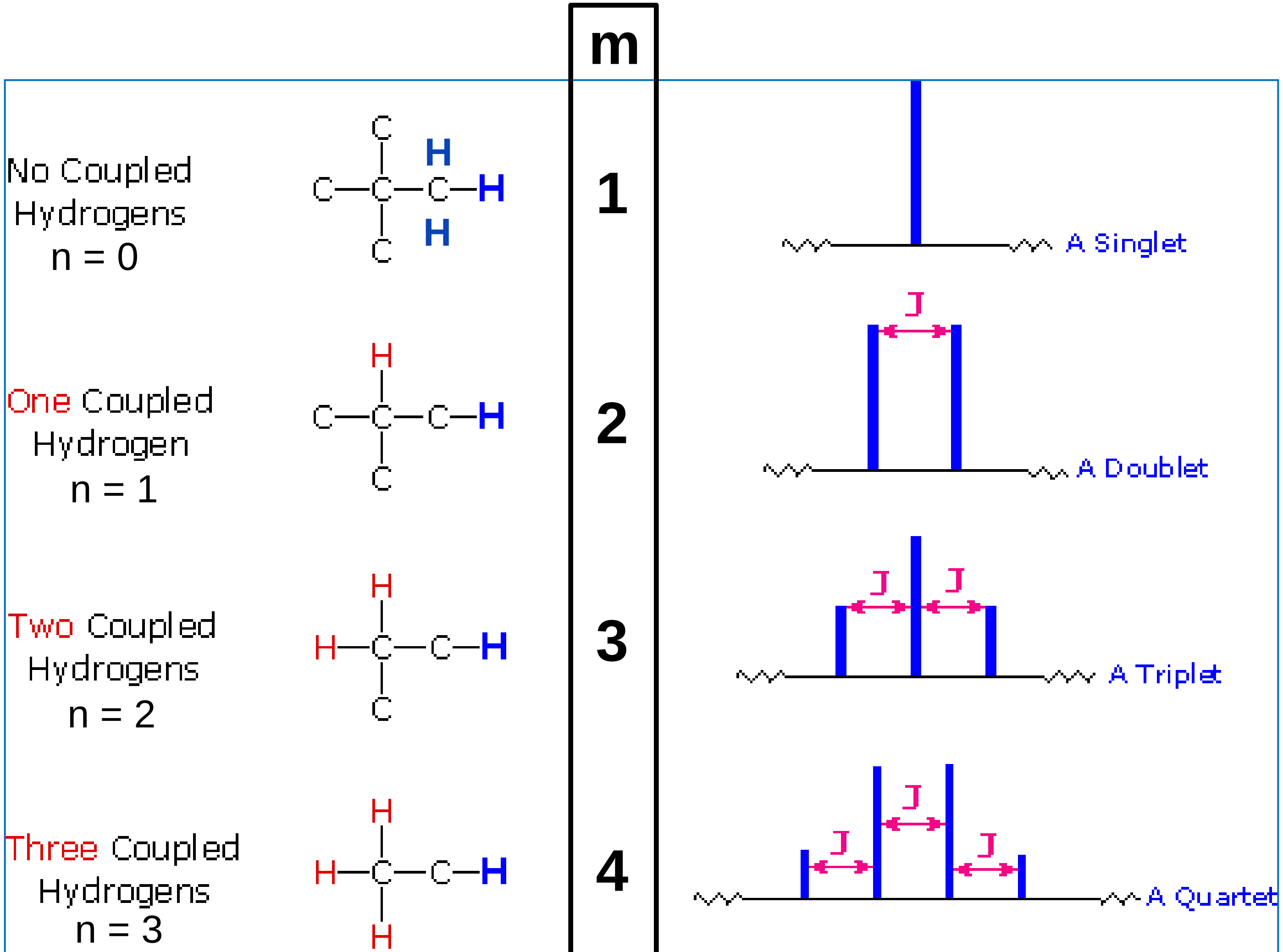
Multiplicity, m = n + 1

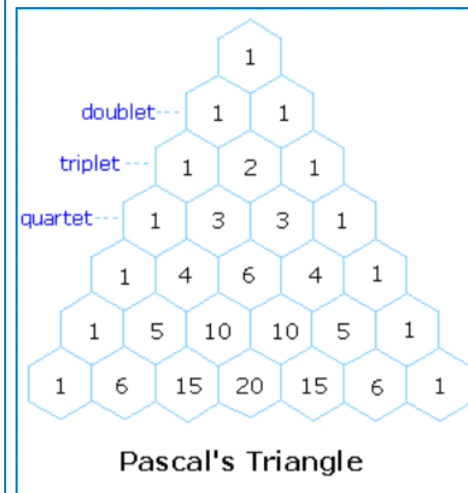
Pattern follows Pascal's triangle

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

Number of Equivalent Protons, *n*	Multiplicity, ($n + 1$)	Relative Peak Areas
0	1	1
1	2	1 1
2	3	1 2 1
3	4	1 3 3 1
4	5	1 4 6 4 1
5	6	1 5 10 10 5 1
6	7	1 6 15 20 15 6 1
7	8	1 7 21 35 35 21 7 1

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





Proximity is important

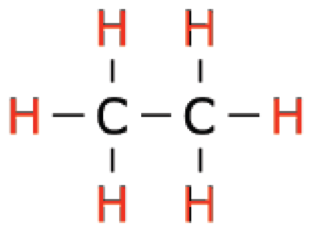
The splitting is called J coupling

Do they split – or not?

Determining Equivalent Hydrogens in ^{1}H NMR Spectroscopy

The hydrogens in the structure of a molecule can be grouped together based on their individual molecular environments (*i.e.*, where each hydrogen is located in the molecule's structure). Hydrogens that are in identical molecular environments in a molecule are **chemically equivalent**. Chemically equivalent hydrogens have the same chemical shift in a ^{1}H NMR spectrum, so they show up as a single signal.

For example, all six hydrogens in ethane are chemically equivalent; they are all in the same molecular environment, so only one signal is seen in ethane's ^{1}H NMR spectrum.



This will yield a spectrum with one NMR singlet.

Protons are not split by identical neighbors.

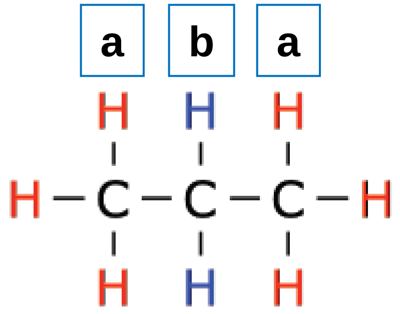
Chemically equivalent hydrogens are called **homotopic hydrogens**. Two hydrogens must be in identical molecular environments for them to be homotopic.

http://cobalt.rocky.edu/~barbaroj/equivalent_hydrogens.pdf

Do they split – or not?

Hydrogens in a molecule that are in different molecular environments are **chemically nonequivalent**. Chemically nonequivalent hydrogens have different chemical shifts in the ^{1}H NMR spectrum of the compound and show separate signals. For example, the eight hydrogens in propane are not chemically equivalent. The six methyl hydrogens are chemically equivalent, as are the two methylene hydrogens, but the two methylene hydrogens are in a different molecular environment than the six methyl hydrogens.

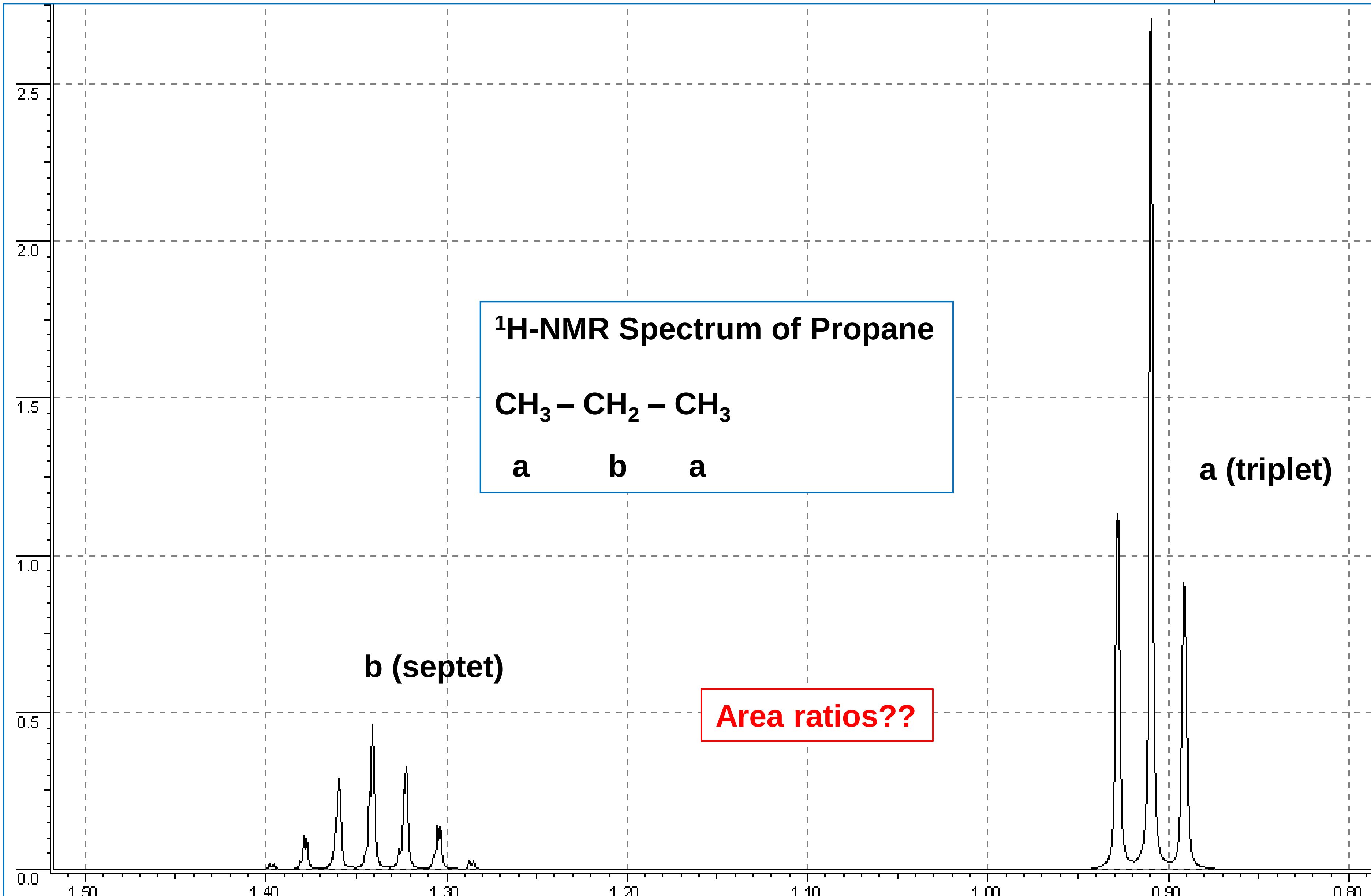
Propane:



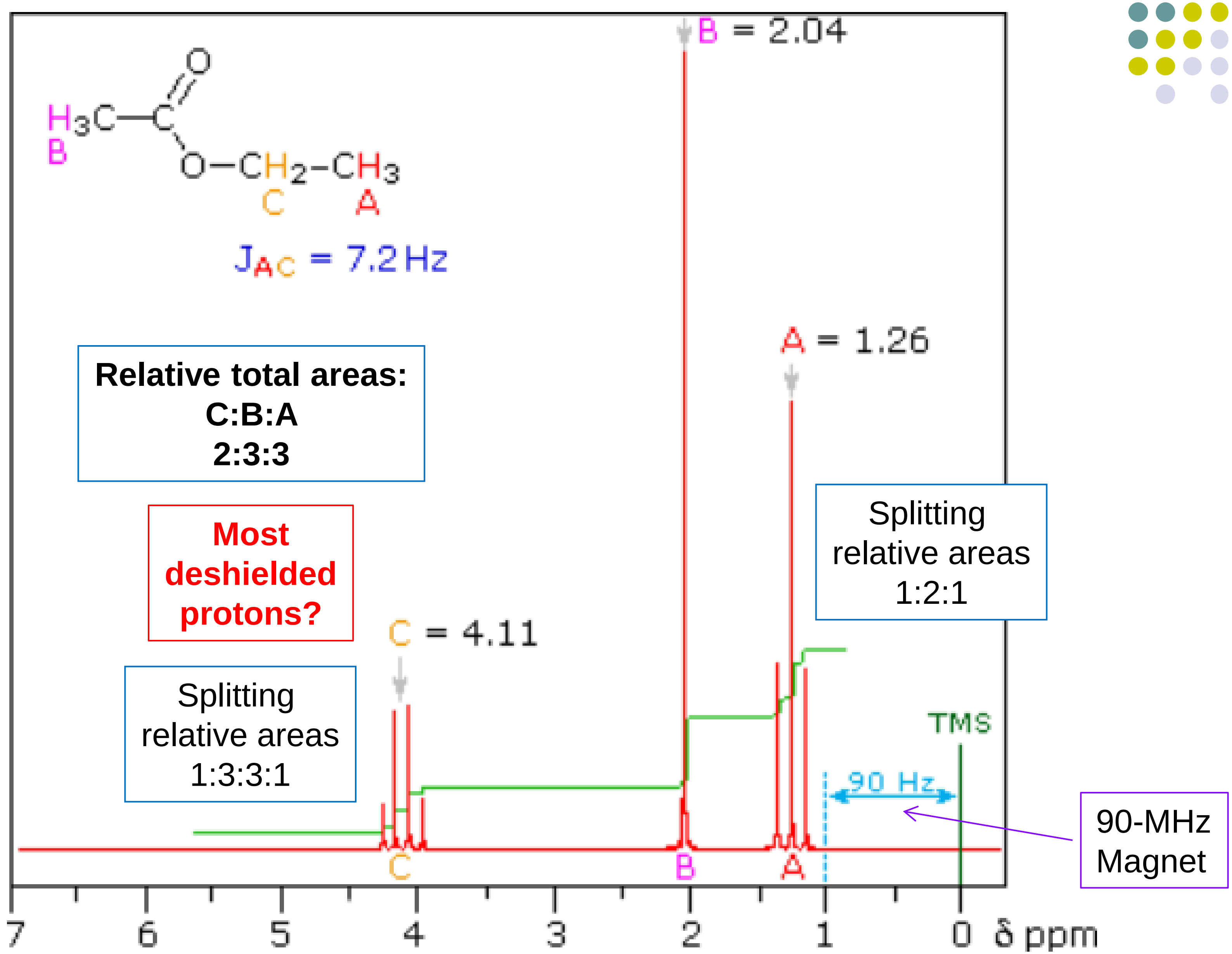
See next panel for spectrum of propane

The methyl hydrogens and the methylene hydrogens in propane are chemically nonequivalent. These two groups of nonequivalent hydrogens have different chemical shifts and will show up as two separate signals in a ^{1}H NMR spectrum. Chemically nonequivalent hydrogens are called **heterotopic hydrogens**. In order for two hydrogens to be heterotopic, they must be in different molecular environments. (In theory, every group of nonequivalent hydrogens gives rise to a separate signal in the ^{1}H NMR spectrum.

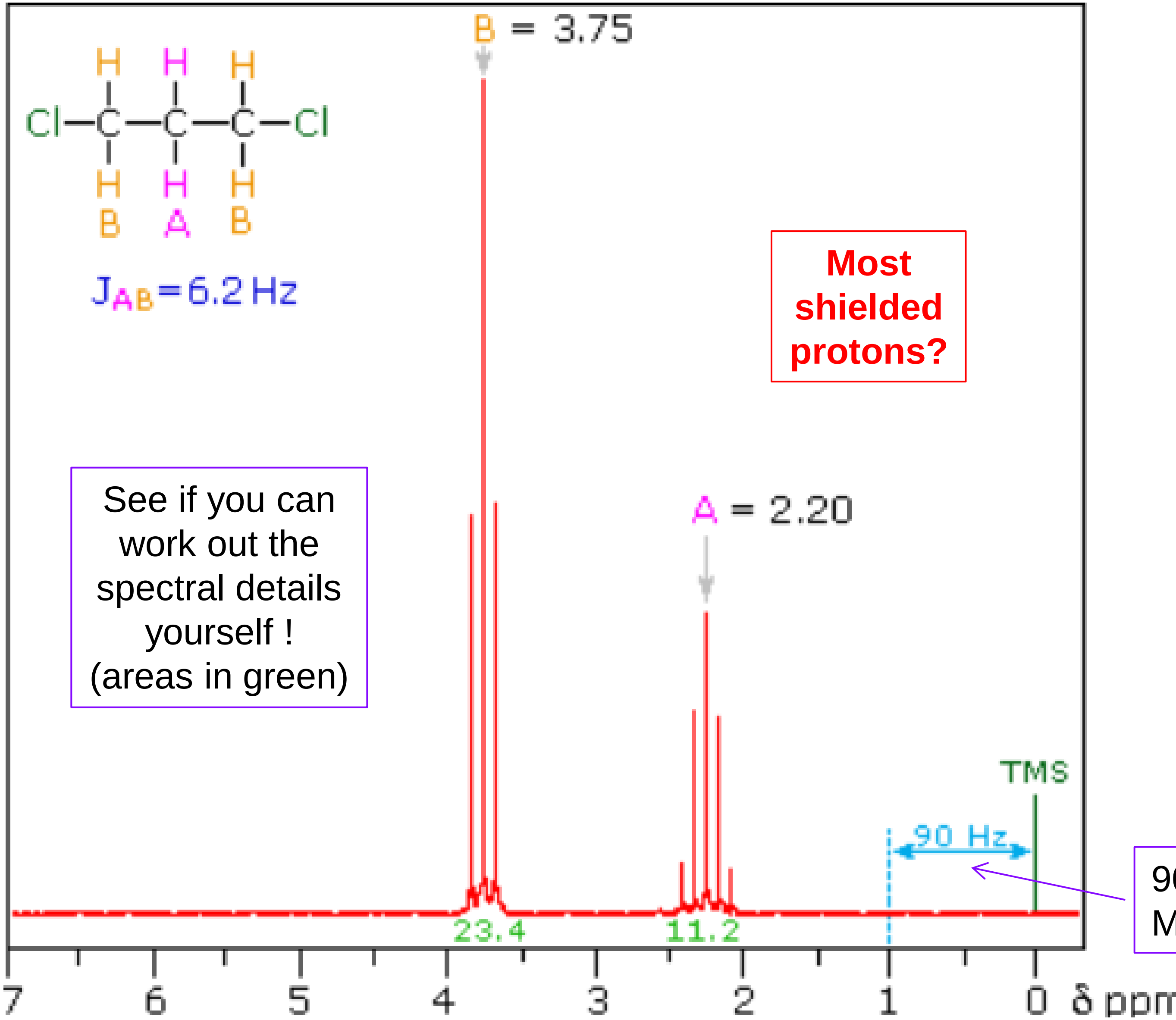
http://cobalt.rocky.edu/~barbaroj/equivalent_hydrogens.pdf


1H-NMR Spectrum of Propane
CH3 – CH2 – CH3
a b a
a (triplet)
b (septet)
Area ratios??
2.5
2.0
1.5
1.0
0.5
0.0
1.50
1.40
1.30
1.20
1.10
1.00
0.90
0.80

NMR Data Interpretation – Example 1



NMR Data Interpretation – Example 2

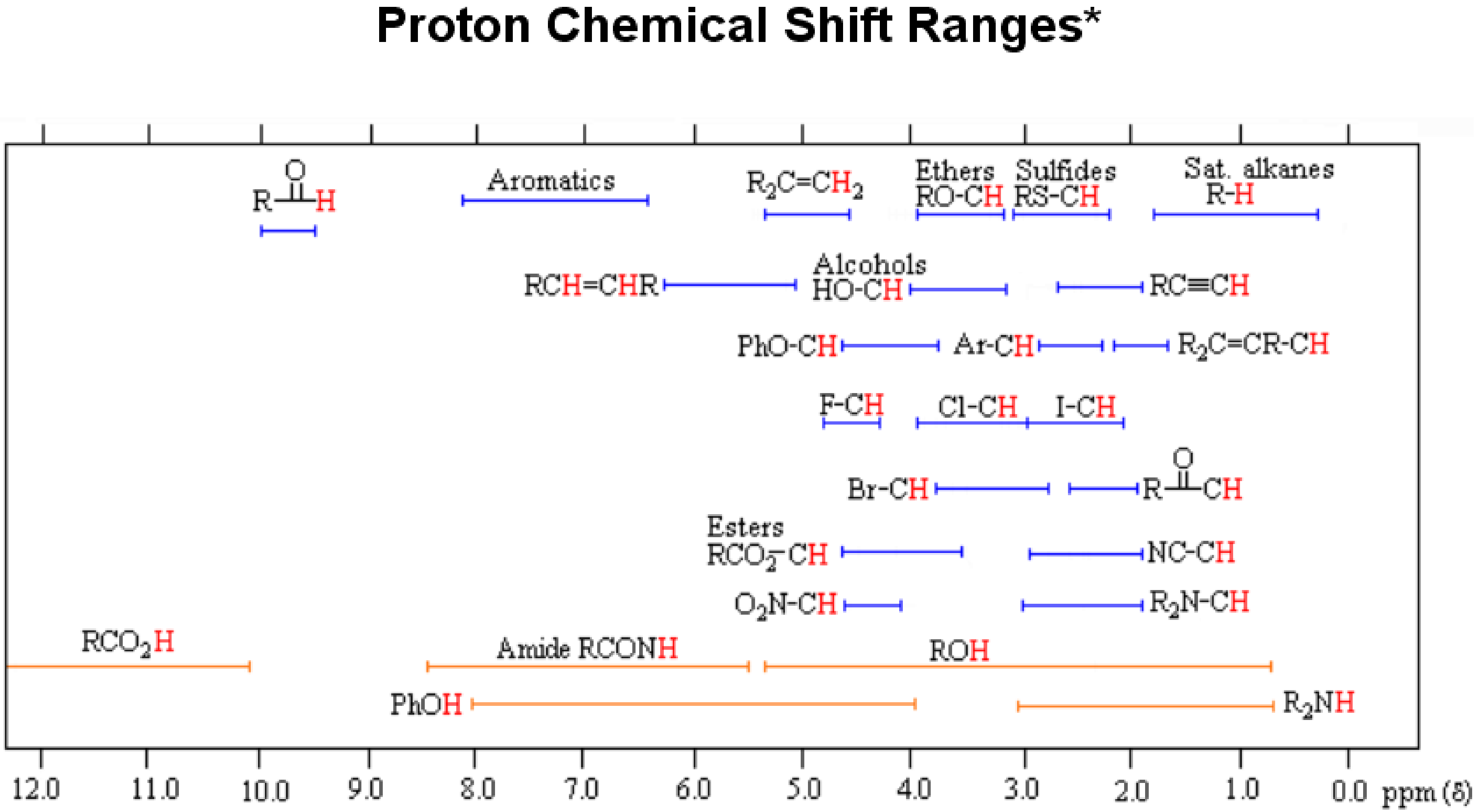


Most shielded protons?

See if you can work out the spectral details yourself ! (areas in green)

90-MHz Magnet

NMR Chemical Shifts – helps interpret data



* For samples in $CDCl_3$ solution. The δ scale is relative to TMS at δ = 0.

NMR data interpretation – watch the video!

http://mestrelab.com/software/mnova-nmrpredict-desktop/

Other Things NMR Can Mean

NMR
National Mileage Register

no membership required

NIGHTMARE RECORDS

nmr
national mileage register

NMR
National Medical Reviews
Independent Review Organization since 1996

North Munster Region

NEW MEDIA RIGHTS

New Moon Rising
A Magickal Pagan Journal

NM&R
NICHOLS MELBURG ROSSETTO
ARCHITECTS/ENGINEERS

nightingale moon records

NEW MEDIA ROCKSTARS

NEW MUSIC
RALEIGH

NEWBERG
MAIL ROOM