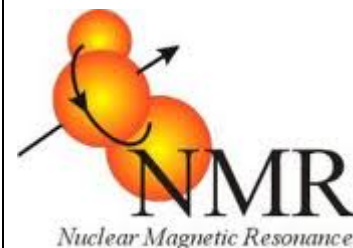
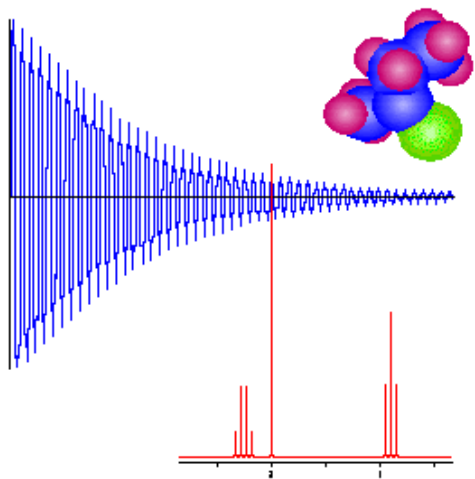
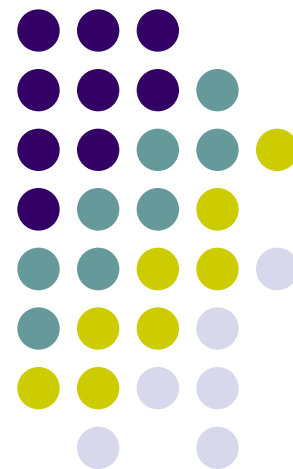


Introduction to Nuclear Magnetic Resonance Spectroscopy

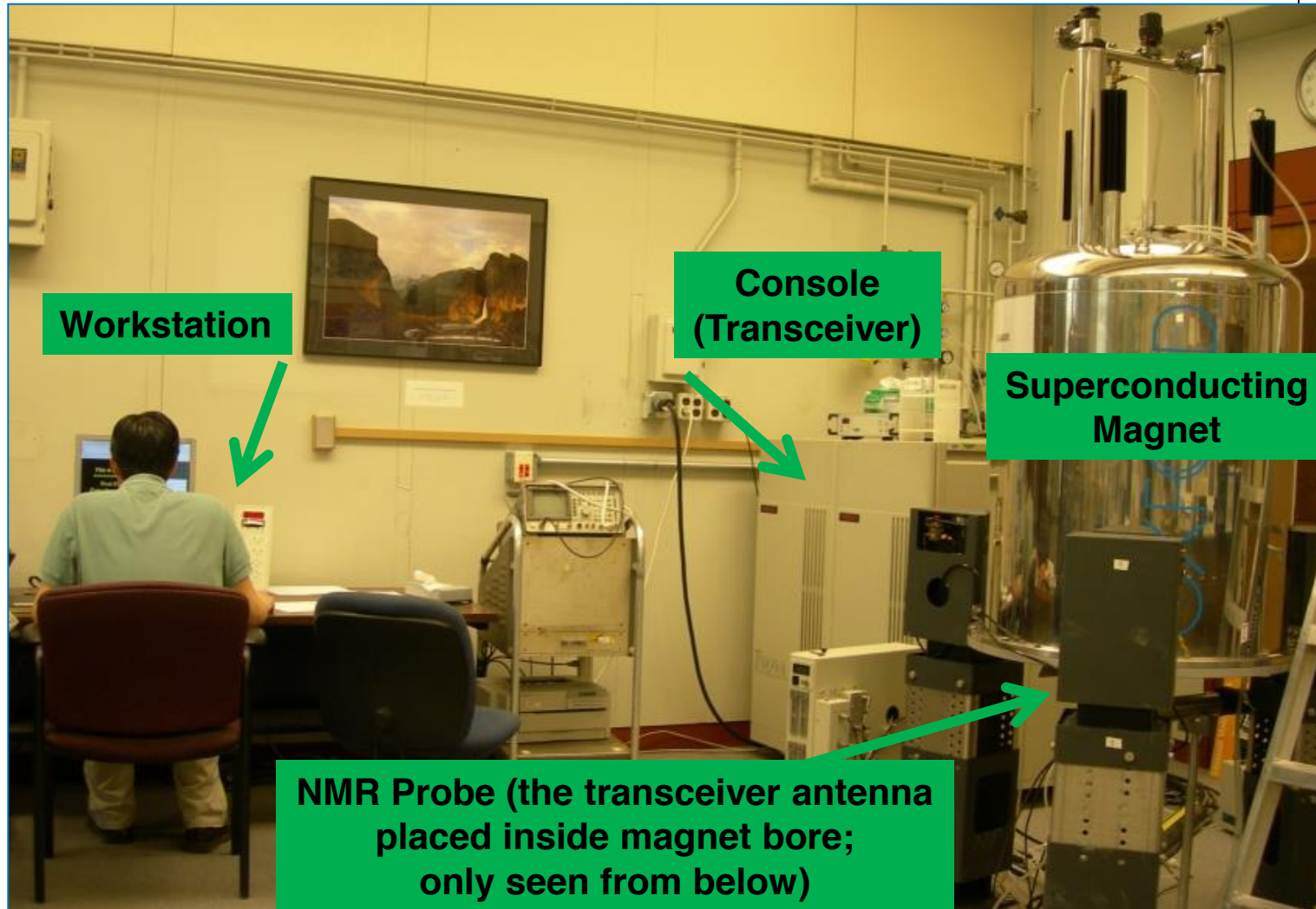


Dr. Dean L. Olson, NMR Lab Director
School of Chemical Sciences
University of Illinois



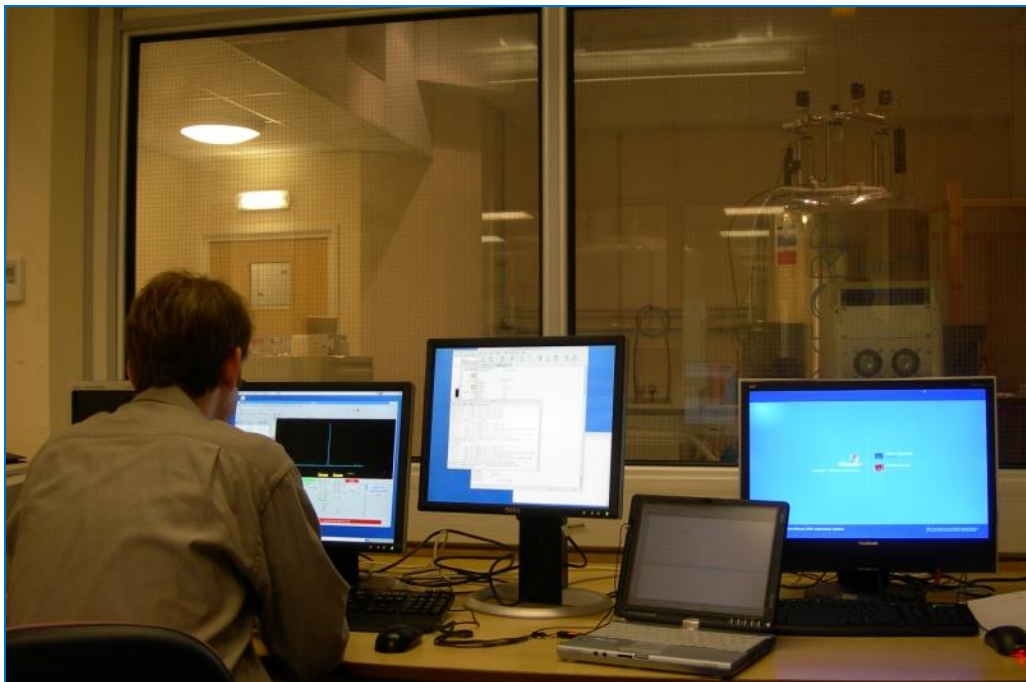
Called figures, equations, and tables are from
“Principles of Instrumental Analysis, 6th Ed.”
Skoog, Holler, and Crouch, 2007;
Thompson Corp.

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



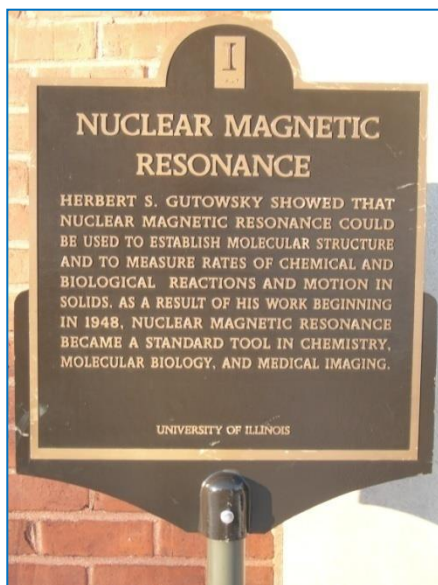
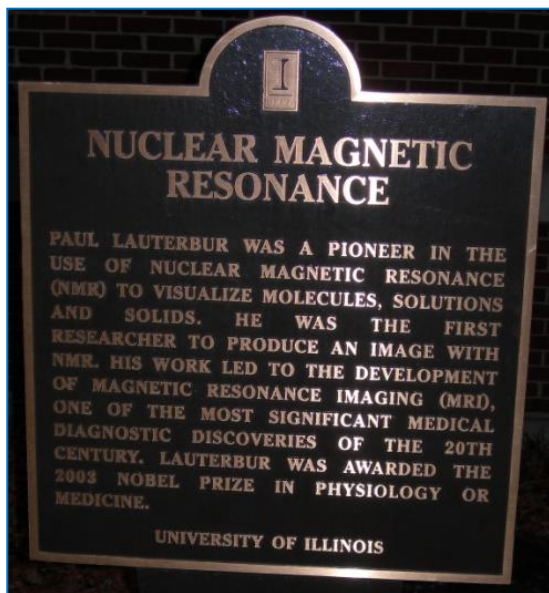
- NMR is based on the behavior of a **sample placed in an electromagnet and irradiated with radiofrequency waves**: 60 – 900 MHz ($\lambda \approx 0.5$ m)
 - The magnet is typically large, strong, \$\$\$, and delivers a *stable, uniform* field – required for the best NMR data
 - A transceiver antenna, 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.**”

NMR components

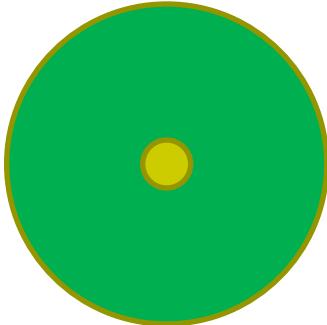


**Workstation
computer**

NMR Console

**(creates and
receives pulses)**

**Magnet
(inside a Dewar)**

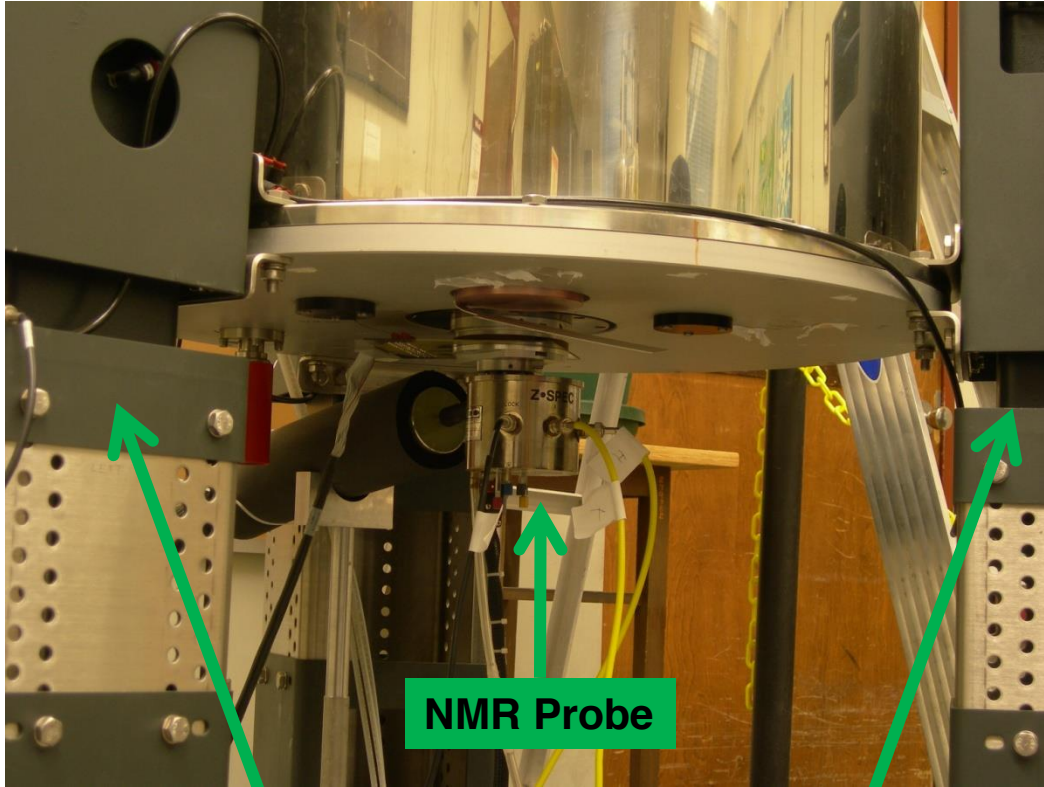


**Overhead
perspective;
solenoid inside**

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



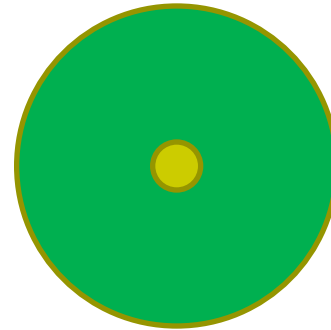
NMR components



NMR Probe

**Pneumatic Legs
(to stabilize vibrations)**

**Magnet
(inside a Dewar)**



Overhead
perspective;
solenoid inside

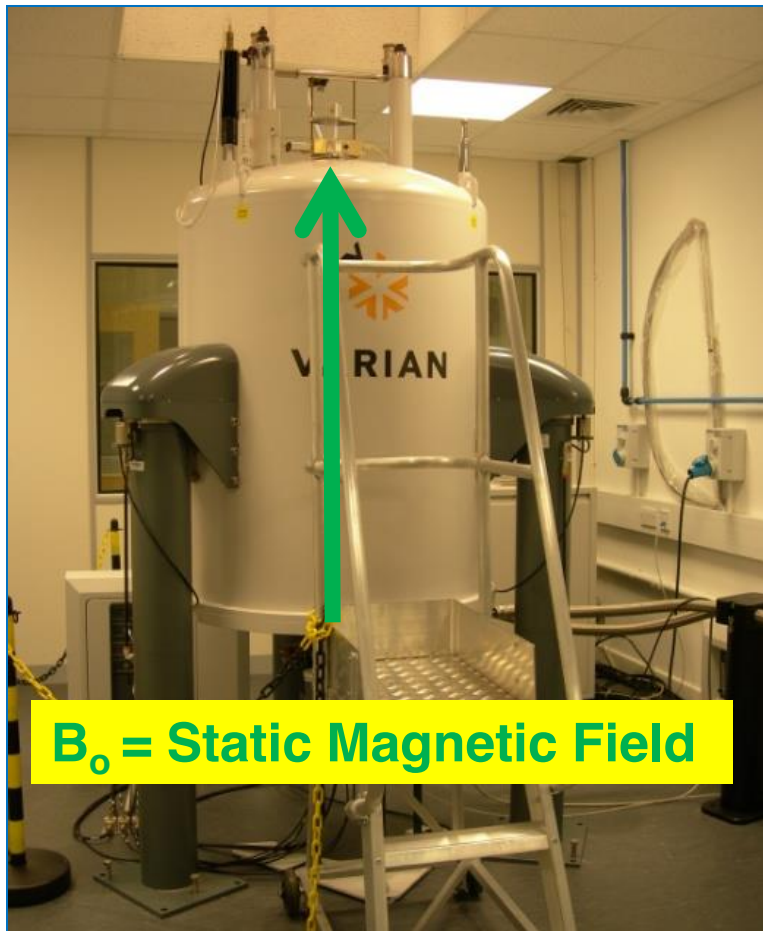
**NMR Probe
(inside magnet)**





**U. Bristol, United Kingdom
14.1 Tesla magnet**

**Termed a
“600 MHz” magnet**



$B_0 = \text{Static Magnetic Field}$

Varian is now Agilent
as of late 2010

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

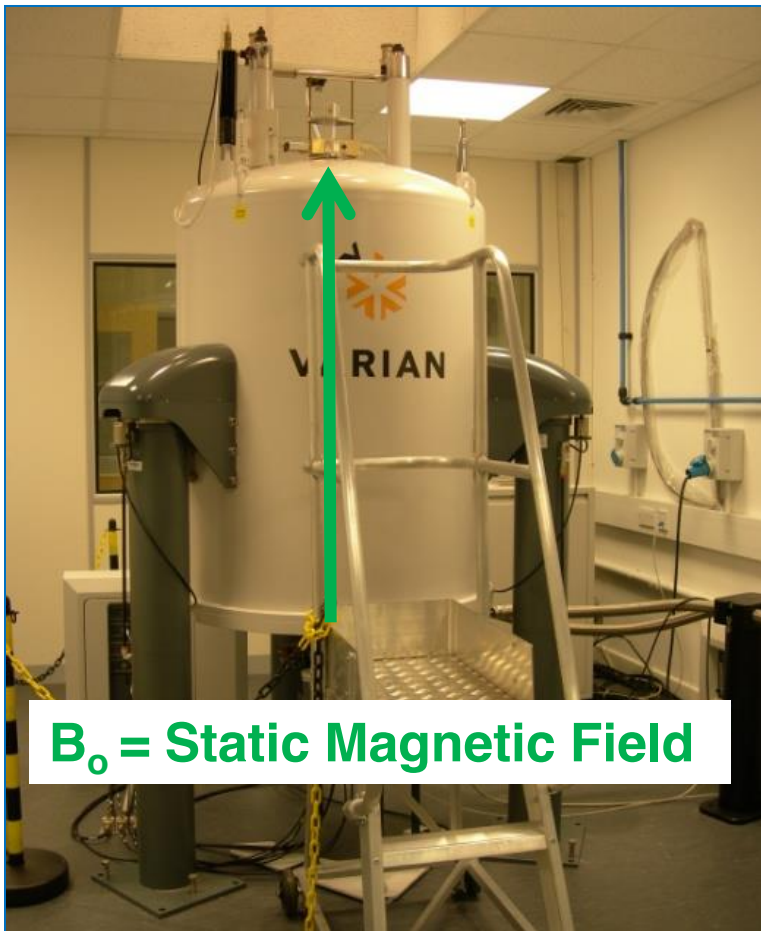
1000 MHz is equivalent to 23.5 Tesla



**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*.



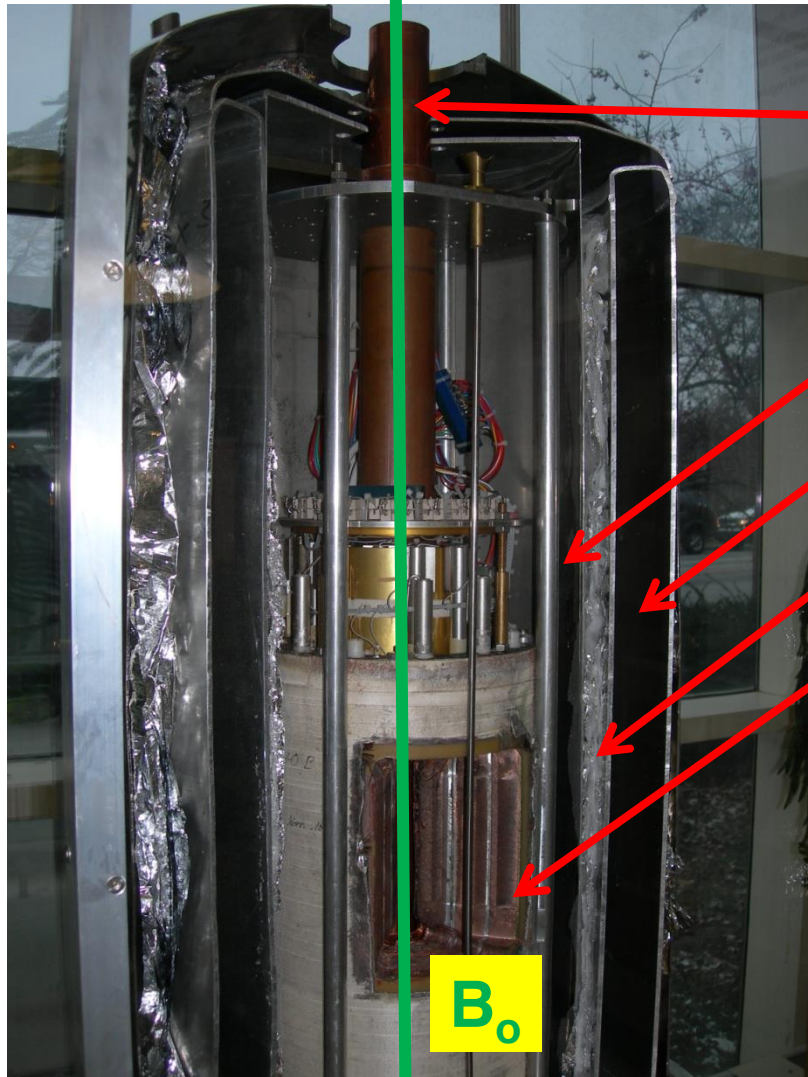
B_0 = Static Magnetic Field

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



Bore

Liquid Helium sleeve

Liquid Nitrogen sleeve

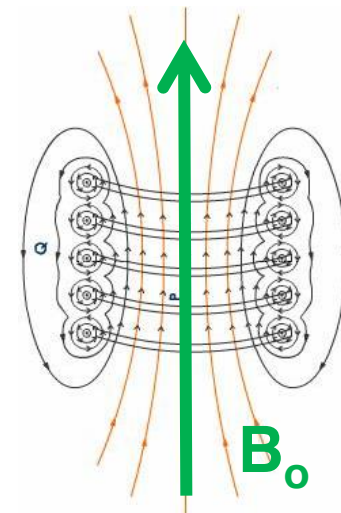
Vacuum sleeve

Solenoid (cut-away)

Superconducting coil

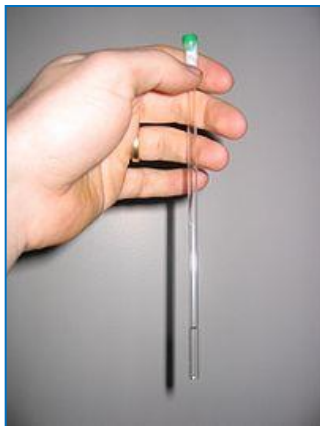
B_0

In the Atrium of
Chemical Life Sciences Lab A



NMR sample handling options

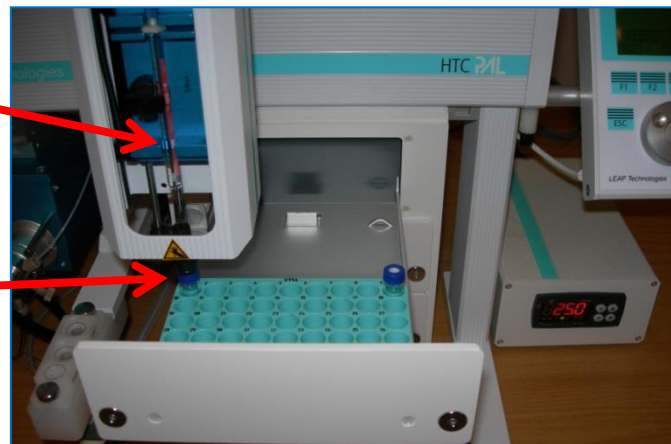
Spinning tube NMR



A typical NMR sample tube:
7 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

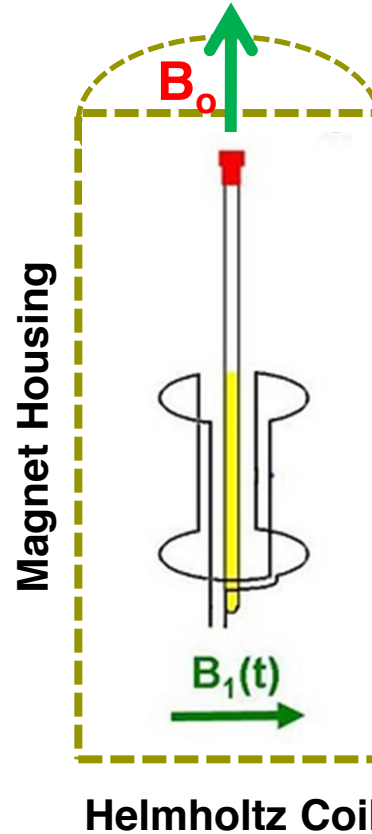


How does NMR work?



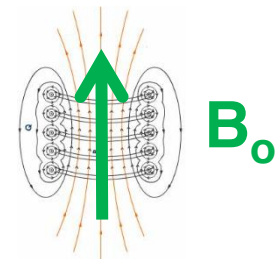
B_0 = **Static** Magnetic Field
from the big supercon
magnet: persistent field

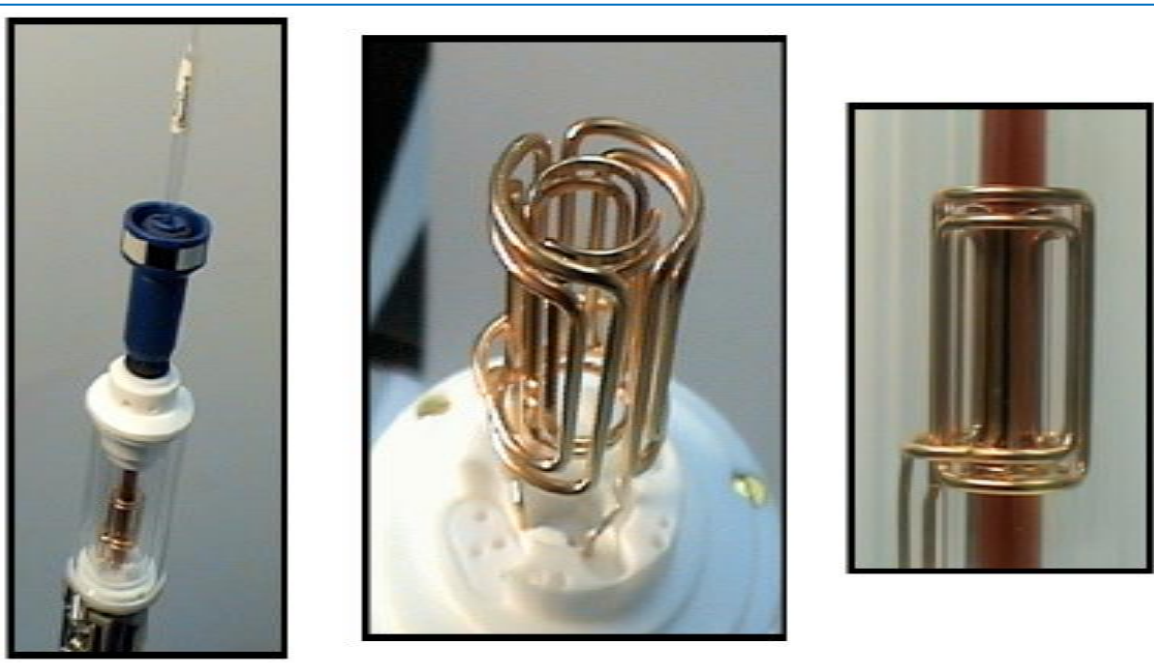
Probe Coils create the **Transverse (B_1)** Field
from a current pulse of **time t**



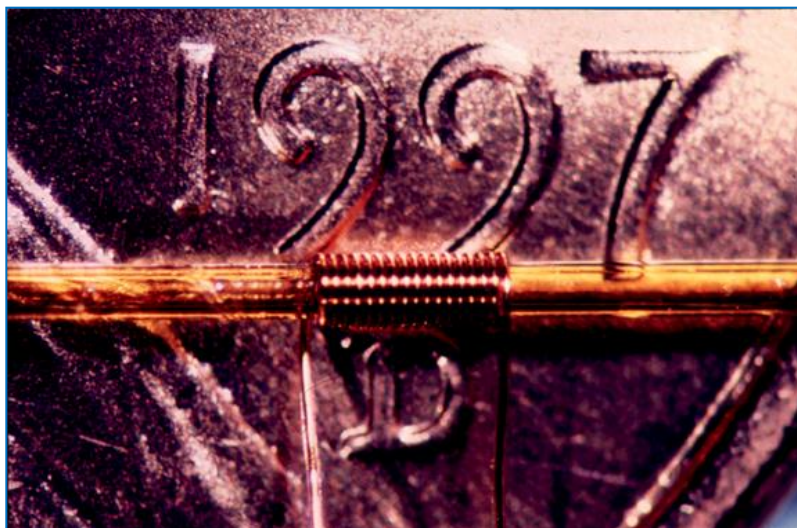
The transverse magnetic field **tips the spin**. A 90° pulse aligns the spin with the transverse field. The spin is not usually flipped 180° .

Solenoid Coil
makes up the
superconducting
magnet inside the
housing





**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**

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

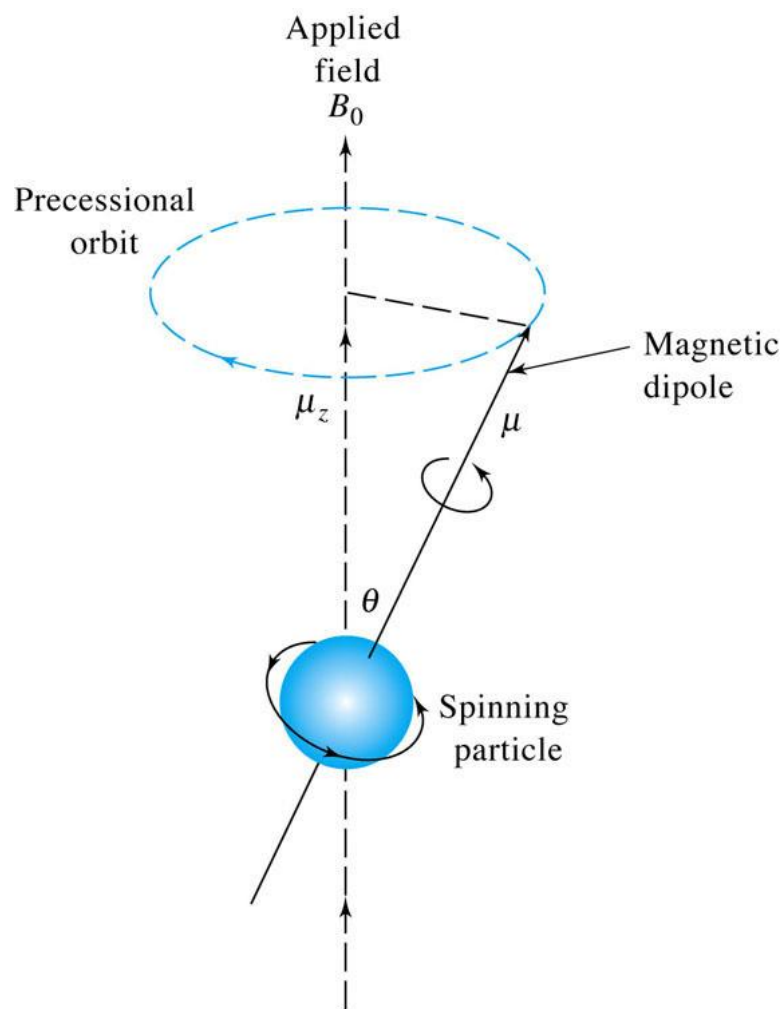


Fig. 19-2

- **Nuclear spin in an applied magnetic field**
 - A magnetic dipole, μ , is produced
 - The spin precesses
 - The spin is quantized
 - ^1H has a **spin quantum number** of either **$+1/2$ (low E)** or **$-1/2$ (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
1H	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

^aAt constant field for equal number of nuclei.

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



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

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

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

m = spin quantum number
m = - 1/2 for high energy; opposed
m = + 1/2 for low energy; aligned

High E; opposed

Low E; aligned

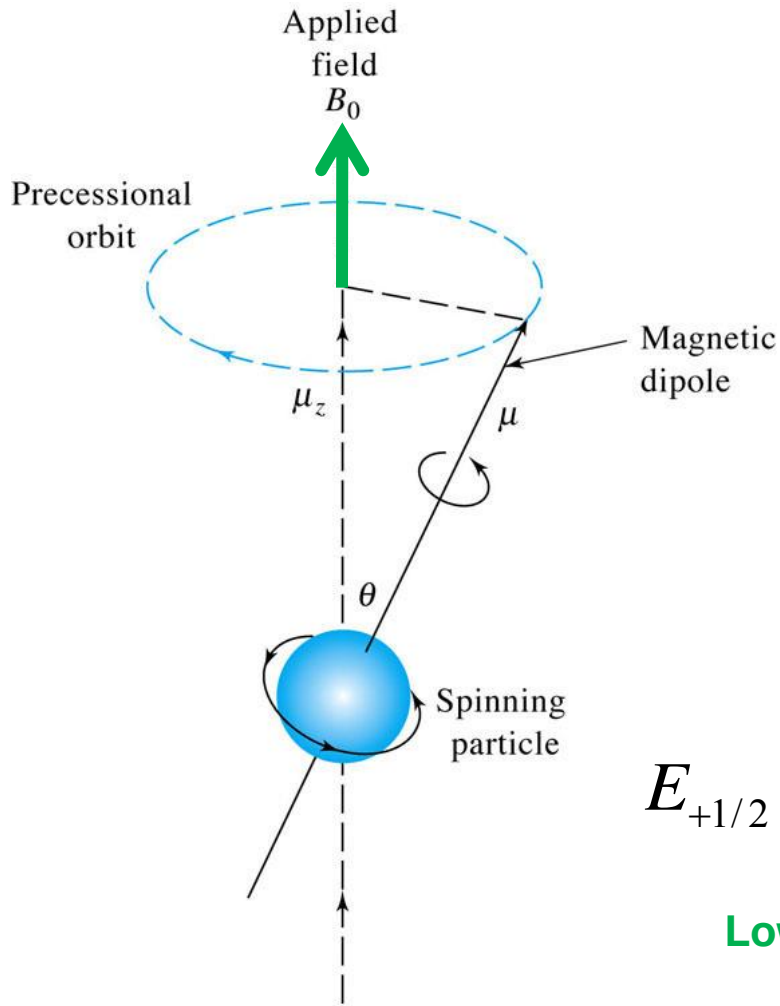
$$\Delta E = \frac{\gamma h}{2\pi} B_o$$

$\Delta E = \text{high} - \text{low}$

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

The spin *precesses*
between the two states.

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



m = spin quantum number
m = - 1/2 for high energy; opposed
m = + 1/2 for low energy; aligned

$$E_{+1/2} = -\frac{\gamma h}{4\pi} B_0$$

Low E; aligned

Fig. 19-2

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

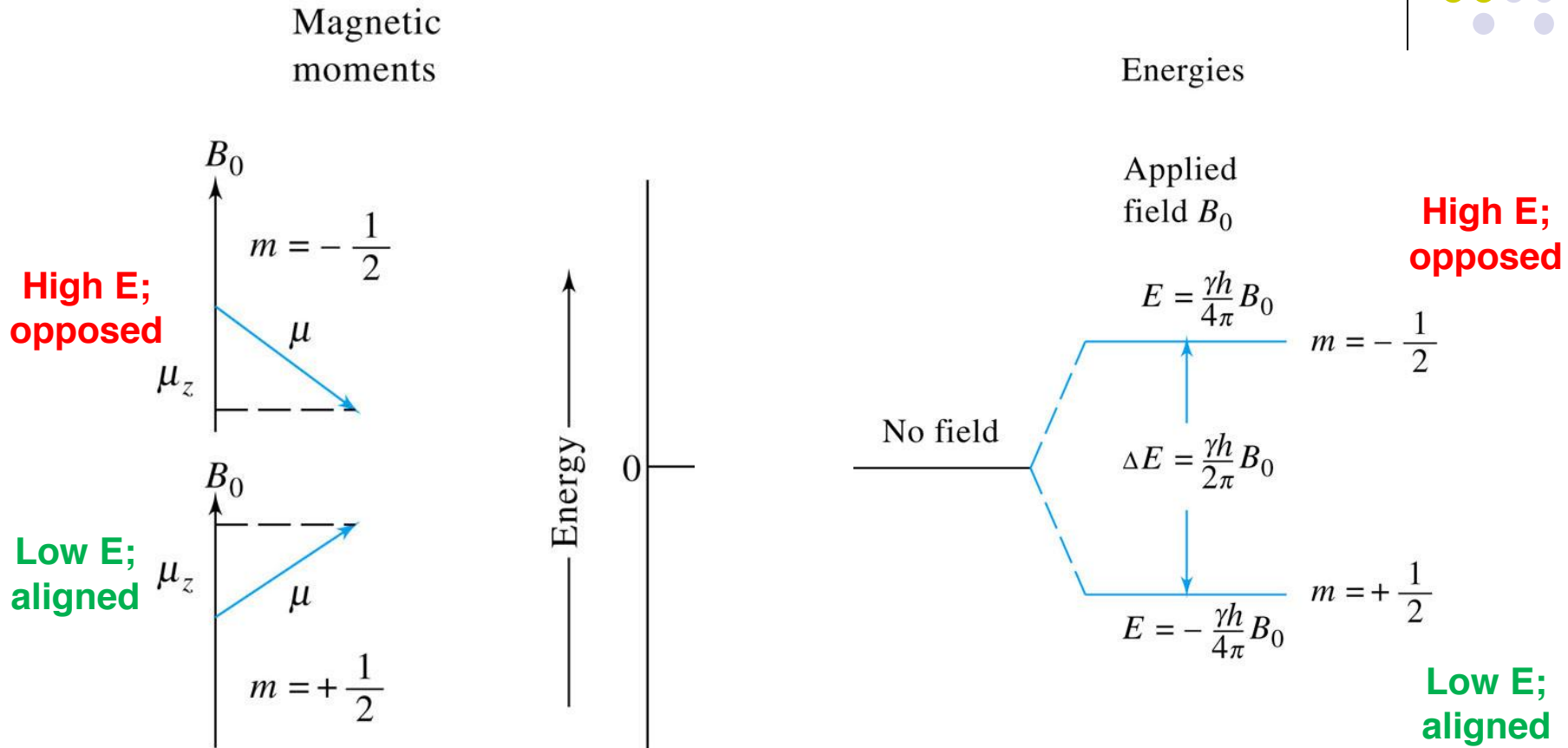
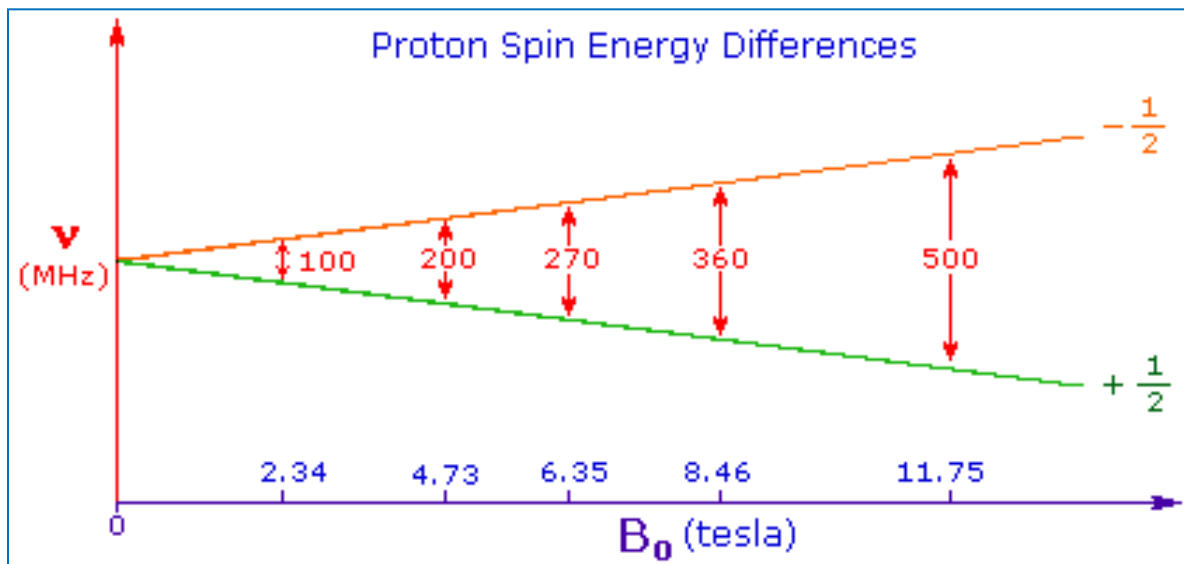
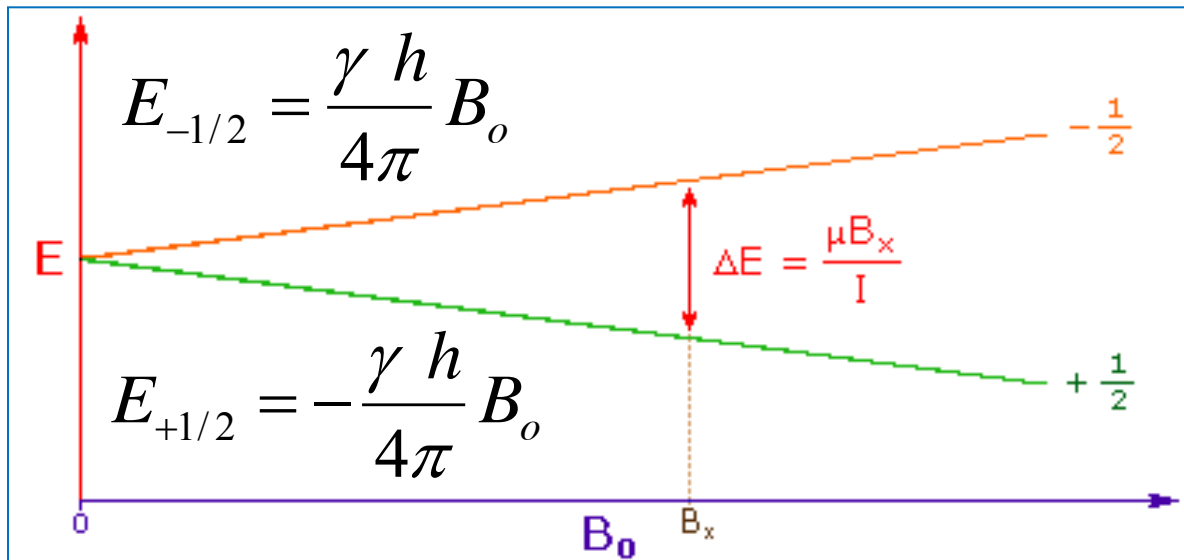


Fig. 19-1

ΔE depends on the applied B_0



The stronger the magnet, the larger the ΔE



So, where does the NMR signal come from?

The transverse magnetic field **tips the spin**. A 90° pulse aligns the spin with the transverse field. The spin is not usually flipped 180°.

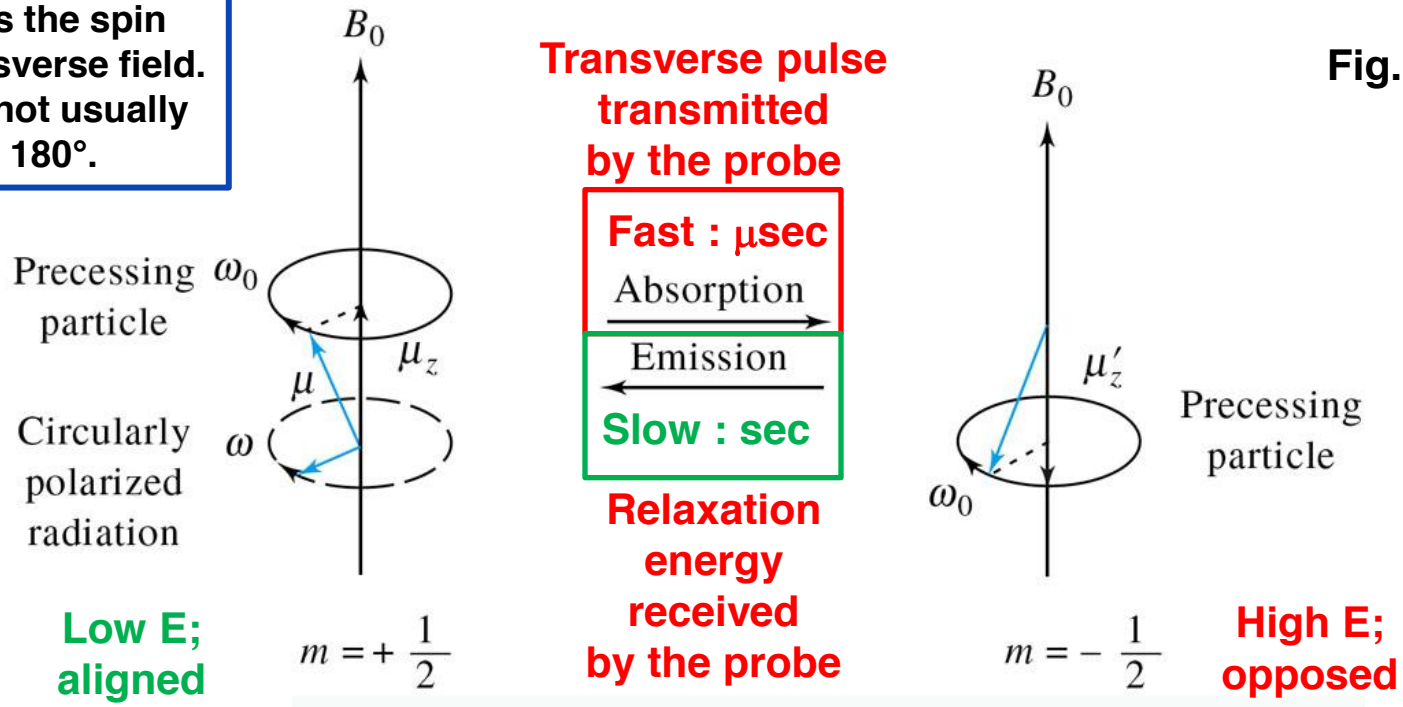


Fig. 19-3

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.



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

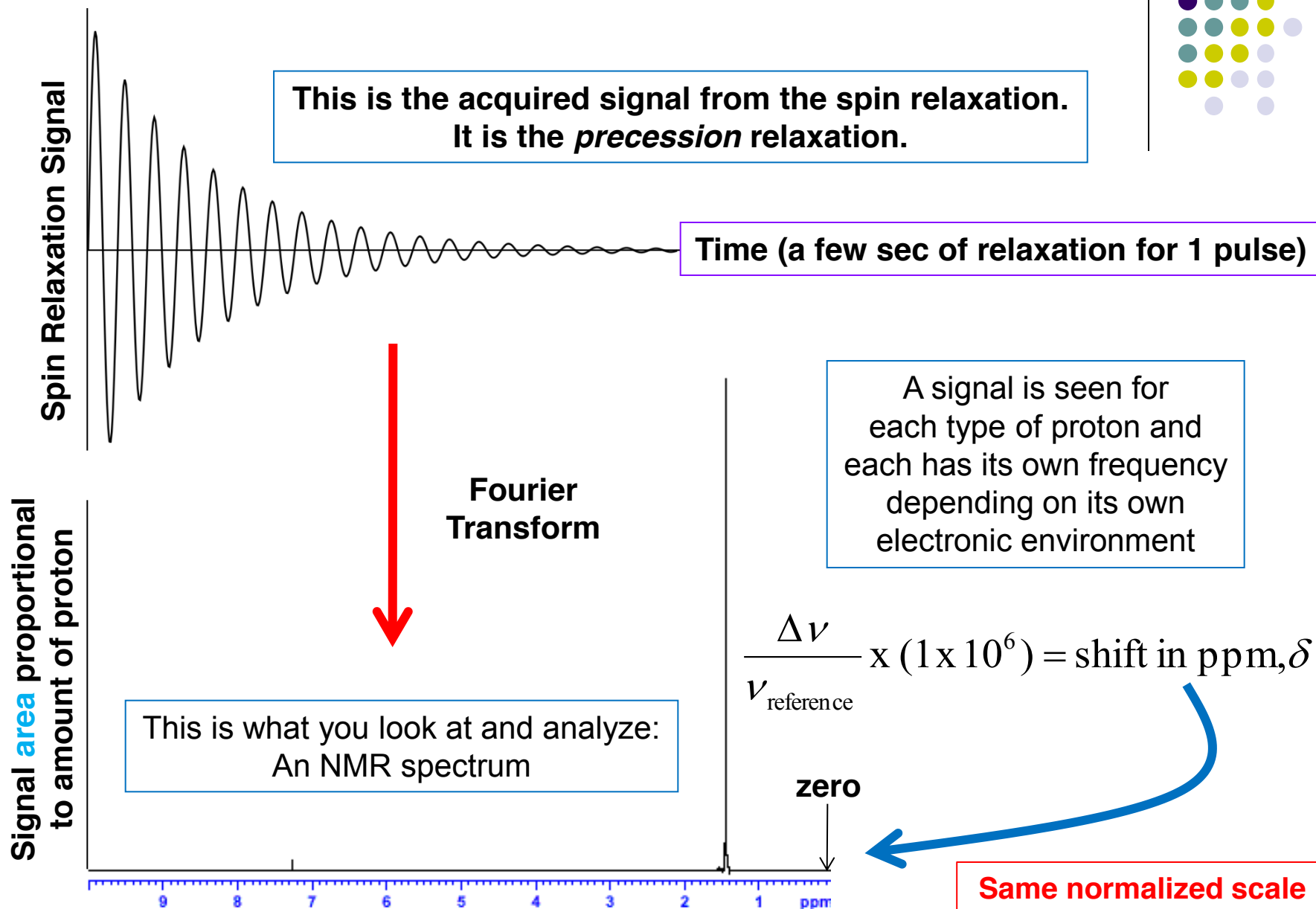
**Boltzmann Distribution Equation
for quantum spin states
in a magnetic field**

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

- $B_o = 4.69$ Tesla
- $T = 20^\circ\text{C}$
- $\gamma = 2.6752 \times 10^8 \text{ T}^{-1} \text{ sec}^{-1}$
- $N_{\text{Hi}} / N_{\text{Lo}} = 0.999967$
- For $N_{\text{Hi}} = 1,000,000$ then $N_{\text{Lo}} = 1,000,033$
- $\Delta N = 33$ 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?



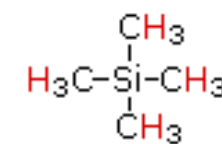
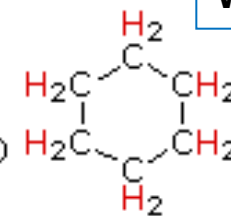
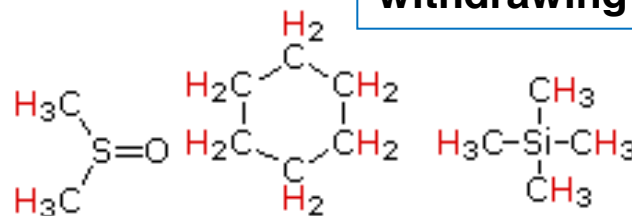
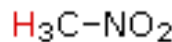
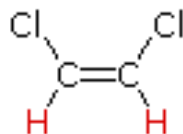
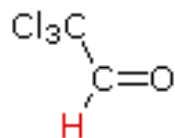
Understanding NMR Spectra



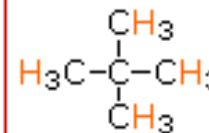
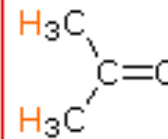
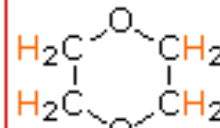
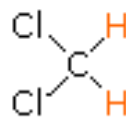
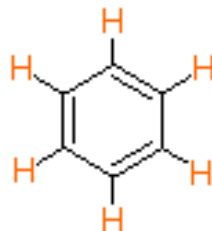
Deshielded protons absorb more energy*

← Increasing Frequency at Fixed Magnetic Field —
 — Increased Shielding by Extranuclear electrons →

Si is not electron withdrawing



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

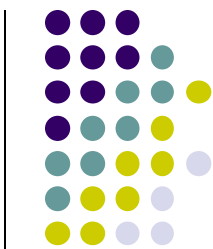


¹H NMR Resonance Signals for some Different Compounds

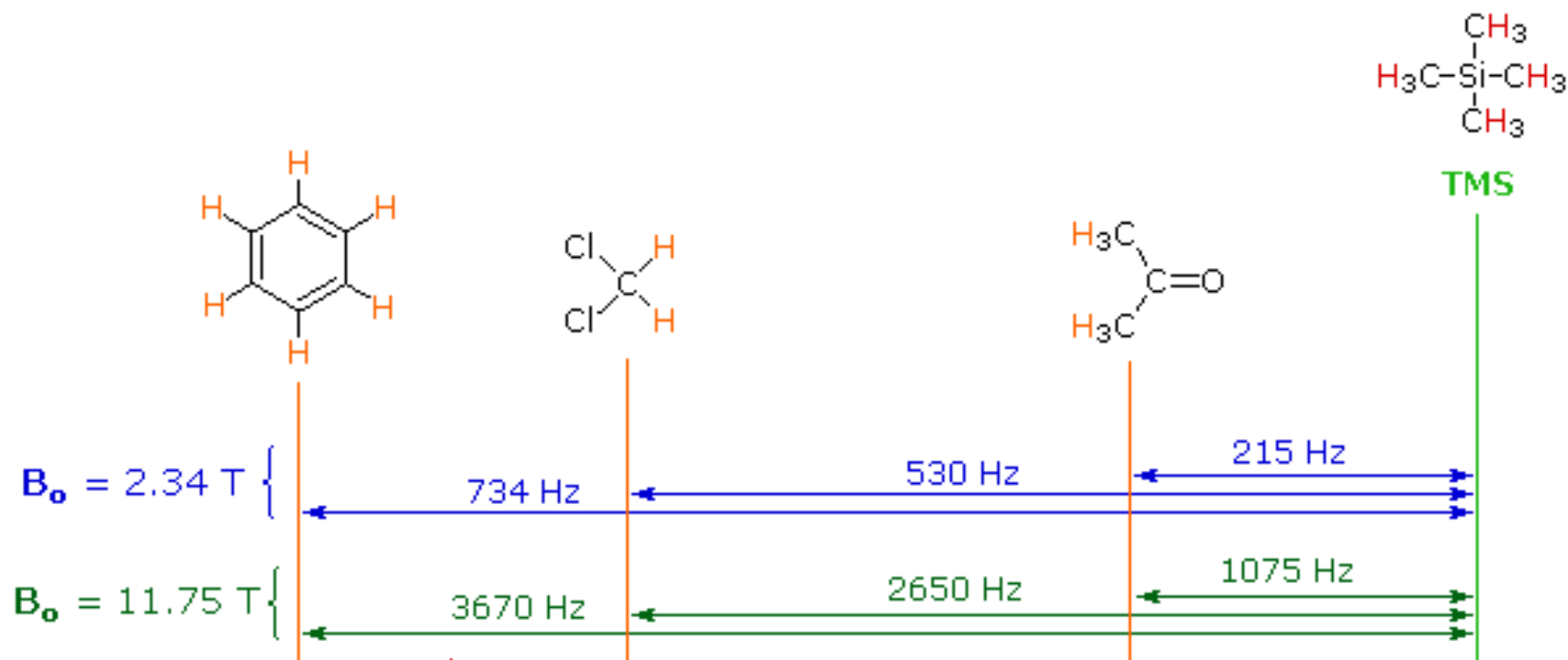
Oxygen is electron withdrawing

zero set by TMS (tetramethyl silane)

Understanding NMR Spectra



← Increasing Frequency at Fixed Magnetic Field →



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

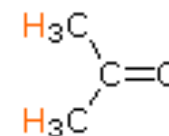
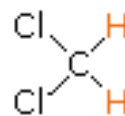
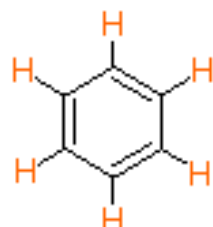
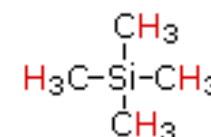
Understanding NMR Spectra



← Increasing Frequency at Fixed Magnetic Field →

Chemical Shift

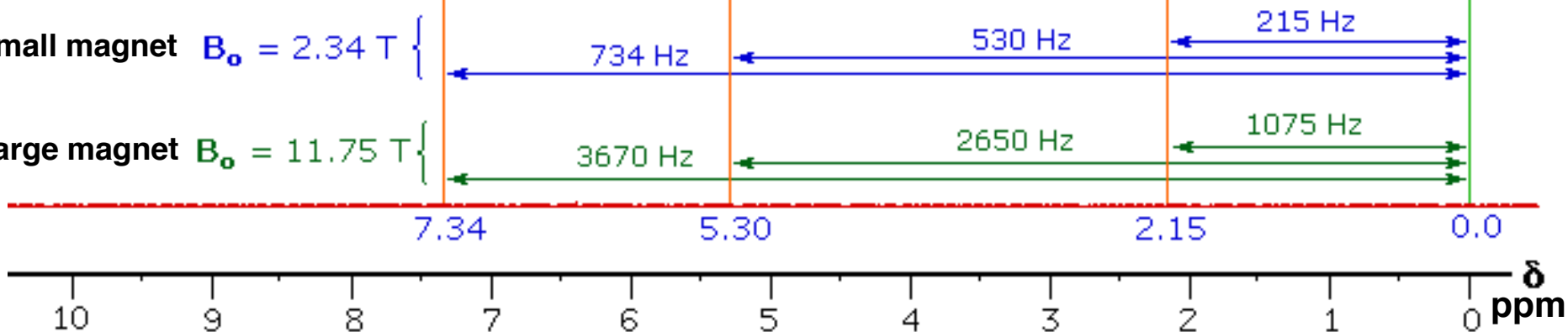
$$\delta = \left(\frac{V_{\text{samp}} - V_{\text{ref}}}{V_{\text{ref}}} \right) \times 10^6$$



TMS

Small magnet $B_0 = 2.34 \text{ T}$

Large magnet $B_0 = 11.75 \text{ T}$

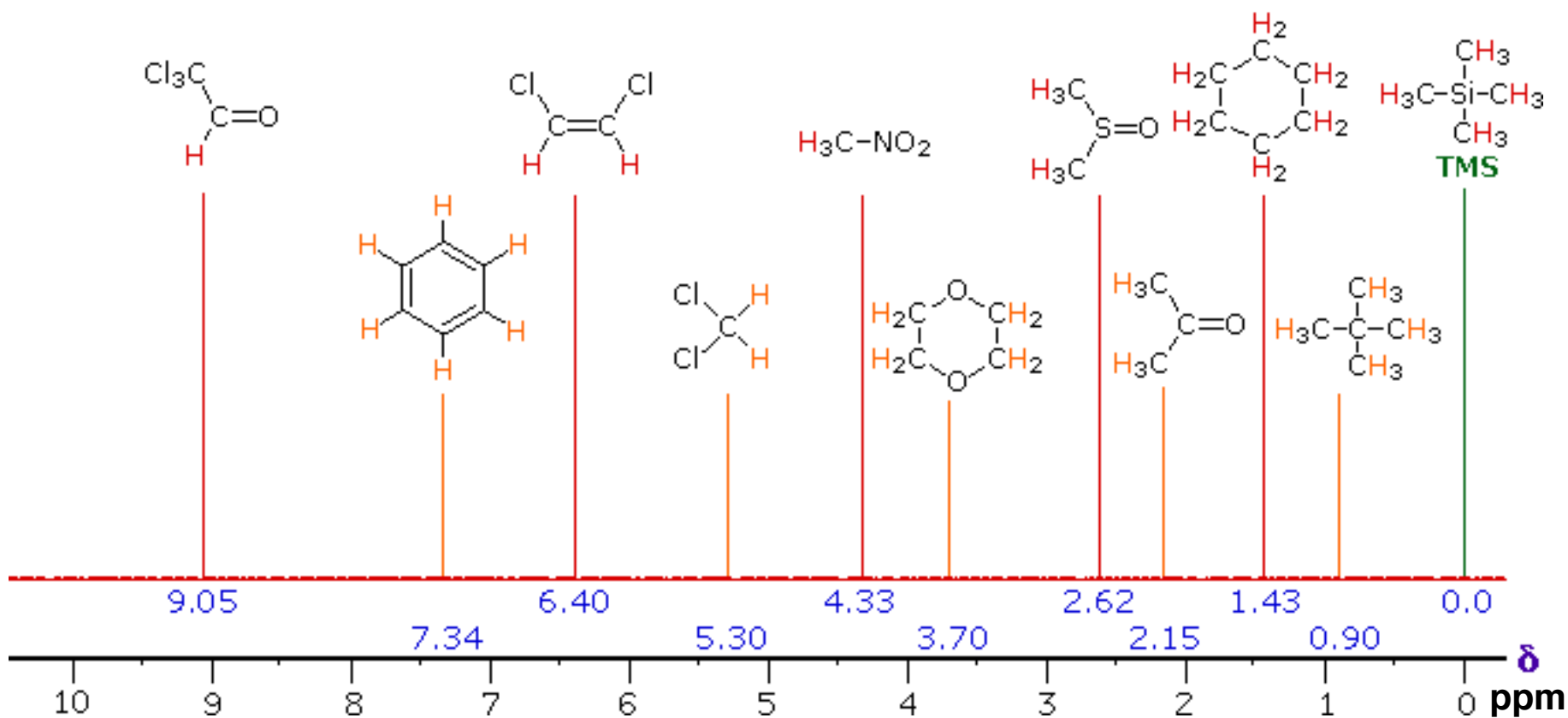


Understanding NMR Spectra



← Increasing Frequency at Fixed Magnetic Field →

→ Increased Shielding by Extranuclear electrons →



These ppm are for ALL magnets

But, the spins couple - they interact

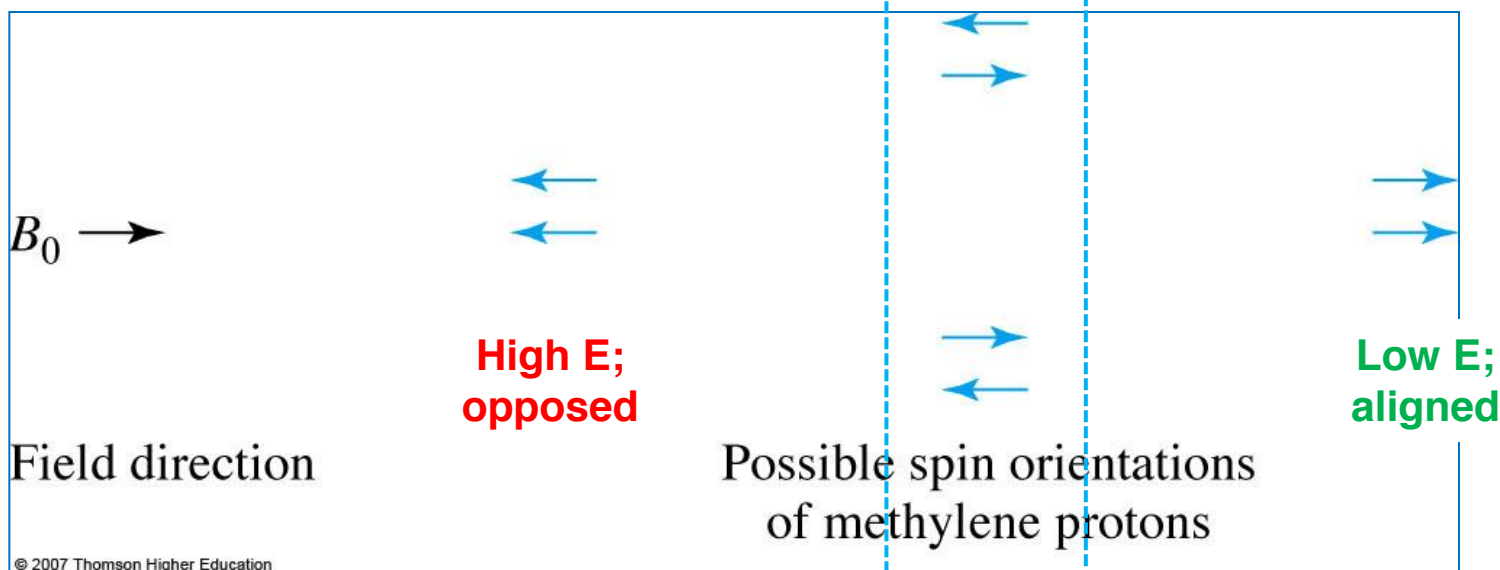


For 2 protons:

- Each proton has its own spin
- The spin can be $+1/2$ or $-1/2$
- 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

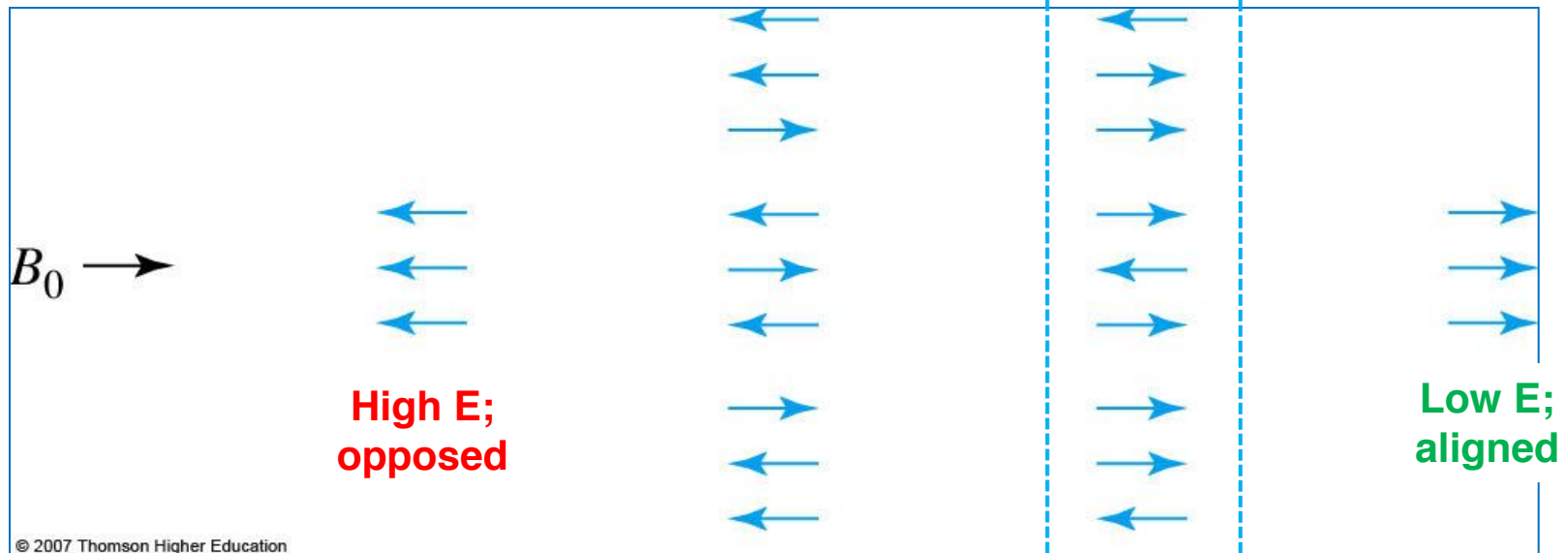


For 3 protons:

- Each proton has its own spin
- The spin can be $+1/2$ or $-1/2$
- We can draw all the combinations:

Degenerate:
all 3 cases have
the same energy

Page 517



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

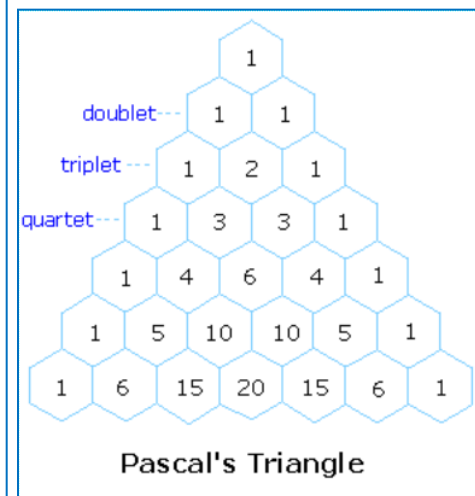
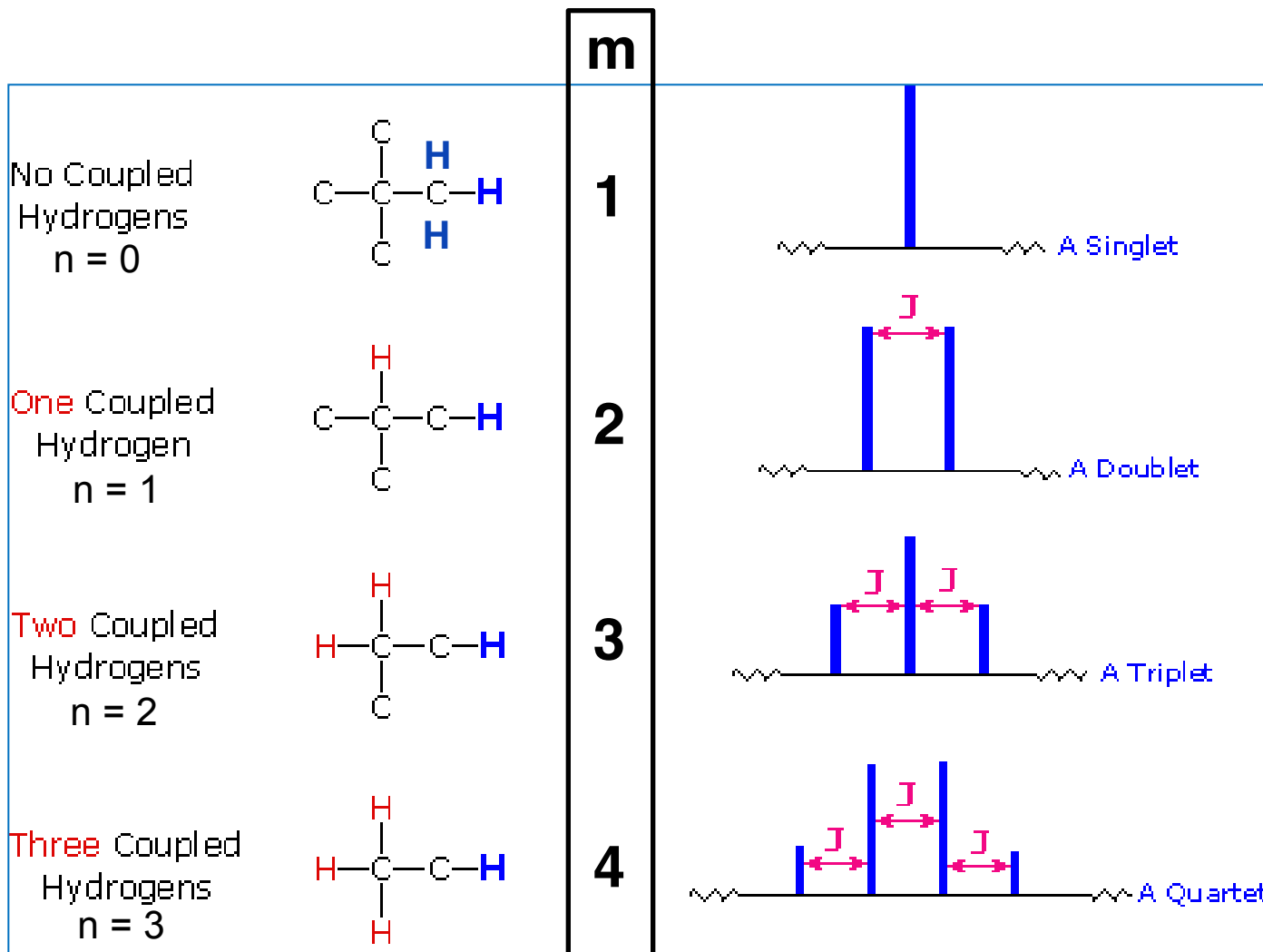
Multiplicity, $m = n + 1$

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

Pattern follows Pascal's triangle

Number of Equivalent Protons, n	Multiplicity, $(n + 1)$	Relative Peak Areas												
0	1													
1	2													
2	3													
3	4													
4	5													
5	6													
6	7													
7	8													

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



Proximity is important

The splitting is called J coupling

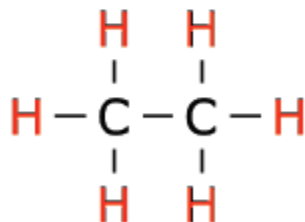
Do they split – or not?



Determining Equivalent Hydrogens in ^1H 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 ^1H 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 ^1H NMR spectrum.



This will yield a spectrum with one NMR singlet.

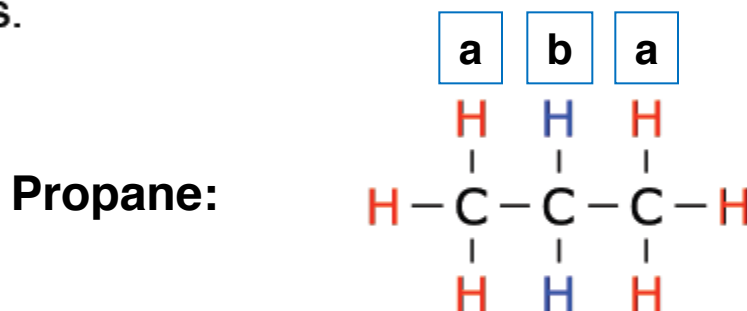
Protons are not split by identical neighbors.

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

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 ^1H 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.

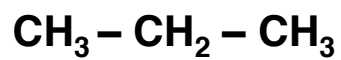


See next panel
for spectrum
of propane

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 ^1H 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 ^1H NMR spectrum)



$^1\text{H-NMR}$ Spectrum of Propane

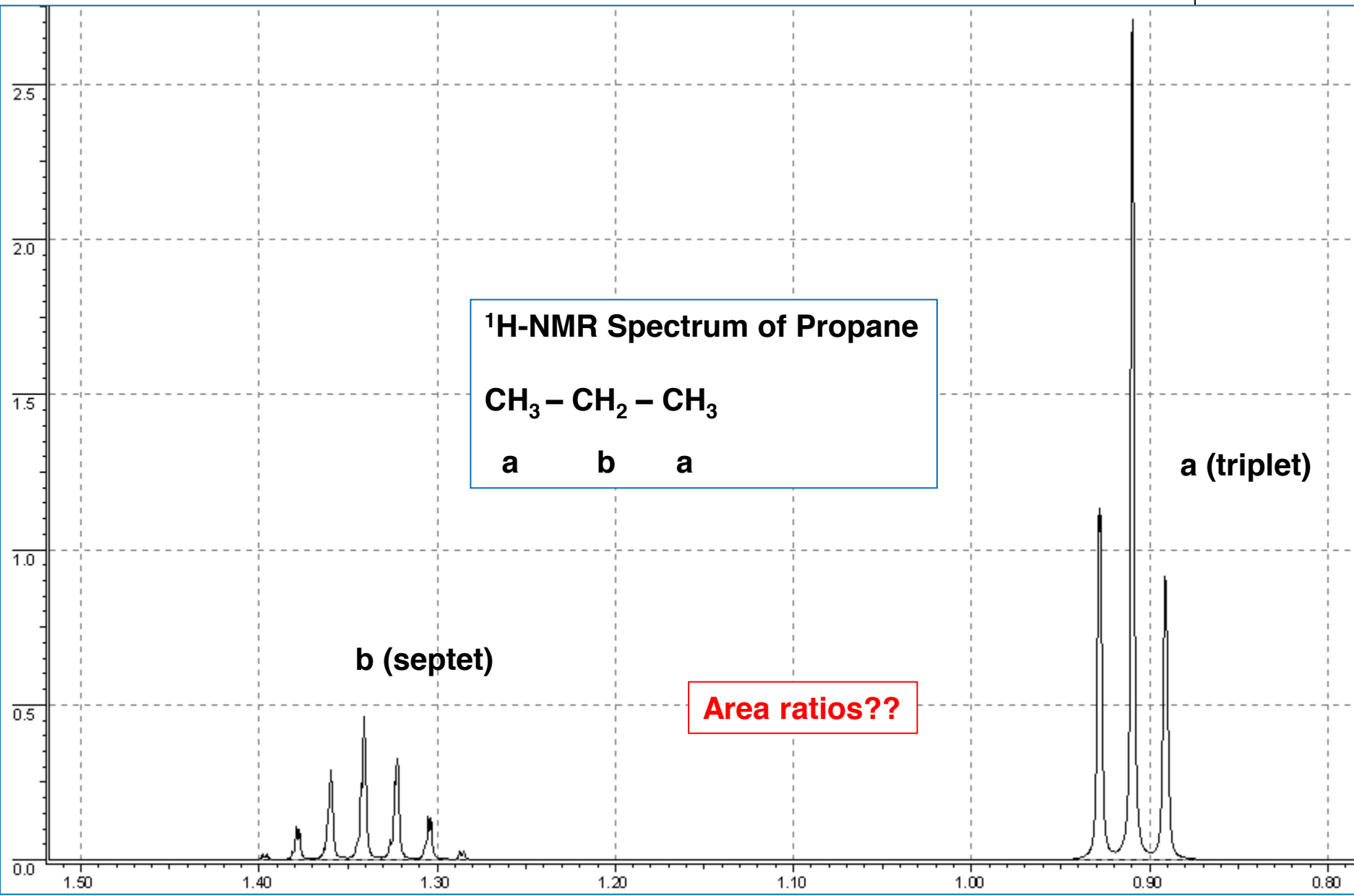


a b a

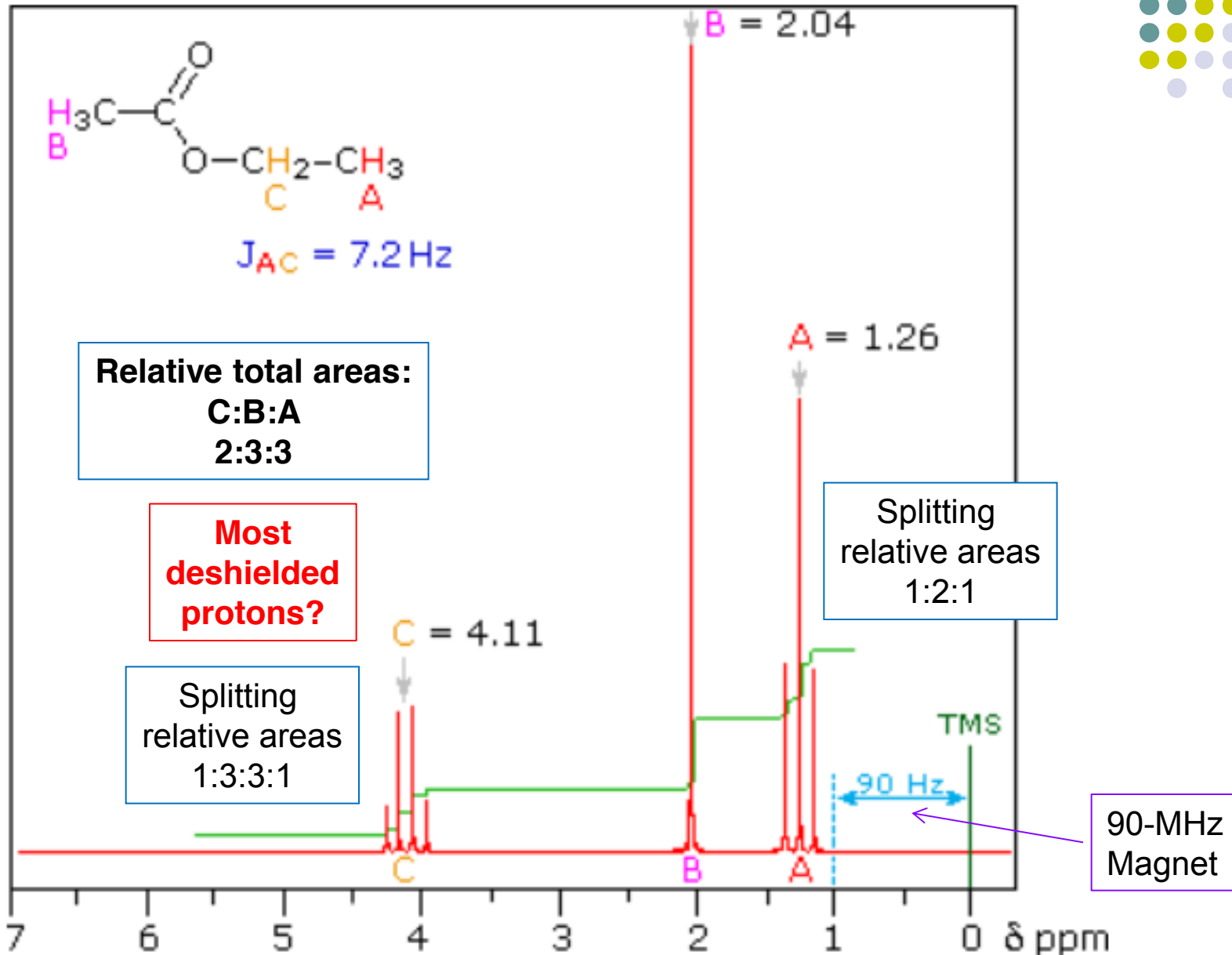
a (triplet)

b (septet)

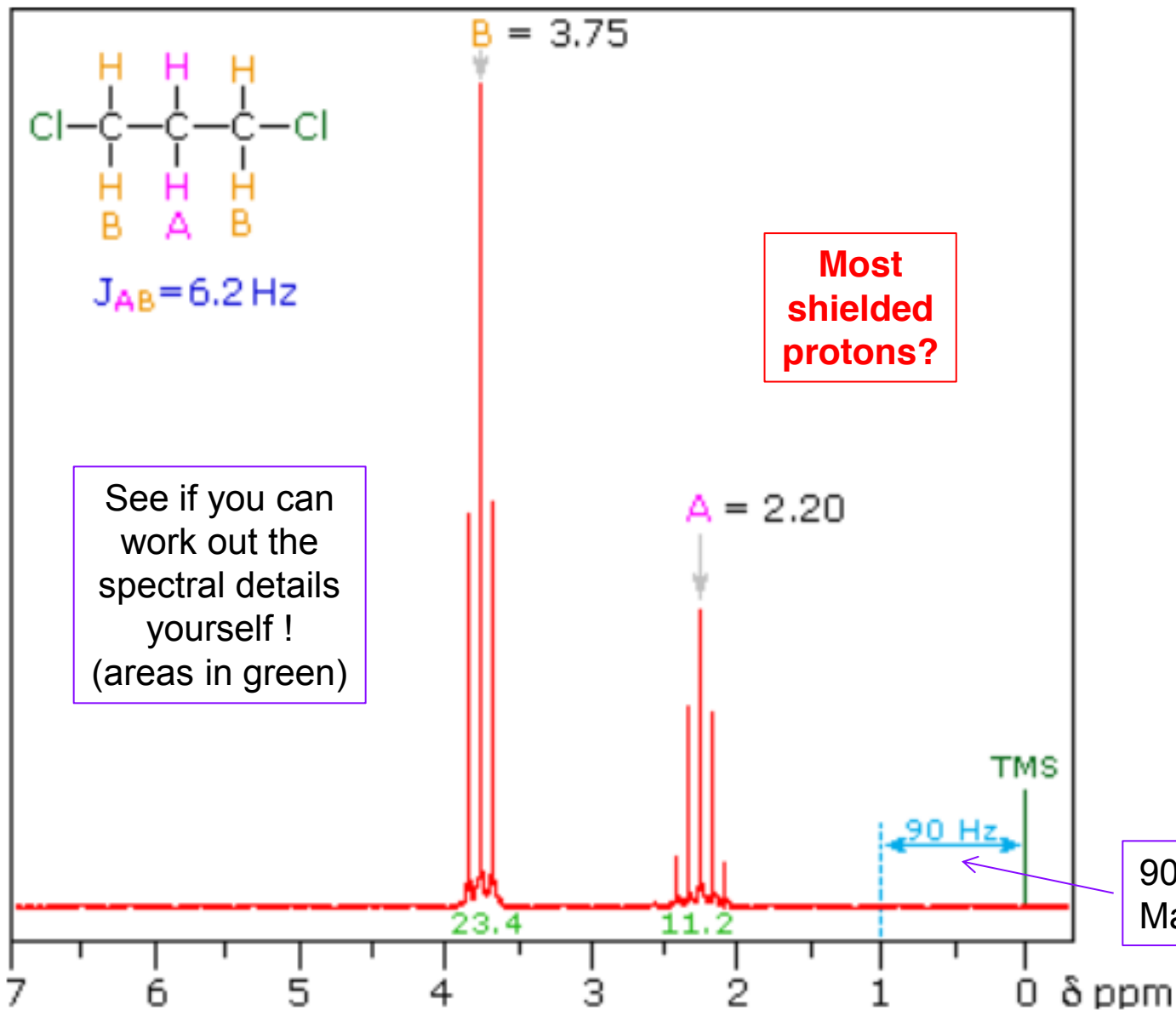
Area ratios??



NMR Data Interpretation – Example 1



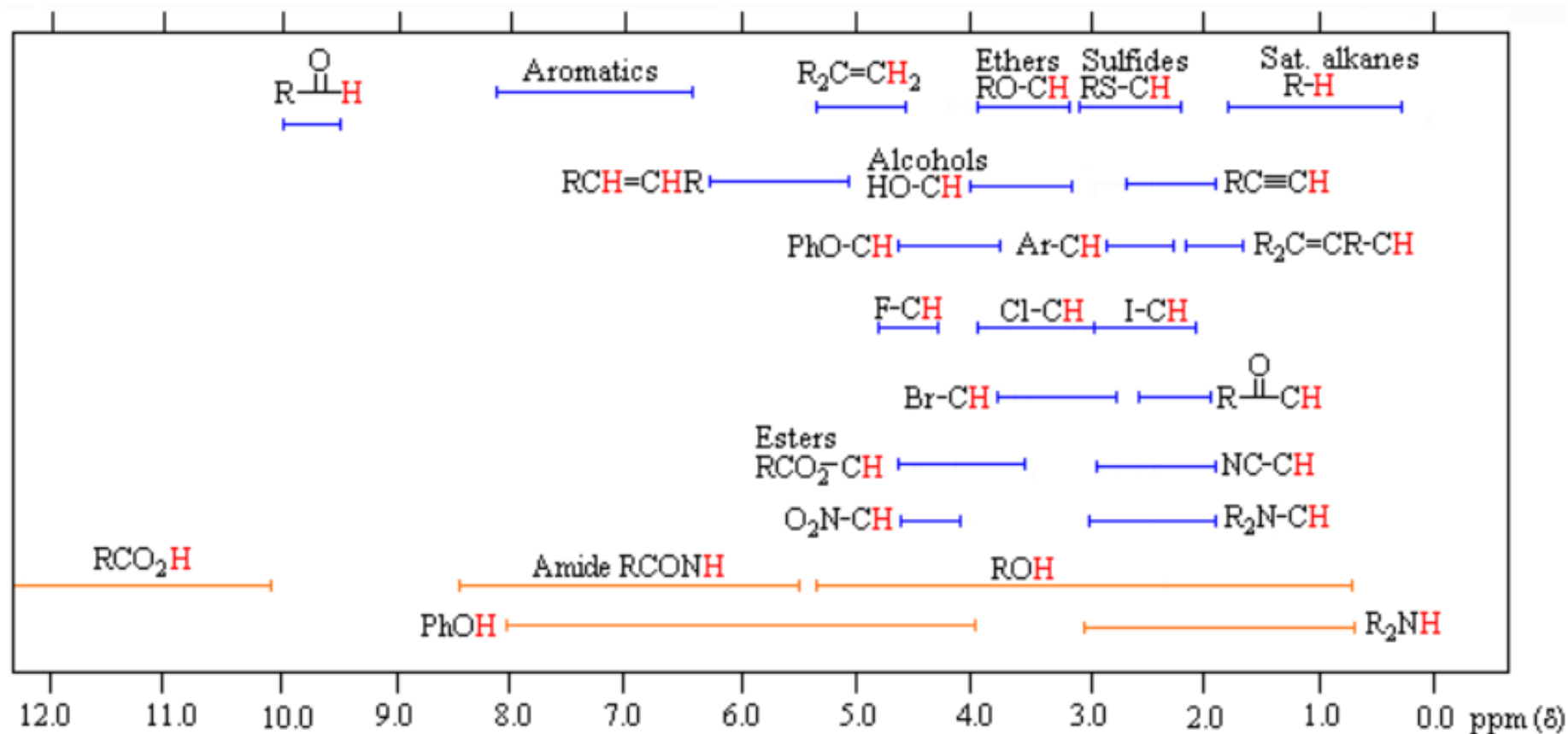
NMR Data Interpretation – Example 2



NMR Chemical Shifts – helps interpret data



Proton Chemical Shift Ranges*



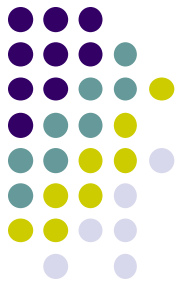
* For samples in CDCl_3 solution. The δ scale is relative to TMS at $\delta = 0$.

NMR data interpretation – watch the video!



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

Other Things NMR Can Mean



no membership required

