Nuclear Magnetic Resonance (NMR) Spectroscopy

Introduction:

Nuclear magnetic resonance spectroscopy (NMR) is the most powerful tool available for organic structure determination. Like IR spectroscopy, NMR can be used with a very small sample, and it does not harm the sample. The NMR spectrum provides a great deal of information about the structure of the compound, and some structures can be determined using only the NMR spectrum. More commonly, however, the NMR spectrum is used in conjunction with other forms of spectroscopy and chemical analysis to determine the structures of complicated organic molecules.

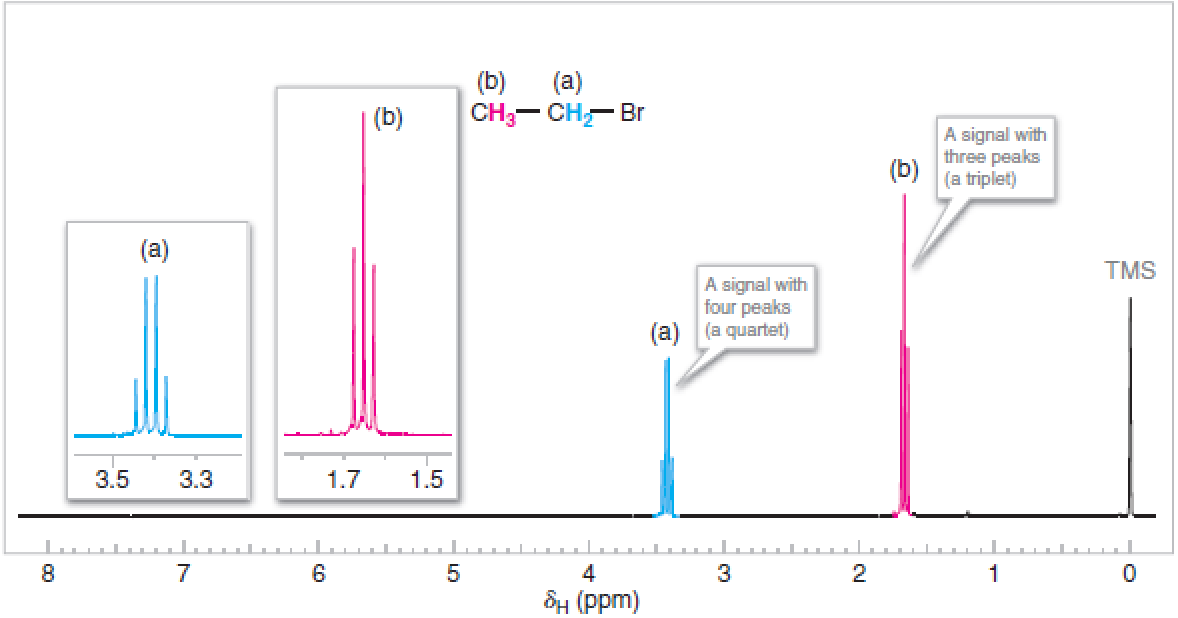
NMR is used to study a wide variety of nuclei, including ^{1}H, ^{13}C, ^{15}N, ^{19}F, and ^{31}P. Organic chemists find proton (^{1}H) and carbon-13 (^{13}C) NMR to be most useful because hydrogen and carbon are major components of organic compounds.

Historically, NMR was first used to study protons (the nuclei of hydrogen atoms), and proton magnetic resonance (^{1}H NMR) spectrometers are the most common. "Nuclear magnetic resonance" is assumed to mean "proton magnetic resonance" unless a different nucleus is specified.

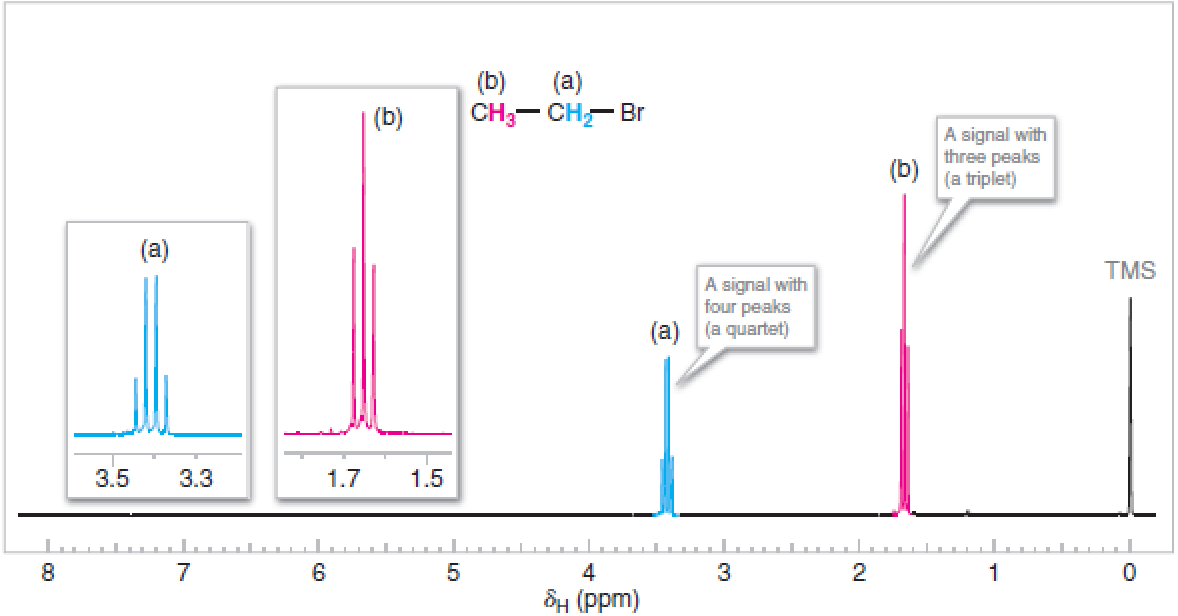
When a compound containing protons or carbon-13 nuclei is placed in a very strong magnetic field and simultaneously irradiated with electromagnetic energy of the appropriate frequency, nuclei of the compound absorb energy through a process called **magnetic resonance**. The absorption of energy is quantized.

Nuclear Magnetic Resonance (NMR) Spectrum:

A graph that shows the characteristic energy absorption frequencies and intensities for a sample in a magnetic field.



^{1}H NMR spectrum of 1-bromoethane (ethyl bromide). Zoomed-in expansions of the signals are shown in the offset plots.



1. The number of signals in the spectrum tells us **how many different sets of protons there are in the molecule**. In the spectrum for 1-bromoethane there are *two signals arising from two different sets of protons*. One signal (consisting of four peaks) is shown in blue and labeled (a). The other signal (consisting of three peaks) is in red and is labeled (b). [Don't worry now about the signal at the far right of the spectrum (labeled TMS); it comes from a compound (tetramethylsilane) that was added to the 1-bromoethane so as to calibrate the positions of the other signals.]

2. The position of the signals in the spectrum along the *x*-axis tells us about the magnetic environment of each set of protons arising largely from the electron density in their environment.

3. The area under the signal tells us about **how many protons there are in the set being measured**.

4. The multiplicity (or splitting pattern) of each signal tells us about about **the number of protons on atoms adjacent to the one whose signal is being measured**. In 1-bromoethane, signal (a) is split into a *quartet* of peaks by the three protons of set (b), and signal (b) is split into a *triplet* of peaks by the two protons of set (a).

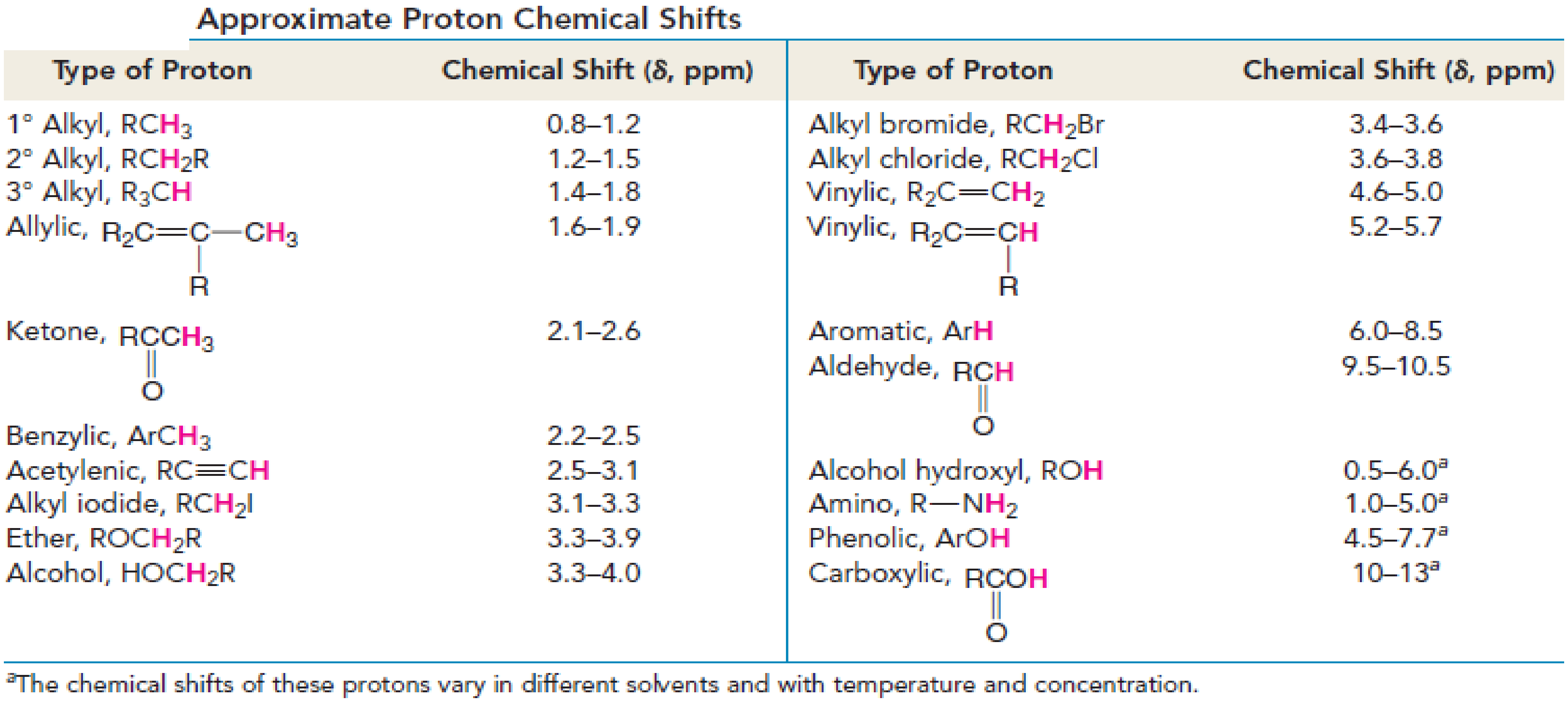
Chemical Shift:

The position of a signal along the *x*-axis of an NMR spectrum is called its **chemical shift**.

The chemical shift of each signal gives information about the structural environment of the nuclei producing that signal.

Counting the number of signals in a ^1H NMR spectrum indicates, at a first approximation, the number of distinct proton environments in a molecule.

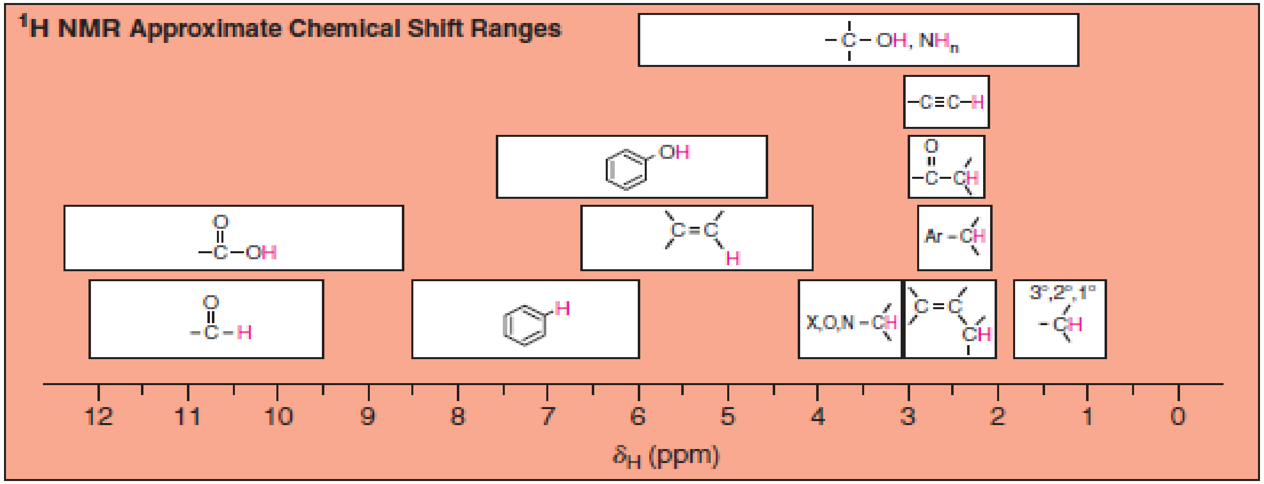
Tables and charts have been developed that allow us to correlate chemical shifts of NMR signals with likely structural environments for the nuclei producing the signals. The below Table and Figure, for example, are useful for this purpose. ^1H NMR chemical shifts generally fall in the range of 13–0 ppm (δ).



Approximate Proton Chemical Shifts

Type of Proton	Chemical Shift (δ, ppm)	Type of Proton	Chemical Shift (δ, ppm)
1° Alkyl, RCH_3	0.8–1.2	Alkyl bromide, RCH_2Br	3.4–3.6
2° Alkyl, RCH_2R	1.2–1.5	Alkyl chloride, RCH_2Cl	3.6–3.8
3° Alkyl, R_3CH	1.4–1.8	Vinylic, $R_2C{=}CH_2$	4.6–5.0
Allylic, $R_2C{=}\underset{\underset{R}{\vert}}{C}{-}CH_3$	1.6–1.9	Vinylic, $R_2C{=}\underset{\underset{R}{\vert}}{C}H$	5.2–5.7
Ketone, $R\underset{\underset{O}{\Vert}}{C}CH_3$	2.1–2.6	Aromatic, ArH	6.0–8.5
		Aldehyde, $R\underset{\underset{O}{\Vert}}{C}H$	9.5–10.5
Benzylic, $ArCH_3$	2.2–2.5		
Acetylenic, $RC{\equiv}CH$	2.5–3.1	Alcohol hydroxyl, ROH	0.5–6.0[a]
Alkyl iodide, RCH_2I	3.1–3.3	Amino, $R{-}NH_2$	1.0–5.0[a]
Ether, $ROCH_2R$	3.3–3.9	Phenolic, ArOH	4.5–7.7[a]
Alcohol, $HOCH_2R$	3.3–4.0	Carboxylic, $R\underset{\underset{O}{\Vert}}{C}OH$	10–13[a]

[a]The chemical shifts of these protons vary in different solvents and with temperature and concentration.



Approximate proton chemical shifts

The chemical shift of a signal in an NMR spectrum depends on the local magnetic environment of the nucleus producing the signal. The local magnetic environment of a nucleus is influenced by electron density and other factors we shall discuss shortly.

The physical meaning of chemical shift values relates to the actual frequency of the NMR signals produced by the nuclei. The *practical* importance of chemical shift information is that it gives important clues about molecular structure. Each NMR signal indicates the presence of nuclei in a different magnetic environment.

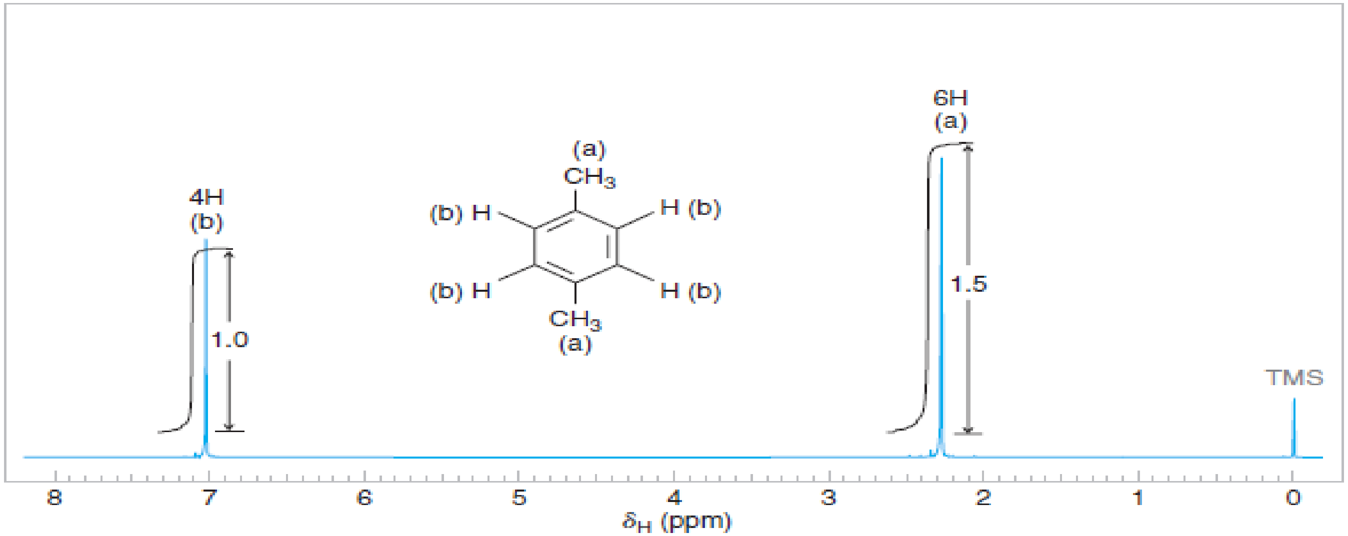
Chemical shifts are measured along the spectrum axis using a delta (δ) scale, in units of parts per million (ppm). When comparing one signal with another:

A signal that occurs further to the left in the spectrum than another (i.e., at a higher δ or ppm value) is said to occur **downfield**.

A signal to the right is said to occur **upfield**.

The terms upfield and downfield relate to the strength of the magnetic field (higher versus lower, respectively) that is required to bring the nuclei into resonance.

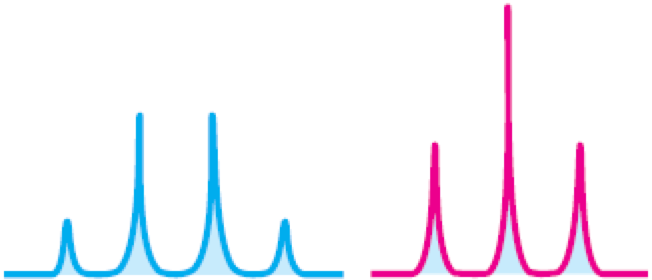
The ^1H NMR spectrum of 1,4-dimethylbenzene (*p*-xylene), is a simple example that we can use to learn how to interpret chemical shifts.



Integration of Signal Areas:

The area under each signal in a ^1H NMR spectrum is proportional to the number of hydrogen atoms producing that signal.

The area under each signal (shown with blue shading above) is what is measured (integrated) and taken as a ratio to compare the relative numbers of hydrogen atoms producing each signal in an NMR spectrum.



Coupling (Signal Splitting):

Coupling, also referred to as **signal splitting** or signal multiplicity, is a third feature of ^1H NMR spectra that provides very useful information about the structure of a compound.

Coupling is caused by the magnetic effect of nonequivalent hydrogen atoms that are within 2 or 3 bonds of the hydrogens producing the signal.

The effect of the nearby hydrogens is to split (or couple with) the energy levels of the hydrogens whose signal is being observed, and the result is a signal with multiple peaks. (Notice that we have been careful to differentiate use of the words signal and peak. A group of equivalent atoms produces one *signal* that may be split into multiple *peaks*.)

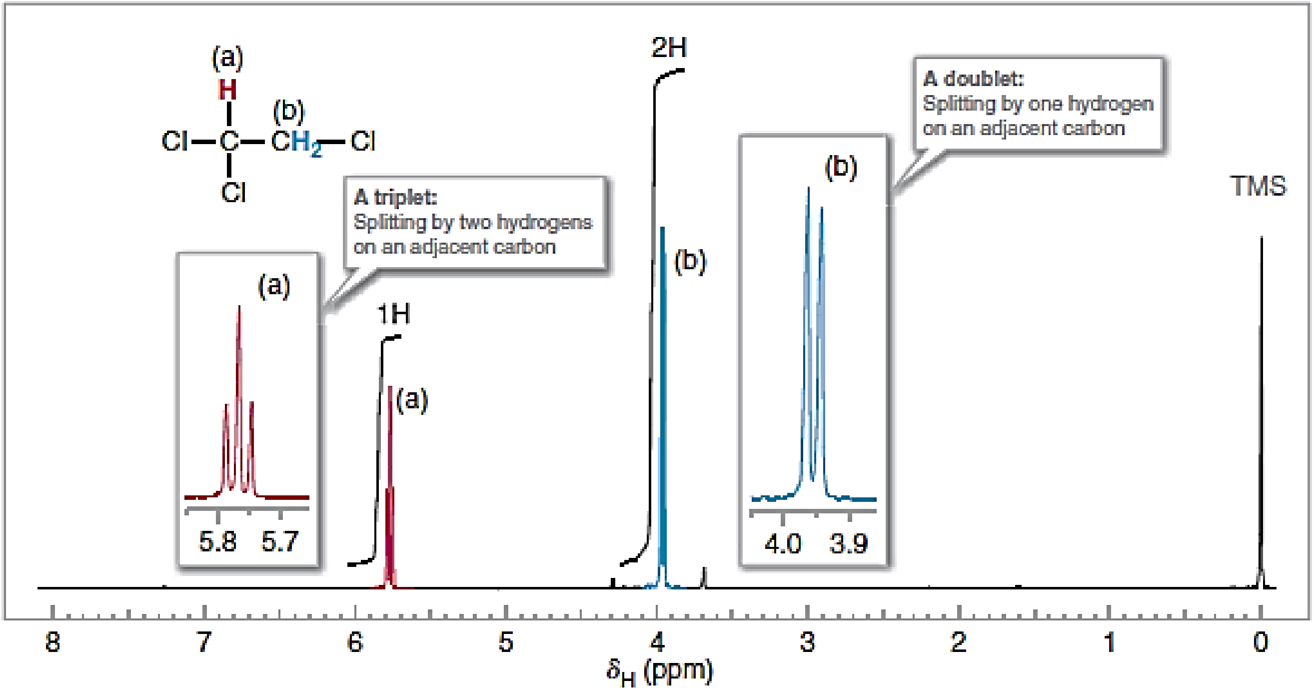
The importance of coupling is that it is predictable, and it gives us specific information about the constitution of the molecule under study.

The typical coupling we observe is from nonequivalent, **vicinal** hydrogens, that is, from hydrogens on adjacent carbons, separated by three bonds from the hydrogens producing the signal. Coupling can also occur between nonequivalent **geminal** hydrogens (hydrogens bonded to the same carbon) if the geminal hydrogens are in a chiral or conformationally restricted molecule.

A simple rule exists for predicting the number of peaks expected from vicinal coupling in ^{1}H NMR:

Number of peaks from vicinal coupling = $n + 1$ in a ^{1}H NMR signal

Where n is the number of vicinal hydrogen atoms that are nonequivalent to those producing the signal



A triplet: Splitting by two hydrogens on an adjacent carbon

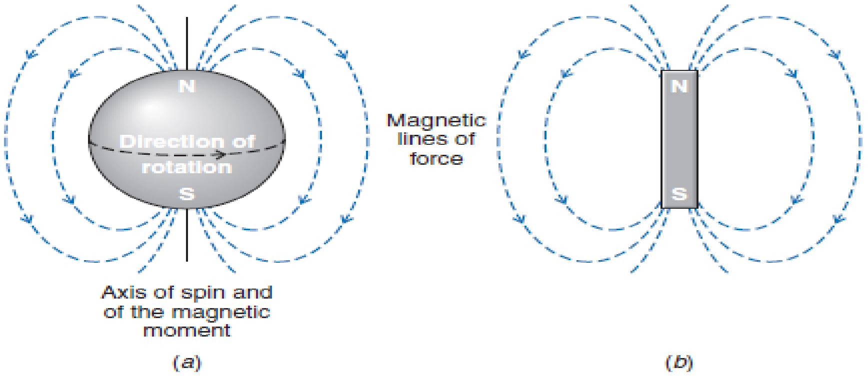
A doublet: Splitting by one hydrogen on an adjacent carbon

^{1}H NMR spectrum of 1,1,2-trichloroethane. Zoomed-in expansions of the signals are shown in the offset plots.

Nuclear Spin: The Origin of the Signal

The nuclei of certain isotopes possess the quality of spin, and therefore these nuclei have spin quantum numbers, designated ***I***.
The nucleus of ordinary hydrogen, ^{1}H, has a spin quantum number of ½, and it can assume either of two spin states: -½ or +½, These correspond to the magnetic moments (*m*) allowed for *I* = ½, which are m = -½ or +½.

Other nuclei with spin quantum numbers *I* = ½ are ^{13}C, ^{19}F, and ^{31}P. Some nuclei, such as ^{12}C, ^{16}O, and ^{32}S, have no spin (*I* = 0), and these nuclei do not give an NMR spectrum. Other nuclei have spin quantum numbers greater than ½. In our treatment here, however, we are concerned primarily with the spectra that arise from ^{1}H and from ^{13}C, both of which have *I* = ½.
Since the proton is electrically charged, the spinning charge generates a tiny magnetic moment—one that coincides with the axis of spin. This tiny magnetic moment gives the spinning proton properties analogous to those of a tiny bar magnet.



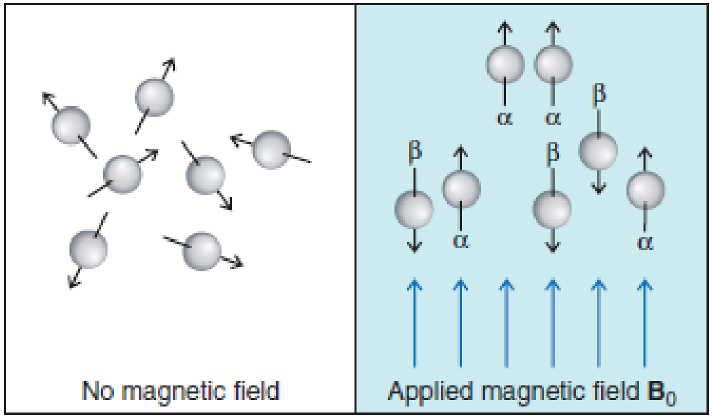
(a) The magnetic field associated with a spinning proton.

(b) The spinning proton resembles a tiny bar magnet.

In the absence of a magnetic field, the magnetic moments of the protons of a given sample are randomly oriented.

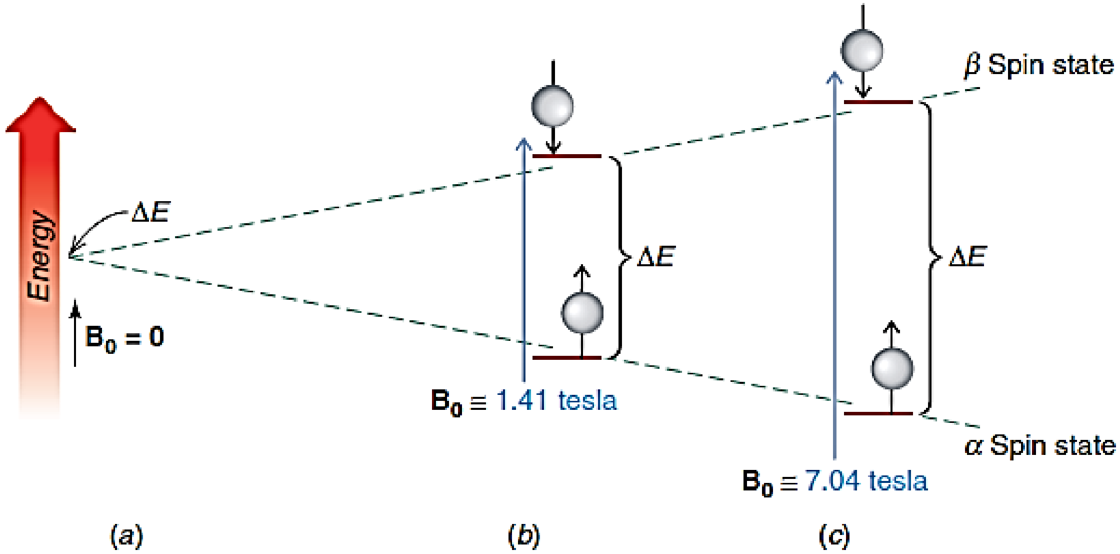
When a compound containing hydrogen (and thus protons) is placed in an applied external magnetic field, however, the magnetic moment of the protons may assume one of two possible orientations with respect to the external magnetic field (other orientations are disallowed on the basis of quantum mechanics).

The magnetic moment of the proton may be aligned “**with**” the external field or “**against**” it. These alignments correspond to the two spin states mentioned earlier.



The two alignments of the proton's magnetic moment in an external field are not of equal energy. When the proton's magnetic moment is aligned with the magnetic field, its energy is lower than when it is aligned against the magnetic field. The lower energy state is slightly more populated in the ground state.

Energy is required to "flip" the proton's magnetic moment from its lower energy state (with the field) to its higher energy state (against the field). In an NMR spectrometer this energy is supplied by electromagnetic radiation in the RF (radio frequency) region. When this energy absorption occurs, the nuclei are said to be *in resonance* with the electromagnetic radiation.



The energy difference between the two spin states of a proton depends on the strength of the applied external magnetic field, B_0. *(a)* If there is no applied field ($B_0 = 0$), there is no energy difference between the two states. *(b)* If $B_0 \cong 1.41$ tesla, the energy difference corresponds to that of electromagnetic radiation of 60×10^6 Hz (60 MHz). *(c)* In a magnetic field of approximately 7.04 tesla, the energy difference corresponds to electromagnetic radiation of 300×10^6 Hz (300 MHz). Instruments are available that operate at these and even higher frequencies (as high as 800 MHz to 1 GHz).

*The relationship between the frequency of the radiation (ν) and the strength of the magnetic field ($\mathbf{B}_0$) is

$$\nu = \frac{\gamma \mathbf{B}_0}{2\pi}$$

where γ is the magnetogyric (or gyromagnetic) ratio. For a proton, $\gamma = 26.753$ rad s^{-1} tesla^{-1}.

Thus, two variables characterize NMR:

- **An applied magnetic field, B_0.** Magnetic field strength is measured in tesla (T).
- **The frequency m of radiation used for resonance,** measured in hertz (Hz) or megahertz (MHz); (1 MHz = 10^6 Hz)

The frequency needed for resonance and the applied magnetic field strength are proportionally related:

$$\boxed{\nu \propto B_0}$$

The stronger the magnetic field, the larger the energy difference between the two nuclear spin states, and the higher the m needed for resonance.

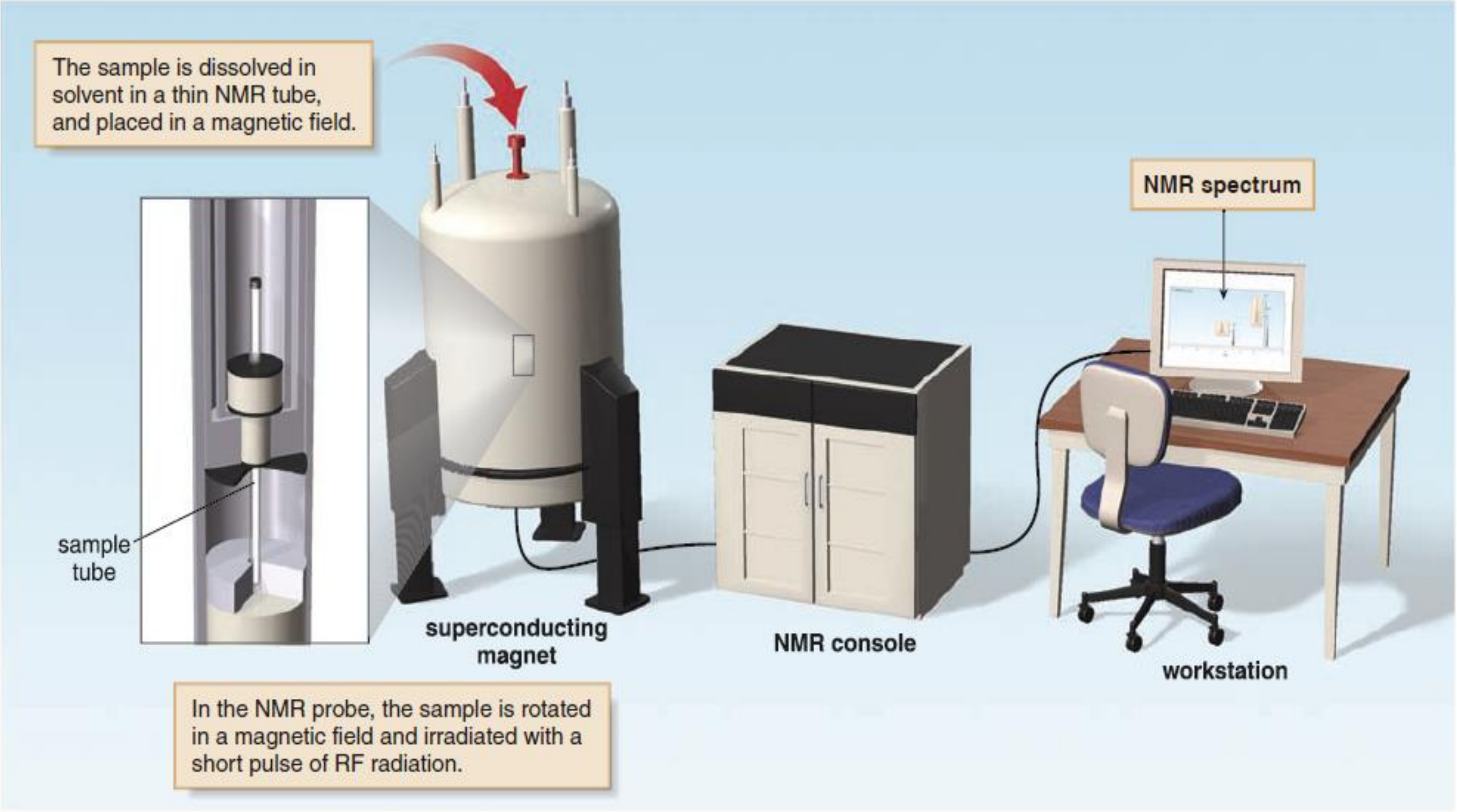
Early NMR spectrometers used a magnetic field strength of ~1.4 T, which required RF radiation of 60 MHz for resonance. Modern NMR spectrometers use stronger magnets, thus requiring higher frequencies of RF radiation for resonance. For example, a magnetic field strength of 7.05 T requires a frequency of 300 MHz for a proton to be in resonance. These spectrometers use very powerful magnetic fields to create a small, but measurable energy difference between the two possible spin states.

If all protons absorbed at the same frequency in a given magnetic field, the spectra of all compounds would consist of a single absorption, rendering NMR useless for structure determination.
Fortunately, however, this is not the case.

- **All protons do *not* absorb at the same frequency. Protons in different environments absorb at slightly different frequencies, and so they are distinguishable by NMR.**

The frequency at which a particular proton absorbs is determined by its electronic environment. Because electrons are moving charged particles, they create a magnetic field opposed to the applied field B_0, and the size of the magnetic field generated by the electrons around a proton determines where it absorbs. Modern NMR spectrometers use a constant magnetic field strength B_0, and then a narrow range of frequencies is applied to achieve the resonance of all protons.

Only nuclei that contain odd mass numbers (such as ^{1}H, ^{13}C, ^{19}F, and ^{31}P) or odd atomic numbers [such as ^{2}H (Deuterium) and ^{14}N] give rise to NMR signals. Because both ^{1}H and ^{13}C, the less abundant isotope of carbon, are NMR active, NMR allows us to map the carbon and hydrogen framework of an organic molecule.



An NMR spectrometer. The sample is dissolved in a solvent, usually $CDCl_3$ (deuterochloroform), and placed in a magnetic field. A radiofrequency generator then irradiates the sample with a short pulse of radiation, causing resonance. When the nuclei fall back to their lower energy state, the detector measures the energy released, and a spectrum is recorded. The superconducting magnets in modern NMR spectrometers have coils that are cooled in liquid helium and conduct electricity with essentially no resistance.