NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

PART ONE

- Nuclear magnetic resonance spectroscopy is a powerful analytical technique used to characterize organic molecules by identifying carbon-hydrogen frameworks within molecules.

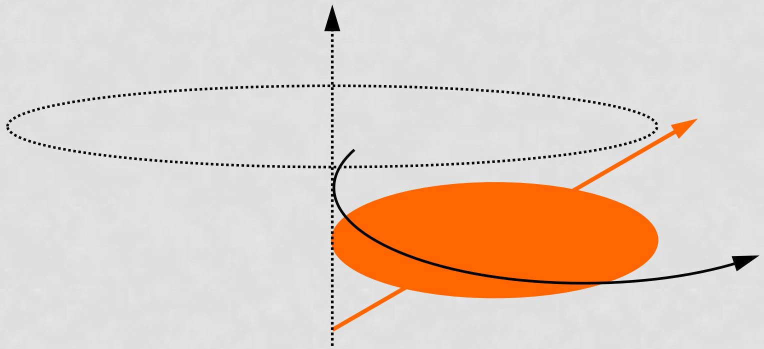
Nuclear Magnetic Resonance Spectroscopy

Introduction to NMR Spectroscopy

- Two common types of NMR spectroscopy are used to characterize organic structure: ^{1}H NMR is used to determine the type and number of H atoms in a molecule; ^{13}C NMR is used to determine the type of carbon atoms in the molecule.
- The source of energy in NMR is radio waves which have long wavelengths, and thus low energy and frequency.
- When low-energy radio waves interact with a molecule, they can change the nuclear spins of some elements, including ^{1}H and ^{13}C.

Introduction to NMR Spectroscopy

We begin by describing some magnetic properties of nuclei. All nuclei carry a charge. In some nuclei this charge "spins" on the nuclear axis, and this circulation of nuclear charge generates a magnetic dipole along the axis (Fig. 4.1). The angular momentum of the spinning charge can be described in terms of quantum spin numbers I; these numbers have values of 0, $\frac{1}{2}$, 1, $\frac{3}{2}$, and so on ($I = 0$ denotes no spin). The intrinsic magnitude of the generated dipole is expressed in terms of nuclear magnetic moment, μ.



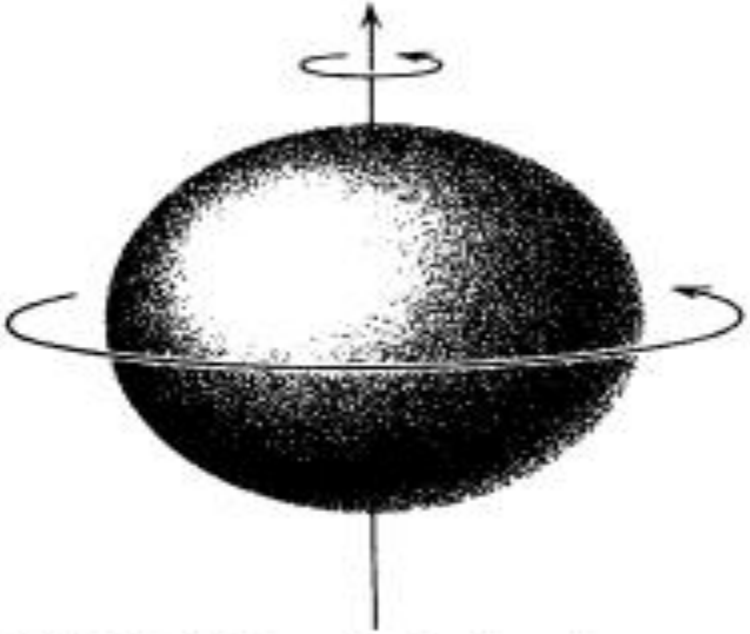
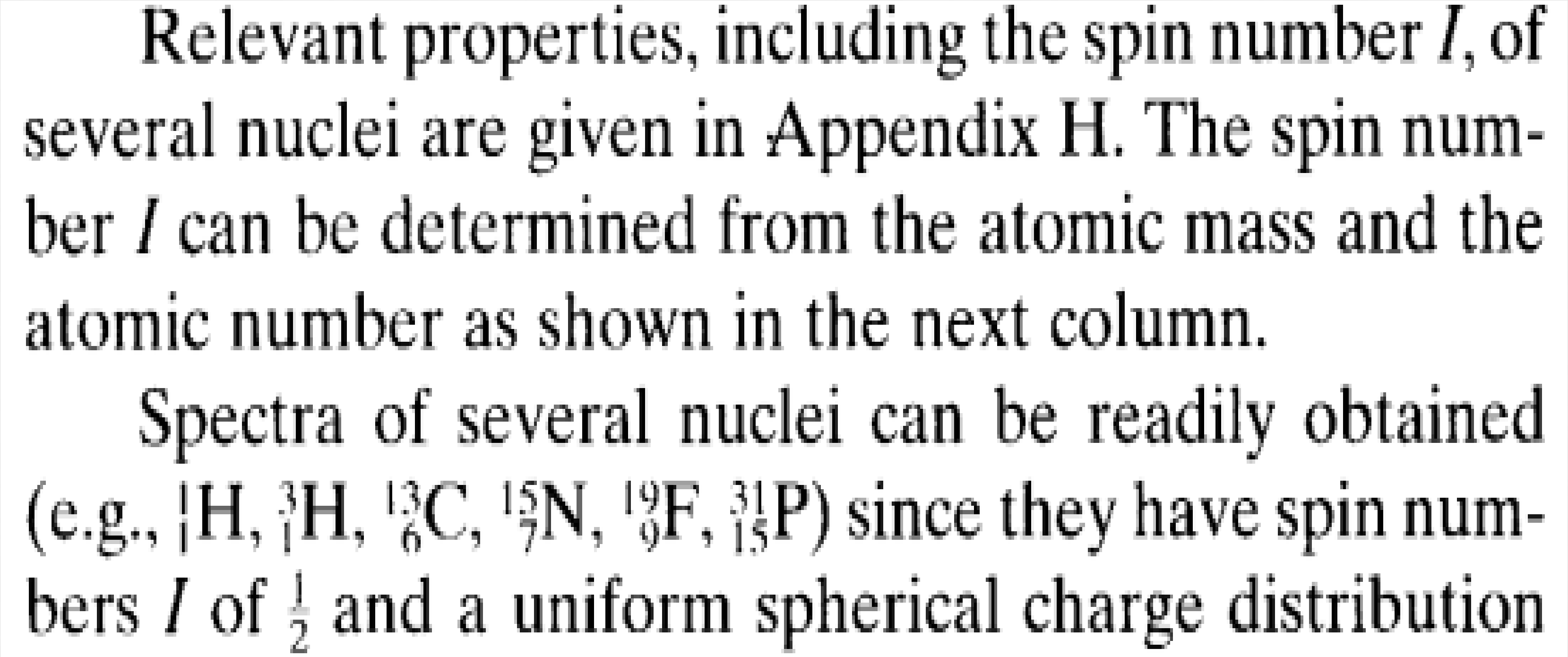
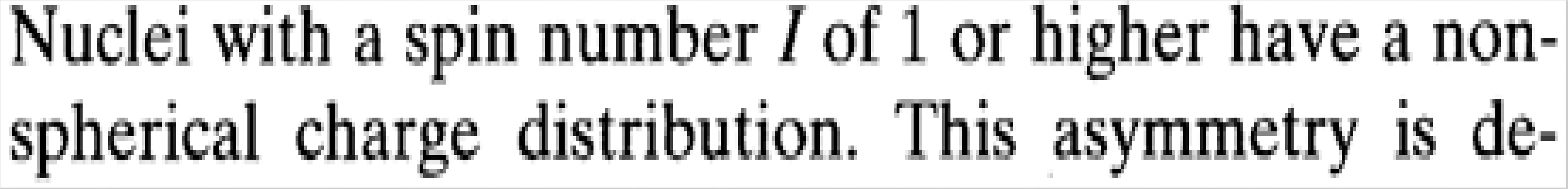


FIGURE 4.1. Spinning charge on proton generates magnetic dipole.

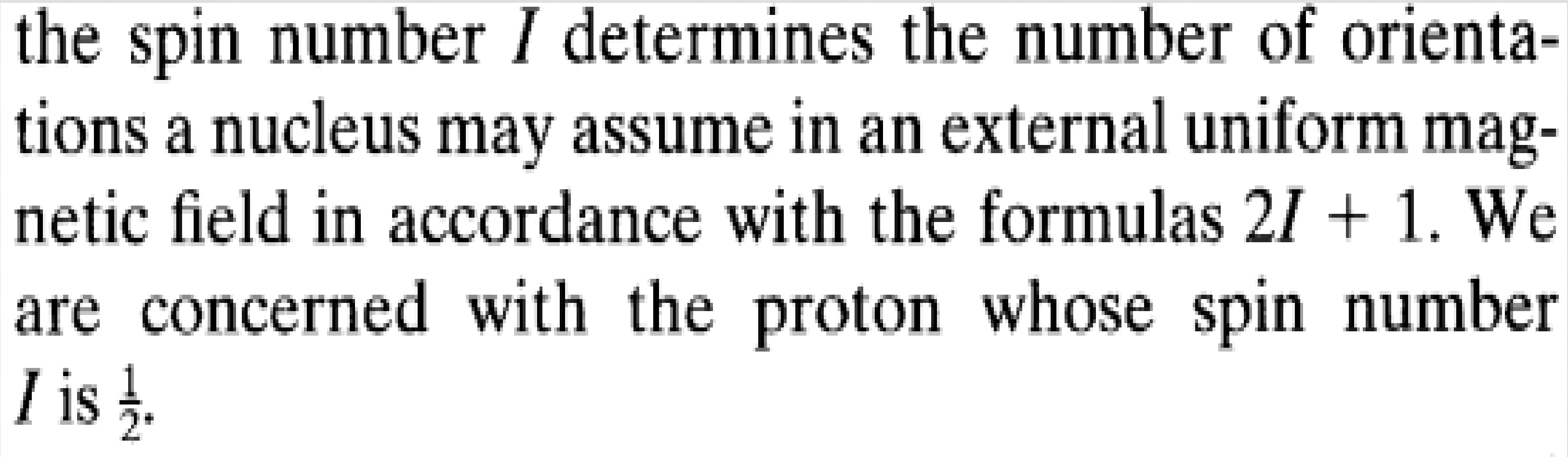


Relevant properties, including the spin number I, of several nuclei are given in Appendix H. The spin number I can be determined from the atomic mass and the atomic number as shown in the next column.

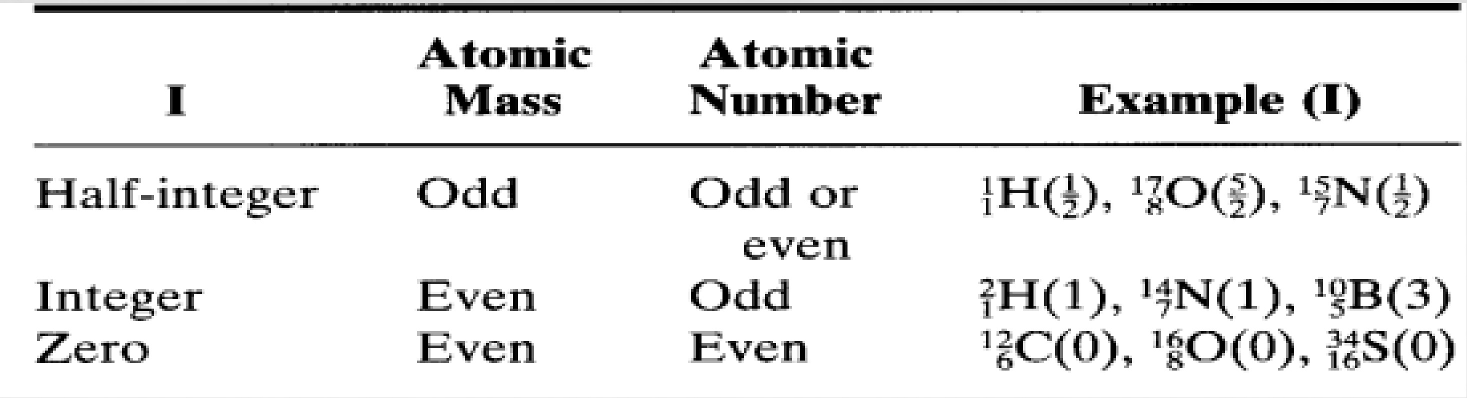
Spectra of several nuclei can be readily obtained (e.g., $^{1}_{1}H$, $^{3}_{1}H$, $^{13}_{6}C$, $^{15}_{7}N$, $^{19}_{9}F$, $^{31}_{15}P$) since they have spin numbers I of $\frac{1}{2}$ and a uniform spherical charge distribution



Nuclei with a spin number I of 1 or higher have a non-spherical charge distribution. This asymmetry is de-



the spin number I determines the number of orientations a nucleus may assume in an external uniform magnetic field in accordance with the formulas $2I + 1$. We are concerned with the proton whose spin number I is $\frac{1}{2}$.



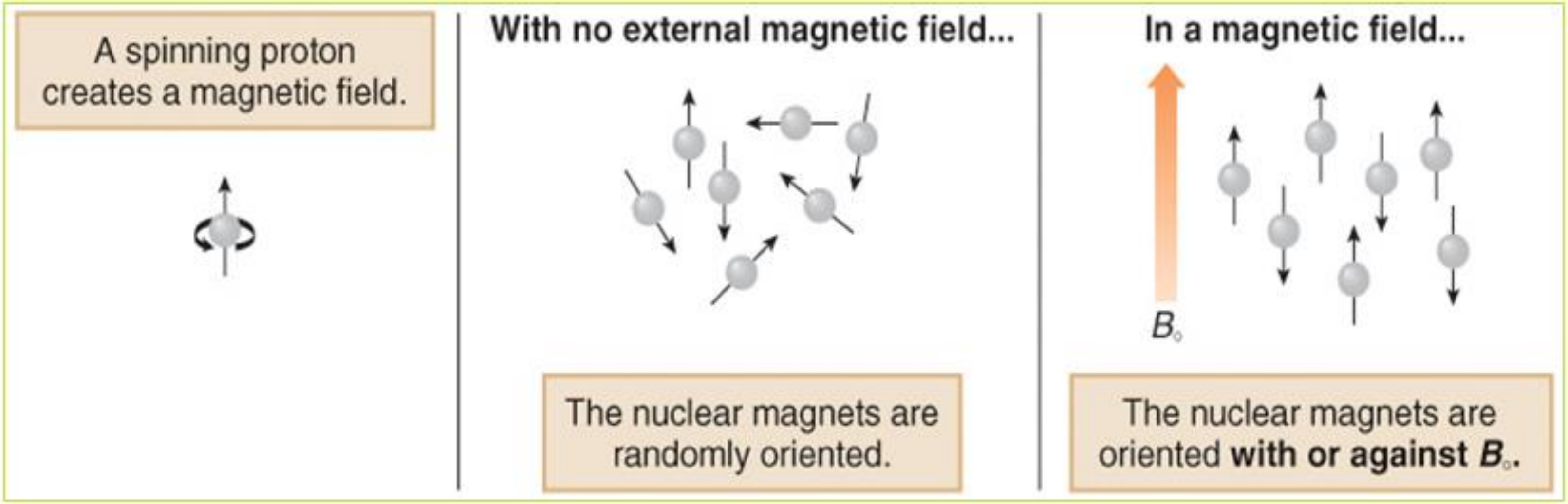
I	Atomic Mass	Atomic Number	Example (I)
Half-integer	Odd	Odd or even	$^{1}_{1}H(\frac{1}{2})$, $^{17}_{8}O(\frac{5}{2})$, $^{15}_{7}N(\frac{1}{2})$
Integer	Even	Odd	$^{2}_{1}H(1)$, $^{14}_{7}N(1)$, $^{10}_{5}B(3)$
Zero	Even	Even	$^{12}_{6}C(0)$, $^{16}_{8}O(0)$, $^{34}_{16}S(0)$

In the case of ^{1}H nuclei only two orientations are allowed; the nuclear magnetic moments may be aligned with or aligned against the direction of the applied magnetic field.

Nuclear Magnetic Resonance Spectroscopy

Introduction to NMR Spectroscopy

- When a charged particle such as a proton spins on its axis, it creates a magnetic field. Thus, the nucleus can be considered to be a tiny bar magnet.
- Normally, these tiny bar magnets are randomly oriented in space. However, in the presence of a magnetic field B_0, they are oriented with or against this applied field. More nuclei are oriented with the applied field because this arrangement is lower in energy.
- The energy difference between these two states is very small (<0.1 cal).



Energy Differentiation

Difference in energy between the two states is given by:

$$\Delta E = \gamma\ h\ B_o\ /\ 2\pi$$

where:

B_o – external magnetic field
h – Planck’s constant
γ – gyromagnetic ratio

When the energy of the photon matches the energy difference between the two spin states , an absorption of energy occurs. We call that phenomenon *Resonance*

$\Delta E = h\upsilon = \gamma h B_o / 2\pi$ So, $\upsilon = \gamma\ B_o / 2\pi$

THE ORIGIN OF NMR SIGNALS:
(THE NUCLEI OF NMR –"ACTIVE NUCLEI " BEHAVE LIKE TINY BAR MAGNETS)

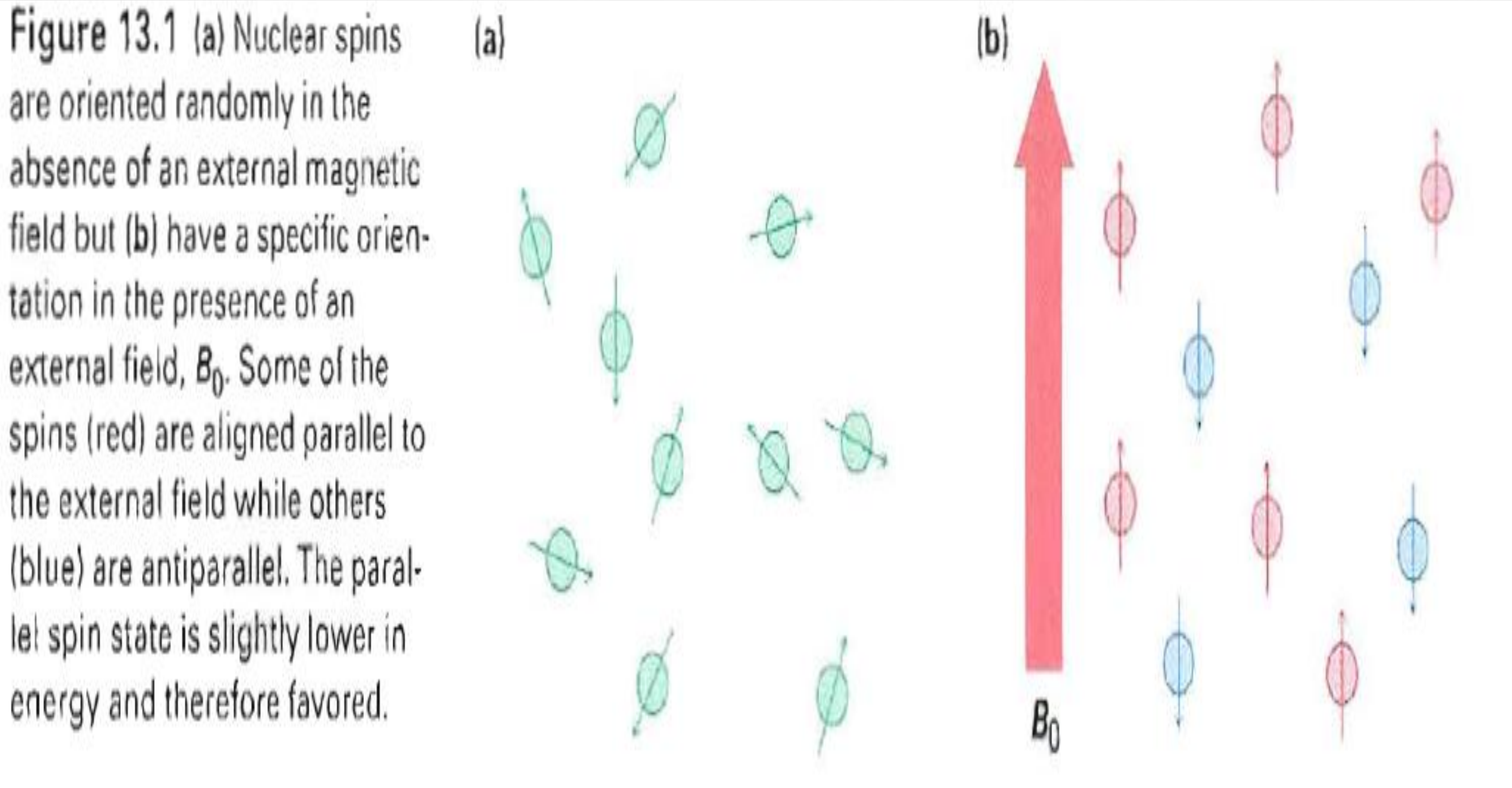


Figure 13.1 (a) Nuclear spins are oriented randomly in the absence of an external magnetic field but (b) have a specific orientation in the presence of an external field, B_0. Some of the spins (red) are aligned parallel to the external field while others (blue) are antiparallel. The parallel spin state is slightly lower in energy and therefore favored.

- Nuclei aligned with the magnetic field are lower in energy than those aligned against the field.
- The nuclei aligned with the magnetic field can be flipped “spin-flip” to the higher-energy state if the right amount of energy is added (DE).
- When this spin-flip occurs, the magnetic nuclei are said to be in resonance with the applied radiation hence the name nuclear magnetic resonance
- The amount of energy required depends on:
- the strength of the external magnetic field
- The identity of the nuclei.

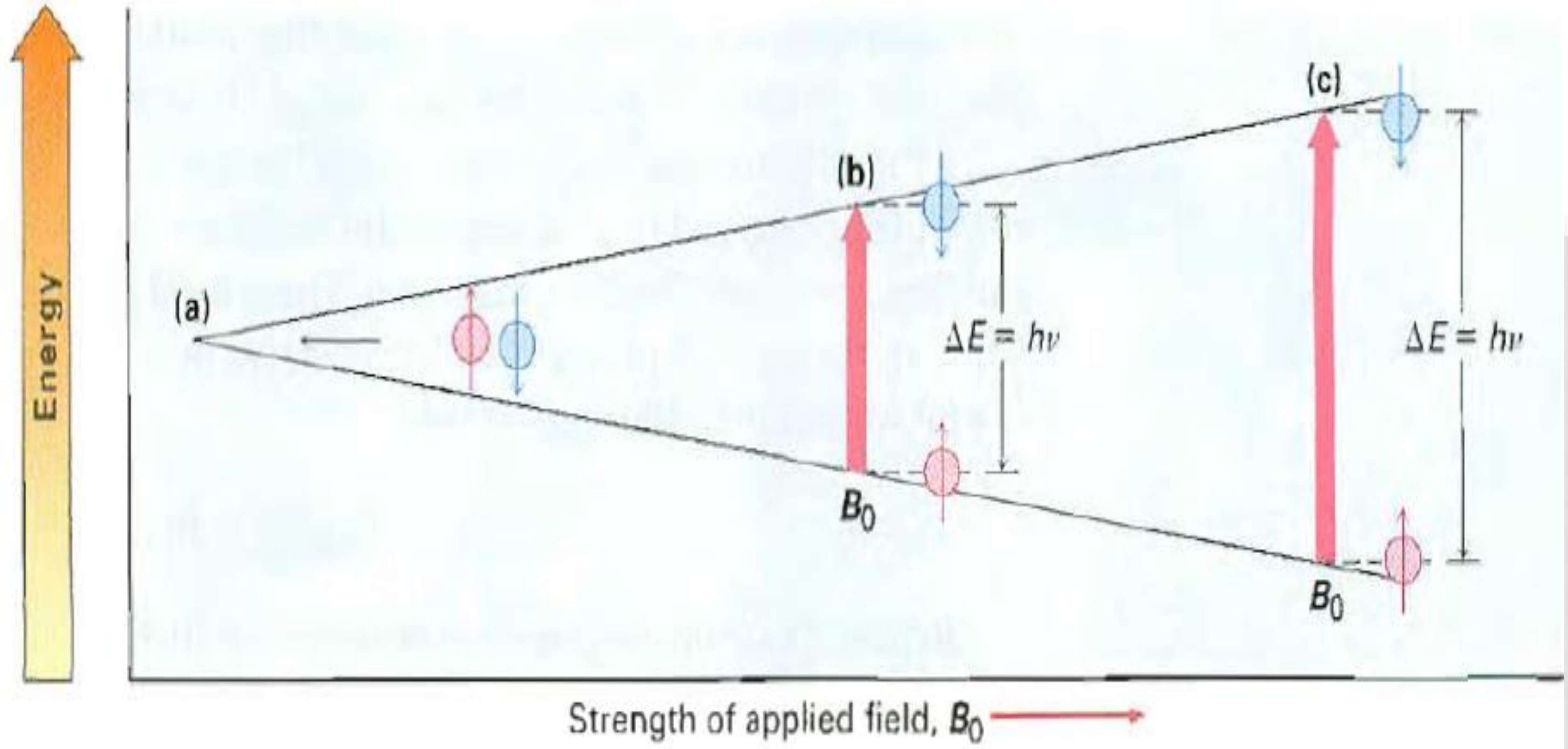
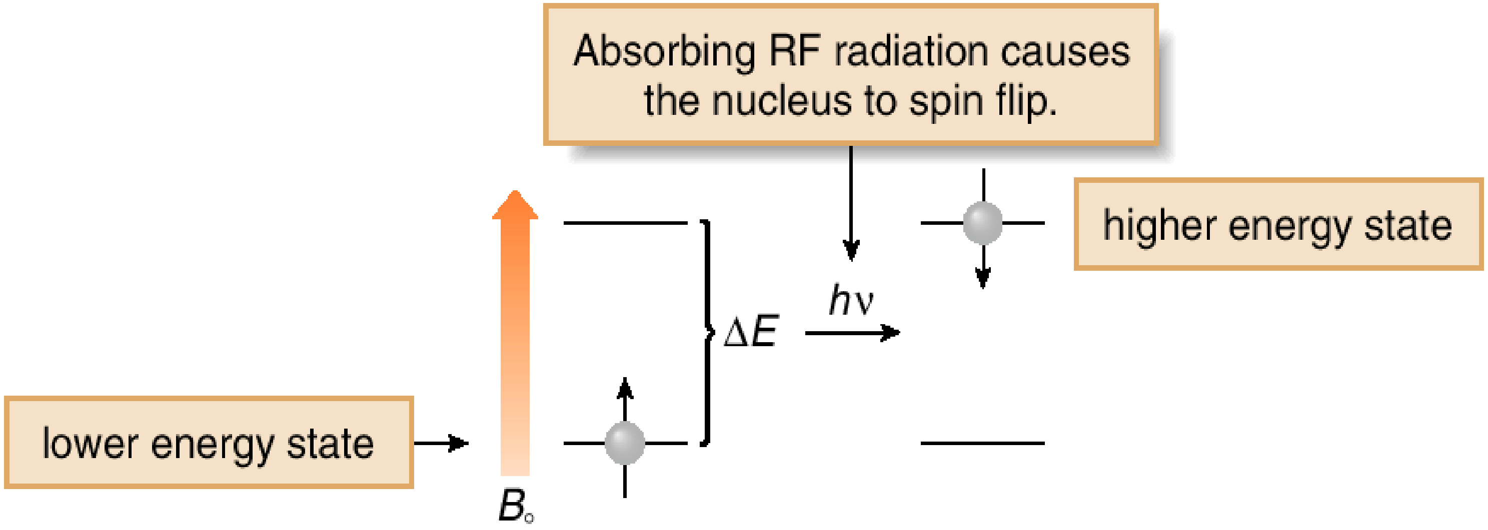


Figure 13.2 The energy difference ΔE between nuclear spin states depends on the strength of the applied magnetic field. Absorption of energy with frequency ν converts a nucleus from a lower spin state to a higher spin state. Spin states (a) have equal energies in the absence of an applied magnetic field but (b) have unequal energies in the presence of a magnetic field. At $\nu = 200$ MHz, $\Delta E = 8.0 \times 10^{-5}$ kJ/mol (1.9×10^{-5} kcal/mol). (c) The energy difference between spin states is greater at larger applied fields. At $\nu = 500$ MHz, $\Delta E = 2.0 \times 10^{-4}$ kJ/mol.

- For NMR spectroscopy the frequencies of interest are in the radio frequency (RF) range, typically 60-500 MHz depending upon the strength of Bo.
- The absorption of energy creates an excited state of the system. The process whereby the system returns to its lowest energy state, i.e. its ground state, is called relaxation.
- One way for the system to relax to the ground state is for it to emit radiation. If a suitable detector is available, e.g. an RF receiver, the emitted radiation may be recorded as a peak on a graph.

Introduction to NMR Spectroscopy

- **Thus, two variables characterize NMR:**
- **an applied magnetic field B_0, the strength of which is measured in tesla (T), and**
- **the frequency ν of radiation used for resonance, measured in hertz (Hz), or megahertz (MHz)—(1 MHz = 10^6 Hz).**

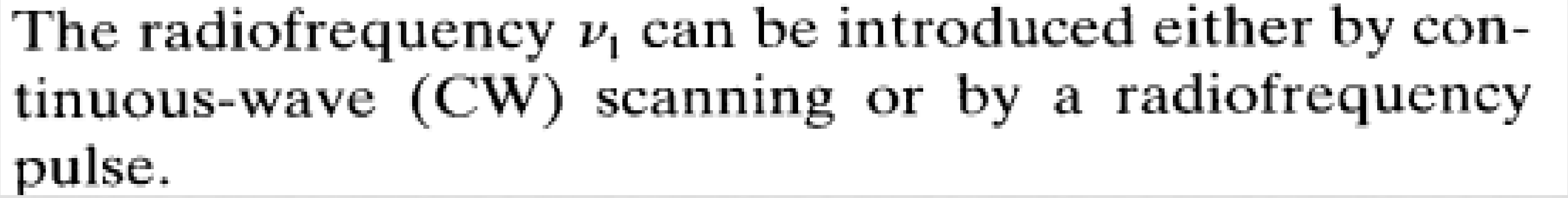


Absorbing RF radiation causes the nucleus to spin flip.

higher energy state

lower energy state

- A nucleus is in *resonance* when it absorbs RF radiation and “spin flips” to a higher energy state.

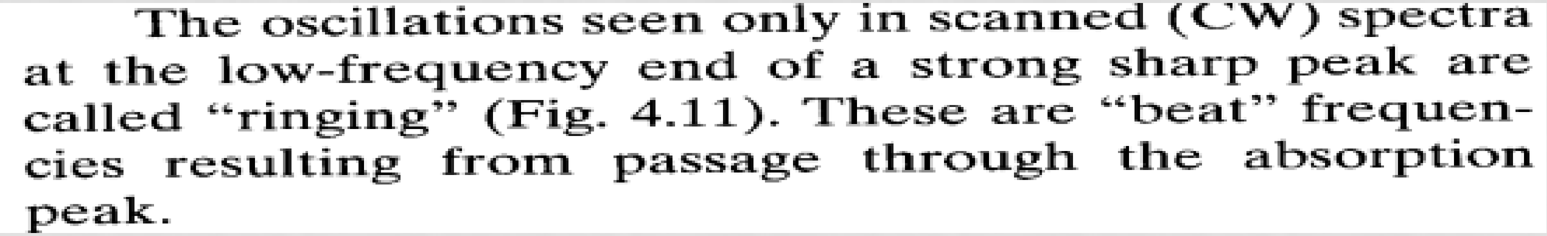


The radiofrequency ν_1 can be introduced either by continuous-wave (CW) scanning or by a radiofrequency pulse.

There are two types of NMR spectrometers continuous wave (CW) and pulsed Fourier transform (FT)

In the CW instruments, the oscillator frequency is kept constant while the magnetic field is changed gradually.

Limitation of the CW NMR spectrometers:

- 1. At any given moment, only protons resonating at a particular chemical shift can be subjected to excitation at the appropriate value of the magnetic field, and it is therefore necessary to *sequentially* excite the protons that have differing processional frequencies in a given molecule.
- 2. Time limitation, since it is often necessary to distinguish splitting that is only a fraction of a hertz in width; a serious time constraint is introduced.
- 3. Small "spinning side bands" are sometimes seen symmetrically disposed on both sides of a strong absorption peak; these result from in homogeneities in the magnetic field and in the spinning tube.
- 4. 

  The oscillations seen only in scanned (CW) spectra at the low-frequency end of a strong sharp peak are called "ringing" (Fig. 4.11). These are "beat" frequencies resulting from passage through the absorption peak.

FOURIER TRANSFORM (FT) NMR SPECTROMETERS

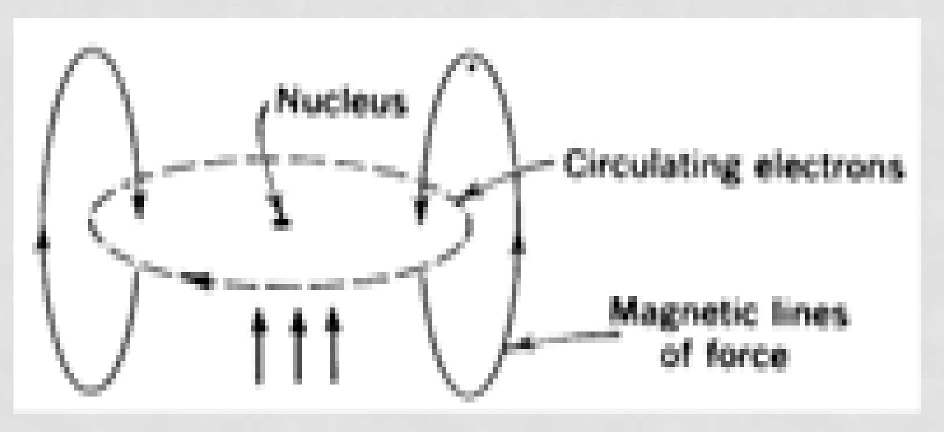
- The sample is placed in a constant, very strong magnetic field
- The sample is irradiated with a short broad pulse of radio frequency energy that excites all nuclei at once
- The resulting signal contains information about all of the absorbing nuclei at once
- This signal is converted to a spectrum by a Fourier transformation
- FT NMR allows signal-averaging, which leads to enhancement of real spectral signals versus noise
- The strong, superconducting magnets used in FTNMR spectrometers lead to greater sensitivity and much higher resolution than continuous wave instruments

The Nature of NMR Absorptions

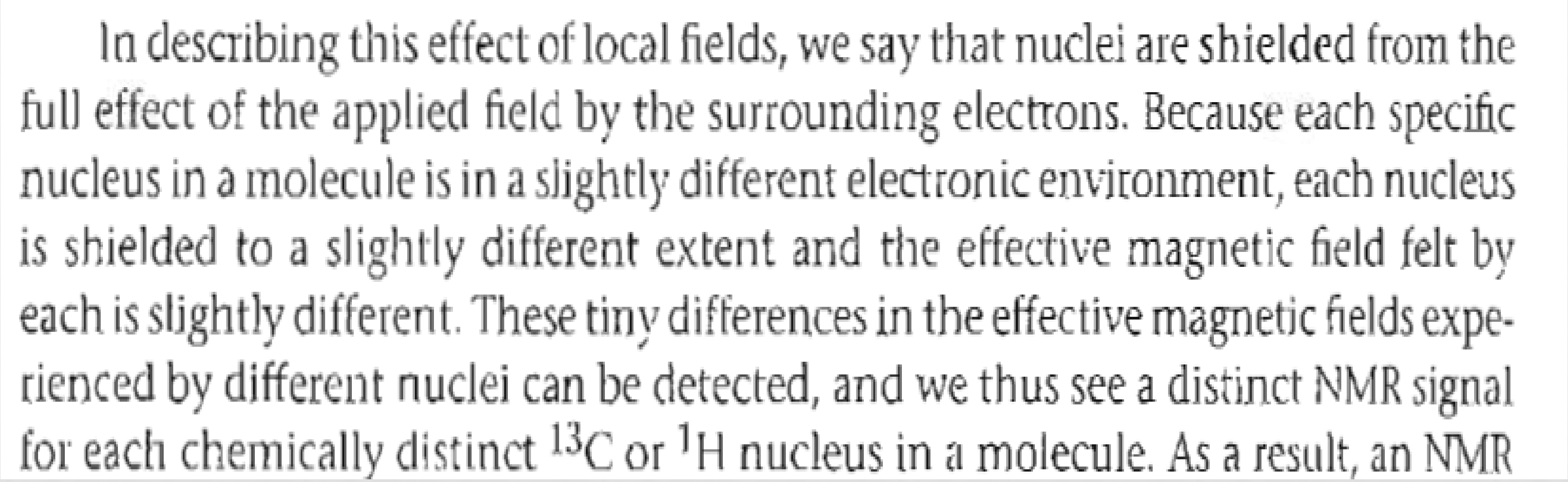
- The absorption frequency is not the same for all ^{1}H or ^{13}C nuclei in a molecule:

When an atom is placed in a magnetic field, its electrons circulate about the direction of the applied magnetic field. This circulation causes a small magnetic field at the nucleus which opposes the externally applied field The magnetic field at the nucleus (the effective field) is therefore generally less than the applied field by a fraction :

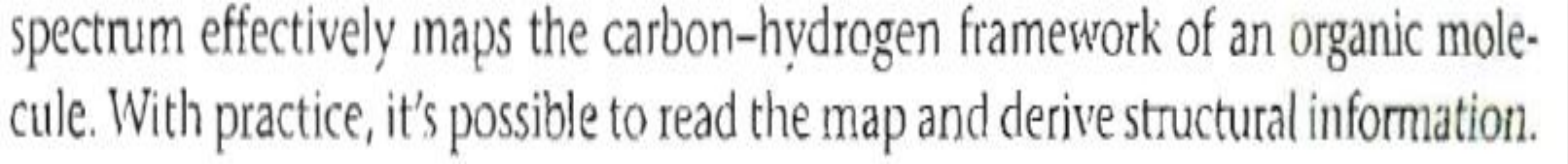
- $B_{effective} = B_{applied} - B_{local}$



Diamagnetic shielding of nucleus by circulating electrons.



In describing this effect of local fields, we say that nuclei are shielded from the full effect of the applied field by the surrounding electrons. Because each specific nucleus in a molecule is in a slightly different electronic environment, each nucleus is shielded to a slightly different extent and the effective magnetic field felt by each is slightly different. These tiny differences in the effective magnetic fields experienced by different nuclei can be detected, and we thus see a distinct NMR signal for each chemically distinct ^{13}C or ^{1}H nucleus in a molecule. As a result, an NMR



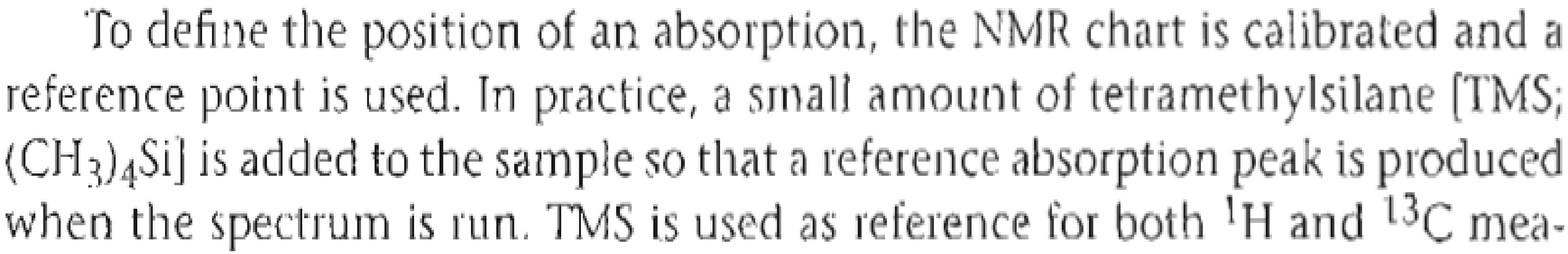
spectrum effectively maps the carbon–hydrogen framework of an organic molecule. With practice, it's possible to read the map and derive structural information.

Chemical Shift-δ

The degree of shielding depends on the density of the circulating electrons, and, as a first, very rough approximation, the degree of shielding of a proton on a carbon atom will depend on the inductive effect of other groups attached to the carbon atom.

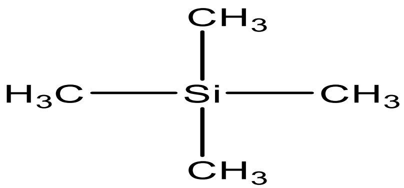
As we can tell from $\nu = \gamma B_0 (1-\sigma) / 2\pi$, the greater the value of B_o, the greater the frequency difference.

The difference in the absorption position of a particular proton from the absorption position of a reference proton is called the chemical shift of the particular proton.



To define the position of an absorption, the NMR chart is calibrated and a reference point is used. In practice, a small amount of tetramethylsilane [TMS; $(CH_3)_4Si$] is added to the sample so that a reference absorption peak is produced when the spectrum is run. TMS is used as reference for both ^1H and ^{13}C mea-

The most generally useful reference compound is tetramethylsilane (TMS).



$$H_3C-\overset{CH_3}{\underset{CH_3}{Si}}-CH_3$$

This material has several advantages:

- it is chemically inert,
- symmetrical,
- volatile (b.p. 27° C),
- soluble in most organic solvents
- it gives a single, intense, sharp, absorption peak,
- its protons are more "shielded" than almost all organic protons.

When water or deuterium oxide is the solvent, TMS can be used as an "external reference" in a concentric capillary or the methyl protons of the water-soluble sodium 2, 2-dimethyl-2-silapentane-5-sulfonate (DSS), (CH3)3SiCH2CH2CH2S03Na, are used as an internal reference (0.015 ppm).

The TMS reference peak is placed at the right-hand edge of the spectrum and designated zero on the either Hz or δ scale

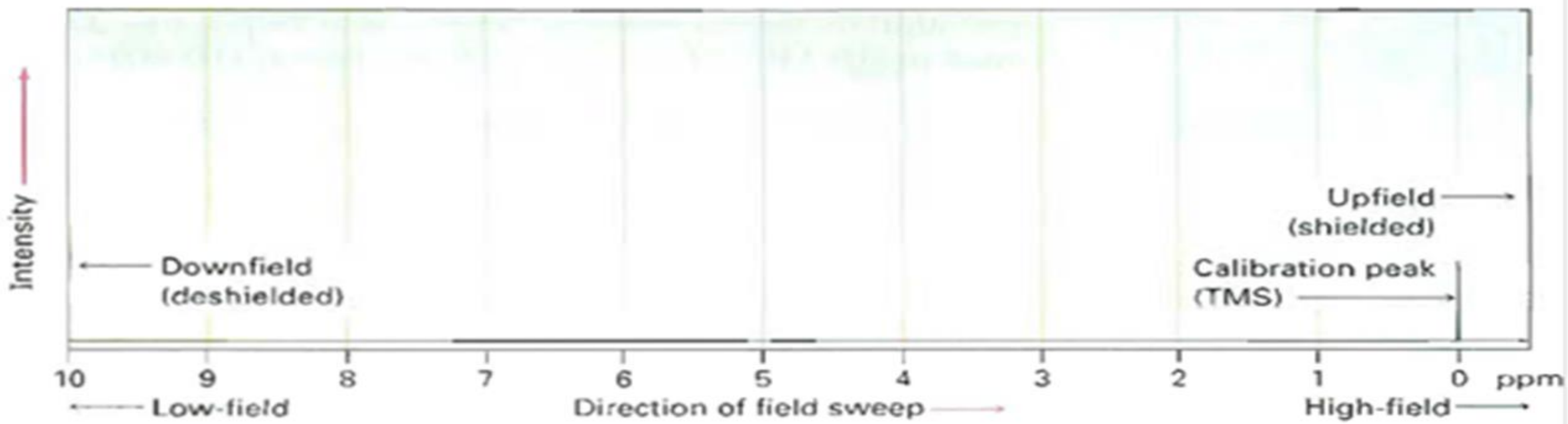


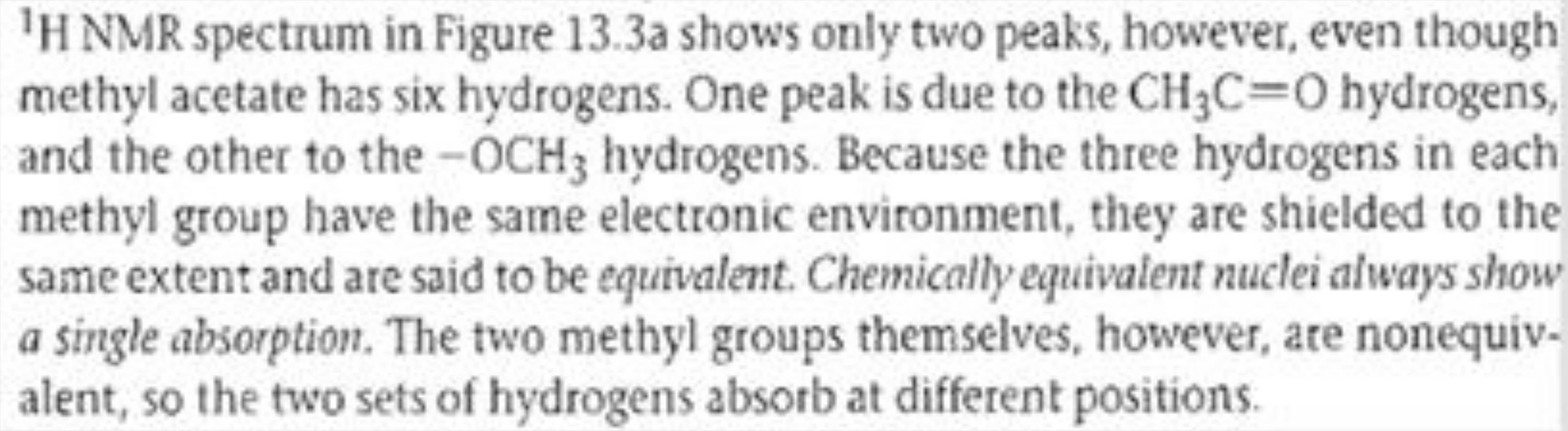
Figure 13.5 The NMR chart. The downfield, deshielded side is on the left, and the upfield, shielded side is on the right. The tetramethylsilane (TMS) absorption is used as reference point.

The term "shielded" means toward the right; "deshielded" means toward the left. It follows that the strongly deshielded protons of dimethyl ether, for example, are more exposed than those of TMS to the applied field;

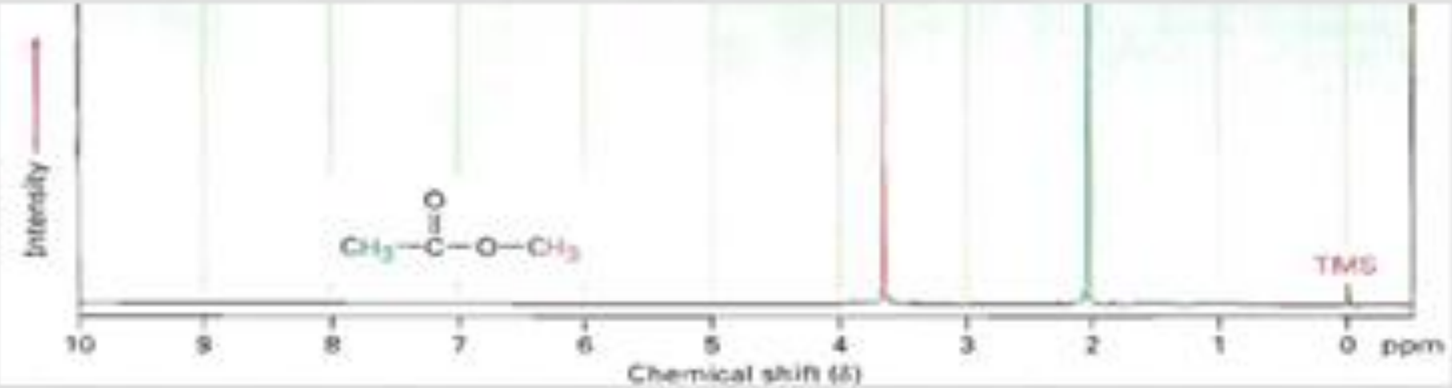
hence, resonance occurs at higher frequency—i.e., to the left —relative to the TMS proton peak.

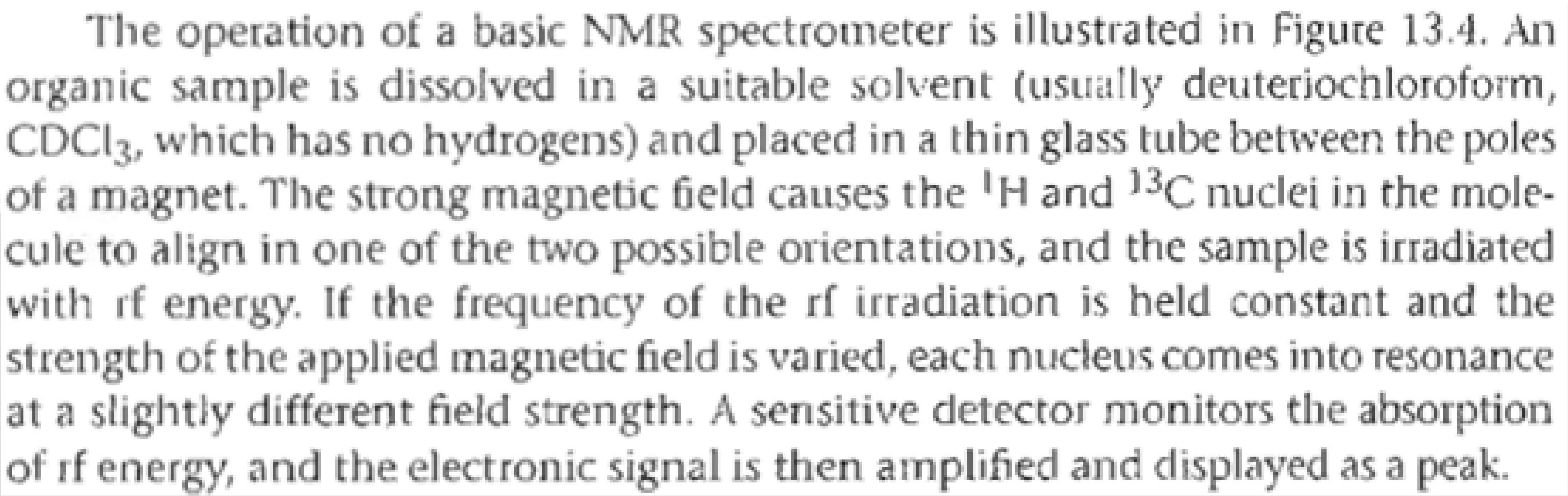
Thus, both the Hz and the δ scales reflect the increase in applied frequency, *at constant field,* toward the left of the TMS resonance frequency, and the decrease in applied frequency toward the right.

The terms "upfield" and "downfield" are now obsolete and have been replaced, respectively, by shielded (lower δ, or to the right) and deshielded (higher δ, or to the left).



^{1}H NMR spectrum in Figure 13.3a shows only two peaks, however, even though methyl acetate has six hydrogens. One peak is due to the $CH_3C{=}O$ hydrogens, and the other to the $-OCH_3$ hydrogens. Because the three hydrogens in each methyl group have the same electronic environment, they are shielded to the same extent and are said to be *equivalent*. *Chemically equivalent nuclei always show a single absorption*. The two methyl groups themselves, however, are nonequivalent, so the two sets of hydrogens absorb at different positions.





The operation of a basic NMR spectrometer is illustrated in Figure 13.4. An organic sample is dissolved in a suitable solvent (usually deuteriochloroform, $CDCl_3$, which has no hydrogens) and placed in a thin glass tube between the poles of a magnet. The strong magnetic field causes the ^1H and ^{13}C nuclei in the molecule to align in one of the two possible orientations, and the sample is irradiated with rf energy. If the frequency of the rf irradiation is held constant and the strength of the applied magnetic field is varied, each nucleus comes into resonance at a slightly different field strength. A sensitive detector monitors the absorption of rf energy, and the electronic signal is then amplified and displayed as a peak.

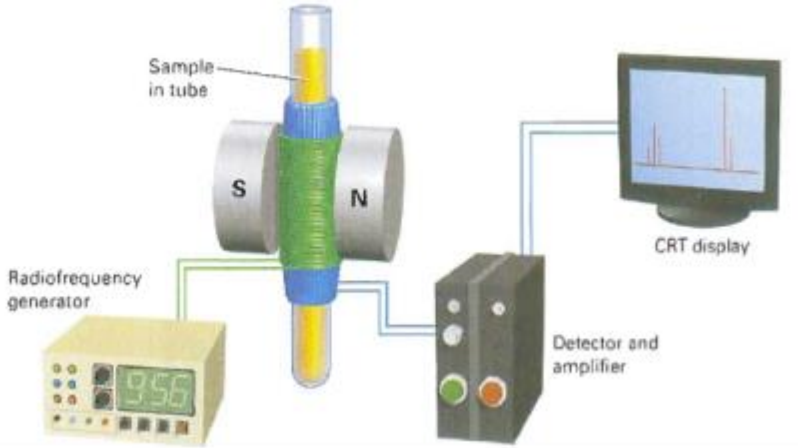


Figure 13.4 Schematic operation of an NMR spectrometer. A thin glass tube containing the sample solution is placed between the poles of a strong magnet and irradiated with rf energy.