

CHAPTER II

LITERATURE SURVEY

2.1 Theoretical background

2.1.1 Introduction

2.1.1.1 Magnetic properties of nuclei

In an electrostatic field (B_0) the component of the nuclear angular momentum in any directions may take the value of $m\hbar$ where \hbar is the Planck constant divided by 2 and m is the discrete spin variable whose range consists of the $2I+1$ values:

$$m = -I, -(I-1), \dots, (I-1), I \quad (2-1)$$

where: $I =$ the spin quantum number.

A nuclei with a non-zero spin quantum number also has a magnetic moment μ , which is proportional to the spin angular momentum P :

$$\mu = \gamma P \quad (2-2)$$

where: γ = magnetogyric ratio of the nuclei is a constant characteristic of particular nuclei.

In the presence of a magnetic induction B_0 , the magnetic moment experiences a torque which is the vector product of μ and B_0 , $\mu \wedge B_0$. According to Newton's law of motion, this torque is equal to the rate of change of the angular momentum:

$$\frac{dP}{dt} = \mu \wedge B_0 \quad (2-3)$$

relate to equation 2:

$$\frac{d\mu}{dt} = \gamma \mu \wedge B_0 \quad (2-4)$$

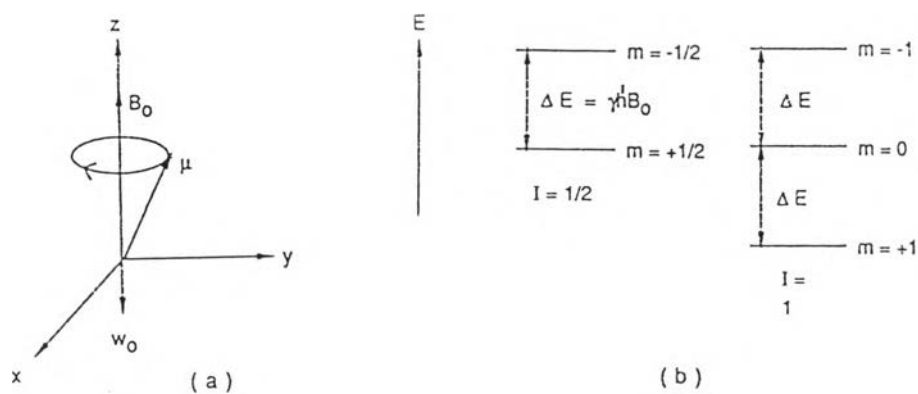


Figure 2-1 (a) Precession of a nuclear magnetic moment μ in a magnetic field B_0 (for $\gamma > 0$).

(b) Energy levels of spin 1/2 and spin 1 nuclei in B_0 (for $\gamma > 0$). m is given a positive values in the field direction.

When placed some nuclei in static magnetic field, they may undergo nuclear magnetic resonance (NMR) and process nuclear spin. Only nuclei with total spin quantum number $I \neq 0$ interact with magnetic fields due to their magnetic moments.

It can be shown that such an equation describes a procession of the vector about B_0 (Fig. 2-1) at the Larmor angular velocity¹:

$$\omega_0 = -\gamma B_0 \quad (2-5)$$

which corresponds to the frequency:

$$\nu_0 = \frac{\gamma B_0}{2\pi} \quad (2-6)$$

and in the field of B_0 , $2I+1$ spin levels are separated into difference energy states (Fig. 2-1). The energy separation between the states in this is proportional to the strength of the field B_0 .

2.1.1.2 The nuclear resonance

The NMR phenomenon relies on the interaction between the nuclear magnetic moment μ which processes about B_0 at the Larmor frequency γ_0 and a small magnetic induction B_1 , perpendicular to B_0 and rotating about B_0 , at frequency ν , in the same direction as μ . Resonance is attained when the frequency of B_1 is equal to ν_0 :

$$\nu = \nu_0 = \frac{\gamma_0 B_0}{2\pi} \quad (2-7)$$

As a result, the spin originally precessing with B_0 flips over, and now precesses against B_0 . Absorption of energy ΔE from B_1 takes place; this is called "nuclear magnetic resonance".

2.1.2 Basic concept of relaxation

2.1.2.1 The equilibrium of nuclear spin in the magnetic field (B_0).

At equilibrium, the nuclear magnetic energy levels are populated according to a Boltzmann distribution which favors the lower state. From the two orientations relative to B_0 of nuclei with $I = 1/2$, the spin population may be symbolized by N_+ and N_- (Fig.2-2). The distribution N_+/N_- can be expressed by the Boltzmann factor, recalling that $\Delta E = 2\mu_0 H_0$:

$$\frac{N_+}{N_-} = e^{\frac{\Delta E}{kT}} \approx 1 + \frac{\Delta E}{kT} = 1 + \frac{2\mu_0 H_0}{kT} \quad (2-8)$$

At room temperature, $\Delta E = 2\mu_0 H_0$ is much less than 4.2 Joules, even at highest field strengths now achievable. As a result, the term $2\mu_0 H_0/kT$ is very small and N_+/N_- is not much greater than 1.

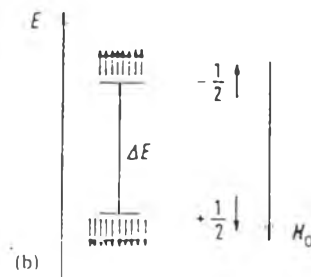


Figure 2-2 Corresponding energy levels and spin populations².

2.1.2.2 The Heisenberg Uncertainty Principle¹⁻²

It is a fundamental property throughout spectroscopy that there is a built-in uncertainty in the accuracy of measurement of the energy of an atomic particle and this uncertainty is inversely proportional to the life-times of the particular energy state.

The Heisenberg Uncertainty Principle is most usually expressed in the form:

$$\Delta E = \Delta t \approx h = 10^{-34} \text{ Js} \quad \text{or} \quad \Delta E \times \Delta t = \text{constant} \quad (2-9)$$

In NMR, if the life-times of any spin state is very short (Δt is small), then ΔE must be large which means a large uncertainty in the measurement of the energy of that spin state then an NMR absorption signal would be a broad line and vice versa.

The significance is that the uncertainty in measured frequency (the limiting line-width) is of the order $1/T_1$ or $1/T_2$.

In viscous solution, $T_1 \approx T_2$, but the inhomogeneities and diffusion processes shorten T_2 and hence give broad lines. Whereas in non-viscous solutions, line-width may be as narrow as 0.1 Hz, in polymer the lines can be several thousand hertz wide. It is the factor which makes line-width studies important in polymer chemistry and biochemistry.

2.1.3 Relaxation processes¹⁻⁵

NMR experiments involves the orientation of nuclei with respect to an applied magnetic field. When a sample is introduced into the magnet of NMR spectrometer, its nuclei becomes magnetically polarized, and an equilibrium is established with a small, but finite excess of nuclei in the ground state. After irradiation with the right amount of the energy (in the form of radio frequency electromagnetic radiation), the nuclei will absorb this energy and flip into the excited state on reaching resonance. Because of the energy difference between the ground state and the excited state is very small, so the excited nuclei would tend to remain there for a very long time. If we put in too much energy, the number of ground state nuclei will tend to equal the number of excited nuclei. At this system there will be no absorption of radiofrequency energy and the signal will collapse. This is known as "saturation". In order to obtain the NMR spectrum, there are two other very important mechanism by which excited nuclei may lose their energy without the emission. The first is called "spin-lattice relaxation" and the other is called 'spin-spin relaxation".

In pulse Fourier transform NMR, the experiments are concerned with the recovery of the magnetization after excitation for a very short period. The recovery time is related to the relaxation time, which can be classified into two terms:

2.1.3.1) spin-lattice relaxation time (T₁) and

2.1.3.2) spin-spin relaxation time (T₂)

2.1.3.1 Spin-lattice relaxation and T₁

Around the nuclei, complex vibrational changes will take place which are both intramolecular and intermolecular motion (including the involvement of solvent molecules); the random tumbling of molecule and the vibration of bonds and electrons set up many fluctuating electric dipoles and a proportion of these will be of appropriate magnitude to interact with the high energy nuclei and absorb the excess of the energy from it.

This process involves transferring spin energy of an excited nuclei to the surrounding lattice (be a crystal lattice or simply an array of solvent molecules), as translational or rotational energy and these two systems are mutually coupled via molecular motion.

This spin-lattice relaxation is assumed to be a first order rate process and the time constant for it is defined as T₁ " the spin-lattice relaxation time" characterizing each kind of nuclei and cover a range of about 10⁻⁴ to 4 seconds.

This process operates so as to re-establish the original Boltzmann distribution i.e. an excess of the nuclei in the ground state. The increased molecular motion caused by this relaxation process raises the temperature of the sample slightly. The magnitude of the population difference between two state is directly proportional to the magnetic field strength in which we place the nuclei and inversely proportional to the absolute temperature.

2.1.3.2 Spin-spin relaxation and T₂

This process is about the loss of the spin states of nuclei by mutual exchange with a close neighbour in the ground state. The slow tumbling molecules experiences internuclear dipole-dipole interaction and energy quanta ($\Delta E = 2\mu_0 B_0$)

are exchanged between nuclei. It is similar to spin-lattice relaxation which tend to shorten the life-time of all spin states and leads to line broadening but spin-spin relaxation leads to no net lose of energy in the system because the energy state of the system is not changed. A corresponding time constant for it is defined as T₂.

$$\Delta\nu = \text{const.}1/T_2 \quad (2-10)$$

The relaxation process take a finite time and has two important practical consequences:

1. Not all groups of nuclei have the same relaxation times; some are more prone to saturation than others, so that we must use a power of radiofrequency sufficiently low so as not to saturate even the most saturation-prone nuclei in the molecule under examination.

2. All NMR signals have a natural line-width which is dependent on the relaxation times. Form the Uncertainty Principle, if T₁ and T₂ are both long (the spin state life-times are long) then we can measure for the NMR absorption with high accuracy and the line-width will be narrow (give rise to sharp spectral lines) and vice versa. Any factors which shorten the spin state life-time and leads to more rapid relaxation process will lead to broader NMR signals. In solid sample general gives very broad spctral lines and their relaxation times are very short (of the order of 10⁻²-10⁻⁴ seconds). In liquids however, it is found that relaxation times are of the order of seconds because molecules in liquid move around relatively freely.

The relationship between life-times with the Heisenberg Uncertainty Principle is important for determining line-width of spectral.

2.1.4 Measurement of spin-lattice relaxation times (T_1)⁵⁻⁷

NMR spectrometer usually detects the magnetization along y-axis, while spin-lattice relaxation time detects the magnetization along z-axis and spin-spin relaxation time detects the magnetization on xy plane. Several methods for measuring spin-lattice (T_1) and spin-spin (T_2) relaxation times have been described. The principle of all of the many methods are similar and the details of some of these methods are described below.

2.1.4.1 Inversion-Recovery Method

Inversion-recovery sequence is known as the most common method of measuring spin-lattice relaxation rates. The experiment is conceptually simple, and serve as a useful introduction to the idea that we can perturb the magnetization vectors.

Spin-lattice relaxation times (T_1) of individual nuclei can be obtained by Fourier transformation of the free induction decay (FID) signal followed by a (180° - τ - 90° -Acq-T) pulse sequence. τ is the variable time between an applied 180° pulse which completely inverts the spin, and a 90° observing pulse which determines the extent of the remaining magnetization after time t . T is the time between acquisition time (Acq) and the next pulse sequence, in which the system is assumed to come to equilibrium after time T. In all measurements, the good T_1 values can be achieved by specifies appropriate values of time and the waiting period between two subsequent sequences or pulse delay (PD) should be at least five times of $T_1(5T_1)$ of the slowest relaxation nuclei in the molecules (having longest T_1). Following Fourier transform of the free induction decay (FID), the

remaining magnetization was determined by measuring the intensity of the peaks. It can be explained by following the pulse driven motion of the magnetization vector M_0 in the rotating frame of reference with the axis x , y and z (Fig. 2-3).

In figure 2-3 starting at equilibrium (a), a 180° pulse along the z -axis rotates the net magnetization vector from (a) to (b) results that the inversion of the magnetization vector $+M_0$ to $-M_0$. At this system there is no signal received in the detector. By sequent longitudinal relaxation, the longitudinal magnetization M_z , reequilibrates going from $-M_0$ through zero to $+M_0$. Before the measuring, 90° pulse is applied and it is effected to the further rotating of the magnetization vector to (c) thus laying it along the negative y -axis: at this point a negative signal is received in the detector, corresponding to the maximum negative z -axis value of M .

Depending on time, the magnetization has partially relaxed to an amount $M_0 < 0$ (c), $M_0 = 0$ (d), or $M_0 > 0$ (e). τ seconds after the 180° pulse, a 90° pulse rotates the partially relaxed magnetization vector towards the negative y' -axis ($M_0 < 0$)(f) or a positive y' -axis (g). The resulting transvers magnetization ($-My'$ for $M_0 < 0$; My' for $M_0 > 0$) processes freely after the 90° pulse, giving rise to an FID signal which is Fourier transformed to the NMR spectrum. The Fourier transformation of the FID arising from this sequence give an inverted absorption spectrum for $M_0 < 0$ ($\tau < T_1 \ln 2$), no signal for $M_0 = 0$ ($\tau = T_1 \ln 2$) and an absorption spectrum for $M_0 > 0$ ($\tau > T_1 \ln 2$).

The sequence can be repeated a sufficient number of times to give a strong enough spectrum by signal summation. The rate of change of signal height is usually exponential, which a first-order rate constant, the reciprocal of which is T_1 . The whole pulse timing operator and the calculation of T_1 values are controlled by a computer programmes.

There are two useful graphical methods for calculating the rate constant k of first-order process (in this case the exponential decline in line height). If $\ln(\text{height})$ is plotted against times, a straight line is produced of slope k . Alternatively, the half-life of the process can be found, and it is known in first-order rate laws that $k(\text{half-life}) = \ln 2$. In the case of T_1 measurements, the half-life is simply the times taken by M_z to relaxed to the point represented in figure 2-3(d) and this point is called "null point". The result of such an experiment which varying τ is shown in figure 2-4; one can extract the T_1 from the varying peak heights.

In Bloch theory of NMR, it assumed that the equilibrium will be approached exponentially, and treating the time constant of this exponential as a parameter which might set out to measure. Fortunately, this hypothesis often turns out to be close to the truth for the molecules in solution and this induced field will build up according to the equation express that the signal intensities I correspond to the transverse magnetization by:

$$\frac{dM_z}{dt} = -\frac{M_z - M_0}{T_1} \quad (2-11)$$

where M_0 is the magnetization at thermal equilibrium. After the $180^\circ\text{-}\tau\text{-}90^\circ$ sequence giving by integration of Bloch equation between $M_z' = -M_0$ at time $t = 0$ and $M_z' = M_z$ at $t = \tau$:

$$\int_{-M_0}^{M_\tau} \frac{dM_z'}{M_z' - M_0} = -\frac{1}{T_1} \int_0^\tau dt \quad (2-12)$$

$$\text{or} \quad \ln \left(\frac{M_0 - M_\tau}{2M_0} \right) = -\frac{\tau}{T_1} \quad (2-13)$$

$$\ln \left(\frac{I_0 - I}{2I_0} \right) = -\frac{\tau}{T_1} \quad (2-14)$$

where I_0 and I_τ are the signal intensities at the equilibrium and pulse interval respectively.

The spin-lattice relaxation time (T_1) can be determined simply from the zero transition τ_0 of the signal intensities ($I=0$) (Fig. 2-4).

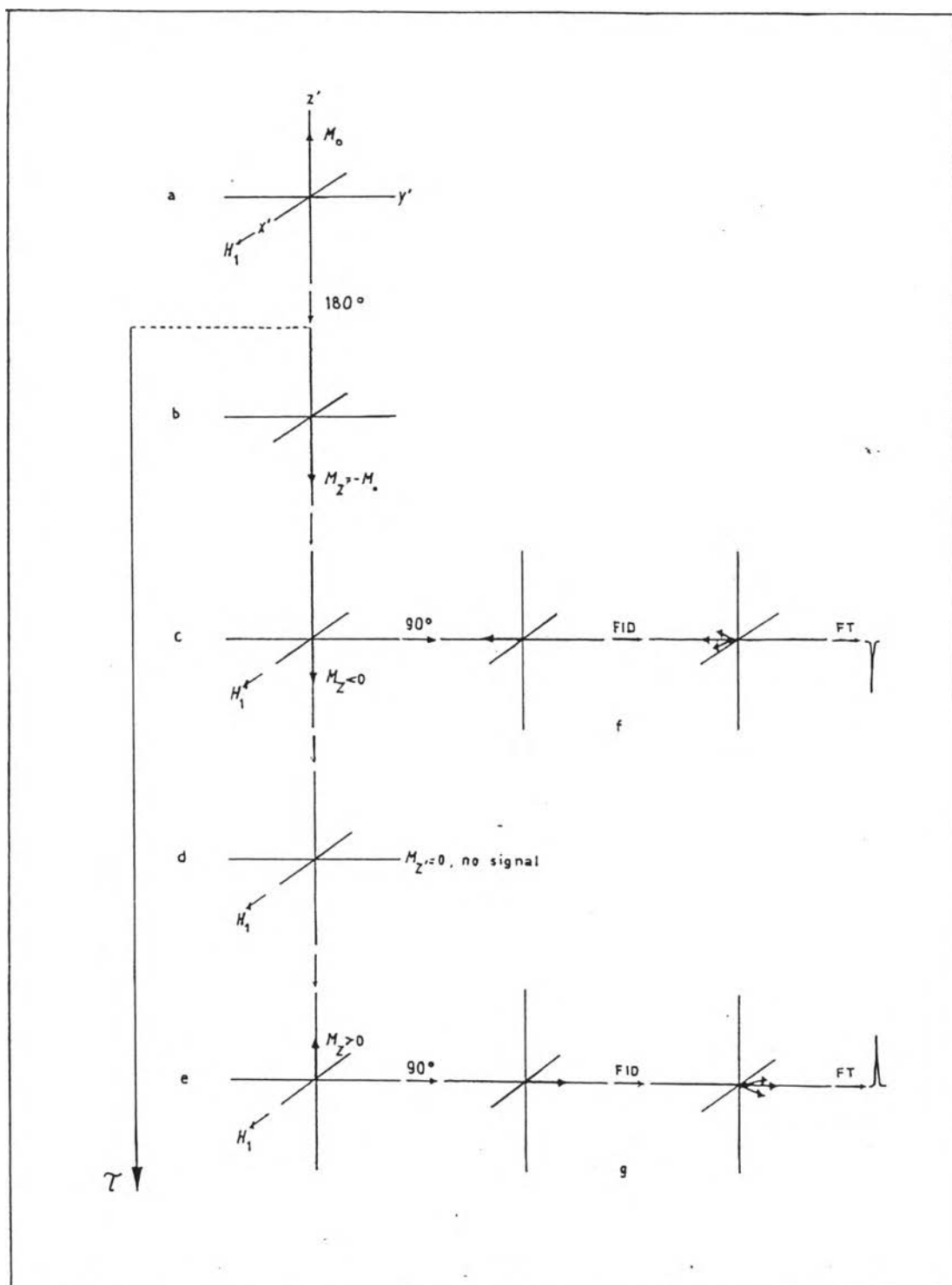


Figure 2-3 (a)-(g) Pulse driven motion of the magnetization vector M_0 in the rotating frame during an inversion-recovery experimental for the measurement of T_1

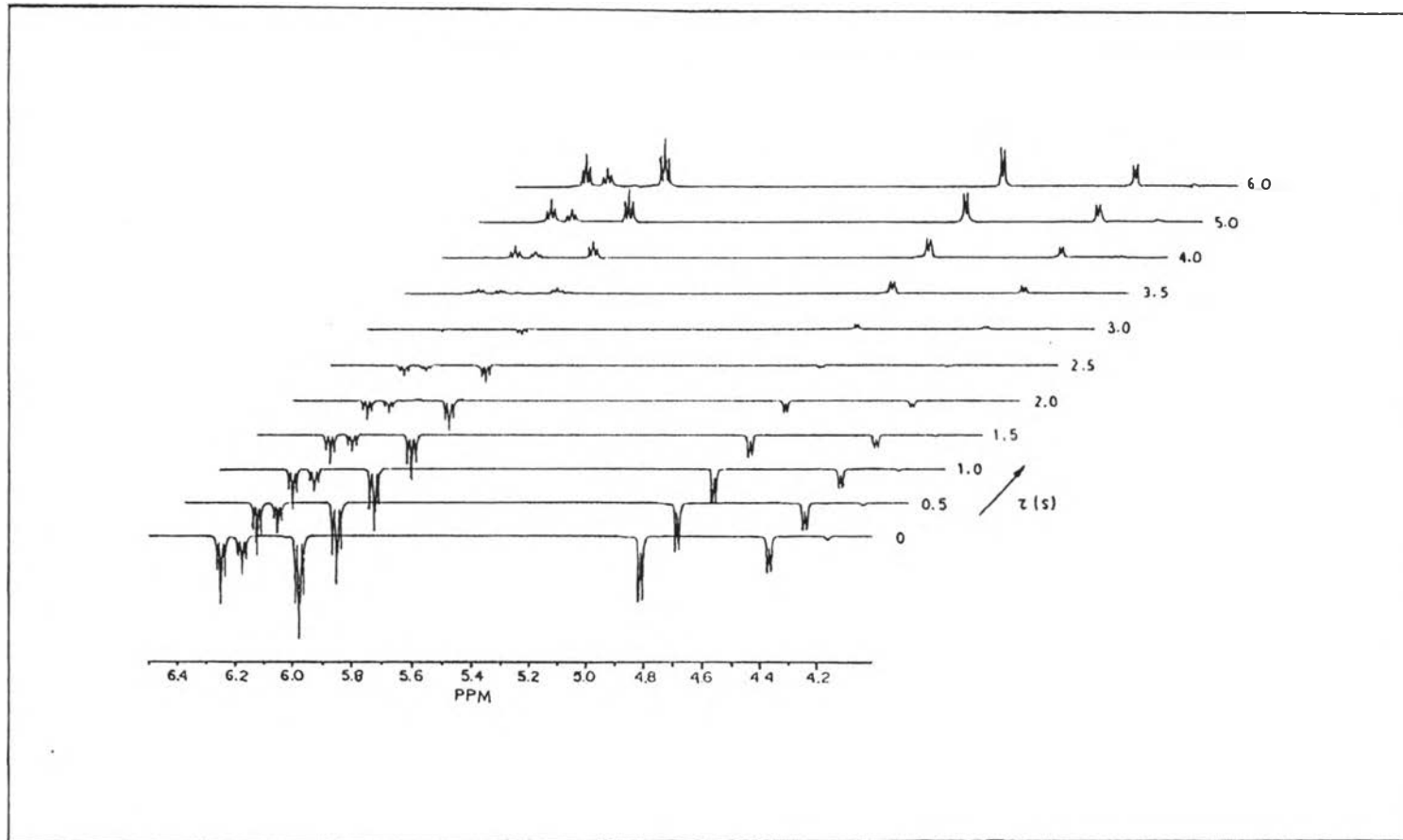


Figure 2-4 Experimental results from an inversion-recovery sequence. The group of peaks at low field (i.e. to the left) all have slightly longer T_1 than those of the high-field group.

2.1.4.2 Progressive Saturation Method

Spin-lattice relaxation time (T_1) of individual nuclei can also be measured by the progressive saturation method by using a sequence $(90^\circ-\tau-90^\circ)_n$ pulse sequence in which the 90° pulse are repeated at relatively short intervals so that saturation is slowly reached. The pulsed interval used for accumulation of FID signal is often short compared to the real value of spin-lattice relaxation. After several 90° pulse, a steady state magnetization M_o' . M_o is established the signal intensities in the Fourier transformation of the FID is attenuated using subsequent 90° pulse, with increasing pulse interval τ , the steady state magnetization M_o' approaches the relaxed magnetization M_o . The 90° pulse rotates the M_o' vector towards the y'-axis, giving rise to transversed magnetization which yields several of FID signals subject to be accumulated and Fourier transformed. In the spectrum obtained from each τ , the signal intensity I_τ corresponds to the steady state magnetization M_o' .

The intensity I_τ as a function of τ is the integral of the Bloch equation between $M_z'=M_o'$ and M_o or from I_τ (at $t = \tau$) to $I_\tau(t=\alpha)$.

$$\ln \frac{(I_o - I)}{2I_o} = -\frac{\tau}{T_1} \quad (2-15)$$

The equilibrium intensity I_α corresponding to the relaxed magnetization M_o is approximated by recording a spectrum arising from a 90° pulse with an interval of at least $\tau = 5 \times T_1$, T_1 accounting for the slowest relaxing nuclei (Fig. 2-5).

The progressive saturation method is normally used to determine T_1 of the nuclei which has long relaxing times ($T_1 > 20$ sec.), and in which the time of experiment is much shorter than inversion-recovery method.

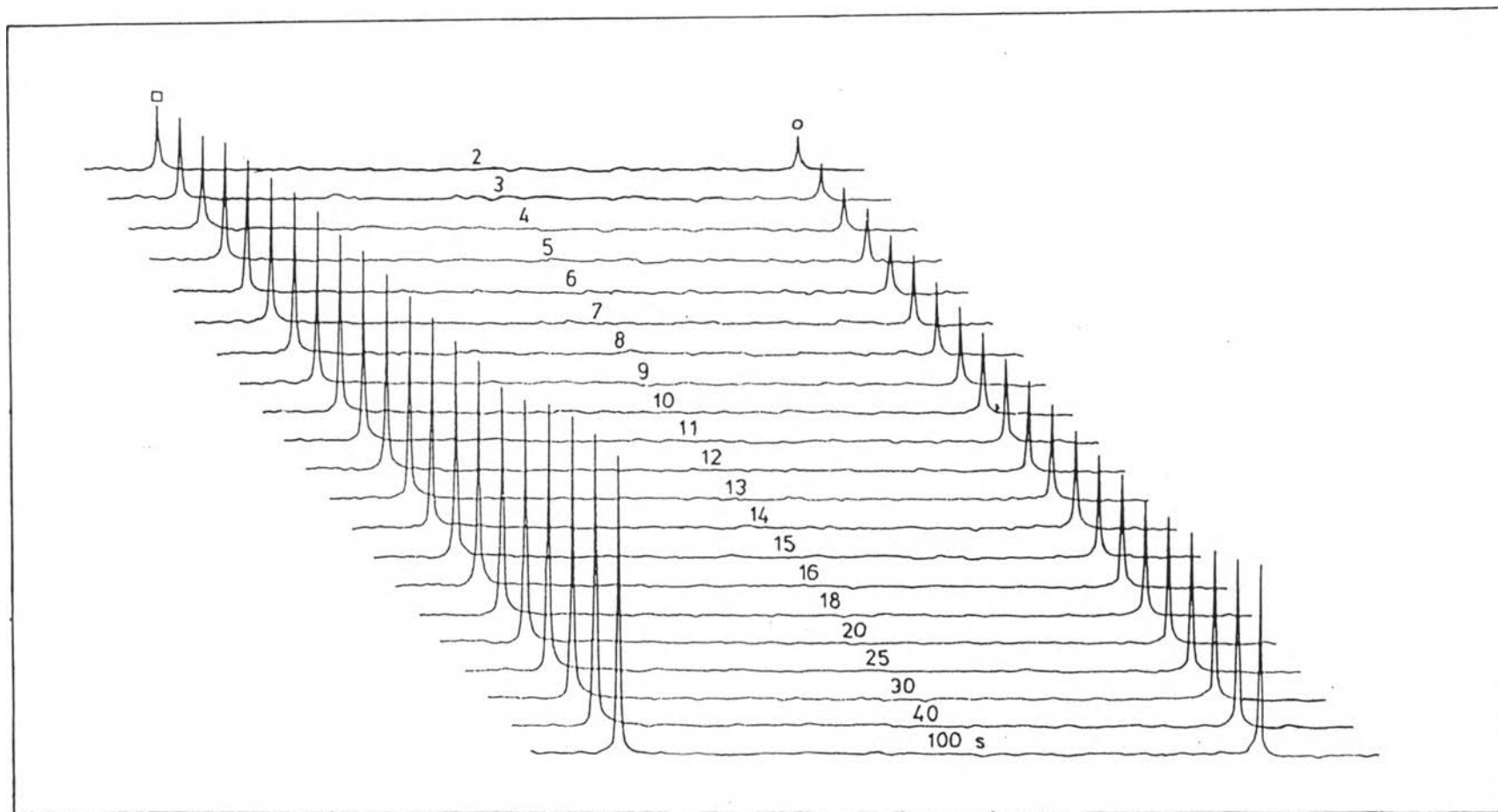


Figure 2-5 Stacked set of progressive saturation spectra.

2.1.5 Measurement of spin-spin relaxation and T₂

The measurement of T₂ is valuable in studying the diffusion processes of the molecules, and like T₁ it is value to polymer chemists and biochemists. The basic pulse method for measuring T₂ is discussed below:

2.1.5.1 Spin Echoes Technique

A signal echo is a result of a rephasing of the nuclear spin in the way which is illustrated in figure 2-6.

In figure 2-6, a 90° pulse rotates the net magnetization vector onto the xy-plane as at (b). Because of field inhomogeneities throughout a macroscopic ensemble of nuclei, so that nuclei in different parts of the sample experiences the different fields and come to resonance at different frequencies (give rise to NMR absorption bands rather than absorption lines), hence respect to the rotating frame, then a time τ the magnetization vector will be as (d). Because of this dephasing, the value of M along the y'-axis is reduced. Then 180° pulse on the system at (d) inverts all of the spin to (e) through a mirror plane on the xz-axis. After a further time τ has elapsed as at (f), all of the nuclei are in phase again and echo signal is received in the detector.

The strength of the echo signal will be less than that corresponding to the original value of M (at (b)): the decay in the signal is the measure of T₂, the random process of the transverse relaxation.

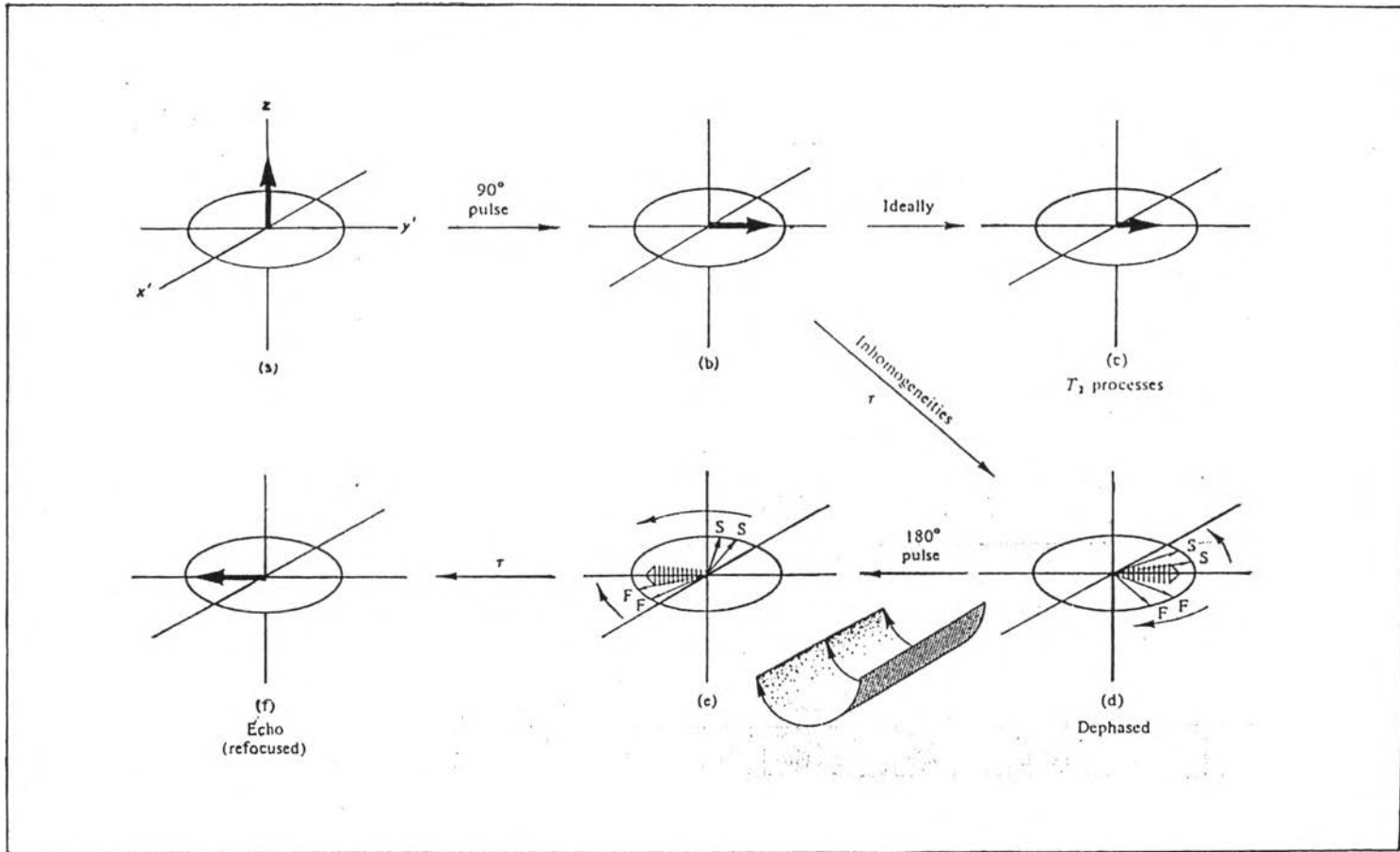


Figure 2-6 Magnetization vectors in the measurement of T_2 : the spin echo pulse sequence.

2.1.5.2 Carr-Purcell-Meiboom-Gill (CPMG) measurement of T₂

Unfortunately, the total rate of transverse relaxation is very sensitive to diffusion effects, which slowly placed the nuclei in different orientation and position with respect to the applied field. To overcome this much more complex multiple pulse programmes named "Carr-Purcell-Meiboom-Gill (CPMG)" are used. This programme modified the basic spin echo method is:

$$90^\circ-\tau-180^\circ-\tau-(\text{echo})-\tau-180^\circ-\tau-(\text{echo})-\tau-180^\circ$$

A sequence of 180° pulse continually inverts the dephased nuclei giving rise to a series of echo at times 2, 4, 6 and until the echo dries away. The exponential decay in the echo intensity is a better measurement of T₂.

When a long series of 180° pulse is used, if the pulse angle is slightly inaccurate, it is effect to refocus the spins inaccurately, with a more rapid decline in magnetization than due purely to T₂. To avoid this problem, this technique is to alter the phase of the 180° pulse is that instead of executing them along the x-axis, they are "phase shifted" by 90° pulse and executed along the y-axis so that the dephased spins are inverted in a mirror plane on the y'z-axis as shown in figure 2-7.

In Fig. 2-7, after the 90° pulse leading to (a), the spins dephase to (b) after time τ ; a 180° pulse then inverts them to (c), and after a further time τ they refocus as at (d).

The echo is always along the positive y'-axis and give a positive NMR signal.

Exponential decay of the echo intensity give a very good measure of the absolute value of T₂.

Because of the difficulty in measuring T_2 values, they have found little applications in structure elucidation and main interest in studying the relaxation processes and the various contributory influences, such as molecular diffusion processes.

From the Heisenberg Uncertainty Principle, the line-width at half height cannot be less than $1/T_2$. The high resolution (narrow line-width) is degraded by all inhomogeneities in the field and T_2 never be greater than T_1 . In non-viscous liquid, and in small molecules in solution, T_1 and T_2 are approximately equal.

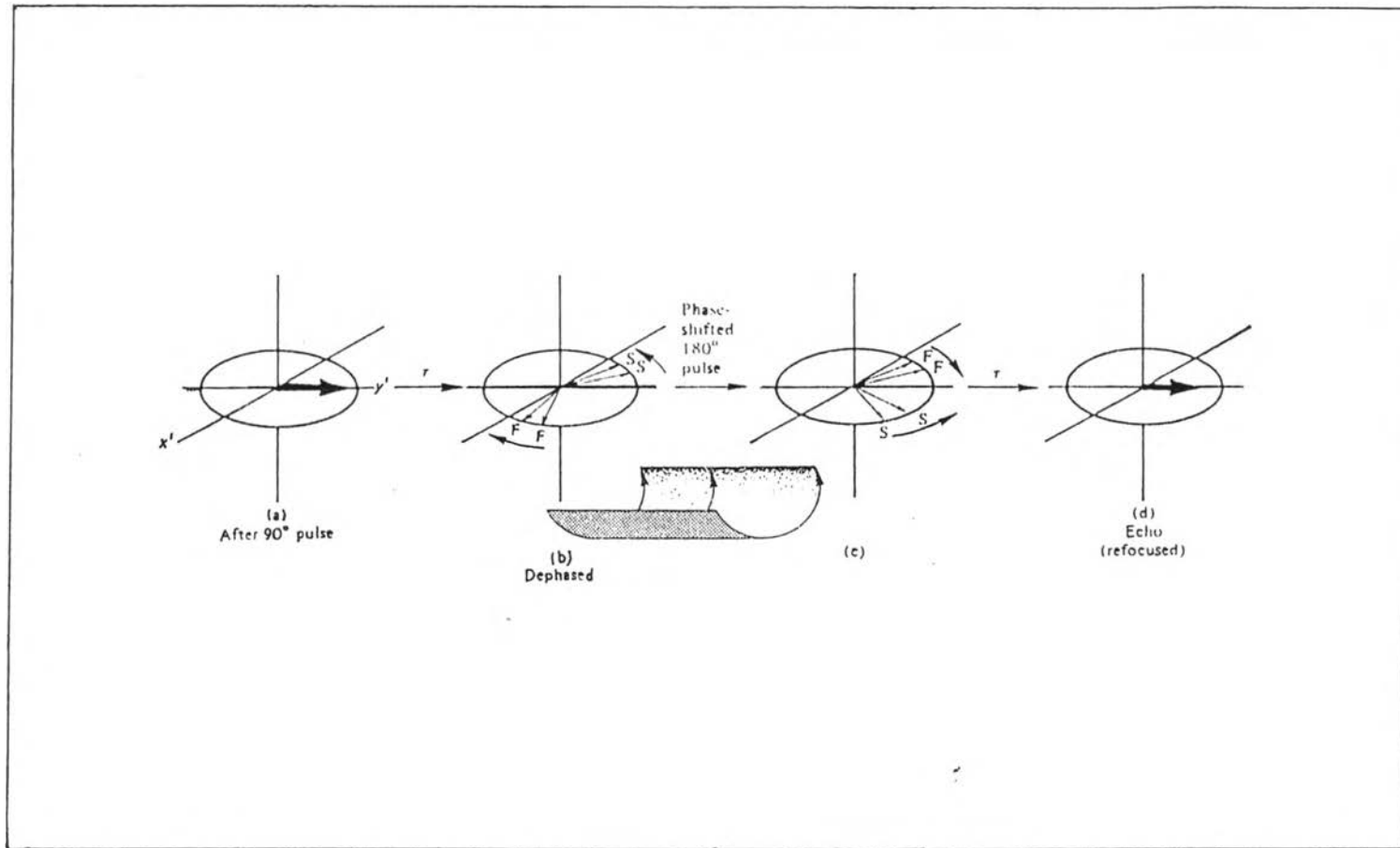


Figure 2-7 Magnetization vectors in the measurement of the T_2 : the Carr-Purcell- Meiboom-Gill (CPMG) pulse sequence.

2.2 The accelerated relaxation times factors

Spin-lattice relaxation of nuclei (e.g. ^1H , ^{13}C) in a molecule may be accelerated by:

1. interaction with adjacent nuclei having spin = 1 or greater (e.g. ^2H , ^{14}N): the electric quadrupole moments of such nuclei result in additional magnetic fields in the tumbling molecules;
2. interaction with unpaired electrons in paramagnetic compounds (radicals, some metal chelates).

Spin-spin relaxation of nuclei is accelerated when they participate in a dipolar bond (O-H, N-H, C-H). Spin-spin relaxation involving dipole-dipole interaction is very effective in solids and viscous liquids with slow molecule motions since the magnetic caused by slowly tumbling dipoles change very slowly.

All these interaction cause considerable line broadening, making the observation of NMR signals rather difficult in some cases (e.g. in paramagnetic compounds).

2.3 Application of relaxation times

1. Use widely in medical sciences for examples, detecting the brain cells or the other cells by magnetic resonance imaging techniques.
2. Use in the quantitative analysis such as investigation of wax in oil etc.
3. Use for determining structure and prove it both organic and inorganic compounds because NMR technique involves the relationship between the observed nuclei and ensembled nuclei.

4. Use in biochemistry, for example in active site determination in biomacromolecules, the study of the lipid double layers, or the determination of the peptide conformations.

5. Because of the relationship between molecular motions and relaxation, so that in many cases we can obtain significant informations about molecular motion and structure by using less time than using from mathematics and arithmetics.

2.4 Spin-lattice relaxation mechanisms

The general requirement for spin-lattice relaxation is a magnetic interaction fluctuating at the resonance frequency. There are a number of physical mechanisms which provide the appropriate conditions which the nuclear spins and the lattice have efficient energy transfer. These are summarized, and the relevant equations given in table 2-1.

a) Dipole-dipole interactions with other nuclei (DD)

Dipolar interaction are of the same type as those observed macroscopically between two small bar magnets. They may be modulated by molecular tumbling (effecting intermolecular and intramolecular interactions) or by translation diffusion (intermolecular interaction), thus causing relaxation, and the equations for the two cases, given in table 2-1 differ. There is also a difference of a factor of $3/2$ between the case where the two nuclei under consideration both contribute to the magnetization being monitored (the homonuclear case) and that where one magnetization is under observation independently of the order (the heteronuclear case).

b) Shielding anisotropy (SA)

The shielding at a nuclei, and therefore the magnetic field acting on it, varies with the molecular orientation in the static field B_0 , except for sites of very high symmetry. Molecular tumbling therefore modulates the local magnetic field, and cause relaxation. The relevant equations are given in table 2-1. It should be noted that the correlation time (in the case of isotropic motion) is exactly the same as that entering into the equation for dipolar relaxation caused by molecular tumbling. As shown by the equation in table 2-1, the relaxation rate arising from shielding anisotropy is proportional to the square of the applied magnetic field B_0 . This effect can cause unacceptable line broadening for some nuclei at high applied field. The SA mechanism is usual in that, even in the extreme narrowing situation, T_1 and T_2 are equal in fact $6T_1 = 7T_2$.

c) Spin-rotation interactions (SR)

Small or highly symmetrical and freely rotating molecules can be effectively relaxed by a mechanism involving interaction between the nuclear magnetic moment and the fluctuating magnetic fields generated by the molecular magnetic moment associated with the charge distribution within the molecules. The correlation time, τ_{sr} therefore related to the time between collisions and clearly differs from the correlation time for molecular tumbling. At high temperature and low viscosity T_1 become shorter as a result of increased molecular motion.

d) Scalar interaction (SC)

A scalar relaxation mechanism may be involved when the observed spin is coupled with a spin S undergoing rapid quadrupolar relaxation. The magnetic field produced via scalar interaction through the bond concerned and through the fluctuations are governed by the quadrupolar relaxation. The two spins, A and X , can couple indirectly (via electrons) leading to a Hamiltonian term of the form:

$$hJ_{AB}I_A I_B$$

Such an interaction, which involves a magnetic field produced by X acting at A (and vice versa), can lead to relaxation of A if a time-dependence occurs. This can happen in one of two ways:

- 1) J_{AX} is time-dependent as a result of exchange
- 2) I_X is time-dependent as a result of relaxation

These two possibilities give what are known as scalar relaxation of the first kind and of the second kind respectively. The correlation times are the exchange rates and the X relaxation rate respectively. It is much more common for scalar relaxation to affect T_2 than T_1 .

e) Interaction with unpaired electrons (UE)

Modulation may either occur by exchange of the electrons between different molecules or by spin-lattice relaxation of the electron itself. Dipolar interactions with electrons are much larger than those with nuclei because the magnetic moment

of the electron is so high. Consequently the presence of paramagnetic impurities can have very severe consequences for nuclear relaxation. Traces of paramagnetic dissolved from the glass of NMR tube by alkaline aqueous solutions can significantly alter relaxation times. So can dissolved oxygen, and it is essential to degas NMR sample by freeze/pump/thaw method if meaningful relaxation measurements are required. Conversely, it is sometimes desirable to add traces of paramagnetic compounds such as $\text{Cr}(\text{acac})_3$ to act as relaxation agents, which assist the efficiency of multipulse FT NMR by allowing interpulse times to be shorter or pulse angles larger.

Table 1 Equation for spin-lattice relaxation rates, T_1^{-1} , of a spin -1/2, A, for various mechanisms in the extreme narrowing approximation.

Mechanism	T_1^{-1}	Notes
1. dd(intra)(homo)	$\left(\frac{\mu_0}{4\pi}\right)^2 \frac{3}{2} \gamma_A^4 h^2 \tau_c / r^6$	for a single pair of spin -1/2 nuclei of separation r
2. dd(intra)(hetero)	$\left(\frac{\mu_0}{4\pi}\right)^2 \gamma_A^2 \gamma_X^2 h^2 \tau_c / r^6$	for a single pair of spin -1/2 nuclei AX of separation r
3. dd(inter)(hetero)	$\left(\frac{\mu_0}{4\pi}\right)^2 \frac{2}{15} N_X \gamma_A^2 \gamma_X^2 h^2 / Da$	for relaxation by a spin -1/2 nucleus X
4. ue(intra)(dipolar)	$\left(\frac{\mu_0}{4\pi}\right)^2 \frac{4}{3} \gamma_A^2 \gamma_e^2 h^2 S(S+1) \tau_c / r^6$	for relaxation by unpaired electrons of total spin S at distance r
5. ue(scalar)	$\frac{8}{3} \pi a_N^2 S(S+1) \tau_c$	for relaxation by unpaired electrons of total spin S
6. sr	$2 I_r k T C^2 \tau_{sr} / h^2$	for isotropic molecular inertia
7. sa	$\frac{2}{15} \gamma_A^2 B_0^2 \Delta \sigma \tau_c$	for cylindrical symmetry of shielding
8. sc	$\frac{8}{3} \pi J_{AX}^2 I_X(I_X+1) \frac{\tau_c}{1 + (\omega_X - \omega_A)^2 \tau_c^2}$	relaxation by coupling to spin, X, of quantum number I_X

Meaning of symbols (where not otherwise defined in this Table)

- τ_c Correlation time for molecular tumbling
- τ_e Correlation time related, *inter alia*, to the spin-lattice relaxation time for the unpaired electrons
- τ_{sc} For scalar relaxation of the first kind this is the exchange lifetime; for scalar relaxation of the second kind this is T_{1X}
- N_X Concentration of spins X (per unit volume)
- D Mutual translational self-diffusion coefficient of the molecule containing A and X
- a Distance of closest approach of A and X
- γ Magnetogyric ratio for the electron
- a_N Nucleus-electron hyperfine splitting constant (in frequency units)
- C Spin-rotation interaction constant (assumed to be isotropic)
- $\Delta\sigma$ Shielding anisotropy ($\sigma_2 - \sigma_1$)

2.5 Research works

After the relaxation processes and their parameters have found to be one of important technique for structural determination and elucidation in both organic and inorganic compounds. The researchers have tried to develop these techniques to have more applications particularly in quantitative analysis of substances because the relaxation rate is dependent on the many factors. Many reports about this development have been described mostly in medical sciences and in the first time they were interested in the effect of some paramagnetic substances to relaxation times⁸⁻¹¹.

Baysal E, Sullivan S.G., and Stern A.⁸ studied about the binding of Fe^{3+} to human red blood cell membranes and evaluated the binding of Fe^{3+} by measurement of NMR water-proton relaxation times. They found that Fe^{3+} binded to the membrane and generated free radicals which influence to decrease both spin-lattice and spin-spin relaxation times. In the same year⁹, from the study of proton NMR relaxation times and water content of red blood cells from normal and chronic alcoholism during the withdrawal phase by Besson J.A.O. and his colleagues was shown that the relaxation times can be used in the investigation of substance quantity.

Bennet H.F., Brown R.D., Keana J.F.W., Koenig S.H., and Swartz H.M.¹⁰ have reported the interaction of nitroxides which was one paramagnetic substance with plasma and blood and found that relaxation of water protons in this case is dominated due to water molecular hydrogen bonded to nitroxide moieties.

In several works later¹¹⁻¹³ were shown that red blood cells proton relaxation times T_1 and T_2 were measured to observe only the change in the water content and other paramagnetic substances except dissolved oxygen and its quantity in red blood cells. The quantity of dissolved oxygen in red blood cells can use in

investigation of the number of red blood cells. Generally, the measuring of number of red blood cells does not necessary to measure in all patients because the measurement is so difficult, long time measurement, and the previous measurement method have error easily. Furthermore, the number of red blood cells is useful to determine the level of blood in patients. So this research, the phenomenon of dissolved oxygen and this application is interesting.